ORGANIC CHEMISTRY I



Jeffrey Turk
Alma College



Organic Chemistry

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CHAPTER OVERVIEW

1: Structure and Bonding

Chapter Objectives

Much of the material in chapter one reviews topics covered CHM 115, while applying those concepts to organic molecules.

- the differences between organic and inorganic chemistry
- ionic and covalent bonding
- polar and nonpolar bonds
- Lewis structures
- hybridization
- molecular geometry and dipole moment
- the structure and geometry of the compounds methane, ethane, ethylene and acetylene.

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1.1: Describing Chemical Bonds - Valence Bond Theory

Objectives

After completing this section, you should be able to

1. explain how covalent bonds are formed as a result of the ability of atoms to share electrons.
2. describe the formation of covalent bonds in terms of the overlapping of atomic orbitals.

Key Terms

Make certain that you can define, and use in context, the key terms below.

- bond strength
- covalent bond
- bond length
- sigma (σ) bond
- valence bond theory

Valence Bond Theory

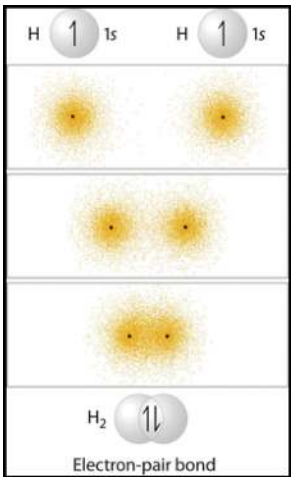
As we have been discussing how to use Lewis structures to depict the bonding in organic compounds, we have been very vague so far in our language about the actual nature of the chemical bonds themselves. We know that a covalent bond involves the 'sharing' of a pair of electrons between two atoms – but how does this happen, and how does it lead to the formation of a bond holding the two atoms together? Two main models have been developed to described how covalent bonds are formed: valence bond theory and molecularly orbital theory.

Valence bond theory is most often used to describe bonding in organic molecules. In this model, covalent bonds are considered to form from the overlap of two atomic orbitals on different atoms, each orbital containing a single electron. The electrons become paired in the orbital overlap bonding the atoms together.

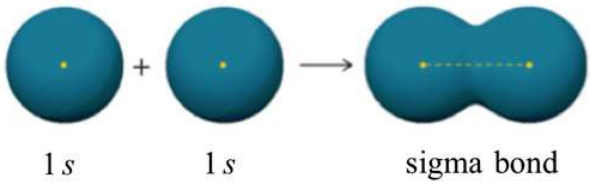
The simplest example valence bond theory can be demonstrated by the H_2 molecule. We can see from the periodic table that each hydrogen atom has a single valence electron. If 2 hydrogen atoms come together to form a bond, then each hydrogen atom effectively has a share in both electrons and thus each resembles the noble gas helium and is more stable. The 2 electrons shared in the orbital overlap are represented by a single dash between the atoms.



Valence bond theory describes a chemical bond as the overlap of atomic orbitals. In the case of the hydrogen molecule, the 1s orbital of one hydrogen atom overlaps with the 1s orbital of the second hydrogen atom to form a molecular orbital called a sigma bond which contains two electrons of opposite spin. The mutual attraction between this negatively charged electron pair and the two atoms' positively charged nuclei serves to physically link the two atoms through a force we define as a covalent bond. The strength of a covalent bond depends on the extent of overlap of the orbitals involved. Orbitals that overlap extensively form bonds that are stronger than those that have less overlap.



One more characteristic of the covalent bond in H_2 is important to consider at this point. The two overlapping 1*s* orbitals can be visualized as two spherical balloons being pressed together. This means that the bond has **cylindrical symmetry**: if we were to take a cross-sectional plane of the bond at any point, it would form a circle. This type of bond is referred to as a **σ(sigma) bond**.



The energy of the system depends on how much the orbitals overlap. The energy diagram below illustrates how the sum of the energies of two hydrogen atoms (the colored curve) changes as they approach each other. When the atoms are far apart there is no overlap, and by convention we set the sum of the energies at zero. As the atoms move together, their orbitals begin to overlap. Each electron begins to feel the attraction of the nucleus in the other atom. In addition, the electrons begin to repel each other, as do the nuclei. While the atoms are still widely separated, the attractions are slightly stronger than the repulsions, and the energy of the system decreases. (A bond begins to form.) As the atoms move closer together, the overlap increases, so the attraction of the nuclei for the electrons continues to increase (as do the repulsions among electrons and between the nuclei). At some specific distance between the atoms, which varies depending on the atoms involved, the energy reaches its lowest (most stable) value. This optimum distance between the two bonded nuclei is called the the bond lengths between the two atoms. The bond is stable because at this point, the attractive and repulsive forces combine to create the lowest possible energy configuration.

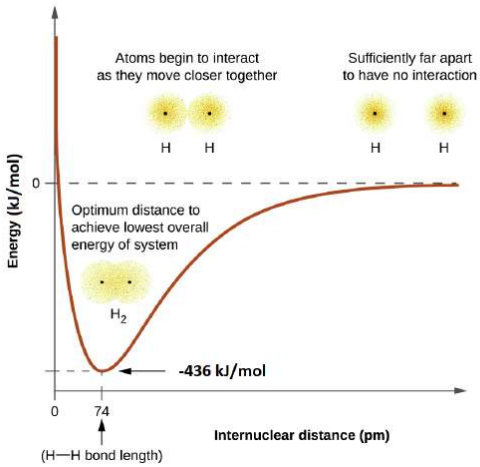


Figure **1.1.2** A Plot of Potential Energy versus Internuclear Distance for the Interaction between Two Gaseous Hydrogen **Atoms**

This optimal internuclear distance is the **bond length**. For the H_2 molecule, the distance is 74 pm (picometers, 10^{-12} meters). Likewise, the difference in potential energy between the lowest energy state (at the optimal internuclear distance) and the state where the two atoms are completely separated is called the **bond dissociation energy,** or, more simply**, bond strength**. For the hydrogen molecule, the H-H bond strength is equal to about 435 kJ/mol. This means it would take 435 kJ to break one mole of H-H bonds.

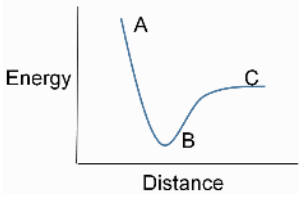
Every covalent bond in a given molecule has a characteristic length and strength. In general, the length of a typical carbon-carbon single bond in an organic molecule is about 150 pm, while carbon-carbon double bonds are about 130 pm, carbon-oxygen double bonds are about 120 pm, and carbon-hydrogen bonds are in the range of 100 to 110 pm. The strength of covalent bonds in organic molecules ranges from about 234 kJ/mol for a carbon-iodine bond (in thyroid hormone, for example), about 410 kJ/mole for a typical carbon-hydrogen bond, and up to over 800 kJ/mole for a carbon-carbon triple bond.

Representative Bond Energies and Lengths

Bond	Length (pm)	Energy (kJ/mol)		Bond	Length (pm)	Energy (kJ/mol)
H-H	74	436		C-O	140.1	358
H-C	106.8	413		C=O	119.7	745
H-N	101.5	391		C≡O	113.7	1072
H-O	97.5	467		H-Cl	127.5	431
C-C	150.6	347		H-Br	141.4	366
C=C	133.5	614		H-I	160.9	298
C≡C	120.8	839		O-O	148	146
C-N	142.1	305		O=O	120.8	498
C=N	130.0	615		F-F	141.2	159
C≡N	116.1	891		Cl-Cl	198.8	243

Exercises

1) For the following energy diagram for energy vs. intermolecular distance is for a fluorine molecule (F_2). Describe the importance for points A, B, & C on the graph.



Solution

A - Repulsive Forces are present, nuclei are too close to one another.

B - Optimal distance between the two orbitals to have a bond (the bond length)

C - Cannot form a bond, the orbitals are too far apart.

Contributors and Attributions

- Dr. Dietmar Kennepohl FCIC (Professor of Chemistry, Athabasca University)
- Richard Banks (Boise State University)

-
- Paul Flowers (University of North Carolina - Pembroke), Klaus Theopold (University of Delaware) and Richard Langley (Stephen F. Austin State University) with contributing authors. Textbook content produced by OpenStax College is licensed under a Creative Commons Attribution License 4.0 license. Download for free at http://cnx.org/contents/85abf193-2bd...a7ac8df6@9.110).

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1.2: Describing Chemical Bonds- Molecular Orbital Theory

Objectives

After completing this section, you should be able to

1. describe the formation of covalent bonds in terms of molecular orbitals.
2. account for differences in bond length and strength in terms of the efficiency with which atomic orbitals overlap.
3. draw simple molecular orbital diagrams (e.g., for the H_2 molecule) showing the formation of bonding and anti-bonding orbitals.

Key Terms

Make certain that you can define, and use in context, the key terms below.

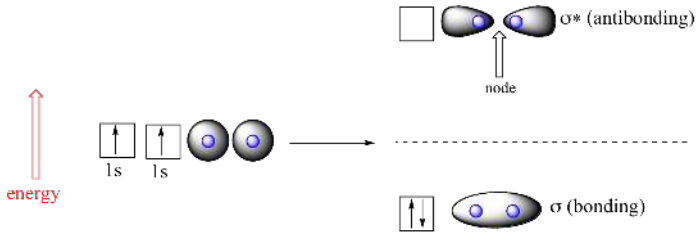
- anti-bonding molecular orbital
- bonding molecular orbital
- molecular orbital (MO) theory

As we have seen, valence bond theory does a remarkably good job of explaining the bonding geometry and properties of many organic compounds. There are some areas, however, where the valence bond theory falls short. It fails to adequately account, for example, for some interesting properties of compounds that contain alternating double and single bonds. In order to understand these properties, we need to think about chemical bonding in a new way, using the ideas of molecular orbital (MO) theory.

Another look at the H_2 molecule: bonding and anti-bonding sigma molecular orbitals

Let's consider again the simplest possible covalent bond: the one in molecular hydrogen (H_2). When we described the hydrogen molecule using valence bond theory, we said that the two 1*s* orbitals from each atom overlap, allowing the two electrons to be shared and thus forming a covalent bond. In molecular orbital theory, we make a further statement: we say that the two atomic 1*s* orbitals don't just overlap, they actually *combine to form two completely new orbitals*. These two new orbitals, instead of describing the likely location of an electron around a single nucleus, describe the location of an electron pair around two or more nuclei. The bonding in H_2, then, is due to the formation of a new **molecular orbital** (MO), in which a pair of electrons is delocalized around two hydrogen nuclei.

An important principle of quantum mechanical theory is that when orbitals combine, the number of orbitals before the combination takes place must equal the number of new orbitals that result – orbitals don't just disappear! We saw this previously when we discussed hybrid orbitals: one *s* and three *p* orbitals make four sp^3 hybrids. When two atomic 1*s* orbitals combine in the formation of H_2, the result is two molecular orbitals called **sigma (σ) orbitals**. According to MO theory, the first sigma orbital is lower in energy than either of the two isolated atomic 1*s* orbitals – thus this sigma orbital is referred to as a **bonding molecular orbital**. The second, **sigma-star (σ*) orbital** is higher in energy than the two atomic 1*s* orbitals, and is referred to as an **anti-bonding molecular orbital**. In MO theory, a star (*) sign always indicates an anti-bonding orbital.



Following the *aufbau* ('building up') principle, we place the two electrons in the H_2 molecule in the lowest energy molecular orbital, which is the (bonding) sigma orbital.

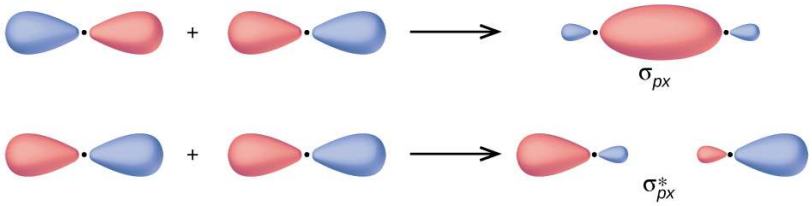
The bonding sigma orbital, which holds both electrons in the ground state of the molecule, is egg-shaped, encompassing the two nuclei, and with the highest likelihood of electrons being in the area between the two nuclei. The high-energy, anti-bonding sigma-

star orbital can be visualized as a pair of droplets, with areas of higher electron density near each nucleus and a ‘node’, (area of zero electron density) midway between the two nuclei.

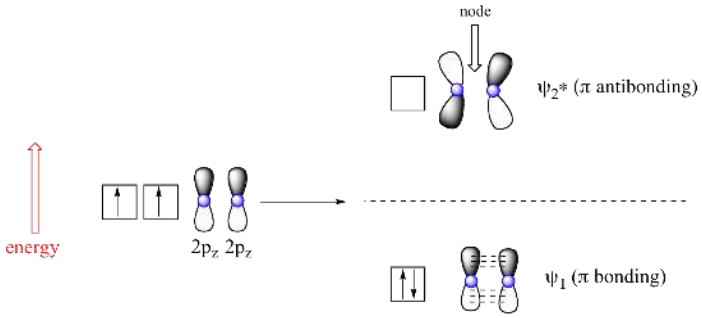
Remember that we are thinking here about electron behavior as *wave behavior*. When two separate waves combine, they can do so with what is called constructive interference, where the two amplitudes reinforce one another, or destructive interference, where the two amplitudes cancel one another out. Bonding MO’s are the consequence of constructive interference between two atomic orbitals which results in an attractive interaction and an increase in electron density between the nuclei. Anti-bonding MO’s are the consequence of destructive interference which results in a repulsive interaction and a ‘canceling out’ of electron density between the nuclei (in other words, a node).

MO theory and pi bonds

In p orbitals, the wave function gives rise to two lobes with opposite phases, analogous to how a two-dimensional wave has both parts above and below the average. We indicate the phases by shading the orbital lobes different colors. When orbital lobes of the same phase overlap, constructive wave interference increases the electron density. When regions of opposite phase overlap, the destructive wave interference decreases electron density and creates nodes. When p orbitals overlap end to end, they create σ and σ* orbitals. If two atoms are located along the x-axis in a Cartesian coordinate system, the two px orbitals overlap end to end and form σp_x (bonding) and $\sigma * p_x$ (antibonding) (read as "sigma-p-x" and "sigma-p-x star," respectively). Just as with s-orbital overlap, the asterisk indicates the orbital with a node between the nuclei, which is a higher-energy, antibonding orbital.



The advantage of MO theory becomes more apparent when we think about pi bonds, especially in those situations where two or more pi bonds are able to interact with one another. Let’s first consider the pi bond in ethene from an MO theory standpoint (in this example we will be disregarding the various sigma bonds, and thinking *only* about the pi bond). According to MO theory, the two atomic $2p_z$ orbitals combine to form two **pi (π) molecular orbitals**, one a low-energy π bonding orbital and one a high-energy **π-star (π*) anti-bonding molecular orbital**. These are sometimes denoted, in MO diagrams like the one below, with the Greek letter psi (Ψ) instead of π.



In the bonding Ψ_1 orbital, the two shaded lobes of the $2p_z$ orbitals interact constructively with each other, as do the two unshaded lobes (remember, the shading choice represents mathematical (+) and (-) signs for the wavefunction). Therefore, there is increased electron density between the nuclei in the molecular orbital – this is why it is a bonding orbital.

In the higher-energy anti-bonding Ψ_2* orbital, the shaded lobe of one $2p_z$ orbital interacts destructively with the unshaded lobe of the second $2p_z$ orbital, leading to a node between the two nuclei and overall repulsion.

By the *aufbau* principle, the two electrons from the two atomic orbitals will be paired in the lower-energy Ψ_1 orbital when the molecule is in the ground state.

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1.3: Polar Covalent Bonds - Electronegativity

Objectives

After completing this section, you should be able to

1. describe how differences in electronegativity give rise to bond polarity.
2. arrange a given series of the elements most often encountered in organic chemistry (C, H, O, N, S, P and the halogens) in order of increasing or decreasing electronegativity, without referring to a table of electronegativities.
3. predict whether a bond is covalent or ionic.
4. predict the partial positive and partial negative ends of a given bond formed between any two elements.

Key Terms

Make certain that you can define, and use in context, the key terms below.

- electronegativity and inductive effect
- polar covalent bond

Study Notes

Students often wonder why it is important to be able to tell whether a given bond is polar or not, and why they need to know which atoms carry a partial positive charge and which a partial negative charge. Consider the chloromethane (CH_3Cl) molecule. The carbon atom is shown as carrying a partial positive charge. Now, recall that opposite charges attract. Thus, it seems reasonable that the slightly positive carbon atom in chloromethane should be susceptible to attack by a negatively charged species, such as the hydroxide ion, OH^-. This theory is borne out in practice: hydroxide ions react with chloromethane by attacking the slightly positive carbon atom in the latter. It is often possible to rationalize chemical reactions in this manner, and you will find the knowledge of bond polarity indispensable when you start to write reaction mechanisms.

Note: Because of the small difference in electronegativity between carbon and hydrogen, the **C-H** bond is normally assumed to be nonpolar.

Electronegativity

Because the tendency of an element to gain or lose electrons is so important in determining its chemistry, various methods have been developed to quantitatively describe this tendency. The most important method uses a measurement called **electronegativity** (represented by the Greek letter *chi*, χ, pronounced “ky” as in “sky”), which is defined as the *relative* ability of an atom to attract electrons to itself *in a chemical compound*. Elements with high electronegativities tend to acquire electrons in chemical reactions and are found in the upper right corner of the periodic table. Elements with low electronegativities tend to lose electrons in chemical reactions and are found in the lower left corner of the periodic table.

Electronegativity of an atom is not a simple, fixed property that can be directly measured in a single experiment. In fact, an atom’s electronegativity should depend to some extent on its chemical environment because the properties of an atom are influenced by the neighboring atoms in a chemical compound. Nevertheless, when different methods for measuring the electronegativity of an atom are compared, they all tend to assign similar relative values to a given element. ***Figure* 1.3.1** shows the electronegativity values of the elements as proposed by one of the most famous chemists of the twentieth century: Linus Pauling. In this scale a value of 4.0 is arbitrarily given to the most electronegative element, fluorine, and the other electronegativities are scaled relative to this value. In general, electronegativity increases from left to right across a period in the periodic table and decreases down a group. Thus, the nonmetals, which lie in the upper right, tend to have the highest electronegativities, with fluorine the most electronegative element of all (EN = 4.0 as previously noted). It is important to notice that the elements most important to organic chemistry, carbon, nitrogen, and oxygen have some of the highest electronegativities in the periodic table (EN = 2.5, 3.0, 3.5 respectively). Metals, on the left, tend to be less electronegative elements, with cesium having the lowest (EN = 0.7). Note that noble gases are excluded from this figure because these atoms usually do not share electrons with others atoms since they have a full valence shell.

*Electronegativity is defined as the ability of an atom in a particular molecule to attract electrons to itself. The **larger** the electronegativity value, the **greater** the attraction.*

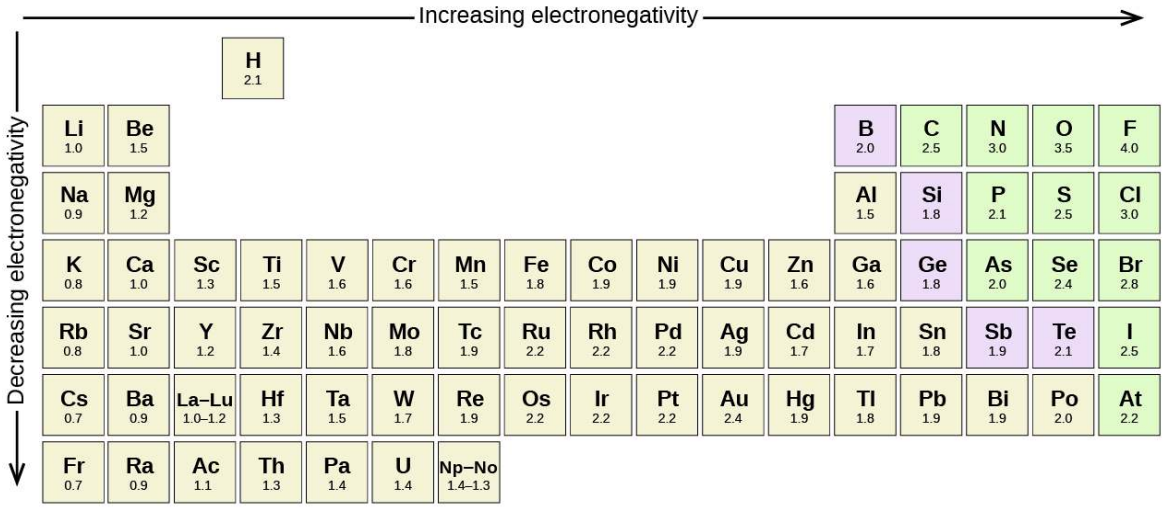


Figure **1.3.1**: Pauling scale electronegativities of elements

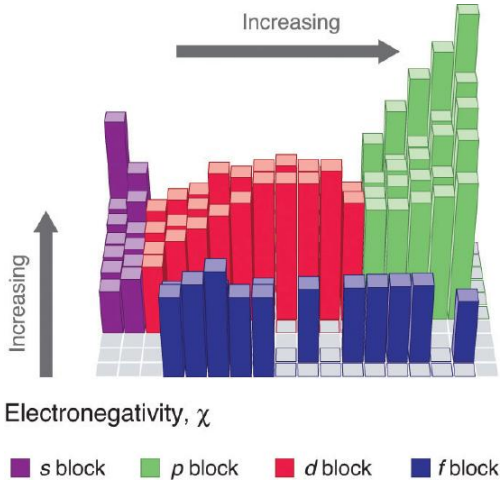


Figure **1.3.2**: Visual representation of electronegativities.

Electronegativity and Bond Type

The two idealized extremes of chemical bonding: (1) **ionic bonding**—in which one or more electrons are transferred completely from one atom to another, and the resulting ions are held together by purely electrostatic forces—and (2) **covalent bonding**, in which electrons are shared equally between two atoms. Most compounds, however, have **polar covalent bonds**, which means that electrons are shared unequally between the bonded atoms. Electronegativity determines how the shared electrons are distributed between the two atoms in a polar covalent bond. The more strongly an atom attracts the electrons in its bonds, the larger its electronegativity. Electrons in a polar covalent bond are shifted toward the more electronegative atom; thus, the more electronegative atom is the one with the partial negative charge. The greater the difference in electronegativity, the more polarized the electron distribution and the larger the partial charges of the atoms. Recall that a lowercase Greek delta (δ) is used to indicate that a bonded atom possesses a partial positive charge, indicated by δ^+ , or a partial negative charge, indicated by δ^- , and a bond between two atoms that possess partial charges is a polar bond.

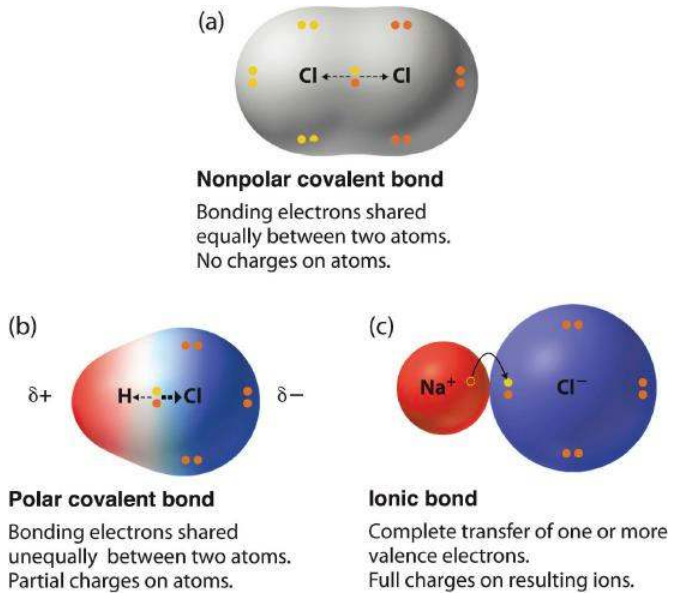
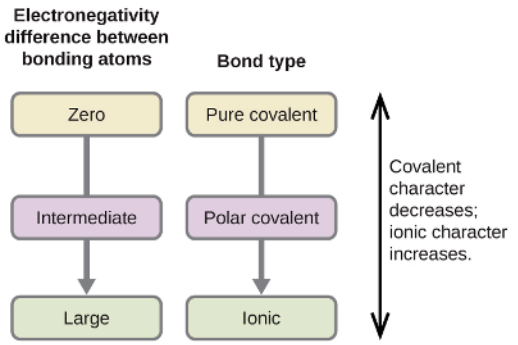


Figure **1.3.3**: The Electron Distribution in a Nonpolar Covalent Bond, a Polar Covalent Bond, and an Ionic Bond Using Lewis Electron Structures. Electron-rich (negatively charged) regions are shown in blue; electron-poor (positively charged) regions are shown in red.

Whether a bond is **ionic**, **nonpolar covalent**, or **polar covalent** can be estimated by by calculating the absolute value of the difference in electronegativity (ΔEN) of two bonded atoms. When the difference is very small or zero, the bond is covalent and nonpolar. When it is large, the bond is polar covalent or ionic. The absolute values of the electronegativity differences between the atoms in the bonds H–H, H–Cl, and Na–Cl are 0 (nonpolar), 0.9 (polar covalent), and 2.1 (ionic), respectively. The degree to which electrons are shared between atoms varies from completely equal (pure covalent bonding) to not at all (ionic bonding). Figure 7.2.4 shows the relationship between electronegativity difference and bond type. This table is just a general guide, however, with many exceptions. The best guide to the covalent or ionic character of a bond is to consider the types of atoms involved and their relative positions in the periodic table. Bonds between two nonmetals are generally covalent; bonding between a metal and a nonmetal is often ionic.



Bond Type	Electronegativity Difference
pure covalent	< 0.4
polar covalent	between 0.4 and 1.8
ionic	> 1.8

Figure **1.3.4**: As the electronegativity difference increases between two atoms, the bond becomes more ionic.

Some compounds contain both covalent and ionic bonds. The atoms in polyatomic ions, such as OH^-, NO_3^-, and NH_4^+, are held together by polar covalent bonds. However, these polyatomic ions form ionic compounds by combining with ions of opposite charge. For example, potassium nitrate, KNO_3, contains the K^+ cation and the polyatomic NO_3^- anion. Thus, bonding in potassium nitrate is ionic, resulting from the electrostatic attraction between the ions K^+ and NO_3^-, as well as covalent between the nitrogen and oxygen atoms in NO_3^-.

Bond polarities play an important role in determining the structure of proteins. Using the electronegativity values in Table A2, arrange the following covalent bonds—all commonly found in amino acids—in order of increasing polarity. Then designate the positive and negative atoms using the symbols δ+ and δ–:

C–H, C–N, C–O, N–H, O–H, S–H

Solution

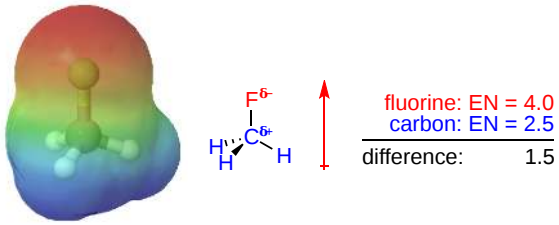
The polarity of these bonds increases as the absolute value of the electronegativity difference increases. The atom with the δ– designation is the more electronegative of the two. Table **1.3.1** shows these bonds in order of increasing polarity.

Table **1.3.1**: Bond Polarity and Electronegativity Difference

Bond	ΔEN	Polarity
C–H	0.4	$\overset{\delta-}{\mathrm{C}}-\overset{\delta+}{\mathrm{H}}$
S–H	0.4	$\overset{\delta-}{\mathrm{S}}-\overset{\delta+}{\mathrm{H}}$
C–N	0.5	$\overset{\delta+}{\mathrm{C}}-\overset{\delta-}{\mathrm{N}}$
N–H	0.9	$\overset{\delta-}{\mathrm{N}}-\overset{\delta+}{\mathrm{H}}$
C–O	1.0	$\overset{\delta+}{\mathrm{C}}-\overset{\delta-}{\mathrm{O}}$
O–H	1.4	$\overset{\delta-}{\mathrm{O}}-\overset{\delta+}{\mathrm{H}}$

Visualizing Bonding

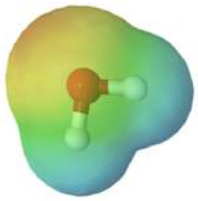
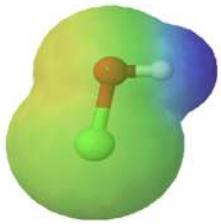
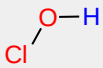
Calculated charge distributions in molecules can easily be visualized by using electrostatic potential maps. The color red is used to indicate electron-rich regions of a molecule while the color blue is used to indicated electron-poor regions. An easier method for visually representing electron displacement in a molecule uses a crossed arrow. By convention the arrow point in the direction of the electron-rich region of a molecule and away from the electron-poor. An example is shown in the molecule fluoromethane. The C-F bond is polarized drawing the bonding electrons toward the more electronegative fluorine giving it a partial negative charge. Consequently, the bonding electrons are drawn away from the less electronegative carbon giving it a partial positive charge. The the electron-rich fluorine is shown as red in the electrostatic potential map and while the electron-poor carbon is shown as blue. The crossed arrow points in the direction of the electron-rich fluorine.



Electrostatic Potential Map and Dipole Moment of Fluoromethane

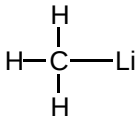
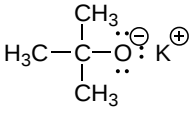
Chemists often use the term, **inductive effect**, to describe the shifting of electrons in a sigma by the electronegativity of atoms. Relatively electronegative atoms, such as fluorine, tend to inductively draw electrons towards themselves and away from nearby atoms. The inductive effect will be used to explain chemical reactivity in many situations in organic chemistry. An excellent example of the inductive effect is seen when comparing the O-H bond polarities of water (H_2O) and hypochlorous acid (ClOH). Replacing the less electronegative hydrogen (EN = 2.1) in water with the more electronegative chlorine (EN = 3.0) in hypochlorous

acid creates a greater bond polarity. The chlorine draws electrons away giving the hydrogen a greater partial positive charge. This is shown in the electrostatic potential map as an increase in the blue color around hydrogen.

	
	
water	hypochlorous acid

A "spectrum" of bonds

There is no clear-cut division between covalent and ionic bonds. In a pure non-polar covalent bond, the electrons are held on average exactly half way between the atoms. In a polar bond, the electrons have been dragged slightly towards one end. How far does this dragging have to go before the bond counts as ionic? There is no real answer to that. Sodium chloride is typically considered an ionic solid, but even here the sodium has not completely lost control of its electron. Because of the properties of sodium chloride, however, we tend to count it as if it were purely ionic. Lithium iodide, on the other hand, would be described as being "ionic with some covalent character". In this case, the pair of electrons has not moved entirely over to the iodine end of the bond. Lithium iodide, for example, dissolves in organic solvents like ethanol - not something which ionic substances normally do. Many bonds between metals and non-metal atoms, are considered ionic, however some of these bonds cannot be simply identified as one type of bond. Examples of this are the lithium - carbon bond in methyllithium which is usually considered as polar covalent (somewhat between covalent and ionic) and the potassium - oxygen bond in potassium *tert*-butoxide which is considered more ionic than covalent.

	
methyllithium	potassium *tert*-butoxide

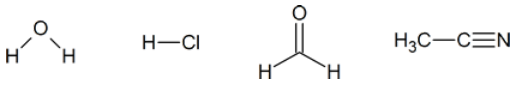
Summary

Covalent bonds form when electrons are shared between atoms and are attracted by the nuclei of both atoms. In pure covalent bonds, the electrons are shared equally. In polar covalent bonds, the electrons are shared unequally, as one atom exerts a stronger force of attraction on the electrons than the other. The ability of an atom to attract a pair of electrons in a chemical bond is called its electronegativity. The difference in electronegativity between two atoms determines how polar a bond will be. In a diatomic molecule with two identical atoms, there is no difference in electronegativity, so the bond is nonpolar or pure covalent. When the electronegativity difference is very large, as is the case between metals and nonmetals, the bonding is characterized as ionic.

- No electronegativity difference between two atoms leads to a non-polar covalent bond.
- A small electronegativity difference leads to a polar covalent bond.
- A large electronegativity difference leads to an ionic bond.

Exercises

1. Identify the partial positive and partial negative ends of each of the bonds shown below.



2. Which of the following atoms is the more electronegative?

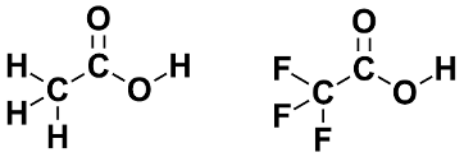
a) Br or C

b) C or H

c) Cl or I

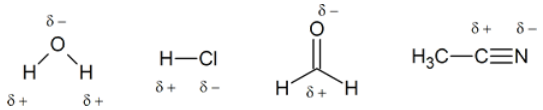
d) C or Li

3. Which of the following molecules would you expect to have the more polarized O-H bond?



Solutions

1.



2.

a) Br

b) C

c) Cl

d) C

3.

The molecule on the right would have the more polarized O-H bond. The presence of the highly electronegative fluorines would draw electrons away by the inductive effect

2.1 Polar Covalent Bonds: Electronegativity

2.1 Exercises

Questions

Q2.1.1

Rank the following from least polar to most polar using knowledge of electronegativity

CH_3CH_2-Li CH_3CH_2-K CH_3CH_2-F CH_3CH_2-OH

Solutions

S2.1.1

(least polar) OH < F < Li < K (most polar)

1.3: Polar Covalent Bonds - Electronegativity is shared under a CC BY-SA 4.0 license and was authored, remixed, and/or curated by Jim Clark, Steven Farmer, Dietmar Kennepohl, Krista Cunningham, Tim Soderberg, Ed Vitz, & Ed Vitz.

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1.4: Development of Chemical Bonding Theory

Objectives

After completing this section, you should be able to

1. draw Lewis Dot Symbols for elements and ions.
2. draw Lewis structures of organic molecules.
3. describe the three-dimensional nature of molecules.
4. sketch a tetrahedral molecule, CX_4, using the "wedge-and-broken-line" method of representation.
5. make a ball-and-stick model of a simple tetrahedral molecules such as methane, ethane... including water and ammonia.

Key Terms

Make certain that you can define, and use in context, the key terms below.

- bond strength
- covalent bond
- ionic bond
- Lewis structure
- lone-pair electron
- non-bonding electron

Study Notes

To draw Lewis structures successfully, you need to know the number of valence electrons present in each of the atoms involved. Memorize the number of valence electrons possessed by each of the elements commonly encountered in organic chemistry: C, H, O, N, S, P and the halogens.

When drawing any organic structure, you must remember that a neutral carbon atom will almost always have four bonds. Similarly, hydrogen always has one bond; neutral oxygen atoms have two bonds; and neutral nitrogen atoms have three bonds. By committing these simple rules to memory, you can avoid making unnecessary mistakes later in the course.

The "wedge-and-broken-line" type of representation, which helps to convey the three-dimensional nature of organic compounds, will be used throughout the course.

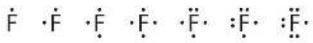
Lewis Symbols

At the beginning of the 20th century, the American chemist G. N. Lewis (1875–1946) devised a system of symbols—now called Lewis electron dot symbols, often shortened to *Lewis dot symbols*—that can be used for predicting the number of bonds formed by most elements in their compounds. Each Lewis dot symbol consists of the chemical symbol for an element surrounded by dots that represent its valence electrons.

Lewis Dot symbols:

- provide a convenient representation of valence electrons
- allows you to keep track of valence electrons during bond formation
- consists of the chemical symbol for the element plus a dot for each valence electron

To write an element's Lewis dot symbol, we place dots representing its valence electrons, one at a time, around the element's chemical symbol. Up to four dots are placed above, below, to the left, and to the right of the symbol (in any order, as long as elements with four or fewer valence electrons have no more than one dot in each position). The next dots, for elements with more than four valence electrons, are again distributed one at a time, each paired with one of the first four. Fluorine, for example, with the electron configuration [He]$2s^2 2p^5$, has seven valence electrons, so its Lewis dot symbol is constructed as follows:



Group	1	2	13	14	15	16	17	18
Electron Configuration	[He]$2s^1$	[He]$2s^2$	[He]$2s^2 2p^1$	[He]$2s^2 2p^2$	[He]$2s^2 2p^3$	[He]$2s^2 2p^4$	[He]$2s^2 2p^5$	[He]$2s^2 2p^6$
Lewis Dot Symbol	Li ·	·Be·	· B ·	· C ·	· N ·	: O ·	: F ·	:Ne:

Figure **1.4.2**: Lewis Dot Symbols for the Elements in Period 2

Lewis used the unpaired dots to predict the number of bonds that an element will form in a compound. Consider the symbol for nitrogen in Figure **1.4.2**. The Lewis dot symbol explains why nitrogen, with three unpaired valence electrons, tends to form compounds in which it shares the unpaired electrons to form three bonds. Boron, which also has three unpaired valence electrons in its Lewis dot symbol, also tends to form compounds with three bonds, whereas carbon, with four unpaired valence electrons in its Lewis dot symbol, tends to share all of its unpaired valence electrons by forming compounds in which it has four bonds. Lewis symbols are a tool to help draw structures. We will see why bonding in molecular compounds follow Lewis' theory in the next section.

Elements in the same group have the same number of valence electrons and similar Lewis symbols. For example, the electron configuration for atomic sulfur is [Ne]$3s^2 3p^4$, thus there are ***six*** valence electrons. Its Lewis symbol would therefore be similar to oxygen and look like:



The Octet Rule

Lewis's major contribution to bonding theory was to recognize that atoms tend to lose, gain, or share electrons to reach a total of eight valence electrons, called an *octet*. This so-called octet rule explains the stoichiometry of most compounds in the *s* and *p* blocks of the periodic table. We now know from quantum mechanics that the number eight corresponds to one *ns* and three *np* valence orbitals, which together can accommodate a total of eight electrons. Remarkably, though, Lewis's insight was made nearly a decade before Rutherford proposed the nuclear model of the atom. Common exceptions to the octet rule are helium, whose $1s^2$ electron configuration gives it a full $n = 1$ shell, and hydrogen, which tends to gain or share its one electron to achieve the electron configuration of helium.

Lewis's idea of an octet explains why noble gases rarely form compounds. They have the stable s^2p^6 configuration (full octet, no charge), so they have no reason to react and change their configuration. All other elements attempt to gain, lose, or share electrons to achieve a noble gas configuration. This explains why atom combine together to form compounds. By forming bond the makes the atoms more stable and lower in energy. Making bonds releases energy and represents a driving force for the formation of compounds.

Atoms often gain, lose, or share electrons to achieve the same number of electrons as the noble gas closest to them in the periodic table.

Lewis Structures

Lewis structures represent how Lewis symbols gain, lose, or share electrons to obtain an octet by forming compounds.

Lewis Structures of Ionic Compounds

Whenever there is a metal present in the structure of an organic compound, there is a high likelihood that at least one ionic bond is present. Ionic bonds are represented differently in Lewis structures than covalent bonds. Great care should be taken whenever drawing the Lewis structure of an organic compounds which contains and ionic bond. Ionic bonds typically are formed when a metal and a nonmetal are part of a compound. Some atoms achieve an octet by fully gaining or losing electrons to form ions. Ionic bonds form through the eletrostatic attraction of the created ions. The formula for table salt is NaCl. It is the result of Na^+ ions and Cl^- ions bonding together. If sodium metal and chlorine gas mix under the right conditions, they will form salt. The sodium loses an

electron, and the chlorine gains that electron. In the process, a great amount of light and heat is released. The resulting salt is mostly unreactive — it is stable. It will not undergo any explosive reactions, unlike the sodium and chlorine that it is made of. Why? Referring to the octet rule, atoms attempt to get a noble gas electron configuration, which is eight valence electrons. Sodium ($1s^2 2s^2 2p^6 3s^1$) has one valence electron, so giving it up would result in the same electron configuration as neon ($1s^2 2s^2 2p^6$). Chlorine ($1s^2 2s^2 2p^6 3s^2 3p^7$)has seven valence electrons, so if it takes one it will have eight (an octet). Chlorine has the electron configuration of argon ($1s^2 2s^2 2p^6 3s^2 3p^8$) when it gains an electron.

The Lewis structure of an ionic compound show the movement of electrons. For NaCl, sodium is in group 1 and has one valence electron and chlorine is in group 17 and has seven valence electrons. Sodium loses its sole valence electron thereby becomes positively charged. Chlorine gains this electron, gaining a full octet, and a negative charge. After the gain/loss of an electron the new Lewis structures of Na^+ and Cl^- are written next to each other representing the ionic bond in NaCl.

Examples of Lewis Structures of Ionic Compounds

Metal		Nonmetal		Ionic Compound
$Na\cdot$	+	$:\ddot{Cl}\cdot$	→	$Na^+[:\ddot{Cl}:]^-$
sodium atom		chlorine atom		sodium chloride (sodium ion and chloride ion)
$\cdot Mg\cdot$	+	$:\ddot{O}\cdot$	→	$Mg^{2+}[:\ddot{O}:]^{2-}$
magnesium atom		oxygen atom		magnesium oxide (magnesium ion and oxide ion)
$\cdot Ca\cdot$	+	$2:\ddot{F}\cdot$	→	$Ca^{2+}[:\ddot{F}:]^-_2$
calcium atom		fluorine atoms		calcium fluoride (calcium ion and two fluoride ions)

Covalent Bonds and the Lewis Structures of Molecular Compounds

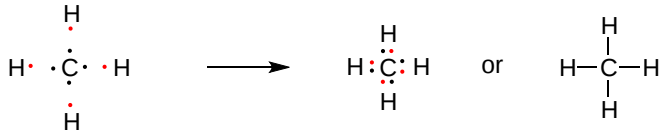
While alkali metals (such as sodium and potassium), alkaline earth metals (such as magnesium and calcium), and halogens (such as fluorine and chlorine) often form ions in order to achieve a full octet, the principle elements of organic chemistry - carbon, hydrogen, nitrogen, and oxygen - instead tend to fill their octet by *sharing* electrons with other atoms, forming covalent bonds. Consider the simplest case of hydrogen gas. An isolated hydrogen atom has only one electron, located in the 1*s* orbital. If two hydrogen atoms come close enough so that their respective 1*s* orbitals overlap, the two electrons can be shared between the two nuclei, and a covalently bonded H_2 molecule is formed. In the Lewis structure of H_2, each pair of electrons that is shared between two atoms is drawn as a single line, designating a single covalent bond.

$$H\cdot \quad \cdot H \longrightarrow H:H \quad \text{or} \quad H\text{—}H$$

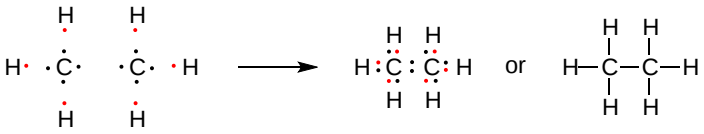
two hydrogen atoms — a hydrogen molecule (H_2)

Hydrogen represents a special case, because a hydrogen atom cannot fulfill the octet rule; it needs only two electrons to have a full shell. This is often called the ‘doublet rule’ for hydrogen.

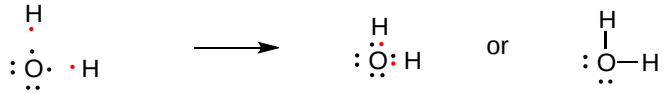
One of the simplest organic molecules is methane with the molecular formula CH_4. Methane is the ‘natural gas’ burned in home furnaces and hot water heaters, as well as in electrical power generating plants. To illustrate the covalent bonding in methane using a Lewis structure, we first must recognize that, although a carbon atom has a total of six electrons it's Lewis symbol has four unpaired electrons. Following Lewis' theory the carbon atom wants to form four covalent bonds to fill its octet. In a methane molecule, the central carbon atom shares its four valence electrons with four hydrogen atoms, thus forming four bonds and fulfilling the octet rule (for the carbon) and the ‘doublet rule’ (for each of the hydrogens).



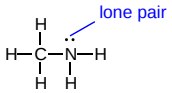
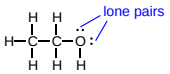
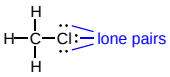
The next relatively simple organic molecule to consider is ethane, which has the molecular formula C_2H_6. If we draw each atom's Lewis symbol separately, we can see that the octet/doublet rule can be fulfilled for all of them by forming one carbon-carbon bond and six carbon-hydrogen bonds.



The same approach can be used for molecules in which there is no carbon atom. In a water molecule, the Lewis symbol of the oxygen atom has two unpaired electrons. These are paired with the single electron in the Lewis symbols of the hydrogens' two O-H covalent bonds. The remaining four non-bonding electrons on oxygen called ‘lone pairs’.

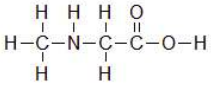


Since the lone pair electrons are often NOT shown in chemical structures, it is important to see mentally add the lone pairs. In the beginning, it can be helpful to physically add the lone pair electrons.

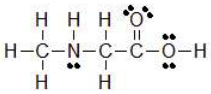
					
methylamine	ethanol	chloromethane			

Exercise

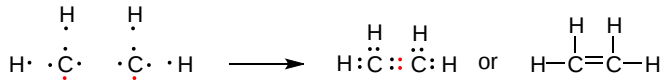
For the following structure, please fill in all of the missing lone pair electrons.



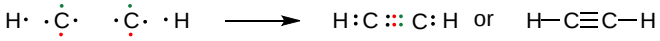
Answer



When two or more electrons are shared between atoms a multiple covalent bond is formed. The molecular formula for ethene (also known as ethylene, a compound found in fruits, such as apples, that signals them to ripen) is C_2H_4. Arranging Lewis symbols of the atoms, you can see that the octet/doublet rule can be fulfilled for all atoms only if the two carbons share *two* pairs of electrons between them. Ethene contains a carbon/carbon double bond.



Following this pattern, the triple bond in ethyne molecular formula C_2H_2, (also known as acetylene, the fuel used in welding torches), is formed when the two carbon atoms share *three* pairs of electrons between them.



Exercise 1.4.1

Draw the Lewis structure for ammonia, NH_3.

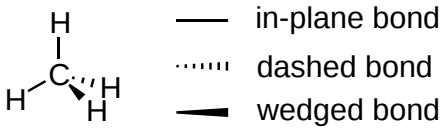
Answer



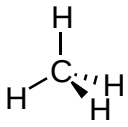
ammonia

Molecular Shape

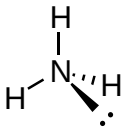
A stick and wedge drawing of methane shows the tetrahedral angles...(The wedge is coming out of the paper and the dashed line is going behind the paper. The solid lines are in the plane of the paper.)



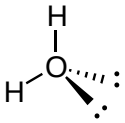
The following examples make use of this notation, and also illustrate the importance of including non-bonding valence shell electron pairs when viewing such configurations.



Methane



Water



Ammonia

Bonding configurations are readily predicted by valence-shell electron-pair repulsion theory, commonly referred to as **VSEPR** in most introductory chemistry texts. This simple model is based on the fact that electrons repel each other, and that it is reasonable to expect that the bonds and non-bonding valence electron pairs associated with a given atom will prefer to be as far apart as possible. The bonding configurations of carbon are easy to remember, since there are only three categories.

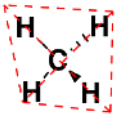
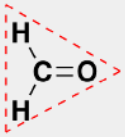
Configuration	Bonding Partners	Bond Angles	Example
Tetrahedral	4	109.5º	
Trigonal Planar	3	120º	
Linear	2	180º	

Figure 1.4.3

In the three examples shown above, the central atom (carbon) does not have any non-bonding valence electrons; consequently the configuration may be estimated from the number of bonding partners alone. However, for molecules of water and ammonia, the non-bonding electrons must be included in the calculation. In each case there are four regions of electron density associated with the valence shell so that a tetrahedral bond angle is expected. The measured bond angles of these compounds (H_2O 104.5º & NH_3 107.3º) show that they are closer to being tetrahedral than trigonal planar or linear. Of course, it is the configuration of atoms (not electrons) that defines the the shape of a molecule, and in this sense ammonia is said to be pyramidal (not tetrahedral). The compound boron trifluoride, BF_3, does not have non-bonding valence electrons and the configuration of its atoms is trigonal. Nice treatments of VSEPR theory have been provided by Oxford and Purdue. The best way to study the three-dimensional shapes of molecules is by using molecular models. Many kinds of model kits are available to students and professional chemists.

Two Electron Groups

Our first example is a molecule with two bonded atoms and no lone pairs of electrons, .

AX_2: BeH_2

1. The central atom, beryllium, contributes two valence electrons, and each hydrogen atom contributes one. The Lewis electron structure is



Figure 1.4.4: Lewis Structure for BeH_2

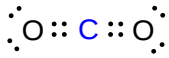
2. There are two electron groups around the central atom. We see from Figure 1.4.3 that the arrangement that minimizes repulsions places the groups 180° apart.

3. Both groups around the central atom are bonding pairs (BP). Thus BeH_2 is designated as AX_2.

4. From Figure 1.4.3 we see that with two bonding pairs, the molecular geometry that minimizes repulsions in BeH_2 is *linear*.

AX_2: CO_2

1. The central atom, carbon, contributes four valence electrons, and each oxygen atom contributes six. The Lewis electron structure is



2. The carbon atom forms two double bonds. Each double bond is a group, so there are two electron groups around the central atom. Like BeH_2, the arrangement that minimizes repulsions places the groups 180° apart.

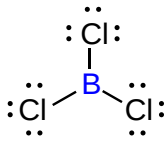
3. Once again, both groups around the central atom are bonding pairs (BP), so CO_2 is designated as AX_2.

4. VSEPR only recognizes groups around the *central* atom. Thus the lone pairs on the oxygen atoms do not influence the molecular geometry. With two bonding pairs on the central atom and no lone pairs, the molecular geometry of CO_2 is linear (Figure 1.4.3).

Three Electron Groups

AX_3: BCl_3

1. The central atom, boron, contributes three valence electrons, and each chlorine atom contributes seven valence electrons. The Lewis electron structure is



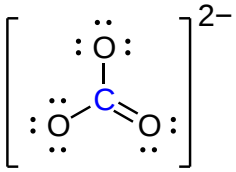
2. There are three electron groups around the central atom. To minimize repulsions, the groups are placed 120° apart (Figure 1.4.3).

3. All electron groups are bonding pairs (BP), so the structure is designated as AX_3.

4. From Figure 1.4.3 we see that with three bonding pairs around the central atom, the molecular geometry of BCl_3 is *trigonal planar*.

AX_3: CO_3^{2-}

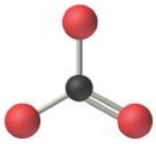
1. The central atom, carbon, has four valence electrons, and each oxygen atom has six valence electrons. As you learned previously, the Lewis electron structure of one of three resonance forms is represented as



2. The structure of CO_3^{2-} is a resonance hybrid. It has three identical bonds, each with a bond order of 4/3. We minimize repulsions by placing the three groups 120° apart (Figure 1.4.3).

3. All electron groups are bonding pairs (BP). With three bonding groups around the central atom, the structure is designated as AX_3.

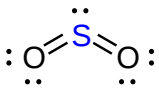
4. We see from Figure 1.4.3 that the molecular geometry of CO_3^{2-} is trigonal planar.



In our next example we encounter the effects of lone pairs and multiple bonds on molecular geometry for the first time.

- ### AX_2E: SO_2

  1. The central atom, sulfur, has 6 valence electrons, as does each oxygen atom. With 18 valence electrons, the Lewis electron structure is shown below.



  2. There are three electron groups around the central atom, two double bonds and one lone pair. We initially place the groups in a trigonal planar arrangement to minimize repulsions (Figure 1.4.3).

  3. There are two bonding pairs and one lone pair, so the structure is designated as AX_2E. This designation has a total of three electron pairs, two X and one E. Because a lone pair is not shared by two nuclei, it occupies more space near the central atom than a bonding pair (Figure 1.4.4). Thus bonding pairs and lone pairs repel each other electrostatically in the order BP–BP < LP–BP < LP–LP. In SO_2, we have one BP–BP interaction and two LP–BP interactions.

  4. The molecular geometry is described only by the positions of the nuclei, *not* by the positions of the lone pairs. Thus with two nuclei and one lone pair the shape is *bent*, or *V shaped*, which can be viewed as a trigonal planar arrangement with a missing vertex (Figures 1.4.2.1 and 1.4.3).

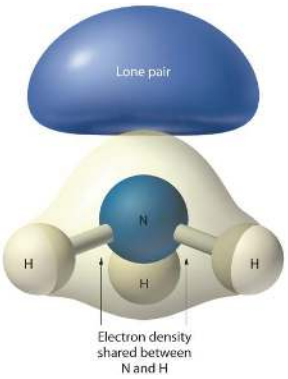
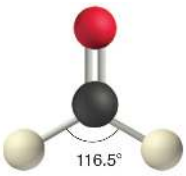


Figure 1.4.4: The Difference in the Space Occupied by a Lone Pair of Electrons and by a Bonding Pair

As with SO_2, this composite model of electron distribution and negative electrostatic potential in ammonia shows that a lone pair of electrons occupies a larger region of space around the nitrogen atom than does a bonding pair of electrons that is shared with a hydrogen atom.

Like lone pairs of electrons, multiple bonds occupy more space around the central atom than a single bond, which can cause other bond angles to be somewhat smaller than expected. This is because a multiple bond has a higher electron density than a single bond, so its electrons occupy more space than those of a single bond. For example, in a molecule such as CH_2O (AX_3), whose structure is shown below, the double bond repels the single bonds more strongly than the single bonds repel each other. This causes a deviation from ideal geometry (an H–C–H bond angle of 116.5° rather than 120°).

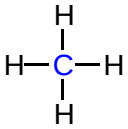


Four Electron Groups

One of the limitations of Lewis structures is that they depict molecules and ions in only two dimensions. With four electron groups, we must learn to show molecules and ions in three dimensions.

AX_4: CH_4

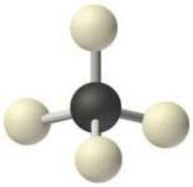
1. The central atom, carbon, contributes four valence electrons, and each hydrogen atom has one valence electron, so the full Lewis electron structure is



2. There are four electron groups around the central atom. As shown in Figure 1.4.2, repulsions are minimized by placing the groups in the corners of a tetrahedron with bond angles of 109.5°.

3. All electron groups are bonding pairs, so the structure is designated as AX_4.

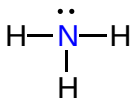
4. With four bonding pairs, the molecular geometry of methane is *tetrahedral* (Figure 1.4.3).



Molecular geometry
(tetrahedral)

AX_3E: NH_3

1. In ammonia, the central atom, nitrogen, has five valence electrons and each hydrogen donates one valence electron, producing the Lewis electron structure



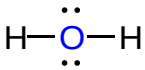
2. There are four electron groups around nitrogen, three bonding pairs and one lone pair. Repulsions are minimized by directing each hydrogen atom and the lone pair to the corners of a tetrahedron.

3. With three bonding pairs and one lone pair, the structure is designated as AX_3E. This designation has a total of four electron pairs, three X and one E. We expect the LP–BP interactions to cause the bonding pair angles to deviate significantly from the angles of a perfect tetrahedron.

4. There are three nuclei and one lone pair, so the molecular geometry is *trigonal pyramidal*. In essence, this is a tetrahedron with a vertex missing (Figure 1.4.3). However, the H–N–H bond angles are less than the ideal angle of 109.5° because of LP–BP repulsions.

AX_2E_2: H_2O

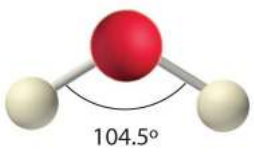
1. Oxygen has six valence electrons and each hydrogen has one valence electron, producing the Lewis electron structure



2. There are four groups around the central oxygen atom, two bonding pairs and two lone pairs. Repulsions are minimized by directing the bonding pairs and the lone pairs to the corners of a tetrahedron Figure 1.4.3.

3. With two bonding pairs and two lone pairs, the structure is designated as AX_2E_2 with a total of four electron pairs. Due to LP–LP, LP–BP, and BP–BP interactions, we expect a significant deviation from idealized tetrahedral angles.

4. With two hydrogen atoms and two lone pairs of electrons, the structure has significant lone pair interactions. There are two nuclei about the central atom, so the molecular shape is *bent*, or *V shaped*, with an H–O–H angle that is even less than the H–N–H angles in NH_3, as we would expect because of the presence of two lone pairs of electrons on the central atom rather than one.. This molecular shape is essentially a tetrahedron with two missing vertices.



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1.5: Formal Charges

Objectives

After completing this section, you should be able to

1. calculate the formal charge of an atom in an organic molecule or ion.
2. identify and recognize the bonding patterns for atoms of carbon, hydrogen, oxygen, nitrogen and the halogens that have a formal charge of zero.

Key Terms

Make certain that you can define, and use in context, the key term below.

- valence electrons
- bonding and non-bonding electrons
- formal charge
- carbocations

Study Notes

It is more important that students learn to easily identify atoms that have formal charges of zero, than it is to actually calculate the formal charge of every atom in an organic compound. Students will benefit by memorizing the "normal" number of bonds and non-bonding electrons around atoms whose formal charge is equal to zero.

Determining the Formal Charge on an Atom

A **formal charge** (*FC*) compares the number of electrons around a "neutral atom" (an atom not in a molecule) versus the number of electrons around an atom in a molecule. Formal charge is assigned to an atom in a molecule by assuming that electrons in all chemical bonds are shared equally between atoms, regardless of relative electronegativity. To calculate formal charges, we assign electrons in the molecule to individual atoms according to these rules:

- Non-bonding electrons are assigned to the atom on which they are located.
- Bonding electrons are divided equally between the two bonded atoms, so one electron from each bond goes to each atom.

The formal charge of each atom in a molecule can be calculated using the following equation:

Misplaced '#'

To illustrate this method, let's calculate the formal charge on the atoms in ammonia ($\mathbf{NH_3}$) whose Lewis structure is as follows:



A neutral nitrogen atom has five valence electrons (it is in group 15). From the Lewis structure, the nitrogen atom in ammonia has one lone pair and three bonds with hydrogen atoms. Substituting into Equation ???, we obtain

$$\begin{aligned} FC(N) &= (\text{5 valence electrons}) - (\text{2 non-bonding electrons}) - \frac{1}{2}(\text{3 bonds}) \\ &= 0 \end{aligned}$$

A neutral hydrogen atom has one valence electron. Each hydrogen atom in the molecule has no non-bonding electrons and one bond. Using Equation ??? to calculate the formal charge on hydrogen, we obtain

$$\begin{aligned} FC(H) &= (\text{1 valence electron}) - (\text{0 non-bonding electrons}) - \frac{1}{2}(\text{1 bond}) \\ &= 0 \end{aligned}$$

The sum of the formal charges of each atom must be equal to the overall charge of the molecule or ion. In this example, the nitrogen and each hydrogen has a formal charge of zero. When summed the overall charge is zero, which is consistent with the overall neutral charge of the NH_3 molecule.

Typically, the structure with the most formal charges of zero on atoms is the more stable Lewis structure. In cases where there MUST be positive or negative formal charges on various atoms, the most stable structures generally have negative formal charges on the more electronegative atoms and positive formal charges on the less electronegative atoms. The next example further demonstrates how to calculate formal charges for polyatomic ions.

Example 2.3.1

Calculate the formal charges on each atom in the NH_4^+ ion.

Given: chemical species

Asked for: formal charges

Strategy:

Identify the number of valence electrons in each atom in the NH_4^+ ion. Use the Lewis electron structure of NH_4^+ to identify the number of bonding and non-bonding electrons associated with each atom and then use Equation ??? to calculate the formal charge on each atom.

Solution:

The Lewis electron structure for the NH_4^+ ion is as follows:



The nitrogen atom in ammonium has zero non-bonding electrons and 4 bonds. Using Equation ???, the formal charge on the nitrogen atom is therefore

$$\begin{aligned} FC(N) &= (5 \text{ valence electrons}) - (0 \text{ non-bonding electrons}) - \frac{1}{2}(4 \text{ bonds}) \\ &= +1 \end{aligned}$$

Each hydrogen atom in has one bond and zero non-bonding electrons. The formal charge on each hydrogen atom is therefore

$$\begin{aligned} FC(H) &= (1 \text{ valence electron}) - (0 \text{ non-bonding electrons}) - \frac{1}{2}(1 \text{ bond}) \\ &= 0 \end{aligned}$$

The formal charges on the atoms in the NH_4^+ ion are thus

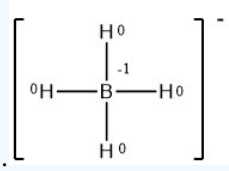


Adding together the formal charges on the atoms should give us the total charge on the molecule or ion. In this case, the sum of the formal charges is 0 + 1 + 0 + 0 + 0 = 1+, which is the same as the total charge of the ammonium polyatomic ion.

Exercise 1.5.1

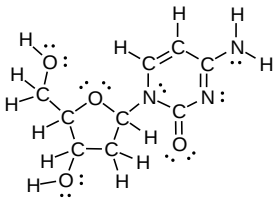
Write the formal charges on all atoms in BH_4^-.

Answer



Determining the Charge of Atoms in Organic Structures

The calculation method reviewed above for determining formal charges on atoms is an essential starting point for a novice organic chemist, and works well when dealing with small structures. But this method becomes unreasonably time-consuming when dealing with larger structures. It would be exceptionally tedious to determine the formal charges on each atom in 2'-deoxycytidine (one of the four nucleoside building blocks that make up DNA) using Equation ???. As you get more experience with organic structures, you will be able to quickly look at this type of complicated structure and determine charges on each atom.



2'-deoxycytidine

You need to develop the ability to quickly and efficiently draw large structures and determine formal charges. Fortunately, this only requires some practice with recognizing common bonding patterns.

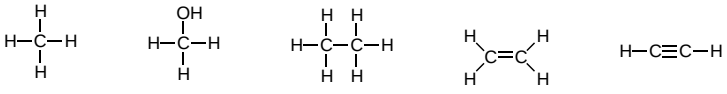
Organic chemistry only deals with a small part of the periodic table, so much so that it becomes convenient to be able to recognize the bonding forms of these atoms. The figure below contains the most important bonding forms. These will be discussed in detail below. An important idea to note is most atoms in a molecule are neutral. Pay close attention to the neutral forms of the elements below because that is how they will appear most of the time.

Figure 1.5.1: Structures of common organic atoms and ions.

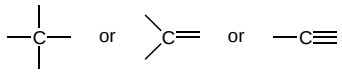
Atom	Positive	Neutral	Negative
C			
N			
O			
Cl (halogens)			

Carbon

Carbon, the most important element for organic chemists. In the structures of methane, methanol, ethane, ethene, and ethyne, there are four bonds to the carbon atom. And each carbon atom has a formal charge of zero. In other words, carbon is ***tetravalent***, meaning that it commonly forms four bonds.



methane methanol ethane ethene ethyne



Carbon usually makes four bonds

Carbon is tetravalent in most organic molecules, but there are exceptions. Later in this chapter and throughout this book are examples of organic ions called 'carbocations' and carbanions', in which a carbon atom has a positive or negative formal charge, respectively. ***Carbocations*** occur when a carbon has only three bonds and no lone pairs of electrons. Carbocations have only 3 valence electrons and a formal charge of 1+. ***Carbanions*** occur when the carbon atom has three bonds plus one lone pair of electrons. Carbanions have 5 valence electrons and a formal charge of 1−.

		
carbocation: 3 bonds & no lone pair	carbanion: 3 bonds & one lone pair	carbon radical: 3 bonds & one unpaired electron

Two other possibilities are carbon radicals and carbenes, both of which have a formal charge of zero. A ***carbon radical*** has three bonds and a single, unpaired electron. Carbon radicals have 4 valence electrons and a formal charge of zero. ***Carbenes*** are a highly reactive species, in which a carbon atom has two bonds and one lone pair of electrons, giving it a formal charge of zero. Though carbenes are rare, you will encounter them in section 8.10 Addition of Carbenes to Alkenes.

You should certainly use the methods you have learned to check that these formal charges are correct for the examples given above. More importantly, you will need, before you progress much further in your study of organic chemistry, to simply recognize these patterns (and the patterns described below for other atoms) and be able to identify carbons that bear positive and negative formal charges by a quick inspection.

Hydrogen

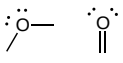
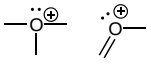
The common bonding pattern for hydrogen is easy: hydrogen atoms in organic molecules typically have only one bond, no unpaired electrons and a formal charge of zero. The exceptions to this rule are the proton, H^+, the hydride ion, H^-, and the hydrogen radical, $H^\cdot$. The ***proton*** is a hydrogen with no bonds and no lone pairs and a formal charge of 1+. The ***hydride ion*** is a is a hydrogen with no bonds, a pair of electrons, and a formal charge of 1−. The ***hydrogen radical*** is a hydrogen atom with no bonds, a single unpaired electron and a formal charge of 0. Because this book concentrates on organic chemistry as applied to living things, however, we will not be seeing 'naked' protons and hydrides as such, because they are too reactive to be present in that form in aqueous solution. Nonetheless, the *idea* of a proton will be very important when we discuss acid-base chemistry, and the *idea* of a hydride ion will become very important much later in the book when we discuss organic oxidation and reduction reactions. As a rule, though, all hydrogen atoms in organic molecules have one bond, and no formal charge.



Neutral Hydrogen: one bond, no lone pair

Oxygen

The common arrangement of oxygen that has a formal charge of zero is when the oxygen atom has 2 bonds and 2 lone pairs. Other arrangements are oxygen with 1 bond and 3 lone pairs, that has a 1− formal charge, and oxygen with 3 bonds and 1 lone pair that has a formal charge of 1+. All three patterns of oxygen fulfill the octet rule.

		
neutral oxygen: 2 bonds & 2 lone pairs	negative oxygen: 1 bond & 3 lone pairs	positive oxygen: 3 bonds & one lone pair

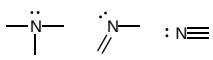
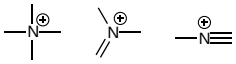
If it has two bonds and two lone pairs, as in water, it will have a formal charge of zero. If it has one bond and three lone pairs, as in hydroxide ion, it will have a formal charge of 1−. If it has three bonds and one lone pair, as in hydronium ion, it will have a formal

charge of 1+.

Oxygen can also exist as a radical, such as where an oxygen atom has one bond, two lone pairs, and one unpaired (free radical) electron, giving it a formal charge of zero. For now, however, concentrate on the three main non-radical examples, as these will account for most oxygen containing molecules you will encounter in organic chemistry.

Nitrogen

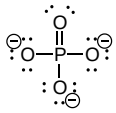
Nitrogen has two major bonding patterns, both of which fulfill the octet rule:

		
neutral nitrogen: 3 bonds & 1 lone pair	positive nitrogen: 4 bonds	negative nitrogen: 2 bonds & 2 lone pairs

If a nitrogen has three bonds and a lone pair, it has a formal charge of zero. If it has four bonds (and no lone pair), it has a formal charge of 1+. In a fairly uncommon bonding pattern, negatively charged nitrogen has two bonds and two lone pairs.

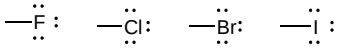
Phosphorus and Sulfur

Two third row elements are commonly found in biological organic molecules: phosphorus and sulfur. Although both of these elements have other bonding patterns that are relevant in laboratory chemistry, in a biological context sulfur almost always follows the same bonding/formal charge pattern as oxygen, while phosphorus is present in the form of phosphate ion (PO_4^{3-}), where it has five bonds (almost always to oxygen), no lone pairs, and a formal charge of zero. Remember that elements in the third row of the periodic table have *d* orbitals in their valence shell as well as *s* and *p* orbitals, and thus are not bound by the octet rule.



Halogens

The halogens (fluorine, chlorine, bromine, and iodine) are very important in laboratory and medicinal organic chemistry, but less common in naturally occurring organic molecules. Halogens in organic compounds usually are seen with one bond, three lone pairs, and a formal charge of zero. Sometimes, especially in the case of bromine, we will encounter reactive species in which the halogen has two bonds (usually in a three-membered ring), two lone pairs, and a formal charge of 1+.



Common Neutral Bonding Patterns for Halogens



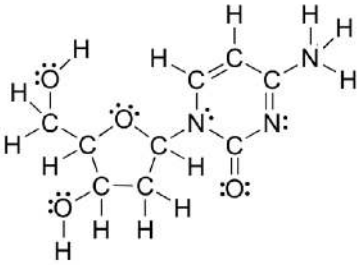
Common Positive Bonding Pattern for Halogens

These rules, if learned and internalized so that you don't even need to think about them, will allow you to draw large organic structures, complete with formal charges, quite quickly.

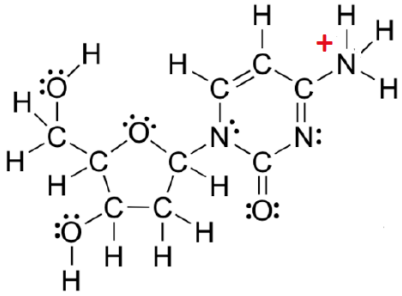
Once you have gotten the hang of drawing Lewis structures, it is not always necessary to draw lone pairs on heteroatoms, as you can assume that the proper number of electrons are present around each atom to match the indicated formal charge (or lack thereof). Occasionally, though, lone pairs are drawn if doing so helps to make an explanation more clear.

? Exercise 1.5.2

Please identify an atom with a non-neutral charge in the following atom:

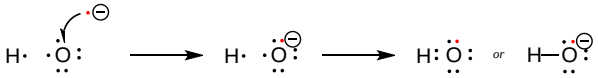


Answer

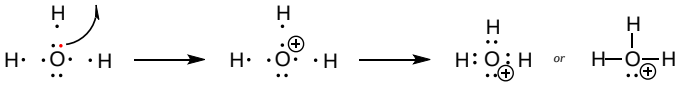


Drawing the Lewis Structure of Ionic Molecular Compounds

The hydroxide ion, OH^-, is drawn simply by showing the oxygen atom with its six valence electrons, then adding one more electron to account for the negative charge. By changing the number of valence electrons the bonding characteristic of oxygen are now changed. Now the oxygen has three non-bonding lone pairs, and can only form one bond to a hydrogen.



To draw a Lewis structure of the hydronium ion, H_3O^+, you again start with the oxygen atom with its six valence electrons, then take one away to account for the positive charge to give oxygen five valence electrons. The oxygen has one non-bonding lone pair and three unpaired electrons which can be used to form bonds to three hydrogen atoms.



Using Formal Charges to Distinguish between Lewis Structures

As an example of how formal charges can be used to determine the most stable Lewis structure for a substance, we can compare two possible structures for CO_2. Both structures conform to the rules for Lewis electron structures.

CO_2

1. C gets more bonds when neutral, so it is the central atom.
2. C has 4 valence electrons and each O has 6 valence electrons, for a total of 16 valence electrons.
3. Placing one electron pair between the C and each O gives O–C–O, with 12 electrons left over.
4. Dividing the remaining electrons between the O atoms gives three lone pairs on each atom:



This structure has an octet of electrons around each O atom but only 4 electrons around the C atom.

5. No electrons are left for the central atom.

6. To give the carbon atom an octet of electrons, we can convert two of the lone pairs on the oxygen atoms to bonding electron pairs. There are, however, two ways to do this. We can either take one electron pair from each oxygen to form a symmetrical structure or take both electron pairs from a single oxygen atom to give an asymmetrical structure:



Both Lewis electron structures give all three atoms an octet. How do we decide between these two possibilities? The formal charges for the two Lewis electron structures of CO2 are as follows:



Both Lewis structures have a net formal charge of zero, but the structure on the right has a 1+ charge on the more electronegative atom (O). Thus the symmetrical Lewis structure on the left is predicted to be more stable, and it is, in fact, the structure observed experimentally. Remember, though, that formal charges do *not* represent the actual charges on atoms in a molecule or ion. They are used simply as a bookkeeping method for predicting the most stable Lewis structure for a compound.

Note

The Lewis structure with the set of formal charges closest to zero is usually the most stable.

Example 2.3.2: Thiocyanate Ion

The thiocyanate ion (SCN^-), which is used in printing and as a corrosion inhibitor against acidic gases, has at least two possible Lewis electron structures. Draw two possible structures, assign formal charges on all atoms in both, and decide which is the preferred arrangement of electrons.

Given: chemical species

Asked for: Lewis electron structures, formal charges, and preferred arrangement

Strategy:

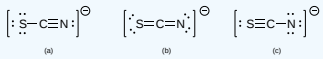
A Use the step-by-step procedure to write two plausible Lewis electron structures for SCN^-.

B Calculate the formal charge on each atom using Equation ???.

C Predict which structure is preferred based on the formal charge on each atom and its electronegativity relative to the other atoms present.

Solution:

A Possible Lewis structures for the SCN^- ion are as follows:



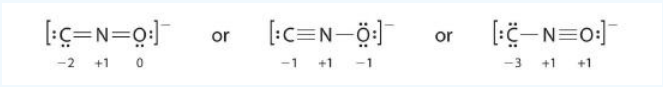
B We must calculate the formal charges on each atom to identify the more stable structure. If we begin with carbon, we notice that the carbon atom in each of these structures shares four bonding pairs, the number of bonds typical for carbon, so it has a formal charge of zero. Continuing with sulfur, we observe that in (a) the sulfur atom shares one bonding pair and has three lone pairs and has a total of six valence electrons. The formal charge on the sulfur atom is therefore 6 - (6 + 2/2) = 1−. In (b), the sulfur atom has a formal charge of 0. In (c), the sulfur atom has a formal charge of 1+. Continuing with the nitrogen, we observe that in (a) the nitrogen atom shares three bonding pairs and has one lone pair and has a total of 5 valence electrons. The formal charge on the nitrogen atom is therefore 5 - (2 + 6/2) = 0. In (b), the nitrogen atom has a formal charge of 1−. In (c), the nitrogen atom has a formal charge of 2−.

C Which structure is preferred? Structure (b) is preferred because the negative charge is on the more electronegative atom (N), and it has lower formal charges on each atom as compared to structure (c): 0, 1− versus 1+, 2−.

? Exercise 1.5.2: Fulminate Ion

Salts containing the fulminate ion (CNO^-) are used in explosive detonators. Draw three Lewis electron structures for CNO^- and use formal charges to predict which is more stable. (Note: **N** is the central atom.)

Answer

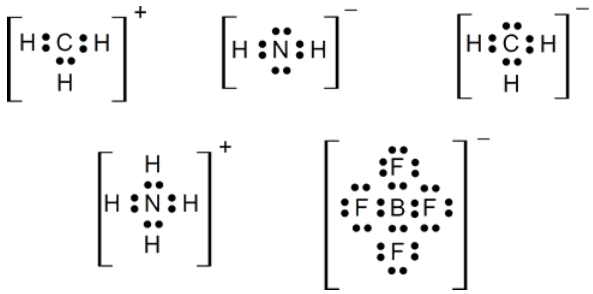


The second structure is predicted to be the most stable.

Exercises

1. Draw the Lewis structure of each of these molecules: CH_3^+, NH_2^-, CH_3^-, NH_4^+, BF_4^-. In each case, use the method of calculating formal charge described to satisfy yourself that the structures you have drawn do in fact carry the charges shown.

Answer

1. 

2.3: Formal Charges

2.3 Exercises

Questions

Q2.3.1

Give the formal charges for all non-hydrogen atoms in the following molecules: BH_4^-, H_2O, CH_3O^-

Solutions

S2.3.1

BH_4^- (B = −1)

H_2O (O = 0)

CH_3O^- (C = 0, O = −1)

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1.6: Drawing Chemical Structures

Objectives

After completing this section, you should be able to

1. propose one or more acceptable Kekulé structures (structural formulas) for any given molecular formula
2. write the molecular formula of a compound, given its Kekulé structure.
3. draw the shorthand structure of a compound, given its Kekulé structure.
4. interpret shorthand structures and convert them to Kekulé structures.
5. write the molecular formula of a compound, given its shorthand structure.

Study Notes

When drawing the structure of a neutral organic compound, you will find it helpful to remember that

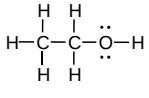
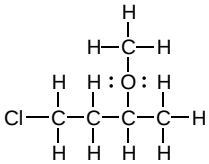
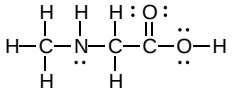
- each carbon atom has four bonds.
- each nitrogen atom has three bonds.
- each oxygen atom has two bonds.
- each hydrogen atom has one bond.

Through general chemistry, you may have already experienced looking at molecular structures using Lewis structures. Because organic chemistry can involve large molecules it would be beneficial if Lewis structures could be abbreviated. The three different ways to draw organic molecules include Kekulé Formulas, Condensed Formulas, and Skeletal structures (also called line-bond structures or line formulas). During this course, you will view molecules written in all three forms. It will be more helpful if you become comfortable going from one style of drawing to another, and look at drawings and understanding what they represent. Developing the ability to convert between different types of formulas requires practice, and in most cases the aid of molecular models. Many kinds of model kits are available to students and professional chemists, and the beginning student is encouraged to obtain one.

Simplification of structural formulas may be achieved without any loss of the information they convey. Kekule formulas is just organic chemistry's term for Lewis structures you have previously encountered. In **condensed structural formulas**, the bonds to each carbon are omitted, but each distinct structural unit (group) is written with subscript numbers designating multiple substituents, including the hydrogens. **Line formulas** omit the symbols for carbon and hydrogen entirely (unless the hydrogen is bonded to an atom other than carbon). Each straight line segment represents a bond, the ends and intersections of the lines are carbon atoms, and the correct number of hydrogens is calculated from the tetravalency of carbon. Non-bonding valence shell electrons are omitted in these formulas.

Kekulé (a.k.a. Lewis Structures)

A Kekulé Formula or structural formula displays the atoms of the molecule in the order they are bonded. It also depicts how the atoms are bonded to one another, for example single, double, and triple covalent bond. Covalent bonds are shown using lines. The number of dashes indicate whether the bond is a single, double, or triple covalent bond. All atom labels are shown and all lone pairs are shown.

		
A	**B**	**C**

Condensed Formula

A condensed formula is made up of the elemental symbols. Condensed structural formulas show the order of atoms like a structural formula but are written in a single line to save space and make it more convenient and faster to write out. The order of the atoms suggests the connectivity in the molecule. Condensed structural formulas are also helpful when showing that a group of atoms is connected to a single atom in a compound. When this happens, parenthesis are used around the group of atoms to show they are together. Also, if more than one of the same substituent is attached to a given atom, it is show with a subscript number. An example is CH_4, which represents four hydrogens attached to the same carbon. Condensed formulas can be read from either direction and H_3C is the same as CH_3, although the latter is more common.

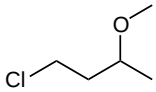
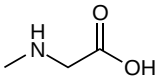
Look at the examples below and match them with their identical molecule under the Kekulé structures and the line formulas.

CH_3CH_2OH	$ClCH_2CH_2CH(OCH_3)CH_3$	CH_3NHCH_2COOH
A	**B**	**C**

Let's look closely at example B. As you go through a condensed formula, you want to focus on the carbons and other elements that aren't hydrogen. The hydrogen's are important, but are usually there to complete octets. Also, notice the $-OCH_3$ is in written in parentheses which tell you that it not part of the main chain of carbons. As you read through a a condensed formula, if you reach an atom that doesn't have a complete octet by the time you reach the next hydrogen, then it's possible that there are double or triple bonds. In example C, the carbon is double bonded to oxygen and single bonded to another oxygen. Notice how COOH means C(=O)-O-H instead of CH_3-C-O-O-H because carbon does not have a complete octet and oxygens.

Line Formula

Because organic compounds can be complex at times, line-angle formulas are used to write carbon and hydrogen atoms more efficiently by replacing the letter "C" with lines. A carbon atom is present wherever a line intersects another line. Hydrogen atoms are omitted but are assumed to be present to complete each of carbon's four bonds. Hydrogens that are attached to elements other than carbon are shown. Atom labels for all other elements are shown. Lone pair electrons are usually omitted. They are assumed to be present to complete the octet of non-carbon atoms. Line formulas help show the structure and order of the atoms in a compound.

		
A	**B**	**C**

These molecules correspond to the exact same molecules depicted for Kekulé structures and condensed formulas. Notice how the carbons are no longer drawn in and are replaced by the ends and bends of a lines. In addition, the hydrogens have been omitted, but could be easily drawn in (see practice problems). Although we do not usually draw in the H's that are bonded to carbon, we do draw them in if they are connected to other atoms besides carbon (example is the OH group above in example A) . This is done because it is not always clear if the non-carbon atom is surrounded by lone pairs or hydrogens. Also in example A, notice how the OH is drawn with a bond to the second carbon, but it does not mean that there is a third carbon at the end of that bond/ line.

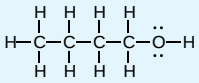
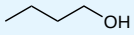
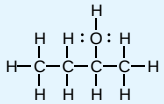
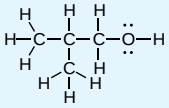
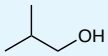
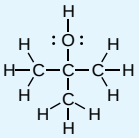
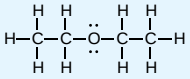
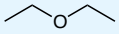
Kekulé Formula	Condensed Formula	Line Formula
	$CH_3(CH_2)_3OH$	
	$CH_3CH_2CH(OH)CH_3$	
	$(CH_3)_2CHCH_2OH$	
	$(CH_3)_3COH$	
	$CH_3CH_2OCH_2CH_3$	

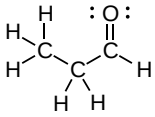
Table 1.6.1: Structural Formulas for $C_4H_{10}O$ isomers

Example: Converting between Structural Formulas

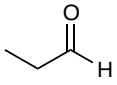
It is helpful to convert compounds into different structural formulas (Kekule, Line, and Condensed) depending on the type of question that is asked. Standardized exams frequently include a high percentage of condensed formulas because it is easier and cheaper to type letters and numbers than to import figures. Initially, it can be difficult writing a Line structure directly from a condensed formula. First, write the Kekule structure from the condensed formula and then draw the Line structure from the Kekule.

a) The condensed formula for propanal is CH_3CH_2CHO. Draw the Kekule structure.

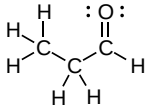
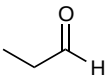
The Kekule structure for propanal is shown below. Remember that every carbon will have four bonds and oxygens octet is filled with lone pairs.



The bond-line structure for propanal is shown below. First, remove hydrogens. The hydrogen attached to the aldehyde group remains because it is part of a functional group. The remove the "C" labels from the structure and keep the lines in place. Lastly, remove any lone pairs.



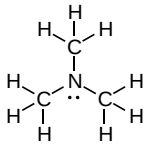
All three structures represent the same compound, propanal.

CH_3CH_2CHO =  = 

b) The following is the line structure of the molecule trimethyl amine.



To convert it to a Kekule structure first identify the carbons in the molecule. The will be at the corners and ends of line without an atom label. Trimethyl amine has three carbons. Next, add hydrogens to the carbons until four bonds are present. Each carbon in trimethyl amine is singly bonded to nitrogen. This means each carbon will need three additional C-H bonds to create its octet. Lastly, add lone pairs to other elements to fill their octets. The nitrogen in trimethyl amine is bonded to three carbons. This means it will require one of lone pair electrons to complete its octet.



Exercises

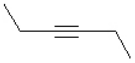
1. How many carbons are in the following drawing? How many hydrogens?



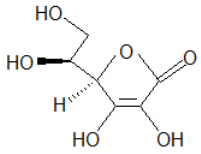
2. How many carbons are in the following drawing? How many hydrogens?



3. How many carbons are in the following drawing? How many hydrogens?

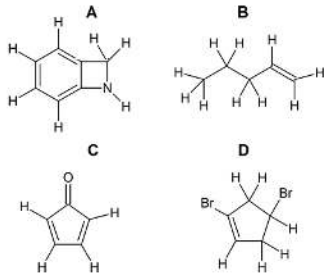


4. Look at the following molecule of vitamin A and draw in the hidden hydrogens and electron pairs.



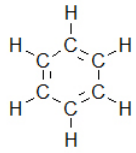
(hint: Do all of the carbons have 4 bonds? Do all the oxygens have a full octet?)

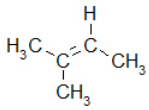
5. Draw $ClCH_2CH_2CH(OCH_3)CH_3$ in Kekulé and line form.
6. Write down the molecular formula for each of the compounds shown here.



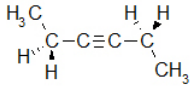
Answers:

1. Remember the octet rule and how many times carbons and hydrogens are able to bond to other atoms.



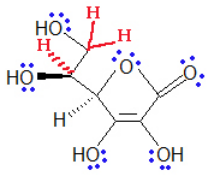


2.

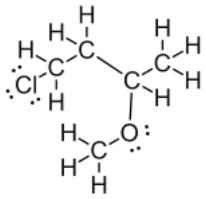


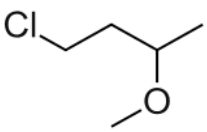
3.

4. Electron pairs drawn in blue and hydrogens draw in red.



5.





6.

A. C_7H_7N
B. C_5H_{10}
C. C_5H_4O
D. $C_5H_6Br_2$

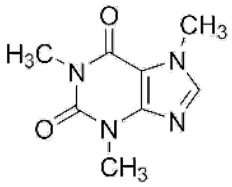
1.12: Drawing Chemical Structures

1.12 Exercises

Questions

Q1.12.1

Below is the molecule for caffeine. Give the molecular formula for it.



Solutions

S1.12.1

$C_8H_{10}O_2N_4$

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1.7: sp³ Hybrid Orbitals and the Structure of Methane

Objective

After completing this section, you should be able to describe the structure of methane in terms of the sp^3 hybridization of the central carbon atom.

Key Terms

Make certain that you can define, and use in context, the key terms below.

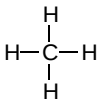
- bond angle
- hybridization
- sp^3 hybrid

Study Notes

The tetrahedral shape is a very important one in organic chemistry, as it is the basic shape of all compounds in which a carbon atom is bonded to four other atoms. Note that the tetrahedral bond angle of **H — C — H** is 109.5°.

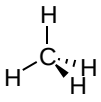
Valence Bond Theory

Valence bond theory's use of overlapping atomic orbitals to explain how chemical bonds form works well in simple diatomic molecules such as H_2. However, when molecules with more than two atoms form stable bonds, we require a more detailed model. A good example is methane (CH_4). According to valence bond theory, the structure of a covalent species can be depicted using a Lewis structure.



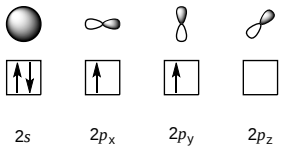
1

Experimentally, it has been shown that the four carbon-hydrogen bonds in the methane molecule are identical, meaning they have the same bond energy and the same bond length. Also, VSEPR theory suggests that the geometry at the carbon atom in the methane molecule is tetrahedral **(2)**, and there exists a large body of both theoretical and experimental evidence supporting this prediction.



2

According to valence bond theory, to form a covalent bond forms when an unpaired electron in one atom overlaps with an unpaired electron in a different atom. Now, consider the the electron configuration of the four valence electrons in carbon.



There is a serious mismatch between the electron configuration of carbon ($1s^2 2s^2 2p^2$) and the predicted structure of methane. The modern structure shows that there are only 2 unpaired electrons to share with hydrogens, instead of the 4 needed to create methane. Also, the p_x and p_y orbitals are at 90° to each other. They would form perpendicular bonds instead of the tetrahedral 109.5° bond angle predicted by VSEPR and experimental data. Lastly, there are two different orbitals, 2*s* and 2*p*, which would create different types of C-H bonds. As noted earlier, experimentally, the four carbon-hydrogen bonds in the methane molecule are identical.

Hybrid Orbitals

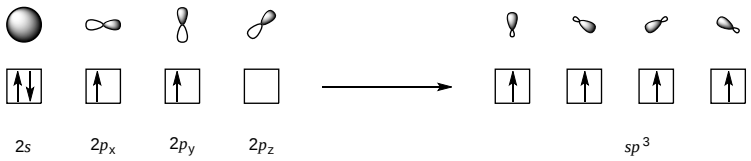
An answer to the problems posed above was offered in 1931 by Linus Pauling. He showed mathematically that an *s* orbital and three *p* orbitals on an atom can combine to form four equivalent hybrid atomic orbitals.

Important Ideals in Understanding Hybridization

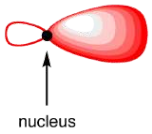
1. Hybrid orbitals do not exist in isolated atoms. They are formed only in covalently bonded atoms.
2. Hybrid orbitals have shapes and orientations that are very different from those of the atomic orbitals in isolated atoms.
3. A set of hybrid orbitals is generated by combining atomic orbitals. The number of hybrid orbitals in a set is equal to the number of atomic orbitals that were combined to produce the set.
4. All orbitals in a set of hybrid orbitals are equivalent in shape and energy.
5. The type of hybrid orbitals formed in a bonded atom create the molecular geometry as predicted by the VSEPR theory.
6. Hybrid orbitals overlap to form σ bonds.
7. Lone pair electrons are often contained in hybrid orbitals

sp^3 Hybridization in Methane

In order to explain this observation, valence bond theory relies on a concept called **orbital hybridization**. In this picture, the four valence orbitals of the carbon (one 2*s* and three 2*p* orbitals) combine mathematically (remember: orbitals are described by equations) to form four equivalent **hybrid orbitals**, which are named ***sp*^{3} orbitals** because they are formed from mixing one *s* and three *p* orbitals. In the new electron configuration, each of the four valence electrons on the carbon occupies a single sp^3 orbital creating four unpaired electrons.



The shape of an sp^3 hybridized orbital is a combination of *s* and *p* atomic orbitals.



Each sp^3-hybridized orbital bears an electron, and electrons repel each other. To minimize the repulsion between electrons, the four sp^3-hybridized orbitals arrange themselves around the carbon nucleus so that they are as far away as possible from each other, resulting in the tetrahedral arrangement predicted by VSPER. The carbon atom in methane is called an "sp^3-hybridized carbon atom." The larger lobes of the sp^3 hybrids are directed towards the four corners of a tetrahedron, meaning that the angle between any two orbitals is 109.5°.

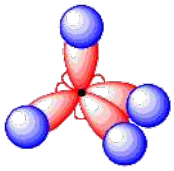


5

Bonding in Methane

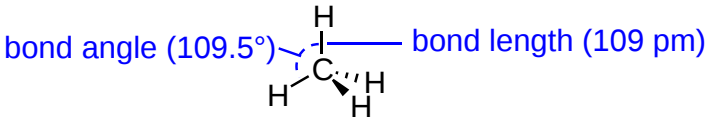
Each C-H bond in methane, then, can be described as an overlap between a half-filled 1*s* orbital in four hydrogen atoms and the larger lobe of one of the four half-filled sp^3 hybrid orbitals form a four equivalent sigma (σ) bond. This orbital overlap is often described using the notation: sp^3(C)-1*s*(H). The formation of sp^3 hybrid orbitals successfully explains the tetrahedral structure of methane and the equivalency of the the four C-H bonds.

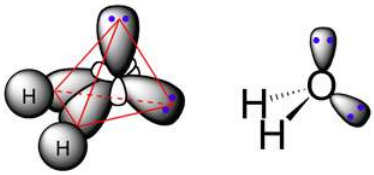
What remains is an explanation of why the sp^3 hybrid orbitals form. When the *s* and 3 *p* orbitals in carbon hybridize the resulting sp^3 hybrid orbital is unsymmetrical with one lobe larger than the other. This means the larger lobe can overlap more effectively with orbitals from other bonds making them stronger. Hybridizing allows for the carbon to form stronger bonds than it would with unhybridized *s* or *p* orbitals.



6

The four carbon-hydrogen bonds in methane are equivalent and all have a bond length of 109 pm (1.09 x 10-10 m), bond strength of of 429 kJ/mol. All of the H-C-H bond angles are 109.5°.



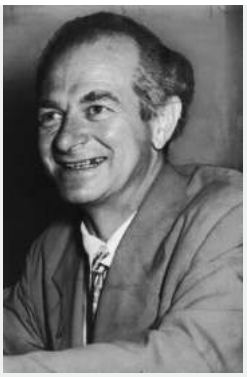


Looking Closer: Linus Pauling

Arguably the most influential chemist of the 20th century, Linus Pauling (1901–1994) is the only person to have won two individual (that is, unshared) Nobel Prizes. In the 1930s, Pauling used new mathematical theories to enunciate some fundamental principles of the chemical bond. His 1939 book *The Nature of the Chemical Bond* is one of the most significant books ever published in chemistry.

Pauling's big contribution to chemistry was valence bond theory, which combined his knowledge of quantum mechanical theory with his knowledge of basic chemical facts, like bond lengths and and bond strengths and shapes of molecules. Valence bond theory, like Lewis's bonding theory, provides a simple model that is useful for predicting and understanding the structures of molecules, especially for organic chemistry. .

By 1935, Pauling's interest turned to biological molecules, and he was awarded the 1954 Nobel Prize in Chemistry for his work on protein structure. (He was very close to discovering the double helix structure of DNA when James Watson and James Crick announced their own discovery of its structure in 1953.) He was later awarded the 1962 Nobel Peace Prize for his efforts to ban the testing of nuclear weapons.



Linus Pauling was one of the most influential chemists of the 20th century.

In his later years, Pauling became convinced that large doses of vitamin C would prevent disease, including the common cold. Most clinical research failed to show a connection, but Pauling continued to take large doses daily. He died in 1994, having spent a lifetime establishing a scientific legacy that few will ever equal

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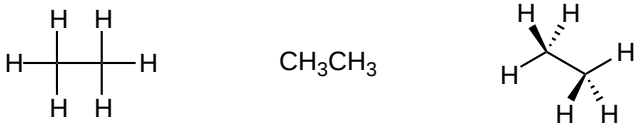
1.8: sp³ Hybrid Orbitals and the Structure of Ethane

Objective

After completing this section, you should be able to describe the structure of ethane in terms of the sp^3 hybridization of the two carbon atoms present in the molecule ethane.

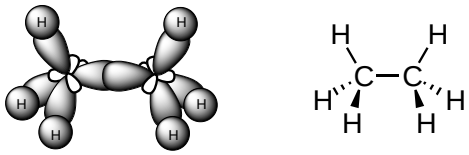
Bonding in Ethane

The simplest molecule with a carbon-carbon bond is ethane, C_2H_6.

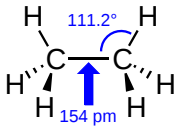


Representations of Ethane

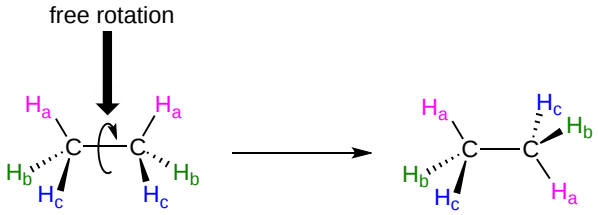
In ethane (CH_3CH_3), both carbons are sp^3-hybridized, meaning that both have four bonds with tetrahedral geometry. An sp^3 orbital of one carbon atom overlaps end to end with an sp^3 orbital of the second carbon atom to form a carbon-carbon σ bond. This orbital overlap is often described using the notation: sp^3(C)-sp^3(C). Each of the remaining sp^3 hybrid orbitals overlaps with the ***S*** orbital of a hydrogen atom to form carbon–hydrogen σ bonds.



The σ carbon-carbon bond has a bond length of 154 pm, and a bond strength of 377 kJ/mol. The carbon-hydrogen σ bonds are slightly weaker, 421 kJ/mol, than those of methane. The C-C-H bond angles in ethane are 111.2° which is close to the what is expected for tetrahedral molecules.



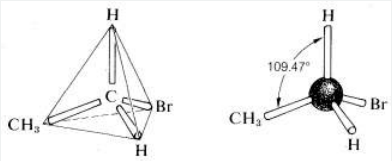
The orientation of the two CH_3 groups is not fixed relative to each other. Because they are formed from the end-on-end overlap of two orbitals, *sigma bonds are free to rotate*. This means, in the case of ethane molecule, that the two methyl (CH_3) groups can be pictured as two wheels on a hub, each one able to rotate freely with respect to the other. In Section 3.7 we will learn more about the implications of rotational freedom in sigma bonds, when we discuss the 'conformation' of organic molecules

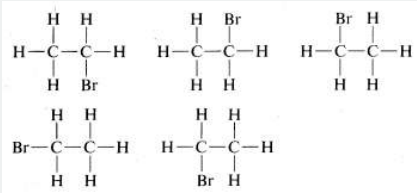


How did they know?

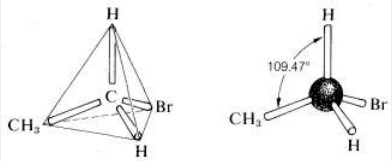
The tetrahedral geometry of carbon was predicted as far back as 1874. But how did they know? A question came up when looking at ethane with a bromine substituent (C_2H_5Br). When looking at the possible structures of the compound C_2H_5Br there are several possible structural formulas.here was a serious problem as to whether these formulas represent the same or different

compounds. All that was known in the early days was that every purified sample of C_2H_5Br, no matter how prepared, had a boiling point of 38 °C and density of 1.460 gml^{-1}. Furthermore, all looked the same, all smelled the same, and all underwent the same chemical reactions. There was no evidence that C_2H_5Br was a mixture or that more than one compound of this formula could be prepared. One might conclude, therefore, that all of the structural formulas above represent a single substance but how? A brilliant solution to the problem came when J. H. van 't Hoff proposed that all four bonds of carbon are equivalent and directed to the corners of a regular tetrahedron. If we redraw the structures for C_2H_5Br with both carbons having tetrahedral geometry, we see that there is only one possible arrangement. This theory hints at the idea of free rotation around sigma bonds which will be discussed later.





There was a serious problem as to whether these formulas represent the same or different compounds. All that was known in the early days was that every purified sample of C_2H_5Br, no matter how prepared, had a boiling point of 38 °C and density of 1.460 gml^{-1}. Furthermore, all looked the same, all smelled the same, and all underwent the same chemical reactions. There was no evidence that C_2H_5Br was a mixture or that more than one compound of this formula could be prepared. One might conclude, therefore, that all of the structural formulas above represent a single substance but how? A brilliant solution to the problem came when J. H. van 't Hoff proposed that all four bonds of carbon are equivalent and directed to the corners of a regular tetrahedron. If we redraw the structures for C_2H_5Br with both carbons having tetrahedral geometry, we see that there is only one possible arrangement. This theory hints at the idea of free rotation around sigma bonds which will be discussed later.



Exercise

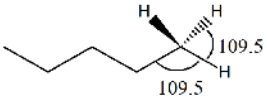
Questions

Q1.7.1

Draw pentane, $CH_3CH_2CH_2CH_2CH_3$, predict the bond angles within this molecule.

Solutions

S1.7.1



All the bond angles will be the same size.

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1.9: sp² Hybrid Orbitals and the Structure of Ethylene

Objectives

After completing this section, you should be able to

1. account for the formation of carbon-carbon double bonds using the concept of sp^2 hybridization.
2. describe a carbon-carbon double bond as consisting of one σ bond and one π bond.
3. explain the difference between a σ bond and a π bond in terms of the way in which *p* orbitals overlap.

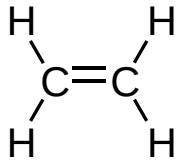
Key Terms

Make certain that you can define, and use in context, the key terms below.

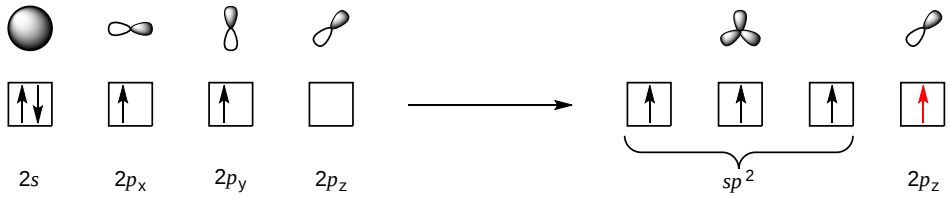
- pi (π) bond
- sp^2 hybrid

Bonding in Ethylene

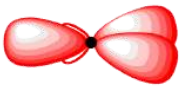
Thus far valence bond theory has been able to describe the bonding in molecules containing only single bonds. However, when molecules contain double or triple bonds the model requires more details. Ethylene (commonly knows as ethene), CH_2CH_2, is the simplest molecule which contains a carbon carbon double bond. The Lewis structure of ethylene indicates that there are one carbon-carbon double bond and four carbon-hydrogen single bonds. Experimentally, the four carbon-hydrogen bonds in the ethylene molecule have been shown to be identical. Because each carbon is surrounded by three electron groups, VSEPR theory says the molecule should have a trigonal planar geometry. Although each carbon has fulfilled its tetravalent requirement, one bond appears different. Clearly, a different type of orbital overlap is involved.



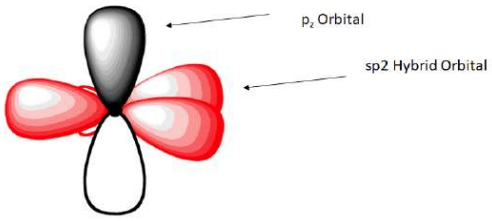
The sigma bonds formed in ethene is by the participation of a different kind of hybrid orbital. Three atomic orbitals on each carbon – the 2*s*, $2p_x$ and $2p_y$ – combine to form three sp^2 hybrids, leaving the $2p_z$ orbital unhybridized. Three of the four valence electrons on each carbon are distributed to the three sp^2 hybrid orbitals, while the remaining electron goes into the unhybridized p_z orbital. Each carbon in ethene is said to be a "sp^2-hybridized carbon." The electron configuration of the sp^2 hybridized carbon shows that there are four unpaired electrons to form bonds. However, the unpaired electrons are contained in two different types of orbitals so it is to be expected that two different types of bonds will form.



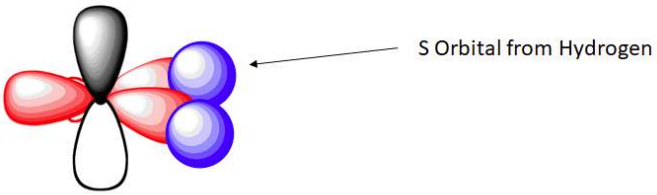
The shape of the sp^2-hybridized orbital has be mathematically shown to to be roughly the same as that of the sp^3-hybridized orbital. To minimize the repulsion between electrons, the three sp^2-hybridized orbitals are arranged with a trigonal planar geometry. Each orbital lobe is pointing to the three corners of an equilateral triangle, with angles of 120° between them. Again, geometry and hybrization can be tied together. Atoms surrounded by three electron groups can be said to have a trigonal planar geometry and sp^2 hybridization.



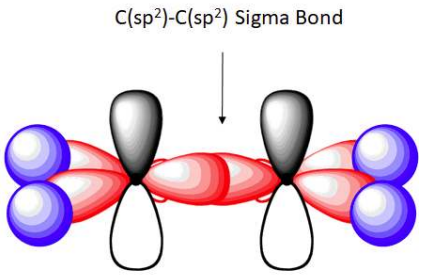
The unhybridized $2p_z$ orbital is *perpendicular* to the plane of the trigonal planar sp^2 hybrid orbtals.



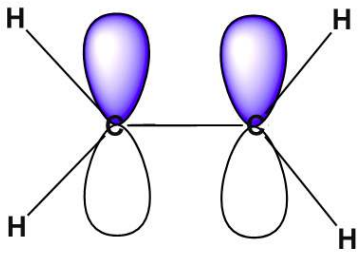
In the ethylene molecule, each carbon atom is bonded to two hydrogen atoms. Thus, overlap two sp^2-hybridized orbitals with the 1s orbitals of two hydrogen atoms for the C-H sigma bonds in ethylene (sp^2(C)-1s(H). Consequently, consistent with the observations, the four carbon-hydrogen bonds in ethylene are identical.



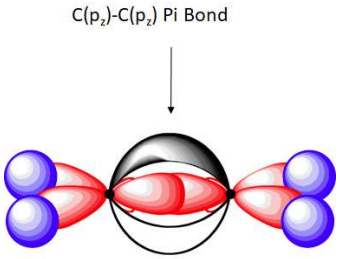
The C-C sigma bond in ethylene is formed by the overlap of an sp^2 hybrid orbital from each carbon.



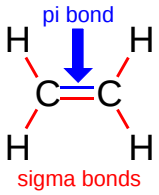
The overlap of hybrid orbitals or a hybrid orbital and a 1s orbtial from hydrogen creates the sigma bond framework of the ethylene molecule. However the unhybridized p_z orbital on each carbon remains.



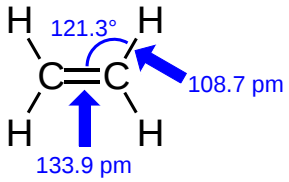
The unhybridized pz orbitals on each carbon overlap to a π bond (pi). The orbital overlap is commonly written as p_z(C)-1p_z(C). In general multiple bonds in molecular compound are formed by the overlap of unhybridized p orbitals. It should be noted that the carbon-carbon double bond in ethlene is made up of two different types of bond, a sigma and a pi.



Overall, ethylene is said to contain five sigma bonds and one pi bond. Pi bonds tend to be weaker than sigma bonds because the side-by-side overlap the p orbitals give a less effective orbital overlap when compared to the end-to-end orbital overlap of a sigma bond. This makes the pi much easier to break which is one of the most important ideas in organic chemistry reactions as we will see in Chapter 7 and subsequent chapters.

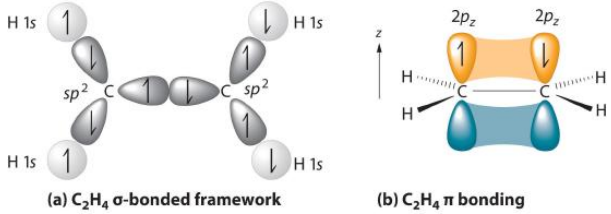


An ethylene molecule is said to be made up of five sigma bonds and one pi bond. The three sp^2 hybrid orbitals on each carbon orient to create the basic trigonal planer geometry. The H-C-C bond angle in ethylene is 121.3° which is very close to the 120° predicted by VSEPR. The four C-H sigma bonds in ethylene . The carbon-carbon double bond in ethylene is both shorter (133.9 pm) and almost twice as strong (728 kJ/mol) than the carbon- carbon single bond in ethylene (154 pm & 377 kJ/mol). Each of the four carbon-hydrogen bond in ethylene are equivalent has have a length of 108.7 pm



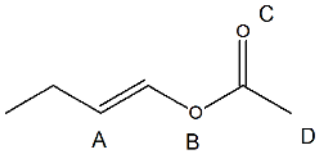
Rigidity in Ethene

Because they are the result of side-by-side overlap (rather then end-to-end overlap like a sigma bond), *pi bonds are not free to rotate.* If rotation about this bond were to occur, it would involve disrupting the side-by-side overlap between the two $2p_z$ orbitals that make up the pi bond. If free rotation were to occur the p-orbitals would have to go through a phase where they are 90° from each other, which would break the pi bond because there would be no overlap. Since the pi bond is essential to the structure of ethene it must not break, so there can be not free rotation about the carbon-carbon sigma bond. The presence of the pi bond thus 'locks' the six atoms of ethene into the same plane.



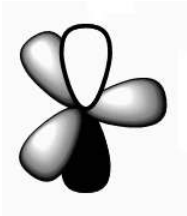
Exercise

1) Consider the following molecule:



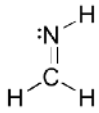
At each atom, what is the hybridization and the bond angle and the bond angle predicted by VSPER?

2) Please identify the types of orbitals shown in the following diagram:



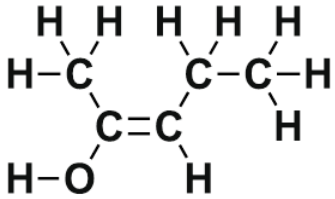
3)

a: Describe the orbitals which overlap to the carbon-nitrogen sigma bond and pie bond in the molecule below:



b: What kind of orbital holds the nitrogen lone pair?

4) For the following molecule please indicate with atoms are being held in the same plane by the carbon-carbon double bond:



Solutions

1)

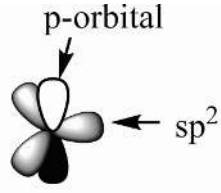
A - sp^2, 120°

B - sp^3, 109°

C - sp^2, 120° (with the lone pairs present)

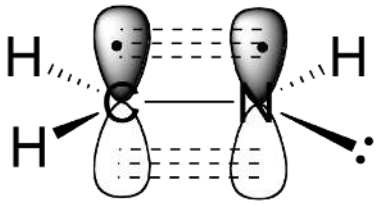
D - sp^3, 109°

2)



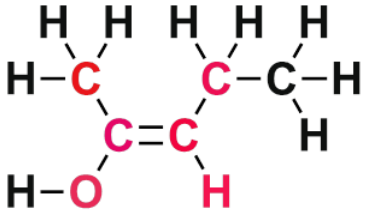
3)

a) The carbon and nitrogen atoms are both sp^2 hybridized. The carbon-nitrogen double bond is composed of a sigma bond formed from two sp^2 orbitals, and a pi bond formed from the side-by-side overlap of two unhybridized *2p* orbitals.



b) As shown in the figure above, the nitrogen lone pair electrons occupy one of the three sp^2 hybrid orbitals.

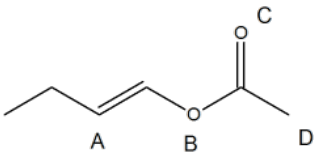
4)



Questions

Q1.8.1

Consider the following molecule:



At each atom, what is the hybridization and the bond angle? At atom A draw the molecular orbital.

Solutions

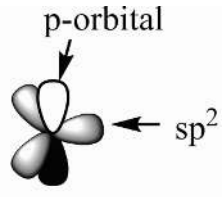
S1.8.1

A - sp^2, 120°

B - sp^3, 109°

C - sp^2, 120° (with the lone pairs present)

D - sp^3, 109°



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1.10: sp Hybrid Orbitals and the Structure of Acetylene

Objectives

After completing this section, you should be able to

1. use the concept of *sp* hybridization to account for the formation of carbon-carbon triple bonds, and describe a carbon-carbon triple bond as consisting of one σ bond and two π bonds.
2. list the approximate bond lengths associated with typical carbon-carbon single bonds, double bonds and triple bonds. [You may need to review Sections 1.7 and 1.8.]
3. list the approximate bond angles associated with sp^3-, sp^2- and *sp*-hybridized carbon atoms and predict the bond angles to be expected in given organic compounds. [If necessary, review Sections 1.6, 1.7 and 1.8.]
4. account for the differences in bond length, bond strength and bond angles found in compounds containing sp^3-, sp^2- and sp-hybridized carbon atoms, such as ethane, ethylene and acetylene.

Key Terms

Make certain that you can define, and use in context, the key term below.

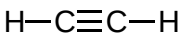
- *sp* hybrid orbital

Study Notes

The bond angles associated with sp^3-, sp^2- and *sp*-hybridized carbon atoms are approximately 109.5°, 120° and 180°, respectively.

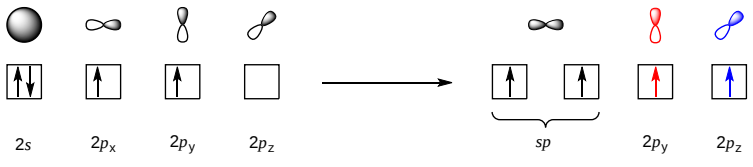
Bonding in acetylene

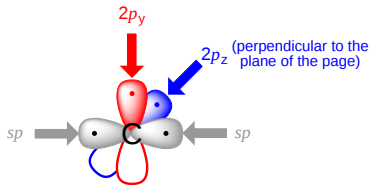
Finally, the hybrid orbital concept applies well to triple-bonded groups, such as alkynes and nitriles. Consider, for example, the structure of ethyne (another common name is acetylene), the simplest alkyne.



ethyne
(acetylene)

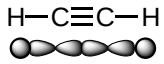
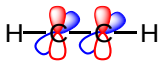
This molecule is linear: all four atoms lie in a straight line. The carbon-carbon triple bond is only 1.20Å long. In the hybrid orbital picture of acetylene, both carbons are ***sp*-hybridized**. In an *sp*-hybridized carbon, the 2*s* orbital combines with the $2p_x$ orbital to form two *sp* hybrid orbitals that are oriented at an angle of 180°with respect to each other (eg. along the x axis). The $2p_y$ and $2p_z$ orbitals remain non-hybridized, and are oriented perpendicularly along the y and z axes, respectively.



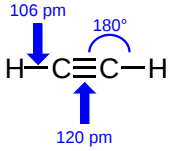


The C-C sigma bond is formed by the overlap of one *sp* orbital from each of the carbons, while the two C-H sigma bonds are formed by the overlap of the second *sp* orbital on each carbon with a 1*s* orbital on a hydrogen. Each carbon atom still has two half-

filled $2p_y$ and $2p_z$ orbitals, which are perpendicular both to each other and to the line formed by the sigma bonds. These two perpendicular pairs of *p* orbitals form two pi bonds between the carbons, resulting in a triple bond overall (one sigma bond plus two pi bonds).

	
sigma bonding in ethylene	pi bonding in ethylene

Acetylene is said to have three sigma bonds and two pi bonds. The carbon-carbon triple bond in acetylene is the shortest (120 pm) and the strongest (965 kJ/mol) of the carbon-carbon bond types. Because each carbon in acetylene has two electron groups, VSEPR predicts a linear geometry and and H-C-C bond angle of 180°.

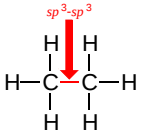
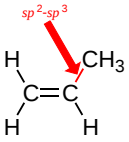
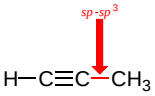


Comparison of C-C bonds Ethane, Ethylene, and Acetylene

Molecule	Bond	Bond Strength (kJ/mol)	Bond Length (pm)
Ethane, CH_3CH_3	(sp^3) C-C (sp^3)	376	154
Ethylene, $H_2C{=}CH_2$	(sp^2) C=C (sp^2)	728	134
Acetylene, HC≡CH	(*sp*) C≡C (*sp*)	965	120

Notice that as the bond order increases the bond length decreases and the bond strength increases.

The hybrid orbital concept nicely explains another experimental observation: single bonds adjacent to double and triple bonds are progressively shorter and stronger than 'normal' single bonds, such as the one in a simple alkane. The carbon-carbon bond in ethane (structure A below) results from the overlap of two sp^3 orbitals.

		
A	B	C

In propene (B), however, the carbon-carbon single bond is the result of overlap between an sp^2 orbital and an sp^3 orbital, while in propyne (C) the carbon-carbon single bond is the result of overlap between an sp orbital and an sp^3 orbital. These are all single bonds, but the single bond in molecule C is shorter and stronger than the one in B, which is in turn shorter and stronger than the one in A.

The explanation here is relatively straightforward. An sp orbital is composed of one *s* orbital and one *p* orbital, and thus it has 50% *s* character and 50% *p* character. sp^2 orbitals, by comparison, have 33% *s* character and 67% *p* character, while sp^3 orbitals have 25% *s* character and 75% *p* character. Because of their spherical shape, 2*s* orbitals are smaller, and hold electrons closer and 'tighter' to the nucleus, compared to 2*p* orbitals. Consequently, bonds involving sp + sp^3 overlap (as in alkyne C) are shorter and stronger than bonds involving sp^2 + sp^3 overlap (as in alkene B). Bonds involving sp^3-sp^3overlap (as in alkane A) are the longest and weakest of the group, because of the 75% '*p*' character of the hybrids.

Hybridization Summary

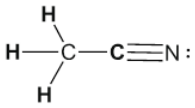
- A single bond is a sigma bond.
- A double bond is made up of a sigma bond and a pi bond.
- A triple bond is made up of a sigma bond and two pi bonds.
- Sigma bonds are made by the overlap of two hybrid orbitals or the overlap of a hybrid orbital and a s orbital from hydrogen.
- Pi bonds are made by the overlap of two unhybridized p orbitals.
- Lone pair electrons are usually contained in hybrid orbitals.

The hybrid orbitals used (and hence the hybridization) depends on how many electron groups are around the atom in question. An electron group can mean either a bonded atom or a lone pair. Molecular geometry is also decided by the number of electron groups so it is directly linked to hybridization.

# of Electron Groups	Hybrid Orbital Used	Example	Basic Geometry	Basic Bond Angle
2	sp		Linear	180°
3	sp^2		Trigonal Planar	120°
4	sp^3		Tetrahedral	109.5°

Exercises

1) For the molecule acetonitrile:



Acetonitrile

a) How many sigma and pi bonds does it have?

b) What orbitals overlap to form the C-H sigma bonds?

c) What orbitals overlap to form the C-C sigma bond?

d) What orbitals overlap to form the C-N sigma bond?

e) What orbitals overlap to the form the C-N pi bonds?

f) What orbital contains the lone pair electrons on nitrogen?

Solutions

1)

a) 5 sigma and 2 pi

b) An sp^3 hybrid orbital from carbon and an a s orbital from hydrogen.

c) An sp^3 hybrid orbital from one carbon and an a sp^3 orbital from the other carbon.

d) An sp hybrid orbital from carbon and an a sp orbital from nitrogen.

e) An p_y and p_z orbital from carbon and an p_y and p_z orbital from nitrogen.

f) An sp hybrid orbital.

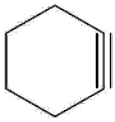
1.9: spsp Hybrid Orbitals and the Structure of Acetylene

1.9 Exercises

Questions

Q1.9.1

1-Cyclohexyne is a very strained molecule. By looking at the molecule explain why there is such a intermolecular strain using the knowledge of hybridization and bond angles.



Solutions

S1.9.1

The alkyne is a sp hybridized orbital. By looking at a sp orbital, we can see that the bond angle is 180°, but in cyclohexane the regular angles would be 109.5°. Therefore the molecule would be strained to force the 180° to be a 109°.

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1.11: Hybridization of Nitrogen, Oxygen, Phosphorus and Sulfur

Objective

After completing this section, you should be able to apply the concept of hybridization of atoms such as N, O, P and S to explain the structures of simple species containing these atoms.

Key Terms

Make certain that you can define, and use in context, the key term below.

- lone pair electrons

Study Notes

Nitrogen is frequently found in organic compounds. As with carbon atoms, nitrogen atoms can be sp^3-, sp^2- or *sp*-hybridized.

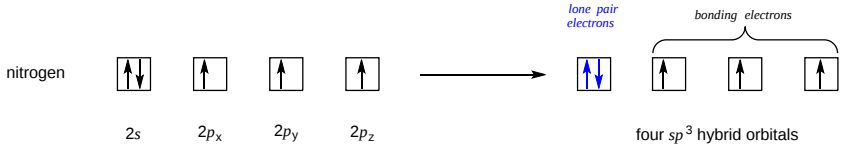
Note that, in this course, the term “lone pair” is used to describe an unshared pair of electrons.

The valence-bond concept of orbital hybridization can be extrapolated to other atoms including nitrogen, oxygen, phosphorus, and sulfur. In other compounds, covalent bonds that are formed can be described using hybrid orbitals.

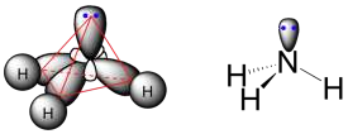
Nitrogen

Bonding in NH_3

The nitrogen in NH_3 has five valence electrons. After hybridization these five electrons are placed in the four equivalent sp^3 hybrid orbitals. The electron configuration of nitrogen now has one sp^3 hybrid orbital completely filled with two electrons and three sp^3 hybrid orbitals with one unpaired electron each. The two electrons in the filled sp^3 hybrid orbital are considered non-bonding because they are already paired. These electrons will be represented as a lone pair on the structure of NH_3. The three unpaired electrons in the hybrid orbitals are considered bonding and will overlap with the s orbitals in hydrogen to form N-H sigma bonds. Note! This bonding configuration was predicted by the Lewis structure of NH_3.

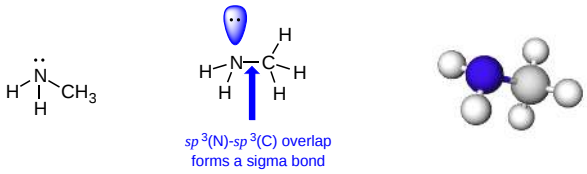


The four sp^3 hybrid orbitals of nitrogen orientate themselves to form a tetrahedral geometry. The three N-H sigma bonds of NH_3 are formed by sp^3(N)-1s(H) orbital overlap. The fourth sp^3 hybrid orbital contains the two electrons of the lone pair and is not directly involved in bonding.



Methyl amine

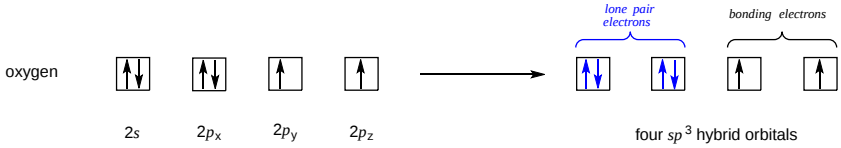
The nitrogen is sp^3 hybridized which means that it has four sp^3 hybrid orbitals. Two of the sp^3 hybridized orbitals overlap with s orbitals from hydrogens to form the two N-H sigma bonds. One of the sp^3 hybridized orbitals overlap with an sp^3 hybridized orbital from carbon to form the C-N sigma bond. The lone pair electrons on the nitrogen are contained in the last sp^3 hybridized orbital. Due to the sp^3 hybridization the nitrogen has a tetrahedral geometry. However, the H-N-H and H-N-C bonds angles are less than the typical 109.5º due to compression by the lone pair electrons.



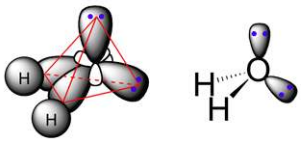
Oxygen

Bonding in H_2O

The oxygen in H_2O has six valence electrons. After hybridization these six electrons are placed in the four equivalent sp^3 hybrid orbitals. The electron configuration of oxygen now has two sp^3 hybrid orbitals completely filled with two electrons and two sp^3 hybrid orbitals with one unpaired electron each. The filled sp^3 hybrid orbitals are considered non-bonding because they are already paired. These electrons will be represented as a two sets of lone pair on the structure of H_2O . The two unpaired electrons in the hybrid orbitals are considered bonding and will overlap with the s orbitals in hydrogen to form O-H sigma bonds. Note! This bonding configuration was predicted by the Lewis structure of H_2O.

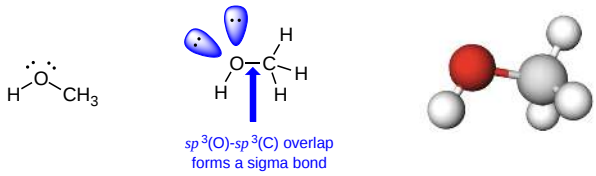


The four sp^3 hybrid orbitals of oxygen orientate themselves to form a tetrahedral geometry. The two O-H sigma bonds of H_2O are formed by sp^3(O)-1s(H) orbital overlap. The two remaining sp^3 hybrid orbitals each contain two electrons in the form of a lone pair.



Methanol

The oxygen is sp^3 hybridized which means that it has four sp^3 hybrid orbitals. One of the sp^3 hybridized orbitals overlap with s orbitals from a hydrogen to form the O-H sigma bonds. One of the sp^3 hybridized orbitals overlap with an sp^3 hybridized orbital from carbon to form the C-O sigma bond. Both the sets of lone pair electrons on the oxygen are contained in the remaining sp^3 hybridized orbital. Due to the sp^3 hybridization the oxygen has a tetrahedral geometry. However, the H-O-C bond angles are less than the typical 109.5° due to compression by the lone pair electrons.

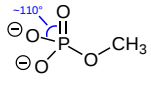


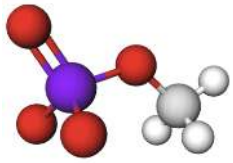
Phosphorus

Methyl phosphate

The bond pattern of phosphorus is analogous to nitrogen because they are both in period 15. However, phosphorus can have have expanded octets because it is in the n = 3 row. Typically, phosphorus forms five covalent bonds. In biological molecules, phosphorus is usually found in organophosphates. Organophosphates are made up of a phosphorus atom bonded to four oxygens, with one of the oxygens also bonded to a carbon. In methyl phosphate, the phosphorus is sp^3 hybridized and the O-P-O bond angle varies from 110° to 112°.

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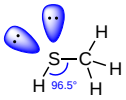


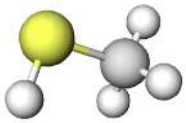
Sulfur

Methanethiol & Dimethyl Sulfide

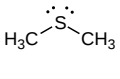
Sulfur has a bonding pattern similar to oxygen because they are both in period 16 of the periodic table. Because sulfur is positioned in the third row of the periodic table it has the ability to form an expanded octet and the ability to form more than the typical number of covalent bonds. In biological system, sulfur is typically found in molecules called thiols or sulfides. In a thiol, the sulfur atom is bonded to one hydrogen and one carbon and is analogous to an alcohol O-H bond. In a sulfide, the sulfur is bonded to two carbons. The simplest example of a thiol is methane thiol (CH_3SH) and the simplest example of a sulfide is dimethyl sulfide [$(CH_3)_3S$]. In both cases the sulfur is sp^3 hybridized, however the sulfur bond angles are much less than the typical tetrahedral 109.5° being 96.6° and 99.1° respectively.

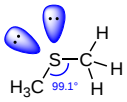


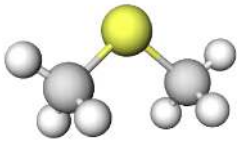




methanethiol





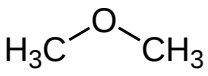


dimethyl sulfide

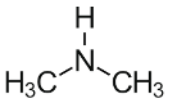
Exercises

1) Insert the missing lone pairs of electrons in the following molecules, and tell what hybridization you expect for each of the indicated atoms.

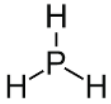
a) The oxygen is dimethyl ether:



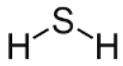
b) The nitrogen in dimethyl amine:



c) The phosphorus in phosphine:



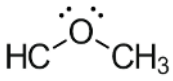
d) The sulfur in hydrogen sulfide:



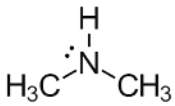
Solutions

1)

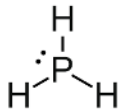
a) sp^3 hybridization



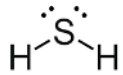
b) sp^3 hybridization



c) sp^3 hybridization



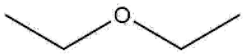
d) sp^3 hybridization



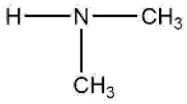
Questions

Q1.10.1

Identify geometry and lone pairs on each heteroatom of the molecules given.



Diethyl Ether



Dimethylamine

Solutions

S1.10.1

Diethyl ether would have two lone pairs of electrons and would have a bent geometry around the oxygen.

Dimethyl amine would have one lone pair and would show a pyramidal geometry around the nitrogen.

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1.12: Polar Covalent Bonds - Dipole Moments

Learning Objectives

After completing this section, you should be able to

- explain how dipole moments depend on both molecular shape and bond polarity.
- predict whether a molecule will possess a dipole moment from the molecular formula or structure.
- use the presence or absence of a dipole moment as an aid to deducing the structure of a given compound.

Key Terms

Make certain that you can define, and use in context, the key term below.

- dipole moment

Study Notes

You must be able to combine your knowledge of molecular shapes and bond polarities to determine whether or not a given compound will have a dipole moment. Conversely, the presence or absence of a dipole moment may also give an important clue to a compound's structure. BCl_3, for example, has no dipole moment, while NH_3 does. This suggests that in BCl_3 the chlorines around boron are in a trigonal planar arrangement, while the hydrogens around nitrogen in NH_3 have a less symmetrical arrangement - trigonal pyramidal.

Remember that the C-H bond is assumed to be non-polar.

Molecular Dipole Moments

In molecules containing more than one polar bond, the molecular dipole moment is just the vector combination of what can be regarded as individual "**bond dipole moments**". Mathematically, dipole moments are *vectors*; they possess both a *magnitude* and a *direction*. The dipole moment of a molecule is therefore the *vector sum* of the dipole moments of the individual bonds in the molecule. If the individual bond dipole moments cancel one another, there is no net dipole moment. Such is the case for CO_2, a linear molecule (Figure **1.12.1*a***). Each C–O bond in CO_2 is polar, yet experiments show that the CO_2 molecule has no dipole moment. Because the two C–O bond dipoles in CO_2 are equal in magnitude and oriented at 180° to each other, they cancel. As a result, the CO_2 molecule has no *net* dipole moment even though it has a substantial separation of charge. In contrast, the H_2O molecule is not linear (Figure **1.12.1*b***); it is bent in three-dimensional space, so the dipole moments do not cancel each other. Thus a molecule such as H_2O has a net dipole moment. We expect the concentration of negative charge to be on the oxygen, the more electronegative atom, and positive charge on the two hydrogens. This charge polarization allows H_2O to hydrogen-bond to other polarized or charged species, including other water molecules.

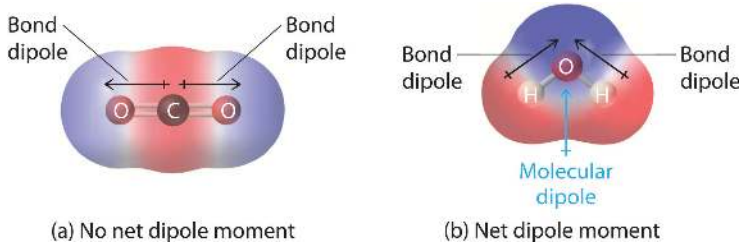


Figure **1.12.1**: How Individual Bond Dipole Moments Are Added Together to Give an Overall Molecular Dipole Moment for Two Triatomic Molecules with Different Structures. (a) In CO_2, the C–O bond dipoles are equal in magnitude but oriented in opposite directions (at 180°). Their vector sum is zero, so CO_2 therefore has no net dipole. (b) In H_2O, the O–H bond dipoles are also equal in magnitude, but they are oriented at 104.5° to each other. Hence the vector sum is not zero, and H_2O has a net dipole moment. (CC BY-SA-NC 3.0; anonymous)

The following is a simplified equation for a simple separated two-charge system that is present in diatomic molecules or when considering a bond dipole within a molecule.

$$\mu_{diatomic} = Q \times r \tag{1.12.1}$$

This bond dipole, μ (Greek mu) is interpreted as the dipole from a charge separation over a distance r between the partial charges Q^+ and Q^- (or the more commonly used terms δ^+ - δ^-); the orientation of the dipole is along the axis of the bond. The units on dipole moments are typically debyes (D) where one debye is equal to 3.336 x 10^{30} coulomb meters (C · m) in SI units. Consider a simple system of a single electron and proton separated by a fix distance. The unit charge on an electron is 1.60 X 1019 C and the proton & electron are 100 pm apart (about the length of a typical covalent bond), the dipole moment is calculated as:

$$\begin{aligned} \mu &= Qr \\ &= (1.60 \times 10^{-19}\, C)(1.00 \times 10^{-10}\, m) \\ &= 1.60 \times 10^{-29}\, C \cdot m \end{aligned} \tag{1.12.2}$$

$$\begin{aligned} \mu &= (1.60 \times 10^{-29}\, C \cdot m)\left(\frac{1\ D}{3.336 \times 10^{-30}\, C \cdot m}\right) \\ &= 4.80\ D \end{aligned} \tag{1.12.3}$$

4.80 D is a key reference value and represents a pure charge of +1 and -1 separated by 100 pm. However, if the charge separation were increased then the dipole moment increases (linearly):

- If the proton and electron were separated by 120 pm:

$$\mu = \frac{120}{100}(4.80\ D) = 5.76\, D$$

- If the proton and electron were separated by 150 pm:

$$\mu = \frac{150}{100}(4.80\ D) = 7.20\, D$$

- If the proton and electron were separated by 200 pm:

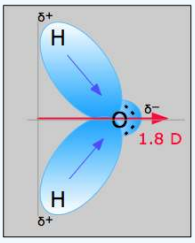
$$\mu = \frac{200}{100}(4.80\ D) = 9.60\, D$$

Example 1.12.1: Water

The water molecule in Figure **1.12.1** can be used to determine the direction and magnitude of the dipole moment. From the electronegativities of oxygen and hydrogen, the difference is 1.2e for each of the hydrogen-oxygen bonds. Next, because the oxygen is the more electronegative atom, it exerts a greater pull on the shared electrons; it also has two lone pairs of electrons. From this, it can be concluded that the dipole moment points from between the two hydrogen atoms toward the oxygen atom. Using the equation above, the dipole moment is calculated to be 1.85 D by multiplying the distance between the oxygen and hydrogen atoms by the charge difference between them and then finding the components of each that point in the direction of the net dipole moment (the angle of the molecule is 104.5˚).

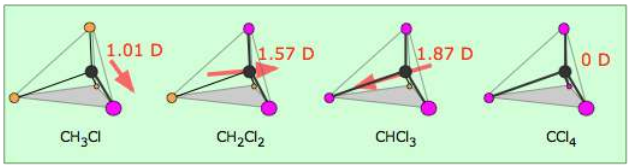
The bond moment of O-H bond =1.5 D, so the net dipole moment is

$$\mu = 2(1.5)\cos\left(\frac{104.5^\circ}{2}\right) = 1.84\ D$$



Dipoles with Differing Atoms

In more complex molecules with more than one polar covalent bonds, the three-dimensional geometry and the compound's symmetry determine whether the molecule has a net dipole moment. The manner in which the individual bonds contribute to the dipole moment of the molecule is nicely illustrated by the series of chloromethanes shown below. The electronegative chlorine draws electrons towards itself.



Consider CCl_4, (left panel in figure below), which as a molecule is not polar - in the sense that it doesn't have an end (or a side) which is slightly negative and one which is slightly positive. The whole of the outside of the molecule is somewhat negative, but there is no overall separation of charge from top to bottom, or from left to right. In contrast, $CHCl_3$ is a polar molecule (right panel in figure above). However, although a molecule like $CHCl_3$ has a tetrahedral geometry, the atoms bonded to carbon are not identical. Consequently, the bond dipole moments do not cancel one another, and the result is a molecule which has a dipole moment. The hydrogen at the top of the molecule is less electronegative than carbon and so is slightly positive. This means that the molecule now has a slightly positive "top" and a slightly negative "bottom", and so is overall a polar molecule.

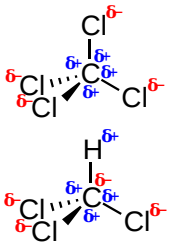


Figure **1.12.3**: Bond polarities for CCl_4 (left) and $CHCl_3$(right)

Electron densities in a molecule (and the dipole moments that unbalanced electron distributions can produce) are easily visualized with electrostatic potential maps. In this example, $CHCl_3$, the blue area centered on carbon represents a electron-deficient positive area, of the molecule, the red area centered on the chlorine, represents a electron-abundant negative area. This charge separation creates a net dipole moment of 1.87 D which points in the direction of the chlorine. In, CCl_4 the evenly spaced red areas represent that there is no separation of charge in the molecule. CCl_4 has a net dipole moment of zero which makes it a nonpolar molecule.

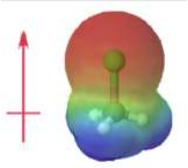
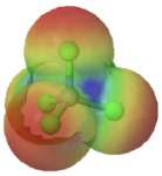
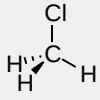
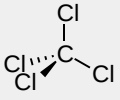
	
	
chloromethane	tetrachloromethane
(μ = 1.87 D)	(μ = 0 D)

Figure* 1.12.4*: Electrostatic potential maps and dipole moments for chloromethane and tetrachloromethane (carbon tetrachloride).

Molecules with asymmetrical charge distributions have a net dipole moment

Other examples of molecules with polar bonds are shown in Figure **1.12.2**. In molecules like BCl_3 and CCl_4, that have only one type of bond and a molecular geometries that are highly symmetrical (trigonal planar and tetrahedral), the individual bond dipole

moments completely cancel, and there is no net dipole moment. However, although a molecule like $CHCl_3$ has a tetrahedral geometry, the atoms bonded to carbon are not identical. Consequently, the bond dipole moments do not cancel one another, and the result is a molecule which has a dipole moment.

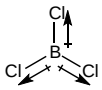
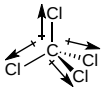
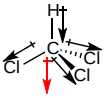
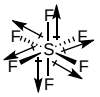
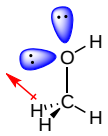
							
net dipole	no net dipole	net dipole	net dipole	no net dipole	net dipole	no net dipole	no net dipole
HCl	BCl_3	CH_2O	NH_3	CCl_4	$CHCl_3$	PF_5	SF_6

***Figure* 1.12.5**: *Molecules with Polar Bonds. Individual bond dipole moments are indicated in black. Due to their different three-dimensional structures, some molecules with polar bonds have a net dipole moment (HCl, CH_2O, NH_3, and $CHCl_3$), indicated in red, whereas others do not because the bond dipole moments cancel (BCl_3, CCl_4, PF_5, and SF_6).*

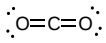
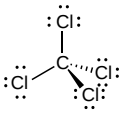
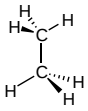
Table **1.12.1**: Dipole Moments of Some Compounds

Compound	Dipole Moment (Debyes)
NaCl	9.0 (measured in the gas phase)
CH_2O	2.33
CH_3Cl	1.87
H_2O	1.85
CH_3OH	1.70
NH_3	1.47
CH_3NH_2	1.31
CO_2	0
CCl_4	0
CH_4	0
CH_3CH_3	0

The table above give the dipole moment of some common substances. Sodium chloride has the largest dipole listed (9.00 D) because it is an ionic compounds. Even small organic compounds such as formaldehyde (CH_2O, 2.33 D) and methanol (CH_3OH, 1.70 D) have significant dipole moments. Both of these molecules contain the strongly electronegative oxygen atom lone pair electrons which gives rise to considerable dipole moments.

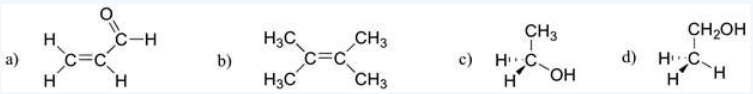
	
methanol	formaldehyde
(μ = 1.70 D)	(μ = 2.33 D)

In contrast many organic molecule have a zero dipole moment despite the fact that they are made up of polar covalent bonds. In, structures with highly symmetrical molecular geometries, the polar bonds and the lone pair electrons can can exactly cancel leaving no overall charge separation.

		
carbon dioxide	carbon tetrachloride	ethane
(μ = 0 D)	(μ = 0 D)	(μ = 0 D)

? Exercise 1.12.1

Which of the molecules below have molecular dipole moments?



Answer

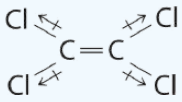
Only molecule (b) does *not* have a molecular dipole, due to its symmetry (bond dipoles are equal and in opposite directions). Add texts here.

? Exercise 1.12.2

Draw out the line structure of the molecule with a molecular formula of C_2Cl_4. Indicate all of the individual bond polarities and predict if the molecule is polar or nonpolar.

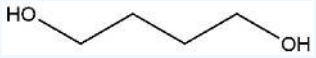
Answer

Although the C–Cl bonds are rather polar, the individual bond dipoles cancel one another in this symmetrical structure, and \(\ce{Cl2C=CCl2}\) moment.



? Exercise 1.12.3

The following molecule has no net dipole moment, explain.

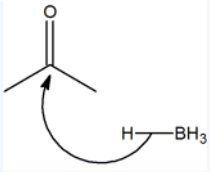


Answer

The hydroxyl groups are oriented opposite of one another and therefore the dipole moments would “cancel” one another out. Therefore having a zero net-dipole.

? Exercise 1.12.4

Within reactions with carbonyls, such as a hydride reduction reaction, the carbonyl is attacked from the carbon side and not the oxygen side. Using knowledge of electronegativity explain why this happens.



Answer

The oxygen is more electronegative than the carbon and therefore creates a dipole along the bond. This leads to having a partial positive charge on the carbon and the reduction can take place.



Exercise 1.12.1

Which molecule(s) has a net dipole moment?

a. H_2S
b. NHF_2
c. BF_3

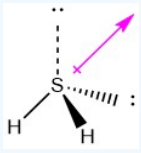
Answer

Strategy:

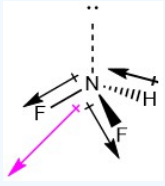
For each three-dimensional molecular geometry, predict whether the bond dipoles cancel. If they do not, then the molecule has a net dipole moment.

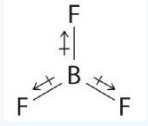
Solution:

The total number of electrons around the central atom, S, is eight, which gives four electron pairs. Two of these electron pairs are bonding pairs and two are lone pairs, so the molecular geometry of H_2S is bent. The bond dipoles cannot cancel one another, so the molecule has a net dipole moment.



Difluoroamine has a trigonal pyramidal molecular geometry. Because there is one hydrogen and two fluorines, and because of the lone pair of electrons on nitrogen, the molecule is not symmetrical, and the bond dipoles of NHF_2 cannot cancel one another. This means that NHF_2 has a net dipole moment. We expect polarization from the two fluorine atoms, the most electronegative atoms in the periodic table, to have a greater affect on the net dipole moment than polarization from the lone pair of electrons on nitrogen.



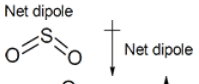


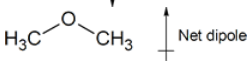
The molecular geometry of BF_3 is trigonal planar. Because all the B–F bonds are equal and the molecule is highly symmetrical, the dipoles cancel one another in three-dimensional space. Thus BF_3 has a net dipole moment of zero:

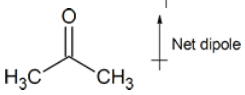
Additional Exercises

1. Determine whether each of the compounds listed below possesses a dipole moment. For the polar compounds, indicate the direction of the dipole moment.
   a. O=C=O
   b. *ICl*
   c. SO_2
   d. $CH_3–O–CH_3$
   e. $CH_3C(=O)CH_3$

Answers:

1. a. CO_2 nonpolar
   b. I—Cl
   
   Net dipole
   c. 

   d. 

   e. 

Questions

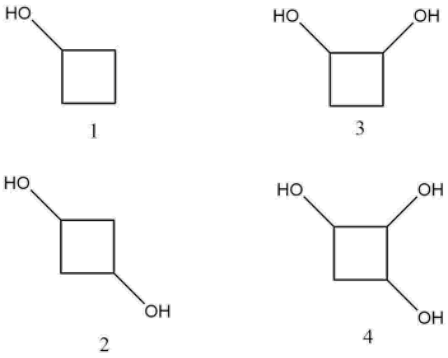
Q2.2.1

The following molecule has no dipole moment in the molecule itself, explain.



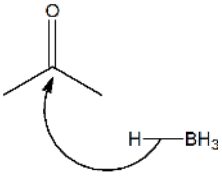
Q2.2.2

Which of the following molecules has a net dipole?



Q2.2.3

Within reactions with carbonyls, such as a reduction reaction, the carbonyl is attacked from the carbon side and not the oxygen side. Using knowledge of electronegativity explain why this happens.



Solutions

S2.2.1

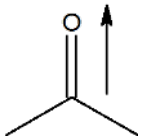
The hydroxyl groups are oriented opposite of one another and therefore the dipole moments would “cancel” one another out. Therefore having a zero net-dipole.

S2.2.2

1, 3, and 4 have a net dipoles.

S2.2.3

The oxygen is more electronegative than the carbon and therefore creates a dipole along the bond. This leads to having a partial positive charge on the carbon and the reduction can take place.



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CHAPTER OVERVIEW

2: Conjugation, Resonance, and Aromaticity

Learning Objectives

After Chapter 2, you should be able to

1. identify conjugated and non-conjugated bonding in molecules
2. use the information presented in this chapter, along with material from earlier chapters, to solve problems, particularly road-map problems and those requiring an understanding of spectroscopy.
3. explain the concept of aromaticity and the stability of aromatic compounds.
4. define, and use in context, the key terms introduced.

In Chapter 2, we describe conjugation within molecules and how it relates to electronic communication. Lewis' method for drawing organic molecules does not always accurately predict some chemical and/or physical phenomenon. Resonance theory is a way to represent molecules as a combination of multiple Lewis structures - the hybrid of which best describes the chemical and physical properties of the molecule. Molecules that are considered aromatic 1) are conjugated, 2) can be represented using a combination of Lewis structures, and 3) have chemical properties that make them uniquely stable.

2.1: Conjugation, Color, and the Chemistry of Vision
2.2: Stability of Conjugated Dienes- Molecular Orbital Theory
2.3: Resonance
2.4: Rules for Resonance Forms
2.5: Drawing Resonance Forms
2.5.1: Orbital Picture of Delocalization
2.6: Structure and Stability of Benzene
2.7: Aromaticity and the Hückel 4n + 2 Rule
2.8: Aromatic Ions
2.9: Aromatic Heterocycles - Pyridine and Pyrrole
2.10: Polycyclic Aromatic Compounds

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2.1: Conjugation, Color, and the Chemistry of Vision

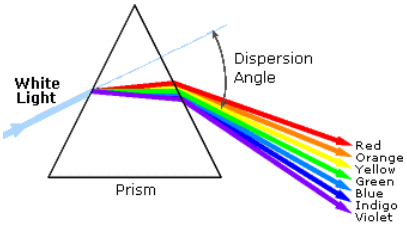
Objectives

After completing this section, you should be able to

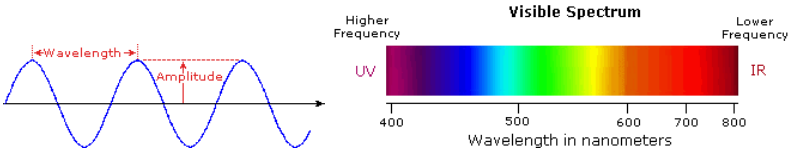
1. explain why some organic compounds have different colors based on compound structure and our perception of light.
2. state the relationship between frequency of light absorbed and the extent of conjugation in an extended pi electron system.

Introduction

An obvious difference between certain compounds is their color. Thus, quinone is yellow; chlorophyll is green; and aspirin is colorless. In this respect the human eye is functioning as a spectrometer analyzing the light reflected from the surface of a solid or passing through a liquid. Although we see sunlight (or white light) as uniform or homogeneous in color, it is actually composed of a broad range of radiation wavelengths in the ultraviolet (UV), visible and infrared (IR) portions of the spectrum. As shown on the image below, the component colors of the visible portion can be separated by passing sunlight through a prism, which acts to bend the light in differing degrees according to wavelength.

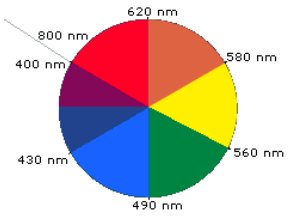


Visible wavelengths cover a range from approximately 400 to 800 nm. The longest visible wavelength is red and the shortest is violet. The wavelengths of what we perceive as particular colors in the visible portion of the spectrum are displayed and listed below.

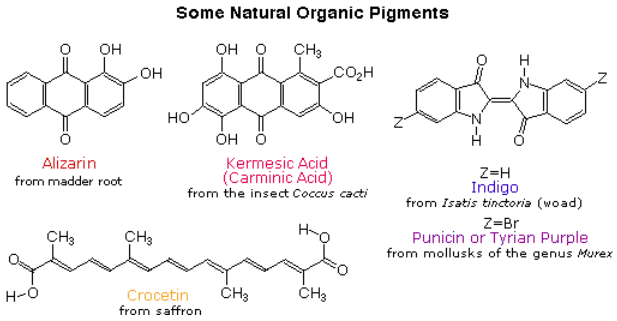


- **Violet:** 400 - 420 nm
- **Indigo:** 420 - 440 nm
- **Blue:** 440 - 490 nm
- **Green:** 490 - 570 nm
- **Yellow:** 570 - 585 nm
- **Orange:** 585 - 620 nm
- **Red:** 620 - 780 nm

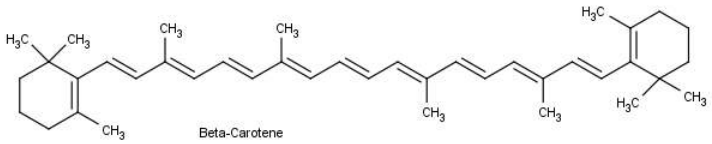
When white light passes through or is reflected by a colored substance, a characteristic portion of the mixed wavelengths is absorbed. The remaining light will then assume the complementary color to the wavelength(s) absorbed. This relationship is demonstrated by the color wheel shown below. Here, complementary colors are diametrically opposite each other. Thus, absorption of violet (400-440 nm) light renders a substance yellow, and absorption of 490-560 nm (green) light makes it red. Green is unique in that it can be created by absorption close to 400 nm as well as absorption near 800 nm.

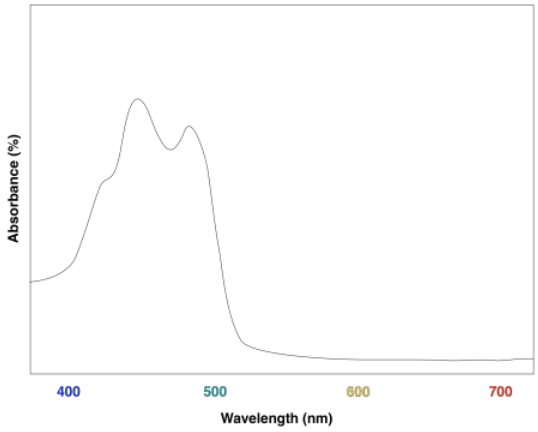


Early humans valued colored pigments, and used them for decorative purposes. Many of these were inorganic minerals, but several important organic dyes were also known. These included the crimson pigment, kermesic acid, the blue dye, indigo, and the yellow saffron pigment, crocetin. A rare dibromo-indigo derivative, punicin, was used to color the robes of the royal and wealthy. A common feature of all these colored compounds, displayed below, is a system of **extensively conjugated π-electrons**.

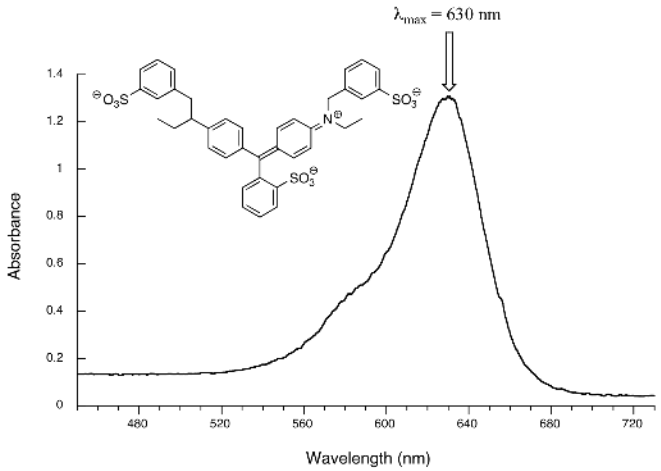


By understanding visible light, complementary colors, and adsorption the color of organic compounds can be understood. Beta-carotene, a compound found in carrots, is a deep orange color. Beta-carotene has 11 conjugated double bonds which places its λ_{max} at 455 nm which is within the blue region of the visible spectrum. The Beta-carotene compound absorbs blue from white light so it appears orange which is the the complementary color of blue.





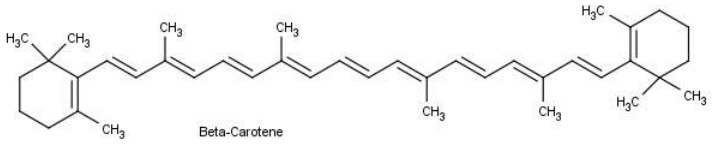
Another example is seen in the absorption spectrum of another food coloring, Blue #1:

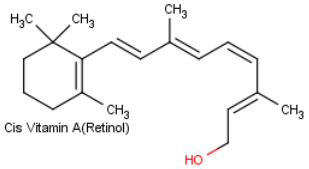


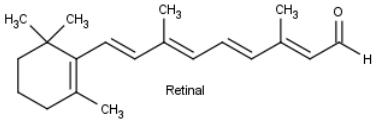
Blue #1 absorbs at a λ_{max} at 630 nm which is the color red in the visible spectrum. Blue is the complementary color of red.

Mechanism of Vision

Conjugation is also important in light sensitive compounds used for vision. Beta carotene, found in carrots and other natural products is cleaved into the liver and converted into Vitamin A, also known as retinol. Vitamin A is critical for vision because it is needed by the retina of eye. Retinol can be oxidized to an aldehyde called retinal which is also important for vision.





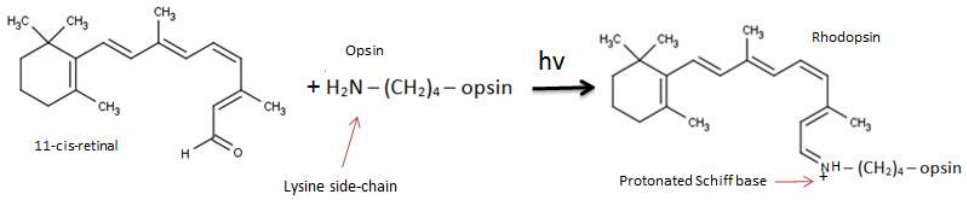


The eye is an extraordinarily sensitive instrument. Although its wavelength response is restricted to 400-800 nm, but its degree of sensitivity is such that a fully dark-adapted eye can clearly detect objects in light so dim as to correspond to a light input over the retina of only about 10,000 quanta per second - one light quantum per three minutes per receptor cell in the retina!

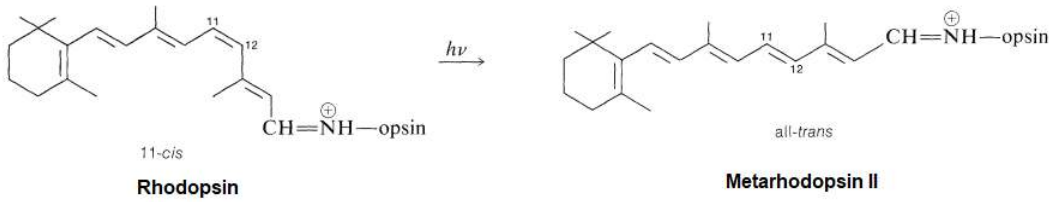
The retina is made up of two kinds of light-sensitive (photoreceptor) cells, known as rods and cones. The rods are the more sensitive and are responsible for vision in dim light. The cones are much fewer in number than the rods and provide detail and color vision in good light. The part of the retina that corresponds to the center of the visual field contains only cones. A red pigment called **rhodopsin** is the photosensitive substance in the rod cells of the retina. It absorbs most strongly in the blue-green region of the visible spectrum (λ_{max} = 500nm) and is essentially unaffected by the far-red end of the spectrum. Cone vision appears to involve a different pigment called **iodopsin**, which absorbs farther toward the red than does rhodopsin.

Rhodopsin, is made up of a protein (opsin) and retinal. Opsin does not absorb visible light, but when it is bonded with 11-cis-retinal to from rhodopsin, the new molecule has a very broad absorption band in the visible region of the spectrum. Rhodopsin is formed

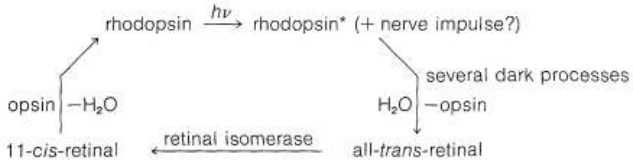
by an an imine (Schiff base) functional group formed between the aldehyde group of the retinal and the side-chain amino function of a lysine unit of opsin.



Opsin itself is colorless, whereas 11-cis-retinal absorbs strongly at 370 nm. The combination of opsin with 11-cis-retinal produces a remarkable shift of λ_{max} to longer wavelengths (430 nm to 620 nm, depending on the species). Light striking the retina changes the color of rhodopsin from red to yellow. The primary photochemical event in this process was established by G. Wald (Nobel Laureate in Physiology and Medicine, 1967), who showed that light absorption led to a change of configuration about the C_{11}-C_{12} double bond of the retinal moiety fo rhodopsin from *cis* to *trans* to form a compound called metarhodopsin II. The new form of trans-retinal does not fit as well into the opsin protein, and so a series of geometry changes in the protein begins. As the protein changes its geometry, it initiates a cascade of biochemical reactions that result in changes in charge so that a large potential difference builds up across the neuron membranes. This potential difference is passed along to an adjoining nerve cell as an electrical impulse. The nerve cell carries this impulse to the brain, where the visual information is interpreted.

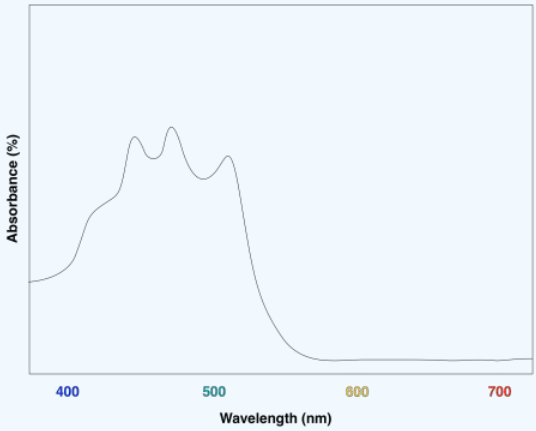


Metarhodopsin II can then be recycled back to rhodopsin by first cleaving to form all-*trans*-retinal and the isomerization back to 11-*cis*-retinal by the enzyme retinal isomerase. Finally, 11-*cis*-retinal is once again coupled with opsin to form rhodopsin.



? Exercise 2.1.1

Lycopene is conjugated compound found in tomatoes. What colors correspond to the UV-Vis absorption maxima of lycopene? What color do we see when we look at lycopene?



Answer

The absorption maxima of lycopene are regions of blue and green in the visible spectrum. Lycopene would be expected to appears orange and red.

? Exercise 2.1.2

Asprin has a λ_{max} of 220 nm. Briefly explain why Asprin appears white.

Answer

Asprin absorbs in the ultraviolet portion of the electromagnetic spectrum. Asprin cannot remove any colors from white light by absorption so the compound itself appears white. Many compounds with a relatively small amount of conjugation appear white because they only absorb in the ultraviolet and not the visible region.

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2.2: Stability of Conjugated Dienes- Molecular Orbital Theory

Objectives

After completing this section, you should be able to

1. write a reaction sequence to show a convenient method for preparing a given conjugated diene from an alkene, allyl halide, alkyl dihalide or alcohol (diol).
2. identify the reagents needed to prepare a given diene from one of the starting materials listed in Objective 1, above.
3. compare the stabilities of conjugated and non-conjugated dienes, using evidence obtained from hydrogenation experiments.
4. discuss the bonding in a conjugated diene, such as 1,3-butadiene, in terms of the hybridization of the carbon atoms involved.
5. discuss the bonding in 1,3-butadiene in terms of the molecular orbital theory, and draw a molecular orbital for this and similar compounds.

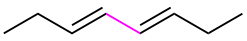
Key Terms

Make certain that you can define, and use in context, the key terms below.

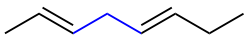
- delocalized electrons
- node

Conjugated vs. Non-conjugated Dienes

Dienes are compounds which contain two double bonds. These dienes can be non-conjugated (the two double bonds are separated by at least one sp^3 hybridized atom. Conjugated dienes have the two double bonds separated by a single bond. Conjugated dienes have properties and reactivity which are distinctly different than non-conjugated dienes. Determining if double bonds are conjugated represents an important skill in organic chemistry.



3,5-Octadiene
(Conjugated)



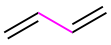
2,5-Octadiene
(Non-Conjugated)



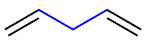
1,3-Cyclohexadiene
(Conjugated)



1,4-Cyclohexadiene
(Non-Conjugated)



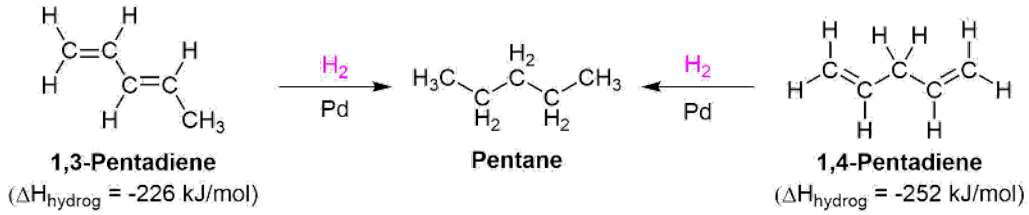
1,3-Butadiene
(Conjugated)



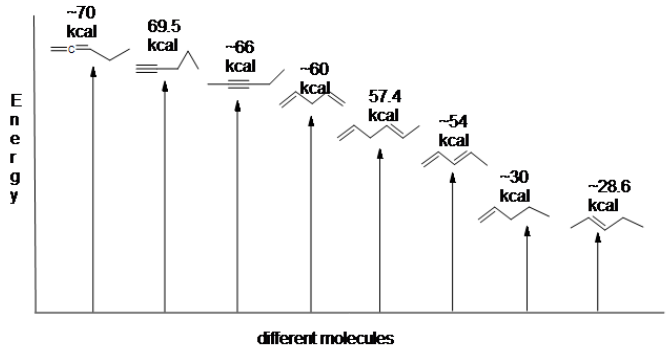
1,4-Pentadiene
(Non-Conjugated)

Stability of Conjugated Dienes

Conjugated dienes are known to be more stable than non-conjugated dienes as shown by their experimentally determined heats of hydrogenation. As alkenes become more stable, they contain less energy, and therefore release less heat during hydrogenation. Experiments have shown that conjugated dienes have a lower heat of hydrogenation (-226 kJ/mol) than non-conjugated dienes (-251 kJ/mol). Using the differences in heats of hydrogenation the stabilization energy in conjugated dienes can be estimate to be roughly 25 kJ/mol.

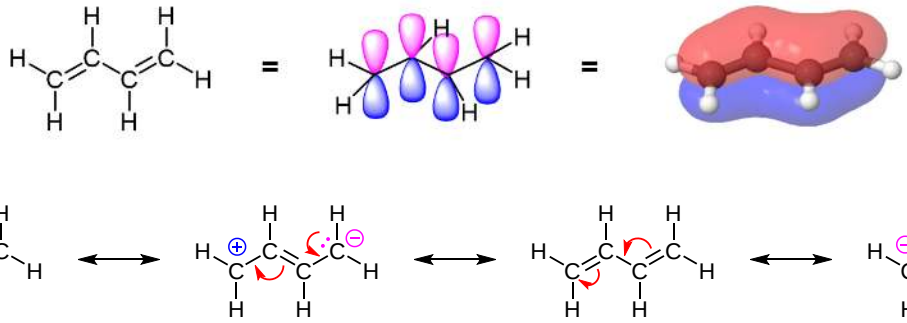


Here is an energy diagram comparing different types of bonds with their heats of hydrogenation to show relative stability of each molecule:

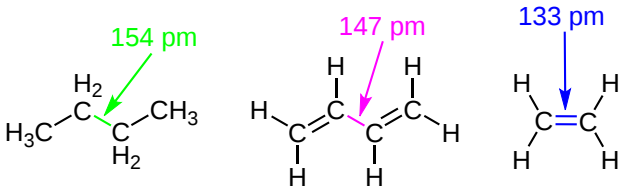


The stabilization of dienes by conjugation is less dramatic than the aromatic stabilization of benzene. Nevertheless, similar resonance and molecular orbital descriptions of conjugation may be written.

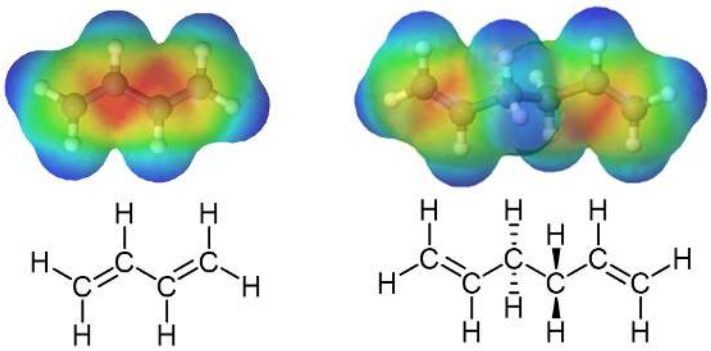
Each alkene carbon in 1,3 dienes are sp^2 hybridized and therefore have one unhybridized *p* orbital. The four *p* orbitals in 1,3-butadiene overlap to form a conjugated system which can be represented by the resonance forms shown below. This delocalization of charges stabilizes conjugated diene making them more stable than non-conjugated dienes.



Evidence of conjugation in 1,3 dienes is seen in the single bond being stronger and shorter (147 pm) than an ordinary alkane C-C bond (154 pm). The resonance hybrid of a 1,3-butadiene shows this bond to contain significant double bond character with its bond length being roughly the average of a single and double bond.

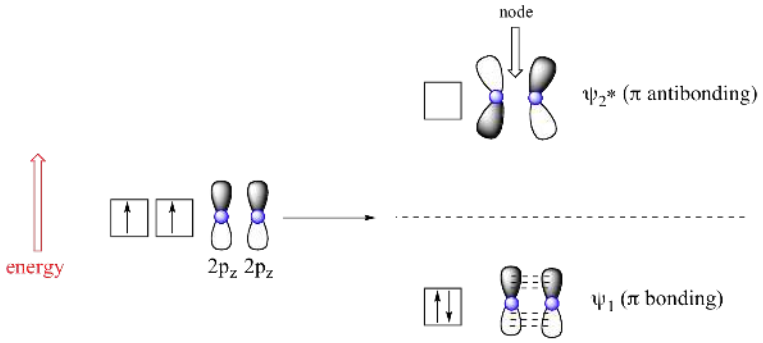


The delocalized electron density of a 1,3 diene can be seen when viewing an electrostatic potential maps. In conjugated dienes, it is observed that the pi electron density overlap (shown in red) is closer together and delocalized in conjugated dienes, while in non-conjugated dienes the pi electron density is located completely on the double bonds.

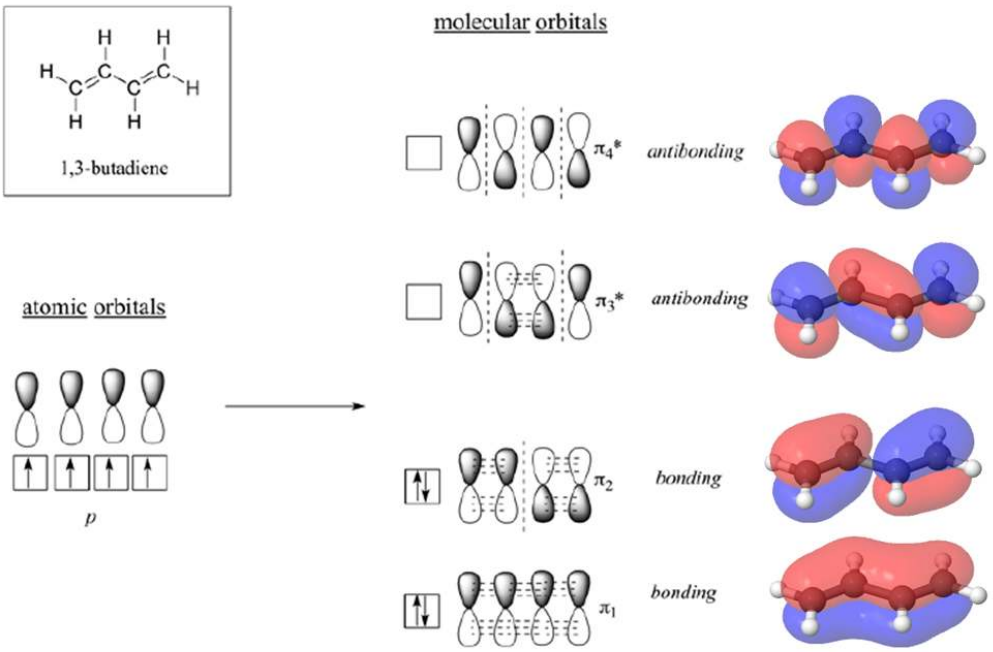


Molecular Orbitals of 1,3 Dienes

According to MO theory, when a double bond is non-conjugated, the two atomic $2p_z$ orbitals combine to form two **pi (π) molecular orbitals**, one a low-energy π bonding orbital and one a high-energy **π-star (π*) anti-bonding molecular orbital**. These are sometimes denoted, in MO diagrams like the one below, with the Greek letter psi (Ψ) instead of π. In the bonding Ψ_1 orbital, the two (+) lobes of the $2p_z$ orbitals interact constructively with each other, as do the two (-) lobes. Therefore, there is increased electron density between the nuclei in the molecular orbital – this is why it is a bonding orbital. In the higher-energy anti-bonding Ψ_2* orbital, the (+) lobes of one $2p_z$ orbital interacts destructively with the (-) lobe of the second $2p_z$ orbital, leading to a node between the two nuclei and overall repulsion. By the *aufbau* principle, the two electrons from the two atomic orbitals will be paired in the lower-energy $\Psi_1$orbital when the molecule is in the ground state.



With a conjugated diene, such as 1,3-butadiene, the four *2p* atomic orbitals combine to form four pi molecular orbitals of increasing energy. Two bonding pi orbitals and two anti-bonding pi* orbitals. The combination of four pi molecular orbitals allow for the formation of a bonding molecular orbital that is lower in energy than those created by an unconjugated alkene. The 4 pi electrons of 1,3-butadiene completely fill the bonding molecular orbitals giving is the additional stability associated with conjugated double bonds.



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2.3: Resonance

Objective

After completing this section, you should be able to

- draw resonance forms for molecules and ions.

Key Terms

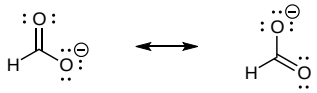
Make certain that you can define, and use in context, the key term below.

- resonance form
- delocalization

Resonance Delocalization

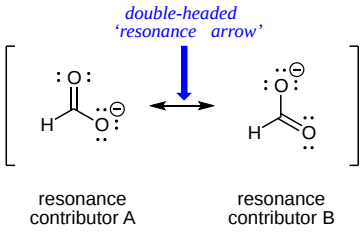
Sometimes, even when formal charges are considered, the bonding in some molecules or ions cannot be described by a single Lewis structure. **Resonance** is a way of describing **delocalized** electrons within certain molecules or polyatomic ions where the bonding cannot be expressed by a single Lewis formula. A molecule or ion with such delocalized electrons is represented by several contributing structures (also called resonance contributors or canonical forms). Resonance contributors involve the 'imaginary movement' of pi-bonded electrons or of lone-pair electrons that are adjacent to pi bonds. Note, sigma bonds cannot be broken during resonance – if you show a sigma bond forming or breaking, you are showing a chemical reaction taking place. Likewise, the positions of atoms in the molecule **cannot change** between resonance contributors.

When looking at the structure of the molecule, formate, we see that there are two equivalent structures possible. Which one is correct? There are two simple answers to this question: 'both' and 'neither one'. Both ways of drawing the molecule are equally acceptable approximations of the bonding picture for the molecule, but neither one, by itself, is an accurate picture of the delocalized pi bonds. The two alternative drawings, however, when considered together, give a much more accurate picture than either one on its own. This is because they imply, together, that the carbon-carbon bonds are not double bonds, not single bonds, but about halfway in between.



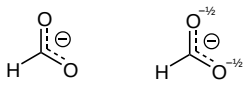
Formate Ion Structures are Equivalent in Energy

When it is possible to draw more than one valid structure for a compound or ion, we have identified **resonance contributors**: two or more different Lewis structures depicting the same molecule or ion that, when considered together, do a better job of approximating delocalized pi-bonding than any single structure. By convention, resonance contributors are linked by a double-headed arrow, and are sometimes enclosed by brackets:

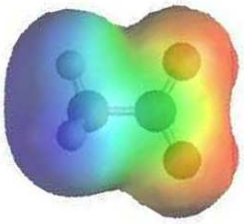


The depiction of formate using the two resonance contributors A and B in the figure above does *not* imply that the molecule at one moment looks like structure A, then at the next moment shifts to look like structure B. Rather, at all moments, the molecule is a combination, or **resonance hybrid** of both A and B. Each individual resonance contributor of the formate ion is drawn with one carbon-oxygen double bond (120 pm) and one carbon-oxygen single bond (135 pm), with a negative formal charge located on the single-bonded oxygen. However, the two carbon-oxygen bonds in formate are actually the same length (127 pm) which implies that

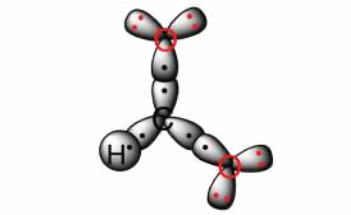
neither resonance contributor is correct. Although there is an overall negative formal charge on the formate ion, it is shared equally between the two oxygens. Therefore, the formate ion can be more accurately depicted by a *pair* of resonance contributors. Alternatively, a single structure can be used, with a dashed line depicting the resonance-delocalized pi bond and the negative charge located in between the two oxygens.



The electrostatic potential map of formate shows that there is an equal amount of electron density (shown in red) around each oxygen.

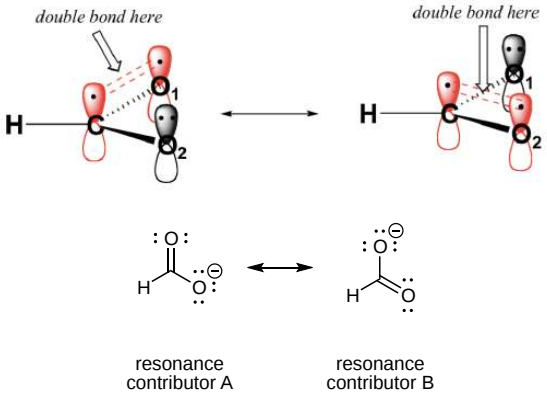


Valence bond theory can be used to develop a picture of the bonding in a carboxylate group. We know that the carbon must be sp^2-hybridized, (the bond angles are close to 120˚, and the molecule is planar), and we will treat both oxygens as being sp^2-hybridized as well. Both carbon-oxygen sigma bonds, then, are formed from the overlap of carbon sp^2 orbitals and oxygen sp^2 orbitals.



the σ-bonding framework of formate

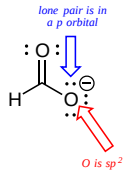
In addition, the carbon and both oxygens each have an un-hybridized $2p_z$ orbital situated perpendicular to the plane of the sigma bonds. These three $2p_z$ orbitals are parallel to each other, and can overlap in a side-by-side fashion to form a delocalized pi bond.



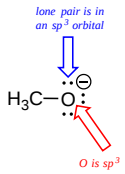
Overall, the situation is one of *three parallel, overlapping $2p_z$ orbitals sharing four delocalized pi electrons*. Because there is one more electron than there are $2p_z$ orbitals, the system has an overall charge of 1–. Resonance contributors are used to approximate

overlapping $2p_z$ orbitals and delocalized pi electrons. Molecules with resonance are usually drawn showing only one resonance contributor for the sake of simplicity. However, identifying molecules with resonance is an important skill in organic chemistry.

This example shows an important exception to the general rules for determining the hybridization of an atom. The oxygen with the negative charge appears to be sp^3 hybridized because it is surrounded by four electron groups. However, this representation of the oxygen atom is not correct because it is actually part of a resonance hybrid. A pair of lone pair of electrons on the negatively charged oxygen are not localized in an sp^3 orbital, rather, they are delocalized as part of a conjugated pi system. The stability gained though resonance is enough to cause the expected sp^3 to become sp^2. The sp^2 hybridization gives the oxygen a p orbital allowing it to participate in conjugation. As a general rule sp^3 hybridized atoms with lone pair electrons tend to become sp^2 hybridized when adjacent to a conjugated system.



oxygen is *conjugated*



oxygen is *not conjugated*

Example: Carbonate (CO_3^{2-})

Like formate, the electronic structure of the carbonate ion cannot be described by a single Lewis electron structure. Unlike O_3, though, the Lewis structures describing CO_3^{2-} has *three* equivalent representations.

1. Because carbon is the least electronegative element, we place it in the central position:

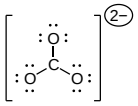


2. Carbon has 4 valence electrons, each oxygen has 6 valence electrons, and there are 2 more for the 2− charge. This gives 4 + (3 × 6) + 2 = 24 valence electrons.

3. Six electrons are used to form three bonding pairs between the oxygen atoms and the carbon:

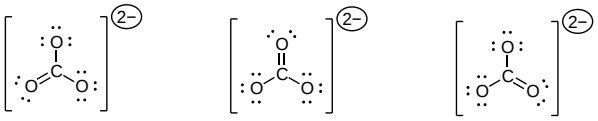


4. We divide the remaining 18 electrons equally among the three oxygen atoms by placing three lone pairs on each and indicating the 2− charge:

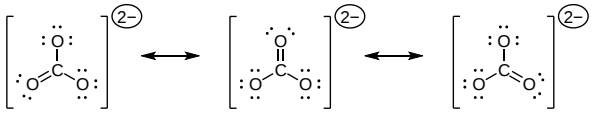


5. There are no electrons left for the central atom.

6. At this point, the carbon atom has only 6 valence electrons, so we must take one lone pair from an oxygen and use it to form a carbon–oxygen double bond. In this case, however, there are *three* possible choices:



As with formate, none of these structures describes the bonding exactly. Each predicts one carbon–oxygen double bond and two carbon–oxygen single bonds, but experimentally all C–O bond lengths are identical. We can write resonance structures (in this case, three of them) for the carbonate ion:



As the case for formate, the actual structure involves the formation of a molecular orbital from p_z orbitals centered on each atom and sitting above and below the plane of the CO_3^{2-} ion.

Example 2.4.1

Benzene is a common organic solvent that was previously used in gasoline; it is no longer used for this purpose, however, because it is now known to be a carcinogen. The benzene molecule (C_6H_6) consists of a regular hexagon of carbon atoms, each of which is also bonded to a hydrogen atom. Use resonance structures to describe the bonding in benzene.

Given: molecular formula and molecular geometry

Asked for: resonance structures

Strategy:

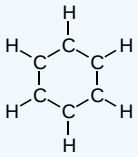
A Draw a structure for benzene illustrating the bonded atoms. Then calculate the number of valence electrons used in this drawing.

B Subtract this number from the total number of valence electrons in benzene and then locate the remaining electrons such that each atom in the structure reaches an octet.

C Draw the resonance structures for benzene.

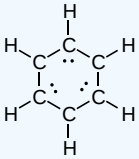
Solution:

A Each hydrogen atom contributes 1 valence electron, and each carbon atom contributes 4 valence electrons, for a total of (6 × 1) + (6 × 4) = 30 valence electrons. If we place a single bonding electron pair between each pair of carbon atoms and between each carbon and a hydrogen atom, we obtain the following:



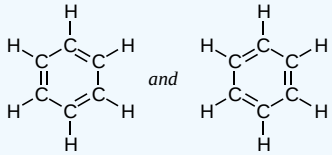
Each carbon atom in this structure has only 6 electrons and has a formal charge of 1+, but we have used only 24 of the 30 valence electrons.

B If the 6 remaining electrons are uniformly distributed pair-wise on alternate carbon atoms, we obtain the following:

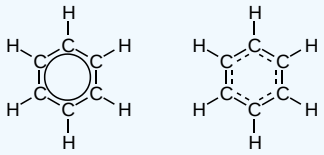


Three carbon atoms now have an octet configuration and a formal charge of 1−, while three carbon atoms have only 6 electrons and a formal charge of 1+. We can convert each lone pair to a bonding electron pair, which gives each atom an octet of electrons and a formal charge of 0, by making three C=C double bonds.

C There are, however, two ways to do this:

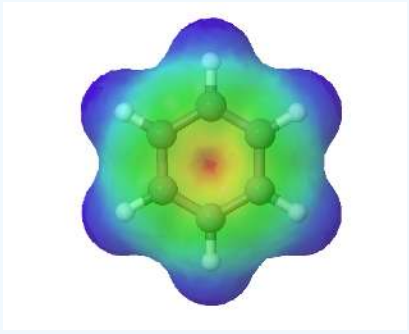


Each structure has alternating double and single bonds, but experimentation shows that each carbon–carbon bond in benzene is identical, with bond lengths (139.9 pm) intermediate between those typically found for a C–C single bond (154 pm) and a C=C double bond (134 pm). We can describe the bonding in benzene using the two resonance structures, but the actual electronic structure is an average of the two. The existence of multiple resonance structures for aromatic hydrocarbons like benzene is often indicated by drawing either a circle or dashed lines inside the hexagon:



benzene

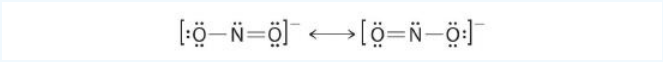
This combination of *p* orbitals for benzene can be visualized as a ring with a node in the plane of the carbon atoms. As can be seen in an electrostatic potential map of benzene, the electrons are distributed symmetrically around the ring.



? Exercise 2.3.1

The sodium salt of nitrite is used to relieve muscle spasms. Draw two resonance structures for the nitrite ion (NO_2^-).

Answer



Exercises

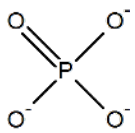
2.4 Resonance

2.4 Exercises

Questions

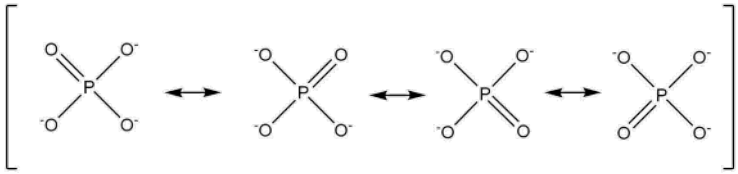
Q2.4.1

Draw the resonance structures for the following molecule:



Solutions

S2.4.1



Extra example - O_3

A molecule or ion with such delocalized electrons is represented by several contributing structures (also called resonance structures or canonical forms). Such is the case for ozone (O_3), an allotrope of oxygen with a V-shaped structure and an O–O–O angle of 117.5°.

1. We know that ozone has a V-shaped structure, so one O atom is central:



2. Each O atom has 6 valence electrons, for a total of 18 valence electrons.

3. Assigning one bonding pair of electrons to each oxygen–oxygen bond gives



with 14 electrons left over.

4. If we place three lone pairs of electrons on each terminal oxygen, we obtain

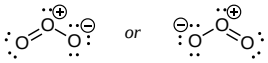


and have 2 electrons left over.

5. At this point, both terminal oxygen atoms have octets of electrons. We therefore place the last 2 electrons on the central atom:



6. The central oxygen has only 6 electrons. We must convert one lone pair on a terminal oxygen atom to a bonding pair of electrons —but which one? Depending on which one we choose, we obtain either

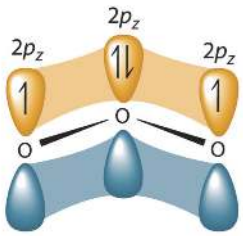


Which is correct? In fact, neither is correct. Both predict one O–O single bond and one O=O double bond. If the bonds were of different types (one single and one double, for example), they would have different lengths. It turns out, however, that both O–O bond distances are identical, 127.2 pm, which is shorter than a typical O–O single bond (148 pm) and longer than the O=O double bond in O_2 (120.7 pm).

Equivalent Lewis dot structures, such as those of ozone, are called resonance structures . The position of the *atoms* is the same in the various resonance structures of a compound, but the position of the *electrons* is different. Double-headed arrows link the different resonance structures of a compound:



Figure 2.4.1).



The resonance structure of ozone involves a molecular orbital extending all three oxygen atoms.In ozone, a molecular orbital extending over all three oxygen atoms is formed from three atom centered p_z orbitals. Similar molecular orbitals are found in every resonance structure.

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2.4: Rules for Resonance Forms

Objectives

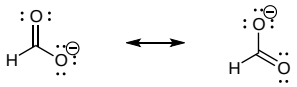
After completing this section, you should be able to

- use the concept of resonance to explain structural features of molecules and ions.
- understand the relationship between resonance and relative stability of molecules and ions.

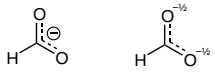
Rules for Drawing and Working with Resonance Contributors

Recognizing, drawing, and evaluating the relative stability of resonance contributors is essential to understanding organic reaction mechanisms. When learning to draw and interpret resonance structures, there are a few basic guidelines to help. .

1) There is ONLY ONE REAL STRUCTURE for each molecule or ion. This real structure (the **resonance hybrid**) takes its character from the average of all the individual **resonance contributors**. When looking at a resonance contributors, we are seeing the exact same molecule or ion depicted in different ways. Resonance hybrids are really a single, unchanging structure.



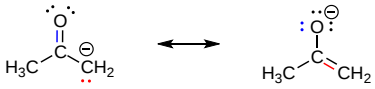
Major resonance contributors of the formate ion



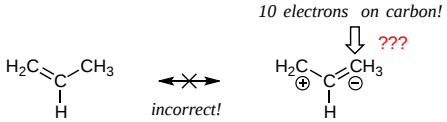
Representations of the formate resonance hybrid

2) The resonance hybrid is more stable than any individual resonance structures. Often, resonance structures represent the movement of a charge between two or more atoms. The charge is spread out amongst these atoms and therefore more stabilized. When looking at the picture above the resonance contributors represent the negative charge as being on one oxygen or the other. The resonance hybrid shows the negative charge being shared equally between two oxygens. In the resonance hybrid, the negative charge is spread out over a larger part of the molecule and is therefore more stable.

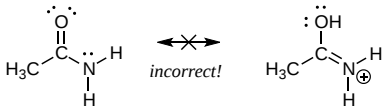
3) Resonance contributors do not have to be equivalent. Because of this, resonance structures do necessarily contribute equally to the resonance hybrid. The two resonance structures shown below are not equivalent because one show the negative charge on an oxygen while the other shows it on a carbon. Later, we will show that the contributor with the negative charge on the oxygen is the more stable of the two. Also, this means that the resonance hybrid will not be an exact mixture of the two structures.



4) All resonance contributors must be correct Lewis structures. Each atom should have a complete valence shell and be shown with correct formal charges. A carbocation (carbon with only 6 valence electrons) is the only allowed exception to the valence shell rules. The structure below is an invalid resonance structure even though it only shows the movement of a pi bond. The resulting structure contains a carbon with ten electrons, which violates the octet rule, making it invalid.



5) All resonance contributors must have the same molecular formula, the same number of electrons, and same net charge. The molecules in the figure below are not resonance structures of the same molecule because then have different molecular formulas (C_2H_5NO Vs. C_2H_6NO). Also, the two structures have different net charges (neutral Vs. positive).

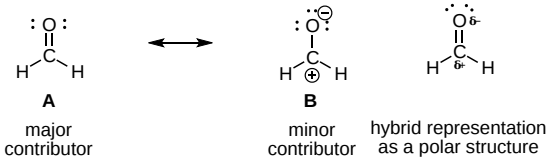


6) Resonance contributors only differ by the positions of pi bond and lone pair electrons. Sigma bonds are never broken or made, because of this atoms must maintain their same position. The molecules in the figure below are not resonance structures of the same molecule even though they have the same molecular formula (C_3H_6O). These molecules are considered structural isomers because their difference involves the breaking of a sigma bond and moving a hydrogen atom.



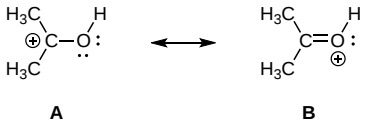
Major and Minor Resonance Contributors

As previously state the true structure of a resonance hybrid is the combination of all the possible resonance structures. If the resonance structures are equal in stability they the contribute equally to the structure of the hybrid. However, if the resonance structures have different stabilities they contribute to the hybrid's structure in proportions related to their relative stabilities. It can be said the the resonance hybrid's structure resembles the most stable resonance structure. Because of this it is important to be able to compare the stabilities of resonance structures. In the example below, structure **B** is much less important in terms of its contribution to the hybrid because it contains the violated octet of a carbocation. The relative stabilities of the two structures are so vastly different that molecules which contain a C=O bond are almost exclusively written in a form like structure **A**. However, as we will learn, the positively charged carbon created by structure **B** will explain how the C=O bond will react with electron rich species.

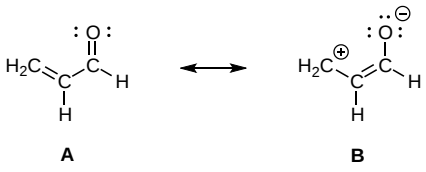


Rules for Estimating Stability of Resonance Structures

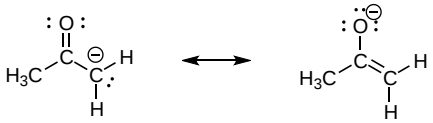
1. The resonance structures in which all atoms have complete valence shells is more stable. This means most atoms have a full octet. In the example below structure **A** has a carbon atom with a positive charge and therefore an incomplete octet. Based on this criterion, structure **A** is less stable and is a more minor contributor to the resonance hybrid than structure **B**.



2. The structures with the **least number of formal charges** is more stable. Based on this, structure **B** is less stable because is has two atoms with formal charges while structure **A** has none. Structure **A** would be the major resonance contributor.



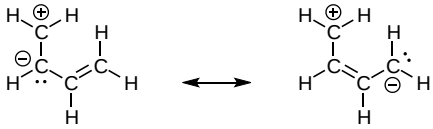
3. The structures with a **negative charge on the more electronegative atom** will be more stable. The difference between the two resonance structures is the placement of a negative charge. Structure **B** is the more stable and the major resonance contributor, because it places the negative charge on the more electronegative oxygen.



A **B**

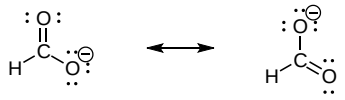
4. The structures with a **positive charges on the least electronegative atom** (most electropositive) is more stable.

5. The structures with the **least separation of formal charges** is more stable. The only difference between the two structures below are the relative positions of the positive and negative charges. In structure **A** the charges are closer together making it more stable.



A **B**

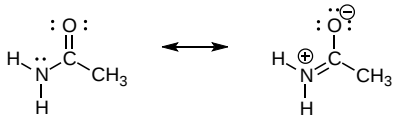
6. **Resonance forms that are equivalent have no difference in stability**. When looking at the two structures below no difference can be made using the rules listed above. This means the two structures are equivalent in stability and would make equal structural contributions to the resonance hybrid.



A **B**

Examples of major and minor contributors

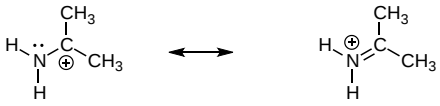
Example 1:



major contributor
(neutral structure)

minor contributor
(charge separation)

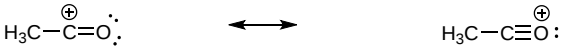
Example 2:



minor contributor
(Incomplete octet on carbon.)

major contributor
(All atoms have octets, even though there is a positive charge on nitrogen.)

Example 3:

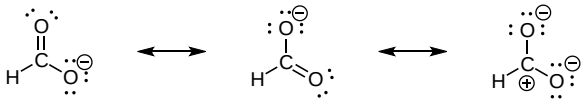


minor contributor
(Incomplete octet on carbon, but more important in terms of reactivity.)

major contributor
(All atoms have octets, even though there is a positive charge on oxygen.)

Carboxylate example

In the case of carboxylates, contributors **A** and **B** below are equivalent in terms of their relative contribution to the hybrid structure. However, there is also a third resonance contributor **C**, in which the carbon bears a positive formal charge (a carbocation) and both oxygens are single-bonded and bear negative charges.



A **B** **C**

minor contributor
(separation of charge)

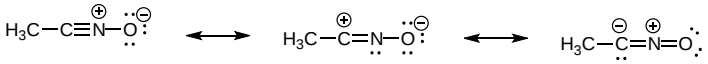
Structure **C** makes a less important contribution to the overall bonding picture of the group relative to **A** and **B**. How do we know that structure **C** is the 'minor' contributor? Apply the rules below

- The carbon in contributor **C** does not have an octet. In general, resonance contributors in which a carbon does not fulfill the octet rule are relatively less important. (rule #1)
- In structure **C**, there are only three bonds, compared to four in **A** and **B**. In general, a resonance structure with a lower number of total bonds is relatively less important. (rule #2)
- Structure **C** also has more formal charges than are present in **A** or **B**. In general, resonance contributors in which there is more/greater separation of charge are relatively less important. (rule #3)
- Structures **A** and **B** are equivalent and will be equal contributors to the resonance hybrid. (rule #5).
- The resonance contributor in which a negative formal charge is located on a more electronegative atom, usually oxygen or nitrogen, is more stable than one in which the negative charge is located on a less electronegative atom such as carbon. An example is in the upper left expression in the next figure. (rule #4)

Example with 3 resonance structures

Molecules with more than 2 resonance structures can also be considered using the rules listed above. Of the resonance structures listed below, structure **A** would be the most stable because all the non-hydrogen atoms have a full octet and the negative charge is on the more electronegative atom (oxygen). Structure **C** would be next in stability because all of the non-hydrogen atoms have full octets, though now the negative charge is on carbon rather than oxygen. Structure **B** would be the least stable of the three because it has the carbocation does not have an octet. Of the three, structure **A** would be the major resonance structure and would most resemble the structure of the true resonance hybrid. Structure **B** is considered a minor resonance contributor and would have very little effect on the structure of the resonance hybrid.

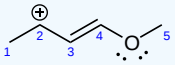
- **2.4: Rules for Resonance Forms** by Dietmar Kennepohl, Krista Cunningham, Steven Farmer, Tim Soderberg, William Reusch is licensed CC BY-SA 4.0.



A **B** **C**

Example 2.4.1

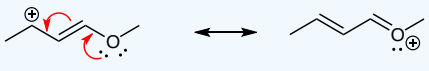
Draw the major resonance contributor of the structure below. Include in your figure the appropriate curved arrows showing how you got from the given structure to your structure. Explain why your contributor is the major one. In what kind of orbitals are the two lone pairs on the oxygen?



Solution

In the structure above, the carbon with the positive formal charge does not have a complete octet of valence electrons. Using the curved arrow convention, a lone pair on the oxygen can be moved to the adjacent bond to the left, and the electrons in the

double bond shifted over to the left (see the rules for drawing resonance contributors to convince yourself that these are 'legal' moves).

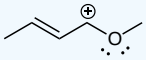


minor
(Carbon does not have a complete octet.)

major
(All atoms have a complete octet.)

The resulting resonance contributor, in which the oxygen bears the formal charge, is the major one because all atoms have a complete octet, and there is one additional bond drawn (resonance rules #1 and #2 both apply). This system can be thought of as four parallel *2p* orbitals (one each on C_2, C_3, and C_4, plus one on oxygen) sharing four pi electrons. One lone pair on the oxygen is in an unhybridized *2p* orbital and is part of the conjugated pi system, and the other is located in an sp^2 orbital.

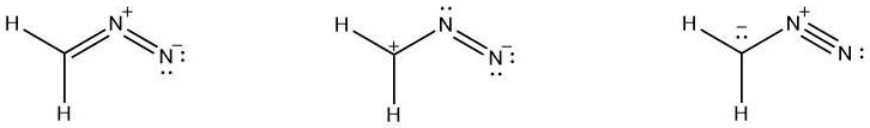
Also note that one additional contributor can be drawn, but it is also minor because it has a carbon with an incomplete octet:



minor

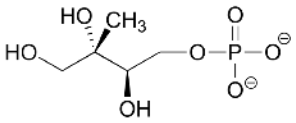
Exercises

1) For the following resonance structures please rank them in order of stability. Indicate which would be the major contributor to the resonance hybrid.



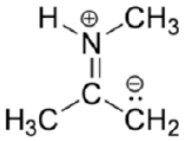
I II III

2) Draw four additional resonance contributors for the molecule below. Label each one as major or minor (the structure below is of a major contributor).

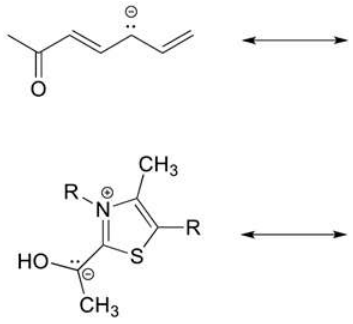


3) Draw three resonance contributors of methyl acetate (an ester with the structure CH_3COOCH_3), and order them according to their relative importance to the bonding picture of the molecule. Explain your reasoning.

4) Below is a minor resonance contributor of a species known as an ‘enamine’, which we will study more later. Draw the major resonance contributor for the enamine, and explain why your contributor is the major one.



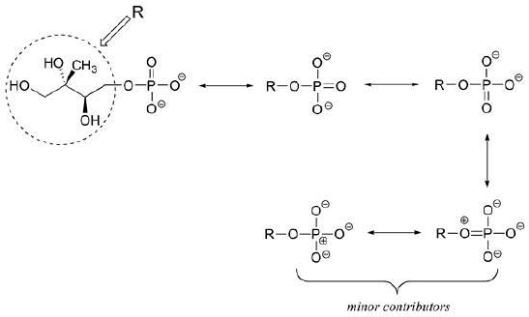
5) Draw the major resonance contributor for each of the anions below:



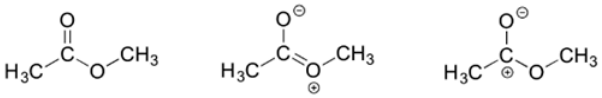
Solutions

1) Structure I would be the most stable because all the non-hydrogen atoms have a full octet and the negative charge is on the more electronegative nitrogen. Structure III would be the next in stability because all of the non-hydrogen atoms have full octets. Structure II would be the least stable because it has the violated octet of a carbocation.

2)



3)

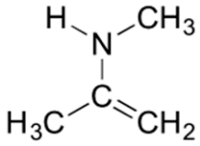


The contributor on the left is the most stable: there are no formal charges.

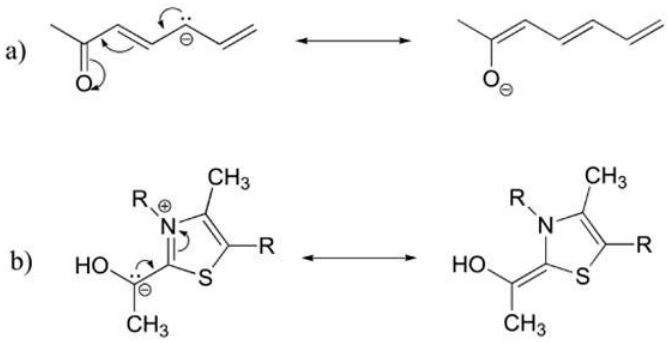
The contributor on the right is least stable: there are formal charges, and a carbon has an incomplete octet.

The contributor in the middle is intermediate stability: there are formal charges, but all atoms have a complete octet.

4) This contributor is major because there are no formal charges.



5)



Exercises

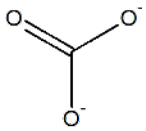
2.5 Rules for Resonance Forms

2.5 Exercises

Questions

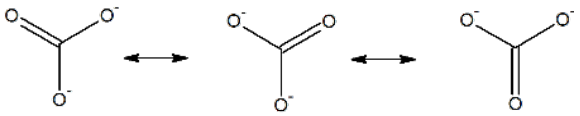
Q2.5.1

Are all the bond lengths the same in the carbonate ion, CO_3^{2-}?



Solutions

S2.5.1 Yes, the bond lengths in carbonate ion are all the same. Carbonate ion exists as the resonance hybrid of the three resonance forms below.



Additional resonance topics

Recognizing Resonance

Resonance contributors involve the 'imaginary movement' of pi-bonded electrons or of lone-pair electrons that are adjacent to (i.e. conjugated to) pi bonds. You can never shift the location of electrons in sigma bonds – if you show a sigma bond forming or breaking, you are showing a chemical reaction taking place. Likewise, the positions of atoms in the molecule cannot change between two resonance contributors.

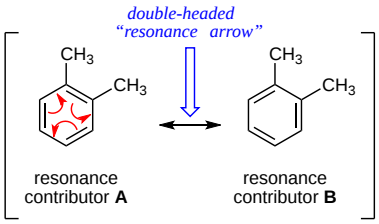
Because benzene will appear throughout this course, it is important to recognize the stability gained through the resonance delocalization of the six pi electrons throughout the six carbon atoms. Benzene also illustrates one way to recognize resonance - when it is possible to draw two or more equivalent Lewis structures. If we were to draw the structure of an aromatic molecule such as 1,2-dimethylbenzene, there are two ways that we could draw the double bonds:



Is this correct… *…or is this?*

Which way is correct? There are two simple answers to this question: 'both' and 'neither one'. Both ways of drawing the molecule are equally acceptable approximations of the bonding picture for the molecule, but neither one, by itself, is an accurate picture of the delocalized pi bonds. The two alternative drawings, however, when considered together, give a much more accurate picture than either one on its own. This is because they imply, together, that the carbon-carbon bonds are not double bonds, not single bonds, but about halfway in between.

When it is possible to draw more than one valid structure for a compound or ion, we have identified **resonance contributors**: two or more different Lewis structures depicting the same molecule or ion that, when considered together, do a better job of approximating delocalized pi-bonding than any single structure. By convention, resonance contributors are linked by a double-headed arrow, and are sometimes enclosed by brackets:

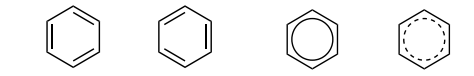


In order to make it easier to visualize the difference between two resonance contributors, small, curved arrows are often used. Each of these arrows depicts the 'movement' of two pi electrons. In the drawing of resonance contributors, however, this electron 'movement' occurs only in our minds, as we try to visualize delocalized pi bonds. Nevertheless, use of the curved arrow notation is an essential skill that you will need to develop in drawing resonance contributors.

The depiction of benzene using the two resonance contributors A and B in the figure above does *not* imply that the molecule at one moment looks like structure A, then at the next moment shifts to look like structure B. Rather, at all moments, the molecule is a combination, or **resonance hybrid** of both A and B.

Caution! It is very important to be clear that in drawing two (or more) resonance contributors, we are not drawing two different molecules: they are simply *different depictions of the exact same molecule*. Furthermore, the double-headed resonance arrow does NOT mean that a chemical reaction has taken place.

Benzene is often drawn as only one of the two possible resonance contributors (it is assumed that the reader understands that resonance hybridization is implied). However, sometimes benzene will be drawn with a circle inside the hexagon, either solid or dashed, as a way of drawing a resonance hybrid.



Examples of Resonance

Molecules with a Single Resonance Configuration

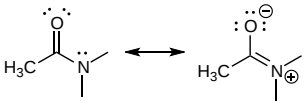
Example 1:



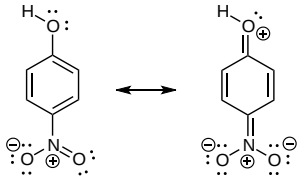
Example 2:



Example 3:



Example 4:

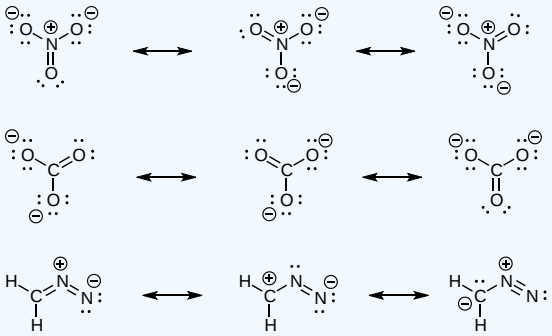


The above resonance structures show that the electrons are delocalized within the molecule and through this process the molecule gains extra stability. Ozone with both of its opposite formal charges creates a neutral molecule and through resonance it is a stable molecule. The extra electron that created the negative charge one terminal oxygen can be delocalized by resonance through the other terminal oxygen.

Benzene is an extremely stable molecule due to its geometry and molecular orbital interactions, but most importantly, due to its resonance structures. The delocalized electrons in the benzene ring make the molecule very stable and with its characteristics of a nucleophile, it will react with a strong electrophile only and after the first reactivity, the substituted benzene will depend on its resonance to direct the next position for the reaction to add a second substituent.

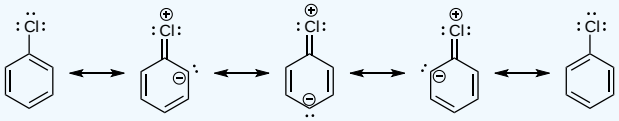
Example 2.5.1: Multiple Resonance of other Molecules

Molecules and ions with more than one resonance form:



Some structural resonance conformations are the major contributor or the dominant forms that the molecule exists. For example, if we look at the above rules for estimating the stability of a molecule, we see that for the third molecule the first and second forms are the major contributors for the overall stability of the molecule. The nitrogen is more electronegative than carbon so, it can handle the negative charge more than carbon. A carbon with a negative charge is the least favorable conformation for the molecule to exist, so the last resonance form contributes very little for the stability of the Ion.

Hybrid Resonance



The different resonance forms of the molecule help predict the reactivity of the molecule at specific sites.

The Hybrid Resonance forms show the different Lewis structures with the electron been delocalized. This is very important for the reactivity of chloro-benzene because in the presence of an electrophile it will react and the formation of another bond will be directed and determine by resonance. The lone pair of electrons delocalized in the aromatic substituted ring is where it can potentially form a new bond with an electrophile, as it is shown there are three possible places that reactivity can take place, the first to react will take place at the *para* position with respect to the chloro- substituent and then to either *ortho*- position.

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2.5: Drawing Resonance Forms

Objectives

After completing this section, you should be able to

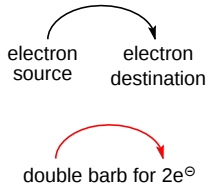
- draw the resonance structures of molecules or ions that exhibit delocalization.
- determine the relative stability of resonance structures using a set of rules.
- use the concept of resonance to explain structural features of molecules and ions.

key words

- resonance structure
- resonance hybrid

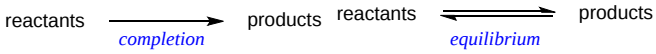
Curved Arrows Communicate Electron Flow (movement)

Organic chemistry has developed a system to show how electrons move between resonance structures. This system will also be used to help describe how electrons from in reactions. Curved double barbed arrows indicates the flow of two electrons. The base of the curved arrow is placed at the source of the electrons that are moving. The head of the arrow is placed at the destination of the electrons.

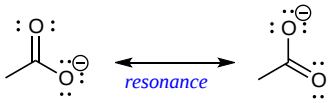


It is also important to consciously use the correct type of arrow. There are four primary types of arrows used by chemists to communicate one of the following: completion reaction, equilibrium reaction, electron movement, and resonance forms. The three other types of arrows are shown below to build discernment between them. Note, the electron movement arrows are the only ones that are curved.

Reaction Arrows



Resonance Arrows

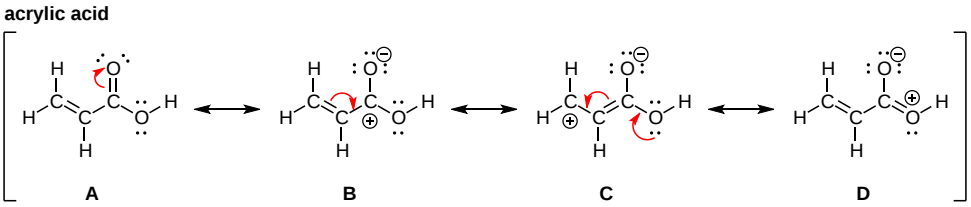


Using Curved Arrows to Show Electron Movement

Because the double barbed arrow represents the movement of two electrons, they usually involve lone pair electrons or pi bonds. There are only three types of electron "motion" in resonance. They are:

1. **A lone pair forms a pi bond to an adjacent atom**
2. **A pi bond forms a new pi bond to an adjacent atom**
3. **A pi bond forms a lone pair on adjacent atom**

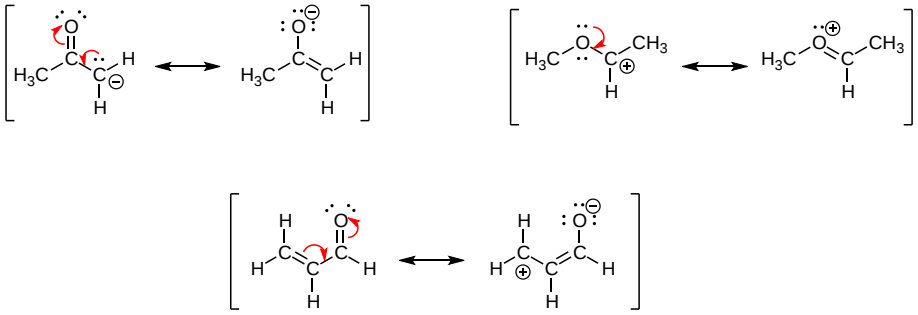
Let's look at the resonance within acrylic acid to demonstrate these three types of resonance.



The curved arrow in structure A represents the type 3 resonance "motion" - the pi bond between the carbon and oxygen breaks to form another lone pair on the oxygen. The curved arrow in structure B represents type 2 resonance "motion" - the pi bond breaks to form a new pi bond to the carbocation carbon. In structure C, there are two curved arrows. The curved arrow from the oxygen lone pair is type 1 resonance motion - the lone pairs forms a new pi bond between the oxygen and carbon. The other arrow in structure C moves the pi bond to the end of the chain and represents resonance type 2. By combining these three basic types of electron movement we can describe virtually any type of resonance.

Example:

Below are a few more examples of 'legal' resonance expressions. Confirm for yourself that the octet rule is not exceeded for any atoms, that formal charges are correct, and identify which type of electron movement is being represented by each arrow.

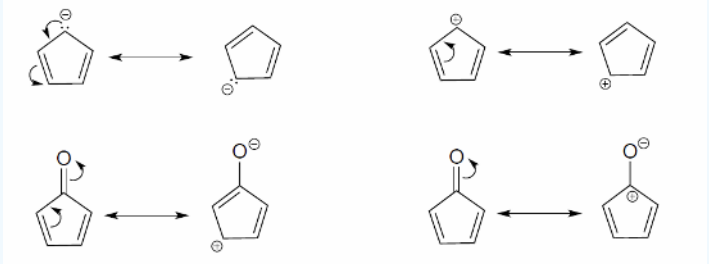


? Exercise 2.5.1

Draw the resonance contributors that correspond to the curved, two-electron movement arrows in the resonance expressions below. Then identify the type of resonance motion in each structure below.

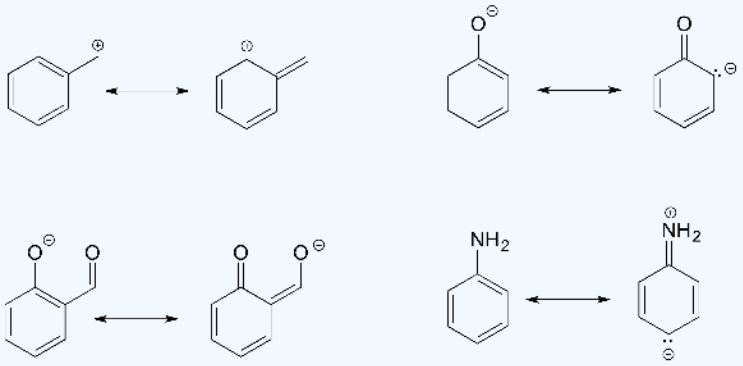


Answer

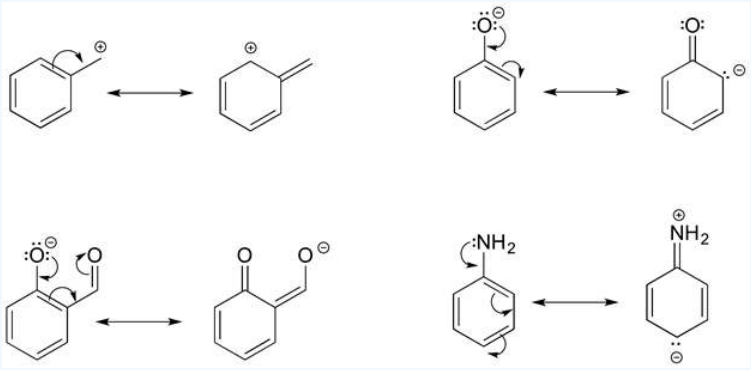


Exercise 2.5.2

In each resonance expression, identify the type of resonance motion. Then draw curved arrows on the left-side contributor that shows how we get to the right-side contributor.



Answer



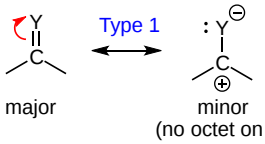
Recognizing Common Patterns of Resonance

If you examine a large number of resonance examples, you will begin to notice that they nearly always match common patterns, of which there are only three. It is important to be able to identify atoms that participate in resonance. In complex resonance cases, multiple types of resonance may occur simultaneously.

Type I - Neutral Species

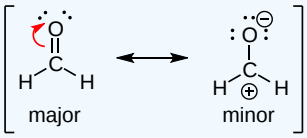
The electrons of a pi bond move to become a set of lone pair electrons on a electronegative atom. The resonance structure made has a carbon with a violated octet which make it a minor contributor. This type of resonance is commonly used to the polarity in certain double bonds.

Neutral Species



Note: Y is an electronegative atom, usually N, O, or S.

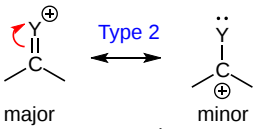
Type I Example



Type II - Charged Species

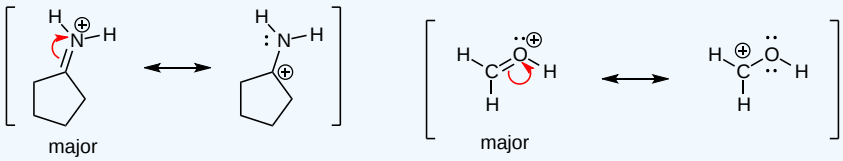
Type II resonance is only seen with a + charge, and usually involves a positive charge on oxygen or nitrogen being shared onto a carbon; the carbocation form has only six valence electrons on the carbon, so it is a less stable form than the major form (which has complete octets).

Charged Species



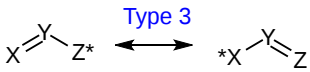
Note: Y is an electronegative atom, usually N, O, S, sometimes halogen

Type II Example



Type III - Allylic Resonance

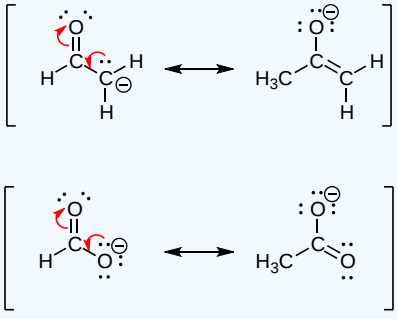
Type III resonance is very common and important because is serves to stabilize positive charges, negative charges, or lone pairs. It is sometimes referred to as “allylic” resonance, especially in cases with all carbon. This type of resonance can be identified by a three-atom group of atoms each with sp^2 hybridization and a *p* orbital.

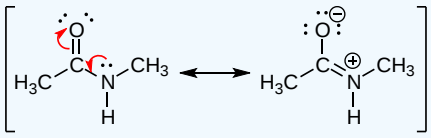


* represents a charge or an unpaired electron

Type III Example

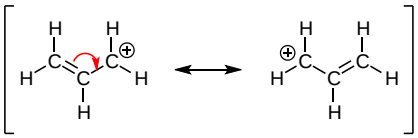
Atoms with lone pair electrons next to a pi bond can be sp^2 hybridized and have the lone pair of electrons in a p orbital despite the fact that they are surrounded by four electron groups. The lone pair electrons contained in the p orbital cause the ion to be stabilized due to resonance.

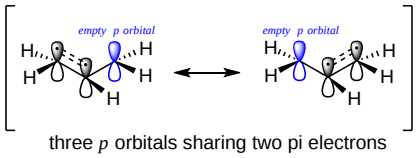




Similarly, carbocations are sp^2-hybridized, with an empty *2p* orbital oriented perpendicular to the plane formed by three sigma bonds. If a carbocation is adjacent to a double bond, then three *2p* orbitals can overlap and share the two pi electrons - another kind of conjugated pi system in which the positive charge is shared over two carbons.

charge is delocalized over two carbons

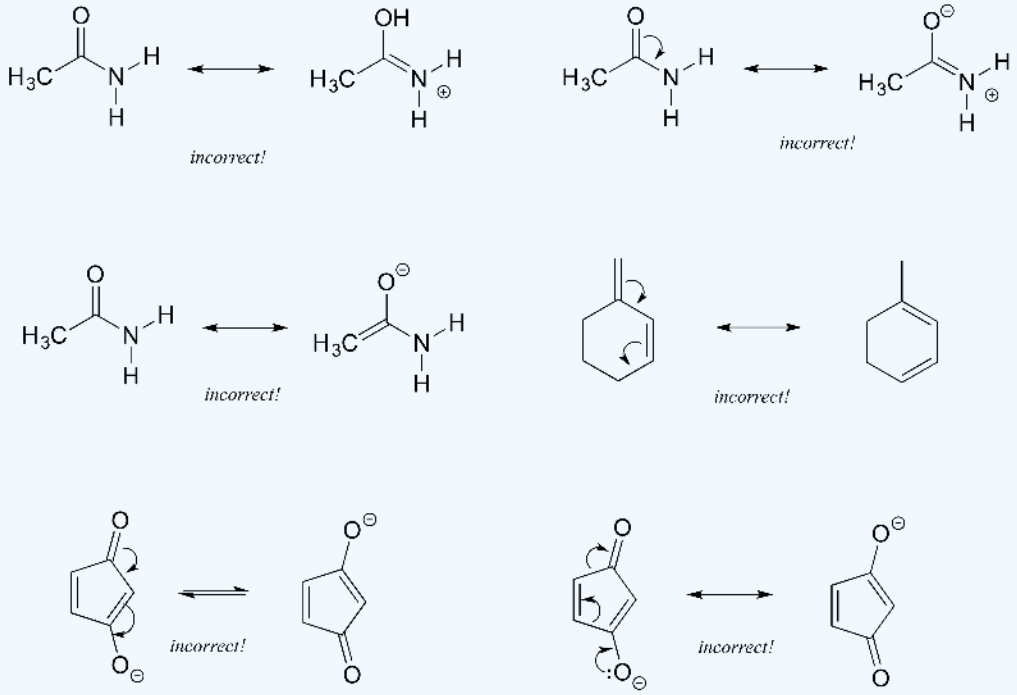




three *p* orbitals sharing two pi electrons

Exercise 2.5.3

Each of the 'illegal' resonance expressions below contains one or more mistakes. Explain what is incorrect in each.



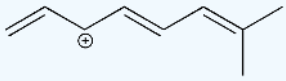
Answer

The first pair are not resonance structures since there is an additional hydrogen on the second structure oxygen. The second pair pushed electrons toward nitrogen which already has a lone pair and would exceed its octet. The third pair includes a structure with 5 bonds to carbon. The fourth pair requires moving carbon-hydrogen bonds, therefore is not resonance. The

fifth pair show electrons moving toward the negatively charged oxygen which would exceed an octet. The fifth pair shows a sigma bond breaking on the ring, rather than pi bond.

Exercise 2.5.4

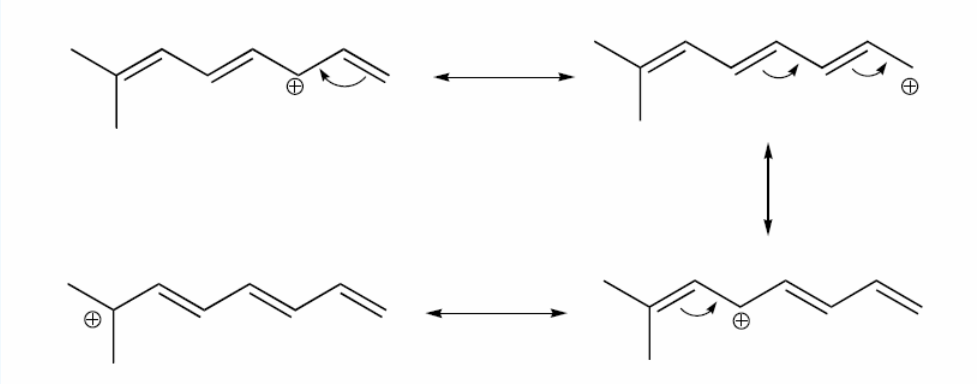
a) Draw three additional resonance contributors for the carbocation below. Include in your figure the appropriate curved arrows showing how one contributor is converted to the next.



b) Fill in the blanks: the conjugated pi system in this carbocation is composed of _____ *2p* orbitals sharing _____ delocalized pi electrons.

Answer

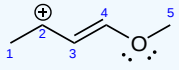
a)



b) The conjugated pi system in this carbocation is composed of seven p orbitals containing six delocalized pi electrons.

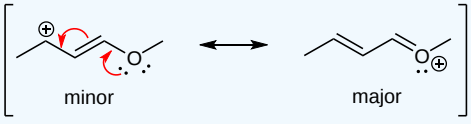
Example 2.5.1

Draw the major resonance contributor of the structure below. Include in your figure the appropriate curved arrows showing how you got from the given structure to your structure. Explain why your contributor is the major one. In what kind of orbitals are the two lone pairs on the oxygen?



Solution

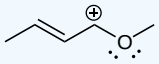
In the structure above, the carbon with the positive formal charge does not have a complete octet of valence electrons. Using the curved arrow convention, a lone pair on the oxygen can be moved to the adjacent bond to the left, and the electrons in the double bond shifted over to the left (see the rules for drawing resonance contributors to convince yourself that these are 'legal' moves).



The resulting resonance contributor, in which the oxygen bears the formal charge, is the major one because all atoms have a complete octet, and there is one additional bond drawn (resonance rules #1 and #2 both apply). This system can be thought of

as four parallel *2p* orbitals (one each on C_2, C_3, and C_4, plus one on oxygen) sharing four pi electrons. One lone pair on the oxygen is in an unhybridized *2p* orbital and is part of the conjugated pi system, and the other is located in an sp^2 orbital.

Also note that one additional contributor can be drawn, but it is also minor because it has a carbon with an incomplete octet:



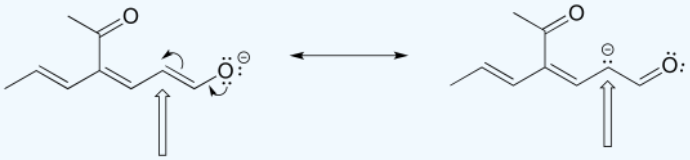
minor

Exercise 2.5.5

The figure below shows how the negative formal charge on an oxygen (of an enol) can be delocalized to the carbon indicated by an arrow. More resonance contributors can be drawn in which negative charge is delocalized to three other atoms on the molecule.

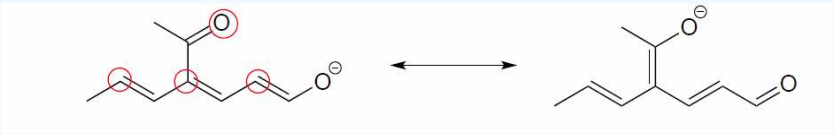
a) Circle these atoms that can also have a resonance structure with a negative charge.

b) Draw the two most important resonance contributors for the enolate ion.



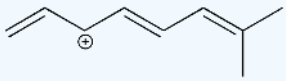
Answer

The two major contributors are those in which the negative formal charge is located on an oxygen rather than on a carbon.



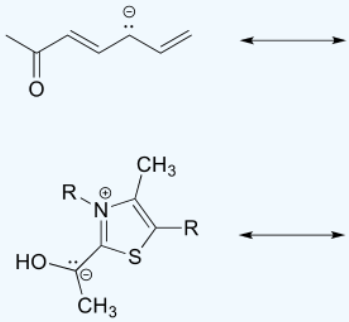
Exercise 2.6.5:

a) Draw three additional resonance contributors for the carbocation below. Include in your figure the appropriate curved arrows showing how one contributor is converted to the next.



b) Fill in the blanks: the conjugated pi system in this carbocation is composed of _____ *2p* orbitals sharing _____ delocalized pi electrons.

Exercise 2.6.6: Draw the major resonance contributor for each of the anions below.

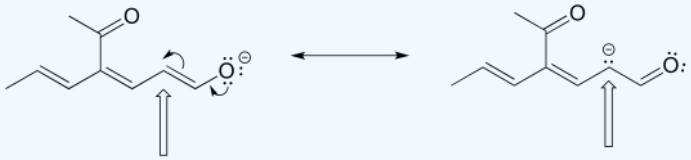


c) Fill in the blanks: the conjugated pi system in part (a) is composed of _____ *2p* orbitals containing _____ delocalized pi electrons.

Exercise 2.6.7: The figure below shows how the negative formal charge on the oxygen can be delocalized to the carbon indicated by an arrow. More resonance contributors can be drawn in which negative charge is delocalized to three other atoms on the molecule.

a) Circle these atoms.

b) Draw the two most important resonance contributors for the molecule.



A word of advice

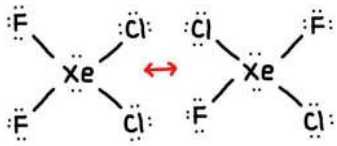
Becoming adept at drawing resonance contributors, using the curved arrow notation to show how one contributor can be converted to another, and understanding the concepts of conjugation and resonance delocalization are some of the most challenging but also most important jobs that you will have as a beginning student of organic chemistry. If you work hard now to gain a firm grasp of these ideas, you will have come a long way toward understanding much of what follows in your organic chemistry course. Conversely, if you fail to come to grips with these concepts now, a lot of what you see later in the course will seem like a bunch of mysterious and incomprehensible lines, dots, and arrows, and it will be difficult to be successful in organic chemistry.

References

1. Petrucci, Ralph H., et al. *General Chemistry: Principles and Modern Applications*. New Jersey: Pearson Prentice Hall, 2007. Print.
2. Ahmad, Wan-Yaacob and Zakaria, Mat B. "Drawing Lewis Structures from Lewis Symbols: A Direct Electron Pairing Approach." Journal of Chemical Education: Journal 77.3: n. pag. Web. March 2000. Link to this journal: pkukmweb.ukm.my/~mbz/c_penerb...83%29/p329.pdf

Problems

1. True or False, The picture below is a resonance structure?

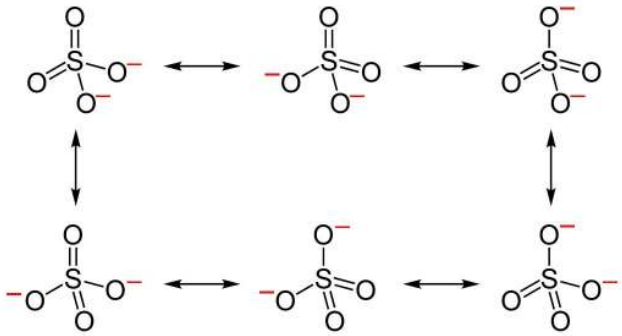


2. Draw the Lewis Dot Structure for $\mathbf{SO_4^{2-}}$ and all possible resonance structures. Which of the following resonance structure is not favored among the Lewis Structures? Explain why. Assign Formal Charges.
3. Draw the Lewis Dot Structure for $\mathbf{CH_3COO^-}$ and all possible resonance structures. Assign Formal Charges. Choose the most favorable Lewis Structure.
4. Draw the Lewis Dot Structure for $\mathbf{HPO_3^{2-}}$ and all possible resonance structures. Assign Formal Charges.
5. Draw the Lewis Dot Structure for $\mathbf{CHO_2^{1-}}$ and all possible resonance structures. Assign Formal Charges.
6. Draw the Resonance Hybrid Structure for $\mathbf{PO_4^{3-}}$.
7. Draw the Resonance Hybrid Structure for $\mathbf{NO_3^-}$.

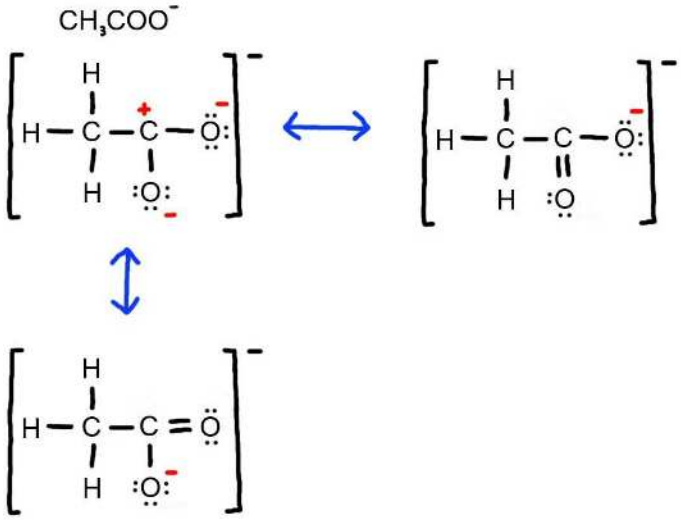
Answers

1. False, because the electrons were not moved around, only the atoms (this violates the Resonance Structure Rules).

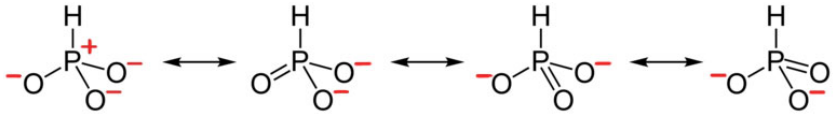
2. Below are the all Lewis dot structure with formal charges (in red) for Sulfate ($\mathbf{SO_4^{2-}}$). There isn't a most favorable resonance of the Sulfate ion because they are all identical in charge and there is no change in Electronegativity between the Oxygen atoms.



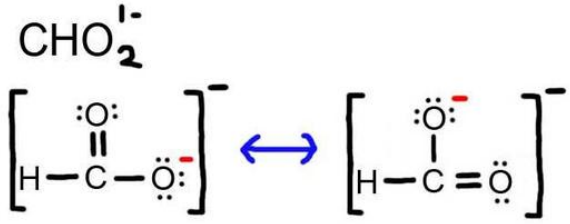
3. Below is the resonance for $\mathbf{CH_3COO^-}$, formal charges are displayed in red. The Lewis Structure with the most formal charges is not desirable, because we want the Lewis Structure with the least formal charge.



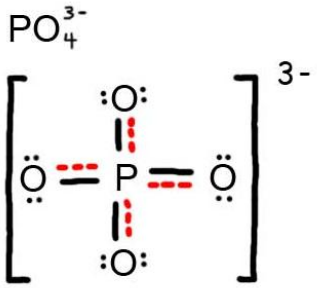
4. The resonance for $\mathbf{HPO_3^{2-}}$, and the formal charges (in red).



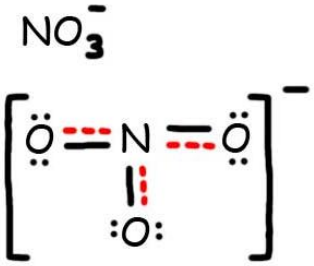
5. The resonance for $\mathbf{CHO_2^{1-}}$, and the formal charges (in red).



6. The resonance hybrid for $\mathbf{PO_4^{3-}}$, hybrid bonds are in red.



7. The resonance hybrid for $\mathbf{NO_3^-}$, hybrid bonds are in red.

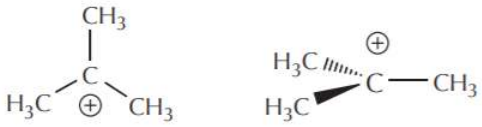


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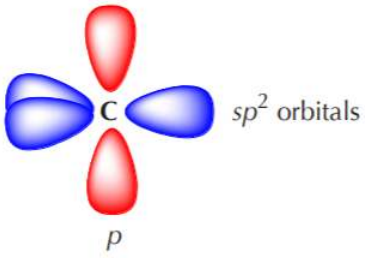
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2.5.1: Orbital Picture of Delocalization

The orbital view of delocalization can get somewhat complicated. For now we're going to keep it at a basic level. We start by noting that sp^2 carbons actually come in several varieties. Two of the most important and common are neutral sp^2 carbons and positively charged sp^2 carbons. Substances containing neutral sp^2 carbons are regular alkenes. Species containing positively charged sp^2 carbons are called **carbocations**. The central carbon in a carbocation has trigonal planar geometry, and the unhybridized *p* orbital is empty. The following representations convey these concepts.

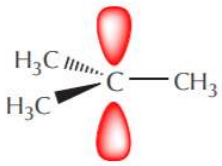


Top and side view of a carbocation in Lewis and 3-D notation



Orbital view of a carbocation. The unhybridized *p* orbital is empty

A combination of orbital and Lewis or 3-D formulas is a popular means of representing certain features that we may want to highlight. For example, if we're not interested in the sp^2 orbitals and we just want to focus on what the *p* orbitals are doing we can use the following notation.



Let's now focus on two simple systems where we know delocalization of *pi* electrons exists. One is a system containing two *pi* bonds in conjugation, and the other has a *pi* bond next to a positively charged carbon. We can represent these systems as follows.

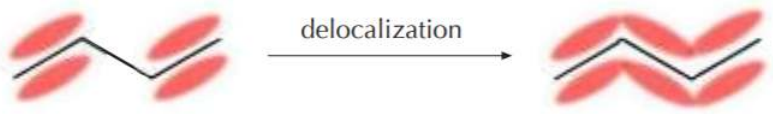


Line angle and orbital picture of a simple conjugated system

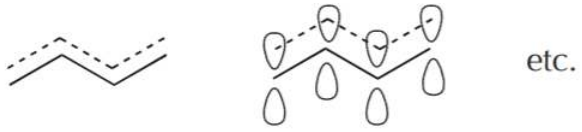


Line angle and orbital picture of a system containing a carbocation next to a *pi* bond

If we focus on the orbital pictures, we can immediately see the potential for electron delocalization. The two *pi* molecular orbitals shown in red on the left below are close enough to overlap. Overlapping is a good thing because it delocalizes the electrons and spreads them over a larger area, bringing added stability to the system.



It is however time-consuming to draw orbitals all the time. The following representations are used to represent the delocalized system.



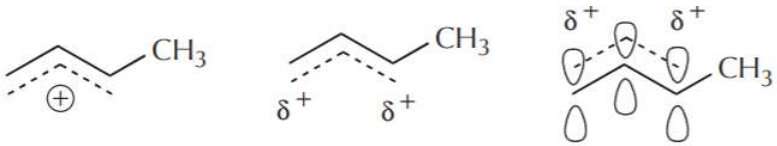
A similar process applied to the carbocation leads to a similar picture.



The resonance representation conveys the idea of delocalization of charge and electrons rather well.



Finally, the following representations are sometimes used, but again, the simpler they are, the less accurately they represent the delocalization picture.



There will be plenty of opportunity to observe more complex situations as the course progresses.

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2.6: Structure and Stability of Benzene

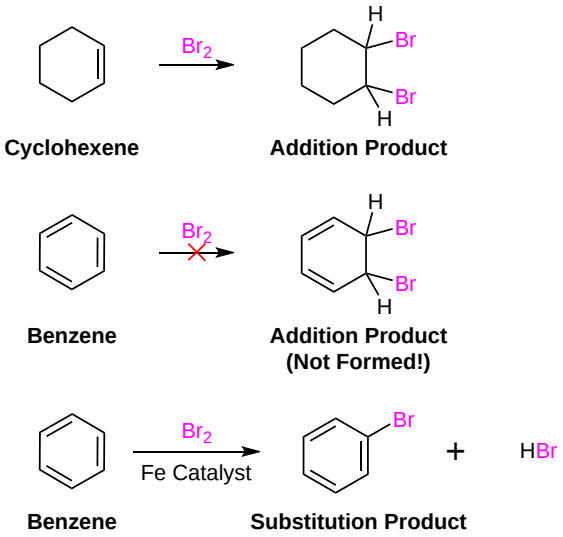
Objectives

After completing this section, you should be able to

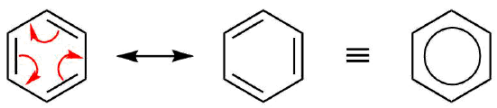
1. compare the reactivity of a typical alkene with that of benzene.
2. Use the heat of hydrogenation data to show that benzene is more stable than might be expected for “cyclohexatriene.”
3. state the length of the carbon-carbon bonds in benzene, and compare this length with those of bonds found in other hydrocarbons.
4. describe the geometry of the benzene molecule.
5. describe the structure of benzene in terms of resonance.
6. describe the structure of benzene in terms of molecular orbital theory.
7. draw a molecular orbital diagram for benzene.

Structure of Benzene

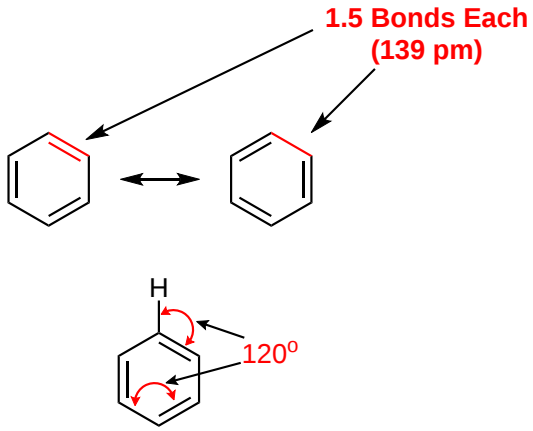
When benzene (C_6H_6) was first discovered its low hydrogen to carbon ratio (1:1) led chemists to believe it contained double or triple bonds. Since double and triple bonds rapidly add bromine (Br_2), this reaction was applied to benzene. Surprisingly, benzene was entirely unreactive toward bromine. In addition, if benzene is forced to react with bromine through the addition of a catalyst, it undergoes **substitution reactions** rather than the addition reactions that are typical of alkenes. These experiments suggested that the six-carbon benzene core is unusually stable to chemical modification.



The conceptual contradiction presented by a high degree of unsaturation (low H:C ratio) and high chemical stability for benzene and related compounds remained an unsolved puzzle for many years. Eventually, the presently accepted structure of benzene as a hexagonal, planar ring of carbons with alternating single and double bonds was adopted, and the exceptional chemical stability of this system was attributed to special resonance stabilization of the conjugated cyclic triene. No single structure provides an accurate representation of benzene as it is a combination of two structurally and energetically equivalent resonance forms representing the continuous cyclic conjugation of the double bonds. In the past, the benzene resonance hybrid was represented by a hexagon with a circle in the center to represent the benzene's pi-electron delocalization. This method has largely been abandoned because it does not show the pi electrons contained in benzene. Currently, the structure of benzene is usually represented by drawing one resonance form with the understanding that it does not completely represent the true structure of benzene.

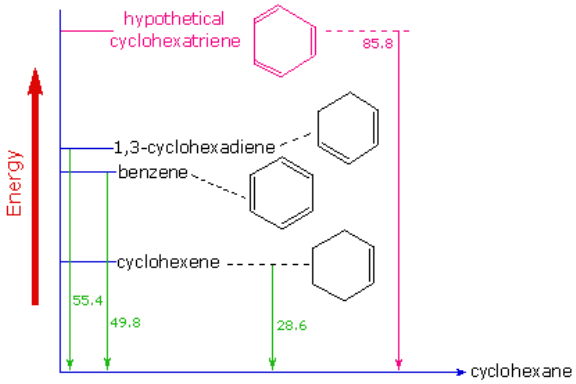


The six-membered ring in benzene is a perfect hexagon with all carbon-carbon bonds having an identical length of 139 pm[1]. The 139 pm bond length is roughly in between those of a C=C double bond (134 pm) and a C-C single (154 pm) which agrees with the benzene ring being a resonance hybrid made up of 1.5 C-C bonds. Each carbon in the benzene ring is sp^2 hybridized which makes all the C-C-C and H-C-C bond angles in benzene 120^o and makes the overall molecule planar.



The High Stability of Benzene

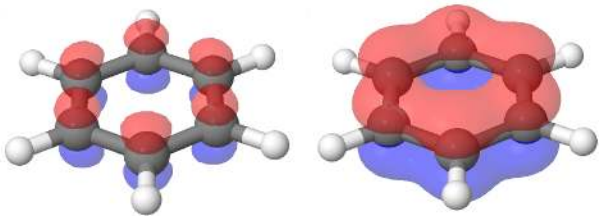
In previous polyalkene, examples the electron delocalization described by resonance enhanced the stability of the molecule. However, benzene's stability goes beyond this. Evidence for the enhanced thermodynamic stability of benzene was obtained from measurements of the heat released when double bonds in a six-carbon ring are hydrogenated (hydrogen is added catalytically) to give cyclohexane as a common product. In the following diagram cyclohexane represents a low-energy reference point. Addition of hydrogen to cyclohexene produces cyclohexane and releases heat amounting to 28.6 kcal per mole. If we take this value to represent the energy cost of introducing one double bond into a six-carbon ring, we would expect a cyclohexadiene to release 57.2 kcal per mole on complete hydrogenation, and 1,3,5-cyclohexatriene to release 85.8 kcal per mole. These **heats of hydrogenation** would reflect the relative thermodynamic stability of the compounds. In practice, 1,3-cyclohexadiene is slightly more stable than expected, by about 2 kcal, presumably due to conjugation of the double bonds. **Benzene, however, is an extraordinary 36 kcal/mole more stable than expected**. This sort of stability enhancement is called **aromaticity** and molecules with aromaticity are called aromatic compounds. Benzene is the most common aromatic compound but there are many others. Aromatic stabilization explains benzene's lack of reactivity compared to typical alkenes.



Atomic Orbitals of Benzene

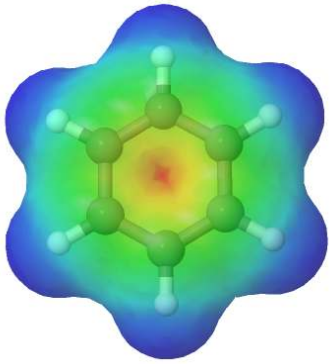
Also, each of benzene's six carbon atoms are sp^2 hybridized and have an unhybridized p orbital perpendicular to plane of the ring. Because each of the six carbon atoms and their corresponding p orbitals are equivalent, it is impossible for them to only overlap with one adjacent p orbital to create three defined double bonds. Instead each p orbital overlaps equally with both adjacent orbitals creating a cyclic overlap involving all six p orbitals. This allows the p orbitals to be delocalized in molecular orbitals that extend all the way around the ring allowing for more overlap than would be obtained from the linear 1,3,5-hexatriene equivalent. For this to

happen, of course, the ring must be planar – otherwise the *p* orbitals couldn't overlap properly and benzene is known to be a flat molecule. An electrostatic potential map of benzene, shown below, shows that the pi electrons are evenly distributed around the ring and that every carbon equivalent.



Each carbon in the benzene ring is sp^2 hybrized with a p orbital perpendicular to the ring plane (Left)

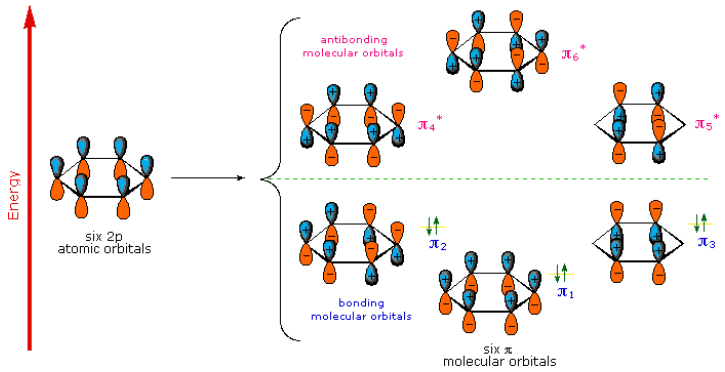
Being planar and cyclic allows benzene's p orbitals to undergo cyclic overlap (Right)



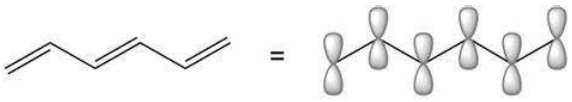
An electrostatic potential map of benzene

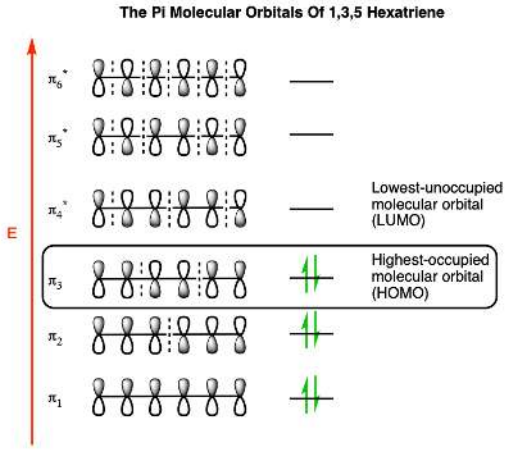
The Molecular Orbitals of Benzene

A molecular orbital description of benzene provides a more satisfying and more general treatment of "aromaticity". We know that benzene has a planar hexagonal structure in which all the carbon atoms are sp^2 hybridized, and all the carbon-carbon bonds are equal in length. As shown below, the remaining cyclic array of six p-orbitals (one on each carbon) overlap to generate six molecular orbitals, three bonding and three antibonding. The plus and minus signs shown in the diagram do not represent electrostatic charge, but refer to phase signs in the equations that describe these orbitals (in the diagram the phases are also color coded). When the phases correspond, the orbitals overlap to generate a common region of like phase, with those orbitals having the greatest overlap (e.g. π_1) being lowest in energy. The remaining carbon valence electrons then occupy these molecular orbitals in pairs, resulting in a fully occupied (6 electrons) set of bonding molecular orbitals. It is this completely filled set of bonding orbitals, or **closed shell**, that gives the benzene ring its thermodynamic and chemical stability, just as a filled valence shell octet confers stability on the inert gases.

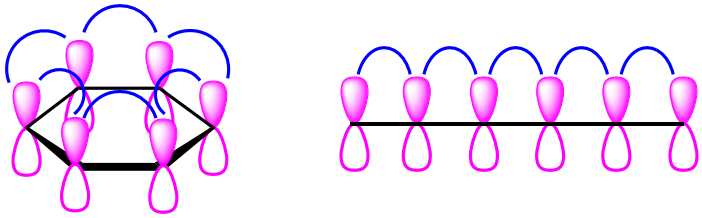


To better see source of the stabilizing aromaticity effect created by the cyclic p orbitals of benzene, the molecular orbitals of 1,3,5-hexatriene must be investigated. The molecule 1,3,5-hexatriene contains six p orbitals which all overlap but in a linear fashion. As with benzene, this overlap creates 3 stabilized bonding molecular which are completely filled with six p electron. As expected, the conjugation creates a marked increase of stability in 1,3,5-hexatriene but not as much as in benzene.





The main difference in stability can be seen when comparing the lowest energy molecular orbital of 1,3,5-hexatriene and benzene: pi_1. In pi_1 molecular orbital of 1,3,5-hexatriene there are 5 stabilizing bonding interactions where there are 6 stabilizing bonding interactions in the pi_1 of benzene. The sixth bonding interaction is made possible by benzene's p orbitals being in a ring. Because benzene's pi_1 molecular orbital has more stabilizing bonding interactions it is lower in energy than the pi_1 molecular orbital of 1,3,5-hexatriene. This gives benzene the additional aromatic stability not seen in the acyclic 1,3,5-hexatriene.



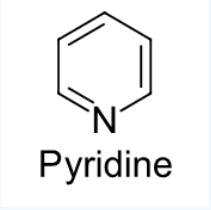
The pi_1 molecular obrital of benzene (Left) has 6 stabilizing bonding interaction

where 1,3,5-hexatriene's (Right) only has 5

Exercises

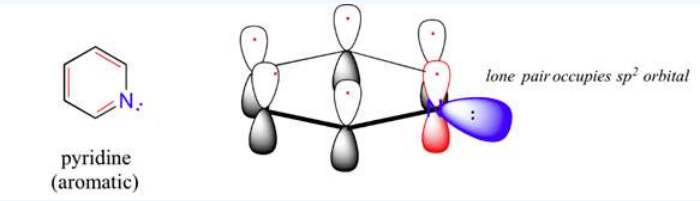
? Exercise 2.6.1

1) The molecule, pyridine, is planar with bond angles of 120^o. Pyridine has many other characteristics similar to benzene. Draw a diagram showing the p orbitals in pyridine and use it to explain its similarity to benzene.



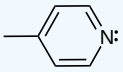
Answer

The nitrogen and each carbon in the pyridine ring is sp^2 hybridized. In the bonding picture for pyridine, the nitrogen is sp^2-hybridized, with two of the three sp^2 orbitals forming sigma overlaps with the sp^2 orbitals of neighboring carbon atoms, and the third nitrogen sp^2 orbital containing the lone pair electrons. The unhybridized p orbital contains a single electron, which is part of the 6 pi-electron system delocalized around the ring. Pyridine is most likely aromatic which gives it its planar shape and 120º bond angles.

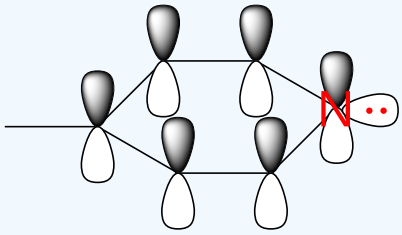


Exercise 2.6.2

The molecule shown, *p*-methylpyridine, has similar properties to benzene (flat, 120° bond angles). Draw the pi-orbitals for this compound.



Answer



References

https://royalsocietypublishing.org/d...rspa.1964.0092 "A crystallographic study of solid benzene by neutron diffraction" G.E. Bacon, N. A. Curry, and S.A. Wilson, 1964

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2.7: Aromaticity and the Hückel 4n + 2 Rule

Objectives

After completing this section, you should be able to

1. define aromaticity in terms of the Hückel 4*n* + 2 rule.
2. use the Hückel 4*n* + 2 rule to determine whether or not a given polyunsaturated cyclic hydrocarbon should exhibit aromatic properties.
3. describe the difference in properties between an aromatic hydrocarbon, such as benzene, and a non-aromatic polyunsaturated cyclic hydrocarbon, such as cyclobutadiene or cyclooctatetraene.
4. draw molecular orbital diagrams for aromatic species, such as benzene, the cyclopentadienyl anion and pyridine, and compare these diagrams with those obtained for non-aromatic species, such as cyclobutadiene and the cyclopentadienyl cation.

In 1931, German chemist and physicist Erich Hückel proposed a theory to help determine if a planar ring molecule would have aromatic properties. His rule states that if a cyclic, planar molecule has $4n + 2\ \pi$ electrons, it is considered aromatic. This rule would come to be known as **Hückel's Rule**.

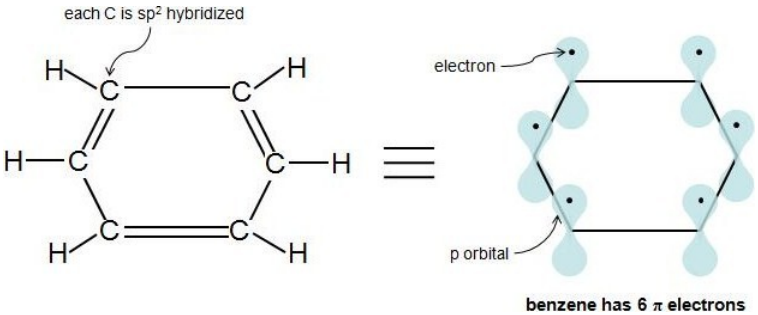
Four Criteria for Aromaticity

When deciding if a compound is aromatic, go through the following checklist. If the compound does not meet all the following criteria, it is likely not aromatic.

1. The molecule is cyclic (a ring of atoms)
2. The molecule is planar (all atoms in the molecule lie in the same plane)
3. The molecule is fully conjugated (p orbitals at every atom in the ring)
4. The molecule has 4n+2 π electrons (n=0 or any positive integer)

Counting π Electrons?

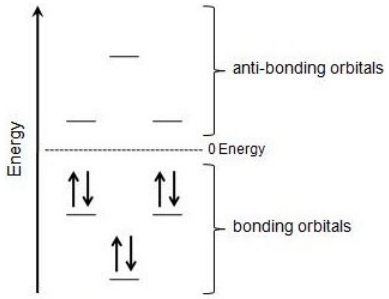
Perhaps the toughest part of Hückel's Rule is figuring out which electrons in the compound are actually π electrons. Once this is figured out, the rule is quite straightforward. Pi electrons lie in the p orbitals and sp^2 hybridized atoms have 1 of these p orbitals each. When looking at a C=C double bond we know that there is one sigma bond and one pi bond. The pi bond is formed by the overlap of 1 p orbital from each carbon in the double bond. Each p orbital contains one electron so when the two p orbitals overlap the two electrons become a pi bond and are thus called pi electrons. Because aromaticity deals directly with double bonds and conjugation it is simpler to just count the number pi electrons in a compound. Each double bond (π bond) always contributes 2 π electrons. Benzene has 3 double bonds, so it has 6 π electrons.



Why 4n+2 π Electrons?

According to Hückel's Molecular Orbital Theory, a compound is particularly stable if all of its bonding molecular orbitals are filled with paired electrons. This is true of aromatic compounds, meaning they are quite stable. With aromatic compounds, 2 electrons fill the lowest energy molecular orbital, and 4 electrons fill each subsequent energy level (the number of subsequent energy levels is

denoted by n), leaving all bonding orbitals filled and no anti-bonding orbitals occupied. This gives a total of 4n+2 π electrons. You can see how this works with the molecular orbital diagram for the aromatic compound, benzene, below. Benzene has 6 π electrons. Its first 2 π electrons fill the lowest energy orbital, and it has 4 π electrons remaining. These 4 fill in the orbitals of the succeeding energy level. Notice how all of its bonding orbitals are filled, but none of the anti-bonding orbitals have any electrons.



molecular orbital diagram for benzene

To apply the 4n+2 rule, first count the number of π electrons in the molecule. Then, set this number equal to 4n+2 and solve for n. If is 0 or any positive integer (1, 2, 3,...), the rule has been met. For example, benzene has six π electrons:

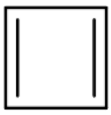
$$4n + 2 = 6 \quad (2.7.1)$$
$$4n = 4 \quad (2.7.2)$$
$$n = 1 \quad (2.7.3)$$

For benzene, we find that $n = 1$, which is a positive integer, so the rule is met.

With Hückel's theory we can assume that if a molecule meets the other criteria for aromaticity and also has 2, 6, 10, 14, 18 ect. pi electrons it will most likely be aromatic.

Antiaromaticity

More than 100 years ago, chemists recognized the possible existence of other conjugated cyclic polyalkenes, which at least superficially would be expected to have properties like benzene. The most interesting of these are cyclobutadiene, whose shape and alignment of p orbitals suggested it should have substantial electron-delocalization energies.



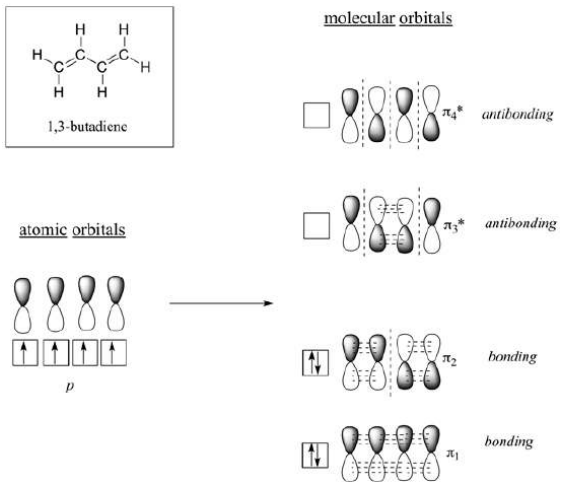
Cyclobutadiene

However, cyclobutadiene was found to be an extremely unstable molecules. In fact, cyclobutadiene is even more reactive than most alkenes. The synthesis of cyclobutadiene eluded chemists for almost 100 years. As more work was done, it became increasingly clear that the molecule, when formed in reactions, was immediately converted to something else. Finally, cyclobutadiene was captured in an essentially rigid matrix of argon at 8K. On warming to even 35K , it dimerizes through a Diels Alder reaction to yield a tricyclicdiene.



Due to the square ring, cyclobutadiene was expected to have some degree of destabilization associated with ring strain. However, estimations of the strain energies, though substantial, did not account for cyclobutadiene's high degree of instability. Also, why was it not being stabilized through cyclic conjugation in the same way as benzene. The answer can be seen in the molecular orbitals.

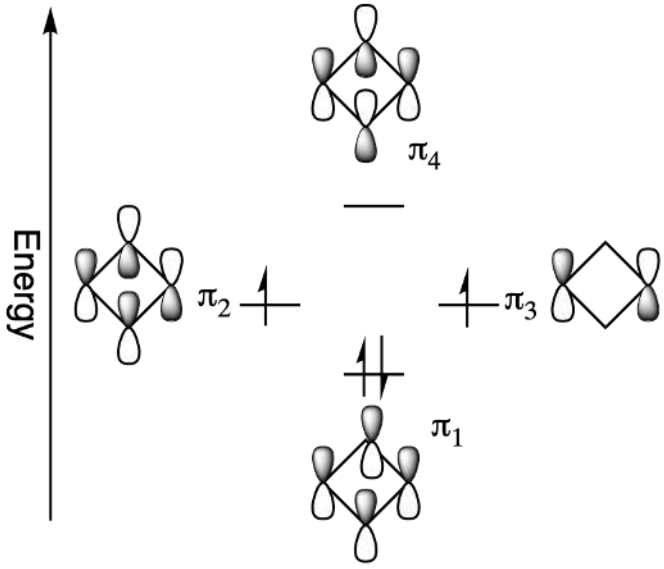
We considering the molecular orbitals diagram of the analogous 1,3-butadiene, the four *2p* atomic orbitals combine to form four pi molecular orbitals of increasing energy. Two bonding pi orbitals and two antibonding pi* orbitals. The 4 pi electrons of 1,3-butadiene completely fill the bonding molecular orbitals giving is the additional stability associated with conjugated double bonds.



However, when placed into a ring the molecular orbitals undergo a significant change. The four p orbitals of cyclobutadiene combine to form the following 4 molecular orbitals:

- a bonding molecular orbital which is lower in energy than the atomic orbitals
- two degenerate non-bonding molecular orbitals which are of equivalent energy to the atomic orbitals
- one antibonding molecular orbital which is higher in energy

The non-bonding orbitals represent that there is no direct interaction between adjacent atoms. When adding cyclobutadiene's 4 pi electrons to the molecular orbital diagram, the bonding orbital is filled and both non-bonding orbitals are singly occupied. If cyclobutadiene's double bonds were delocalized, all the pi electrons would be in low energy bonding orbitals. However, only two of the pi electrons are in bonding orbitals; the other two are non-bonding. In addition, the molecular orbital diagram shows that two of the electrons are unpaired, a situation called a triplet state, which usually makes organic molecules very reactive. For cyclobutadiene cyclic conjugation has made the molecule less stable. This unexpected instability in 4n π-electron cyclic conjugated compounds is termed **antiaromaticity** and the compounds are called antiaromatic.



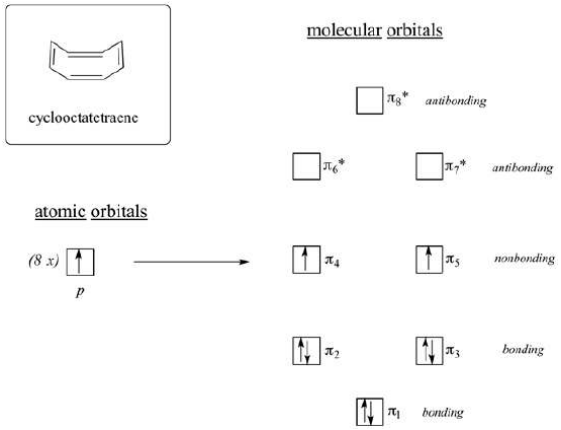
Antiaromaticity gives cyclobutadiene some interesting structural features. Cyclobutadiene's single and double bonds have different bond lengths, 158 pm and 135 pm respectively which give it a rectangular shape. If the double bonds were conjugated, there would only be one average bond length, like benzene, and shape would be square. In fact, cyclobutadiene's double bonds are not conjugated but locked into position.

Just like 4n + 2 rule with aromaticity, compounds which are flat, cyclic, have a p orbital at every member of the ring, and 4n pi electrons should be antiaromatic. Another potentially antiaromatic molecule is 1,3,5,7-cyclooctatetraene.

Cyclooctatetraene was first synthesized in 1911 by a German chemist, R. Willstatter (Nobel Prize 1915), who reported an extraordinary thirteen-step synthesis of cyclooctatetraene from a rare alkaloid called pseudopelletierine isolated from the bark of pomegranate trees. However, during the Second World War, the German chemist W. Reppe found that cyclooctatetraene can be made in reasonable yields by the tetramerization of ethyne under the influence of a nickel cyanide catalyst:



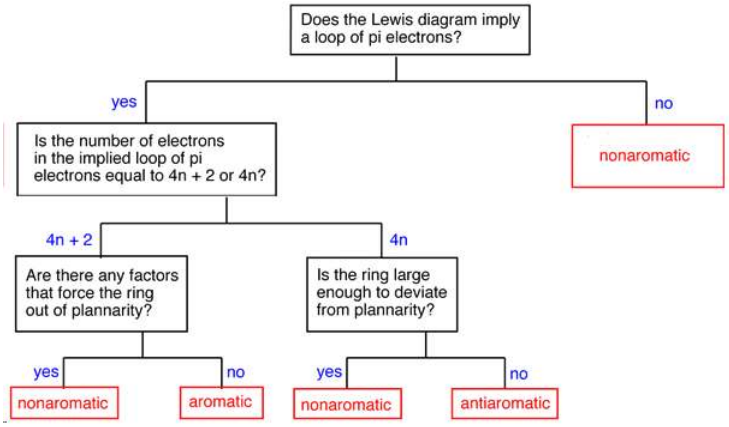
If cyclooctatetraene was flat it would have all the requirements to be antiaromatic. It is cyclic, has a p orbital in every member of the ring, and has 8 pi electrons. When looking at the molecular orbital diagram of cyclooctatetraene we see it shares certain characteristics in common with cyclobutadiene. Two of the molecular orbitals are degenerate non-bonding orbitals. When the molecular orbitals are fill with cyclooctatetraene's 8 pi electrons the last two electrons are unpaired in the two nonbonding orbitals creating a triplet state. Based off the molecular orbital diagram cyclooctatetraene should be antiaromatic.



However, cyclooctatetraene is easily prepared and relatively stable. Also, it undergoes addition reactions typical of alkenes. In reality, cyclooctatetraene is not flat but has a tub-like shape. By assuming this shape, the p orbtials between double bond are out of alignment for overlap. Because the double bonds are not conjugated, cyclooctatetraene escapes the destabilizing effects of antiaromaticity. This makes its its pi bonds react like 'normal' alkenes. Because cyclooctatetraene is not flat nor conjugated it is properly defined as non-aromatic. In general, if an antiaromatic compound has the ability to form a non-planar shape it will do so to avoid destabilization by becoming non-aromatic.

Determining if a Compound is Aromatic, Antiaromatic, or Nonaromatic

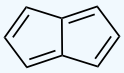
To make this determination it is important to first as if the compound has the possibility of cyclic conjugation. This requires that the compound be cyclic and have a p orbital at every atom in the ring. If the compound does not have both of these criteria it cannot be aromatic or antiaromatic and must therefore be nonaromatic. Next the number of pi electrons in the ring is determined to see if it follows the count of aromaticity (4n + 2) or antiaromaticity (4n). Before making the final determination, it is vital to know the actual geometry of the molecule. Despite the number of pi electrons, a compound cannot be aromatic or antiaromatic if its geometry is not planar to allow for p orbital overlap.



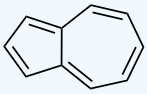
Example 2.7.1



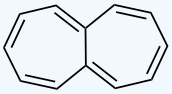
Cyclopentadiene (planar)
4 p Electrons
Nonaromatic



Pentalene (planar)
8 p Electrons
Antiaromatic



Azulene (planar)
10 p Electrons
Aromatic



Heptalene (planar)
12 p Electrons
Antiaromatic

A Common Misconception

A very common misconception is that hybridization can be used to predict the geometry, or that hybridization somehow involves an energy cost associated with 'promoting' electrons into the hybrid orbitals. **This is entirely wrong.** Hybridization is always determined by geometry. You can only assign hybridization states to an atom if you already know its geometry, based on some experimental or theoretical evidence. The geometry of the oxygen in furan is trigonal planar and therefore the hybridization must be sp^2.

The *specific* rule is that if you have an sp^2 conjugated system, the lone pair will be involved ***if it makes the system more stable.*** In this case, conferring Hückel 4n+2 aromaticity. For furan with *two* lone pairs on the oxygen atom, if we count electrons from the carbon atoms, we have 4 (one per carbon). So adding two electrons from one of the lone pairs will give 6 = 4(1)+2, so Hückel rule is applicable and furan is aromatic.

Exercise 2.7.1

Using the criteria for aromaticity, determine if the following molecules are aromatic:



a)



b)



c)



d)



e)



f)



g)



h)



i)



j)

Answer

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a) Aromatic - only 1 of S's lone pairs counts as π electrons, so there are 6 π electrons, n=1

b) Not aromatic - not fully conjugated, top C is sp^3 hybridized

c) Not aromatic - top C is sp^2 hybridized, but there are 4 π electrons, n=1/2

d) Aromatic - N is using its 1 p orbital for the electrons in the double bond, so its lone pair of electrons are not π electrons, there are 6 π electrons, n=1

e) Aromatic - there are 6 π electrons, n=1

f) Not aromatic - all atoms are sp^2 hybridized, but only 1 of S's lone pairs counts as π electrons, so there 8 π electrons, n=1.5

g) Not aromatic - there are 4 π electrons, n=1/2

h) Aromatic - only 1 of N's lone pairs counts as π electrons, so there are 6 π electrons, n=1

i) Not aromatic - not fully conjugated, top C is sp^3 hybridized

j) Aromatic - O is using its 1 p orbital for the elections in the double bond, so its lone pair of electrons are not π electrons, there are 6 π electrons, n=1

? Exercise 2.7.2

To be aromatic, a molecule must be planar conjugated, and obey the 4n+2 rule. The following is the following molecule aromatic?



Answer

No, it is not. It does not obey the 4n+2 rule. Also it is not planar.

References

1. Vollhardt, Peter, and Neil E. Schore. Organic Chemistry: Structure and Function. 5th ed. New York: W. H. Freeman & Company, 2007.
2. Berson, Jerome. Chemical Creativity: Ideas from the Work of Woodward, Hückel, Meerwein, and Others. New York: Wiley-VCH, 1999.
3. Badger, G.M. Aromatic Character and Aromaticity. London, England: Cambridge University Press, 1969.
4. Lewis, David and David Peters. Facts and Theories of Aromaticity. London, England: Macmillan Press, 1975.

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2.8: Aromatic Ions

Objectives

After completing this section, you should be able to

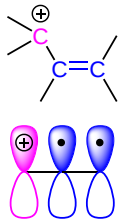
1. use the Hückel 4*n* + 2 rule to explain the stability of the cyclopentadienyl anion, the cycloheptatrienyl cation and similar species.
2. use the Hückel 4*n* + 2 rule to determine whether or not a given unsaturated cyclic hydrocarbon anion or cation is aromatic.
3. draw the resonance contributors for the cyclopentadienyl anion, cation and radical, and similar species.

Aromatic Ions

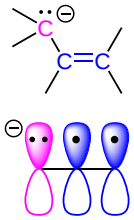
As previously, noted a ring must be fully conjugated to have the potential to be aromatic. This means that every atom in the ring must have a *p* orbital which can overlap with adjacent *p* orbitals. Until now the atoms providing the *p* orbitals have been neutral sp^2 hybridized carbons, however it is also possible for sp^2 hybridized carbons to have a charge. There are several examples of cationic and anionic compounds with unexpected stabilities that suggest that they are aromatic. It is important to understand how charged carbons in these compounds will affect the determination of aromaticity.

There are two main situations which need to be considered: The conjugation of a carbocation and the conjugation of a carbanion. A carbocation carbon is surrounded by three electron groups giving it sp^2 hybridization. The remaining unhybridized *p* orbital holds the carbocation's positive charge and is vacant of pi electrons. Although a carbocation is capable of extending conjugation it does not add to the compound's pi electron count.

A carbanion carbon is surrounded by four electron groups and would normally be sp^3 hybridized. However, to obtain the stabilizing effects of conjugation, carbanion carbons can becomes sp^2 hybridized putting the set of lone pair electrons into the unhybridized *p* orbital. Because the carbanion's *p* orbital contains two electrons in the form of a set of lone pair electrons, it increases a compound's pi electron count by 2.



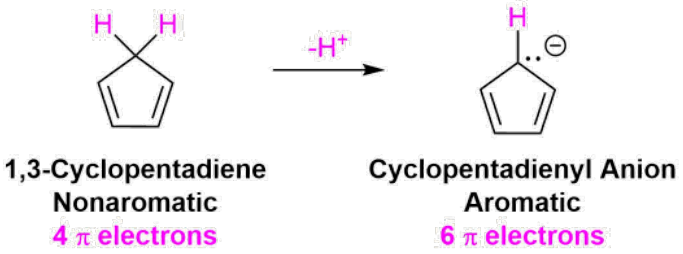
2 p Electrons Total
The carbocation adds
0 p Electrons



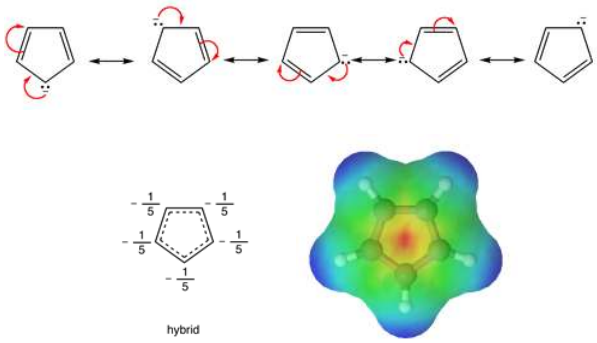
4 p Electrons Total
The carbanion adds
2 p Electrons

Cyclopentadiene Ion

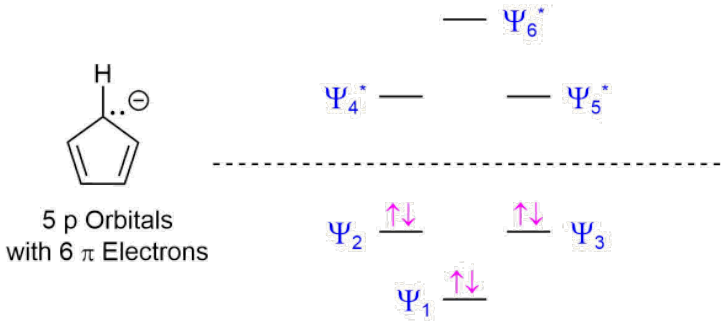
One of the most well know examples of an aromatic ion is the 1,3-cyclopentadiene ion. 1,3-Cyclopentadiene is nonaromatic due to the presence of an intervening sp^3 hybridized -CH_2- carbon atom which prevents pi electrons from delocalizing about the entire ring. Also, it only has 4 pi electrons which does not follow Hückel's 4n + 2 rule. However, if a proton is removed form the CH_2 group to form the cyclopentadienyl anion, the carbon atom becomes sp^2 hybridized and the two electrons of the resulting lone pair occupy the newly produced *p* orbital. This increases the number of pi electrons in the cyclopentadienyl anion to 6 which follows the 4n +2 rule. Moreover, this new *p* orbital overlaps with the *p* orbitals already present allowing for cyclic delocalization of pi electrons about the entire ring.



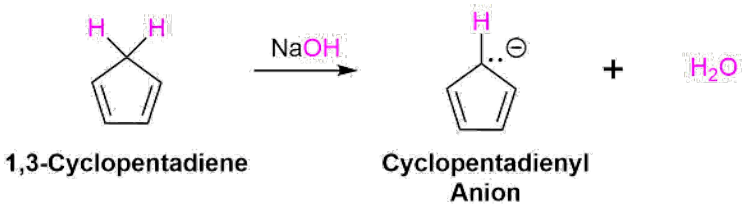
The lone pair electrons and the negative charge are conjugated about the entire ring making each carbon in the cyclopentadienyl anion equivalent with 1/5 the negative charge. The resonance hybrid can be shown by drawing a series of five resonance form. Also, the electrostatic potential map of the cyclopentadienyl anion show the negative charge, seen in red/yellow is distributed over the entire ring. The fact that the red/yellow color is held in the center of the ring indicates that the extra electrons of the ion are involved in the aromatic p-electron system.



The reason why the 4n +2 rule still works for a 5 p orbital ring system can be seen by looking the molecular orbital diagram of the cyclopentadienyl anion. As discussed in **Section 15.3**, the molecular orbital diagram of a 5 p orbital system is made up of 3 bonding MO's and 2 antibonding MO's. The 6 pi electrons gained by forming an anion is enough to completely fill the bonding MO's in the diagram giving the cyclopentadienyl anion aromaticity.



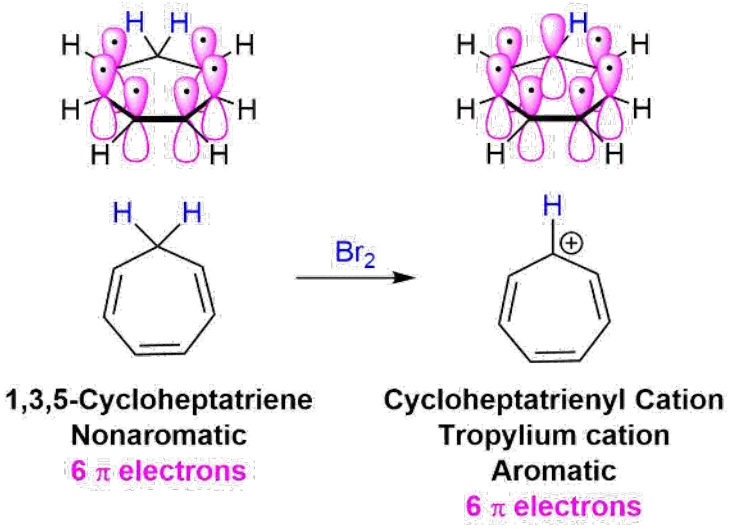
One of the effects of the aromaticity of the cyclopentadienyl anion is that the acidity of 1,3-cyclopentadiene is unusually strong. As previously discussed, stabilizing the conjugate base increases the acidity of the corresponding acid. In this case, the conjugate base of 1,3-cyclopentadiene, the cyclopentadienyl anion, is stabilized through aromaticity. This makes 1,3-cyclopentadiene one of the most acidic hydrocarbons known with a pK_a of 16. This is almost 10^{30} times more acidic than cyclopentane. Because of its acidity, cyclopentadiene can be deprotonated by moderately strong bases such as NaOH.



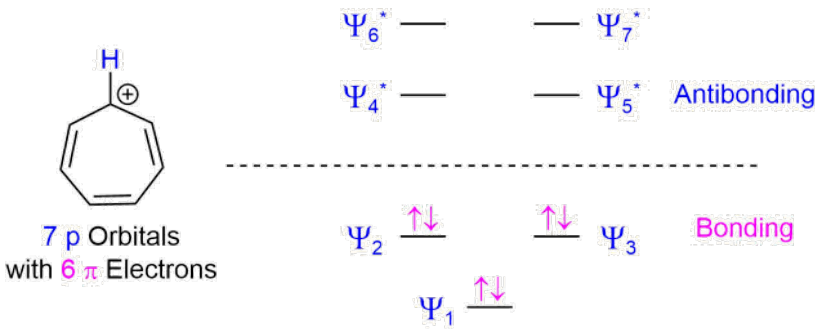
Tropylium ion

The molecule 1,3,5-cycloheptatriene has six pi electrons but is nonaromatic due the presence of an sp^3 hybridized -CH_2- group which prevents cyclic delocalization. When 1,3,5-cycloheptatriene is reacted with a reagent that can remove a hydride ion ($H:^-$), the 1,3,5-cycloheptatrienyl cation, which is commonly known as the tropylium cation, is formed with unexpected ease. Despite the presence of an electron deficient carbocation, the tropylium cation, is unusually stable and can be isolated as a salt.

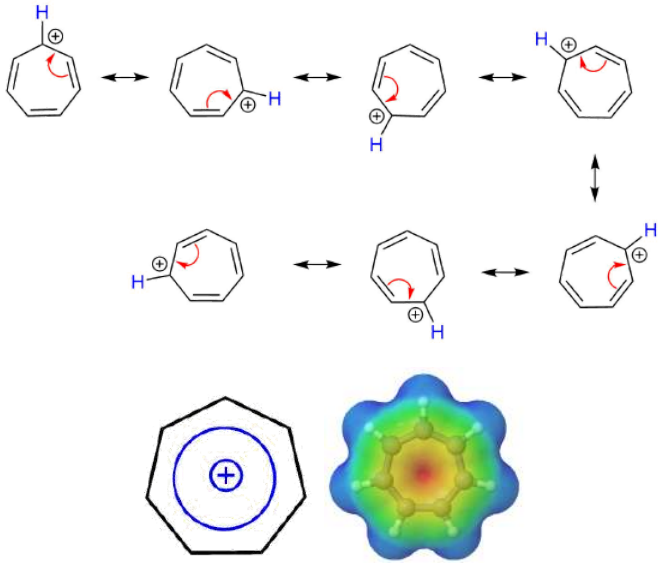
Removal of a hydride from the -CH_2- group in 1,3,5-cycloheptatriene creates an sp^2 hybridized carbocation with a vacant *p* orbital. The new *p* orbital allows for cyclic conjugation to occur among the seven *p* orbitals in the tropylium cation. The vacant *p* orbital does not change the pi electron count so the tropylium cation has 6 pi electrons which obeys the 4n + 2 rule for aromaticity.



The molecular orbital diagram for the 7 *p* orbitals in the tropylium cation has three bonding MO's and 4 antibonding MO's. The tropylium cation's 6 pi electrons completely fill the bonding molecular orbitals which is consistent with the tropylium cation being aromatic and therefore unusually stable.

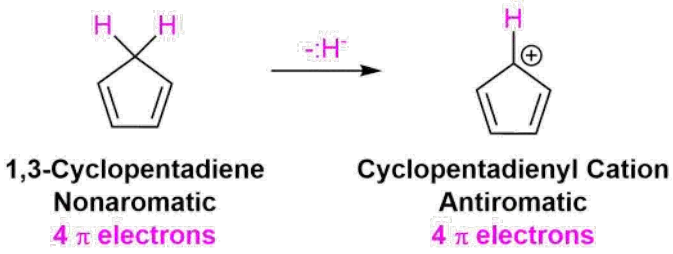


As predicted with aromaticity, the positive charge is completely conjugated about the entire ring giving each carbon +1/7 charge. The true resonance hybrid can be depicted by drawing a series of seven resonance form. Also, the electrostatic potential map of the tropylium cation shows the positive charge is evenly distributed over the entire ring. The equivalency of the carbons in the seven membered ring is experimentally supported by an ^1H NMR spectrum of the tropylium cation which contains one peak showing that all seven protons are equivalent.

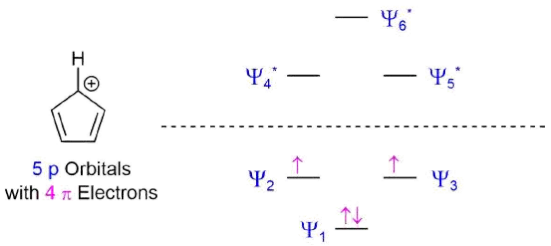


Antiaromatic Ions

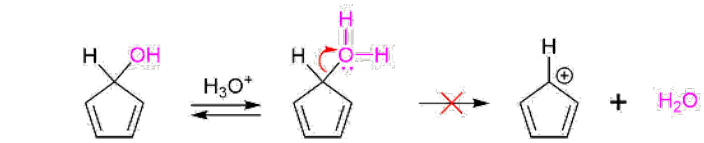
In a similar fashion, cyclically conjugated ions with 4n pi electrons can be predicted to be antiaromatic and therefore highly unstable. An excellent example is the cyclopentadienyl cation. Above, the cyclopentadienyl anion was shown to be aromatic, however, the formation of a carbocation produces a different result. Although the vacant *p* orbital provided by the carbocation allows for cyclic conjugation to occur the compound only has 4 pi electrons.



After placing these 4 pi electrons into the molecular orbital for a cyclic 5 *p* orbital species the bonding molecular orbitals remain unfilled. Two of the pi electrons are unpaired in degenerate molecular orbitals creating the highly unstable triplet state. As predicted by Hückel's Rule, the cyclopentadienyl cation has 4n pi electrons and should be anitaromatic and very unstable.



Although there is some discussion as to whether the cyclopentadienyl cation is truly antiaromatic, there is experimental evidence which shows it is usually unstable. In particular, the compound 2,4-cyclopentadien-1-ol is usually resistant to S_N1 reactions with acid halides. The carbocation intermediate created during the mechanism of this reaction would be expected to easily form due to the resonance stabilization provided by the two double bonds. Because the carbocation intermediate is antiaromatic it does not form so the reaction does not occur.



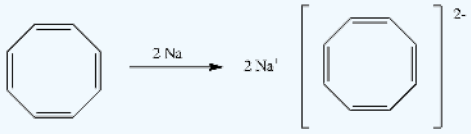
2,4-Cyclopentadien-1-ol

4 π Electrons
Antiaromatic
Not Formed

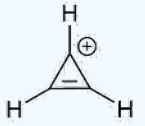
Exercise 2.8.1

1) Are all bonds equivalent cyclopentadienyl anion? How many lines (signals) would you expect to see in a H^1 and C^{13} NMR spectrum?

2) The following reaction occurs readily. Propose a reason why this occurs?



3) Is the cyclopropenium ion aromatic? Use the 4n + 2 rule and the MO diagram for a 3 p orbital ring system to explain your answer.



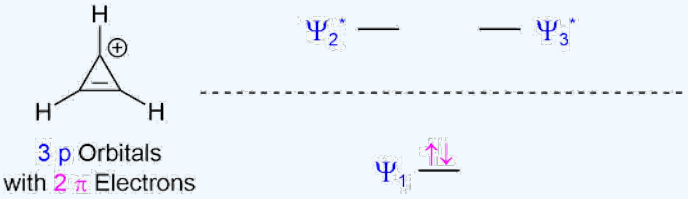
Cyclopropenium Ion

Answer

1) Due to the cyclopentadienyl anion being fully conjugated a protons and carbons are equivalent. Both the ^1H and ^{13}C NMR spectrum would only have one signal.

2) The addition of two electrons gives the ring system 10 pi electrons which follows the 4n+2 rule making the dianion aromatic. When looking at the MO diagram for an 8 p orbital ring system, 10 pi electrons completely fills the three bonding MO's and the two nonbonding MO's allowing for aromaticity.

3) The cyclopropenium ion has 2 pi electrons which follows the 4n + 2 rule when n = 0. When considering the molecular orbital diagram for a 3 p orbital ring system the is one bonding MO and two antibonding MO's. The two pi electrons completely fill the bonding MO allowing for aromaticity.



3 p Orbitals
with 2 π Electrons

Exercises

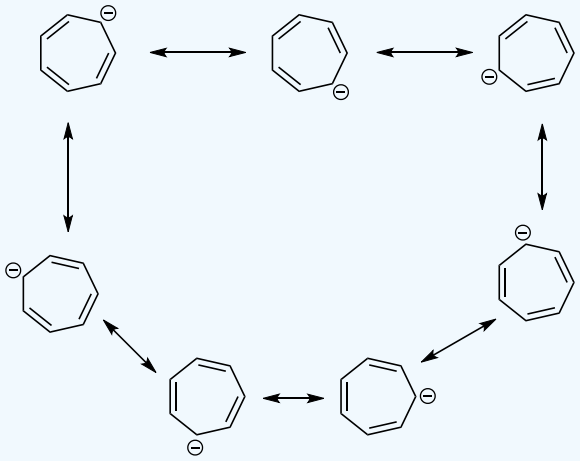
Exercise 2.8.2

Draw the resonance structures for cycloheptatriene anion. Are all bonds equivalent? How many lines (signals) would you see in a H^1 NMR? C^{13} NMR?

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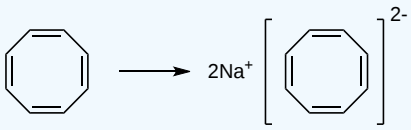
Answer

All protons and carbons are the same, so therefore each spectrum will only have one signal each in the proton NMR and carbon NMR.



? Exercise 2.8.3

The following reaction occurs readily. Propose a reason why this occurs?



Answer

The ring becomes aromatic with the addition of two electrons. Thereby obeying the 4n+2 rule.

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2.9: Aromatic Heterocycles - Pyridine and Pyrrole

Objectives

After completing this section, you should be able to

1. draw the structure of the common aromatic heterocycles pyridine and pyrrole.
2. use the Hückel $4n + 2$ rule to explain the aromaticity of each of pyridine and pyrrole.
3. draw a diagram to show the orbitals involved in forming the conjugated six-pi-electron systems present in aromatic heterocycles such as pyridine, pyrrole, etc.

Key Terms

Make certain that you can define, and use in context, the key terms below.

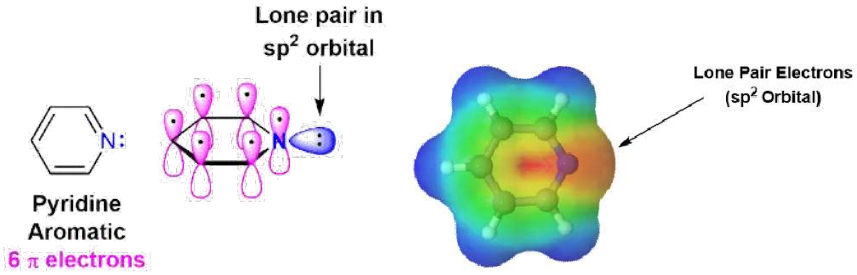
- carbocycles
- heterocycles

Aromatic Heterocycles

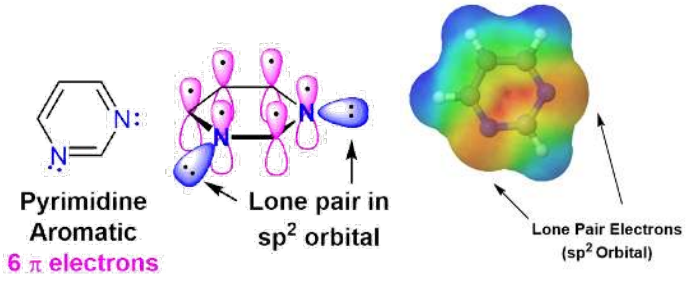
Many cyclic compounds have an element other than carbon present in the ring. Cyclic compounds that include one or more elements other than carbon are called a heterocycle. The most common heterocyclic compounds contain carbon along with nitrogen, oxygen, or sulfur. Because some heterocyclic compounds are aromatic, it is important to discuss how the inclusion of non-carbon atoms affects the determination of aromaticity.

Pyridine & Pyrimidine

Pyridine is an example of a six-membered aromatic heterocycle and has an electronic structure similar to benzene. In the bonding picture of pyridine the five carbons and single nitrogen are all sp^2 hybridized. All six of these atoms have a p orbital perpendicular to the plane of the ring and each contains one pi electron which allows the ring to be fully conjugated. This makes the pi electron count for pyridine 6 pi electrons. In much the same fashion as benzene, the 6 pi electrons follow the 4n + 2 rule and completely fill the bonding molecular orbitals which fulfills the electronic requirement for aromaticity. The lone pair electrons on pyridine's nitrogen are contained in a sp^2 orbital that lies in the same plane as the ring and does not overlap with the p orbitals of the ring. The lone pair electrons are not part of the aromatic system and do not affect the p electron count. Pyridine's electrostatic potential map shows that the lone pair electrons, shown in a yellow/red color, are locked onto the nitrogen and not distributed around the ring.

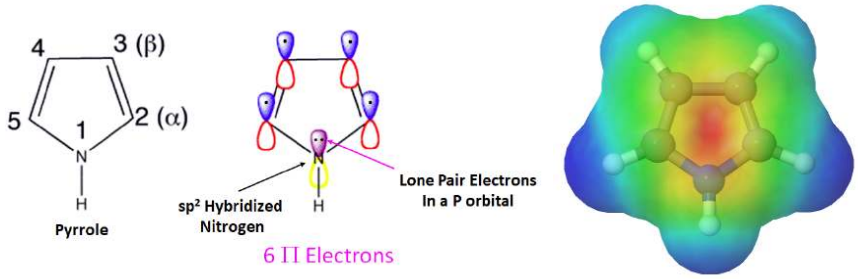


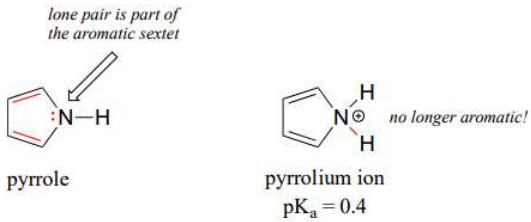
Pyrimidine is an another six-membered aromatic heterocycle that is analogous to pyridine. Pyrimidine has four carbons atoms and two nitrogen atoms that are sp^2 hybridized. Each of these atoms contributes a p orbital and a pi election allowing pyrimidine to be fully conjugated and aromatic. Both of the nitrogens in pyrimidine have lone pair electrons contained in a sp^2 orbitals and are not involved in the aromatic system. An electrostatic potential map of pyrimidine shows that neither set of lone pair electrons is distributed around the ring.



Pyrrole

Pyrrole is a five-membered heterocyclic ring which has 5 p orbitals and six pi electrons contributing to its aromaticity. Each carbon in pyrrole contributes one p orbital and pi electron. The nitrogen in pyrrole contributes two pi electrons by becoming sp^2 hybridized and placing its lone pair electrons into a p orbital. The electrostatic potential map of pyrrole show the nitrogen's lone pair electrons are distributed in the ring. Because the nitrogen lone pair *is* part of the aromatic sextet the electrons are very stable and are much less available for bonding to a proton (and if they *do* pick up a proton, the molecule loses aromaticity). Pyrrole is a very weak base: the conjugate acid, the pyrrolium ion, is a strong acid with a pK_a of 0.4.

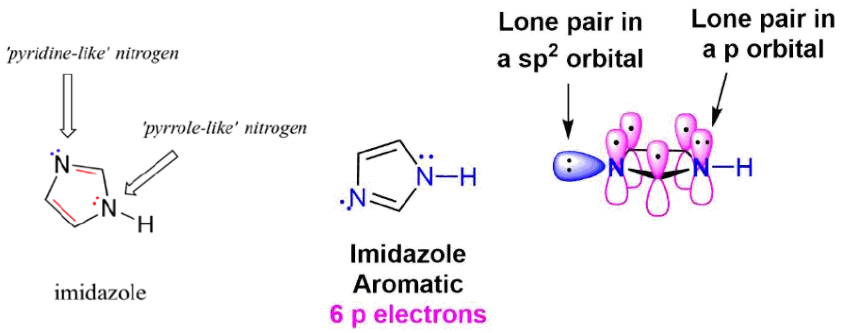


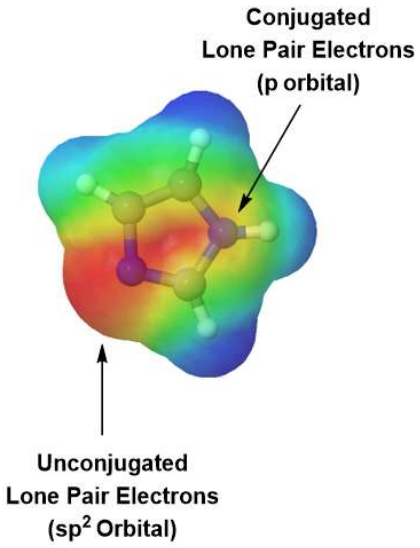


Imidazole

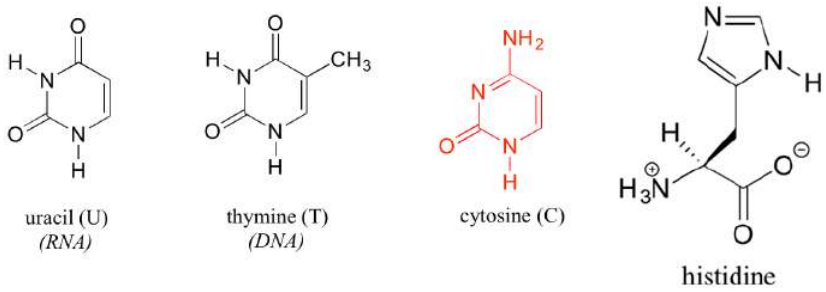
Imidazole is another five-membered heterocyclic ring which has 6 pi electrons and is aromatic. Both of the nitrogen atoms are sp^2 hybridized. One nitrogen is pyridine-like because it is part of a double bond and adds one pi electron to the aromatic pi ring. The other nitrogen is not part of a double bond making it pyrrole-like allowing it to contribute 2 pi electrons from it lone pair electrons. When looking at the electrostatic potential map of imidazole, the lone pair electrons on the pyrrole-like nitrogen are distributed around the ring while the lone pair electrons on the pyridine-like nitrogen are non-conjugated and locked into place.

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Pyrimidine and imidazole rings are particularly important in biological chemistry. Pyrimidine, for instance, is the parent ring system in cytosine, thymine, and uracil, three of the five heterocyclic amine bases found in nucleic acids. An aromatic imidazole ring is present in histidine, one of the amino acids found in proteins.



? Worked Example 2.9.1

Determine if furan is aromatic. Draw an orbital diagram to support your answer.

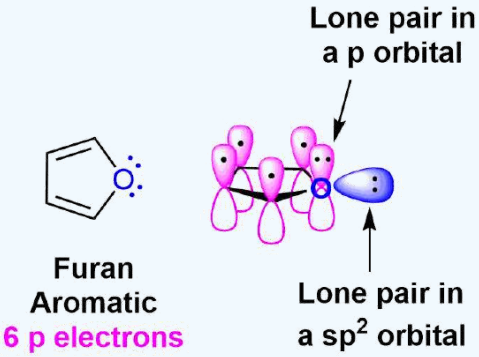


Furan

Answer

For a molecule to be aromatic it must: Be cyclic, be planar, be fully conjugated, and have 4n+2 π electrons.

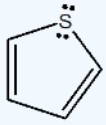
Furan is obviously cyclic and can be assumed to be planar due to the constrains of having a five membered ring with two double bonds. To be fully conjugated each atom in the ring must have a p orbital. Although the oxygen has 4 electron groups and appears to be sp^3 hybridized, it will become sp^2 hybridized to gain the stability of conjugation. Becoming sp^2 hybridized allows the oxygen atom to put a set of lone pair electrons into a p orbital allowing it to be part of the cyclic conjugation. These two pi electrons along with the 4 pi electrons provided by the two double bonds gives furan 6 pi electrons total. This follows the 4n + 2 rule making furan aromatic.



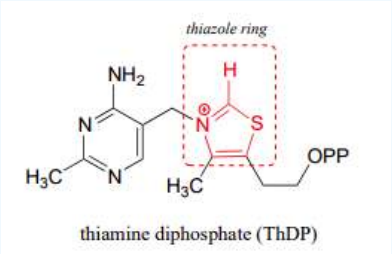
Exercises

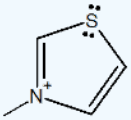
? Exercise 2.9.1

1) Draw the orbitals of thiophene to show that it is aromatic.



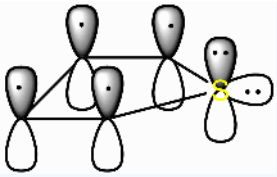
2) The thiazolium ring is a five-membered sulfur containing aromatic ring system which is found in biological systems, such as thiamine diphosphate (ThDP). Describe how thiazolium ring is aromatic.



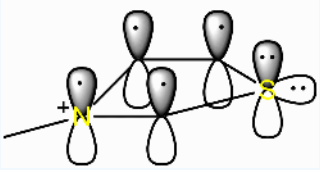


Answer

1) This drawing shows thiophene has 6 electrons in the pi-orbital.



2) Similar to the last question, the drawing shows that there is only 6 electrons in the pi-system.



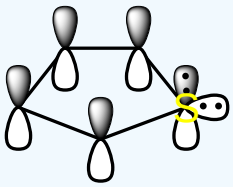
Exercise 2.9.2

Draw the orbitals of thiophene to show that is aromatic.



Answer

This drawing shows it has 6 electrons in the pi-orbital.



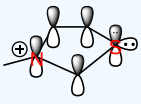
Exercise 2.9.3

The following ring is called a thiazolium ring. Describe how it is aromatic.



Answer

Similar to the last question, the drawing shows that there is only 6 electrons in the pi-system.



2.9: Aromatic Heterocycles - Pyridine and Pyrrole is shared under a CC BY-SA 4.0 license and was authored, remixed, and/or curated by Steven Farmer, Dietmar Kennepohl, Tim Soderberg, William Reusch, James Kabrhel, & James Kabrhel.

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2.10: Polycyclic Aromatic Compounds

Objectives

After completing this section, you should be able to draw the resonance contributors for polycyclic aromatic compounds, such as naphthalene, anthracene, etc.

Key Terms

Make certain that you can define, and use in context, the key term below.

- polycyclic aromatic compounds

Study Notes

As their name indicates, *polycyclic aromatic hydrocarbons* are aromatic hydrocarbons which contain more than one benzenoid (i.e., benzene-like) ring. This section deals only with those compounds in which the benzenoid rings are fused together; in other words, compounds in which at least one carbon-carbon bond is common to two aromatic rings. Another type of polycyclic aromatic hydrocarbon contains two or more benzenoid rings joined by a carbon-carbon single bond. The simplest compound of this type is biphenyl, the compound from which PCBs (polychlorinated biphenyls) are derived.

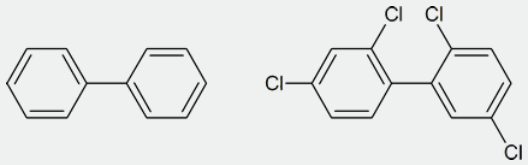


Figure 15.3: Structures of biphenyl and a typical PCB

Polycyclic Aromatic Compounds

Hückel's 4n +2 rule for aromaticity does not only apply to mono-cyclic compounds. Benzene rings may be joined together (fused) to give larger polycyclic aromatic compounds. A few examples are drawn below, together with the approved numbering scheme for substituted derivatives. The peripheral carbon atoms (numbered in all but the last three examples) are all bonded to hydrogen atoms. Unlike benzene, all the C-C bond lengths in these fused ring aromatics are not the same, and there is some localization of the pi-electrons. The six benzene rings in coronene are fused in a planar ring; whereas the six rings in hexahelicene are not joined in a larger ring, but assume a helical turn, due to the crowding together of the terminal ring atoms (in the structure below, note that the top right and center right rings are not attached to one another). This helical configuration renders the hexahelicene molecule chiral, and it has been resolved into stable enantiomers.

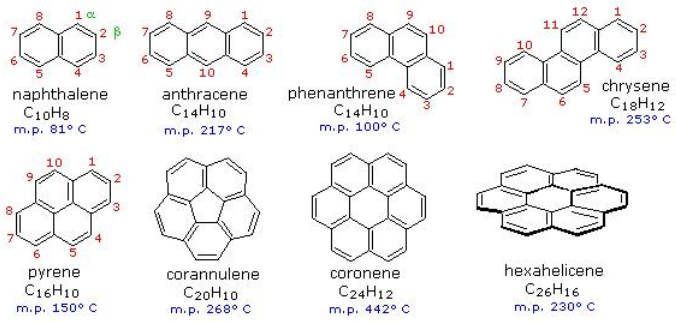
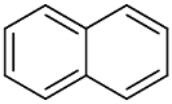
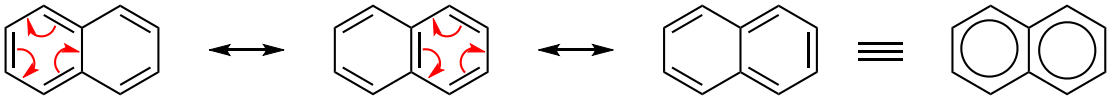


***Figure 2**: Examples of Polycyclic Aromatic Hydrocarbons (PAHs).*

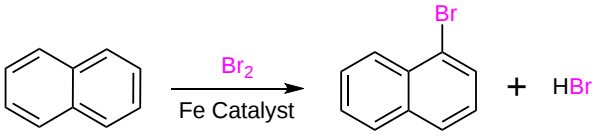
Probably the most well know polycyclic aromatic compound which only contains carbon is naphthalene ($C_{10}H_8$). Naphthalene shares many of the same characteristic as benzene. Naphthalene is cyclic and known to be flat. Each carbon in naphthalene is sp^2 hybridized so it is completely conjugated. The true structure of naphthalene is a combination of three resonance hybrids.



Naphthalene

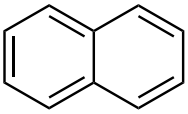


Heat of hydrogenation experiments with naphthalene shows an unusual "aromatic" stabilization energy. Also, naphthalene prefers to react with electrophiles to give substitution products rather than the typical double bond addition products.

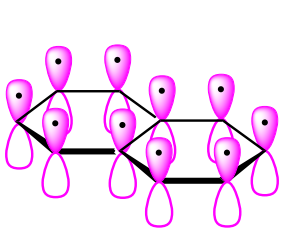


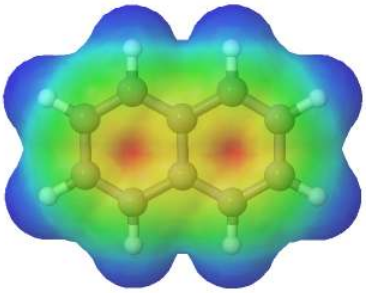
Naphthalene **1-Bromonaphthalene Substitution Product**

Every carbon in naphthalene is sp^2 hybridized so there is conjugated p orbital overlap over the entire ring system. The electrostatic potential map shows that pi electrons in naphthalene are evenly distributed making each carbon equivalent.

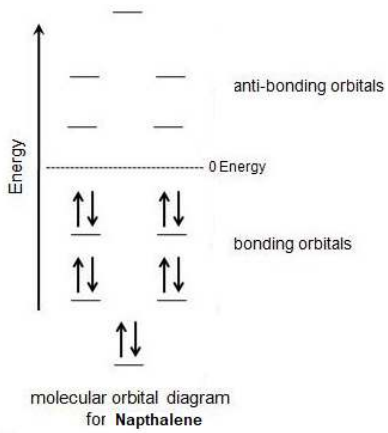


Naphthalene
Aromatic
10 p electrons





Lastly, naphthalene has 10 pi electrons which fulfills Hückel's rule. The importance of the 4n + 2 rule can be seen when considering the molecular orbital diagram of naphthalene. Naphthalene has 10 p orbitals which is 4 more than benzene. In the molecular orbital diagram of naphthalene, the 4 additional p orbitals become 2 bonding orbitals and two anti-bonding orbitals. The two additional bonding orbitals require 4 additional pi electrons to be filled so naphthalene needs 10 pi electrons in total to fill all of the bonding molecular orbitals.



molecular orbital diagram for **Napthalene**

Polycyclic Aromatic Heterocycles

There is a wide variety of polycyclic aromatic heterocycles, many of which contain nitrogen, oxygen, or sulfur. Some of the biologically important structures, are the nitrogen containing polycyclic aromatic heterocycles indole, quinoline, isoquinoline, and purine which are all polycyclic aromatic heterocycles commonly found in nature. Notice that these compound all have 10 pi electrons.

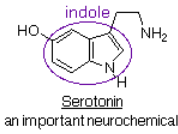

Indole

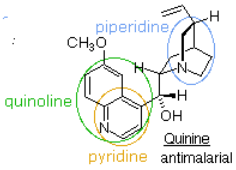

Quinoline

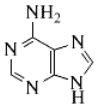

Isoquinoline

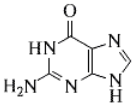

Purine

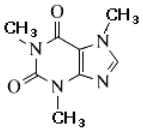
Indole, quinoline, and isoquinoline all contain a hetrocyclic ring fused to benzene. Purine is made up to two heterocyclic rings, imidazole and pyrimidine, fused together. Quinoline is found in the antimalarial drug quinine. Indole is found in the neurotransmitter serotonin. The purine ring structure is found in adenine and guanine, two important parts of DNA and in the stimulant caffeine.






adenine

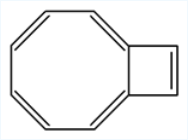

guanine


caffeine

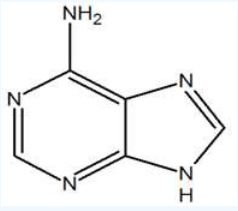
Exercises

? Exercise 2.10.1

1) The following molecule is an isomer of naphthalene. Is it aromatic? Draw a resonance structure for it.



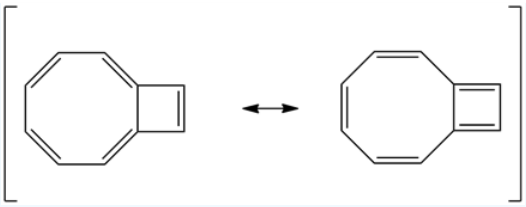
2) The following molecule is adenine. It has a purine core. Of the nitrogen in the core, how many electrons are donated into the pi system?



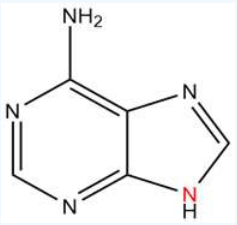
Answer

1) It has 10 pi electrons which follows the 4n+2 rule making it aromatic.

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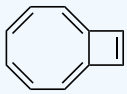


2) There is only one nitrogen of the core that contributes a set of lone pair electrons as 2 pi electrons (in red). All of the other nitrogens are sp2 hybrized and contribute 1 pi electron each. In total, the core is aromatic with 10 electrons in the pi-system.



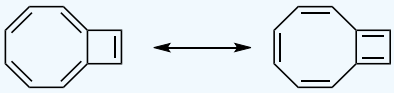
Exercise 2.10.2

This is an isomer of naphthalene. Is it aromatic? Draw a resonance structure for it.



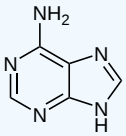
Answer

Yes, it is aromatic. 4n+2 pi-electrons.



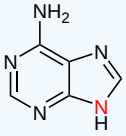
Exercise 2.10.3

The following molecule is adenine. It has a purine core. Of the nitrogen in the core, how many electrons are donated into the pi system?



Answer

There is only one nitrogen of the core that contributes to the pi-system (in red). With this one lone pair the core is aromatic with 10 electrons in the pi-system.



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CHAPTER OVERVIEW

3: Organic Compounds- Alkanes and Their Stereochemistry

Learning Objectives

After you have completed Chapter 3, you should be able to

1. fulfill the detailed objectives listed under each section.
2. identify some of the commonest functional groups.
3. write the structures and names of the first ten straight-chain alkanes.
4. recognize and name the simple alkyl substituents, and give the systematic names for branched-chain alkanes.
5. briefly describe some of the processes used during the refining of petroleum.
6. briefly describe the physical properties of alkanes.
7. draw a number of possible conformations of some simple alkanes and alkane-like compounds, and represent the energies of such conformations on energy versus rotation diagrams.
8. define, and use in context, the key terms introduced in this chapter.

This chapter begins with an introduction to the concept of the functional group, a concept that facilitates the systematic study of organic chemistry. Next, we introduce the fundamentals of organic nomenclature (i.e., the naming of organic chemicals) through examination of the alkane family of compounds. We then discuss, briefly, the occurrence and properties of alkanes, and end with a description of *cis-trans* isomerism in cycloalkanes.

3.1: Gasoline - A Deeper Look
3.2: Properties of Alkanes
3.3: Alkanes and Alkane Isomers
3.4: Alkyl Groups
3.5: Naming Alkanes
3.6: Conformations of Ethane
3.7: Conformations of Other Alkanes

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3.1: Gasoline - A Deeper Look

Objectives

After completing this section, you should be able to

1. describe the general nature of petroleum deposits, and recognize why petroleum is such an important source of organic compounds.
2. explain, in general terms, the processes involved in the refining of petroleum.
3. define the octane number of a fuel, and relate octane number to chemical structure.

Key Terms

Make certain that you can define, and use in context, the key terms below.

- catalytic cracking
- catalytic reforming
- fractional distillation
- octane number (octane rating)

Study Notes

The refining of petroleum into usable fractions is a very important industrial process. In the laboratory component of this course, you will have the opportunity to compare this industrial process to the distillation procedure as it is performed in the student laboratory.

Petroleum

The petroleum that is pumped out of the ground is a complex mixture of several thousand organic compounds, including straight-chain alkanes, cycloalkanes, alkenes, and aromatic hydrocarbons with four to several hundred carbon atoms. The identities and relative abundance of the components vary depending on the source - Texas crude oil is somewhat different from Saudi Arabian crude oil. In fact, the analysis of petroleum from different deposits can produce a “fingerprint” of each, which is useful in tracking down the sources of spilled crude oil. For example, Texas crude oil is “sweet,” meaning that it contains a small amount of sulfur-containing molecules, whereas Saudi Arabian crude oil is “sour,” meaning that it contains a relatively large amount of sulfur-containing molecules.

Gasoline

Petroleum is converted to useful products such as gasoline in three steps: distillation, cracking, and reforming. Recall from Chapter 1 that distillation separates compounds on the basis of their relative volatility, which is usually inversely proportional to their boiling points. Part (a) in Figure 3.8.1 shows a cutaway drawing of a column used in the petroleum industry for separating the components of crude oil. The petroleum is heated to approximately 400°C (750°F) and becomes a mixture of liquid and vapor. This mixture, called the feedstock, is introduced into the refining tower. The most volatile components (those with the lowest boiling points) condense at the top of the column where it is cooler, while the less volatile components condense nearer the bottom. Some materials are so nonvolatile that they collect at the bottom without evaporating at all. Thus the composition of the liquid condensing at each level is different. These different fractions, each of which usually consists of a mixture of compounds with similar numbers of carbon atoms, are drawn off separately. Part (b) in Figure 3.8.1 shows the typical fractions collected at refineries, the number of carbon atoms they contain, their boiling points, and their ultimate uses. These products range from gases used in natural and bottled gas to liquids used in fuels and lubricants to gummy solids used as tar on roads and roofs.

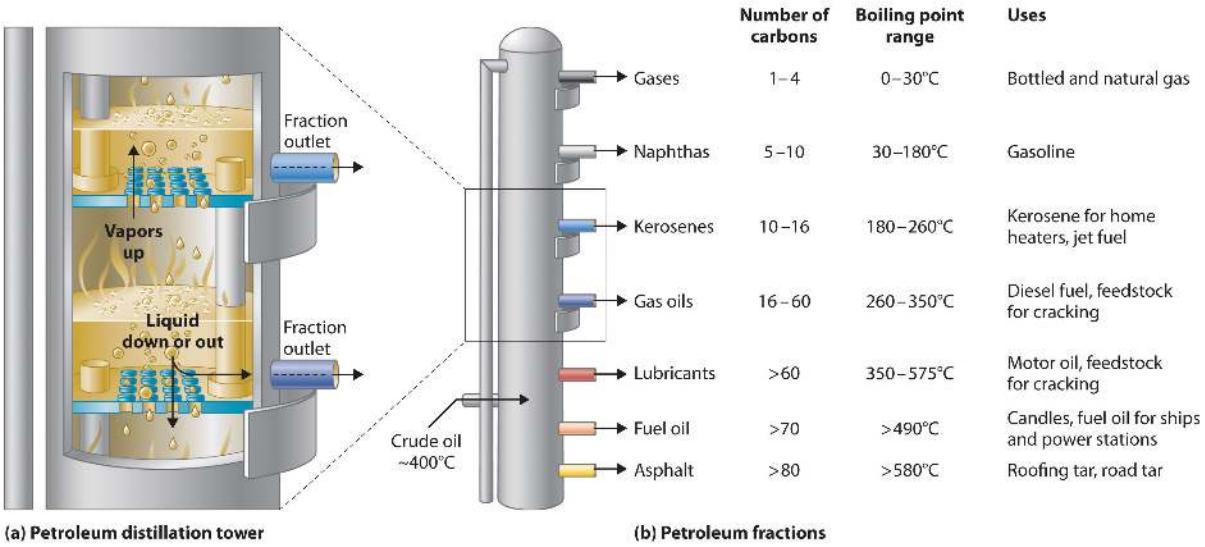


Figure 3.8.1: The Distillation of Petroleum. (a) This is a diagram of a distillation column used for separating petroleum fractions. (b) Petroleum fractions condense at different temperatures, depending on the number of carbon atoms in the molecules, and are drawn off from the column. The most volatile components (those with the lowest boiling points) condense at the top of the column, and the least volatile (those with the highest boiling points) condense at the bottom. (CC BY-NC-SA; anonymous)

The economics of petroleum refining are complex. For example, the market demand for kerosene and lubricants is much lower than the demand for gasoline, yet all three fractions are obtained from the distillation column in comparable amounts. Furthermore, most gasolines and jet fuels are blends with very carefully controlled compositions that cannot vary as their original feedstocks did. To make petroleum refining more profitable, the less volatile, lower-value fractions are converted to more volatile, higher-value mixtures that have carefully controlled formulas. The first process used to accomplish this transformation is cracking, in which the larger and heavier hydrocarbons in the kerosene and higher-boiling-point fractions are heated to temperatures as high as 900°C. High-temperature reactions cause the carbon–carbon bonds to break, which converts the compounds to lighter molecules similar to those in the gasoline fraction. Thus in cracking, a straight-chain alkane with a number of carbon atoms corresponding to the kerosene fraction is converted to a mixture of hydrocarbons with a number of carbon atoms corresponding to the lighter gasoline fraction. The second process used to increase the amount of valuable products is called reforming; it is the chemical conversion of straight-chain alkanes to either branched-chain alkanes or mixtures of aromatic hydrocarbons. Using metals such as platinum brings about the necessary chemical reactions. The mixtures of products obtained from cracking and reforming are separated by fractional distillation.

Octane Ratings

The quality of a fuel is indicated by its octane rating, which is a measure of its ability to burn in a combustion engine without knocking or pinging. Knocking and pinging signal premature combustion (Figure 3.8.2), which can be caused either by an engine malfunction or by a fuel that burns too fast. In either case, the gasoline-air mixture detonates at the wrong point in the engine cycle, which reduces the power output and can damage valves, pistons, bearings, and other engine components. The various gasoline formulations are designed to provide the mix of hydrocarbons least likely to cause knocking or pinging in a given type of engine performing at a particular level.

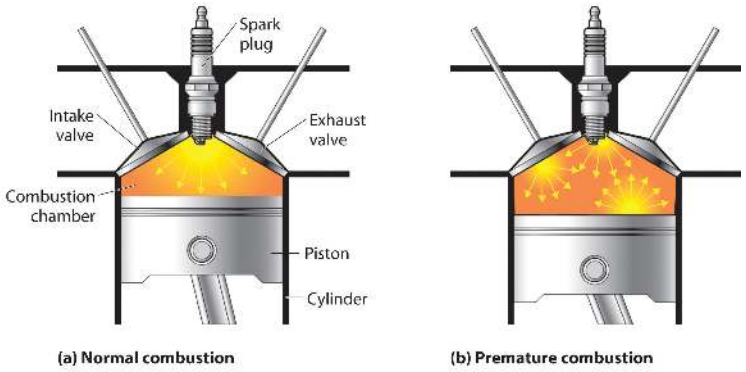


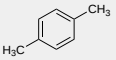
Figure 3.8.2: The Burning of Gasoline in an Internal Combustion Engine. (a) Normally, fuel is ignited by the spark plug, and combustion spreads uniformly outward. (b) Gasoline with an octane rating that is too low for the engine can ignite prematurely, resulting in uneven burning that causes knocking and pinging. (CC BY-NC-SA; anonymous)

The octane scale was established in 1927 using a standard test engine and two pure compounds: n-heptane and isooctane (2,2,4-trimethylpentane). n-Heptane, which causes a great deal of knocking on combustion, was assigned an octane rating of 0, whereas isooctane, a very smooth-burning fuel, was assigned an octane rating of 100. Chemists assign octane ratings to different blends of gasoline by burning a sample of each in a test engine and comparing the observed knocking with the amount of knocking caused by specific mixtures of n-heptane and isooctane. For example, the octane rating of a blend of 89% isooctane and 11% n-heptane is simply the average of the octane ratings of the components weighted by the relative amounts of each in the blend. Converting percentages to decimals, we obtain the octane rating of the mixture:

$$0.89(100) + 0.11(0) = 89 \tag{3.1.1}$$

As shown in Table **3.1.1**, many compounds that are now available have octane ratings greater than 100, which means they are better fuels than pure isooctane. In addition, anti-knock agents, also called octane enhancers, have been developed. One of the most widely used for many years was **tetraethyl lead** [$(C_2H_5)_4Pb$], which at approximately 3 g/gal gives a 10–15-point increase in octane rating. Since 1975, however, lead compounds have been phased out as gasoline additives because they are highly toxic. Other enhancers, such as methyl t-butyl ether (MTBE), have been developed to take their place. They combine a high octane rating with minimal corrosion to engine and fuel system parts. Unfortunately, when gasoline containing MTBE leaks from underground storage tanks, the result has been contamination of the groundwater in some locations, resulting in limitations or outright bans on the use of MTBE in certain areas. As a result, the use of alternative octane enhancers such as ethanol, which can be obtained from renewable resources such as corn, sugar cane, and, eventually, corn stalks and grasses, is increasing.

Table **3.1.1**: The Octane Ratings of Some Hydrocarbons and Common Additives

Name	Condensed Structural Formula	Octane Rating	Name	Condensed Structural Formula	Octane Rating
n-heptane	$CH_3CH_2CH_2CH_2CH_2CH_2CH_3$	0	*o*-xylene	skeletal structure of o-xylene.cdxml	107
n-hexane	$CH_3CH_2CH_2CH_2CH_2CH_3$	25	ethanol	CH_3CH_2OH	108
n-pentane	$CH_3CH_2CH_2CH_2CH_3$	62	*t*-butyl alcohol	$(CH_3)_3COH$	113
isooctane	$(CH_3)_3CCH_2CH(CH_3)_2$	100	*p*-xylene		116
benzene		106	methyl *t*-butyl ether	$H_3COC(CH_3)_3$	116
methanol	CH_3OH	107	toluene		118

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3.2: Properties of Alkanes

Objectives

After completing this section, you should be able to

1. arrange a number of given straight-chain alkanes in order of increasing or decreasing boiling point or melting point.
2. arrange a series of isomeric alkanes in order of increasing or decreasing boiling point.
3. explain the difference in boiling points between a given number of alkanes.

Key Terms

Make certain that you can define, and use in context, the key term below.

- van der Waals force (also known as London Dispersion force)

Alkanes are not very reactive and have little biological activity; all alkanes are colorless and odorless non-polar compounds. The relative weak London dispersion forces of alkanes result in gaseous substances for short carbon chains, volatile liquids with densities around 0.7 g/mL for moderate carbon chains, and solids for long carbon chains. For molecules with the same functional groups, there is a direct relationship between the size and shape of molecules and the strength of the intermolecular forces (IMFs) causing the differences in the physical states.

Boiling Points

Table **3.2.1** describes some of the properties of some straight-chain alkanes. There is not a significant electronegativity difference between carbon and hydrogen, thus, there is not any significant bond polarity. The molecules themselves also have very little polarity. A totally symmetrical molecule like methane is completely non-polar, meaning that the only attractions between one molecule and its neighbors will be Van der Waals dispersion forces. These forces will be very small for a molecule like methane but will increase as the molecules get bigger. Therefore, the boiling points of the alkanes increase with molecular size.

For isomers, the more branched the chain, the lower the boiling point tends to be. Van der Waals dispersion forces are smaller for shorter molecules and only operate over very short distances between one molecule and its neighbors. It is more difficult for short, fat molecules (with lots of branching) to lie as close together as long, thin molecules.

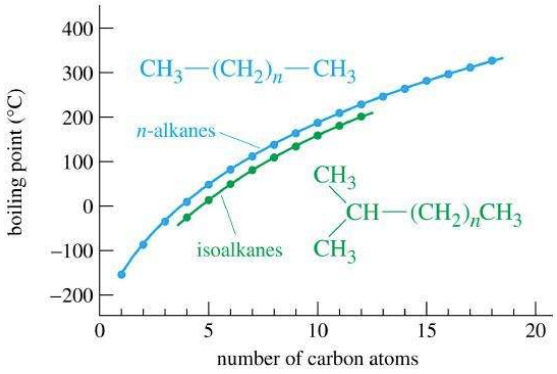
The boiling points shown are for the "straight chain" isomers of which there is more than one. The first four alkanes are gases at room temperature, and solids do not begin to appear until about $C_{17}H_{36}$, but this is imprecise because different isomers typically have different melting and boiling points.

Table **3.2.1**: Physical Properties of Some Alkanes

Molecular Name	Formula	Melting Point (°C)	Boiling Point (°C)	Density (20°C)*	Physical State (at 20°C)
methane	CH_4	–182	–164	0.668 g/L	gas
ethane	C_2H_6	–183	–89	1.265 g/L	gas
propane	C_3H_8	–190	–42	1.867 g/L	gas
butane	C_4H_{10}	–138	–1	2.493 g/L	gas
pentane	C_5H_{12}	–130	36	0.626 g/mL	liquid
hexane	C_6H_{14}	–95	69	0.659 g/mL	liquid
octane	C_8H_{18}	–57	125	0.703 g/mL	liquid
decane	$C_{10}H_{22}$	–30	174	0.730 g mL	liquid

*Note the change in units going from gases (grams per liter) to liquids (grams per milliliter). Gas densities are at 1 atm pressure.

The boiling points for the "straight chain" isomers and isoalkanes isomers are shown to demonstrate that branching decreases the surfaces area, weakens the IMFs, and lowers the boiling point.



Example 3.2.1: Boiling Points of Alkanes

For example, the boiling points of the three isomers of C_5H_{12} are:

- pentane: 309.2 K
- 2-methylbutane: 301.0 K
- 2,2-dimethylpropane: 282.6 K

The slightly higher boiling points for the cycloalkanes are presumably because the molecules can get closer together because the ring structure makes them better able!

Exercise 3.2.1

For each of the following pairs of compounds, select the substance which you expect to have the higher boiling point:

a. octane and nonane.
b. octane and 2,2,3,3-tetramethylbutane.

Solution

a. nonane, since it has more atoms it will have greater IMF
b. octane, since it is not branched, the molecules can pack closer together increasing IMF

Solubility

Alkanes are virtually insoluble in water, but dissolve in organic solvents. However, liquid alkanes are good solvents for many other non-ionic organic compounds.

Solubility in Water

When a molecular substance dissolves in water, the following must occur:

- break the intermolecular forces within the substance. In the case of the alkanes, these are the Van der Waals dispersion forces.
- break the intermolecular forces in the water so that the substance can fit between the water molecules. In water, the primary intermolecular attractions are hydrogen bonds.

Breaking either of these attractions requires energy, although the amount of energy to break the Van der Waals dispersion forces in something like methane is relatively negligible; this is not true of the hydrogen bonds in water.

As something of a simplification, a substance will dissolve if there is enough energy released when new bonds are made between the substance and the water to compensate for what is used in breaking the original attractions. The only new attractions between the alkane and the water molecules are Van der Waals forces. These forces do not release a sufficient amount of energy to compensate for the energy required to break the hydrogen bonds in water. The alkane does not dissolve.

> This is a simplification because entropic effects are important when things dissolve.

Solubility in organic solvents

In most organic solvents, the primary forces of attraction between the solvent molecules are Van der Waals. Therefore, when an alkane dissolves in an organic solvent, the Van der Waals forces are broken and are replaced by new Van der Waals forces. The two processes more or less cancel each other out energetically; thus, there is no barrier to solubility.

? Exercise 3.2.1

For each of the following pairs of compounds, select the substance you expect to have the higher boiling point.

a. octane and nonane.
b. octane and 2,2,3,3-tetramethylbutane.

Answer

Nonane will have a higher boiling point than octane, because it has a longer carbon chain than octane. Octane will have a higher boiling point than 2,2,3,3-tetramethylbutane, because it branches less than 2,2,3,3-tetramethylbutane, and therefore has a larger “surface area” and more van der Waals forces.

Note: The actual boiling points are:

- nonane, 150.8°C
- octane, 125.7°C
- 2,2,3,3-tetramethylbutane, 106.5°C

Reactions of Alkanes

Alkanes undergo very few reactions. There are two important reactions that are still possible, combustion and halogenation. The halogenation reaction is very important in organic chemistry because it opens a gateway to further chemical reactions.

Combustion

Complete combustion (given sufficient oxygen) of any hydrocarbon produces carbon dioxide, water, and a significant amount of heat. Due to the exothermic nature of these combustion reactions, alkanes are commonly used as a fuel source (for example: propane for outdoor grills, butane for lighters). The hydrocarbons become harder to ignite as the molecules get bigger. This is because the larger molecules don't vaporize as easily. If the liquid is not very volatile, only those molecules on the surface can react

with the oxygen. Larger molecules have greater Van der Waals attractions which makes it more difficult for them to break away from their neighbors and become a gas. An example combustion reaction is shown for propane:

$$C_3H_8 + O_2 \longrightarrow 3\,CO_2 + 4\,H_2O + 2044\,kJ/mol$$

Halogenation

Halogenation is the replacement of one or more hydrogen atoms in an organic compound by a halogen (fluorine, chlorine, bromine or iodine). Unlike the complex transformations of combustion, the halogenation of an alkane appears to be a simple **substitution reaction** in which a C-H bond is broken and a new C-X bond is formed.

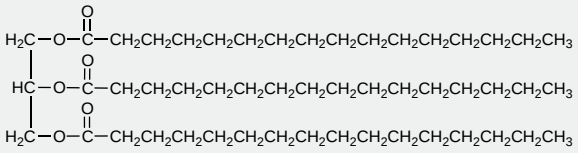
Since only two covalent bonds are broken (C-H & Cl-Cl) and two covalent bonds are formed (C-Cl & H-Cl), this reaction seems to be an ideal case for mechanistic investigation and speculation. However, one complication is that all the hydrogen atoms of an alkane may undergo substitution, resulting in a mixture of products, as shown in the following unbalanced equation. The relative amounts of the various products depend on the proportion of the two reactants used. In the case of methane, a large excess of the hydrocarbon favors formation of methyl chloride as the chief product; whereas, an excess of chlorine favors formation of chloroform and carbon tetrachloride.

$$CH_4 + Cl_2 \rightarrow CH_3Cl + CH_2Cl + CHCl_3 + CCl_4 + HCl$$

Looking Closer: An Alkane Basis for Properties of Other Compounds

An understanding of the physical properties of alkanes is important since petroleum and natural gas and the many products derived from them—gasoline, bottled gas, solvents, plastics, and more—are composed primarily of alkanes. This understanding is also vital because it is the basis for describing the properties of other organic and biological compound families. For example, large portions of the structures of lipids consist of nonpolar alkyl groups. Lipids include the dietary fats and fat like compounds called phospholipids and sphingolipids that serve as structural components of living tissues. These compounds have both polar and nonpolar groups, enabling them to bridge the gap between water-soluble and water-insoluble phases. This characteristic is essential for the selective permeability of cell membranes.

(a)



(b)

Tripalmitin (a), a typical fat molecule, has long hydrocarbon chains typical of most lipids. Compare these chains to hexadecane (b), an alkane with 16 carbon atoms.

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3.3: Alkanes and Alkane Isomers

Objectives

After completing this section, you should be able to

1. draw the Kekulé structure, condensed structure and shorthand structure of each of the first ten straight-chain alkanes.
2. name each of the first ten straight-chain alkanes, given its molecular formula, Kekulé structure, condensed structure or shorthand structure.
3. explain the difference in structure between a straight- and a branched-chain alkane, and illustrate the difference using a suitable example.
4. explain why the number of possible isomers for a given molecular formula increases as the number of carbon atoms increases.
5. draw all the possible isomers that correspond to a given molecular formula of the type $C_n H_{2n+2}$, where *n* is ≤ 7.

Key Terms

Make certain that you can define, and use in context, the key terms below.

- branched-chain alkane
- constitutional or structural isomer
- homologous series
- isomer
- saturated hydrocarbon
- straight-chain alkane (or normal alkane)

Study Notes

A series of compounds in which successive members differ from one another by a CH_2 unit is called a homologous series. Thus, the series CH_4, C_2H_6, C_3H_8 . . . C_nH_{2n+2}, is an example of a homologous series.

It is important that you commit to memory the names of the first 10 straight-chain alkanes (i.e., from CH_4 to $C_{10}H_{22}$). You will use these names repeatedly when you begin to learn how to derive the systematic names of a large variety of organic compounds. You need not remember the number of isomers possible for alkanes containing more than seven carbon atoms. Such information is available in reference books when it is needed. When drawing isomers, be careful not to deceive yourself into thinking that you can draw more isomers than you are supposed to be able to. Remember that it is possible to draw each isomer in several different ways and you may inadvertently count the same isomer more than once.

Alkanes are organic compounds that consist entirely of single-bonded carbon and hydrogen atoms and lack any other functional groups. Alkanes are often called saturated hydrocarbons because they have the maximum possible number of hydrogens per carbon. In Section 1.7, thealkane molecule, ethane, was shown to contain a C-C sigma bond. By adding more C-C sigma bond larger and more complexed alkanes can be formed. Methane (CH_4), ethane (C_2H_6), and propane (C_3H_8) are the beginning of a series of compounds in which any two members in a sequence differ by one carbon atom and two hydrogen atoms—namely, a CH_2 unit. Any family of compounds in which adjacent members differ from each other by a definite factor (here a CH_2 group) is called a homologous series. The members of such a series, called *homologs*, have properties that vary in a regular and predictable manner.

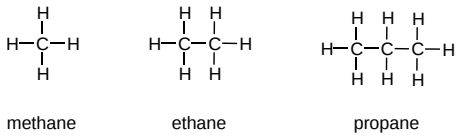


Figure 25.3.1 : The Three Simplest Alkanes

Methane (CH_4), ethane (C_2H_6), and propane (C_3H_8) are the beginning of a series of compounds in which any two members in a sequence differ by one carbon atom and two hydrogen atoms—namely, a CH_2 unit. Consider the series in Figure 25.3.3. The sequence starts with C_3H_8, and a CH_2 unit is added in each step moving up the series. Any family of compounds in which adjacent members differ from each other by a definite factor (here a CH_2 group) is called a homologous series. The members of such a series, called *homologs*, have properties that vary in a regular and predictable manner.

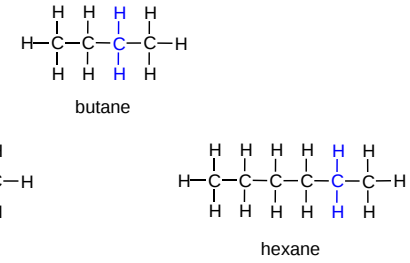


Figure 25.3.2: Members of a Homologous Series. Each succeeding formula incorporates one carbon atom and two hydrogen atoms more than the previous formula.

The homologous series allows us to write a general formula for alkanes: $C_nH_{2n\ +\ 2}$. Using this formula, we can write a molecular formula for any alkane with a given number of carbon atoms. For example, an alkane with eight carbon atoms has the molecular formula $C_8H_{(2\ \times\ 8)\ +\ 2} = C_8H_{18}$.

Molecular Formulas

Alkanes are the simplest family of hydrocarbons - compounds containing carbon and hydrogen only. Alkanes only contain carbon-hydrogen bonds and carbon-carbon single bonds. The first six alkanes are as follows:

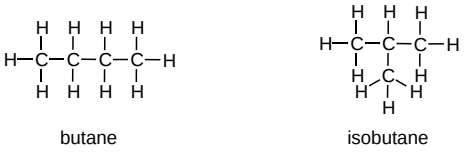
Table 3.3.1: Molecular formulas for small alkanes

methane	CH_4
ethane	C_2H_6
propane	C_3H_8
butane	C_4H_{10}
pentane	C_5H_{12}
hexane	C_6H_{14}

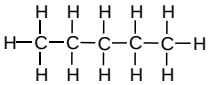
You can work out the formula of any of the alkanes using the general formula C_nH_{2n+2}

Isomerism

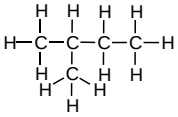
All of the alkanes containing 4 or more carbon atoms show structural isomerism, meaning that there are two or more different structural formulas that you can draw for each molecular formula. Isomers (from the Greek *isos* + *meros*, meaning "made of the same parts") are molecules that have the same molecular formula, but have a different arrangement of the atoms in space. Alkanes with 1-3 carbons, methane (CH_4), ethane (C_2H_6), and propane (C_3H_8,) do not exist in isomeric forms because there is only one way to arrange the atoms in each formula so that each carbon atom has four bonds. However, C_4H_{10}, has more than possible structure. The four carbons can be drawn in a row to form butane or the can branch to form isobutane. The two compounds have different properties—for example, butane boils at −0.5°C, while isobutane boils at −11.7°C.



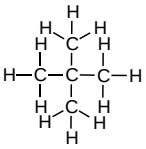
Likewise the molecular formula: C_5H_{12} has three possible isomer. The compound at the far left is pentane because it has all five carbon atoms in a continuous chain. The compound in the middle is isopentane; like isobutane, it has a one CH_3 branch off the second carbon atom of the continuous chain. The compound at the far right, discovered after the other two, was named neopentane (from the Greek *neos*, meaning "new"). Although all three have the same molecular formula, they have different properties, including boiling points: pentane, 36.1°C; isopentane, 27.7°C; and neopentane, 9.5°C.



pentane



isopentane



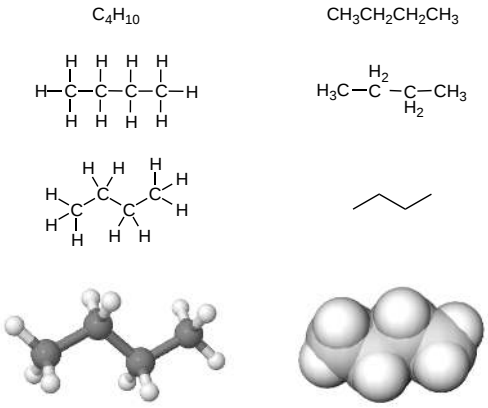
neopentane

Of the structures show above, butane and pentane are called **normal alkanes** or **straight-chain alkanes**, indicating that all contain a single continuous chain of carbon atoms and can be represented by a projection formula whose carbon atoms are in a straight line. The other structures, isobutane, isopentane, and neopentane are called called branched-chain alkanes. As the number of carbons in an akane increases the number of possible isomers also increases as shown in the table below.

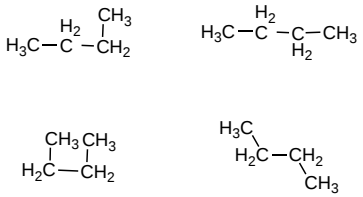
Table 3.3.2: Number of isomers for hydrocarbons

Molecular Formula	Number of Structural Isomers
CH_4	1
C_2H_6	1
C_3H_8	1
C_4H_{10}	2
C_5H_{12}	3
C_6H_{14}	5
C_7H_{16}	9
C_8H_{18}	18
C_9H_{20}	35
$C_{10}H_{22}$	75
$C_{14}H_{30}$	1858
$C_{18}H_{38}$	60,523
$C_{30}H_{62}$	4,111,846,763

Akanes can be represented in many different ways. The figure below shows some of the different ways straight-chain butane can be represented. Most often chemists refer to butane by the condensed structure $CH_3CH_2CH_2CH_3$ or *n*-C_4H_{10} where n denotes a normal straight alkane.



Note that many of these structures only imply bonding connections and do not indicate any particular geometry. The bottom two structures, referred to as "ball and stick" and "space filling" do show 3D geometry for butane. Because the four-carbon chain in butane may be bent in various ways the groups can rotate freely about the C–C bonds. However, this rotation does not change the identity of the compound. It is important to realize that bending a chain does *not* change the identity of the compound; all of the following represent the same compound, butane:



The nomenclature of straight alkanes is based on the number of carbon atoms they contain. The number of carbons are indicated by a prefix and the suffix -ane is added to indicate the molecules is an alkane. The prefix for three carbons is prop so adding -ane, the IUPAC name for C_3H_8 is propane. Likewise, the prefix for six is hex so the name for the straight chain isomer of C_6H_{14} is called hexane. The first ten prefixes should be memorized, because these alkane names from the basis for naming many other organic compounds.

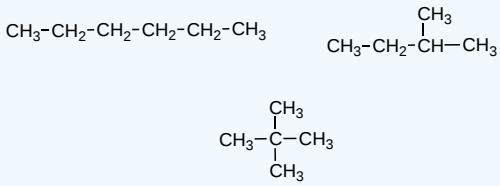
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Table **3.3.3**: The First 10 Straight-Chain Alkanes

Molecular Formula	Prefix	Condensed Structural Formula	Name
CH_4	Meth	CH_4	methane
C_2H_6	Eth	CH_3CH_3	ethane
C_3H_8	Prop	$CH_3CH_2CH_3$	propane
C_4H_{10}	But	$CH_3CH_2CH_2CH_3$	butane
C_5H_{12}	Pent	$CH_3CH_2CH_2CH_2CH_3$	pentane
C_6H_{14}	Hex	$CH_3(CH_2)_4CH_3$	hexane
C_7H_{16}	Hept	$CH_3(CH_2)_5CH_3$	heptane
C_8H_{18}	Oct	$CH_3(CH_2)_6CH_3$	octane
C_9H_{20}	Non	$CH_3(CH_2)_7CH_3$	nonane
$C_{10}H_{22}$	Dec	$CH_3(CH_2)_8CH_3$	decane

Example 3.3.1: Chain Isomers in Pentane

Pentane, C_5H_{12}, has three chain isomers. If you think you can find any others, they are simply twisted versions of the ones below. If in doubt make some models.

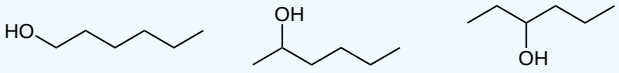


Exercises

Exercise 3.3.1

Draw all of the isomers for $C_6H_{14}O$ that contain a 6 carbon chain and an alcohol (-OH) functional group.

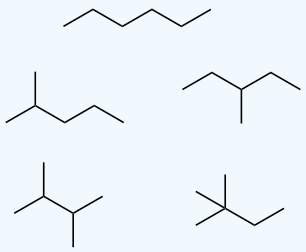
Answer



Exercise 3.3.2

Draw all possible isomers for C_6H_{14} (There are five total).

Answer



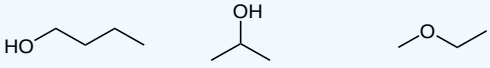
The top structure is when it is a 6 carbon chain. The middle row contains the 5 carbon chained isomers with branching at the 2nd and 3rd carbon. The bottom row contains the two 4 carbon chain isomers that can be drawn.

Exercise 3.3.3

Draw all possible isomers for C_3H_8.

Answer

The first structure is when an alcohol comes off the first carbon. The second structure is when the alcohol is coming off the central carbon. The third structure is the only possible ether form of C_3H_8.

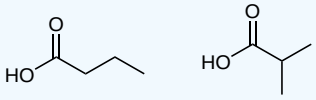


Exercise 3.3.4

Draw all possible isomers for $C_4H_8O_2$ that contain a carboxylic acid.

Answer

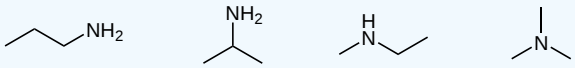
There are only 2 possibilities.



Exercise 3.3.5

Draw all possible isomers for C_3H_9N and indicate whether each amine is primary, secondary, or tertiary.

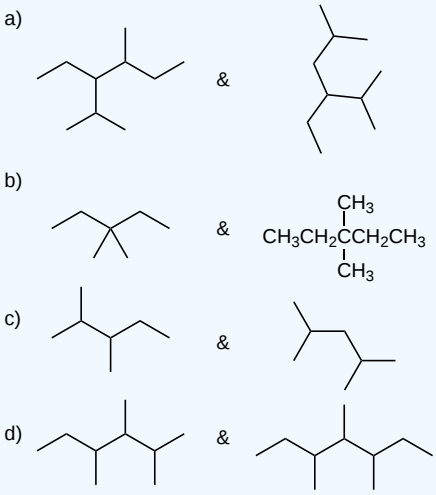
Answer



The first and second structures are primary amines. The third structure is a secondary amine. The last structure is a tertiary amine.

Exercise 3.3.6

Indicate whether each of the following sets are constitutional isomers, the same compound, or different compounds.



Answer

a) Both structures have formulas of $C_{10}H_{22}$ and have different connectivity which makes these **constitutional isomers**.

b) Both structures have formulas of C_7H_{16} and have the same connectivity which makes these the **same compound**.

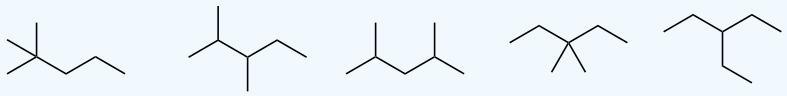
c) Both structure have formulas of C_7H_{16} and have different connectivity which makes these **constitutional isomers**.

d) The structure on the left has a formula of C_9H_{20} and the structure on the right has a formula of $C_{10}H_{22}$ so these are **different compounds**.

Exercise 3.3.7

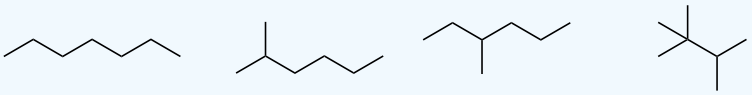
Draw the 5 constitutional isomers of C_7H_{16} (of the 9 total isomers possible) that have 5 carbons as the longest carbon chain length.

Answer



The 5 constitutional isomers with a 5 carbon chain length are shown above. Since there needs to be 7 carbons total, the 2 extra carbons are added as substituents. From left to right, the methyl group substitution pattern is 2,2, 2,3, 2,4, and 3,3, and the last one (on right) has a 3-ethyl substituent.

The other 4 possible constitutional isomers (with different length carbon chains) are shown below.



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3.4: Alkyl Groups

Objectives

After completing this section, you should be able to

1. recognize and name any alkyl group that can be considered to have been formed by the removal of a terminal hydrogen atom from a straight-chain alkane containing ten or fewer carbon atoms.
2. explain what is meant by a primary, secondary, tertiary or quaternary carbon atom.
3. represent the various types of organic compounds using the symbol “R” to represent any alkyl group.

Key Terms

Make certain that you can define, and use in context, the key terms below.

- alkyl group
- methyl group
- isopropyl group
- *sec*-butyl group
- isobutyl group
- *tert*-butyl group
- primary carbon
- secondary carbon
- tertiary carbon
- quaternary carbon

Study Notes

The differences among primary, secondary, tertiary and quaternary carbon atoms are explained in the following discussion. A convenient way of memorizing this classification scheme is to remember that a primary carbon atom is attached directly to only one other carbon atom, a secondary carbon atom is attached directly to two carbon atoms, and so on.

The **IUPAC** system requires first that we have names for simple unbranched chains and second, that we have names for simple alkyl groups that may be attached to the chains. An **alkyl group** is formed by removing one hydrogen from the alkane chain. The removal of this hydrogen results in a stem change from **-ane** to **-yl** to indicate an alkyl group. The removal of a hydrogen from methane, CH_4, creates a methyl group -CH_3. Likewise, the removal of a hydrogen from ethane, CH_3CH_3, creates an ethyl group -CH_2CH_3. The nomenclature pattern can continue to provide a series of straight-chain alkyl groups from straight chain alkanes with a hydrogen removed from the end. Note, the letter **R** is used to designate a generic (unspecified) alkyl group.

CH_4	⟹	$\mathbf{CH_3}$–R
methane		methyl
$CH_3CH_2CH_3$	⟹	$\mathbf{CH_3CH_2CH_2}$–R
propane		propyl

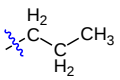
Table **3.4.2**: Straight chain alkane and alkyl group names

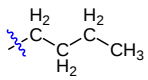
Alkane	Name	Alkyl Group	Name (Abbreviation)
CH_4	Methane	$-CH_3$	Methyl (Me)
CH_3CH_3	Ethane	$-CH_2CH_3$	Ethyl (Et)
$CH_3CH_2CH_3$	Propane	$-CH_2CH_2CH_3$	Propyl (Pr)
$CH_3CH_2CH_2CH_3$	Butane	$-CH_2CH_2CH_2CH_3$	Butyl (Bu)
$CH_3CH_2CH_2CH_2CH_3$	Pentane	$-CH_2CH_2CH_2CH_2CH_3$	Pentyl
$CH_3CH_2CH_2CH_2CH_2CH_3$	Hexane	$-CH_2CH_2CH_2CH_2CH_2CH_3$	Hexyl

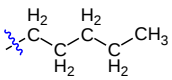
Prior to the systematic nomenclature developed for organic chemistry, prefixes were used to specify the connection point of straight-chain and branched-chain alkyl groups. Although the modern nomenclature system, discussed in the next section, is preferred these older terms are still often used, especially in solvents and reagents. Thus, an understanding of these prefixes is important to understanding organic chemistry. Notice that the total number of carbons in the alkyl subsistent is still indicated with the **prefix + yl**. For methyl and ethyl alkyl groups there is only one possible connection point so connection prefixes are not necessary. Starting with a three carbon alkyl group (propyl) the possibility of multiple connection points necessitates connection prefixes. These prefixes are often abbreviated with a letter which is italicized.

Normal (*n*)

The prefix "n" is used to indicate a connection at the end of a straight-chain alkane. This prefix is not commonly used to just indicate alkyl subsistent as discussed above. However it is sometime used to indicate the connection of a functional group onto a straight alkane.

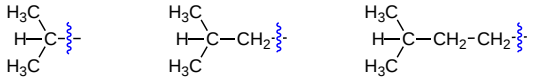

n-propyl
or propyl


n-butyl
or butyl


n-pentyl
or pentyl

Iso (*i*)

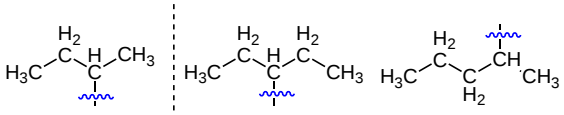
Starting with propyl alkyl groups there is the possibility of a connection other than the very end. The prefix "iso" implies that the connection ends with a $(CH_3)_2CH$- group.



isopropyl or *i*-propyl | isobutyl or *i*-butyl | isopentyl or *i*-pentyl

Secondary (*Sec*)

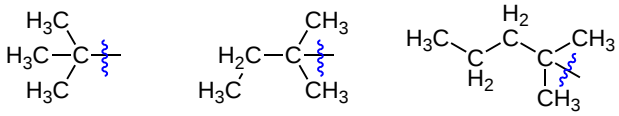
With butyl straight-chain alkyl groups there is the possibility of a connection on the second carbon from the end of the chain. These alkyl groups are given the prefix "*Sec*." This is not used for pentyl or hexyl groups because there is more than one structure that are not identical that could be named as sec-pentyl or sec-hexyl.



sec -butyl | NOT *sec* -pentyl

Tertiary (*tert* or *t*)

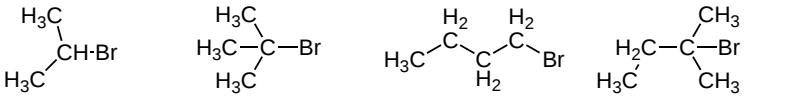
Starting with four carbon alkyl groups, there is an isomer which can have a connection to a tertiary carbon. These alkyl groups get the prefix "*t*."



tert-butyl or *t*-butyl | *tert*-pentyl or *t*-pentyl | *tert*-hexyl or *t*-hexyl

Example:

The naming system described above is often used to describe halogens which contain only a few carbons. The halogen is shown as bonded to the connection point of the alkyl group.



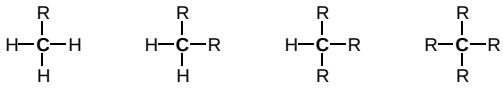
isopropyl bromide | *t*-butyl bromide | *n*-butyl bromide | *tert*-pentyl bromide

Classification of carbon atoms

Carbons have a special terminology to describe how many other carbons they are attached to. This allows for an easy description of branching in alkanes. Also, we will find that the number of carbons attached to a given atom will have subtle effects on its chemistry.

- Primary carbons (1^o) attached to one other C atom.
- Secondary carbons (2^o) are attached to two other C's.
- Tertiary carbons (3^o) are attached to three other C's.
- Quaternary carbons (4^o) are attached to four C's.

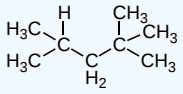
The figure below use the group "R" to represent an alkyl group of unspecified length. R typically used to represent alkyl groups but an also represent a part of a molecule which is either unspecified or not germane to the discussion.



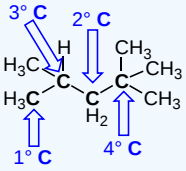
This terminology will be used repeatedly in organic chemistry to describe the number of carbons attached to a specific atom, however, the atom will not always a carbon.

Example 3.4.1

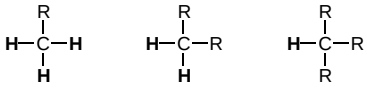
Please indicate the the number of 1^o, 2^o, 3^o, and 4^o carbons in the following molecule:



- The molecule has five Primary carbons (1^o).
- The molecule has one Secondary carbon (2^o).
- The molecule has one Tertiary carbon (3^o).
- The molecule has one Quaternary carbon (4^o)



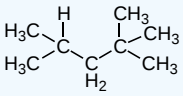
Hydrogen atoms are also classified in this manner. A hydrogen atom attached to a primary carbon atom is called a primary hydrogen ect.



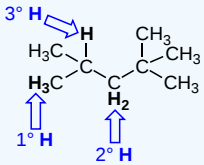
- Primary hydrogens (1^o) are attached to carbons bonded to one other C atom
- Secondary hydrogens (2^o) are attached to carbons bonded to two other C's
- Tertiary hydrogens (3^o) are attached to carbons bonded to three other C's
- It is not possible to have a quaternary hydrogen (4^o).

Example 3.4.2

Please indicate the the number of 1^o, 2^o, and 3^o, hydrogens are in the following molecule:



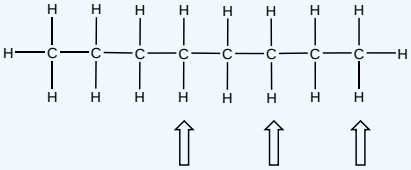
- The molecule has fifteen Primary (1^o) hydrogens.
- The molecule has two Secondary (2^o) hydrogens.
- The molecule has one Tertiary (3^o) hydrogen.



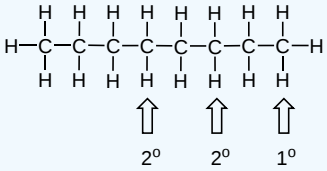
Exercises

Exercise 3.4.1

Determine whether the H's indicated in the following structure are 1°, 2°, or 3°.

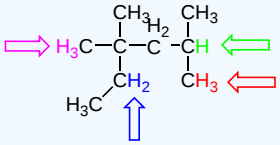


Answer

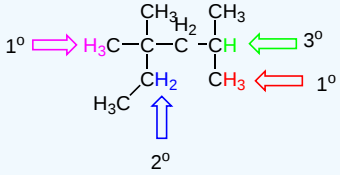


Exercise 3.4.2

Determine whether the H's indicated in the following structure is 1°, 2°, or 3°.

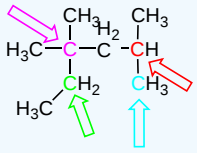


Answer

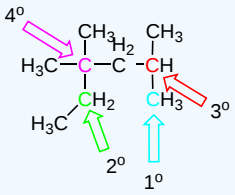


Exercise 3.4.3

Determine whether the carbons indicated in the structure below are 1°, 2°, 3°, or 4°.

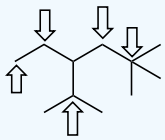


Answer

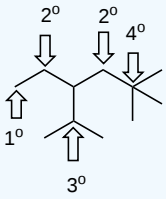


Exercise 3.4.4

Determine whether the carbons indicated in the structure below are 1°, 2°, 3°, or 4°.

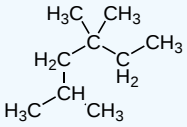


Answer



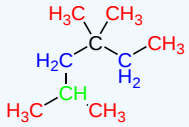
Exercise 3.4.5

Please indicate the total number of each type 1°, 2°, 3°, and 4° carbons in the following molecule.



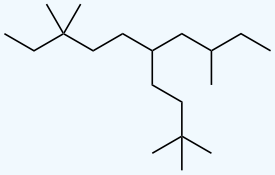
Answer

There are 5 primary (1°) C's, 2 secondary (2°) C's, 1 tertiary (3°) C and 1 quaternary (4°) C in the structure (seen color coded below).



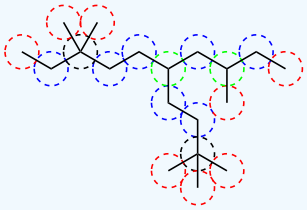
Exercise 3.4.6

Please indicate the total number of each type 1°, 2°, 3°, and 4° carbons in the following molecule.



Answer

There are 8 primary (1^o) C's, 7 secondary (2^o) C's, 2 tertiary (3^o) C's and 2 quaternary (4^o) C's in the structure (seen color coded below).



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3.5: Naming Alkanes

Objectives

After completing this section, you should be able to

1. provide the correct IUPAC name for any given alkane structure (Kekulé, condensed or shorthand).
2. draw the Kekulé, condensed or shorthand structure of an alkane, given its IUPAC name.

Key Terms

Make certain that you can define, and use in context, the key term below.

- IUPAC system

Study Notes

The IUPAC system of nomenclature aims to ensure

1. that every organic compound has a unique, unambiguous name.
2. that the IUPAC name of any compound conveys the structure of that compound to a person familiar with the system.

One way of checking whether the name you have given to an alkane is reasonable is to count the number of carbon atoms implied by the chosen name. For example, if you named a compound 3-ethyl-4-methylheptane, you have indicated that the compound contains a total of 10 carbon atoms—seven carbon atoms in the main chain, two carbon atoms in an ethyl group, and one carbon atom in a methyl group. If you were to check the given structure and find 11 carbon atoms, you would know that you had made a mistake. Perhaps the name you should have written was 3-ethyl-4,4-dimethylheptane!

When naming alkanes, a common error of beginning students is a failure to pick out the longest carbon chain. For example, the correct name for the compound shown below is 3-methylheptane, not 2-ethylhexane.

Remember that every substituent must have a number, and do not forget the prefixes: di, tri, tetra, etc.

You must use commas to separate numbers, and hyphens to separate numbers and substituents. Notice that 3-methylhexane is one word.

Hydrocarbons having no double or triple bond functional groups are classified as **alkanes** or **cycloalkanes**, depending on whether the carbon atoms of the molecule are arranged only in chains or also in rings. Although these hydrocarbons have no functional groups, they constitute the framework on which functional groups are located in other classes of compounds, and provide an ideal starting point for studying and naming organic compounds. The alkanes and cycloalkanes are also members of a larger class of compounds referred to as **aliphatic**. Simply put, aliphatic compounds are compounds that do not incorporate any aromatic rings in their molecular structure.

The following table lists the IUPAC names assigned to simple continuous-chain alkanes from C-1 to C-10. A common **"ane"** suffix identifies these compounds as alkanes. Longer chain alkanes are well known, and their names may be found in many reference and text books. The names **methane** through **decane** should be memorized, since they constitute the root of many IUPAC names. Fortunately, common numerical prefixes are used in naming chains of five or more carbon atoms.

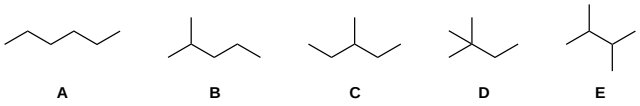
Table 3.4.1 : Simple Unbranched Alkanes

Name	Molecular Formula	Structural Formula	Isomers		Name	Molecular Formula	Structural Formula	Isomers
meth**ane**	CH_4	CH_4	1		hex**ane**	C_6H_{14}	$CH_3(CH_2)_4CH_3$	5
eth**ane**	C_2H_6	CH_3CH_3	1		hept**ane**	C_7H_{16}	$CH_3(CH_2)_5CH_3$	9
prop**ane**	C_3H_8	$CH_3CH_2CH_3$	1		oct**ane**	C_8H_{18}	$CH_3(CH_2)_6CH_3$	18
but**ane**	C_4H_{10}	$CH_3CH_2CH_2CH_3$	2		non**ane**	C_9H_{20}	$CH_3(CH_2)_7CH_3$	35
pent**ane**	C_5H_{12}	$CH_3(CH_2)_3CH_3$	3		dec**ane**	$C_{10}H_{22}$	$CH_3(CH_2)_8CH_3$	75

Some important behavior trends and terminologies

1. The formulas and structures of these alkanes increase uniformly by a CH_2 increment.
2. A uniform variation of this kind in a series of compounds is called **homologous**.
3. These formulas all fit the $\mathbf{C_nH_{2n+2}}$ rule. This is also the highest possible H/C ratio for a stable hydrocarbon.
4. Since the H/C ratio in these compounds is at a maximum, we call them **saturated** (with hydrogen).

Beginning with butane (C_4H_{10}), and becoming more numerous with larger alkanes, we note the existence of alkane isomers. For example, there are five C_6H_{14} isomers, shown below as abbreviated line formulas (**A** through **E**):



Although these distinct compounds all have the same molecular formula, only one (**A**) can be called hexane. How then are we to name the others?

The **IUPAC** system requires first that we have names for simple unbranched chains, as noted above, and second that we have names for simple alkyl groups that may be attached to the chains. Examples of some common **alkyl groups** are given in the following table. Note that the "ane" suffix is replaced by "**yl**" in naming groups. The symbol **R** is used to designate a generic (unspecified) alkyl group.

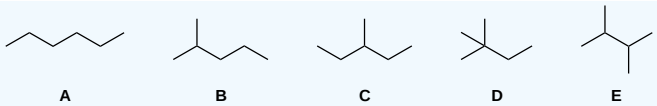
Table 3.4.2 : Alkyl Groups Names

Group	$CH_3–$	$C_2H_5–$	$CH_3CH_2CH_2–$	$(CH_3)_2CH–$	$CH_3CH_2CH_2CH_2–$	$(CH_3)_2CHCH_2–$	$CH_3CH_2CH(CH_3)–$	$(CH_3)_3C–$	R–
Name	Methyl	Ethyl	Propyl	Isopropyl	Butyl	Isobutyl	sec-Butyl	tert-Butyl	Alkyl

IUPAC Rules for Alkane Nomenclature

1. Find and name the longest continuous carbon chain.
2. Identify and name groups attached to this chain.
3. Number the chain consecutively, starting at the end nearest a substituent group.
4. Designate the location of each substituent group by an appropriate number and name.
5. Assemble the name, listing groups in alphabetical order.
6. The prefixes di, tri, tetra etc., used to designate several groups of the same kind, are not considered when alphabetizing.

Example 3.4.1 : Alkanes



The IUPAC names of the isomers of hexane are: **A** hexane **B** 2-methylpentane **C** 3-methylpentane **D** 2,2-dimethylbutane **E** 2,3-dimethylbutane

Halogen Groups

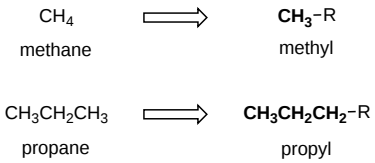
Halogen substituents are easily accommodated, using the names: fluoro (F-), chloro (Cl-), bromo (Br-) and iodo (I-).

Example 3.4.2 : Halogen Substitution

For example, $(CH_3)_2CHCH_2CH_2Br$ would be named 1-bromo-3-methylbutane. If the halogen is bonded to a simple alkyl group an alternative "alkyl halide" name may be used. Thus, C_2H_5Cl may be named chloroethane (no locator number is needed for a two carbon chain) or ethyl chloride.

Alkyl Groups

Alkanes can be described by the general formula C_nH_{2n+2}. An alkyl group is formed by removing one hydrogen from the alkane chain and is described by the formula C_nH_{2n+1}. The removal of this hydrogen results in a stem change from **-ane** to **-yl**. Take a look at the following examples.



The same concept can be applied to any of the straight chain alkane names provided in the table below.

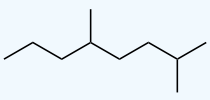
Name	Molecular Formula	Condensed Structural Formula
Methane	CH_4	CH_4
Ethane	C_2H_6	CH_3CH_3
Propane	C_3H_8	$CH_3CH_2CH_3$
Butane	C_4H_{10}	$CH_3(CH_2)_2CH_3$
Pentane	C_5H_{12}	$CH_3(CH_2)_3CH_3$
Hexane	C_6H_{14}	$CH_3(CH_2)_4CH_3$
Heptane	C_7H_{16}	$CH_3(CH_2)_5CH_3$
Octane	C_8H_{18}	$CH_3(CH_2)_6CH_3$
Nonane	C_9H_{20}	$CH_3(CH_2)_7CH_3$
Decane	$C_{10}H_{22}$	$CH_3(CH_2)_8CH_3$
Undecane	$C_{11}H_{24}$	$CH_3(CH_2)_9CH_3$
Dodecane	$C_{12}H_{26}$	$CH_3(CH_2)_{10}CH_3$
Tridecane	$C_{13}H_{28}$	$CH_3(CH_2)_{11}CH_3$
Tetradecane	$C_{14}H_{30}$	$CH_3(CH_2)_{12}CH_3$
Pentadecane	$C_{15}H_{32}$	$CH_3(CH_2)_{13}CH_3$
Hexadecane	$C_{16}H_{34}$	$CH_3(CH_2)_{14}CH_3$
Heptadecane	$C_{17}H_{36}$	$CH_3(CH_2)_{15}CH_3$
Octadecane	$C_{18}H_{38}$	$CH_3(CH_2)_{16}CH_3$
Nonadecane	$C_{19}H_{40}$	$CH_3(CH_2)_{17}CH_3$
Eicosane	$C_{20}H_{42}$	$CH_3(CH_2)_{18}CH_3$

Three Rules for Naming Alkanes

1. Choose the longest, most substituted carbon chain containing a functional group.
2. A carbon bonded to a functional group must have the lowest possible carbon number. If there are no functional groups, then any substituent present must have the lowest possible number.
3. Take the alphabetical order into consideration; that is, after applying the first two rules given above, make sure that your substituents and/or functional groups are written in alphabetical order.

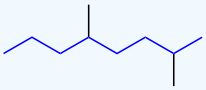
Example 3.4.3

What is the name of the follow molecule?

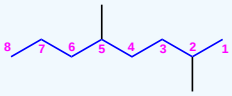


Solution

Rule #1: Choose the longest, most substituted carbon chain containing a functional group. This example does not contain any functional groups, so we only need to be concerned with choosing the longest, most substituted carbon chain. The longest carbon chain has been highlighted in blue and consists of eight carbons.



Rule #2: Carbons bonded to a functional group must have the lowest possible carbon number. If there are no functional groups, then any substitute present must have the lowest possible number. Because this example does not contain any functional groups, we only need to be concerned with the two substitutes present, that is, the two methyl groups. If we begin numbering the chain from the left, the methyls would be assigned the numbers 4 and 7, respectively. If we begin numbering the chain from the right, the methyls would be assigned the numbers 2 and 5. Therefore, to satisfy the second rule, numbering begins on the right side of the carbon chain as shown below. This gives the methyl groups the lowest possible numbering.

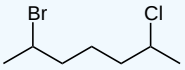


Rule 3: In this example, there is no need to utilize the third rule. Because the two substitutes are identical, neither takes alphabetical precedence with respect to numbering the carbons. This concept will become clearer in the following examples.

The name of this molecule is **2,5-dimethyloctane**

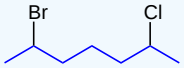
Example 3.4.4

What is the name of the follow molecule?



Solution

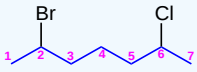
Rule #1: Choose the longest, most substituted carbon chain containing a functional group. This example contains two functional groups, bromine and chlorine. The longest carbon chain has been highlighted in blue and consists of seven carbons.



Rule #2: Carbons bonded to a functional group must have the lowest possible carbon number. If there are no functional groups, then any substituent present must have the lowest possible number. In this example, numbering the chain from either the left or the right would satisfy this rule. If we number the chain from the left, bromine and chlorine would be assigned the second and sixth carbon positions, respectively. If we number the chain from the right, chlorine would be assigned the second position and bromine would be assigned the sixth position. In other words, whether we choose to number from the left or right, the functional groups occupy the second and sixth positions in the chain. To select the correct numbering scheme, we need to utilize the third rule.



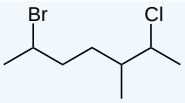
Rule #3: After applying the first two rules, take the alphabetical order into consideration. Alphabetically, bromine comes before chlorine. Therefore, bromine is assigned the second carbon position, and chlorine is assigned the sixth carbon position.



The name of this molecule is: **2-bromo-6-chloroheptane**

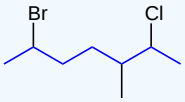
Example 3.4.5

What is the name of the follow molecule?

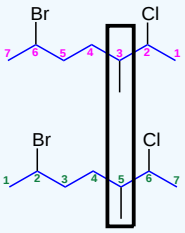


Solution

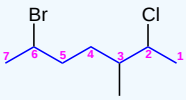
Rule #1: Choose the longest, most substituted carbon chain containing a functional group. This example contains two functional groups, bromine and chlorine, and one substitute, the methyl group. The longest carbon chain has been highlighted in blue and consists of seven carbons.



Rule #2: Carbons bonded to a functional group must have the lowest possible carbon number. After taking functional groups into consideration, any substitutes present must have the lowest possible carbon number. This particular example illustrates the **point of difference principle**. If we number the chain from the left, bromine, the methyl group and chlorine would occupy the second, fifth and sixth positions, respectively. This concept is illustrated in the second drawing below. If we number the chain from the right, chlorine, the methyl group and bromine would occupy the second, third and sixth positions, respectively, which is illustrated in the first drawing below. The position of the methyl, therefore, becomes a **point of difference**. In the first drawing, the methyl occupies the third position. In the second drawing, the methyl occupies the fifth position. To satisfy the second rule, we want to choose the numbering scheme that provides the lowest possible numbering of this substitute. Therefore, the first of the two carbon chains shown below is correct.



Therefore, the first numbering scheme is the appropriate one to use.



Once you have determined the correct numbering of the carbons, it is often useful to make a list, including the functional groups, substitutes, and the name of the parent chain.

Rule #3: After applying the first two rules, take the alphabetical order into consideration. Alphabetically, bromine comes before chlorine. Therefore, bromine is assigned the second carbon position, and chlorine is assigned the sixth carbon position.

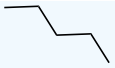
Parent chain: heptane Substitutents: 2-chloro 3-methyl 6-bromo

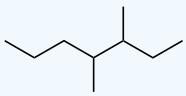
The name of this molecule is: **6-bromo-2-chloro-3-methylheptane**

Exercises

? Exercise 3.4.1

Give the proper IUPAC names of the following compounds.

a) 

b) 

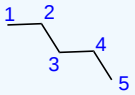
c) 

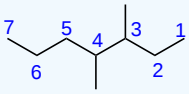
Answer

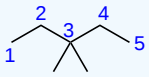
a) Since this structure is an unbranched alkane (all single bonds) with a 5 carbon chain length, its name would be **pentane**.

b) This alkane has a 7 carbon longest continuous chain length that we number from right to left to get the first methyl substituent we encounter to have the lowest possible number (3 versus being 4 if numbering from left to right). This causes it to have 2 methyl substituents at positions 3 & 4 so we would name it indicating those numbers and the prefix dimethyl which gives a proper IUPAC name of **3,4-dimethylheptane**.

c) This alkane has a 5 carbon longest continuous chain length (which could be numbered from left to right or right to left due to the symmetry at C-3). It has two methyl substituents off of C-3 so the proper IUPAC name is **3,3-dimethylpentane.**

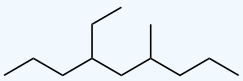
a) 

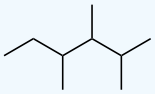
b) 

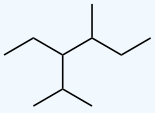
c) 

Exercise 3.4.2

Give the proper IUPAC names of the following compounds.

a) 

b) 

c) 

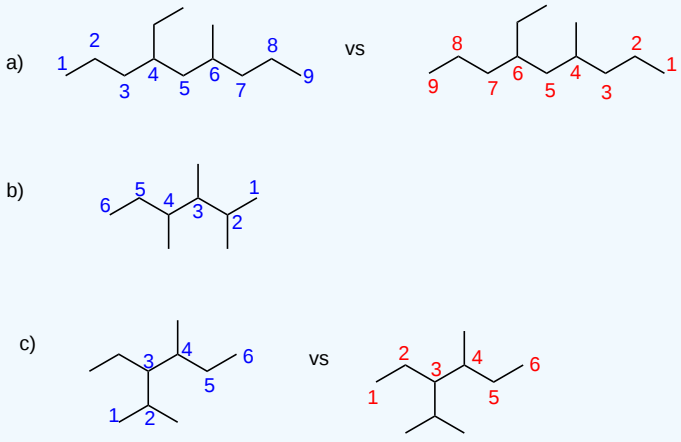
Answer

a) This alkane has a 9 carbon longest continuous chain length that we number from left to right (structure on left numbered in blue) to make the ethyl substituent be number 4. For the structure on the right (numbered in red) going from right to left,

the methyl substituent is number 4. Since ethyl is higher in the alphabetical order, you want to make it have the lower number so the structure on the left (blue numbering) takes priority and the name is **4-ethyl-6-methylnonane**.

b) This alkane has a 6 carbon longest continuous chain length that we number from right to left to make the first methyl be C-2 (versus the opposite direction which would make the first methyl C-3). Since there are 3 methyl substituents at positions 2,3, & 4, this compound would have the name **2,3,4-trimethylhexane**.

c) This 6 carbon alkane can be numbered along different chains (see below) as well as in the opposite directions. This shows the two different chains that can be drawn (making the first substituent in that chain the lowest number). The structure on the left (numbered in blue) is the correct choice since it causes more substituents to be on the longest continuous chain (3 vs 2 in the structure on the right). This would make the IUPAC name of the structure **3-ethyl-2,4-dimethylhexane**. (Notice how ethyl takes priority over methyl and the di- is not considered for alphabetizing.)



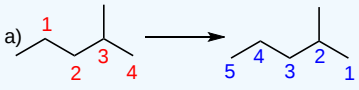
Exercise 3.4.3

All of the following names represent a compound that has been named improperly. Draw out the structure from the name and give the proper IUPAC name for the compounds.

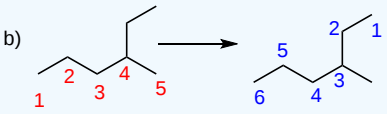
a. 1,3-dimethylbutane
b. 4-ethylpentane
c. 2-ethyl-3-methylpentane

Answer

a) The structure that can be drawn for the improper name is shown below on the left. When you renumber it properly (structure on the right), the correct name should be **2-methylpentane**.

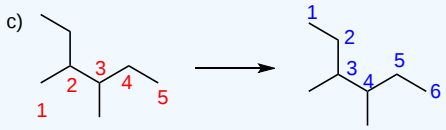


b) The structure that can be drawn for the improper name is shown below on the left. When you renumber it properly (structure on the right), notice that the longest chain is 6 C's and we start the numbering on the end to the right to make the methyl substituent come off at C-3 (instead of beong at C-4 if we numbered it the opposite direction) the correct name should be **3-methyl hexane**.



c) The structure that can be drawn for the improper name is shown below on the left. When you renumber it properly (structure on the right), notice that the longest chain is 6 C's and since this molecule is symmetrical (between carbon 3 &

4), you can start the numbers from either end. In this case, we have methyl substituents coming off of carbons 3 & 4 so the proper name is **3,4-dimethyl hexane**.



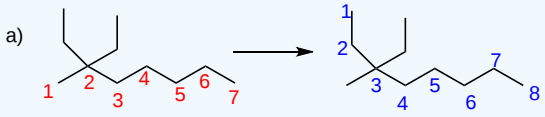
Exercise 3.4.4

All of the following names represent a compound that has been named improperly. Draw out the structure from the name and give the proper IUPAC name for the compounds.

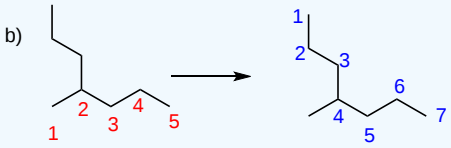
a. 2,2-diethylheptane
b. 2-propylpentane
c. 4,4-diethylbutane

Answer

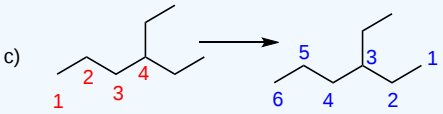
a) The structure that can be drawn for the improper name is shown below on the left. When you renumber it properly (structure on the right), notice that the longest chain is now 8 C's and you have an ethyl substituent at C-3 and a methyl substituent also at C-3 so the proper name is **3- ethyl-3-methyloctane**.



b) The structure that can be drawn for the improper name is shown below on the left. When you renumber it properly (structure on the right), notice that the longest chain is now 7 C's and since this molecule is symmetrical (at carbon 4), you can start the numbers from either end. There is a methyl substituent at C-4 so the proper name is **4-methylheptane**.



c) The structure that can be drawn for the improper name is shown below on the left. When you renumber it properly (structure on the right) going from right to left (to make the ethyl substituent have the lowest number possible), the correct name is **3-ethylhexane**



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3.6: Conformations of Ethane

Objectives

After completing this section, you should be able to

1. explain the concept of free rotation about a carbon-carbon single bond.
2. explain the difference between conformational isomerism and structural isomerism.
3. draw the conformers of ethane using both sawhorse representation and Newman projection.
4. sketch a graph of energy versus bond rotation for ethane, and discuss the graph in terms of torsional strain.

Key Terms

Make certain that you can define, and use in context, the key terms below.

- conformation (conformer, conformational isomer)
- dihedral angle
- eclipsed conformation
- Newman projection
- staggered conformation
- strain energy
- torsional strain (eclipsing strain)

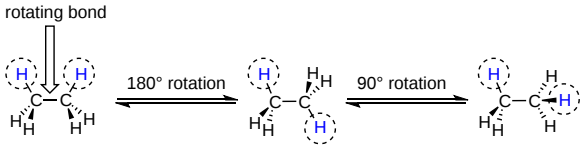
Study Notes

You should be prepared to sketch various conformers using both sawhorse representations and Newman projections. Each method has its own advantages, depending upon the circumstances. Notice that when drawing the Newman projection of the eclipsed conformation of ethane, you cannot clearly draw the rear hydrogens exactly behind the front ones. This is an inherent limitation associated with representing a 3-D structure in two dimensions.

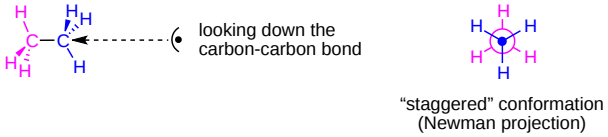
Conformational isomerism involves rotation about sigma bonds, and does not involve any differences in the connectivity of the atoms or geometry of bonding. Two or more structures that are categorized as conformational isomers, or **conformers**, are really just two of the exact same molecule that differ only in rotation of one or more sigma bonds.

Ethane Conformations

Although there are seven sigma bonds in the ethane molecule, rotation about the six carbon-hydrogen bonds does not result in any change in the shape of the molecule because the hydrogen atoms are essentially spherical. Rotation about the carbon-carbon bond, however, results in many different possible molecular conformations.



In order to better visualize these different conformations, it is convenient to use a drawing convention called the **Newman projection**. In a Newman projection, we look lengthwise down a specific bond of interest – in this case, the carbon-carbon bond in ethane. We depict the 'front' atom as a dot, and the 'back' atom as a larger circle.



The six carbon-hydrogen bonds are shown as solid lines protruding from the two carbons at 120°angles, which is what the actual tetrahedral geometry looks like when viewed from this perspective and flattened into two dimensions.

Figure 3.6.1: A 3D Model of Staggered Ethane.

The lowest energy conformation of ethane, shown in the figure above, is called the 'staggered' conformation. In the staggered conformation, all of the C-H bonds on the front carbon are positioned at an angle of 60° relative to the C-H bonds on the back carbon. This angle between a sigma bond on the front carbon compared to a sigma bond on the back carbon is called the dihedral angle. In this conformation, the distance between the bonds (and the electrons in them) is maximized. Maximizing the distance between the electrons decreases the electrostatic repulsion between the electrons and results in a more stable structure.

If we now rotate the front CH_3 group 60° clockwise, the molecule is in the highest energy 'eclipsed' conformation, and the hydrogens on the front carbon are as close as possible to the hydrogens on the back carbon.



"eclipsed" conformation

This is the highest energy conformation because of unfavorable electrostatic repulsion between the electrons in the front and back C-H bonds. The energy of the eclipsed conformation is approximately 3 kcal/mol (12 kJ/mol) higher than that of the staggered conformation. **Torsional strain** (or eclipsing strain) is the name give to the energy difference caused by the increased electrostatic repulsion of eclipsing bonds.

Another 60° rotation returns the molecule to a second staggared conformation. This process can be continued all around the 360° circle, with three possible eclipsed conformations and three staggered conformations, in addition to an infinite number of variations in between. We will focus on the staggered and eclipsed conformers since they are, respectively, the lowest and highest energy conformers.

Unhindered (Free) Rotations Do Not Exist in Ethane

The carbon-carbon bond is not *completely* free to rotate – the 3 kcal/mol torsional strain in ethane creates a barrier to rotation that must be overcome for the bond to rotate from one staggered conformation to another. This rotational barrier is not large enough to prevent rotation except at extremely cold temperatures. So at normal temperatures, the carbon-carbon bond is constantly rotating. However, at any given moment the molecule is more likely to be in a staggered conformation - one of the rotational 'energy valleys' - than in any other conformer. The potential energy associated with the various conformations of ethane varies with the dihedral angle of the bonds, as shown in Figure 3.6.2.

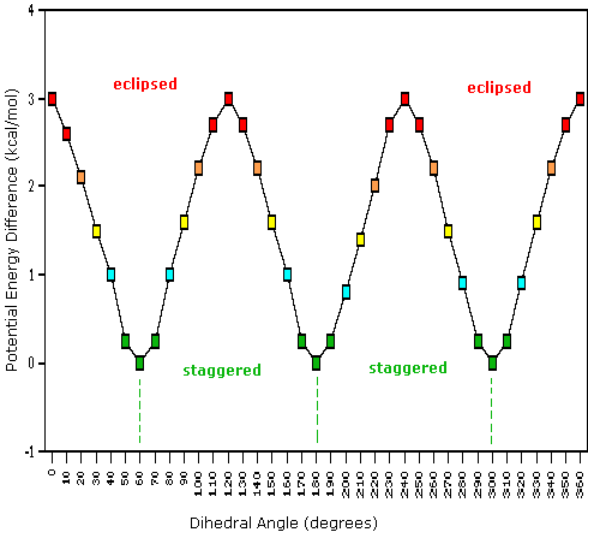


Figure 3.6.2: The potential energy associated with the various conformations of ethane varies with the dihedral angle of the bonds. Valleys in the graph represent the low energy staggered conformers, while peaks represent the higher energy eclipsed conformers.

Although the conformers of ethane are in rapid equilibrium with each other, the 3 kcal/mol energy difference leads to a substantial preponderance of staggered conformers (> 99.9%) at any given time. The animation below illustrates the relationship between ethane's potential energy and its dihedral angle

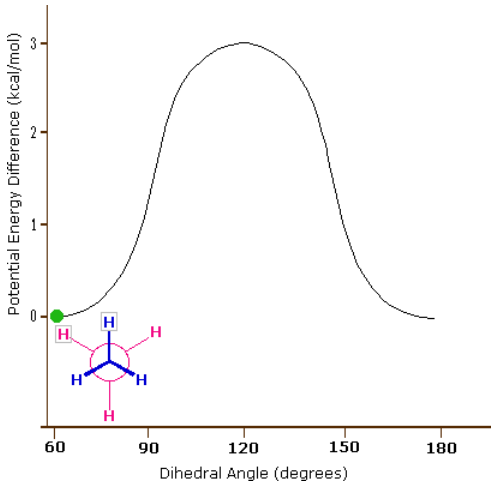


Figure 3.6.2: Animation of potential energy vs. dihedral angle in ethane

Exercises

1) What is the most stable rotational conformation of ethane and explain why it is preferred over the other conformation?

Solutions

1) Staggered, as there is less repulsion between the hydrogen atoms.

Questions

Q3.6.1

What is the most stable rotational conformation of ethane and explain why it is preferred over the other conformation?

Solutions

S3.6.1

Staggered, as there is less repulsion between the hydrogen atoms.

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3.7: Conformations of Other Alkanes

Objectives

After completing this section, you should be able to

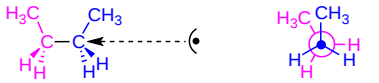
1. depict the staggered and eclipsed conformers of propane (or a similar compound) using sawhorse representations and Newman projections.
2. sketch a graph of energy versus bond rotation for propane (or a similar compound) and discuss the graph in terms of torsional strain.
3. depict the anti, gauche, eclipsed and fully eclipsed conformers of butane (or a similar compound), using sawhorse representations and Newman projections.
4. sketch a graph of energy versus C_2-C_3 bond rotation for butane (or a similar compound), and discuss it in terms of torsional and steric repulsion.
5. assess which of two (or more) conformers of a given compound is likely to predominate at room temperature from a semi-quantitative knowledge of the energy costs of the interactions involved.

Key Terms

Make certain that you can define, and use in context, the key terms below.

- anti conformation
- gauche conformation
- eclipsed conformation
- steric repulsion (strain)

In butane, there are three rotating carbon-carbon sigma bonds to consider, but we will focus on the middle bond between C_2 and C_3. Below are two representations of butane in a conformation which puts the two CH_3 groups (C_1 and C_4) in the eclipsed position.

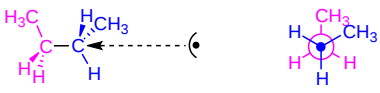


"eclipsed" (A)

Eclipsed interaction	Energy (kcal/mol)	Energy (kJ/mol)
H-H	1.0	4.0
H-CH_3	1.4	6.0
CH_3-CH_3	2.6	11.0

The CH_3-CH_3 groups create the significantly larger eclipsed interaction of 11.0 kJ/mol. There are also two H-H eclipsed interactions at 4.0 kJ/mol each to create a total of 2(4.0 kJ/mol) + 11.0 kJ/mol = 19.0 kJ/mol of strain. This is the highest energy conformation for butane, due to torsional strain caused by the electrostatic repulsion of electrons in the eclipsed bonds, but also because of another type of strain called '**steric repulsion'**, between the two rather bulky methyl groups. Steric strain comes about when two large groups, such as two methyl groups, try to occupy the same space. What results is a repulsive non-covalent interaction caused by their respective electron densities.

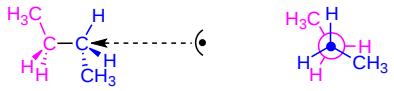
If we rotate the front, (blue) carbon by 60°clockwise, the butane molecule is now in a staggered conformation.



gauche

This is more specifically referred to as the '**gauche'** conformation of butane. Notice that although they are staggered, the two methyl groups are not as far apart as they could possibly be. There is still significant steric repulsion between the two bulky groups.

A further rotation of 60° gives us a second eclipsed conformation (B) in which both methyl groups are lined up with hydrogen atoms.



Due to steric repulsion between methyl and hydrogen substituents, this eclipsed conformation B is higher in energy than the gauche conformation. However, because there is no methyl-to-methyl eclipsing, it is lower in energy than eclipsed conformation A. One more 60° rotation produces the **'anti**' conformation, where the two methyl groups are positioned opposite each other and steric repulsion is minimized.



The anti conformation is the lowest energy conformation for butane. The diagram below summarizes the relative energies for the various eclipsed, staggered, and gauche conformations.

Figure* 3.7.1:* A 3D Structure of the Anti Butane Conformer.

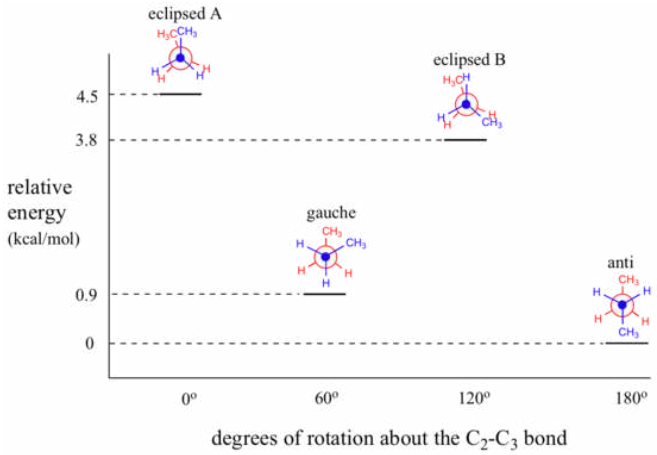


Figure **3.7.2**: Potential curve vs dihedral angle of the C_2-C_3 bond of butane.

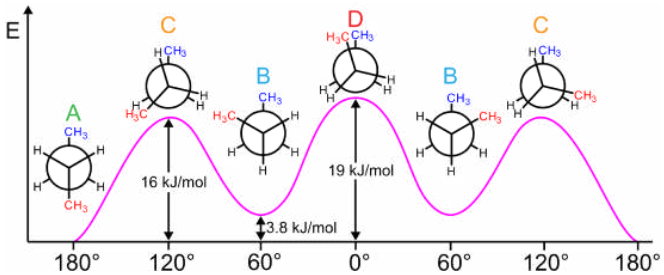
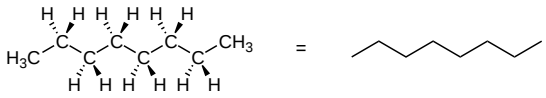


Figure **3.7.2**: Newman projections of butane conformations & their relative energy differences (not total energies). Conformations form when butane rotates about one of its single covalent bond. Torsional/dihedral angle is shown on x-axis. Torsional/dihedral angle is shown on x-axis. Conformation names (according to IUPAC): **A**: anti-periplanar, anti or trans **B**: synclinal or gauche **C**: anticlinal or eclipsed **D**: syn-periplanar or cis. Source for conformation names & conformer classification: Pure & Appl. Chem., Vol. 68, No. 12, pp. 2193-2222, 1996. (Public Domain; Keministi).

At room temperature, butane is most likely to be in the lowest-energy anti conformation at any given moment in time, although the energy barrier between the anti and eclipsed conformations is not high enough to prevent constant rotation except at very low

temperatures. For this reason (and also simply for ease of drawing), it is conventional to draw straight-chain alkanes in a zigzag form, which implies the anti conformation at all carbon-carbon bonds. For example octane is commonly drawn as:



octane

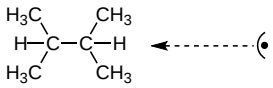
Drawing Newman Projections

Newman projections are a valuable method for viewing the relative positions of groups within molecule. Being able to draw the Newman projection for a given molecule is a valuable skill and will be used repeatedly throughout organic chemistry. Because organic molecules often contain multiple carbon-carbon bonds it is important to precisely know which bond and which direction is being sighted for the Newman projection. The details of the Newman projection change given the molecule but for typical alkanes a full conformational analysis involves a full 360^o rotation in 60^o increments. This will produce three staggered conformers and three eclipsed conformers. Typically, the staggered conformers are more stable and the eclipsed conformers are less stable. The least stable conformer will have the largest groups eclipsed while the most stable conformer will have the largest groups anti (180^o) to each other.

Example

Draw the Newman projection of 2,3 dimethylbutane along the C_2-C_3 bond. Then determine the least stable conformation.

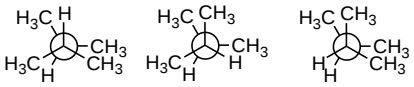
First draw the molecule and locate the indicated bond:



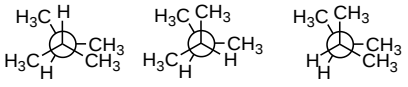
Because the question asks for the least stable conformation, focus on the three possible eclipsed Newman projections. Draw out three eclipsed Newman projections as a template. Because it is difficult to draw a true staggered Newman projection, it is common to show the bonds slightly askew.



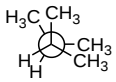
Place the substituents attached to the second carbon (C_3) on the back bonds of all three Newman projections. In this example they are 2 CH_3s and an H. Place the substituents in the same position on all three Newman projections.



Then place the substituents attached to the first carbon (C_2) on the front bonds of the Newman projection. In this example, the substituents are also 2 CH_3s and an H. Move the substituents through two 60^o rotations to create the remaining two eclipsed Newman projections. Leave the substituents on the back carbon in place. Attempting to rotate the front and back carbons simultaneously is a common mistake and often leads to incorrect Newman projections.



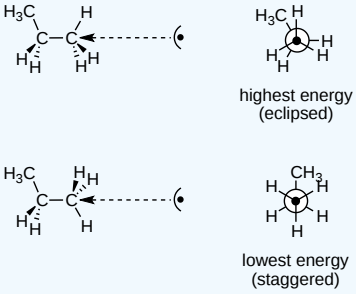
Compare the Newman projections by looking the eclipsed interactions. Remember that the order of torsional strain interactions are CH_3-CH_3 > CH_3-H > H-H. The third structure has two CH_3-CH_3 torsional interactions which will make it the least stable conformer of 2,3 dimethyl butane.



Example 3.7.1

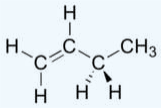
Draw Newman projections of the eclipsed and staggered conformations of propane, as if viewed down the C_1-C_2 bond.

Answer

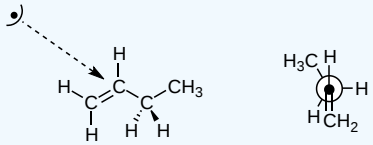


Example 3.7.2

Draw a Newman projection, looking down the C_2-C_3 bond, of 1-butene in the conformation shown below.



Answer



Exercises

Questions

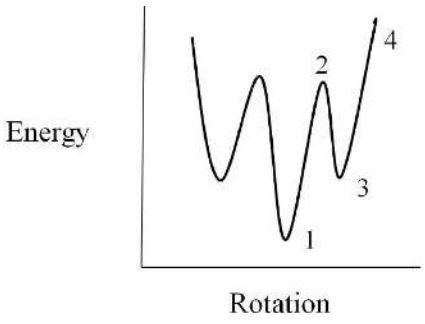
Q3.7.1

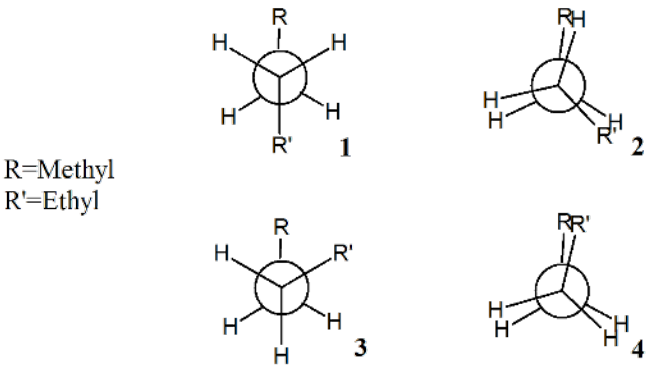
Draw the energy diagram for the rotation of the bond highlighted in pentane.



Solutions

S3.7.1





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CHAPTER OVERVIEW

4: Organic Compounds - Cycloalkanes and their Stereochemistry

Learning Objectives

After you have completed Chapter 4, you should be able to

1. fulfill all of the detailed objectives listed under each individual section.
2. draw the *cis-trans* isomers of some simple disubstituted cycloalkanes, and write the IUPAC names of such compounds.
3. define, and use in context, the key terms introduced in this chapter.

This chapter deals with the concept of stereochemistry and conformational analysis in cyclic compounds. The causes of various ring strains and their effects on the overall energy level of a cycloalkane are discussed. We shall stress the stereochemistry of alicyclic compounds.

4.1: Naming Cycloalkanes
4.2: Cis-Trans Isomerism in Cycloalkanes
4.3: Stability of Cycloalkanes - Ring Strain
4.4: Conformations of Cycloalkanes
4.5: Conformations of Cyclohexane
4.6: Axial and Equatorial Bonds in Cyclohexane
4.7: Conformations of Monosubstituted Cyclohexanes
4.8: Conformations of Disubstituted Cyclohexanes
4.9: Conformations of Polycyclic Molecules

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4.1: Naming Cycloalkanes

Objectives

After completing this section, you should be able to:

- Name a substituted or unsubstituted cycloalkane, given its Kekulé structure, shorthand structure or condensed structure.
- Draw the Kekulé, shorthand or condensed structure for a substituted or unsubstituted cycloalkane, given its IUPAC name.

Key Terms

Make certain that you can define, and use in context, the key terms below.

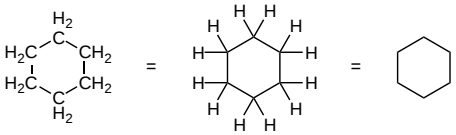
- cycloalkane

Study Notes

Provided that you have mastered the IUPAC system for naming alkanes, you should find that the nomenclature of cycloalkanes does not present any particular difficulties.

Many organic compounds found in nature contain rings of carbon atoms. These compounds are known as **cycloalkanes**. Cycloalkanes only contain carbon-hydrogen bonds and carbon-carbon single bonds. The simplest examples of this class consist of a single, un-substituted carbon ring, and these form a homologous series similar to the unbranched alkanes.

Like alkanes, cycloalkane molecules are often drawn as skeletal structures in which each intersection between two lines is assumed to have a carbon atom with its corresponding number of hydrogens. Cyclohexane, one of the most common cycloalkanes is shown below as an example.



Cyclic hydrocarbons have the prefix "cyclo-". The IUPAC names, molecular formulas, and skeleton structures of the cycloalkanes with 3 to 10 carbons are given in Table **4.1.1**. Note that the general formula for a cycloalkane composed of **n** carbons is C_nH_{2n}, and not C_nH_{2n+2} as for alkanes. Although a cycloalkane has two fewer hydrogens than the equivalent alkane, each carbon is bonded to four other atoms so are still considered to be **saturated** with hydrogen.

Table **4.1.1**: Examples of Simple Cycloalkanes

Cycloalkane	Molecular Formula	Skeleton Structure
Cyclopropane	C_3H_6	
Cyclobutane	C_4H_8	
Cyclopentane	C_5H_{10}	
Cyclohexane	C_6H_{12}	
Cycloheptane	C_7H_{14}	
Cyclooctane	C_8H_{16}	
Cyclononane	C_9H_{18}	
Cyclodecane	$C_{10}H_{20}$	

IUPAC Rules for Nomenclature

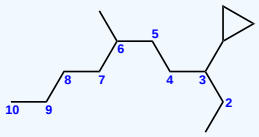
The naming of substituted cycloalkanes follows the same basic steps used in naming alkanes.

1. Determine the parent chain.
2. Number the substituents of the ring beginning at one substituent so that the nearest substituent is numbered the lowest possible. If there are multiple choices that are still the same, go to the next substituent and give it the lowest number possible.
3. Name the substituents and place them in alphabetical order.

More specific rules for naming substituted cycloalkanes with examples are given below.

1. Determine the cycloalkane to use as the parent. If there is an alkyl straight chain that has a greater number of carbons than the cycloalkane, then the alkyl chain must be used as the primary parent chain. Cycloalkanes substituents have an ending "-yl". If there are two cycloalkanes in the molecule, use the cycloalkane with the higher number of carbons as the parent.

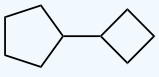
Example 4.1.1



The longest straight chain contains 10 carbons, compared with cyclopropane, which only contains 3 carbons. The parent chain in this molecule is decane and cyclopropane is a substituent. The name of this molecule is 3-cyclopropyl-6-methyldecane.

Example 4.1.2

Name the cycloalkane structure.

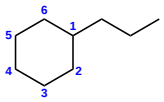


Solution

There are two different cycloalkanes in this molecule. Because it contains more carbons, the cyclopentane ring will be named as the parent chain. The smaller ring, cyclobutane, is named as a substituent on the parent chain. The name of this molecule is cyclobutylcyclopentane.

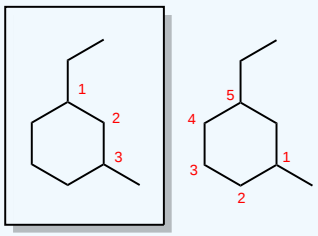
2. When there is only one substituent on the ring, the ring carbon attached to the substituent is automatically carbon #1. Indicating the number of the carbon with the substituent in the name is optional.

Example 4.1.3

	
1-chlorocyclobutane or cholorocyclobutane	1-propylcyclohexane or propylcyclohexane

3. If there are multiple substituents on the ring, number the carbons of the cycloalkane so that the carbons with substituents have the lowest possible number. A carbon with multiple substituents should have a lower number than a carbon with only one substituent or functional group. One way to make sure that the lowest number possible is assigned is to number the carbons so that when the numbers corresponding to the substituents are added, their sum is the lowest possible.
4. When naming the cycloalkane, the substituents must be placed in alphabetical order. Remember the prefixes di-, tri-, etc. , are not used for alphabetization.

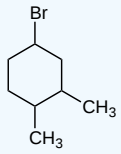
Example 4.1.4



In this example, the ethyl or the methyl subsistent could be attached to carbon one. The ethyl group attachment is assigned carbon 1 because ethyl comes before methyl alphabetically. After assigning carbon 1 the cyclohexane ring can be numbered going clockwise or counterclockwise. When looking at the numbers produced going clockwise produces lower first substituent numbers (1,3) than when numbered counterclockwise (1,5). So the correct name is 1-ethyl-3-methylcyclohexane.

Example 4.1.5

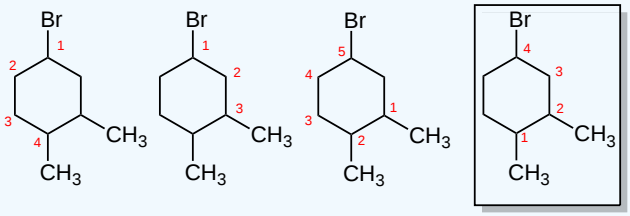
Name the following structure using IUPAC rules.



Solution

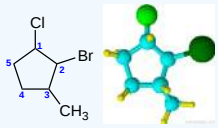
Remember when dealing with cycloalkanes with more than two substituents, finding the lowest possible 2nd substituent numbering takes precedence. Consider a numbering system with each substituent attachment point as being carbon one. Compare them and whichever produces the lowest first point of difference will be correct.

The first structure would have 1,4 for the relationship between the first two groups. The next structure would have 1,3. The final 2 structures both have 1,2 so those are preferable to the first two. Now we have to determine which is better between the final 2 structures. The 3rd substituent on structure 3 would be at the 5 position leading to 1,2,5 while in the final structure the 3rd methyl group is on carbon 4 leading to 1,2,4. This follows the rules of giving the lowest numbers at the first point of difference.



The correct name for the molecule is 4-Bromo-1,2-dimethylcyclohexane.

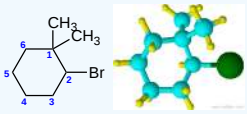
Example 4.1.6



2-bromo-1-chloro-3-methylcyclopentane

Notice that "b" of bromo alphabetically precedes the "m" of methyl. Also, notice that the chlorine attachment point is assigned carbon 1 because it comes first alphabetically and the overall sum of numbers would be the same if the methyl attachment carbon was assigned as 1 and the chlorine attachment as 3.

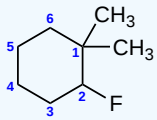
Example 4.1.7



(2-bromo-1,1-dimethylcyclohexane)

Although "di" alphabetically precedes "f", "di" is not used in determining the alphabetical order.

Example 4.1.8



2-fluoro-1,1,-dimethylcyclohexane **NOT** 1,1-dimethyl-2-fluorocyclohexane also 2-fluoro-1,1,-dimethylcyclohexane **NOT** 1-fluoro-2,2-dimethylcyclohexane (as that would give a larger number to the first point of difference)

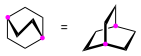
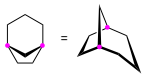
Although "di" alphabetically precedes "f", "di" is not used in determining the alphabetical order of the substituents. Notice that the attachment point of the two methyl groups is assigned carbon 1 despite the fact that fluorine comes first alphabetically. This is because this assignment allows for a lower overall numbering of substituents, so assigning alphabetical priority is not necessary.

Polycyclic Compounds

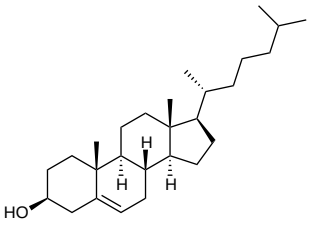
Hydrocarbons having more than one ring are common, and are referred to as **bicyclic** (two rings), **tricyclic** (three rings) and in general, **polycyclic compounds**. The molecular formulas of such compounds have H/C ratios that decrease with the number of rings. In general, for a hydrocarbon composed of n carbon atoms associated with m rings the formula is: $\mathbf{C_nH_{2n+2-2m}}$. The structural relationship of rings in a polycyclic compound can vary. They may be separate and independent, or they may share one or two common atoms. Some examples of these possible arrangements are shown in the following table.

Table **4.1.2**: Examples of Isomeric $\mathbf{C_8H_{14}}$ Bicycloalkanes

https://chem.libretexts.org/@go/page/418098

Isolated Rings	Spiro Rings	Fused Rings	Bridged Rings
No common atoms	One common atom	One common bond	Two common atoms
			
			

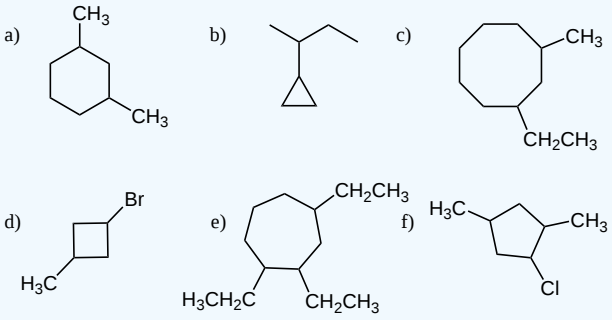
Polycyclic compounds, like cholesterol shown below, are biologically important and typically have common names accepted by IUPAC. However, the common names do not generally follow the basic IUPAC nomenclature rules, and will not be covered here.



Cholesterol (polycyclic)

Exercise 4.1.1

Give the IUPAC names for the following cycloalkane structures.



Answer

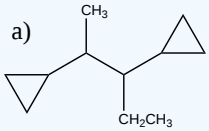
a. 1,3-Dimethylcyclohexane
b. 2-Cyclopropylbutane
c. 1-Ethyl-3-methylcyclooctane
d. 1-Bromo-3-methylcyclobutane
e. 1,2,4-Triethylcycloheptane
f. 1-Chloro-2,4-dimethylcyclopentane

Exercise 4.1.2

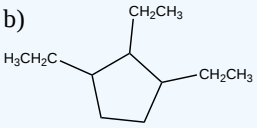
Draw the structures for the IUPAC names below.

a. 2,3-dicyclopropylpentane
b. 1,2,3-triethylcyclopentane
c. 3-cyclobutyl-2-methylhexane
d. 2-bromo-1-chloro-4-methylcyclohexane
e. 1-bromo-5-propylcyclododecane

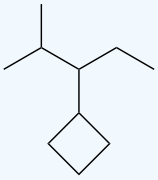
Answer

a) 

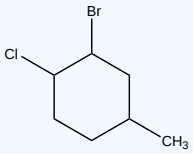
2,3-dicyclopropylpentane

b) 

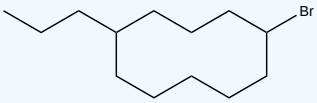
1,2,3-triethylcyclopentane

c) 

3-cyclobutyl-2-methylhexane

d) 

2-bromo-1-chloro-4-methylcyclohexane

e) 

1-bromo-5-propylcyclodecane

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4.2: Cis-Trans Isomerism in Cycloalkanes

Objectives

After completing this section, you should be able to

1. draw structural formulas that distinguish between *cis* and *trans* disubstituted cycloalkanes.
2. construct models of *cis* and *trans* disubstituted cycloalkanes using ball-and-stick molecular models.

Key Terms

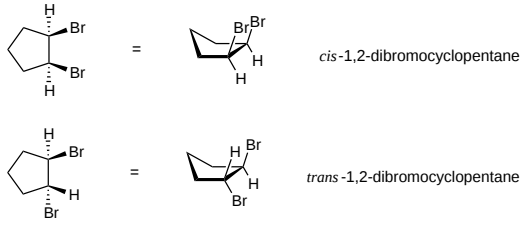
Make certain that you can define, and use in context, the key terms below.

- constitutional isomer
- stereoisomer
- *cis*-*trans* isomers

Previously, constitutional isomers have been defined as molecules that have the same molecular formula, but different atom connectivity. In this section, a new class of isomers, stereoisomers, will be introduced. **Stereoisomers** are molecules that have the same molecular formula, the same atom connectivity, but they differ in the relative spatial orientation of the atoms.

Cycloalkanes are similar to open-chain alkanes in many respects. They both tend to be nonpolar and relatively inert. One important difference, is that cycloalkanes have much less freedom of movement than open-chain alkanes. As discussed in **Sections 3.6 and 3.7**, open-chain alkanes are capable of rotation around their carbon-carbon sigma bonds. The ringed structures of cycloalkanes prevent such free rotation, causing them to be more rigid and somewhat planar.

Di-substituted cycloalkanes are one class of molecules that exhibit stereoisomerism. 1,2-dibromocyclopentane can exist as two different stereoisomers: *cis*-1,2-dibromocyclopentane and *trans*-1,2-dibromocyclopentane. The *cis*-1,2-dibromocyclopentane and *trans*-1,2-dibromocyclopentane stereoisomers of 1,2-dibromocyclopentane are shown below. Both molecules have the same molecular formula and the same atom connectivity. They differ only in the relative spatial orientation of the two bromines on the ring. In *cis*-1,2-dibromocyclopentane, both bromine atoms are on the same "face" of the cyclopentane ring, while in *trans*-1,2-dibromocyclopentane, the two bromines are on opposite faces of the ring. Stereoisomers require an additional nomenclature prefix be added to the IUPAC name in order to indicate their spatial orientation. Di-substituted cycloalkane stereoisomers are designated by the nomenclature prefixes ***cis*** (Latin, meaning on this side) and ***trans*** (Latin, meaning across).

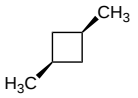


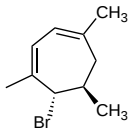
The 3D Structure of *cis*-1,2-dibromocyclopentane

***The 3D Structure of trans*-1,2-dibromocyclopentane**

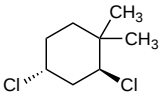
Representing 3D Structures

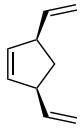
By convention, chemists use heavy, wedge-shaped bonds to indicate a substituent located above the plane of the ring (coming out of the page), a dashed line for bonds to atoms or groups located below the ring (going back into the page), and solid lines for bonds in the plane of the page.





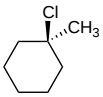
cis-1,3-dimethylcyclobutane *trans*-5-bromo-1,4,6-trimethyl-1,3-cycloheptadiene





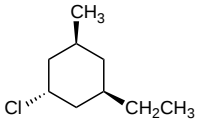
trans-2,4-dichloro-1,1-dimethylcyclohexane *cis*-3,5-divinylcyclopentene

In general, if any two sp^3 carbons in a ring have two different substituent groups (not counting other ring atoms) cis/trans stereoisomerism is possible. However, the cis/trans designations are not used if both groups are on the same carbon. For example, the chlorine and the methyl group are on the same carbon in 1-chloro-1-methylcyclohexane and the *trans* prefix should not be used.



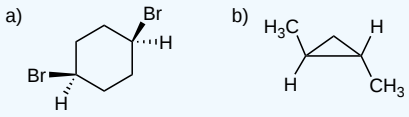
1-chloro-1-methylcyclohexane

If more than two ring carbons have substituents, the stereochemical notation distinguishing the various isomers becomes more complex and the prefixes *cis* and *trans cannot be used to formally name the molecule*. However, the relationship of any two substituents can be informally described using *cis* or *trans*. For example, in the tri-substituted cyclohexane below, the methyl group is *cis* to the ethyl group, and also *trans* to the chlorine. However, the entire molecule cannot be designated as either a *cis* or trans *isomer*.



Example 4.2.1

Name the following cycloalkanes:



Solution

These two example represent the two main ways of showing spatial orientation in cycloalkanes.

a) In example "a" the cycloalkane is shown as being flat and in the plane of the page. The positioning of the substituents is shown by using dash-wedge bonds. Cis/trans positioning can be determined by looking at the type of bonds attached to the substituents. If the substituents are both on the same side of the ring (Cis) they would both have either dash bonds or wedge bonds. If the the substituents are on opposite side of the ring (Trans) one substituent would have a dash bond and the other a wedge bond. Because both bromo substituents have a wedge bond they are one the same side of the ring and are cis. The name of this molecule is cis-1,4-Dibromocyclohexane.

b) Example "b" shows the cycloalkane ring roughly perpendicular to the plane of the page. When this is done, the upper and lower face of the ring is defined and each carbon in the ring will have a bond one the upper face and a bond on the lower face. Cis substituents will either both be on the upper face or the lower face. Trans substituents will have one on the upper face and one one the lower face. In example "b", one of the methyl substituents is on the upper face of the ring and one is on the lower face which makes them trans to each other. The name of this molecule is *trans*-1,2-Dimethylcyclopropane.

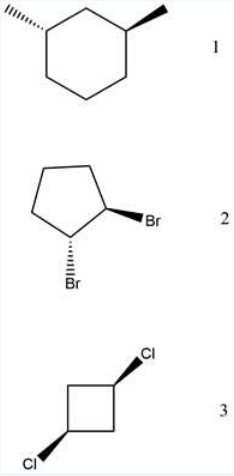
Exercises

Exercise 4.2.1

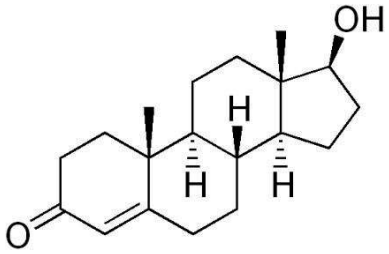
Draw the following molecules:

1. *trans*-1,3-dimethylcyclohexane
2. *trans*-1,2-dibromocyclopentane
3. *cis*-1,3-dichlorocyclobutane

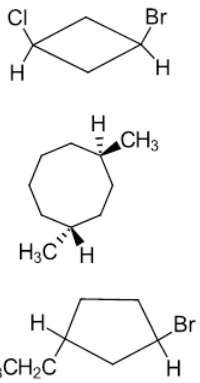
Answer



2) Cis/Trans nomenclature can be used to describe the relative positioning of substituents on molecules with more complex ring structures. The molecule below is tesosterone, the primary male sex hormone. Is the OH and the adjacent methyl group cis or trans to each other? What can you deduce about the relative positions of the indicated hydrogens?



3) Name the following compounds:



Solutions

2) Both the OH and the methyl group have wedge bonds. This implies that they are both on the same side of the testosterone ring making them cis. Two of the hydrogens have wedge bonds while one has a wedge. This means two of the hydrogens are on one side of the testosterone ring while one is on the other side.

3)

Cis-1-Bromo-3-Chlorocyclobutane

Trans-1,4-Dimethylcyclooctane

Trans-1-Bromo-3-ethylcyclopentane

Exercises

4.2 Cis-Trans Isomerism in Cycloalkanes

4.2 Exercises

Questions

Q4.2.1

Draw the following molecules:

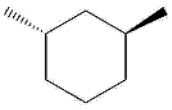
trans-1,3-dimethylcyclohexane

trans-1,2-dibromocyclopentane

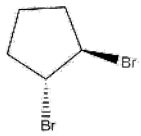
cis-1,3-dichlorocyclobutane

Solutions

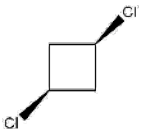
S4.2.1



1



2



3

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4.3: Stability of Cycloalkanes - Ring Strain

Objectives

After completing this section, you should be able to:

- Describe the Baeyer strain theory.
- Describe how the measurement of heats of combustion provides information about the amount of strain present in a cycloalkane ring.
- Determine the relative stability of cyclic compounds, by assessing such factors as angle strain, torsional strain and steric strain.

Key Terms

Make certain that you can define, and use in context, the key terms below.

- angle strain
- steric strain
- torsional strain
- ring strain
- heat of combustion

Heat of Combustion as a Measure of Bond Strength

The combustion of carbon compounds, especially hydrocarbons, has been the most important source of heat energy for human civilizations throughout recorded history. The practical importance of this reaction cannot be denied, but the massive and uncontrolled chemical changes that take place in combustion make it difficult to deduce mechanistic paths. Using the combustion of propane as an example, we see from the following equation that every covalent bond in the reactants has been broken and an entirely new set of covalent bonds have formed in the products. No other common reaction involves such a profound and pervasive change, and the mechanism of combustion is so complex that chemists are just beginning to explore and understand some of its elementary features.

$$\mathrm{CH_3CH_2CH_3 + 5\,O_2 \longrightarrow 3\,CO_2 + 4\,H_2O + heat}$$

Since all the covalent bonds in the reactant molecules are broken, the quantity of heat evolved in this reaction, and any other combustion reaction, is related to the strength of these bonds (and, of course, the strength of the bonds formed in the products). Precise heat of combustion measurements can provide useful information about the structure of molecules and their relative stability.

For example, heat of combustion is useful in determining the relative stability of isomers. Pentane has a heat of combustion of -782 kcal/mol, while that of its isomer, 2,2-dimethylpropane (neopentane), is –777 kcal/mol. These values indicate that 2,3-dimethylpentane is 5 kcal/mol more stable than pentane, since it has a lower heat of combustion.

Ring Strain

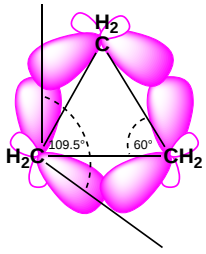
Table **4.3.1** lists the heat of combustion data for some simple cycloalkanes. These cycloalkanes do not have the same molecular formula, so the heat of combustion per each CH_2 unit present in each molecule is calculated (the fourth column) to provide a useful comparison. From the data, cyclopropane and cyclobutane have significantly higher heats of combustion per CH_2, while cyclohexane has the lowest heat of combustion. This indicates that cyclohexane is more stable than cyclopropane and cyclobutane, and in fact, that cyclohexane has a same relative stability as long chain alkanes that are not cyclic. This difference in stability is seen in nature where six membered rings are by far the most common. What causes the difference in stability or the strain in small cycloalkanes?

Table **4.3.1**: Heats of combustion of select hydrocarbons

Cycloalkane $(CH_2)_n$	CH_2 Units n	ΔH^{25° kcal/mol	ΔH^{25° per CH_2 Unit	Ring Strain kcal/mol
Cyclopropane	n = 3	468.7	156.2	27.6
Cyclobutane	n = 4	614.3	153.6	26.4
Cyclopentane	n = 5	741.5	148.3	6.5
Cyclohexane	n = 6	882.1	147.0	0.0
Cycloheptane	n = 7	1035.4	147.9	6.3
Cyclooctane	n = 8	1186.0	148.2	9.6
Cyclononane	n = 9	1335.0	148.3	11.7
Cyclodecane	n = 10	1481	148.1	11.0
$CH_3(CH_2)_mCH_3$	m = large	—	147.0	0.0

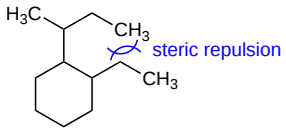
The Baeyer Theory on the Strain in Cycloalkane Rings

In 1890, the famous German organic chemist, A. Baeyer, suggested that cyclopropane and cyclobutane are less stable than cyclohexane, because the the smaller rings are more "strained". There are many different types of strain that contribute to the overall ring strain in cycloalkanes, including angle strain, torsional strain, and steric strain. **Torsional strain** and **steric strain** were previously defined in the discussion of conformations of butane. **Angle Strain** occurs when the sp^3 hybridized carbons in cycloalkanes do not have the expected ideal bond angle of 109.5°, causing an increase in the potential energy. An example of angle strain can be seen in the diagram of cyclopropane below in which the bond angle is 60° between the carbons. The compressed bond angles causes poor overlap of the hybrid orbitals forming the carbon-carbon sigma bonds which in turn creates destabilization.



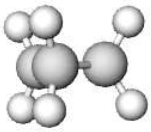
The C-C-C bond angles in cyclopropane (diagram above) (60°) and cyclobutane (90°) are much different than the ideal bond angle of 109.5°. This bond angle causes cyclopropane and cyclobutane to be less stable than molecules such as cyclohexane and cyclopentane, which have a much lower ring strain because the bond angle between the carbons is much closer to 109.5°. Changes in chemical reactivity as a consequence of angle strain are dramatic in the case of cyclopropane, and are also evident for cyclobutane.

In addition to angle strain, there is also steric (transannular) strain and torsional strain in many cycloalkanes. Transannular strain exists when there is steric repulsion between atoms.



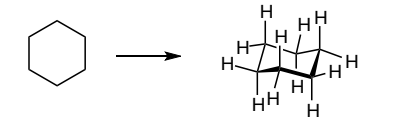
transannular strain

Because cycloalkane lack the ability to freely rotate, torsional (eclipsing) strain exists when a cycloalkane is unable to adopt a staggered conformation around a C-C bond. Torsional strain is especially prevalent in small cycloalkanes, such as cyclopropane, whose structures are nearly planar.



The Eclipsed C-H Bonds in Cyclopropane

Larger rings like cyclohexane, deal with torsional strain by forming conformers in which the rings are not planar. A conformer is a stereoisomer in which molecules of the same connectivity and formula exist as different isomers, in this case, to reduce ring strain. The ring strain is reduced in conformers due to the rotations around the sigma bonds, which decreases the angle and torsional strain in the ring. The non-planar structures of cyclohexane are very stable compared to cyclopropane and cyclobutane, and will be discussed in more detail in the next section.



The Types of Strain Which Contribute to Ring Strain in Cycloalkanes

- Angle Strain - The strain caused by the increase or reduction of bond angles
- Torsional Strain - The strain caused by eclipsing bonds on adjacent atoms
- Steric Strain - The strain caused by the repulsive interactions of atoms trying to occupy the same space

Exercise 4.3.1

trans-1,2-Dimethylcyclobutane is more stable than *cis*-1,2-dimethylcyclobutane. Explain this observation.

Answer

The trans form does not have eclipsing methyl groups, therefore lowering the energy within the molecule. It does however have hydrogen-methyl eclipsing interactions which are not as high in energy as methyl-methyl interactions.

Exercise 4.3.2

Cyclobutane has more torsional stain than cyclopropane. Explain this observation.

Answer

Cyclobutane has 4 CH_2 groups while cyclopropane only has 3. More CH2 groups means cyclobutane has more eclipsing H-H interactions and therefore has more torsional strain.

Exercises

1. *Trans*-1,2-Dimethylcyclobutane is more stable than *cis*-1,2-dimethylcyclobutane. Explain this observation.
2. The trans form does not have eclipsing methyl groups, therefore lowering the energy within the molecule. It does however have hydrogen-methyl interactions, but are not as high in energy than methyl-methyl interactions.

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4.4: Conformations of Cycloalkanes

Objectives

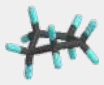
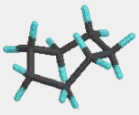
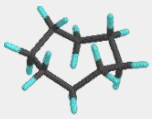
After completing this section, you should be able to

1. describe, and sketch the conformation of cyclopropane, cyclobutane, and cyclopentane.
2. describe the bonding in cyclopropane, and use this to account for the high reactivity of this compound.
3. analyze the stability of cyclobutane, cyclopentane and their substituted derivatives in terms of angular strain, torsional strain and steric interactions.

Study Notes

Notice that in both cyclobutane and cyclopentane, torsional strain is reduced at the cost of increasing angular (angle) strain.

Although the customary line drawings of simple cycloalkanes are geometrical polygons, the actual shape of these compounds in most cases is very different.

cyclopropane	cyclobutane	cyclopentane	cyclohexane	cycloheptane	cyclooctane
					

Cyclopropane is necessarily planar (flat), with the carbon atoms at the corners of an equilateral triangle. The 60º bond angles are much smaller than the optimum 109.5º angles of a normal tetrahedral carbon atom, and the resulting angle strain dramatically influences the chemical behavior of this cycloalkane. Cyclopropane also suffers substantial eclipsing strain, since all the carbon-carbon bonds are fully eclipsed. Cyclobutane reduces some bond-eclipsing strain by folding (the out-of-plane dihedral angle is about 25º), but the total eclipsing and angle strain remains high. Cyclopentane has very little angle strain (the angles of a pentagon are 108º), but its eclipsing strain would be large (about 40 kJ/mol) if it remained planar. Consequently, the five-membered ring adopts non-planar puckered conformations whenever possible.

Rings larger than cyclopentane would have angle strain if they were planar. However, this strain, together with the eclipsing strain inherent in a planar structure, can be relieved by puckering the ring. Cyclohexane is a good example of a carbocyclic system that virtually eliminates eclipsing and angle strain by adopting non-planar conformations. Cycloheptane and cyclooctane have greater strain than cyclohexane, in large part due to transannular crowding (steric hindrance by groups on opposite sides of the ring).

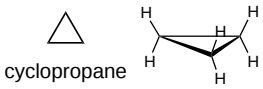
Cyclic systems are a little different from open-chain systems. In an open chain, any bond can be rotated 360º, going through many different conformations. That complete rotation isn't possible in a cyclic system, because the parts that would be trying to twist away from each other would still be connected together. Thus cyclic systems have fewer "degrees of freedom" than aliphatic systems; they have "restricted rotation".

Because of the restricted rotation of cyclic systems, most of them have much more well-defined shapes than their aliphatic counterparts. Let's take a look at the basic shapes of some common rings. Many biologically important compounds are built around structures containing rings, so it's important that we become familiar with them. In nature, three- to six-membered rings are frequently encountered, so we'll focus on those.

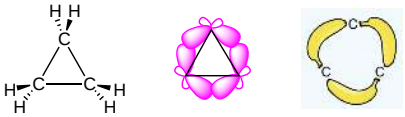
Cyclopropane

A three membered ring has no rotational freedom whatsoever. A plane is defined by three points, so the three carbon atoms in cyclopropane are all constrained to lie in the same plane. This lack of flexibility does not allow cyclopropane to form more stable

conformers which are non-planar.



The main source of ring strain in cyclopropane is angle strain. All of the carbon atoms in cyclopropane are tetrahedral and would prefer to have a bond angle of 109.5^o The angles in an equilateral triangle are actually 60^o, about half as large as the optimum angle. The large deviation from the optimal bond angle means that the C-C sigma bonds forming the cyclopropane ring are bent. Maximum bonding occurs when the overlapping orbitals are pointing directly toward each other. The severely strained bond angles in cyclopropane means that the orbitals forming the C-C bonds overlap at a slight angle making them weaker. This strain is partially overcome by using so-called “banana bonds”, where the overlap between orbitals is no longer directly in a line between the two nuclei, as shown here in three representations of the bonding in cyclopropane:



The constrained nature of cyclopropane causes neighboring C-H bonds to all be held in eclipsed conformations. Cyclopropane is always at maximum torsional strain. This strain can be illustrated in a Newman projections of cyclopropane as shown from the side.



Newman Projection of cyclopropane

Cyclopropane isn't large enough to introduce any steric strain. Steric strain does not become a factor until we reach six membered rings. Before that point, rings are not flexible enough to allow for two ring substituents to interact with each other.

The combination of torsional and angle strain creates a large amount of ring strain in cyclopropane which weakens the C-C ring bonds (255 kJ/mol) when compared to C-C bonds in open-chain propane (370 kJ/mol).

Cyclobutane

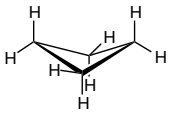
Cyclobutane is a four membered ring. The larger number of ring hydrogens would cause a substantial amount of torsional strain if cyclobutane were planar.



cyclobutane

In three dimensions, cyclobutane is flexible enough to buckle into a "puckered" shape which causes the C-H ring hydrogens to slightly deviate away from being completely eclipsed. This conformation relives some of the torsional strain but increases the angle strain because the ring bond angles decreases to 88^o.

In a line drawing, this butterfly shape is usually shown from the side, with the near edges drawn using darker lines.



The deviation of cyclobutane's ring C-H bonds away from being fully eclipsed can clearly be seen when viewing a Newman projections signed down one of the C-C bond.



Newman projection of cyclobutane

- With bond angles of 88^o rather than 109.5^o degrees, cyclobutane has significant amounts of angle strain, but less than in cyclopropane.
- Although torsional strain is still present, the neighboring C-H bonds are not exactly eclipsed in the cyclobutane's puckered conformation.
- Steric strain is very low. Cyclobutane is still not large enough that substituents can reach around to cause crowding.
- Overall the ring strain in cyclobutane (110 kJ/mol) is slightly less than cyclopropane (115 kJ/mol).

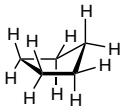
Cyclopentane

Cyclopentanes are even more stable than cyclobutanes, and they are the second-most common cycloalkane ring in nature, after cyclohexanes. Planar cyclopentane has virtually no angle strain but an immense amount of torsional strain. To reduce torsional strain, cyclopentane addops a non-planar conformation even though it slightly increases angle strain.



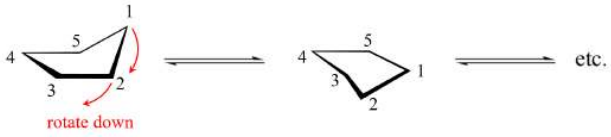
cyclopentane

The lowest energy conformation of cyclopentane is known as the ‘envelope’, with four of the ring atoms in the same plane and one out of plane (notice that this shape resembles an envelope with the flap open). The out-of-plane carbon is said to be in the ***endo*** position (‘*endo*’ means ‘inside’). The envelope removes torsional strain along the sides and flap of the envelope. However, the neighboring carbons are eclipsed along the "bottom" of the envelope, away from the flap.

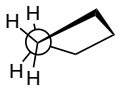


3D structure of cyclopentane (notice that the far top right carbon is the endo position).

At room temperature, cyclopentane undergoes a rapid bond **rotation** process in which each of the five carbons takes turns being in the *endo* position.



Cyclopentane distorts only very slightly into an "envelope" shape in which one corner of the pentagon is lifted up above the plane of the other four. The envelope removes torsional strain along the sides and flap of the envelope by allowing the bonds to be in an almost completely staggered position. However, the neighboring bonds are eclipsed along the "bottom" of the envelope, away from the flap. Viewing a Newman projections of cyclopentane signed down one of the C-C bond show the staggered C-H bonds.

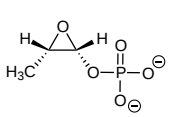


Newman projection of cyclopentane

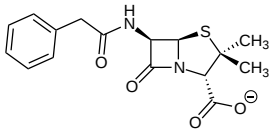
- The angle strain in the envelope conformation of cyclopentane is low. The ideal angle in a regular pentagon is about 107^o, very close to the preferred 109.5^o tetrahedral bond angle.
- There is some torsional strain in cyclopentane. The envelope conformation reduces torsional strain by placing some bonds in nearly staggered positions. However, other bonds are still almost fully eclipsed.
- Cyclopentane is not large enough to allow for steric strain to be created.
- Overall, cyclopentane has very little ring strain (26 kJ/mol) when compared to cyclopropane and cyclobutane.

C_3-C_5 Cycloalkanes in Nature

If one of the carbon-carbon bonds is broken in cyclopropane or cyclobutane, the ring will 'spring' open, releasing energy as the bonds reassume their preferred tetrahedral geometry. The effectiveness of two antibiotic drugs, fosfomycin and penicillin, is due in large part to the high reactivity of the three- and four-membered rings in their structures.

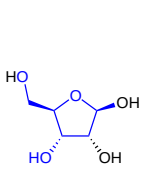


fosfomycin

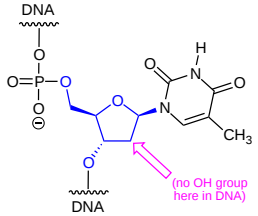


penicillin G

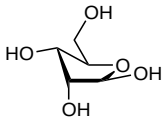
One of the most important five-membered rings in nature is a sugar called ribose – DNA and RNA are both constructed upon 'backbones' derived from ribose. Pictured below is one thymidine (T) deoxy-nucleotide from a stretch of DNA. Since the ribose has lost one of the OH groups (at carbon 2 of the ribose ring), this is part of a deoxyribonucleic acid (DNA). If the OH at carbon 2 of the ribose ring was present, this would be part of a ribonucleic acid (RNA).



ribose



The lowest-energy conformations for ribose are envelope forms in which either C_3 or C_2 are *endo*, on the same side as the C_5 substituent.



? Exercise 4.4.1

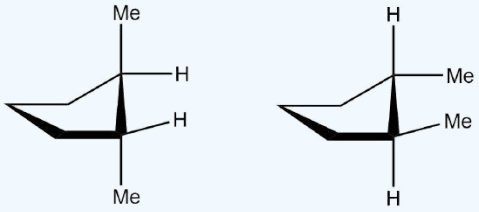
If cyclobutane were to be planar, how many H-H eclipsing interactions would there be? Assuming 4 kJ/mol per H-H eclipsing interaction what would the strain be on this "planar" molecule?

Answer

There are eight eclipsing interactions (two per C-C bond). The extra strain on this molecule would be 32 kJ/mol (4 kJ/mol x 8).

? Exercise 4.4.1

In the two conformations of *trans*-1,2-Dimethylcyclopentane one is more stable than the other. Explain why this is.



Answer

The first conformation is more stable. Even though the methyl groups are *trans* in both models, they are anti to one another in the first structure (which is lower energy) while they are gauche in the second structure increasing strain within the

molecule.

Exercise 4.4.3

In methylcyclopentane, which carbon would most likely be in the *endo* position?

Answer

The ring carbon attached to the methyl group would most likely be the endo carbon. The large methyl group would create the most torsional strain if eclipsed. Being in the *endo* position would place the bonds is a more staggered position which would reduce strain.

Exercise 4.4.4

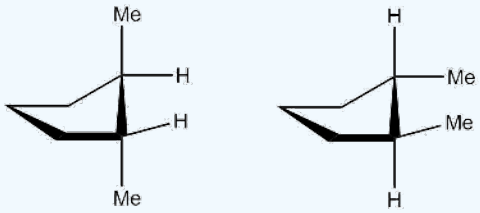
If cyclobutane were to be planar how many H-H eclipsing interactions would there be, and assuming 4 kJ/mol per H-H eclipsing interaction what is the strain on this “planar” molecule?

Answer

There are eight eclipsing interactions (two per C-C bond). The extra strain on this molecule would be 32 kJ/mol (4 kJ/mol x 8).

Exercise 4.4.5

In the two conformations of *trans*-cyclopentane one is more stable than the other. Explain why this is.



Answer

The first conformation is more stable. Even though the methyl groups are *trans* in both models, in the second structure they are eclipsing one another, therefore increasing the strain within the molecule compared to the first structure where the larger methyl groups are anti to one another.

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4.5: Conformations of Cyclohexane

Objectives

After completing this section, you should be able to

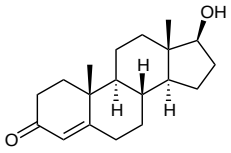
1. explain why cyclohexane rings are free of angular strain.
2. draw the structure of a cyclohexane ring in the chair conformation.

Key Terms

Make certain that you can define, and use in context, the key terms below.

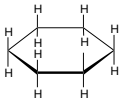
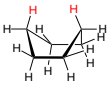
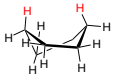
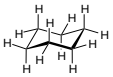
- chair conformation
- twist-boat conformation

We will find that cyclohexanes tend to have the least angle strain and consequently are the most common cycloalkanes found in nature. A wide variety of compounds including, hormones, pharmaceuticals, and flavoring agents have substituted cyclohexane rings.



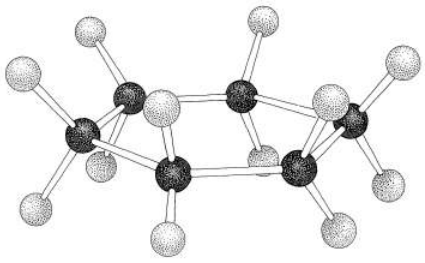
testosterone, which contains three cyclohexane rings and one cyclopentane ring

Rings larger than cyclopentane would have angle strain if they were planar. However, this strain, together with the eclipsing strain inherent in a planar structure, can be relieved by puckering the ring. Cyclohexane is a good example of a carbocyclic system that virtually eliminates eclipsing and angle strain by adopting non-planar conformations. Cycloheptane and cyclooctane have greater strain than cyclohexane, in large part due to transannular crowding (steric hindrance by groups on opposite sides of the ring). Cyclohexane has the possibility of forming multiple conformations each of which have structural differences which lead to different amounts of ring strain.

			
planar structure severe angle strain (120°) severe eclipsing strain (all bonds) small steric strain	**boat conformation** slight angle strain eclipsing strain at two bonds steric crowding of two hydrogens	**twist boat conformation** slight angle strain small eclipsing strain small steric strain	**chair conformation** no angle strain no eclipsing strain small steric strain

Conformations of Cyclohexane

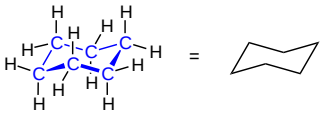
A planar structure for cyclohexane is clearly improbable. The bond angles would necessarily be 120º, 10.5º larger than the ideal tetrahedral angle. Also, every carbon-hydrogen bond in such a structure would be eclipsed. The resulting angle and eclipsing strains would severely destabilize this structure. The ring strain of planar cyclohexane is in excess of 84 kJ/mol so it rarely discussed other than in theory.



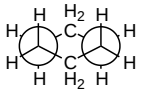
Cyclohexane in the strained planar configuration showing how the hydrogens become eclipsed.

Chair Conformation of Cyclohexane

The flexibility of cyclohexane allows for a conformation which is almost free of ring strain. If two carbon atoms on opposite sides of the six-membered ring are bent out of the plane of the ring, a shape is formed that resembles a reclining beach chair. This **chair conformation** is the lowest energy conformation for cyclohexane with an overall ring strain of 0 kJ/mol. In this conformation, the carbon-carbon ring bonds are able to assume bonding angles of ~111º which is very near the optimal tetrahedral 109.5º so angle strain has been eliminated.

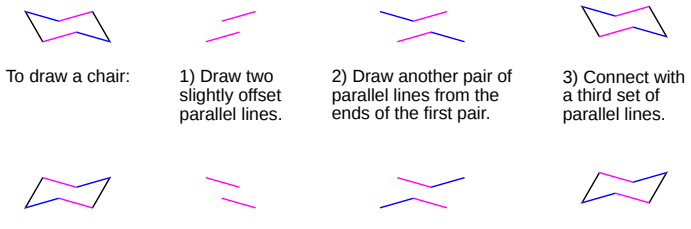


Also, the C-H ring bonds are staggered so torsional strain has also been eliminated. This is clearly seen when looking at a Newman projection of chair cyclohexane sighted down the two central C-C bonds.



Newman projection of cyclohexane

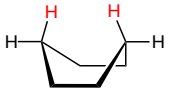
How to Draw the Chair Conformation



To draw its ring-flip conformer, just start the first pair of lines at the opposite angle.

Boat Conformation of Cyclohexane

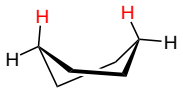
The **Boat Conformation** of cyclohexane is created when two carbon atoms on opposite sides of the six-membered ring are both lifted up out of the plane of the ring creating a shape which slightly resembles a boat. The boat conformation is less stable than the chair form for two major reasons. The boat conformation has unfavorable steric interactions between a pair of 1,4 hydrogens (the so-called "flagpole" hydrogens) that are forced to be very close together (1.83Å). This steric hindrance creates a repulsion energy of about 12 kJ/mol. An additional cause of the higher energy of the boat conformation is that adjacent hydrogen atoms on the 'bottom of the boat' are forced into eclipsed positions. For these reasons, the boat conformation about 30 kJ/mol less stable than the chair conformation.



A boat structure of cyclohexane (the interfering "flagpole" hydrogens are shown in red)

Twist-Boat Conformation of Cyclohexane

The boat form is quite flexible and by twisting it at the bottom created the **twist-boat conformer**. This conformation reduces the strain which characterized the boat conformer. The flagpole hydrogens move farther apart (the carbons they are attached to are shifted in opposite directions, one forward and one back) and the eight hydrogens along the sides become largely but not completely staggered. Though more stable than the boat conformation, the twist-boat (sometimes skew-boat) conformation is roughly 23 kJ/mol less stable than the chair conformation.



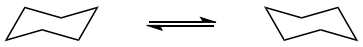
A twist-boat structure of cyclohexane

Half Chair Conformation of Cyclohexane

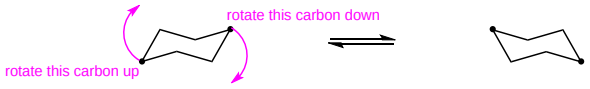
Cyclohexane can obtain a partially plane conformation called "half chair" but with only with excessive amounts of ring strain. The half chair conformation is formed by taking planar cyclohexane and lifting one carbon out of the plane of the ring. The half chair conformation has much of the same strain effects predicted by the fully planar cyclohexane. In the planar portion of half chair cyclohexane the C-C bond angles are forced to 120^{o} which creates significant amounts of angle strain. Also, the corresponding C-H bonds are fully eclipsed which create torsional strain. The out-of-plane carbon allows for some of the ring's bond angles to reach 109.5^{o} and for some of C-H bonds to not be fully eclipsed. Overall, the half chair conformation is roughly 45 kJ/mol less stable than the chair conformation.

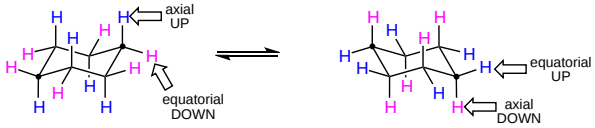
Conformation Changes in Cyclohexane - "Ring Flips"

Cyclohexane is rapidly rotating between the two most stable conformations known as the chair conformations in what is called the "ring flip" shown below. The importance of the ring flip will be discussed in the next section.

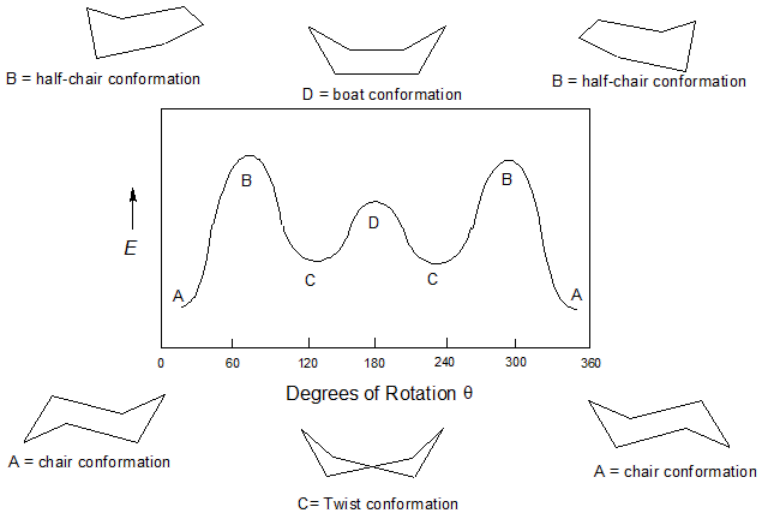


"Ring flip" describes the rapid equilibrium of cyclohexane rings between the two chair conformations





It is important to note that one chair does not immediately become the other chair, rather the ring must travel through the higher energy conformations as transitions. At room temperature the energy barrier created by the half chair conformation is easily overcome allowing for equilibration between the two chair conformation on the order of 80,000 times per second. Although cyclohexane is continually converting between these different conformations, the stability of the chair conformation causes it to comprises more than 99.9% of the equilibrium mixture at room temperature.



1" id="MathJax-Element-12-Frame" role="presentation" style="position:relative;" tabindex="0">Image of energy diagram of cyclohexane conformations

1" role="presentation" style="position:relative;" tabindex="0">

Exercises

1) Consider the conformations of cyclohexane: half chair, chair, boat, twist boat. Order them in increasing ring strain in the molecule.

Solutions

1) Chair < Twist Boat < Boat < half chair (most ring strain)

Questions

Q4.5.1

Consider the conformations of cyclohexane, chair, boat, twist boat. Order them in increasing strain in the molecule.

Solutions

S4.5.1

Chair < Twist Boat < Boat (most strain)

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4.6: Axial and Equatorial Bonds in Cyclohexane

Objectives

After completing this section, you should be able to

1. Draw the chair conformation of cyclohexane, with axial and equatorial hydrogen atoms clearly shown and identified.
2. identify the axial and equatorial hydrogens in a given sketch of the cyclohexane molecule.
3. explain how chair conformations of cyclohexane and its derivatives can interconvert through the process of ring flip.

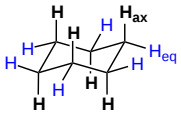
Key Terms

Make certain that you can define, and use in context, the key terms below.

- axial position
- equatorial position
- ring flip

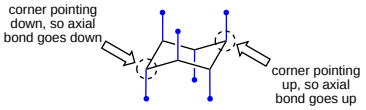
Axial and Equatorial Positions in Cyclohexane

Careful examination of the chair conformation of cyclohexane, shows that the twelve hydrogens are not structurally equivalent. Six of them are located about the periphery of the carbon ring, and are termed **equatorial**. The other six are oriented above and below the approximate plane of the ring (three in each location), and are termed **axial** because they are aligned parallel to the symmetry axis of the ring.

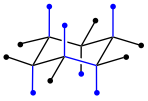


In the figure above, the equatorial hydrogens are colored blue, and the axial hydrogens are black. Since there are two equivalent chair conformations of cyclohexane in rapid equilibrium, all twelve hydrogens have 50% equatorial and 50% axial character.

How To Draw Axial and Equatorial Bonds

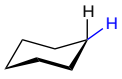


Draw axial bonds **straight up** or **straight down.**



Draw equatorial bonds **up and out** or **down and out.**

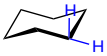
How **not** to draw the chair:



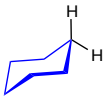
Incorrect. Equatorial bond should be **down** and **out**.



Incorrect. Axial bond should be **straight up**.



Incorrect. Axial bond should be **straight down,** equatorial bond should be **up** and **out**.



Incorrect. Ring should be tilted slightly.

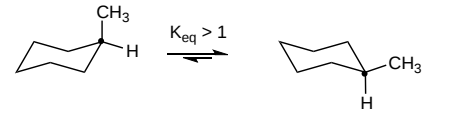
Aside from drawing the basic chair, the key points are:

- Axial bonds alternate up and down, and are shown "vertical".
- Equatorial groups are approximately horizontal, but actually somewhat distorted from that (slightly up or slightly down), so that the angle from the axial group is a bit more than a right angle -- reflecting the common 109.5^{o} bond angle.
- Each carbon has an axial and an equatorial bond.
- Each face of the cyclohexane ring has three axial and three equatorial bonds.

- Each face alternates between axial and equatorial bonds. Then looking at the "up" bond on each carbon in the cyclohexane ring they will alternate axial-equatorial-axial ect.
- When looking down at a cyclohexane ring:
  - the equatorial bonds will form an "equator" around the ring.
  - The axial bonds will either face towards you or away. These will alternate with each axial bond. The first axial bond will be coming towards with the next going away. There will be three of each type.
- Note! The terms cis and trans in regards to the stereochemistry of a ring are not directly linked to the terms axial and equatorial. It is very common to confuse the two. It typically best not to try and directly inter convert the two naming systems.

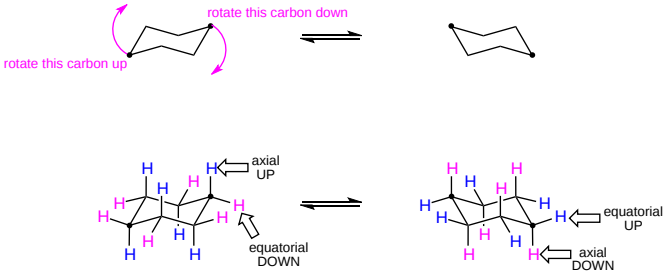
Axial vs. Equatorial Substituents

When a substituent is added to cyclohexane, the ring flip allows for two distinctly different conformations. One will have the substituent in the axial position while the other will have the substituent in the equatorial position. In the next section will discuss the energy differences between these two possible conformations. Below are the two possible chair conformations of methylcyclohexane created by a ring-flip. Although the conformation which places the methyl group in the equatorial position is more stable by 7 kJ/mol, the energy provided by ambient temperature allows the two conformations to rapidly interconvert.



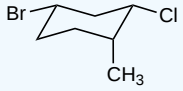
methyl group axial — methyl group equatorial (more stable by **7 kJ/mol**)

The figure below illustrates how to convert a molecular model of cyclohexane between two different chair conformations - this is something that you should practice with models. Notice that a 'ring flip' causes equatorial groups to become axial, and vice-versa.



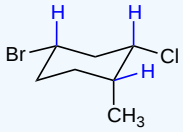
Example 4.6.1

For the following please indicate if the substituents are in the axial or equatorial positions.



Solution

Due to the large number of bonds in cyclohexane it is common to only draw in the relevant ones (leaving off the hydrogens unless they are involved in a reaction or are important for analysis). It is still possible to determine axial and equatorial positioning with some thought. With problems such as this it is important to remember that each carbon in a cyclohexane ring has one axial and one equatorial bond. Also, remember that axial bonds are perpendicular with the ring and appear to be going either straight up or straight down. Equatorial bonds will be roughly in the plane of the cyclohexane ring (only slightly up or down). Sometimes it is valuable to draw in the additional bonds on the carbons of interest.



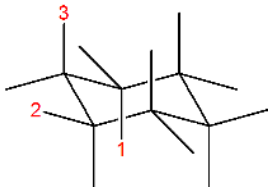
With this it can be concluded that the bromine and chlorine substituents are attached in equatorial positions and the CH_3 substituent is attached in an axial position.

Exercises

1) Draw two conformations of cyclohexyl amine ($C_6H_{11}NH_2$). Indicate axial and equatorial positions.

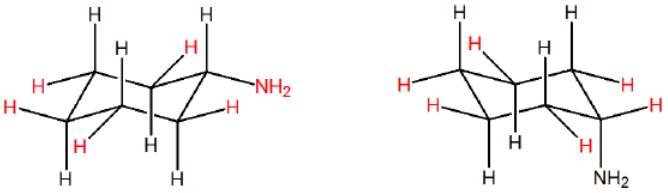
2) Draw the two isomers of 1,4-dihydroxylcyclohexane, identify which are equatorial and axial.

3) In the following molecule, label which are equatorial and which are axial, then draw the chair flip (showing labels 1,2,3).



Solutions

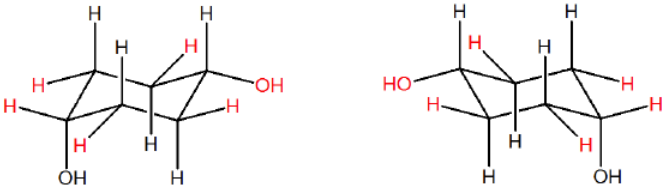
1)



Axial

Equatorial

2)

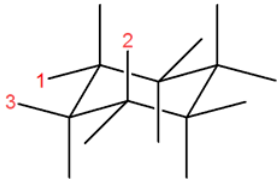


Axial

Equatorial

3) Original conformation: 1 = axial, 2 = equatorial, 3 = axial

Flipped chair now looks like this.



Questions

Q4.6.1

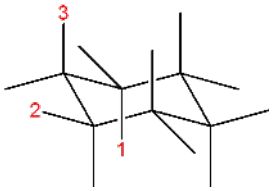
Draw two conformations of cyclohexyl amine ($C_6H_{11}NH_2$). Indicate axial and equatorial positions.

Q4.6.2

Draw the two isomers of 1,4-dihydroxylcyclohexane, identify which are equatorial and axial.

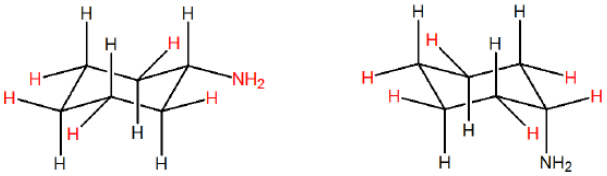
Q4.6.3

In the following molecule, label which are equatorial and which are axial, then draw the chair flip (showing labels 1,2,3).



Solutions

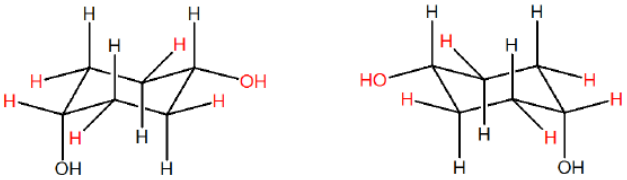
S4.6.1



Axial

Equatorial

S4.6.2



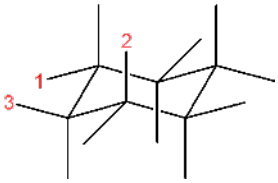
Axial

Equatorial

S4.6.3

Original conformation: 1 = axial, 2 = equatorial, 3 = axial

Flipped chair now looks like this.



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4.7: Conformations of Monosubstituted Cyclohexanes

Objectives

After completing this section, you should be able to

1. account for the greater stability of the equatorial conformers of monosubstituted cyclohexanes compared to their axial counterparts, using the concept of 1,3-diaxial interaction.
2. compare the gauche interactions in butane with the 1,3-diaxial interactions in the axial conformer of methylcyclohexane.
3. arrange a given list of substituents in increasing or decreasing order of 1,3-diaxial interactions.

Key Terms

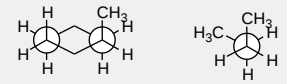
Make certain that you can define, and use in context, the key term below.

- 1,3-diaxial interaction

Study Notes

1,3-Diaxial interactions are steric interactions between an axial substituent located on carbon atom 1 of a cyclohexane ring and the hydrogen atoms (or other substituents) located on carbon atoms 3 and 5.

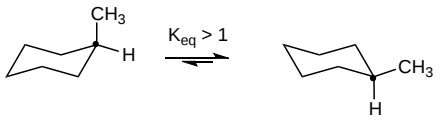
Be prepared to draw Newman-type projections for cyclohexane derivatives as the one shown for methylcyclohexane. Note that this is similar to the Newman projections from chapter 3 such as *n*-butane.



methylcyclohexane *n*-butane

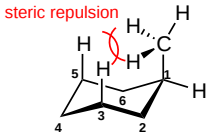
Newman projections of methylcyclohexane and *n*-butane

When a substituent is added to a cyclohexane ring, the two possible chair conformations created during a ring flip are not equally stable. In the example of methylcyclohexane the conformation where the methyl group is in the equatorial position is more stable than the axial conformation by 7.6 kJ/mol at 25° C. The percentages of the two different conformations at equilibrium can be determined by solving the following equation for K (the equilibrium constant): $\Delta E = -RT\ln K$. In this equation ΔE is the energy difference between the two conformations, R is the gas constant (8.314 J/mol•K), T is the temperature in Kelvin, and K is the equilibrium constant for the ring flip conversion. Using this equation, we can calculate a K value of 21 which means about 95% methylcyclohexane molecules have the methyl group in the equatorial position at 25° C.

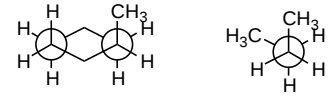


methyl group axial methyl group equatorial (more stable by **7 kJ/mol**)

The energy difference between the two conformations comes from strain, called 1,3-diaxial interactions, created when the axial methyl group experiences steric crowding with the two axial hydrogens located on the same side of the cyclohexane ring. Because axial bonds are parallel to each other, substituents larger than hydrogen experience greater steric crowding when they are oriented axial rather than equatorial. Consequently, ***substituted cyclohexanes will preferentially adopt conformations in which the larger substituents are in the equatorial orientation***. When the methyl group is in the equatorial position this strain is not present which makes the equatorial conformer more stable and favored in the ring flip equilibrium.



Actually, 1,3-diaxial steric strain is directly related to the steric strain created in the gauche conformer of butane discussed in Section: 3-7. When butane is in the gauche conformation 3.8 kJ/mol of strain was created due the steric crowding of two methyl group with a 60° dihedral angle. When looking at the a Newman projection of axial methylcyclohexane the methyl group is at a 60° dihedral angle with the ring carbon in the rear. This creates roughly the same amount of steric strain as the gauche conformer of butante. Given that there is actually two such interactions in axial methylcyclohexane, it makes sense that there is 2(3.8 kJ/mol) = 7.6 kJ/mol of steric strain in this conformation. The Newman projection of equatorial methylcyclohexane shows no such interactions and is therefore more stable.



methylcyclohexane *n*-butane

Newman projections of methyl cyclohexane and butane showing similarity of 1,3-diaxial and gauche interactions.

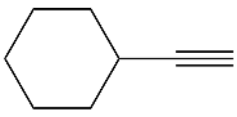
Strain values for other cyclohexane substituents can also be considered. The relative steric hindrance experienced by different substituent groups oriented in an axial versus equatorial location on cyclohexane determined the amount of strain generated. The strain generated can be used to evaluate the relative tendency of substituents to exist in an equatorial or axial location. Looking at the energy values in this table, it is clear that as the size of the substituent increases, the 1,3-diaxial energy tends to increase, also. Note that it is the size and not the molecular weight of the group that is important. Table 4.7.1 summarizes some of these strain values values.

Table 4.7.1: A Selection of ΔG° *Values for the Change from Axial to Equatorial Orientation of Substituents for Monosubstituted Cyclohexanes*

Substituent	-ΔG° (kcal/mol)	Substituent	-ΔG° (kcal/mol)
CH_3–	1.7	O_2N–	1.1
CH_2H_5–	1.8	N≡C–	0.2
$(CH_3)_2CH$–	2.2	CH_3O–	0.5
$(CH_3)_3C$–	≥ 5.0	HO_2C–	0.7
F–	0.3	H_2C=CH–	1.3
Cl–	0.5	C_6H_5–	3.0
Br–	0.5		
I–	0.5		

Exercises

1) In the molecule, cyclohexyl ethyne there is little steric strain, why?



2) Calculate the energy difference between the axial and equatorial conformations of bromocyclohexane?

3) Using your answer from Question 2) estimate the percentages of axial and equatorial conformations of bromocyclohexane at 25° C.



Bromo group axial **Bromo** group equitorial

4) There very little in 1,3-diaxial strain when going from a methyl substituent (3.8 kJ/mol) to an ethyl substituent (4.0 kJ/mol), why? It may help to use molecular model to answer this question.

Solutions

1) The ethyne group is linear and therefore does not affect the hydrogens in the 1,3 positions to say to the extent as a bulkier or a bent group (e.g. ethene group) would. This leads to less of a strain on the molecule.



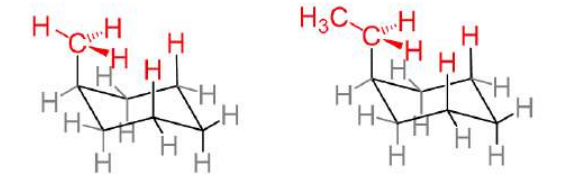
2) The equatorial conformation of bromocyclohexane will have two 1,3 diaxial interactions. The table above states that each interaction accounts for 1.2 kJ/mol of strain. The total strain in equatorial bromocyclohexane will be 2(1.2 kJ/mol) = 2.4 kJ/mol.

3) Remembering that the axial conformation is higher in energy, the energy difference between the two conformations is ΔE = (E equatorial - E axial) = (0 - 2.4 kJ/mol) = -2.4 kJ/mol. After converting ^{o}C to Kelvin and kJ/mol to J/mol we can use the equation $\Delta E = -RT \ln K$ to find that $-\Delta E/RT = \ln K$ or (2.4 x 10^3 J/mol) / (8.313 kJ/mol K • 298 K) = lnK. From this we calculate that K = 2.6. Because the ring flip reaction is an equilibrium we can say that K = [Equatorial] / [Axial]. If assumption is made that [Equatorial] = X then [Axial] must be 1-X. Plugging these values into the equilibrium expression produces K = [X] / [1-X]. After plugging in the calculated value for K, X can be solved algebraically. 2.6 = [X] / [1-X] → 2.6 - 2.6X = X → 2.6 = 3.6X → 2.6/3.6 = X = 0.72. This means that bromocyclohexane is in the equatorial position 72% of the time and in the axial position 28% of the time.



Bromo group axial **Bromo** group equitorial

4) The fact that C-C sigma bonds can freely rotate allows the ethyl subsistent to obtain a conformation which places the bulky CH_3 group away from the cyclohexane ring. This forces the ethyl substituent to have only have 1,3- diaxial interactions between hydrogens, which only provides a slight difference to a methyl group.



Exercises

Questions

Q4.7.1

In the molecule, cyclohexyl ethyne there is little steric strain, why?

Solutions

S4.7.1

The ethyne group is linear and therefore does not affect the hydrogens in the 1,3 positions to say to the extent as a bulkier or a bent group (e.g. ethene group) would. This leads to less of a strain on the molecule.



4.7: Conformations of Monosubstituted Cyclohexanes is shared under a CC BY-SA 4.0 license and was authored, remixed, and/or curated by Steven Farmer, Dietmar Kennepohl, Layne Morsch, Krista Cunningham, Tim Soderberg, Robert Bruner, & Robert Bruner.

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4.8: Conformations of Disubstituted Cyclohexanes

Objective

After completing this section, you should be able to use conformational analysis to determine the most stable conformation of a given disubstituted cyclohexane.

Key Terms

Make certain that you can define, and use in context, the key term below.

- conformational analysis

Study Notes

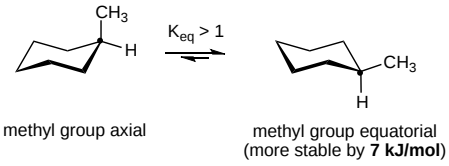
When faced with the problem of trying to decide which of two conformers of a given disubstituted cyclohexane is the more stable, you may find the following generalizations helpful.

1. A conformation in which both substituents are equatorial will always be more stable than a conformation with both groups axial.
2. When one substituent is axial and the other is equatorial, the most stable conformation will be the one with the bulkiest substituent in the equatorial position. Steric bulk decreases in the order

   tert-butyl > isopropyl > ethyl > methyl > hydroxyl > halogens

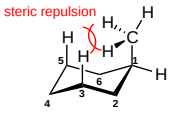
Monosubstituted Cyclohexanes

In the previous section, it was stated that the chair conformation in which the methyl group is equatorial is more stable because it minimizes steric repulsion, and thus the equilibrium favors the more stable conformer. This is true for all monosubstituted cyclohexanes. The chair conformation which places the substituent in the equatorial position will be the most stable and be favored in the ring flip equilibrium.



methyl group axial

methyl group equatorial
(more stable by **7 kJ/mol**)



Disubstituted Cyclohexanes

Determining the more stable chair conformation becomes more complex when there are two or more substituents attached to the cyclohexane ring. To determine the stable chair conformation, the steric effects of each substituent, along with any additional steric interactions, must be taken into account for both chair conformations.

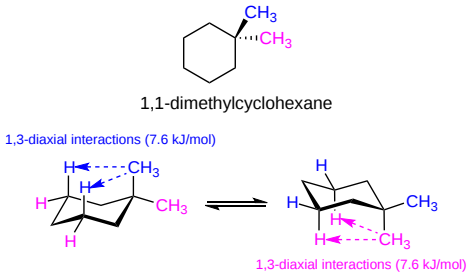
In this section, the effect of conformations on the relative stability of disubstituted cyclohexanes is examined using the two principles:

i. Substituents prefer equatorial rather than axial positions in order to minimize the steric strain created of 1,3-diaxial interactions.
ii. The more stable conformation will place the larger substituent in the equatorial position.

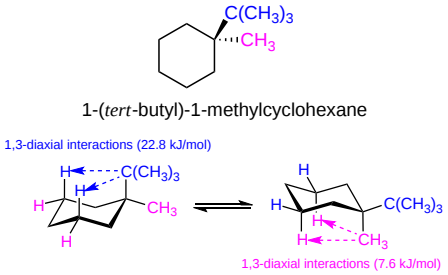
1,1-Disubstituted Cyclohexanes

The more stable chair conformation can often be determined empirically or by using the energy values of steric interactions previously discussed in this chapter. Note, in some cases there is no discernable energy difference between the two chair conformations which means they are equally stable.

1,1-dimethylcyclohexane does not have *cis* or *trans* isomers, because both methyl groups are on the same ring carbon. Both chair conformers have one methyl group in an axial position and one methyl group in an equatorial position giving both the same relative stability. The steric strain created by the 1,3-diaxial interactions of a methyl group in an axial position (versus equatorial) is 7.6 kJ/mol (from Table 4.7.1), so both conformers will have equal amounts of steric strain. Thus, the equilibrium between the two conformers does not favor one or the other. Note, that both methyl groups cannot be equatorial at the same time without breaking bonds and creating a different molecule.

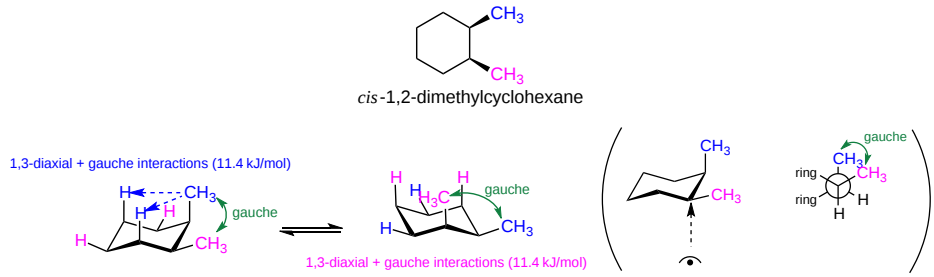


However, if the two groups are different, as in 1-*tert*-butyl-1-methylcyclohexane, then the equilibrium favors the conformer in which the larger group (*tert*-butyl in this case) is in the more stable equatorial position. The energy cost of having one tert-butyl group axial (versus equatorial) can be calculated from the values in table 4.7.1 and is approximately 22.8 kJ/mol. The conformer with the *tert*-butyl group axial is approximately 15.2 kJ/mol (22.8 kJ/mol - 7.6 kJ/mol) less stable then the conformer with the *tert*-butyl group equatorial. Solving for the equilibrium constant K shows that the equatorial is preferred about 460:1 over axial. This means that 1-*tert*-butyl-1-methylcyclohexane will spend the majority of its time in the more stable conformation, with the *tert*-butyl group in the equatorial position.



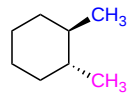
Cis and *trans* stereoisomers of 1,2-dimethylcyclohexane

In *cis*-1,2-dimethylcyclohexane, both chair conformations have one methyl group equatorial and one methyl group axial. As previously discussed, the axial methyl group creates 7.6 kJ/mol of steric strain due to 1,3-diaxial interactions. It is important to note, that both chair conformations also have an additional 3.8 kJ/mol of steric strain created by a gauche interaction between the two methyl groups. Overall, both chair conformations have 11.4 kJ/mol of steric strain and are of equal stability.

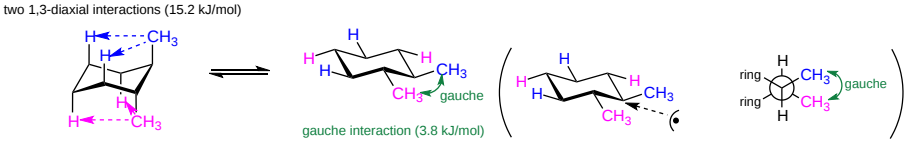


https://chem.libretexts.org/@go/page/418105

In *trans*-1,2-dimethylcyclohexane, one chair conformer has both methyl groups axial and the other conformer has both methyl groups equatorial. The conformer with both methyl groups equatorial has no 1,3-diaxial interactions however there is till 3.8 kJ/mol of strain created by a gauche interaction. The conformer with both methyl groups axial has four 1,3-Diaxial interactions which creates 2 x 7.6 kJ/mol (15.2 kJ/mol) of steric strain. This conformer is (15.2 kJ/mol -3.8 kJ/mol) 11.4 kJ/mol less stable than the other conformer. The equilibrium will therefore favor the conformer with both methyl groups in the equatorial position.

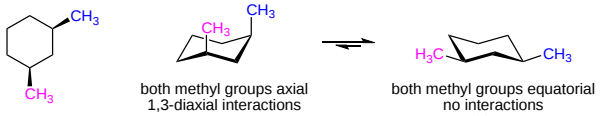


trans -1,2-dimethylcyclohexane

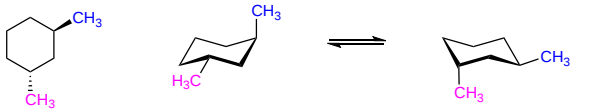


Cis and *trans* stereoisomers of 1,3-dimethylcyclohexane

A similar conformational analysis can be made for the *cis* and *trans* stereoisomers of 1,3-dimethylcyclohexane. For *cis*-1,3-dimethylcyclohexane one chair conformation has both methyl groups in axial positions creating 1,3-diaxial interactions. The other conformer has both methyl groups in equatorial positions thus creating no 1,3-diaxial interaction. Because the methyl groups are not on adjacent carbons in the cyclohexane rings gauche interactions are not possible. Even without energy calculations it is simple to determine that the conformer with both methyl groups in the equatorial position will be the more stable conformer.



For *trans*-1,3-dimethylcyclohexane both conformations have one methyl axial and one methyl group equatorial. Each conformer has one methyl group creating a 1,3-diaxial interaction so both are of equal stability.



both conformers have equal stability

Summary of Disubstitued Cyclohexane Chair Conformations

When considering the conformational analyses discussed above a pattern begins to form. There are only two possible relationships which can occur between ring-flip chair conformations:

1) AA/EE: One chair conformation places both substituents in axial positions creating 1,3-diaxial interactions. The other conformer places both substituents in equatorial positions creating no 1,3-diaxial interactions. This diequatorial conformer is the more stable regardless of the substituents.

2) AE/EA: Each chair conformation places one substituent in the axial position and one substituent in the equatorial position. If the substituents are the same, there will be equal 1,3-diaxial interactions in both conformers making them equal in stability. However,

if the substituents are different then different 1,3-diaxial interactions will occur. The chair conformation which places the larger substituent in the equatorial position will be favored.

Substitution type	Chair Conformation Relationship
cs-1,2-disubstituted cyclohexanes	AE/EA
trans-1,2-disubstituted cyclohexanes	AA/EE
cis-1,3-disubstituted cyclohexanes	AA/EE
trans-1,3-disubstituted cyclohexanes	AE/EA
cis-1,4-disubstituted cyclohexanes	AE/EA
trans-1,4-disubstituted cyclohexanes	AA/EE

Example 4.8.1

For *cis*-1-chloro-4-methylcyclohexane, draw the most stable chair conformation and determine the energy difference between the two chair conformers.

Solution

Based on the table above, *cis*-1,4-disubstitued cyclohexanes should have two chair conformations each with one substituent axial and one equatorial. Based on this, we can surmise that the energy difference of the two chair conformations will be based on the difference in the 1,3-diaxial interactions created by the methyl and chloro substituents.



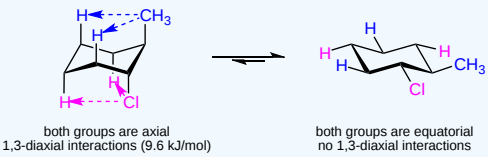
As predicted, each chair conformer places one of the substituents in the axial position. Because the methyl group is larger and has a greater 1,3-diaxial interaction than the chloro, the most stable conformer will place it the equatorial position, as shown in the structure on the right. Using the 1,3-diaxial energy values given in the previous sections we can calculate that the conformer on the right is (7.6 kJ/mol - 2.0 kJ/mol) 5.6 kJ/mol more stable than the other.

Example 4.8.2

For *trans*-1-chloro-2-methylcyclohexane, draw the most stable chair conformation and determine the energy difference between the two chair conformers.

Solution

Based on the table above, *trans*-1,2-disubstitued cyclohexanes should have one chair conformation with both substituents axial and one conformation with both substituents equatorial. Based on this, we can predict that the conformer which places both substituents equatorial will be the more stable conformer. The energy difference of the two chair conformations will be based on the 1,3-diaxial interactions created by both the methyl and chloro substituents.



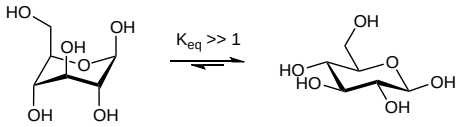
As predicted, one chair conformer places both substituents in the axial position and other places both substituents equatorial. The more stable conformer will place both substituents in the equatorial position, as shown in the structure on the right. Using

the 1,3-diaxial energy values given in the previous sections we can calculate that the conformer on the right is (7.6 kJ/mol + 2.0 kJ/mol) 9.6 kJ/mol more stable than the other.

Conformational Analysis of Complex Six Membered Ring Structures

Cyclohexane can have more than two substituents. Also, there are multiple six membered rings which contain atoms other than carbon. All of these systems usually form chair conformations and follow the same steric constraints discussed in this section. Because the most commonly found rings in nature are six membered, conformational analysis can often help in understanding the usual shapes of some biologically important molecules. In complex six membered ring structures a direct calculation of 1,3-diaxial energy values may be difficult. In these cases a determination of the more stable chair conformer can be made by empirically applying the principles of steric interactions.

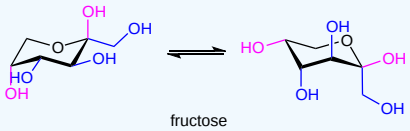
A later chapter will discuss how many sugars can exist in cyclic forms which are often six remembered rings. When in an aqueous solution the six carbon sugar, glucose, is usually a six membered ring adopting a chair conformation. When looking at the two possible ring-clip chair conformations, one has all of the substituents axial and the other has all the substutents equatorial. Even without a calculation, it is clear that the conformation with all equatorial substituents is the most stable and glucose will most commonly be found in this conformation.



glucose
(β-glucopyranose form)

Example 4.8.3

The six carbon sugar, fructose, in aqueous solution is also a six-membered ring in a chair conformation. Which of the two possible chair conformations would be expected to be the most stable?



fructose
(β-fructopyranose form)

Solution

The lower energy chair conformation is the one with three of the five substituents (including the bulky $–CH_2OH$ group) in the equatorial position (pictured on the right). The left structure has 3 equatorial substituents while the structure on the right only has two equatorial substituents.

Exercises

1. Draw the two chair conformations for *cis*-1-ethyl-2-methylcyclohexane using bond-line structures and indicate the more energetically favored conformation.

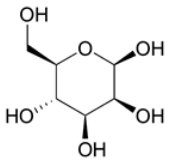
2. Draw the most stable conformation for *trans*-1-ethyl-3-methylcyclohexane using bond-line structures.

3. Draw the most stable conformation for trans-1-*t*-butyl-4-methylcyclohexane using bond-line structures.

4. Draw the most stable conformation fo *trans*-1-isopropyl-3-methylcyclohexane.

5. Can a ‘ring flip’ change a *cis*-disubstituted cyclohexane to *trans*? Explain.

6. Draw the two chair conformations of the six-carbon sugar mannose, being sure to clearly show each non-hydrogen substituent as axial or equatorial. Predict which conformation is likely to be more stable, and explain why.

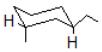


mannose

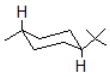
Solutions

1. 

larger ethyl group in equatorial position is favored

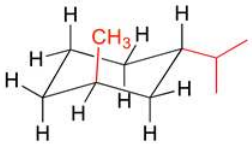
2. 

larger ethyl group in equatorial position is favored

3. 

both alkyl groups in equatorial position

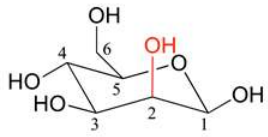
4.



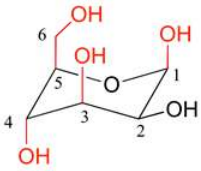
The bulkier isopropyl groups is in the equatorial position.

5. No. In order to change the relationship of two substituents on a ring from *cis* to *trans*, you would need to break and reform two covalent bonds. Ring flips involve only *rotation* of single bonds.

6.



major chair form of mannose
(only one substituent axial)



minor chair form of mannose
(four substituents axial)

Exercises

Questions

Q4.8.1

For the following molecules draw the most stable chair conformation and explain why you chose this as an answer

1 = *trans*-1,2-dimethylcyclohexane

2 = *cis*-1,3-dimethylcyclohexane

Solutions

S4.8.1

1 – The most stable conformation would be to have the methyl groups equatorial reducing steric interaction

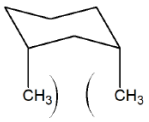
2 – The most stable conformation would be to have the groups equatorial this would reduce the strain if they were axial



1



2



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4.9: Conformations of Polycyclic Molecules

Objective

After completing this section, you should be able to draw the structures and construct molecular models of simple polycyclic molecules.

Key Terms

Make certain that you can define, and use in context, the key terms below.

- bridgehead carbon atom
- polycyclic molecule

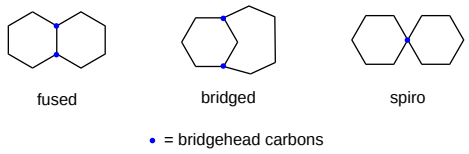
Study Notes

A *bridgehead carbon atom* is a carbon atom which is shared by at least two rings. The hydrogen atom which is attached to a bridgehead carbon may be referred to as a bridgehead hydrogen.

Note that bicyclo[2.2.1]heptane is the systematic name of norborane. You need not be concerned over the IUPAC name of norbornane. The nomenclature of compounds of this type is beyond the scope of this course.

Nomenclature of Bicyclic Ring Systems

There are many hydrocarbons and hydrocarbon derivatives with two rings having common carbon atoms. There are three main ways that the two rings can be connected. The first is called a **fused bicyclic** ring structure where the two rings share a covalent bond and a have two **bridgehead** carbons (marked in red on the structures below). A bridgehead is defined as a carbon that is part of two or more rings. Hydrogens attached to bridge head carbons are often referred to as bridge head hydrogens. The two rings can also be connected by a bridge containing one or more carbons to form a **bridged bicyclic** molecule. Lastly, the two rings can be joined with a singe bridge head carbon to form **spiro bicyclic** molecules.



Bicyclic Isomers of $C_{10}H_{18}$

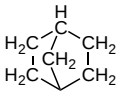
Naming Fused and Bridged Compounds

Fused and bridged bicyclic compounds are follow similar naming conventions:

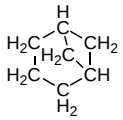
1. Count the total number of carbons in both rings. This is the parent name. (eg. ten carbons in the system would be decane)
2. Count the number of carbons between the bridgeheads, then place the numbers in square brackets in descending order separated by periods. Fused and bridged bycyclic compounds should have three numbers such as [2.2.0]. For fused compounds one of the numbers should be zero.
3. Place the word **bicyclo** at the beginning of the name.



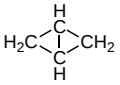
Examples with carbons and hydrogens explicitly shown:



bicyclo[2.2.1]heptane



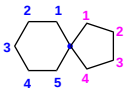
bicyclo[3.1.1]heptane



bicyclo[1.1.0]butane

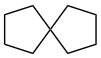
Naming Spiro Compounds

Spiro bicyclics are named using the same basic rules. Because there is only one bridgehead carbon only two numbers will be required in the brackets. Also, the word **spiro** is placed at the beginning.



spiro[5.4]decane

Examples



spiro[4.4]nonane



spiro[3.2]hexane

Conformations in Bicyclic Ring Systems

As expected, the connection of two rings has defined effects on the possible conformations. However, the ideas previously discussed in this chapter can be used for conformational analysis. Fused rings have the possibility of two isomers where the bridgehead hydrogens are either *cis* or *trans* along the shared bond. These two isomers have significant differences in flexibility and stability as seen in bicyclo[4,4,0]decane more commonly known as decalin. If the positioning of the bridgehead hydrogens are shown in a fused ring the prefix cis or trans should be included in the name.

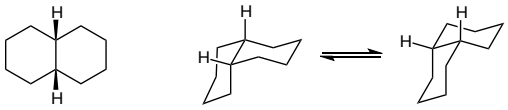
The trans-isomer is the easiest to describe because the fusion of the two rings creates a rigid, roughly planar, structure made up of two chair conformations. Unlike cyclohexane, the two rings cannot flip from one chair form to another. Accordingly, the orientation of the any substituents is fixed in either an axial or equatorial position in *trans*-decalin. This means that the C-C bonds coming away from the fused edge are held in equatorial positions relative to each ring thus preventing the possibility of any 1,3-diaxial interactions occurring between ring atoms.



***trans* -decalin**
(rigid)

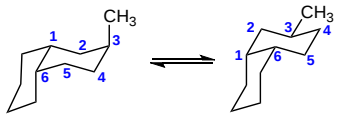
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The two rings in *cis*-decalin are also both held in a chair conformations. In comparison, the chair-chair forms of *cis*-decalin are relatively flexible, and inversion of both rings at once occurs fairly easily.



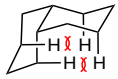
***cis* -decalin**
(more flexible)

The flexibility of *cis*-decalin allows for a substituent to interconvert between axial and equatorial conformations. In much the same fashion as cyclohexane, equatorial substituents tend to create less steric strain and create a more stable conformer.



(Note: atoms are mapped in blue for clarity.)

A major difference in *cis*-decalin is the fact that one of C-C bonds coming away from the fused edge is held an an axial position. This is true in both ring-flip conformations. This axial C-C bond causes 1,3-diaxial interactions to occur in *cis*-decalin making it roughly 8.4 kJ/mol less stable than *trans*-decalin. This amount of 1,3-diaxial steric strain is roughly equivalent to that of an ethyl substituent attached to a cyclohexane ring (8.0 kJ/mol)



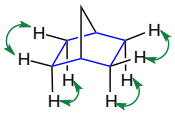
= steric strain

Bicyclic compounds with a bridge typically have very little flexibility and are often held in a ridged conformation. The molecule norbornane represent a cyclohexane ring connected by a single carbon bridge.



norbornane, or
bicyclo[2.2.1]heptane

Norbornane is estimated to have 72 kJ/mol of ring strain which can be understood when viewing the contained rings. The carbon bridge in norbornane holds the cyclohexane ring at the bottom in a boat conformation creating torsional strain from eclipsing bonds along the edge.



(green arrows used to illustrate
eclipsing hydrogens)

Also, the carbon bridge forms a cyclopentane ring (shown in red below making up the right side of the structure) with increased angle strain throughout the whole molecule.



Polycyclic Systems in Nature

Fused ring systems like decalin are very common in natural products. In fact, similar ring systems are found in steroids, which are an important class of lipids. Steroids generally have structures that include three six-membered rings and a five-membered ring connected by three fused bonds. Most natural steroids have a *trans* configuration at all three fusion points. This tends to give steroids a rigid and semi-flat structure.

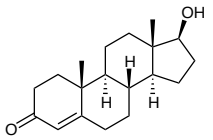


basic steroid ring confguration
(fused bonds highlighted in purple)

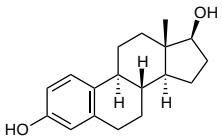
trans-trans-trans

Sex hormones are an example of steroids. The primary male hormone, testosterone, is responsible for the development of secondary sex characteristics. Two female sex hormones, progesterone and estrogen (or estradiol) control the ovulation cycle. Notice that the male and female hormones have only slight differences in structures, but yet have very different physiological

effects. Testosterone promotes the normal development of male genital organs and is synthesized from cholesterol in the testes. It also promotes secondary male sexual characteristics such as deep voice, facial and body hair.

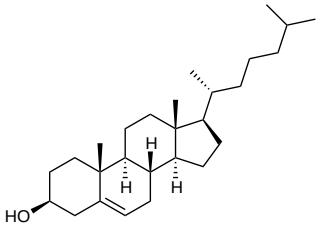


testosterone



estradiol

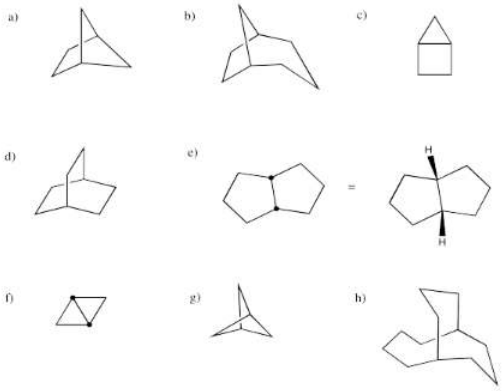
The best known and most abundant steroid in the body is cholesterol. Cholesterol is formed in brain tissue, nerve tissue, and the blood stream. It is the major compound found in gallstones and bile salts. Cholesterol also contributes to the formation of deposits on the inner walls of blood vessels. These deposits harden and obstruct the flow of blood. This condition, known as atherosclerosis, results in various heart diseases, strokes, and high blood pressure.



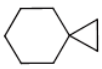
cholesterol

Exercises

1)



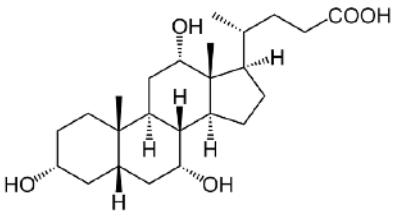
i)



j)



3) The following molecule is cholic acid. Determine if the three fused bonds have a *cis* or *trans* configuration.



Solutions

1)

a) Bicyclo[2.1.1]hexane

b) Bicyclo[3.2.1]octane

c) Bicyclo[2.1.0]pentane (more commonly called "housane")

d) Bicyclo[2.2.2]octane

e) cis-Bicyclo[3.3.0]octane

f) cis-Bicyclo[1.1.0]butane

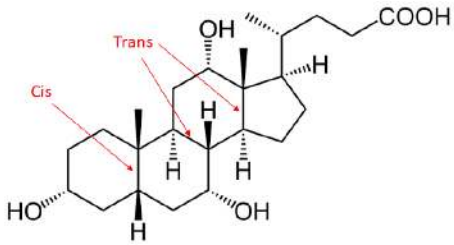
g) Bicyclo[1.1.1]pentane

h) Bicyclo[4.3.3]dodecane

i) Spiro[5.2]octane

j) Spiro[3.3]heptane

2)



Questions

Q4.9.1

Someone stated that *trans*-decalin is more stable than *cis*-decalin. Explain why this is incorrect.

Solutions

S4.9.1

Cis-decalin has fewer steric interactions than *trans*-decalin.

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CHAPTER OVERVIEW

5: Stereochemistry at Tetrahedral Centers

Learning Objectives

After you have completed Chapter 5, you should be able to

- fulfill all of the detailed objectives listed under each individual section.
- use molecular models in solving problems on stereochemistry.
- solve road-map problems that include stereochemical information.
- define, and use in context, the new key terms.

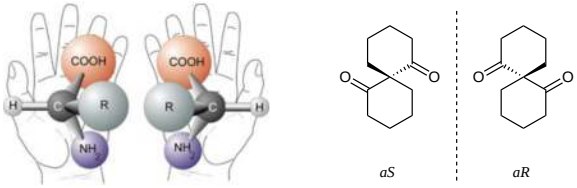
This chapter introduces the concept of chirality, and discusses the structure of compounds containing one or two chiral centers. A convenient method of representing the three-dimensional arrangement of the atoms in chiral compounds is explained; furthermore, throughout the chapter , considerable emphasis is placed on the use of molecular models to assist in the understanding of the phenomenon of chirality. The chapter continues with an examination of stereochemistry—the three-dimensional nature of molecules. The subject is introduced using the experimental observation that certain substances have the ability to rotate plane-polarized light. Finally, certain reactions of alkenes are re-examined in the light of the new material encountered in this chapter.

5.1: Chapter Objectives and Introduction
5.2: Optical Activity
5.3: Chirality in Nature and Chiral Environments
5.4: Enantiomers and the Tetrahedral Carbon
5.5: The Reason for Handedness in Molecules - Chirality
5.6: Sequence Rules for Specifying Configuration
5.7: Diastereomers
5.8: Meso Compounds
5.9: Racemic Mixtures and the Resolution of Enantiomers
5.10: Chirality at Nitrogen, Phosphorus, and Sulfur
5.11: Prochirality

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5.1: Chapter Objectives and Introduction

The opposite of chiral is **achiral**. Achiral objects are superimposable with their mirror images. If the molecules are superimposable, they are identical to each other. For example, two pieces of paper are achiral. In contrast, **chiral** objects, like our hands, are non-superimposable mirror images of each other. Try to line up your left hand perfectly with your right hand, so that the palms are both facing in the same directions. Spend about a minute doing this. Do you see that they cannot line up exactly?



The same thing applies to some molecules. A chiral molecule has a mirror image that cannot line up with it perfectly - the mirror images are non-superimposable. This pair of non-superimposable mirror image molecules are called **enantiomers**. But why are chiral molecules so interesting? Just like your left hand will not fit properly in your right glove, one of the enantiomers of a molecule may not work the same way in your body, as the other. It turns out that many of the biological molecules such as our DNA, amino acids and sugars, are chiral molecules.

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5.2: Optical Activity

Objectives

After completing this section, you should be able to

1. describe the nature of plane-polarized light.
2. describe the features and operation of a simple polarimeter.
3. calculate the specific rotation of a compound, given the relevant experimental data.

Key Terms

Make certain that you can define, and use in context, the key terms below.

- analyzer
- dextrorotatory
- levorotatory
- optically active
- plane-polarized light
- polarimeter
- polarizer
- specific rotation, $[\alpha]_D^{20}$

Study Notes

A *polarizer* is a device through which only light waves oscillating in a single plane may pass. A *polarimeter* is an instrument used to determine the angle through which plane-polarized light has been rotated by a given sample. You will have the opportunity to use a polarimeter in the laboratory component of the course. An *analyzer* is the component of a polarimeter that allows the angle of rotation of plane-polarized light to be determined.

Specific rotations are normally measured at 20°C, and this property may be indicated by the symbol $[\alpha]_D^{20}$. Sometimes the solvent is specified in parentheses behind the specific rotation value, for example,

$$[\alpha]_D^{20} = +12^o\,(\text{chloroform})$$

For liquids, the specific rotation may be obtained using the neat liquid rather than a solution; in such cases the formula is

$$[\alpha]_D^{\text{temp}}\,(\text{neat}) = \alpha \times l \times d$$

where α is the observed rotation, l is the path length of the cell (measured in decimetres, dm), and d is the density of the liquid.

Identifying and distinguishing enantiomers is inherently difficult, since their physical and chemical properties are largely identical. Fortunately, a nearly two hundred year old discovery by the French physicist Jean-Baptiste Biot has made this task much easier. This discovery disclosed that the right- and left-handed enantiomers of a chiral compound perturb plane-polarized light in opposite ways. This perturbation is unique to chiral molecules, and has been termed **optical activity**.

Polarimetry

Plane-polarized light is created by passing ordinary light through a polarizing device, which may be as simple as a lens taken from polarizing sun-glasses. Such devices transmit selectively only that component of a light beam having electrical and magnetic field vectors oscillating in a single plane. The plane of polarization can be determined by an instrument called a **polarimeter** (Figure 5.2.1).

Monochromatic (single wavelength) light, is polarized by a fixed polarizer next to the light source. A sample cell holder is located in line with the light beam, followed by a movable polarizer (the analyzer) and an eyepiece through which the light intensity can be observed. In modern instruments an electronic light detector takes the place of the human eye. In the absence of a sample, the light

intensity at the detector is at a maximum when the second (movable) polarizer is set parallel to the first polarizer (α = 0º). If the analyzer is turned 90º to the plane of initial polarization, all the light will be blocked from reaching the detector.

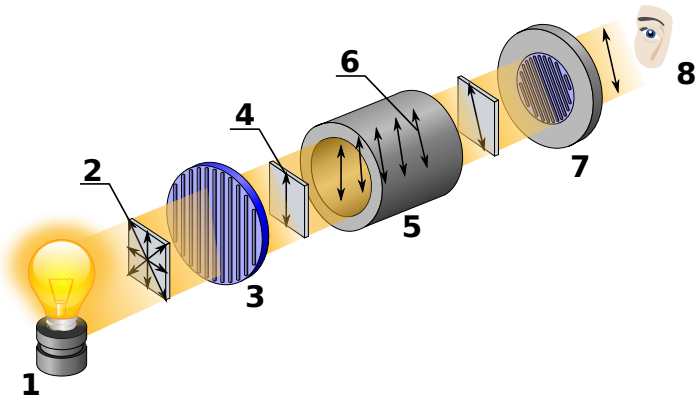


Figure 5.2.1: Operating principle of an optical polarimeter. 1. Light source 2. Unpolarized light 3. Linear polarizer 4. Linearly polarized light 5. Sample tube containing molecules under study 6. Optical rotation due to molecules 7. Rotatable linear analyzer 8. Detector. (CC BY-SA 3.0 Unported; Kaidor via Wikipedia)

Chemists use polarimeters to investigate the influence of compounds (in the sample cell) on plane polarized light. Samples composed only of achiral molecules (e.g. water or hexane), have no effect on the polarized light beam. However, if a single enantiomer is examined (all sample molecules being right-handed, or all being left-handed), the plane of polarization is rotated in either a clockwise (positive) or counter-clockwise (negative) direction, and the analyzer must be turned an appropriate matching angle, **α**, if full light intensity is to reach the detector. In the above illustration, the sample has rotated the polarization plane clockwise by +90º, and the analyzer has been turned this amount to permit maximum light transmission.

The observed rotations (α) of enantiomers are opposite in direction. One enantiomer will rotate polarized light in a clockwise direction, termed **dextrorotatory** or (+), and its mirror-image partner in a counter-clockwise manner, termed **levorotatory** or (–). The prefixes dextro and levo come from the Latin *dexter*, meaning right, and *laevus*, for left, and are abbreviated *d* and *l* respectively. If equal quantities of each enantiomer are examined , using the same sample cell, then the magnitude of the rotations will be the same, with one being positive and the other negative. To be absolutely certain whether an observed rotation is positive or negative it is often necessary to make a second measurement using a different amount or concentration of the sample. In the above illustration, for example, α might be –90º or +270º rather than +90º. If the sample concentration is reduced by 10%, then the positive rotation would change to +81º (or +243º) while the negative rotation would change to –81º, and the correct α would be identified unambiguously.

Since it is not always possible to obtain or use samples of exactly the same size, the observed rotation is usually corrected to compensate for variations in sample quantity and cell length. Thus it is common practice to convert the observed rotation, α, to a **specific rotation**, by the following formula:

$$[\alpha]_D = \frac{\alpha}{lc} \tag{5.3.1}$$

where

- $[\alpha]_D$ is the specific rotation
- l is the cell length in dm
- c is the concentration in g/ml
- D designates that the light used is the 589 line from a sodium lamp

Compounds that rotate the plane of polarized light are termed **optically active**. Each enantiomer of a stereoisomeric pair is optically active and has an equal but opposite-in-sign specific rotation. Specific rotations are useful in that they are experimentally determined constants that characterize and identify pure enantiomers. For example, the lactic acid enantiomers have the following specific rotations:

- Carvone from caraway: $[\alpha]_D^{20} = +62.5^o$ (this isomer may be referred to as (+)-carvone or d-carvone)
- Carvone from spearmint: $[\alpha]_D^{20} = -62.5^o$ (this isomer may be referred to as (–)-carvone or l-carvone)

and carvone enantiomers have the following specific rotations:

- Lactic acid from muscle tissue: $[\alpha]_D^{20} = +2.5^o$ (this isomer may be referred to as (+)-lactic acid or d-lactic acid)
- Lactic acid from sour milk: $[\alpha]_D^{20} = -2.5^o$ (this isomer may be referred to as (–)-lactic acid or l-lactic acid)

A 50:50 mixture of enantiomers has no observable optical activity. Such mixtures are called **racemates** or racemic modifications, and are designated (±). When chiral compounds are created from achiral compounds, the products are racemic unless a single enantiomer of a chiral co-reactant or catalyst is involved in the reaction. The addition of **HBr** to either cis- or trans-2-butene is an example of racemic product formation (the chiral center is colored red).

$$CH_3CH{=}CHCH_3 + HBr \longrightarrow (\pm)\ CH_3CH_2\color{red}{C}HBrCH_3$$

Chiral organic compounds isolated from living organisms are usually optically active, indicating that one of the enantiomers predominates (often it is the only isomer present). This is a result of the action of chiral catalysts we call enzymes, and reflects the inherently chiral nature of life itself. Chiral synthetic compounds, on the other hand, are commonly racemates, unless they have been prepared from enantiomerically pure starting materials.

There are two ways in which the condition of a chiral substance may be changed:

1. A racemate may be separated into its component enantiomers. This process is called **resolution**.
2. A pure enantiomer may be transformed into its racemate. This process is called **racemization**.

Enantiomeric Excess

The "optical purity" is a comparison of the optical rotation of a pure sample of unknown stereochemistry versus the optical rotation of a sample of pure enantiomer. It is expressed as a percentage. If the sample only rotates plane-polarized light half as much as expected, the optical purity is 50%.

$$\%\ \text{optical purity} = \frac{\text{specific rotation of mixture}}{\text{specific rotation of pure enantiomer}} \times 100\%$$

Because *R* and *S* enantiomers have equal but opposite optical activity, it naturally follows that a 50:50 racemic mixture of two enantiomers will have no observable optical activity. If we know the specific rotation for a chiral molecule, however, we can easily calculate the ratio of enantiomers present in a mixture of two enantiomers, based on its measured optical activity. When a mixture contains more of one enantiomer than the other, chemists often use the concept of **enantiomeric excess (ee)** to quantify the difference. Enantiomeric excess can be expressed as:

$$ee = \frac{(\%\ \text{more abundant enantiomer} - 50) \times 100\%}{50}$$

For example, a mixture containing 60% *R* enantiomer (and 40% *S* enantiomer) has a 20% enantiomeric excess of R: ((60-50) x 100) / 50 = 20 %.

? Exercise 5.2.1

The specific rotation of (*S*)-carvone is (+)61°, measured 'neat' (pure liquid sample, no solvent). The optical rotation of a neat sample of a mixture of *R* and *S* carvone is measured at (-)23°. Which enantiomer is in excess, and what is its ee? What are the percentages of (*R*)- and (*S*)-carvone in the sample?

Answer

The observed rotation of the mixture is levorotary (negative, counter-clockwise), and the specific rotation of the pure *S* enantiomer is given as dextrorotary (positive, clockwise), meaning that the pure *R* enantiomer must be levorotary, and the mixture must contain more of the *R* enantiomer than of the *S* enantiomer.

Rotation (*R*/*S* Mix) = [Fraction(*S*) × Rotation (*S*)] + [Fraction(*R*) × Rotation (*R*)]

Let Fraction (*S*) = x, therefore Fraction (*R*) = 1 – x.

Rotation (*R*/*S* Mix) = x[Rotation (*S*)] + (1 – x)[Rotation (*R*)].

$$-23 = x(+61) + (1 - x)(-61)$$

Solve for x: x = 0.3114 and (1 – x) = 0.6885

Therefore the percentages of (*R*)- and (*S*)-carvone in the sample are 68.9% and 31.1%, respectively.

ee = [(% more abundant enantiomer – 50) × 100]/50. = [68.9 – 50) × 100]/50 = 37.8%.

Chiral molecules are often labeled according to the sign of their specific rotation, as in (S)-(+)-carvone and (R)-(-)-carvone, or (±)-carvone for the racemic mixture. However, there is no relationship whatsoever between a molecule's R/S designation and the sign of its specific rotation. Without performing a polarimetry experiment or looking in the literature, we would have no idea that (-)-carvone has the R configuration and (+)-carvone has the S configuration

Chiral molecules are often labeled according to the sign of their specific rotation, as in (S)-(+)-carvone and (R)-(-)-carvone, or (±)-carvone for the racemic mixture. However, there is no relationship whatsoever between a molecule's R/S designation and the sign of its specific rotation. Without performing a polarimetry experiment or looking in the literature, we would have no idea that (-)-carvone has the R configuration and (+)-carvone has the S configuration.

Separation of Chiral Compounds

As noted earlier, chiral compounds synthesized from achiral starting materials and reagents are generally racemic (i.e. a 50:50 mixture of enantiomers). Separation of racemates into their component enantiomers is a process called resolution. Since enantiomers have identical physical properties, such as solubility and melting point, resolution is extremely difficult. Diastereomers, on the other hand, have different physical properties, and this fact is used to achieve resolution of racemates. Reaction of a racemate with an enantiomerically pure chiral reagent gives a mixture of diastereomers, which can be separated. For example, if a racemic mixture of a chiral alcohol is reacted with a enantiomerically pure carboxylic acid, the result is a mixture of diastereomers: in this case, because the pure (R) entantiomer of the acid was used, the product is a mixture of (R-R) and (R-S) diastereomeric esters, which can, in theory, be separated by their different physical properties. Subsequent hydrolysis of each separated ester will yield the 'resolved' (enantiomerically pure) alcohols. The used of this technique is known as chiral resolution.

? Exercise 5.2.2

A 3.20 g sample of morphine ($[\alpha]_D$ = -132) was dissolved in 10.0 mL of acetic acid ($[\alpha]_D$ = 0). If it is put into a sample tube with a path length of 2.00 cm, what would be its observed rotation (α)?

Answer

The specific rotation, $[\alpha]_D$ = (observed rotation, α (degrees))/ [(pathlength, *l* (dm)) x (concentration, c (g/cm^3))] = α/(*l* x c)

Solving for α, α = $[\alpha]_D$ x *l* x c

($[\alpha]_D$ = -132) x (*l* = 2.00 cm = 0.200 dm) x (c = 3.20 g / 10.0 cm^3 = 0.320 g/cm^3)

α = -132 x 0.200 dm x 0.320 g/cm^3 = -8.45 °

? Exercise 5.2.3

Is the morphine in the previous excercise dextrorotatory or levorotatory?

Answer

Since morphine has a (-) rotation, it indicates that it rotates light to the left (counterclockwise) and morphine is levorotatory.

? Exercise 5.2.4

Label the following compounds as dextrorotatory or levorotatory.

a. sucrose ($[\alpha]_D$ = + 66.7)
b. cholesterol ($[\alpha]_D$ = - 31.5)

c. cocaine ($[\alpha]_D$ = - 16)
d. chloroform ($[\alpha]_D$ = 0)

Answer

a. sucrose ($[\alpha]_D$ = + 66.7) dextrorotatory
b. cholesterol ($[\alpha]_D$ = - 31.5) levorotatory
c. cocaine ($[\alpha]_D$ = - 16) levorotatory
d. chloroform ($[\alpha]_D$ = 0) neither, not optically active

? Exercise 5.2.5a

The specific rotation of (*S*)-carvone is (+) 61^o when measured neat (pure liquid sample with no solvent). The optical rotation of a neat sample of a mixture of R and S carvone is measured at (-) 23 ^{o}.

a) Which enantiomer is in excess?

Answer

Since the pure *S* enantiomer ((+) 61^o) is dextrorotatory (positive, clockwise), the *R* enantiomer must be levorotatory. The observed rotation of the mixture is levorotatory since its negative (counterclockwise). This means the mixture must contain more of the *R* enantiomer than the *S* enantiomer.

? Exercise 5.2.5b

b) What are the percentages of (*S*)- and (*R*)- carvone in the sample mixture?

Answer

Optical rotation (α) of the (*R*/*S* mixture) = [fraction (*S*) x $[\alpha]_D$ (*S*)] + [fraction (*R*) x $[\alpha]_D$ (*R*)]

To determine the fraction of S and R, we make y = fraction (*S*) and 1 – y = fraction (*R*)

-23^o = y x (61^o) + (1 – y) x (-61^o) solving for y: y = 0.3114 and (1-y) = 0.6885

Therefore the percentage of (*S*)-carvone is 31.1 % and (*R*)-carvone is 68.9 %

? Exercise 5.2.5c

c) What is the ee (enantiomeric excess)?

Answer

ee = [(% more abundant isomer – 50) x 100]/50 = [(68.9 – 50) x100]/50 = 37.8 % ee

? Exercise 5.2.6a

Determine the ee's of the following from the percentages

- 95 % (*R*)- tartaric acid and 5.0 % (*S*)- tartaric acid

Answer

[(95 – 50) x 100] / 50 = 90 % ee (*R*)-tartaric acid

Exercise 5.2.6b

Determine the ee's of the following from the percentages

- 75 % (*S*)- limonene and 25 % (*R*)- limonene

Answer

[(75 – 50) x 100] / 50 = 50 % ee (*S*)- limonene

Exercise 5.2.6c

Determine the ee's of the following from the percentages

- 85 % (*R*) cysteine

Answer

(85 – 50) x 100] / 50 = 70 % ee (*R*)-cysteine

Exercise 5.2.6d

Determine the ee's of the following from the percentages

- 50 % (*S*) alanine

Answer

(50 – 50) x 100] / 50 = 0 % ee, racemic mixture

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5.3: Chirality in Nature and Chiral Environments

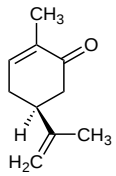
Objective

After completing this section, you should be able to explain how chiral molecules in nature can have such dramatically different biological properties.

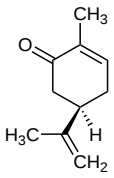
Some Chiral Organic Molecules

There are a number of important biomolecules that could occur as enantiomers, including amino acids and sugars. In most cases, only one enantiomer occurs naturally (although some fungi, for example, are able to produce mirror-image forms of these compounds). We will look later at some of these biomolecules, but first we will look at a compound that occurs naturally in both enantiomeric forms.

Carvone is a secondary metabolite. That means it is a naturally-occurring compound that is not directly connected to the very basic functions of a cell, such as self-replication or the production of energy. The role of secondary metabolites in nature is often difficult to determine. However, these compounds often play roles in self-defense, acting as deterrents against competitor species in a sort of small-scale chemical warfare scenario. They are also frequently used in communications; this role has been studied most extensively among insects, which use lots of compounds to send information to each other.



(*S*)-carvone
oil at 25 °C
bp: 230-231 °C
d: 0.965 g/mL
n: 1.4988
insol H_2O, misc EtOH, MeOH
$[\alpha]_D$ = +61.2°



(*R*)-carvone
oil at 25 °C
bp: 230-231 °C
d: 0.965 g/mL
n: 1.4988
insol H_2O, misc EtOH, MeOH
$[\alpha]_D$= −62.46°

Figure **5.3.1**: The two naturally-occurring enantiomers of carvone.

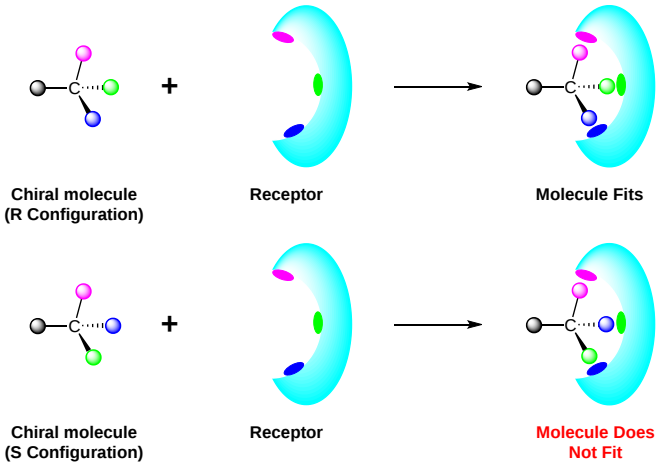
Carvone is produced in two enantiomeric forms. One of these forms, called (-)-carvone, is found in mint leaves, and it is a principal contributor to the distinctive odor of mint. The other form, (+)-carvone, is found in caraway seeds. This form has a very different smell, and is typically used to flavor rye bread and other Eastern European foods.

Note that (+)-carvone is another name for (S)-carvone. The (+) designation is based on its positive optical rotation value, which is experimentally measured. This means the (-)-carvone is (R)-carvone and would have a negative optical rotation value.

How different, exactly, are these two compounds, (+)- and (-)-carvone? Are they completely different isomers, with different physical properties? In most ways, the answer is no. These two compounds have the same appearance (colorless oil), the same boiling point (230 °C), the same refractive index (1.499) and specific gravity (0.965). However, they have optical rotations that are almost exactly opposite values.

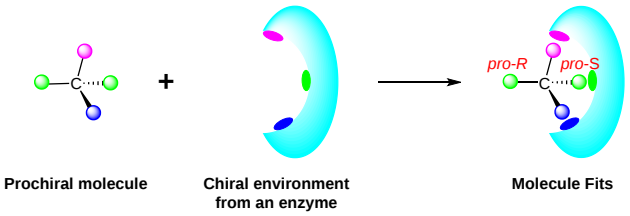
- Two enantiomers have the same physical properties.
- Enantiomers have opposite optical rotations.

Clearly they have different biological properties; since they have slightly different odors, they must fit into slightly different nasal receptors, signaling to the brain whether the person next to you is chewing a stick of gum or a piece of rye bread. This is much like how a left hand only fits into a left handed baseball glove and not into a right handed one. Receptors which allow for a biological effect, in this case to perceive a certain smell, are often chiral and will only allow one enantiomer of a chiral substrate to fit. An example of this is shown in the figure below. The receptor as a complementary three-dimension shape to allow the R configuration of the chiral substrate to fit. When the S configuration of the chiral substrate attempts to fit the configuration does not match that of the receptor as shown in the second drawing where the bottom two groups do not fit the receptor site.



Chiral Environments

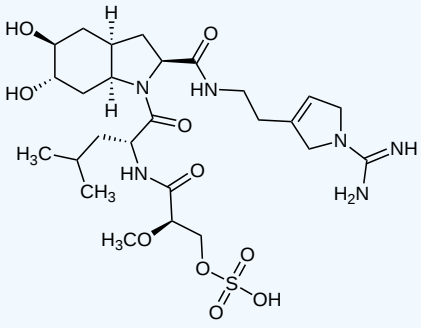
In the previous section, enzymes were shown to be capable of converting a prochiral substrate into a single enantiomer product. Enzymes can provides such an effect because they create a **chiral environment**. The figure below shows a prochiral substrate. The magenta and blue balls represent substituents while the two green balls represent two of the same substituent which is available for a given reaction. One of these substituents is *pro*-R and the other is *pro*-S. Without the presence of a chiral environment the two green substituents are chemically identical. However, as the prochiral molecule interacts with the chiral environment provided by an enzyme the two green substituents become chemically distinct. Despite being achiral, the prochiral molecule can only interact with the chiral environment in one specific position. The figure below shows that the *pro*-S green substituent of the prochiral molecule is protected by the enzyme, while the pro-R green substituent is exposed and can undergo a reaction. In this case the enzyme would provide a product that is predominantly the R enantiomer.



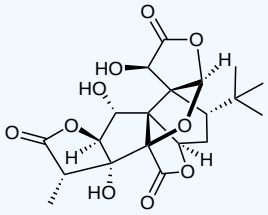
Exercise 5.3.1

The following are three molecules found in nature. Please identify four chiral centers in each, mark them with asterisks, and identify each center as having a R or S configuration. Each molecule contains more than four chiral centers.

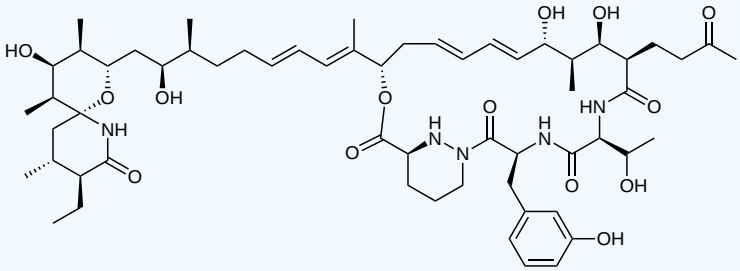
a) The following is the structure of dysinosin A, a potent thrombin inhibitor that consequently prevents blood clotting.



b) Ginkgolide B (below) is a secondary metabolite of the ginkgo tree, extracts of which are used in Chinese medicine.

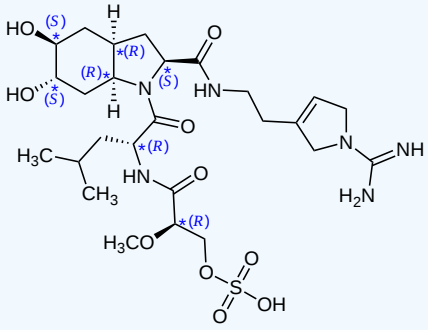


c) Sanglifehrin A, shown below, is produced by a bacteria that may be found in the soil of coffee plantations in Malawi. It is also a promising candidate for the treatment of organ transplant patients owing to its potent immuno-suppressant activity.

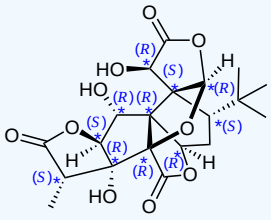


Answer

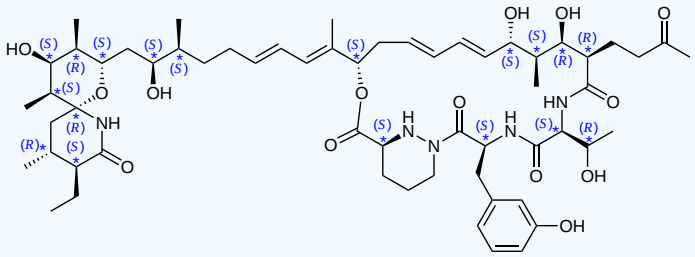
a)



b)



c)



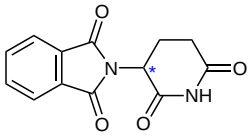


Figure \(\PageIndex{2}\): Thalidomide.

There are other reasons that we might concern ourselves with an understanding of enantiomers, apart from dietary and olfactory preferences. Perhaps the most dramatic example of the importance of enantiomers can be found in the case of thalidomide. Thalidomide was a drug commonly prescribed during the 1950's and 1960's in order to alleviate nausea and other symptoms of morning sickness. In fact, only one enantiomer of thalidomide had any therapeutic effect in this regard. The other enantiomer, apart from being therapeutically useless in this application, was subsequently found to be a teratogen, meaning it produces pronounced birth defects. This was obviously not a good thing to prescribe to pregnant women. Workers in the pharmaceutical industry are now much more aware of these kinds of consequences, although of course not all problems with drugs go undetected even through the extensive clinical trials required in the United States. Since the era of thalidomide, however, a tremendous amount of research in the field of synthetic organic chemistry has been devoted to methods of producing only one enantiomer of a useful compound and not the other. This effort probably represents the single biggest aim of synthetic organic chemistry through the last quarter century.

- Enantiomers may have very different biological properties.
- Obtaining enantiomerically pure compounds is very important in medicine and the pharmaceutical industry.

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5.4: Enantiomers and the Tetrahedral Carbon

Objectives

After completing this section, you should be able to

1. use molecular models to show that only a tetrahedral carbon atom satisfactorily accounts for the lack of isomerism in molecules of the type CH_2XY, and for the existence of optical isomerism in molecules of the type CHXYZ.
2. determine whether two differently oriented wedge-and-broken-line structures are identical or represent a pair of enantiomers.

Key Terms

Make certain that you can define, and use in context, the key term below.

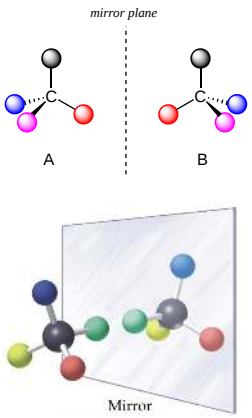
- enantiomer

Study Notes

Stereoisomers are isomers that differ in spatial arrangement of atoms, rather than order of atomic connectivity. One of the most interesting types of isomer is the mirror-image stereoisomer, a non-superimposable set of two molecules that are mirror images of one another. The existence of these molecules are determined by a a concept known as **chirality**. The word “chiral” was derived from the Greek word for hand, because our hands are a good example of chirality since they are non-superimposable mirror images of each other.

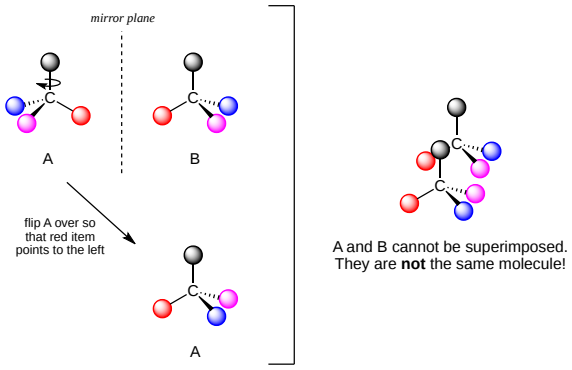
Chiral Molecules

The term **chiral**, from the Greek work for 'hand', refers to anything which cannot be superimposed on its own mirror image. Certain organic molecules are chiral meaning that they are not superimposable on their mirror image. Chiral molecules contain one or more **chiral centers**, which are almost always tetrahedral (sp^3-hybridized) carbons with four different substituents. Consider the molecule A below: a tetrahedral carbon, with four different substituents denoted by balls of four different colors.



The mirror image of A, which we will call B, is drawn on the right side of the figure, and an imaginary mirror is in the middle. Notice that every point on A lines up through the mirror with the same point on B: in other words, if A looked in the mirror, it would see B looking back.

Now, if we flip compound A over and try to superimpose it point for point on compound B, we find that we cannot do it: if we superimpose any two colored balls, then the other two are misaligned.



A is not superimposable on its mirror image (B), thus by definition A is a chiral molecule. It follows that B also is not superimposable on *its* mirror image (A), and thus it is also a chiral molecule.

A and B are called **stereoisomers or optical isomers**: molecules with the same molecular formula and the same bonding arrangement, but *a different arrangement of atoms in space*. **Enantiomers** are pairs of stereoisomers which are mirror images of each other: thus, A and B are enantiomers. It should be self-evident that a chiral molecule will always have one (and *only* one) enantiomer: enantiomers come in pairs. Enantiomers have identical physical properties (melting point, boiling point, density, and so on). However, enantiomers do differ in how they interact with polarized light (we will learn more about this soon) and they may also interact in very different ways with other chiral molecules - proteins, for example. We will begin to explore this last idea in later in this chapter, and see many examples throughout the remainder of our study of biological organic chemistry.

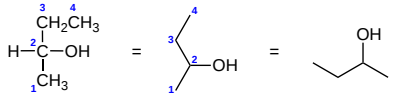
The Many Synonyms of the Chiral Carbon

Be aware - all of the following terms can be used to describe a chiral carbon.

chiral carbon = asymmetric carbon = optically active carbon = stereo carbon = stereo center = chiral center

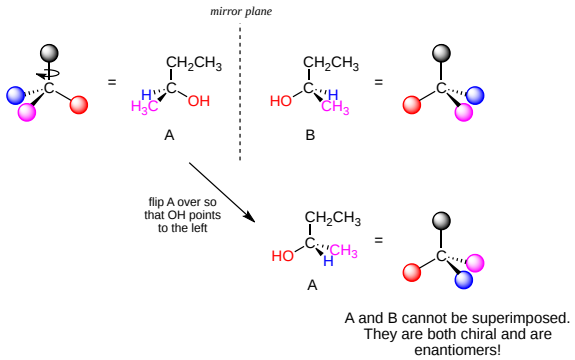
Let's apply our chirality discussion to real molecules.

Consider 2-butanol, drawn in two dimensions below.



2-butanol
(drawn in 2D)

Carbon #2 is a chiral center: it is sp^3-hybridized and tetrahedral (even though it is not drawn that way above), and the four substituents attached to is are different: a hydrogen (H) , a methyl ($-CH_3$) group, an ethyl ($-CH_2CH_3$) group, and a hydroxyl (OH) group. If the bonding at C_2 of 2-butanol is drawn in three dimensions and this structure called A. Then the mirror image of A can be drawn to form structure B.

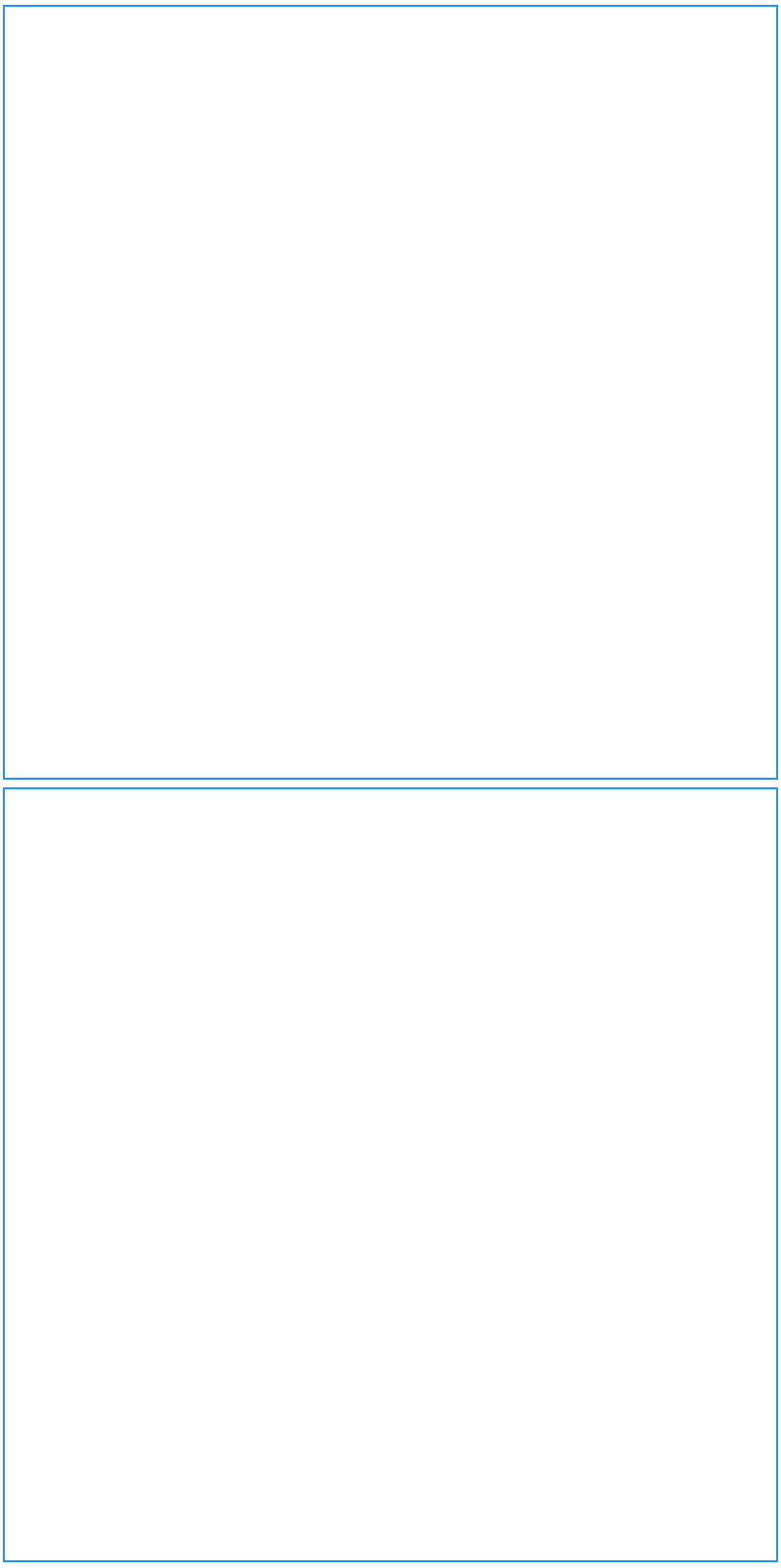


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When we try to superimpose A onto B, we find that we cannot do it. Because structure A and B are not superimposable on their mirror image they are both chiral molecules. Because A and B are different due only to the arrangement of atoms in space they are stereoisomers. Because A and B are mirror images of each other they are also enantiomers. When looking at simplified line structures is clear that there are two distinct ways of drawing 2-butanol which only differ in their spatial arrangement around a chiral carbon.



two enantiomers of 2-butanol

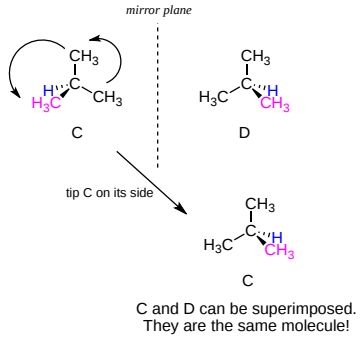


The 3D Structures of the Two Enantiomers of 2-Butanol

For comparison, 2-propanol, is an achiral molecule because is lacks a chiral carbon. Carbon #2 is bonded to two identical substituents (methyl groups), and so it is not a chiral carbon. Being achiral means that 2-propanol should be superimposable on its

mirror image which is shown in the figure below. A more detailed explaination on why 2-propanol is achiral will be given in the next section.

2-propanol is achiral:



Stereoisomers

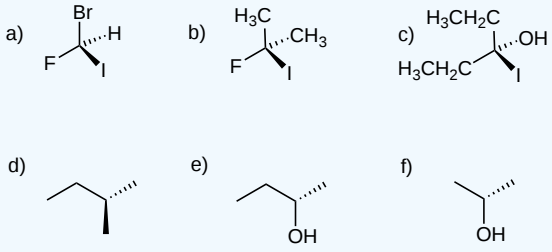
Stereoisomers have been defined as molecules with the same connectivity but different arrangements of the atoms in space. It is important to note that there are two types of stereoisomers: geometric and optical.

Optical isomers are molecules whose structures are mirror images but cannot be superimposed on one another in any orientation. Optical isomers have identical physical properties, although their chemical properties may differ in asymmetric environments. Molecules that are nonsuperimposable mirror images of each other are said to be chiral. 25.7.1a" id="MathJax-Element-1-Frame" role="presentation" style="position:relative;" tabindex="0">

Geometric isomers differ in the relative position(s) of substituents in a rigid molecule. Simple rotation about a C–C σ bond in an alkene, for example, cannot occur because of the presence of the π bond. The substituents are therefore rigidly locked into a particular spatial arrangement. Thus a carbon–carbon multiple bond, or in some cases a ring, prevents one geometric isomer from being readily converted to the other. The members of an isomeric pair are identified as either cis or trans, and interconversion between the two forms requires breaking and reforming one or more bonds. Because their structural difference causes them to have different physical and chemical properties, cis and trans isomers are actually two distinct chemical compounds.mers have the same connectivity, but different arrangements of atoms in space. Geometric isomers will be discussed in more detain in **Sections 7.4 and 7.5**.

Exercise 5.4.1

Identify the following molecules as chiral or achiral.



Answer

a) chiral (4 different groups off C)

b) achiral (2 identical -CH_3 substituents off central C)

c) achiral (2 identical -CH_2CH_3 substituents off central C)

d) achiral (2 identical CH_3 substituents off carbon 2)

e) chiral (4 different groups off carbon 2)

f) achiral (2 identical CH_3 substituents off central C)

Exercise 5.4.2

Determine if the following sets of compounds in each group are enantiomers or the same compound.

a) 

b) 

c) 

d) 

Answer

a) enantiomers – non superimposable mirror images

b) same compound – when you rotate the molecule on the right it is identical to the one on the left

c) enantiomers – non superimposable mirror images

d) enantiomers – non superimposable mirror images

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5.5: The Reason for Handedness in Molecules - Chirality

Objectives

After completing this section, you should be able to

1. determine whether or not a compound is chiral, given its Kelulé, condensed or shorthand structure, with or without the aid of molecular models.
2. label the chiral centres (carbon atoms) in a given Kelulé, condensed or shorthand structure.

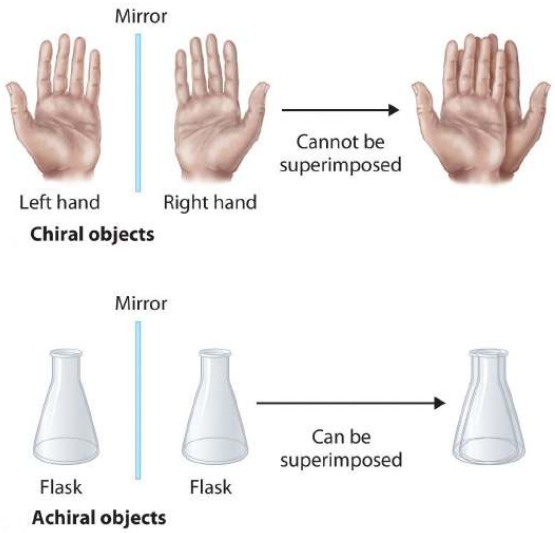
Key Terms

Make certain that you can define, and use in context, the key terms below.

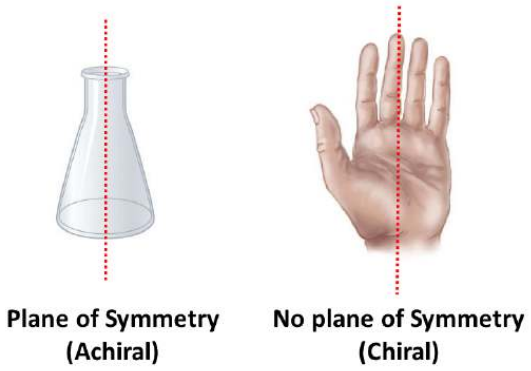
- achiral
- chiral
- chiral (stereogenic) centre
- plane of symmetry

Symmetry and Chirality

Molecules that are nonsuperimposable mirror images of each other are said to be chiral (pronounced “ky-ral,” from the Greek cheir, meaning “hand”). Examples of some familiar chiral objects are your hands. Your left and right hands are nonsuperimposable mirror images. (Try putting your right shoe on your left foot—it just doesn’t work.) An achiral object is one that can be superimposed on its mirror image, as shown by the superimposed flasks 25.7.1b in the figure below. .

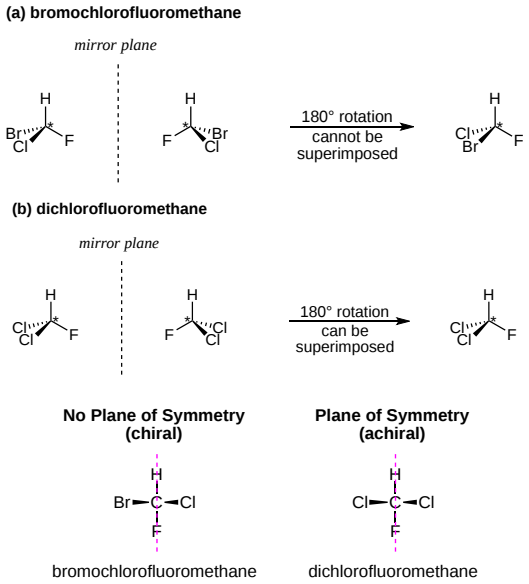


An an important questions is why is one chiral and the other not? The answer is that the flask has a plane of symmetry and your hand does not. A plane of symmetry is a plane or a line through an object which divides the object into two halves that are mirror images of each other. When looking at the flask, a line can be drawn down the middle which separates it into two mirror image halves. However, a similar line down the middle of a hand separates it into two non-mirror image halves. This idea can be used to predict chirality. If an object or molecule has a plane of symmetry it is achiral. If if lacks a plane of symmetry it is chiral.



Symmetry can be used to explain why a carbon bonded to four different substituents is chiral. When a carbon is bonded to fewer than four different substituents it will have a plane of symmetry making it achiral. A carbon atom that is bonded to four different substituents loses all symmetry, and is often referred to as an asymmetric carbon. The lack of a plane of symmetry makes the carbon chiral. The presence of a single chiral carbon atom sufficient to render the molecule chiral, and modern terminology refers to such groupings as chiral centers or stereo centers.

An example is shown in the bromochlorofluoromethane molecule shown in part (a) of the figure below. This carbon, is attached to four different substituents making it chiral. which is often designated by an asterisk in structural drawings. If the bromine atom is replaced by another chlorine to make dichlorofluoromethane, as shown in part (b) below, the molecule and its mirror image can now be superimposed by simple rotation. Thus the carbon is no longer a chiral center. Upon comparison, bromochlorofluoromethane lacks a plane of symmetry while dichlorofluoromethane has a plane of symmetry.



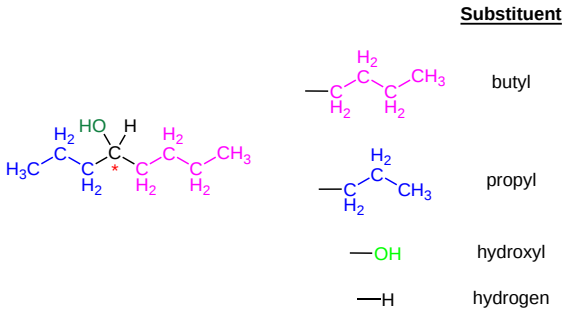
Identifying Chiral carbons

Identifying chiral carbons in a molecule is an important skill for organic chemists. The presence of a chiral carbon presents the possibility of a molecule having multiple stereoisomers. Most of the chiral centers we shall discuss in this chapter are asymmetric carbon atoms, but it should be recognized that other tetrahedral or pyramidal atoms may become chiral centers if appropriately substituted. Also, when more than one chiral center is present in a molecular structure, care must be taken to analyze their relationship before concluding that a specific molecular configuration is chiral or achiral. This aspect of stereoisomerism will be treated later. Because an carbon requires four different substituents to become asymmertric, it can be said, with few exceptions, that

sp^2 and sp hybridized carbons involved in multiple bonds are achiral. Also, any carbon with more than one hydrogen, such as a -CH_3 or -CH_2- group, are also achiral.

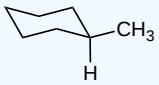
Looking for planes of symmetry in a molecule is useful, but often difficult in practice. It is difficult to illustrate on the two dimensional page, but you will see if you build models of these achiral molecules that, in each case, there is at least one **plane of symmetry**, where one side of the plane is the mirror image of the other. In most cases, the easiest way to decide whether a molecule is chiral or achiral is to look for one or more stereocenters - with a few rare exceptions, the general rule is that molecules with at least one stereocenter are chiral, and molecules with no stereocenters are achiral.

Determining if a carbon is bonded to four distinctly different substituents can often be difficult to ascertain. Remember even the slightest difference makes a substituent unique. Often these difference can be distant from the chiral carbon itself. Careful consideration and often the building of molecular models may be required. A good example is shown below. It may appear that the molecule is achiral, however, when looking at the groups directly attached to the possible chiral carbon, it is clear that they all different. The two alkyl groups are differ by a single -CH_2- group which is enough to consider them different.



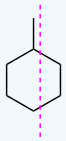
Example 5.5.1

Predict if the following molecule would be chiral or achiral:



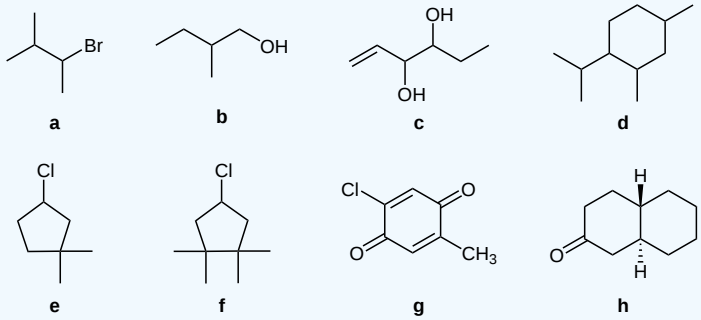
Answer

Achiral. When determining the chirality of a molecule, it best to start by locating any chiral carbons. An obvious candidate is the ring carbon attached to the methyl substituent. The question then becomes: does the ring as two different substituents making the substituted ring carbon chiral? With an uncertainty such as this, it is then helpful try to identify any planes of symmetry in the molecule. This molecule does have a plane of symmetry making the molecule achiral. The plane of symmetry would be easier see if the molecule were view from above. Typically, monosubstituted cycloalkanes have a similar plane of symmetry making them all achiral.

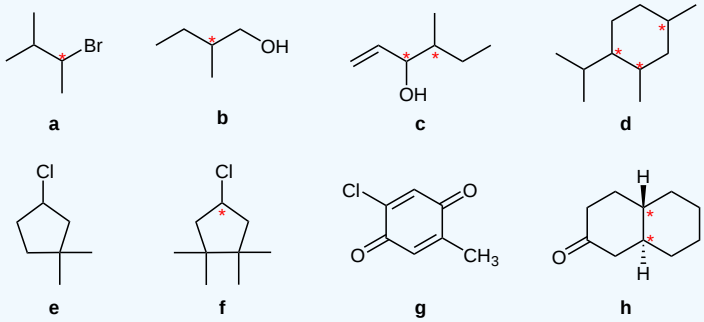


Exercise 5.2.1

Determine if each of the following molecules are chiral or achiral. For chiral molecules indicate any chiral carbons.



Answer

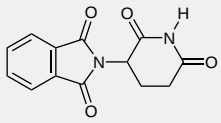


Explanation

Structures F and G are achiral. The former has a plane of symmetry passing through the chlorine atom and bisecting the opposite carbon-carbon bond. The similar structure of compound E does not have such a symmetry plane, and the carbon bonded to the chlorine is a chiral center (the two ring segments connecting this carbon are not identical). Structure G is essentially flat. All the carbons except that of the methyl group are sp^2 hybridized, and therefore trigonal-planar in configuration. Compounds C, D & H have more than one chiral center, and are also chiral.

Note

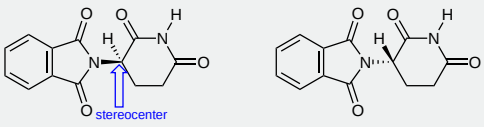
In the 1960's, a drug called thalidomide was widely prescribed in the Western Europe to alleviate morning sickness in pregnant women.



thalidomide

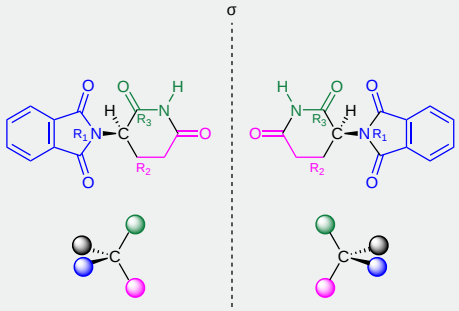
Thalidomide had previously been used in other countries as an antidepressant, and was believed to be safe and effective for both purposes. The drug was not approved for use in the U.S.A. It was not long, however, before doctors realized that something had gone horribly wrong: many babies born to women who had taken thalidomide during pregnancy suffered from severe birth defects.

Researchers later realized the problem lay in the fact that thalidomide was being provided as a mixture of two different isomeric forms.



effective isomer mutagenic isomer

One of the isomers is an effective medication, the other caused the side effects. Both isomeric forms have the same molecular formula and the same atom-to-atom connectivity, so they are not constitutional isomers. Where they differ is in the arrangement in three-dimensional space about one tetrahedral, sp^3-hybridized carbon. These two forms of thalidomide are **stereoisomers**. If you make models of the two stereoisomers of thalidomide, you will see that they too are mirror images, and cannot be superimposed.

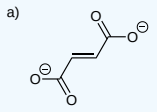


As a historical note, thalidomide was never approved for use in the United States. This was thanks in large part to the efforts of Dr. Frances Kelsey, a Food and Drug officer who, at peril to her career, blocked its approval due to her concerns about the lack of adequate safety studies, particularly with regard to the drug's ability to enter the bloodstream of a developing fetus. Unfortunately, though, at that time clinical trials for new drugs involved widespread and unregulated distribution to doctors and their patients across the country, so families in the U.S. were not spared from the damage caused.

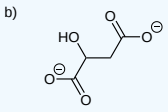
Very recently a close derivative of thalidomide has become legal to prescribe again in the United States, with strict safety measures enforced, for the treatment of a form of blood cancer called multiple myeloma. In Brazil, thalidomide is used in the treatment of leprosy - but despite safety measures, children are still being born with thalidomide-related defects.

Example 5.2.2

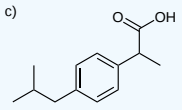
Label the molecules below as chiral or achiral, and locate all stereocenters.



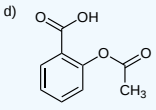
fumarate
(a citric acid cycle intermediate)



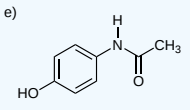
malate
(a citric acid cycle intermediate)



ibuprofen

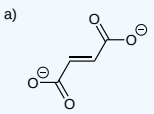


acetylsalicylic acid
(aspirin)

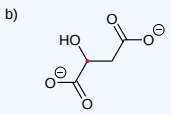


acetaminophen
(active ingredient in Tylenol)

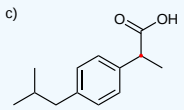
Answer



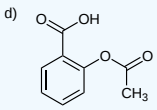
fumarate
(achiral)



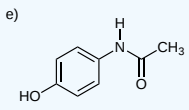
malate
(chiral)



ibuprofen
(chiral)



acetylsalicylic acid
(achiral)

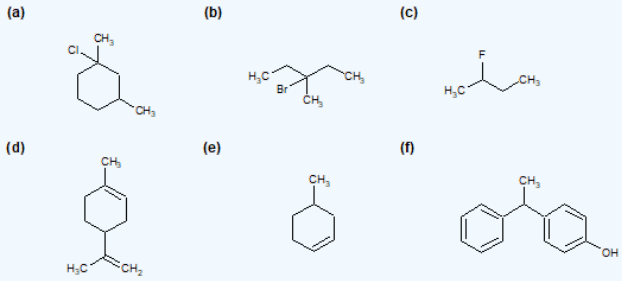


acetaminophen
(achiral)

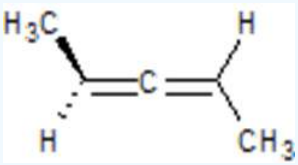
https://chem.libretexts.org/@go/page/418111

Exercise 5.2.2

1) For the following compounds, star (*) each chiral center, if any.



2) Explain why the following compound is chiral.



3) Determine which of the following objects is chiral.

a) A Glove.

b) A nail.

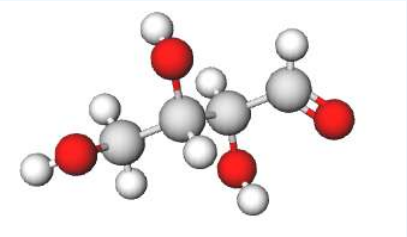
c) A pair of sunglasses.

d) The written word "Chiral".

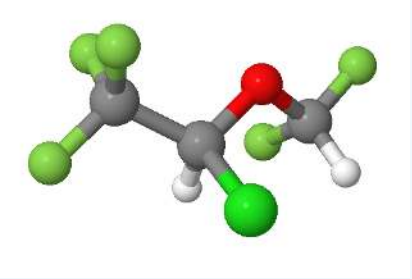
4) Place an "*" by all of the chrial carbons in the following molecules.

a)

Erythrose, a four carbon sugar.

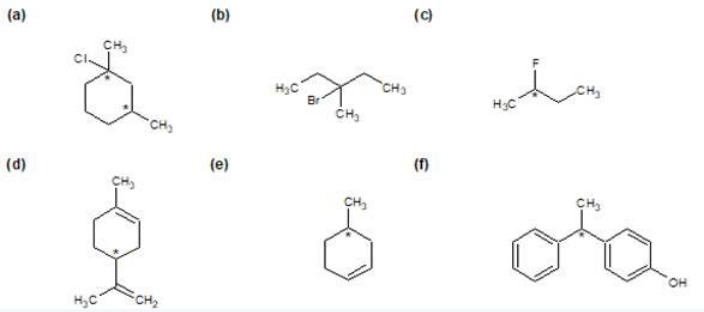


b) Isoflurane, an anestetic. Bright green = Chlorine, Pale green = Fluorine.



Answer

1)



2) Though the molecule does not contain a chiral carbon, it is chiral as it is non-superimposable on its mirror image due to its twisted nature (the twist comes from the structure of the double bonds needing to be at 90° angles to each other, preventing the molecule from being planar).

3)

a) Just as hands are chiral a glove must also be chiral.

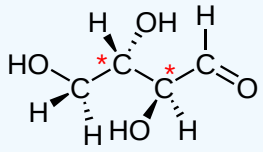
b) A nail has a plane of symmetry which goes down the middle making it a achiral.

c) A pair of sunglasses has a plane of symmetry which goes through the nose making it achiral.

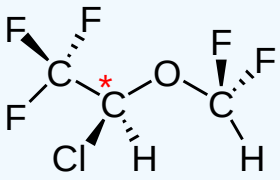
d) Most written words are chiral. Look one in a mirror to confirm this.

4

a)

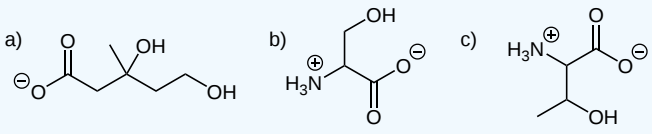


b)



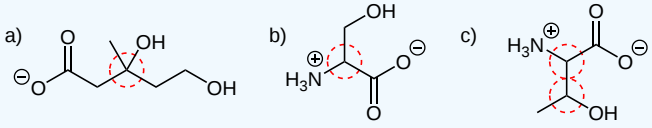
Exercise 5.2.3

Circle all of the carbon stereocenters in the molecules below.



mevalonate serine threonine

Answer

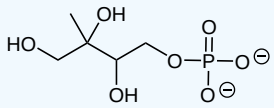


mevalonate serine threonine

Exercise 5.2.4

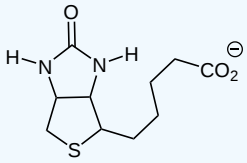
Circle all of the carbon stereocenters in the molecules below.

a)



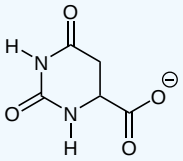
2-methylerythritol-4-phopshate

b)



biotin

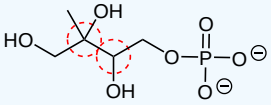
c)



dihydroorotate

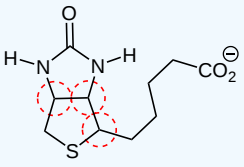
Answer

a)



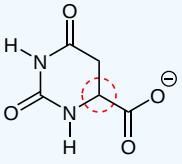
2-methylerythritol-4-phopshate

b)



biotin

c)

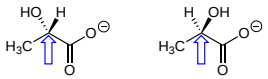


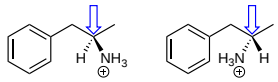
dihydroorotate

Here are some more examples of chiral molecules that exist as pairs of enantiomers. In each of these examples, there is a single stereocenter, indicated with an arrow. (Many molecules have more than one stereocenter, but we will get to that that a little later!)

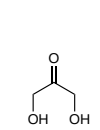

glyceraldehyde

alanine

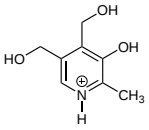

lactate

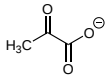

amphetamine

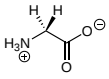
Here are some examples of molecules that are **achiral** (*not* chiral). Notice that none of these molecules has a stereocenter.

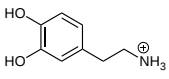

dihydroxyacetone


citrate


pyridoxine (vitamin B_6)


pyruvate


glycine (amino acid)


dopamine (neurotransmitter)

It is difficult to illustrate on the two dimensional page, but you will see if you build models of these achiral molecules that, in each case, there is at least one **plane of symmetry**, where one side of the plane is the mirror image of the other. Chirality is tied conceptually to the idea of asymmetry, and *any molecule that has a plane of symmetry cannot be chiral*. When looking for a plane of symmetry, however, we must consider all possible conformations that a molecule could adopt. Even a very simple molecule like ethane, for example, is asymmetric in many of its countless potential conformations – but it has obvious symmetry in both the eclipsed and staggered conformations, and for this reason it is achiral.

Looking for planes of symmetry in a molecule is useful, but often difficult in practice. In most cases, the easiest way to decide whether a molecule is chiral or achiral is to look for one or more stereocenters - with a few rare exceptions (see section 3.7B), the general rule is that molecules with at least one stereocenter are chiral, and molecules with no stereocenters are achiral. Carbon stereocenters are also referred to quite frequently as **chiral carbons**.

When evaluating a molecule for chirality, it is important to recognize that the question of whether or not the dashed/solid wedge drawing convention is used is irrelevant. Chiral molecules are sometimes drawn without using wedges (although obviously this means that stereochemical information is being omitted). Conversely, wedges may be used on carbons that are not stereocenters – look, for example, at the drawings of glycine and citrate in the figure above. Just because you see dashed and solid wedges in a structure, do not automatically assume that you are looking at a stereocenter.

Other elements in addition to carbon can be stereocenters. The phosphorus center of phosphate ion and organic phosphate esters, for example, is tetrahedral, and thus is potentially a stereocenter.

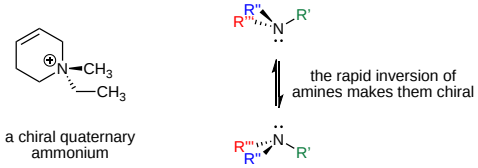

phosphate (achiral)


labeled phosphate ester (chiral)


a chiral phosphate triester

We will see in chapter 10 how researchers, in order to investigate the stereochemistry of reactions at the phosphate center, incorporated sulfur and/or ^{17}O and ^{18}O isotopes of oxygen (the 'normal' isotope is ^{16}O) to create chiral phosphate groups. Phosphate triesters are chiral if the three substituent groups are different.

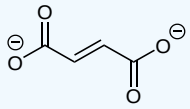
Asymmetric quaternary ammonium groups are also chiral. Amines, however, are not chiral, because they rapidly invert, or turn 'inside out', at room temperature.



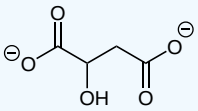
Exercise 5.2.5

Label the molecules below as chiral or achiral, and circle all stereocenters.

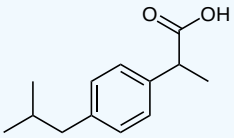
a) fumarate (a citric acid cycle intermediate)



b) malate (a citric acid cycle intermediate)

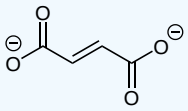


b) malate (a citric acid cycle intermediate)

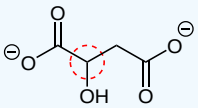


Answer

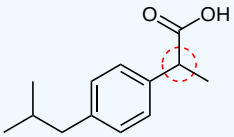
a) achiral (no stereocenters)



b) chiral



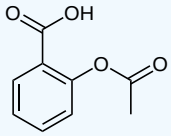
c) chiral



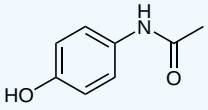
Exercise 5.2.6

Label the molecules below as chiral or achiral, and circle all stereocenters.

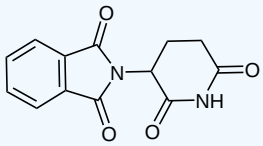
a) acetylsalicylic acid (aspirin)



b) acetaminophen (active ingredient in Tylenol)

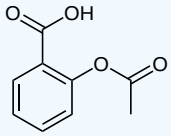


c) thalidomide (drug that caused birth defects in pregnant mothers in the 1960's)

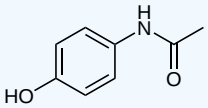


Answer

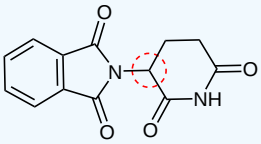
a) achiral (no stereocenters)



b) achiral (no stereocenters)

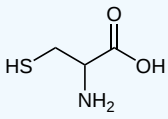


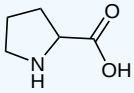
c) chiral



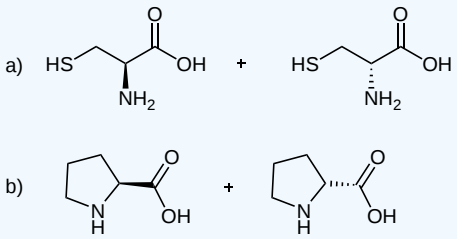
Exercise 5.2.7

Draw both enantiomers of the following chiral amino acids.

a) Cysteine 

b) Proline 

Answer



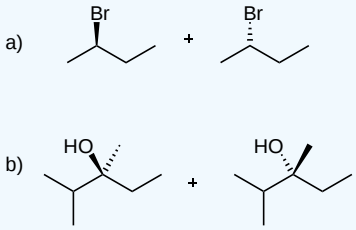
Exercise 5.2.8

Draw both enantiomers of the following compounds from the given names.

a) 2-bromobutane

b) 2,3-dimethyl-3-pentanol

Answer



Exercise 5.2.9

Which of the following body parts are chiral?

a) Hands b) Eyes c) Feet d) Ears

Answer

a) Hands- chiral since the mirror images cannot be superimposed (think of the example in the beginning of the section)

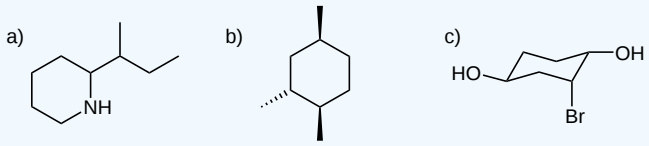
b) Eyes- achiral since mirror images that are superimposable

c) Feet- chiral since the mirror images cannot be superimposed (Does your right foot fit in your left shoe?)

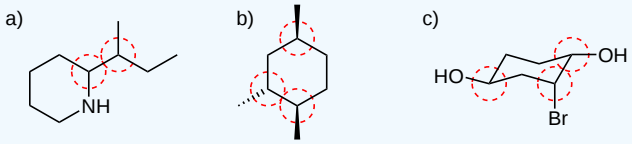
d) Ears- chiral since the mirror images cannot be superimposed

Exercise 5.2.10

Circle the chiral centers in the following compounds.



Answer

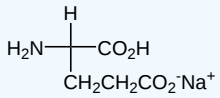


https://chem.libretexts.org/@go/page/418111

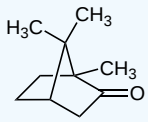
Exercise 5.2.11

Identify the chiral centers in the following compounds.

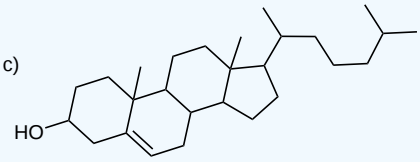
a)



b)

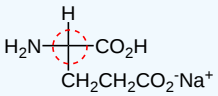


c)

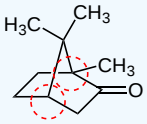


Answer

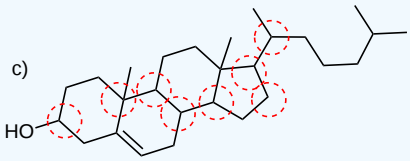
a)



b)



c)



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5.6: Sequence Rules for Specifying Configuration

Objectives

After completing this section, you should be able to

1. assign Cahn-Ingold-Prelog priorities to a given set of substituents.
2. determine whether a given wedge-and-broken-line structure corresponds to an *R* or an *S* configuration, with or without the aid of molecular models.
3. draw the wedge-and-broken-line structure for a compound, given its IUPAC name, complete with *R* or *S* designation.
4. construct a stereochemically accurate model of a given enantiomer from either a wedge-and-broken-line structure or the IUPAC name of the compound, complete with *R* or *S* designation.

Key Terms

Make certain that you can define, and use in context, the key terms below.

- absolute configuration
- *R* configuration
- *S* configuration

Study Notes

When designating a structure as *R* or *S*, you must ensure that the atom or group with the lowest priority is pointing away from you, the observer. The easiest way to show this is to use the wedge-and-broken-line representation. You can then immediately determine whether you are observing an *R* configuration or an *S* configuration.

To name the enantiomers of a compound unambiguously, their names must include the "handedness" of the molecule. The method for this is formally known as *R*/*S* nomenclature.

Introduction

The method of unambiguously assigning the handedness of molecules was originated by three chemists: R.S. Cahn, C. Ingold, and V. Prelog and, as such, is also often called the Cahn-Ingold-Prelog rules. In addition to the Cahn-Ingold system, there are two ways of experimentally determining the absolute configuration of an enantiomer:

1. X-ray diffraction analysis. Note that there is no correlation between the sign of rotation and the structure of a particular enantiomer.
2. Chemical correlation with a molecule whose structure has already been determined via X-ray diffraction.

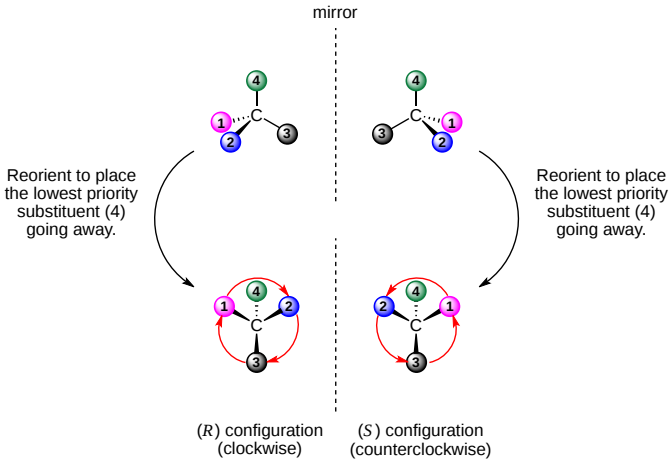
However, for non-laboratory purposes, it is beneficial to focus on the (*R*)/(*S*) system. The sign of optical rotation, although different for the two enantiomers of a chiral molecule,at the same temperature, **cannot** be used to establish the absolute configuration of an enantiomer; this is because the sign of optical rotation for a particular enantiomer may change when the temperature changes.

Stereocenters are labeled (*R*) or (*S*)

The "right hand" and "left hand" nomenclature is used to name the enantiomers of a chiral compound. The stereocenters are labeled as (*R*) or (*S*).

The **Cahn-Ingold-Prelog** rules of assign priorities the groups directly bonded to the chiral carbon. Having ranked the four groups attached to a chiral carbon, we describe the stereochemical configuration around the carbon by orienting the molecule so that the group with the lowest ranking (4) is given a dash bond to indicate it points directly away from us. We then look at the three remaining substituents, which now appear to radiate toward us which is shown by using wedge bonds. If a curved arrow drawn from the highest to second-highest to third-highest ranked substituent is clockwise, we say that the chirality center has the (R) configuration (Latin rectus, meaning “right”). If an arrow from is counterclockwise, the chirality center has the (S) configuration

(Latin sinister, meaning “left”). To remember these assignments, think of a car’s steering wheel when making a Right (clockwise) turn. Note, the (R) or (S) configurations represent the two enantiomers of a chiral molecule. The (R) or (S) configuration is often added as a prefix, in parenthesis, to a chiral molecule's name to indicate which enantiomer is being discussed (e.g., (R)-2-bromobutane). If more than chiral carbon is present in a chiral molecule, each carbon's number is included before the (R) or (S) configuration. Ex: (2R,4S,6R)-2-bromo-6-chloro-4-methylheptane.



Sequence Rules to Assign Priorities to Substituents

Before applying the (*R*) and (*S*) nomenclature to a stereocenter, the substituents must be prioritized according to the following rules:

Rule 1

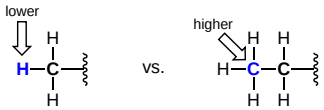
First, examine at the atoms directly attached to the stereocenter of the compound. A atom with a higher atomic number takes precedence over a atom with a lower atomic number. Hydrogen is the lowest possible priority atom, because it has the lowest atomic number.

1. The atom with higher atomic number has higher priority (I > Br > Cl > S > P > F > O > N > C > H).
2. When comparing isotopes, the atom with the higher mass number has higher priority [^{18}O > ^{16}O or ^{15}N > ^{14}N or ^{13}C > ^{12}C or T (^{3}H) > D (^{2}H) > H].

Rule 2

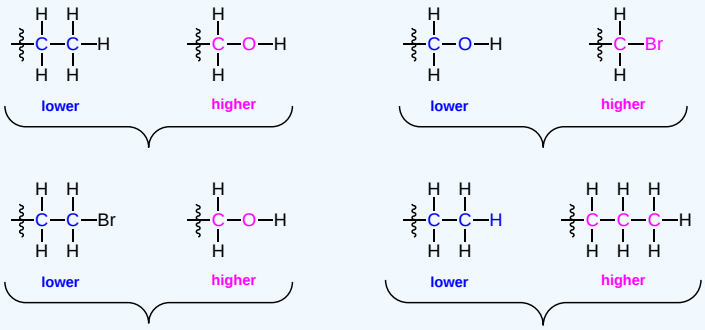
If there are two or more substituents which have the same element directly attached to chiral carbon, proceed along the substituent chains until a point of difference is found. Determine which of the chains has the first connection to an atom with the highest priority (the highest atomic number). That chain has the higher priority.

For example: an ethyl substituent takes priority over a methyl substituent. At the connectivity of the stereocenter, both have a carbon atom, which are equal in rank. Going down the chains, a methyl has only has hydrogen atoms attached to it, whereas the ethyl has two hydrogen atoms and a carbon atom. The carbon atom on the ethyl is the first point of difference and has a higher atomic number than hydrogen; therefore the ethyl takes priority over the methyl.



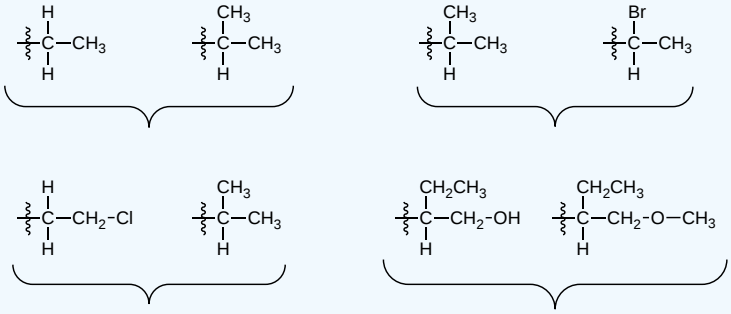
The "-H" (left) ranks lower than the "C-" (right) based on the relative molecular weights at the first point of difference.

Example 5.6.1



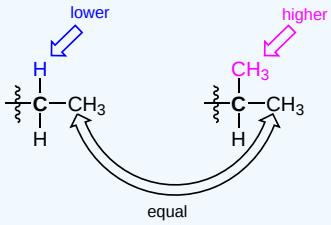
Worked Exercise 5.6.1

For the following pairs of substituents, determine which would have the higher and lower priority based on the **Cahn-Ingold-Prelog** rules. Explain your answer.



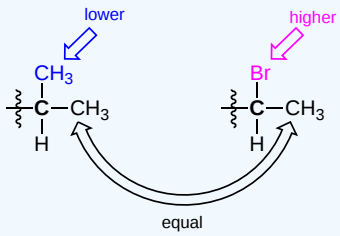
Answer

A 1-methylethyl substituent takes precedence over an ethyl substituent. Connected to the first carbon atom, ethyl only has one other carbon, whereas the 1-methylethyl has two carbon atoms attached to the first; this is the first point of difference. Therefore, 1-methylethyl ranks higher in priority than ethyl, as shown below:



The "C-" (right) ranks higher than the "H-" (left) based on the first point of difference and their relative atomic numbers.

However:

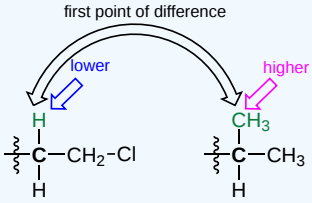


In this case, even though the bold carbon on the right structure has two connections to a non-hydrogen atom (C), it is the lower priority.

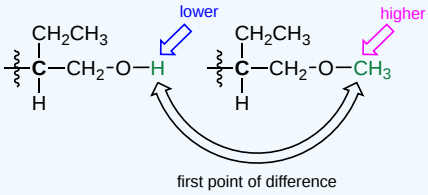
This is because one of the atoms attached to the bold carbon on the left molecule ranks higher than any of the atoms attached to the bold carbon on the right structure, since Br has a higher atomic number than C.

Caution!!

Keep in mind that priority is determined by the **first** point of difference along the two similar substituent chains. After the first point of difference, the rest of the chain is irrelevant.

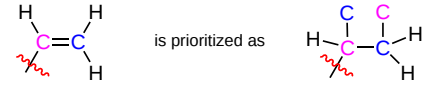


When looking for the first point of difference on similar substituent chains, one may encounter branching. If there is branching, choose the branch that is higher in priority. If the two substituents have similar branches, rank the elements within the branches until a point of difference.

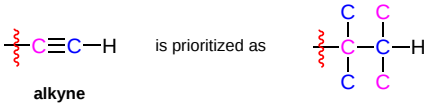


Rule 3

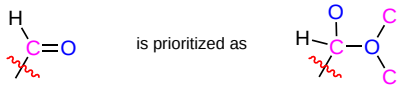
For assigning priority, multiple bonds are treated as if each bond of the multiple bond is bonded to a unique atom. For example, an alkene substituent (CH_2=CH-) has higher priority than an ethyl substituent (CH_3CH_2-). The alkene carbon priority is "two" bonds to carbon atoms and one bond to a hydrogen atom compared with the ethyl carbon that has only one bond to a carbon atom and two bonds to two hydrogen atoms. Similarly, alkyne substituent (HCC-) would have an even higher priority because the alkyne carbon is treated as if it is bonded to three carbons. This method remains the same with compounds containing a carbonyl (C=O) group. The carbon of an aldehyde substituent (O=CH-) is treated as if it is bonded to a hydrogen and two oxygen atoms.



alkene



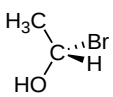
alkyne



aldehyde

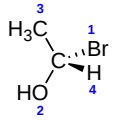
Determining (*R*) or (*S*) Configuration Using a Molecular Model

In order to demonstrate how to determine the (*R*)/(*S*) configuration of the chiral carbon in the following molecule using molecular models, first construct a model of the bromoethanol structure:

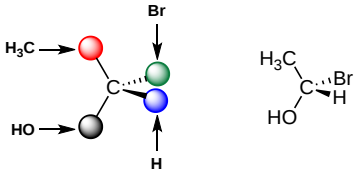


First make a molecular model of a tetrahedral carbon with four different substituents. In many cases, this will appear as a carbon with four bonds with a different colored ball attached to each bond.

For the molecule in question, determine the location of the chiral carbon and assign CIP priorities to the substituents. In this case, Br gets the highest priority because it has the highest atomic number. The O in the OH substituent gets priority 2 and the C in CH_3 gets priority 3. Lastly, H gets the lowest priority, 4, because it has the smallest atomic number.



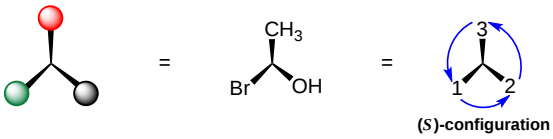
Now take your molecular model and orientate it to match the molecule in question. Remember in the dash/wedge representation, two regular bonds are in the plane of the page. The wedge bond is coming toward you and the dashed bond is going away from you. If you were to hold a piece of paper directly in front of you, the substituents with the regular bond should both be touching the piece of paper. The dashed bond should be pointing behind the piece of paper and the wedge bond should be pointing in front.



In this structure, the bromine is going away from you, the hydrogen is coming toward you and the hydroxide and methyl groups are in the plane of the page.

Then based on the position, assign each substituent on the chiral carbon a colored ball on your molecular model. In this case, bromine is going away so it is assigned the green ball. The hydrogen is coming toward you so it is assigned the blue ball. The last two substituents are in the plane of the page, however, the CH_3 is positioned higher so it is assigned the red ball which leaves OH being assigned the black ball.

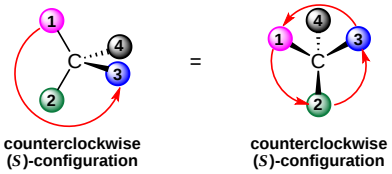
Lastly, grab onto the ball for the lowest priority substitutent, in this case the blue one, and point the other three substituents towards you. The three bonds should be angled towards you as if they all have wedge bonds. Assign the original substituents and their corresponding CIP priorities to the three colored balls. The green ball was assigned to bromine which was given priority one. The OH was assigned to the black ball and given priority two. The CH_3 was assigned to the red ball and given priority three. In this case the priorities are going counter clockwise so the chiral carbon has an ***(S)*** configuration.



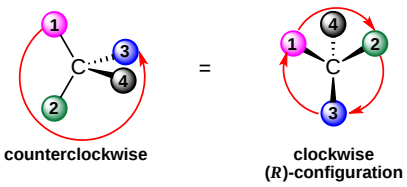
Determining (*R*) or (*S*) Configuration Without a Molecular Model

If a molecular model cannot be used there are a couple of simple methods which can be applied if the dash/wedge bond system is being used.

After assigning CIP priorities, if the lowest priority substituent (4) is on the dash bond the configuration of substituents 1-3 can be assigned directly. As shown in the figure below, the configuration of substituents 1-3 does not change when moving to sight down the bond of substituent 4. In both cases, substituents 1-3 are ordered in a counterclockwise fashion which gives the chiral carbon an (*S*) configuration.



The opposite is true if the lowest priority substituent (4) is on the wedge bond. As shown in the figure below, the configuration of substituents 1-3 is inverted when moving to sight down the bond of substituent 4. When the lowest priority substituent is on the wedge bond, the configuration of substituents 1-3 can be assigned directly only if the direction is inverted. i.e. clockwise = (*S*) and counterclockwise = (*R*).

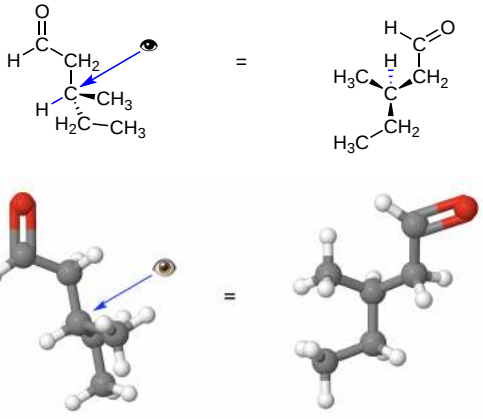


With the lowest priority group in front, drawing an arc from 1 to 2 to 3 gives the reverse of the configuration.

However, if the lowest priority substituent is on one of the regular bonds when the dash/wedge system is being used then configurations are best assigned by changing perspectives. This method can also be used if the three-dimensional configuration of the chiral carbon is represented. First, locate the chiral carbon and assign CIP priorities to its substituents. Then while perceiving the drawn molecule as a three-dimensional image, mentally change your perspective such that you are looking down the bond between the chiral carbon and the lowest CIP ranked substituent (#4). If done correctly, the bonds for substituents 1-3 should be coming towards you as wedge bonds. You can then follow the direction of the CIP priority numbers to determine the (*R*)/(*S*) configuration of the chiral carbon.

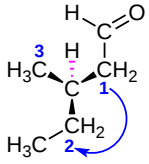


Locate the chiral carbon and assign CIP priorities to its substituents.



Mentally sight down the bond between the chiral carbon and the lowest CIP ranked substituent.

This bond is shown in magenta.



clockwise

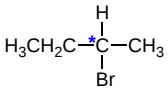
(*R*)-configuration

Follow the direction of the CIP priority numbers to determine the (*R*)/(*S*) configuration.

Drawing the Structure of a Chiral Molecule from its Name

Draw the structure of (*S*)-2-Bromobutane:

1) Draw the basic structure of the molecule and determine the location of the chiral carbon.



2) Determine the chiral carbon's substituents and assign them a CIP priority.

-H (Priority 4)

-CH_3 (Priority 3)

-CH_2CH_3 (Priority 2)

-Br (Priority 1)

3) Draw the chiral carbon in a dash/wedge form and add the lowest priority substituent to the dash bond. In this case, the lowest priority substituent is -H.



4) Add the remaining substituents in a clockwise fashion for (*R*) and a counterclockwise fashion for (*S*).



clockwise (*R*)-configuration

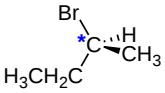


counterclockwise (*S*)-configuration

The molecule posed in this question has an (*S*) configuration so the remaining substituents are added in a counterclockwise fashion.



counterclockwise (*S*)-configuration



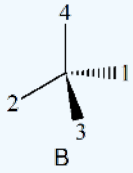
(*S*)-2-bromobutane

? Exercise 5.6.1

1) Orient the following so that the least priority (4) atom is paced behind, then assign stereochemistry ((*R*) or (*S*)).



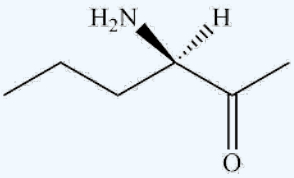
A



B

2) Draw (*R*)-2-bromobutan-2-ol.

3) Assign (*R*)/(*S*) to the following molecule.



4) Which in the following pairs would have a higher CIP priority?

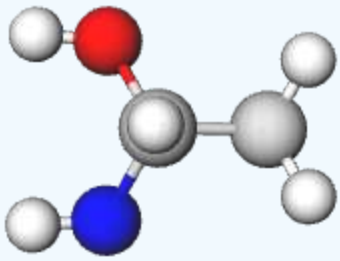
a. -H or -Cl
b. -Br or -I
c. $-CH_2OH$ or $-OCH_3$
d. $-CH_2CH_3$ or $-CH=CH_2$
e. $-NH_2$ or -OH

5) Rank the following substituents in order of their CIP priority:

a. -H, $-OCH_3$, $-CH_2OH$, -OH
b. -OH, $-CO_2H$, -CH=O, $-CH_2OH$
c. -CN, $-NH_2$, -CH=O, $-NHCH_3$
d. -SH, $-SCH_3$, -OH, $-OOCH_3$

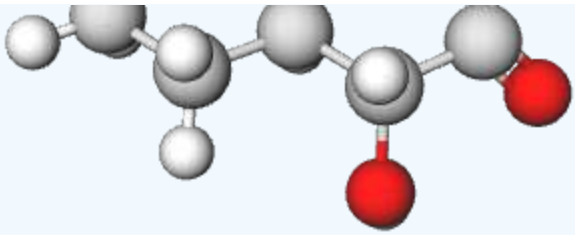
6) Determine if the chiral carbon in the following molecules have an (*R*) or (*S*) configuration. Red = Oxygen & Blue = Nitrogen.

a)



b)

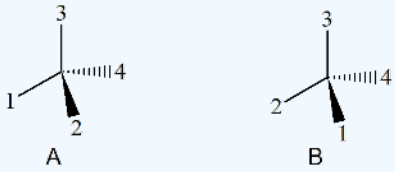




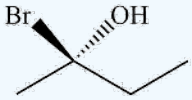
GLmol

Answer

1) A is (*S*) and B is (*R*).



2)



3) The stereocenter is (*R*).

4)

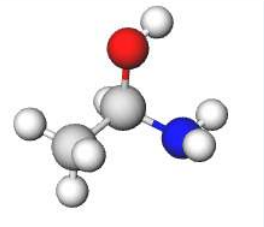
a. -Cl
b. -I
c. $-OCH_3$
d. $-CH=CH_2$
e. -OH

5) Rank the following substituents in order of their CIP priority:

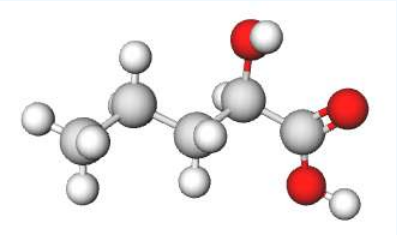
a. $-OCH_3$, -OH, $-CH_2OH$, -H,
b. -OH, $-CO_2H$, -CH=O, $-CH_2OH$
c. $-NHCH_3$, $-NH_2$, -CH=O, -CN
d. $-SCH_3$, -SH, $-OOCH_3$, -OH

6)

a) The chiral carbon is (*R*). The four substituents of the chiral carbon are -OH (1), $-NH_2$ (2), $-CH_3$ (3), and -H (4). Then looking down the lowest priority bond, you should roughly see what appears in the picture below. The substituents with priorities 1-3 are ordered in a clockwise fashion so the chiral carbon is (*R*).



b) The chiral carbon is (*S*). The four substituents of the chiral carbon are -CO_2H (1), -OH (2), -$CH_2CH_2CH_3$ (3), and -H (4). Then looking down the lowest priority bond, you should roughly see what appears in the picture below. The substituents with priorities 1-3 are ordered in a counterclockwise fashion so the chiral carbon is (*S*).



? Exercise 5.6.2

Identify which substituent in the following sets has a higher ranking.

a. -H or -CH_3
b. -$CH_2CH_2CH_3$ or CH_2CH_3
c. -CH_2Cl or CH_2OH

Answer

a. **-CH_3**
b. **-$CH_2CH_2CH_3$**
c. **-CH_2Cl**

? Exercise 5.6.3

Identify which substituent in the following sets has a higher ranking.

a. -NH_2 or -N=NH
b. -CH_2CH_2OH or -CH_2OH
c. -$CH=CH_2$ or -CH_2CH_3

Answer

a) **-N=NH**

b) **-CH_2OH**

c) **-$CH=CH_2$**

? Exercise 5.6.4

Place the following sets of substituents in each group in order of lowest priority (1^{st}) to highest priority (4^{th})

a. -NH_2, -F, -Br, -CH_3
b. -SH, -NH_2, -F, -H

Answer

a) $-CH_3 < -NH_2 < -F, < -Br$

b) $-H < -NH_2 < -F, < -SH$

Exercise 5.6.5

Place the following sets of substituents in each group in order of lowest priority (1st) to highest priority (4th)

a. $-CH_2CH_3$, -CN, $-CH_2CH_2OH$, $-CH_2CH_2CH_2OH$
b. $-CH_2NH_2$, $-CH_2SH$, $-C(CH_3)_3$, -CN

Answer

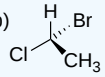
a) $-CH_2CH_3 < -CH_2CH_2OH < -CH_2CH_2CH_2OH, < -CN$

b) $-C(CH_3)_3 < -CH_2NH_2 < -CN < -CH_2SH$

Exercise 5.6.6

Assign the following chiral centers as (*R*) or (*S*).

a) 

b) 

c) 

Answer

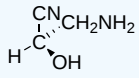
a) **(*S*)**: I > Br > F > H. The lowest priority substituent is going backwards so following the highest priority, it goes left (counterclockwise).

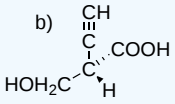
b) **(*R*)**: Br > Cl > CH_3 > H. Using a model kit, you need to rotate the H to the back position where the Br is. This causes the priority to go to the left (clockwise) when looking at it with the H in the back position. Alternatively, if you do not have a model kit, you can imagine the structure 3-dimensionally and since the lowest priority (H) is facing up (as drawn), if you look at it from below, starting with Br (1st priority) and moving towards Cl (2nd priority), you are moving right (clockwise) which represents (*R*) stereochemistry.

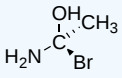
c) **Neither (*R*) or (*S*)**: Since there are two identical substituents (H's) the molecule is achiral and cannot be assigned (*R*) or (*S*).

Exercise 5.6.7

Assign the following chiral centers as (*R*) or (*S*).

a) 

b) 

c) 

Answer

a) **(*R*)**: OH > CN (C triple bonded to N) > CH_2NH_2 > H. The H needs to be moved to the back position which causes the priority to go to the right (clockwise) which indicates (*R*).

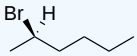
b) **(*S*)**: COOH > CH_2OH > C ≡ CH > H. Since the H is coming forward, you can assign the priority and it goes to the right (clockwise which would be (*R*)) but since the lowest priority is forward, you have to switch it to (*S*). Alternatively, you can rotate the molecule to put the lowest priority to the back and you'll see that it rotates left (or counterclockwise) for (*S*).

c) **(*S*)**: Br > OH > NH_2 > CH_3. Since the lowest priority is going back, you can follow the priority and see that it is going left (counterclockwise) and therefore (*S*).

? Exercise 5.6.8

Draw the structure of (*R*)-2-bromohexane.

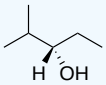
Answer



? Exercise 5.6.9

Draw the structure of (*S*)-2-methyl-3-pentanol.

Answer



References

1. Schore and Vollhardt. *Organic Chemistry Structure and Function.* New York:W.H. Freeman and Company, 2007.
2. McMurry, John and Simanek, Eric. *Fundamentals of Organic Chemistry*. 6th Ed. Brooks Cole, 2006.

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5.7: Diastereomers

Objectives

After completing this section, you should be able to

1. calculate the maximum number of stereoisomers possible for a compound containing a specified number of chiral carbon atoms.
2. draw wedge-and-broken-line structures for all possible stereoisomers of a compound containing two chiral carbon atoms, with or without the aid of molecular models.
3. assign (*R*)/(*S*) configurations to wedge-and-broken-line structures containing two chiral carbon atoms, with or without the aid of molecular models.
4. determine, with or without the aid of molecular models, whether two wedge-and-broken-line structures containing two chiral carbon atoms are identical, represent a pair of enantiomers, or represent a pair of diastereomers.
5. draw the wedge-and-broken-line structure of a specific stereoisomer of a compound containing two chiral carbon atoms, given its IUPAC name and (*R*)/(*S*) configuration.

Key Terms

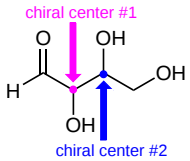
Make certain that you can define, and use in context, the key term below.

- diastereomer

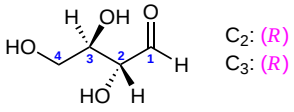
Diastereomers are two molecules which are stereoisomers (same molecular formula, same connectivity, different arrangement of atoms in space) but are *not* enantiomers. Unlike enantiomers which **are mirror images** of each other and **non-superimposable**, diastereomers are **not mirror images** of each other and **non-superimposable**. Diastereomers can have different physical properties and reactivity. They have different melting points and boiling points and different densities. In order for diastereomer stereoisomers to occur, a compound must have **two or more** stereocenters.

Introduction

So far, we have been analyzing compounds with a single chiral center. Next, we turn our attention to those which have multiple chiral centers. We'll start with some stereoisomeric four-carbon sugars with two chiral centers.



We will start with a common four-carbon sugar called D-erythrose.

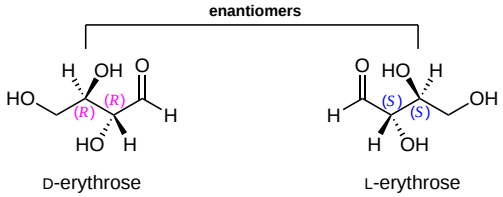


D-erythrose

A note on sugar nomenclature: biochemists use a special system to refer to the stereochemistry of sugar molecules, employing names of historical origin in addition to the designators '*D*' and '*L*'. You will learn about this system if you take a biochemistry class. We will use the *D*/*L* designations here to refer to different sugars, but we won't worry about learning the system.

As you can see, *D*-erythrose is a chiral molecule: C_2 and C_3 are stereocenters, both of which have the (*R*) configuration. In addition, you should make a model to convince yourself that it is impossible to find a plane of symmetry through the molecule, regardless of the conformation. Does D-erythrose have an enantiomer? Of course it does – if it is a chiral molecule, it must. The

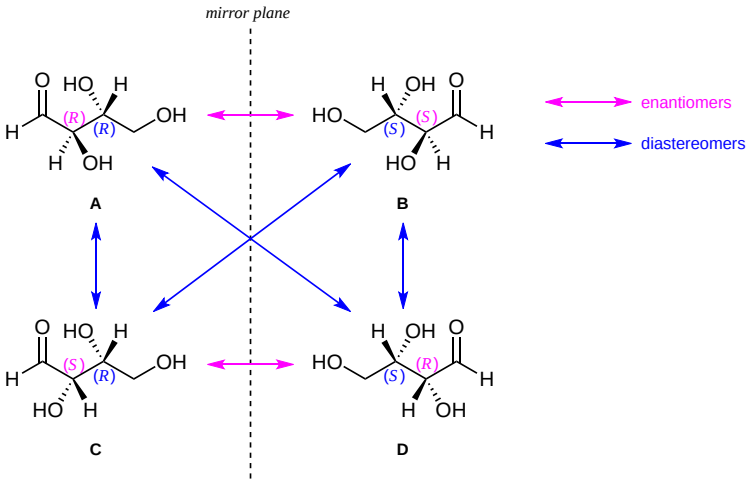
enantiomer of erythrose is its mirror image, and is named L-erythrose (once again, you should use models to convince yourself that these mirror images of erythrose are not superimposable).



Notice that both chiral centers in L-erythrose both have the (*S*) configuration. To avoid confusion, we will simply refer to the different stereoisomers by capital letters.

Now let's consider all the possible stereoisomers.

Look first at compound A below. Both chiral centers in have the (*R*) configuration (you should confirm this for yourself!). The mirror image of Compound A is compound B, which has the (*S*) configuration at both chiral centers. If we were to pick up compound A, flip it over and put it next to compound B, we would see that they are *not* superimposable (again, confirm this for yourself with your models!). A and B are nonsuperimposable mirror images: in other words, enantiomers.



Now, look at compound C, in which the configuration is (*S*) at chiral center 1 and (*R*) at chiral center 2. Compounds A and C are stereoisomers: they have the same molecular formula and the same bond connectivity, but a different arrangement of atoms in space (recall that this is the definition of the term 'stereoisomer). However, they are *not* mirror images of each other (confirm this with your models!), and so they are *not* enantiomers. By definition, they are **diastereomers** of each other.

Notice that compounds C and B also have a diastereomeric relationship, by the same definition.

So, compounds A and B are a pair of enantiomers, and compound C is a diastereomer of both of them. Does compound C have its own enantiomer? Compound D is the mirror image of compound C, and the two are not superimposable. Therefore, C and D are a pair of enantiomers. Compound D is also a diastereomer of compounds A and B.

This can also seem very confusing at first, but there some simple shortcuts to analyzing stereoisomers:

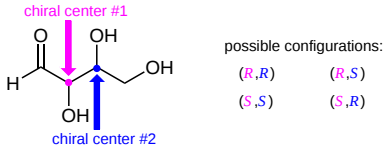
Stereoisomer Shortcuts

If ***all*** of the chiral centers are of opposite (*R*)/(*S*) configuration between two stereoisomers, they are enantiomers.

If ***at least one, but not all*** of the chiral centers are opposite between two stereoisomers, they are diastereomers.

> These shortcuts to not take into account the possibility of additional stereoisomers due to alkene groups: we will come to that later

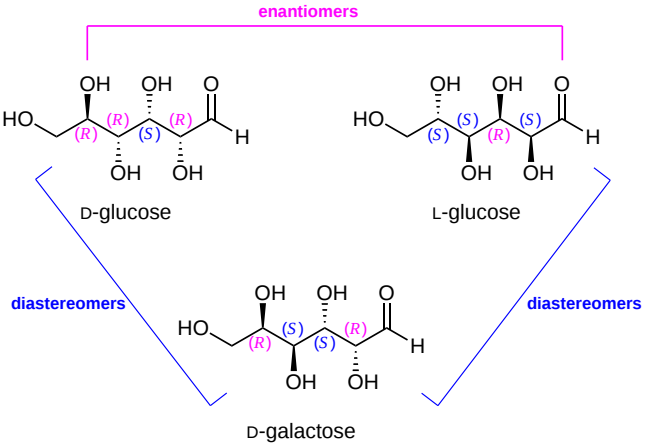
Here's another way of looking at the four stereoisomers, where one chiral center is associated with red and the other blue. Pairs of enantiomers are stacked together.



We know, using the shortcut above, that the enantiomer of (*R*,*R*) must be (*S*,*S*) - both chiral centers are different. We also know that (*R*,*S*) and (*S*,*R*) are diastereomers of (*R*,*R*), because in each case one - but not both - chiral centers are different.

Determining the Maximum Number of Stereoisomers for a Compound

In general, a structure with *n* stereocenters will have a maximum of 2^n different stereoisomers. (We are not considering, for the time being, the stereochemistry of double bonds – that will come later). For example, let's consider the glucose molecule in its open-chain form (recall that many sugar molecules can exist in either an open-chain or a cyclic form). There are two enantiomers of glucose, called D-glucose and L-glucose. The D-enantiomer is the common sugar that our bodies use for energy. It has $n = 4$ stereocenters, so therefore there are $2^n = 2^4 = 16$ possible stereoisomers (including D-glucose itself).

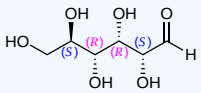


In L-glucose, all of the stereocenters are inverted relative to *D*-glucose. That leaves 14 diastereomers of D-glucose: these are molecules in which at least one, but not all, of the stereocenters are inverted relative to D-glucose. One of these 14 diastereomers, a sugar called *D*-galactose, is shown above: in D-galactose, one of four stereocenters is inverted relative to D-glucose. Diastereomers which differ in only one stereocenter (out of two or more) are called **epimers**. D-glucose and D-galactose can therefore be refered to as epimers as well as diastereomers.

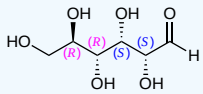
Example 5.7.1

- Draw the structure of L-galactose, the enantiomer of D-galactose.
- Draw the structure of two more diastereomers of D-glucose. One should be an epimer.

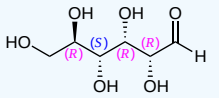
Answer



L-galactose

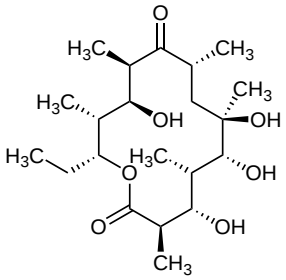


L-mannose
(epimer of D-glucose)



L-gulose
(diasteromer of D-glucose)

Erythronolide B, a precursor to the 'macrocyclic' antibiotic erythromycin, has 10 stereocenters. It's enantiomer is that molecule in which all 10 stereocenters are inverted.



erythronolide B

In total, there are 2^{10} = 1024 stereoisomers in the erythronolide B family: 1022 of these are diastereomers of the structure above, one is the enantiomer of the structure above, and the last ***is*** the structure above.

We know that enantiomers have identical physical properties and equal but opposite degrees of specific rotation. Diastereomers, in theory at least, have different physical properties – we stipulate 'in theory' because sometimes the physical properties of two or more diastereomers are so similar that it is very difficult to separate them. In addition, the specific rotations of diastereomers are unrelated – they could be the same sign or opposite signs, and similar in magnitude or very dissimilar.

? Exercise 5.7.1

Determine the number of stereoisomers a molecule can have with…

a. 3 chiral centers
b. 1 chiral center
c. 6 chiral centers

Answer

Since a molecule with n chiral centers can have 2^n stereoisomers…

a. 2^3 = 8 possible stereoisomers
b. 2^1 = 2 possible stereoisomers
c. 2^6 = 64 possible stereoisomers

? Exercise 5.7.2*a*

What is the relationship between enantiomers?

Answer

They are mirror images of each other and when 2 or more chiral centers are present, every stereocenter is the opposite in its enantiomer.

? Exercise 5.7.2*b*

How does the stereochemistry in diastereomers differ from each other?

Answer

In diastereomers, one or more of the chiral centers is the opposite but they all can't be the opposite or else they'd be enantiomers.

? Exercise 5.7.2c

What are epimers?

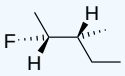
Answer

Epimers are when **only one** chiral center is the opposite (in molecules with 2 or more chiral centers) in its diastereomer.

? Exercise 5.7.3a

Draw the structure of (2R,3R) 2-fluoro-3-methylhexane.

Answer

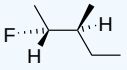


2R,3R

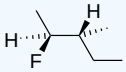
? Exercise 5.7.3b

Draw both diastereomers of (2R,3R) 2-fluoro-3-methylhexane.

Answer



2R,3S

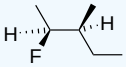


2S,3R

? Exercise 5.7.3c

Draw the enantiomer of (2R,3R) 2-fluoro-3-methylhexane.

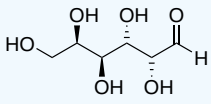
Answer



2S,3S

? Exercise 5.7.4a

Draw the structure of L-galactose, the enantiomer of D-galactose.

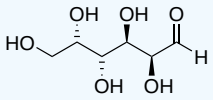


S, R, R, S

D-galactose

Answer

https://chem.libretexts.org/@go/page/418115



S, *R*, *R*, *S*

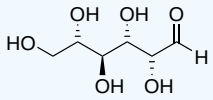
L-galactose

? Exercise 5.7.4*b*

Draw a diastereomer of D-galactose that is an epimer.

Answer

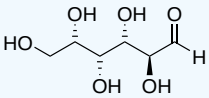
You can draw an epimer by drawing D-galactose with 1 (and only 1) of its chiral centers reversed. Here's an example when you switch only the first chiral center (in red). (There are 3 other epimers that could be drawn as long as you only swap a single chiral center in the diastereomer that you use.)



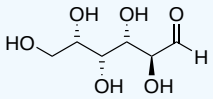
R, *R*, *R*, *S*

? Exercise 5.7.4*c*

Identify if the following diastereomer of galactose is an epimer of D- galactose or L- galactose.



Answer

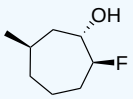


S, *R*, *S*, *S*

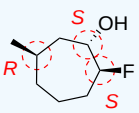
Since the diastereomer above only varies from L-galactose by 1 chiral center, the above is an epimer in relationship to L-galactose. Since it varies from D-galactose by 3 chiral centers, it is not an epimer but a diastereomer. Since not all of the chiral centers are swapped, it is not an enantiomer!

? Exercise 5.7.5*a*

For the compound shown below, label each chiral center as R or S.



Answer



Exercise 5.7.5b

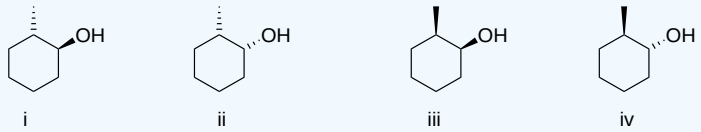
How many stereoisomers are possible for the compound in part a)?

Answer

Since there are 3 chiral centers, $2^3 = 8$ possible stereoisomers.

Exercise 5.7.6

Consider the stereoisomers below.



i ii iii iv

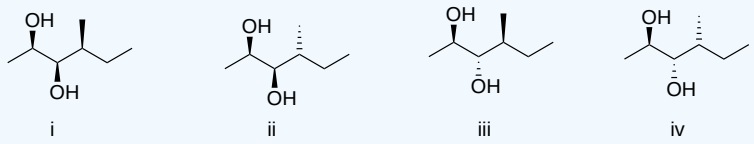
a. Which is/are an enantiomer of i?
b. Which is/are a diastereomer of ii?
c. Which is/are an epimer of i?

Answer

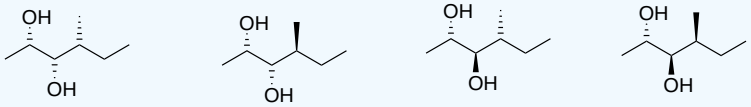
a. iv is an enantiomer of i since both chiral centers are switched and they are non superimposable mirror images.
b. i & iv are diastereomers of ii since they are stereoisomers that are not mirror images.
c. ii and iii are epimers of i since they are diastereomers with only 1 chiral center switched and the other one the same.

Exercise 5.7.7

Consider the 8 stereoisomers below.



i ii iii iv



v vi vii viii

a. Which is/are an enantiomer of i?
b. Which is/are a diastereomer of i?
c. Which is/are an epimer of i?

Answer

a. v is an enantiomer since all three chiral centers are switched and they are non superimposable mirror images.
b. ii, iii, iv, vi, vii & viii are diastereomers of i since they are stereoisomers that are not mirror images.
c. ii,iii & viii are epimers of i since they are diastereomers with only 1 chiral center switched and the other chiral centers the same.

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5.8: Meso Compounds

Objectives

After completing this section, you should be able to

1. determine whether or not a compound containing two chiral carbon atoms will have a meso form, given its Kekulé, condensed or shorthand structure, or its IUPAC name.
2. draw wedge-and-broken-line structures for the enantiomers and meso form of a compound such as tartaric acid, given its IUPAC name, or its Kekulé, condensed or shorthand structure.
3. make a general comparison of the physical properties of the enantiomers, meso form and racemic mixture of a compound such as tartaric acid.

Key Terms

Make certain that you can define, and use in context, the key term below.

- meso compound

Study Notes

You may be confused by the two sets of structures showing “rotations.” Of course in each case the two structures shown are identical, they represent the same molecule looked at from two different perspectives. In the first case, there is a 120° rotation around the single carbon-carbon bond. In the second, the whole molecule is rotated 180° top to bottom.

Introduction

A meso compound is an achiral compound that has chiral centers. A meso compound contains an internal plane of symmetry which makes it superimposable on its mirror image and is optically **inactive** although it contains two or more stereocenters. Remember, an internal plane of symmetry was shown to make a molecule achiral in **Section 5.2**.

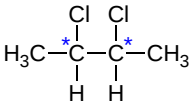
In general, a meso compound should contain two or more identical substituted stereocenters. Also, it has an internal symmetry plane that divides the compound in half. These two halves reflect each other by the internal mirror. The stereochemistry of reflected stereocenters should "cancel out". What it means here is that when we have an internal plane that splits the compound into two symmetrical sides, the stereochemistry of both left and right side should be opposite to each other, and therefore, resulting the molecule being **optically inactive**.

Identification

A meso compound must have:

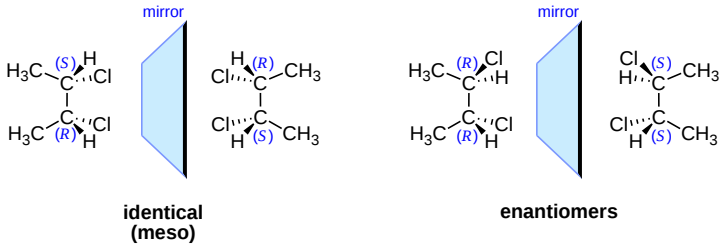
1. Two or more stereocenters.
2. An internal plane of symmetry, or internal mirror, that lies in the compound.
3. Stereochemistry that cancels out. This means reflected stereocenter should have the same substituents and be inverted. For instance, in a meso compound with two stereocenters one should be R and the other S.

The compounds 2,3-dichlorobutane contains two chiral carbons and therefore would be expected to provide $2^2 = 4$ different stereoisomers. These stereoisomers should be made up of two pairs of enantiomers.



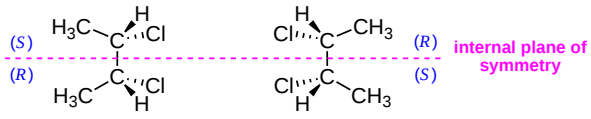
2,3-dichlorobutane

After drawing out all the possible stereoisomers of 2,3-dichlorobutane, the pair on the right in the figure below are mirror images. Also, they are non-superimposable because they have distinctly different conformation (R,R & S,S). This makes the pair enantiomers of each other. However, the pair on the left represent a meso compound, they both are identical despite being mirror images.



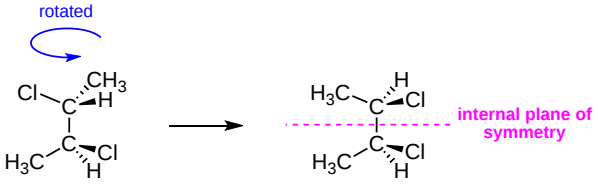
identical (meso) **enantiomers**

Upon further investigation, the meso compound has an internal plane of symmetry which is not present in the pair of enantiomers. The plane of symmetry in the meso compound comes about because there are two chiral carbons present, both chiral carbons are identically substituted (Cl, H, CH_3), and one chiral carbon is R and the other is S. Despite being represented as mirror images, both structures represent the same compound. This is best proven by making molecular models of both representations and then superimposing them. Overall, 2,3-dichlorobutane only has three possible stereosiomers, the pair of enantiomers and the meso compound.



identical (meso)

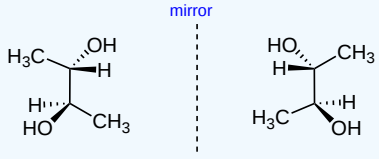
When looking for an internal plane of symmetry, it is important to remember that sigma bonds (single bonds) can rotate. Just because the immediate representation of a molecule does not have a plane of symmetry does not mean that one cannot be obtained through rotation. Often the substituents attached to a stereocenter need to be rotated to recognize the internal plane of symmetry. As the stereocenter is rotated, its configuration does not change. Building a molecular model when considering a possible meso compound is an invaluable tool because it allows for easy rotation of chiral carbons. An example of how rotation of a chiral carbon can reveal an internal plane of symmetry is shown below.



meso compound

Example 5.8.1

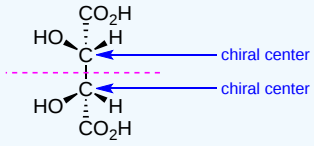
Below are the two mirror images of (meso)-2,3-Butanediol. Because it is a meso compound, the two structures are identical. Show that both mirror images can be obtained by simply rotating the three-dimensional structure provided below.



(meso)-2,3-butanediol

GLmol

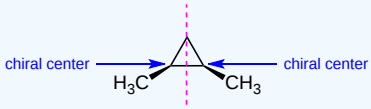
Example 5.8.2



1

1 has a plane of symmetry (the horizontal plane going through the red broken line) and, therefore, is achiral; 1 has chiral centers. Thus, 1 is a meso compound.

Example 5.8.3

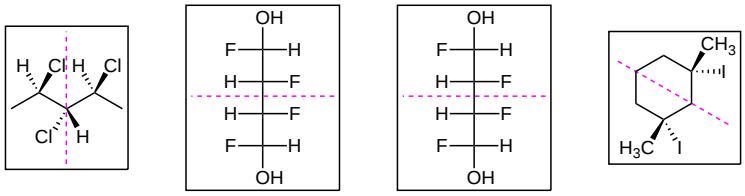


2

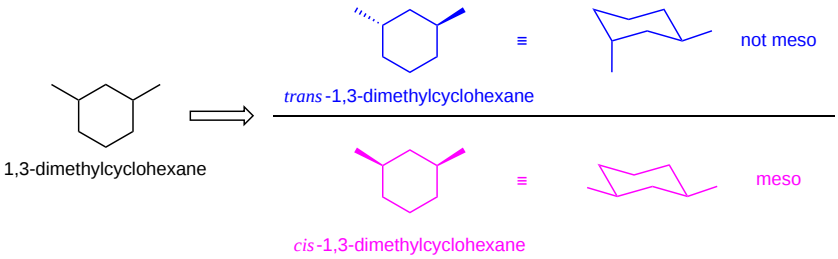
This molecules has a plane of symmetry (the vertical plane going through the red broken line perpendicular to the plane of the ring) and, therefore, is achiral, but has has two chiral centers. Thus, its is a meso compound.

Other Examples of Meso Compounds

Meso compounds can exist in many different forms such as pentane, butane, heptane, and even cycloalkanes. Although two chiral carbons must be present, meso compounds can have many more. Notice that in every case a plane of symmetry is present.

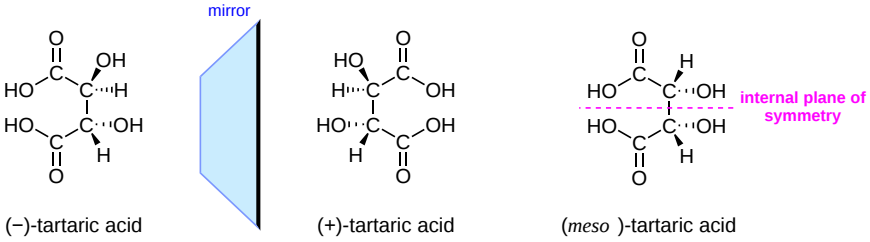


In general, a disubstituted cycloalkane is meso if the two substituents are the same and they are in a *cis* conformation. *Trans* disubstituted cycloalkanes are not meso regardless if the two substituents are the same.



Optical Activity Analysis of a Meso Compound

When the optical activity of a meso compound is attempted to be determined with a polarimeter, the indicator will not show (+) or (-). It simply means there is no certain direction of rotation of the polarized light, neither levorotatory (-) and dexorotatory (+) because a meso compound is achiral (optically inactive). Investigations of isomeric tartaric acid (2,3-dihydroxybutanedioic acid), carried out by Louis Pasteur in the mid 19th century, were instrumental in elucidating some of the subtleties of stereochemistry. Tartaric acid, has two chiral but only three stereoisomers. Two of these stereoisomers are enantiomers and the third is an achiral a **meso** compound. Some physical properties of these stereoisomers of tartaric acid are given in the table below. Notice that the enantiomers have the same amount of optical rotation but in different directons. Meso-tartaric acid produces no optical rotation because it is achiral and not optically active. Meso-tartaric acid is actually a diastereomer of both (-) and (+)-tartaric acid, which gives it a distinctly different melting point.

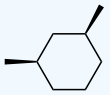


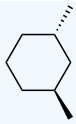
(+)-tartaric acid:	$[\alpha]_D = +13^o$	m.p. 172 ºC
(–)-tartaric acid:	$[\alpha]_D = -13^o$	m.p. 172 ºC
meso-tartaric acid:	$[\alpha]_D = 0^o$	m.p. 140 ºC

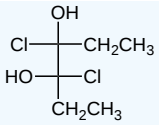
Exercise 5.8.1

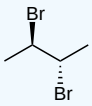
1) Determine which of the following molecules are meso.

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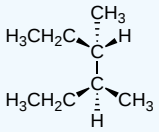
a) 

b) 

c) 

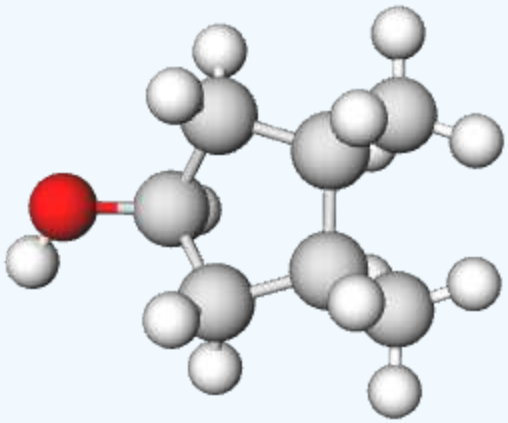
d) 

e) 

f) 

2) Explain why 2,3-dibromobutane has the possibility of being a meso compound while 2,3-dibromopentane does not.

3) Observe the following compound and determine if it is a meso compound. If so indicate the plane of symmetry. Red = oxygen. Remember sigma bonds are able to rotate.

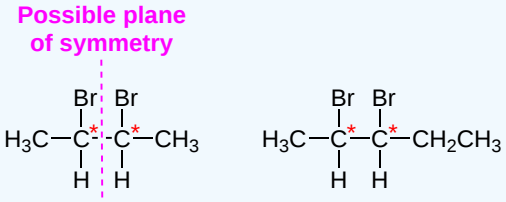


GLmol

Answer

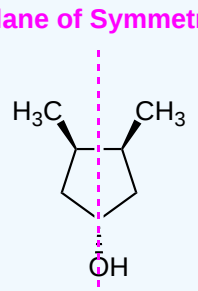
1) A C, D, E are meso compounds.

2) One of the requirements of a meso compound is that the reflected chiral carbons have the same substituents. The compound 2,3-dibromobutane, fulfills this requirement (Br, H, CH_3) and can possibly be a meso compound if the two chiral carbons have the appropriate configuration (R & S). The substituents of the two chiral carbons in 2,3-dibromopentane do not have the same substituents (Br, H, CH_3 vs. Br, H, CH_2CH_3). This 2,3-dibromopentane cannot form a meso compound regardless of the configurations of its chiral carbons.



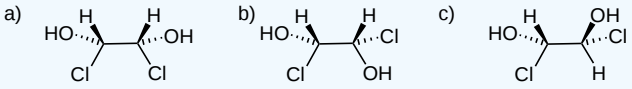
2,3-Dibromobutane **2,3-Dibromopentane**

3) The compound is meso.



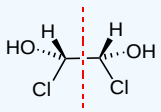
Exercise 5.8.1

Which of the following are meso compounds?



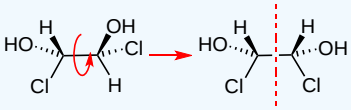
Answer

a) This is a meso compound. There is an internal plane of symmetry (dashed line shown in red) between the C's (and it has stereochemistry of *S* & *R*).



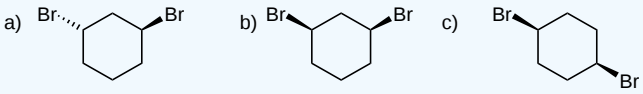
b) This is not a meso compound. No matter how you rotate the C-C bond, you do not see a plane of symmetry (and its stereochemistry is *S* & *S*)

c) This is a meso compound. There is an internal plane of symmetry (dashed line shown in red) that can be seen when you rotate the C-C bond (and it has stereochemistry of *S* & *R*).



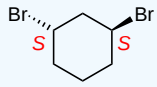
? Exercise 5.8.2

Which of the following are meso compounds?

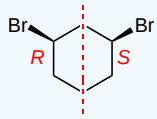


Answer

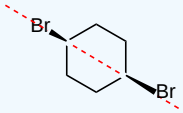
a) This is not a meso compound. There is no plane of symmetry and has stereochemistry of *S* & *S*.



b) This is a meso compound. There is an internal plane of symmetry (dashed line shown in red) and it has stereochemistry of *R* & *S*.

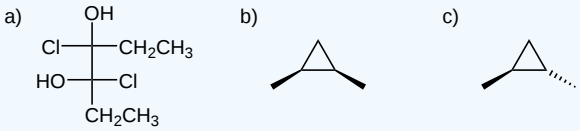


c) This is not a meso compound (even though it has planes of symmetry). The plane of symmetry shown in red makes it so that both chiral centers have symmetrical groups (the ring) and thus the compound is not chiral (so it can't be a meso compound).



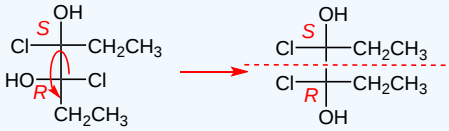
Exercise 5.8.3

Which of the following are meso compounds?



Answer

a) This is a meso compound. If you rotate between the C-C bond, you can see that it has a mirror plane between the C's (shown in red on the structure to the right). Notice how rotating a C-C bond doesn't change the stereochemistry of the molecule (*S* & *R*).



b) This is a meso compound. You can see the plane of symmetry in red and the compound has stereochemistry of *S* & *R*.



c) This is not a meso compound. There is no plane of symmetry and it has stereochemistry of *S* & *S*.



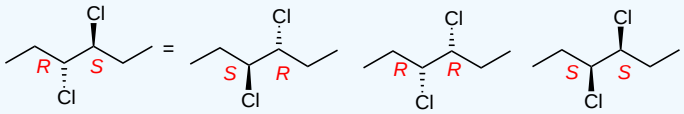
https://chem.libretexts.org/@go/page/418116

Exercise 5.8.4

Determine (and draw) if any of the forms of 3,4-dichlorohexane are a meso compound.

Answer

Looking at the 4 different possibilities below, i & ii are equivalent structures (with R & S stereochemistry) so it is a meso compound. iii & iv are not meso compounds but are enantiomers to each other.



i ii iii iv

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5.9: Racemic Mixtures and the Resolution of Enantiomers

Objectives

After completing this section, you should be able to

1. describe a common process for separating a mixture of enantiomers.
2. explain why racemic mixtures do not rotate plane-polarized light.

Key Terms

Make certain that you can define, and use in context, the key terms below.

- racemic mixture (or racemate)
- resolve

Study Notes

A *racemic mixture* is a 50:50 mixture of two enantiomers. Because they are mirror images, each enantiomer rotates plane-polarized light in an equal but opposite direction and is optically inactive. If the enantiomers are separated, the mixture is said to have been *resolved*. A common experiment in the laboratory component of introductory organic chemistry involves the resolution of a racemic mixture.

The dramatic biochemical consequences of chirality are illustrated by the use, in the 1950s, of the drug Thalidomide, a sedative given to pregnant women to relieve morning sickness. It was later realized that while the (+)-form of the molecule, was a safe and effective sedative, the (−)-form was an active teratogen. The drug caused numerous birth abnormalities when taken in the early stages of pregnancy because it contained a mixture of the two forms.

As noted earlier, chiral compounds synthesized from achiral starting materials and reagents are generally racemic (i.e. a 50:50 mixture of enantiomers). Separation of racemates into their component enantiomers is a process called resolution. Since enantiomers have identical physical properties, such as solubility and melting point, resolution is extremely difficult. Diastereomers, on the other hand, have different physical properties, and this fact is used to achieve resolution of racemates. Reaction of a racemate with an enantiomerically pure chiral reagent gives a mixture of diastereomers, which can be separated. For example, if a racemic mixture of a chiral alcohol is reacted with a enantiomerically pure carboxylic acid, the result is a mixture of diastereomers: in this case, because the pure (R) entantiomer of the acid was used, the product is a mixture of (R-R) and (R-S) diastereomeric esters, which can, in theory, be separated by their different physical properties. Subsequent hydrolysis of each separated ester will yield the 'resolved' (enantiomerically pure) alcohols. The used in this technique are known as 'Moscher's esters', after Harry Stone Moscher, a chemist who pioneered the method at Stanford University.

As noted earlier, chiral compounds synthesized from achiral starting materials and reagents are generally racemic (i.e. a 50:50 mixture of enantiomers). Separation of racemates into their component enantiomers is a process called **resolution**. Since enantiomers have identical physical properties, such as solubility and melting point, resolution is extremely difficult. Diastereomers, on the other hand, have different physical properties, and this fact is used to achieve resolution of racemates. Reaction of a racemate with an enantiomerically pure chiral reagent gives a mixture of diastereomers, which can be separated. Reversing the first reaction then leads to the separated enantiomers plus the recovered reagent.

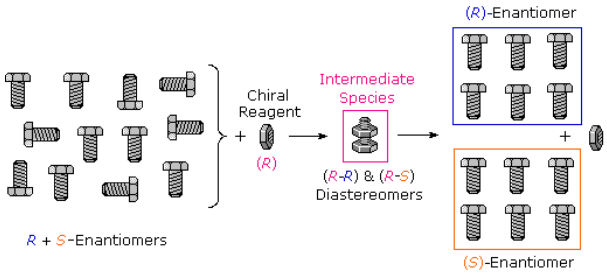


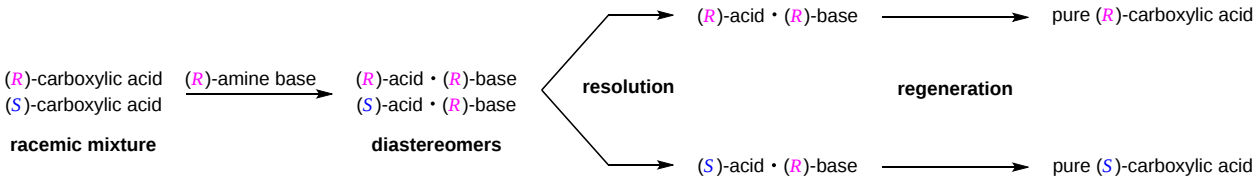
Figure 5.8.1:

Many kinds of chemical and physical reactions, including salt formation, may be used to achieve the diastereomeric intermediates needed for separation. Figure 5.8.1 illustrates this general principle by showing how a nut having a right-handed thread (R) could serve as a "reagent" to discriminate and separate a mixture of right- and left-handed bolts of identical size and weight. Only the two right-handed partners can interact to give a fully-threaded intermediate, so separation is fairly simple. The resolving moiety, i.e. the nut, is then removed, leaving the bolts separated into their right and left-handed forms. Chemical reactions of enantiomers are normally not so dramatically different, but a practical distinction is nevertheless possible.

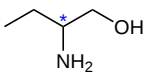
Because the physical properties of enantiomers are identical, they seldom can be separated by simple physical methods, such as fractional crystallization or distillation. It is only under the influence of another chiral substance that enantiomers behave differently, and almost all methods of resolution of enantiomers are based upon this fact. We include here a discussion of the primary methods of resolution.

Chiral Amines as Resolving Agents and Resolution of Racemic Acids

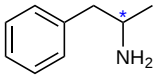
The most commonly used procedure for separating enantiomers is to convert them to a mixture of diastereomers that will have different physical properties: melting point, boiling point, solubility, and so on (Section 5-5). For example, if you have a racemic or (*R*)/(*S*) mixture of enantiomers of a carboxylic acid and convert this to a salt with a chiral amine base having the (*R*) configuration, the salt will be a mixture of two diastereomers, ((*R*)-acid • (*R*)-base) and ((*S*)-acid • (*R*)-base). These diastereomeric salts are *not* identical and they are not mirror images. Therefore they will differ to some degree in their physical properties, and a separation by physical methods, such as crystallization, may be possible. If the diastereomeric salts can be completely separated, the carboxylic acid regenerated from each salt will be either exclusively the (*R*) or the (*S*) enantiomer.



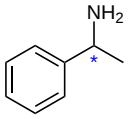
Resolution of chiral acids through the formation of diastereomeric salts requires adequate supplies of suitable chiral bases. Brucine, strychnine, and quinine frequently are used for this purpose because they are readily available, naturally occurring chiral bases. Simpler amines of synthetic origin, such as 2-amino-1-butanol, amphetamine, and 1-phenylethanamine, also can be used, but first they must be resolved themselves.



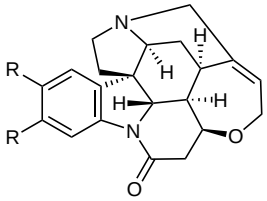
2-amino-1-butanol



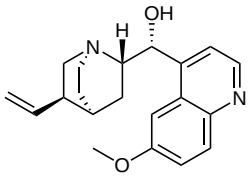
1-phenyl-2-propanamine
(amphetamine)



1-phenylethanamine



R = H,strychnine
R = OCH_3, brucine

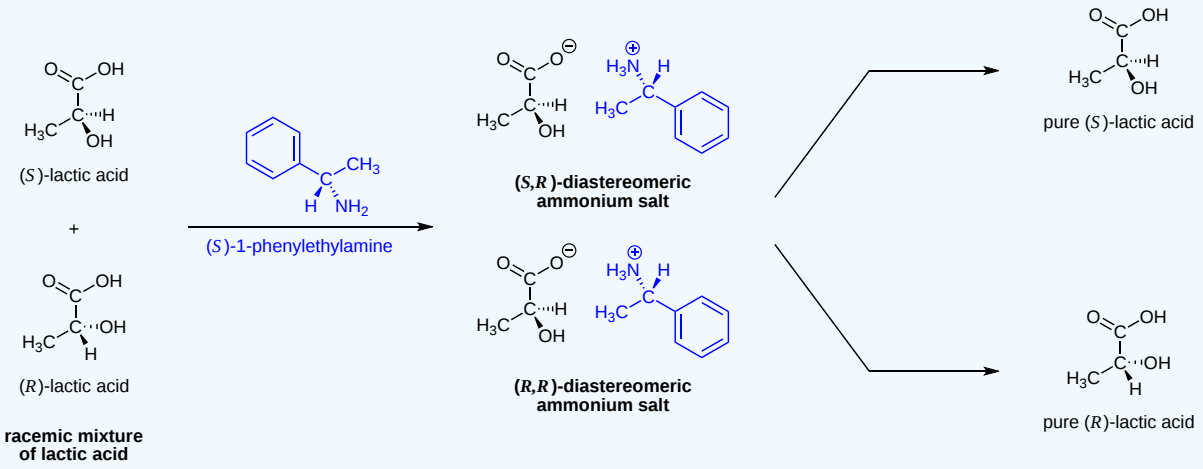


quinine
(antimicrobial)
(antimalarial)

Worked Example 5.9.1

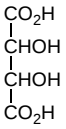
Show how (*S*)-1-phenylethylamine can be used to resolve a racemic mixture of lactic acid. Please draw all the structures involved.

Answer

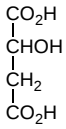


Resolution of Racemic Bases

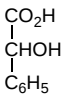
Chiral acids, such as (+)-tartaric acid, (-)-malic acid, (-)-mandelic acid, and (+)-camphor- 10-sulfonic acid, are used for the resolution of a racemic base.



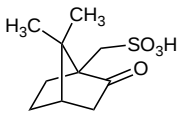
tartaric acid
(2,3-dihydroxy-
butanedioic acid)



malic acid
(2-hydroxybutane-
dioic acid)



mandelic acid
(2-hydroxy-2-
phenylethanoic acid)



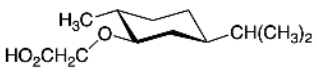
camphor-10-
sulfonic acid

The principle is the same as for the resolution of a racemic acid with a chiral base, and the choice of acid will depend both on the ease of separation of the diastereomeric salts and, of course, on the availability of the acid for the scale of the resolution involved. Resolution methods of this kind can be tedious, because numerous recrystallizations in different solvents may be necessary to progressively enrich the crystals in the less-soluble diastereomer. To determine when the resolution is complete, the mixture of

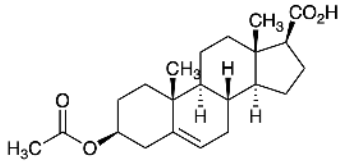
diastereomers is recrystallized until there is no further change in the measured optical rotation of the crystals. At this stage it is hoped that the crystalline salt is a pure diastereomer from which one pure enantiomer can be recovered. The optical rotation of this enantiomer will be a maximum value if it is "optically" pure because any amount of the other enantiomer could only reduce the magnitude of the measured rotation α.

Resolution of Racemic Alcohols

To resolve a racemic alcohol, a chiral acid can be used to convert the alcohol to a mixture of diastereomeric esters. This is not as generally useful as might be thought because esters tend to be liquids unless they are very high-molecularweight compounds. If the diastereomeric esters are not crystalline, they must be separated by some other method than fractional crystallization (for instance, by chromatography methods, Section 9-2). Two chiral acids that are useful resolving agents for alcohols are:

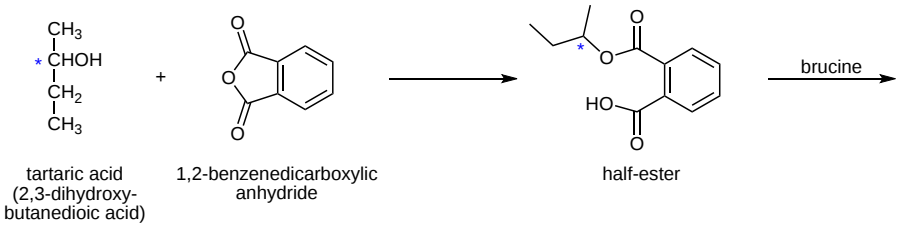


menthoxyethanoic acid



3-β-acetoxy-Δ^5-etienic acid

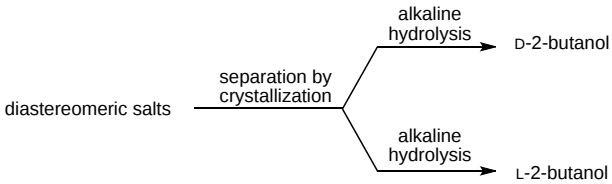
The most common method of resolving an alcohol is to convert it to a half-ester of a dicarboxylic acid, such as butanedioic (succinic) or 1,2-benzenedicarboxylic (phthalic) acid, with the corresponding anhydride. The resulting half-ester has a free carboxyl function and may then be resolvable with a chiral base, usually brucine:



tartaric acid (2,3-dihydroxy-butanedioic acid)

1,2-benzenedicarboxylic anhydride

half-ester



Other Methods of Resolution

One of the major goals in the field of organic chemistry is the development of reagents with the property of "chiral recognition" such that they can affect a clean separation of enantiomers in one operation without destroying either of the enantiomers. We have not achieved that ideal yet, but it may not be far in the future. Chromatographic methods, whereby the stationary phase is a chiral reagent that adsorbs one enantiomer more strongly than the other, have been used to resolve racemic compounds, but such resolutions seldom have led to both pure enantiomers on a preparative scale. Other methods, called kinetic resolutions, are excellent when applicable. The procedure takes advantage of differences in reaction rates of enantiomers with chiral reagents. One enantiomer may react more rapidly, thereby leaving an excess of the other enantiomer behind. For example, racemic tartaric acid can be resolved with the aid of certain penicillin molds that consume the dextrorotatory enantiomer faster than the levorotatory enantiomer. As a result, almost pure (-)-tartaric acid can be recovered from the mixture:

$$(\pm)\text{-tartaric acid} + \text{mold} \rightarrow (-)\text{-tartaric acid} + \text{more mold}$$

The crystallization procedure employed by Pasteur for his classical resolution of (±)-tartaric acid (**Section 5.4**) has been successful only in a very few cases. This procedure depends on the formation of individual crystals of each enantiomer. Thus if the crystallization of sodium ammonium tartrate is carried out below 27", the usual racemate salt does not form; a mixture of crystals of the (+) and (-) salts forms instead. The two different kinds of crystals, which are related as an object to its mirror image, can be

separated manually with the aid of a microscope and subsequently may be converted to the tartaric acid enantiomers by strong acid. A variation on this method of resolution is the seeding of a saturated solution of a racemic mixture with crystals of one pure enantiomer in the hope of causing crystallization of just that one enantiomer, thereby leaving the other in solution. Unfortunately, very few practical resolutions have been achieved in this way.

Predicating the Chirality of the Product of a Reaction

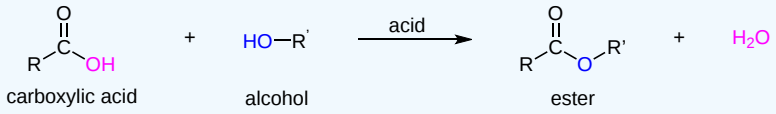
It important to understand the changes in chirality which occur during the formation of product during a reaction. A chiral reaction product, has the possibility of forming multiple stereoisomers which all need to be considered. Changes in chirality, if possible, will be discussed with each individual reaction as this textbook moves forward. Some possible situations which can occur are:

- **A new chiral carbon is formed during a reaction.** This commonly occurs when an sp^2 hybridized carbon in the reactant is converted to sp^3 hybridized chiral carbon in the product. When this occurs, a racemic mixture of the new chiral carbon is formed.
- **A chiral carbon is lost during a reaction.** This commonly occurs when an sp^3 hybridized chiral carbon in the reactant is converted to either a sp^2 or sp hybridized carbon in the product.
- **An enantiomerically pure starting material is converted to a racemic mixture in the product.** This commonly occurs when a sp^3 hybridized chiral carbon is temporarily converted to an sp^2 hybridized carbon during a reaction's mechanism. The chiral carbon is reformed as a racemic mixture.
- **Chiral carbons remain unchanged during a reaction.** If a chiral carbon is not directly involved in a reaction, it will move from a reactant to a product unchanged.

Determining if a chiral carbon is involved in a given reaction is vital for determining which of these four situations is occurring.

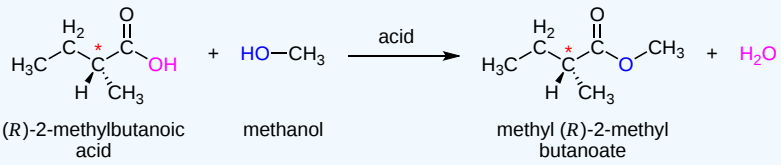
? Worked Example 5.9.2

The following reaction involves the conversion of a carboxylic acid reacting with an alcohol to form an ester. If a pure sample of (R)-2-methylbutanoic acid is reacted with methanol to form an ester, what would be the stereochemistry of the product?



Answer

First it is important to identify the location of the chiral carbon and determine if it is directly involved in the reaction. In this case, the chiral carbon is not involved so the stereochemistry will be carried over into the product unchanged.



? Exercise 5.9.1

Indicate the reagents you could use to resolve the following compounds. Show the reactions involved and specify the physical method you believe would be the best to separate the diastereomers of 1 -phenyl-2-propanamine.

Answer

You could react the 1-phenyl-2-propanamine racemic mixture with a chiral acid such as (+)-tartaric acid (*R*, *R*). The reaction will produce a mixture of diastereomeric salts (i.e. *R*, *R*, *R* and *S*, *R*, *R*). You can separate the diastereomers through crystallization and treat the salt with a strong base (e.g. KOH) to recover the pure enantiomeric amine.

? Exercise 5.9.2

Indicate the reagents you would use to resolve the following and discuss the reactions involved and specify the physical method you believe would be the best to separate the diastereomers of 2,3-pentadienedioic acid.

Answer

You could react the 2,3-pentadienedioic acid mixture with a chiral base such as (*R*)-1-phenylethylamine. The reaction will produce a mixture of diastereomeric salts. Separate the diastereomers through crystallization and treat the resulting salt with strong acid (e.g. HCl) to recover the pure enantiomeric acid.

? Exercise 5.9.3

Indicate the reagents you would use to resolve the following and discuss the reactions involved and specify the physical method you believe would be the best to separate the diastereomers of 1 -phenylethanol.

Answer

You could react the 1-phenylethanol mixture with 1,2-benzenedicarboxylic anhydride. The reaction will produce a mixture of diastereomeric salts. You could then separate the diastereomers through crystallization and then alkaline hydrolysis treatment should recover the pure enantiomeric alcohol.

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5.10: Chirality at Nitrogen, Phosphorus, and Sulfur

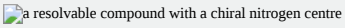
Objectives

After completing this section, you should be able to

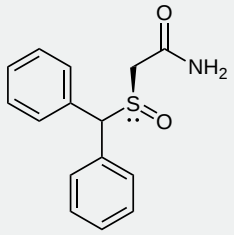
1. recognize that atoms other than carbon can be chiral centres.
2. explain why enantiomers of compounds such as ethylmethylamine cannot normally be isolated.

Study Notes

The first example of a resolvable compound containing a chiral nitrogen atom was resolved by William Pope and Stanley Peachey in 1899. It had the structure shown below.



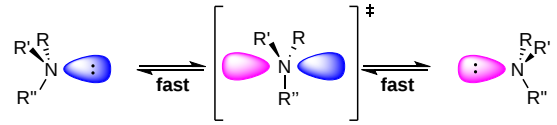
Chiral sulfoxides find application in certain drugs such as esomeprazole and armodafinil and are a good example of a stereogenic sulfur center.



armodafinil

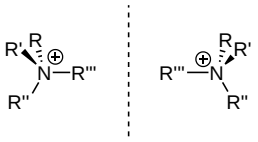
Chirality at Nitrogen

Due to their tetrahedral configuration, amines with three different substituents are chiral. The R and S enantiomeric forms of chiral amines cannot be resolved due to their rapid interconversion by a process called pyramidal or nitrogen inversion. During the inversion, the sp^3 hybridized amine momentarily rehybridizes to a sp^2 hybridized, trigonal planar, transition state where the lone pair electrons occupy a p orbital. The nitrogen then returns to tetrahedral sp^3 hybridization causing the lone pair electrons to enter to a hybrid orbital on the opposite side of the nitrogen. During this process substituents invert to form the enantiomer, analogous to the Walden inversion seen in S_N2 reactions. The thermodynamic barrier for this inversion (~25 kJ/mol) is low enough to allow rapid inversion at room temperature, leading to a mixture of interconverting R and S configurations. At room temperature a nitrogen atom exists as a racemic mixture of R and S configurations.



sp^3-hybridized (tetrahedral) | sp^2-hybridized (trigonal planar) | sp^3-hybridized (tetrahedral)

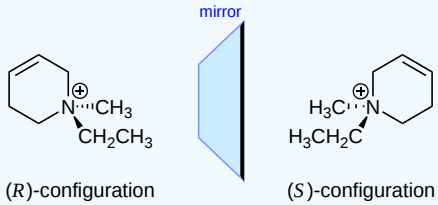
Quaternary amines lack lone pair electrons and therefore do not undergo pyramidal inversions. Quaternary amines with four different substituents are chiral and are readily resolved into separate enantiomers.



enantiomers of a chiral quaternary amine

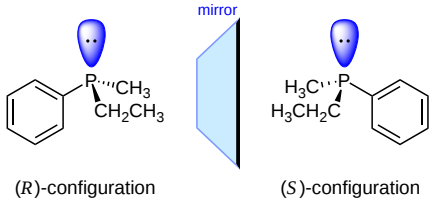
Example 5.10.1

The Enantiomers of a chiral quaternary amine.



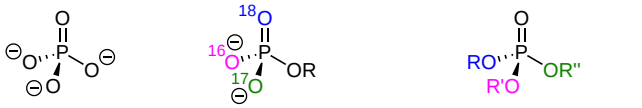
Chirality at Phosphorus

Trivalent phosphorus compounds called phosphines have a tetrahedral electron-group geometry which makes them structurally analogous to amines. The rate of inversion for phosphines are so much slower than amines that chiral phosphines can be isolated. In this case the set of lone pair electrons are considered a substituent and given the lowest Cahn-Ingold-Prelog priority.



enantiomers of ethylmethylphenylphosphine

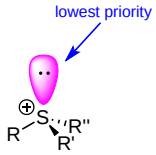
The phosphorus center of phosphate ions and organic phosphate esters is also tetrahedral, and thus potentially a stereocenter. In order to investigate the stereochemistry of reactions at the phosphate center, ^{17}O and ^{18}O isotopes of oxygen (the 'normal' isotope is ^{16}O) can be incorporated to create chiral phosphate groups. Phosphate triesters are chiral if the all four substituent groups are different (including the carbonyl oxygen).



phosphate (achiral) | labeled phosphate ester (chiral) | a chiral phosphate triester

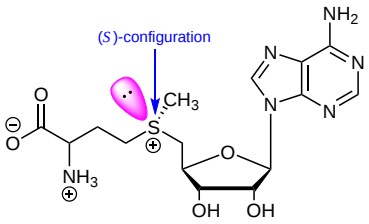
Chirality at Sulfur

Trivalent sulfur compounds called sulfonium salts (R_3S^+) have a tetrahedral electron-group geometry similar to amines and can be chiral if the R groups are all different. In a similar fashion as phosphorus, the inversion rates are slow enough for chiral sulfonium salts to be isolated. Here again the set of lone pair electrons are considered a substituent and given the lowest CIP priority. Sulfonium salts will be discussed in greater detail in **Section 18.8**.



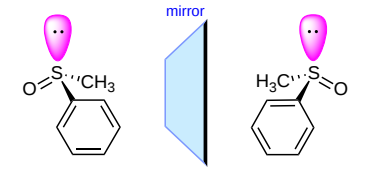
a chiral sulfur in the form of a sulfonium ion

An excellent example of a chiral sulfonium salt in biological systems is the coenzyme (*S*)-adenosylmethionine (SAM). The presence of a sulfonium allows SAM to be a biological methyl group donor in many metabolic pathways. Note that SAM has an (*S*) configuration at the sulfur atom.



(*S*)-S-adenosylmethionine

The sulfur in sulfoxides (R'SOR") can be chiral if both R groups are different. Here again the inversion rate is slow enough to allow chiral sulfoxides to be isolated. An excellent example is methyl phenyl sulfoxide. Sulfoxides will also be discussed in greater detail in **Section 18.8**.



(*R*)-configuration (*S*)-configuration

enantiomers of methyl phenyl sulfoxide

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5.11: Prochirality

Objectives

After completing this section, you should be able to

1. identify a compound as being prochiral.
2. identify the *Re* and *Si* faces of prochiral sp^2 centre.
3. identify atoms (or groups of atoms) as *pro-R* or *pro-S* on a prochiral sp^3 centre.

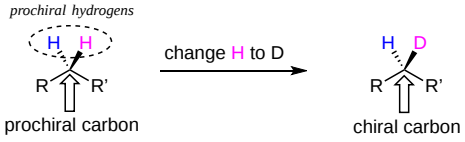
Key Terms

Make certain that you can define, and use in context, the key terms below.

- prochiral
- *pro-R*
- *pro-S*
- *Re*
- *Si*

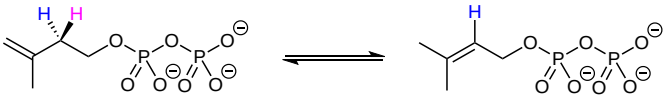
Prochiral Carbons

When a tetrahedral carbon can be converted to a chiral center by changing only one of the attached groups, it is referred to as a '**prochiral**' carbon. The two hydrogens on the prochiral carbon can be described as 'prochiral hydrogens'.



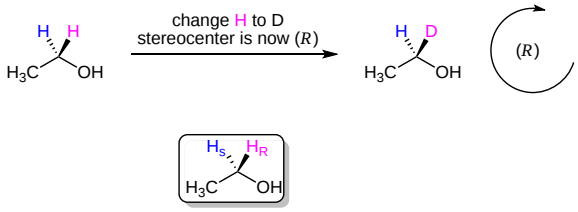
Note that if, in a 'thought experiment', we were to change either one of the prochiral hydrogens on a prochiral carbon center to a deuterium (the ^{2}H isotope of hydrogen), the carbon would now have four different substituents and thus would be a chiral center.

Prochirality is an important concept in biological chemistry, because enzymes can distinguish between the two 'identical' groups bound to a prochiral carbon center due to the fact that *they occupy different regions in three-dimensional space*. Consider the isomerization reaction below, which is part of the biosynthesis of isoprenoid compounds. We do not need to understand the reaction itself (it will be covered in chapter 14); all we need to recognize at this point is that the isomerase enzyme is able to distinguish between the prochiral 'red' and the 'blue' hydrogens on the isopentenyl diphosphate (IPP) substrate. In the course of the left to right reaction, IPP specifically loses the 'red' hydrogen and keeps the 'blue' one.



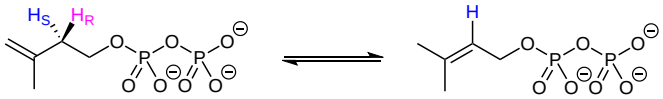
isopentenyl diphosphate dimethylallyl diphosphate

Prochiral hydrogens can be unambiguously designated using a variation on the *R/S* system for labeling chiral centers. For the sake of clarity, we'll look at a very simple molecule, ethanol, to explain this system. To name the 'red' and 'blue' prochiral hydrogens on ethanol, we need to engage in a thought experiment. If we, in our imagination, were to arbitrarily change red H to a deuterium, the molecule would now be chiral and the chiral carbon would have the *R* configuration (D has a higher priority than H).



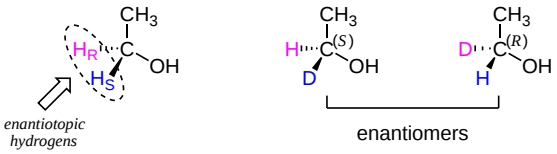
For this reason, we can refer to the red H as the *pro-R* hydrogen of ethanol, and label it H_R. Conversely, if we change the blue H to D and leave red H as a hydrogen, the configuration of the molecule would be *S*, so we can refer to blue H as the *pro-S* hydrogen of ethanol, and label it H_S.

Looking back at our isoprenoid biosynthesis example, we see that it is specifically the *pro-R* hydrogen that the isopentenyl diphosphate substrate loses in the reaction.



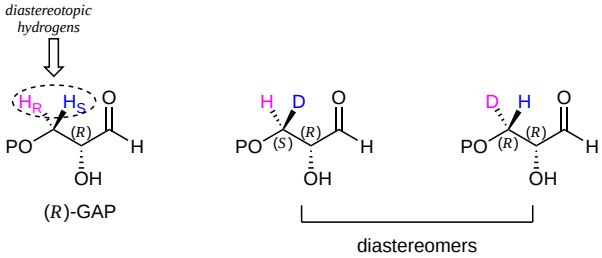
isopentenyl diphosphate dimethylallyl diphosphate

Prochiral hydrogens can be designated either enantiotopic or diastereotopic. If either H_R or H_S on ethanol were replaced by a deuterium, the two resulting isomers would be enantiomers (because there are no other stereocenters anywhere on the molecule).



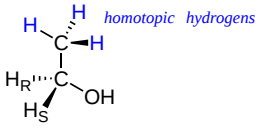
Thus, these two hydrogens are referred to as **enantiotopic**.

In (*R*)-glyceraldehyde-3-phosphate ((*R*)-GAP), however, we see something different:



R)-GAP already has one chiral center. If either of the prochiral hydrogens H_R or H_S is replaced by a deuterium, a second chiral center is created, and the two resulting molecules will be diastereomers (one is *S*,*R*, one is *R*,*R*). Thus, in this molecule, H_R and H_S are referred to as **diastereotopic** hydrogens.

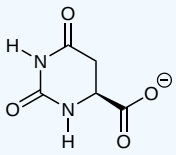
Finally, hydrogens that can be designated neither enantiotopic nor diastereotopic are called **homotopic**. If a homotopic hydrogen is replaced by deuterium, a chiral center is *not* created. The three hydrogen atoms on the methyl (CH_3) group of ethanol (and on *any* methyl group) are homotopic. An enzyme cannot distinguish among homotopic hydrogens.



Example 5.11.1

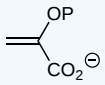
Identify in the molecules below all pairs/groups of hydrogens that are homotopic, enantiotopic, or diastereotopic. When appropriate, label prochiral hydrogens as H_R or H_S.

a)



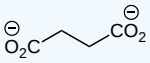
dihydroorotate
(a nucleotide biosynthesis intermediate)

b)



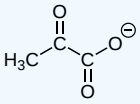
phosphoenolpyruvate
(a glycolysis intermediate)

c)



succinate
(a citric acid cycle intermediate)

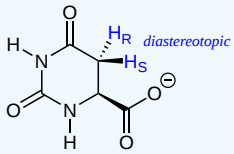
d)



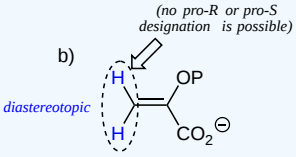
pyruvate
(endpoint of glycolysis)

Answer

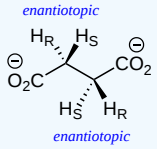
a)



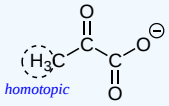
b)



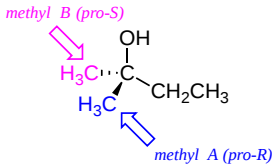
c)



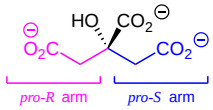
d)



Groups other than hydrogens can be considered prochiral. The alcohol below has two prochiral methyl groups - the red one is *pro-R*, the blue is *pro-S*. How do we make these designations? Simple - just arbitrarily assign the red methyl a higher priority than the blue, and the compound now has the *R* configuration - therefore red methyl is *pro-R*.

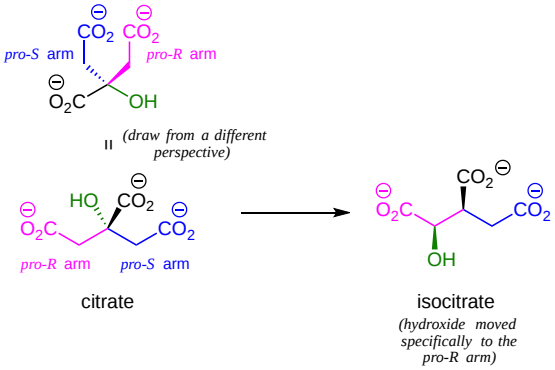


Citrate is another example. The central carbon is a prochiral center with two 'arms' that are identical except that one can be designated *pro-R* and the other *pro-S*.



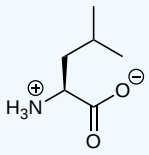
citrate

In an isomerization reaction of the citric acid (Krebs) cycle, a hydroxide is shifted specifically to the *pro-R* arm of citrate to form isocitrate: again, the enzyme catalyzing the reaction distinguishes between the two prochiral arms of the substrate (we will study this reaction in chapter 13).



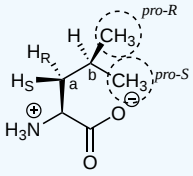
? Exercise 5.11.1

Assign *pro-R* and *pro-S* designations to all prochiral groups in the amino acid leucine. (*Hint*: there are two pairs of prochiral groups!). Are these prochiral groups diastereotopic or enantiotopic?



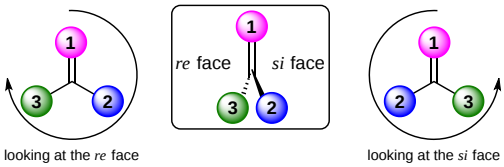
leucine

Answer



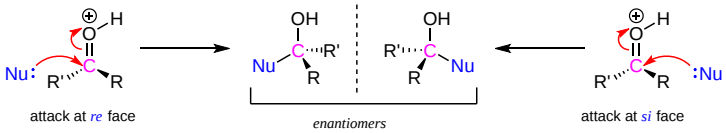
Prochiral Carbonyl and Imine Groups

Trigonal planar, sp^2-hybridized carbons are not, as we well know, chiral centers– but they can be prochiral centers if they are bonded to three different substitutuents. We (and the enzymes that catalyze reactions for which they are substrates) can distinguish between the two planar 'faces' of a prochiral sp^2 - hybridized group. These faces are designated by the terms ***re*** and ***si***. To determine which is the *re* and which is the *si* face of a planar organic group, we simply use the same priority rankings that we are familiar with from the R/S system, and trace a circle: *re* is clockwise and *si* is counterclockwise.



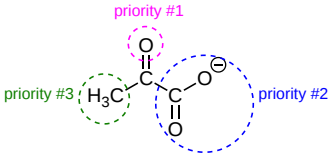
When the two groups adjacent to a carbonyl (C=O) are not the same, we can distinguish between the re and si 'faces' of the planar structure. The concept of a trigonal planar group having two distinct faces comes into play when we consider the stereochemical outcome of a nucleophilic addition reaction. Nucleophilic additions to carbonyls will be covered in greater detail in **Chapter 19**. Notice that in the course of a carbonyl addition reaction, the hybridization of the carbonyl carbon changes from sp^2 to sp^3, meaning that the bond geometry changes from trigonal planar to tetrahedral. If the two R groups are not equivalent, then a chiral center is created upon addition of the nucleophile. The configuration of the new chiral center depends upon which side of the carbonyl plane the nucleophile attacks from. Reactions of this type often result in a 50:50 racemic mixture of stereoisomers, but it is also possible

that one stereoisomer may be more abundant, depending on the structure of the reactants and the conditions under which the reaction takes place.

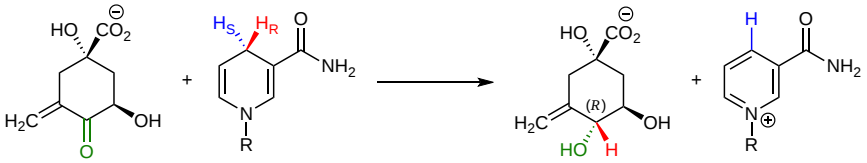


Note: R is higher priority than R'

Below, for example, we are looking down on the *re* face of the ketone group in pyruvate. If we flipped the molecule over, we would be looking at the *si* face of the ketone group. Note that the carboxylate group does not have *re* and *si* faces, because two of the three substituents on that carbon are identical (when the two resonance forms of carboxylate are taken into account).



As we will see in chapter 10, enzymes which catalyze reactions at carbonyl carbons act specifically from one side or the other.

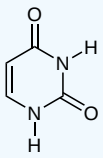


*looking at the **si** face of the ketone*

We need not worry about understanding the details of the reaction pictured above at this point, other than to notice the stereochemistry involved. The *pro-R* hydrogen (along with the two electrons in the C-H bond) is transferred to the *si* face of the ketone (in green), forming, in this particular example, an alcohol with the *R* configuration. If the transfer had taken place at the *re* face of the ketone, the result would have been an alcohol with the *S* configuration.

? Exercise 5.11.2

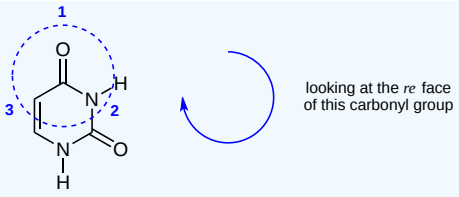
For each of the carbonyl groups in uracil, state whether we are looking at the *re* or the *si* face in the structural drawing below.

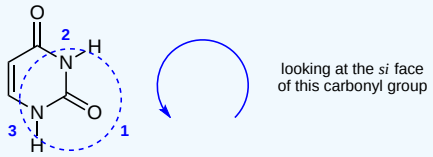


uracil

Answer

https://chem.libretexts.org/@go/page/418120



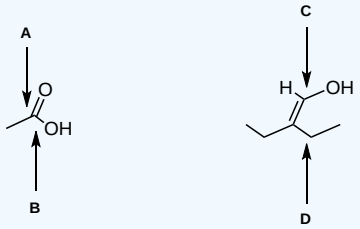


Exercise 5.11.3

a) State which of the following hydrogen atoms are *pro-R* or *pro-S*.



b) Identify which side is Re or Si.



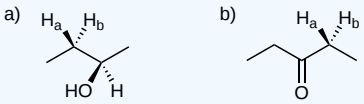
Answer

a) Left compound: H_a = *pro-S* and H_b = *pro-R*; Right compound: H_a = *pro-R* and H_b = *pro-S*

b) A – Re; B – Si; C – Re; D – Si\)

Exercise 5.11.4

State whether the H's indicated below are pro-*R* or pro-*S* for the following structures.



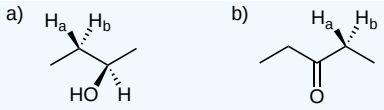
Answer

a) H_a is pro-R; H_b is pro-S

H_a is pro-R; H_b is pro-S

Exercise 5.11.5

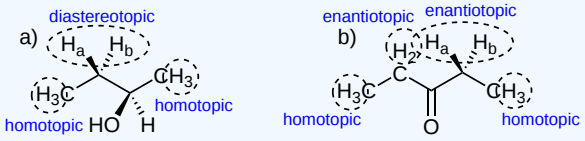
In the structures below, determine if the H's are homotopic, enantiotopic, or diastereotopic.



Answer

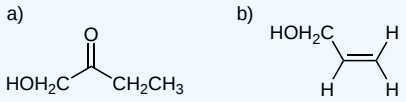
In a), the CH_2 is diastereotopic since there is another chiral center on the molecule. Both CH_3's are homotopic since replacing one of them doesn't create a chiral center.

IN b), the CH_2's are enantiotopic since it would create the only chiral center on the molecule. Both CH_3's are homotopic since replacing one of them doesn't create a chiral center.



Exercise 5.11.6

State whether you are looking down at the molecule from the re face or si face.



Answer

a. You are looking at the **si face**. The re face would be if you were facing the molecule from the back.
b. You are looking at the **re face**. The si face would be if you were facing the molecule from the back.

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CHAPTER OVERVIEW

6: An Overview of Organic Reactions

Learning Objectives

After you have completed Chapter 6, you should be able to

1. fulfill the detailed objectives listed under each individual section.
2. identify the polarity pattern in the common functional groups, and explain the importance of being able to do so.
3. describe the essential differences between polar and radical reactions, and assign a given reaction to one of these two categories.
4. discuss how kinetic and thermodynamic factors determine the rate and extent of a chemical reaction.
5. use bond dissociation energies to calculate the $\Delta H°$ of simple reactions, and *vice versa*.
6. draw and interpret reaction energy diagrams.
7. define, and use in context, the new key terms.

This chapter is designed to provide a gentle introduction to the subject of reaction mechanisms. Two types of reactions are introduced—polar reactions and radical reactions. The chapter briefly reviews a number of topics you should be familiar with, including rates and equilibria, elementary thermodynamics and bond dissociation energies. You must have a working knowledge of these topics to obtain a thorough understanding of organic reaction mechanisms. Reaction energy diagrams are used to illustrate the energy changes that take place during chemical reactions, and to emphasize the difference between a reaction intermediate and a transition state.

6.1: Kinds of Organic Reactions
6.2: How Organic Reactions Occur - Mechanisms
6.3: Radical Reactions
6.4: Polar Reactions
6.5: An Example of a Polar Reaction - Addition of HBr to Ethylene
6.6: Using Curved Arrows in Polar Reaction Mechanisms
6.7: Describing a Reaction - Equilibria, Rates, and Energy Changes
6.8: Describing a Reaction - Bond Dissociation Energies
6.9: Describing a Reaction - Energy Diagrams and Transition States
6.10: Describing a Reaction- Intermediates
6.11: A Comparison between Biological Reactions and Laboratory Reactions
6.12: Oxidation and Reduction in Organic Chemistry

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6.1: Kinds of Organic Reactions

Objective

After completing this section, you should be able to list and describe the four important “kinds” of reactions that occur in organic chemistry.

Key Terms

Make certain that you can define, and use in context, the key terms below.

- addition reaction
- elimination reaction
- rearrangement reaction
- substitution reaction

Study Notes

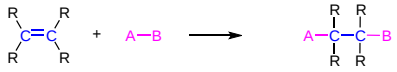
It is sufficient that you know the general form of each kind of reaction. However, given a chemical equation, you should be able to recognize which kind of reaction it involves.

If you scan any organic textbook you will encounter what appears to be a very large, often intimidating, number of reactions. These are the "tools" of a chemist, and to use these tools effectively, we must organize them in a sensible manner and look for patterns of reactivity that permit us make plausible predictions. Most of these reactions occur at special sites of reactivity known as functional groups, and these constitute one organizational scheme that helps us catalog and remember reactions.

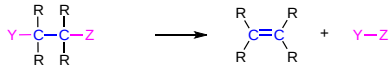
> *Ultimately, the best way to achieve proficiency in organic chemistry is to understand how reactions take place, and to recognize the various factors that influence their course.*

First, we identify four broad classes of reactions based solely on the **structural change** occurring in the reactant molecules. This classification does not require knowledge or speculation concerning reaction paths or mechanisms. The four main reaction classes are additions, eliminations, substitutions, and rearrangements.

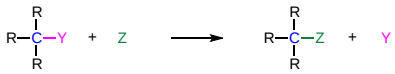
Addition Reaction



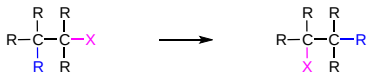
Elimination Reaction



Substitution Reaction



Rearrangement Reaction



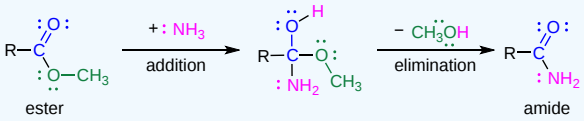
In an **addition** reaction the number of σ-bonds in the substrate molecule increases, usually at the expense of one or more π-bonds. The reverse is true of **elimination** reactions, *i.e.*the number of σ-bonds in the substrate decreases, and new π-bonds are often formed. **Substitution** reactions, as the name implies, are characterized by replacement of an atom or group (Y) by another atom or

group (Z). Aside from these groups, the number of bonds does not change. A **rearrangement** reaction generates an isomer, and again the number of bonds normally does not change.

The examples illustrated above involve simple alkyl and alkene systems, but these reaction types are general for most functional groups, including those incorporating carbon-oxygen double bonds and carbon-nitrogen double and triple bonds. Some common reactions may actually be a combination of reaction types.

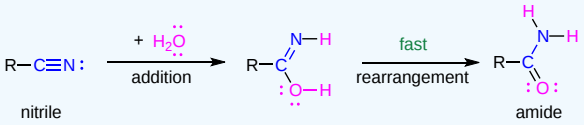
Example 6.1.1: Reaction of an Ester with Ammonia

The reaction of an ester with ammonia to give an amide, as shown below, appears to be a substitution reaction (Y = CH_3O & Z = NH_2); however, it is actually two reactions, an addition followed by an elimination.



Example 6.1.2: The Addition of water to a Nitrile

The addition of water to a nitrile does not seem to fit any of the above reaction types, but it is simply a slow addition reaction followed by a rapid rearrangement, as shown in the following equation. Rapid rearrangements of this kind are called **tautomerizations**.



Exercise 6.1.3

Classify each reaction as addition, elimination, substitution, or rearrangement.

A) $CH_3CH_2Br + LiOH \longrightarrow CH_3CH_2OH + LiBr$

B) $CH_3CH_2CH_2Cl \longrightarrow CH_3CH{=}CH_2 + HCl$

C) $CH_3CH{=}CH_2 + H_2 \longrightarrow CH_3CH_2CH_3$

Answer

A = Substitution; B = Elimination; C = Addition

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6.2: How Organic Reactions Occur - Mechanisms

Objectives

After completing this section, you should be able to

- explain the difference between heterolytic and homolytic bond breakage, and between heterogenic and homogenic bond formation.
- state the two reaction types involved in symmetrical and unsymmetrical processes.

Key Terms

Make certain that you can define, and use in context, the key terms below.

- heterogenic
- heterolytic
- homogenic
- homolytic
- polar reaction
- radical reaction
- reaction mechanism

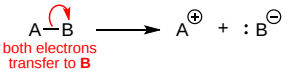
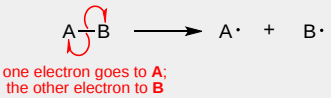
Study Notes

Upon first reading first four key terms, it is easy to be puzzled. The ending of the word tells you whether a bond is being formed (-genic) or broken (-lytic), while the root of the word describes the nature of that formation or decomposition. So hetero (meaning different) reactions involve asymmetrical bond making (or breaking) and homo (meaning same) involve symmetrical processes.

Because one pair of electrons constitutes a single bond, the unsymmetrical making or breaking of that bond in a hetero processes are described as polar reactions. Similarly, symmetrical homo processes of bond making and breaking are called radical reactions. Radicals (sometimes referred to as free radicals) are highly reactive neutral chemical species with one unpaired electron. In later sections we discuss radical and polar reactions in more detail.

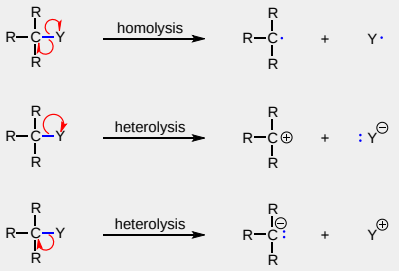
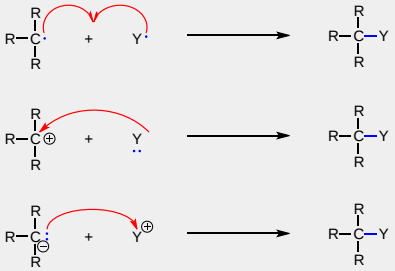
The Arrow Notation in Mechanisms

Since chemical reactions involve the breaking and making of bonds, a consideration of the movement of bonding (and non-bonding) valence shell electrons is essential to this understanding. It is now common practice to show the movement of electrons with curved arrows, and a sequence of equations depicting the consequences of such electron shifts is termed a **mechanism**. In general, two kinds of curved arrows are used in drawing mechanisms:

A full head on the arrow indicates the movement or shift of an electron pair:		
A partial head (fishhook) on the arrow indicates the shift of a single electron:		

The use of these symbols in bond-breaking and bond-making reactions is illustrated below. If a covalent single bond is broken so that one electron of the shared pair remains with each fragment, as in the first example, this bond-breaking is called **homolysis**. If

the bond breaks with both electrons of the shared pair remaining with one fragment, as in the second and third examples, this is called **heterolysis**.

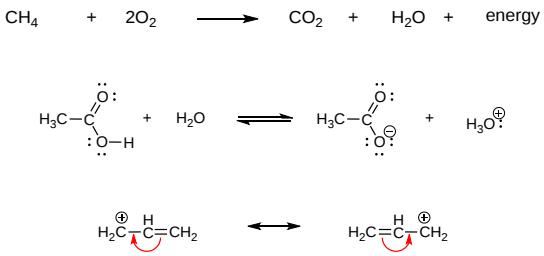
Bond-Breaking	Bond-Making
	

Other Arrow Symbols

Chemists also use arrow symbols for other purposes, and it is essential to use them correctly.

The Reaction Arrow	The Equilibrium Arrow	The Resonance Arrow
		

The following equations illustrate the proper use of these symbols:



Reactive Intermediates

The products of bond breaking, shown above, are not stable in the usual sense, and cannot be isolated for prolonged study. Such species are referred to as **reactive intermediates**, and are believed to be transient intermediates in many reactions. The general structures and names of four such intermediates are given below.

Charged Intermediates	Uncharged Intermediates
 a carbocation	 a radical
 a carbanion	 a carbene

A pair of widely used terms, related to the Lewis acid-base notation, should also be introduced here.

- Electrophile: An electron deficient atom, ion or molecule that has an affinity for an electron pair, and will bond to a base or nucleophile.

- Nucleophile: An atom, ion or molecule that has an electron pair that may be donated in bonding to an electrophile (or Lewis acid).

Using these definitions, it is clear that carbocations (called carbonium ions in the older literature) are electrophiles and carbanions are nucleophiles. Carbenes have only a valence shell sextet of electrons and are therefore electron deficient. In this sense they are electrophiles, but the non-bonding electron pair also gives carbenes nucleophilic character. As a rule, the electrophilic character dominates carbene reactivity. Carbon radicals have only seven valence electrons, and may be considered electron deficient; however, they do not in general bond to nucleophilic electron pairs, so their chemistry exhibits unique differences from that of conventional electrophiles. Radical intermediates are often called **free radicals**.

The importance of electrophile / nucleophile terminology comes from the fact that many organic reactions involve at some stage the bonding of a nucleophile to an electrophile, a process that generally leads to a stable intermediate or product. Reactions of this kind are sometimes called **ionic reactions**, since ionic reactants or products are often involved. Some common examples of ionic reactions and their mechanisms may be examined below.

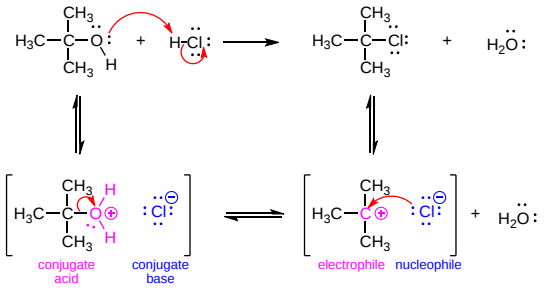
The shapes ideally assumed by these intermediates becomes important when considering the stereochemistry of reactions in which they play a role. A simple tetravalent compound like methane, CH_4, has a tetrahedral configuration. Carbocations have only three bonds to the charge bearing carbon, so it adopts a planar trigonal configuration. Carbanions are pyramidal in shape (tetrahedral if the electron pair is viewed as a substituent), but these species invert rapidly at room temperature, passing through a higher energy planar form in which the electron pair occupies a p-orbital. Radicals are intermediate in configuration, the energy difference between pyramidal and planar forms being very small. Since three points determine a plane, the shape of carbenes must be planar; however, the valence electron distribution varies.

Ionic Reactions

The principles and terms introduced in the previous sections can now be summarized and illustrated by the following three examples. Reactions such as these are called **ionic** or **polar** reactions, because they often involve charged species and the bonding together of **electrophiles and nucleophiles**. Ionic reactions normally take place in liquid solutions, where solvent molecules assist the formation of charged intermediates.

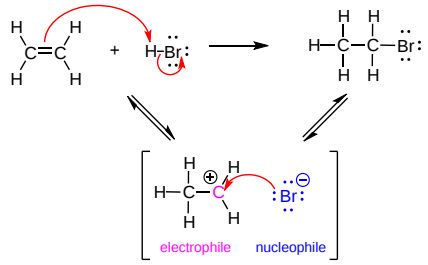
Substitution Reaction

The substitution reaction shown below can be viewed as taking place in three steps. The first is an acid-base equilibrium, in which HCl protonates the oxygen atom of the alcohol. The resulting conjugate acid then loses water in a second step to give a carbocation intermediate. Finally, this electrophile combines with the chloride anion nucleophile to give the final product.



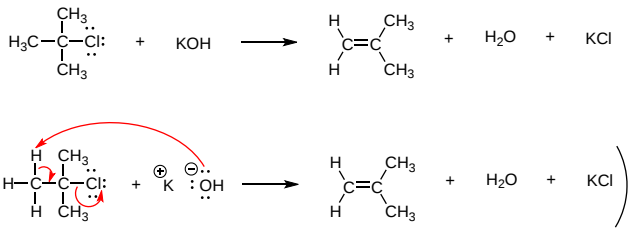
Addition Reaction

The addition reaction shown below can be viewed as taking place in two steps. The first step can again be considered an acid-base equilibrium, with the pi-electrons of the carbon-carbon double bond functioning as a base. The resulting conjugate acid is a carbocation, and this electrophile combines with the nucleophilic bromide anion.



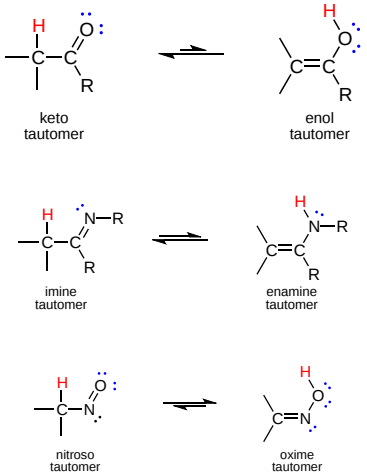
Elemination Reaction

The elimination reaction shown below takes place in one step. The bond breaking and making operations that take place in this step are described by the curved arrows. The initial stage may also be viewed as an acid-base interaction, with hydroxide ion serving as the base and a hydrogen atom component of the alkyl chloride as an acid. **rearrangement** (tautomerism)



Tautomerization Reaction

There are many kinds of molecular rearrangements. The examples shown below are from an important class called **tautomerization** or, more specifically, keto-enol tautomerization. Tautomers are rapidly interconverted constitutional isomers, usually distinguished by a different bonding location for a labile hydrogen atom (colored red here) and a differently located double bond. The equilibrium between tautomers is not only rapid under normal conditions, but it often strongly favors one of the isomers (acetone, for example, is 99.999% keto tautomer). Even in such one-sided equilibria, evidence for the presence of the minor tautomer comes from the chemical behavior of the compound. Tautomeric equilibria are catalyzed by traces of acids or bases that are generally present in most chemical samples.



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6.3: Radical Reactions

Objectives

After completing this section, you should be able to

- give an example of a radical substitution reaction.
- identify the three steps (initiation, propagation and termination) that occur in a typical radical substitution reaction.
- write out the steps involved in a simple radical substitution reaction, such as the chlorination of methane.
- explain why the halogenation of an alkane is not a particularly useful method of preparing specific alkyl halides.

Key Terms

Make certain that you can define, and use in context, the key terms below.

- chain reaction
- initiation step
- propagation step
- radical substitution
- termination step

Study Notes

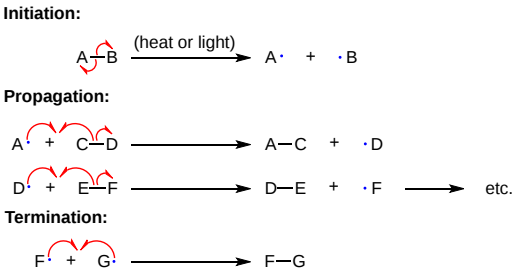
A *radical substitution reaction* is a reaction which occurs by a free radical mechanism and results in the substitution of one or more of the atoms or groups present in the substrate by different atoms or groups.

The *initiation step* in a radical chain reaction is the step in which a free radical is first produced. A *termination step* of a radical chain reaction is one in which two radicals react together in some way so that the chain can no longer be propagated.

While radical halogenation of very simple alkanes can be an effective synthetic strategy, it cannot be employed for larger more complex alkanes to yield specific alkyl halides, since the reactive nature of radicals always leads to mixtures of single- and multiple-halogenated products.

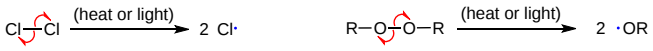
The Three Phases of Radical Chain Reactions

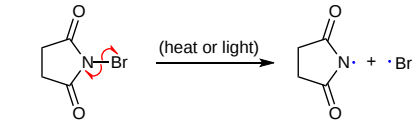
Because of their high reactivity, free radicals have the potential to be both extremely powerful chemical tools and extremely harmful contaminants. Much of the power of free radical species stems from the natural tendency of radical processes to occur in a chain reaction fashion. **Radical chain reactions** have three distinct phases: initiation, propagation, and termination.



The **initiation phase** describes the step that initially creates a radical species. In most cases, this is a homolytic cleavage event, and takes place very rarely due to the high energy barriers involved. Often the influence of heat, UV radiation, or a metal-containing catalyst is necessary to overcome the energy barrier.

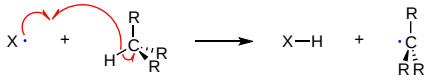
Molecular chlorine and bromine will both undergo homolytic cleavage to form radicals when subjected to heat or light. Other functional groups which also tend to form radicals when exposed to heat or light are chlorofluorocarbons, peroxides, and the halogenated amide N-bromosuccinimide (NBS).

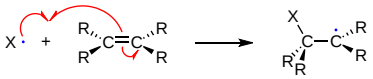




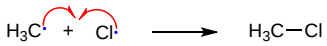
N-bromosuccinimide
(NBS)

The **propagation phase** describes the 'chain' part of chain reactions. Once a reactive free radical is generated, it can react with stable molecules to form new free radicals. These new free radicals go on to generate yet more free radicals, and so on. Propagation steps often involve hydrogen abstraction or addition of the radical to double bonds.





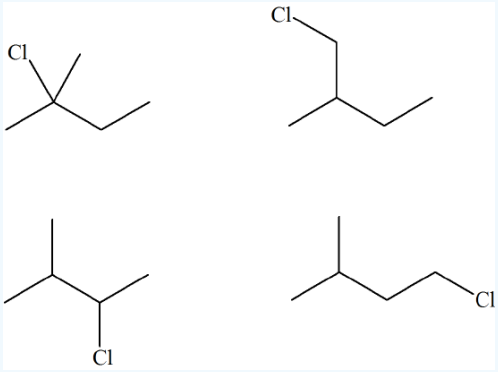
Chain termination occurs when two free radical species react with each other to form a stable, non-radical adduct. Although this is a very thermodynamically downhill event, it is also very rare due to the low concentration of radical species and the small likelihood of two radicals colliding with one another. In other words, the Gibbs free energy barrier is very high for this reaction, mostly due to entropic rather than enthalpic considerations. The active sites of enzymes, of course, can evolve to overcome this entropic barrier by positioning two radical intermediates adjacent to one another.



? Exercise 6.3.1

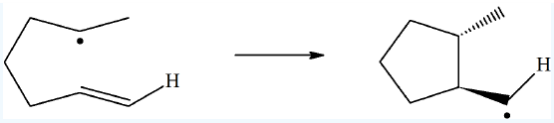
Radical chlorination of alkanes are not useful due to uncontrolled substitution. Draw the mono-substituted products of Cl_2 reacting with 2-methylbutane.

Answer



? Exercise 6.3.2

Propose a radical mechanism for the following reaction:



Answer



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6.4: Polar Reactions

Objectives

After completing this section, you should be able to

- identify the positive and negative ends of the bonds present in the common functional groups.
- explain how bond polarity can be enhanced by the interaction of a functional group with a solvent, metal cation or acid.
- explain how the polarizability of an atom can be an important factor in determining the reactivity of a bond.
- describe the heterolytic bond-breaking process.
- use curved (curly) arrows to indicate the movement of electron pairs during bond breakage and bond formation.
- predict whether a given species (compound or ion) is likely to behave as a nucleophile or as an electrophile.

Key Terms

Make certain that you can define, and use in context, the key terms below.

- electrophile
- nucleophile
- polar reaction
- polarizability

Study Notes

You may wish to review Section 2.1 before you begin this section. The relative electronegativities of the elements shown in the periodic table should already be familiar. Remember that it is the relative electronegativities that are important, not the actual numerical values.

Make sure that you understand the polarity patterns of the common functional groups. Do not try to memorize these polarities; rather, concentrate on why they arise. You will encounter these group polarities so frequently that they will soon become "second nature" to you.

Halogens and the Character of the Carbon-Halogen Bond

With respect to electronegativity, most halogens are more electronegative than carbon. This results in a carbon-halogen bond that is polarized. As shown in the image below, the carbon atom has a partial positive charge, while the halogen has a partial negative charge.



The following table shows the relationship between the halogens and electronegativity. Notice, as we move up the periodic table from iodine to fluorine, electronegativity increases.

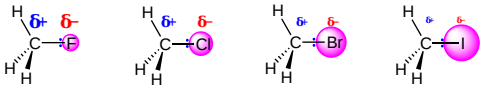
Electronegativity	I < Br < Cl < F

The following table shows the relationships between bond length, bond strength, and molecular size. As we progress down the periodic table from fluorine to iodine, molecular size increases. As a result, we also see an increase in bond length. Conversely, as molecular size increases and we get longer bonds, the strength of those bonds decreases.

Bond length	C–F < C–Cl < C–Br < C–I
Bond strength	C–I < C–Br < C–Cl < C–F
Molecular size	F < Cl < Br < I

The influence of bond polarity

Of the four halogens, fluorine is the most electronegative and iodine the least. That means that the electron pair in the carbon-fluorine bond will be dragged most towards the halogen end. Looking at the methyl halides as simple examples:



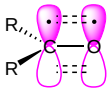
The electronegativities of carbon and iodine are not very different, and so there will be little separation of charge on the bond. One of the important set of reactions of alkyl halides involves replacing the halogen by something else - substitution reactions. These reactions can involve the carbon-halogen bond breaking to give positive and negative ions. The ion with the positively charged carbon atom then reacts with something either fully or slightly negatively charged. Alternatively, something either fully or negatively charged is attracted to the slightly positive carbon atom and pushes off the halogen atom.

You might have thought that either of these would be more effective in the case of the carbon-fluorine bond with the quite large amounts of positive and negative charge already present. But that's not so - quite the opposite is true! The thing that governs the reactivity is the strength of the bonds which have to be broken. It is difficult to break a carbon-fluorine bond, but easy to break a carbon-iodine one.

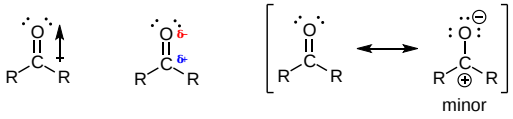
The Carbonyl Group

C=O is prone to additions and nucleophillic attack because or carbon's positive charge and oxygen's negative charge. The resonance of the carbon partial positive charge allows the negative charge on the nucleophile to attack the Carbonyl group and become a part of the structure and a positive charge (usually a proton hydrogen) attacks the oxygen. Just a reminder, the nucleophile is a good acid therefore "likes protons" so it will attack the side with a positive charge.

Before we consider in detail the reactivity of aldehydes and ketones, we need to look back and remind ourselves of what the bonding picture looks like in a carbonyl. Carbonyl carbons are sp^2 hybridized, with the three sp^2 orbitals forming overlaps with orbitals on the oxygen and on the two carbon or hydrogen atoms. These three bonds adopt trigonal planar geometry. The remaining unhybridized 2p orbital on the central carbonyl carbon is perpendicular to this plane, and forms a ‘side-by-side’ pi bond with a 2p orbital on the oxygen.



The carbon-oxygen double bond is polar: oxygen is more electronegative than carbon, so electron density is higher on the oxygen side of the bond and lower on the carbon side. Recall that bond polarity can be depicted with a dipole arrow, or by showing the oxygen as holding a partial negative charge and the carbonyl carbon a partial positive charge.



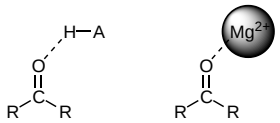
A third way to illustrate the carbon-oxygen dipole is to consider the two main resonance contributors of a carbonyl group: the major form, which is what you typically see drawn in Lewis structures, and a minor but very important contributor in which both electrons in the pbond are localized on the oxygen, giving it a full negative charge. The latter depiction shows the carbon with an empty 2p orbital and a full positive charge.

Some Carbonyl Compounds

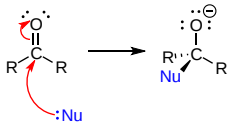
Compound	aldehyde	ketone	formaldehyde	carboxylic acid	ester	amide	enone	acyl halide	acid anhydride
Structure									
General Formula	RCHO	RCOR'	CH_2O	RCOOH	RCOOR'	RCONR'R''	RC(O)C(R')CR''R'''	RCOX	RCO_2COR'

Nucleophilic Addition to Aldehydes and Ketones

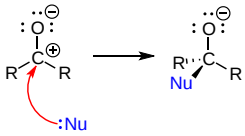
The result of carbonyl bond polarization, however it is depicted, is straightforward to predict. The carbon, because it is electron-poor, is an electrophile: it is a great target for attack by an electron-rich nucleophilic group. Because the oxygen end of the carbonyl double bond bears a partial negative charge, anything that can help to stabilize this charge by accepting some of the electron density will increase the bond's polarity and make the carbon more electrophilic. Very often a general acid group serves this purpose, donating a proton to the carbonyl oxygen.



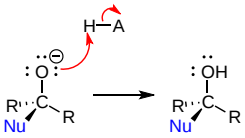
The same effect can also be achieved if a Lewis acid, such as a magnesium ion, is located near the carbonyl oxygen. Unlike the situation in a nucleophilic substitution reaction, when a nucleophile attacks an aldehyde or ketone carbon there is no leaving group – the incoming nucleophile simply 'pushes' the electrons in the pi bond up to the oxygen.



Alternatively, if you start with the minor resonance contributor, you can picture this as an attack by a nucleophile on a carbocation.



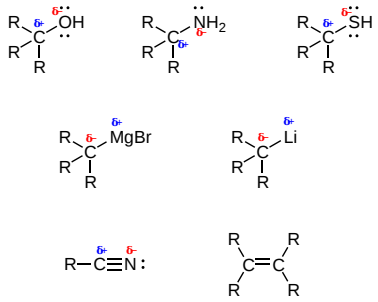
After the carbonyl is attacked by the nucleophile, the negatively charged oxygen has the capacity to act as a nucleophile. However, most commonly the oxygen acts instead as a base, abstracting a proton from a nearby acid group in the solvent or enzyme active site.



This very common type of reaction is called a **nucleophilic addition**. In many biologically relevant examples of nucleophilic addition to carbonyls, the nucleophile is an alcohol oxygen or an amine nitrogen, or occasionally a thiol sulfur. In one very important reaction type known as an aldol reaction, the nucleophile attacking the carbonyl is a resonance-stabilized carbanion. In this chapter, we will concentrate on reactions where the nucleophile is an oxygen or nitrogen.

1. Nucleophilic Addition to Aldehydes and Ketones
2. Nucleophilic Substitution of RCOZ (Z = Leaving Group)
3. General reaction
4. General mechanism

Polarity Patterns in Other Common Functional Groups



Nucleophile?

Nucleophilic functional groups are those which have electron-rich atoms able to donate a pair of electrons to form a new covalent bond. In both laboratory and biological organic chemistry, the most relevant nucleophilic atoms are oxygen, nitrogen, and sulfur, and the most common nucleophilic functional groups are water, alcohols, phenols, amines, thiols, and occasionally carboxylates.

More specifically in laboratory reactions, halide and azide (N_3^-) anions are commonly seen acting as nucleophiles.

Of course, carbons can also be nucleophiles - otherwise how could new carbon-carbon bonds be formed in the synthesis of large organic molecules like DNA or fatty acids? Enolate ions (section 7.5) are the most common carbon nucleophiles in biochemical reactions, while the cyanide ion (CN^-) is just one example of a carbon nucleophile commonly used in the laboratory. Reactions with carbon nucleophiles will be dealt with in chapters 13 and 14, however - in this chapter and the next, we will concentrate on non-carbon nucleophiles.

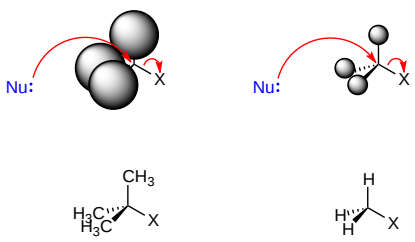
When thinking about nucleophiles, the first thing to recognize is that, for the most part, the same quality of 'electron-richness' that makes a something nucleophilic also makes it basic: *nucleophiles can be bases, and bases can be nucleophiles*. It should not be surprising, then, that most of the trends in basicity that we have already discussed also apply to nucleophilicity.

Neutral Nucleophiles	Charged Nucleophiles
H_2O, NH_3, RNH_2, R_2NH, R_3N, ROH, RCOOH, RSH, and PR_3	$^{\ominus}OH$, $^{\ominus}OR$, $^{\ominus}NH_2$, $^{\ominus}NHR$, $^{\ominus}NR_2$, $^{\ominus}SH$, $^{\ominus}SR$, $^{\ominus}SeR$, $^{\ominus}Cl$, $^{\ominus}Br$, $^{\ominus}I$, $^{\ominus}F$, $^{\ominus}CN$, $RCOO^{\ominus}$

Electrophiles

In the vast majority of the nucleophilic substitution reactions you will see in this and other organic chemistry texts, the electrophilic atom is a carbon which is bonded to an electronegative atom, usually oxygen, nitrogen, sulfur, or a halogen. The concept of electrophilicity is relatively simple: an electron-poor atom is an attractive target for something that is electron-rich, *i.e.* a nucleophile. However, we must also consider the effect of steric hindrance on electrophilicity. In addition, we must discuss how the nature of the electrophilic carbon, and more specifically the stability of a potential carbocationic intermediate, influences the S_N1 vs. S_N2 character of a nucleophilic substitution reaction.

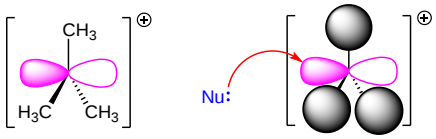
Consider two hypothetical S_N2 reactions: one in which the electrophile is a methyl carbon and another in which it is tertiary carbon.



Because the three substituents on the methyl carbon electrophile are tiny hydrogens, the nucleophile has a relatively clear path for backside attack. However, backside attack on the tertiary carbon is blocked by the bulkier methyl groups. Once again, steric

hindrance - this time caused by bulky groups attached to the electrophile rather than to the nucleophile - hinders the progress of an associative nucleophilic (S_N2) displacement.

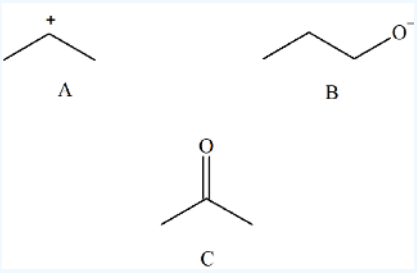
The factors discussed in the above paragraph, however, do not prevent a sterically-hindered carbon from being a good electrophile - they only make it less likely to be attacked in a *concerted S_N2 reaction*. Nucleophilic substitution reactions in which the electrophilic carbon is sterically hindered are more likely to occur by a two-step, dissociative (S_N1) mechanism. This makes perfect sense from a geometric point of view: the limitations imposed by sterics are significant mainly in an S_N2 displacement, when the electrophile being attacked is a sp^3-hybridized tetrahedral carbon with its relatively 'tight' angles of 109.4°. Remember that in an S_N1 mechanism, the nucleophile attacks an sp^2-hybridized carbocation intermediate, which has trigonal planar geometry with 'open' 120 angles.



With this open geometry, the empty p orbital of the electrophilic carbocation is no longer significantly shielded from the approaching nucleophile by the bulky alkyl groups. A carbocation is a very potent electrophile, and the nucleophilic step occurs very rapidly compared to the first (ionization) step.

? Exercise 6.4.1

Label the following either an electrophile or a nucleophile.



Answer

A = Electrophile

B = Nucleophile

C = Both (carbonyl carbon is electrophile and oxygen is nucleophile)

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6.5: An Example of a Polar Reaction - Addition of HBr to Ethylene

Objectives

After completing this section, you should be able to

- give an example of a simple polar reaction (e.g., a electrophilic addition).
- identify the electrophile and nucleophile in a simple polar reaction.

Key Terms

Make certain that you can define, and use in context, the key terms below.

- electrophilic addition
- carbocation

Study Notes

The curved arrows introduced in this section are used throughout the course to indicate the movement of electron pairs. It takes practice for the beginning student to feel comfortable using these arrows. Remember that the head of the arrow indicates where the electron pair moves to; its tail shows where the electron pair comes from. (Chemists often refer to the use of curved arrows as “electron pushing.")

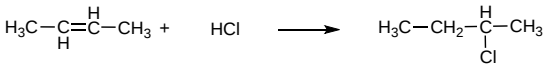
This page looks at the reaction of the carbon-carbon double bond in alkenes such as ethene with hydrogen halides such as hydrogen chloride and hydrogen bromide. Symmetrical alkenes (like ethene or but-2-ene) are dealt with first. These are alkenes where identical groups are attached to each end of the carbon-carbon double bond.

Addition to symmetrical alkenes

All alkenes undergo addition reactions with the hydrogen halides. A hydrogen atom joins to one of the carbon atoms originally in the double bond, and a halogen atom to the other. For example, with ethene and hydrogen chloride, you get chloroethane:



With but-2-ene you get 2-chlorobutane:

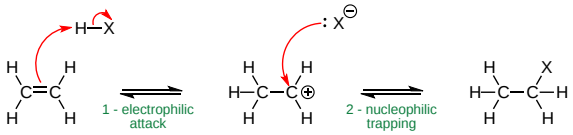


What happens if you add the hydrogen to the carbon atom at the right-hand end of the double bond, and the chlorine to the left-hand end? You would still have the same product. The chlorine would be on a carbon atom next to the end of the chain - you would simply have drawn the molecule flipped over in space. That would be different of the alkene was unsymmetrical - that's why we have to look at them separately.

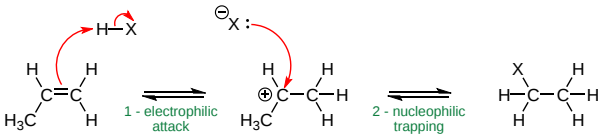
Mechanism

The addition of hydrogen halides is one of the easiest electrophilic addition reactions because it uses the simplest electrophile: the proton. Hydrogen halides provide both an electrophile (proton) and a nucleophile (halide). First, the electrophile will attack the double bond and take up a set of pi electrons, attaching it to the molecule (1). This is basically the reverse of the last step in the E1 reaction (deprotonation step). The resulting molecule will have a single carbon-carbon bond with a positive charge on one of them (carbocation). The next step is when the nucleophile (halide) bonds to the carbocation, producing a new molecule with both the original hydrogen and halide attached to the organic reactant (2). The second step will only occur if a good nucleophile is used.

Mechanism of Electrophilic Addition of Hydrogen Halide to Ethene



Mechanism of Electrophilic Addition of Hydrogen Halide to Propene

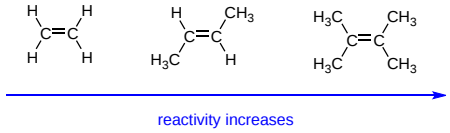


All of the halides (HBr, HCl, HI, HF) can participate in this reaction and add on in the same manner. Although different halides do have different rates of reaction, due to the H-X bond getting weaker as X gets larger (poor overlap of orbitals)s.

Reaction rates

Reaction rates increase in the order HF - HCl - HBr - HI. Hydrogen fluoride reacts much more slowly than the other three, and is normally ignored in talking about these reactions. When the hydrogen halides react with alkenes, the hydrogen-halogen bond has to be broken. The bond strength falls as you go from HF to HI, and the hydrogen-fluorine bond is particularly strong. Because it is difficult to break the bond between the hydrogen and the fluorine, the addition of HF is bound to be slow.

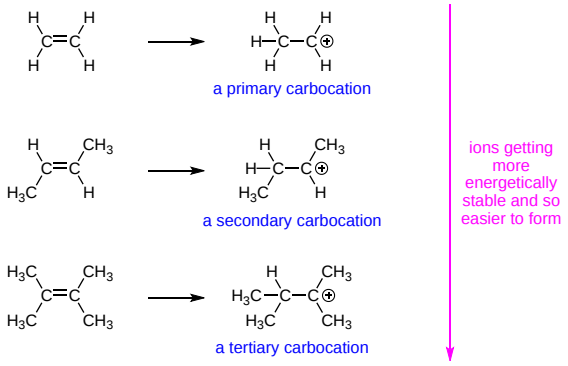
This applies to unsymmetrical alkenes as well as to symmetrical ones. For simplicity the examples given below are all symmetrical ones- but they don't have to be. Reaction rates increase as the alkene gets more complicated - in the sense of the number of alkyl groups (such as methyl groups) attached to the carbon atoms at either end of the double bond. For example:



There are two ways of looking at the reasons for this - both of which need you to know about the mechanism for the reactions.

Alkenes react because the electrons in the pi bond attract things with any degree of positive charge. Anything which increases the electron density around the double bond will help this. Alkyl groups have a tendency to "push" electrons away from themselves towards the double bond. The more alkyl groups you have, the more negative the area around the double bonds becomes.

The more negatively charged that region becomes, the more it will attract molecules like hydrogen chloride. The more important reason, though, lies in the stability of the intermediate ion formed during the reaction. The three examples given above produce these carbocations (carbonium ions) at the half-way stage of the reaction:

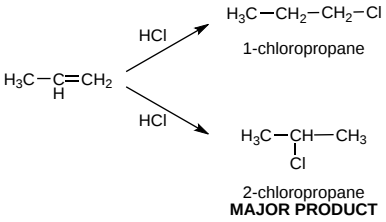


The stability of the intermediate ions governs the activation energy for the reaction. As you go towards the more complicated alkenes, the activation energy for the reaction falls. That means that the reactions become faster.

Addition to unsymmetrical alkenes

In terms of reaction conditions and the factors affecting the rates of the reaction, there is no difference whatsoever between these alkenes and the symmetrical ones described above. The problem comes with the orientation of the addition - in other words, which way around the hydrogen and the halogen add across the double bond.

If HCl adds to an unsymmetrical alkene like propene, there are two possible ways it could add. However, in practice, there is only one major product.



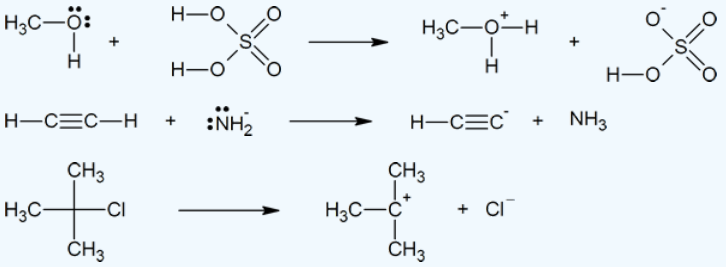
This is in line with Markovnikov's Rule which says:

> When a compound HX is added to an unsymmetrical alkene, the hydrogen becomes attached to the carbon with the most hydrogens attached to it already.

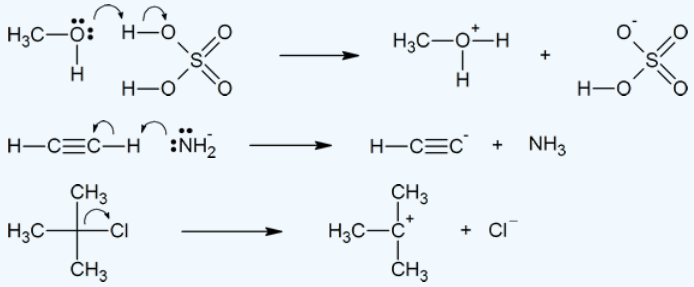
In this case, the hydrogen becomes attached to the CH_2 group, because the CH_2 group has more hydrogens than the CH group. Notice that only the hydrogens directly attached to the carbon atoms at either end of the double bond count. The ones in the CH_3 group are totally irrelevant.

? Exercise 6.5.1

Supply the missing curved arrows in the equations given below.

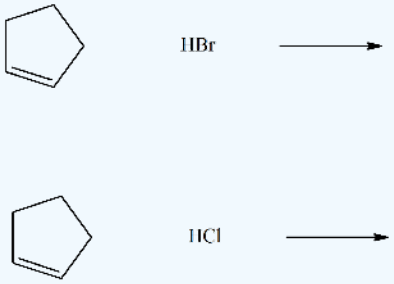


Answer

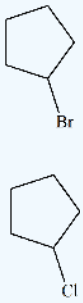


Exercise 6.5.2

Predict the product of the following reactions:



Answer



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6.6: Using Curved Arrows in Polar Reaction Mechanisms

Objective

After completing this section, you should be able to use curved (curly) arrows, in conjunction with a chemical equation, to show the movement of electron pairs in a simple polar reaction, such as electrophilic addition.

Key Terms

Make certain that you can define, and use in context, the key terms below.

- electrophlic
- nucleophlic

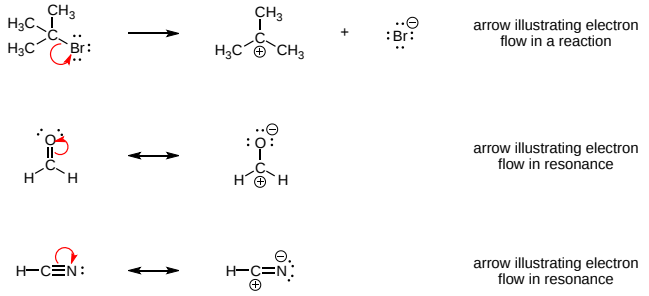
Pushing Electrons and Curved Arrows

Understanding the location of electrons and being able to draw the curved arrows that depict the mechanisms by which the reactions occur is one of the most critical tools for learning organic chemistry since they allow you to understand what controls reactions, and how reactions proceed.

Before you can do this you need to understand that a **bond** is due to a pair of electrons shared between atoms. When asked to draw a mechanism, curved arrows should be used to show all the bonding changes that occur. A few simple lessons that illustrate these concepts can be found below.

Lesson 1

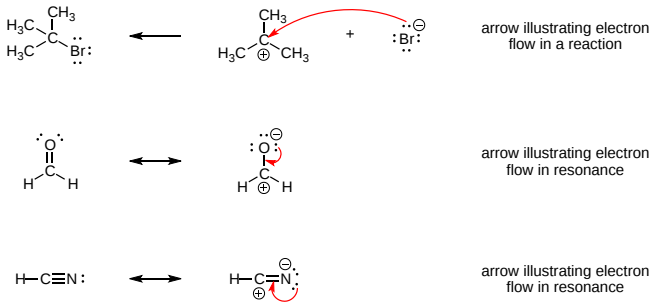
If we remove the pair of electrons in a bond, then we BREAK that bond. This is true for single and multiple bonds as shown below:



Notice that since the starting materials were *neutral*, the products are also *neutral*. In general terms, the *sum of the charges* on the starting materials MUST equal the *sum of the charges* on the products since we have the **same number of electrons**.

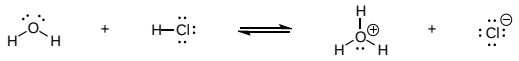
The first example is a REACTION since we broke a sigma bond. In the second two examples, we moved pi electrons into long pairs. This is RESONANCE.

If we move electrons between two atoms, then we MAKE a new bond:

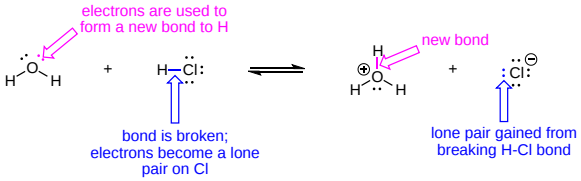


We always show electrons moving from **electron rich** to **electron poor**.

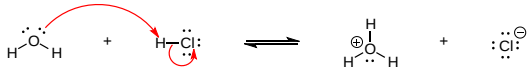
Lesson 2



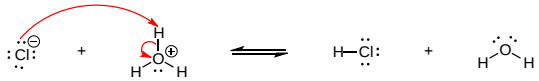
This is a simple acid/base reaction, showing the formation of the hydronium ion produced when hydrochloric acid is dissolved in water. It is useful to analyze the bond changes that are occurring. Water is functioning as a **base** and hydrochloric acid as an **acid**. Consider the differences in bonding between the starting materials and the products:



One of the lone pairs on the oxygen atom of water was used to form a bond to a hydrogen atom, creating the hydronium ion (H_3O^+) seen in the products. The hydrogen-chlorine bond of HCl was broken, and the electrons in this bond became a lone pair on the chlorine atom, thus generating a chloride ion. We can illustrate these changes in bonding using the curved arrows shown below.



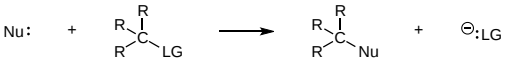
Note that in this diagram, the overall charge of the reactants is the same as the overall charge of the products. We can also show the curved arrows for the reverse reaction:



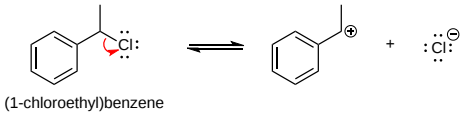
This shows the formation of the new H-Cl bond by using a lone pair of electrons from the electron-rich chloride ion to form a bond to an electron poor hydrogen atom of the hydronium ion. Because hydrogen can only form one bond, the oxygen-hydrogen bond is broken and its electrons become a lone pair on the electron-poor oxygen atom. Notice that the charges balance!

Lesson 3

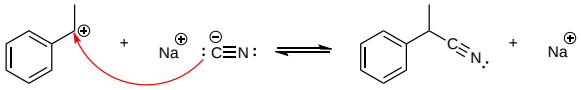
In this section, we will look at the curved arrows for some nucleophilic substitution reactions. Overall, the processes involved are similar to those for the acid/base reactions described above. In a nucleophilic substitution reaction, an electron-rich nucleophile (Nu) becomes bonded to an electron-poor carbon atom, and a leaving group (LG) is displaced. In bonding terms, we must *make* a Nu-C bond and *break* a C-LG bond.



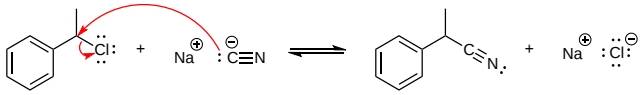
Let's consider the stepwise S_N1 reaction between (1-chloroethyl)benzene and sodium cyanide. The first step of this process is breaking the C-Cl bond, where the electrons in that bond become a lone pair on the chlorine atom. The carbon atom has lost electrons and therefore becomes positive, generating a secondary carbocation. Because the chlorine atom gained an additional lone pair of electrons, it becomes a negatively charged chloride ion.


(1-chloroethyl)benzene

In the second step, the electron-rich nucleophile donates electrons to form a new C-C bond with the electron-poor secondary carbocation.



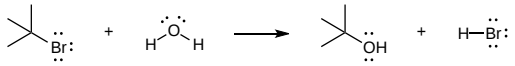
In an S_N2 reaction, the bond forming and breaking processes occur simultaneously. The scheme below shows the Nu donating electrons to form a new C-C bond at the same time that the C-Cl bond is breaking. The electrons in the C-Cl bond become a long pair on the chlorine atom, generating a chloride ion. Forming and breaking the bonds simultaneously allows carbon to obey the octet rule throughout this process.



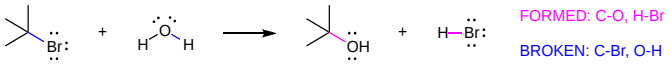
Notice that in all steps for the processes above, the overall charges of the starting materials match those of the products.

Lesson 4

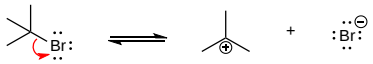
This section will dissect another substitution reaction, although it is more involved. Let's consider the S_N1 reaction of *tert*-butyl bromide with water.



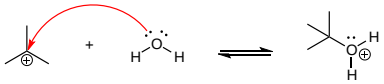
It can be helpful to take inventory of which bonds have been formed, and which bonds have been broken.



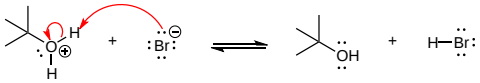
The curved arrows we draw must account for ALL of these bonding changes. Since we are dealing with an S_N1 reaction process, the first step will be cleavage of the C-Br bond to give a carbocation and and a bromide anion.



Water then acts as a nucleophile, using one of its lone pairs to form a bond to the electron-poor *t*-butyl cation. This generates an oxonium ion, where oxygen has three bonds and a positive formal charge.

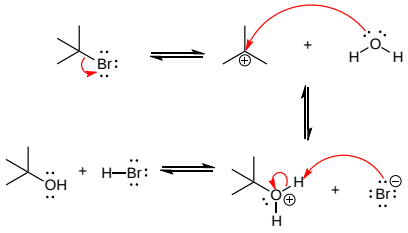


The final step is an acid/base reaction between the bromide anion generated in step 1 and the oxonium product of step 2. The bromide anion acts as a base, using a lone pair to form a bond to one of the hydrogen atoms. The O-H bond then breaks, and its electrons become a lone pair on oxygen. This gives the final products of HBr and *t*-butyl alcohol.

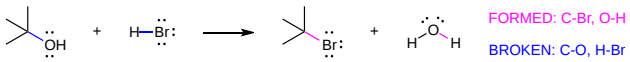


Notice that in each of the mechanistic steps above, the overall charge of the reactant side balances with the overall charge of the product side.

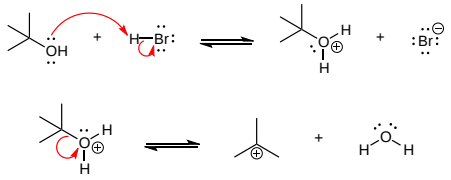
While the above process was broken down into distinct steps, however it is important to note that mechanisms are almost always shown as a continuous process. The overall mechanism for this processes can be found below:



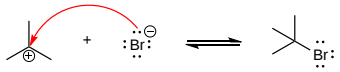
Now consider the reverse reaction, i.e. the reaction of *t*-butyl alcohol with hydrobromic acid to generate *t*-butyl bromide and water. The scheme is shown below, along with an analysis of the bonds formed and broken in this process:



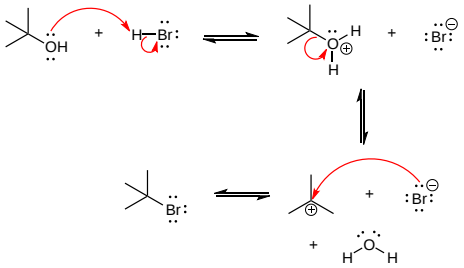
The mechanism must occur via the same pathway as shown above (Law of Macroscopic Reversibility), however this mechanism can still be deduced without knowing that. First, it is known that HBr is a strong acid and can donate a proton to a base. The most basic sites in the whole system are the lone pairs on the oxygen atom of *t*-butanol. Since the lone pairs are the electron-rich area of the molecule, the arrow starts at a lone pair and ends at the proton of HBr. The H-Br bond breaks, pushing its electrons onto the bromine atom and generating a bromide ion.



The bromide ion generated in the first step can then react with the *t*-butyl cation to generate *t*-butyl bromide.



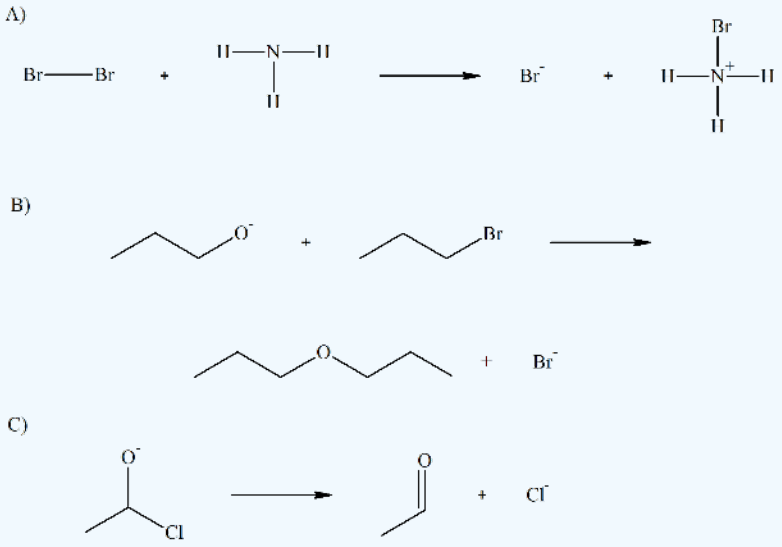
Once again, the above the overall process is broken down into individual steps, however it is more common to illustrate this as one overall process:



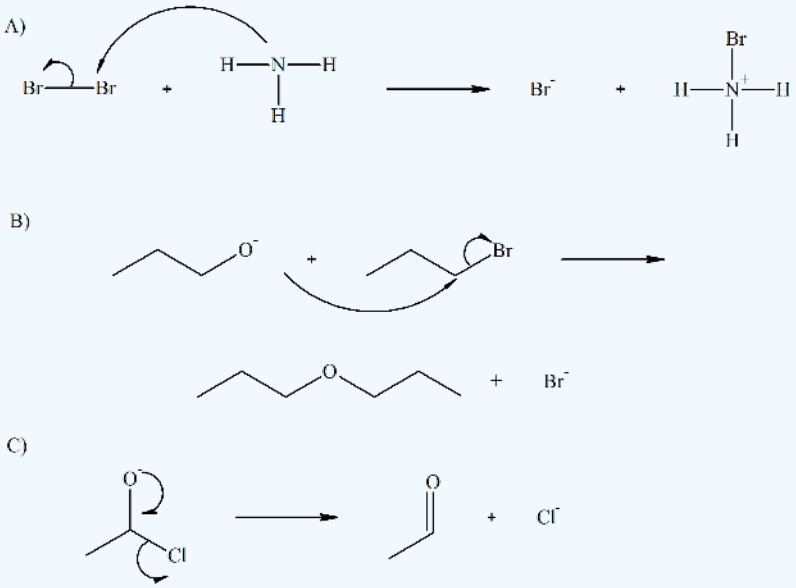
Curved Arrow Summary

- Curved arrows flow from electron rich to electron poor.
- Therefore they start from lone pairs or bonds.
- The charges in any particular step should always be balanced.
- Remember to obey the rules of valence (*eg*. octet rule for C,N,O,F *etc*.)
- If electrons are taken out of a bond, then that bond is broken.
- If electrons are placed between two atoms then it implies a bond is being made.

Exercise 6.6.1



Answer



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6.7: Describing a Reaction - Equilibria, Rates, and Energy Changes

Objectives

After completing this section, you should be able to

- write the equilibrium constant expression for a given reaction.
- assess, qualitatively, how far a reaction will proceed in a given direction, given the value of K_{eq}.
- explain the difference between rate and equilibrium.
- state the relationship between $\Delta G°$ and K_{eq}, and use this relationship to determine the value of either of the two variables, given the other.
- state the relationship between Gibbs free-energy, enthalpy and entropy, and use the relationship to calculate any one of $\Delta G°$, $\Delta H°$ and $\Delta S°$, given the other two.
- make a qualitative assessment of whether $\Delta S°$ for a given process is expected to be positive or negative.

Key Terms

Make certain that you can define, and use in context, the key terms below.

- exergonic
- endergonic
- exothermic
- endothermic
- enthalpy change (heat of reaction), $\Delta H°$
- entropy change, $\Delta S°$
- reaction mechanism
- standard Gibbs free-energy change, $\Delta G°$

Study Notes

Throughout this course you will be paying a great deal of attention to the mechanisms of the reactions that you study. Some students see this as a laborious task of little practical use. However, you will find that a knowledge of reaction mechanisms can help reduce the number of reactions to memorize, provide a connecting link between apparently unrelated reactions, and enable someone with a basic knowledge of organic chemistry to deduce how a previously unseen reaction might proceed. The investigation of reaction mechanisms is a popular research area for organic chemists.

Equilibrium Constant

For the hypothetical chemical reaction:

$$aA + bB \rightleftharpoons cC + dD$$

the equilibrium constant is defined as:

$$K_C = \frac{[C]^c[D]^d}{[A]^a[B]^b}$$

The notation [A] signifies the molar concentration of species A. An alternative expression for the equilibrium constant involves partial pressures:

$$K_P = \frac{P_C^c P_D^d}{P_A^a P_B^b}$$

Note that the expression for the equilibrium constant includes only solutes and gases; pure solids and liquids do not appear in the expression. For example, the equilibrium expression for the reaction

$$CaH_2(s) + 2H_2O(g) \rightleftharpoons Ca(OH)_2(s) + 2H_2(g)$$

is the following:

$$K_C = \frac{[H_2]^2}{[H_2O]^2}$$

Observe that the gas-phase species H_2O and H_2 appear in the expression but the solids CaH_2 and $Ca(OH)_2$ do not appear.

The equilibrium constant is most readily determined by allowing a reaction to reach equilibrium, measuring the concentrations of the various solution-phase or gas-phase reactants and products, and substituting these values into the Law of Mass Action.

Free Energy

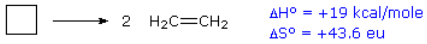
The interaction between enthalpy and entropy changes in chemical reactions is best observed by studying their influence on the equilibrium constants of reversible reactions. To this end a new thermodynamic function called Free Energy (or Gibbs Free Energy), symbol ΔG, is defined as shown in the first equation below. Two things should be apparent from this equation. First, in cases where the entropy change is small, $\Delta G \cong \Delta H$. Second, the importance of ΔS in determining ΔG increases with increasing temperature.

$$\Delta G^o = \Delta H^o - T\Delta S^o$$

where the temperature is measured in absolute temperature (K).

The free energy function provides improved insight into the thermodynamic driving forces that influence reactions. A negative ΔG^o is characteristic of an **exergonic reaction**, one which is thermodynamically favorable and often spontaneous, as is the melting of ice at 1 ºC. Likewise a positive ΔG^o is characteristic of an **endergonic reaction**, one which requires an input of energy from the surroundings.

For an example of the relationship of free energy to enthalpy consider the decomposition of cyclobutane to ethene, shown in the following equation. The standard state for all the compounds is gaseous.



This reaction is endothermic, but the increase in number of molecules from one (reactants) to two (products) results in a large positive ΔSº.

At 25 ºC (298 K):

ΔGº = 19 kcal/mol – 298(43.6) cal/mole = 19 – 13 kcal/mole = +6 kcal/mole.

Thus, the entropy change opposes the enthalpy change, but is not sufficient to change the sign of the resulting free energy change, which is endergonic. Indeed, cyclobutane is perfectly stable when kept at room temperature.

Because the entropy contribution increases with temperature, this energetically unfavorable transformation can be made favorable by raising the temperature. At 200 ºC (473 K),

$$\Delta G^o = 19\,kcal/mol - 473(43.6)\,cal/mole \quad (6.7.1)$$
$$= 19 - 20.6\,kcal/mole \quad (6.7.2)$$
$$= -1.6 kcal/mole. \quad (6.7.3)$$

This is now an **exergonic reaction**, and the thermal cracking of cyclobutane to ethene is known to occur at higher temperatures.

$$\Delta G^o = -RT \ln K = -2.303 RT \log_{10} K \quad (6.7.4)$$

where R = 1.987 cal/ K mole T = temperature in K and K = equilibrium constant

Note

Equation 6.7.4 is important because it demonstrates the fundamental relationship of ΔG^o to the equilibrium constant, K. Because of the negative logarithmic relationship between these variables, a negative ΔGº generates a K>1, whereas a positive ΔGº generates a K<1. When ΔGº = 0, K = 1. Furthermore, small changes in ΔGº produce large changes in K. A change of 1.4

kcal/mole in ΔG° changes K by approximately a factor of 10. This interrelationship may be explored with the calculator on the right. Entering free energies outside the range -8 to 8 kcal/mole or equilibrium constants outside the range 10^{-6} to 900,000 will trigger an alert, indicating the large imbalance such numbers imply.

? Exercise 6.7.1

At 155°C, the equilibrium constant, K_{eq}, for the reaction

$$\mathrm{CH3CO2H + CH3CH2OH <=> CH3CO2CH2CH3 + H2O}$$

has a value of 4.0. Calculate $\Delta G°$ for this reaction at 155°C.

? Exercise 6.7.2

Acetylene (C_2H_2) can be converted into benzene (C_6H_6) according to the equation:

You can't use 'macro parameter character #' in math mode

At 25°C, $\Delta G°$ for this reaction is −503 kJ and $\Delta H°$ is −631 kJ. Determine $\Delta S°$ and indicate whether the size of $\Delta S°$ agrees with what you would have predicted simply by looking at the chemical equation.

Answer

The entropy change is negative, as one would expect from looking at the chemical equation, since three moles of reactants yield one mole of product; that is, the system becomes much more “ordered” as it goes from reactants to products.

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6.8: Describing a Reaction - Bond Dissociation Energies

Objectives

After completing this section, you should be able to

- predict the value of $\Delta H°$ for a gas-phase reaction, given the necessary bond dissociation energy data.
- predict the dissociation energy of a particular bond, given $\Delta H°$ for a reaction involving the bond and any other necessary bond dissociation energy data.
- outline the limitations of using bond dissociation energies to predict whether or not a given reaction will occur.

Key Terms

Make certain that you can define, and use in context, the key terms below.

- bond dissociation energy
- solvation

Study Notes

The idea of calculating the standard enthalpy of a reaction from the appropriate bond dissociation energy data should be familiar to you from your first-year chemistry course.

Solvation is the interaction between solvent molecules and the ions or molecules dissolved in that solvent.

The homolytic bond dissociation energy is the amount of energy needed to break apart one mole of covalently bonded gases into a pair of radicals. The SI units used to describe bond energy are kiloJoules per mole of bonds (kJ/Mol). It indicates how strongly the atoms are bonded to each other.

Introduction

Breaking a covalent bond between two partners, A-B, can occur either heterolytically, where the shared pair of electron goes with one partner or another

$$A - B \rightarrow A^+ + B:^-$$

or

$$A - B \rightarrow A:^- + B^+$$

or homolytically, where one electron stays with each partner.

$$A - B \rightarrow A^\bullet + B^\bullet$$

The products of homolytic cleavage are radicals and the energy that is required to break the bond homolytically is called the Bond Dissociation Energy (BDE) and is a measure of the strength of the bond.

Calculation of the BDE

The BDE for a molecule A-B is calculated as the difference in the enthalpies of formation of the products and reactants for homolysis

$$BDE = \Delta_f H(A^\bullet) + \Delta_f H(B^\bullet) - \Delta_f H(A - B)$$

Officially, the IUPAC definition of bond dissociation energy refers to the energy change that occurs at 0 K, and the symbol is D_o. However, it is commonly referred to as BDE, the bond dissociation energy, and it is generally used, albeit imprecisely, interchangeably with the bond dissociation *enthalpy*, which generally refers to the enthalpy change at room temperature (298K).

Although there are technically differences between BDEs at 0 K and 298 K, those difference are not large and generally do not affect interpretations of chemical processes.

Bond Breakage/Formation

Bond dissociation energy (or enthalpy) is a state function and consequently does not depend on the path by which it occurs. Therefore, the specific mechanism in how a bond breaks or is formed does not affect the BDE. Bond dissociation energies are useful in assessing the energetics of chemical processes. For chemical reactions, combining bond dissociation energies for bonds formed and bonds broken in a chemical reaction using Hess's Law can be used to estimate reaction enthalpies.

Example 6.8.1: Chlorination of Methane

Consider the chlorination of methane

$$CH_4 + Cl_2 \rightarrow CH_3Cl + HCl$$

the overall reaction thermochemistry can be calculated exactly by combining the BDEs for the bonds broken and bonds formed

$$CH_4 \rightarrow CH_3\bullet + H\bullet \quad BDE(CH_3\text{-}H)$$

$$Cl_2 \rightarrow 2Cl\bullet \quad BDE(Cl_2) \nonumber \]$$

$$H\bullet + Cl\bullet \rightarrow HCl \quad -BDE(HCl)$$

$$CH_3\bullet + Cl\bullet \rightarrow CH_3Cl \quad -BDE(CH_3\text{-}Cl)$$

$$CH_4 + Cl_2 \rightarrow CH_3Cl + HCl$$

$$\Delta H = BDE(R-H) + BDE(Cl_2) - BDE(HCl) - BDE(CH_3-Cl)$$

Because reaction enthalpy is a state function, it does not matter what reactions are combined to make up the overall process using Hess's Law. However, BDEs are convenient to use because they are readily available.

Alternatively, BDEs can be used to assess individual steps of a mechanism. For example, an important step in free radical chlorination of alkanes is the abstraction of hydrogen from the alkane to form a free radical.

$$RH + Cl\bullet \rightarrow R\bullet + HCl$$

The energy change for this step is equal to the difference in the BDEs in RH and HCl

$$\Delta H = BDE(R-H) - BDE(HCl)$$

This relationship shows that the hydrogen abstraction step is more favorable when BDE(R-H) is smaller. The difference in energies accounts for the selectivity in the halogenation of hydrocarbons with different types of C-H bonds.

Table 6.8.1: Representative C-H BDEs in Organic Molecules

R-H	D_o, kJ/mol	D_{298}, kJ/mol	R-H	D_o, kJ/mol	D_{298}, kJ/mol
CH_3-H	432.7±0.1	439.3±0.4	H_2C=CH-H	456.7±2.7	463.2±2.9
CH_3CH_2-H		423.0±1.7	C_6H_5-H	465.8±1.9	472.4±2.5
$(CH_3)_2$CH-H		412.5±1.7	HCCH	551.2±0.1	557.8±0.3
$(CH_3)_3$C-H		403.8±1.7			
			H_2C=CHCH_2-H		371.5±1.7
HC(O)-H		368.6±0.8	$C_6H_5CH_2$-H		375.3±2.5
CH_3C(O)-H		374.0±1.2			

Trends in C-H BDEs

It is important to remember that C-H BDEs refer to the energy it takes to break the bond, and is the difference in energy between the reactants and the products. Therefore, it is not appropriate to interpret BDEs solely in terms of the "stability of the radical products" as is often done.

Analysis of the BDEs shown in the table above shows that there are some systematic trends:

1. **BDEs vary with hybridization:** Bonds with sp^3 hybridized carbons are weakest and bonds with sp hybridized carbons are much stronger. The vinyl and phenyl C-H bonds are similar, reflecting their sp^2 hybridization. The correlation with hybridization can be viewed as a reflection of the C-H bond lengths. Longer bonds formed with sp^3 orbitals are consequently weaker. Shorter bonds formed with orbitals that have more s-character are similarly stronger.
2. **C-H BDEs vary with substitution:** Among sp^3 hybridized systems, methane has the strongest C-H bond. C-H bonds on primary carbons are stronger than those on secondary carbons, which are stronger than those on tertiary carbons.

Interpretation of C-H BDEs for sp^3 Hybridized Carbons

The interpretation of the BDEs in saturated molecules has been subject of recent controversy. As indicated above, the variation in BDEs with substitution has traditionally been interpreted as reflecting the stabilities of the alkyl radicals, with the assessment that more highly substituted radicals are more stable, as with carbocations. Although this is a popular explanation, it fails to account fo the fact the bonds to groups other than H do not show the same types of variation.

R	BDE(R-CH_3)	BDE(R-Cl)	BDE(R-Br)	BDE(R-OH)
CH_3-	377.0±0.4	350.2±0.4	301.7±1.3	385.3±0.4
CH_3CH_2-	372.4±1.7	354.8±2.1	302.9±2.5	393.3±1.7
$(CH_3)_2CH$-	370.7±1.7	356.5±2.1	309.2±2.9	399.6±1.7
$(CH_3)_3C$-	366.1±1.7	355.2±2.9	303.8±2.5	400.8±1.7

Therefore, although C-CH_3 bonds get weaker with more substitution, the effect is not nearly as large as that observed with C-H bonds. The strengths of C-Cl and C-Br bonds are not affected by substitution, despite the fact that the same radicals are formed as when breaking C-H bonds, and the C-OH bonds in alcohols actually *increase* with more substitution.

Gronert has proposed that the variation in BDEs is alternately explained as resulting from destabilization of the reactants due to steric repulsion of the substituents, which is released in the nearly planar radicals.[1] Considering that BDEs reflect the relative energies of reactants and products, either explanation can account for the trend in BDEs.

Another factor that needs to be considered is the electronegativity. The Pauling definition of electronegativity says that the bond dissociation energy between unequal partners is going to be dependent on the difference in electrongativities, according to the expression

$$D_o(A-B) = \frac{D_o(A-A) + D_o(B-B)}{2} + (X_A - X_B)^2$$

where X_A and X_B are the electronegativities and the bond energies are in eV. Therefore, the variation in BDEs can be interpreted as reflecting variation in the electronegativities of the different types of alkyl fragments.

There is likely some merit in all three interpretations. Since Gronert's original publication of his alternate explanation, there have been many desperate attempts to defend the radical stability explanation.

? Exercise 6.8.1

Given that $\Delta H°$ for the reaction

CH_4 (g) + $4F_2$ (g) → CF_4 (g) + 4HF (g)

is −1936 kJ, use the following data to calculate the average bond energy of the C-F bonds in CF_4.

Bond	Average Bond Energy
C – H	413 kJ · mol^{-1}
F – F	155 kJ · mol^{-1}
H – F	567 kJ · mol^{-1}

Answer

Bonds broken:

$$4 \text{ mol C-H bonds} \times \frac{(413\ \text{kJ})}{(1\ \text{mol})} = 1652\ \text{kJ}$$

$$4 \text{ mol F-F bonds} \times \frac{(155\ \text{kJ})}{(1\ \text{mol})} = 620\ \text{kJ}$$

Bonds formed:

$$4 \text{ mol CF bonds} \times \frac{(x\ \text{kJ})}{(1\ \text{mol})} = 4x\ \text{kJ}$$

(where x = the average energy of one mole of C-F bonds in CF_4, expressed in kJ)

$$4 \text{ mol H-F bonds} \times \frac{(567\ \text{kJ})}{(1\ \text{mol})} = 2268\ \text{kJ}$$

$\Delta H° = \Delta H°(\text{bonds broken}) - \Delta H°(\text{bonds formed}) = (1652\ \text{kJ} + 620\ \text{kJ}) - (4x + 2268\ \text{kJ}) = 1652\ \text{kJ} + 620\ \text{kJ} - 4x - 2268\ \text{kJ} = -1936\ \text{kJ}$

Thus,

$$4x = 1936\ \text{kJ} - 2268\ \text{kJ} + 620\ \text{kJ} + 1652\ \text{kJ}$$
$$= 1940\ \text{kJ}$$

and

$$x = \frac{1940\ \text{kJ}}{4\ \text{mol}}$$
$$= 385\ \text{kJ} \cdot \text{mol}^{-1}$$

The average energy of a C-F bond in CF_4 is 385 kJ · mol^{-1}

Exercise 6.8.1

Calculate $\Delta H°$ for the reactions given below. [Access bond energy tables via left-hand blue column Resources > Reference Tables > Reference Tables > Thermodynamic Tables > T3: Bond Energies]

a. $CH_3CH_2OCH_3 + HI \rightarrow CH_3CH_2OH + CH_3I$
b. $CH_3Cl + NH_3 \rightarrow CH_3NH_2 + HCl$

Answer

$CH_3CH_2OCH_3 + HI \rightarrow CH_3CH_2OH + CH_3I$

Reactant bonds broken	D	Product bonds formed	D
$CH_3CH_2O-CH_3$	339 kJ/mol	CH_3CH_2O-H	438 kJ/mol
H—I	298 kJ/mol	CH_3-I	238 kJ/mol
	637 kJ/mol		676 kJ/mol

$$\Delta H° = D_{\text{bonds broken}} + D_{\text{bonds formed}}$$
$$= 637\ \text{kJ/mol} - 676\ \text{kJ/mol}$$
$$= -39\ \text{kJ/mol}$$

$CH_3Cl + NH_3 \rightarrow CH_3NH_2 + HCl$

Reactant bonds broken	D		Product bonds formed	D
CH_3-Cl	356 kJ/mol		CH_3-NH_2	364 kJ/mol
NH_2-H	450 kJ/mol		$H-Cl$	432 kJ/mol
	806 kJ/mol			796 kJ/mol

$$\Delta H^\circ = D_{\text{bonds broken}} + D_{\text{bonds formed}}$$
$$= 806 \text{ kJ/mol} - 796 \text{ kJ/mol}$$
$$= +10 \text{ kJ/mol}$$

References

1. Gronert, S. *J. Org. Chem.* **2006**, *13*, 1209

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6.9: Describing a Reaction - Energy Diagrams and Transition States

Objectives

After completing this section, you should be able to

- sketch the reaction energy diagram for a single-step reaction, given some indication of whether the reaction is fast or slow, exothermic or endothermic.
- interpret the reaction energy diagram for a single-step process (e.g., use the diagram to decide whether the reaction is exothermic or endothermic).
- suggest possible transition-state structures for simple one-step processes.
- assess the likelihood of a reaction occurring at room temperature, given the value of the activation energy $\Delta G^{\ddagger}$.

Key Terms

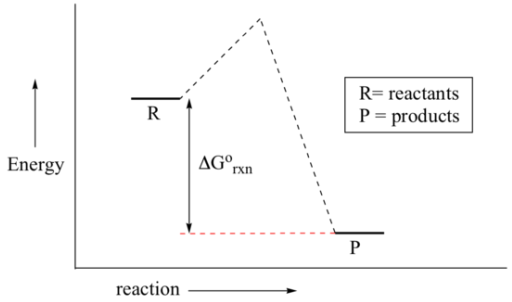
Make certain that you can define, and use in context, the key terms below.

- activation energy, $\Delta G^{\ddagger}$
- reaction energy diagram
- transition state

Study Notes

You may have been taught to use the term “activated complex” rather than “transition state,” as the two are often used interchangeably. Similarly, the activation energy of a reaction is often represented by the symbol E_{act} or E_a.

You may recall from general chemistry that it is often convenient to describe chemical reactions with energy diagrams. In an energy diagram, the vertical axis represents the overall energy of the reactants, while the horizontal axis is the ‘reaction coordinate’, tracing from left to right the progress of the reaction from starting compounds to final products. The energy diagram for a typical one-step reaction might look like this:



Despite its apparent simplicity, this energy diagram conveys some very important ideas about the thermodynamics and kinetics of the reaction. Recall that when we talk about the **thermodynamics** of a reaction, we are concerned with the difference in energy between reactants and products, and whether a reaction is ‘downhill’ (exergonic, energy releasing) or ‘uphill (endergonic, energy absorbing). When we talk about **kinetics**, on the other hand, we are concerned with the *rate* of the reaction, regardless of whether it is uphill or downhill thermodynamically.

First, let’s review what this energy diagram tells us about the thermodynamics of the reaction illustrated by the energy diagram above. The energy level of the products is *lower* than that of the reactants. This tells us that the change in standard Gibbs Free Energy for the reaction (ΔG°_{rnx}) is negative. In other words, the reaction is exergonic, or ‘downhill’. Recall that the ΔG°_{rnx} term encapsulates both ΔH°_{rnx}, the change in enthalpy (heat) and ΔS°_{rnx} , the change in entropy (disorder):

$$\Delta G^{\circ} = \Delta H^{\circ} - T\Delta S^{\circ}$$

where T is the absolute temperature in Kelvin. For chemical processes where the entropy change is small (~0), the enthalpy change is essentially the same as the change in Gibbs Free Energy. Energy diagrams for these processes will often plot the enthalpy (H) instead of Free Energy for simplicity.

The standard Gibbs Free Energy change for a reaction can be related to the reaction's equilibrium constant (\(K_{eq}_) by a simple equation:

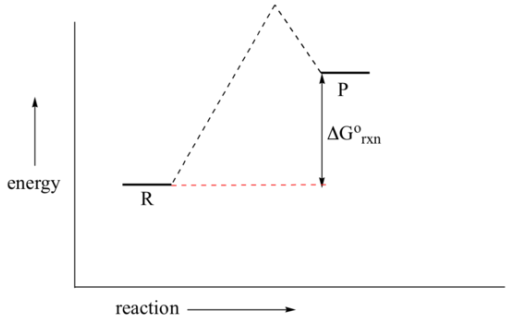
$$\Delta G^\circ = -RT \ln K_{eq}$$

where:

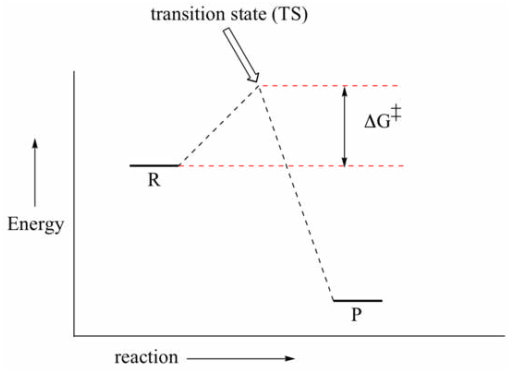
- K_{eq} = [product] / [reactant] at equilibrium
- R = 8.314 J×K^{-1}×mol^{-1} *or* 1.987 cal× K^{-1}×mol^{-1}
- T = temperature in Kelvin (K)

If you do the math, you see that a negative value for ΔG°_{rnx} (an exergonic reaction) corresponds - as it should by intuition - to K_{eq} being greater than 1, an equilibrium constant which favors product formation.

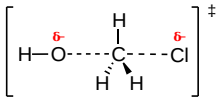
In a hypothetical endergonic (energy-absorbing) reaction the products would have a higher energy than reactants and thus ΔG°_{rnx} would be positive and K_{eq} would be less than 1, favoring reactants.



Now, let's move to kinetics. Look again at the energy diagram for exergonic reaction: although it is 'downhill' overall, it isn't a straight downhill run.



First, an 'energy barrier' must be overcome to get to the product side. The height of this energy barrier, you may recall, is called the '**activation energy'** ($\Delta G^\ddagger$). The activation energy is what determines the kinetics of a reaction: the higher the energy hill, the slower the reaction. At the very top of the energy barrier, the reaction is at its **transition state** (TS), which is the point at which the bonds are in the process of breaking and forming. The transition state is an '**activated complex'**: a transient and dynamic state that, unlike more stable species, does not have any definable lifetime. It may help to imagine a transition state as being analogous to the exact moment that a baseball is struck by a bat. Transition states are drawn with dotted lines representing bonds that are in the process of breaking or forming, and the drawing is often enclosed by brackets. Here is a picture of a likely transition state for a substitution reaction between hydroxide and chloromethane:



Note that this species is absent from the chemical equation (that is it is neither a reactant nor product)

$$CH_3Cl + HO^- \rightarrow CH_3OH + Cl^-$$

This reaction involves a collision between *two* molecules: for this reason, we say that it has **second order kinetics**. The **rate expression** for this type of reaction is:

$$\text{rate} = k[\text{reactant 1}][\text{reactant 2}]$$

... which tells us that the rate of the reaction depends on the **rate constant** k as well as on the concentration of *both* reactants. The rate constant can be determined experimentally by measuring the rate of the reaction with different starting reactant concentrations. The rate constant depends on the activation energy, of course, but also on temperature: a higher temperature means a higher k and a faster reaction, all else being equal. This should make intuitive sense: when there is more heat energy in the system, more of the reactant molecules are able to get over the energy barrier.

Here is one more interesting and useful expression. Consider a simple reaction where the reactants are **A** and **B**, and the product is **AB** (this is referred to as a **condensation reaction**, because two molecules are coming together, or condensing). If we know the rate constant k for the forward reaction and the rate constant $k_{reverse}$ for the reverse reaction (where AB splits apart into **A** and **B**), we can simply take the quotient to find our equilibrium constant K_{eq}:

$$A + B \rightleftharpoons AB$$

with

$$K_{eq} = \frac{[AB]}{[A][B]} = \frac{k_{\text{forward}}}{k_{\text{reverse}}}$$

This too should make some intuitive sense; if the forward rate constant is higher than the reverse rate constant, equilibrium should lie towards products.

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6.10: Describing a Reaction- Intermediates

Objectives

After completing this section, you should be able to

- explain the difference between a transition state and an intermediate.
- draw a reaction energy diagram for a given multistep process.
- interpret the reaction energy diagram of a multistep process (e.g., determine which of the steps is rate-determining).

Key Terms

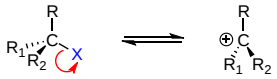
Make certain that you can define, and use in context, the key term below.

- reaction intermediate

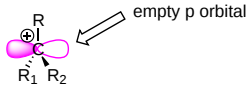
Study Notes

Each step in a multistep reaction has its own activation energy. The overall activation energy is the difference in energy between the reactants and the transition state of the slowest (rate-determining) step. The rate-determining step, that is, the one that controls the overall rate of reaction, is the step with the highest activation energy.

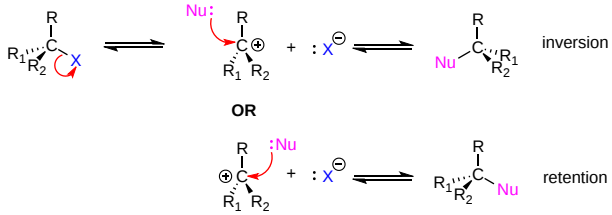
A second model for a nucleophilic substitution reaction is called the '**dissociative**', or '**S_N1**' mechanism: in this picture, the C-X bond breaks *first*, before the nucleophile approaches:



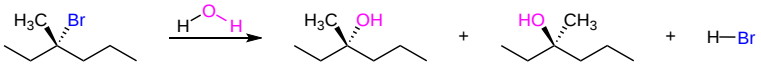
This results in the formation of a carbocation: because the central carbon has only three bonds, it bears a formal charge of +1. Recall that a carbocation should be pictured as sp^2 hybridized, with trigonal planar geometry. Perpendicular to the plane formed by the three sp^2 hybrid orbitals is an empty, unhybridized *p* orbital.



In the second step of this two-step reaction, the nucleophile attacks the empty, 'electron hungry' *p* orbital of the carbocation to form a new bond and return the carbon to tetrahedral geometry.



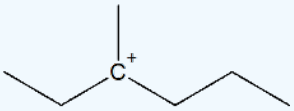
We saw that S_N2 reactions result specifically in inversion of stereochemistry at the electrophilic carbon center. What about the stereochemical outcome of S_N1 reactions? In the model S_N1 reaction shown above, the leaving group dissociates completely from the vicinity of the reaction before the nucleophile begins its attack. Because the leaving group is no longer in the picture, the nucleophile is free to attack from either side of the planar, sp^2-hybridized carbocation electrophile. This means that about half the time the product has the same stereochemical configuration as the starting material (retention of configuration), and about half the time the stereochemistry has been inverted. In other words, *racemization* has occurred at the carbon center. As an example, the tertiary alkyl bromide below would be expected to form a racemic mix of *R* and *S* alcohols after an S_N1 reaction with water as the incoming nucleophile.



Exercise 6.10.1

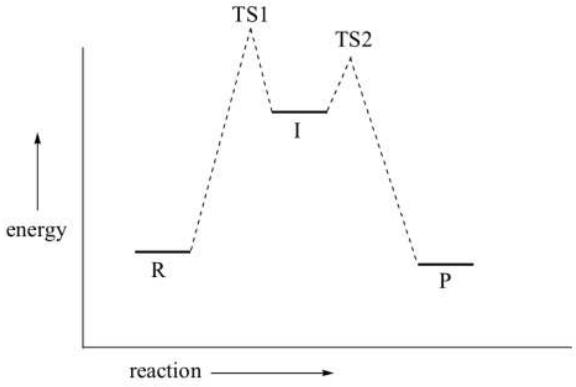
Draw the structure of the intermediate in the two-step nucleophilic substitution reaction above.

Answer



S_N1 intermediate (sp^2)

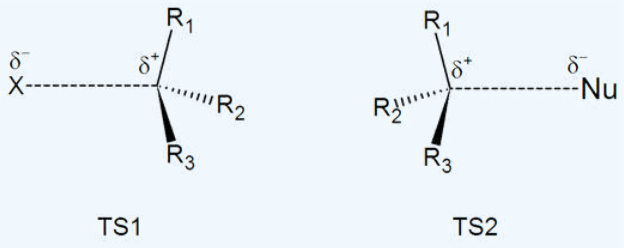
The S_N1 reaction we see an example of a **reaction intermediate**, a very important concept in the study of organic reaction mechanisms that was introduced earlier in the module on organic reactivity Recall that many important organic reactions do not occur in a single step; rather, they are the sum of two or more discreet bond-forming / bond-breaking steps, and involve transient intermediate species that go on to react very quickly. In the S_N1 reaction, the carbocation species is a reaction intermediate. A potential energy diagram for an S_N1 reaction shows that the carbocation **intermediate** can be visualized as a kind of valley in the path of the reaction, higher in energy than both the reactant and product but lower in energy than the two transition states.



Exercise 6.10.2

Draw structures representing TS1 and TS2 in the reaction above. Use the solid/dash wedge convention to show three dimensions.

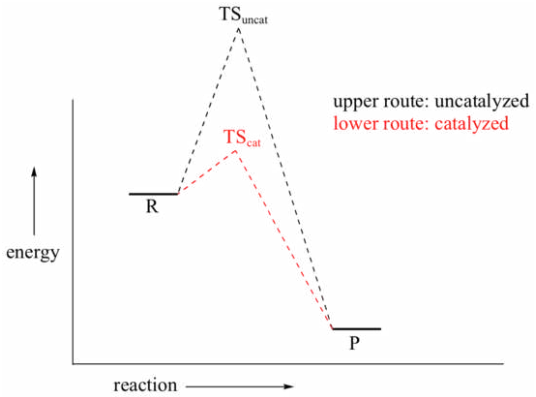
Answer



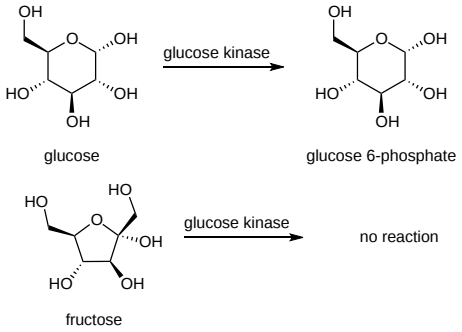
Recall that the first step of the reaction above, in which two charged species are formed from a neutral molecule, is much the slower of the two steps, and is therefore rate-determining. This is illustrated by the energy diagram, where the activation energy for the first step is higher than that for the second step. Also recall that an S_N1 reaction has *first order* kinetics, because the rate determining step involves one molecule splitting apart, not two molecules colliding

We come now to the subject of catalysis. Our hypothetical bowl of sugar (from section 6.2) is still stubbornly refusing to turn into carbon dioxide and water, even though by doing so it would reach a much more stable energy state. There are, in fact, two ways that we could speed up the process so as to avoid waiting several millennia for the reaction to reach completion. We could supply enough energy, in the form of heat from a flame, to push some of the sugar molecules over the high energy hill. Heat would be released from the resulting exothermic reaction, and this energy would push more molecules over their energy hills, and so on - the sugar would literally burn up.

A second way to make the reaction go faster is to employ a **catalyst**. You probably already know that a catalyst is an agent that causes a chemical reaction to go faster by lowering its activation energy.



How might you catalyze the conversion of sugar to carbon dioxide and water? It's not too hard – just eat the sugar, and let your digestive enzymes go to work catalyzing the many biochemical reactions involved in breaking it down. Enzymes are proteins, and are very effective catalysts. 'Very effective' in this context means very specific, and very fast. Most enzymes are very selective with respect to reactant molecules: they have evolved over millions of years to catalyze their specific reactions. An enzyme that attaches a phosphate group to glucose, for example, will not do anything at all to fructose (the details of these reactions are discussed in section 10.2B).



Glucose kinase is able to find and recognize glucose out of all of the other molecules floating around in the 'chemical soup' of a cell. A different enzyme, fructokinase, specifically catalyzes the phosphorylation of fructose.

We have already learned (section 3.9) that enzymes are very specific in terms of the stereochemistry of the reactions that they catalyze . Enzymes are also highly **regiospecific**, acting at only one specific part of a molecule. Notice that in the glucose kinase reaction above only one of the alcohol groups is phosphorylated.

Finally, enzymes are capable of truly amazing rate acceleration. Typical enzymes will speed up a reaction by anywhere from a million to a billion times, and the most efficient enzyme currently known to scientists is believed to accelerate its reaction by a

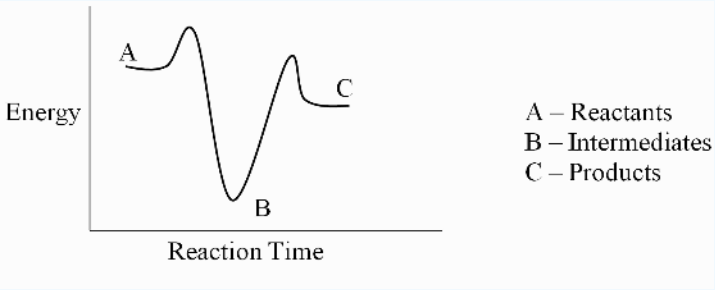
factor of about 10^{17} (see *Chemical and Engineering News*, March 13, 2000, p. 42 for an interesting discussion about this enzyme, orotidine monophosphate decarboxylase).

We will now begin an exploration of some of the basic ideas about how enzymes accomplish these amazing feats of catalysis, and these ideas will be revisited often throughout the rest of the text as we consider various examples of enzyme-catalyzed organic reactions. But in order to begin to understand how enzymes work, we will first need to learn (or review, as the case may be) a little bit about protein structure.

? Exercise 6.10.3

Draw an energy diagram with a exergonic first step and an endergonic second step. Label the diagram.

Answer



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6.11: A Comparison between Biological Reactions and Laboratory Reactions

Objectives

- No objectives have been identified for this section

Key Terms

Make certain that you can define, and use in context, the key term below.

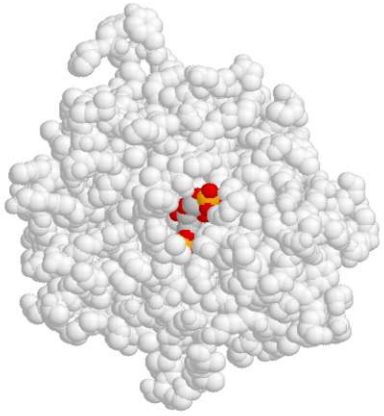
- enzyme

Study Notes

This section is a brief (but perhaps interesting) overview of some of the key differences between reactions performed in the lab and those in living systems. At this point, do not concern yourself with memorizing large biological molecules and reactions.

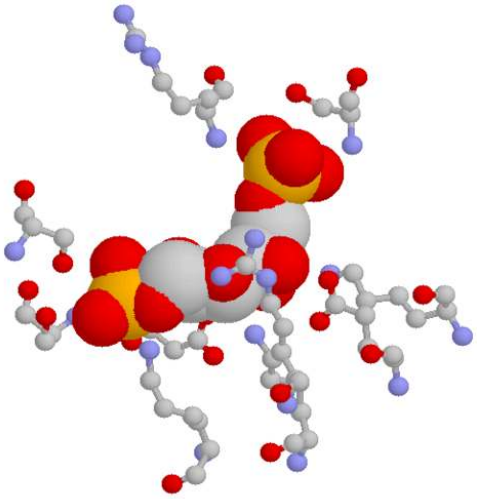
The Active Site

A critical element in the three-dimensional structure of any enzyme is the presence of an '**active site'**, which is a pocket, usually located in the interior of the protein, that serves as a docking point for the enzyme's **substrate**(s) ('substrate' is the term that biochemists use for a reactant molecule in an enzyme-catalyzed reaction). It is inside the active site pocket that enzymatic catalysis occurs. Shown below is an image of the glycolytic enzyme fructose-1,6-bisphosphate aldolase, with its substrate bound inside the active site pocket.

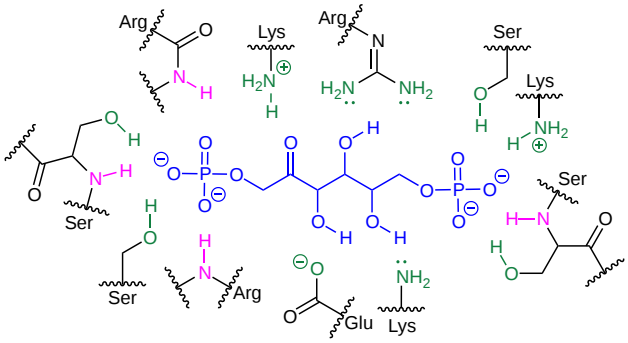


When the substrate binds to the active site, a large number of noncovalent interactions form with the amino acid residues that line the active site. The shape of the active site, and the enzyme-substrate interactions that form as a result of substrate binding, are *specific to the substrate-enzyme pair*: the active site has evolved to 'fit' one particular substrate and to catalyze one particular reaction. Other molecules do not fit in this active site nearly so well as fructose 1,6-bisphosphate.

Here are two close-up views of the same active site pocket, showing some of the specific hydrogen-bonding interactions between the substrate and active site amino acids. The first image below is a three-dimensional rendering directly from the crystal structure data. The substrate is shown in 'space-filling' style, while the active site amino acids are shown in the 'ball and stick' style. Hydrogens are not shown. The color scheme is grey for carbon, red for oxygen, blue for nitrogen, and orange for phosphorus.



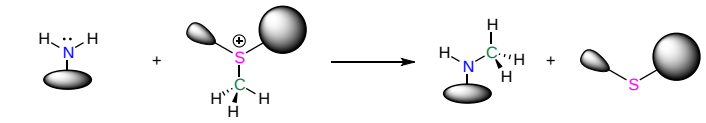
Below is a two-dimensional picture of the substrate (colored blue) surrounded by hydrogen-bonding active site amino acids. Notice that both main chain and side chain groups contribute to hydrogen bonding: in this figure, main chain H-bonding groups are colored purple, and side chain H-bonding groups are colored green.



Looking at the last three images should give you some appreciation for the specific manner in which a substrate fits inside its active site.

Transition State Stabilization

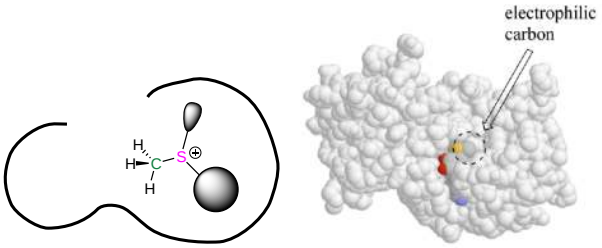
One of the most important ways that an enzyme catalyzes any given reaction is through entropy reduction: by bringing order to a disordered situation (remember that entropy is a component of Gibbs Free Energy, and thus a component of the activation energy). Let's turn again to our previous example (from section 6.1C) of a biochemical nucleophilic substitution reaction, the methylation of adenosine in DNA. The reaction is shown below with non-reactive sections of the molecules depicted by variously shaped 'bubbles' for the sake of simplicity.



In order for this reaction to occur, the two substrates (reactants) must come into contact in precisely the right way. If they are both floating around free in solution, the likelihood of this occurring is very small – the entropy of the system is simply too high. In other words, this reaction takes place *very* slowly without the help of a catalyst.

Here's where the enzyme's active site pocket comes into play. It is lined with various functional groups from the amino acid main and side chains, and has a very specific three-dimensional architecture that has evolved to bind to both of the substrates. If the

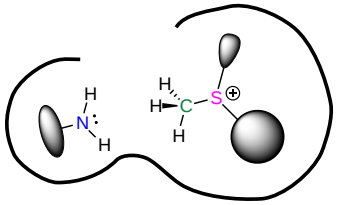
SAM molecule, for example, diffuses into the active site, it can replace its (favorable) interactions with the surrounding water molecules with (even more favorable) new interactions with the functional groups lining the active site.



Depiction of SAM bound in active site of enzyme

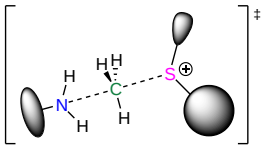
In a sense, SAM is moving from one solvent (water) to another 'solvent' (the active site), where many new energetically favorable interactions are possible. Remember: these new contacts between SAM and the active site groups are *highly specific* to SAM and SAM alone – no other molecule can ‘fit’ so well in this precise active site environment, and thus no other molecule will be likely to give up its contacts to water and bind to the active site.

The second substrate also has a specific spot reserved in the active site. (Because in this case the second substrate is a small segment of a long DNA molecule, the DNA-binding region of the active site is more of a 'groove' than a 'pocket').



So now we have both substrates bound in the active site. But they are not just bound in any random orientation – they are specifically positioned relative to one another so that the nucleophilic nitrogen is held very close to the electrophilic carbon, with a free path of attack. What used to be a very disordered situation – two reactants diffusing freely in solution – is now a very highly ordered situation, with everything set up for the reaction to proceed. This is what is meant by entropy reduction: the entropic component of the energy barrier has been lowered.

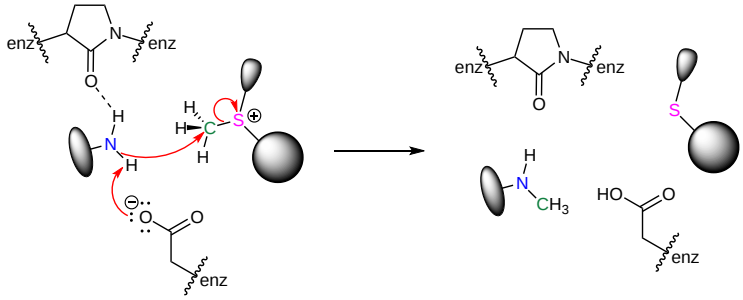
Looking a bit deeper, though, it is not really the noncovalent interaction between enzyme and *substrate* that are responsible for catalysis. Remember: all catalysts, enzymes included, accelerate reactions by lowering the energy of the *transition state*. With this in mind, it should make sense that the primary job of an enzyme is to maximize favorable interactions with the transition state, *not* with the starting substrates. This does not imply that enzyme-substrate interactions are not strong, rather that enzyme-TS interactions are far *stronger*, often by several orders of magnitude. Think about it this way: if an enzyme were to bind to (and stabilize) its substrate(s) more tightly than it bound to (and stabilized) the transition state, it would actually *slow down* the reaction, because it would be *increasing* the energy difference between starting state and transition state. ***The enzyme has evolved to maximize favorable noncovalent interactions to the transition state***: in our example, this is the state in which the nucleophilic nitrogen is already beginning to attack the electrophilic carbon, and the carbon-sulfur bond has already begun to break.



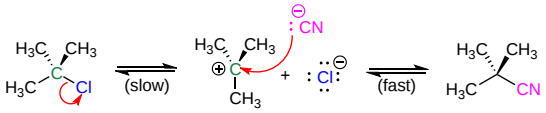
enzyme binds best to
the transition state

In many enzymatic reactions, certain active site amino acid residues contribute to catalysis by *increasing the reactivity of the substrates*. Often, the catalytic role is that of acid and/or base. In our DNA methylation example, the nucleophilic nitrogen is deprotonated by a nearby aspartate side chain as it begins its nucleophilic attack on the methyl group of SAM. We will study nucleophilicity in greater detail in chapter 8, but it should make intuitive sense that deprotonating the amine increases the electron

density of the nitrogen, making it *more nucleophilic*. Notice also in the figure below that the main chain carbonyl of an active site proline forms a hydrogen bond with the amine, which also has the effect of increasing the nitrogen's electron density and thus its nucleophilicity (*Nucleic Acids Res.* **2000**, *28*, 3950).

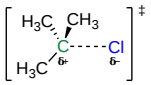


How does our picture of enzyme catalysis apply to multi-step reaction mechanisms? Although the two-step nucleophilic substitution reaction between 2-chloro-2-methylpropane and the cyanide anion is not a biologically relevant process, let's pretend just for the sake of illustration that there is a hypothetical enzyme that catalyzes this reaction.

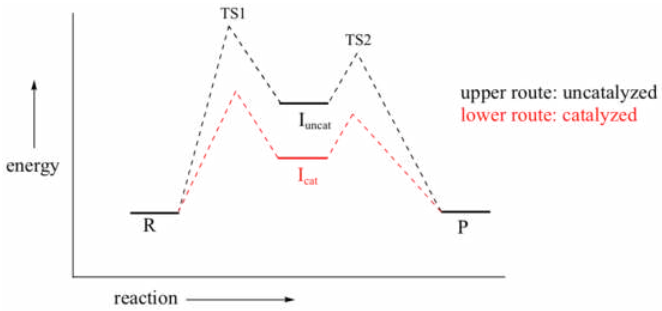


The same basic principles apply here: the enzyme binds best to the transition state. But therein lies the problem: there are two transition states! To which TS does the enzyme maximize its contacts?

Recall that the first step – the loss of the chloride leaving group to form the carbocation intermediate – is the slower, rate-limiting step. It is this step that our hypothetical enzyme needs to accelerate if it wants to accelerate the overall reaction, and it is thus the energy of TS1 that needs to be lowered.



By Hammond's postulate, we also know that the intermediate I is a close approximation of TS1. So the enzyme, by stabilizing the intermediate, will also stabilize TS1 (as well as TS2) and thereby accelerate the reaction.



If you read scientific papers about enzyme mechanisms, you will often see researchers discussing how an enzyme stabilizes a reaction intermediate. By virtue of Hammond's postulate, they are, at the same time, talking about how the enzyme lowers the energy of the transition state.

An additional note: although we have in this section been referring to SAM as a 'substrate' of the DNA methylation reaction, it is also often referred to as a **coenzyme**, or **cofactor**. These terms are used to describe small (relative to protein and DNA) biological organic molecules that bind specifically in the active site of an enzyme and help the enzyme to do its job. In the case of SAM, the job is methyl group donation. In addition to SAM, we will see many other examples of coenzymes in the coming chapters, a number of which - like ATP (adenosine triphosphate), coenzyme A, thiamine, and flavin - you have probably heard of before. The full structures of some common coenzymes are shown in table 6 in the tables section.

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6.12: Oxidation and Reduction in Organic Chemistry

Objectives

After completing this section, you should be able to

- identify organic reactions as being oxidations, reductions, or neither.
- rank given compounds in order of their oxidation level.

Key Terms

Make certain that you can define, and use in context, the terms below.

- oxidation
- reduction
- heteroatom

General Redox Reactions

General chemistry courses describe oxidation and reduction - when a compound or atom is oxidized it loses electrons, and when it is reduced it gains electrons. Also, oxidation and reduction half reactions occur in pairs: if one species is oxidized, another must be reduced at the same time. Thus, the combination of an oxidation and a reduction half reaction is termed a 'redox reaction.' Most of the redox reactions you have seen previously in general chemistry typically involved the flow of electrons from one metal to another, such as the reaction between copper ion in solution and metallic zinc:

$$\mathrm{Cu^{+2}(aq) + Zn(s) \longrightarrow Cu(s) + Zn^{+2}(aq)}$$

$$\mathrm{Cu^{+2}(aq) + 2\,e^- \longrightarrow Cu(s)}$$

Reduction

$$\mathrm{Zn(s) \longrightarrow Zn^{+2}(aq) + 2\,e^-}$$

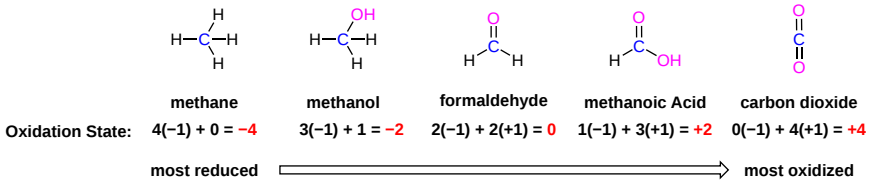
Oxidation

In order, to keep track of electrons in organic molecules an oxidation state formalism is used. Oxidation states do not represent the actual charge on an atom, but it will allow the number of electrons being gained or lost by a particular atom to be determined during a reaction.

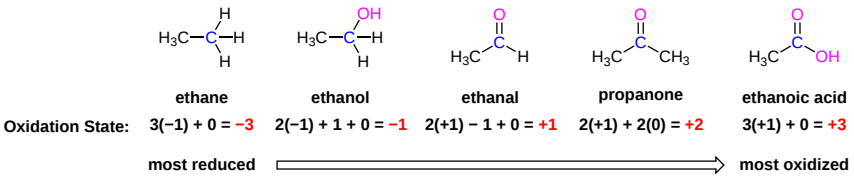
To calculate the oxidation state of a carbon atom the following rules are used:

1. A C-C bond does not affect the oxidation state of a carbon. So a carbon attached to 4 carbons has an oxidation state of zero.
2. Every C-H bond will **decrease** the oxidation state of the carbon by 1.
3. Each C-X bond will **increase** the oxidation state of the carbon by 1. Where X is an electronegative atom, such as nitrogen, oxygen, sulfur, or a halogen.

When looking at the oxidation states of carbon in the common functional groups shown below it can be said that carbon loses electron density as it becomes more oxidized. We'll take a series of single carbon compounds as an example. Methane (CH_4) is at the lowest oxidation level of carbon because is has the maximum possible number of bonds to hydrogen. Carbon dioxide (CO_2) is at the highest oxidation level because it has the maximum number of bonds to an electronegative atom.



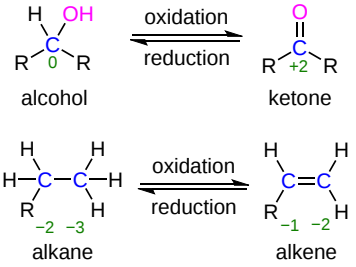
This pattern holds true for the relevant functional groups on organic molecules with two or more carbon atoms:



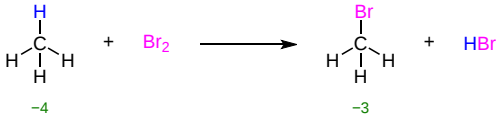
Organic Redox Reactions

It is important to be able to recognize when an organic molecule is being oxidized or reduced, because this information tells you to look for the participation of a corresponding redox agent that is being reduced or oxidized. If a reaction converts a compound to a higher oxidation level that is an oxidation. If it converts a compound to a lower oxidation level it is a reduction. If the oxidation level of the reactant does not change it is not a redox reaction.

Two examples of organic redox reactions are shown below. The conversion of an alcohol to a ketone is considered an oxidation because the oxidation level of the carbon increases from 0 to +2. This implies that the reaction would require an oxidizing agent. Likewise, the conversion of a ketone to an alcohol is a reduction and would require a reducing agent. The conversion of an alkane to alkene is an oxidation because the oxidation state on both carbons is increasing while the reverse reaction would be a reduction.

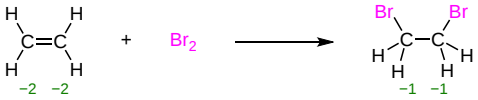


Now reaction previously discussed in this textbook can be considered to determine if they are in fact redox reaction. The free radical bromination of methane to bromomethane would be an oxidation because the oxidation level of carbon is raised from -4 to -3.

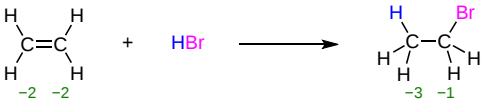


free radical halogenation: **oxidation**

The electrophilic addition of Br_2 to an alkene to provide a 1,2-dibromide is an oxidation because both carbons increase their oxidation level from -2 to -1. However, the electrophilic addion of HBr to an alkene to provide an alkyl halide is not a redox reaction because the overall oxidation state of carbons involved are not changed. One carbon has its oxidation level decreased from -2 to -3 while the other carbon's oxidation level is increased from -2 to -1. Overall, the change in oxidation level cancels out to leave an overall change of oxidcation level in the compound of 0.



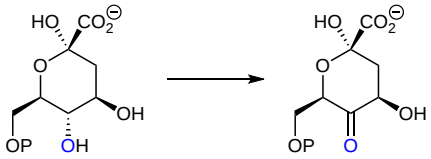
electrophilic addition of Br_2: **oxidation**



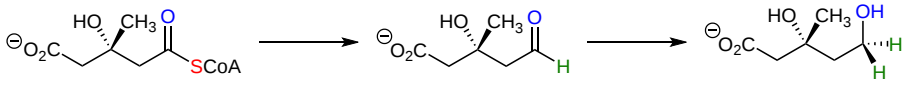
electrophilic addition of HBr: **not redox**

You should learn to recognize when a reaction involves a change in oxidation state in an organic reactant . Looking at the following transformation, for example, you should be able to quickly recognize that it is an oxidation: an alcohol functional group is

converted to a ketone, which is one step up on the oxidation ladder.

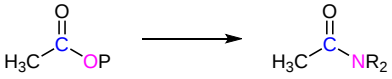


Likewise, this next reaction involves the transformation of a carboxylic acid derivative (a thioester) first to an aldehyde, then to an alcohol: this is a *double* reduction, as the substrate loses two bonds to heteroatoms and gains two bonds to hydrogens.



thioester aldehyde alcohol

An acyl transfer reaction (for example the conversion of an acyl phosphate to an amide) is *not* considered to be a redox reaction - the oxidation state of the organic molecule is does not change as substrate is converted to product, because a bond to one heteroatom (oxygen) has simply been traded for a bond to another heteroatom (nitrogen).



carbon is in same oxidation state: **not redox**

It is important to be able to recognize when an organic molecule is being oxidized or reduced, because this information tells you to look for the participation of a corresponding redox agent that is being reduced or oxidized- remember, oxidation and reduction always occur in tandem! We will soon learn in detail about the most important biochemical and laboratory redox agents.

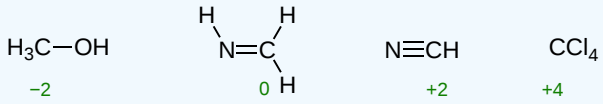
Worked Example 6.12.1

Rank the following compounds in order of increasing oxidation level:



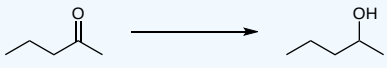
Answer

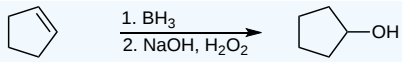
The easiest way to solve this problem is to calculate the oxidation level of the carbon in each compound. Remembering that hydrogens decrease the oxidation level by one, electronegative elements increase the oxidation level by one, and carbons do not change the oxidation level, the oxidation level of each carbon can be calculate. The carbon in CH_3OH has three bonds to hydrogens and one bond to oxygen so it oxidation level is 3(-1) + 1(+1) = -2. The carbon in HCN has one bond to hydrogens and three bonds to nitrogen so it oxidation level is 1(-1) + 3(+1) = +2. The carbon in CH_2NH has two bonds to hydrogens and two bond to nitrogen so it oxidation level is 2(-1) + 2(+1) = 0. The carbon in CCl_4 has zero bonds to hydrogens and four bonds to chlorine so it oxidation level is o(-1) + 4(+1) = +4. The compounds now can be listing in the following order of increasing oxidation level.



? Exercise 6.12.2

In each case state whether the reaction is an oxidation or reduction of the organic compound.

A - 

B - 

Answer

A – Reduction

B – Oxidation

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CHAPTER OVERVIEW

7: Acids and Bases

Chapter Objectives

This chapter provides a review of the more advanced material covered in a standard introductory chemistry course through a discussion of the following topics:

- the use of electronegativity to determine bond polarity, and the application of this knowledge to determine whether a given molecule possesses a dipole moment.
- the drawing and interpretation of organic chemical structures.
- the concept and determination of formal charge.
- resonance and drawing of resonance forms
- the Brønsted-Lowry and Lewis definitions of acids and bases, acidity constants and acid-base reactions.
- acid-base equilibria

7.1: Acids and Bases - The Brønsted-Lowry Definition

7.2: Acid and Base Strength

7.3: Predicting Acid-Base Reactions from pKa Values

7.4: Organic Acids and Organic Bases

7.5: Acids and Bases - The Lewis Definition

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7.1: Acids and Bases - The Brønsted-Lowry Definition

Objectives

After completing this section, you should be able to

1. state the Brønsted-Lowry definition of an acid and a base.
2. identify the Brønsted-Lowry acid and base in a given acid-base reaction.
3. identify the conjugate base of an acid and identify the conjugate acid of a base.

Key Terms

Make certain that you can define, and use in context, the key terms below.

- Brønsted-Lowry acid
- Brønsted-Lowry base
- conjugate acid
- conjugate base

Study Notes

You should already be familiar with the Brønsted-Lowry concept of acidity and the differences between strong and weak acids. You may wish to review this topic before proceeding.

In 1923, chemists Johannes Brønsted and Martin Lowry independently developed definitions of acids and bases based on compounds abilities to either donate or accept protons (H^+ ions). Here, acids are defined as being able to donate protons in the form of hydrogen ions; whereas bases are defined as being able to accept protons. This took the Arrhenius definition one step further as water is no longer required to be present in the solution for acid and base reactions to occur.

Brønsted-Lowry Definition

J.N. Brønsted and T.M. Lowry independently developed the theory of proton donors and proton acceptors in acid-base reactions, coincidentally in the same region and during the same year. The Arrhenius theory where acids and bases are defined by whether the molecule produces hydrogen ion or hydroxide ion when dissolved in water was too limiting, because not all chemical reactions, especially organic reactions, occur in water. The Brønsted-Lowry Theory defines an acid a proton donor, while a base is a proton acceptor. This is illustrated in the following reactions:

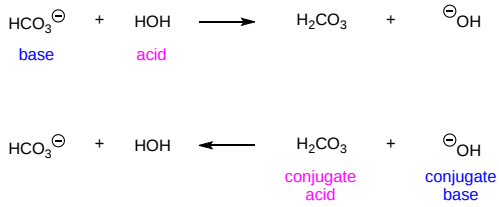
$$HCl + HOH \rightarrow H_3O^+ + Cl^-$$

$$HOH + NH_3 \rightarrow NH_4^+ + OH^-$$

Acid	Base	
Donates hydrogen ions	**Accepts hydrogen ions.**	
HCl	HOH →	$H_3O^+ + Cl^-$
HOH	NH_3 →	$NH_4^+ + {}^-OH$

The determination of a substance as a Brønsted-Lowry acid or base can only be done by examining the reaction, since many chemicals can be either an acid or a base. For example, HOH is a base in the first reaction and an acid in the second reaction.

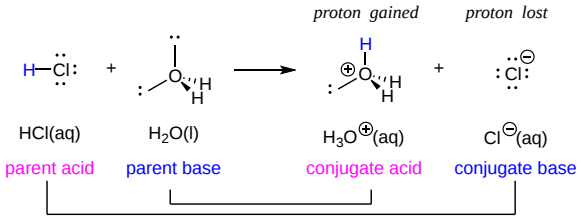
Bronsted-Lowry Acids and Bases



To determine whether a substance is an acid or a base, count the hydrogens on each substance before and after the reaction. If the number of hydrogens has decreased, then that substance is the acid (donates hydrogen ions). If the number of hydrogens has increased, then that substance is the base (accepts hydrogen ions). These definitions are normally applied to the reactants on the left. If the reaction is viewed in reverse a new acid and base can be identified. The substances on the right side of the equation are called the conjugate acid and conjugate base compared to those on the left. Also note that an acid turns into a conjugate base, and the base turns into the conjugate acid after the reaction is over.

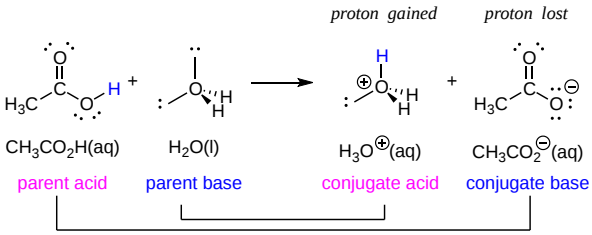
Conjugate Acid–Base Pairs

In aqueous solutions, acids and bases can be defined in terms of the transfer of a proton from an acid to a base. Thus for every acidic species in an aqueous solution, there exists a species derived from the acid by the loss of a proton. These two species that differ by only a proton constitute a conjugate acid–base pair. For example, in the reaction of HCl with water shown below, HCl , the parent acid, donates a proton to a water molecule, the parent base, thereby forming Cl-. Thus HCl and Cl- constitute a conjugate acid–base pair. By convention, we always write a conjugate acid–base pair as the acid followed by its conjugate base. In the reverse reaction, the Cl- ion in solution acts as a base to accept a proton from H_3O^+, forming H_2O and HCl. Thus H_3O^+ and H_2O constitute a second conjugate acid–base pair. In general, any acid–base reaction must contain two conjugate acid–base pairs, which in this case are HCl/Cl- and H_3O^+/H_2O.

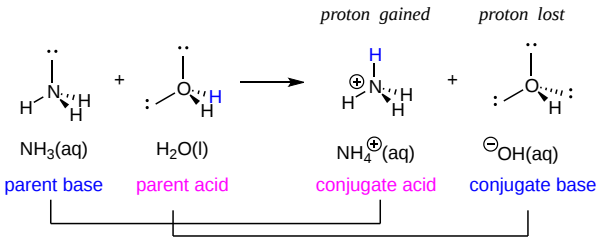


> *All acid–base reactions contain two conjugate acid–base pairs.*

Similarly, in the reaction of acetic acid with water, acetic acid donates a proton to water, which acts as the base. In the reverse reaction, H_3O^+ is the acid that donates a proton to the acetate ion, which acts as the base. Once again, we have two conjugate acid–base pairs: the parent acid and its conjugate base ($CH_3CO_2H/CH_3CO_2^-$) and the parent base and its conjugate acid (H_3O^+/H_2O).



In the reaction of ammonia with water to give ammonium ions and hydroxide ions, ammonia acts as a base by accepting a proton from a water molecule, which in this case means that water is acting as an acid. In the reverse reaction, an ammonium ion acts as an acid by donating a proton to a hydroxide ion, and the hydroxide ion acts as a base. The conjugate acid–base pairs for this reaction are NH_4^+/NH_3 and H_2O/OH^-.



Example 7.1.1

Aniline ($C_6H_5NH_2$) is slightly soluble in water. It has a nitrogen atom that can accept a hydrogen ion from a water molecule just like the nitrogen atom in ammonia does. Write the chemical equation for this reaction and identify the Brønsted-Lowry acid and base.

Solution

$C_6H_5NH_2$ and H_2O are the reactants. When $C_6H_5NH_2$ accepts a proton from H_2O, it gains an extra H and a positive charge and leaves an OH^- ion behind. The reaction is as follows:

$$\mathbf{C_6H_5NH_2\,(aq) + H_2O(\ell) \rightleftharpoons C_6H_5NH_3{}^+\,(aq) + OH^-\,(aq)}$$

Because $C_6H_5NH_2$ accepts a proton, it is the Brønsted-Lowry base. The H_2O molecule, because it donates a proton, is the Brønsted-Lowry acid.

Example 7.1.1

Identify the conjugate acid-base pairs in this equilibrium.

$$\mathbf{(CH_3)_3N + H_2O \rightleftharpoons (CH_3)_3NH^+ + OH^-}$$

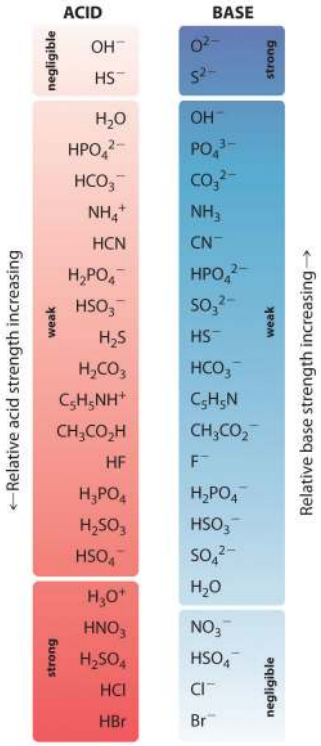
Solution

One pair is H2O and OH^-, where H2O has one more H^+ and is the conjugate acid, while OH^- has one less H^+ and is the conjugate base.

The other pair consists of (CH3)3N and $(CH_3)_3NH^+$, where $(CH_3)_3NH^+$ is the conjugate acid (it has an additional proton) and (CH3)3N is the conjugate base.

Some common conjugate acid–base pairs are shown in Figure 2.7.1. The strongest acids are at the bottom left, and the strongest bases are at the top right. The conjugate base of a strong acid is a very weak base, and, conversely, the conjugate acid of a strong base is a very weak acid.

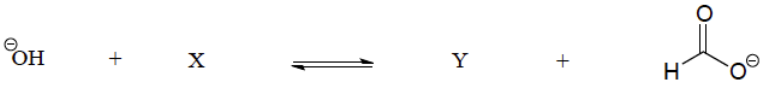
Figure 2.7.1 *The Relative Strengths of Some Common Conjugate Acid–Base Pairs*



Exercises

1. Identify the Brønsted-Lowry acids and bases in the reactions given below.
   a. $CH3CH2O^- + H2O <=> CH3CH2OH + OH^-$
   b. $CH3CH2OH + H2SO4 <=> CH3CH2OH2 + +HSO4-$
2. Show the structures of species X and Y in the following acid-base reactions:

a)



b)

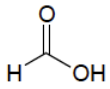


Answer:

1. a. $CH_3CH_2O^- + H_2O \rightleftharpoons CH_3CH_2OH + OH^-$

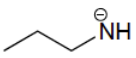
   b. $\underset{\text{base}}{CH_3CH_2OH} + \underset{\text{acid}}{H_2SO_4} \rightleftharpoons \underset{\text{acid}}{CH_3CH_2OH_2^+} + \underset{\text{base}}{HSO_4^-}$

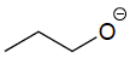
2. a)

   X: 

   Y: H_2O

   b)

   X: 

   Y: 

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Questions

Q2.7.1

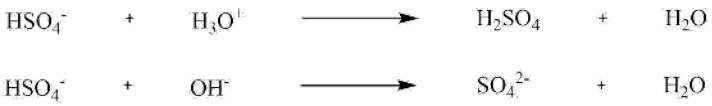
Is the following molecule a Brønsted acid or base?

HSO_4^-

Solutions

S2.7.1

It can be both, consider the following schemes:



7.1: Acids and Bases - The Brønsted-Lowry Definition is shared under a CC BY-SA 4.0 license and was authored, remixed, and/or curated by Steven Farmer, Dietmar Kennepohl, Krista Cunningham, Tim Soderberg, & Tim Soderberg.

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7.2: Acid and Base Strength

Objectives

After completing this section, you should be able to

- write the expression for the K_a of a weak acid.
- convert a given K_a value into a pK_a value, and *vice versa*.
- arrange a series of acids in order of increasing or decreasing strength, given their K_a or pK_a values.
- arrange a series of bases in order of increasing or decreasing strength, given the K_a or pK_a values of their conjugate acids.

Key Terms

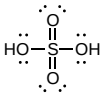
Make certain that you can define, and use in context, the key terms below.

- acidity constant, K_a
- equilibrium constant, K_{eq}

Study Notes

Calculations and expressions involving K_a and pK_a were covered in detail in your first-year general chemistry course. Note that acidity constant is also known as the acid dissociation constant.

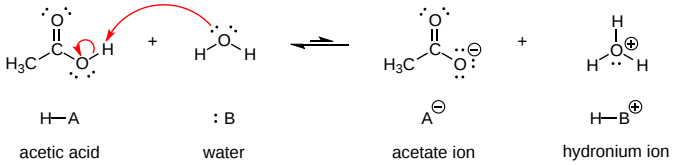
You are no doubt aware that some acids are stronger than others. Sulfuric acid is strong enough to be used as a drain cleaner, as it will rapidly dissolve clogs of hair and other organic material.



Not surprisingly, concentrated sulfuric acid will also cause painful burns if it touches your skin, and permanent damage if it gets in your eyes (there's a good reason for those safety goggles you wear in chemistry lab!). Acetic acid (vinegar), will also burn your skin and eyes, but is not nearly strong enough to make an effective drain cleaner. Water, which we know can act as a proton donor, is obviously not a very strong acid. Even hydroxide ion could *theoretically* act as an acid – it has, after all, a proton to donate – but this is not a reaction that we would normally consider to be relevant in anything but the most extreme conditions.

The relative acidity of different compounds or functional groups – in other words, their relative capacity to donate a proton to a common base under identical conditions – is quantified by a number called the **acid dissociation constant**, abbreviated $\mathbf{K_a}$. The common base chosen for comparison is water.

We will consider acetic acid as our first example. When a small amount of acetic acid is added to water, a proton-transfer event (acid-base reaction) occurs to some extent.



Notice the phrase 'to some extent' – this reaction does *not* run to completion, with all of the acetic acid converted to acetate, its conjugate base. Rather, a *dynamic equilibrium* is reached, with proton transfer going in both directions (thus the two-way arrows) and finite concentrations of all four species in play. The nature of this equilibrium situation, as you recall from General Chemistry, is expressed by an equilibrium constant, K.

The equilibrium constant is actually a ratio of activities (represented by the symbol a), but activities are rarely used in courses other than analytical or physical chemistry. To simplify the discussion for general chemistry and organic chemistry courses, the activities

of all of the solutes are replaced with molarities, and the activity of the solvent (usually water) is defined as having the value of 1.

In our example, we added a small amount of acetic acid to a large amount of water: water is the *solvent* for this reaction. Therefore, in the course of the reaction, the concentration of water changes very little, and the water can be treated as a pure solvent, which is always assigned an activity of 1. The acetic acid, acetate ion and hydronium ion are all *solutes*, and so their activities are approximated with molarities. The acid dissociation constant, or K_a, for acetic acid is therefore defined as:

$$K_{eq} = \frac{a_{CH_3COO^-} \cdot a_{H_3O^+}}{a_{CH_3COOH} \cdot a_{H_2O}} \approx \frac{[CH_3COO^-][H_3O^+]}{[CH_3COOH][1]}$$

Because dividing by 1 does not change the value of the constant, the "1" is usually not written, and K_a is written as:

$$K_{eq} = K_a = \frac{[CH_3COO^-][H_3O^+]}{[CH_3COOH]} = 1.75 \times 10^{-5}$$

In more general terms, the dissociation constant for a given acid is expressed as:

$$K_a = \frac{[A^-][H_3O^+]}{[HA]} \tag{7.2.1}$$

or

$$K_a = \frac{[A][H_3O^+]}{[HA^+]} \tag{7.2.2}$$

Equation 7.2.1 applies to a neutral acid such as like HCl or acetic acid, while Equation 7.2.2 applies to a cationic acid like ammonium (NH_4^+).

The value of $K_a = 1.75 \times 10^{-5}$ for acetic acid is very small - this means that very little dissociation actually takes place, and there is much more acetic acid in solution at equilibrium than there is acetate ion. Acetic acid is a relatively weak acid, at least when compared to sulfuric acid ($K_a = 10^9$) or hydrochloric acid ($K_a = 10^7$), both of which undergo essentially complete dissociation in water.

A number like 1.75×10^{-5} is not very easy either to say or to remember. Chemists often use $\mathbf{pK_a}$ values as a more convenient term to express relative acidity. $\mathbf{pK_a}$ is related to $\mathbf{K_a}$ by the following equation

$$pK_a = -\log K_a$$

Doing the math, we find that the pK_a of acetic acid is 4.8. The use of pK_a values allows us to express the acidity of common compounds and functional groups on a numerical scale of about –10 (very strong acid) to 50 (not acidic at all). Table **7.2.1** at the end of the text lists exact or approximate pK_a values for different types of protons that you are likely to encounter in your study of organic and biological chemistry. Looking at Table **7.2.1**, you see that the pK_a of carboxylic acids are in the 4-5 range, the pK_a of sulfuric acid is –10, and the pK_a of water is 14. Alkenes and alkanes, which are not acidic at all, have pK_a values above 30. *The lower the pK_a value, the stronger the acid.*

Table 7.2.1: *Representative acid constants*

 sulfuric acid pK_a −10	 hydrochloric acid pK_a −7	 hydronium pK_a 0.00	 protonated ketone pK_a ~ −7	 protonated alcohol pK_a ~ −3
 phosphate monoester pK_a ~ 1	 phosphate diester pK_a ~ 1.5	 phosphoric acid pK_a 2.2	 protonated aniline pK_a ~ 4.6	 carboxylic acid pK_a ~ 4-5
 pyridinium pK_a 5.3	 carbonic acid pK_a 6.4	hydrogen cyanide pK_a ~ 9.2	 ammonium pK_a 9.2	 phenol pK_a 9.9
 thiol pK_a ~ 10-11	 water pK_a 14.00	 amide pK_a ~ 17	 alcohol pK_a ~ 16-18	 alpha-proton pK_a ~ 18-20
	terminal alkyne pK_a ~ 25	 terminal alkene pK_a ~ 35	 ammonia pK_a ~ 35	

It is important to realize that pK_a is *not* the same thing as pH: pK_a is an inherent property of a compound or functional group, while pH is the measure of the hydronium ion concentration in a particular aqueous solution:

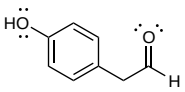
$$pH = -\log[H_3O^+]$$

Any particular acid will always have the same pK_a (assuming that we are talking about an aqueous solution at room temperature) but different aqueous solutions of the acid could have different pH values, depending on how much acid is added to how much water.

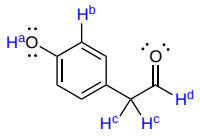
Our table of pK_a values will also allow us to compare the strengths of different bases by comparing the pK_a values of their conjugate acids. The key idea to remember is this: *the stronger the conjugate acid, the weaker the conjugate base*. Sulfuric acid is the strongest acid on our list with a pK_a value of –10, so HSO_4^- is the weakest conjugate base. You can see that hydroxide ion is a stronger base than ammonia (NH_3), because ammonium (NH_4^+, pK_a = 9.2) is a stronger acid than water (pK_a = 14.00).

> *The stronger the conjugate acid, the weaker the conjugate base.*

While Table **7.2.1** provides the pK_a values of only a limited number of compounds, it can be very useful as a starting point for estimating the acidity or basicity of just about any organic molecule. Here is where your familiarity with organic functional groups will come in very handy. What, for example, is the pK_a of cyclohexanol? It is not on the table, but as it is an alcohol it is probably somewhere near that of ethanol (pK_a = 16). Likewise, we can use Table **7.2.1** to predict that para-hydroxyphenyl acetaldehyde, an intermediate compound in the biosynthesis of morphine, has a pK_a in the neighborhood of 10, close to that of our reference compound, phenol.



Notice in this example that we need to evaluate the potential acidity at *four* different locations on the molecule.



pK_a H^a ~ 10

pK_a H^b = not on table (not acidic)

pK_a H^c ~ 19

pK_a H^d = not on table (not acidic)

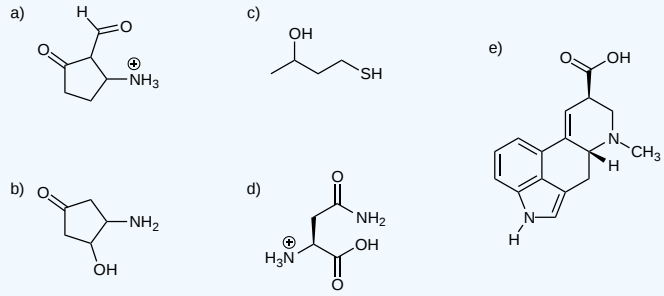
Aldehyde and aromatic protons are not at all acidic (pK_a values are above 40 – not on our table). The two protons on the carbon next to the carbonyl are slightly acidic, with pK_a values around 19-20 according to the table. The most acidic proton is on the phenol group, so if the compound were to be reacted with a single molar equivalent of strong base, this is the proton that would be donated first.

As you continue your study of organic chemistry, it will be a very good idea to commit to memory the approximate pK_a ranges of some important functional groups, including water, alcohols, phenols, ammonium, thiols, phosphates, carboxylic acids and carbons next to carbonyl groups (so-called a-carbons). These are the groups that you are most likely to see acting as acids or bases in biological organic reactions.

A word of caution: when using the pK_a table, be absolutely sure that you are considering the correct conjugate acid/base pair. If you are asked to say something about the basicity of ammonia (NH_3) compared to that of ethoxide ion ($CH_3CH_2O^-$), for example, the relevant pK_a values to consider are 9.2 (the pK_a of ammonium ion) and 16 (the pK_a of ethanol). From these numbers, you know that ethoxide is the stronger base. Do not make the mistake of using the pK_a value of 38: this is the pK_a of ammonia *acting as an acid*, and tells you how basic the NH_2^- ion is (very basic!)

Example 7.2.1: Acidic Groups

Using the pK_a table, estimate pK_a values for the most acidic group on the compounds below, and draw the structure of the conjugate base that results when this group donates a proton. Use the pKa table above and/or from the Reference Tables.



Answer

a. The most acidic group is the protonated amine, pKa ~ 5-9

b. Alpha proton by the C=O group, pKa ~ 18-20

c. Thiol, pKa ~ 10

d. Carboxylic acid, pKa ~ 5

e. Carboxylic acid, pKa ~ 5

Example 7.2.2

Acetic acid (CH_3COOH) is known to have a pK_a of 4.76. Please determine the Ka for acetic acid.

Solution

Solving for K_a algebraically you get the following:

$pK_a = -Log(K_a)$

$-pK_a = Log(K_a)$

$10^{-pK_a} = K_a$

Using a calculator first enter in the value for the pK_a (4.76). The make the number negative (-4.76). Next, use the inverse log function. All calculators are slightly different so this function may appear as: ANTILOG, INV LOG, or 10^X. Often it is the second function of the LOG button.

K_a for acetic acid = $10^{-pK_a} = 1.74 \times 10^{-5}$

Exercises

1. Write down an expression for the acidity constant of acetic acid, CH_3COOH.
2. The pK_a of acetic acid is 4.72; calculate its K_a.
3. The K_a of benzoic acid is 6.5×10^{-5}; determine its pK_a.
4. From your answers to the questions above, determine whether acetic acid or benzoic acid is stronger

Answers

1. $K_a = \frac{[CH_3CO_2^-][H^+]}{[CH_3CO_2H]}$ or $K_a = \frac{[CH_3CO_2^-][H_3O^+]}{[CH_3CO_2H]}$
2. $pK_a = -\log_{10} K_a = 4.74$ Thus, $\log_{10} K_a = -4.72$ and K_a = anti-log$(-4.72) = 1.9 \times 10^{-5}$
3. $pK_a = -\log_{10} K_a = -\log_{10} 6.5 \times 10^{-5} = -(-4.19) = 4.19$
4. Benzoic acid is stronger than acetic acid. [Benzoic acid has a higher K_a and a lower pK_a.]

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7.3: Predicting Acid-Base Reactions from pKa Values

Template:HideTOC

Objective

After completing this section, you should be able to

- use pK_a values to calculate K_{eq}
- use pK_a values to predict the equilibrium direction of an acid-base reaction.

Key Terms

Make certain that you can define, and use in context, the key term below.

- pK_a

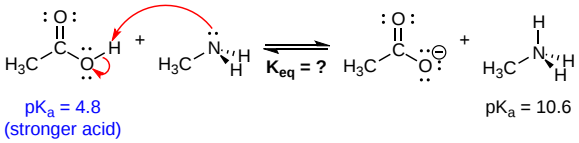
Using pK_a values to predict reaction Equilibria

By definition, the pK_a value tells us the extent to which an acid will react with water as the base, but by extension, we can also calculate the equilibrium constant for a reaction between any acid-base pair. Mathematically, it can be shown that:

$$K_{eq} \text{ (for the acid base reaction in question)} = 10^{\Delta pKa}$$

where ΔpK_a is the pK_a of product acid minus pK_a of reactant acid

Consider a reaction between methylamine and acetic acid:



First, we need to identify the acid species on either side of the equation. On the left side, the acid is of course acetic acid, while on the right side the acid is methyl ammonium. The specific pK_a values for these acids are not on our very generalized pK_a table, but are given in the figure above. Without performing any calculations, you should be able to see that this equilibrium lies far to the right-hand side: acetic acid has a lower pK_a, is a stronger acid, and thus it wants to give up its proton more than methyl ammonium does. Doing the math, we see that

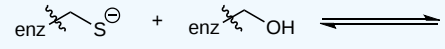
$$K_{eq} = 10^{\Delta pK_a} = 10^{10.6-4.8} = 10^{5.8} = 6.3 \times 10^5$$

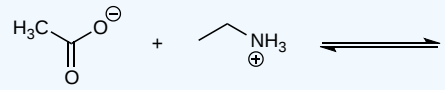
So K_{eq} is a very large number (much greater than 1) and the equilibrium lies far to the right-hand side of the equation, just as we had predicted.

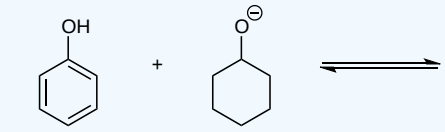
If you had just wanted to approximate an answer without bothering to look for a calculator, you could have noted that the difference in pK_a values is approximately 6, so the equilibrium constant should be somewhere in the order of 10^6, or one million. Using the pK_a table in this way, and making functional group-based pK_a approximations for molecules for which we don't have exact values, we can easily estimate the extent to which a given acid-base reaction will proceed.

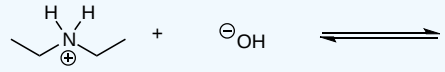
Example 7.3.1

Show the products of the following acid-base reactions, and estimate the value of K_{eq}. Use the pK_a table from Section 2.8 and/or from the Reference Tables.

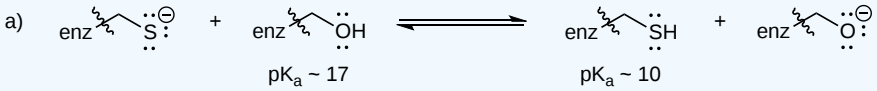
a) 

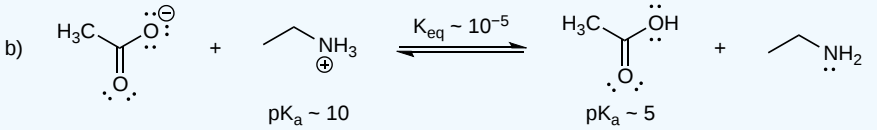
b) 

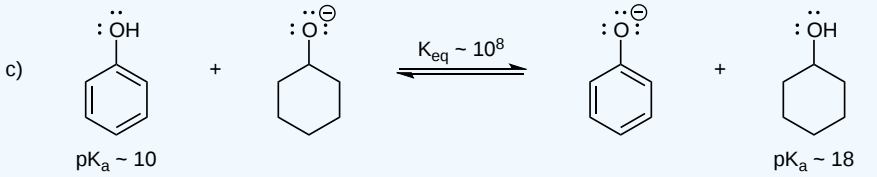
c) 

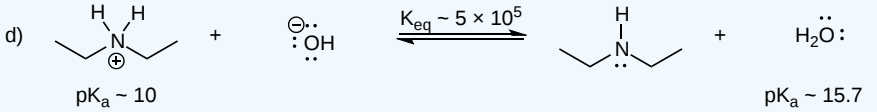
d) 

Answer

a) 

b) 

c) 

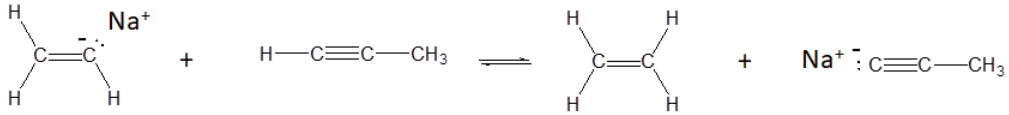
d) 

The pK_a of water is 14.0. Thus the K_{eq} for reaction d) is ~ 10^4.

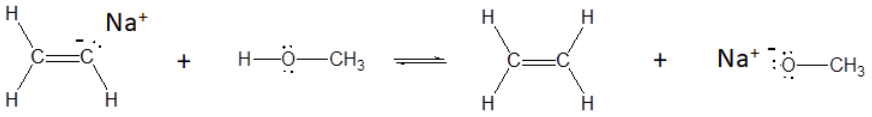
Exercises

? Exercise 7.3.1

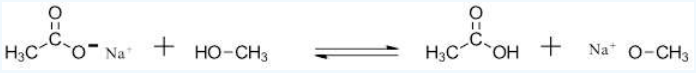
Use the pKa table from Section 2.8 and/or from the Reference Tables to determine if the following reactions would be expected to occur:

a) 

b)



c)



Answer

a) Yes - alkenes have pK_a values of ~35 while alkynes have pK_a values of ~25. This means that alkynes are more acidic and more likely to donate a proton.

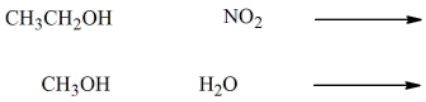
b) Yes - alkenes have pK_a values of ~35 while alcohols have pK_a values of ~16-18. This means that alcohols are more acidic and more likely to donate a proton.

c) No - carboxylic acids have pK_a values of ~4-5 while alcohols have pK_a values of ~16-18. This means that carboxylic acids are more acidic and more likely to donate a proton (so the reverse reaction would be expected to occur).

Questions

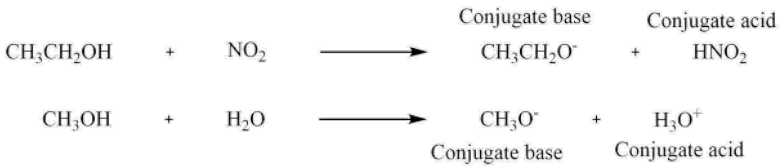
Q2.9.1

In the following reactions give the resulting products and label the conjugate acid and bases.



Solutions

S2.9.1



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7.4: Organic Acids and Organic Bases

Objective

After completing this section, you should be able to

- predict the relative acidity of two organic molecules from their structures.
- predict the relative basicity of two organic molecules from their structures.

This page explains the acidity of simple organic acids and looks at the factors which affect their relative strengths.

Organic acids as weak acids

For the purposes of this topic, we are going to take the definition of an acid as "a substance which donates hydrogen ions (protons) to other things". We are going to get a measure of this by looking at how easily the acids release hydrogen ions to water molecules when they are in solution in water.

An acid in solution sets up this equilibrium:

$$AH_{(aq)} + H_2O_{(l)} \rightleftharpoons A^-_{(aq)} + H_3O^+_{(aq)}$$

A hydronium ion is formed together with the anion (negative ion) from the acid. This equilibrium is sometimes simplified by leaving out the water to emphasize the ionization of the acid.

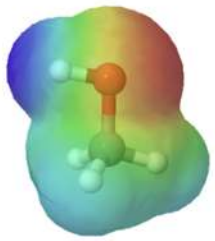
$$AH_{(aq)} \rightleftharpoons A^-_{(aq)} + H^+_{(aq)}$$

If you write it like this, you must include the state symbols - "(aq)". Writing $H^+_{(aq)}$ implies that the hydrogen ion is attached to a water molecule as H_3O^+. Hydrogen ions are always attached to something during chemical reactions.

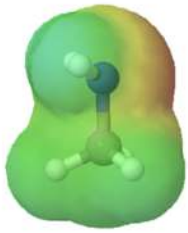
The organic acids are weak in the sense that this ionization is very incomplete. At any one time, most of the acid will be present in the solution as un-ionized molecules. For example, in the case of dilute ethanoic acid, the solution contains about 99% of ethanoic acid molecules - at any instant, only about 1% have actually ionized. The position of equilibrium therefore lies well to the left.

Weak acid polarization

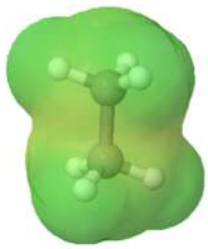
Organic acids can usually can be characterized in electrostatic potential maps by the presence of of a positively polarized hydrogen atom shown in blue. When looking at the maps below, methanol has a slightly polarized O-H bond and is considered very weakly acidic. The O-H bond in methyl amine is less polarized, as shown by the lighter blue color around the hydrogen, making it less acidic than methanol. However, the C-H bond in ethane lack virtually any polarity, as shown by the lack of a blue color, making it non-acidic. The following discussion will explain the difference in acidity of these and other organic molecules molecules.



methanol



methylamine



ethane

Comparing the strengths of weak acids

Acid strength is strongly correlated to stability of the conjugate base that will form by removing a proton. In order to analyze how acidic a molecule is likely to be, then you need to estimate the stability of its conjugate base.

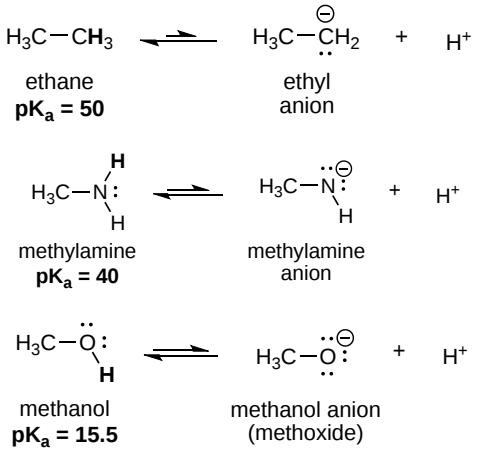
Stabilization of the Conjugate Base - Four Main Considerations:

1. Size and electronegativity of the atom holding the charge
2. Can the charge be delocalized by resonance?
3. Are there any inductive effects?
4. Hybridization of orbital holding the charge

These considerations are listed in order of importance and are explained individually, but must be looked at collectively.

1. Size and Electronegativity Effects in Acidity

When comparing elements, it depends on the positional relationship of the elements on the periodic table. When moving a period (aka across a row) of the main group elements, the valence electrons all occupy orbitals in the same shell. These electrons have comparable energy, so this factor does not help us discern differences relative stability. Differences in electronegativity are now the dominant factor. This trend is shown when comparing the pKa values of ethane, methyl amine, and methanol which reflects the relative electronegativities of the C < N < O. The key to understanding this trend is to consider the hypothetical conjugate base in each case*: the more stable the conjugate base, the stronger the acid*. In general, the more electronegative an atom, the better it is able to bear a negative charge. In the ethyl anion, the negative charge is borne by carbon, in the methylamine anion by nitrogen, and in the methoxide anion by an oxygen. Remember the periodic trend in electronegativity: it also increases as we move from left to right along a row, meaning that oxygen is the most electronegative of three elements being considered. This makes the negative charge on the methoxide anion the most stable of the three conjugate bases and methanol the strongest of the three acids. Likewise, carbon is the least electronegative making ethane the weakest of the three acids.



Within a Group (aka down a column) As we move down the periodic table, the electrons are occupying higher energy subshells creating a larger atomic size and volume. As the volume of an element increases, any negative charge present tends to become more spread out which decreases electron density and increases stability. The figure below shows spheres representing the atoms of the *s* and *p* blocks from the periodic table to scale, showing the two trends for the atomic radius.

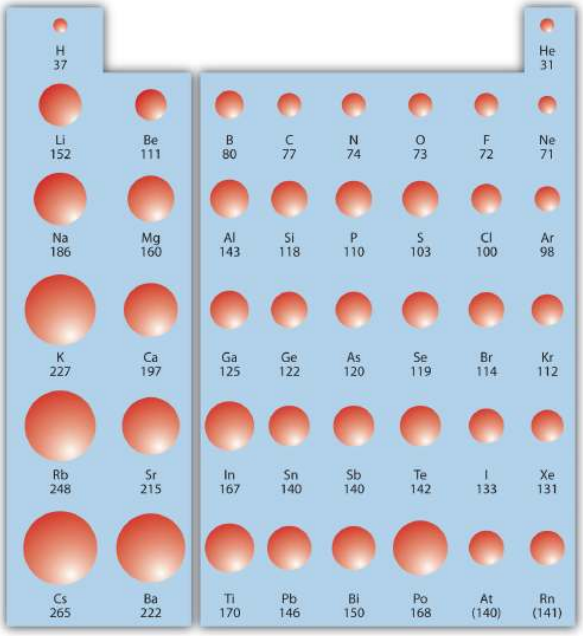
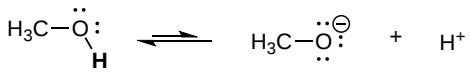
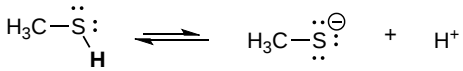


Figure **7.4.1**: Atomic Radii Trends on the Periodic Table. Although there are some reversals in the trend (e.g., see Po in the bottom row), atoms generally get smaller as you go across the periodic table and larger as you go down any one column. Numbers are the radii in pm.

This relationship of atomic size and electron density is illustrated when we compare the relative acidities of methanol, CH_3OH, with methanethiol, CH_3SH. The lower pKa value of 10.4 for methanethiol indicates that it is a stronger acid than methanol with a pKa value of 15.5. It is important to remember that neither compound is considered an acid. These relationships become useful when trying to deprotonate compounds to increase their chemical reactivity in non-aqueous reaction conditions.

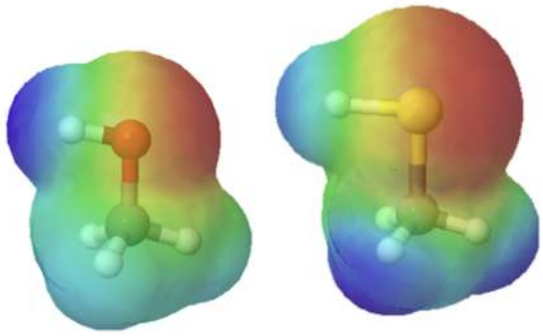


methanol
pK_a = 15.5

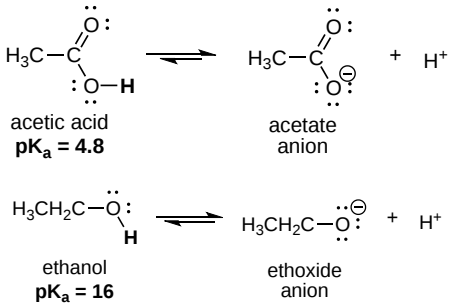


methanethiol
pK_a = 10.4

The difference in size can easily be seen when looking at the electrostatic potential maps for methanol (Left) and methanethiol (Right). The sulfur atom methanethiol is larger than the oxygen atom in methanol. The larger size of sulfur will be better able to delocalize and stabilize the negative charge in its conjugate base metanethiolate.



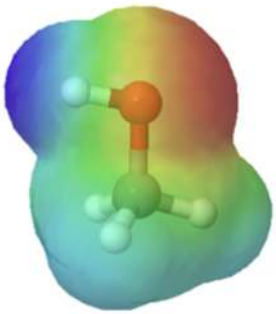
This section will focus on how the resonance structures of different organic groups contributes to their relative acidity even though the same element acts as the proton donor. When evaluating conjugate bases for the presence of resonance contributors, remember to look for movable electrons (lone pairs and pi bonding electrons). Delocalizing electrons over two or more atoms spreads out the electron density, increasing the stability of the conjugate base, and increasing the acidity of the corresponding acid. A classic example compares the relative acidity of ethanol and acetic acid, but the conclusions we reach will be equally valid for all alcohol and carboxylic acid groups. Despite the fact that they are both oxygen acids, the pK_a values of ethanol and acetic acid are very different.

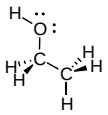


In both species, the negative charge on the conjugate base is held by an oxygen, so periodic trends cannot be invoked. For acetic acid, however, there is a key difference: a resonance contributor can be drawn in which the negative charge is drawn on the second oxygen of the group. The two resonance forms for the conjugate base are equal in energy, according to our 'rules of resonance' (Section 2.5). What this means is that the negative charge on the acetate ion is not located on one oxygen or the other: rather it is shared between the two. Chemists use the term 'delocalization of charge' to describe this situation. In the ethoxide ion, by contrast, the negative charge is 'locked' on the single oxygen. This stabilization leads to a markedly increased acidity.

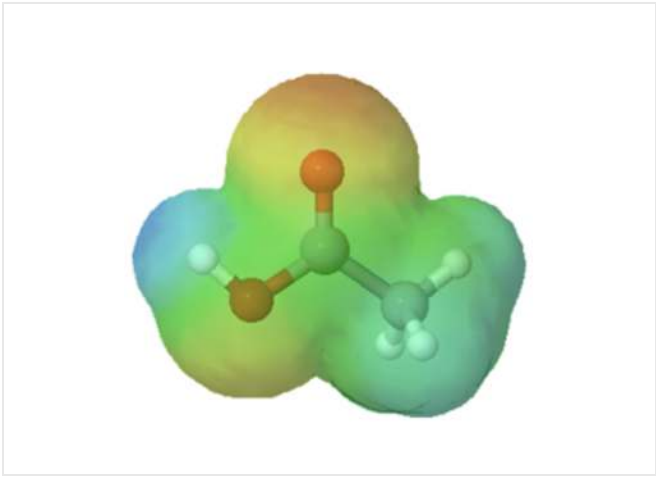
The delocalization of charge by resonance has a very powerful effect on the reactivity of organic molecules, enough to account for the difference of nearly 12 pK_a units between ethanol and acetic acid (and remember, pK_a is a log expression, so we are talking about a difference of over 10^{12} between the acidity constants for the two molecules). The acetate ion is much more stable than the ethoxide ion, due to the effects of resonance delocalization.

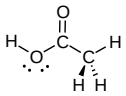
The effects of conjugation can be seen when comparing the electrostatic potential maps of ethanol and acetic acid. Conjugation creates a greater polarization in the O-H bond in acetic acid as shown by its darker blue color.





ethanol

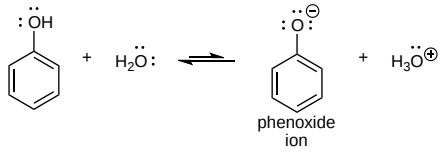




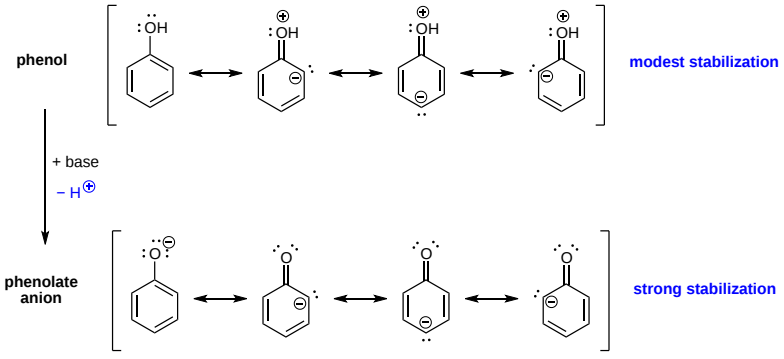
acetic acid

Why is Phenol Acidic?

Compounds like alcohols and phenol which contain an -OH group attached to a hydrocarbon are very weak acids. Alcohols are so weakly acidic that, for normal lab purposes, their acidity can be virtually ignored. However, phenol is sufficiently acidic for it to have recognizably acidic properties - even if it is still a very weak acid. A hydrogen ion can break away from the -OH group and transfer to a base. For example, in aqueous solution:

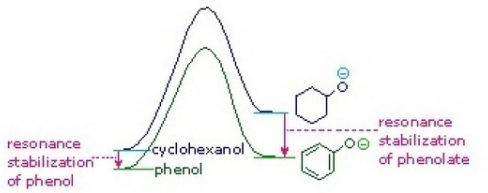


Since phenol is a very weak acid, the position of equilibrium lies well to the left. However, phenol can lose a hydrogen ion because the phenoxide ion (or phenolate ion - the two terms can be used interchangeably) formed is stabilized due to resonance. The negative charge on the oxygen atom is delocalized around the ring since one of the lone pairs on the oxygen atom can be in a p orbital and overlap with the pi electrons on the benzene ring.



This overlap leads to a delocalization which extends from the ring out over the oxygen atom. As a result, the negative charge is no longer entirely localized on the oxygen, but is spread out around the whole ion. Spreading the charge around makes the ion more stable than it would be if all the charge remained on the oxygen. However, oxygen is the most electronegative element in the ion and the delocalized electrons will be drawn towards it. That means that there will still be a lot of charge around the oxygen which will tend to attract the hydrogen ion back again. That is why phenol is only a very weak acid.

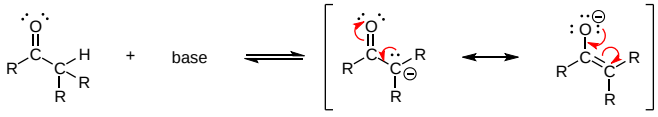
This explains why phenol is a much stronger acid than cyclohexanol. As can be seen in the following energy diagram, resonance stabilization is increased for the conjugate base of phenol vs. cyclohexanol after removal of a proton.



The resonance stabilization in these two cases is very different. An important principle of resonance is that charge separation diminishes the importance of contributors to the resonance hybrid. The contributing structures to the phenol hybrid all suffer charge separation, resulting in very modest stabilization of this compound. On the other hand, the phenolate anion is already charged, and the canonical contributors act to disperse the charge, resulting in a substantial stabilization of this species. The conjugate bases of simple alcohols are not stabilized by charge delocalization, so the acidity of these compounds is similar to that of water. An energy diagram showing the effect of resonance on cyclohexanol and phenol acidities is shown on the right. Since the resonance stabilization of the phenolate conjugate base is much greater than the stabilization of phenol itself, the acidity of phenol relative to cyclohexanol is increased. Supporting evidence that the phenolate negative charge is delocalized on the ortho and para carbons of the benzene ring comes from the influence of electron-withdrawing substituents at those sites.

Acidity of hydrogen α (alpha) to carbonyl

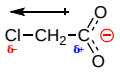
Alkyl hydrogen atoms bonded to a carbon atom in a α (alpha) position (directly adjacent) relative to a C=O group display unusual acidity. While the pKa values for alkyl C-H bonds in is typically on the order of 40-50, pKa values for these alpha hydrogens is more on the order of 19-20. This is almost exclusively due to the resonance stabilization of the product carbanion, called an enolate, as illustrated in the diagram below. The effect of the the stabilizing C=O is seen when comparing the pKa for the α hydrogens of aldehydes (~16-18), ketones (~19-21), and esters (~23-25).



enolate ion

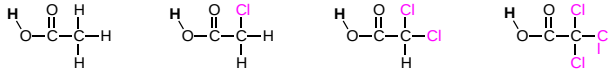
3. Inductive Effects

The inductive effect is an experimentally observed effect of the transmission of charge through a chain of atoms in a molecule, resulting in a permanent dipole in a bond. For example, in a carboxylic acid group the presence of chlorine on adjacent carbons increases the acidity of the carboxylic acid group. A chlorine atom is more electronegative than hydrogen, and thus is able to 'induce', or 'pull' electron density towards itself, away from the carboxylate group. This further spreads out the electron density of the conjugate base, which has a stabilizing effect. In this context, the chlorine substituent is called an **electron-withdrawing group**. Notice that the pK_a-lowering effect of each chlorine atom, while significant, is not as dramatic as the delocalizing resonance effect illustrated by the difference in pK_a values between an alcohol and a carboxylic acid. In general, *resonance effects are more powerful than inductive effects*.



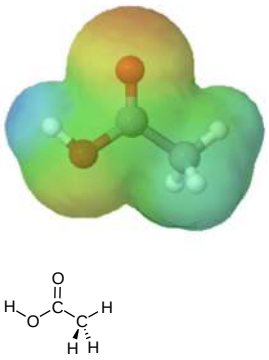
negative charge is delocalized by being pulled out onto chlorine atom

Compare the pK_a values of acetic acid and its mono-, di-, and tri-chlorinated derivatives:

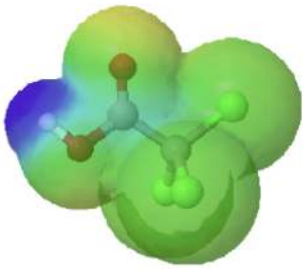


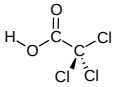
pK_a = 4.8 **pK_a = 2.8** **pK_a = 1.3** **pK_a = 0.64**

The inductive effects of chlorine can be clearly seen when looking at the electrostatic potential maps of acetic acid (Left) and trichloroacetic acid (Right). The O-H bond in trichloroacetic acid is highly polarized as shown by the dark blue color. This illustrates that tricholoracetic acid is a much stronger acid than acetic acid.



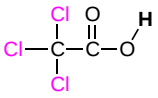
acetic acid



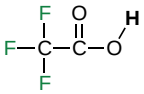


trichloroacetic acid

Because the inductive effect depends on electronegativity, fluorine substituents have a more pronounced pK_a-lowering effect than chlorine substituents.

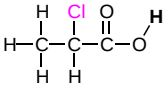


trichloroacetic acid
pK_a = 0.64

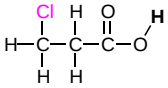


trifluoroacetic acid
pK_a = −0.25

In addition, the inductive takes place through covalent bonds, and its influence decreases markedly with distance – thus a chlorine two carbons away from a carboxylic acid group has a decreased effect compared to a chlorine just one carbon away. 2-chloropropanoic acid has a pK_a of 2.8 while for 3-chloropropanoic acid, the pK_a is 4.0.

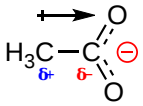


2-chloropropanoic acid
pK_a = 2.8
stronger acid



3-chloropropanoic acid
pK_a = 4.0

Alkyl groups (hydrocarbons) are weak inductive electron donators. In this case the inductive effect pushes electron density onto the conjugate base, causing the electron density to become more concentrated and producing a destabilizing effect.



more negative charge pushed towards already negative end

The inductive effects of alkyl groups causes a significant variation in the acidities of different carboxylic acids. Notice that the inductive effect drops off after the alkyl chain is about three carbons long.

	pK_a
HCOOH (Methanoic Acid or Formic Acid)	3.75
CH_3COOH (Ethanoic Acid or Acetic Acid)	4.76
CH_3CH_2COOH (Propanoic Acid)	4.87
$CH_3CH_2CH_2COOH$ (Butanoic Acid)	4.82

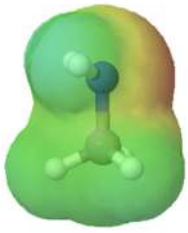
4. Orbital Hybridization

The hybridization of an orbital affects its electronegativity. Within a shell, the s orbitals occupy the region closer to the nucleus than the p orbitals. Therefore, the spherical s orbitals are more electronegative than the lobed p orbitals. The relative electronegativity of hybridized orbitals is $sp > sp^2 > sp^3$ since the percentage of s-character is decreasing as more p-orbitals are added to the hybrids. This trend indicates the sp hybridized orbitals are more stable with a negative charge than sp^3 hybridized orbitals. The table below shows how orbital hybridization influences relative acidity.

compound	conjugate base	hybridization	*s* character	pK_a	
		sp^3	25%	50	weakest acid
		sp^2	33%	44	↓
				36	↓
		sp	50%	25	↓
				16	strongest acid

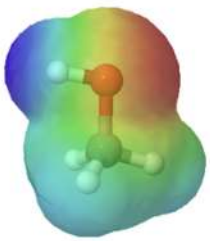
Comparing the Strengths of Weak Bases

Technically, organic bases are characterized by the presence of an atom with lone pair electrons. These lone pairs contain a high electron density, which is shown red in the electrostatic potential maps, and can bond to H^+. Below are the maps of methanol, methyl amine, and acetone. All three compounds can be protonated with a sufficiently strong acid. Note, that all three of these compounds also have the ability to donate a proton when reacted with a strong enough base. Whether these compounds act as a acid or base depends on the conditions.



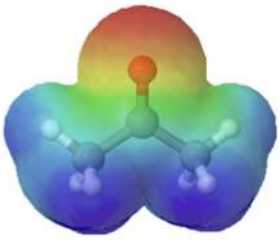


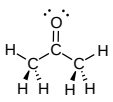
methylamine





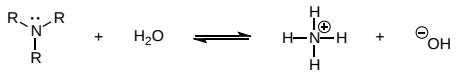
methanol



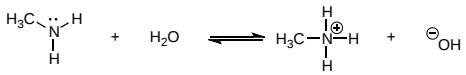


acetone

It is common to compare basicity's quantitatively by using the pK_a's of their conjugate acids rather than their pK_b's. Since pK_a + pK_b = 14, **the higher the pK_a the stronger the base**, in contrast to the usual inverse relationship of pK_a with acidity. Recall that ammonia (NH_3) acts as a base because the nitrogen atom has a lone pair of electrons that can accept a proton. The conjugate acid of most simple alkyl amines have pK_a's in the range 9.5 to 11.0, and their water solutions are basic (have a pH of 11 to 12, depending on concentration). This can be illustrated by the reaction below where an amine removes a proton from water to form substituted ammonium (e.g. NH_4^+) ions and hydroxide (OH^-) ions:



Amines are one of the only neutral functional groups which are considered basic. This is a direct consequence of the presence of the unshared electron pair on the nitrogen. The unshared electron pair is less tightly held by the nitrogen of an amine than the corresponding oxygen of an alcohol, which makes it more available to act as a base. As a specific example, methylamine reacts with water to form the methylammonium ion and the OH^- ion.



Example: Ammonia

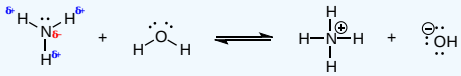
All of the have similarities to ammonia and so we'll start by looking at the reason for its basic properties. For the purposes of this topic, we are going to take the definition of a base as "a substance which combines with hydrogen ions (protons)". We are going to get a measure of this by looking at how easily the bases take hydrogen ions from water molecules when they are in solution in water.

Ammonia in solution sets up this equilibrium:

$$NH_3 + H_2O \rightleftharpoons NH_4^+ + OH^- \tag{2.10.1}$$

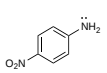
An ammonium ion is formed together with hydroxide ions. Because the ammonia is only a weak base, it doesn't hang on to the extra hydrogen ion very effectively and so the reaction is reversible. At any one time, about 99% of the ammonia is present as unreacted molecules. The position of equilibrium lies well to the left.

The ammonia reacts as a base because of the active lone pair on the nitrogen. Nitrogen is more electronegative than hydrogen and so attracts the bonding electrons in the ammonia molecule towards itself. That means that in addition to the lone pair, there is a build-up of negative charge around the nitrogen atom. That combination of extra negativity and active lone pair attracts the new hydrogen from the water.



When looking at the table below, it is clear that the basicity of nitrogen containing compounds is greatly influenced by their structures. The variance in the basicity of these compounds can mostly be explained by the effects of electron delocalization discussed above.

Table **7.4.1**: pKa of conjugate acids of a series of amines.

Compound										
pK_a	11.0	10.7	10.7	9.3	5.2	4.6	1.0	0.0	-1.0	-10.0

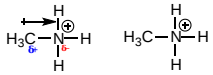
Inductive Effects in Nitrogen Basicity

Alkylamines are more basic than ammonia since alkyl groups donate electrons to the more electronegative nitrogen. This inductive effect makes the electron density on the alkylamine nitrogen greater than the nitrogen of ammonium. That means that there will be a small amount of extra negative charge built up on the nitrogen atom. That extra negativity around the nitrogen makes the lone pair even more attractive towards hydrogen ions. Correspondingly, primary, secondary, and tertiary alkyl amines are more basic than ammonia.



methyl group pushes electron density toward the nitrogen, making it more basic

Making the nitrogen more negative helps the lone pair to pick up a hydrogen ion. What about the effect on the positive methylammonium ion formed? Is this more stable than a simple ammonium ion? Compare the methylammonium ion with an ammonium ion:



CH_3 group pushes electron density toward nitrogen

In the methylammonium ion, the positive charge is spread around the ion by the "electron-pushing" effect of the methyl group. The more you can spread charge around, the more stable an ion becomes. In the ammonium ion there is not any way of spreading the charge.

To summarize:

- The nitrogen is more negative in methylamine than in ammonia, and so it picks up a hydrogen ion more readily.
- The ion formed from methylamine is more stable than the one formed from ammonia, and so is less likely to shed the hydrogen ion again.

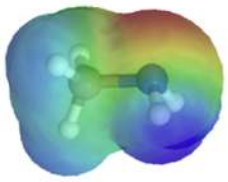
Taken together, these mean that methylamine is a stronger base than ammonia.

Compound	pK_a
NH_3	9.3
CH_3NH_2	10.66
$(CH_3)_2NH$	10.74
$(CH_3)_3N$	9.81

Resonance Effects in Nitrogen Basicity

The resonance effect also explains why a nitrogen atom is basic when it is in an amine, but *not* significantly basic when it is part of an amide group. While the lone pair of electrons in an amine nitrogen is localized in one place, the lone pair on an amide nitrogen is delocalized by resonance. The lone pair is stabilized by resonance delocalization. Here's another way to think about it: the lone pair on an amide nitrogen is not available for bonding with a proton – these two electrons are too stable being part of the delocalized pi-bonding system. The electrostatic potential map show the effect of resonance on the basicity of an amide. The map

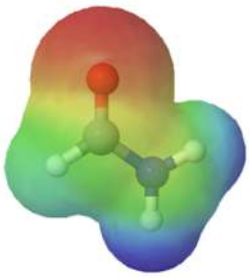
shows that the electron density, shown in red, is almost completely shifted towards the oxygen. This greatly decreases the basicity of the lone pair electrons on the nitrogen in an amide.





amine

pK_a of conjugate acid ~ 11





amide

pK_a of conjugate acid ~ −1

Aniline, the amine analog of phenol, is substantially less basic than an amine (as evidenced by the pK_a of the conjugate acids).



cyclohexylamine

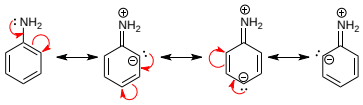
pK_a of conjugate acid ~ 10



aniline

pK_a of conjugate acid ~ 5

We can use the same reasoning that we used when comparing the acidity of a phenol to that of an alcohol. In aniline, the lone pair on the nitrogen atom is stabilized by resonance with the aromatic pi system, making it less available for bonding and thus less basic.



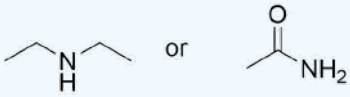
lone pair is stabilized through resonance

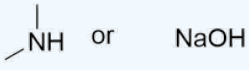
In these cases, you seem to be breaking the same oxygen-hydrogen bond each time, and so you might expect the strengths to be similar. The most important factor in determining the relative acid strengths of these molecules is the nature of the ions formed. You always get a hydronium ion - so that's constant - but the nature of the anion (the negative ion) varies markedly from case to case.

Exercises

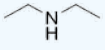
? Exercise 7.4.1

Select the more basic from each of the following pairs of compounds.

(a) 

(b) 

Answer

a)  The lone pair of electrons on the amide nitrogen are less available to react with a proton.

(b) NaOH -- The hydroxide has a negative charge with three lone pairs of electrons that can react with a proton.

Exercise 7.4.2

The 4-methylbenzylammonium ion has a pK_a of 9.51, and the butylammonium ion has a pK_a of 10.59. Which is more basic? What's the pK_b for each compound?

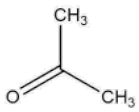
Answer

The butylammonium is more basic. Remember that $pK_a+pK_b = 14$. The pK_b for butylammonium is 3.41, the pK_b for 4-methylbenzylammonium is 4.49.

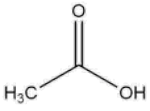
Questions

Q2.10.1

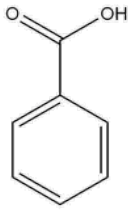
Determine which of the one of the molecules is an acid or a base.



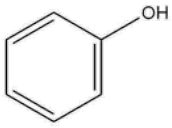
1



2



3



4

Solutions

S2.10.1

1 = Base

2 = Acid

3 = Acid

4 = Acid

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7.5: Acids and Bases - The Lewis Definition

Objectives

After completing this section, you should be able to

1. state the Lewis definition of an acid and a base.
2. identify a given compound as being a Lewis acid or Lewis base, given its Lewis structure or its Kekulé structure.
3. identify an organic molecule or ion in a reaction as either an electrophile or nucleophile.

Key Terms

Make certain that you can define, and use in context, the key terms below.

- Lewis acid
- Lewis base
- Electrophile
- Nucleophile

Study Notes

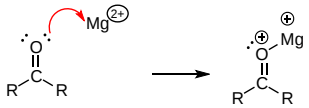
The Lewis concept of acidity and basicity will be of great use to you when you study reaction mechanisms. The realization that an ion such as



is electron deficient, and is therefore a Lewis acid, should help you understand why this ion reacts with substances which are Lewis bases (e.g., H_2O).

Introduction to Lewis Acid-Base Theory

The Brønsted acid-base theory has been used throughout the history of acid and base chemistry. However, this theory is very restrictive and focuses primarily on acids and bases acting as proton donors and acceptors. Sometimes conditions arise where the theory doesn't necessarily fit, such as in solids and gases. In 1923, G.N. Lewis from UC Berkeley proposed an alternate theory to describe acids and bases. His theory gave a generalized explanation of acids and bases based on structure and bonding. Through the use of the Lewis definition of acids and bases, chemists are now able to predict a wider variety of acid-base reactions. Lewis' theory used electrons instead of proton transfer and specifically stated that an acid is a species that accepts an electron pair while a base donates an electron pair.



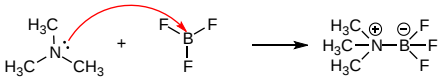
Example of Lewis base (oxygen atom from carbonyl) reacting with Lewis Acid (Mg^{2+} ion).

The reaction of a Lewis acid and a Lewis base will produce a coordinate covalent bond. A coordinate covalent bond is just a type of covalent bond in which one reactant donates both electrons to form the bond. In this case the Lewis base donates its electrons to form a bond to the Lewis acid. The resulting product is called an addition compound, or more commonly a complex. The electron-pair flow from Lewis base to Lewis acid is shown using curved arrows much like those used for resonance structures in Section 2.5. Curved arrows always mean that an electron pair moves from the atom at the tail of the arrow to the atom at the head of the arrow. In this case the lone pair on the Lewis base attacks the Lewis acid forming a bond. This new type of electron pair movement, along with those described in Section 2.5 will be used throughout this text to describe electron flow during reactions.

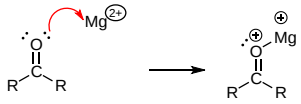
- Lewis Acid: a species that accepts an electron pair and will typically either have vacant orbitals or a polar bond involving hydrogen such that it can donate H^+ (which has an empty 1s orbital)
- Lewis Base: a species that donates an electron pair and will have lone-pair electrons of pi bonding electrons.

Lewis Acids

Neutral compounds of boron, aluminum, and the other Group 13 elements, (BF_3, $AlCl_3$), which possess only six valence electrons, have a very strong tendency to gain an additional electron pair. Because these compounds are only surrounded by three electron groups, they are sp^2 hybridized, contained a vacant p orbital, and are potent Lewis acids. Trimethylamine's lone pair elections are contained in an sp^3 hybrid orbital making it a Lewis base. These two orbitals overlap, creating a covalent bond in a boron trifluoride-trimethylamine complex. The movement of electrons during this interaction is show by by an arrow.



Positive ions are often Lewis acids because they have an electrostatic attraction for electron donors. Examples include alkali and alkaline earth metals in the group IA and IIA columns. K^+, Mg^{2+} and Ca^{2+} are sometimes seen as Lewis acidic sites in biology, for example. These ions are very stable forms of these elements because of their low electron ionization potentials. However, their positive charges do attract electron donors.The interaction between a magnesium cation (Mg^{+2}) and a carbonyl oxygen is a common example of a Lewis acid-base reaction. The carbonyl oxygen (the Lewis base) donates a pair of electrons to the magnesium cation (the Lewis acid). As we will see in Chapter 19 when we begin the study of reactions involving carbonyl groups, this interaction has the very important effect of increasing the polarity of the carbon-oxygen double bond.



The eight-electron rule does not hold throughout the periodic table. In order to obtain noble gas configurations, some atoms may need eighteen electrons in their valence shell. Transition metals such as titanium, iron and nickel may have up to eighteen electrons and can frequently accept electron pairs from Lewis bases. Transition metals are often Lewis acids. For example, titanium has four valence electrons and can form four bonds in compounds such as titanium tetrakis (isopropoxide), below, or titanium tetrachloride, $TiCl_4$. However, the titanium atom in that compound has only eight valence electrons, not eighteen. It can easily accept electrons from donors.

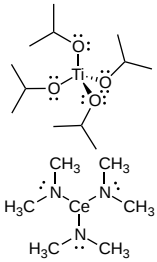


Figure **7.5.1**: *Although titanium has eight electrons in this molecule, titanium tetrakis(isopropoxide), it can accommodate up to eighteen. It is a Lewis acid. The cerium atom in cerium tris(dimethylamide) comes from a similar part of the periodic table and is also a Lewis acid.*

For example, when THF and $TiCl_4$ are combined, a Lewis acid-base complex is formed, $TiCl_4(THF)_2$. $TiCl_4(THF)_2$ is a yellow solid at room temperature.

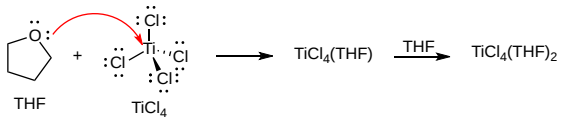


Figure **7.5.2**: *A Lewis acid-base complex between tetrahydrofuran (THF) and titanium tetrachloride.*

The Proton as a Common Lewis Acid

Perhaps the most common example of a Lewis acid is also the simplest. It is the hydrogen cation (H^+) or proton. It is called a proton because, in most hydrogen atoms, the only particle in the nucleus is a proton. If an electron is removed to make a cation, a proton is all that is left. A proton is a Lewis acid for a number of reasons. It has a positive charge, and so it will attract electrons, which are negative. Also, it lacks the electron configuration of its noble gas neighbor, helium. Helium has two electrons. If a Lewis base or nucleophile donates a pair of electrons to a proton, the proton will obtain a helium noble gas configuration.

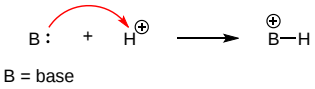


Figure **7.5.3**: *Proton reacting as a Lewis acid.*

There is something about hydrogen cations that is not so simple, however. They are actually not so common. Instead, protons are generally always bound to a Lewis base. Hydrogen is almost always covalently (or coordinately) bonded to another atom. Many of the other elements commonly found in compounds with hydrogen are more electronegative than hydrogen. As a result, hydrogen often has a partial positive charge making is still act as a Lewis Acid.

A acid-base reaction involving protons might better be expressed as:

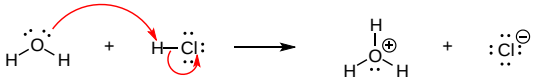


Figure **7.5.4**: *Proton transfer from one site to another.*

The Lewis acid-base interactions we have looked at so far are slightly different here. Instead of two compounds coming together and forming a bond, we have one Lewis base replacing another at a proton. Two specific movements of electrons are shown in the reaction both of which are show by arrows. Lone pair electrons on oxygen attack the hydrogen to form an O-H bond in the product. Also, the electrons of the H-Cl bond move to become a lone pair on chlorine as the H-Cl bond breaks. These two arrows together are said to represent the mechanism of this acid-base reaction.

Lewis Bases

What makes a molecule (or an atom or ion) a Lewis base? It must have a pair of electrons available to share with another atom to form a bond. The most readily available electrons are those that are not already in bonds. Bonding electrons are low in energy. Non-bonding electrons are higher in energy and may be stabilized when they are delocalized in a new bond. Lewis bases usually have non-bonding electrons or lone pairs this makes oxygen and nitrogen compounds common Lewis bases. Lewis bases may be anionic or neutral. The basic requirement is that they have a pair of electrons to donate.

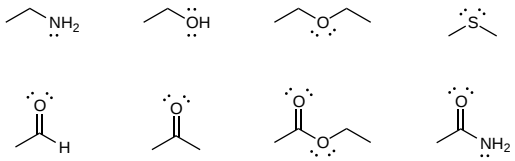


Figure **7.5.5**: Some common organic examples of Lewis bases. Most oxygen, nitrogen and sulfur containing compounds can act as Lewis Bases.

Note 1: Ammonia

Ammonia, NH_3, has a lone pair and is a Lewis base. It can donate to compounds that will accept electrons.



Ammonia donating to an electron acceptor or Lewis acid.

Not all compounds can act as a Lewis base. For example, methane, CH_4, has all of its valence electrons in bonding pairs. These bonding pairs are too stable to donate under normal conditions therefore methane is not a Lewis base. Neutral boron compounds also have all electrons in bonding pairs. For example, borane, BH_3 has no lone pairs; all its valence electrons are in bonds. Boron compounds are not typically Lewis bases.

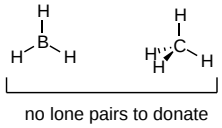


Figure 7.5.6: *Carbon and boron compounds with all sigma bonds do not have lone pairs, and do not act as Lewis bases.*

? Exercise 7.5.1

Which of the following compounds would you expect to be Lewis bases?

a) SiH_4 b) AlH_3 c) PH_3 d) SH_2 e) ^-SH

Answer

a) No, silicon has 4 valence electrons (like carbon) and all 4 are involved in sigma bonds

b) No, aluminum has 3 valence electrons and all 3 are involved in sigma bonds

c) Yes, phosphorus has 5 valence electrons, so there is one lone pair available

d) Yes, sulfur has 6 valence electrons, so there are two lone pairs available

e) Yes, this ion has 3 lone pairs available

Lewis Acid-Base Complexes

What happens when a Lewis base donates a pair of electrons to a Lewis acid? The electron pushing formalism (arrows) we have been using to illustrate the behavior of Lewis acids and Lewis bases is meant to show the direction of electron movement from the donor to the acceptor. However, given that a bond can be thought of as a pair of electrons that are shared between two atoms (in this case, between the donor and the acceptor), these arrows also show where bonds are forming.

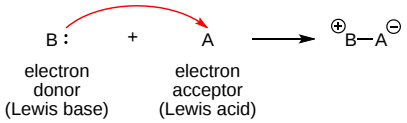


Figure 7.5.7: Donation of electrons from a Lewis base to a Lewis acid.

The electrons donated from a Lewis base to a Lewis acid form a new bond. A new, larger compound is formed from the smaller Lewis acid and Lewis base. This compound is called a Lewis acid-base complex. A simple example of Lewis acid-base complexation involves ammonia and boron trifluoride. The nitrogen atom has a lone pair and is an electron donor. The boron has no octet and is an electron acceptor. The two compounds can form a Lewis acid-base complex or a coordination complex together.

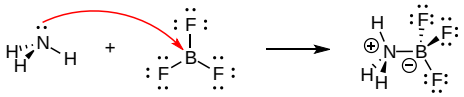


Figure 7.5.8: *Formation of a Lewis acid-base complex from ammonia and boron trifluoride.*

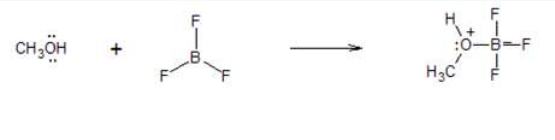
When the nitrogen donates a pair of electrons to share with the boron, the bond that forms is sometimes called a coordinate bond. A coordinate bond is any covalent bond that arose because one atom brought a pair of its electrons and donated them to another.

In organic chemistry terminology, the electron donor is called a **nucleophile** and the electron acceptor is called an **electrophile**. Ammonia is a nucleophile and boron trifluoride is an electrophile.

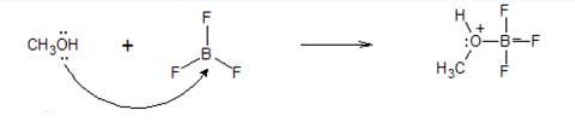
- Because Lewis bases are attracted to electron-deficient atoms, and because positive charge is generally associated with the nucleus of an atom, Lewis bases are sometimes refered to as "nucleophiles". Nucleophile means nucleus-loving.
- Because Lewis acids attract electron pairs, Lewis acids are sometimes called "electrophiles". Electrophile means electron-loving.

Exercise 7.5.2

For the following reaction, add curved arrows (electron pushing formalism) to indicate the electron flow.



Answer



Exercise 7.5.3

A Lewis acid-base complex is formed between THF (tetrahyrofuran) and borane, BH_3.

a) Which compound is the Lewis acid? Which one is the Lewis base?

b) Which atom in the Lewis acid is the acidic site? Why?

c) Which atom in the Lewis base is the basic site? Why?

d) How many donors would be needed to satisfy the acidic site?

e) Show, using arrow notation, the reaction to form a Lewis acid-base complex.

f) Borane is highly pyrophoric; it reacts violently with air, bursting into flames. Show, using arrow notation, what might be happening when borane contacts the air.

g) Borane-THF complex is much less pyrophoric than borane. Why do you suppose that is so?

Add exercises text here.

Answer

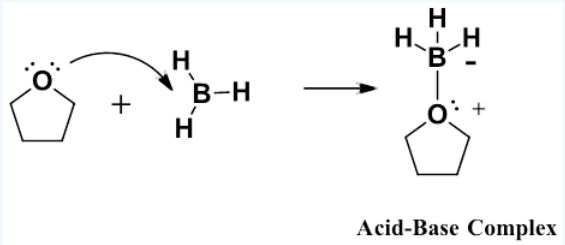
a) Borane is the Lewis acid. THF has lone pair electrons so it is the Lewis base.

b) The Boron atom has an unfilled octet so it has an empty p orbital that can accept electrons.

c) The oxygen atom in THF has lone pair electrons contained in a sp^3 hybridized orbital.

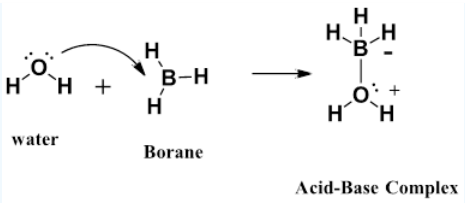
d) The boron in borane has six electrons around it so it would only need one lone pair donor to reach an octet.

e) Show, using arrow notation, the reaction to form a Lewis acid-base complex.



Acid-Base Complex

f) The Borane initially reacts with water in air.



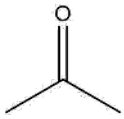
g) After the Borane-THF complex is formed, the boron atom has a complete octet making it less reactive.

Exercises

Questions

Q2.11.1

For the following molecules state wither they are Lewis acid or base and wither or not they are a Brønsted acid or base.



NH_4^+

Solutions

S2.11.1

Acetone is a Lewis base and a Brønsted base. Ammonium cation is both a Lewis acid and a weak Brønsted acid.

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CHAPTER OVERVIEW

8: Organohalides- Radical Halogenation of Alkanes and Alkenes

Learning Objectives

After you have completed this Chapter, you should be able to

- draw all steps of a chain reaction involving radical halogenation of an alkane
- predict radical halogenation outcomes of alkanes and alkenes
- determine how best to synthesize certain organohalides from alkanes and alkenes

8.1: Introduction to Organohalides

8.2: Names and Properties of Alkyl Halides

8.3: Preparing Alkyl Halides from Alkanes - Radical Halogenation

8.4: Preparing Alkyl Halides from Alkenes - Allylic Bromination

8.5: Stability of the Allyl Radical - Resonance Revisited

Contributors and Attributions

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8.1: Introduction to Organohalides

Objectives

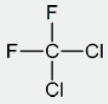
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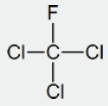
1. list the industrial uses of some important halogenated hydrocarbons including 1,1,1-trichloroethane, tetrafluoroethylene and dichlorodifluoromethane.
2. outline, briefly, how the chemistry of vinyl halides and aryl halides differs from that of the alkyl halides discussed.

Study Notes

There are several different types of halogen-substituted organic compounds, including aryl halides, acyl halides, vinyl halides and alkynyl halides. The primary focus of this chapter is on alkyl halides.

Freons™, also called fluorocarbons or chlorofluorocarbons, have been a source of concern to environmentalists since 1974, when Frank S. Rowland and Mario J. Molina suggested that these substances might be contributing to the destruction of Earth's ozone layer. The stratospheric ozone layer filters out much of the ultraviolet radiation from the sun's rays. It is believed that extensive depletion of this layer, and the consequent increase in the amount of ultraviolet radiation reaching Earth, could result in the destruction of certain crops, in climate modification, and in an increase in the incidence of skin cancer. In recent years, the manufacture and use of freons has declined sharply as the general public has become more aware of the problems that might be caused by these substances.

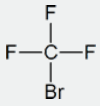


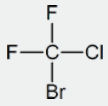


Note: "Freon" is a DuPont trademark.

Related to the freons are the halons—now used in some fire extinguishers, particularly in areas where foams or dry-chemical extinguishers cannot be used (e.g., in and around computers). If you examine such extinguishers, you will find that the halon is identified by a number; for example, halon 1301 or halon 1211. The first number represents the number of carbon atoms present, the second is the number of fluorines, the third is the number of chlorines and the fourth is the number of bromines.

Thus the halons given as examples above have the following structures:





You need not remember the names of the various freons and halons, but you should be prepared to name them by the IUPAC system according to the rules developed in the next section.

Many organic compounds are closely related to the alkanes. Alkanes react with halogens to produce halogenated hydrocarbons, the simplest of which have a single halogen atom substituted for a hydrogen atom of the alkane. Even more closely related are the cycloalkanes, compounds in which the carbon atoms are joined in a ring, or cyclic fashion.

The reactions of alkanes with halogens produce **halogenated hydrocarbons**, compounds in which one or more hydrogen atoms of a hydrocarbon have been replaced by halogen atoms:



The replacement of only one hydrogen atom gives an **alkyl halide (or haloalkane)**. A wide variety of interesting and often useful compounds have one or more halogen atoms per molecule. For example, methane (CH_4) can react with chlorine (Cl_2), replacing one, two, three, or all four hydrogen atoms with Cl atoms. Several halogenated products derived from methane and ethane (CH_3CH_3) are listed in Table 10.1, along with some of their uses.

Table 10.1: Some Halogenated Hydrocarbons

Formula	Common Name	IUPAC Name	Some Important Uses
Derived from CH_4			
CH_3Cl	methyl chloride	chloromethane	refrigerant; the manufacture of silicones, methyl cellulose, and synthetic rubber
CH_2Cl_2	methylene chloride	dichloromethane	laboratory and industrial solvent
$CHCl_3$	chloroform	trichloromethane	industrial solvent
CCl_4	carbon tetrachloride	tetrachloromethane	dry-cleaning solvent and fire extinguishers (but no longer recommended for use)
$CBrF_3$	halon-1301	bromotrifluoromethane	fire extinguisher systems
CCl_3F	chlorofluorocarbon-11 (CFC-11)	trichlorofluoromethane	foaming plastics
CCl_2F_2	chlorofluorocarbon-12 (CFC-12)	dichlorodifluoromethane	refrigerant
Derived from CH_3CH_3			
CH_3CH_2Cl	ethyl chloride	chloroethane	local anesthetic
$ClCH_2CH_2Cl$	ethylene dichloride	1,2-dichloroethane	solvent for rubber
CCl_3CH_3	methylchloroform	1,1,1-trichloroethane	solvent for cleaning computer chips and molds for shaping plastics

To Your Health: Halogenated Hydrocarbons

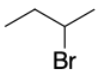
Once widely used in consumer products, many chlorinated hydrocarbons are suspected carcinogens (cancer-causing substances) and also are known to cause severe liver damage. An example is carbon tetrachloride (CCl_4), once used as a dry-cleaning solvent and in fire extinguishers but no longer recommended for either use. Even in small amounts, its vapor can cause serious illness if exposure is prolonged. Moreover, it reacts with water at high temperatures to form deadly phosgene ($COCl_2$) gas, which makes the use of CCl_4 in fire extinguishers particularly dangerous.

Ethyl chloride, in contrast, is used as an external local anesthetic. When sprayed on the skin, it evaporates quickly, cooling the area enough to make it insensitive to pain. It can also be used as an emergency general anesthetic.

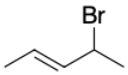
Bromine-containing compounds are widely used in fire extinguishers and as fire retardants on clothing and other materials. Because they too are toxic and have adverse effects on the environment, scientists are engaged in designing safer substitutes for them, as for many other halogenated compounds.

Reactivity of Halides

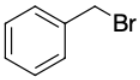
Alkyl halides have an sp^3 carbon atom with a halogen attached, this is also true for allylic halides and benzylic halides. These types of halides are all reactive toward most substitution and elimination reactions. Allyl and benzyl halides tend to form carbocations more easily due to resonance stabilization.



alkyl halide



allyl halide

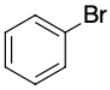


benzyl halide

However, halogens bonded to sp^2 carbon atoms are not typically reactive. Examples of this are vinyl and aryl halides.



vinyl halide



aryl halide

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8.2: Names and Properties of Alkyl Halides

Objectives

After completing this section, you should be able to

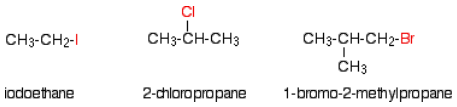
1. write the IUPAC name of a halogenated aliphatic hydrocarbon, given its Kekulé, condensed, or shorthand structure.
2. draw the Kekulé, condensed, or shorthand structure of a halogenated aliphatic hydrocarbon, given its IUPAC name.
3. write the IUPAC name and draw the Kekulé, condensed, or shorthand structure of a simple alkyl halide, given a systematic, non-IUPAC name (e.g., *sec*-butyl iodide).
4. arrange a given series of carbon-halogen bonds in order of increasing or decreasing length and strength.

Study Notes

This section contains little that is new. If you mastered the IUPAC nomenclature of alkanes, you should have little difficulty in naming alkyl halides. Notice that when a group such as CH_2Br must be regarded as a substituent, rather than as part of the main chain, we may use terms such as bromomethyl.

You will find it easier to understand the reactions of the alkyl halides if you keep the polarity of the C-X bond fixed permanently in your mind (see "The Polar C-X Bond" shown in the reading below).

Alkyl halides are also known as haloalkanes. This page explains what they are and discusses their physical properties. Alkyl halides are compounds in which one or more hydrogen atoms in an alkane have been replaced by halogen atoms (fluorine, chlorine, bromine or iodine). For example:

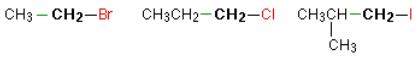


Halide Designations

Alkyl halides fall into different classes depending on how many alkyl groups are attached to the carbon which holds the halogen. There are some chemical differences between the various types. When there are **no** alkyl groups attached to the carbon holding the halogen, these are considered methyl halides (CH_3X).

Primary alkyl halides

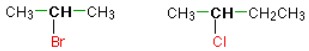
In a primary (1°) haloalkane, the carbon which carries the halogen atom is only attached to one other alkyl group. Some examples of primary alkyl halides include:



Notice that it doesn't matter how complicated the attached alkyl group is. In each case there is only one linkage to an alkyl group from the CH_2 group holding the halogen. There is an exception to this: CH_3Br and the other methyl halides are often counted as primary alkyl halides even though there are **no** alkyl groups attached to the carbon with the halogen on it.

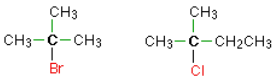
Secondary alkyl halides

In a secondary (2°) haloalkane, the carbon with the halogen attached is joined directly to two other alkyl groups, which may be the same or different. Examples:



Tertiary alkyl halides

In a tertiary (3°) haloalkane, the carbon atom holding the halogen is attached directly to three alkyl groups, which may be any combination of same or different. Examples:



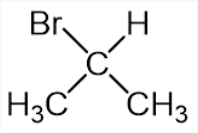
Example 8.2.1

Please indicate if the following haloalkanes are methyl, 1^o, 2^o, or 3^o:

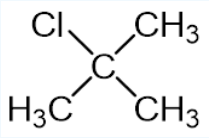
a) CH_3I

b) CH_3CH_2Br

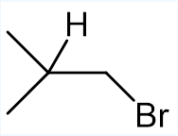
c)



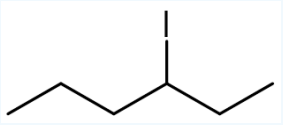
d)



e)



f)



Solution

a) methyl

b) 1^o

c) 2^o

d) 3^o

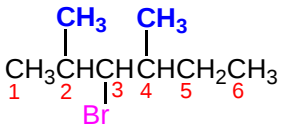
e) 1^o

f) 2^o

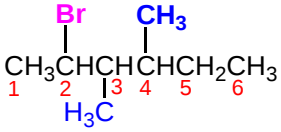
Nomenclature of Alkyl Halides

Alkyl halides are systematically named as alkanes (Section 3-4) where the halogen is a substituent on the parent alkane chain. To summarize the rules discussed in detail in **Section 3-4**, there are three basic steps to naming alkyl halides.

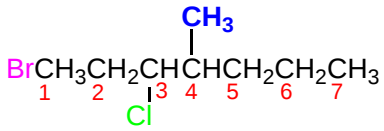
1. Find and name the longest carbon chain and name it as the parent chain. Remember is an alkene or alkyne is present, the parent chain must contain both carbons of the multiple bond.
2. Number the parent chain consecutively, starting at the end nearest a substituent group. Then assign each substituent a number. Remember the IUPAC system uses a prefix to indicate the halogen followed by the suffix -ide. The prefixes are *fluoro-* for fluorine, *chloro-* for chlorine, *bromo-* from bromine, and *iodo-* for iodine. The name of a halogen is preceded by a number indicating the substituent's location on the parent chain.



3-Bromo-2,4-Dimethylhexane

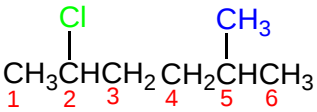


2-Bromo-3,4-Dimethylhexane



1-Bromo-3-Chloro-4-methylheptane

3. If there is an ambiguity in numbering the parent chain, begin on the end which is closer to the substituent which comes first alphabetically.



2-Chloro-5-methylhexane
(Not 5-Chloro-2-methylhexane)

Common Names of Alkyl Halides

Alkyl halides with simple alkyl groups are often called by common names. Those with a larger number of carbon atoms are usually given IUPAC names. The *common names* of alkyl halides consist of two parts: the name of the alkyl group plus the first syllable of the name of the halogen, with the ending *-ide*. The names of common alkyl groups are listed in Section 3.3.



IUPAC Name:	Bromomethane	2-Iodopropane	Chlorocyclohexane
Common Name:	Methyl bromide	Isopropy iodide	Cyclohexyl chloride

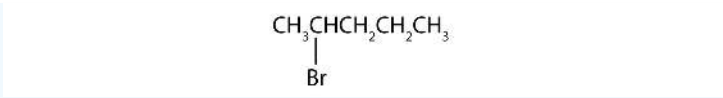
? Exercise 8.2.1

1) Give the common and IUPAC names for each compound.

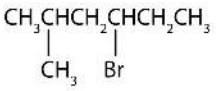
a. $CH_3CH_2CH_2Br$
b. $(CH_3)_2CHCl$
c. CH_3CH_2I
d. $CH_3CH_2CH_2CH_2F$

2) Give the IUPAC name for each compound.

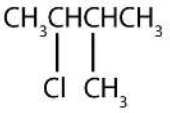
a)



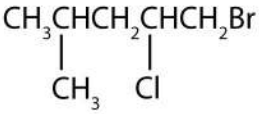
b)



c)



d)



Answer

1) a) The alkyl group ($CH_3CH_2CH_2$–) is a propyl group, and the halogen is bromine (Br). The common name is therefore propyl bromide. For the IUPAC name, the prefix for bromine (bromo) is combined with the name for a three-carbon chain (propane), preceded by a number identifying the carbon atom to which the Br atom is attached, so the IUPAC name is 1-bromopropane.

b) The alkyl group [$(CH_3)_2CH$–] has three carbon atoms, with a chlorine (Cl) atom attached to the middle carbon atom. The alkyl group is therefore isopropyl, and the common name of the compound is isopropyl chloride. For the IUPAC name, the Cl atom (prefix *chloro*-) attached to the middle (second) carbon atom of a propane chain results in 2-chloropropane.

c) The alkyl group (CH_3CH_2–) is a ethyl group, and the halogen is iodine (I). The common name is therefore ethyl iodide. For the IUPAC name, the prefix for iodine (iodo) is combined with the name for a two-carbon chain (ethane), preceded by a number identifying the carbon atom to which the I atom is attached, so the IUPAC name is 1-iodoethane.

d) The alkyl group ($CH_3CH_2CH_2CH_2$–) is a butyl group, and the halogen is fluorine (F). The common name is therefore butyl fluoride. For the IUPAC name, the prefix for fluorine (Fluoro) is combined with the name for a four-carbon chain (butane), preceded by a number identifying the carbon atom to which the F atom is attached, so the IUPAC name is 1-fluorobutane.

2) a) The parent alkane has five carbon atoms in the longest continuous chain; it is pentane. A bromo (Br) group is attached to the second carbon atom of the chain. The IUPAC name is 2-bromopentane.

b) The parent alkane is hexane. Methyl (CH_3) and bromo (Br) groups are attached to the second and fourth carbon atoms, respectively. Listing the substituents in alphabetical order gives the name 4-bromo-2-methylhexane.

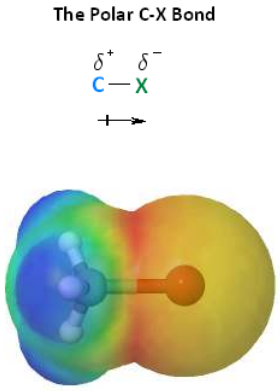
c) 2-Chloro-3-methylbutane

d) 1-Bromo-2-chloro-4-methylpentane.

There is a fairly large distinction between the structural and physical properties of haloalkanes and the structural and physical properties of alkanes. As mentioned above, the structural differences are due to the replacement of one or more hydrogens with a halogen atom. The differences in physical properties are a result of factors such as electronegativity, bond length, bond strength, and molecular size.

Halogens and the Character of the Carbon-Halogen Bond

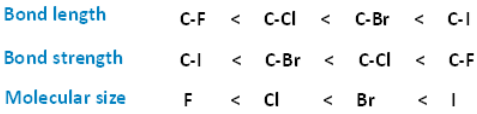
As discussed in Section 6.4, halogens are more electronegative than carbon. This results in a carbon-halogen bond that is polarized with the carbon atom bearing a partial positive charge and the halogen a partial negative charge. This polarity can be distinctly seen when viewing the electrostatic potential map of a methyl halide. Electron density is shown by a red/yellow color which is almost exclusively around the halogen atom. The methyl portion of the compound lacks electron density which is shown by a blue/green color.



The following image shows the relationship between the halogens and electronegativity. Notice, as we move up the periodic table from iodine to fluorine, electronegativity increases.



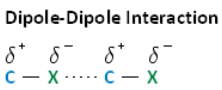
The following image shows the relationships between bond length, bond strength, and molecular size. As we progress down the periodic table from fluorine to iodine, molecular size increases. As a result, we also see an increase in bond length. Conversely, as molecular size increases, the bonds get longer, and the strength of those bonds decreases.



Haloalkanes Have Higher Boiling Points than Alkanes

When comparing alkanes and haloalkanes, we will see that haloalkanes have higher boiling points than alkanes containing the same number of carbons. London dispersion forces are the first of two types of forces that contribute to this physical property. You might recall from general chemistry that London dispersion forces increase with molecular surface area. In comparing haloalkanes with alkanes, haloalkanes exhibit an increase in surface area due to the substitution of a halogen for hydrogen. The increase in surface area leads to an increase in London dispersion forces, which then results in a higher boiling point.

Dipole-dipole interaction is the second type of force that contributes to a higher boiling point. As you may recall, this type of interaction is a coulombic attraction between the partial positive and partial negative charges that exist between carbon-halogen bonds on separate haloalkane molecules. Similar to London dispersion forces, dipole-dipole interactions establish a higher boiling point for haloalkanes in comparison to alkanes with the same number of carbons.



The table below illustrates how boiling points are affected by some of these properties. Notice that the boiling point increases when hydrogen is replaced by a halogen, a consequence of the increase in molecular size, as well as an increase in both London dispersion forces and dipole-dipole attractions. The boiling point also increases as a result of increasing the size of the halogen, as well as increasing the size of the carbon chain.

Boiling Points of Haloalkanes (°C)						
R	X =	H	F	Cl	Br	I
CH_3		-161.7	-78.4	-24.2	3.6	42.4
CH_3CH_2		-88.6	-37.7	12.3	38.4	72.3
$CH_3(CH_2)_2$		-42.1	-2.5	46.6	71.0	102.5
$CH_3(CH_2)_3$		-0.5	32.5	78.4	101.6	130.5
$CH_3(CH_2)_4$		36.1	62.8	107.8	129.6	157.0
$CH_3(CH_2)_7$		125.7	142.0	182.0	200.3	225.5

Solubility

Solubility in water

The alkyl halides are at best only slightly soluble in water. For a haloalkane to dissolve in water the attractions between the haloalkane molecules (van der Waals dispersion and dipole-dipole interactions) and hydrogen bonds between water molecules must be broken. Both of these cost energy. Energy is released when new intermolecular forces are generated between the haloalkane molecules and water molecules. These will only be dispersion forces and dipole-dipole interactions. These are not as strong as the original hydrogen bonds in the water, and so not as much energy is released as was used to separate the water molecules. The energetics of the changes are sufficiently "unprofitable" such that very little dissolves.

Solubility in organic solvents

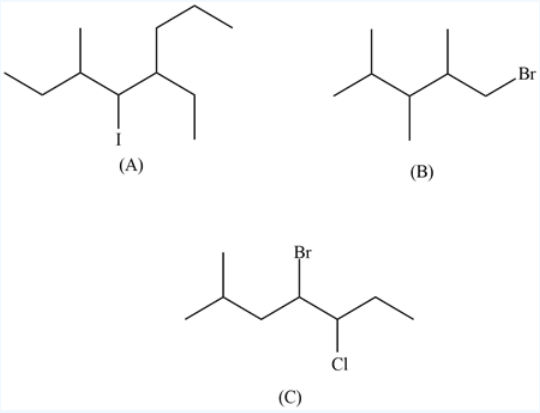
Alkyl halides tend to dissolve in organic solvents because the new intermolecular attractions have roughly the same strength as the ones being broken in the separate haloalkane and solvent.

Chemical Reactivity

The pattern in chemical reactiviy lies in the strength of the bond between the carbon atom and the halogen atom. Previously in this section, it was noted that the trend for bond strength increases from C-I to C-Br to C-Cl with C-F bonds being the strongest. To react with the alkyl halides, the carbon-halogen bond has got to be broken. Because that gets easier as you go from fluoride to chloride to bromide to iodide, the compounds get more reactive in that order. Iodoalkanes are the most reactive and fluoroalkanes are the least. In fact, fluoroalkanes are so unreactive that we will ignore them completely from now on in this section!

? Exercise 8.2.2

1) Give the names of the following organohalides:



2) Draw the structures of the following compounds:

a) 2-Chloro-3,3-dimethylpentane

b) 1,1-Dichloro-4-isopropylcyclohexane

c) 3-bromo-3-ethylhexane

Answer

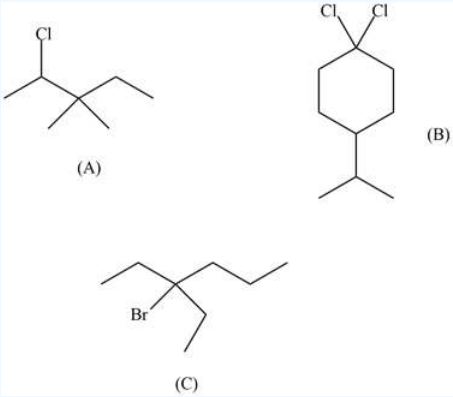
1)

a) 5-ethyl-4-iodo-3-methyloctane

b) 1-bromo-2,3,4-trimethylpentane

c) 4-bromo-5-chloro-2-methylheptane

2)



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8.3: Preparing Alkyl Halides from Alkanes - Radical Halogenation

Objectives

After completing this section, you should be able to

1. explain why the radical halogenation of alkanes is not usually a particularly good method of preparing pure samples of alkyl halides.
2. use **C — H** bond energies to account for the fact that in radical chlorinations, the reactivity of hydrogen atoms decreases in the order

$$\textbf{tertiary} > \textbf{secondary} > \textbf{primary}.$$

3. predict the approximate ratio of the expected products from the monochlorination of a given alkane.

Study Notes

The following terms are synonymous:

1. methyl hydrogens, primary hydrogens, and 1° hydrogens.
2. methylene hydrogens, secondary hydrogens, and 2° hydrogens.
3. methine hydrogens, tertiary hydrogens, and 3° hydrogens.

Note that in radical chlorination reactions, the reactivity of methine, methylene and methyl hydrogens decreases in the ratio of approximately 5 : 3.5 : 1. This will aid in the prediction of expected products from the monochlorination of a given alkane.

Radical Halogenation

Alkanes (the simplest of all organic compounds) undergo very few reactions. One of these reactions is halogenation, or the substitution of a single hydrogen on the alkane for a single halogen (Cl_2 or Br_2) to form a haloalkane. This reaction is very important in organic chemistry because it functionalizes alkanes which opens a gateway to further chemical reactions.

General Reaction

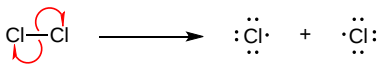
$$CH_4 + Cl_2 + energy \rightarrow CH_3Cl + HCl$$

Radical Chain Mechanism

The reaction proceeds through the radical chain mechanism which is characterized by three steps: **initiation**, **propagation,** and **termination**. Initiation requires an input of energy but after that the reaction is self-sustaining.

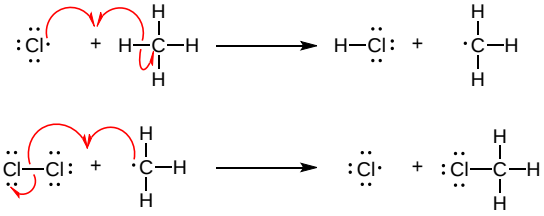
Step 1: Initiation

During the initiation step free radicals are created when ultraviolet light or heat causes the X-X halogen bond to undergo homolytic to create two halogen free radicals. It is important to note that this step is not energetically favorable and cannot occur without some external energy input. After this step, the reaction can occur continuously (as long as reactants provide) without input of more energy.



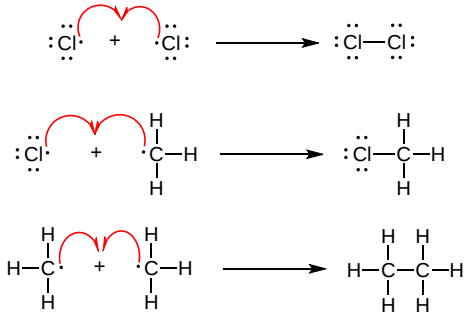
Step 2: Propagation

The next two steps in the mechanism are called propagation steps. In the first propagation step, a chlorine radical abstracts hydrogen atom from methane. This gives hydrochloric acid (HCl, the inorganic product of this reaction) and the methyl radical. In the second propagation step, the methyl radical reacts with more of the chlorine starting material (Cl_2). One of the chlorine atoms becomes a radical and the other combines with the methyl radical to form the alkyl halide product.

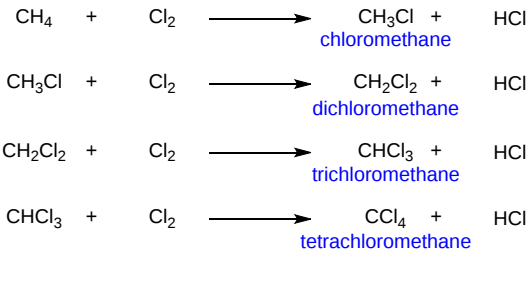


Step 3: Termination

In the three termination steps of this mechanism, radicals produced in the mechanism an undergo radical coupling to form a sigma bond. These are called termination steps because a free radical is not produced as a product, which prevents the reaction from continuing. Combining the two types of radicals produced can be combined to from three possible products. Two chlorine radicals and couple to form more halogen reactant (Cl_2). A chlorine radical and a methyl radical can couple to form more product (CH_3Cl). An finally, two methyl radicals can couple to form a side product of ethane (CH_3CH_3).



This reaction is a poor synthetic method due to the formation of polyhalogenated side products. The desired product occurs when one of the hydrogen atoms in the methane has been replaced by a chlorine atom. However, the reaction doesn't stop there, and all the hydrogens in the methane can in turn be replaced by chlorine atoms to produce a mixture of chloromethane, dichloromethane, trichloromethane and tetrachloromethane.

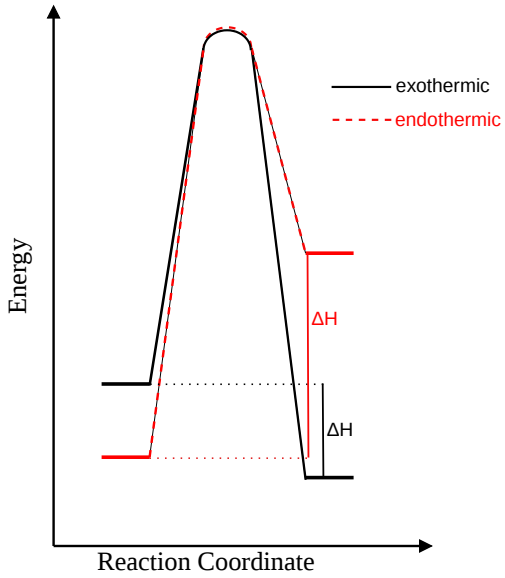


Energetics

Why do these reactions occur? Is the reaction favorable? A way to answer these questions is to look at the change in enthalpy ΔH that occurs when the reaction takes place.

$$\Delta H = (\text{Energy put into reaction}) - (\text{Energy given off from reaction})$$

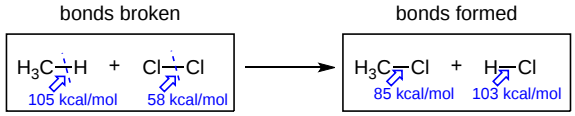
If more energy is put into a reaction than is given off, the ΔH is positive, the reaction is endothermic and not energetically favorable. If more energy is given off in the reaction than was put in, the ΔH is negative, the reaction is said to be exothermic and is considered favorable. The figure below illustrates the difference between endothermic and exothermic reactions.



ΔH can also be calculated using bond dissociation energies (ΔH°):

$$\Delta H = \sum \Delta H^\circ \text{ of bonds broken} - \sum \Delta H^\circ \text{ of bonds formed}$$

Let's look at our specific example of the chlorination of methane to determine if it is endothermic or exothermic:



change in enthalpy = (105 kcal/mol + 58 kcal/mol) − (85 kcal/mol + 103 kcal/mol)
= −25 kcal/mol

Since, the ΔH for the chlorination of methane is negative, the reaction is exothermic. Energetically this reaction is favorable. In order to better understand this reaction we need to look at the mechanism (a detailed step by step look at the reaction showing how it occurs) by which the reaction occurs.

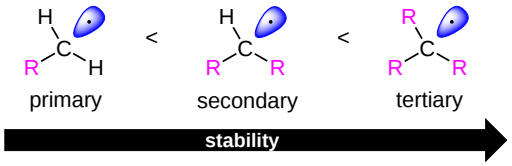
Chlorination of Other Alkanes

When alkanes larger than ethane are halogenated, isomeric products are formed. Thus chlorination of propane gives both 1-chloropropane and 2-chloropropane as mono-chlorinated products. The halogenation of propane discloses an interesting feature of these reactions. **All the hydrogens in a complex alkane do not exhibit equal reactivity**. For example, propane has eight hydrogens, six of them being structurally equivalent **primary**, and the other two being **secondary**. If all these hydrogen atoms were equally reactive, halogenation should give a 3:1 ratio of 1-halopropane to 2-halopropane mono-halogenated products, reflecting the primary/secondary numbers. This is not what we observe. Light-induced gas phase chlorination at 25 ºC gives 45% 1-chloropropane and 55% 2-chloropropane.

$$CH_3\text{-}CH_2\text{-}CH_3 + Cl_2 \rightarrow 45\%\ CH_3\text{-}CH_2\text{-}CH_2Cl + 55\%\ CH_3\text{-}CHCl\text{-}CH_3$$

These results suggest strongly that 2º-hydrogens are inherently more reactive than 1º-hydrogens, by a factor of about 3.5:1. Further experiments showed that 3º-hydrogens are about 5 times more toward halogen atoms 1º-hydrogens. Thus, light-induced chlorination of 2-methylpropane gave predominantly (65%) 2-chloro-2-methylpropane, the substitution product of the sole 3º-hydrogen, despite the presence of nine 1º-hydrogens in the molecule.

$$(CH_3)_3CH + Cl_2 \rightarrow 65\%\ (CH_3)_3CCl + 35\%\ (CH_3)_2CHCH_2Cl$$



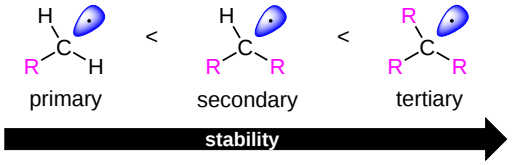
The Relative Reactivity of Hydrogens to

Radical Chlorination

This difference in reactivity can only be attributed to differences in C-H bond dissociation energies. In our previous discussion of bond energy we assumed average values for all bonds of a given kind, but now we see that this is not strictly true. In the case of carbon-hydrogen bonds, there are significant differences, and the specific dissociation energies (energy required to break a bond homolytically) for various kinds of C-H bonds have been measured. These values are given in the following table.

R (in R–H)	methyl	ethyl	i-propyl	t-butyl
Bond Dissociation Energy (kcal/mole)	103	98	95	93

This data shows that a tertiary C-H bond (93 kcal/mole) is easier to break than a secondary (95 kcal/mole) and primary (98 kcal/mole) C-H bond. These bond dissociation energies can be used to estimate the relative stability of the radicals formed after homolytic cleavage. Because a tertiary C-H bond requires less energy to undergo homolytic cleavage than a secondary or primary C-H bond, it can be inferred that a tertiary radical is more stable than secondary or primary.



Relative Stability of Free Radicals

? Exercise 8.3.1

Write out the complete mechanism for the chlorination of methane.

Answer

The answer to this problem is actually above in the initiation, propagation and termination descriptions.

? Exercise 8.3.2

Explain, in your own words, how the first propagation step can occur without input of energy if it is energetically unfavorable.

Answer

Since the second step in propagation is energetically favorable and fast, it drives the equilibrium toward products, even though the first step is not favorable.

? Exercise 8.3.3

Which step of the radical chain mechanism requires outside energy? What can be used as this energy?

Answer

Initiation step requires energy which can be in the form of light or het.

Exercise 8.3.4

Having learned how to calculate the change in enthalpy for the chlorination of methane apply your knowledge and using the table provided below calculate the change in enthalpy for the bromination of ethane.

Compound	Bond Dissociation Energy (kcal/mol)
CH_3CH_2-H	101
CH_3CH_2-Br	70
H-Br	87
Br_2	46

Answer

To calculate the enthalpy of reaction, you subtract the BDE of the bonds formed from the BDE of the bonds broken.

Bonds broken are C-H and Br-Br.

Bonds formed are H-Br adn C-Br.

Bonds broken - bonds formed = change in enthalpy

(101 kcal/mol + 46 kcal/mol) - (87 kcal/mol + 70 kcal/mol) = change in enthalpy

-10 kcal/mol = change in enthalpy for bromination of ethane.

Exercise 8.3.5

1) Predict the mono-substituted halogenated product(s) of chlorine gas reacting with 2-methylbutane.

2) Predict the relative amount of each mono-brominated product when 3-methylpentane is reacted with Br_2. Consider 1°, 2°, 3° hydrogen.

3) For the following compounds, give all possible monochlorinated derivatives.

a) 

b) 

c) 

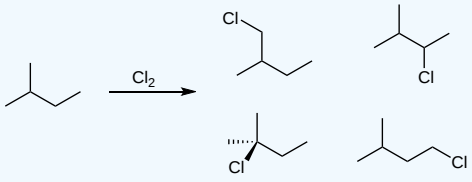
d) 

e) 

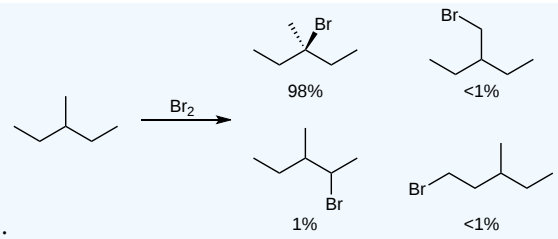
f) 

Answer

1)

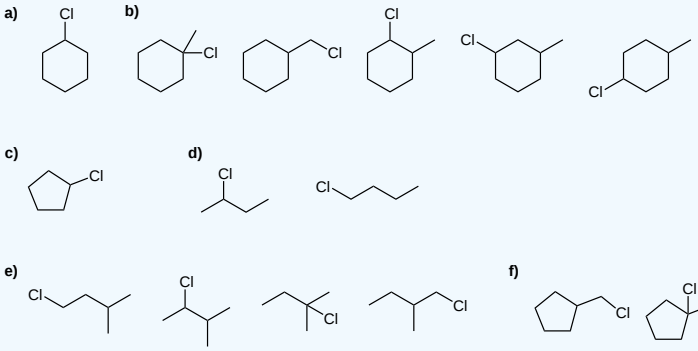


2)



.

3)



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8.4: Preparing Alkyl Halides from Alkenes - Allylic Bromination

Objectives

After completing this section, you should be able to

1. write the equation for the bromination of a symmetrical alkene using N-bromosuccinimide.
2. predict the product formed when a given symmetrical alkene is treated with N-bromosuccinimide.
3. identify the reagent, the symmetrical alkene, or both, needed to produce a given allyl halide by allylic bromination.
4. list the following radicals in order of increasing or decreasing stability: allyl, vinyl, primary alkyl, secondary alkyl, tertiary alkyl, methyl.
5. explain the ease of forming an allyl radical, and the difficulty of forming a vinyl radical, in terms of relative $\ce{\sf{C–H}}$ bond dissociation energies.

Key Terms

Make certain that you can define, and use in context, the key term below.

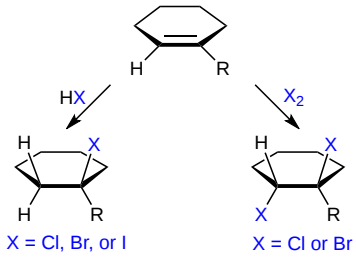
- allylic carbon

Study Notes

We have discussed the electrophilic addition of X_2 and HX to alkenes as a route to forming alkyl halides (Sections 7.8 and 8.2). In this section we introduce bromination at the allyic position with N-bromosuccinimide (NBS). Notice that at the moment we are restricting our studies to the allylic bromination of symmetrical alkenes, such as cyclohexene. When we introduce an element of asymmetry, we find that more than one allyl radical can be formed; therefore, we must assess the relative stability of each radical when trying to predict which product will predominate. The method of doing this assessment is described in the next section.

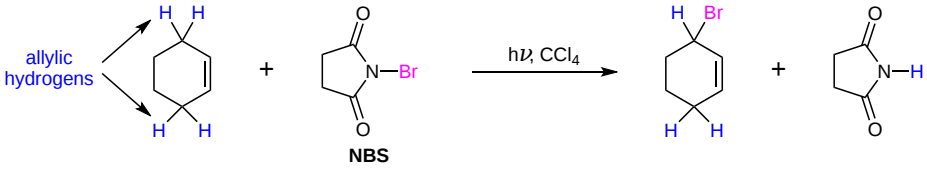
Allylic Bromination

Previously, alkyl halides have been produced though reactions with alkenes. Hydrogen halides (HCl, HBr, and HI) react with alkenes in an electrophilic addition reaction discussed in **Section 7-8** to yield alkyl halides as products. Also, Bromine (Br_2) and chlorine (Cl_2) can react with alkenes to provide dihalogenated products as discussed in **Section 8-2**.



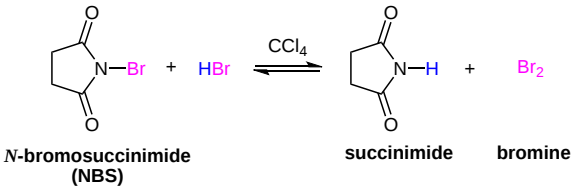
Another method for preparing alkyl halides from alkenes is with **N-bromosuccinimide (NBS)** in carbon tetrachloride (CCl_4) solution with the presence of light. The reaction specifically causes the substitution of bromine with a hydrogen attached to a carbon adjacent to the double bond - the allylic position.

General Reaction

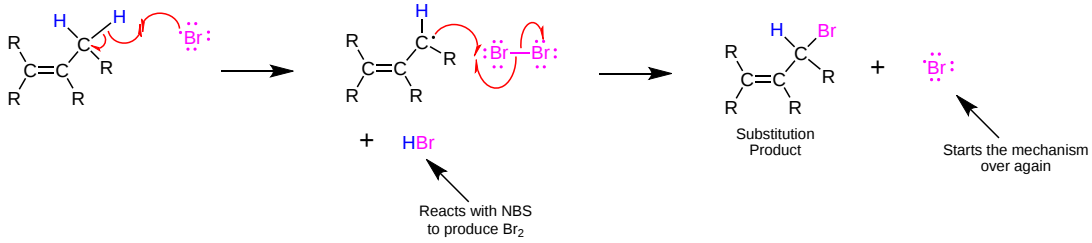


Mechanism

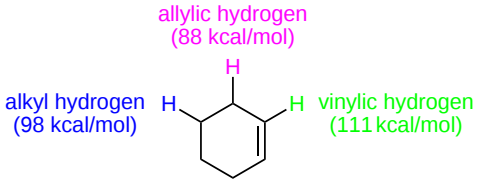
The allylic bromination with NBS is analagous to the alkane halogenation reaction (Section 10.2) since it also occurs as a radical chain reaction. NBS is the most commonly used reagent to produce low concentrations of bromine. When suspended in tetrachloride (CCl_4), NBS reacts very rapidly with the HBr formed during the reaction mechanism to provide bromine (Br_2) which is required for the reaction to continue. Under the correct conditions, NBS provides a constant but very low concentration of Br_2 in the reaction mixture. The low concentration of Br_2 helps to prevent the formation of unwanted side-products.



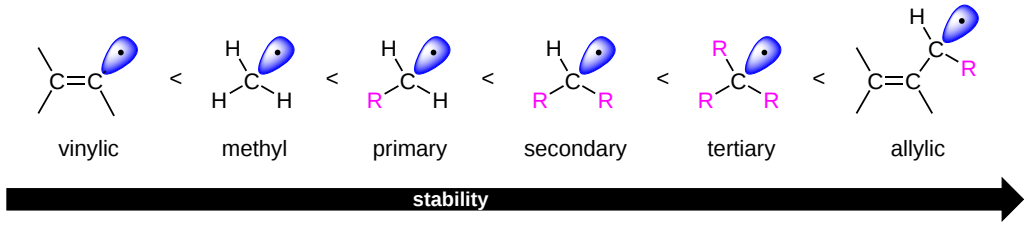
The mechanism starts with the formation of a small amount of bromine radical which then abstracts an allylic hydrogen to form an allylic radical and HBr. The HBr can then react with NBS to form the Br_2 required for the reaction. The allylic radical then abstracts a bromine atom from Br_2 to form the allyl halide product and a bromine radical. The bromine radical produced allows the reaction to continue.



The predominance of allylic substitution over other positions is based on bond dissociation energies. An allylic C-H bond has a strength of about 88 kcal/mol which is much weaker than a typical alkyl C-H bond (98 kcal/mol) or vinylic C-H bond (111 kcal/mol). Therefore, an allylic C-H bond is most likely to form a free radical and react.



Because a allylic C-H bond requires less energy to undergo homolytic cleavage than even a tertiary C-H bond, it can be inferred that a allylic radical is more stable than a tertiary radical. The ordering of stability in radicals can be expanded to include vinylic and allylic radicals. The enhanced stability of allyl radicals can be attributed to resonance stabilization which will be discussed in the next section.



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8.5: Stability of the Allyl Radical - Resonance Revisited

Objectives

After completing this section, you should be able to

1. explain the stability of the allyl radical in terms of resonance.
2. explain the difference between resonance and tautomerism.
3. write an equation for the reaction of an unsymmetrical alkene with N-bromosuccinimide.
4. draw the structure of each of the possible products that could be obtained from the reaction of a given unsymmetrical alkene with N-bromosuccinimide, and predict which product will predominate.
5. explain the formation of more than one product from the reaction of N-bromosuccinimide with a given unsymmetrical alkene.
6. explain the observed product ratio when a given unsymmetrical alkene is treated with N-bromosuccinimide.

Key Terms

Make certain that you can define, and use in context, the key terms below.

- delocalized
- resonance forms
- resonance hybrid

Study Notes

You will have encountered the concept of resonance if you have taken general first-year chemistry course. You should also briefly review Section 2.5.

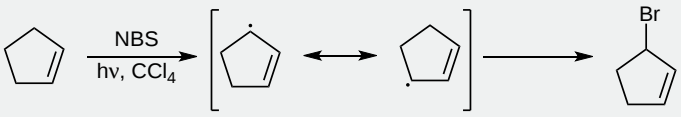
When we can represent a species by two or more different Lewis or Kekulé structures, neither of which represents the true structure of the species, these structures are referred to as *resonance forms*. A common example used in general chemistry courses to illustrate the concept of resonance is ozone, O_3. The two resonance forms of ozone may be represented as follows:



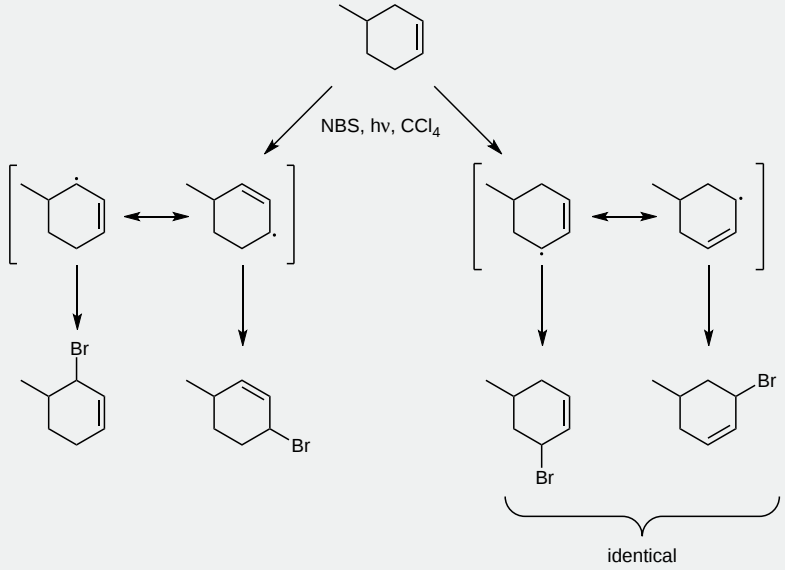
The concept of resonance is quite important, and will be used frequently throughout the remainder of this course. The guidelines below may assist you in drawing resonance contributors.

1. Resonance occurs whenever a molecule, radical or ion can be represented by two or more structures differing only in the arrangement of electrons (no atoms may be moved).
2. The true structure of a species is a hybrid of the resonance contributors and is more stable (i.e., lower in energy) than any of the contributors.
3. The most important contributors are those containing the most covalent bonds. Another way of saying the same thing is that the most important contributors have the least amount of charge separation.
4. Contributors in which all the atoms (except hydrogen) have a complete octet (i.e., are surrounded by eight electrons) are particularly important.

In the previous section we discussed the allylic bromination of a symmetrical alkene with NBS such as this cyclopentene, which affords one product.

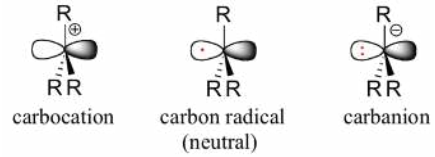


However, with an unsymmetrical alkene and the delocalized unpaired electron forming various allylic resonances, several products are possible. For example, the NBS bromination of 4-methyl-cyclohexene leads to three products.



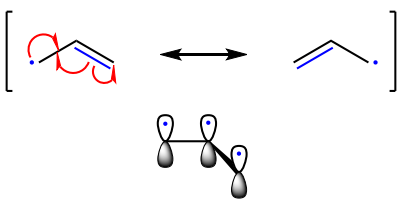
The geometry and relative stability of carbon radicals

As organic chemists, we are particularly interested in radical intermediates in which the unpaired electron resides on a carbon atom. Experimental evidence indicates that the three bonds in a carbon radical have trigonal planar geometry, and therefore the carbon is considered to be sp^2-hybridized with the unpaired electron occupying the perpendicular, unhybridized $2p_z$orbital. Contrast this picture with carbocation and carbanion intermediates, which are both also trigonal planar but whose $2p_z$ orbitals contain zero or two electrons, respectively.



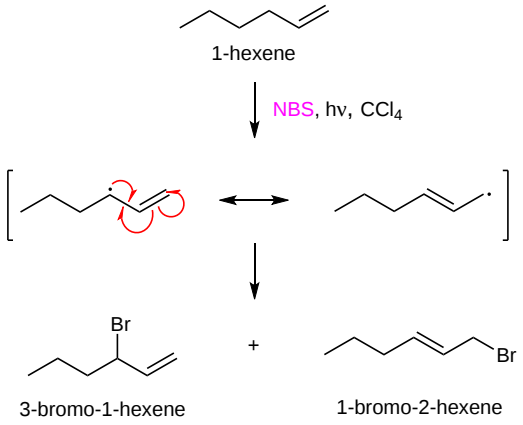
The trend in the stability of carbon radicals parallels that of carbocations (section 8.4B): tertiary radicals, for example, are more stable than secondary radicals, followed by primary and methyl radicals. This should make intuitive sense, because radicals, like carbocations, can be considered to be electron deficient, and thus are stabilized by the electron-donating effects of nearby alkyl groups.

Benzylic and allylic radicals are more stable than alkyl radicals due to resonance effects - an unpaired electron can be delocalized over a system of conjugated pi bonds. An allylic radical, for example, can be pictured as a system of three parallel $2p_z$ orbitals sharing three electrons. With two resonance forms, the allylic radical is electronically symmetrical. Due to resonance hybrid theory, neither structure is correct, but instead the structure lies somewhere between the two resonance forms. Another way to phrase this is that the unpaired electron is delocalized across all the carbon atoms through the pi system and not localized on one site. The more resonance structures, the more stable the molecule. This is why the allylic radical is more stable than the alkyl radical.



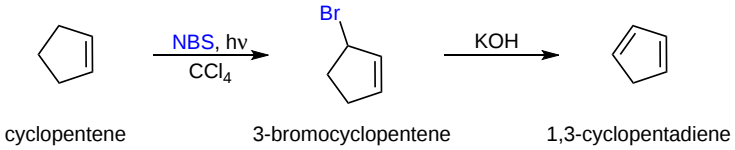
Because the allylic radical is symmetrical, a reaction can occur on either side. Therefore if reacting with bromine, the bromination could occur on either end of the allylic radical. When the allyl radical is symmetrical, this yields the same product. However, if you

have an unsymmetrical allyl radical, it would lead to a mixture of products and not necessarily in equal amounts. This is because the intermediate radical is unsymmetrical. The reaction will occur at the less hindered site. An example would be 1-octene as a starting material in a bromination. The products the reaction would yield would be 3-bromo-1-octene and 1-bromo-2-octene.



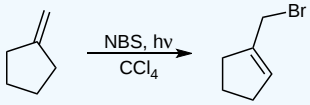
Further Reactions

The products from allylic bromination reactions can easily be converted into dienes by elimination using a base. If the alkyl chain is long enough, alkenes can be converted to dienes through a two-step process: allylic bromination followed by elimination.

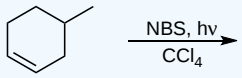


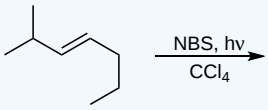
Exercise 8.5.1

1) The following reaction shows the major product. Explain why this would be the final product and why the 2° bromo product is not the major product.



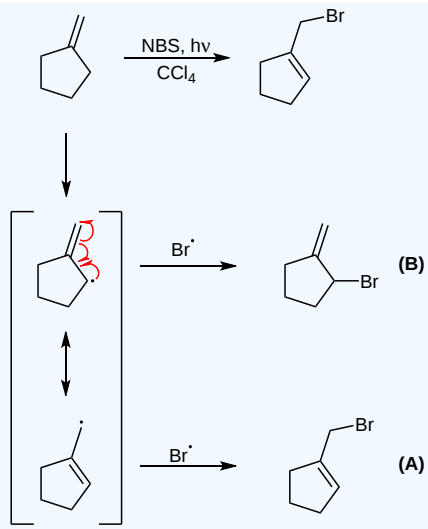
2) Predict the products of the following reactions:



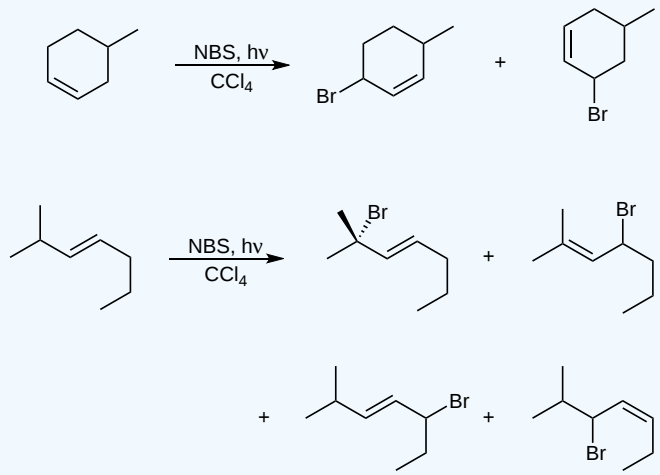


Answer

1) The product (A) is a 1° halogen which is more predominant product even though the (B) had a better transition state with a 2° radical. The 1° radical intermediate is not as sterically hindered.



2)



8.5: Stability of the Allyl Radical - Resonance Revisited is shared under a CC BY-SA 4.0 license and was authored, remixed, and/or curated by Steven Farmer, Dietmar Kennepohl, Sharon Wei, Liza Chu, & Liza Chu.

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CHAPTER OVERVIEW

9: Reactions of Alkyl Halides- Nucleophilic Substitutions and Eliminations

Learning Objectives

After you have completed Chapter 9, you should be able to

- fulfill all of the detailed objectives listed under each individual section.
- use the reactions studied in this chapter with those from earlier ones when designing multistep syntheses.
- use the reactions and concepts discussed in this chapter to solve road map problems.
- define, and use in context, the key terms introduced.

In this course, you have already seen several examples of nucleophilic substitution reactions; now you will see that these reactions can occur by two different mechanisms. You will study the factors that determine which mechanism will be in operation in a given situation, and examine possible ways for increasing or decreasing the rates at which such reactions occur. The stereochemical consequences of both mechanisms will also be discussed. Elimination reactions often accompany nucleophilic substitution; so these reactions are also examined in this chapter. Again you will see that two different mechanisms are possible, and, as in the case of nucleophilic substitution reactions, chemists have learned a great deal about the factors that determine which mechanism will be observed when a given alkyl halide undergoes such a reaction.

9.1: Introduction
9.2: The Discovery of Nucleophilic Substitution Reactions
9.3: The SN2 Reaction
9.4: Characteristics of the SN2 Reaction
9.5: The SN1 Reaction
9.6: Characteristics of the SN1 Reaction
9.7: Biological Substitution Reactions
9.8: Elimination Reactions- Zaitsev's Rule
9.9: The E2 Reaction and the Deuterium Isotope Effect
9.10: The E2 Reaction and Cyclohexane Conformation
9.11: The E1 and E1cB Reactions
9.12: Biological Elimination Reactions
9.13: A Summary of Reactivity - SN1, SN2, E1, E1cB, and E2

9: Reactions of Alkyl Halides- Nucleophilic Substitutions and Eliminations is shared under a CC BY-SA 4.0 license and was authored, remixed, and/or curated by Steven Farmer & Dietmar Kennepohl.

9.1: Introduction

Objective

After completing this section, you should be able to identify substitution and elimination as being the two most important reactions of alkyl halides.

Study Notes

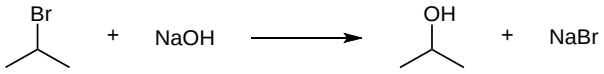
Alkyl halides are electrophiles, which means they can undergo nucleophilic substitution and base-induced elimination reactions. These reaction types offer a large and useful range of reactions for organic synthesis in the laboratory.

The Reactions

Two reactions are shown her with both involving heating a halogenoalkane under reflux with sodium or potassium hydroxide solution. Two different reactions can occur.

Nucleophilic substitution

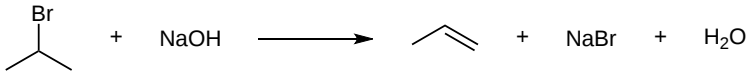
The hydroxide ions present are good nucleophiles, and one possibility is a replacement of the halogen atom by an -OH group to give an alcohol via a nucleophilic substitution reaction.



In the example, 2-bromopropane is converted into propan-2-ol.

Elimination

Hydroxide ions are also strong bases, therefore halogenoalkanes also undergo elimination reactions in the presence of sodium or potassium hydroxide.



In this reaction, the 2-bromopropane has reacted to form an alkene - propene.

Notice that a hydrogen atom has been removed from one of the end carbon atoms together with the bromine from the centre one. In all simple elimination reactions the things being removed are on adjacent carbon atoms, and a double bond is set up between those carbons.

What decides whether you get substitution or elimination?

The reagents you are using are the same for both substitution or elimination - the halogenoalkane and either sodium or potassium hydroxide solution. In all cases, you will get a mixture of both reactions happening - some substitution and some elimination. What you get most of depends on a number of factors.

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9.2: The Discovery of Nucleophilic Substitution Reactions

Objectives

After completing this section, you should be able to

1. write an equation to represent the Walden inversion.
2. write a short paragraph describing the Walden inversion.
3. describe, using equations, a series of reactions interconverting two enantiomers of 1-phenyl-2-propanol which led to the conclusion that nucleophilic substitution of primary and secondary alkyl halides proceeds with inversion of configuration.

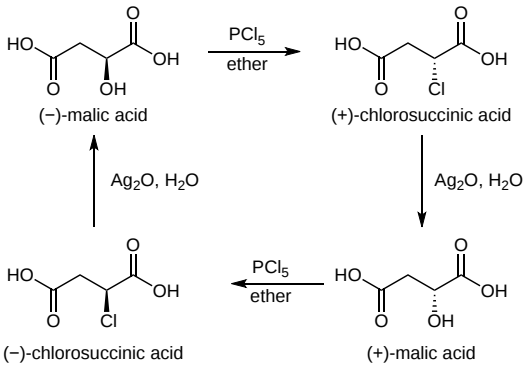
Study Notes

The IUPAC name for malic acid is 2-hydroxybutanedioic acid. This acid is produced by apples, a fact which seems to have been appreciated by the British novelist Thomas Hardy in *The Woodlanders*:

Up, upward they crept, a stray beam of the sun alighting every now and then like a star on the blades of the pomace-shovels, which had been converted to steel mirrors by the action of the malic acid.

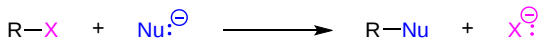
In 1896, the German chemist Paul Walden discovered that he could interconvert pure enantiomeric (+) and (-) malic acids through a series of reactions. This conversion meant that there was some kind of change in the stereochemistry made during the series of reactions. First, (−)-malic acid was reacted with **phosphorus pentachloride (PCl_5)** to provide (+)-chlorosuccinic acid.

This was reacted with **silver(I)oxide (Ag_2O)** to provide (+)-malic acid. These two combined steps caused an inversion of stereochemistry of (−)-malic acid to (+)-malic acid. The reaction series was then continued to convert (+)-malic acid back into (−)-malic acid by further reaction with PCl_5 and Ag_2O.

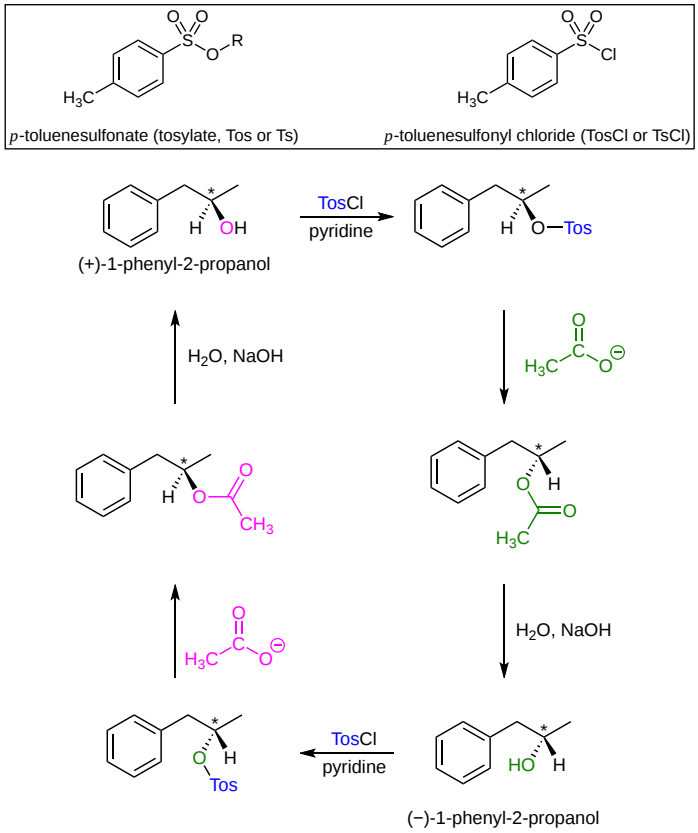


These results were considered astonishing. The fact that (−)-malic acid was converted into (+)-malic acid meant that the configuration of the chiral center has somehow been changed during the reaction series.

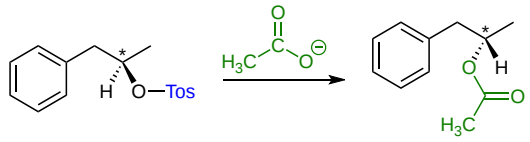
These reactions are currently referred to as nucleophilic substitution reactions because each step involves the substitution of one nucleophile by another. These are among the most common and versatile reaction types in organic chemistry.



Further investigations into these reaction were undertaken during the 1920's and 1930's to clarify the mechanism and clarify how the inversion of configurations occur. These reactions involved nucleophilic substitution of an alkyl p-toluenesulfonate (called a tosylate group). For this purpose the tosylate groups act similarly to a halogen substituent. In the series of reactions (+)-1-phenyl-2-propanol is interconverted with (-)-1-phenyl-2-propanol.



Somewhere in this three-step series of reactions the configuration at a chiral center is being inverted. In the first step the tosylate is formed without breaking the C-O bond of the chiral center, which means the configuration is unchanged. Similarly, the cleavage of the ester in step three occurs without breaking the C-O bond of the chiral center, which also means the configuration of the chiral carbon is unaffected. It was determined that the second step where acetate nucleophile undergoes a substitution with tosylate was causing the stereochemical configuration to be inverted.



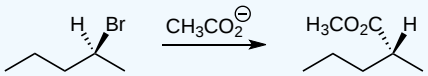
inversion of configuration

Exercise 9.2.1

1) Predict the product of a nucleophilic substitution of (S)-2-bromopentane reacting with $CH_3CO_2^-$, Show stereochemistry.

Answer

1)



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9.3: The SN2 Reaction

Objectives

After completing this section, you should be able to

1. write an expression relating reaction rate to the concentration of reagents for a second-order reaction.
2. determine the order of a chemical reaction from experimentally obtained rate data.
3. describe the essential features of the S_N2 mechanism, and draw a generalized **transition state** for such a reaction.

Key Terms

Make certain that you can define, and use in context, the key terms below.

- bimolecular
- kinetics
- rate coefficient
- rate equation
- reaction rate
- second-order reaction
- S_N2

Study Notes

Most of the key terms introduced in this section should already be familiar to you from your previous general chemistry course.

Reaction rate refers to the change in concentration of a reactant or product per unit of time. Using strict SI units, reaction rates are expressed in mol $\cdot$ L^{-1} $\cdot$ s^{-1}, but in some textbooks you will find this value written as M/s. In general, the reaction rate of a given reaction changes with time, as it is dependent on the concentration of one or more of the reactants.

An equation which shows the relationship between the reaction rate and the concentrations of the reactants is known as the rate equation. All rate equations contain a proportionality constant, usually given the symbol *k*, which is known as the rate coefficient. Some textbooks refer to this value as the "rate constant," but this name is a little misleading as it is not a true constant. The rate coefficient of a given reaction depends on such factors as temperature and the nature of the solvent.

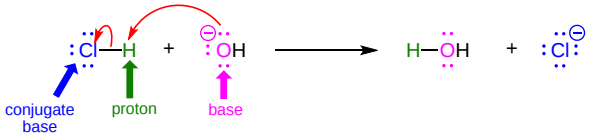
S_N2 is short for "bimolecular nucleophilic substitution." You will encounter abbreviations for other types of reactions later in this chapter.

If you are unclear on the point about the inversion of configuration during an S_N2 reaction, construct a molecular model of a chiral alkyl halide, the **transition state** formed when this substance reacts with a nucleophile in an S_N2 process, and the product obtained from this reaction.

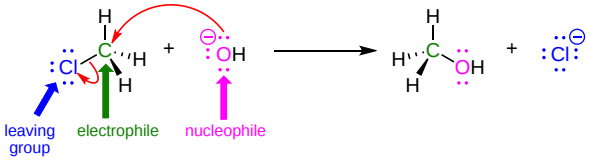
Brønsted-Lowry acid-base reactions

In many ways, the proton transfer process in a Brønsted-Lowry acid-base reaction can be thought of as simply a special kind of nucleophilic substitution reaction, one in which the electrophile is a hydrogen rather than a carbon.

Acid-base reaction:

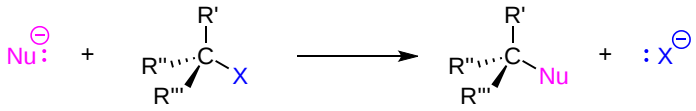


Nucleophilic substitution:



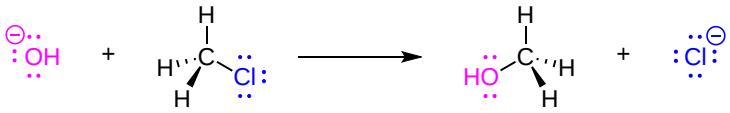
In both reaction types, we are looking at very similar players: an electron-rich species (the nucleophile/base) attacks an electron-poor species (the electrophile/proton), driving off the leaving group/conjugate base. Instead of showing a specific nucleophile like hydroxide, we will simply refer to the nucleophilic reactant as 'Nu'. In a similar fashion, we will call the leaving group 'X'. We will see as we study actual reactions that leaving groups are sometimes negatively charged, sometimes neutral, and sometimes positively charged. We will also see some examples of nucleophiles that are negatively charged and some that are neutral. Therefore, in this general picture we will not include a charge designation on the 'X' or 'Nu' species. We will generalize the three other groups bonded on the electrophilic central carbon as R_1, R_2, and R_3: these symbols could represent hydrogens as well as alkyl groups. Here, then, is the generalized picture of a concerted (single-step) nucleophilic substitution reaction.

General S_N2 Reaction



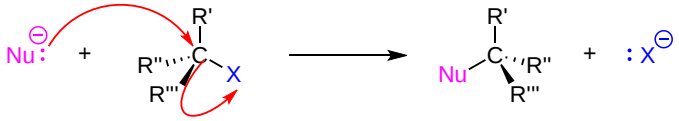
R = alkyl or H

Example



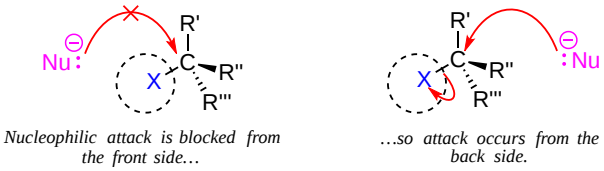
The S_N2 Mechanism

Bimolecular nucleophilic substitution (S_N2) reactions are **concerted**, meaning they are a **one step process**. This means that the process whereby the nucleophile attacks and the leaving group leaves is simultaneous. Hence, the bond-making between the nucleophile and the electrophilic carbon occurs at the same time as the bond-breaking between the electrophilic carbon and the halogen. This is called an '**S_N2**' mechanism. In the term S_N2, S stands for 'substitution', the subscript N stands for 'nucleophilic', and the number 2 refers to the fact that this is a **bimolecular reaction**: the overall rate depends on a step in which two separate molecules (the nucleophile and the electrophile) collide. The mechanism starts when lone pair electrons from the nucleophile attacks the electrophilic carbon of the alkyl halide to form a C-Nu sigma bond. Simultaneously, X-C bond is broken when the electrons are pushed onto the leaving group. Overall during this mechanism, a set of lone pair electrons are transferred from the nucleophile to the leaving groups.



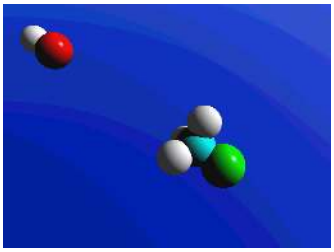
If you look carefully at the progress of the S_N2 reaction, you will realize something very important about the outcome. The nucleophile, being an electron-rich species, must attack the electrophilic carbon from the *back side* relative to the location of the

leaving group. Approach from the front side simply doesn't work: the leaving group - which is also an electron-rich group - blocks the way.

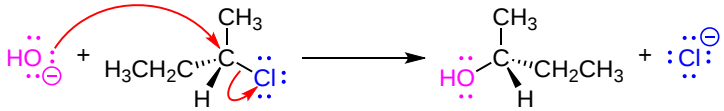


The result of this backside attack is that the stereochemical configuration at the central carbon *inverts* as the reaction proceeds. In a sense, the molecule is turned inside out. S_N2 reactions that begin with the R enantiomer as the substrate will form the S enantiomer as the product. Those that begin with the S enantiomer as the substrate will form the R enantiomer as the product. This concept also applies to substrates that are *cis* and substrates that are *trans*. If the *cis* configuration is the substrate, the resulting product will be *trans*. Conversely, if the *trans* configuration is the substrate, the resulting product will be *cis*.

What this means is that S_N2 reactions whether enzyme catalyzed or not, are inherently stereoselective: when the substitution takes place at a stereocenter, we can confidently predict the stereochemical configuration of the product. Below is an animation illustrating the principles we have just learned, showing the S_N2 reaction between hydroxide ion and methyl iodide. Notice how backside attack by the hydroxide nucleophile results in inversion at the tetrahedral carbon electrophile.



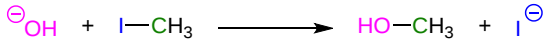
Example



(*S*)-2-chlorobutane (*R*)-2-butanol

Bimolecular Nucleophilic Substitution Reactions and Kinetics

In the term S_N2, (as previously stated) the number two stands for bimolecular, meaning there are two molecules involved in the rate determining step. The rate of bimolecular nucleophilic substitution reactions depends on the concentration of both the haloalkane and the nucleophile. To understand how the rate depends on the concentrations of both the haloalkane and the nucleophile, let us look at the following example. The hydroxide ion is the nucleophile and methyl iodide is the haloalkane.



Rate = k [CH_3–I] [$^{\ominus}OH$]

If we were to double the concentration of either the haloalkane or the nucleophile, we can see that the rate of the reaction would proceed twice as fast as the initial rate.

$$\text{Rate}_1 = k\,[CH_3\text{–}I]\,[^{\ominus}OH]$$
$$\text{Rate}_2 = 2k\,[CH_3\text{–}I]\,[^{\ominus}OH]$$
$$\text{Rate}_2 = 2\text{Rate}_1$$

If we were to double the concentration of both the haloalkane and the nucleophile, we can see that the rate of the reaction would proceed four times as fast as the initial rate.

$$\text{Rate}_1 = k\,[CH_3{-}I]\,[^{\ominus}OH]$$
$$\text{Rate}_2 = 4k\,[CH_3{-}I]\,[^{\ominus}OH]$$
$$\text{Rate}_2 = 4\text{Rate}_1$$

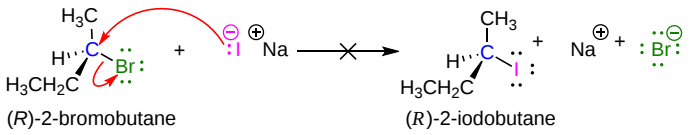
The bimolecular nucleophilic substitution reaction follows second-order kinetics; that is, the rate of the reaction depends on the concentration of two first-order reactants. In the case of bimolecular nucleophilic substitution, these two reactants are the haloalkane and the nucleophile. For further clarification on reaction kinetics, the following links may facilitate your understanding of rate laws, rate constants, and second-order kinetics:

- Definition of a Reaction Rate
- Rate Laws and Rate Constants
- The Determination of the Rate Law
- Second-Order Reactions

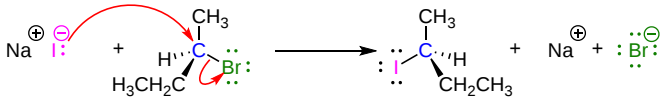
S_N2 Reactions Are Stereospecific

The S_N2 reaction is stereospecific. A stereospecific reaction is one in which different stereoisomers react to give different stereoisomers of the product. For example, if the substrate is an (*R*) enantiomer, a frontside nucleophilic attack results in retention of configuration, and the formation of the (*R*) enantiomer. A backside nucleophilic attack results in inversion of configuration, and the formation of the (*S*) enantiomer.

Frontside attack with retention of configuration:

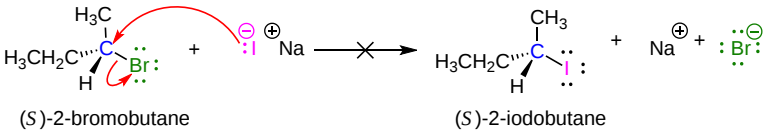


Backside attack with inversion of configuration:

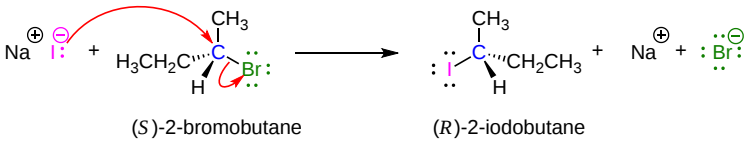


Conversely, if the substrate is an (*S*) enantiomer, a frontside nucleophilic attack results in retention of configuration, and the formation of the (*S*) enantiomer. A backside nucleophilic attack results in inversion of configuration, and the formation of the (*R*) enantiomer.

Frontside attack with retention of configuration:



Backside attack with inversion of configuration:

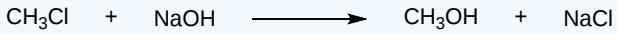


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In conclusion, S_N2 reactions that begin with the (*R*) enantiomer as the substrate will form the (*S*) enantiomer as the product. Those that begin with the (*S*) enantiomer as the substrate will form the (*R*) enantiomer as the product. This concept also applies to substrates that are *cis* and substrates that are *trans*. If the *cis* configuration is the substrate, the resulting product will be *trans*. Conversely, if the *trans* configuration is the substrate, the resulting product will be *cis*.

? Exercise 9.3.1

1) The reaction below follows the S_N2 mechanism.



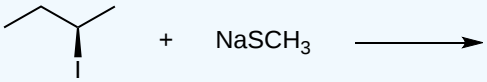
a) Write the rate law for this reaction.

b) Determine the value of the rate coefficient, k, if the initial concentrations are 0.01 M CH_3Cl, 0.01 M NaOH, and the initial reaction rate is 6 x 10^{-10} M/s.

c) Calculate the initial reaction rate if the initial reactant concentrations are changed to 0.02 M CH_3Cl and 0.0005 M NaOH.

2) Predict the product of a nucleophilic substitution of (S)-2-bromopentane reacting with $CH_3CO_2^-$, Show stereochemistry.

3) Predict the structure of the product in this S_N2 reaction. Be sure to specify stereochemistry.



4) Since everything is relative in chemistry, one reaction's nucleophile can be another reaction's leaving group. Some functional groups can only react as a nucleophile or electrophile, while other functional groups can react as either a nucleophile or electrophile depending on the reaction conditions. Classify the following compounds as nucleophile, electrophile, or leaving groups. More than one answer may be possible.

a) bromoethane

b) hydroxide

c) water

d) chlorocyclohexane

e) ethanol

f) bromide

Answer

1) a) rate = k [CH_3Cl] [OH^-]

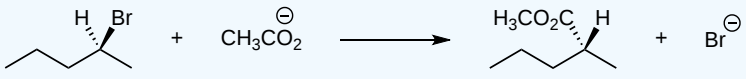
b) substitute the data into the rate expression above and apply algebra to solve for k

k = 6 x 10^{-6} $Lmol^{-1}s^{-1}$

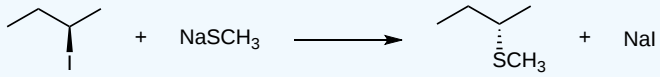
c) Using the rate law above, substitute the value for k from the previous question along with the new concentrations to determine the new initial rate.

rate = 6 x 10^{-10} M/s

2)



3)



4)

a) electrophile (Alkyl halides are always electrophiles - one reason they are an o-chem student's best friend.)

b) strong nucleophile

c) weak nucleophile and good leaving group

d) electrophile (Alkyl halides are always electrophiles - one reason they are an o-chem student's best friend.)

e) weak nucleophile, a poor electrophile without clever chemistry (stay tuned for future chapters), good leaving group

f) good nucleophile and a good leaving group

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9.4: Characteristics of the SN2 Reaction

Objectives

After completing this section, you should be able to

1. discuss the role of steric effects in S_N2 reactions.
2. arrange a given series of alkyl halides in order of increasing or decreasing reactivity towards nucleophilic substitution through the S_N2 mechanism.
3. suggest a reason why vinyl halides and aryl halides do not undergo S_N2 reactions.
4. discuss how the nature of the nucleophile affects the rate of an S_N2 reaction.
5. arrange a given series of common nucleophiles (e.g., CN^-, I^-, Br^- Cl^-, H_2O) in order of increasing or decreasing nucleophilicity.
6. discuss how the nature of the leaving group affects the rate of an S_N2 reaction.
7. arrange a given series of leaving groups in order of increasing or decreasing ability to leave during an S_N2 reaction.
8. discuss the role played by the solvent in an S_N2 reaction.
9. give examples of the solvents which are commonly used for S_N2 reactions, and identify those that promote a high reaction rate.
10. predict which of two given S_N2 reactions will proceed faster, by taking into account the structure of the substrates, the nucleophiles involved, leaving-group ability, solvent effects, or any combination of these factors.

Key Terms

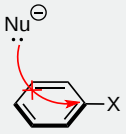
Make certain that you can define, and use in context, the key terms below.

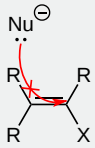
- leaving group
- polar aprotic solvent
- solvation

Study Notes

You may wish to review the discussion of acid-base theory given in Sections 2.7-2.11.

Both aryl and vinylic halides are relatively unreactive in S_N2 displacement mechanisms, mostly because during the backside attack of the molecule the incoming nucleophile is sterically hindered by both substituents and electron density from any double bonds present. Also, leaving groups on sp^2-hybridized carbons tend to be held tighter than sp^3-hybridized carbons.

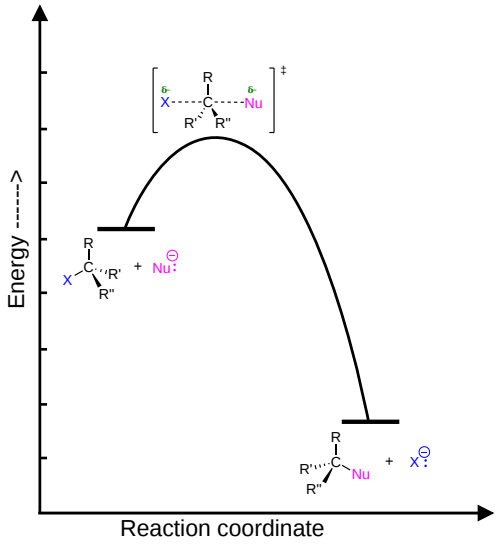




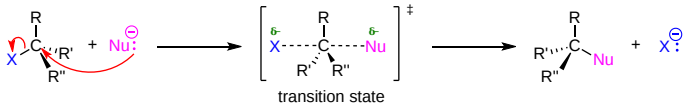
Solvation may be defined as the interaction between molecules of solvent and particles of solute. The result of solvation is to stabilize (i.e., lower the energy of) the solute particles. Solvents with lone pairs of electrons are good at solvating cations. Protic (i.e., hydroxylic) solvents are able to solvate anions through hydrogen bonding. As water has two lone pairs of electrons and is also protic, it is good at solvating both anions and cations.

Potential Energy Diagram for an S_N2 Reaction

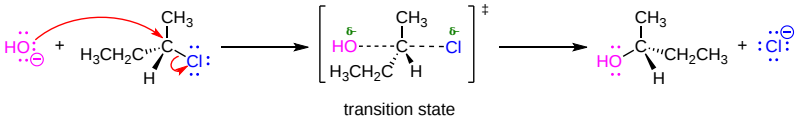
The potential energy diagram for an S_N2 reaction is shown below. This is a single-step, concerted process so a single transition state is formed. A transition state, unlike a reaction intermediate, is a very short-lived species that cannot be isolated or directly observed. For an S_N2 reaction the transition state directly determines the energy of activation which must be overcome for the reaction to occur. Factors which affect the stability of the transition state affect the rate of the S_N2 reaction.



For an S_N2 reaction, the transition state represents the half way point of the reaction. The C-Nu bond is in the process of forming and is represented by a dashed bond. The X-C bond is in the process of breaking and is also represented by a dash bond. The negative charge of the nucleophile is in the process of being transfered to the leaving groups. This is represented by both the nucleophile and the leaving group having a partial negative charge. The electrophilic carbon and the three 'R' substituents all lie on the same plane. Brackets and a double-dagger are placed around the structure to represent that it is a transition state.

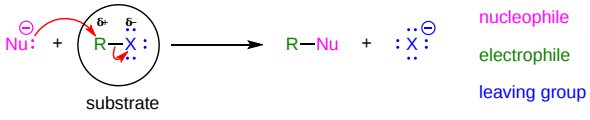


Example

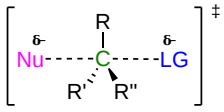


Sterically Hindered Substrates Will Reduce the S_N2 Reaction Rate

Steric hindrance about the electrophilic carbon, is one of the most important factors Determining the rate of S_N2 reactions. Although the substrate, in the case of nucleophilic substitution of haloalkanes, is considered to be the entire molecule circled below we are most interested in the electrophilic carbon that bears the leaving group.



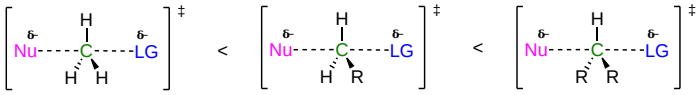
The S_N2 **transition state** is very crowded. Recall that there are a total of five groups around the electrophilic center, the nucleophile, the leaving group, and three substituents.



S_N2 Transition State

If each of the three substituents were hydrogen atoms, as illustrated in the first example below, there would be little steric repulsion created in the planar portion of the transition state thereby increasing the ease at which the nucleophilic substitution reaction occurs. If one of the hydrogens, however, were replaced with an R group, such as a methyl or ethyl group, there would be an increase in steric repulsion created in the planar portion of the transition state. If two of the hydrogens were replaced by R groups, there would be an even greater increase in steric repulsion in the transition state.

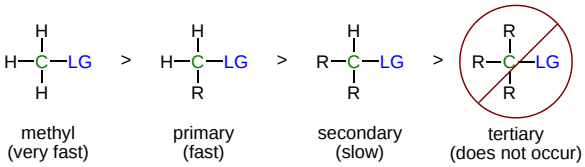
Steric repulsion of S_N2 Transition States



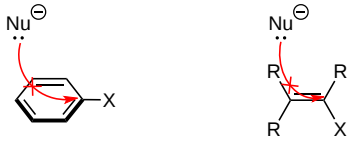
How does steric hindrance affect the rate at which an S_N2 reaction will occur? As each hydrogen is replaced by an R group, the rate of reaction is significantly diminished. The increases steric hindrance destabilizes the transition state causing it to become higher in energy. This in turn increases the energy of activation and decreases the reaction rate.

The diagram below illustrates this concept, showing that electrophilic carbons attached to three hydrogen atoms results in faster nucleophilic substitution reactions, in comparison to primary and secondary haloalkanes, which result in nucleophilic substitution reactions that occur at slower or much slower rates, respectively. Notice that a tertiary haloalkane, that which has three R groups attached, does not undergo nucleophilic substitution reactions at all. The addition of a third R group to this molecule creates a carbon that is entirely blocked.

S_N2 Displacement Reactivity of Haloalkanes



Vinyl and aryl halides are unreactive toward S_N2 displacement due to extreme steric factors. To perform an S_N2 reaction, the incoming nucleophile would have to enter the plane of the C-C double bond and move through the molecule to achieve the backside displacement required.



In addition to alkyl groups being added to the electrophilic carbon, it turns out that the addition of substitutes on neighboring carbons will slow nucleophilic substitution reactions as well.

In the example below, 1-bromo-2-methylpropane differs from 1-bromopropane in that it has a methyl group attached to the carbon that neighbors the electrophilic carbon. The addition of this methyl group results in a significant decrease in the rate of a nucleophilic substitution reaction.



1-bromo-2-methylpropane 1-bromopropane

If R groups were added to carbons farther away from the electrophilic carbon, we would still see a decrease in the reaction rate. However, branching at carbons farther away from the electrophilic carbon would have a much smaller effect.

The Nucleophile

Nucleophilic functional groups are those which have electron-rich atoms able to donate a pair of electrons to form a new covalent bond. In both laboratory and biological organic chemistry, the most relevant nucleophilic atoms are oxygen, nitrogen, and sulfur,

and the most common nucleophilic functional groups are water, alcohols, phenols, amines, thiols, and occasionally carboxylates.

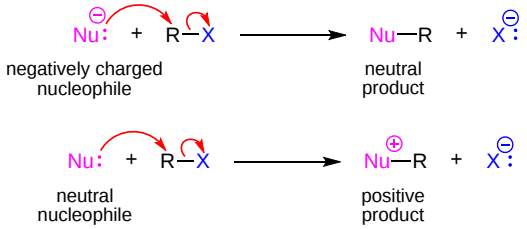
When thinking about nucleophiles, the first thing to recognize is that, for the most part, the same quality of 'electron-richness' that makes a something nucleophilic also makes it basic: *nucleophiles can be bases, and bases can be nucleophiles*. It should not be surprising, then, that most of the trends in basicity that we have already discussed also apply to nucleophilicity.

Some confusion in distinguishing basicity (base strength) and nucleophilicity (nucleophile strength) is inevitable. Since basicity is a less troublesome concept; it is convenient to start with it. Basicity refers to the ability of a base to accept a proton. Basicity may be related to the pK_a of the corresponding conjugate acid, as shown below. The strongest bases have the weakest conjugate acids and vice versa. The range of basicities included in the following table is remarkable, covering over fifty powers of ten! In general, as the pKa of the conjugate acid increases the base becomes a stronger nuclophile. This, however, is not always the case.

Base	$I^{(-)}$	$Cl^{(-)}$	H_2O	$CH_3CO_2^{(-)}$	$RS^{(-)}$	$CN^{(-)}$	$RO^{(-)}$	$NH_2^{(-)}$	$CH_3^{(-)}$
Conj. Acid	HI	HCl	$H_3O^{(+)}$	CH_3CO_2H	RSH	HCN	ROH	NH_3	CH_4
pK_a	-9	-7	0.0	4.8	8	9.1	16	33	48

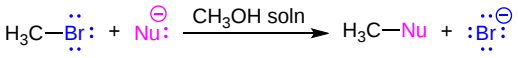
increasing base strength

Nucleophilicity is a more complex property. Any compound, neutral or charged, which has lone pair electrons can act a neuclophile. After a S_N2 reaction neutral nucleophiles make a positively charges products and negatively charged nucleophiles make neutral products. In general, negatively charges compound tend to make better nucleophilies.



Specifically, nucleophilicity refers to the rate of substitution reactions at the halogen-bearing **carbon atom** of a reference alkyl halide, such as CH_3-Br. The nucleophilicity of the $Nu:^{(-)}$ reactant in the following substitution reaction varies as shown in the chart below:

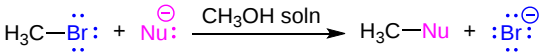
Nucleophilicity is a more complex property. It commonly refers to the rate of substitution reactions at the halogen-bearing **carbon atom** of a reference alkyl halide, such as CH_3-Br. Thus the nucleophilicity of the $Nu:^{(-)}$ reactant in the following substitution reaction varies as shown in the chart below:



Nucleophilicity: $H_2O < CH_3CO_2^{(-)} < NH_3 < Cl^{(-)} < Br^{(-)} < HO^{(-)} < CH_3O^{(-)} < I^{(-)} < CN^{(-)} < CH_3S^{(-)}$

increasing nucleophile strength

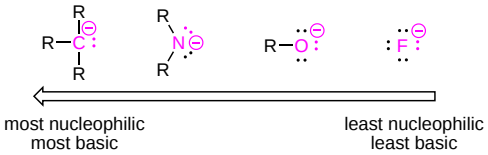
The versatility of the S_N2 reaction is shown by the wide variety of functional groups which can be formed.



Nucleophile		Products		
Formula	**Name**	**Formula**	**Name**	**Functional Group**
$CH_3S^{(-)}$	Methanethiolate	**CH_3SCH_3**	Dimethylsulfide	Sulfide
$CN^{(-)}$	Cyanide	**CH_3CN**	Acetonitrile	Nitrile
$I^{(-)}$	Iodide	**CH_3I**	Iodomethane	Alkyl Halide
$CH_3O^{(-)}$	Methoxide	**CH_3OCH_3**	Diethylether	Ether
$HO^{(-)}$	Hydroxide	**CH_3OH**	Methanol	Alcohol
$Br^{(-)}$	Bromide	**CH_3Br**	Bromomethane	Alkyl Halide
$Cl^{(-)}$	Chloride	**CH_3Cl**	Chloromethane	Alkyl Halide
NH_3	Ammonia	**$CH_3NH_3^{(+)}$**	Methylammonium ion	Ammonium
$CH_3CO_2^{(-)}$	Acetate	**$CH_3O_2CH_3$**	Methyl acetate	Ester
H_2O	Water	**$CH_3OH_2^{(+)}$**	Methylhydronium ion	Protonated Alcohol

Periodic Trends in Nucleophilicity

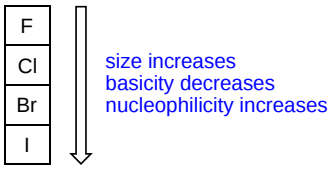
There are predictable periodic trends in nucleophilicity. Moving horizontally across the second row of the table, the trend in nucleophilicity parallels the trend in basicity:



The reasoning behind the horizontal nucleophilicity trend is the same as the reasoning behind the basicity trend: more electronegative elements hold their electrons more tightly, and are less able to donate them to form a new bond. This horizontal trend also tells us that amines are more nucleophilic than alcohols, although both groups commonly act as nucleophiles in both laboratory and biochemical reactions.

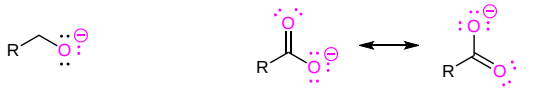
Recall that the basicity of atoms decreases as we move vertically down a column on the periodic table: thiolate ions are less basic than alkoxide ions, for example, and bromide ion is less basic than chloride ion, which in turn is less basic than fluoride ion. Recall also that this trend can be explained by considering the increasing size of the 'electron cloud' around the larger ions: the electron density inherent in the negative charge is spread around a larger area, which tends to increase stability (and thus reduce basicity).

As Size Increases, Basicity Decreases: In general, if we move from the top of the periodic table to the bottom of the periodic table as shown in the diagram below, the size of an atom will increase. As size increases, basicity will decrease, meaning a species will be less likely to act as a base; that is, the species will be less likely to share its electrons and act as a nucleophile.



Resonance Effects on Nucleophilicity

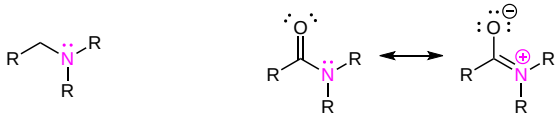
Resonance effects also come into play when comparing the inherent nucleophilicity of different molecules. The reasoning involved is the same as that which we used to understand resonance effects on basicity. If the electron lone pair on a heteroatom is delocalized by resonance, it is inherently less reactive - meaning less nucleophilic, and also less basic. An alkoxide ion, for example, is more nucleophilic and more basic than a carboxylate group, even though in both cases the nucleophilic atom is a negatively charged oxygen. In the alkoxide, the negative charge is localized on a single oxygen, while in the carboxylate the charge is delocalized over two oxygen atoms by resonance.



alkoxide ion
charge is localized on oxygen
more nucleophilic

carboxylate ion
charge is delocalized over both oxygens
less nucleophilic

The nitrogen atom on an amide is less nucleophilic than the nitrogen of an amine, due to the resonance stabilization of the nitrogen lone pair provided by the amide carbonyl group.



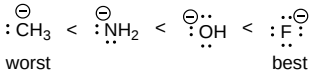
amine
more nucleophilic

amide
less nucleophilic

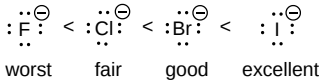
The Leaving Group

As Electronegativity Increases, The Ability of the Leaving Group to Leave Increases

As mentioned previously, if we move from left to right on the periodic table, electronegativity increases. With an increase in electronegativity, basicity decreases, and the ability of the leaving group to leave increases. This is because an increase in electronegativity results in a species that wants to hold onto its electrons rather than donate them. The following diagram illustrates this concept, showing $^{-}CH_3$ to be the worst leaving group and F^- to be the best leaving group. This particular example should only be used to facilitate your understanding of this concept. In real reaction mechanisms, these groups are not good leaving groups at all. For example, fluoride is such a poor leaving group that S_N2 reactions of fluoroalkanes are rarely observed.



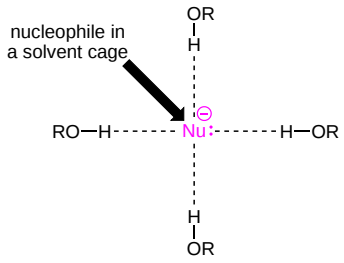
As Size Increases, The Ability of the Leaving Group to Leave Increases: Here we revisit the effect size has on basicity. If we move down the periodic table, size increases. With an increase in size, basicity decreases, and the ability of the leaving group to leave increases. The relationship among the following halogens, unlike the previous example, is true to what we will see in upcoming reaction mechanisms.



Influence of the Solvent in an S_N2 Reaction

The rate of an S_N2 reaction is significantly influenced by the solvent in which the reaction takes place. The use of **protic solvents** (those, such as water or alcohols, with hydrogen-bond donating capability) decreases the power of the nucleophile, because of

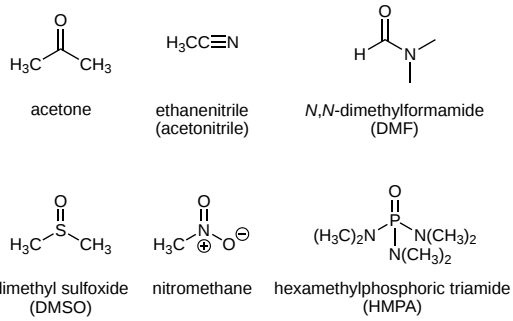
strong hydrogen-bond interactions between solvent protons and the reactive lone pairs on the nucleophile. Protic solvent molecules form very strong ion-dipole interactions with the negatively-charged nucleophile, essentially creating a 'solvent cage' around the nucleophile. In order for the nucleophile to attack the electrophile, it must break free, at least in part, from its solvent cage. A less powerful nucleophile in turn means a slower S_N2 reaction. S_N2 reactions are faster in **polar, aprotic solvents:** those that lack hydrogen-bond donating capability.



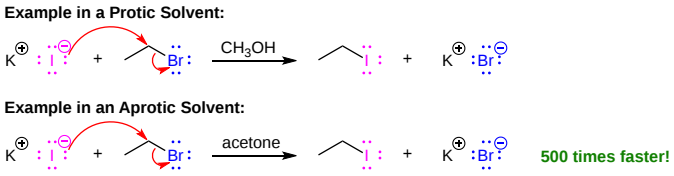
Why not use a completely nonpolar solvent, such as hexane, for this reaction, so that the solvent cage is eliminated completely? The answer to this is simple - the nucleophile needs to be in solution in order to react at an appreciable rate with the electrophile, and a solvent such as hexane will not solvate an a charged (or highly polar) nucleophile at all. That is why chemists use polar aprotic solvents for nucleophilic substitution reactions in the laboratory: they are polar enough to solvate the nucleophile, but not so polar as to lock it away in an impenetrable solvent cage. In addition to acetone, three other commonly used polar aprotic solvents are acetonitrile, dimethylformamide (DMF), and dimethyl sulfoxide (DMSO).

Below are several polar aprotic solvents that are commonly used in the laboratory:

Polar Aprotic Solvents



These aprotic solvents are polar but, because they do not form hydrogen bonds with the anionic nucleophile, there is a relatively weak interaction between the aprotic solvent and the nucleophile. By using an aprotic solvent we can raise the reactivity of the nucleophile. This can sometimes have dramatic effects on the rate at which a nucleophilic substitution reaction can occur. For example, if we consider the reaction between bromoethane and potassium iodide, the reaction occurs 500 times faster in acetone than in methanol.



Summary of Factors in Affecting S_N2 Reactions

There are four main factors which affect S_N2 reaction:

1) The structure of the alkyl portion of the substrate: S_N2 reactions are affected by steric hindrance around the electrophilic carbon. As steric hindrance increases the rate of S_N2 reactions decrease. Methyl and primary substrates work well for S_N2 reactions, secondary substrates react slowly, and teritary substrates do not undergo S_N2 reactions at all.

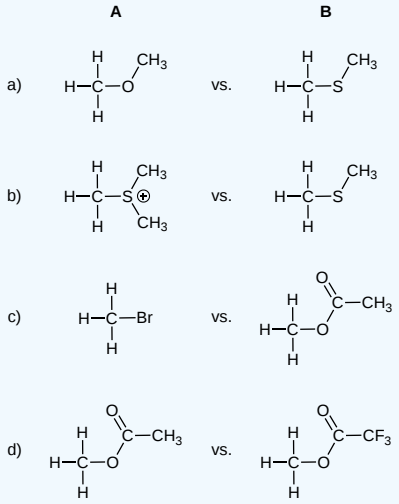
2) The reactivity of the nucleophile: The rate of S_N2 reaction is increased when strong nucleophiles are used. Strong nucleophiles tend to be negatively charged and good bases. Also, being of an increases size tends to increase the nucleopihlicity of an atom.

3) The nature of the leaving group: The rate of S_N2 reaction is increased when leaving groups are used in the substrate. Good leaving groups tend to stabilize the electrons gained during an S_N2 reaction. High electronegativity, resonance, and an increases size all can stabilize electrons.

4) The solvent: S_N2 reaction are severely hindered when a polar protic solvent is used for the reaction. Instead, polar aprotic solvents tend to be used for S_N2 reaction.

Example **9.4.1**

In each pair (A and B) below, which electrophile would be expected to react more rapidly in an S_N2 reaction with the thiol group of cysteine as the common nucleophile?



Solution (8.13)

? Exercise **9.4.1**

1) What product(s) do you expect from the reaction of 1-bromopentane with each of the following reagents in an S_N2 reaction?

a) KI

b) NaOH

c) $CH_3C{\equiv}C\text{-}Li$

d) NH_3

2)

Which in the following pairs is a better nuceophile?

a) $(CH_3CH_2)_2N^-$ or $(CH_3CH_2)_2NH$

b) $(CH_3CH_2)_3N$ or $(CH_3CH_2)_3B$

c) H_2O or H_2S

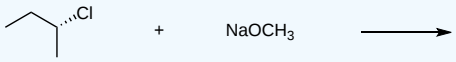
3) Order the following in increasing reactivity for an S_N2 reaction.

CH_3CH_2Br CH_3CH_2OTos $(CH_3CH_2)_3CCl$ $(CH_3CH_2)_2CHCl$

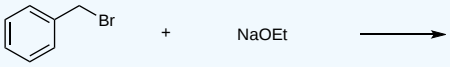
4) Solvents benzene, ether, chloroform are non-polar and not strongly polar solvents. What effects do these solvents have on an S_N2 reaction?

5) Predict the products of these nucleophilic substitution reactions, including stereochemistry when appropriate.

a)



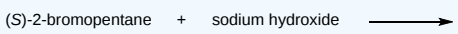
b)



d)

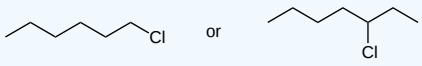


d)

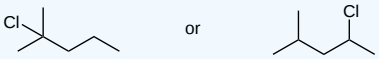


6) Predict which compound in each pair would undergo the S_N2 reaction faster.

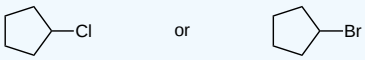
a)



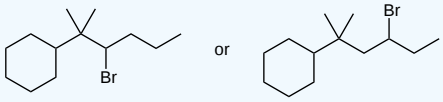
b)



c)

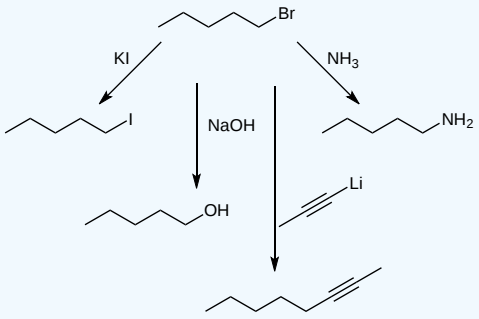


d)



Answer

1)



2)

a) $(CH_3CH_2)_2N^-$ as there is a charge present on the nitrogen.

b) $(CH_3CH_2)_3N$ because a lone pair of electrons is present.

c) H_2O as oxygen is more electronegative.

3)

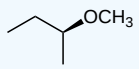
$(CH_3CH_2)_3CCl$ OR $(CH_3CH_2)_2CHCl < CH_3CH_2Br < CH_3CH_2OTos$

4) They will decrease the reactivity of the reaction.

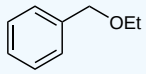
5)

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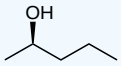
a)



b)

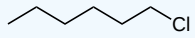


c) No reaction

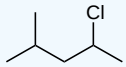
d) 

6)

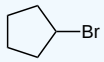
a)



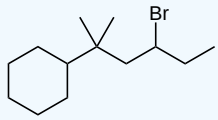
b)



c)



d)



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9.5: The SN1 Reaction

Objectives

After completing this section, you should be able to

- write an expression relating reaction rate and reactant concentration for a first-order reaction.
- compare the kinetics of S_N1 and S_N2 reactions.
- identify the rate-limiting step for a reaction, given the reaction energy diagram.
- sketch a reaction energy diagram for a reaction, given the mechanism and sufficient information to identify the rate-limiting step.
- write the mechanism of a typical S_N1 reaction, and discuss the important features of the mechanism.
- discuss the stereochemistry of an S_N1 reaction, and explain why a racemic mixture is expected when substitution takes place at the chiral carbon atom of an optically pure substrate.
- explain why unimolecular nucleophilic substitution at the chiral carbon atom of an optically pure substrate does not result in complete racemization.
- compare the stereochemical consequences of the S_N1 mechanism with those of the S_N2 mechanism.

Key Terms

Make certain that you can define, and use in context, the key terms below.

- first-order reaction
- rate-limiting step
- S_N1

Study Notes

You should recognize that certain compounds (notably tertiary alkyl halides) which react very slowly by the S_N2 mechanism can undergo rapid nucleophilic substitution by an alternative mechanism.

The abbreviation S_N1 refers to “unimolecular nucleophilic substitution.” In a *first-order reaction*, the rate of the reaction depends on the concentration of only one of the reactants. Thus, when an alkyl halide reacts by an S_N1 mechanism, the rate of reaction is dependent on the concentration of the alkyl halide, but is independent of the concentration of the attacking nucleophile.

Note: In many textbooks the “rate-limiting step” is called the “rate-determining step.”

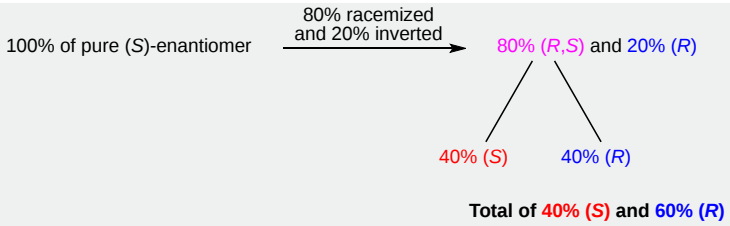
Racemization problems can be a potential source of confusion. Most students entering an introductory organic chemistry course have a reasonable background in mathematics, and feel comfortable if they have a formula or equation they can use in this type of situation. Thus, we recommend that you consider the following approach.

1. In a given mixture of enantiomers, let x = the fraction of the (+)-enantiomer, and $1 - x$ = the fraction of the (−)-enantiomer. [Remember that the fraction can be obtained by dividing the percentage by 100%.]
2. The observed $[\alpha]_D$ of the mixture is then given by:

   Observed $[\alpha]_D = x$ ($[\alpha]_D$ of the (+)-enantiomer)

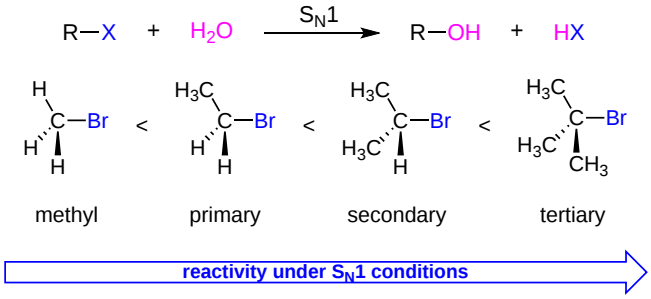
   + $(1 - x)$($[\alpha]_D$ of the (−)-enantiomer)

Another source of confusion is the way in which the terms “percentage racemization” and “percentage inversion” are used. To illustrate this idea, consider a given reaction that is said to be 80% racemized and 20% inverted. You must be clear in your mind that 80% racemized means that we have 40% of the original configuration and 60% (40% + 20%) of the inverted configuration. This point is illustrated in the diagram below.



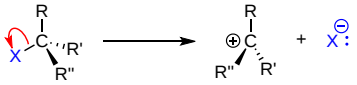
General S_N1 Reaction

When looking at the following substitution reaction it would be expected to be extremely slow. The reaction represents a worst case scenario based off the rules of an S_N2 reaction. The substrate is sterically hindered, the nucleophile is relatively weak, and the solvent is polar protic. However, the reaction proceeds quickly and prefers tertiary substrates over methyl, which is opposite to the trend seen in S_N2 reactions. It makes sense that this substitution reaction occurs using a different mechanism than S_N2.

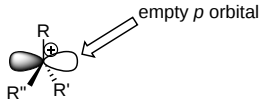


The S_N1 mechanism

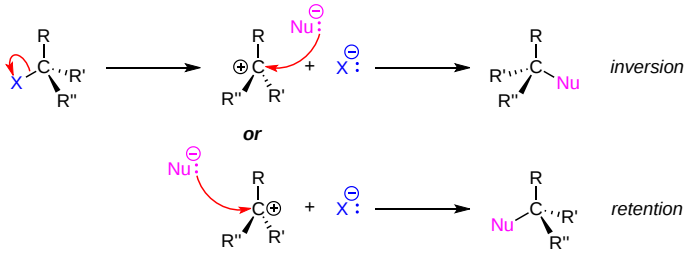
A second model for a nucleophilic substitution reaction is called the '**dissociative**', or '**S_N1**' mechanism. In the S_N1 reaction, the bond between the substrate and the leaving group is broken when the leaving group departs with the pair of electrons that formerly composed the bond.



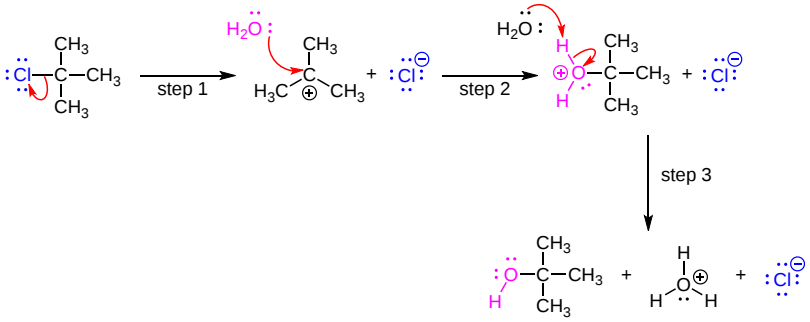
This results in the formation of a **carbocation** (from "carbon" and "cation") the word for a positively charged carbon atom. Because the carbocation has only three bonds, it bears a formal charge of +1. Recall that a carbocation is sp^2 hybridized, with trigonal planar geometry. The positive charge is contained in an empty, unhybridized *p* orbital perpendicular to the plane formed by the three sigma bonds. The formation of a carbocation is not energetically favored, so this step in the reaction is the slowest step and determines the overall rate of the reaction. The step which controls the overall rate of a reaction is called the **rate-determining step**.



In the second step of this two-step reaction, the nucleophile attacks the empty, 'electron hungry' *p* orbital of the carbocation to form a new bond and return the carbon to tetrahedral geometry. Since the nucleophile attacks the carbocation only after the leaving group has departed, there is no need for back-side attack. The carbocation and its substituents are all in the same plane, meaning that the nucleophile can attack from either side. As a result, both enantiomers are formed in an the S_N1 reaction, leading to a **racemic mixture** of both enantiomers.

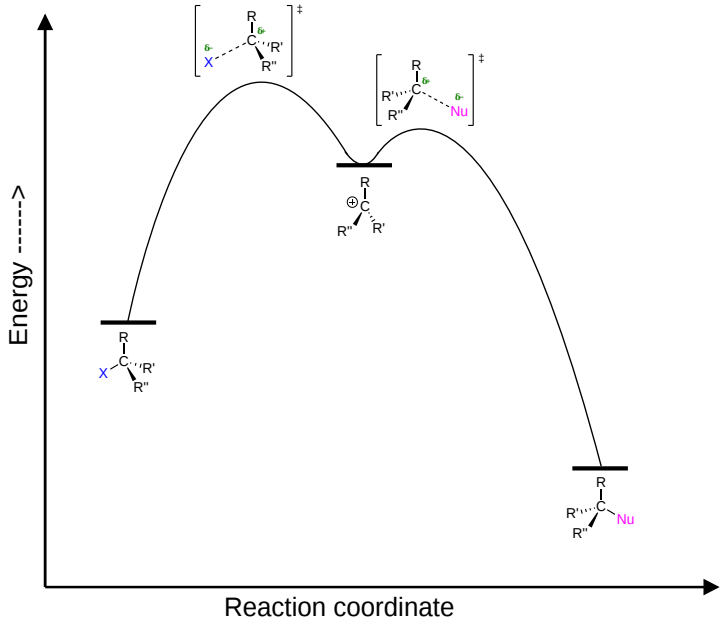


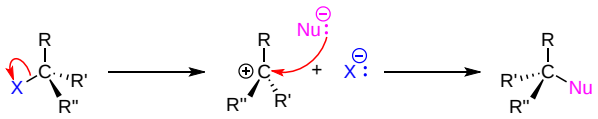
Because S_N1 reactions almost exclusively involve neutral nucleophile the product of this second step of the mechanism is often positively charged. The neutral substitution product is usually formed after a third, deprotonation step.



Reaction Coordinate Diagrams and S_N1 Mechanism

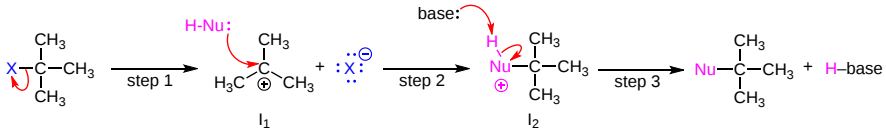
During the S_N1 reaction we see an example of a reaction intermediate, a very important concept in the study of organic reaction mechanisms that was introduced earlier in the module on organic reactivity Recall that many important organic reactions do not occur in a single step; rather, they are the sum of two or more discreet bond-forming / bond-breaking steps, and involve transient intermediate species that go on to react very quickly. In the S_N1 reaction, the carbocation species is a reaction intermediate. A potential energy diagram for an S_N1 reaction shows that the carbocation intermediate can be visualized as a kind of valley in the path of the reaction, higher in energy than both the reactant and product but lower in energy than the two transition states. The following reaction coordinate diagram shows an example of a an S_N1 reaction with a negatively charged nucleophile.



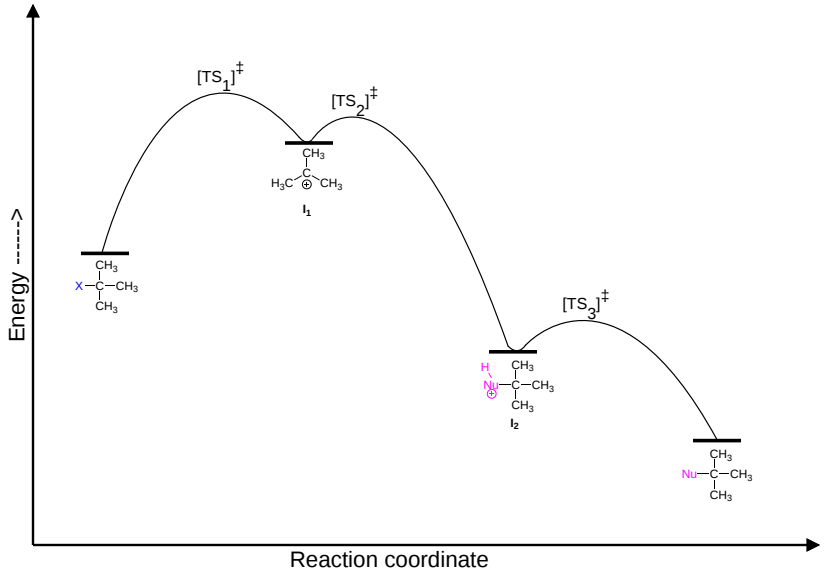


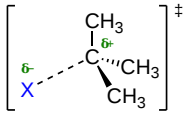
There are several important consequences to the **unimolecular** nature of the rate-determining step in the the S_N1 reaction. The first step (dissociation) is the rate determining step, so the rate is controlled only by the loss of the leaving group and does not involve any participation of the nucleophile. Therefore, the rate of the reaction is dependent only on the concentration of the substrate, not on the concentration of the nucleophile.

This can also be shown for the reactions with a neutral nucleophile which includes an extra step of deprotonation. A potential energy diagram for this mechanism shows that each of the two positively-charged intermediates (I_1 and I_2) can be visualized as a valley in the path of the reaction, higher in energy than both the reactant and product but lower in energy than the transition states. The first, bond-breaking step is the slowest, rate-determining step - notice it has the highest activation energy and leads to the highest-energy species, I_1, the carbocation intermediate. Step 2 is rapid: a new covalent bond forms between a carbocation and a water nucleophile, and no covalent bonds are broken. The third step represents a Bronsted-Lowry proton transfer which is rapid, with low activation energy.



Because the first step of the mechanism is the rate determining step, the first transition state will be the most important. During the first step, a carbon-leaving group bond in a neutral substrate is broken to form a carbocation intermediate and a leaving group anion. The breaking bond is represented as a dashed-partial bond in the transition state. A partial positive charge is shown on the carbon to represent the formation of a carbocation and a partial negative charge is shown on the leaving group to represent the formation of an anion.





Transition State 1 ([TS_1]‡)

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S_N1 Reaction Kinetics

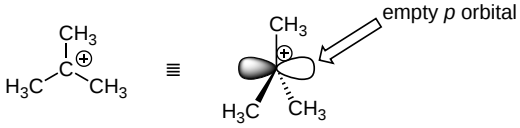
In the first step of an S_N1 mechanism, two charged species are formed from a neutral molecule. This step is much the slower of the three steps, and is therefore rate-determining. In the reaction energy diagram, the activation energy for the first step is higher than that for the second step indicating that the S_N1 reaction has *first order*, *unimolecular* kinetics because the rate determining step involves one molecule splitting apart, not two molecules colliding. It is important to remember that first order refers to the rate law expression where the generic term substrate is used to describe the alkyl halide.

$$\text{rate} = k\,[\text{substrate}]$$

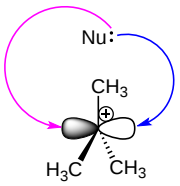
Because an S_N1 reaction is first order overall the concentration of the nucleophile does not affect the rate. Since the nucleophile is not involved in the rate-limiting first step, the nature of the nucleophile does not affect the rate of an S_N1 reaction.

Stereochemical Considerations

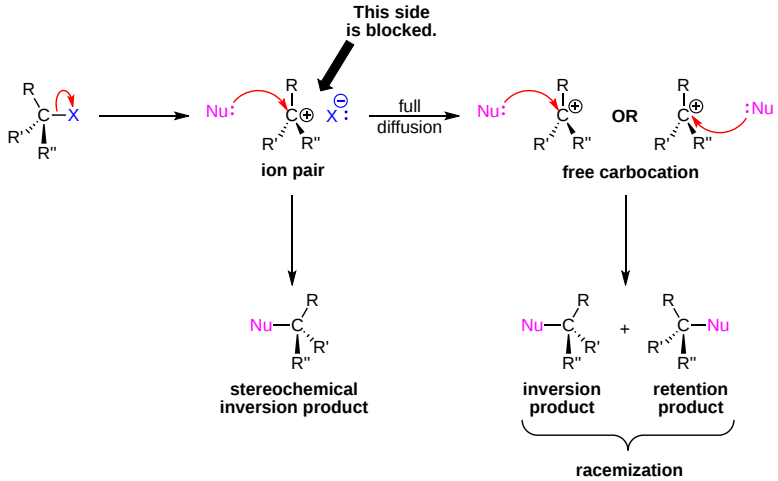
We saw that S_N2 reactions result in inversion of stereochemical configuration at the carbon center. The difference in mechanisms means the stereochemical outcome of S_N1 can be different than S_N2. Recall that a carbocation intermediate produced during an S_N1 reaction is sp^2-hybridized, with an empty p orbital perpendicular to the plane formed by the three sigma bonds:



Because the nucleophile is free to attack from either side of the carbocation electrophile, the reaction leads to a 50:50 mixture of two stereoisomeric products. In other words: the S_N1 reaction occurs with both retention or inversion of configuration at the electrophilic carbon, leading to racemization if the carbon is chiral after the substitution.

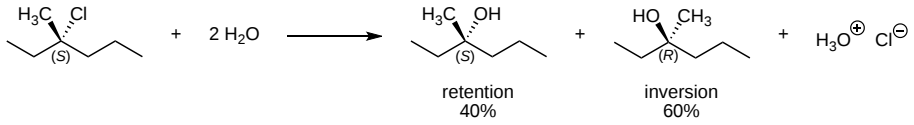


However, often chemical reactions are more complicated than the mechanisms that represent limiting cases like S_N1 and S_N2. Experimental data has shown that the inversion product is favored over racemization due to the formation of **ion pairs**. After dissociation during the rate determining step the carbocation and the leaving group are still electrostatically associated. The leaving group anion is temporarily held in place which provides a shield to one side of the carbocation. If substitution occurs before the leaving group anion fully diffuses away the stereochemical inversion substitution product is created. Only after the leaving group fully diffuses away can racemization occur. Overall, the product of an S_N1 reaction shows an excess of the stereochemical inversion product.



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For an example, consider the hydrolysis of (*S*)-3-chloro-3-methylhexane.



Exercise 9.5.1

Consider two nucleophilic substitutions that occur uncatalyzed in solution. Assume that reaction A is S_N2, and reaction B is S_N1. Predict, in each case, what would happen to the rate of the reaction if the concentration of the nucleophile were doubled, while all other conditions remained constant.

a) $CH_3I + CH_3S^{\ominus} \xrightarrow{S_N2}$

b) $(CH_3)_3CBr + CH_3SH \xrightarrow{S_N1}$

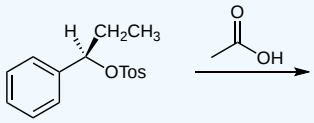
Answer

For Reaction A, the rate law is rate = $k[CH_3I][CH_3S^-]$. Therefore, if the concentration of the nucleophile, CH_3S^-, is doubled and the concentration of the alkyl halide remains the same, then the reaction rate will double.

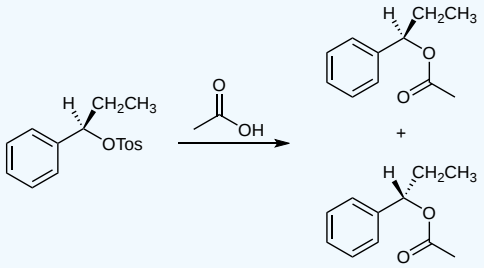
For Reaction B, the rate law is rate = $k[CH_3)_3Br]$. Therefore, if the concentration of the nucleophile, CH_3SH, is doubled and the concentration of the alkyl halide remains the same, then reaction rate stays the same.

Exercise 9.5.2

Give the products of the following S_N1 reaction. Show stereochemistry.



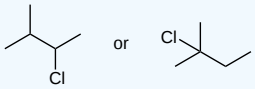
Answer



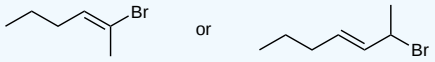
Exercise 9.5.3

Predict with compound in each pair will undergo an S_N1 reaction more quickly.

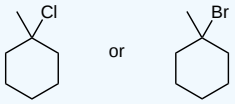
a)



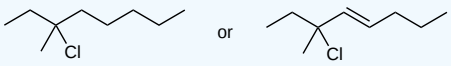
b)



c)

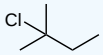


d)

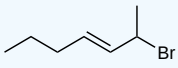


Answer

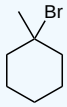
a)



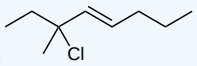
b)



c)



d)



9.5: The SN1 Reaction is shared under a CC BY-SA 4.0 license and was authored, remixed, and/or curated by Jim Clark, Steven Farmer, Dietmar Kennepohl, Tim Soderberg, William Reusch, & William Reusch.

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- **8.2: Two Mechanistic Models for Nucleophilic Substitution** by Tim Soderberg is licensed CC BY-NC-SA 4.0. Original source: https://digitalcommons.morris.umn.edu/chem_facpubs/1/.

9.6: Characteristics of the SN1 Reaction

Objectives

After completing this section, you should be able to

1. discuss how the structure of the substrate affects the rate of a reaction occurring by the S_N1 mechanism.
2. arrange a given list of carbocations (including benzyl and allyl) in order of increasing or decreasing stability.
3. explain the high stability of the allyl and benzyl carbocations.
4. arrange a given series of compounds in order of increasing or decreasing reactivity in S_N1 reactions, and discuss this order in terms of the Hammond postulate.
5. discuss how the nature of the leaving group affects the rate of an S_N1 reaction, and in particular, explain why S_N1 reactions involving alcohols are carried out under acidic conditions.
6. explain why the nature of the nucleophile does not affect the rate of an S_N1 reaction.
7. discuss the role played by the solvent in an S_N1 reaction, and hence determine whether a given solvent will promote reaction by this mechanism.
8. compare the roles played by the solvent in S_N1 and in S_N2 reactions.
9. determine which of two S_N1 reactions will occur faster, by taking into account factors such as the structure of the substrate and the polarity of the solvent.
10. determine whether a given reaction is most likely to occur by an S_N1 or S_N2 mechanism, based on factors such as the structure of the substrate, the solvent used, etc.

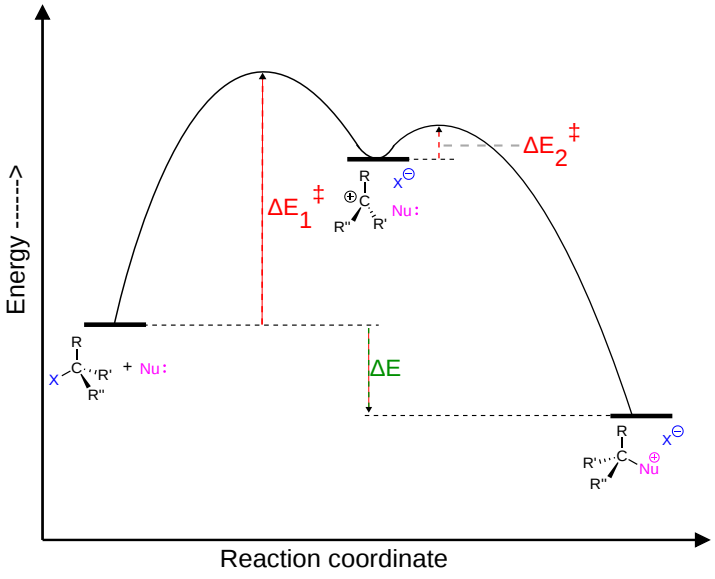
Key Terms

Make certain that you can define, and use in context, the key terms below.

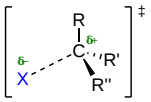
- benzylic
- dielectric constant
- polarity

The Substrate in S_N1Reactions

As discussed in the previous section S_N1 reactions follow first order kinetics due to a multi-step mechanism in which the rate-determining step consists of the ionization of the alkyl halide to form a carbocation.

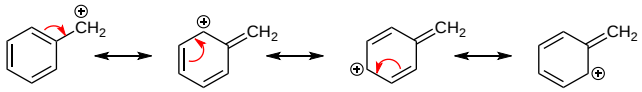


The transition state for the rate determining step shows the transition of an alkyl halide to a carbocation. Because the rate determining step is endothermic, the Hammond postulate says that the transition state more closely resembles the carbocation intermediate. Factors which stabilize this intermediate will lower the energy of activation for the rate determining step and cause the rate of reaction to increase. In general, a more stable carbocation intermediate formed during the reaction allows for a faster the S_N1 reaction rate.

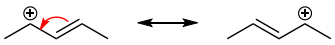


Transition State 1
($TS_1^{\ddagger}$)

In Section 7-9, the stability of alky carbocations was shown to be $3^o > 2^o > 1^o >$ methyl. Two special cases of resonance-stabilized carbocations, allyl and benzyl, must be considered and added to the list. The delocalization of the positive charge over an extended p orbital system allows for allyl and benzyl carbocations to be exceptionally stable. The resonance hybrid of an allyic cation is made up of two resonance forms while the resonance hybrid of the benzylic carbocation is made up of five.

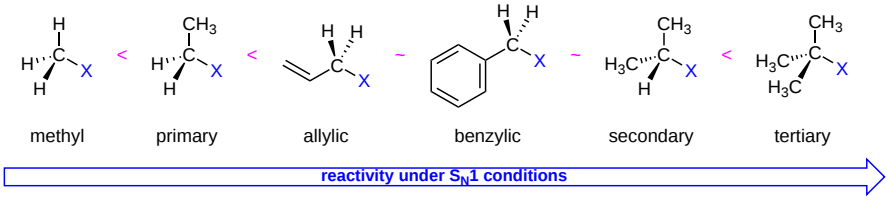


Resonance Structures for a Benzyl Carbocation



Resonance Structures for an Allylic Carbocation

Carbocation Stability	$CH_3^{(+)}$	<	$CH_3CH_2^{(+)}$	<	$(CH_3)_2CH^{(+)}$	≈	$CH_2{=}CH{-}CH_2^{(+)}$	≈	$C_6H_5CH_2^{(+)}$	≈	$(CH_3)_3C^{(+)}$

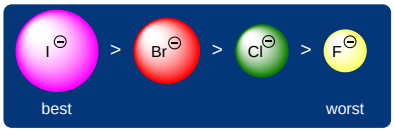


Effects of Leaving Group

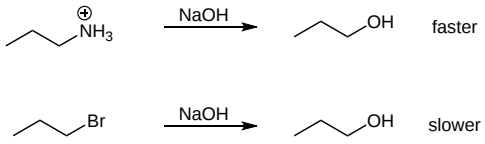
Since leaving group removal is involved in the rate-determining step of the S_N1 mechanism, reaction rates increase with a good leaving group. A good leaving group can stabilize the electron pair it obtains after the breaking of the C-Leaving Group bond faster. Once the bond breaks, the carbocation is formed and the faster the carbocation is formed, the faster the nucleophile can come in and the faster the reaction will be completed.

Because weak bases tend to strongly hold onto their electrons, they are lower energy molecules and they tend to make good leaving groups. Strong bases, on the other hand, donate electrons readily because they are high energy, reactive molecules. Therefore, they are not typically good leaving groups. As you go from left to right on the periodic table, electron donating ability decreases and thus ability to be a good leaving group increases. Halides are an example of a good leaving group whose leaving-group ability increases as you go down the halogen column of the periodic table.

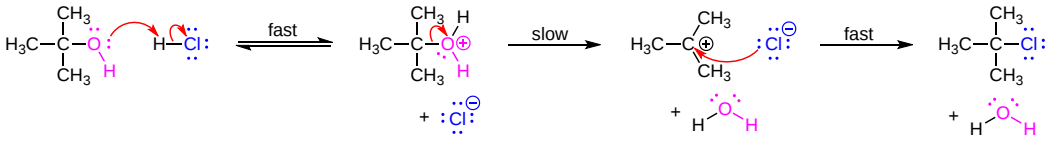




The two reactions below only vary by the different leaving groups in each reaction. The reaction with a more stable leaving group is significantly faster than the other. This is because the better leaving group leaves faster and thus the reaction can proceed faster.

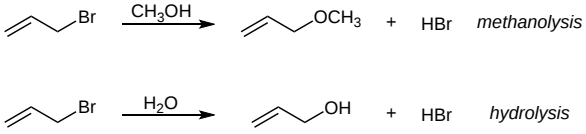


Under acidic conditions, the -OH group of an alcohol can be converted into a neutral water leaving group through protonation. As discussed in **Section 10-5**, this occurs during the conversion of a tertiary alcohol to an alkyl halide through reaction with HCl or HBr. Because the -OH group itself is a poor nucleophile, the mechanism starts with protonation to form a hydronium ion. Neutral water is then lost as a leaving group to create the carbocation intermediate which then reacts with the halide ion nucleophile to provide the alkyl halide product. This reaction works best when a tertiary alcohol is used because it produces a stable carbocation intermediate.



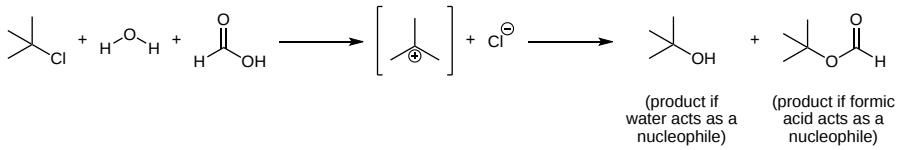
The Nucleophile

Since nucleophiles only participate in the fast second step, their relative molar concentrations rather than their nucleophilicities should be the primary product-determining factor. If a nucleophilic solvent such as water is used, its high concentration will assure that alcohols are the major product. While recombination of the halide anion with the carbocation intermediate can occur, it simply reforms the starting compound. Also this is less likely since there are less molecules of the leaving group in solution than there are of the solvent. Note that S_N1 reactions in which the nucleophile is also the solvent are commonly called **solvolysis** reactions. The S_N1 reaction of allyl bromide in methanol is an example of what we would call **methanolysis**, while if water is the solvent the reaction would be called **hydrolysis**:



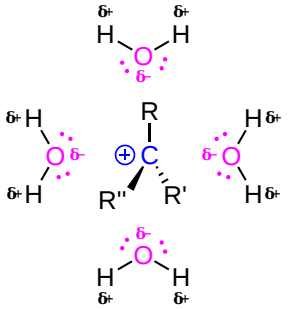
The strength of the nucleophile does not affect the reaction rate of S_N1 because, as described previously, the nucleophile is not involved in the rate-determining step. However, if you have more than one nucleophile competing to bond to the carbocation, the

strengths and concentrations of those nucleophiles affects the distribution of products that you will get. For example, if you have $(CH_3)_3CCl$ reacting in water and formic acid where the water and formic acid are competing nucleophiles, you will get two different products: $(CH_3)_3COH$ and $(CH_3)_3COCOH$. The relative yields of these products depend on the concentrations and relative reactivities of the nucleophiles.



Solvent Effects on the S_N1 Reaction

Since the hydrogen atom in a polar protic solvent is highly positively charged, it can interact with the anionic nucleophile which would negatively affect an S_N2 reaction which depends on nucleophilic attack during the rate-determining step of the reaction. However, this does not affect an S_N1 reaction because the nucleophile is not a part of the rate-determining step. Polar protic solvents actually speed up the rate of the unimolecular substitution reaction because the large dipole moment of the solvent helps to stabilize the carbocation-like transition state. Since the carbocation is unstable, anything that can stabilize this even a little will speed up the reaction.



The polarity and the ability of the solvent to stabilize the intermediate carbocation is very important as shown by the relative rate data for a solvolysis (see table below). The dielectric constant of a solvent roughly provides a measure of the solvent's polarity. A dielectric constant below 15 is usually considered non-polar. Basically, the dielectric constant can be thought of as the solvent's ability to reduce the internal charge of the solvent. So for our purposes, the higher the dielectric constant the more polar the substance and in the case of S_N1 reactions, the faster the rate.

Solvent	Dielectric Constant	Relative Rate
CH_3CO_2H	6	1
CH_3OH	33	4
H_2O	78	150,000

(note that even though acetic acid is a highly polar molecule, it tends to make a dimer with itself greatly reducing its dielectric constant)

Predicting S_N1 vs. S_N2 mechanisms

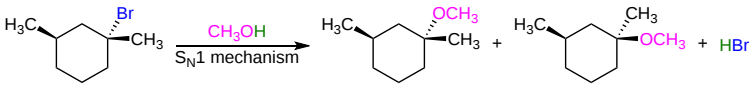
When considering whether a nucleophilic substitution is likely to occur via an S_N1 or S_N2 mechanism, we really need to consider three factors:

1) **The electrophile:** when the leaving group is attached to a methyl group or a primary carbon, an S_N2 mechanism is favored (here the electrophile is unhindered by surrounded groups, and any carbocation intermediate would be high-energy and thus unlikely). When the leaving group is attached to a tertiary, allylic, or benzylic carbon, a carbocation intermediate will be relatively stable and thus an S_N1 mechanism is favored.

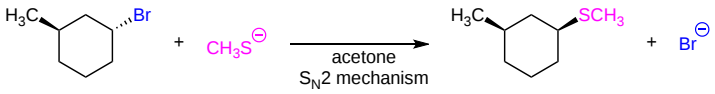
2) **The nucleophile**: powerful nucleophiles, especially those with negative charges, favor the S_N2 mechanism. Weaker nucleophiles such as water or alcohols favor the S_N1 mechanism.

3) **The solvent**: Polar aprotic solvents favor the S_N2 mechanism by enhancing the reactivity of the nucleophile. Polar protic solvents favor the S_N1 mechanism by stabilizing the carbocation intermediate. S_N1 reactions are frequently solvolysis reactions.

For example, the reaction below has a tertiary alkyl bromide as the electrophile, a weak nucleophile, and a polar protic solvent (we'll assume that methanol is the solvent). Thus we'd confidently predict an S_N1 reaction mechanism. Because substitution occurs at a chiral carbon, we can also predict that the reaction will proceed with racemization.

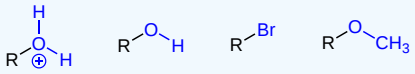


In the reaction below, on the other hand, the electrophile is a secondary alkyl bromide – with these, both S_N1 and S_N2 mechanisms are possible, depending on the nucleophile and the solvent. In this example, the nucleophile (a thiolate anion) is strong, and a polar aprotic solvent is used – so the S_N2 mechanism is heavily favored. The reaction is expected to proceed with inversion of configuration.



Exercise 9.6.1

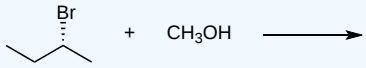
1. Put the following leaving groups highlighted in blue in order of decreasing leaving group ability



2. Which solvent would an S_N1 reaction occur faster in? H_2O or CH_3CN

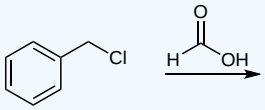
3. What kind of conditions disfavor S_N1 reactions?

4. What are the products of the following reaction and does it proceed via S_N1 or S_N2?

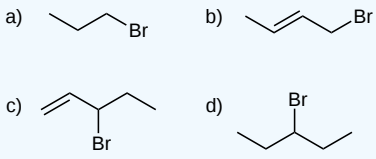


5. How could you change the reactants in the problem 4 to favor the other substitution reaction?

6. Indicate the expected product and list why it occurs through S_N1 instead of S_N2?

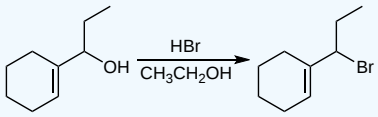


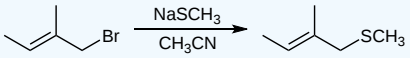
7. Rank the following by increasing reactivity in an S_N1 reaction.



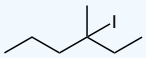
8. 3-bromo-1-pentene and 1-bromo-2-pentene undergo S_N1 reaction at almost the same rate, but one is a secondary halide while the other is a primary halide. Explain why this is.

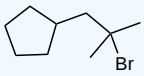
9. Label the following reactions as most likely occuring by an S_N1 or S_N2 mechanism. Suggest why.

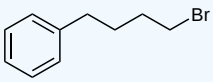
a) 

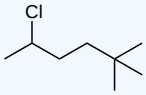
b) 

10. Give the solvolysis product expected when the compound is heated in methanol.

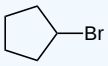
a) 

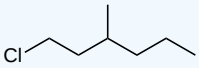
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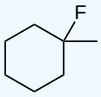
c) 

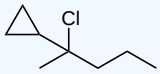
d) 

11. Predict whether each compound below would be more likely to undergo a S_N2 or S_N1 reaction.

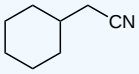
a) 

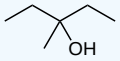
b) 

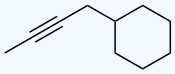
c) 

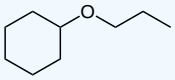
d) 

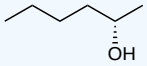
12. Show how each compound may be synthesized using nucleophilic substitution reactions.

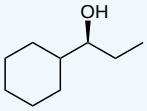
a) 

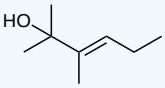
b) 

c) 

d) 

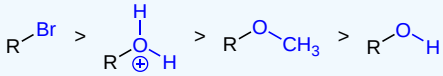
e) 

f) 

g) 

Answers

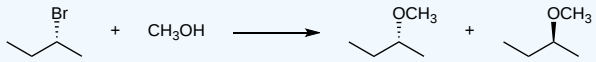
1.



2. An S_N1 reaction would occur faster in H_2O because it's polar protic and would stabilize the carbocation and CH_3CN is polar aprotic.

3. Polar aprotic solvents, a weak leaving group and primary substrates disfavor S_N1 reactions.

4.

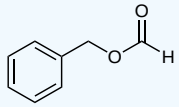


racemic mixture

Reaction proceeds via S_N1 because a secondary carbocation was formed, the solvent is polar protic and Br- is a good leaving group.

5. You could change the solvent to something polar aprotic like CH_3CN or DMSO, and you could use a stronger nucleophile such as $NaOCH_3$. Note that this would give only the inverted product, and not a racemic mixture.

6.

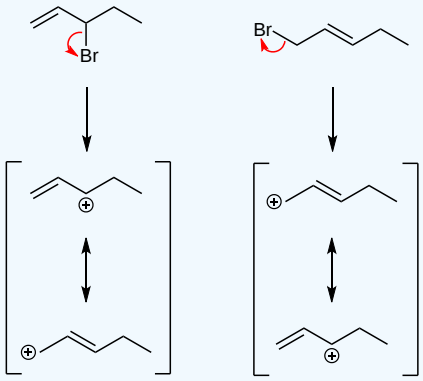


This reaction occurs via S_N1 because Cl^- is a good leaving group, the intermediate carbocation is a stable benzylic cation, and the solvent is polar protic. This is an example of a solvolysis reaction because the nucleophile is also the solvent.

7. Consider the stability of the intermediate, the carbocation.

A < D < B < C (most reactive)

8. They have the same intermediates when you look at the resonance forms.

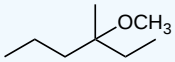


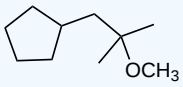
9.

A – S_N1 *poor leaving group, protic solvent, secondary cation intermediate

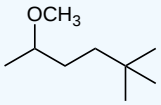
B – S_N2 *good leaving group, polar solvent, primary position.

10.

a) 

b) 

c) no reaction

d) 

11.

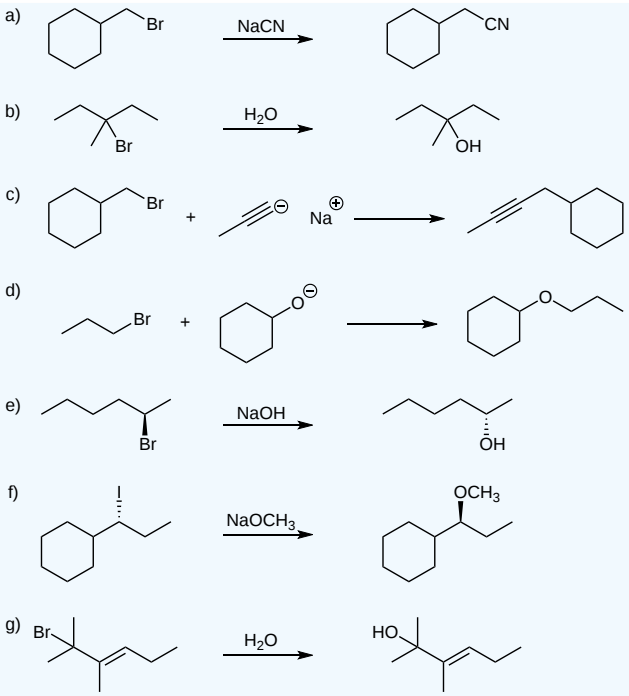
a) Can undergo S_N1 or S_N2, depending on reaction conditions

b) S_N2

c) S_N1

d) S_N1

12.



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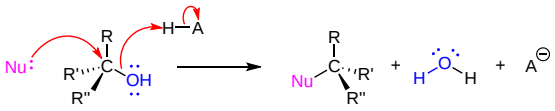
9.7: Biological Substitution Reactions

Objective

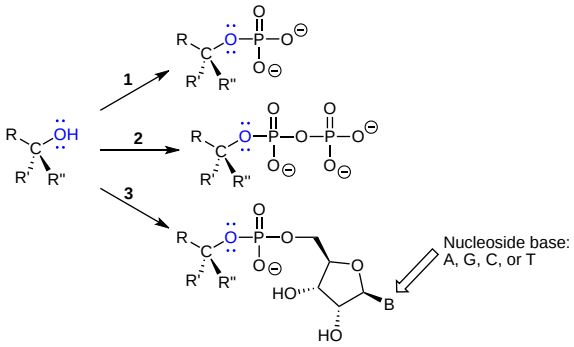
After completing this section, you should have an appreciation that S_N1 and S_N2 mechanisms exist and are well-known in biological chemistry.

Leaving Groups in Biochemical Reactions

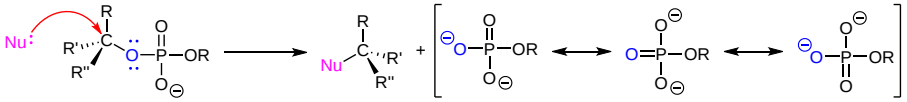
In biological reactions, we do not often see halides serving as leaving groups (in fact, outside of some marine organisms, halogens are fairly unusual in biological molecules). More common leaving groups in biochemical reactions are phosphates, water, alcohols, and thiols. In many cases, the leaving group is protonated by an acidic group on the enzyme as bond-breaking occurs. For example, hydroxide ion itself seldom acts as a leaving group – it is simply too high in energy (too basic). Rather, the hydroxide oxygen is generally protonated by an enzymatic acid before or during the bond-breaking event, resulting in a (very stable) water leaving group.



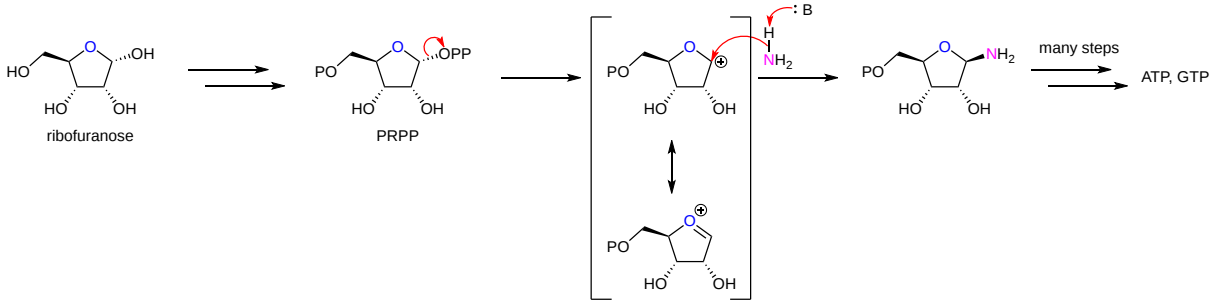
More often, however, the hydroxyl group of an alcohol is first converted enzymatically to a phosphate ester in order to create a better leaving group. This phosphate ester can take the form of a simple monophosphate (arrow 1 in the figure below), a diphosphate (arrow 2), or a nucleotide monophosphate (arrow 3).



Due to resonance delocalization of the developing negative charge, phosphates are excellent leaving groups.



Here's a specific example (from DNA nucleotide biosynthesis) that we will encounter in more detail in this section:

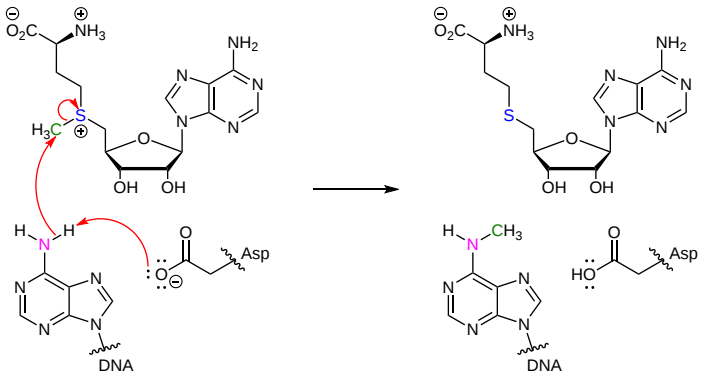


Here, the OH group on ribofuranose is converted to a diphosphate, a much better leaving group. Ammonia is the nucleophile in the second step of this S_N1-like reaction.

We will learn much more about phosphates in this section. What is important for now is that in each case, an alcohol has been converted into a much better leaving group, and is now primed for a nucleophilic substitution reaction.

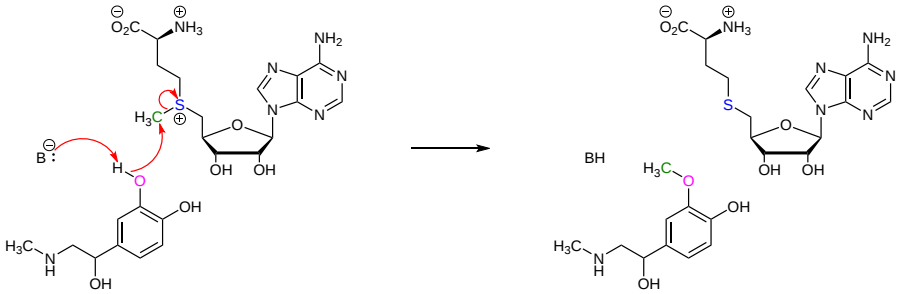
SAM Methyltransferases

Some of the most important examples of S_N2 reactions in biochemistry are those catalyzed by S-adenosyl methionine (SAM) – dependent methyltransferase enzymes. We have already seen, in chapter 6 and again in chapter 8, how a methyl group is transferred in an S_N2 reaction from SAM to the amine group on the nucleotide base adenosine:



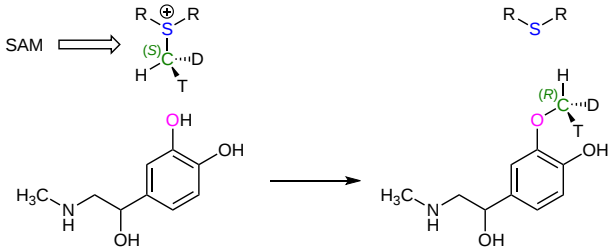
(*Nucleic Acids Res.* **2000**, *28*, 3950).

Another SAM-dependent methylation reaction is catalyzed by an enzyme called catechol-O-methyltransferase. The substrate here is epinephrine, also known as adrenaline.



Notice that in this example, the attacking nucleophile is an alcohol rather than an amine (that's why the enzyme is called an O-methyltransferase). In both cases, though, a basic amino acid side chain is positioned in the active site in just the right place to deprotonate the nucleophilic group as it attacks, increasing its nucleophilicity. The electrophile in both reactions is a methyl carbon, so there is little steric hindrance to slow down the nucleophilic attack. The methyl carbon is electrophilic because it is bonded to a positively-charged sulfur, which is a powerful electron withdrawing group. The positive charge on the sulfur also makes it an excellent leaving group, as the resulting product will be a neutral and very stable sulfide. All in all, in both reactions we have a reasonably good nucleophile, an electron-poor, unhindered electrophile, and an excellent leaving group.

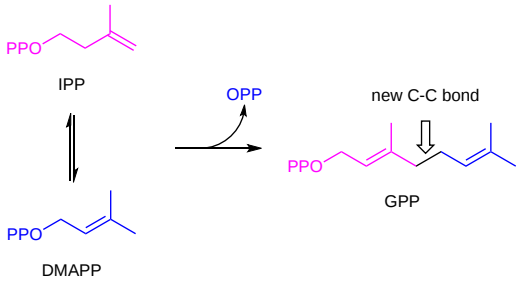
Because the electrophilic carbon in these reactions is a methyl carbon, a stepwise S_N1-like mechanism is extremely unlikely: a methyl carbocation is very high in energy and thus is not a reasonable intermediate to propose. We can confidently predict that this reaction is S_N2. Does this S_N2 reaction occur, as expected, with inversion of stereochemistry? Of course, the electrophilic methyl carbon in these reactions is achiral, so inversion is not apparent. To demonstrate inversion, the following experiment has been carried out with catechol-O-methyltransferase:



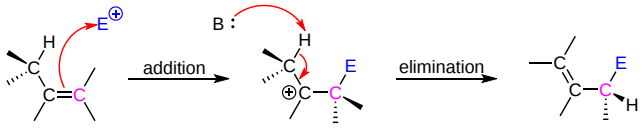
Here, the methyl group of SAM was made to be chiral by incorporating hydrogen isotopes tritium (^{3}H, T) and deuterium (^{2}H, D). The researchers determined that the reaction occurred with inversion of configuration, as expected for an S_N2 displacement (*J. Biol. Chem.* **1980,** *255,* 9124).

Substitution by Electrophilic Addition/Elimination

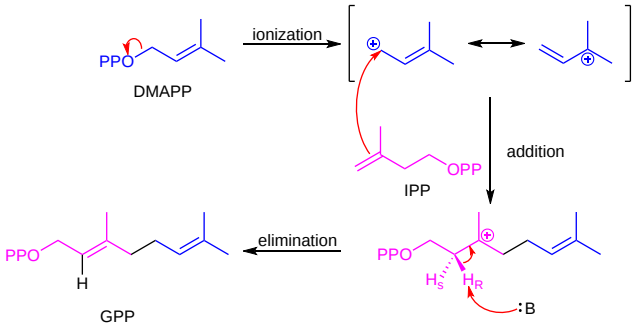
The electrophilic double bond isomerization catalyzed by IPP isomerase is a highly reversible reaction, with an equilibrium IPP:DMAPP ratio of about 6:1. In the next step of isoprenoid biosynthesis, the two five-carbon isomers condense to form a 10-carbon isoprenoid product called geranyl diphosphate (GPP).



This is a nice example of an electrophilic addition/elimination mechanism, which we saw in general form in this section:

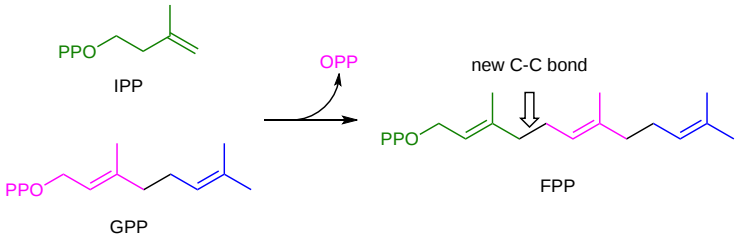


The first step is ionization of the electrophile - in other words, the leaving group departs and a carbocation intermediate is formed. In this case, the pyrophosphate group on DMAPP is the leaving group, and the electrophilic species is the resulting allylic carbocation.

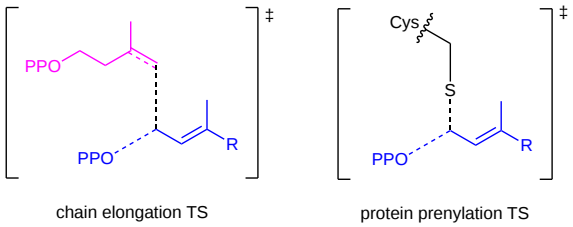


In the condensation (addition) step, the C_3-C_4 double bond in IPP attacks the positively-charged C_1 of DMAPP, resulting in a new carbon-carbon bond and a second carbocation intermediate, this time at a tertiary carbon. In the elimination phase, proton abstraction leads to re-establishment of a double bond in the GPP product. Notice that the enzyme specifically takes the *pro-R* proton in this step.

To continue the chain elongation process, another IPP molecule can then condense, in a very similar reaction, with C_1 of geranyl diphosphate to form a 15-carbon product called farnesyl diphosphate (FPP).

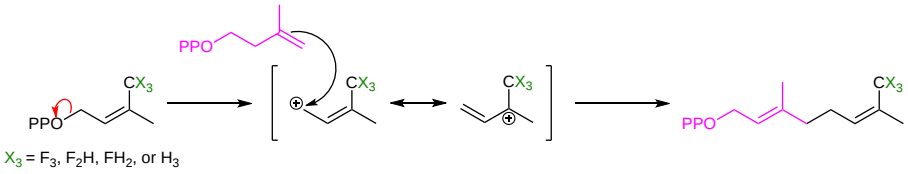


How do we know that these are indeed S_N1-like mechanisms with carbocation intermediates, rather than concerted S_N2-like mechanisms? First of all, recall that the question of whether a substitution is dissociative (S_N1-like) or associative (S_N2-like) is not always clear-cut - it could be somewhere in between, like the protein prenyltransferase reaction (section 9.3). The protein prenyltransferase reaction and the isoprenoid chain elongation reactions are very similar: the electrophile is the same, but in the former the nucleophile is a thiolate, while in the latter the nucleophile is a pi bond.



This difference in the identity of the nucleophilic species would lead one to predict that the chain elongation reaction has more S_N1-like character than the protein prenylation reaction. A thiolate is a very powerful nucleophile, and thus is able to *push* the pyrophosphate leaving group off, implying some degree of S_N2 character. The electrons in a pi bond, in contrast, are only weakly nucleophilic, and thus need to be *pulled* in by a powerful electrophile - *ie*. a carbocation.

So it makes perfect sense that the chain elongation reaction should more S_N1-like than S_N2-like. Is this in fact the case? We know how to answer this question experimentally - just run the reaction with fluorinated DMAPP or GPP substrates and observe how much the fluorines slow things down (see section 9.3B).



If the reaction is S_N1-like, the electron-withdrawing fluorines should destabilize the allylic carbocation intermediate and thus slow the reaction down considerably. If the mechanism is S_N2-like, the fluorine substitutions should not have a noticeable effect, because a carbocation intermediate would not be formed. When this experiment was performed with FPP synthase, the results were dramatic: the presence of a single fluorine slowed down the rate of the reaction by a factor of about 60, while two and three fluorines resulted in a reaction that was 500,000 and 3 million times slower, respectively (*J. Am. Chem. Soc.* **1981**, *103*, 3926.) These results strongly suggest indicate the formation of a carbocation intermediate in an S_N1-like displacement.

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9.8: Elimination Reactions- Zaitsev's Rule

Objective

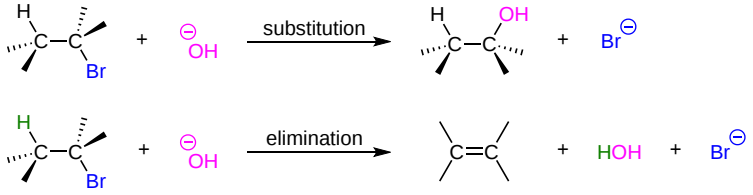
After completing this section, you should be able to apply Zaitsev's rule to predict the major product in a base-induced elimination of an unsymmetrical halide.

Key Terms

Make certain that you can define, and use in context, the key term below.

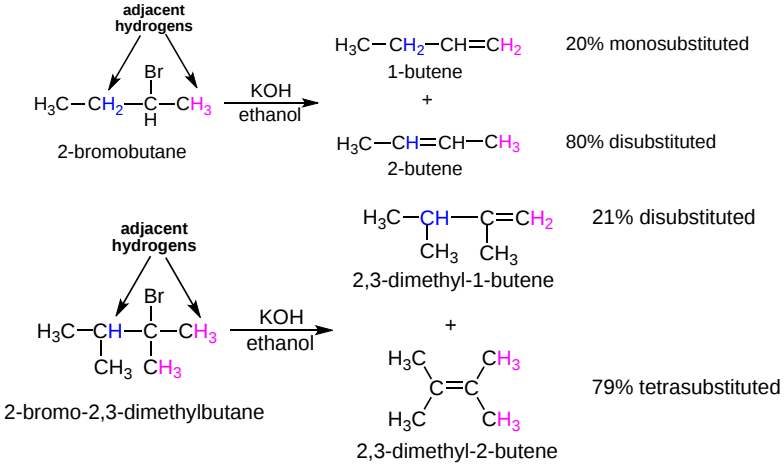
- Zaitsev's rule

When an alkyl halide is reacted with a nucleophile/Lewis base two major types of reaction can occur. Thus far in this chapter, we have discussed substitution reactions where a nucleophile displaces a leaving group at the electrophilic carbon of a substrate. Alternatively, the nucleophile could act as a Lewis base and cause an elimination reaction by removing a hydrogen adjacent to the leaving group. These reaction are similar and are often in competition with each other.



Introduction

The prefix "regio" indicates the interaction of reactants during bond making and/or bond breaking occurs preferentially by one orientation. If two or more structurally distinct groups of adjacent hydrogens are present in a given reactant, then multiple constitutionally isomeric alkenes may be formed by an elimination. **Zaitsev's rule** is an empirical rule used to predict the major products of elimination reactions. It states that in an elimination reaction the major product is the more stable alkene with the more highly substituted double bond. This situation is illustrated by the 2-bromobutane and 2-bromo-2,3-dimethylbutane elimination examples given below.



By using the strong base hydroxide, we direct these reactions toward elimination (rather than substitution). In both cases there are two different sets of adjacent hydrogens available to the elimination reaction (these are colored blue and magenta). If the rate of each possible elimination was the same, we might expect the amounts of the isomeric elimination products to reflect the number of hydrogens that could participate in that reaction. For example, since there are three 1°-hydrogens (magenta) and two 2°-hydrogens (blue) on beta-carbons in 2-bromobutane, statistics would suggest a 3:2 ratio of 1-butene and 2-butene in the products. This is not

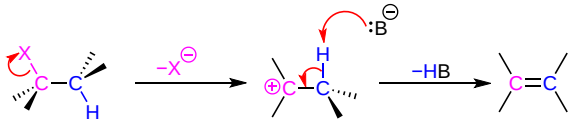
observed, and the latter predominates by 4:1. This departure from statistical expectation is even more pronounced in the second example, where there are six adjacent 1° hydrogens (magenta) compared with one 3°-hydrogen (blue). These results point to a strong favoring the more highly substituted product double bond predicted by **Zaitsev's Rule**.

The E1, E2, and E1cB Reactions

Elimination reaction take place by three common mechanism, E1, E2, and E1cB, all of which break the H-C and X-C bonds at different points of their mechanism. In addition, the different mechanisms will have subtle effects on the reaction products which will be discussed later in this chapter.

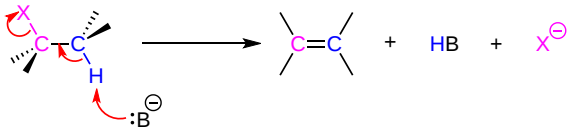
E1 Mechanism

This mechanism starts the breaking of the C-X to provide a carbocation intermediate. A base removes a hydrogen adjacent to the original electrophilic carbon. The electrons from the broken H-C bond move to form the pi bond of the alkene. In much the same fashion as the S_N1 mechanism, the first step of the mechanism is slow making it the rate determining step. This means that the reaction kinetics are unimolecular and first-order with respect to the substrate.



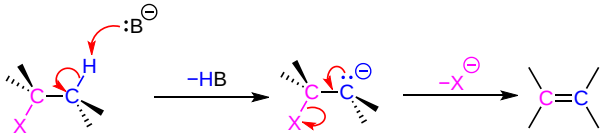
E2 Mechanism

The E2 mechanism takes place in a single concerted step. The rate at which this mechanism occurs follows second order kinetics, and depends on the concentration of both the base and alkyl halide. The base removes a hydrogen from a carbon adjacent to the leaving group. The electrons of the broken H-C move to form the pi bond of the alkene. In doing this the C-X bond is broken causing the removal of the leaving group.



E1cB Mechanism

The E1cB mechanism starts with the base deprotonating a hydrogen adjacent to the leaving to form a carbanion. In the second step of the mechanism the lone pair electrons of the carbanion move to become the pi bond of the alkene. This causes the C-X bond to break and the leaving group to be removed.



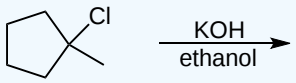
Predicting the Products of an Elimination Reaction

For most elimination reactions, the formation of the product involves the breaking of a C-X bond from the electrophilic carbon, the breaking of a C-H bond from a carbon adjacent to the electrophilic carbon, and the formation of a pi bond between these two carbons. Which elimination mechanism is being followed has little effect on these steps. The limitations of each elimination mechanism will be discussed later in this chapter.

To determining the possible products, it is vital to first identify the electrophilic carbon in the substrate. Next identify all hydrogens on carbons directly adjacent to the electrophilic carbon. Each unique adjacent hydrogen has the possibility of forming a unique elimination product. Break a C-H bond from each unique group of adjacent hydrogens then break the C-X bond. Finally connect the adjacent carbon and the electrophilic carbon with a double bond. Repeat this process for each unique group of adjacent hydrogens. Finally, compare all of the possible elimination products. The product whose double bond has the most alkyl substituents will most likely be the preferred product.

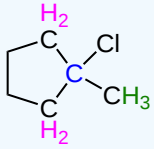
Worked Example 9.8.1

What would be the expected products of the following reaction? Which would be expected to be the major product?



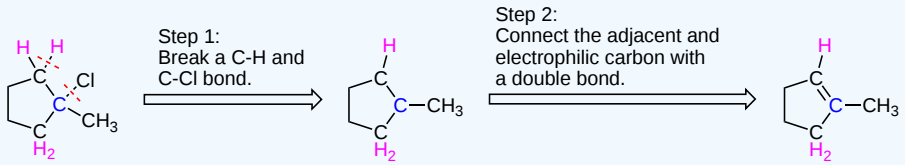
Solution

To solve this problem, first find the electrophilic carbon in the starting compound. This carbon is directly attached to the chlorine leaving groups and is shown in blue in the structure below. Next, identify all unique groups of hydrogens on carbons directly adjacent to the electrophilic carbon. In the starting compound, there are two distinct groups of hydrogens which can create a unique elimination product if removed. They are shown as magenta and green in the structure below.

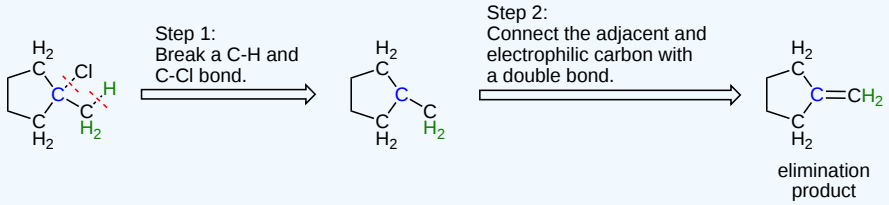


Create the possible elimination product by breaking a C-H bond from each unique group of adjacent hydrogens then breaking the C-Cl bond. Then connect the adjacent carbon and the electrophilic carbon with a double bond to create an alkene elimination product. Repeat this process for each unique group of adjacent hydrogens. Because the starting compound in this example has two unique groups of adjacent hydrogens, two elimination products can possibly be made.

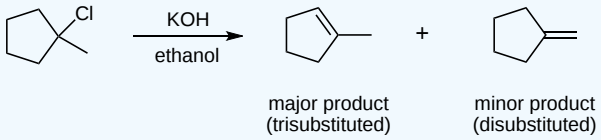
Product 1



Product 2



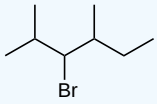
Finally, compare the possible elimination products to determine which has the most alkyl substituents. This product will most likely be the preferred. For this example product 1 has three alkyl substituents and product 2 has only two. This means product 1 will likely be the preferred product of the reaction.



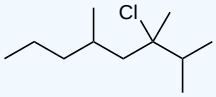
Exercise 9.8.1

1) Ignoring the alkene stereochemistry show the elimination product(s) of the following compounds:

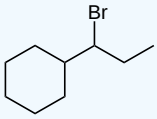
a)



b)

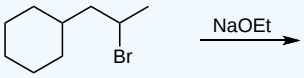


c)

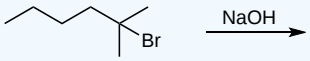


2) Predict the major products of the following reactions.

a)



b)



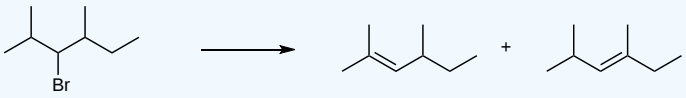
c)



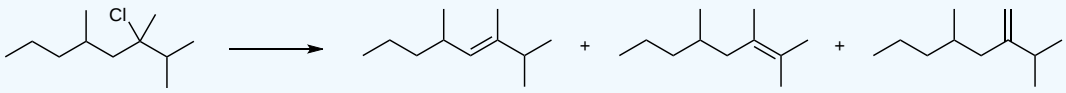
Answer

1)

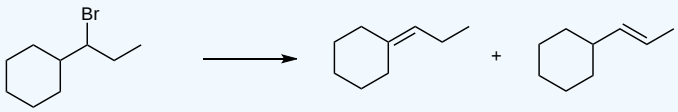
a)



b)

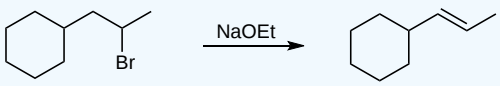


c)

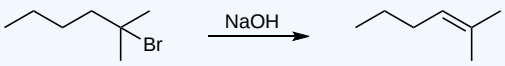


2)

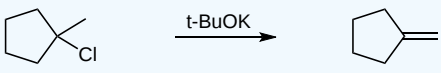
a)



b)



c)



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9.9: The E2 Reaction and the Deuterium Isotope Effect

Objectives

After completing this section, you should be able to

1. write the mechanism of a typical E2 reaction.
2. sketch the transition state of a typical E2 reaction.
3. discuss the kinetic evidence that supports the proposed E2 mechanism.
4. discuss the stereochemistry of an E2 reaction, and explain why the anti periplanar geometry is preferred.
5. determine the structure of the alkene produced from the E2 reaction of a substrate containing two chiral carbon atoms.
6. describe the deuterium isotope effect, and discuss how it can be used to provide evidence in support of the E2 mechanism.

Key Terms

Make certain that you can define, and use in context, the key terms below.

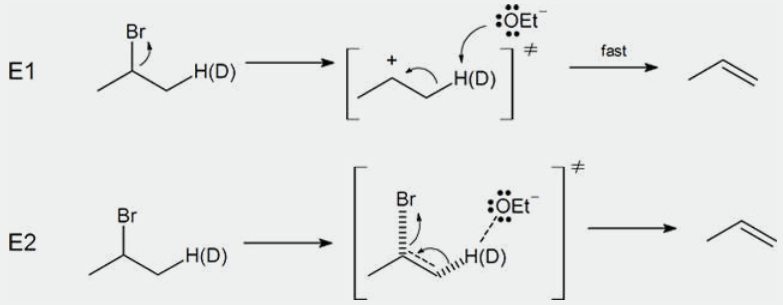
- anti periplanar
- deuterium isotope effect
- E2 reaction
- periplanar
- syn periplanar

Study Notes

An *E2 reaction* is a bimolecular elimination reaction; thus, two molecules are involved in the rate-limiting step. In this section, we are concerned with E2 reactions involving an alkyl halide and a base.

Use molecular models to assist you to understand the difference between syn periplanar and anti periplanar, and to appreciate why E2 eliminations are stereospecific.

Note that when deuterium is used the kinetic isotope effect (KIE) is referred to as the deuterium isotope effect. A C–H bond is about 5 kJ/mol weaker than a C–D bond. So if the rate-limiting step involves a breaking of this bond as it does at the E2 transition state there will be a substantial difference in reaction rates when comparing deuterated and non-deuterated analogues. Indeed, the reaction of 2-bromopropane with sodium ethoxide (NaOEt) is 6.7 times faster than its deuterated counterpart, providing evidence consistent with an E2 mechanism.

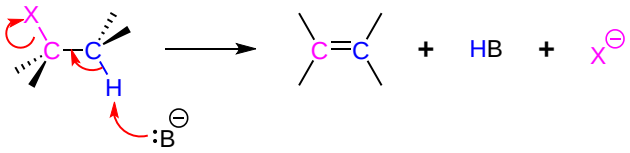


Introduction

E2, bimolecular elimination, was proposed in the 1920s by British chemist Christopher Kelk Ingold. E2 reactions are typically seen with secondary and tertiary alkyl halides, in the presence of a base (OH-, RO-, R_2N-). For a primary halide to undergo an E2 reaction a strong sterically hindered base is usually required. The products of an E2 reaction follow Zaitsev's rule, the most substituted alkene is usually the major product.

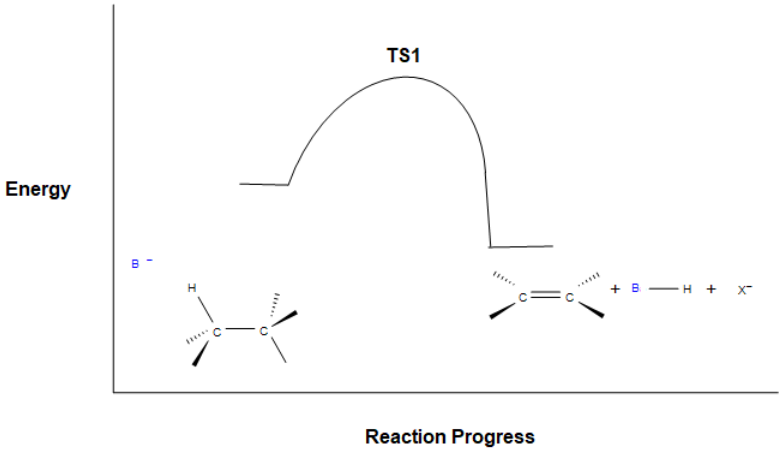
E2 Mechanism

The E2 mechanism takes place in a single concerted step. The rate at which this mechanism occurs follows second order kinetics, and depends on the concentration of both the base and alkyl halide. The base removes a hydrogen from a carbon adjacent to the carbon with the leaving group. The electrons of the broken H-C bond move to form the pi bond of the neutral product alkene. In doing this, the C-X bond is broken causing the removal of the leaving group. Overall during this reaction an electron pair is transferred from the base to the leaving group.

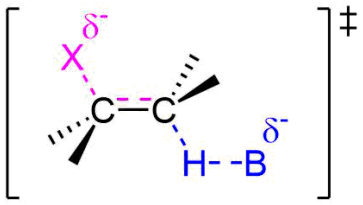


E2 Reaction Transition State

Because the E2 reaction is predicted to follow a concerted mechanism only one transition state is expected in its energy coordinate diagram.



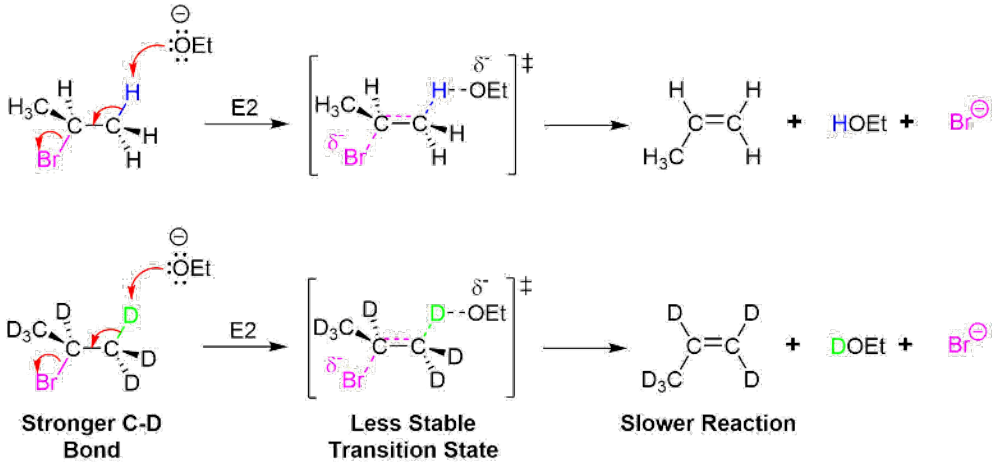
As the base begins to remove a hydrogen adjacent to the leaving group an H-B is starting to form and an H-C bond is in the process of breaking. Simultaneously, a C=C pi bond forms and the C-X bond breaks. During this reaction a set of electrons and a negative charge are transferred from the base to the leaving group. This is represented by a partial negative charge being present on both the base and the leaving group in the transition state.



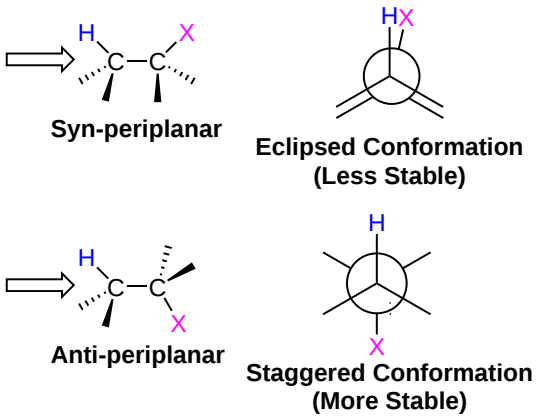
Evidence for the E2 Mechanism and Transition State

Kinetic studies of E2 reactions show that they are second order overall and follow the rate law: rate = k[RX][Base]. This data is consistent with the predicted bimolecular E2 mechanism that includes both the alkyl halide and the base participating in the mechanism's rate-determining step.

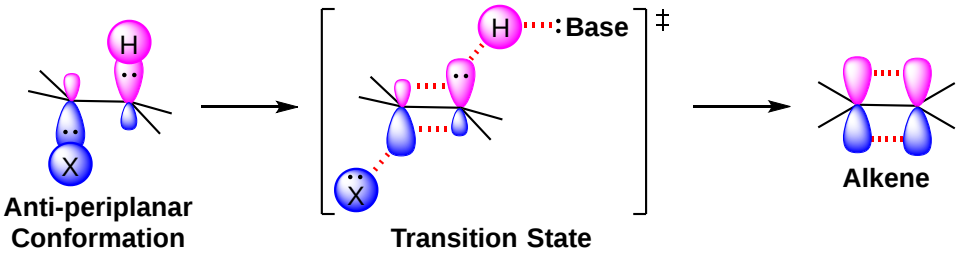
Further evidence for the predicted mechanism for the E2 reaction was provided by experiments involving the **deuterium isotope effect** (DIE). The **deuterium isotope effect** (DIE) is a phenomenon associated with molecules which have had hydrogen (H) atoms isotopically substituted with deuterium (D) atoms, exhibiting different reaction rates. The bond dissociation energy for C-D bonds is about 5 kJ/mol stronger than the bond dissociation energy of C-H bonds. This difference in energy results in a reduction in the rate of reaction, if the deuterium replacement occurs at a site of bond breaking in the rate determining step of a reaction. So if the rate-limiting step involves a breaking of this bond, as it does at the E2 transition state, there will be a substantial decrease in reaction rates when comparing deuterated and non-deuterated analogues. Indeed, the reaction of 2-bromopropane with sodium ethoxide (NaOEt) is 6.7 times faster than its deuterated counterpart, providing evidence that the C-H bond is broken during the rate determining step of the E2 mechanism. This is consistent with the predicted mechanism of the E2 reaction consisting of a single concerted step. If the rate-determining step was the leaving group bond breaking first (as in an E1 reaction) the deuterium substitution would not have caused an observable change in reaction rate.



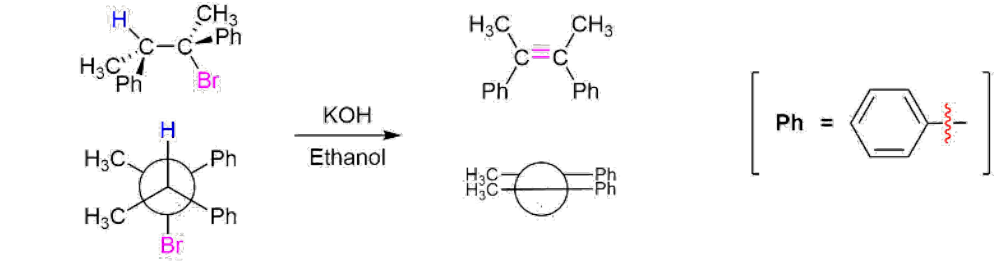
Yet another piece of evidence which supports the E2 mechanism comes when considering the stereochemistry of the elimination products. In the transition state of the E2 mechanism there are two carbons rehybridization from sp^3 to sp^2 while forming a π-bond. For good orbital overlap to occur during this change all the atoms involved in the reaction, the two carbons, the hydrogen, and the leaving group need to all lie in the same plane or **periplanar**. There are two possible ways this geometry can be achieved: **syn-periplanar** where the hydrogen and the leaving group are on the same side of the C-C bond and **anti-periplanar** where the hydrogen and the leaving group are on opposite sides of the C-C bond. To obtain a syn-periplanar geometry the substituents attached to the C-C bond must adopt an energetically unfavorable eclipsed conformation. The energy barrier to syn-orientation is such that syn-elimination is rarely observed in E2 reactions. E2 eliminations typically take place from the anti-periplanar conformation, as this is the most stable conformation due to the substituents attached to the C-C bond being staggered.



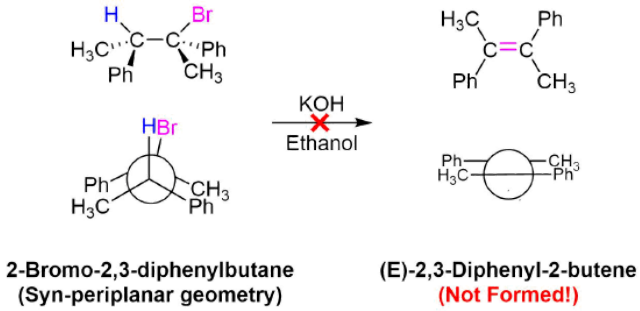
When viewing the transition state of the E2 mechanism when in the anti-periplanar conformation, the two sp^3 hybridized orbitals making up the C-H and C-X sigma bonds are in the same plane. When these two carbons rehybridization from sp^3 to sp^2, the p orbitals forming the π-bond will also have good overlap.



The stereochemical consequences of reactant molecules obtaining anti-periplanar geometry prior to E2 reactions has been observed in numerous experiments and provides further evidence of the proposed mechanism. For example, (2S, 3R)-2-bromo-2,3-diphenylbutane only forms (Z)-2,3-diphenyl-2-butene as a product of E2 elimination. To form the Z alkene isomer, the starting material must obtain the anti-periplanar geometry preferred for E2 reactions.



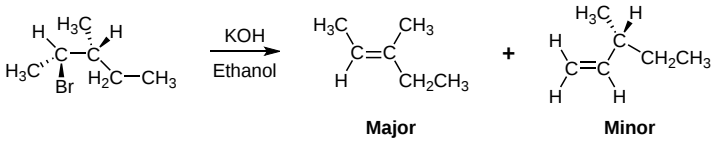
No isomeric E alkene product is formed because the starting materials would need to obtain a staggard, syn-periplanar geometry. The syn-periplanar geometry would be transferred to the transition state making it higher in energy and harder to form. The fact that only the Z alkene isomer forms provides further evidence that the E2 mechanism takes place by a single bimolecular step.



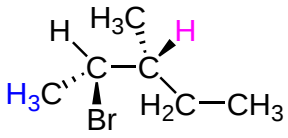
Predicting the Stereochemical Product of E2 Reactions

E2 reactions have the requirements of a leaving group and a hydrogen on a carbon adjacent to the leaving group carbon. For non-ringed compounds, the C-C can usually undergo free rotation to place the C-X and C-H bonds anti-periplaner to each other. Stereochemical considerations usually come into play when both of the carbons in the C-C bond are chiral. When these carbons are achiral but contain the other requirements for an E2 reaction, products lacking stereochemistry are usually produced.

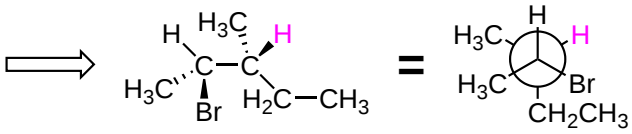
When both of the carbons in the C-C bond are chiral, one carbon will have a leaving group and the other carbon will have a single hydrogen. To consider the stereochemistry of an E2 product, start by creating a Newman projection looking down the C-C bond. Then rotate the C-C bond until the C-X and C-H bonds are in the anti position. The Newman projection now shows the relative positioning of the substituents on the C-C bond as they will appear in the double bond formed. It should be noted that if syn elimination was possible, a positional isomer of the double bond will be created. Consider the elimination products for (2R, 3R)-2-bromo-3-methylpentane.



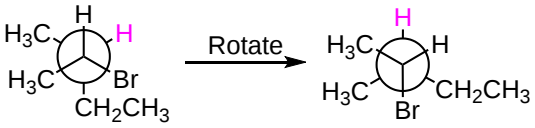
First, locate hydrogens on carbons adjacent to the leaving group. The compound used in this example has two unique sets of hydrogens.



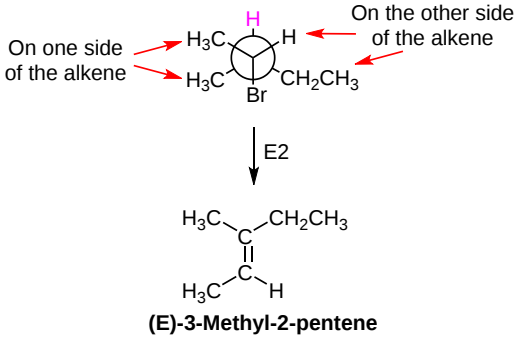
Because the adjacent hydrogen colored fuchsia is attached to a chiral carbon it require special consideration. Convert the structure into a Newman projection along the C-C bond that will for the alkene elimination product. The C-C bond can be view down either direction and still product the correct product.



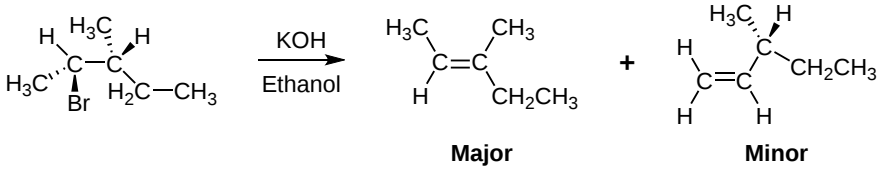
Then rotate such the the adjacent H and the leaving group are in the anti position.



This Newman projection shows the relative positioning of the substituents on the double bond formed. Note, none of the Z isomer is formed because it would require syn orientation of the H and Br.



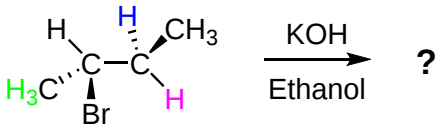
Lastly, consider the products made by other adjacent hydrogens and apply Zaitsev's rule to predict the preferred product.



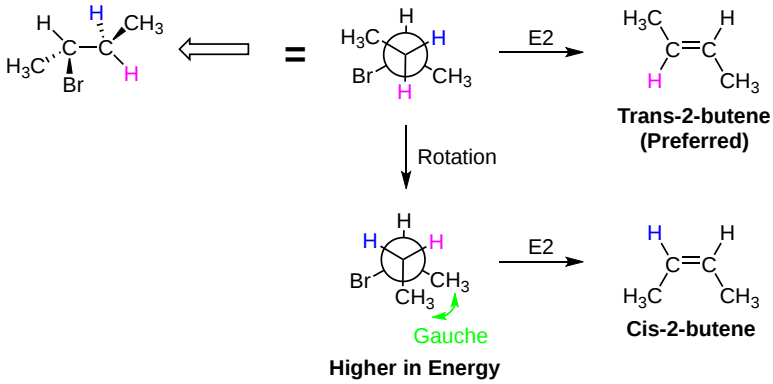
Determining *Cis* and *Trans* Products in Elimination Reaction

Understanding that E2 reactions require an anti-periplanar geometry can explain cis and trans alkene isomers can form as products. This occurs as an important exception to the rule that stereoisomers only form as elimination products when both of the carbons in

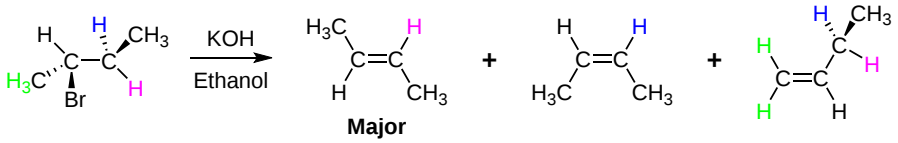
the C-C bond forming the alkene are chiral. When considering the E2 reaction products of (R)-2-butane, there are two groups of hydrogens on carbons adjacent to the leaving group a CH_3 and a CH_2.



The carbon in the CH_2 group is achiral so both the H's appear to be equivalent. However, when the anti-periplanar geometry requirement is applied each hydrogen will produce its own unique product. Once the reactant is converted into a Newman projection it can be seen that the Br leaving group and the hydrogen colored blue are in the anti orientation and are ready to be eliminated. It should also be noted that the two CH_3 groups are also in the anti position which gives them the least amount of steric interaction possible. Because the CH_3 groups are on opposite sides of the Newman projection the CH_3 groups will be on opposite sides of the alkene thus creating the product *trans*-2-butene. When the Newman projection is rotated such that the fuchsia colored hydrogen is anti to the Br leaving group, the two CH_3 groups are now on the same. This orientation creates the isomer *cis*-2-butene. However, to obtain this orientation the two CH_3 groups must overcome the steric strain associated with a gauche conformation. This makes the transition state leading the cis isomer higher in energy and more difficult to form. Because of this, the trans isomer will be the major product. It is clear that the two hydrogens of the CH_2 group are not equivalent despite their not being attached to a chiral carbon.

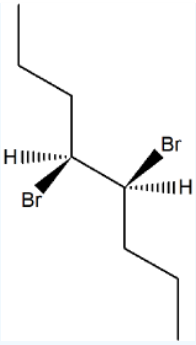


After considering all the products made during this E2 reaction the preferred product can be determined. The *cis* and *trans* isomer both have two alkene substituents while the third product only has one. Of the *cis* and *trans* isomer, the *trans* isomer is expected to be easier to form. Zaitsev's rule says that trans-2-butene will be the major product of this reaction.



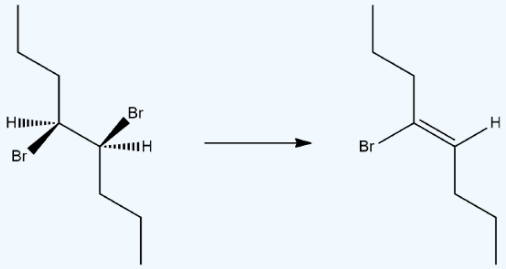
? Exercise 9.9.1

1) What is the product of the following molecule in an E2 reaction? What is the stereochemistry?



Answer

The stereochemistry is (*Z*) for the reaction.



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9.10: The E2 Reaction and Cyclohexane Conformation

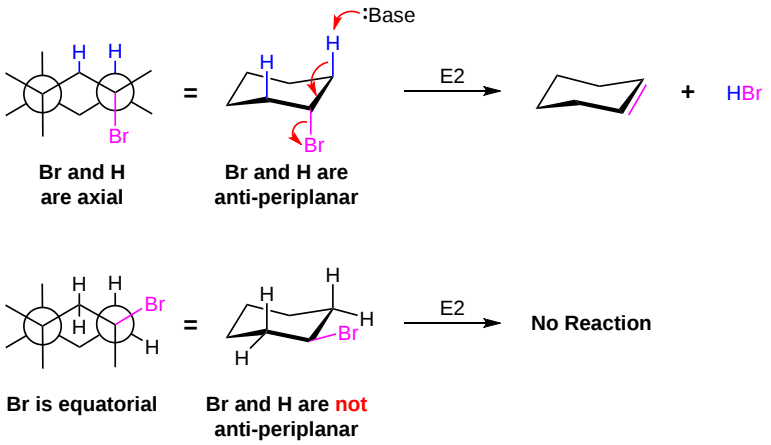
Objectives

After completing this section, you should be able to

1. identify anti periplanar arrangements of atoms in substituted cyclohexanes.
2. determine which cyclohexane conformation will generate a specific anti periplanar arrangement.

Stereochemical Requirements of the E2 Reaction

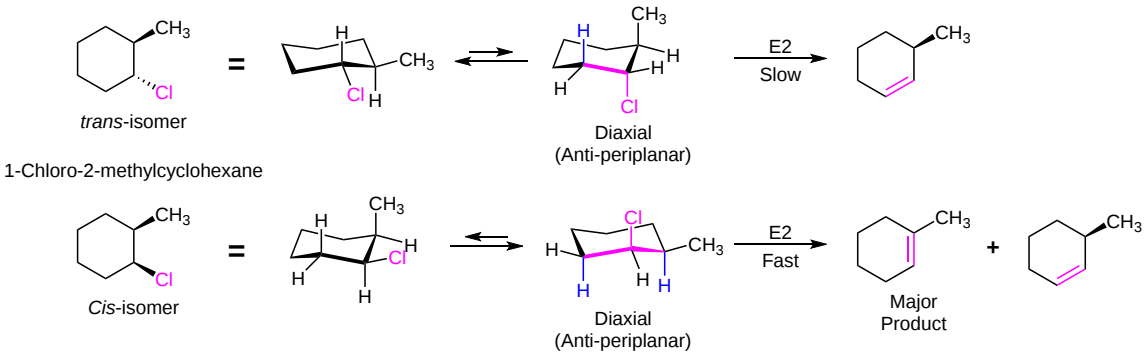
E2 elimination reactions of certain isomeric cycloalkyl halides show unusual rates and regioselectivity which can provide important supporting evidence that anti-periplanar is the preferred orientation of reactant species in the E2 transition state. Unlike open chain structures, cyclic compounds generally restrict the spatial orientation of ring substituents to relatively few arrangements. The compounds used here all have six-membered rings, so to achieve the anti-periplanar orientation required for the E2 reaction both the halogen and the adjacent hydrogen much assume an axial conformation.



For the compound, 2-methyl-1-chlorocyclohexane, the *cis* to the *trans* isomers have distinctly different reaction rates and form different preferred products. For example, *trans*-2-methyl-1-chlorocyclohexane reacts with alcoholic KOH at a much slower rate than does its *cis*-isomer. For trans-methyl-1-chlorocyclohexane, to obtains a chair conformation which places the chlorine substituent in the axial orientation required for E2 elimination, the methyl substituents is also forced into an axial position. Having both substituents in the axial position makes this chair conformer of the *trans*-isomer much less stable and presents an energy barrier that must be overcome for an E2 reaction to occur. When *cis*-2-methyl-1-chlorocyclohexane obtains a chair conformation which places its chlorine substituent in an axial orientation, the methyl substituent is forced into an equatorial orientation. Having one substituent axial and one equatorial makes this chair conformation of the cis-isomer lower in energy and thus easier to form. Consequently, the E2 reaction rates with the *trans*-isomer are slower than with the *cis*-isomer.

Furthermore, the product from E2 elimination of the *trans*-isomer is 3-methylcyclohexene (not predicted by Zaitsev's rule), whereas the *cis*-isomer gives the 1-methylcyclohexene as the preferred product (as predicted by Zaitsev's rule). The trans-isomer only has one adjacent hydrogen which can obtain an axial orientation along with the chlorine. The adjacent hydrogen which would lead to a 1-methylcyclohexene product cannot obtain the diaxial, anti-periplanar orientation with chlorine so an E2 reaction cannot occur. This makes 3-methylcyclohexene the preferred E2 elimination product of the *trans*-isomer showing that the anti-periplanar orientation requirement of E2 reactions is more important in determining products for this reaction than Zaitsev's rule.

In the *cis*-isomer the smaller chlorine atom assumes an axial position in the more stable chair conformation, and here there are two adjacent axial hydrogens. Removing one hydrogen forms the product, 3-methylcyclohexene, while removing the other hydrogen forms 1-methylcyclohexene. Here Zaitsev's rule determines that the more substituted alkene, 1-methylcyclohexene, is the preferred product.

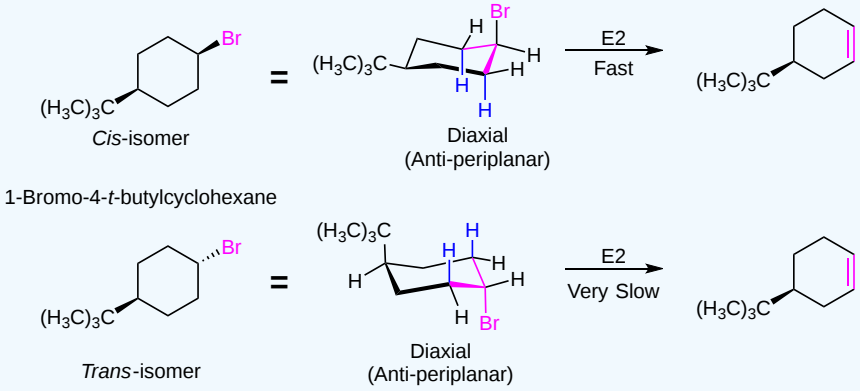


Worked Exercise 9.10.1

Which isomer would be expected to undergo E2 elimination quicker cis or trans-1-bromo-4-tert-butylcyclohexane? Explain your answer.

Answer

In the case of the 1-bromo-4-tert-butylcyclohexane isomers, the tert-butyl group is so large that it will always assume an equatorial orientation, leaving the bromine to be axial in the *cis*-isomer and equatorial in the *trans*-isomer. Because of symmetry, the two axial adjacent hydrogens in the *cis*-isomer react equally with base, resulting in rapid elimination to the same alkene (actually a racemic mixture). This reflects the fixed anti orientation of these hydrogens to the bromine atom. To assume a conformation having an axial bromine, the *trans*-isomer must tolerate serious crowding distortions. Such conformers are therefore present in extremely low concentration, and the rate of elimination is very slow. Indeed, substitution by hydroxide anion predominates in this situation.



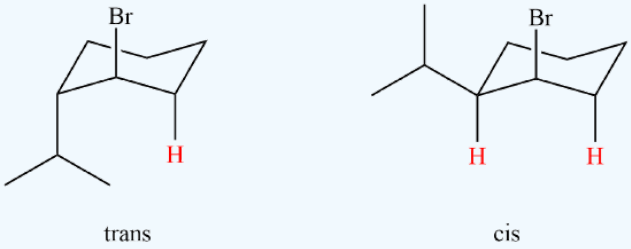
Exercise 9.10.1

Which of the following compounds will react faster in an E2 reaction; *trans*-1-bromo-2-isopropylcyclohexane or *cis*-1-bromo-2-isopropylcyclohexane?

Answer

The *cis* isomer will react faster than the *trans*. The *cis* isomer has two possible perpendicular hydrogen in which it can eliminate from.

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trans cis

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9.11: The E1 and E1cB Reactions

Objectives

After completing this section, you should be able to

1. write the mechanism for a typical E1 reaction.
2. explain why E1 elimination often accompanies S_N1 substitution.
3. write an equation to describe the kinetics of an E1 reaction.
4. discuss the stereochemistry of E1 reactions.
5. account for the lack of a deuterium isotope effect in E1 reactions.

Key Terms

Make certain that you can define, and use in context, the key terms below.

- E1 reaction
- E1cB reaction

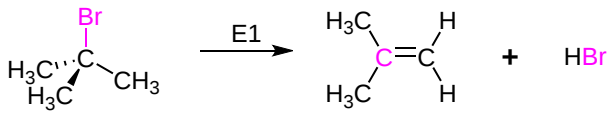
Study Notes

The abbreviation E1 stands for “unimolecular elimination”; that is, an E1 reaction is an elimination reaction in which only one species is involved in the rate-limiting step.

Unimolecular Elimination (E1) is a reaction in which the removal of an HX substituent results in the formation of a double bond. It is similar to a unimolecular nucleophilic substitution reaction (S_N1) in various ways. One being the formation of a carbocation intermediate. Also, the only rate determining (slow) step is the dissociation of the leaving group to form a carbocation, hence the name unimolecular. Thus, since these two reactions behave similarly, they compete against each other. Many times, both these reactions will occur simultaneously to form different products from a single reaction. However, one can be favored over another through thermodynamic control. Although Elimination entails two types of reactions, E1 and E2, we will focus mainly on E1 reactions with some reference to E2.

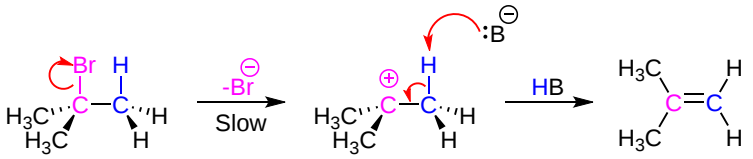
General E1 Reaction

An E1 reaction involves the removal of the halogen leaving group followed by the deprotonation of an adjacent hydrogen to produce an alkene product. In order to accomplish this, a Lewis base is required.



Mechanism

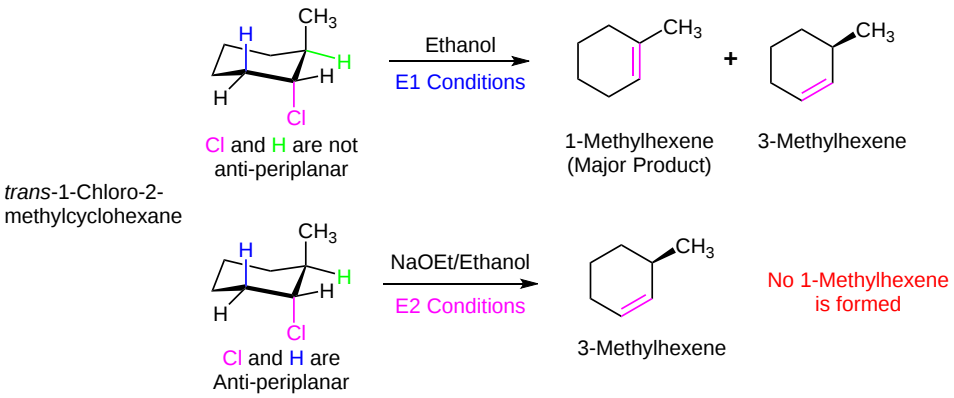
This mechanism starts with the spontaneous removal of the leaving group. The leaving group also removes the electrons from the C-Br bond, making the attached carbon a carbocation. In much the same fashion as the S_N1 mechanism, the first step of the E1 mechanism is slow thus making it the rate determining step. This makes E1 reaction kinetics unimolecular and first-order with respect to the substrate. Next, a Lewis Base (B^-) deprotonates an adjacent hydrogen from the carbocation. The electrons of the C-H bond are donated to the adjacent C-C bond, forming a double bond. Unlike E2 reactions, which require the adjacent proton to be *anti* to the leaving group, E1 reactions only require a neighboring hydrogen. This is due to the fact that the leaving group has left the molecule to form an achiral, trigonal planar carbocation.



Evidence for the E1 Mechanism

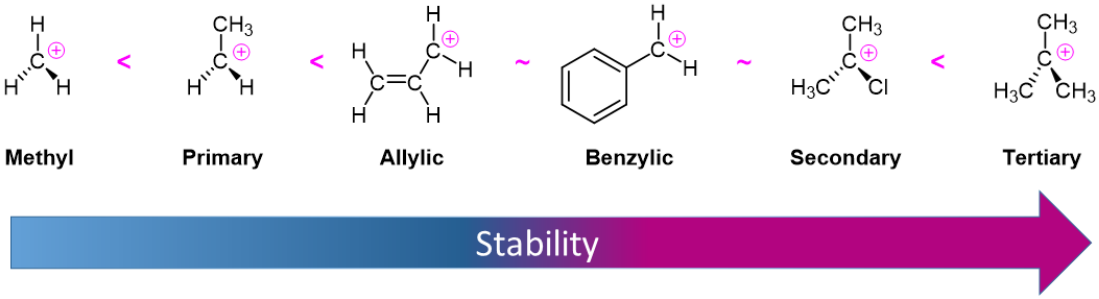
The primary evidence in support of the E1 mechanism is the fact that E1 reaction follow first-order kinetics which is consistent with the reaction mechanism containing a unimolecular dissociation as the rate determining step. Another piece of evidence is seen in the fact that E1 reactions show no deuterium isotope effect. Experiments have shown that there is no difference in reaction rate when deuterated and nondeuterated substrates are used. This is consistent with the E1 mechanism because a C-H bond is not broken in the rate determining step.

Lastly, because the halogen and hydrogen are removed in different steps, the mechanism of E1 reactions predicts that they will not require the anti-periplanar geometry required for E2 reactions. E1 reactions do not have the geometric constraints of E2 reactions discussed in **Sections 11-8** and **11-9**. In Section 11-9 an example showed that trans-1-Chloro-2-methylcyclohexane was capable of only forming the product 3-methylhexene during an E2 reaction due to the anti-periplanar constraints. When the same substrate is reacted under E1 conditions two elimination products (1-methylhexene and 3-methylhexene) are produced. In the substrate, the hydrogen marked as green cannot obtain anti-periplanar geometry with the Cl leaving group. Under E2 conditions this hydrogen and the Cl cannot be eliminated to form an elimination product. However, under E1 conditions the hydrogen and the Cl eliminate, despite the lack of anti-periplanar geometry, to form 1-methylhexene.

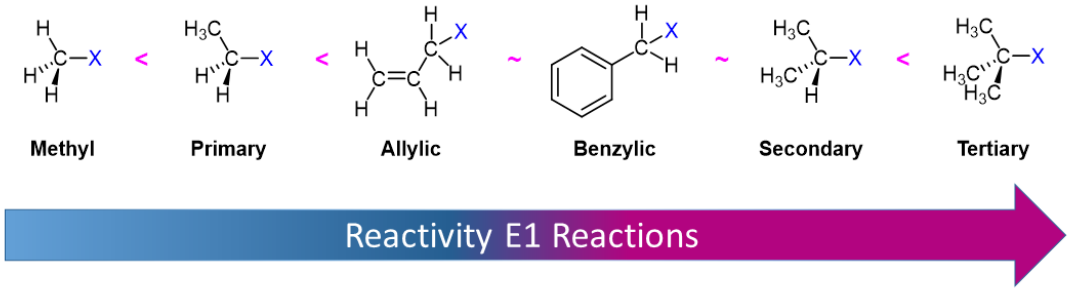


Alkyl Halide Reactivity in E1 Reactions

Due to the fact that E1 reactions create a carbocation intermediate, reactivity of alkyl halides toward E1 reaction mirror those present in S_N1 reactions.



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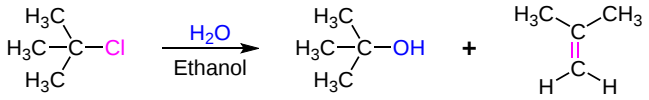


As expected, tertiary carbocations are favored over secondary, primary and methyl carbocations. This is due to the phenomena of hyperconjugation, which essentially allows a nearby C-C or C-H bond to interact with the p orbital of the carbon to bring the electrons down to a lower energy state. Thus, this has a stabilizing effect on the molecule as a whole. In general, primary and methyl carbocations do not proceed through the E1 pathway for this reason, unless there is a means of carbocation rearrangement to move the positive charge to a nearby carbon that is more stable. Secondary and Tertiary carbons form more stable carbocations, thus E1 reactions occur quite rapidly at these atoms.

Secondary carbocations can be subject to the E2 reaction pathway, but this generally occurs in the presence of a good/strong base. Adding a weak base to the reaction disfavors E2, essentially pushing towards the E1 pathway. In many instances, solvolysis occurs rather than using a base to deprotonate. This means heat is added to the solution, and the solvent itself deprotonates a hydrogen. The medium can effect the pathway of the reaction as well. Polar protic solvents may be used to hinder nucleophiles, thus disfavoring E2/S_N2 from occurring.

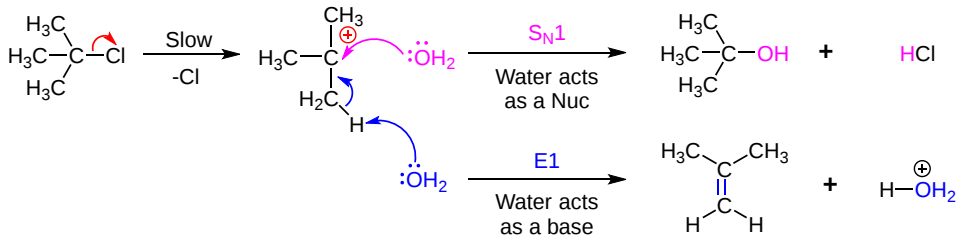
The Connection Between S_N1 and E1 Reactions

The E1 and S_N1 mechanisms both begin with the rate-determing step, the unimolecular removal of a leaving group to form a carbocation intermediate. Sharing the rate-determining step causes alkyl halides to produce both S_N1 substitution and E1 elimination products whenever they are reacted with nonbasic nucleophiles in a protic solvent. For example, the hydrolysis of *tert*-butyl chloride in a solution of water and ethanol gives a mixture of 2-methyl-2-propanol (60%) and 2-methylpropene (40%) at a rate independent of the water concentration.



2-Chloro-2-methylpropane → **2-Methyl-2-propanol (60%)** + **2-Methylpropene (40%)**

To produce the alcohol product, water attacks the carbocation as a nucleophile as part of an S_N1 reaction. To produce the alkene product, water acts as a base and deprotonates an adjacent hydrogen as part of an E1 reaction. As expected, the mechanism of the two reactions have similar characteristics. They both show first order kinetics; neither is much influenced by a change in the nucleophile/base; and both are relatively non-stereospecific.



To summarize, when carbocation intermediates are formed one can expect them to react further by one or more of the following modes:

1. The cation may bond to a nucleophile to give a substitution product.

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2. The cation may transfer a adjacent proton to a base, giving an alkene product.
3. The cation may rearrange to a more stable carbocation, and then react by mode #1 or #2.

Comparing E1 and E2 Mechanisms

When considering whether an elimination reaction is likely to occur via an E1 or E2 mechanism, we really need to consider three factors:

1) **The base:** strong bases favor the E2 mechanism, whereas, E1 mechanisms only require a weak base.

2) **The solvent**: good ionizing solvents (polar protic) favor the E1 mechanism by stabilizing the carbocation intermediate.

3) **The alkyl halide:** primary alkyl halides have the only structure useful in distinguishing between the E2 and E1 pathways. Since primary carbocations do not form, only the E2 mechanism is possible.

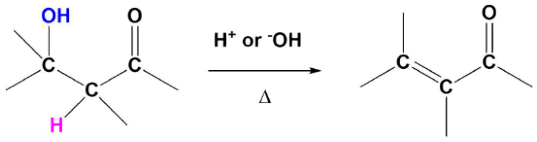
Ultimately, whether the elimination mechanism is E1 or E2 is not very important, since the product is the same alkene. We need to remember, however, that Zeitzev´s rule always determines the most likely alkene to be formed.

Reaction Parameter	E2	E1
alkyl halide structure	tertiary > secondary > primary	tertiary > secondary >>>> primary
nucleophile	high concentration of a strong base	weak base
mechanism	1-step	2-step
rate limiting step	bimolecular transition state	carbocation formation
rate law	rate = k[R-X][Base]	rate = k[R-X]
solvent	not important	polar protic

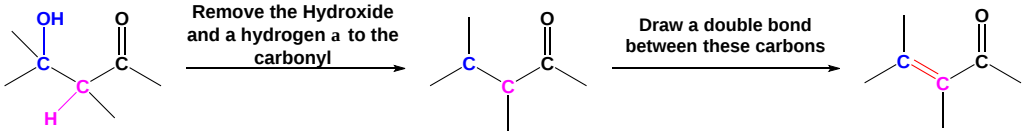
The E1cB Reaction

Although E1 reactions typically involve a carbocation intermediate, the E1cB reaction utilizes a carbanion intermediate. A proton adjacent to a carbonyl group is removed using a strong base. This proton is acidic because the resulting conjugate base anion is stabilized by delocalization on to the carbonyl group. This anion causes the expulsion of an adjacent leaving group to create an alkene which is conjugated with the carbonyl which is called an enone. This reaction is generally utilized when a poor leaving group, such as a hydroxide, is involved. This poor leaving group makes the direct E1 or E2 reactions difficult. This reaction is used later in a reaction called an aldol condensation which will be discussed in **Section 23-3**.

General Reaction

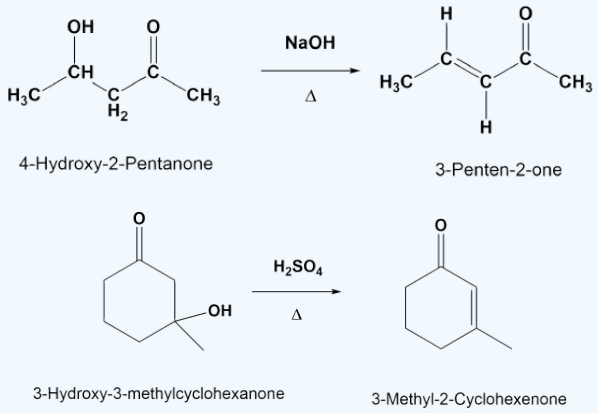


Predicting the Product of an E1cB Reaction



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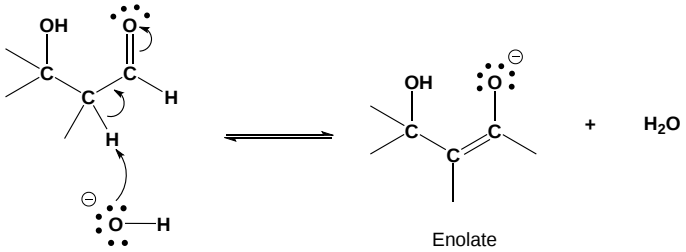
Example 11.10.1



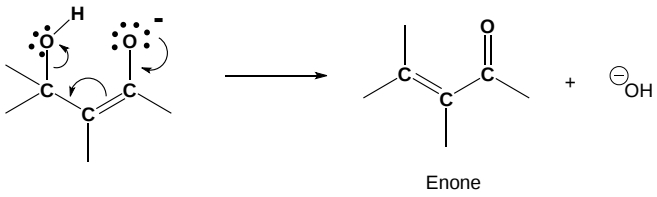
E1cB Mechanism

The mechanism starts with the base removing a hydrogen to form an alkoxide anion. The alkoxide reforms the carbonyl C=O bond promoting the elimination of alcohol OH as a leaving group which also reforms the base catalyst. Although the base catalyzed elimination of alcohols is rare, it happens in this case in part due to the stability of the conjugated enone product.

1) Deprotonation to form the anion



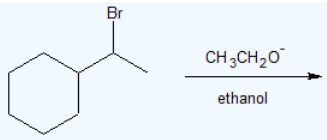
2) Leaving Group Removal

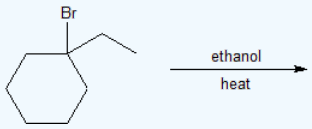


Note! The double bond always forms in conjugation with the carbonyl.

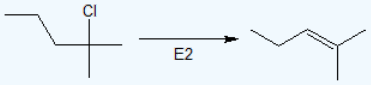
Exercise 9.11.1

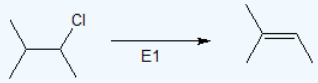
1. Predict the dominant elimination mechanism (E1 or E2) for each reaction below. Explain your reasoning.

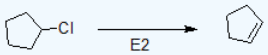
a) 

b) 

2) Specify the reaction conditions to favor the indicated elimination mechanism.

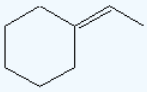
a) 

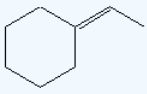
b) 

c) 

Answer

1)

a)  E2 reaction b/c secondary alkyl halide with a strong base.

b)  E1 reaction b/c tertiary alkyl halide with a weak base.

2)

a) strong base, such as hydroxide, an alkoxide, or equivalent

b) water or alcohol or equivalent weak base with heat

c) strong base, such as hydroxide, an alkoxide, or equivalent

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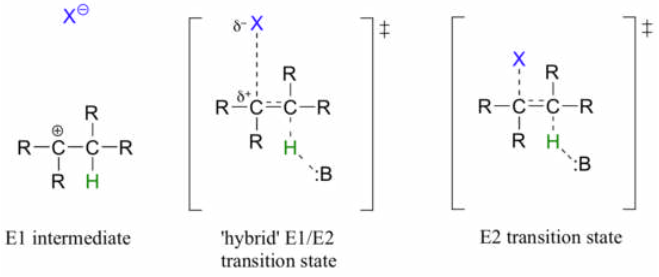
9.12: Biological Elimination Reactions

Objective

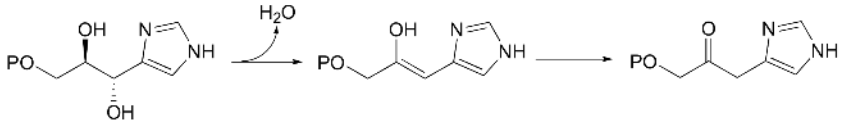
After completing this section, you should have an appreciation that E1, E2 and E1cB mechanisms exist and are well-known in biological chemistry.

Enzymatic E1 and E2 reactions

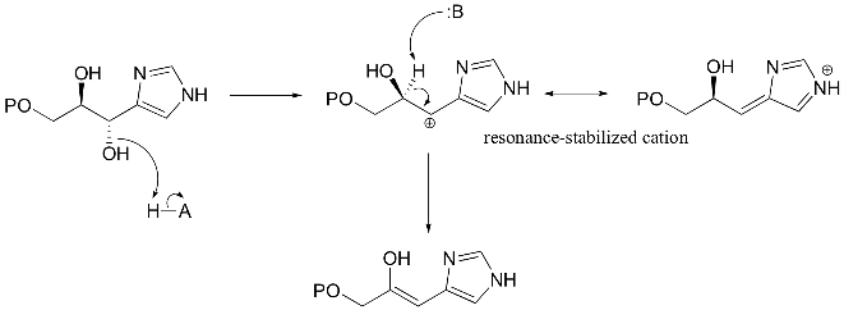
While most biochemical b-elimination reactions are of the E1cb type, some enzymatic E2 and E1 reactions are known. Like the enzymatic S_N2 and S_N1 substitution mechanisms discussed in chapters 8 and 9, the E2 and E1 models represent two possible mechanistic extremes, and actual enzymatic elimination reactions may fall somewhere in between. In an E1/E2 hybrid elimination, for example, C_β-X bond cleavage may be quite advanced (but not complete) before proton abstraction takes place - this would lead to the build-up of transient *partial* positive charge on C_β, but a discreet carbocation intermediate would not form. The extent to which partial positive charge builds up determines whether we refer to the mechanism as 'E1-like' or 'E2-like'.



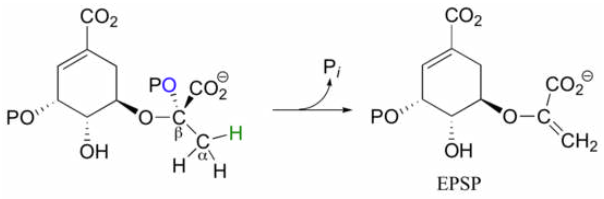
A reaction in the histidine biosynthetic pathway provides a good example of a biological E1-like elimination step (we're looking specifically here at the first, enol-forming step in the reaction below - the second step is simply a tautomerization from the enol to the ketone product (section 13.1A)).



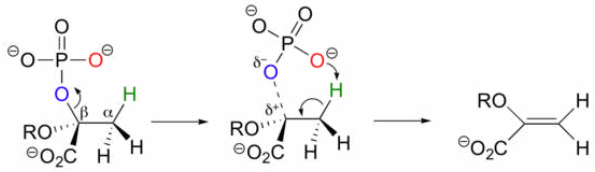
Notice in this mechanism that an E1cb elimination is not possible - there is no electron-withdrawing group (like a carbonyl) to stabilize the carbanion intermediate that would form if the proton were abstracted first. There is, however, an electron-*donating* group (the lone pair on a nitrogen) that can stabilize a positively-charged intermediate that forms when the water leaves.



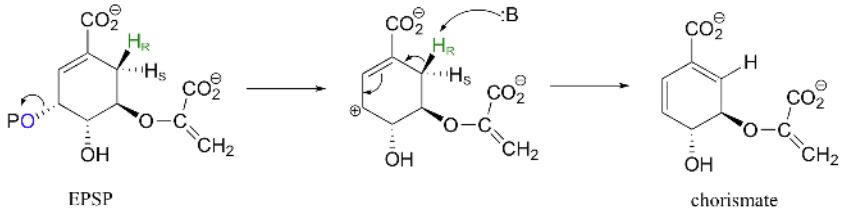
Another good example of a biological E1-like reaction is the elimination of phosphate in the formation of 5-enolpyruvylshikimate-3-phosphate (EPSP), an intermediate in the synthesis of aromatic amino acids.



Experimental evidence indicates that significant positive charge probably builds up on C_β of the starting compound, implying that C-O bond cleavage is advanced before proton abstraction occurs (notice the parallels to the Cope elimination in the previous section):

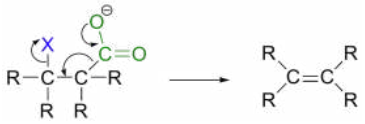


The very next step in the aromatic acid biosynthesis pathway is also an elimination, this time a 1,6-conjugated elimination rather than a simple beta-elimination.

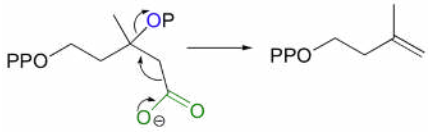


An E1-like mechanism (as illustrated above) has been proposed for this step, but other evidence suggests that a free-radical mechanism may be involved.

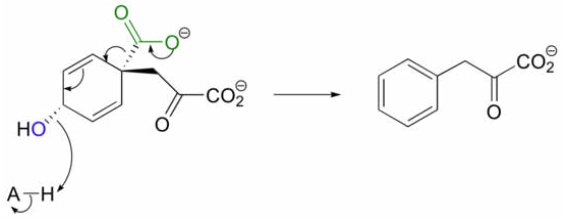
While most E1 and E2 reactions involve proton abstraction, eliminations can also incorporate a decarboxylation step.



Isopentenyl diphosphate, the 'building block' for all isoprenoid compounds, is formed from a decarboxylation-elimination reaction.



Phenylpyruvate, a precursor in the biosynthesis of phenylalanine, results from a conjugated 1,6 decarboxylation-elimination.



9.12: Biological Elimination Reactions is shared under a CC BY-SA 4.0 license and was authored, remixed, and/or curated by Tim Soderberg.

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9.13: A Summary of Reactivity - SN1, SN2, E1, E1cB, and E2

Objectives

After completing this section, you should be able to

1. determine whether a specified substrate is most likely to undergo an E1, E2, S_N1 or S_N2 reaction under a given set of conditions.
2. describe the conditions under which a given substrate is most likely to react by a specified mechanism (E1, E2, S_N1 or S_N2).

Study Notes

This section summarizes much of what has been discussed in the chapter. It focuses on how a given substrate will behave under certain conditions, but does not deal with the stereochemistry of the products.

Having discussed the many factors that influence nucleophilic substitution and elimination reactions of alkyl halides, we must now consider the practical problem of predicting the most likely outcome when a given alkyl halide is reacted with a given nucleophile. As we noted earlier, there are multiple variables to be considered, **the most important being the substitution of the alkyl halide**. S_N2 reactions favor alkyl halides with little steric hindrance such as methyl halides and primary halides. In general, in order for an S_N1 or E1 reaction to occur, the relevant carbocation intermediate must be relatively stable such as with tertiary halides, secondary allylic halides, and secondary benzylic halides.

The next most import variable for predicting the outcome of a reaction is **the nature of the nucleophilic reactant**. Strong nucleophiles favor S_N2 substitution, and strong bases, especially strong hindered bases (such as tert-butoxide) favor E2 elimination. Weak nucleophiles that are also weak bases tend to favor S_N1 and E1 reactions.

- **Good Nucleophiles Which are Weak Bases:** I^-, Br^-, SCN^-, N_3^-, $CH_3CO_2^-$, RS^-, CN^-, Amines, etc.
- **Good Nucleophiles Which are Strong Bases:** HO^-, RO^-.
- **Poor Nucleophiles which are Weak Bases:** H_2O, ROH, RSH.

General Rules For Predicting a Reaction

Consider these in the order listed.

Methyl Alkyl Halides

- An S_N2 substitution occurs regardless if a good or poor nucleophile is used.

Primary Alkyl Halides

- An E2 elimination occurs if a strong, sterically hindered base is used.
- An E1cB elimination occurs if a strong base is used and the leaving group is two carbons away from a carbonyl group.
- An S_N2 substitution occurs if a good nucleophile is used.

Secondary Alkyl Halides

- An E1cB elimination occurs if a strong base is used and the leaving group is two carbons away from a carbonyl group.
- An E2 elimination occurs if a strong base is used.
- An S_N2 reaction occurs if a good nucleophile that is a weak bases is used in a polar aprotic solvent.
- An S_N1 reaction along with an E1 reaction occurs if a poor nucleophile that is a weak bases is used in a protic solvent.

Tertiary Alkyl Halides

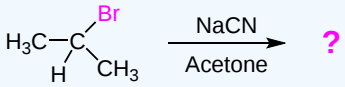
- An E1cB elimination occurs if a strong base is used and the leaving group is two carbons away from a carbonyl group.
- An E2 elimination occurs if a strong base is used.

- An S_N1 reaction along with an E1 reaction occurs if a poor nucleophile that is a weak bases is used in a protic solvent.

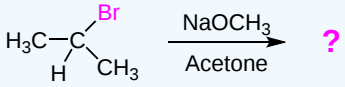
Worked Example 9.13.1

1) For the following, please determine what kind of reaction is occurring and predict the product(s).

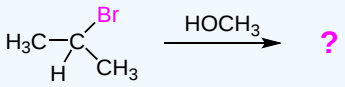
a)



b)

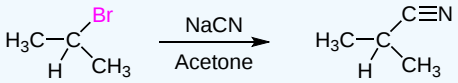


c)

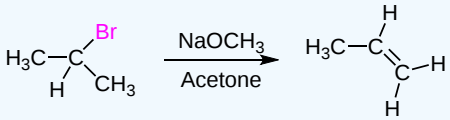


Answer

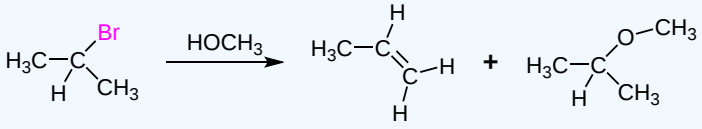
a) The substrate is a secondary halide so the product is determined by the nature of the nucleophile used in the reaction. Cyanide (^-CN) is a good nucleophile which is a weak base. The fact that the nucleophile is a weak base means that an E2 reaction is not favored. Also, the fact that cyanide is a good nucleophile means that S_N2 substitutions are favored over S_N1. When a secondary halide is reacted with a good nucleophile which is a weak base, the preferred reaction is S_N2. After S_N2 substitution the product is a nitrile.



b) The substrate is a secondary halide so the product is determined by the nature of the nucleophile used in the reaction. Methoxide ($^-OCH_3$) is a strong base so it could prefer to remove a hydrogen from the substrate. This makes an E2 elimination the preferred reaction and an alkene the product.

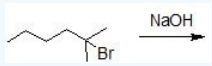


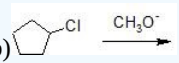
c) The substrate is a secondary halide so the product is determined by the nature of the nucleophile used in the reaction. Methanol ($HOCH_3$) is a weak nucleophile that is a weak base. Being a weak base means that methanol is not capable of actively removing a hydrogen to cause an E2 reaction. Also, because methanol is a weak nucleophile is not capable of attacking the substrate and causing an S_N2 reaction. For the methanol nucleophile to react the substrate must first eject it leaving group to form the highly reactive carbocation intermediate. Formation of the carbocation is the rate determine step for both the S_N1 and E1 reactions so they each form a separate product.

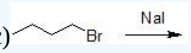


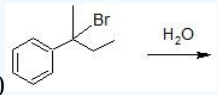
Exercises 9.13.1

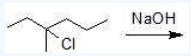
1. Identify the dominant reaction mechanism (S_N1, S_N2, E1, or E2) and predict the major product for the following reactions.

a) 

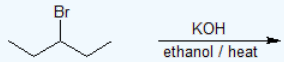
b) 

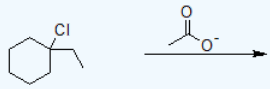
c) 

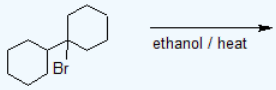
d) 

e) 

a) 

b) 

c) 

d) 

2) Identify the function of the following reagents. The reagents will be a strong/weak nucleophile and/or a strong/weak base.

a) Cl^-

b) NaH

c) t-BuO^-

d) OH^-

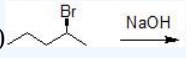
e) H_2O

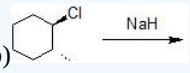
f) HS^-

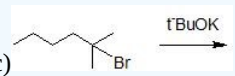
g) MeOH

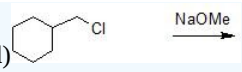
3) Identify which mechanism the following reactions would undergo.

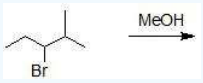
4) Identify all the products of the following reactions and specify the major product.

a) 

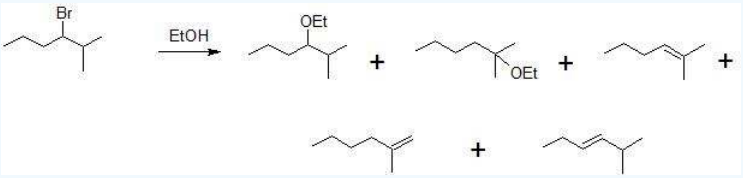
b) 

c) 

d) 

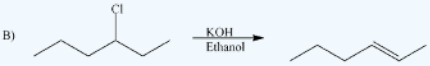
e) 

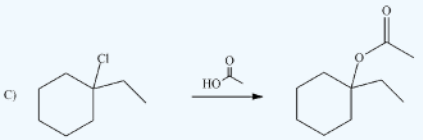
5) The following reaction yields five different products. Give the mechanisms for how each is formed.

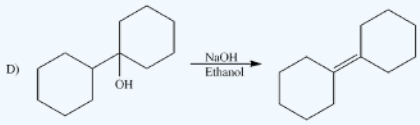


6) Label the following reactions as S_N1, S_N2, E1, or E2.

A) 

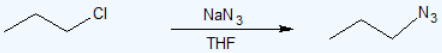
B) 

C) 

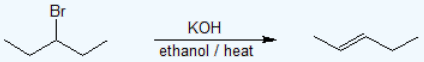
D) 

Answer

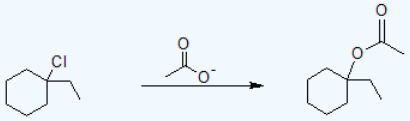
1)

a) 

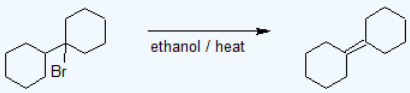
S_N2 b/c primary alkyl halide and strong nucleophile that is a weak base in a polar aprotic solvent

b) 

E2 b/c secondary alkyl halide and a strong base heated

c) 

SN1 b/c tertiary alkyl halide with a weak nucleophile that is a weak base

d) 

E1 b/c tertiary alkyl halide with a weak base heated

2)

a) Cl^- ; strong nucleophile

b) NaH ; strong base

c) t-BuO^- ; strong base

d) OH^- ; strong nucleophile ; strong base

e) H_2O ; weak nucleophile ; weak base

f) HS^- ; strong nucleophile

g) MeOH ; weak nucleophile ; weak base

3)

a) E2, S_N1

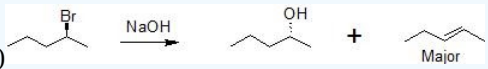
b) S_N2, E2

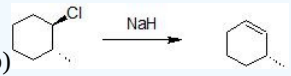
c) S_N2

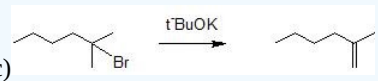
d) S_N1, E1

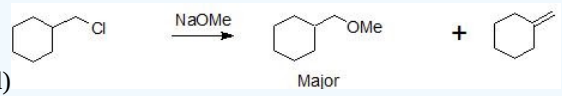
e) E2, S_N1

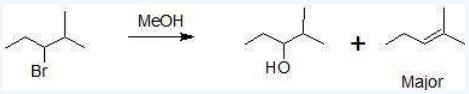
4)

a) 

b) 

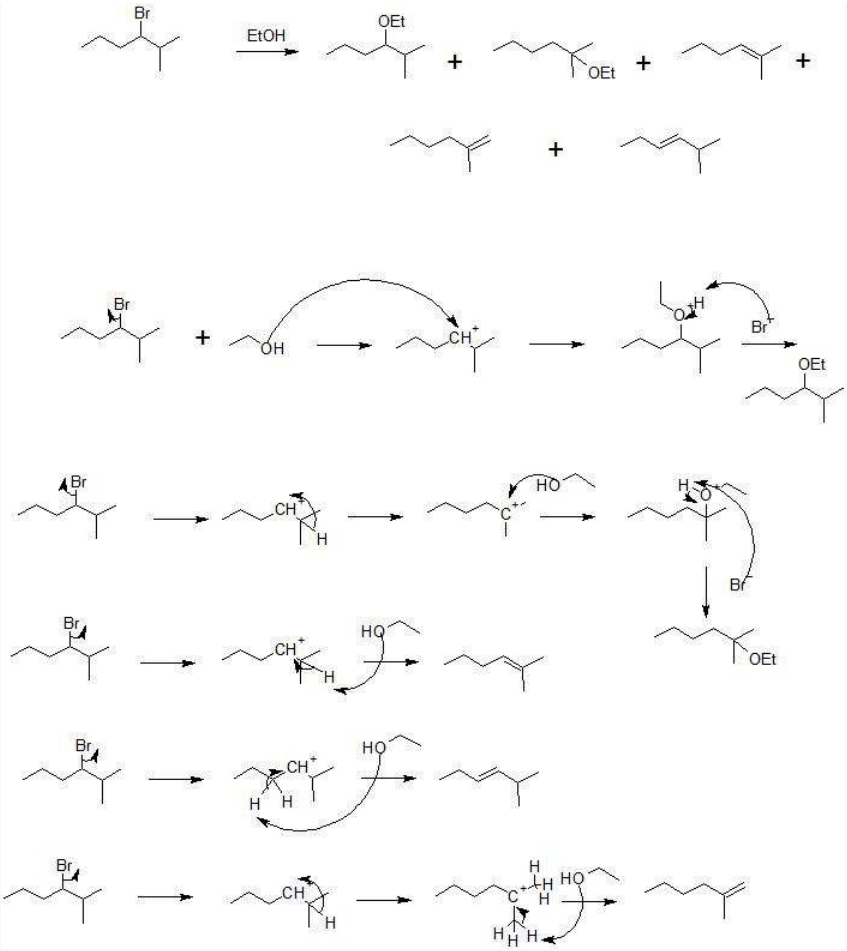
c) 

d) 

e) 

5)

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6)

A – S_N2

B – E1

C – S_N1

D – E2

9.13: A Summary of Reactivity - SN1, SN2, E1, E1cB, and E2 is shared under a CC BY-SA 4.0 license and was authored, remixed, and/or curated by Dietmar Kennepohl & William Reusch.

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CHAPTER OVERVIEW

10: Alkenes- Structure and Reactivity

Learning Objectives

After you have completed Chapter 10, you should be able to

1. fulfill all of the detailed objectives listed under each individual section.
2. describe the importance of alkenes to the chemical industry.
3. use the concept of “degree of unsaturation” in determining chemical structures.
4. describe the electronic structure and geometry of alkenes.
5. describe the factors that influence alkene stability, and determine the relative stability of a number of given alkenes.
6. write the IUPAC name of a given alkene, and draw the structure of any alkene, given its IUPAC name.
7. determine whether a given alkene has an *E* configuration or a *Z* configuration.
8. explain why alkenes are more reactive than alkanes.
9. describe the reaction between an alkene and a hydrogen halide, and explain why one product is formed rather than another. Base your explanation on the concepts of carbocation stability and the Hammond postulate.
10. define, and use in context, the key terms introduced in this chapter.

This, the first of two chapters devoted to the chemistry of alkenes, describes how certain alkenes occur naturally, then shows the industrial importance of ethylene and propylene (the simplest members of the alkene family). The electronic structure of alkenes is reviewed, and their nomenclature discussed in detail. After dealing with the question of cis-trans isomerism in alkenes, Chapter 7 introduces the reactivity of the carbon-carbon double bond. The chapter then focuses on one specific reaction—the addition of hydrogen halides to alkenes—to raise a number of important concepts, including carbocation stability and the Hammond postulate.

10.1: Introduction to Alkenes
10.2: Industrial Preparation and Use of Alkenes
10.3: Naming Alkenes
10.4: Cis-Trans Isomerism in Alkenes
10.5: Sequence Rules - The E,Z Designation
10.6: Stability of Alkenes
10.7: Electrophilic Addition Reactions of Alkenes
10.8: Orientation of Electrophilic Additions - Markovnikov's Rule
10.9: Carbocation Structure and Stability
10.10: The Hammond Postulate
10.11: Evidence for the Mechanism of Electrophilic Additions - Carbocation Rearrangements

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10.1: Introduction to Alkenes

Objective

After completing this section, you should be able to give an example of a naturally occurring compound that contains at least one double bond.

Key Terms

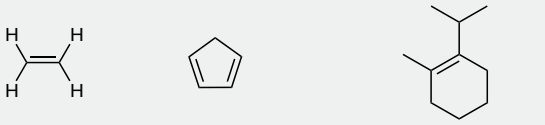
Make certain that you can define, and use in context, the key term below.

- olefin

Study Notes

Alkenes are a class of hydrocarbons (i.e., containing only carbon and hydrogen). They are unsaturated compounds with at least one carbon-to-carbon double bond. The double bond makes Alkenes more reactive than alkanes. Olefin is another term used to describe alkenes.

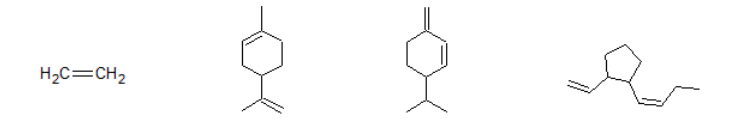
The graphic shows three alkenes. The more complex alkene is commonly known as 1-menthene, but its full proper IUPAC name is 1-methyl-2-(1-methylethyl)-cyclohexene.



ethene | 1,3-cyclopentadiene | 1-menthene (peppermint fragrance)

Alkenes

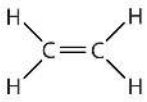
Alkenes are a class of hydrocarbons (i.e., containing only carbon and hydrogen). They are unsaturated compounds with at least one carbon-to-carbon double bond. The double bond makes alkenes more reactive than alkanes. Olefin is another term used to describe alkenes. The alkene group can also be called a vinyl group and the carbons sharing the double bond can be called vinyl carbons.



fruit ripening hormone | oil of eucalyptus | limonene | sex attractanct of brown algae

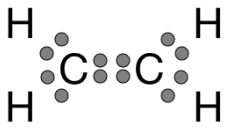
Structure of Ethene - the Simplest Alkene

Ethene is often written as CH_2=CH_2 which stands for:

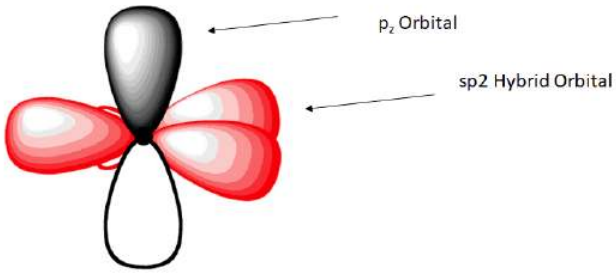


The double bond is shared by the two carbon atoms and does not involve the hydrogen atoms, although the condensed formula does not make this point obvious. Note that the molecular formula for ethene is C_2H_4, whereas that for ethane is C_2H_6.

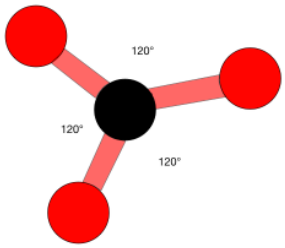
Ethene is not a very complicated molecule. It is made up of four $1s^1$ hydrogen atoms and two $2s^2$ $2p_x^1$ $2p_y^1$ carbon atoms. These carbon atoms already have four electrons, but they each want to get four more so that they have a full eight (octet) in the valence shell. Having eight valence electrons around carbon gives the atom the same electron configuration as neon, a noble gas. Carbon wants to have the same configuration as neon because when it has eight valence electrons carbon is at its most stable, lowest energy state.



This forms a total of three bonds to each carbon atom, giving them an sp^2 hybridization. Since the carbon atom is forming three sigma bonds instead of the four that it can, it only needs to hybridize three of its outer orbitals, instead of four. It does this by using the $2s$ electron and two of the $2p$ electrons, leaving the other unchanged. This new orbital is called an sp^2 hybrid because it is made from one s orbital and two p orbitals.



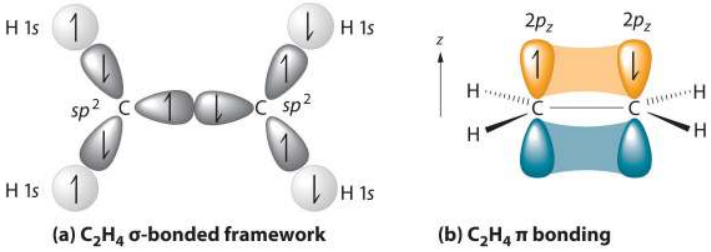
When atoms use sp^2 hybrids they have a trigonal planar structure. These structures are very similar to a 'peace' sign, there is a central atom with three atoms around it, all on one plane. Trigonal planar molecules have an ideal bond angle of 120° on each side.



The H-C-H bond angle is 117°, which is very close to the ideal 120° of a carbon with sp^2 hybridization. The other two angles (H-C=C) are both 121.5°.

Rigidity in Ethene

There is rigidity in the ethene molecule due to the double-bonded carbons. A double bond consists of one sigma bond formed by overlap of sp^2 hybrid orbitals and one pi bond formed by overlap of parallel 2 p orbitals. In ethene there is no free rotation about the carbon-carbon sigma bond because these two carbons also share a π bond. A π bond is only formed when there is adequate overlap between both top and bottom p-orbitals. Rotation of the p-orbitals causes them to be 90° from each other breaking the π bond because there would be no overlap. There is a much larger energy barrier to rotation than there is about a carbon-carbon sigma bond.



(a) C_2H_4 σ-bonded framework (b) C_2H_4 π bonding

(a) The σ-bonded framework is formed by the overlap of two sets of singly occupied carbon sp^2 hybrid orbitals and four singly occupied hydrogen 1s orbitals to form electron-pair bonds. This uses 10 of the 12 valence electrons to form a total of five σ bonds (four C–H bonds and one C–C bond).

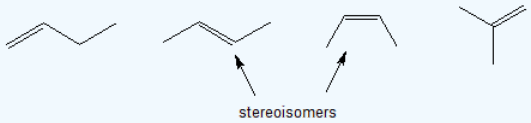
(b) One singly occupied unhybridized $2p_z$ orbital remains on each carbon atom to form a carbon–carbon π bond. (Note: by convention, in planar molecules the axis perpendicular to the molecular plane is the z-axis.)

? Exercise

1. Although there is only one alkene with the formula C_2H_4 (ethene) and only one with the formula C_3H_6 (propene), there are several alkenes with the formula C_4H_8. Draw all of the possible bond line structures for alkenes with the formula C_4H_8 including all possible structural and stereoisomers.

Answer

1. There are three possible structural isomers. 2-butene can exist as two different stereoisomers.



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10.2: Industrial Preparation and Use of Alkenes

Objectives

After completing this section, you should be able to

1. discuss the industrial importance of ethylene (ethene) and propylene (propene).
2. describe, briefly, the industrial process known as thermal cracking.

Study Notes

Among the most important and most abundant organic chemicals produced worldwide are the two simple alkenes, ethylene and propylene. They are used as the starting materials to synthesize numerous valuable compounds.

Produced from ethylene (ethene)

Chemical	Uses
ethanol	solvent; constituent of cleaning preparations; in synthesis of esters
acetaldehyde	slug killer, in the form of methaldehyde $(CH_3CHO)_4$
acetic acid	manufacture of vinyl acetate polymers, ethyl acetate solvent and cellulose acetate polymers
ethylene oxide	“cellosolves” (industrial solvents)
ethylene glycol	anti-freeze; production of DacronOR
ethylene dichloride	solvent; production of vinyl chloride
vinyl chloride	manufacture of poly (vinyl chloride)—PVC
vinyl acetate	manufacture of poly (vinyl acetate) used in paint emulsions, plywood adhesives and textiles
polyethylene	“plastic” bags; toys; packaging

Produced from propylene (propene)

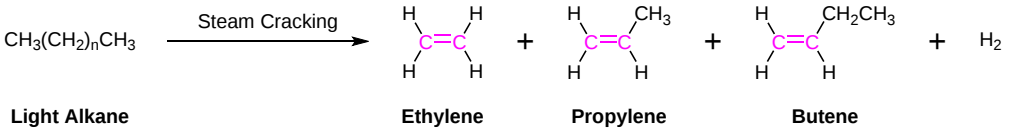
Chemical	Uses
isopropyl alcohol	rubbing alcohol; cosmetics; synthesis of acetone
propylene oxide	manufacture of polyurethanes; polyesters
cumene	industrial preparation of phenol and acetone
polypropylene	molded articles (e.g., kitchenware); fibres for indoor-outdoor carpeting

Industrial Preparation of Ethylene and Propylene

Ethene (CH_2CH_2) and propene (CH_3CHCH_2), are most often called by their common names—ethylene and propylene. Ethylene is a major commercial chemical. The US chemical industry produces about 25 billion kilograms of ethylene annually, more than any other synthetic organic chemical. More than half of this ethylene goes into the manufacture of polyethylene, one of the most familiar plastics. Propylene is also an important industrial chemical. It is converted to plastics, isopropyl alcohol, and a variety of

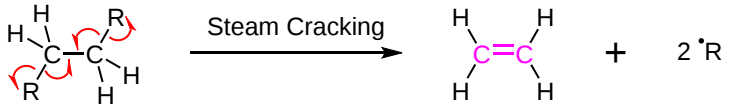
other products. Both ethylene and propylene are the feedstock for the industrial synthesis of a wide variety of small organic molecules.

Ethylene, propylene, and butylene ($CH_3CH_2CHCH_2$) are typically industrially synthesized through the steam cracking of light alkanes (C < 8) obtained from fractional distillation of crude oil. Cracking is the name given to a number of petroleum refining processes which break up large hydrocarbon molecules into smaller fragment. Steam cracking is achieved without a catalyst by using high temperatures (~900 ^oC) and produces a mixtures of products containing high proportions of hydrocarbons with double bonds. There is not any single unique reaction happening during steam cracking. The hydrocarbon molecules are broken up in a fairly random way but the process can be generically represented by the reaction below.



Light Alkane **Ethylene** **Propylene** **Butene**

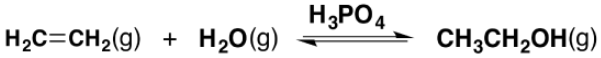
The mechanism of the steam cracking is complex and believed to involve the formation of free radicals. The high temperatures of steam cracking is enough to cause the homolytic cleavage of C-C and C-H bonds in the starting material. The cleavage of C-C bonds inherently creates smaller hydrocarbons as represented below.



Ethylene **Radical**

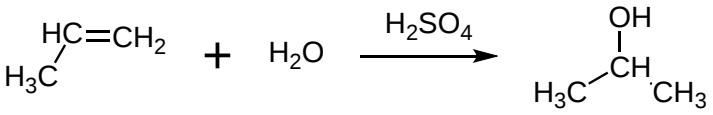
Industrial Preparations of Alcohols from Ethylene and Propylene

Ethanol is manufactured by reacting ethylene with steam. The catalyst used is solid silicon dioxide coated with phosphoric acid. The reaction is reversible.



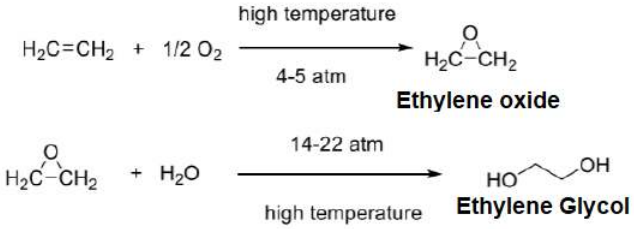
Only 5% of the ethylene is converted into ethanol at each pass through the reactor. By removing the ethanol from the equilibrium mixture and recycling the ethylene, it is possible to achieve an overall 95% conversion.

Isopropyl alcohol is synthesized on an industrial scale using a similar reaction with propylene.



Propylene **Isopropyl Alcohol**

Ethylene is also used in the industrial synthesis of ethylene glycol. Ethylene glycol is a major industrial compound with a wide range of applications. The traditional method to synthesize ethylene glycol is a two step process in which ethylene is directly oxidized to ethylene oxide. Next the three-membered ring of ethylene oxide is opened using water at high temperatures and pressures to form ethylene glycol.



https://chem.libretexts.org/@go/page/418139

Industrial Preparations of Plastics from Ethylene and Propylene

One of the primary uses of industrial synthesized ethylene is the production of the polymer **polyethylene (PE)**. Polyethylene is the most common plastic. As of 2017, over 100 million tons of polyethylene resins are produced annually, accounting for 34% of the total plastics market. Its primary use is in packaging (plastic bags, plastic films, geomembranes, containers including bottles, etc.). Many kinds of polyethylene are known, with most having the chemical formula $(C_2H_4)_n$.

It is the simplest polymer, consisting of random-length (but generally very long) chains made up of two-carbon units. During the polymerization process many ethylene molecules are linked together to form the carbon backbone of polyethylene. In the polyethylene structures are represented below. The squiggly lines at the ends of the long structure indicate that the same pattern extends indefinitely. The more compact notation on the right shows the minimal repeating unit enclosed in brackets; this means the same thing and is the preferred way of depicting polymer structures.

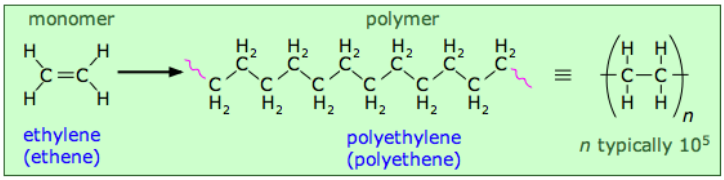


Figure **10.2.1** Polyethylene.

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10.3: Naming Alkenes

Objectives

After completing this section, you should be able to

- provide the correct IUPAC name for an acyclic or cyclic alkene, given its Kekulé, condensed or shorthand structure.
- draw the Kekulé, condensed or shorthand structure of an alkene (cyclic or acyclic), given its IUPAC name.
- give the IUPAC equivalent of the following trivial names: ethylene, propylene, isobutylene and isoprene.
- draw the structure of a vinyl (ethenyl) and allyl (2-propenyl) group, and use these names in alkene nomenclature.

Study Notes

This course uses IUPAC nomenclature; therefore, you need not usually memorize a large number of trivial names. However, you will encounter some trivial names so frequently in books and articles that they soon become familiar.

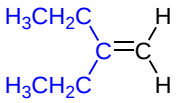
An alkene that can exhibit geometric isomerism has not been properly named unless its name specifies whether the double bond (or bonds) is (or are) cis or trans. The most effective way of giving this information is discussed, and more details of cis and trans follow in Section 7.4.

Alkenes contain carbon-carbon double bonds and are unsaturated hydrocarbons with the molecular formula is C_nH_{2n}; this is also the same molecular formula as cycloalkanes. The parent chain of an alkene is the longest chain containing both carbon atoms of the double bond. Alkenes are named by dropping the **-ane** ending of the parent and adding **-ene**. Also, the position of double bond in the parent chain of the alkene is indicated with a number.

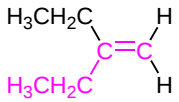
The Basic Rules for Naming Alkenes

For straight chain alkenes, it is the same basic rules as nomenclature of alkanes apply except the **-ane** suffix is changed to **-ene**.

1) Find the longest carbon chain that contains both carbons of the double bond.

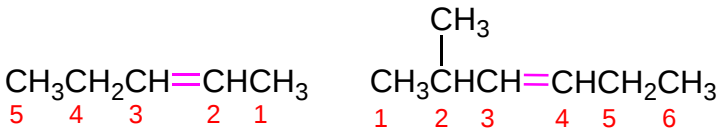


This compound is NOT named as an pentene



This compound is named as a butene because the double bond is contained in the four carbon chain

2) Start numbering from the end of the parent chain which gives the lowest possible number to the double bond. If the double bond is equidistant from both ends of the parent chain, number from the end which gives the substituents the lowest possible number. The double bond in cycloalkenes do not need to number because it is understood that they are in the one position.

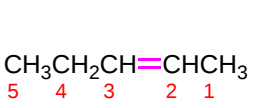


3) Place the location number of the double bond directly before the parent name. The location number indicates the position of the first carbon of the double bond. Add substituents and their position to the alkene as prefixes. Remember substituents are written in alphabetical order.

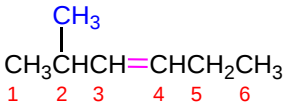
The presence of multiple double bonds is indicated by using the appropriate suffix such as **-diene**, **-triene**, ect. Each of the multiple bonds receives a location number. Also, only **-ne** is removed from the parent alkane chain name leaving an "a" in the name.

Overall, the name of an alkene should look like:

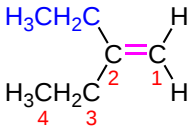
(Location number of substituent)-(Name of substituent)-(Location number of double bond)-(Name of parent chain) + ene



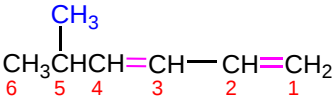
2-Pentene



2-Methyl-3-hexene



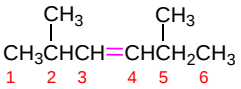
3-Ethyl-1-butene

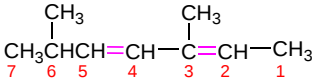


5-Methyl-1,3-hexadiene

Newer IUPAC Nomenclature

In 1993 IUPAC updated their naming recommendation to place the location number of the double bond before the -ene suffix of alkene names. The provides names such as hex-2-ene rather than 2-hexene. The newer system is slowly being accepted so it may occasionally be encountered.

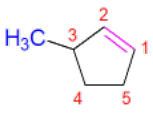




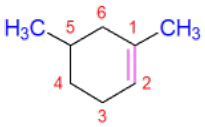
Older Numbering System:	**2,5-Dimethyl-3-hexene**	**5-Methyl-1,3-hexadiene**
Newer Numbering System:	**2,5-Dimethylhex-3-ene**	**5-Methylhexa-1,3-diene**

Naming Cycloalkenes

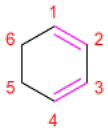
Because there are no chain ends in cycloalkenes, the double bond is assumed to numbered C1 and C2 and its location number is not required in the name. The direction of the numbering is determined by which will give the substituent closest to the double bond the lowest number. If multiple double bonds are present, it may be necessary to include their location numbers in the name. One of the double bonds will be number C1 and C2 and the numbering direction is determined by which gives the remaining double bonds the lowest possible number.



3-Methylcyclopent-1-ene



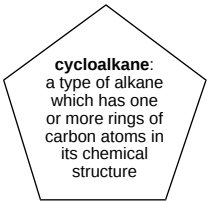
1,5-Dimethylcyclohexene



1,3-Cyclohexadiene
(New:Cyclohexa-1,3-diene)

Endocyclic vs. Exocyclic Alkenes

Endocyclic double bonds have both carbons in the ring and exocyclic double bonds have only one carbon as part of the ring.



Cyclopentene is an example of an endocyclic double bond.



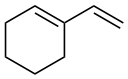
Methylenecylopentane is an example of an exocyclic double bond.



Name the following compounds...



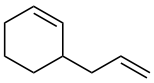
1-methylcyclobutene. The methyl group places the double bond. It is correct to also name this compound as 1-methylcyclobut-1-ene.



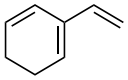
1-ethenylcyclohexene, the methyl group places the double bond. It is correct to also name this compound as 1-ethenylcyclohex-1-ene. A common name would be 1-vinylcyclohexene.

Try to draw structures for the following compounds...

- 3-allylcyclohex-1-ene

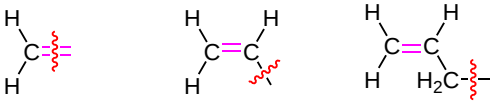


- 2-vinyl-1,3-cyclohexadiene



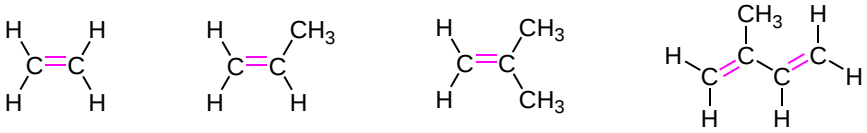
Common Names of Alkene Fragments

Some alkene containing fragments have common names which should be recognized. These common names can be used to simplify naming much the alkyl fragments discussed in **Section: 3.3**. Some of these fragments are the methylene group (H_2C=), the vinyl group (H_2C=CH-), and the allyl group (H_2C=CH-CH_2-).



Methylene Group **Vinyl Group** **Allyl Group**

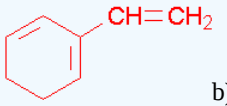
In addition, the common name some small alkene compounds are still accepted by IUPAC. It is important to be able to identify them.

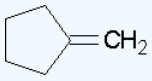


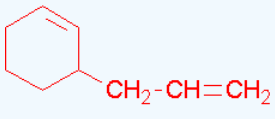
Common Name:	**Ethylene**	**Propylene**	**Isobutylene**	**Isoprene**
IUPAC Name:	**Ethene**	**Propene**	**2-Methylpropene**	**2-Methyl-1,3-butadiene**

? Exercise 10.3.1

Name the following compounds using common fragment names.

a) 

b) 

C) 

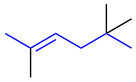
Answer

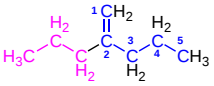
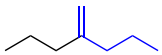
a) 2-Vinyl-cyclohexa-1,3-diene

b) Methylenecylopentane

c) 3-Allylcyclohex-1-ene

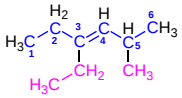
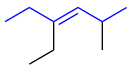
Examples

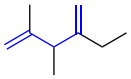
(1)  ≡  ≡ $(CH_3)_2C{=}CHCH_2C(CH_3)_3$
2,5,5-trimethyl-2-hexene

(2)  ≡  ≡ $(CH_3CH_2CH_2)_2C{=}CH_2$
2-propyl-1-pentene

Both these compounds have double bonds, making them alkenes. In example (1) the longest chain consists of six carbons, so the root name of this compound will be hexene. Three methyl substituents (colored red) are present. Numbering the six-carbon chain begins at the end nearest the double bond (the left end), so the methyl groups are located on carbons 2 & 5. The IUPAC name is therefore: 2,5,5-trimethyl-2-hexene.

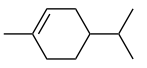
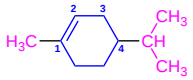
In example (2) the longest chain incorporating both carbon atoms of the double bond has a length of five. There is a seven-carbon chain, but it contains only one of the double bond carbon atoms. Consequently, the root name of this compound will be pentene. There is a propyl substituent on the inside double bond carbon atom (#2), so the IUPAC name is: 2-propyl-1-pentene.

(3)  ≡  ≡ $(CH_3CH_2)_2C{=}CHCH(CH_3)_2$
4-ethyl-2-methyl-3-hexene

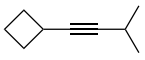
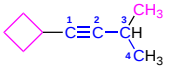
(4)  ≡  ≡ $CH_2{=}C(CH_3)CH(CH_3)C(C_2H_5){=}CH_2$
2-ethyl-3,4-dimethyl-1,4-pentadiene

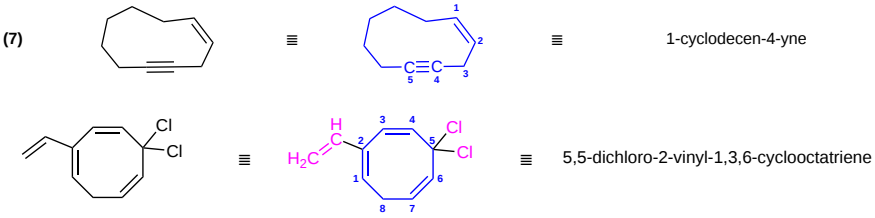
The double bond in example (3) is located in the center of a six-carbon chain. The double bond would therefore have a locator number of 3 regardless of the end chosen to begin numbering. The right hand end is selected because it gives the lowest first-substituent number (2 for the methyl as compared with 3 for the ethyl if numbering were started from the left). The IUPAC name is assigned as shown.

Example (4) is a diene (two double bonds). Both double bonds must be contained in the longest chain, which is therefore five- rather than six-carbons in length. The second and fourth carbons of this 1,4-pentadiene are both substituted, so the numbering begins at the end nearest the alphabetically first-cited substituent (the ethyl group).

(5)  ≡  ≡ 4-isopropyl-1-methylcyclohexene

4-isopropyl-1-methylcyclohex-1-ene

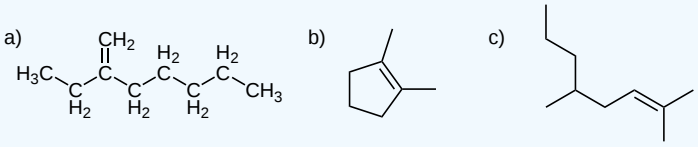
(6)  ≡  ≡ 1-cyclobutyl-3-methyl-1-butyne



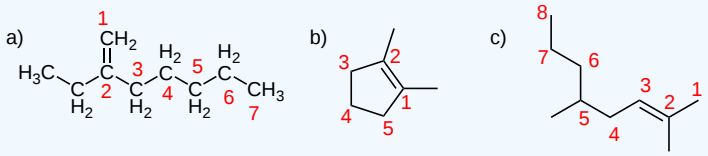
These examples include rings of carbon atoms as well as some carbon-carbon triple bonds. Example (6) is best named as an alkyne bearing a cyclobutyl substituent. Example (7) is simply a ten-membered ring containing both a double and a triple bond. The double bond is cited first in the IUPAC name, so numbering begins with those two carbons in the direction that gives the triple bond carbons the lowest locator numbers. Because of the linear geometry of a triple bond, a-ten membered ring is the smallest ring in which this functional group is easily accommodated. Example (8) is a cyclooctatriene (three double bonds in an eight-membered ring). The numbering must begin with one of the end carbons of the conjugated diene moiety (adjacent double bonds), because in this way the double bond carbon atoms are assigned the smallest possible locator numbers (1, 2, 3, 4, 6 & 7). Of the two ways in which this can be done, we choose the one that gives the vinyl substituent the lower number.

? Exercise 10.3.2

Name the following alkenes.



Answer



a) 2-ethylhept-1-ene or 2-ethyl-1-heptene

b) 1,2-dimethylcyclohept-1-ene

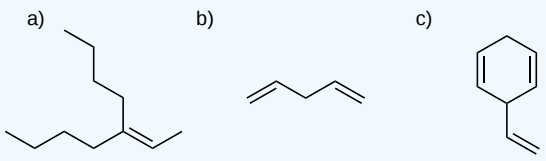
c) 2,5-dimethyloct-2-ene or 2,5-dimethyl-1-octene

? Exercise 10.3.3

Draw structures for the following compounds from the given names.

a. 3-butylhept-2-ene (3-butyl-2-heptene)
b. 1,4-pentadiene (penta-1,4-diene)
c. 3-vinyl-1,4-cyclohexadiene (cyclohexa-1,4-diene)

Answer



References

1. Vollhardt, Peter, and Neil E. Schore. Organic Chemistry: Structure and Function. 5th Edition. New York: W. H. Freeman & Company, 2007.

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10.4: Cis-Trans Isomerism in Alkenes

Objectives

After completing this section, you should be able to

- discuss the formation of carbon-carbon double bonds using the concept of sp^2 hybridization.
- describe the geometry of compounds containing carbon-carbon double bonds.
- compare the molecular parameters (bond lengths, strengths and angles) of a typical alkene with those of a typical alkane.
- explain why free rotation is not possible about a carbon-carbon double bond.
- explain why the lack of free rotation about a carbon-carbon double bond results in the occurrence of cis-trans isomerism in certain alkenes.
- decide whether or not cis-trans isomerism is possible for a given alkene, and where such isomerism is possible, draw the Kekulé structure of each isomer.

Key Terms

Make certain that you can define, and use in context, the key term below.

- cis-trans stereoisomers

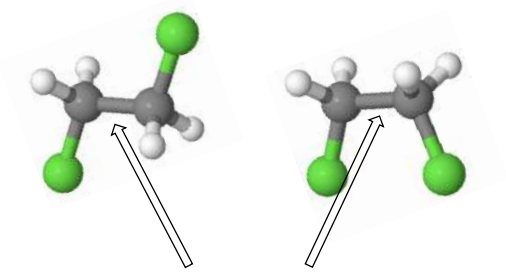
Study Notes

Your previous studies in chemistry may have prepared you to discuss the nature of a carbon-carbon double bond. If not, you should review Section 1.8 of this course before beginning the present section. It is particularly important that you make molecular models of some simple alkenes to gain insight into the geometry of these compounds.

Geometric isomerism (also known as cis-trans isomerism or E-Z isomerism) is a form of stereoisomerism. Isomers are molecules that have the same molecular formula, but have a different arrangement of the atoms in space. That excludes any different arrangements which are simply due to the molecule rotating as a whole, or rotating about particular bonds. Where the atoms making up the various isomers are joined up in a different order, this is known as structural isomerism. Structural isomerism is **not** a form of stereoisomerism, and is dealt with in a separate Module.

Geometric (cis / trans) isomerism

These isomers occur where you have restricted rotation somewhere in a molecule. At an introductory level in organic chemistry, examples usually just involve the carbon-carbon double bond - and that's what this page will concentrate on. Think about what happens in molecules where there is **un**restricted rotation about carbon bonds - in other words where the carbon-carbon bonds are all single. The next diagram shows two possible configurations of 1,2-dichloroethane.

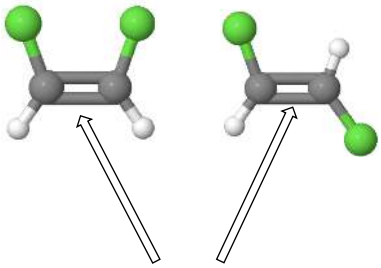


free rotation about carbon-carbon single bond

These two models represent exactly the same molecule. You can get from one to the other just by twisting around the carbon-carbon single bond. These molecules are *not* isomers. If you draw a structural formula instead of using models, you have to bear in mind the possibility of this free rotation about single bonds. You must accept that these two structures represent the same molecule:



But what happens if you have a carbon-carbon double bond - as in 1,2-dichloroethene?



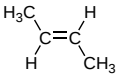
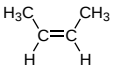
These two molecules are not the same. The carbon-carbon double bond won't rotate and so you would have to take the models to pieces in order to convert one structure into the other one. That is a simple test for isomers. If you have to take a model to pieces to convert it into another one, then you've got isomers. If you merely have to twist it a bit, then you haven't!

Drawing structural formulae for the last pair of models gives two possible isomers:

1. In one, the two chlorine atoms are locked on opposite sides of the double bond. This is known as the ***trans*** isomer. (*trans* : from latin meaning "across" - as in transatlantic).
2. In the other, the two chlorine atoms are locked on the same side of the double bond. This is know as the ***cis*** isomer. (*cis* : from latin meaning "on this side")

	
trans-1,2-dichloroethene	*cis*-1,2-dichloroethene

The most likely example of geometric isomerism you will meet at an introductory level is but-2-ene. In one case, the CH_3 groups are on opposite sides of the double bond, and in the other case they are on the same side.

	
trans-but-2-ene	*cis*-but-2-ene

The importance of drawing geometric isomers properly

It's very easy to miss geometric isomers in exams if you take short-cuts in drawing the structural formulae. For example, it is very tempting to draw but-2-ene as

$$CH_3CH=CHCH_3$$

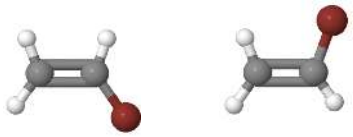
If you write it like this, you will almost certainly miss the fact that there are geometric isomers. If there is even the slightest hint in a question that isomers might be involved, always draw compounds containing carbon-carbon double bonds showing the correct bond angles (120°) around the carbon atoms at the ends of the bond. In other words, use the format shown in the last diagrams above.

How to recognize the possibility of geometric isomerism

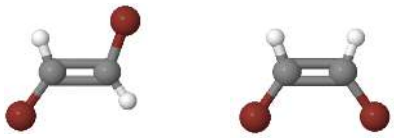
You obviously need to have restricted rotation somewhere in the molecule. Compounds containing a carbon-carbon double bond have this restricted rotation. (Other sorts of compounds may have restricted rotation as well, but we are concentrating on the case you are most likely to meet when you first come across geometric isomers.) If you have a carbon-carbon double bond, you need to think carefully about the possibility of geometric isomers.

What needs to be attached to the carbon-carbon double bond?

Think about this case:



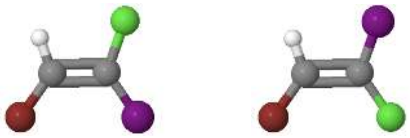
Although we've swapped the right-hand groups around, these are still the same molecule. To get from one to the other, all you would have to do is to turn the whole model over. You won't have geometric isomers if there are two groups the same on one end of the bond - in this case, the two pink groups on the left-hand end. So there must be two different groups on the left-hand carbon and two different groups on the right-hand one. The cases we've been exploring earlier are like this:



But you could make things even more different and still have geometric isomers:

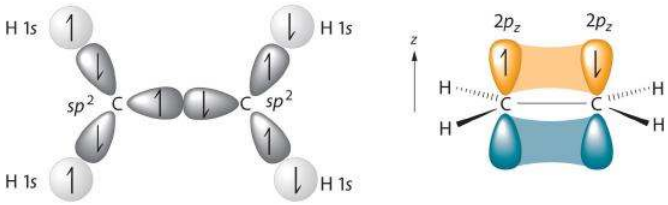


Here, the blue and green groups are either on the same side of the bond or the opposite side. Or you could go the whole hog and make everything different. You still get geometric isomers, but by now the words *cis* and *trans* are meaningless. This is where the more sophisticated *E-Z* notation comes in.



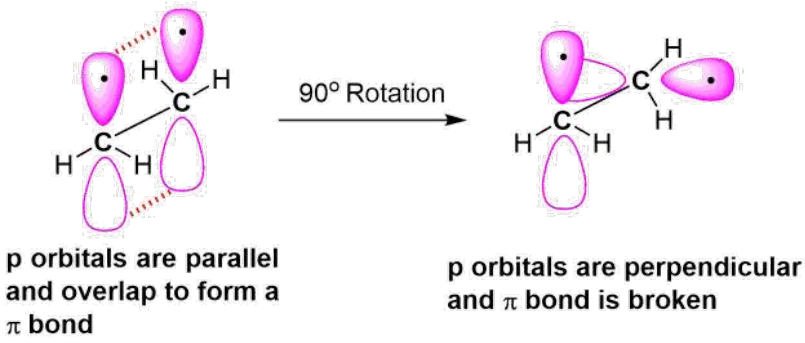
Rigidity of C=C Bonds

As discussed in Section 1.8 the double bond in the molecule ethene ($H_2C=CH_2$) is created by the overlap of two different sets of orbitals. The C-C σ bond is formed when an sp^2 orbital from each carbon atom overlaps end to end. Also, the C-C pi bond is created by the side-to-side overlap of a p_z orbital from each carbon atom.

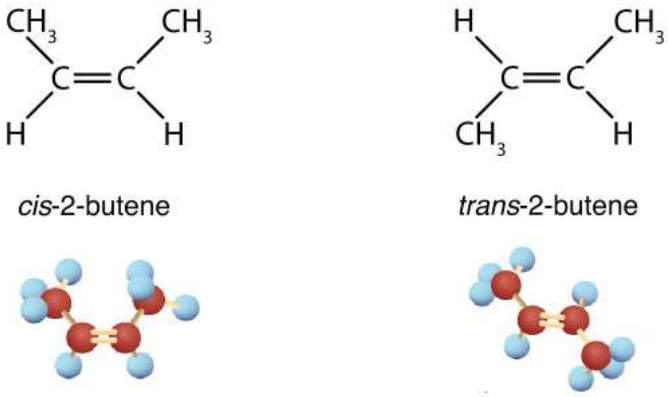


(a) C_2H_4 σ-bonded framework (b) C_2H_4 π bonding

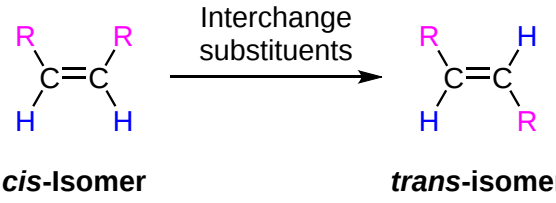
Because they are the result of side-by-side overlap (rather then end-to-end overlap like a sigma bond), *pi bonds are not free to rotate.* If rotation about this bond were to occur, it would involve disrupting the side-by-side overlap between the two $2p_z$ orbitals that make up the pi bond. If free rotation were to occur the p-orbitals would have to go through a phase where they are 90° from each other, which would break the pi bond because there would be no overlap. Since the pi bond is essential to the structure of ethene it must not break, so there can be no free rotation about the carbon-carbon sigma bond. The presence of the pi bond thus 'locks' the six atoms of ethene into the same plane.



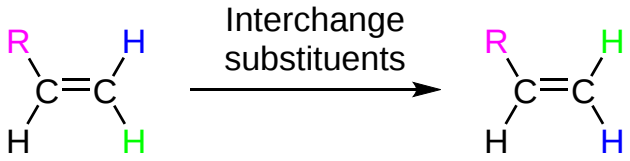
Restricted rotation about the double bond means that the relative positions of substituent groups above or below the double bond become significant. This leads to a special kind of isomerism in double bonds. Consider the alkene with the condensed structural formula $CH_3CH{=}CHCH_3$. We could name it 2-butene, but there are actually two such compounds due to this isomerism. The isomer in which the two methyl (CH_3) groups lie on the same side of the molecule is called the cis isomer (Latin *cis*, meaning "on this side") and is named cis-2-butene. The isomer with the two (CH_3) groups on opposite sides of the molecule is the trans isomer (Latin *trans*, meaning "across") and is named *trans*-2-butene. These two compounds are *cis-trans* isomers (or geometric isomers), compounds that have different configurations (groups permanently in different places in space) because of the presence of a rigid structure in their molecule. In general these isomers have different physical, chemical, and physiological properties.



It is important to note that the presence of a double bond does **not** necessarily lead to *cis-trans* isomerism. Being able to tell if a double bond has the possibility of isomerism is a very important skill. *Cis-trans* can occur whenever both double-bond carbons are directly attached to a carbon and a hydrogen. In this case, interchanging the substituents on one of the double-bond carbons creates a different isomer.



If one of the double-bond carbons of an alkene is attached to two identical groups, *cis-trans* isomerism is not possible. Here, interchanging the substituents on one of the double-bond carbons forms an identical molecule.



These two molecules are identical

Worked Example 10.4.1

Are the following molecules *cis-trans* isomers?

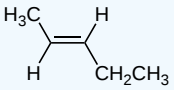


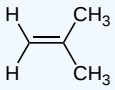
Answer

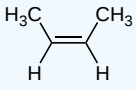
Although the two molecules *are seemingly* different propenes, these two structures are not really different from each other. Because the one of the double-bond carbons is attached to two identical groups (hydrogens) it is incapable of forming *cis-trans* isomers. The interchange of two substituents seen here does not create a new isomer. If either molecule were flipped over top to bottom, the two would you would look identical.

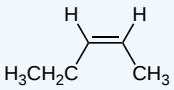
Exercise 10.4.1

Classify each compound as a *cis* isomer, a *trans* isomer, or neither.

a) 

b) 

c) 

d) 

Answer

a) trans isomer

b) neither

c) cis isomer

d) cis isomer

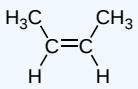
Exercise 10.4.2

Which of the following compounds could exist as cis/trans isomers? Draw (& label) both of the isomers for the ones that can.

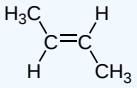
a. $CH_3CH{=}CHCH_3$
b. $(CH_3)_2C{=}CHCH_3$
c. $H_2C{=}CHCH_3$
d. $CH_3CH_2CH{=}CHBr$

Answer

a)

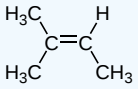


cis isomer &



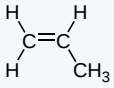
trans isomer

b)



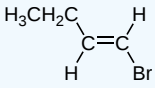
no cis/trans isomers

c)

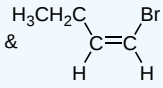


no cis/trans isomers

d)



trans isomer &



cis isomer

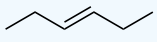
Exercise 10.4.3

Draw (& label) the cis and trans isomer for each of the following compound names. If no cis/trans isomerism is possible, write none.

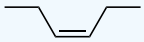
a. 3-hexene
b. 1-hexene
c. 4-methylpent-2-ene (4-methyl-2-pentene)
d. 1,1-dibromobut-2-ene (1,1-dibromo-2-butene)

Answer

a)

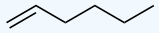


trans isomer &



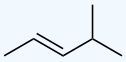
cis isomer

b)

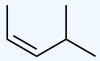


no cis/trans isomers

c)

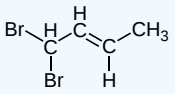


trans isomer &

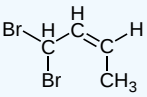


cis isomer

d)



trans isomer &

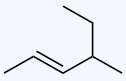


cis isomer

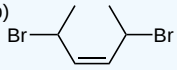
Exercise 10.4.4

Name the following compounds using cis/trans nomenclature

a)



b)



Answer

a) *trans*-4-methylhex-2-ene (*trans*-4-methyl-2-hexene)

b) *cis*-2,5-dibromohex-3-ene (*cis*-2,5-dibromo-3-hexene)

10.4: Cis-Trans Isomerism in Alkenes is shared under a CC BY-SA 4.0 license and was authored, remixed, and/or curated by Jim Clark, Steven Farmer, Dietmar Kennepohl, Zachary Sharrett, Krista Cunningham, & Krista Cunningham.

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10.5: Sequence Rules - The E,Z Designation

Objectives

After completing this section, you should be able to

- illustrate, by means of a suitable example, the limitations of the terms *cis* and *trans* in naming isomeric alkenes.
- use the *E*/*Z* designation to describe the geometry of a given alkene structure.
- incorporate the *E*/*Z* designation into the IUPAC name of a given alkene.
- draw the correct Kekulé, condensed or shorthand structure of an alkene, given its *E*/*Z* designation plus other necessary information (e.g., molecular formula, IUPAC name).

Key Terms

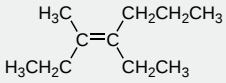
Make certain that you can define, and use in context, the key term below.

- sequence rules (Cahn-Ingold-Prelog rules)

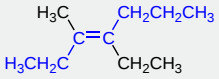
Study Notes

The limitations of the *cis/trans* system are illustrated in the examples given below.

1. From your study of the IUPAC system, you should be able to identify this compound as 4-ethyl-3-methyl-3-heptene, but is it *cis* or *trans*?



   At first you might say *cis*, because it appears that two ethyl groups appear on the same side of the double bond. However, the correct answer is *trans*. The rule is that the designation *cis* or *trans* must correspond to the configuration of the *longest* carbon chain. Tracing out the seven-carbon chain in the compound shown above, you change sides as you pass through the double bond:

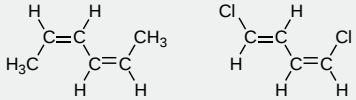


   So, the full name for this compound is *trans*-4-ethyl-3methyl-3-heptene.

2. The *cis*/*trans* system breaks down completely in a compound such as that shown below. The *E*/*Z* system, which is the subject of this section, is designed to accommodate such situations.



   In cases where two or more double bonds are present, you must be prepared to assign an *E* or *Z* designation to each of the double bonds. For example:

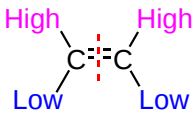


   Another use for these sequence rules will be part of the discussion of optical isomerism in Section 9.5.

E/*Z* nomenclature

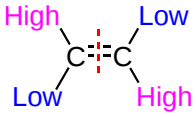
When each carbon in a double bond is attached to a hydrogen and and a non-hydrogen substituent, the geometric isomers can be identified by using the *cis*-*trans* nomenclature discussed in the previous section. However, when a double bond is attached to three

or four non-hydrogen substituents there are some examples where *cis-trans* nomenclature is ineffective in describing the substituents orientation in geometric isomers. In these situations the rigorous IUPAC system for naming alkene isomers, called the E/Z system, is used. The E/Z system analyzes the two substituents attached to each carbon in the double bond and assigns each either a high or low priority. If the higher priority group on both carbons in the double bond the **same** side the alkene is said to have a **Z isomer** (from German zusammen = together). You could think of Z as Zame Zide to help memorize it. If the higher priority group on **opposite** sides the alkene has an **E isomer** (from German entgegen = opposite).



Z Configuration

High priority substituents are on the same side of the double bond



E Configuration

High priority substituents are on opposide sides of the double bond

Note, if both substituents an a double bond carbon are exactly the same there is no E/Z isomerizem is possible. Also, if E/Z isomerism is possible, interchanging the substituents attached on double-bond carbon converts one isomer to the other.

Substituent priority for the E,Z system is assigned using the Cahn–Ingold–Prelog (CIP) sequence rules. These are the same rules used to assign R/S configurations to chiral centers in **Section 5.5**. A brief overview of using CIP rules to determine alkene configuration is given here but CIP rules are discussed in greater detail in **Section 5.5**.

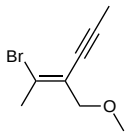
Note

The priority rules are often called the Cahn-Ingold-Prelog (CIP) rules, after the chemists who developed the system

Rule 1: The "first point of difference" rule

First, determine the two substituents on each double-bond carbon separately. Rank these substituents based on **the atom** which directly attached to the double-bond carbon. The substituent whose atom has a higher atomic number takes precedence over the substituent whose atom has a lower atomic number.

Which is higher priority, by the CIP rules: a C with an O and 2 H attached to it or a C with three C? The first C has one atom of high priority but also two atoms of low priority. How do these "balance out"? Answering this requires a clear understanding of how the ranking is done. The simple answer is that the first point of difference is what matters; the O wins.



To illustrate this, consider the molecule at the left. Is the double bond here *E* or *Z*? At the left end of the double bond, Br > C. But the right end of the double bond requires a careful analysis.

At the right hand end, the first atom attached to the double bond is a C at each position. A tie, so we look at what is attached to this first C. For the upper C, it is CCC (since the triple bond counts three times). For the lower C, it is OHH -- listed in order from high priority atom to low. OHH is higher priority than CCC, because of the first atom in the list. That is, the O of the lower group beats the C of the upper group. In other words, the O is the highest priority atom of any in this comparison; thus the O "wins".

Therefore, the high priority groups are "up" on the left end (the -Br) and "down" on the right end (the $-CH_2-O-CH_3$). This means that the isomer shown is opposite = entgegen = *E*. And what is the name? The "name" is (E)-2-Bromo-3-(methoxymethyl)hex-2-en-4-yne.

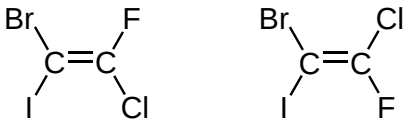
Rule 2

If the first atom on both substituents are the identical, then proceed along both substituent chains until the first point of difference is determined.

Rule 3

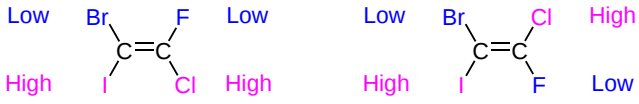
Remember that atoms involved in multiple bonds are considered with a specific set of rules. These atoms are treated as if they have the same number of single-bond atoms as they have attached to multiply bonded atoms.

An easy example which shows the necessity of the E/Z system is the alkene, 1-bromo-2-chloro-2-fluoro-1-iodoethene, which has four different substituents attached to the double bond. The figure below shows that there are two distinctly different geometric isomers for this molecule neither of which can be named using the *cis-trans* system.



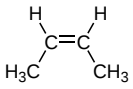
Consider the left hand structure. On the double bond carbon on the left, the two atoms attached to the double bond are Br and I. By the CIP priority rules, I is higher priority than Br (higher atomic number). Now look at carbon on the right. The attached atoms are Cl and F, with Cl having the higher atomic number and the higher priority.

When considering the relative positions of the higher priority groups, the higher priority group is "down" on the left double bond carbon and "down" at right double bond carbon. Since the two higher priority groups are both on the **same** side of the double bond ("down", in this case), they are zusammen = together. Therefore, this is the (Z) isomer. Similarly, the right hand structure is (E).

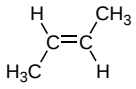


Z Configuration **E Configuration**

Example 7..61: Butene



cis-2-butene
(*Z*)-2-butene



trans-2-butene
(*E*)-2-butene

The Figure above shows the two isomers of 2-butene. You should recognize them as *cis* and *trans*. Let's analyze them to see whether they are *E* or *Z*. Start with the left hand structure (the cis isomer). On C2 (the left end of the double bond), the two atoms attached to the double bond are C and H. By the CIP priority rules, C is higher priority than H (higher atomic number). Now look at C3 (the right end of the double bond). Similarly, the atoms are C and H, with C being higher priority. We see that the higher priority group is "down" at C2 and "down" at C3. Since the two priority groups are both on the **same** side of the double bond ("down", in this case), they are zusammen = together. Therefore, this is (*Z*)-2-butene.

Now look at the right hand structure (the *trans* isomer). In this case, the priority group is "down" on the left end of the double bond and "up" on the right end of the double bond. Since the two priority groups are on **opposite** sides of the double bond, they are entgegen = opposite. Therefore, this is (*E*)-2-butene.

E/*Z* will work – even when *cis*/*trans* fails

In simple cases, such as 2-butene, *Z* corresponds to *cis* and *E* to *trans*. However, that is **not** a rule. This section and the following one illustrate some idiosyncrasies that happen when you try to compare the two systems. The real advantage of the *E*/*Z* system is

that it will always work. In contrast, the *cis*/*trans* system breaks down with many ambiguous cases.

Example 7.6.2

The following figure shows two isomers of an alkene with four different groups on the double bond, 1-bromo-2-chloro-2-fluoro-1-iodoethene.



(*Z*)-1-bromo-2-chloro-2-fluoro-1-iodoethene

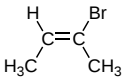


(*E*)-1-bromo-2-chloro-2-fluoro-1-iodoethene

It should be apparent that the two structures shown are distinct chemicals. However, it is impossible to name them as *cis* or *trans*. On the other hand, the *E*/*Z* system works fine... Consider the left hand structure. On C1 (the left end of the double bond), the two atoms attached to the double bond are Br and I. By the CIP priority rules, I is higher priority than Br (higher atomic number). Now look at C2. The atoms are Cl and F, with Cl being higher priority. We see that the higher priority group is "down" at C1 and "down" at C2. Since the two priority groups are both on the **same** side of the double bond ("down", in this case), they are zusammen = together. Therefore, this is the (*Z*) isomer. Similarly, the right hand structure is (*E*).

E/*Z* will work, but may not agree with *cis*/*trans*

Consider the molecule shown below. This is 2-bromo-2-butene -- ignoring the geometric isomerism for now. *Cis* or *trans*? This molecule is clearly *cis*. The two methyl groups are on the same side. More rigorously, the "parent chain" is *cis*.



E or *Z*? There is a methyl at each end of the double bond. On the left, the methyl is the high priority group -- because the other group is -H. On the right, the methyl is the low priority group -- because the other group is -Br. That is, the high priority groups are -CH_3 (left) and -Br (right). Thus the two priority groups are on opposite sides = entgegen = *E*.

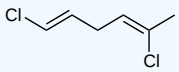
Note

This example should convince you that *cis* and *Z* are not synonyms. *Cis*/*trans* and *E*/*Z* are determined by distinct criteria. There may seem to be a simple correspondence, but it is not a rule. Be sure to determine *cis*/*trans* or *E*/*Z* separately, as needed.

Multiple double bonds

If the compound contains more than one double bond, then each one is analyzed and declared to be *E* or *Z*.

Example 7.6.3

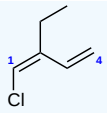


The configuration at the left hand double bond is *E*; at the right hand double bond it is *Z*. Thus this compound is (1*E*,4*Z*)-1,5-dichloro-1,4-hexadiene.

The double-bond rule in determining priorities

Example 7.6.4

Consider the compound below

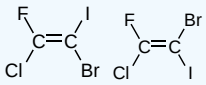


This is 1-chloro-2-ethyl-1,3-butadiene -- ignoring, for the moment, the geometric isomerism. There is no geometric isomerism at the second double bond, at 3-4, because it has 2 H at its far end.

What about the first double bond, at 1-2? On the left hand end, there is H and Cl; Cl is higher priority (by atomic number). On the right hand end, there is $-CH_2-CH_3$ (an ethyl group) and $-CH=CH_2$ (a vinyl or ethenyl group). Both of these groups have C as the first atom, so we have a tie so far and must look further. What is attached to this first C? For the ethyl group, the first C is attached to C, H, and H. For the ethenyl group, the first C is attached to a C twice, so we count it twice; therefore that C is attached to C, C, H. CCH is higher than CHH; therefore, the ethenyl group is higher priority. Since the priority groups, Cl and ethenyl, are on the same side of the double bond, this is the *Z*-isomer; the compound is (*Z*)-1-chloro-2-ethyl-1,3-butadiene.

Example 7.6.5

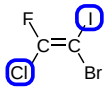
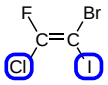
The configuration about double bonds is undoubtedly best specified by the *cis*/*trans* notation when there is no ambiguity involved. Unfortunately, many compounds cannot be described adequately by the *cis*/*trans* system. Consider, for example, configurational isomers of 1-fluoro-1-chloro-2-bromo-2-iodo-ethene, 9 and 10. There is no obvious way in which the *cis*/*trans* system can be used:



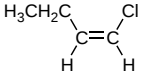
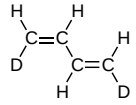
9 **10**

A system that is easy to use and which is based on the sequence rules already described for the *R*,*S* system works as follows:

1. An order of precedence is established for the two atoms or groups attached to each end of the double bond according to the sequence rules of Section 19-6. When these rules are applied to 1-fluoro- 1-chloro-2-bromo-2- iodoethene, the priority sequence is:
    - at carbon atom 1, C1 > F
    - at carbon atom 2, I > Br
2. Examination of the two configurations shows that the two priority groups- one on each end- are either on the same side of the double bond or on opposite sides:

	
priority groups on opposite sides (*E*) configuration	priority groups on same side (*Z*) configuration

The *Z* isomer is designated as the isomer in which the top priority groups are on the same side (*Z* is taken from the German word zusammen- together). The *E* isomer has these groups on opposite sides (*E*, German for entgegen across). Two further examples show how the nomenclature is used:

	
(*Z*)-1-chloro-1-butene	(1*Z*,3*E*)-1,3-butadiene-1,4-*d*2

Exercises

Exercise 10.5.1

Which of the following sets has a higher ranking?

a. $-CH_3$ or $-CH_2Br$
b. -Br or -Cl
c. $-CH{=}CH_2$ or -CH=O

Answer

a) $-CH_2Br$

b) -Br

c) -CH=O

Exercise 10.5.2

Place the following sets of substituents in each group in order of lowest priority (1^{st}) to highest priority (4^{th})

a. $-CH(CH_3)_2$, $-CH_2CH_3$, $-C(CH_3)_3$, $-CH_3$
b. $-NH_2$, -F, -Br, $-CH_3$
c. -SH, $-NH_2$, -F, -H

Answer

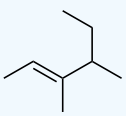
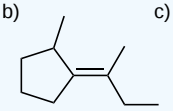
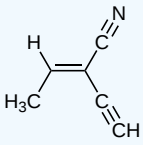
a) (lowest priority) $-CH_3 < -CH_2CH_3 < -CH(CH_3)_2 < -C(CH_3)_3$ (highest priority)

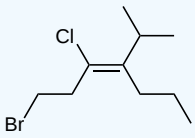
b) (lowest priority) $-CH_3 < -NH_2 < -F <$ -Br (highest priority)

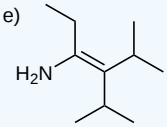
c) (lowest priority) $-H < -NH_2 < -F <$ -SH (highest priority)

Exercise 10.5.3

Label the following alkenes as E, Z, or neither.

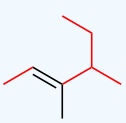
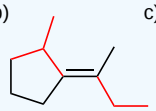
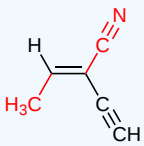
a) 
b) 
c) 

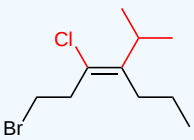
d) 

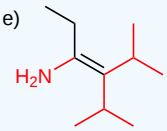
e) 

Answer

The higher priority group is highlighted in red.

a) 
b) 
c) 

d) 

e) 

a) E

b) E

c) E

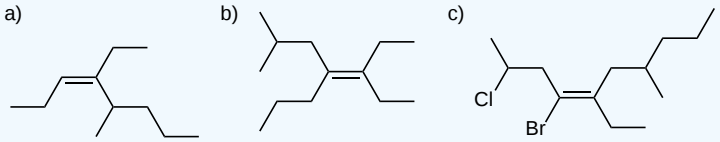
d) Z

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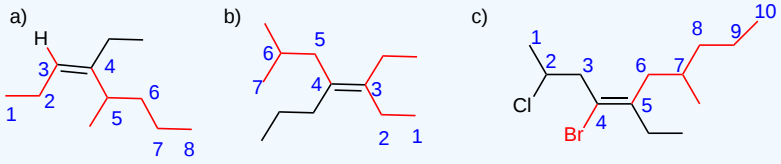
e) neither (both isopropyls on the right have the same priority)

Exercise 10.5.4

Name the following alkenes.



Answer



The higher priority group is highlighted in red.

a. (Z)-4-ethyl-5-methyloct-3-ene or (Z)-4-ethyl-5-methyl-3-octene
b. 3-ethyl-6-methyl-4-propylhept-3-ene or 3-ethyl-6-methyl-4-propyl-3-heptene
c. (E)-4-bromo-2-chloro-5-ethyl-7-methyldec-4-ene or (E)-4-bromo-2-chloro-5-ethyl-7-methyl-4-decene

10.5: Sequence Rules - The E,Z Designation is shared under a CC BY-SA 4.0 license and was authored, remixed, and/or curated by Steven Farmer, Dietmar Kennepohl, Zachary Sharrett, Krista Cunningham, John Roberts, Marjorie C. Caserio, Robert Bruner, & Robert Bruner.

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10.6: Stability of Alkenes

Objectives

After completing this section, you should be able to

- explain why *cis* alkenes are generally less stable than their *trans* isomers.
- explain that catalytic reduction of a *cis* alkene produces the same alkane as the catalytic reduction of the *trans* isomer.
- explain how heats of hydrogenation ($\Delta H°_{hydrog}$) can be used to show that *cis* alkenes are less stable than their *trans* isomers, and discuss, briefly, the limitations of this approach.
- arrange a series of alkenes in order of increasing or decreasing stability.
- describe, briefly, two of the hypotheses proposed to explain why alkene stability increases with increased substitution. [**Note:** This problem is a typical example of those instances in science where there is probably no single "correct" explanation for an observed phenomenon.]

Key Terms

Make certain that you can define, and use in context, the key terms below.

- catalytic hydrogenation
- heat of hydrogenation ($\Delta H°_{hydrog}$)
- hyperconjugation

Study Notes

The two alkenes, *cis*-$CH_3CH{=}CHCH_3$ and $(CH_3)_2C{=}CH_2$ have similar heats of hydrogenation (−120 kJ/mol and −119 kJ/mol, respectively), and are therefore of similar stability. However, they are both less stable than *trans*-$CH_3CH{=}CHCH_3$ (−116 kJ/mol).

You may wonder why an sp^2 -sp^3 bond is stronger than an sp^3-sp^3 bond. Bond strength depends on the efficiency with which orbitals can overlap. In general, *s* orbitals overlap more efficiently than do *p* orbitals; therefore, the *s*-*s* bond in the hydrogen molecule is stronger than the *p*-*p* bond in fluorine. In hybrid orbitals, the greater the *s* character of the orbital, the more efficiently it can overlap: an sp^2 orbital, which has a 33% *s* character, can overlap more effectively than an sp^3 orbital, with only 25% *s* character.

Hydrogenation

Alkene hydrogenation is the addition of hydrogen gas (H_2) to an alkene which saturates the bond and forms an alkane. Alkene hydrogenation reactions require a transition metal catalyst, such as Pt or Pd, to speed up the reaction. The hydrogenation reaction is used in this section to investigate the stability of alkenes, however, it will be discussed in greater detail in **Section 8.7**. Hydrogenation reactions are exothermic and the enthalpy change in this reaction is called the heat of hydrogenation ($\Delta H°_{hydrog}$). Since the double bond is breaking in this reaction, the energy released during hydrogenation is proportional to the energy in the double bond of the molecule. By comparing the heat of hydrogenations from a series of alkenes that produce the same alkane, a quantitative measure of relative alkene stabilities can be produced. These experiments will lead to an general understanding of structural features which tend to stabilize or destabilize alkenes.

The Catalyst

A catalyst increases the reaction rate by lowering the activation energy of the reaction. Although the catalyst is not consumed in the reaction, it is required to accelerate the reaction sufficiently to be observed in a reasonable amount of time. Catalysts commonly used in alkene hydrogenation are: platinum, palladium, and nickel. The metal catalyst acts as a surface on which the reaction takes place. This increases the rate by putting the reactants in close proximity to each other, facilitating interactions between them. With

this catalyst present, the sigma bond of H_2 breaks, and the two hydrogen atoms instead bind to the metal (see #2 in the figure below). The π bond of the alkene weakens as it also interacts with the metal (see #3 below).

Since both the reactants are bound to the metal catalyst, the hydrogen atoms can easily add, one at a time, to the previously double-bonded carbons (see #4 and #5 below). The position of both of the reactants bound to the catalyst makes it so the hydrogen atoms are only exposed to one side of the alkene. This explains why the hydrogen atoms add to same side of the molecule, called syn-addition.

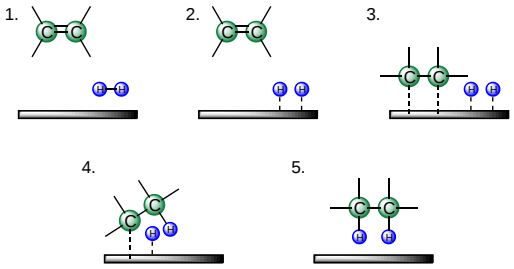
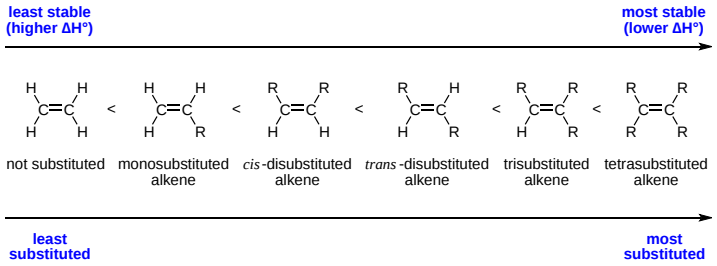


Figure **10.6.1***: Hydrogenation takes place in the presence of a metal catalyst.*

> **Note**
>
> The catalyst remains intact and unchanged throughout the reaction.

Heats of Hydrogenation

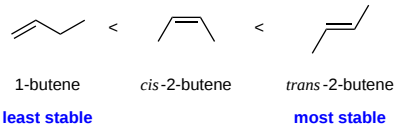
The stability of alkene can be determined by measuring the amount of energy associated with the hydrogenation of the molecule. Since the double bond is breaking in this reaction, the energy released in hydrogenation is proportional to the energy in the double bond of the molecule. This is a useful tool because heats of hydrogenation can be measured very accurately. The ΔH^o is usually around -30 kcal/mol for alkenes. Stability is simply a measure of energy. Lower energy molecules are more stable than higher energy molecules. More substituted alkenes are more stable than less substituted ones due to hyperconjugation. They have a lower heat of hydrogenation. The following illustrates stability of alkenes with various substituents:



Cis/Trans Isomers

Between cis and trans isomers of an alkene, the cis isomer tends to be less stable due to the molecular crowding created nonbonding interaction between two alky groups on the same side of the double bond. The crowding creates steric strain which distorts bond angles creating less effective bond orbital overlap and desabilizing the molecule. Steric strain has previously been seen in gauche interactions in Newman projections (**Section 3.7**) and 1,3-diaxial interactions in substituted cyclohexanes (**Section 4.7**). Steric strain is directly related to the size of the species being crowded. The difference in energy between *cis* and *trans* 2-butene is 5 kJ/mol, however, this difference would be greater if larger group were being held in the *cis* position. Two *cis*-*tert*-butyl group can create over 40 kJ/mol of steric strain.

See the following isomers of butene:



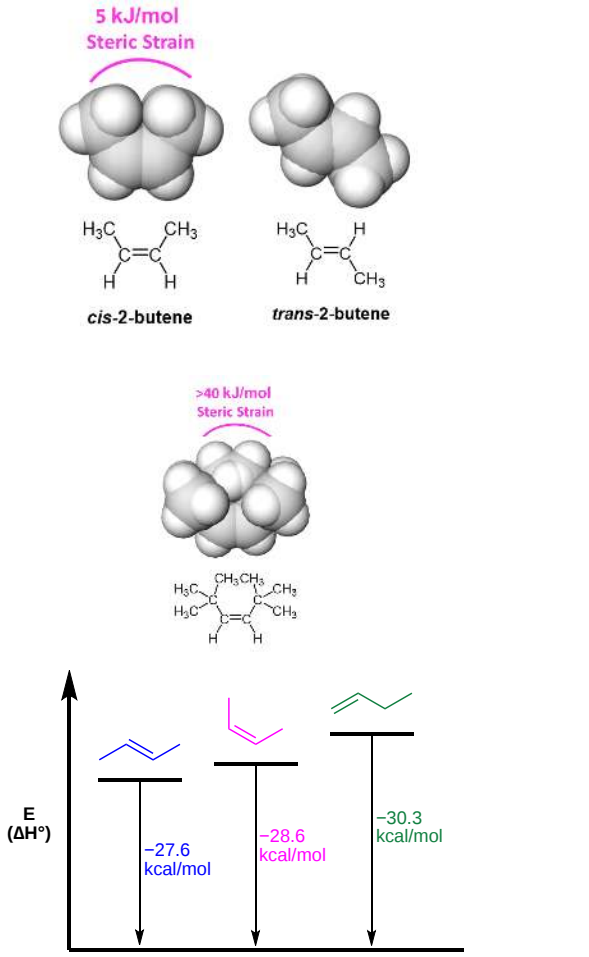


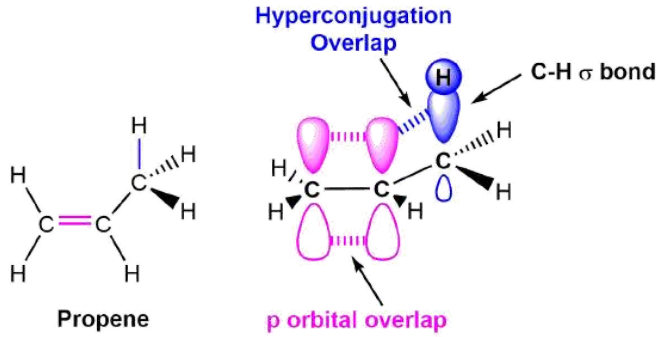
Figure **10.6.2**: *Trans-2-butene is the most stable because it has the lowest heat of hydrogenation.*

Alkene Stabilization by Alkyl Substituents

In general, the stability of an alkene increases with the number of alkyl substituents. This effect is due by the combination of two factors:

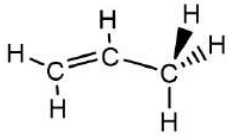
Hyperconjugation

In classical valence-bond theory, electron delocalization can only occur by the parallel overlap of adjacent p orbitals. According to hyperconjugation theory, electron delocalization could also occur by the parallel overlap of p orbitals with adjacent hybridized orbitals participating in sigma bonds. This electron delocalization serves to stabilize the alkene. As the number of alkyl substituents increases, the number of sigma bonds available for hyperconjugation increases, and the alkene tends to become more stabilized. In the example of propene shown below, a p orbital from a sp^2 hybridized carbon involved in the double bond interacts with a sp^3 hybridized orbital participating in an adjacent C-H sigma bond.

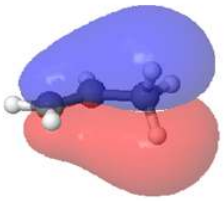


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In a molecular orbital description of hyperconjugation, the electrons in sigma molecular orbitals (C-H or C-C) of alkyl substituens, interact with adjacent unpopulated non-bonding or antibonding molecular orbitals from the double bond. The interaction creates a bonding molecular orbital which extends over the four atom chain (C=C-C-H) involved in hyperconjugation. The expanded molecular orbital helps to stabilize the double bond.



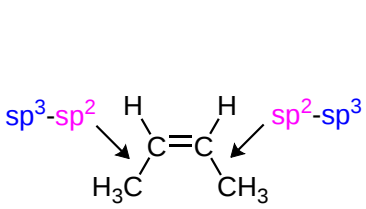
Propene



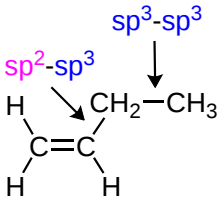
Extended Bonding MO created by hyperconjugation

Bond Stability

Bond strengths play an important part in determining the overall stability of a molecule. A C-C bond between a sp^3 carbon and a sp^2 carbon is slightly stronger than a C-C bond between two sp^3 carbons. Increasing the number alkyl substituents of a double bond also increases the number of sp^3-sp^2 C-C bonds making the alkene more stable. This is idea can be clearly seen when comparing the isomers 1-butene and 2-butene. The molecule 1-butene is monosubstituted and contains a sp^3-sp^3 C-C and a sp^3-sp^2 C-C bond. The disubstituted, 2-butene, contains 2 sp^3-sp^2 C-C bonds which contributes to its greater stability.



2-Butene (More Stable)



1-Butene (Less Stable)

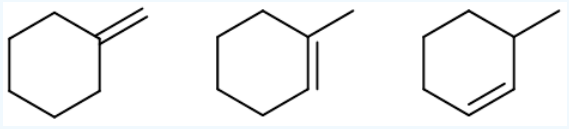
Note

In cycloalkenes smaller than cyclooctene, the cis isomers are more stable than the trans as a result of ring strain.

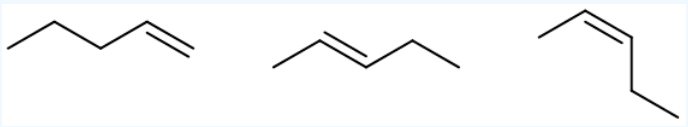
Exercise 10.6.1

Of the three following isomers which would be expected to be the most stable?

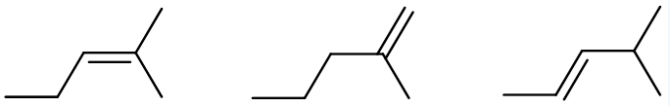
a)



b)



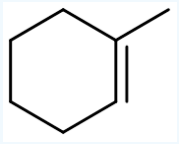
c)



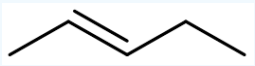
Answer

1)

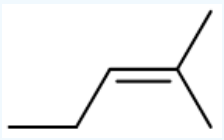
a)



b)

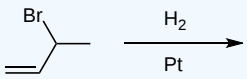


c)



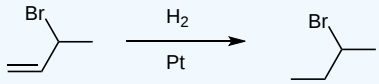
Exercise 10.6.2

3-Bromobut-1-ene reacts with hydrogen gas in the presence of a platinum catalyst. What is the name of the product?



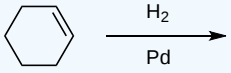
Answer

2-Bromobutane (numbering changes when alkene is no longer present)



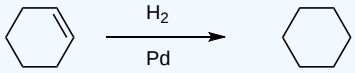
Exercise 10.6.3

Cyclohexene reacts with hydrogen gas in the presence of a palladium catalyst. What is the name of the product?



Answer

Cyclohexane



? Exercise 10.6.4

What is the stereochemistry (syn or anti addition) of an alkene hydrogenation reaction?

Answer

Syn-addition

? Exercise 10.6.5

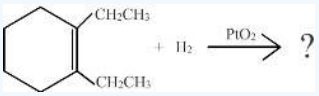
When looking at their heats of hydrogenation, is the cis or the trans isomer generally more stable?

Answer

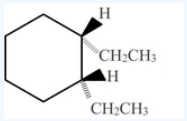
Trans

? Exercise 10.6.6

Show the product for the following



Answer



References

1. Fox, Marye Anne, and James K. Whitesell. Organic Chemistry. 3rd ed. Sudbury, MA: Janes and Bartlett Publishers, 2004.
2. Hanson, James R. Functional Group Chemistry. Bristol, UK: The Royal Society of Chemistry, 2001.
3. Streitwieser, Andrew Jr., and Clayton H. Heathcock. Introduction to Organic Chemistry. 2nd ed. New York, NY: Macmillan Publishing Co., Inc., 1981.
4. Vollhardt, Peter C., and Neil E. Schore. Organic Chemistry: Structure and Function. 5th ed. New York, NY: W.H. Freeman and Company, 2007.
5. Zlatkis, Albert, Eberhard Breitmaier, and Gunther Jung. A Concise Introduction to Organic Chemistry. New York: McGraw-Hill Book Company, 1973.

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10.7: Electrophilic Addition Reactions of Alkenes

Objectives

After completing this section, you should be able to

- explain the term “electrophilic addition reaction,” using the reaction of a protic acid, HX, with an alkene as an example.
- write the mechanism for the reaction of a protic acid, HX, with an alkene.
- sketch a reaction energy diagram for the electrophilic addition of an acid, HX, to an alkene.

Key Terms

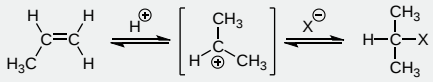
Make certain that you can define, and use in context, the key terms below.

- carbocation (carbonium ion)
- electrophilic addition reaction

Study Notes

An *electrophilic addition reaction* is a reaction in which a substrate is initially attacked by an electrophile, and the overall result is the addition of one or more relatively simple molecules across a multiple bond.

The mechanism for the addition of hydrogen halide to propene shown in the reading is quite detailed. Normally, an organic chemist would write the reaction scheme as follows:



However, the more detailed mechanism shown in the reading does allow you to see the exact fate of all the electrons involved in the reaction.

In your previous chemistry course, you were probably taught the importance of balancing chemical equations. It may come as a surprise to you that organic chemists usually do not balance their equations, and often represent reactions using a format which is quite different from the carefully written, balanced equations encountered in general chemistry courses. In fact, organic chemists are rarely interested in the inorganic products of their reactions; furthermore, most organic reactions are non-quantitative in nature.

In many of the reactions in this course, the percentage yield is indicated beneath the products: you are not expected to memorize these figures. The question of yield is very important in organic chemistry, where two, five, ten or even twenty reactions may be needed to synthesize a desired product. For example, if a chemist wishes to prepare compound D by the following reaction sequence:

$$A \rightarrow B \rightarrow C \rightarrow D$$

and each of the individual steps gives only a 50% yield, one mole of A would give only

$$1 \text{ mol} \times \frac{50\%}{100\%} \times \frac{50\%}{100\%} \times \frac{50\%}{100\%} = 0.125 \text{ mol of D}$$

You will gain first-hand experience of such situations in the laboratory component of this course.

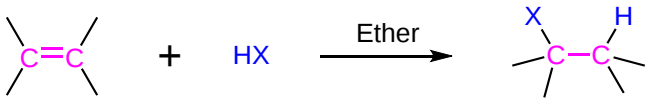
Introduction

One of the most important reactions for alkenes is called electrophilic addition. In this chapter several variations of the electrophilic addition reaction will be discussed. Each case will have aspects common among all electrophilic addition. In this section, the electrophilic addition reaction will be discussed in general to provide a better understanding of subsequent alkene reactions.

As discussed in Section 6-5, the double bond in alkenes is electron rich due to the prescience of 4 electrons instead of the two in a single bond. Also, the pi electrons are positioned above and below the double bond making them more accessibly for reactions. Overall, double bonds can easily donate lone pair electrons to act like a nucleophile (nucleus-loving, electron rich, a Lewis acid). During an electrophilic addition reactions double bonds donate lone pair electrons to an electrophile (Electron-loving, electron poor, a Lewis base). There are many types of electrophilic addition, but this section will focus on the addition of hydrogen halides (HX). Many of the basic ideas discussed will aplicable to subsequent electrophilic addition reactions.

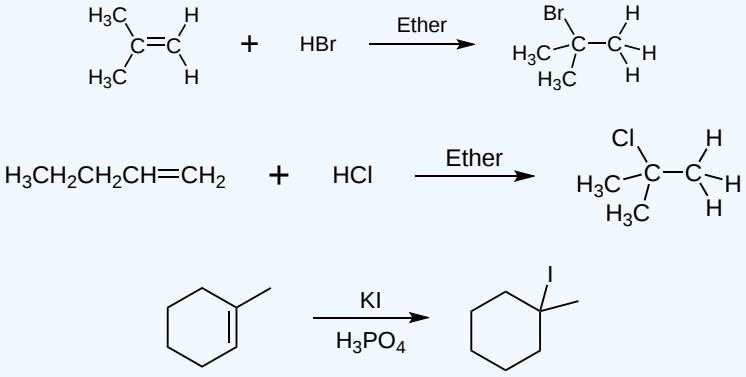
General Reaction

Overall during this reaction the pi bond of the alkene is broken to form two single, sigma bonds. As shown in the reaction mechanism, one of these sigma bonds is connected to the H and the other to the X of the hydrogen halide. This reaction works well with HBr and HCl. HI can also but used but is is usually generated during the reaction by reacting potassium iodidie (KI) with phosphoric acid (H_3PO_4).



Alkene **Hydrogen Halide** **Alkyl Halide**

Example 10.7.1



Addition to symmetrical alkenes

What happens?

All alkenes undergo addition reactions with the hydrogen halides. A hydrogen atom joins to one of the carbon atoms originally in the double bond, and a halogen atom to the other.

For example, with ethene and hydrogen chloride, you get chloroethane:



Figure **10.7.1** Electrophilic addition of HCl to ethene.

With but-2-ene you get 2-chlorobutane:

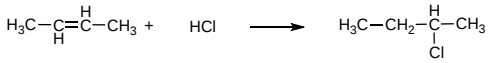


Figure **10.7.2** Electrophilic addition of HCl to but-2-ene.

What happens if you add the hydrogen to the carbon atom at the right-hand end of the double bond, and the chlorine to the left-hand end? You would still have the same product. The chlorine would be on a carbon atom next to the end of the chain - you would

simply have drawn the molecule flipped over in space. That would be different of the alkene was unsymmetrical - that's why we have to look at them separately.

Mechanism

Step 1) Electrophilic Attack

During the first step of the mechanism, the 2 pi electrons from the double bond attack the H in the HBr electrophile which is shown by a curved arrow. The two pi electrons form a C-H sigma bond between the hydrogen from HBr and a carbon from the double bond. Simultaneously the electrons from the H-X bond move onto the halogen to form a halide anion. The removal of pi electrons form the double bond makes one of the carbons become an electron deficient carbocation intermediate. This carbon is sp^2 hybridized and the positive charge is contained in an unhybridized p orbital.

Step 2) Nucleophilic attack by halide anion

The formed carbocation now can act as an electrophile and accept an electron pair from the nucleophilic halide anion. The electron pair becomes a X-C sigma bond to create the neutral alkyl halide product of electrophilic addition.

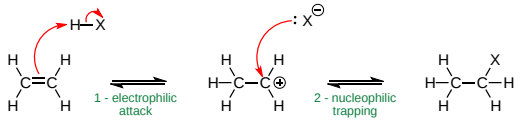


Figure **10.7.3** *Mechanism of Electrophilic Addition of Hydrogen Halide to Ethene*

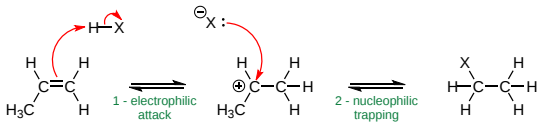
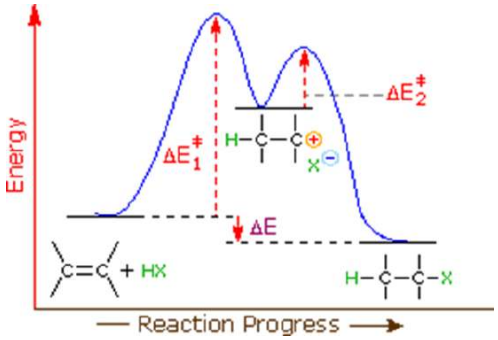


Figure **10.7.4** *Mechanism of Electrophilic Addition of Hydrogen Halide to Propene*

All of the halides (HBr, HCl, HI, HF) can participate in this reaction and add on in the same manner. Although different halides do have different rates of reaction, due to the H-X bond getting weaker as X gets larger (poor overlap of orbitals)s.

Reaction Energy Diagram

An energy diagram for the two-step electrophilic addition mechanism is shown below. The energy diagram has two peaks which represent the transition state for each mechanistic step. The peaks are separated by a valley which represents the high energy carbocation reaction intermediate. Because the energy of activation for the first step of the mechanism ($\Delta E^{\ddagger}_1$) is much larger than the second ($\Delta E^{\ddagger}_1$), the first step of the mechanism is the rate-determining step. Both the alkene and the hydrogen halide are reactants in the first step of the mechanism, this electrophilic addition is a second order reaction and the rate law expression can be written rate = k[Alkene][HX]. Also, any structural feature which can stabilize the transition state between the reactants the carbocation intermediate will lower $\Delta E^{\ddagger}_1$ and thereby increase the reaction rate. Overall, the alkyl halide product of this reaction more stable than the reactants making the reaction exothermic.



Reaction rates

Variation of rates when you change the halogen

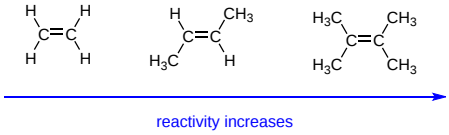
Reaction rates increase in the order HF - HCl - HBr - HI. Hydrogen fluoride reacts much more slowly than the other three, and is normally ignored in talking about these reactions.

When the hydrogen halides react with alkenes, the hydrogen-halogen bond has to be broken. The bond strength falls as you go from HF to HI, and the hydrogen-fluorine bond is particularly strong. Because it is difficult to break the bond between the hydrogen and the fluorine, the addition of HF is bound to be slow.

Variation of rates when you change the alkene

This applies to unsymmetrical alkenes as well as to symmetrical ones. For simplicity the examples given below are all symmetrical ones- but they don't have to be.

Reaction rates increase as the alkene gets more complicated - in the sense of the number of alkyl groups (such as methyl groups) attached to the carbon atoms at either end of the double bond. For example:

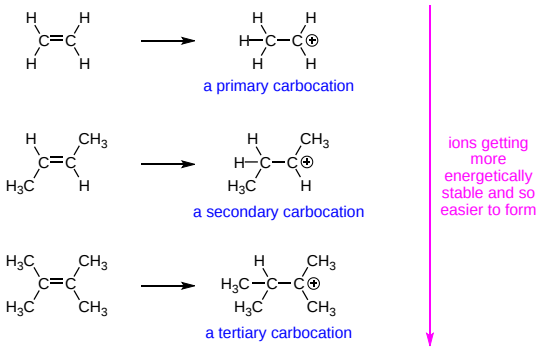


There are two ways of looking at the reasons for this - both of which need you to know about the mechanism for the reactions.

Alkenes react because the electrons in the pi bond attract things with any degree of positive charge. Anything which increases the electron density around the double bond will help this.

Alkyl groups have a tendency to "push" electrons away from themselves towards the double bond. The more alkyl groups you have, the more negative the area around the double bonds becomes. The more negatively charged that region becomes, the more it will attract molecules like hydrogen chloride.

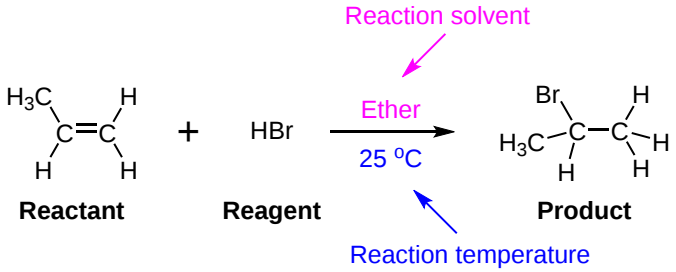
The more important reason, though, lies in the stability of the intermediate ion formed during the reaction. The three examples given above produce these carbocations (carbonium ions) at the half-way stage of the reaction:



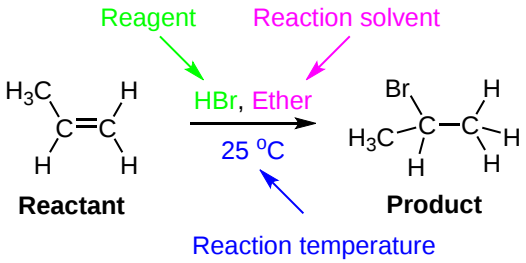
The stability of the intermediate ions governs the activation energy for the reaction. As you go towards the more complicated alkenes, the activation energy for the reaction falls. That means that the reactions become faster.

Representing Organic Reactions

Organic reaction equations are often written in one of two ways. The reactant for the reaction is written to the left of the reaction arrow. The products are written to the right of the arrow. The reagent for the reaction is written above the arrow. Other reaction conditions such as the solvent or the temperature can be written above or below the reaction arrow.



Alternatively the reactant and reagent can both be written to the left of the reaction arrow. This is typically done to highlight the importance of the reactant. The solvent and reaction temperature are still written above or below the reaction arrow. The reaction products are still written to the right of the reaction arrow.



10.7: Electrophilic Addition Reactions of Alkenes is shared under a CC BY-SA 4.0 license and was authored, remixed, and/or curated by Jim Clark, Steven Farmer, Dietmar Kennepohl, Krista Cunningham, Tim Soderberg, William Reusch, John Roberts, Marjorie C. Caserio, & Marjorie C. Caserio.

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10.8: Orientation of Electrophilic Additions - Markovnikov's Rule

Objectives

After completing this section, you should be able to

- use Markovnikov's rule to predict the product formed when a protic acid, HX, reacts with an alkene.
- identify the protic acid, HX, and the alkene that must be reacted together to produce a given alkyl halide. [**Note:** Special conditions are needed if an alkyl iodide is to be produced.]
- distinguish among primary, secondary and tertiary carbocations.

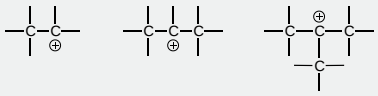
Key Terms

Make certain that you can define, and use in context, the key terms below.

- Markovnikov's rule
- regioselective (regiospecific)

Study Notes

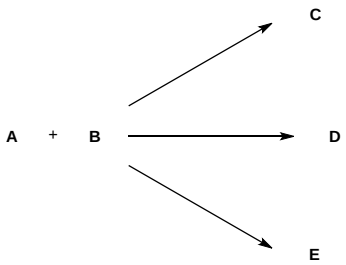
Recall the definitions of primary, secondary and tertiary hydrogen atoms given in Section 3.3. It follows that a "primary carbocation" is a carbocation in which the carbon atom carrying the positive charge is bonded to only one other carbon atom, a "secondary carbocation" is one in which the carbon atom carrying the positive charge is bonded to two other carbon atoms, and so on.



Regioselectivity

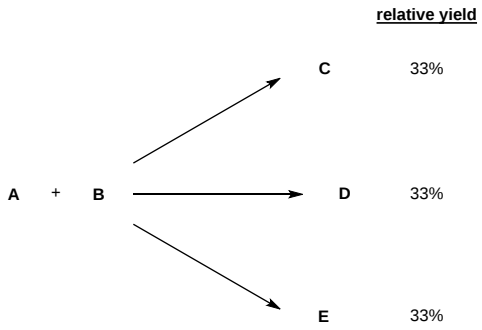
If more than one reaction could occur between a set of reactants under the same conditions giving products that are constitutional isomers and if one product forms in greater amounts than the others, the overall reaction is said to be regioselective.

Say three reactions could occur between the hypothetical reactants **A** and **B** under the same conditions giving the constitutionally isomeric products **C**, **D**, and **E**.



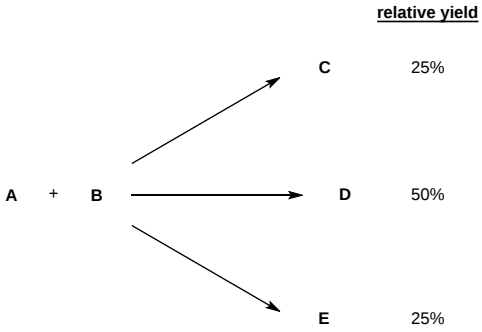
There are two possibilities:

1. The three products form in equal amounts, i.e., of the total product 33% is **C**, another 33% **D**, the remaining 33% **E**. (These percentages are called relative yields of the products.)



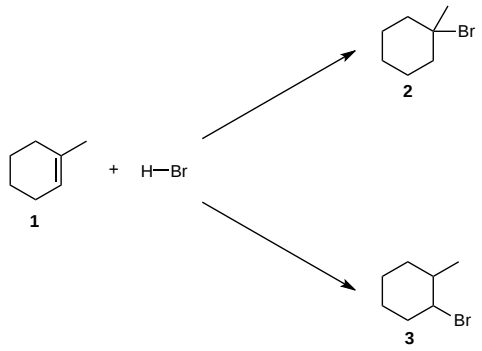
If this is what is observed, the overall reaction between **A** and **B** is not regioselective.

2. One product forms in greater amounts than the others. Say, for example, the relative yields of **C**, **D**, and **E** are 25%, 50%, and 25%, respectively.



If this is what is observed, the overall reaction between **A** and **B** is regioselective.

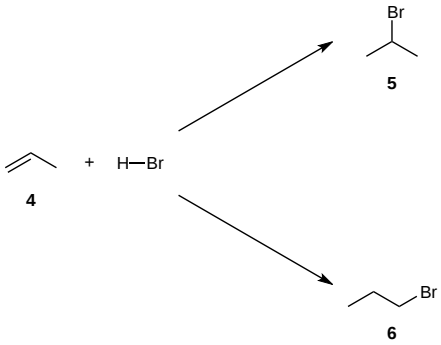
eg:



Experimentally, **2** is the major product; **3** is the minor product. Thus, the overall reaction between **1** and HBr is regioselective toward **2**.

If more than one reaction could occur between a set of reactants under the same conditions giving products that are constitutional isomers and if only one product is observed, the overall reaction is said to be 100% regioselective or regiospecific.

eg:

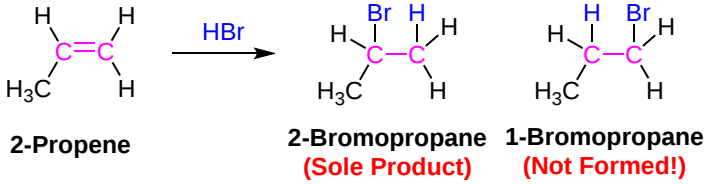


The only observed product is **5**. (Relative yields of **5** and **6** are 100% and 0%, respectively.) Thus the overall reaction between **4** and HBr is regiospecific toward **5**.

Regiospecificity is merely the limiting case of regioselectivity. All regiospecific reactions are regioselective, but not all regioselective reactions are regiospecific.

Addition to unsymmetrical alkenes

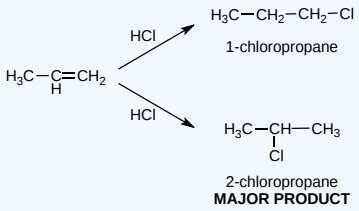
During the electrophilic addition of HX to an alkene, the halide (X) could attach to either carbon in the double bond producing two different isomers as products. But, when an unsymmertrically alkyl substituted alkene undergoes an electrophillic addition with HX a single isomer is typically produced. For example, if propene were reacted with HBr, two products could possibly form: 2-bromolpropane and 1-bromopropane. However, 2-bromopropane is produced as the reaction's only product. Reactions are called regiospecific when only one of multiple possible isomers is exclusively formed.



Example 10.8.1

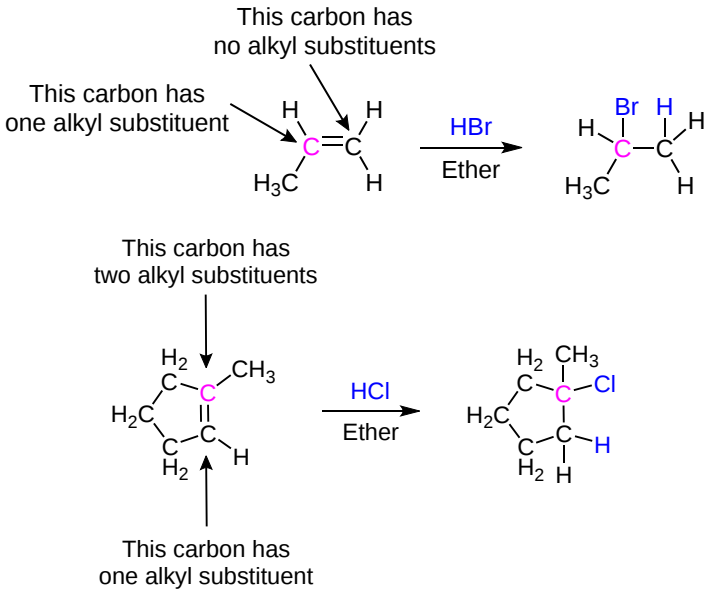
If HCl adds to an unsymmetrical alkene like propene what will the major product be?

Solution

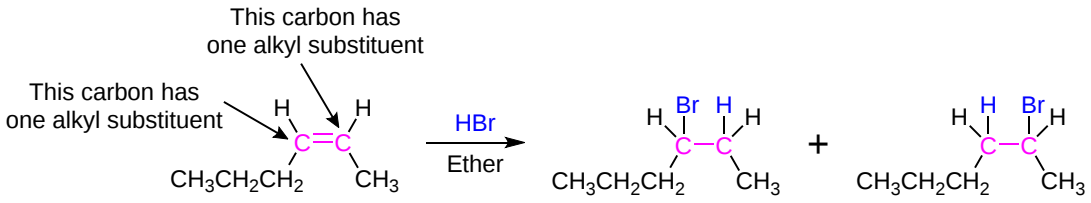


The regiospecificity of electrophilic additions to alkenes is commonly known as **Markovnikov's rule**, after the Russian chemist Vladimir Markovnikov who proposed it in 1869. The electrophilic addition of HX to an alkene is said to follow Markovnikov's rule.

Markovnikov's rule: During the electrophilic addition of HX to an alkene, the H adds to the carbon of the double bond with the fewest number of alkyl substitutent. The halide (X) adds to the double bond carbon with the most alkyl substituents. Although Markovnikov's rule has been specifically stated for the electrophilic addition of HX, later in this chapter many more reaction will be shown to also follow Markovnikov's rule.

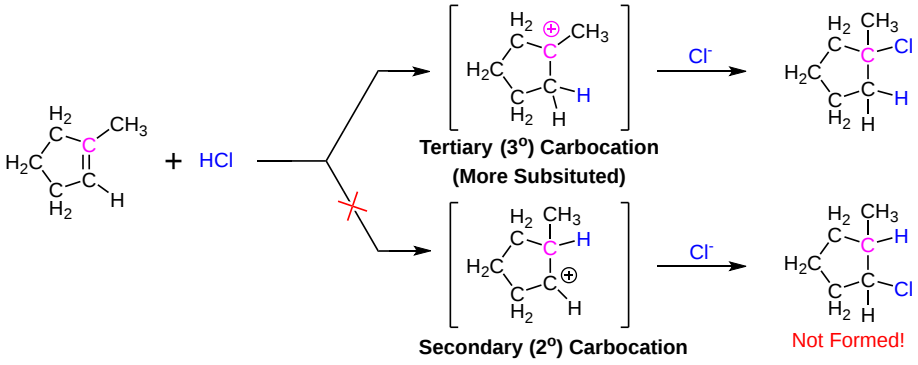


It is important to point out that Markovnikov's rule only truly applies when there is a difference between the number of alky groups attached to each carbon in the double bond. When both carbon of the double bond have the same degree of alkyl substitution, Markovnikovs's rule becomes void and a mixture of both possible isomers is produced.

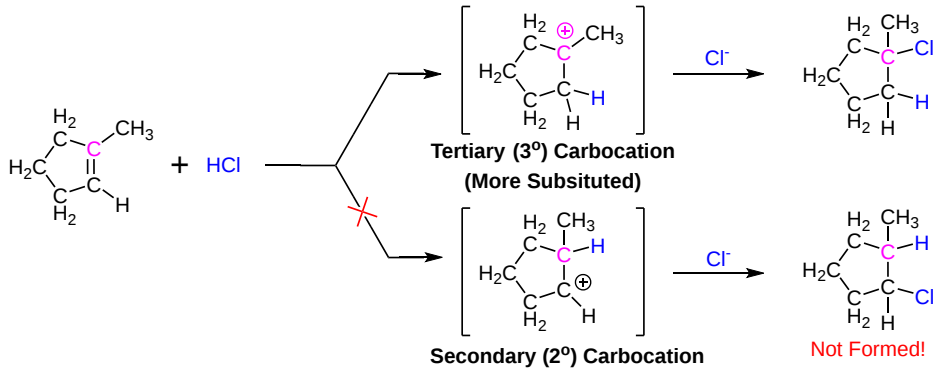


To consider an explanation for why Markovnikov's rule holds true, the mechanism of the reaction needs to be considered. As seen in the previous section, the mechanism starts with the addition of H to a carbon in the double bond. This in turn caused the other double bond carbon to become a carbocation intermediate. In the second step of the mechanism the halide ion attacks the carbocation to form a C-X. Because Markovnikov's rule says that the halogen adds to the carbon in the double bond with the most alky substituents, it can be said the carbocation also prefers to form on the carbon with the most alkyl substituents. The reason for this holds the explaination for Markovnikov's rule. To simplify this idea, Markovnikov's rule can be restated in a different form.

Markovnikov's rule: During the electrophilic addition of HX to an alkene, the carbocation intermediate forms on the double bond carbon with the greatest number of alkyl substitutents.

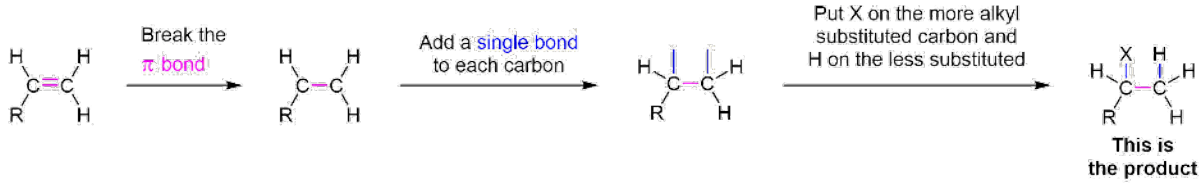


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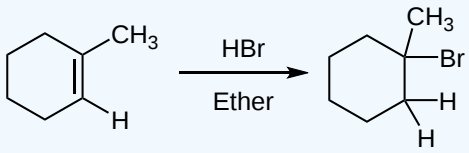
Predicting the Product of an Electrophilic Addition with HX

Overall, during the electrophilic addition of HX to an alkene there are two major changes in the bonding. First, the pi bond of the alkene is broken. Second, a single bond is formed on each carbon that was originally in the double bond. The two single bonds will become attached to and H and an X. If the alkene is unsymmertrically alkyl substituted, Markovnikov's rule is followed and the X will be bonded to the more alky substituted carbon and the H to the less substiuted. If the alkene is symmertrically alkyl substituted a mixture of isomers will be produced in the product.



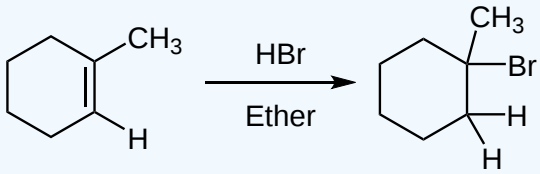
? Worked Example 10.8.1

Please draw the product of the following reaction:



Answer

In answering these types of questions it is always important to first determine which reaction is occurring. Because an alkene is the reactant and HBr is the product this reaction is an electrophilic addition. Overall, the double bond will be broken as H and Br are added. The next step is to determine if Markovnikov's rule needs to be applied. In the reactant's double bond the upper carbon has two alkyl substituents and the lower carbon has only two. Markovnikov's rule says that Br will attach to the upper carbon and H to the lower.

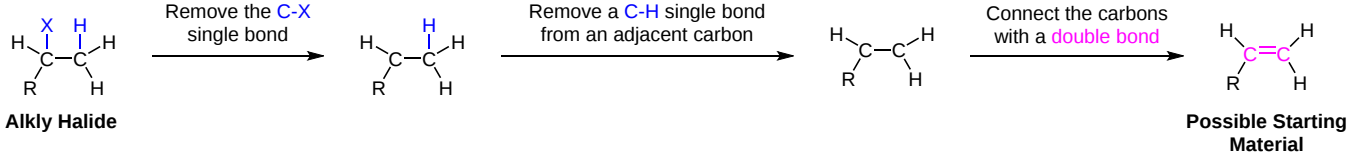


Planning the Synthesis of an Alkyl Halide using Electrophilic Addition

Understanding the starting material and reaction required for the synthesis a specific target molecule is an important concept in organic chemistry. The preferred method for answering these types of questions is to work backwards from the target molecule.

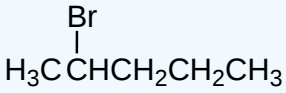
Often there will be multiple variations of reactions and starting materials capable synthesizing the target molecule. Further analysis of these variations can draw out strengths and weaknesses and lead to the pathway with the best chance of success.

To create a possible starting material for a given alkyl halide simply reverse the bonding changes expected during an electrophilic addition. Remove the C-X single bond and a C-H bond from an adjacent carbon. Then connect these two carbons with a double bond.



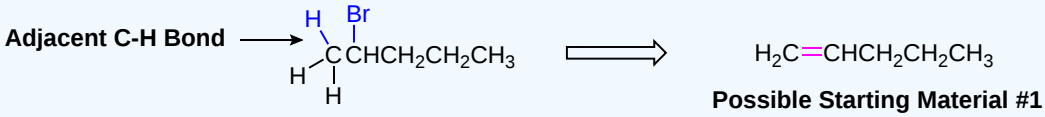
Worked Example 10.8.1

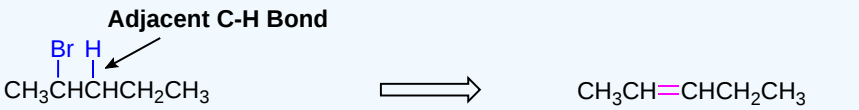
What alkene would be required to make the following 2-bromopentane using an electrophilic addition?



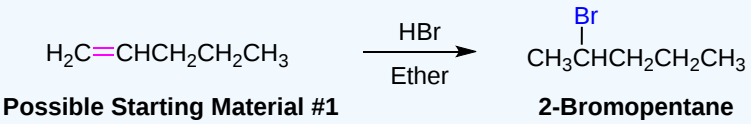
Answer

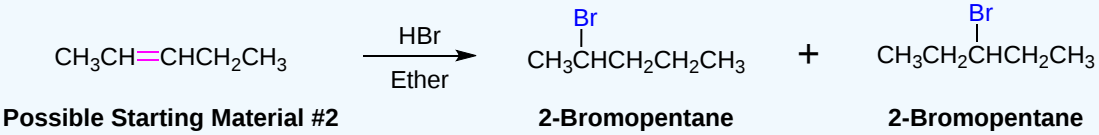
Analysis: Possible starting materials can be made by first removing the C-Br bond and an adjacent C-H bond. Then connecting the two carbons with a double bond. Because there are two different locations where an adjacent C-H bond can be removed there will be two possible starting material.





Solution: When comparing the the possible starting materials, #1 will follow Markovnikov's rule and produce 2-bromopentane as the sole product. Starting material #2 is symmertrically alkyl substituted, so Markovnikov's rule does not apply. A mixture of 2-bromopentane and 3-bromopentane would be produced. Between the two possible starting material #1 would be preferred because only one product is produced.

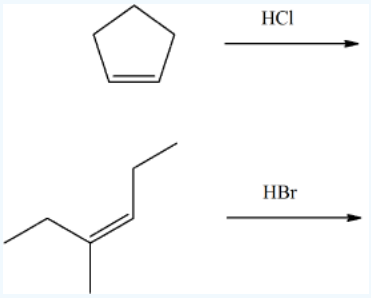




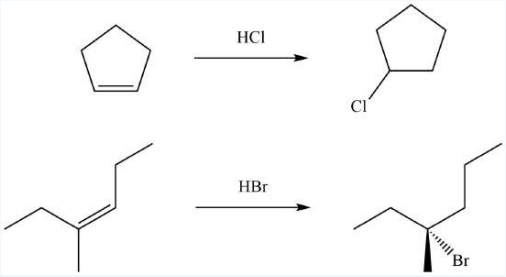
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Exercise 10.8.1

Predict the product(s) for the following reactions:

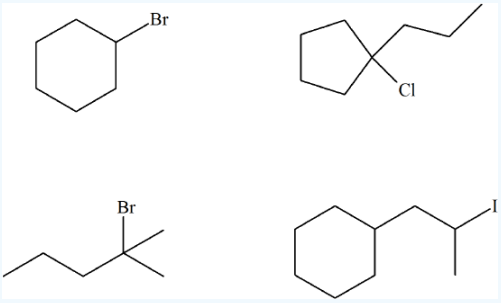


Answer

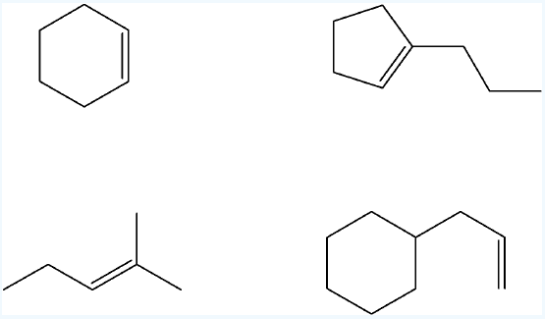


Exercise 10.8.2

In each case, suggest an alkene that would give the product shown.



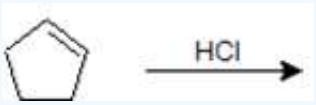
Answer



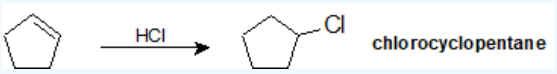
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Exercise 10.8.3

Give the IUPAC name for the product of the following reaction.



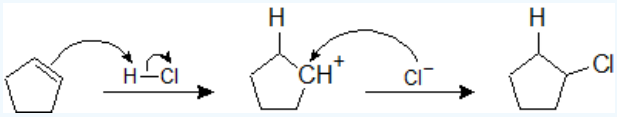
Answer



Exercise 10.8.4

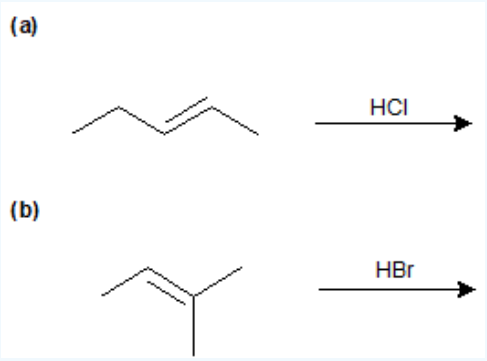
Draw the reaction mechanism of the previous problem

Answer

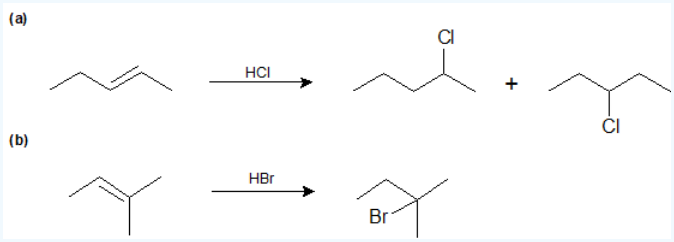


Exercise 10.8.5

Identify the products of the following reactions.



Answer



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10.9: Carbocation Structure and Stability

Objectives

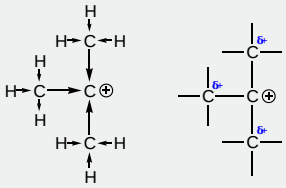
After completing this section, you should be able to

- describe the geometry of a given carbocation.
- arrange a given series of carbocations in order of increasing or decreasing stability.
- explain the relative stability of methyl, primary, secondary and tertiary carbocations in terms of hyperconjugation and inductive effects.

Study Notes

Although hyperconjugation can be used to explain the relative stabilities of carbocations, this explanation is certainly not the only one, and is by no means universally accepted. A more common explanation, involving the concept of an inductive effect, is given below.

It is a general principle in chemistry that the more a charge is dispersed, the more stable is the species carrying the charge. Put simply, a species in which a positive charge is shared between two atoms would be more stable than a similar species in which the charge is borne wholly by a single atom. In a tertiary carbocation, the positively charged carbon atom attracts the bonding electrons in the three carbon-carbon sigma (σ) bonds, and thus creates slight positive charges on the carbon atoms of the three surrounding alkyl groups (and, indeed, on the hydrogen atoms attached to them). Chemists sometimes use an arrow to represent this inductive release:



Note: These diagrams do not reflect the geometry of the carbocation. The overall charge on the carbocation remains unchanged, but some of the charge is now carried by the alkyl groups attached to the central carbon atom; that is, the charge has been dispersed.

In the tertiary carbocation shown above, the three alkyl groups help to stabilize the positive charge. In a secondary carbocation, only two alkyl groups would be available for this purpose, while a primary carbocation has only one alkyl group available. Thus the observed order of stability for carbocations is as follows:

tertiary > secondary > primary > methyl.

Stability of carbocation intermediates

The next step in understanding why Markovnikov's rule is often followed in electrophilic additions, involves understanding the structure and stability of the carboncation intermediate formed during the mechanism.

Carbocation Structure

Carbocations typically have three substituents which makes the carbon sp^2 hybridized and gives the overall molecule a trigonal planar geometry (Figure **10.9.1**). The carbocation's substituents are all in the same plane and have a bond angle of 120^o between them. The carbon atom in the carbocation is electron deficient; it only has six valence electrons which are used to form three sigma covalent bonds with the substituents. The carbocation carbon has an unoccupied p orbital which is perpendicular to the plane created by the substituents. The p orbital can easily accept electron pairs during reactions making carbocations excellent Lewis acids.

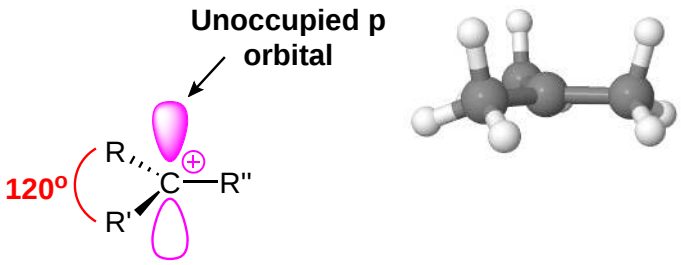
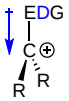


Figure **10.9.1**: (1) Hybridization of a generic carbocation and (2) the structure of the tert-butyl cation ($C_4H_9^+$).

Stability of Carbocation Intermediates

By being a reactive intermediate of the electrophilic addition mechanism, the stability of a carbocation has a direct effect on the reaction. The critical question now becomes, *what stabilizes a carbocation*?

A positively charged species such as a carbocation is very electron-poor, and thus anything which donates electron density will help to stabilize it. Conversely, a carbocation will be *destabilized* by an electron withdrawing group.



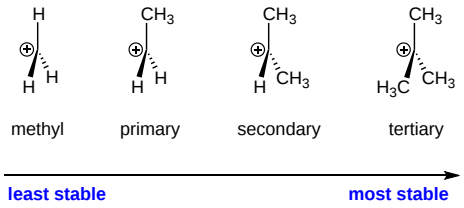
electron donating group *stabilizes* a carbocation



electron withdrawing group *destabilizes* a carbocation

Extensive experimental evidence has shown that a carbocation becomes more stable as the number of alkyl substituents increases. Carbocations can be given a designation based on the number of alkyl groups attached to the carbocation carbon. Three alkyl groups is called a tertiary (3^o) carbocation, 2 alkyl groups is called secondary (2^o), and 1 alkyl group is called primary (1^o). No alkyl groups are attached (3 hydrogen substituents) is called a methyl carbocation.

The overall order of stability is as follows:



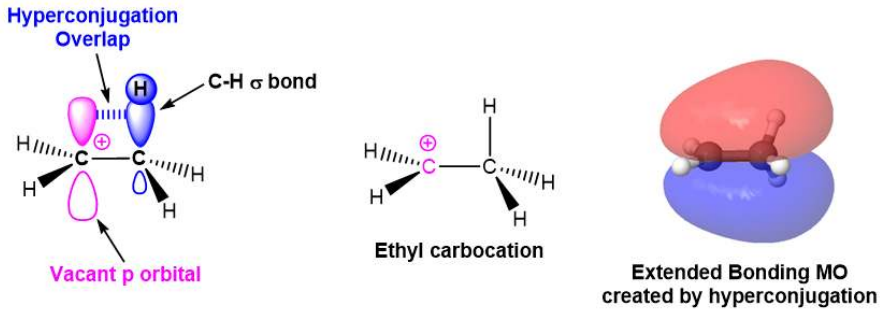
Alkyl groups stabilized carbocations for two reasons. The first is through inductive effects. As discussed in **Section 2-1**, inductive effects occur when the electrons in covalent bonds are shifted towards an nearby atom with a higher electronegativity. In this case, the positively charged carbocation draws in electron density from the surrounding substituents thereby gaining stabilization by slightly reducing its positive charge. Alkyl groups are more effective at inductively donating electron density than a hydrogen because they are larger, more polarizable, and contain more bonding electrons. As more alkyl groups are attached to the carbocation more inductive electron donation occurs and the carbocation becomes more stable.

The second reason alkyl groups stabilize carbocations is through hyperconjugation. As previously discussed in **Section 7.6**, hyperconjugation is an electron donation that occurs from the parallel overlap of p orbitals with adjacent hybridized orbitals participating in sigma bonds. This electron donation serves to stabilize the carbocation. As the number of alkyl substituents increases, the number of sigma bonds available for hyperconjugation increases, and the carbocation tends to become more stabilized.

In the example of ethyl carbocation shown below, the p orbital from a sp^2 hybridized carbocation carbon involved interacts with a sp^3 hybridized orbital participating in an adjacent C-H sigma bond. Electron density from the C-H sigma bond is donated into carbocation's p orbital providing stabilization.

The molecular orbital of the ethyl carbocation shows the interaction of electrons in methyl group's C-H sigma bonds with the adjacent empty p orbital from the carbocation. The interaction creates a bonding molecular orbital which extends over the three

atom chain (C-C-H) involved in hyperconjugation. The expanded molecular orbital helps to stabilize the carbocation.



It is not accurate to say, however, that carbocations with higher substitution are *always* more stable than those with less substitution. Just as electron-donating groups can stabilize a carbocation, electron-withdrawing groups act to destabilize carbocations. Carbonyl groups are electron-withdrawing by inductive effects, due to the polarity of the C=O double bond. It is possible to demonstrate in the laboratory that carbocation A below is more stable than carbocation B, even though A is a primary carbocation and B is secondary.

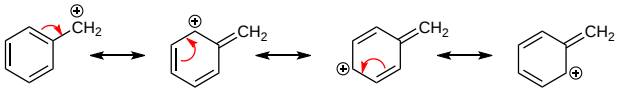


A: more stable **B**: less stable

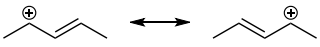
The difference in stability can be explained by considering the electron-withdrawing inductive effect of the ester carbonyl. Recall that inductive effects - whether electron-withdrawing or donating - are relayed through covalent bonds and that the strength of the effect decreases rapidly as the number of intermediary bonds increases. In other words, the effect decreases with distance. In species B the positive charge is closer to the carbonyl group, thus the destabilizing electron-withdrawing effect is stronger than it is in species A.

> In the next chapter we will see how the carbocation-destabilizing effect of electron-withdrawing fluorine substituents can be used in experiments designed to address the question of whether a biochemical nucleophilic substitution reaction is S_N1 or S_N2.

Stabilization of a carbocation can also occur through resonance effects, and as we have already discussed in the acid-base chapter, resonance effects as a rule are more powerful than inductive effects. Consider the simple case of a **benzylic** carbocation:

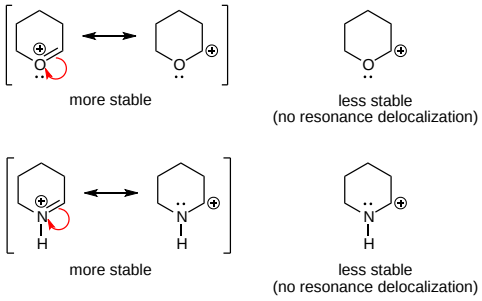


This carbocation is comparatively stable. In this case, electron donation is a resonance effect. Three additional resonance structures can be drawn for this carbocation in which the positive charge is located on one of three aromatic carbons. The positive charge is not isolated on the benzylic carbon, rather it is delocalized around the aromatic structure: this delocalization of charge results in significant stabilization. As a result, benzylic and **allylic** carbocations (where the positively charged carbon is conjugated to one or more non-aromatic double bonds) are significantly more stable than even tertiary alkyl carbocations.



Because heteroatoms such as oxygen and nitrogen are more electronegative than carbon, you might expect that they would by definition be electron withdrawing groups that destabilize carbocations. In fact, the opposite is often true: if the oxygen or nitrogen atom is in the correct position, the overall effect is carbocation stabilization. This is due to the fact that although these heteroatoms are electron *withdrawing* groups by induction, they are electron *donating* groups by resonance, and it is this resonance effect which

is more powerful. (We previously encountered this same idea when considering the relative acidity and basicity of phenols and aromatic amines in section 7.4). Consider the two pairs of carbocation species below:



In the more stable carbocations, the heteroatom acts as an electron donating group by resonance: in effect, the lone pair on the heteroatom is available to delocalize the positive charge. In the less stable carbocations the positively-charged carbon is more than one bond away from the heteroatom, and thus no resonance effects are possible. In fact, in these carbocation species the heteroatoms actually *destabilize* the positive charge, because they are electron withdrawing by induction.

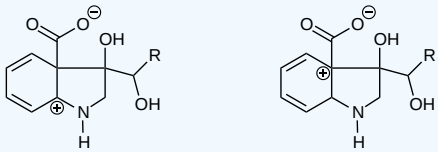
Finally, **vinylic** carbocations, in which the positive charge resides on a double-bonded carbon, are very unstable and thus unlikely to form as intermediates in any reaction.



a vinylic carbocation (very unstable)

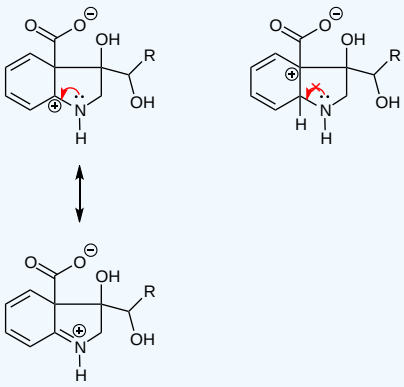
Example 10.9.1

In which of the structures below is the carbocation expected to be more stable? Explain.



Answer

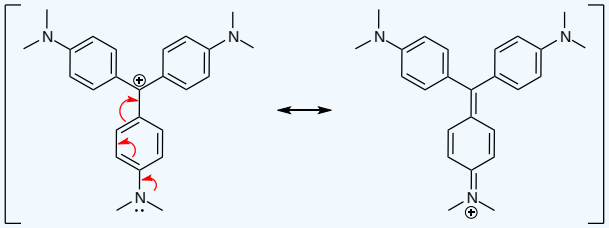
In the carbocation on the left, the positive charge is located in a position relative to the nitrogen such that the lone pair of electrons on the nitrogen can be donated to fill the empty orbital. This is not possible for the carbocation species on the right.



Example 10.9.2

Draw a resonance structure of the crystal violet cation in which the positive charge is delocalized to one of the nitrogen atoms.

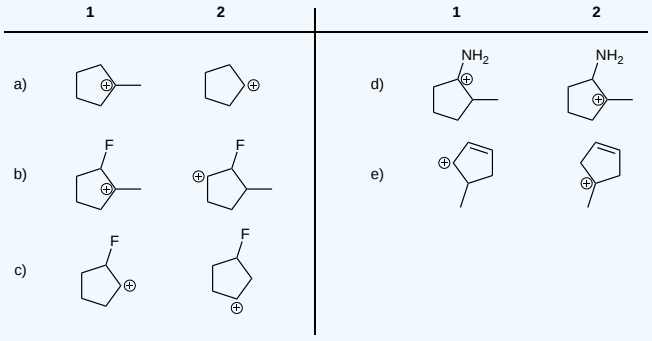
Answer



When considering the possibility that a nucleophilic substitution reaction proceeds *via* an S_N1 pathway, it is critical to evaluate the stability of the hypothetical carbocation intermediate. If this intermediate is not sufficiently stable, an S_N1 mechanism must be considered unlikely, and the reaction probably proceeds by an S_N2 mechanism. In the next chapter we will see several examples of biologically important S_N1 reactions in which the positively charged intermediate is stabilized by inductive and resonance effects inherent in its own molecular structure.

Example 10.9.3

State which carbocation in each pair below is more stable, or if they are expected to be approximately equal. Explain your reasoning.



Answer

a. 1 (tertiary vs. secondary carbocation)
b. 1 (tertiary vs. secondary carbocation)
c. 2 (positive charge is further from electron-withdrawing fluorine)
d. 1 (lone pair on nitrogen can donate electrons by resonance)
e. 1 (allylic carbocation – positive charge can be delocalized to a second carbon)

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10.10: The Hammond Postulate

Objective

After completing this section, you should be able to use the Hammond postulate to explain the formation of the most stable carbocation during the addition of a protic acid, HX, to an alkene.

Key Terms

Make certain that you can define, and use in context, the key term below.

- Hammond postulate

So far in this chapter the following points have been made about the electrophilic addition of HX to a double bond.

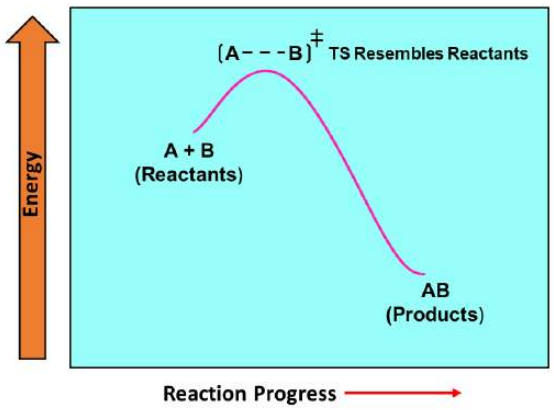
- The reaction takes place through a two step mechanism which forms a carbocation intermediate.
- During electrophilic addition the carbocation intermediate, and the subsequent H-X bond, forms on the double bond carbon with the most alkyl stubstituents *(***Markovnikov's rule)**
- Carbocations become more stable as the number of alkyl substituents increases.

It appears that the stability of the carbocation reactive intermediate has a direct effect on the products of a reaction. However, it is the activation energy required to reach the transition state of the reaction's rate determine step which determines which determines which product is produced. This implies that there is a relationship between the transition state and the carbocation reactive intermediate in the mechanism of electrophilic addition.

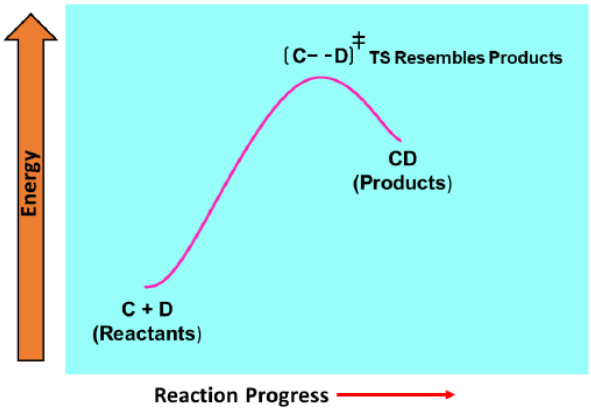
The Hammond Postulate

Chemists are often very interested in the structures of the transition states in a reaction's mechanism. In particular, the transition state for a mechanism's rate determining step directly determines the energy of activation barrier and thereby the rate for the overall reaction. Understanding the structure of a transition state allows chemists to consider structural features which might stabilize or destabilize the transition state causing a corresponding change in the rate of reaction. However, transition state structures cannot be directly observed because they are highly unstable activated complexes which instantly convert to a more stable species. In order to gain some insight into the structure of particular transition state, chemists often invoke the **Hammond postulate**, which states that *a transition state resembles the structure of the nearest stable species* (reactant, intermediate or product).

For an exergonic reaction, the transition state is closer in energy to the reactants. Therefore, the structure of the transition state can assumed to resemble the reactants more than the products. Shown below is a hypothetical exergonic reaction between reactant compounds A and B to form the product AB. The Hammond postulate would theorize that the distance between A and B in the transition state would be relatively large thus resembling the reactants where A and B are two isolated species.

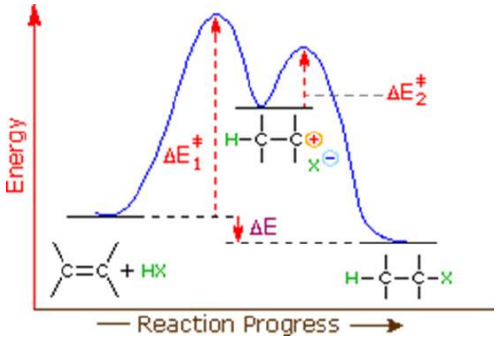


For an endergonic reaction, the transition state is closer in energy to the product. Therefore, the structure of the transition state can assumed to resemble the products more than the reactants. In the hypothetical endergonic reaction shown below, reactant compounds C and D react to form the product CD. The Hammond postulate would predict that the distance between C and D in the transition state would be relatively small thus resembling the products where C and D are bonded together as a single product CD.

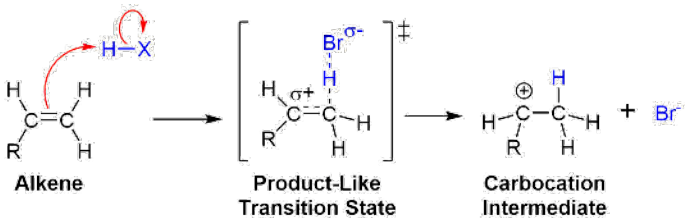


The Hammond Postulate and Electrophilic Addition

By applying the Hammond postulate and other ideas cultivated in this chapter the reason why electrophilic additions tend to follow Markovnikov's rule. When the energy diagram of an electrophilic addition was discussed in **Section 7.2**, it was noted the first step of the mechanism was the rate determining step. The first step of the mechanism also is endergonic and results in the formation of a carbocation intermediate.

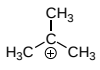


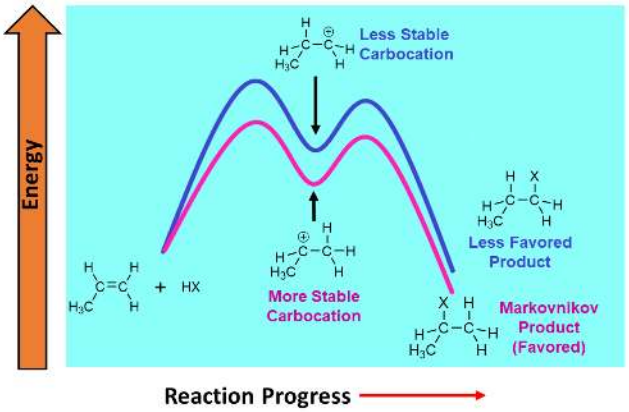
The Hammond postulate suggests that the transition state structure for the first step of the mechanism resembles that of the carbocation intermediate because they are the closest in energy. A transitions state, seen below, is typically drawn as a theoretical structure part way between the reactants and the product. For this transition state the pi bonds and the H-Br bond are in the process of being broken and are represented with a dashed line. The C-H bond is in the process of being formed so it also represented with a dashed line. The bromine is shown with a partial negative charge (sigma-) because it is becoming a bromide ion (Br^-) which has a full negative charge. Most importantly, the carbon is in the process of becoming a carbocation so it is shown to have a partial positive change (sigma+).



Because the Hammond postulate predicts this transitions state closely resembles the carbocation intermediate, the partial positive charge can said to closely resemble the full positive charge of the carbocation. Consequently, any structural feature that stabilized

the carbocation intermediate will also stabilize the transition state. The partial positive charge of the transition state is stabilized by adjacent alkyl groups thorough inductive effects and hyperconjugation much like the carbocation intermediate. Adding more alkyl substituents to the partially positive charged carbon stabilizes the transition state, causing it to become lower in energy. This in turn, decreases the energy of activation and increases the rate of the reaction. In short, during an electrophilic addition, the double bond carbon with the most alkyl substituents will for a carbocation intermediate and therefore its C-X bond faster than the double bond carbon with fewer alkyl substituents. These effects cause electrophillic additions to follow Markovnikov's rule and place the halogen (X) group on the more substituted carbon of asymmetrically alkyl substituted double bond.

Carbocation Stability		<<		<</td>		≈		<</td>		≈	

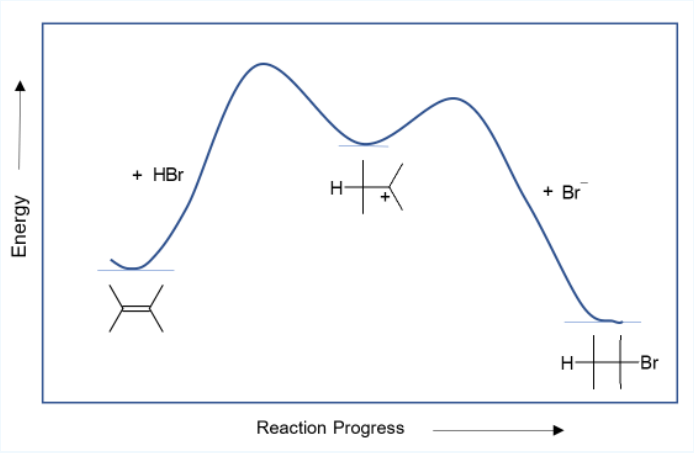


? Exercise 10.10.1

Consider the second step in the electrophilic addition of HBr to an alkene. Is this step exergonic or endergonic and does the transition state represent the product or the reactant (cation)? Draw out an energy diagram of this step reaction.

Answer

Exergonic and the transition state (second step) represents the reactant (cation). As shown to go from intermediate cation to final product the step is exergonic.

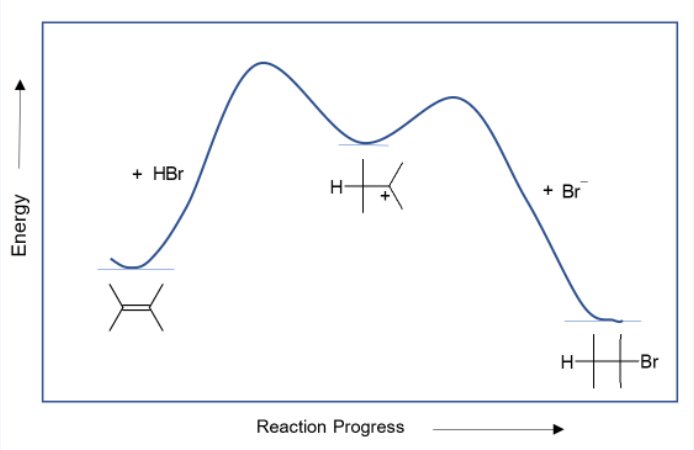


Exercise 10.10.2

Consider the second step in the electrophilic addition of HBr to an alkene. Is this step exergonic or endergonic and does the transition state represent the product or the reactant (cation)? Draw out an energy diagram of this step reaction.

Answer

Exergonic and the transition state (second step) represents the reactant (cation). As shown to go from intermediate cation to final product the step is exergonic.



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10.11: Evidence for the Mechanism of Electrophilic Additions - Carbocation Rearrangements

Objective

After completing this section, you should be able to explain the “unusual” products formed in certain reactions in terms of the rearrangement of an intermediate carbocation.

Key Terms

Make certain that you can define, and use in context, the key terms below.

- alkyl shift
- hydride shift

Study Notes

Whenever possible, carbocations will rearrange from a less stable isomer to a more stable isomer. This rearrangement can be achieved by either a hydride shift, where a hydrogen atom migrates from one carbon atom to the next, taking a pair of electrons with it; or an alkyl shift, in which an alkyl group undergoes a similar migration, again taking a bonding pair of electrons with it. These migrations usually occur between neighbouring carbon atoms, and hence are termed 1,2-hydride shifts or 1,2-alkyl shifts.

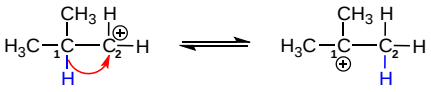
[A hydride ion consists of a proton and two electrons, that is, $[H:]^-$. Hydride ions exist in compounds such as sodium hydride, NaH, and calcium hydride, CaH_2.]

An electrophilic reaction such as HX with an alkene will often yield more than one product. This is strong evidence that the mechanism includes intermediate rearrangement steps of the cation.

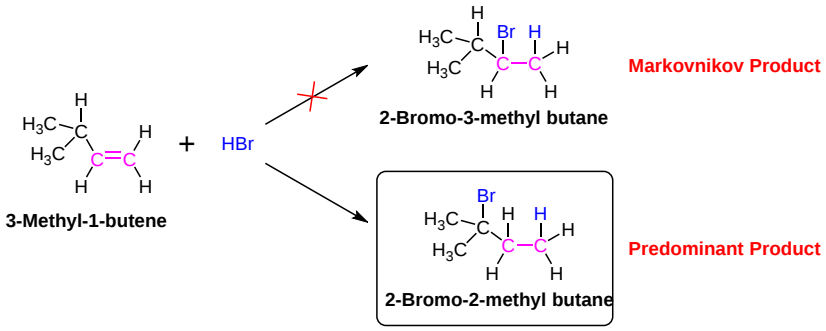
Throughout this textbook many reaction mechanisms will be presented. It is impossible to know with absolute certainty that a mechanism is correct. At best a proposed mechanism can be shown to be consistent with existing experimental data. Virtually all of the mechanisms in this textbook have been carefully studied by experiments designed to test their validity although the details are not usually discussed. An excellent example of experimental evidence which supports the carbocation based mechanism for electrophilic addition, is that structural rearrangements often occur during the reaction.

1,2-Hydride Shift

A 1,2-hydride shift is a carbocation rearrangement in which a hydrogen atom in a carbocation migrates to the carbon atom bearing the formal charge of +1 (carbon 2 in the example below) from an adjacent carbon (carbon 1).

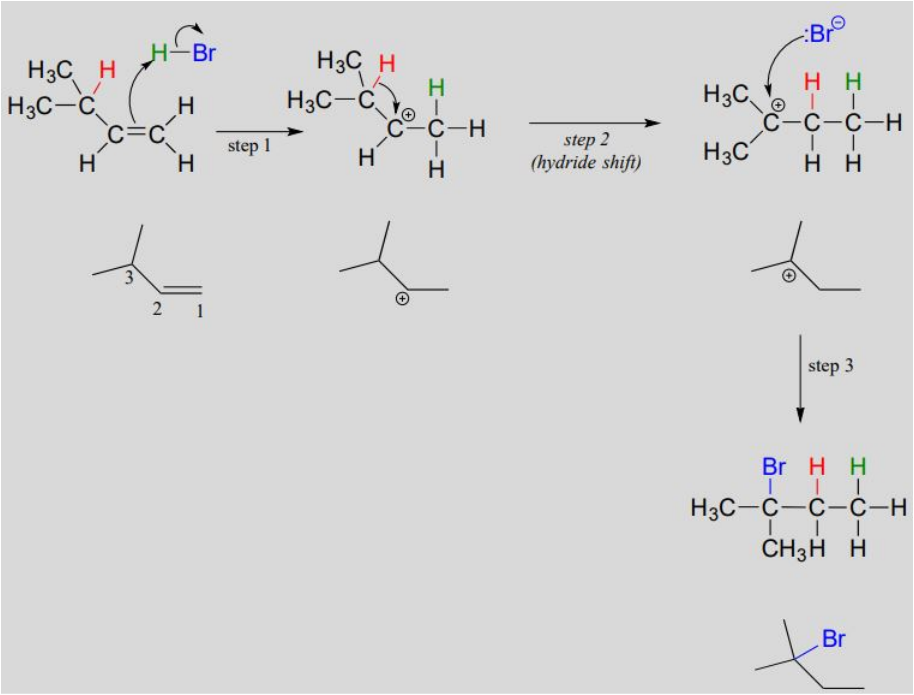


An example of this structural rearrangment occurs during the reaction of 3-methyl-1-butene with HBr. Markovnikov's rule predicts that the preferred product would be 2-bromo-3-methylbutane, however, very little of this product forms. The predominant product is actually 2-bromo-2-methylbutane.

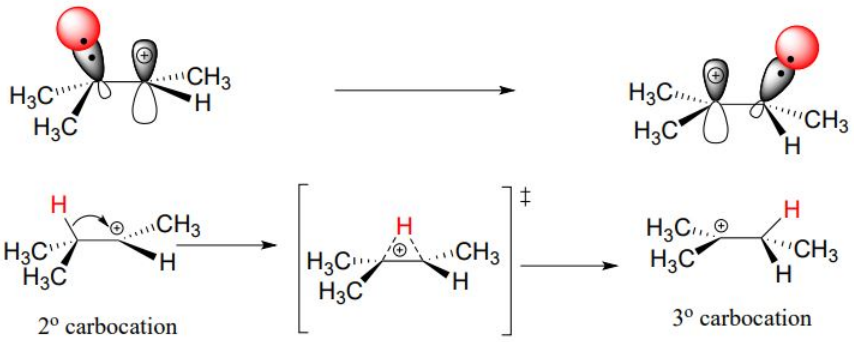


Mechanism of Hydride Shift

This result comes from a **Hydride Shift** during the reaction mechanism. The mechanism begins with protonation of the alkene which places a positive charge on the more alkyl substituted double bond carbon resulting in a secondary carbocation. In step 2, The electrons in the C-H bond on carbon #3 are attracted by the positive charge on carbon #2, and they simply shift over to fill the carbocation's empty *p* orbital, pulling the proton over with them. The process called a carbocation rearrangement, and more specifically, a hydride shift. A hydride ion ($H:^-$) is a proton plus two electrons which not to be confused with H^+, which is just a proton without any electrons. Notice that the hydride, in shifting, is not acting as an actual leaving group - a hydride ion is a very strong base and a very poor leaving group.



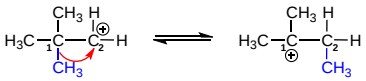
As the hydride shift proceeds, a new $C-H$ σ bond is formed at carbon #2, and carbon #3 is left with an empty p orbital and a positive charge.



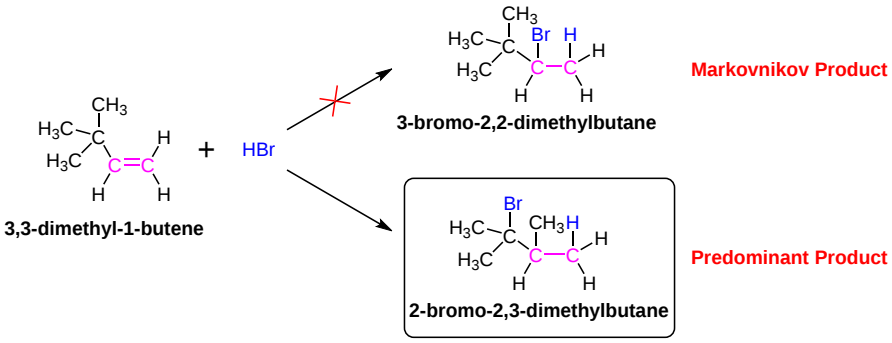
What is the thermodynamic driving force for this process? Notice that the hydride shift results in the conversion of a secondary carbocation (on carbon 2) to a (more stable) tertiary carbocation (on carbon 3) - a thermodynamically downhill step. As it turns out, the shift occurs so quickly that it is accomplished before the bromide nucleophile has time to attack at carbon #2. Rather, the bromide will attack after the hydride shift (step 3) at carbon #3 to complete the addition.

1,2-Alkyl Shift

A 1,2-alkyl shift is a carbocation rearrangement in which an alkyl group migrates to the carbon atom bearing the formal charge of +1 (carbon 2) from an adjacent carbon atom (carbon 1), e.g.



Consider another example. When HBr is added to 3,3-dimethyl-1-butene the preferred product is 2-bromo-2,3-dimethylbutane and not 3-bromo-2,2-dimethylbutane as predicted by Markovnikov's rule.

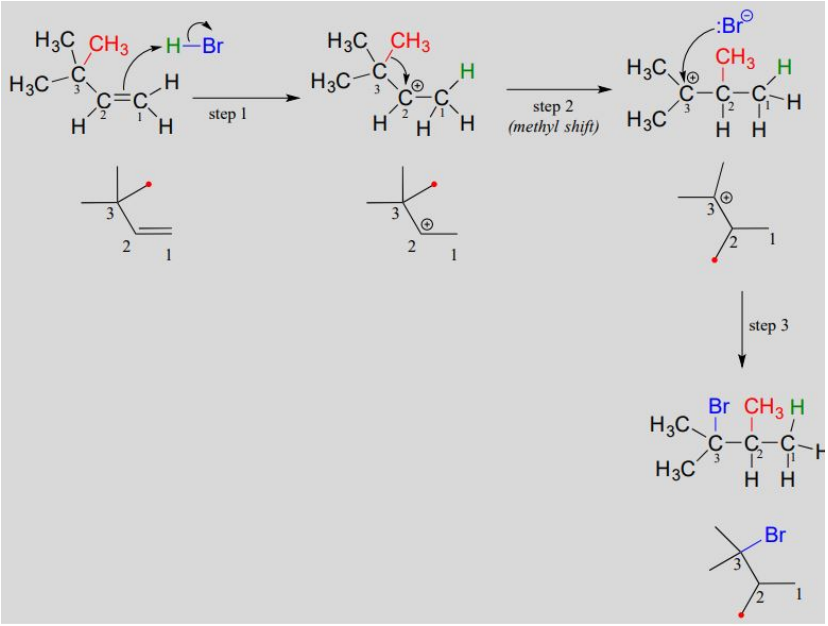


Notice that in the observed product, the carbon framework has been rearranged: a methyl carbon has been shifted. This is an example of another type of carbocation rearrangement, called an **alkyl shift** or more specifically a **methyl shift**.

Mechanism of Alkyl Shift

Below is the mechanism for the reaction. Once again a secondary carbocation intermediate is formed in step 1. In this case, there is no hydrogen on carbon #3 available to shift over create a more stable tertiary carbocation. Instead, it is a methyl group that does the shifting, as the electrons in the carbon-carbon σ bond shift over to fill the empty orbital on carbon #2 (step 2 below). The methyl shift results in the conversion of a secondary carbocation to a more stable tertiary carbocation. It is this tertiary carbocation which is attacked by the bromide nucleophile to make the rearranged end product. The end result is a rearrangement of the carbon framework of the molecule.

Electrophilic addition with methyl shift:



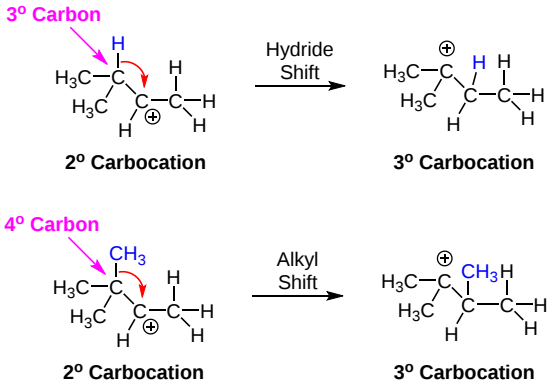
Predicting the Product of a Carbocation Rearrangement

Carbocation shifts occur in many more reactions than just electrophilic additions as some of which will be discussed in subsequent chapters of this textbook. Whenever a carbocation is produced in a reaction's mechanism the possibility of rearrangements should be considered. As discussed in Section 7.9, there are multiple ways to stabilize a carbocation all of which could induce a rearrangement.

The most common situation for a rearrangement to occur during electrophilic addition is:

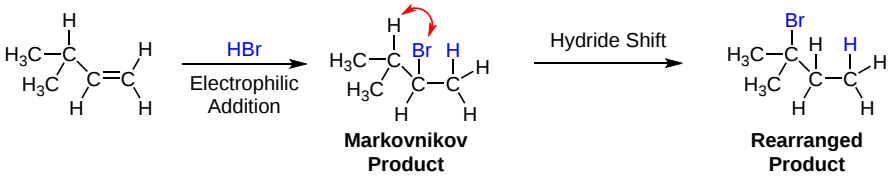
A 2^o Carbocation with a 3^o or 4^o Alkyl Substituent

When considering the possibility of a carbocation rearrangement the most important factors are the designation of the carbocation formed and the designation of the alkyl groups attached to the carbocation. When a 2^o carbocation has a 3^o alkyl substituent a hydride shift will occur to create a more stable 3^o carbocation. When a 2^o carbocation has a 4^o alkyl substituent an alkyl shift will occur to create a more stable 3^o carbocation.



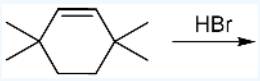
Drawing the Rearranged Product

First, draw the unrearranged product. Add HX to the double bond following Markovnikov's rule if necessary. Then determine if a hydride or alkyl shift is occurring by observing the designation of the alkyl substituent. The switch X ⇔H for a hydride shift and X ⇔ CH_3 for an alkyl shift this will produce the rearranged product.

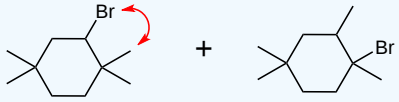


Exercise 10.11.1

Draw the expected products of the following reaction.

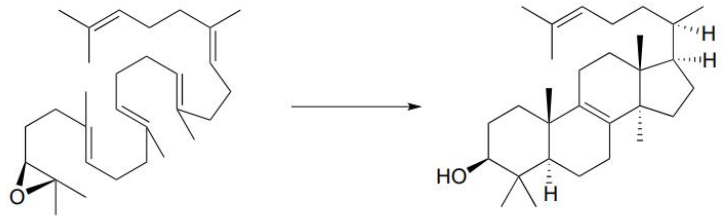


Answer



Biological Carbocation Rearrangement

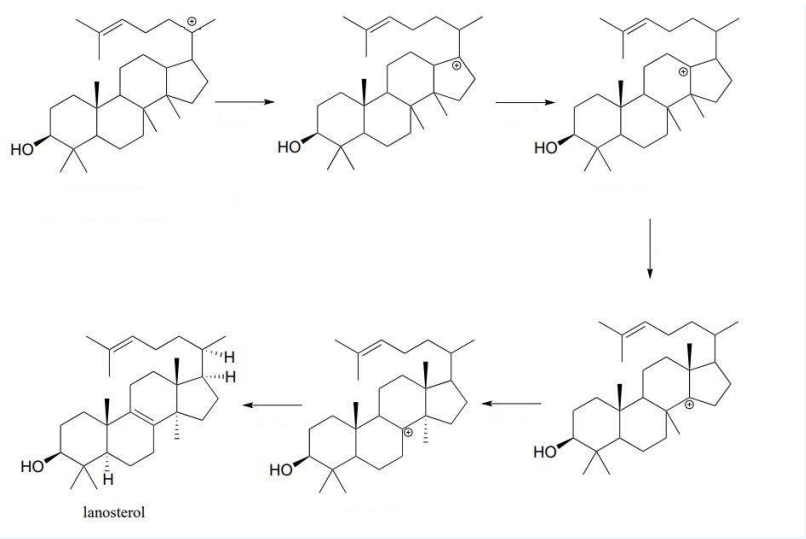
Carbocation rearrangements are involved in many known biochemical reactions. Rearrangements are particularly important in carbocation-intermediate reactions in which isoprenoid molecules cyclize to form complex multi-ring structures. For example, one of the key steps in the biosynthesis of cholesterol is the electrophilic cyclization of oxidosqualene to form a steroid called lanosterol.



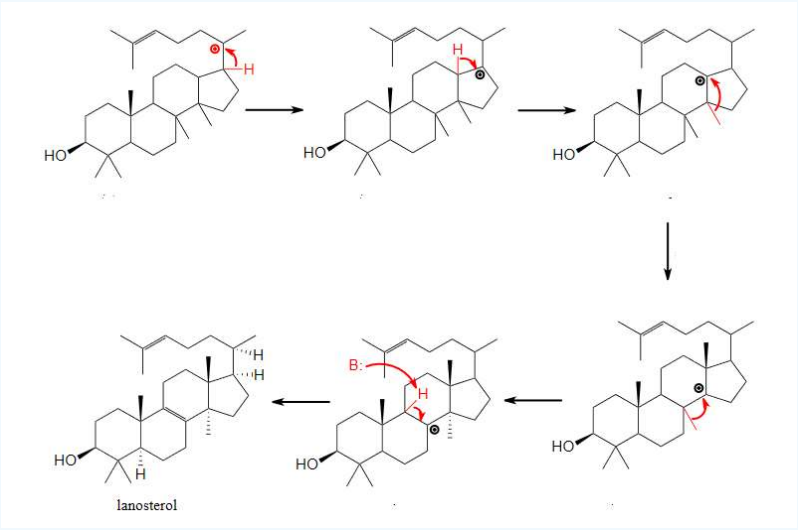
This complex but fascinating reaction has two phases. The first phase is where the actual cyclization takes place, with the formation of four new carbon-carbon bonds and a carbocation intermediate. The second phase involves a series of hydride and methyl shifts culminating in a deprotonation. In the exercise below, you will have the opportunity to work through the second phase of the cyclase reaction mechanism.

Exercise 10.11.1

The second phase of the cyclase reaction mechanism involves multiple rearrangement steps and a deprotonation. Please supply the missing mechanistic arrows.

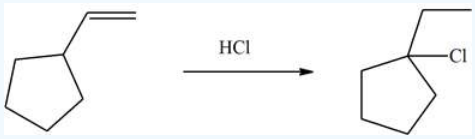


Answer

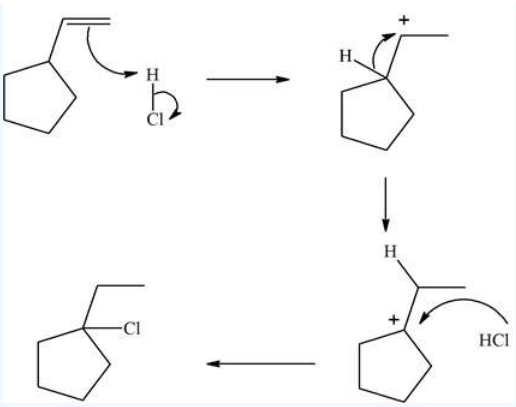


Exercise 10.11.2

The following reaction shows a rearrangement within the mechanism. Propose a mechanism that shows this.

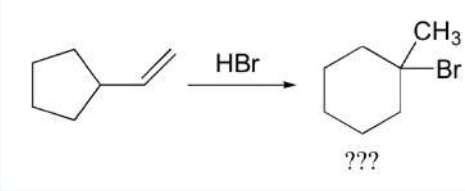


Answer



Exercise 10.11.1

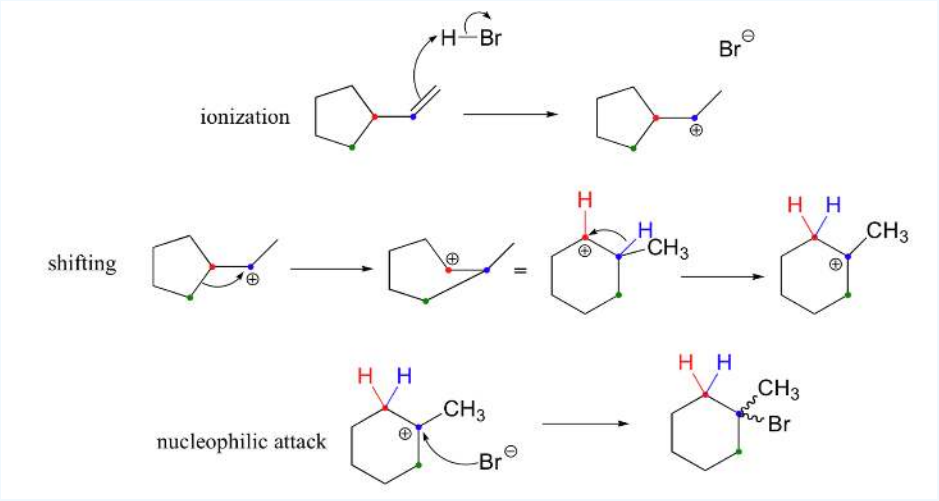
Propose a mechanism for the following reaction. It involves an electrophilic addition and the shift of a C-C and a C-H bond.



Answer

In most examples of carbocation rearrangements that you are likely to encounter, the shifting species is a hydride or methyl group. However, pretty much any alkyl group is capable of shifting. Sometimes, the entire side of a ring will shift over in a ring-expanding rearrangement.

The first 1,2-alkyl shift is driven by the expansion of a five-membered ring to a six-membered ring, which has slightly less ring strain. A hydride shift then converts a secondary carbocation to a tertiary carbocation, which is the electrophile ultimately attacked by the bromide nucleophile.



Once again, the driving force for this process is an increase in stability of the carbocation. Initially, there is a primary carbocation at C2, and this becomes a tertiary carbocation at C1 as a result of the (1,2)-methyl shift.

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CHAPTER OVERVIEW

11: Alkenes- Reactions and Synthesis

As you have seen, addition reactions dominate the chemistry of alkenes. This chapter shows how a variety of reagents can add to alkenes; how hydrogen bromide can be made to add to alkenes in a non-Markovnikov manner; and how alkene molecules can be cleaved into easily identifiable parts. First, you will examine the preparation of alkenes by elimination reactions.

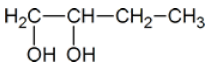
11.1: Chapter Objectives
11.2: Preparation of Alkenes - A Preview of Elimination Reactions
11.3: Halogenation of Alkenes - Addition of X_2
11.4: Halohydrins from Alkenes - Addition of HOX
11.5: Hydration of Alkenes - Addition of H_2O by Oxymercuration
11.6: Hydration of Alkenes - Addition of H_2O by Hydroboration
11.7: Reduction of Alkenes - Hydrogenation
11.8: Oxidation of Alkenes to Vicinal Diols
11.9: Oxidation of Alkenes - Cleavage to Carbonyl Compounds

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11.1: Chapter Objectives

After you have completed Chapter 11, you should be able to

1. fulfill all of the detailed objectives listed under each section.
2. design a relatively simple, multistep synthesis using the reactions introduced in this chapter, given the structure, name, or both, of the starting material and product. For example, show how you would convert 1-bromobutane to



3. deduce the structures of a number of compounds involved in a certain reaction sequence, given sufficient information. In other words, solve so-called road-map problems.
4. define, and use in context, the key terms introduced in this chapter.

Contributors and Attributions

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11.2: Preparation of Alkenes - A Preview of Elimination Reactions

Objectives

After completing this section, you should be able to

- explain the relationship between an addition reaction and an elimination reaction.
- write an equation to describe the dehydrohalogenation of an alkyl halide.
- identify the reagents required to bring about dehydrohalogenation of an alkyl halide.
- write an equation to represent the dehydration of an alcohol.
- identify the reagents required to dehydrate a given alcohol.

Key Terms

Make certain that you can define, and use in context, the key terms below.

- dehydration
- dehydrohalogenation
- elimination reaction

Study Notes

An *elimination reaction* is a reaction in which two or more atoms, one of which is usually hydrogen, are removed from adjacent atoms in the reactant, resulting in the formation of a multiple bond.

The relationship between addition reactions and elimination reactions is shown in Figure 8.1, below.

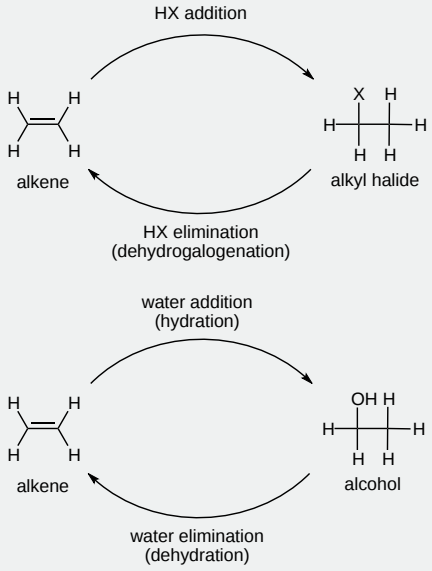
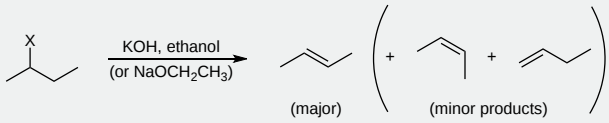
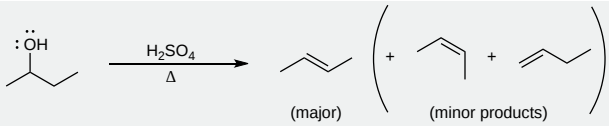


Figure 8.1: Relationship of addition and elimination reactions

Alkenes can be readily prepared from the alkylhalide (X = Cl, Br, I) or the alcohol.



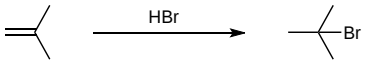


Electrophilic Addition

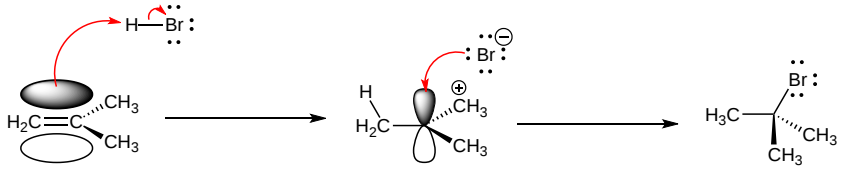
Alkenes are found throughout nature. They form the basis of many natural products, such as terpenes, which play a variety of roles in the lives of plants and insects. The C=C bonds of alkenes are very different from the C=O bonds that are also common in nature. The C=C bonds of alkenes are electron-rich and nucleophilic, in contrast to the electron-poor C=O bonds of carbohydrates, fatty acids and proteins. That difference plays a role in how terpenes form in nature.

Alkenes, or olefins, are also a major product of the petroleum industry. Reactions of alkenes form the basis for a significant portion of our manufacturing economy. Commonly used plastics such as polyethylene, polypropylene and polystyrene are all formed through the reactions of alkenes. These materials continue to find use in our society because of their valuable properties, such as high strength, flexibility and low weight.

Alkenes undergo addition reactions as you will see carbonyls do as well. Most commonly they add a proton to one end of the double bond and another group to the other end. These reactions happen in slightly different ways, however.



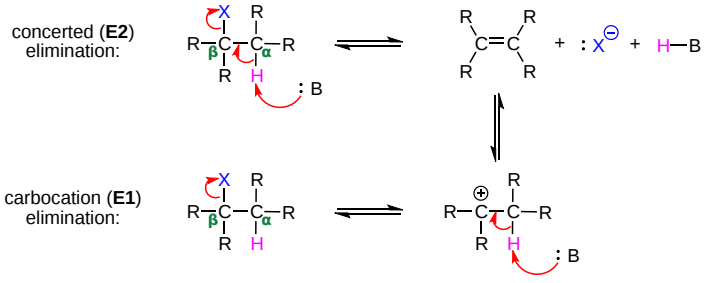
Alkenes are reactive because they have a high-lying pair of π-bonding electrons. These electrons are loosely held, being high in energy compared to σ-bonds. The fact that they are not located between the carbon nuclei, but are found above and below the plane of the double bond, also makes these electrons more accessible.



Alkenes can donate their electrons to strong electrophiles other than protons, too. Sometimes their reactivity pattern is a little different than the simple addition across the double bond, but that straightforward pattern is what we will focus on in this chapter.

Elimination reactions

Elimination reactions are possible by abstraction of a proton at positions that are next to a potential leaving group. This type of elimination can be described by two model mechanisms: it can occur in a single concerted step (proton abstraction at C_α occurring at the same time as C_β-X bond cleavage), or in two steps (C_β-X bond cleavage occurring first to form a carbocation intermediate, which is then 'quenched' by proton abstraction at the alpha-carbon).



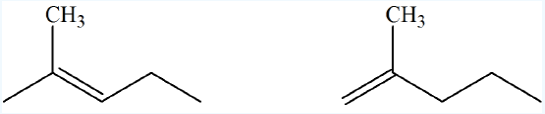
The most common elimination reactions are dehydrohalogenation and dehydration. In the mechanism above, X could be Cl, Br, or I for the dehydrohalogenation where there is a loss of HX from an alkyl halide. For dehydration, X would be an OH group in the above mechanism where the overall loss is water from an alcohol. These mechanisms, termed E2 and E1, respectively, are important in laboratory organic chemistry, but are less common in biological chemistry. As explained below, which mechanism

actually occurs in a laboratory reaction will depend on the identity of the R groups (ie., whether the alkyl halide is primary, secondary, tertiary, etc.) as well as on the characteristics of the base.

Exercise 11.2.1

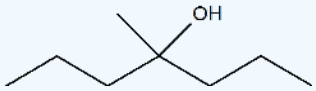
In elimination reactions there tends to have a mixture of products. What are the two possible alkene products for the reaction of 2-bromo-2-methylpentane with NaOH?

Answer

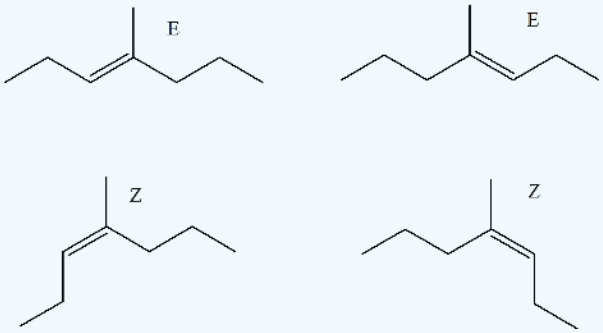


Exercise 11.2.2

Predict the *E/Z* isomers for the following molecule when reacted with H_2SO_4.



Answer



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11.3: Halogenation of Alkenes - Addition of X_2

Objectives

After completing this section, you should be able to

- write the equation for the reaction of chlorine or bromine with a given alkene.
- identify the conditions under which an addition reaction occurs between an alkene and chlorine or bromine.
- draw the structure of the product formed when a given alkene undergoes an addition reaction with chlorine or bromine.
- write the mechanism for the addition reaction that occurs between an alkene and chlorine or bromine, and account for the stereochemistry of the product.

Key Terms

Make certain that you can define, and use in context, the key terms below.

- anti stereochemistry
- bromonium ion

Study Notes

In the laboratory you will test a number of compounds for the presence of a carbon-carbon double bond. A common test is the decolourization of a reddish-brown bromine solution by an alkene.

The two-step mechanism shown in the LibreText pages gives you an idea of how the reaction between an alkene and a halogen occurs. Note the formation of the bridged bromonium ion intermediate and the anti stereochemistry of the final product because the two bromine atoms come from opposite faces of the double bond.

Additional evidence in support of the bromonium ion mechanism comes from the results obtained when an alkene (such as cyclopentene) reacts with bromine in the presence of sodium chloride (see Figure 8.2: Reaction of an alkene with bromine in the presence of sodium chloride, below).

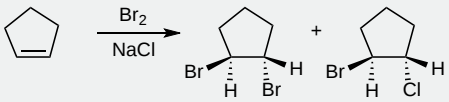


Figure 8.2: *Reaction of an alkene with bromine in the presence of sodium chloride*

Once formed, the bromonium ion is susceptible to attack by two nucleophiles—chloride ion and bromide ion—and, in fact, a mixture of two products (both produced by anti attack) is formed.

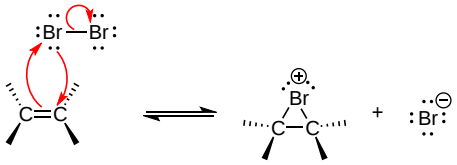
Halogens can act as electrophiles to which can be attacked by a pi bond from an alkene. Pi bonds represents a region of electron density and therefore function as a nucleophiles. How is it possible for a halogen to obtain positive charge to be an electrophile?

Introduction

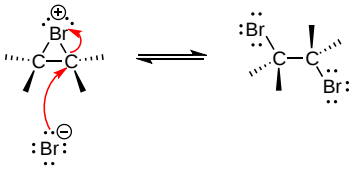
A halogen molecule, for example Br_2, approaches a double bond of the alkene, electrons in the double bond repel electrons in the bromine molecule causing polarization of the halogen-halogen bond. This creates a dipole moment in the halogen-halogen bond. Heterolytic bond cleavage occurs and one of the halogens obtains a positive charge and reacts as an electrophile. The reaction of the addition is not regioselective but is stereoselective. Stereochemistry of this addition can be explained by the mechanism of the reaction. In the first step, the electrophilic halogen (with the positive charge) approaches the pi bond and 2p orbitals of the halogen bond with two carbon atoms creating a cyclic ion with a halogen as the intermediate. In the second step, the remaining halide ion (halogen with the negative charge) attacks either of the two carbons in the cyclic ion from the back side of the cycle as in the S_N2 reaction. Therefore stereochemistry of the product is anti addition of **vicinal dihalides**.

$$\mathbf{R_2C{=}CR_2 + X_2 \rightarrow R_2CX{-}CR_2X} \tag{8.2.1}$$

Step 1: In the first step of the addition the Br-Br bond polarizes, heterolytic cleavage occurs and Br with the positive charge forms a cyclic intermediate with the two carbons from the alkene.



Step 2: In the second step, bromide anion attacks either carbon of the bridged bromonium ion from the back side of the ring. The bromine atom in the bromonium ion acts as a shield in a way, forcing the bromonium anion to attack from the opposite side as it. The result of this is the ring opening up with the two halogens on opposite sides as each other. This is **anti** stereochemistry, which is defined as the two bromine atoms come from opposite faces of the double bond. The product is that the bromines add on trans to each other.



Halogens that are commonly used in this type of the reaction are: ***Br*** and ***Cl***. In thermodynamical terms ***I*** is too slow for this reaction because of the size of its atom, and ***F*** is too vigorous and explosive.

Because the halide ion can attack any carbon from the opposite side of the ring it creates a mixture of steric products. Optically inactive starting material produce optically inactive achiral products (meso) or a racemic mixture.

Electrophilic addition mechanism consists of two steps.

Before constructing the mechanism let us summarize conditions for this reaction. We will use Br_2 in our example for halogenation of ethylene.

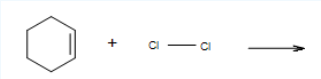
Nucleophile	**Double bond in alkene**
Electrophile	Br_2, Cl_2
Regiochemistry	not relevant
Stereochemistry	**ANTI**

Summary

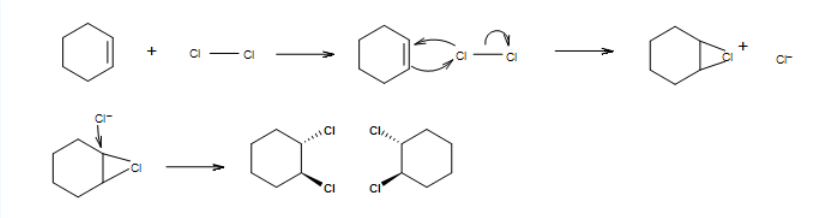
Halogens can act as electrophiles due to polarizability of their covalent bond. Addition of halogens is stereospecific and produces vicinal dihalides with anti addition.

? Exercise 11.3.1

What is the mechanism of adding Cl_2 to the cyclohexene?



Answer



Exercise 11.3.2

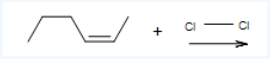
A reaction of Br_2 molecule in an inert solvent with alkene follows?

a. syn addition
b. anti addition
c. Morkovnikov rule

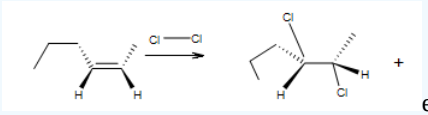
Answer

b

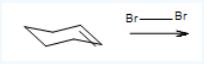
Exercise 11.3.3



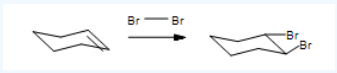
Answer


enantiomer

Exercise 11.3.4



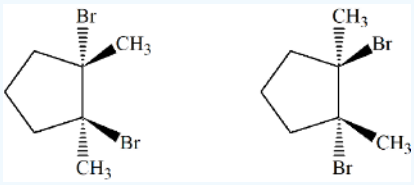
Answer



Exercise 11.3.5

Predict the products for 1,2-dimethylcyclopentene reacting with Br_2 with proper stereochemistry.

Answer

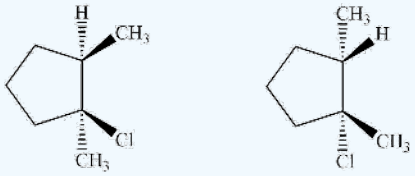


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Exercise 11.3.6

Predict the products for 1,2-dimethylcyclpentene reacting with HCl, give the proper stereochemistry. What is the relationship between the two products?

Answer



These compounds are enantiomers.

References

1. Vollhard,K.Peter C., and Neil E.Schore.Organic Chemistry:Structure and Function. New York: W.H.Freeman and Company 2007
2. Chemistry-A European Journal 9 (2003) :1036-1044

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11.4: Halohydrins from Alkenes - Addition of HOX

Objectives

After completing this section, you should be able to

- write the equation for the formation of a halohydrin from an alkene.
- write the mechanism for the formation of a halohydrin from an alkene and a mixture of halogen and water.
- predict the mechanism of the addition reaction that occurs between a given reagent and an alkene, basing your prediction on mechanisms you have studied in this chapter.
- identify the alkene, the reagents, or both, that should be used to produce a given halohydrin by an addition reaction.
- identify N-bromosuccinimide in aqueous dimethyl sulphoxide as an alternative source of bromine for producing bromohydrins.

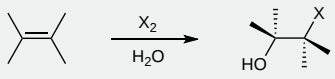
Key Terms

Make certain that you can define, and use in context, the key terms below.

- bromohydrin
- halohydrin

Study Notes

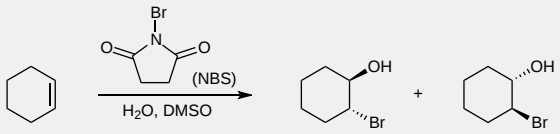
Bromohydrin and chlorohydrin are examples of halohydrins (where X = Br or Cl).



alkene halohydrin

Chemists often abbreviate the names of frequently used chemicals: DMSO for dimethyl sulfoxide, NBS for N-bromosuccinimide, etc. You should already be familiar with some similar examples from everyday life: DDT for dichlorodiphenyltrichloroethane, PCB for polychlorinated biphenyl, and ASA for acetylsalicylic acid (aspirin). You can see how someone with a limited knowledge of chemistry could misinterpret the abbreviation NBS—it is not a compound containing nitrogen, boron and sulfur!

NBS can serve as a less dangerous and easier to handle replacement for Br_2 in the formation of bromohydrins.



The proton is not the only electrophilic species that initiates addition reactions to the double bond of alkenes. Lewis acids like the halogens, boron hydrides and certain transition metal ions are able to bond to the alkene pi-electrons, and the resulting complexes rearrange or are attacked by nucleophiles to give addition products.The electrophilic character of the halogens is well known as discussed in the previous section. Chlorine (Cl_2) and bromine(Br_2) react selectively with the double bond of alkenes, and these reactions are what we will focus on. Fluorine adds uncontrollably with alkenes,and the addition of iodine is unfavorable, so these are not useful preparative methods.

The addition of chlorine and bromine to alkenes, as shown below, proceeds by an initial electrophilic attack on the pi-electrons of the double bond (Section 8.2). Dihalo-compounds in which the halogens are bound to adjacent carbons are called vicinal, from the Latin *vicinalis*, meaning neighboring.

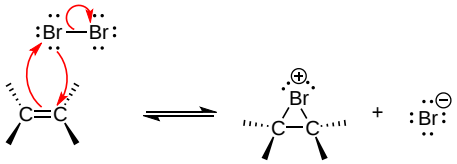
$$R_2C{=}CR_2 + X_2 \longrightarrow R_2CX\text{-}CR_2X$$

Another electrophilic addition to an alkene is the reaction of an alkene with the other halogen-containing reagents like hypohalous acids, HOX, to form halohydrins. However, halohydrins are not formed by directly adding a hypohalous acid, instead the alkene is reacted with Br_2 or Cl_2 in the presence of water. These reagents are unsymmetrical (unlike Br_2 or Cl_2), so their addition to unsymmetrical double bonds may in principle take place in two ways. In practice, these addition reactions are regioselective, with one of the two possible constitutionally isomeric products being favored. The electrophilic moiety in both of these reagents is the halogen.

$$(CH_3)_2C{=}CH_2 + HOBr \longrightarrow (CH_3)_2COH\text{-}CH_2Br$$

The regioselectivity of the above reactions may be explained by the same mechanism we used to rationalize the Markovnikov rule. Thus, bonding of an electrophilic species to the double bond of an alkene should result in preferential formation of the more stable (more highly substituted) carbocation, and this intermediate should then combine rapidly with a nucleophilic species to produce the addition product.

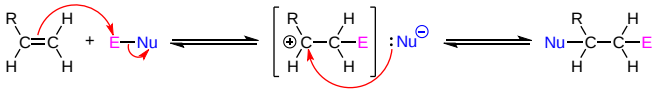
The regioselectivity of the above reactions may be explained by the same mechanism we used to rationalize the Markovnikov rule. Thus, bonding of an electrophilic species to the double bond of an alkene should result in preferential formation of the more stable (more highly substituted) carbocation, and this intermediate should then combine rapidly with a nucleophilic species to produce the addition product.



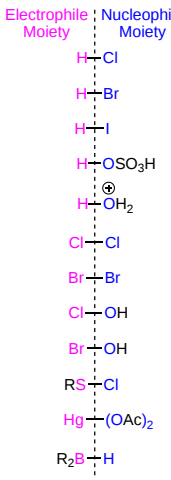
Step one is the same as halogenation of alkenes. The halogen, in this case bromine, reacts with the alkene to form a cyclic bromonium ion.

Step two does not have the bromine ion attack, but instead water acts as the nucleophile. Water is available at a higher concentration than the bromine ion, so is more likely to be available in the correct orientation for the nucleophilic attack. Water is also a better nucleophile than the bromine ion. The better a nucleophile, the more likely it is to attack. You may notice that as oxygen makes a bond it gets a positive formal charge at the completion of this step.

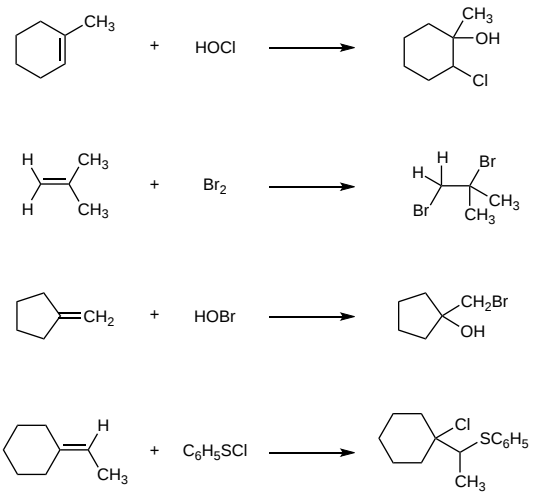
Step 3 is a final acid-base step, where there is a loss of a proton from the oxygen to the solvent (water) to form the neutral halohydrin. In this case, a bromohydrin is the product of the addition reaction.



To apply this mechanism we need to determine the electrophilic moiety in each of the reagents. By using electronegativity differences we can dissect common addition reagents into electrophilic and nucleophilic moieties, **as shown on the right**. In the case of hypochlorous and hypobromous acids (HOX), these weak Brønsted acids (pKa's ~ 8) do not react as proton donors; and since oxygen is more electronegative than chlorine or bromine, the electrophile will be a halide cation. The nucleophilic species that bonds to the intermediate carbocation is then hydroxide ion, or more likely water (the usual solvent for these reagents), and the products are called halohydrins. Sulfenyl chlorides add in the opposite manner because the electrophile is a sulfur cation, RS(+), whereas the nucleophilic moiety is chloride anion (chlorine is more electronegative than sulfur).

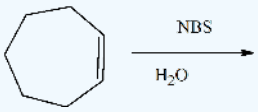


Below are some examples illustrating the addition of various electrophilic halogen reagents to alkene groups. Notice the specific regiochemistry of the products, as explained above.

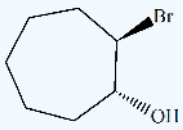


Exercise 11.4.1

Predict the product of the following reaction:



Answer



Exercise 11.4.2

When butene is treated with NBS in the presence of water, the product shows that the bromine is on the least substituted carbon, is this Markovnikov or anti-Markovnikov?

Answer

Since the bromine is the first addition to the alkene, this addition would be an anti-Markovnikov addition.

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11.5: Hydration of Alkenes - Addition of H_2O by Oxymercuration

Objectives

After completing this section, you should be able to

- write an equation for the hydration of an alkene with sulfuric acid.
- write an equation for the formation of an alcohol from an alkene by the oxymercuration-demercuration process.
- identify the alkene, the reagents, or both, that should be used to produce a given alcohol by the oxymercuration-demercuration process.
- write the mechanism for the reaction of an alkene with mercury(II) acetate in aqueous tetrahydrofuran (THF).

Key Terms

Make certain that you can define, and use in context, the key terms below.

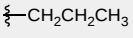
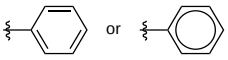
- hydration
- oxymercuration

Study Notes

Oxymercuration is the reaction of an alkene with mercury(II) acetate in aqueous THF, followed by reduction with sodium borohydride. The final product is an alcohol.

It is important that you recognize the similarity between the mechanisms of bromination and oxymercuration. Recognizing these similarities helps you to reduce the amount of factual material that you need to remember.

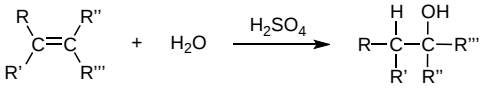
Mercuric acetate, or mercury(II) acetate, to give it the preferred IUPAC name, is written as $Hg(OAc)_2$; by comparing this formula with the formula $Hg(O_2CCH_3)_2$, you can equate Ac with $-COCH_3$. In fact, Ac is an abbreviation used for the acetyl group with the structure shown below as are other similar abbreviations that you will encounter.

Ac (acetyl)	
Me (methyl)	
Et (ethyl)	
Pr^n (*n*-propyl)	
Pr^i (isopropyl)	
Bu^t (*tert*-butyl)	
Ph (phenyl)	

What Is Electrophilic Hydration?

Electrophilic hydration is the act of adding an electrophilic hydrogen from a non-nucleophilic strong acid (a reusable catalyst, examples of which include sulfuric and phosphoric acid) and applying appropriate temperatures to break the alkene's double bond. After a carbocation is formed, water bonds with the carbocation to form a 1º, 2º, or 3º alcohol on the alkane. Electrophilic hydration

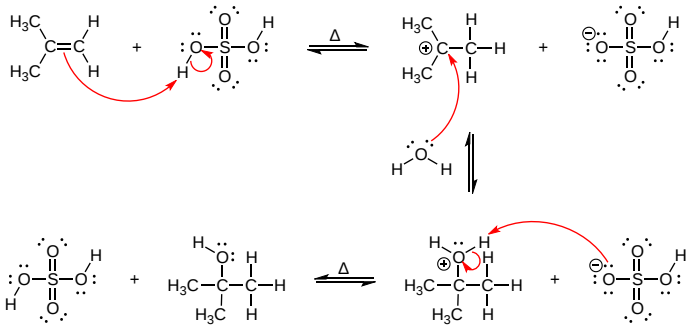
is the reverse dehydration of alcohols and has practical applications in making alcohols for fuels and reagents for other reactions. The basic reaction under certain temperatures (given below) is the following:



An electrophilic hydrogen is essentially a proton: a hydrogen atom stripped of its electron. An electrophilic hydrogen is commonly used to help break double bonds or restore catalysts (see S_N2 for more details).

Mechanism for the formation of a 3º Alcohol (1º and 2º mechanisms are similar)

Hydration is the process where water is added to an alkene to yield an alcohol. Acid-catalyzed hydration is when a strong acid is used as a catalyst to begin the reaction, but let's look at the mechanism below and break down the steps.



Step 1: A hydrogen atom from the acid is attacked by the nucleophilic Pi-electrons in the double bond. This is similar to the other alkene reactions we have seen so far. In this process, a new C-H bond is formed at the location which creates the more stable carbocation.

Step 2: A nucleophilic water attacks or donates a lone pair to the carbocation intermediate created in the first step. A new C-O bond is formed with the O having a formal charge of +1. The product is a protonated alcohol.

Step 3: To obtain the neutral alcohol product, the final step is to deprotonate the oxygen atom with the +1 formal charge using the conjugate base of the acid catalyst. This final step regenerates the acid catalyst and yields the neutral alcohol product.

> Heat is used to catalyze electrophilic hydration; because the reaction is in equilibrium with the dehydration of an alcohol, which requires higher temperatures to form an alkene, lower temperatures are required to form an alcohol. *The exact temperatures used are highly variable and depend on the product being formed.*

What is Regiochemistry and How Does It Apply?

Regiochemistry deals with where the substituent bonds on the product is formed. **Zaitsev's** and **Markovnikov**'s rules address regiochemistry, but Zaitsev's rule applies when synthesizing an alkene while Markovnikov's rule describes where the substituent bond form in the product of an electrophilic additon. In the case of electrophilic hydration, Markovnikov's rule is the only rule that *directly* applies. See the following for an in-depth explanation of regiochemistry: Markovnikov explanation: Radical Additions--Anti-Markovnikov Product Formation

In the mechanism for the formation of a 3º alcohol shown above, the H is added to the least-substituted carbon in the nucleophilic double bond (it has less carbons attached to it). This means that the carbocation forms on the 3º carbon, causing it to be more stabilized by *hyperconjugation*—electrons in nearby sigma (single) bonds help fill the empty p-orbital of the carbocation, which lessens the positive charge. More substitution on a carbon means more sigma bonds are available to "help out" (by using overlap) with the positive charge, which creates greater *carbocation stability*. In other words, **carbocations form on the most substituted carbon** in the double bond.

If the carbocation does originally form on the less substituted part of the alkene, carbocation rearrangements occur to form more substituted products:

- **Hydride shifts:** a hydrogen atom bonded to a carbon atom next to the carbocation leaves that carbon to bond with the carbocation (after the hydrogen has taken both electrons from the single bond, it is known as a hydride). This changes the once neighboring carbon to a carbocation, and the former carbocation becomes a neighboring carbon atom.



- **Alkyl shifts:** if no hydrogen atoms are available for a hydride shift, an entire methyl group performs the same shift.

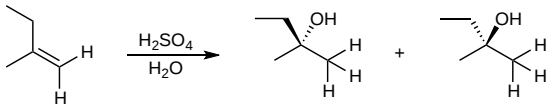


The nucleophile attacks the positive charge formed on the most substituted carbon connected to the double bond, because the nucleophile is seeking that positive charge. In the mechanism for a 3º alcohol shown above, water is the nucleophile. After one H atom is removed from the water molecule, the alcohol is attached to the most substituted carbon. Hence, **electrophilic hydration follows Markovnikov's rule.**

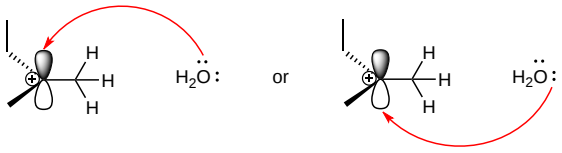
What is Stereochemistry and How Does It Apply?

Stereochemistry deals with how the substituent bonds on the product directionally. Dashes and wedges denote stereochemistry by showing whether the molecule or atom is going into or out of the plane of the board. Whenever the bond is a simple single straight line, the molecule that is bonded is equally likely to be found going into the plane of the board as it is out of the plane of the board. This indicates that **the product is a racemic mixture**.

Electrophilic hydration adopts a stereochemistry wherein the substituent is equally likely to bond pointing into the plane of the board as it is pointing out of the plane of the board. The 3º alcohol product of the following reaction could look like either of the following products:



There is no stereochemical control in acid-catalyzed hydration reactions. This is due to the trigonal planar, sp^2 nature of the carbocation intermediate. Water can act as a nucleophile to form a bond to either face of the carbocation, resulting in a mixture of stereochemical outcomes.



Note: Whenever a straight line is used along with dashes and wedges on the same molecule, it could be denoting that the straight line bond is in the same plane as the board. Practice with a molecular model kit and attempting the practice problems at the end can help eliminate any ambiguity.

Is this a Reversible Synthesis?

Electrophilic hydration is reversible because an alkene in water is in equilibrium with the alcohol product. To sway the equilibrium one way or another, the temperature or the concentration of the non-nucleophilic strong acid can be changed. For example:

- Less sulfuric or phosphoric acid and an excess of water help synthesize more alcohol product.
- Lower temperatures help synthesize more alcohol product.

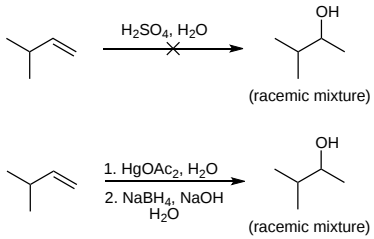
Is There a Better Way to Add Water to Synthesize an Alcohol From an Alkene?

A more efficient pathway does exist: **Oxymercuration - Demercuration**, a special type of electrophilic addition. Oxymercuration does not allow for rearrangements, but it does require the use of mercury, which is highly toxic. Detractions for using electrophilic hydration to make alcohols include:

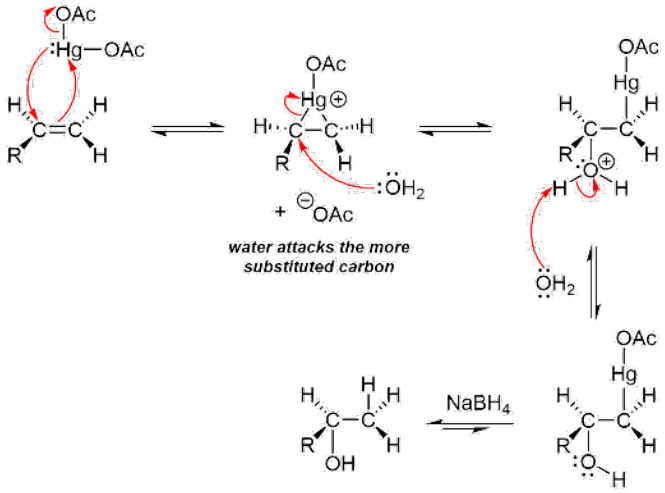
- Allowing for carbocation rearrangements
- Poor yields due to the reactants and products being in equilibrium
- Allowing for product mixtures (such as an (*R*)-enantiomer and an (*S*)-enantiomer)
- Using sulfuric or phosphoric acid

Oxymercuration is a special electrophilic addition. It is anti-stereospecific and regioselective. Regioselectivity is a process in which the substituents choses one direction it prefers to be attached to over all the other possible directions. The good thing about this reaction is that there are no carbocation rearrangement due to stabilization of the reactive intermediate. Similar stabilization is also seen in bromination addition to alkenes.

One of the major advantages to oxymercuration is that carbocation rearrangements cannot occur under these conditions ($Hg(OAc)_2$, H_2O). Carbocation rearrangement is a process in which the carbocation intermediate can undergo a methyl or alkyl shift to form a more stable ion. Due to a possible carbocation rearrangement, the reaction below would not generate the product shown in high yields. In contrast, the oxymercuration reaction would proceed to form the desired product.



This reaction involves a mercury acting as a reagent attacking the alkene double bond to form a *Mercurinium Ion Bridge*. A water molecule will then attack the most substituted carbon to open the mercurium ion bridge, followed by proton transfer to solvent water molecule.



The organomercury intermediate is then reduced by sodium borohydride - the mechanism for this final step is beyond the scope of our discussion here. Notice that overall, the oxymercuration - demercuration mechanism follows Markovnikov's regioselectivity with the OH group is attached to the most substituted carbon and the H is attach to the least substituted carbon. The reaction is useful, however, because strong acids are not required, and carbocation rearrangements are avoided because no discreet carbocation intermediate forms.

It is important to note that for the mechanism shown above, the enantiomer of the product shown is also formed. This is the result of formation of the mercurium ion below the alkene in the first step.

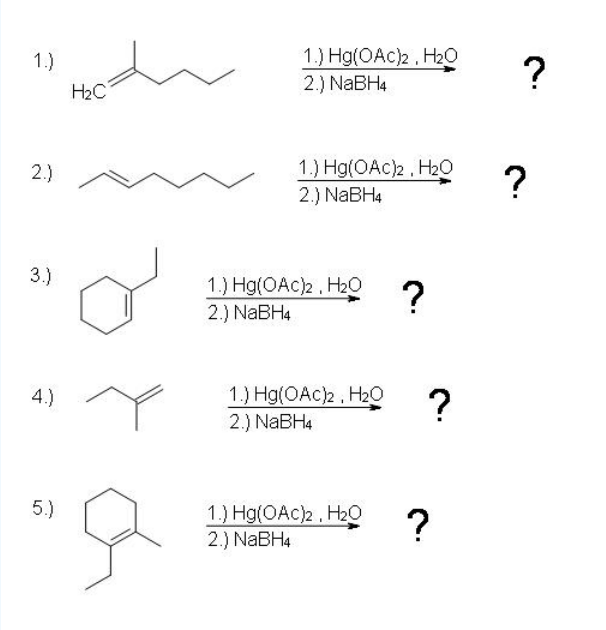
References

1. Vollhardt, K. Peter C. Organic chemistry structure and function. New York: W.H. Freeman, 2007.
2. Smith, Michael B., and Jerry March. March's Advanced Organic Chemistry Reactions, Mechanisms, and Structure (March's Advanced Organic Chemistry). New York: Wiley-Interscience, 2007 2007.
3. Roderic P. Quirk , Robert E. Lea, Reductive demercuration of hex-5-enyl-1-mercuric bromide by metal hydrides. Rearrangement, isotope effects, and mechanism, *J. Am. Chem. Soc.*, 1976, 98 (19), pp 5973–5978.

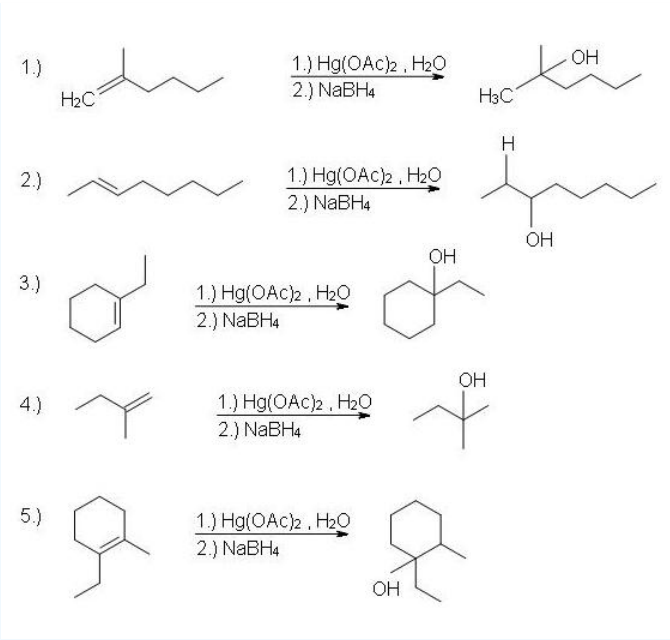
Some Practice Problems

? Practice problems

What are the end products of these reactants?



Answer

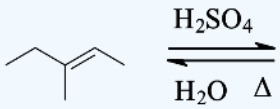


The end product to these practice problems are pretty much very similar. First, you locate where the double bond is on the reactant side. Then, you look at what substituents are attached to each side of the double bond and add the OH group to the more substituent side and the hydrogen on the less substituent side.

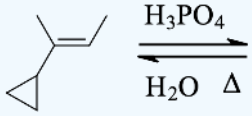
More Problems

Predict the product of each reaction.

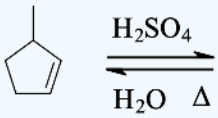
1)



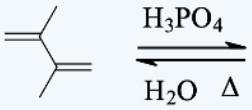
2) How does the cyclopropane group affect the reaction?



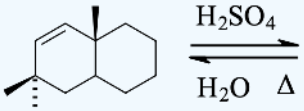
3) (Hint: What is different about this problem?)



4) (Hint: Consider stereochemistry.)

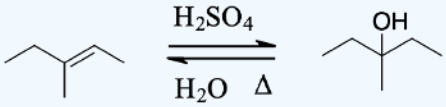


5) Indicate any shifts as well as the major product:

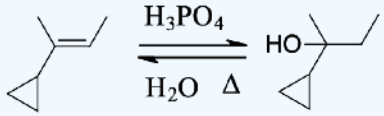


Answer

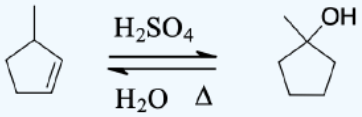
1) This is a simple electrophilic hydration.



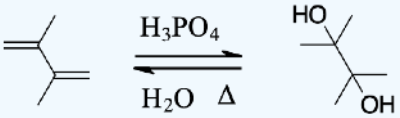
2) The answer is additional side products, but **the major product formed is still the same** (the product shown). Depending on the temperatures used, the cyclopropane may open up into a straight chain, which makes it unlikely that the major product will form (after the reaction, it is unlikely that the 3º carbon will remain as such).



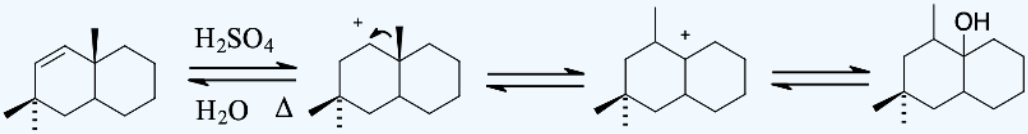
3) A hydride shift actually occurs from the 3 carbon of the 3-methylcyclopentene to where the carbocation had formed.



4) **This reaction will have poor yields due to a very unstable intermediate**. For a brief moment, carbocations can form on the two center carbons, which are more stable than the outer two carbons. The carbocations have an sp^2 hybridization, and when the water is added on, the carbons change their hybridization to sp^3. This makes the methyl and alcohol groups equally likely to be found going into or out of the plane of the paper- the product is racemic.



5) In the first picture shown below, an alkyl shift occurs but a hydride shift (which occurs faster) is possible. Why doesn't a hydride shift occur? The answer is because **the alkyl shift leads to a more stable product**. There is a noticeable amount of side product that forms where the two methyl groups are, but the major product shown below is still the most significant due to the hyperconjugation that occurs by being in between the two cyclohexanes.



11.5: Hydration of Alkenes - Addition of H_2O by Oxymercuration is shared under a CC BY-SA 4.0 license and was authored, remixed, and/or curated by Steven Farmer & Dietmar Kennepohl.

- **8.4: Hydration of Alkenes - Addition of H_2O by Oxymercuration** by Aliza Bother Duke University, Dietmar Kennepohl, Krista Cunningham, Lauren Reutenauer, Layne Morsch, Steven Farmer is licensed CC BY-SA 4.0.

11.6: Hydration of Alkenes - Addition of H_2O by Hydroboration

Objectives

After completing this section, you should be able to

- identify hydroboration (followed by oxidation) as a method for bringing about the (apparently) non-Markovnikov addition of water to an alkene.
- write an equation for the formation of a trialkylborane from an alkene and borane.
- write an equation for the oxidation of a trialkylborane to an alcohol.
- draw the structure of the alcohol produced by the hydroboration, and subsequent oxidation, of a given alkene.
- determine whether a given alcohol should be prepared by oxymercuration-demercuration or by hydroboration-oxidation, and identify the alkene and reagents required to carry out such a synthesis.
- write the detailed mechanism for the addition of borane to an alkene, and explain the stereochemistry and regiochemistry of the reaction.

Key Terms

Make certain that you can define, and use in context, the key term below.

- hydroboration

Study Notes

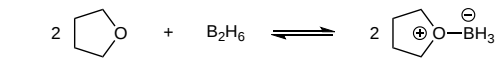
The two most important factors influencing organic reactions are polar (or electronic) effects and steric effects.

Hydroboration-oxidation is a two step pathway used to produce alcohols. The reaction proceeds in an anti-Markovnikov manner, where the hydrogen (from BH_3 or BHR_2) attaches to the more substituted carbon and the boron attaches to the least substituted carbon in the alkene double bond. Furthermore, the borane acts as a Lewis acid by accepting two electrons in its empty p orbital from an alkene that is electron rich. This process allows boron to have an electron octet. A very interesting characteristic of this process is that it does not require any activation by a catalyst. The hydroboration mechanism has the elements of both hydrogenation and electrophilic addition and it is a stereospecific (***syn addition),*** meaning that the hydroboration takes place on the same face of the double bond, this leads ***cis*** stereochemistry.

Introduction

Hydroboration-oxidation of alkenes has been a very valuable laboratory method for the stereoselectivity and regioselectivity of alkenes. An additional feature of this reaction is that it occurs without rearrangement.

First off it is very important to understand little bit about the structure and the properties of the **borane** molecule. Borane exists naturally as a very toxic gas and it exists as dimer of the general formula B_2H_6 (diborane). Additionally, the dimer B_2H_6 ignites spontaneously in air. Borane is commercially available in ether and tetrahydrofuran (THF), in these solutions the borane can exist as a Lewis acid-base complex, which allows boron to have an electron octet.



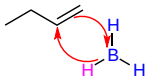
tetrahydrofuran (THF) (BH_3 • THF)

The Mechanism

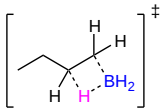
Step 1

- Part 1: Hydroboration of the alkene. In this first step the addition of the borane to the alkene is initiated and proceeds as a concerted reaction because bond breaking and bond formation occurs at the same time. This part consists of the vacant 2p

orbital of the boron electrophile pairing with the electron pair of the pi bond of the nucleophile.

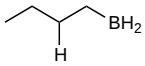


Transition state



*** Note that a carbocation is not formed. Therefore, no rearrangement takes place.**

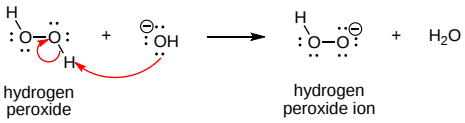
- Part 2: The Anti Markovnikov addition of Boron. The boron adds to the less substituted carbon of the alkene, which then places the hydrogen on the more substituted carbon. Both, the boron and the hydrogen add simultaneously on the same face of the double bond (syn addition).



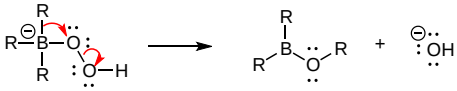
Oxidation of the Trialkylborane by Hydrogen Peroxide

Step 2

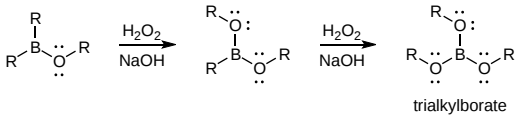
- Part 1: The first part of this mechanism deals with the donation of a pair of electrons from the hydrogen peroxide ion. the hydrogen peroxide is the nucleophile in this reaction because it is the electron donor to the newly formed trialkylborane that resulted from hydroboration.



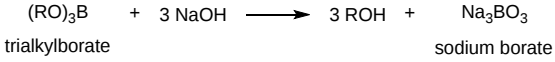
- Part 2: In this second part of the mechanism, a rearrangement of an R group with its pair of bonding electrons to an adjacent oxygen results in the removal of a hydroxide ion.



Two more of these reactions with hydroperoxide will occur in order give a trialkylborate



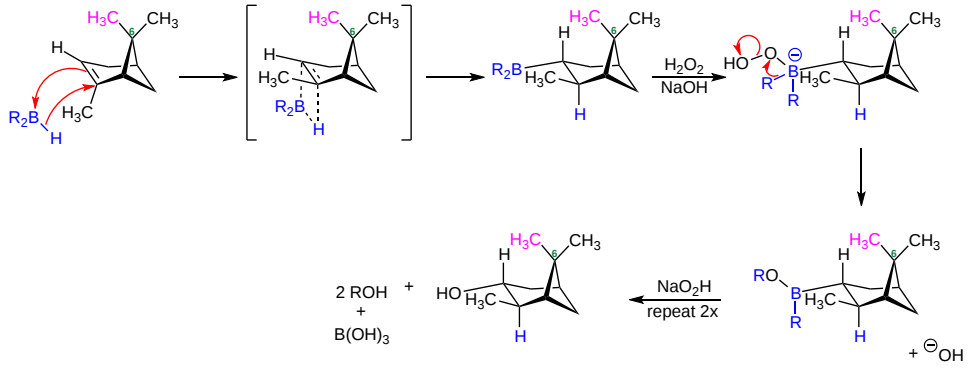
- Part 3: This is the final part of the oxidation process. In this part the trialkylborate reacts with aqueous NaOH to give the alcohol and sodium borate.



If you need additional visuals to aid you in understanding the mechanism, click on the outside links provided here that will take you to other pages and media that are very helpful as well.

Stereochemistry of Hydroboration

The hydroboration reaction is among the few simple addition reactions that proceed cleanly in a *syn* fashion. As noted above, this is a single-step reaction. Since the bonding of the double bond carbons to boron and hydrogen is concerted, it follows that the geometry of this addition must be syn. Furthermore, rearrangements are unlikely inasmuch as a discrete carbocation intermediate is never formed. These features are illustrated for the hydroboration of α-pinene.

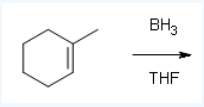


Since the hydroboration procedure is most commonly used to hydrate alkenes in an anti-Markovnikov fashion, we also need to know the stereoselectivity of the second oxidation reaction, which substitutes a hydroxyl group for the boron atom. Independent study has shown this reaction takes place with retention of configuration so the overall addition of water is also syn.

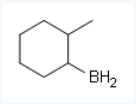
The hydroboration of α-pinene also provides a nice example of steric hindrance control in a chemical reaction. In the less complex alkenes used in earlier examples the plane of the double bond was often a plane of symmetry, and addition reagents could approach with equal ease from either side. In this case, one of the methyl groups bonded to C-6 (colored purple in the equation) covers one face of the double bond, blocking any approach from that side. All reagents that add to this double bond must therefore approach from the side opposite this methyl.

? Exercise 11.6.1

What are the products of this reactions?

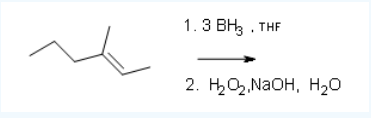


Answer

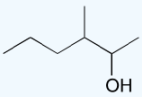


? Exercise 11.6.2

What are the products of this reactions?

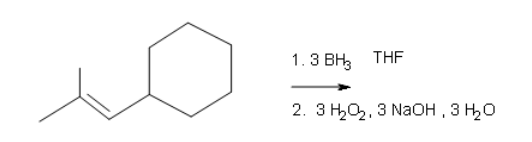


Answer

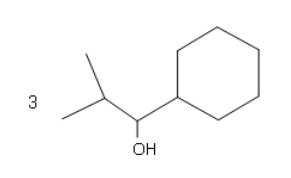


Exercise 11.6.3

What are the products of this reactions?

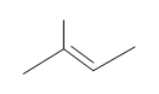


Answer

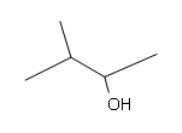


Exercise 11.6.4

Draw the structural formulas for the alcohols that result from hydroboration-oxidation of this alkene.



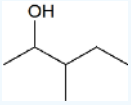
Answer



Exercise 11.6.5

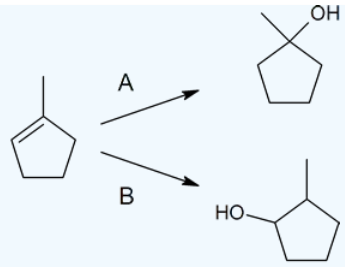
Draw the structural formulas for the alcohols that result from hydroboration-oxidation of (E)-3-methyl-2-pentene. If you need clarification or a reminder on the nomenclature of alkenes refer to the link below on naming the alkenes.

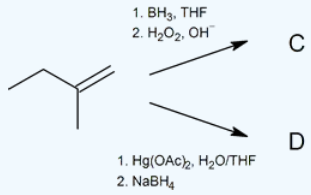
Answer



Exercise 11.6.6

Write out the reagents or products (A–D) shown in the following reaction schemes.

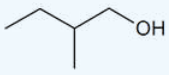


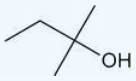


Answer

A 1. $Hg(OAc)_2$, H_2O/THF 2. $NaBH_4$

B 1. BH_3, THF 2. H_2O_2, OH^-

C 

D 

References

1. Vollhardt, Peter, and Neil Shore. Organic Chemistry: Structure and Function. 5th. New York: W.H. Freeman and Company, 2007.
2. Foote, S. Christopher, and William H. Brown. Organic Chemistry. 5th. Belmont, CA: Brooks/Cole Cengage Learning, 2005.
3. Bruice, Paula Yurkanis. Oragnic Chemistry. 5th. CA. Prentice Hall, 2006.
4. Bergbreiter E. David , and David P. Rainville. Stereochemistry of hydroboration-oxidation of terminal alkenes. *J. Org. Chem.*, 1976, 41 (18), pp 3031–3033
5. Ilich, Predrag-Peter; Rickertsen, Lucas S., and Becker Erienne. Polar Addition to C=C Group: Why Is Anti-Markovnikov Hydroboration-Oxidation of Alkenes Not "Anti-"? Journal of Chemical Education., 2006, v83, n11, pg 1681-1685

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11.7: Reduction of Alkenes - Hydrogenation

Objectives

After completing this section, you should be able to

- write an equation for the catalytic hydrogenation of an alkene.
- identify the product obtained from the hydrogenation of a given alkene.
- identify the alkene, the reagents, or both, required to prepare a given alkane by catalytic hydrogenation.
- describe the mechanism of the catalytic hydrogenation of alkenes.
- explain the difference between a heterogeneous reaction and a homogeneous reaction.
- recognize that other types of compounds containing multiple bonds, such as ketones, esters, nitriles and aromatic compounds, do not react with hydrogen under the conditions used to hydrogenate alkenes.

Key Terms

Make certain that you can define, and use in context, the key terms below.

- Adams' catalyst
- hydrogenation

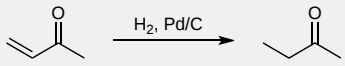
Study Notes

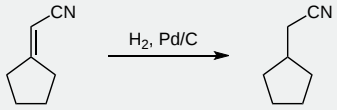
Chemical reactions that are heterogeneous have reactants that are in at least two different phases (e.g. gas with a solid), whereas homogeneous reactions occur in a single phase (e.g. gas with another gas).

Some confusion may arise from the description of the catalyst used in the reaction between alkenes and hydrogen. Three metals—nickel, platinum and palladium—are commonly used, but a chemist cannot simply place a piece of one of these metals in a mixture of the alkene and hydrogen and get a reaction. Each metal catalyst must be prepared in a special way:

- nickel is usually used in a finely divided form called "Raney nickel." It is prepared by reacting a Ni-Al alloy with NaOH.
- palladium is obtained commercially "supported" on an inert substance, such as charcoal, (Pd/C). The alkene is usually dissolved in ethanol when Pd/C is used as the catalyst.
- platinum is used as PtO_2, Adams' catalyst, although it is actually platinum metal that is the catalyst. The hydrogen used to add to the carbon-carbon double bond also reduces the platinum(IV) oxide to finely divided platinum metal. Ethanol or acetic acid is used as the solvent for the alkene.

Other types of compounds containing multiple bonds, such as ketones, esters, and nitriles, do not react with hydrogen under the conditions used to hydrogenate alkenes. The examples below show reduction of an alkene, but the ketone and nitrile groups present remain intact and are not reduced.





Aromatic rings are also not reduced under the conditions used to reduce alkenes, although these rings appear to contain three carbon-carbon double bonds. As you will see later, aromatic rings do not really contain any double bonds, and many chemists prefer to represent the benzene ring as a hexagon with a circle inside it

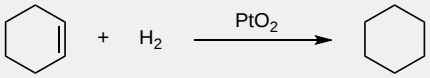


rather than as a hexagon with three alternating double bonds.

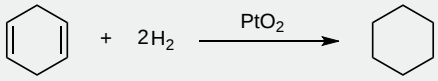


The representation of the benzene ring will be discussed further in Section 15.2.

The reaction between carbon-carbon double bonds and hydrogen provides a method of determining the number of double bonds present in a compound. For example, one mole of cyclohexene reacts with one mole of hydrogen to produce one mole of cyclohexane:



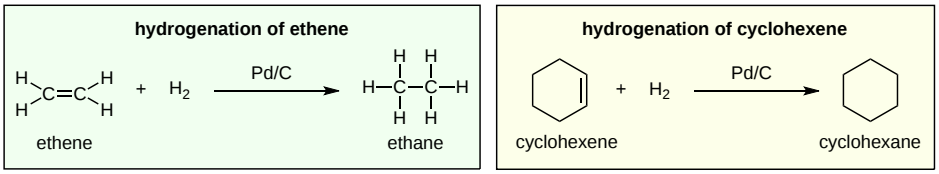
but one mole of 1,4-cyclohexadiene reacts with two moles of hydrogen to form one mole of cyclohexane:



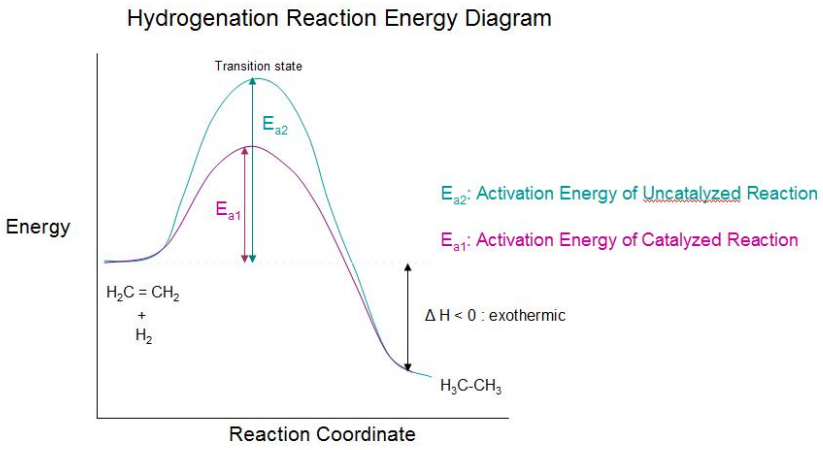
A chemist would say that cyclohexene reacts with one equivalent of hydrogen, and 1,4-cyclohexadiene reacts with two equivalents of hydrogen. If you take a known amount of an unknown, unsaturated hydrocarbon and determine how much hydrogen it will absorb, you can readily determine the number of double bonds present in the hydrocarbon (see question 2, below).

Addition of hydrogen to a carbon-carbon double bond is called hydrogenation. The overall effect of such an addition is the reductive removal of the double bond functional group. Regioselectivity is not an issue, since the same group (a hydrogen atom) is bonded to each of the double bond carbons. The simplest source of two hydrogen atoms is molecular hydrogen (H_2), but mixing alkenes with hydrogen does not result in any discernible reaction. Although the overall hydrogenation reaction is exothermic, a high activation energy prevents it from taking place under normal conditions. This restriction may be circumvented by the use of a catalyst, as shown in the reaction coordinate diagram below.

An example of an alkene addition reaction is a process called hydrogenation. In a hydrogenation reaction, two hydrogen atoms are added across the double bond of an alkene, resulting in a saturated alkane. Hydrogenation of a double bond is a thermodynamically favorable reaction because it forms a more stable (lower energy) product. In other words, the energy of the product is lower than the energy of the reactant; thus it is exothermic (heat is released). The heat released is called the heat of hydrogenation, which is an indicator of a molecule's stability.



Catalysts are substances that changes the rate (velocity) of a chemical reaction without being consumed or appearing as part of the product. Catalysts act by lowering the activation energy of reactions, but they do not change the relative potential energy of the reactants and products. Finely divided metals, such as platinum, palladium and nickel, are among the most widely used hydrogenation catalysts. Catalytic hydrogenation takes place in at least two stages, as depicted in the diagram. First, the alkene must be adsorbed on the surface of the catalyst along with some of the hydrogen. Next, two hydrogens shift from the metal surface to the carbons of the double bond, and the resulting saturated hydrocarbon, which is more weakly adsorbed, leaves the catalyst surface. The exact nature and timing of the last events is not well understood.

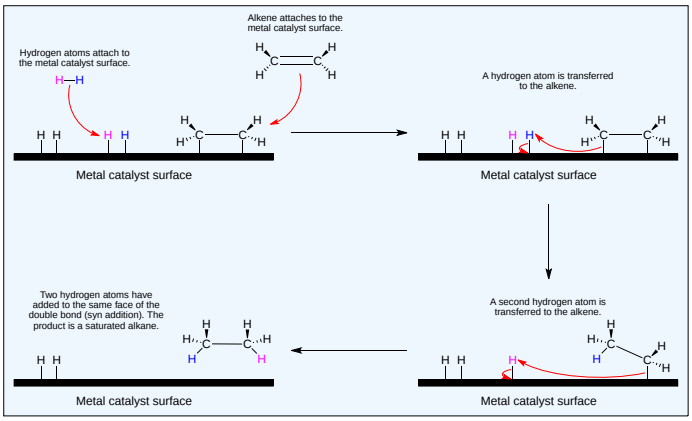


A catalyst lowers the activation energy needed for the reacting molecules to reach the transition state. The addition of a catalyst enables the hydrogenation reaction to occur, that otherwise, would not.

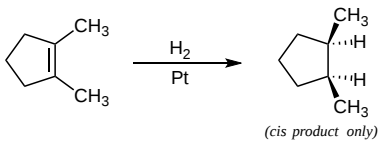
As shown in the energy diagram, the hydrogenation of alkenes is exothermic, and heat is released corresponding to the ΔH in the diagram. This heat of reaction can be used to evaluate the thermodynamic stability of alkenes having different numbers of alkyl substituents on the double bond. For example, the following table lists the heats of hydrogenation for three C_5H_{10} alkenes which give the same alkane product (2-methylbutane). Since a larger heat of reaction indicates a higher energy reactant, these heats are inversely proportional to the stabilities of the alkene isomers. To a rough approximation, we see that each alkyl substituent on a double bond stabilizes this functional group by a bit more than 1 kcal/mole.

Alkene Isomer	$(CH_3)_2CHCH{=}CH_2$ 3-methyl-1-butene	$CH_2{=}C(CH_3)CH_2CH_3$ 2-methyl-1-butene	$(CH_3)_2C{=}CHCH_3$ 2-methyl-2-butene
Heat of Reaction (ΔH^o)	–30.3 kcal/mole	–28.5 kcal/mole	–26.9 kcal/mole

Catalytic Hydrogenation Mechanism



From the mechanism shown here we would expect the addition of hydrogen to occur with syn-stereoselectivity. This is often true, but the hydrogenation catalysts may also cause isomerization of the double bond prior to hydrogen addition, in which case stereoselectivity may be uncertain.



(cis product only)

Exercise 11.7.1

In the reaction

$$H_2C{=}CH_2 \quad + \quad H_2 \xrightarrow{PtO_2} H_3C{-}CH_3$$

a. 0.500 mol of ethene reacts with _____ mol of hydrogen. Thus a chemist might say that ethene reacts with one _____ of hydrogen.
b. ethene is being _____; while _____ is being oxidized.
c. the oxidation number of carbon in ethene is _____; in ethane it is _____.

Answer

a. 0.500 mol of ethene reacts with 0.500 mol of hydrogen. Thus a chemist might say that ethene reacts with one equivalent of hydrogen.
b. ethene is being reduced; while hydrogen is being oxidized.
c. the oxidation number of carbon in ethene is −2; in ethane it is −3.

Exercise 11.7.2

When 1.000 g of a certain triglyceride (fat) is treated with hydrogen gas in the presence of Adams' catalyst, it is found that the volume of hydrogen gas consumed at 99.8 kPa and 25.0°C is 162 mL. A separate experiment indicates that the molar mass of the fat is 914 g mol^{-1}. How many carbon-carbon double bonds does the compound contain?

Answer

Amount of hydrogen consumed

$$= n \text{ mol}$$
$$= \frac{PV}{RT} \qquad ^{-1} \cdot K^{-1} \times 298\ K = 6.53 \times 10^{-3}\ \text{mol}\ H_2$$
$$= \frac{99.8\ \text{kPa} \times 0.162\ \text{L}}{8.31\ \text{kPa}\cdot\text{msup}}$$

Amount of fat used

Math input error

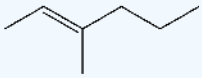
Ratio of moles of hydrogen consumed to moles of fat

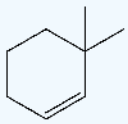
Math input error

Thus, the fat contains six carbon-carbon double bonds per molecule.

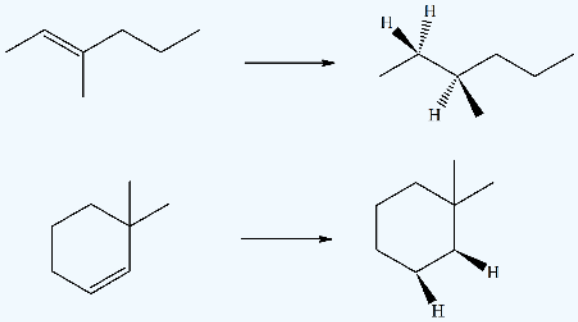
Exercise 11.7.3

Predict the products if the following alkenes were reacted with catalytic hydrogen.





Answer



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11.8: Oxidation of Alkenes to Vicinal Diols

Objectives

After completing this section, you should be able to

1. write the equation for the hydroxylation of an alkene using osmium tetroxide, and draw the structure of the cyclic intermediate.
2. draw the structure of the diol formed from the reaction of a given alkene with osmium tetroxide.
3. identify the alkene, the reagents, or both, that must be used to prepare a given 1,2-diol.

Key Terms

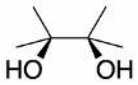
Make certain that you can define, and use in context, the key terms below.

- diol
- glycol
- hydroxylation

The previous section discussed the reduction of a double bond, so adding hydrogen to the the double bond. This section will discuss oxidation. In organic chemistry, this is a reaction that where the carbon atom loses electron density, which happens when new bond to a more electronegative atom occurs or when a double bond is broken between a carbon and a less electronegative atom. A simplified to say this is in organic chemistry a reduction is more bonds to hydrogen and oxidation is more bonds to oxygen often.

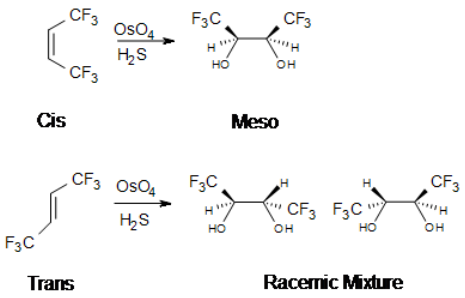
Syn Dihydroxylation

A glycol, also known as a vicinal diol, is a compound with two -OH groups on adjacent carbons. Osmium tetroxide oxidizes alkenes to give glycols through a syn addition, resulting in cis vicinal diols. Next semester in the chapter on ethers, you'll learn how to make trans vicinal diols.



Introduction

The reaction with OsO_4 is a concerted process that has a cyclic intermediate and no rearrangements. When an alkene reacts with osmium tetroxide, stereocenters can form in the glycol product. Cis alkenes give meso products and trans alkenes give racemic mixtures.



OsO_4 is formed slowly when osmium powder reacts with gasoues O_2 at ambient temperature. Reaction of bulk solid requires heating to 400 °C:

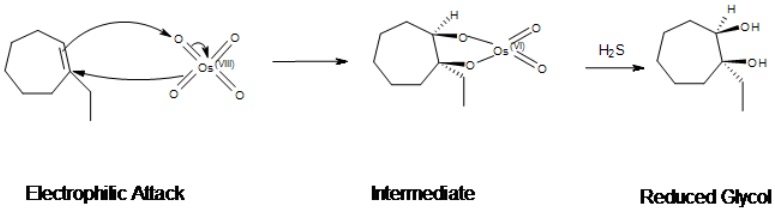
$$Os_{(s)} + 2O_{2\ (g)} \rightarrow OS_4 \tag{11.8.1}$$

Since Osmium tetroxide is expensive and highly toxic, the reaction with alkenes has been modified. Catalytic amounts of OsO_4 and stoichiometric amounts of an oxidizing agent such as hydrogen peroxide are now used to eliminate some hazards. Also, an older reagent that was used instead of OsO_4 was potassium permanganate, $KMnO_4$. Although syn diols will result from the reaction of $KMnO_4$ and an alkene, potassium permanganate is less useful since it gives poor yields of the product because of *overoxidation*.

Mechanism

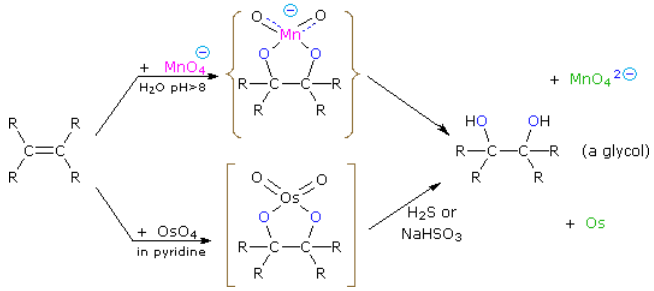
- Electrophilic attack on the alkene
  - Pi bond of the alkene acts as the nucleophile and reacts with osmium (VIII) tetroxide (OsO_4)
  - 2 electrons from the double bond flows toward the osmium metal
    - In the process, 3 electron pairs move simultaneously
  - Cyclic ester with Os (VI) is produced
- Reduction
  - H_2S reduces the cyclic ester
    - $NaHSO_4$ with H_2O may be used
  - Forms the syn-1,2-diol (glycol)

Example: Dihydroxylation of 1-ethyl-1-cycloheptene



Hydroxylation of alkenes

Dihydroxylated products (glycols) are obtained by reaction with aqueous potassium permanganate (pH > 8) or osmium tetroxide in pyridine solution. Both reactions appear to proceed by the same mechanism (shown below); the metallocyclic intermediate may be isolated in the osmium reaction. In basic solution the purple permanganate anion is reduced to the green manganate ion, providing a nice color test for the double bond functional group. From the mechanism shown here we would expect syn-stereoselectivity in the bonding to oxygen, and regioselectivity is not an issue.



When viewed in context with the previously discussed addition reactions, the hydroxylation reaction might seem implausible. Permanganate and osmium tetroxide have similar configurations, in which the metal atom occupies the center of a tetrahedral grouping of negatively charged oxygen atoms. How, then, would such a species interact with the nucleophilic pi-electrons of a double bond? A possible explanation is that an empty d-orbital of the electrophilic metal atom extends well beyond the surrounding oxygen atoms and initiates electron transfer from the double bond to the metal, in much the same fashion noted above for platinum. Back-bonding of the nucleophilic oxygens to the antibonding π*-orbital completes this interaction. The result is formation of a metallocyclic intermediate, as shown above.

Outside links

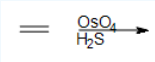
- http://en.Wikipedia.org/wiki/Osmium_tetroxide
- http://www.chm.bris.ac.uk/motm/oso4/oso4v.htm
- http://www.organic-chemistry.org/chemicals/oxidations/osmiumtetroxide.shtm

References

1. Dehestani, Ahmad et al. (2005). Ligand-assisted reduction of osmium tetroxide with molecular hydrogen via a [3+2] mechanism. *Journal of the American Chemical Society, 2005, 127 (10)*, 3423-3432.
2. Sorrell, Thomas, N. Organic Chemistry. New York: University Science Books, 2006.
3. Vollhardt, Peter, and Neil E. Schore. Organic Chemistry: Structure and Function. 5th Edition. New York: W. H. Freeman & Company, 2007.

? Dihydroxylation Exercises

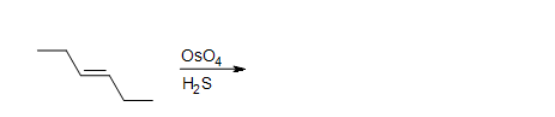
1. Give the major product.



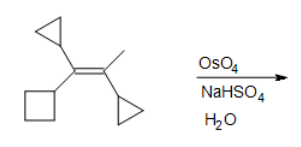
2. What is the product in the dihydroxylation of (Z)-3-hexene?



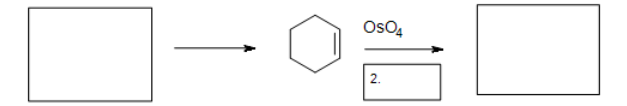
3. What is the product in the dihydroxylation of (E)-3-hexene?



4. Draw the intermediate of this reaction.

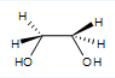


5. Fill in the missing reactants, reagents, and product.

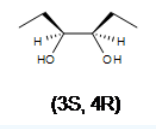


Answers

1. A syn-1,2-ethanediol is formed. There is no stereocenter in this particular reaction. The OH groups are on the same side.



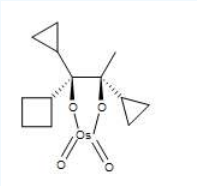
2. Meso-3,4-hexanediol is formed. There are 2 stereocenters in this reaction.



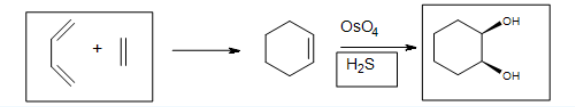
3. A racemic mixture of 3,4-hexanediol is formed. There are 2 stereocenters in both products.



4. A cyclic osmic ester is formed.



5. The Diels-Alder cycloaddition reaction is needed in the first box to form the cyclohexene. The second box needs a reagent to reduce the intermediate cyclic ester (not shown). The third box has the product: 1,2-cyclohexanediol.



Contributors and Attributions

-
-
- Shivam Nand
- Organic Chemistry With a Biological Emphasis by Tim Soderberg (University of Minnesota, Morris)
- Kristen Perano
- Layne Morsch (University of Illinois Springfield)
- Lauren Reutenauer (Amherst College)

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11.9: Oxidation of Alkenes - Cleavage to Carbonyl Compounds

Objective

After completing this section, you should be able to

- write an equation to describe the cleavage of an alkene by ozone, followed by reduction of the ozonide so formed with either sodium borohydride or zinc and acetic acid.
- predict the products formed from the ozonolysis-reduction of a given alkene.
- write an equation to describe the cleavage of an alkene by potassium permanganate.
- predict the products from the oxidative cleavage of a given alkene by potassium permanganate.
- use the results of ozonolysis-reduction, or cleavage with permanganate, to deduce the structure of an unknown alkene.
- identify the reagents that should be used in the oxidative cleavage of an alkene to obtain a given product or products.
- write the equation for the cleavage of a 1,2-diol by periodic acid, and draw the structure of the probable intermediate.
- predict the product or products that will be formed from the treatment of a given 1,2-diol with periodic acid.
- use the results of hydroxylation/1,2-diol cleavage to deduce the structure of an unknown alkene.

Key Terms

Make certain that you can define, and use in context, the key terms below.

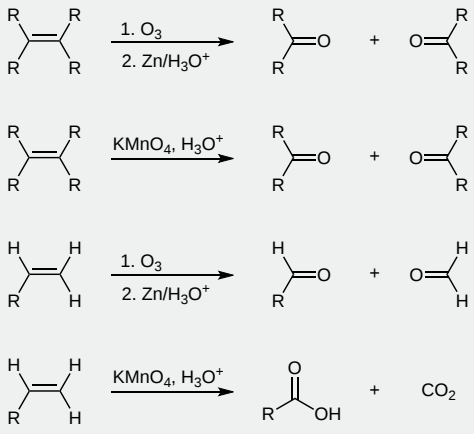
- molozonide
- ozonide
- ozonolysis

Study Notes

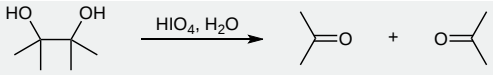
Ozonolysis, or ozonolysis-reduction, refers to the treatment of an alkene with ozone followed by a suitable reducing agent to break down complex double-bond-containing compounds into smaller, more easily identified products. From the identity of the products formed, it may be possible to deduce the structure of the original double-bond-containing substance. Ozonolysis will feature prominently in many of the road-map problems that you will encounter in this course.

A *molozonide* is an unstable, cyclic intermediate that is initially formed when an alkene reacts with ozone.

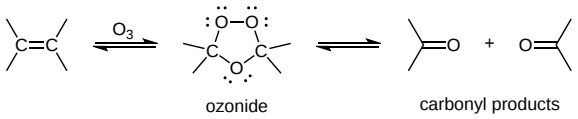
Alkenes can also be cleaved by other oxidizing agents such as potassium permanganate. However, $KMnO_4$ will carry the oxidation further than ozonolysis, so products can be slightly different. Note within the summary of the following reactions that ozonolysis produces aldehydes and ketones, while $KMnO_4$ can oxidize all the way to to carbon dioxide and carboxylic acid.



Diol cleavage is another example of a redox reaction; periodic acid, HIO_4, is reduced to iodic acid, HIO_3.



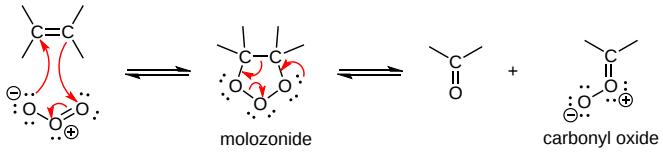
Ozonolysis is a method of oxidatively cleaving alkenes or alkynes using ozone (O_3), a reactive allotrope of oxygen. The process allows for carbon-carbon double or triple bonds to be replaced by double bonds with oxygen. This reaction is often used to identify the structure of unknown alkenes. by breaking them down into smaller, more easily identifiable pieces. Ozonolysis also occurs naturally and would break down repeated units used in rubber and other polymers. On an industrial scale, azelaic acid and pelargonic acids are produced from ozonolysis.



The gaseous ozone is first passed through the desired alkene solution in either methanol or dichloromethane. The first intermediate product is an ozonide molecule which is then further reduced to carbonyl products. This results in the breaking of the Carbon-Carbon double bond and is replaced by a Carbon-Oxygen double bond instead.

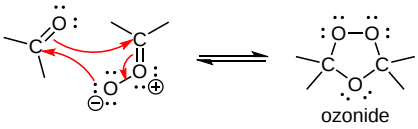
Reaction Mechanism

Step 1:



The first step in the mechanism of ozonolysis is the initial electrophilic addition of ozone to the Carbon-Carbon double bond, which then form the molozonide intermediate. Due to the unstable molozonide molecule, it continues further with the reaction and breaks apart to form a carbonyl and a carbonyl oxide molecule.

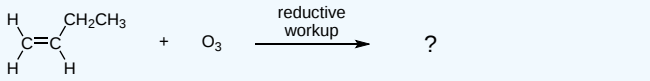
Step 2:

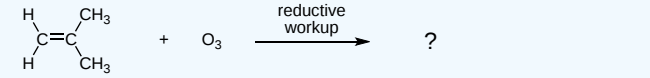


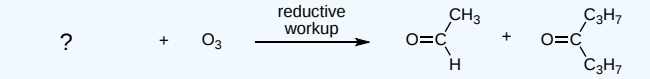
The carbonyl and the carbonyl oxide rearranges itself and reforms to create the stable ozonide intermediate. Since some ozonides are explosive, it is immediately reacted with a reductive workup to then convert the ozonide molecule into the desired carbonyl products. A typical reductive workup is zinc metal in acetic acid. A variety of carbonyl products could result depending on the starting alkene. For example, a tetrasubstituted alkene would yield two ketone products, while a trisubstituted alkene would yield one ketone product and one aldehyde product.

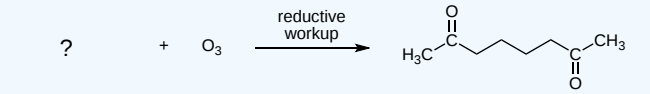
While there are other options for oxidative cleavage of the double bond, this is the most commonly used reaction.

Exercise 11.9.1

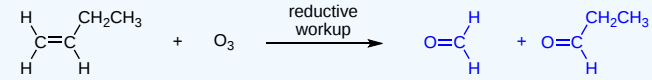
1. 

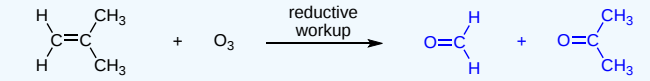
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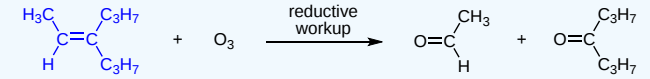
3. 

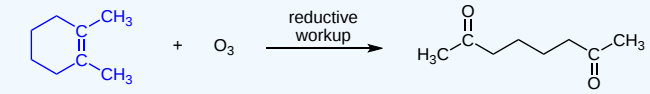
4. 

Answer

1. 

2. 

3. 

4. 

Exercise 11.9.2

Draw the structure of the product or products obtained in each of the following reactions:

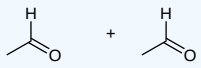
a. *cis*-2-butene $\xrightarrow[2.\ Zn/H_3O^+]{1.\ O_3}$

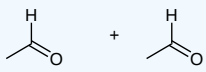
b. *trans*-2-butene $\xrightarrow[2.\ Zn/H_3O^+]{1.\ O_3}$

c. 2-methylpropene $\xrightarrow[2.\ Zn/H_3O^+]{1.\ O_3}$

d. 2-methyl-1-pentene $\xrightarrow[KMnO_4]{\text{hot, acidic}}$

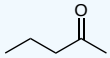
Answer

a. 

b. 

https://chem.libretexts.org/@go/page/418160

c.  +

d.  + CO_2

? Exercise 11.9.3

Exercises 1(*a*) and 1(*b*), above, indicate that it is not possible to distinguish between cis and trans isomers of alkenes using oxidative cleavage.

Answer

Both isomers give the same product or products.

References

1. Vollhardt, K., Schore, N. Organic Chemistry: Structure and Function. 5th ed. New York, NY: W. H. Freeman and Company, 2007.
2. Shore, N. Study Guide and Solutions Manual for Organic Chemistry. 5th ed. New York, NY: W.H. Freeman and Company, 2007.

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CHAPTER OVERVIEW

12: Alkynes - An Introduction to Organic Synthesis

Learning Objectives

After you have completed Chapter 12, you should be able to

1. fulfillall of the detailed objectives listed under each individual section.
2. solve road-map problems involving any of the reactions introduced to this point.
3. design multistep syntheses using any of the reactions introduced to this point, and determine the viability of a given synthesis.
4. define, and use in context, the key terms introduced.

Addition reactions not only dominate the chemistry of alkenes, they are also the major class of reaction you will encounter. This chapter discusses an important difference between (terminal) alkynes and alkenes, that is, the acidity of the former; it also addresses the problem of devising organic syntheses. Once you have completed this chapter you will have increased the number of organic reactions in your repertoire, and should be able to design much more elaborate multistep syntheses.

12.1: Naming Alkynes
12.2: Preparation of Alkynes - Elimination Reactions of Dihalides
12.3: Alkylation of Acetylide Anions
12.4: Alkyne Acidity - Formation of Acetylide Anions
12.5: Reactions of Alkynes - Addition of HX and X_2
12.6: Hydration of Alkynes
12.7: Reduction of Alkynes
12.8: Oxidative Cleavage of Alkynes
12.9: An Introduction to Organic Synthesis

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12.1: Naming Alkynes

Objectives

After completing this section, you should be able to

- provide the correct IUPAC name of an alkyne, given its Kekulé, condensed or shorthand structure.
- provide the correct IUPAC name of a compound containing both double and triple bonds, given its Kekulé, condensed or shorthand structure.
- draw the structure of a compound containing one or more triple bonds, and possibly one or more double bonds, given its IUPAC name.
- name and draw the structure of simple alkynyl groups, and where appropriate, use these names as part of the IUPAC system of nomenclature.

Study Notes

Simple alkynes are named by the same rules that are used for alkenes (see Section 7.3), except that the ending is *-yne* instead of *-ene*. Alkynes cannot exhibit *E*,*Z* (cis-trans) isomerism; hence, in this sense, their nomenclature is simpler than that of alkenes.

Alkynes are organic molecules made of the functional group carbon-carbon triple bonds and are written in the empirical formula of $\mathbf{C_nH_{2n-2}}$. They are unsaturated hydrocarbons. Like alkenes have the suffix –ene, alkynes use the ending –yne; this suffix is used when there is only one alkyne in the molecule.

$$HC{\equiv}CH$$

Introduction

Here are the molecular formulas and names of the first ten carbon straight chain alkynes.

Name	Molecular Formula
Ethyne	C_2H_2
Propyne	C_3H_4
1-Butyne	C_4H_6
1-Pentyne	C_5H_8
1-Hexyne	C_6H_{10}
1-Heptyne	C_7H_{12}
1-Octyne	C_8H_{14}
1-Nonyne	C_9H_{16}
1-Decyne	$C_{10}H_{18}$

The more commonly used name for ethyne is acetylene, which used industrially.

Naming Alkynes

Like previously mentioned, the IUPAC rules are used for the naming of alkynes.

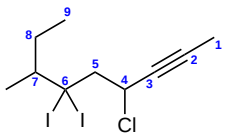
Rule 1

Find the longest carbon chain that includes both carbons of the triple bond.

Rule 2

Number the longest chain starting at the end closest to the triple bond. A 1-alkyne is referred to as a terminal alkyne and alkynes at any other position are called internal alkynes.

For example:

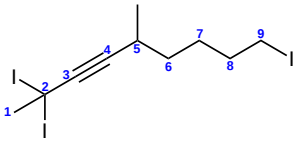


4-chloro-6,6-diiodo-7-methylnon-2-yne

Rule 3

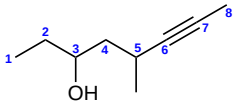
After numbering the longest chain with the lowest number assigned to the alkyne, label each of the substituents at its corresponding carbon. While writing out the name of the molecule, arrange the substituents in alphabetical order. If there are more than one of the same substituent use the prefixes di, tri, and tetra for two, three, and four substituents respectively. These prefixes are not taken into account in the alphabetical order.

For example:



2,2,9-triiodo-5-methylnon-3-yne

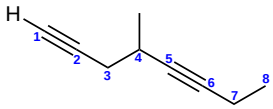
If there is an alcohol present in the molecule, number the longest chain starting at the end closest to it, and follow the same rules. However, the suffix would be –ynol, because the alcohol group takes priority over the triple bond.



5-methyl-6-octyn-3-ol

When there are two triple bonds in the molecule, find the longest carbon chain including both the triple bonds. Number the longest chain starting at the end closest to the triple bond that appears first. The suffix that would be used to name this molecule would be –diyne.

For example:

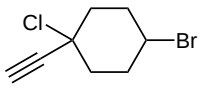


4-methyl-1,5-octadiyne

Rule 4

Substituents containing a triple bond are called alkynyl.

For example:



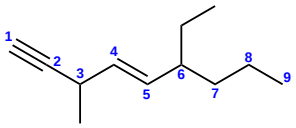
4-bromo-1-chloro-1-ethynylcyclohexane

Here is a table with a few of the alkynyl substituents:

Name	Molecule
Ethynyl	-C≡CH
2- Propynyl	$-CH_2C{\equiv}CH$
2-Butynyl	$-CH_3C{\equiv}CH_2CH_3$

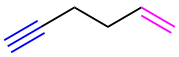
Rule 5

A molecule that contains both double and triple bonds is called an alkenyne. The chain can be numbered starting with the end closest to the functional group that appears first. For example:



(*E*)-6-ethyl-3-methyl-non-4-en-1-yne

If both functional groups are the exact same distance from the ending of the parent chain, the alkene takes precedence in the numbering.

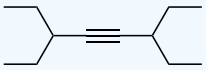


hex-1-en-5-yne

? Exercise 12.1.1

Name the following compounds:

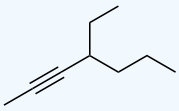
a)



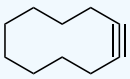
b)



c)



d)



Answer

a. 3,6-diethyl-4-octyne
b. 3-methylbutyne
c. 4-ethyl-2-heptyne
d. cyclodecyne

? Exercise 12.1.2

How many isomers are possible for C_5H_8? Draw them.

Answer

2 possible isomers

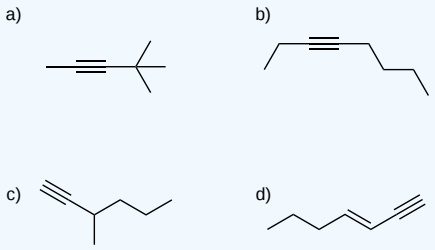


Exercise 12.1.3

Draw the following compounds:

a. 4,4-dimethyl-2-pentyne
b. 3-octyne
c. 3-methyl-1-hexyne
d. *trans* 3-hepten-1-yne

Answer



Exercise 12.1.4

Do alkynes show cis-trans isomerism? Explain.

Answer

No. A triply bonded carbon atom can form only one other bond and has linear electron geometry so there are no "sides". Allkenes have two groups attached to each inyl carbon with a trigonal planar electron geometry that creates the possibility of cis-trans isomerism.

Reference

1. Vollhardt, Peter, and Neil E. Schore. Organic Chemistry: Structure and Function. 5th Edition. New York: W. H. Freeman & Company, 2007.

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12.2: Preparation of Alkynes - Elimination Reactions of Dihalides

Objectives

After completing this section, you should be able to

1. write an equation to describe the preparation of an alkyne by the dehydrohalogenation of a vicinal dihalide or vinylic halide.
2. identify the alkyne produced from the dehydrohalogenation of a given vicinal dihalide or vinylic halide.
3. write a reaction sequence to show how the double bond of an alkene can be transformed into a triple bond.
4. identify the vicinal dihalide (or vinylic halide) needed to synthesize a given alkyne by dehydrohalogenation.

Key Terms

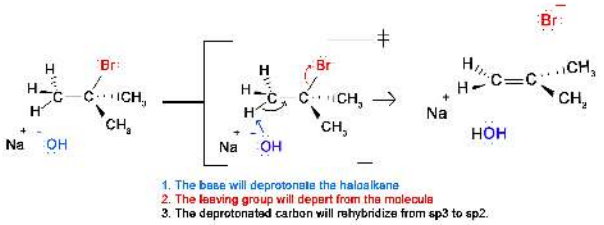
Make certain that you can define, and use in context, the key terms below.

- vicinal dihalide
- vinylic halide

Alkynes can be a useful functional group to synthesize due to some of their antibacterial, antiparasitic, and antifungal properties. One simple method for alkyne synthesis is by double elimination from a dihaloalkane.

E2 Mechanism

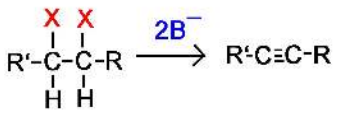
Alkenes can be formed through an elimination reaction. In particular, the synthesis of alkynes will utilize the E2 elimination reaction. During the mechanism of an E2 reaction, a strong base removes a hydrogen adjacent to a halogen. The electrons from the broken C-H bond move to form the C=C double bond. Doing this causes the halogen to be ejected from the compound. Overall, a hydrogen and a halogen are eliminated from the compound to form an alkene. During this mechanism there is a stereoelectronic requirement that the adjacent hydrogen and the halogen be adjacent to each other.



Alkyne Formation Through Dihaloalkane Elimination

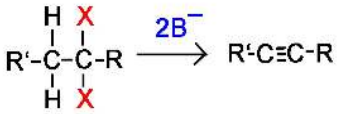
Alkynes are frequently prepared through a double E2 reaction using 2 halides that are vicinal (meaning on adjacent carbons) or geminal (meaning on the same carbon). Because the E2 reaction takes place twice 2 π bonds are formed thus creating an Alkyne. Although hydroxide and alkoxide bases could be used for the strong base required for an E2 reaction, their used opens the possibility of position rearrangement in the alkyne product. Because of this, the stronger base sodium amide in ammonia ($NaNH_2/NH_3$) is commonly used.

General Reaction



Vicinal dihalide converted to an alkyne

or

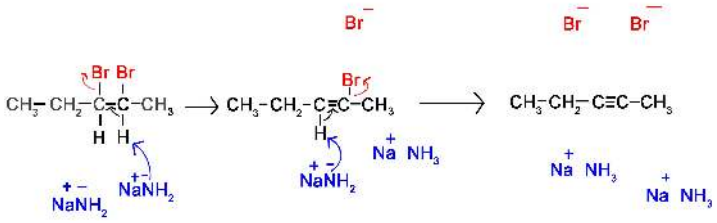


Geminal dihalide converted to an alkyne

Note! If a terminal alkyne is formed during the reaction, 3 equivalents of base are required instead of 2 as discussed below.

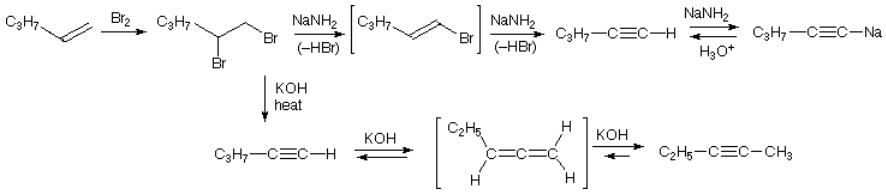
Mechanism

The following mechanism represents the reaction between 2,3-Dibromopentane with sodium amide in liquid ammonia to form pent-2-yne. During this mechanism an intermediate alkene is formed. Notice that in the alkene intermediate, the remaining hydrogen and halogen are anti to each other due to the stereoelectronic requirements of the E2 mechanism. The intermediate alkene is converted to an alkyne by a second E2 elimination of a hydrogen and halogen.



Terminal Alkynes

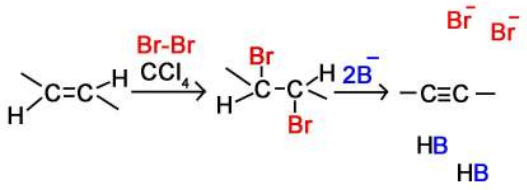
The acidity of terminal alkynes also plays a role in product determination when vicinal (or geminal) dihalides undergo base induced dielimination reactions. The following example illustrates eliminations of this kind starting from 1,2-dibromopentane, prepared from 1-pentene by addition of bromine. The initial elimination presumably forms 1-bromo-1-pentene, since base attack at the more acidic and less hindered 1°-carbon should be favored. The second elimination then produces 1-pentyne. If the very strong base such as sodium amide is used, the terminal alkyne is trapped as its sodium salt, from which it may be released by mild acid treatment. However, if the weaker base KOH with heat is used for the elimination, the terminal alkyne salt is not formed, or is formed reversibly, and the initially generated 1-pentyne rearranges to the more stable 2-pentyne via an allene intermediate. Even though terminal alkynes can be generated using sodium amide as a base, most chemists will prefer to use S_N2 nucleophilic substitution instead of elimination when trying to form a terminal alkyne.



Preparation of Alkynes from Alkenes

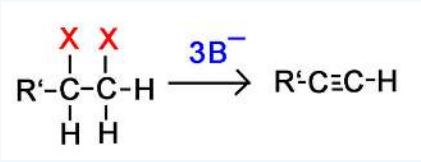
An simple method for the preparation of alkynes utilizes alkenes as starting material. The process begins with the electrophilic addition of a halogen to the alkene bond to form the dihaloalkane. Then the double E2 elimination process is used to form the 2 π bonds of an alkyne.

This first process is gone over in much greater detail in the page on halogenation of an alkene. In general, chlorine or bromine is used with an inert halogenated solvent like chloromethane to create a vicinal dihalide from an alkene. The vicinal dihalide formed is the reactant needed to produce the alkyene using double elimination, as covered previously on this page.



Exercise 12.2.1

1) Why would we need 3 bases for every terminal dihaloalkane instead of 2 in order to form an alkyne?

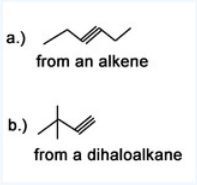


2) What are the major products of the following reactions:

a.) 1,2-Dibromopentane with sodium amide in liquid ammonia

b.) 1-Pentene first with Br_2 and chloromethane, followed by sodium ethoxide ($Na^+ {}^-O\text{-}CH_2CH_3$)

3) What would be good starting molecules for the synthesis of the following molecules:



4) Use a 6 carbon diene to synthesize a 6 carbon molecule with 2 terminal alkynes.

5) Identify the vinyl halide or halides and the vicinal dihalide or dihalides that could be used in the synthesis of:

a) 2,2,5,5-Tetramethyl-3-hexyne.

b) 4-Methyl-2-hexyne.

Answer

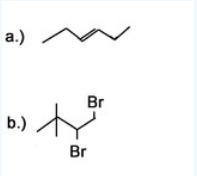
1) Remember that hydrogen atoms on terminal alkynes make the alkyne acidic. One of the base molecules will pull off the terminal hydrogen instead of one of the halides like we want.

2)

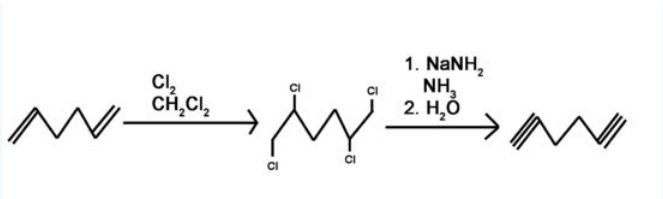
a) 1-Pentyne

b) 1-Pentyne

3)

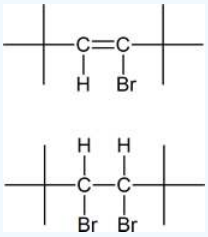


4) Bromine or chlorine can be used with different inert solvents for the halogenation. This can be done using many different bases. Liquid ammonia is used as a solvent and needs to be followed by an aqueous work-up.

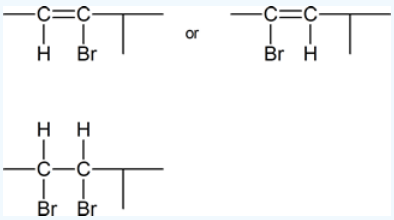


5)

a)



b)



References

1. Vollhardt, Peter, and Neil Shore. Organic Chemistry: Structure and Function. 5th. New York: W.H. Freeman and Company, 2007.
2. Daley, Richard, and Sally Daley. "13.8 Elimination of Organohalogens." Organic Chemistry. Daley. 5 July 2005. 21 Feb. 2009. <https://studylib.net/doc/8721401/13-elimination-reactions>.

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12.3: Alkylation of Acetylide Anions

Objectives

After completing this section, you should be able to

1. write an equation to describe the reaction of an acetylide ion with an alkyl halide.
2. discuss the importance of the reaction between acetylide ions and alkyl halides as a method of extending a carbon chain.
3. identify the alkyne (and hence the acetylide ion) and the alkyl halide needed to synthesize a given alkyne.
4. determine whether or not the reaction of an acetylide ion with a given alkyl halide will result in substitution or elimination, and draw the structure of the product formed in either case.

Key Terms

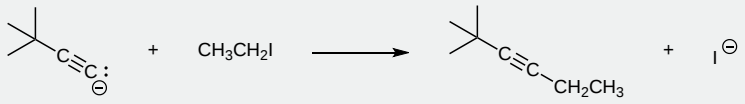
Make certain that you can define, and use in context, the key term below.

- alkylation

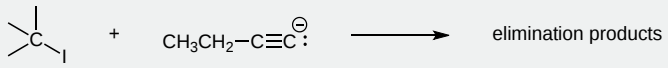
Study Notes

The alkylation of acetylide ions is important in organic synthesis because it is a reaction in which a new carbon-carbon bond is formed; hence, it can be used when an organic chemist is trying to build a complicated molecule from much simpler starting materials.

The alkyl halide used in this reaction must be primary. Thus, if you were asked for a suitable synthesis of 2,2-dimethyl-3-hexyne, you would choose to attack iodoethane with the anion of 3,3- dimethyl-1-butyne



rather than to attack 2-iodo-2-methylpropane with the anion of 1-butyne.



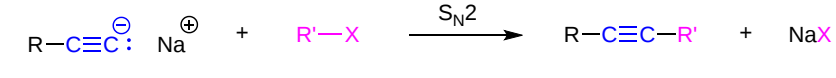
The reasons will be made clear in Chapter 11.

Nucleophilic Substitution Reactions of Acetylides

The presence of lone pair electrons and a negative charge on a carbon, makes acetylide anions are strong bases and strong nucleophiles. Therefore, acetylide anions can attack electrophiles such as alkyl halides to cause a substitution reaction. These substitution reactions will be discussed in detail in **Chapter 11**.

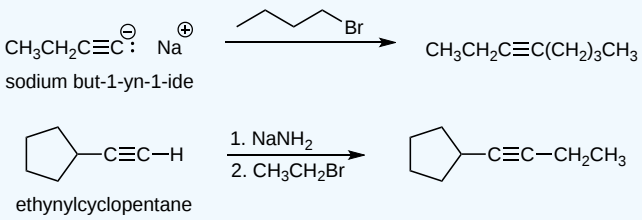
Mechanism

The C-X bonds in 1^o alkyl halides are polarized due to the high electronegativity of the halogen. The electrons of the C-X sigma bond are shifted towards the halogen giving it a partial negative charge. This also causes electrons to be shifted away from the carbon giving it a partial positive and making it electrophilic. During this reaction, the lone pair electrons on the acetylide anion attack the electrophilic carbon in the 1^o alkyl halide forming a new C-C bond. The formation of this new bond causes the expulsion of the halogen as what is called a leaving group. Overall, this reaction forms a C-C bond and converts a terminal alkyne into a internal alkyne. Because a new alkyl group is added to the alkyne during this reaction, it is commonly called an alkylation.

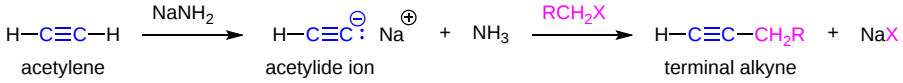


This substitution reaction is often coupled with the acetylide formation, discussed in the previous section, and shown as a single reaction.

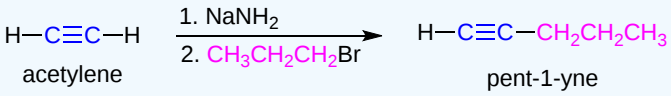
Example 12.3.1



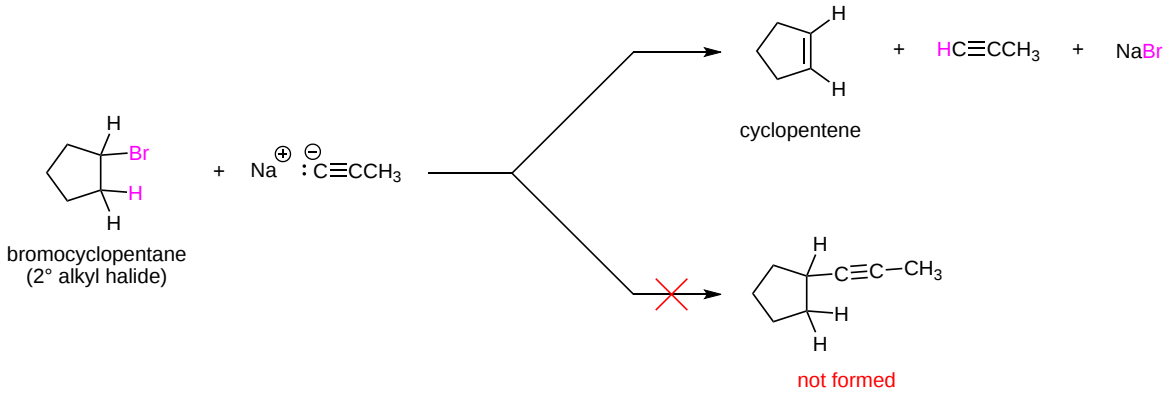
Terminal alkynes can be generated through the reaction of acetylene and a 1º alkyl halide.



Example 12.3.2

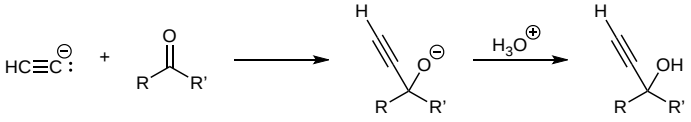


Because the acetylide anion is a very strong base, this substitution reaction is most efficient with methyl or primary halides. Secondary, tertiary, or even bulky primary halogens will give alkenes by the E2 elimination mechanism discussed in **Section 11.10**. An example of this effect is seen in the reaction of bromocyclopentane with a propyne anion. The reaction produces the elimination product cyclopentene rather than the substitution product 1-propynylcyclopentane.



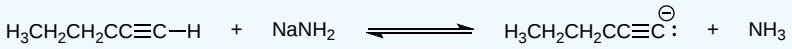
Nucleophilic Addition of Acetylides to Carbonyls

Acetylide anions also add to the electrophilic carbon in aldehydes and ketones to form alkoxides, which, upon protonation, give propargyl alcohols. With aldehydes and non-symmetric ketones, in the absence of chiral catalyst, the product will be a racemic mixture of the two enantiomers. These types of reaction will be discussed in more detail in **Chapter 19**.



Exercise 12.3.1

The pK_a of ammonia is 35. Estimate the equilibrium constant for the deprotonation of pent-1-yne by sodium amide, as shown below.

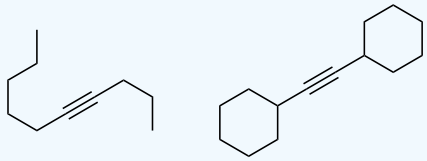


Answer

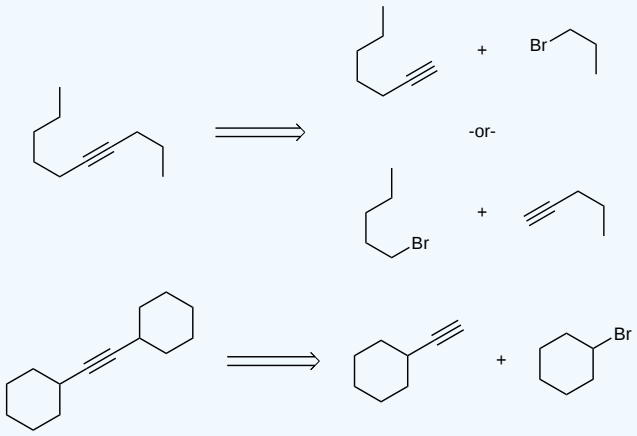
Assuming the pK_a of pent-1-yne is about 25, then the difference in pK_as is 10. Since pentyne is more acidic, the formation of the acetylide will be favored at equilibrium, so the equilibrium constant for the reaction is about 10^{10}.

Exercise 12.3.2

Give the possible reactants which could form the following molecules by an alkylation.



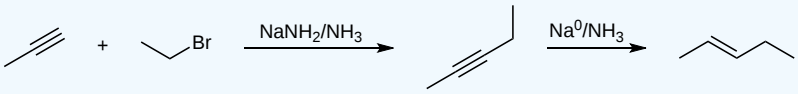
Answer



Exercise 12.3.3

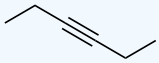
Propose a synthetic route to produce 2-pentene from propyne and an alkyl halide.

Answer



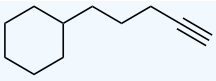
Exercise 12.3.4

Using acetylene as the starting material, show how you would synthesize the following compounds

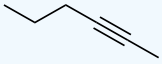
a) 

b) but-2-yne

c)

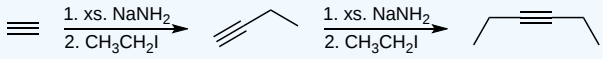


d)



Answer

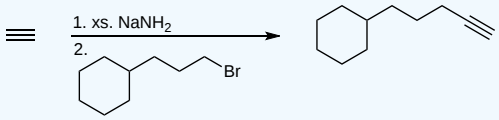
a)



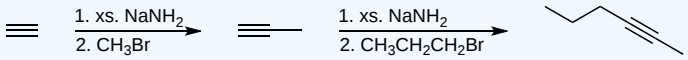
b)



c)

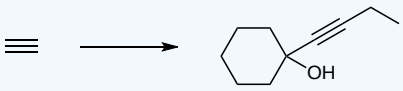


d)

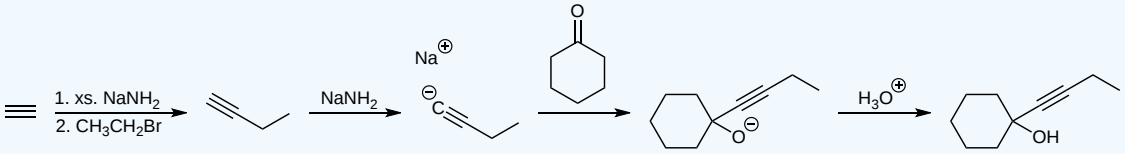


Exercise 12.3.5

Show how you would accomplish the following synthetic transformation.



Answer



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12.4: Alkyne Acidity - Formation of Acetylide Anions

Objectives

After completing this section, you should be able to

1. write an equation for the reaction that occurs between a terminal alkyne and a strong base, such as sodamide, $NaNH_2$.
2. rank a given list of compounds, including water, acetylene and ammonia, in order of increasing or decreasing acidity.
3. rank a given list of hydrocarbons, such as acetylene, ethylene and ethane, in order of increasing or decreasing acidity.
4. describe a general method for determining which of two given compounds is the stronger acid.
5. provide an acceptable explanation of why terminal alkynes are more acidic than alkanes or alkenes.

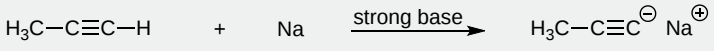
Key Terms

Make certain that you can define, and use in context, the key terms below.

- acetylide anion
- acidity order

Study Notes

An *acetylide anion* is an anion formed by removing the proton from the end carbon of a terminal alkyne:

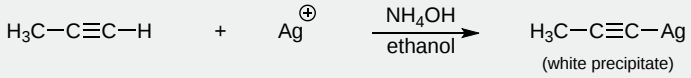


An *acidity order* is a list of compounds arranged in order of increasing or decreasing acidity.

The general ideas discussed in this section should already be familiar to you from your previous exposure to chemistry and from the review in Section 2.8. A slightly different account of why terminal alkynes are stronger acids than are alkenes or alkanes is given below. However, the argument is still based on the differences between *sp*-, sp^2- and sp^3-hybrid orbitals.

The carbons of a triple bond are *sp*-hybridized. An *sp*-hybrid orbital has a 50% *s* character and a 50% *p* character, whereas an sp^2-hybrid orbital is 33% *s* and 67% *p*, and an sp^3-hybrid orbital is 25% *s* and 75% *p*. The greater the *s* character of the orbital, the closer the electrons are to the nucleus. Thus in a C(*sp*)-H bond, the bonding electrons are closer to the carbon nucleus than they are in a C(sp^2)-H bond. In other words, compared to a C(sp^2)-H bond (or a C(sp^3)-H bond), a C(*sp*)-H bond is very slightly polar: $C^{\delta-}$-$H^{\delta+}$. This slight polarity makes it easier for a base to remove a proton from a terminal alkyne than from a less polar or non-polar alkene or alkane.

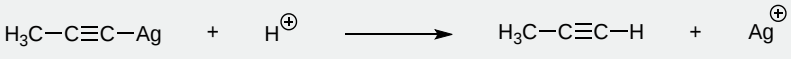
As you will appreciate, the reaction between sodium amide and a terminal alkyne is an acid-base reaction. The sodium acetylide product is, of course, a salt. Terminal alkynes can also form salts with certain heavy-metal cations, notably silver(I) and copper(I). In the laboratory component of this course, you will use the formation of an insoluble silver acetylide as a method for distinguishing terminal alkynes from alkenes and non-terminal alkynes:







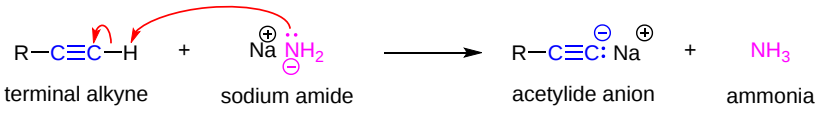
Metal acetylides are explosive when dry. They should be destroyed while still wet by warming with dilute nitric acid:



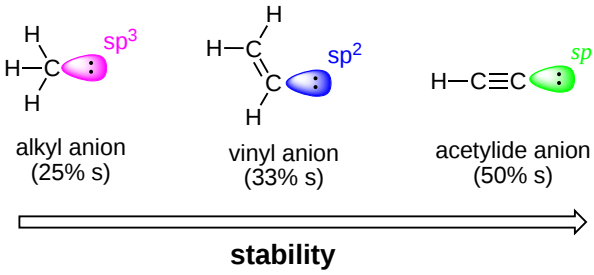
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Acidity of Terminal Alkynes: Formation of Acetylide Anions

Terminal alkynes are much more acidic than most other hydrocarbons. Removal of the terminal proton leads to the formation of an acetylide anion, $RC{\equiv}C{:}^{-}$.



As discussed in **Section 2.10**, acidity typically increases with the stability of the corresponding conjugate base. The origin of the enhanced acidity of terminal alkynes can be attributed to the stability of the acetylide anion, which has the unpaired electrons in an sp hybridized orbital. The hybridization of an orbital affects its electronegativity. Within a shell, the s orbitals occupy the region closer to the nucleus than the p orbitals. Therefore, the spherical s orbitals are more electronegative than the lobed p orbitals. The relative electronegativity of hybridized orbitals increases as the percent s character increases and follows the order sp > sp^2 > sp^3.



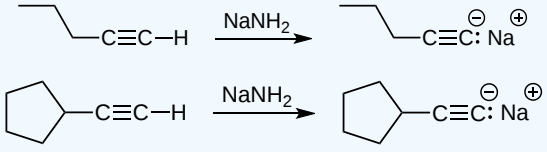
This trend indicates the sp hybridized orbitals of the acetylide anion are more electronegative and better able to stabilize a negative charge than sp^2 or sp^3 hybridized orbitals. There is a strong correlation between s-character in the orbital containing the non-bonding electrons in the anion and the acidity of hydrocarbons. The table below shows how orbital hybridization compares with the identity of the atom when predicting relative acidity. Remember that as the pK_a of a compound decreases its acidity increases.

Table **12.4.1**: Akynes

Compound	Conjugate Base	Hybridization	"s Character"	pKa	C-H BDE (kJ/mol)
CH_3CH_3	$CH_3CH_2^-$	sp^3	25%	50	410
CH_2CH_2	CH_2CH^-	sp^2	33%	44	473
HCCH	HCC^-	sp	50%	25	523

Acetylene, with a pK_a of 25 is shown to be much more acidic than ethylene (pK_a = 44) or ethane (pK_a = 50). Consequently, acetylide anions can be readily formed by deprotonation of a terminal alkynes with a sufficiently strong base. The amide anion (NH_2^-), in the form of sodium amide ($NaNH_2$) is commonly used for the formation of acetylide anions.

Example 12.4.1



Exercise 12.4.1

Given that the p*K*a of water is 14.00, would you expect hydroxide ion to be capable of removing a proton from each of the substances listed below? Justify your answers, briefly.

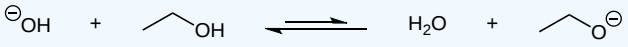
a. ethanol (p*K*a = 16)

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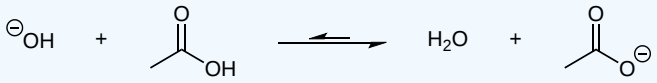
b. acetic acid (p*K*a = 4.72)
c. acetylene (p*K*a = 25)

Answer

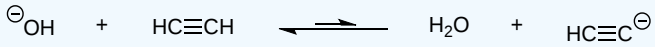
a. No, not very well. The p*K*a of ethanol is greater than that of water, thus the equilibrium lies to the left rather than to the right.Add texts here. Do not delete this text first.



b. Yes, very well. There is a difference of 11 p*K*a units between the p*K*a of water and the p*K*a of acetic acid. The equilibrium lies well to the right.



c. No, hardly at all. The hydroxide ion is too weak a base to remove a proton from acetylene. The equilibrium lies well to the left.



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12.5: Reactions of Alkynes - Addition of HX and X_2

Objectives

After completing this section, you should be able to

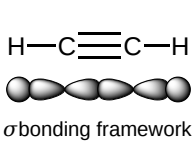
- describe the bonding and geometry of the carbon-carbon triple bond in terms of the *sp*-hybridization of the carbon atoms involved.
- explain the reactivity of alkynes based on the known strengths of carbon-carbon single, double and triple bonds.
- write equations for the reaction of an alkyne with one or two equivalents of halogen (chlorine or bromine) or halogen acid (HCl, HBr or HI).
- draw the structure of the product formed when an alkyne reacts with one equivalent of the halogens and halogen acids listed in Objective 3.
- identify the alkyne which must have been used in an addition reaction with a halogen or halogen acid, given the product of such a reaction.

Study Notes

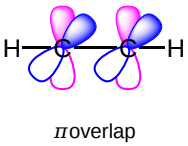
You might find it useful to review Section 1.9 before you begin work on this chapter. If necessary, construct a molecular model of a simple alkyne. Notice the similarity between the behaviour of alkenes and that of alkynes. In the laboratory, you will observe that alkynes readily decolourize a solution of bromine in dichloromethane. Section 9.7 describes a test that allows you to distinguish between a terminal alkyne (i.e., one in which the triple bond occurs between the last two carbons in the chain) and nonterminal alkynes and alkenes.

The Alkyne Triple Bond

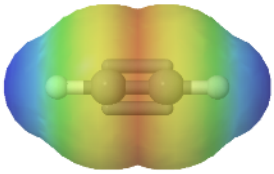
As discussed in **Section 1-9**, the carbon-carbon triple bonds of alkynes are created by the the overlap of orbitals on two sp hybridized carbon atoms. The molecule acetylene (HCCH) is said to contain three sigma bonds and two pi bonds. The C-C sigma bond of acetylene is formed by the overlap an *sp* hybrid orbital from each of the carbon atoms. The two C-H sigma bonds are formed by the overlap of the second *sp* orbital on each carbon atom with a 1*s* orbital from a hydrogen. Each carbon atom still has two half-filled P orbitals, which are perpendicular both to each other and to the line formed by the sigma bonds. These two perpendicular pairs of *p* orbitals form two pi bonds between the carbons, resulting in a triple bond overall (one sigma bond plus two pi bonds). The electrostatic potential map of acetylene shows that the pi electrons of the triple bond form a negative belt (shown in red) around the center of the molecule.



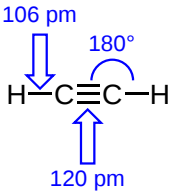
σ bonding framework



π overlap



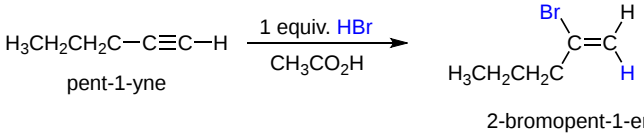
Acetylene is linear, as predicted by VSEPR, with all four atoms lying in a straight line and both H-C-C bond angles being 180°. The triple bond in acetylene is the shortest (120 pm) and the strongest (964 kJ/mol) carbon-carbon bond known.



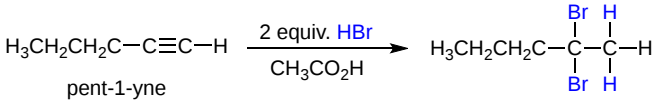
Electrophilic Addition of HX to Alkynes

Alkynes undergo electrophilic addition in much the same manner as alkenes, however, the presence to two pi bonds allows for the possibly of the addition happening twice. The addition of one equivalent of hydrogen chloride or hydrogen bromide converts alkynes to haloalkenes. The addition of two or more equivalents of HCl or HBr converts alkynes to geminal dihalides through an haloalkene intermediate. These additions are regioselective and follow Markovnikov's rule. The double bonds formed during the reaction with internal alkynes tend to have Z stereochemistry although not always.

HBr Addition to a Terminal Alkyne

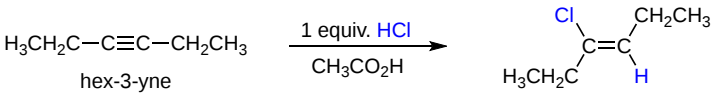


pent-1-yne → 2-bromopent-1-ene

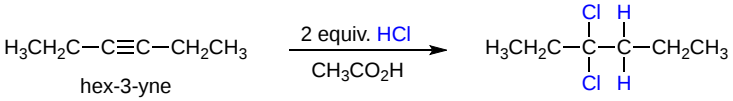


pent-1-yne → 2,2-dibromopentane

HCl Addition to a Symmetrical Internal Alkyne



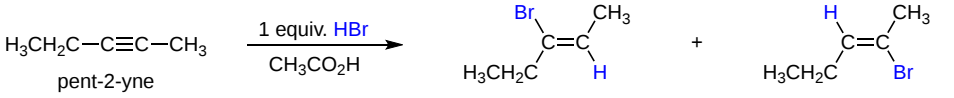
hex-3-yne → (Z)-4-chlorohex-3-ene



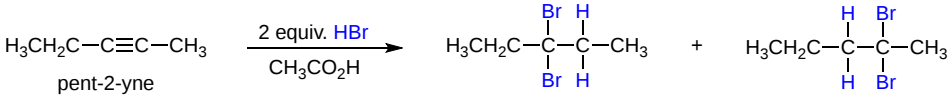
hex-3-yne → 3,3-dichlorohexane

HBr Addition to an Asymmetrical Internal Alkyne

The addition of HX to an asymmetrical internal alkyne tend to make a mixture of isomers as products.



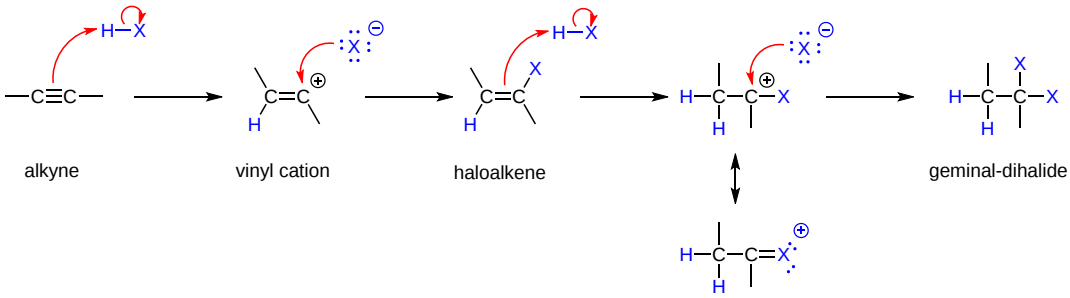
pent-2-yne → (Z)-3-bromopent-2-ene + (Z)-2-bromopent-2-ene



pent-2-yne → 3,3-dibromopentane + 2,2-dibromopentane

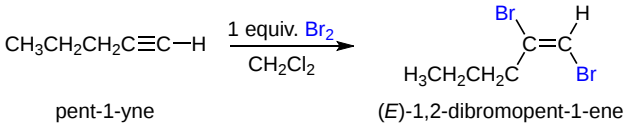
Mechanism

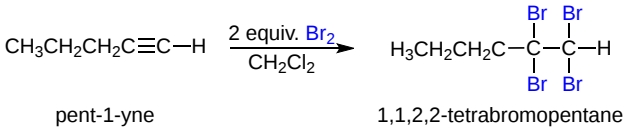
The mechanism for the electrophilic addition of HX to an alkyne is analogous to the HX addition to an alkene. The presence of two pi bonds in the alkyne allows for the addition of HX to occur twice. The addition of H^+ to the alkyne forms a vinyl cation will preferably form on the more substituted side of the alkyne following Markovnikov's rule. The subsequent addition of Br^- forms a haloalkene which undergoes electrophilic addition to a second H^+. The carbocation form will preferably form on the carbon attached to the halogen already in place. The carbocation is stabilized by the halogen through the creation of a resonance structure which obeys the octet rule. This stabilizing effect ensures that a geminal-dihalide is the sole product and no vicinal-dihalide is formed.



Electrophilic Addition of X_2 to Alkynes

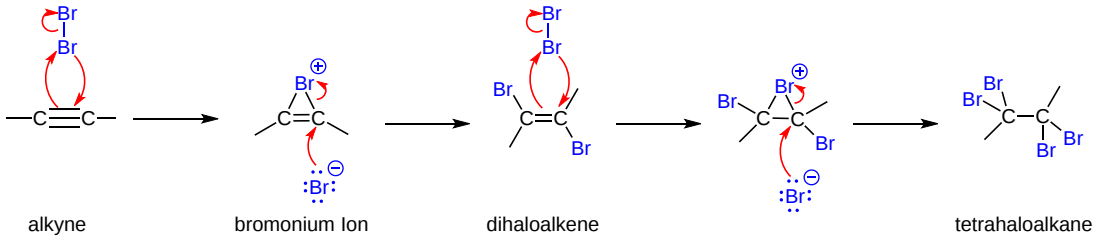
Alkynes undergo the same type of electrophilic addition with chloride and bromine as alkenes. However, with alkynes the halogen addition can occur once or twice depending on the molar equivalents of halogen used in the reaction. If one molar equivalent of halogen is used, a dihaloalkene is formed. The anti addition of the reaction mechanism causes the halogens to be trans in the resulting alkene. The addition of two or more molar equivalents of halogen converts the alkyne to a tetrahaloalkane through a dihaloalkene intermediate.





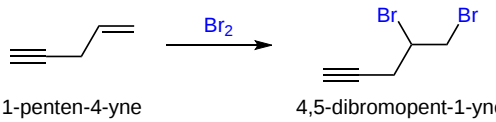
Mechanism

The alkyne undergoes electrophilic addition with bromine to form a bromonium ion in a three-membered ring. The ejected bromide ion performs an S_N2 reaction with the bromonium ion causing the ring to open and the bromines in the resulting alkene to be in a *trans* configuration. The process is repeated with a second pi bond creating a tetrahaloalkane as a product.



Relative Reactivity of Alkynes and Alkenes to Electrophilic Reagents

When the addition reactions of electrophilic reagents, such as strong Brønsted acids and halogens, to alkynes are studied there is a curious paradox. The reactions of alkynes are even more exothermic than the additions to alkenes, and yet the rate of addition to alkynes is slower by a factor of 100 to 1000. This concept is shown in the reaction of one equivalent of bromine with 1-penten-4-yne to produce 4,5-dibromopent-1-yne as the chief product.

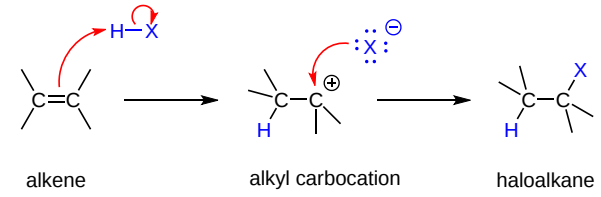


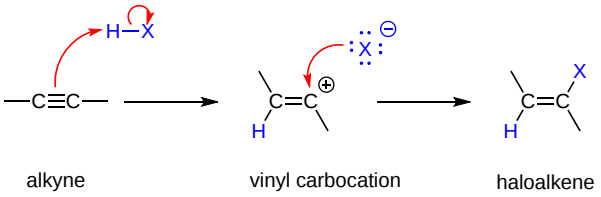
Why are the reactions of alkynes with electrophilic reagents more sluggish than the corresponding reactions of alkenes? Typically, addition reactions to alkynes are more exothermic than additions to alkenes, and there would seem to be a higher π-electron density

about the triple bond (two π-bonds versus one). Two factors are significant in explaining this apparent paradox. First, although there are more π-electrons associated with the triple bond, the sp-hybridized alkyne carbons are more electronegative than the sp^2-hybridized alkene carbons. The alkyne carbons exert a strong attraction for their π-electrons, which are consequently bound more tightly to the functional group than are the π-electrons of a double bond. This is seen in the ionization potentials of ethylene and acetylene. Remember an **ionization potential** is the minimum energy required to remove an electron from a molecule of a compound. Since the initial interaction between an electrophile and an alkene or alkyne involves the donation of electrons, the relatively slower reactions of alkynes becomes understandable.

Acetylene	$HC{\equiv}CH + Energy \rightarrow [HC{\equiv}CH\ \bullet^{(+)} + e^{(-)}$	ΔH = +264 kcal/mole
Ethylene	$H_2C{=}CH_2 + Energy \rightarrow [H_2C{=}CH_2]\ \bullet^{(+)} + e^{(-)}$	ΔH = +244 kcal/mole

A second factor is presumed to be the stability of the carbocation intermediate generated by sigma-bonding of a proton or other electrophile to one of the triple bond carbon atoms. When comparing the mechanism for the addition of HBr to an alkene and an alkyne, the alkyne reaction creates a vinyl carbocation which is less stable than the alkyl carbocation made during the alkene reaction.

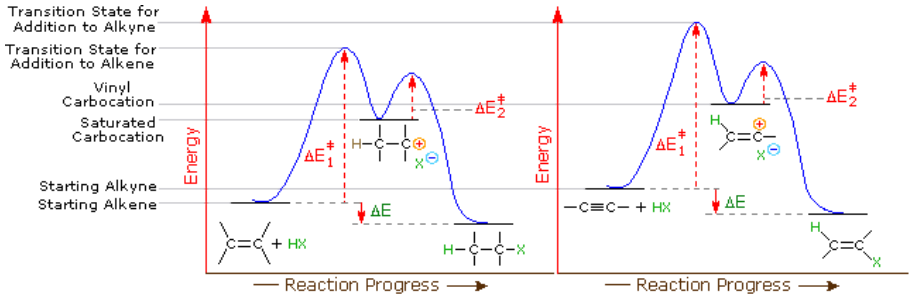




Indeed, we can modify our earlier ordering of carbocation stability to include these vinyl cations in the manner shown below.

Substitution	**Methyl**		**1°-Vinyl**		**1°**		**2°-Vinyl**		**2°**		**1°-Allyl**		**3°**
Stability	$CH_3^{(+)}$	≈	$RCH{=}CH^{(+)}$	<	$RCH_2^{(+)}$	≈	$RCH{=}CR^{(+)}$	<	$R_2CH^{(+)}$	≈	$CH_2{=}CH{-}CH_2^{(+)}$	<	$R_3C^{(+)}$

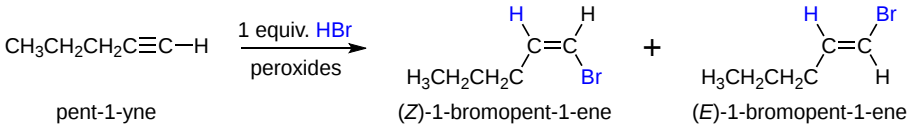
Application of the Hammond postulate indicates that the activation energy for the generation of a vinyl cation intermediate would be higher than that for a lower energy intermediate. Thus, electrophilic reactions with alkenes have a lower activation energy and process faster than the corresponding reaction with an alkyne. This is illustrated for alkenes versus alkynes by the following energy diagrams. Despite these differences, electrophilic additions to alkynes have emerged as exceptionally useful synthetic transforms.



A Comparison of Energy Profiles for Electrophilic Addition to Alkenes and Alkynes

Electrophilic Addition of HX with Peroxides to Alkynes

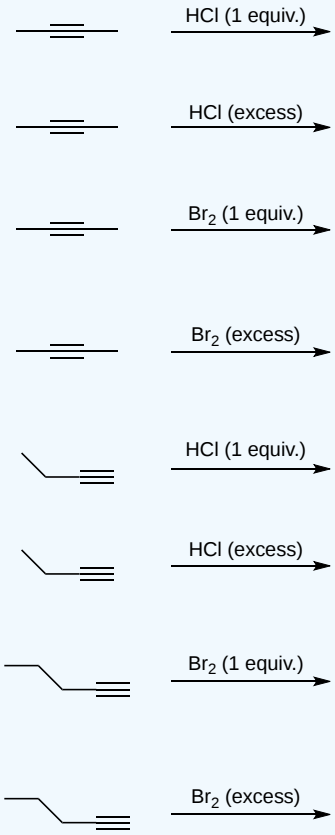
When 1 equivalent of HBr is reacted with alkynes in the presence of peroxides and Anti-Markovnikov addition occurs. The use of peroxides causes the reaction to occur via a free radical mechanism. The bromine adds to the less substituted alkyne carbon while the hydrogen adds to the more substituted creating a haloalkene. Typically, H and Br are added in a syn or anti manner creating a mixture of products.



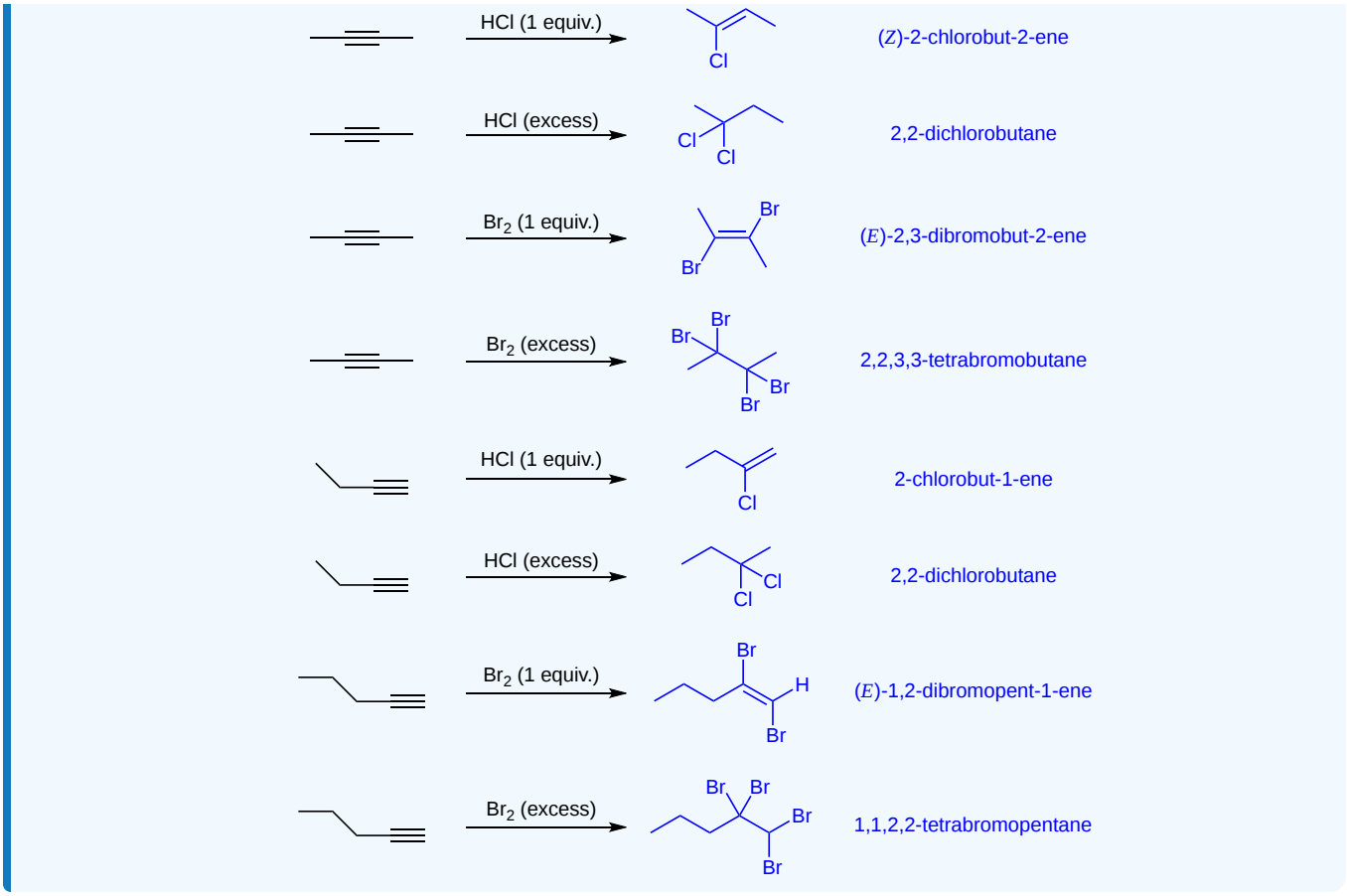
pent-1-yne (*Z*)-1-bromopent-1-ene (*E*)-1-bromopent-1-ene

? Exercise 12.5.1

Draw the structure and give the IUPAC name of the product formed in each of the reactions listed below:



Answer



12.5: Reactions of Alkynes - Addition of HX and X₂ is shared under a CC BY-SA 4.0 license and was authored, remixed, and/or curated by Jim Clark, Steven Farmer, Dietmar Kennepohl, Layne Morsch, Tim Soderberg, William Reusch, & William Reusch.

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12.6: Hydration of Alkynes

Objectives

After completing this section, you should be able to

- write the equation for the reaction of water with an alkyne in the presence of sulfuric acid and mercury(II) sulfate.
- describe keto-enol tautomerism.
- predict the structure of the ketone formed when a given alkyne reacts with sulfuric acid in the presence of mercury(II) sulfate.
- identify the reagents needed to convert a given alkyne to a given ketone.
- identify the alkyne needed to prepare a given ketone by hydration of the triple bond.
- write an equation for the reaction of an alkyne with borane.
- write the equation for the reaction of a vinylic borane with basic hydrogen peroxide or hot acetic acid.
- identify the reagents, the alkyne, or both, needed to prepare a given ketone or a given cis alkene through a vinylic borane intermediate.
- identify the ketone produced when a given alkyne is reacted with borane followed by basic hydrogen peroxide.
- identify the cis alkene produced when a given alkyne is reacted with borane followed by hot acetic acid.
- explain why it is necessary to use a bulky, sterically hindered borane when preparing vinylic boranes from terminal alkynes.
- predict the product formed when the vinylic borane produced from a terminal alkyne is treated with basic hydrogen peroxide.
- identify the alkyne needed to prepare a given aldehyde by a vinylic borane.

Key Terms

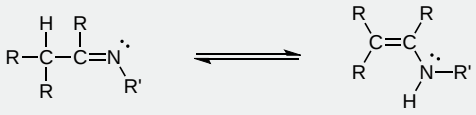
Make certain that you can define, and use in context, the key terms below.

- enol
- keto-enol tautomeric equilibrium
- tautomerism
- tautomers

Study Notes

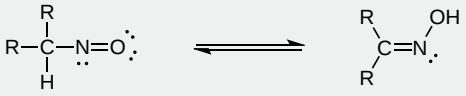
Rapid interconversion between tautomers is called **tautomerism**; however, as the two tautomers are in equilibrium, the term *tautomeric equilibrium* may be used. This section demonstrates the equilibrium between a ketone and an enol; hence, the term *keto-enol tautomeric equilibrium* is appropriate. The term “enol” indicates the presence of a carbon-carbon double bond and a hydroxyl (i.e., alcohol) group. Later in the course, you will see the importance of keto-enol tautomerism in discussions of the reactions of ketones, carbohydrates and nucleic acids.

It is important to note that tautomerism is not restricted to keto-enol systems. Other examples include imine-enamine tautomerism



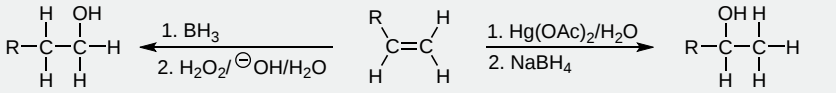
imine enamine

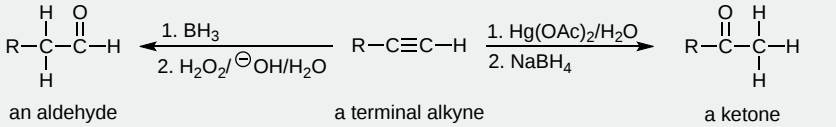
and nitroso-oxime tautomerism



However, at the moment you need only concern yourself with keto-enol tautomerism.

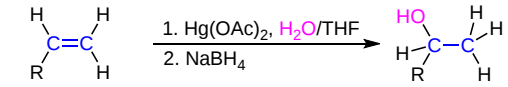
Notice how hydroboration complements hydration in the chemistry of both alkenes and alkynes.



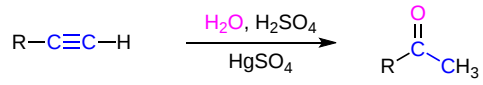


Mercury(II)-Catalyzed Hydration of Alkynes

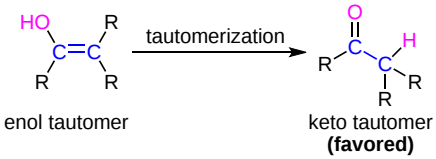
As with alkenes, hydration (addition of water) of alkynes requires a strong acid, usually sulfuric acid, and is facilitated by the mercuric ion (Hg^{2+}). However, the hydration of alkynes gives ketone products while the hydration of alkenes gives alcohol products. Notice that the addition of oxygen in both reactions follows Markovnikov rule.



During the hydration of an alkyne, the initial product is an enol intermediate (a compound having a hydroxyl substituent attached to a double-bond), which immediately rearranges to the more stable ketone through a process called **enol-keto tautomerization**.

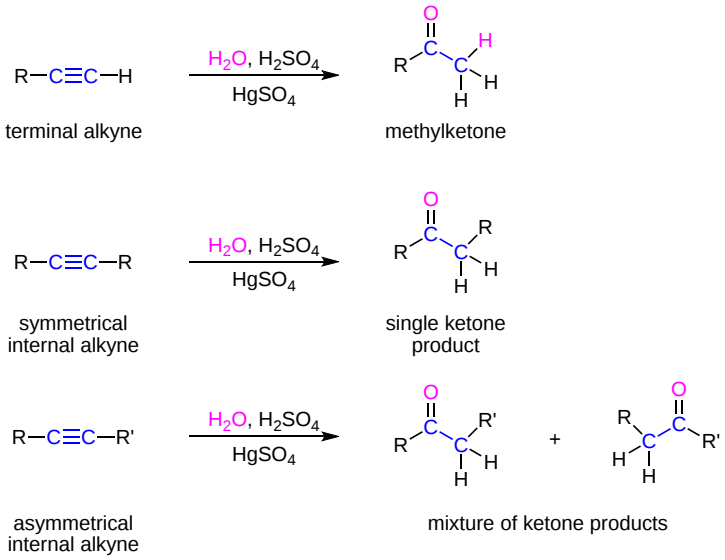


Tautomers are defined as rapidly inter-converted constitutional isomers, usually distinguished by a different bonding location for a labile hydrogen atom and a differently located double bond. The keto and enol tautomers are in equilibrium with each other and with few exceptions the keto tautomer is more thermodynamically stable and therefor favored by the equilibrium. This mechanism for tautomerization will be discussed in greater detail in **Section 22-1**.



General Reaction

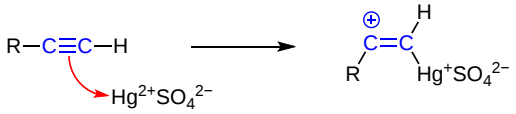
For terminal alkynes, the addition of water follows the Markovnikov rule, and the final product is a methyl ketone. For internal alkynes the addition of water is not regioselective. Hydration of symmetrical internal alkynes produces a single ketone product. However, hydration of asymmetrical alkynes, (i.e. if R & R' are not the same) produces two isomeric ketone products.



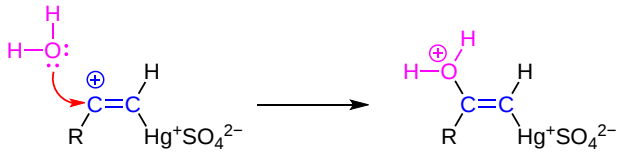
Mechanism

The mechanism starts with the electrophilic addition of the mercuric ion (Hg^{2+}) to the alkyne producing a mercury-containing vinylic carbocation intermediate. Nucleophilic attack of water on the vinylic carbocation forms a C-O bond to produce a protonated enol. Deprotonation of the enol by water then produces a organomercury enol. The mercury is substituted with H^+ to produced a neutral enol and regenerate the Hg^{2+} catalyst. The enol is converted to the ketone product through keto-enol tautomerization the mechanism of which is provided in **Section 22-1**.

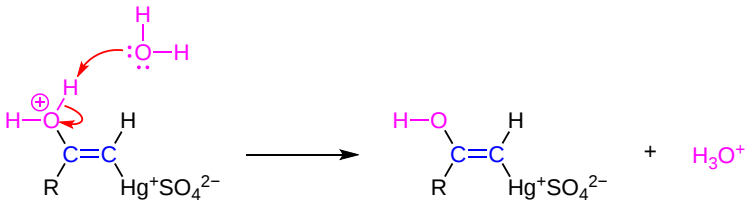
Step 1: Electrophilic addition of Hg^{2+}



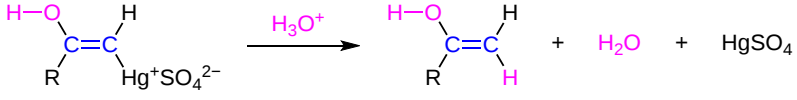
Step 2: Nucleophilic attack by water



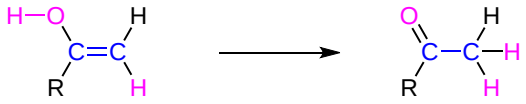
Step 3: Deprotonation



Step 4: Substitution

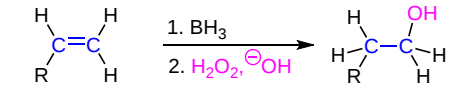


Step 5: Tautomerization

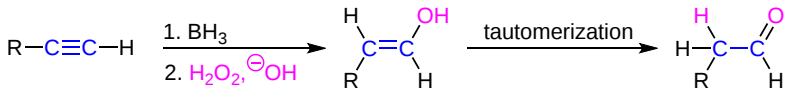


Hydroboration–Oxidation of Alkynes

The hydroboration-oxidation of alkynes is analagous to the reaction with alkenes. However, where alkenes for alcohol products, alkynes for aldehyde or ketone products. In both cases the addition is anti-Markovnikov and an oxygen is placed on the less alkyl substituted carbon. With the hydroboration of an alkyne the presences of a second pi bond allows the initial product to under tautomerization to become the final aldehyde product.

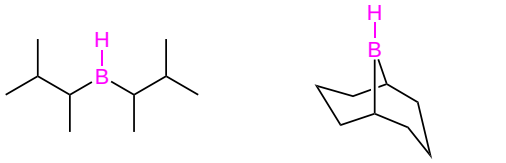


terminal alkene — 1° alcohol



terminal alkyne — enol — aldehyde

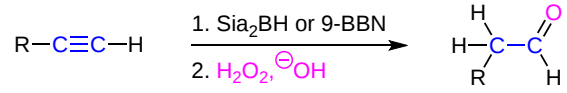
Alkynes have two pi bonds both of which are capable of reacting with borane (BH_3). To limit the reactivity to only one alkyne pi bond, a dialkyl borane reagent (R_2BH) is used. Replacing two of the hydrogens on the borane with alkyl groups also creates steric hindrance which enhances the anti-Markovnikov regioselective of the reaction. Disiamylborane (Sia_2BH) and 9-borabicyclo[3.3.1]nonane (9-BBN) are two common reagents for this hydroboration reaction. The oxidation reagents (a basic hydrogen peroxide solution) are the same for both alkenes and alkynes.



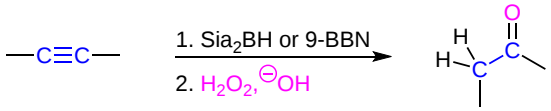
disiamylborane (Sia_2BH) — 9-borabicyclo[3.3.1]nonane (9-BBN)

General Reaction

The hydroboration of terminal alkynes produces aldehyde products while internal alkynes produce ketone products. The hydroboration of symmetrical alkynes produces one ketone product and asymmetrical alkynes produce a mixture of product ketones.



terminal alkyne — aldehyde

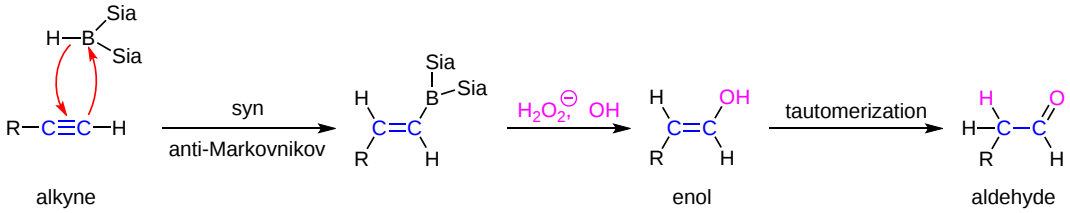


internal alkyne — ketone

Mechanism

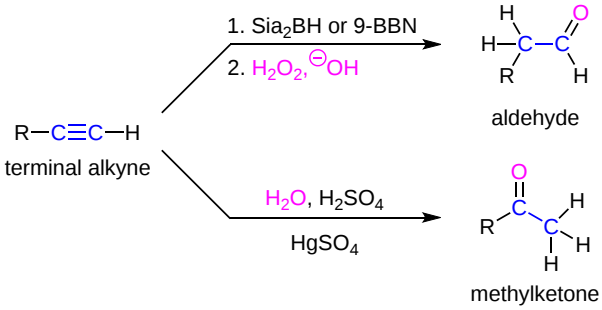
The mechanism starts with the electrophilic addition of the B-H bond of the borane. The hydrogen atom and the borane all on the same side of the alkyne creating a syn addition configuration in the alkene product. Also, the addition is anti-Markovnikov regioselective which means the borane adds to the less substituted carbon of the alkyne and the hydrogen atom adds to the more

substituted. The oxidative work-up replaces the borane with a hydroxy group (-OH) creating an enol intermediate. The enol immediately tautomerizes to the product aldehyde for terminal alkynes and the product ketone for internal alkynes.

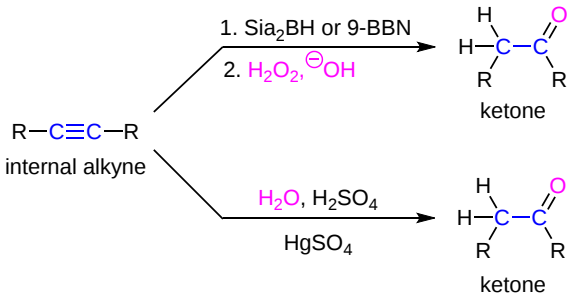


Comparison of Mercury(II)-Catalyzed Hydration and Hydroboration–Oxidation of Alkynes

These two reactions are complementary for the reaction of a terminal alkyne because the produce distinctly different products. The mercury(II) catalyzed hydration of a terminal alkyne produces a methyl ketone, while the hydroboration-oxidation produces an aldehyde.



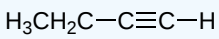
For internal alkynes, the regioslectivity of these reactions are rendered ineffective. The reactions are redundant in that they both produce the same ketone products.



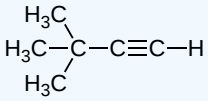
? Exercise 12.6.1

Draw the structure of the product formed when each of the substances below is treated with H_2O/H_2SO_4 in the presence of $HgSO_4$.

a)



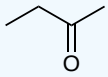
b)

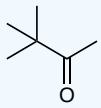


Answer

a)

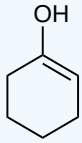
b)



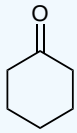


Exercise 12.6.2

Draw the structure of the keto form of the compound shown below. Which form would you expect to be the most stable?



Answer

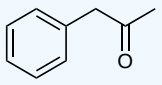


The keto form should be the most stable.

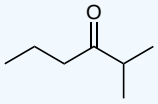
Exercise 12.6.3

What alkyne would you start with to gain the following products?

a)

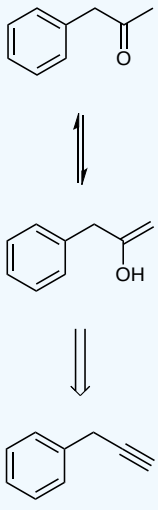


b)

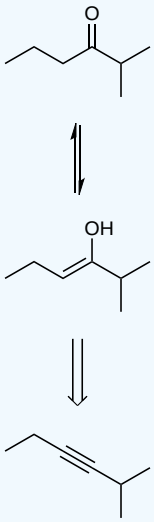


Answer

a)



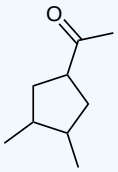
b)



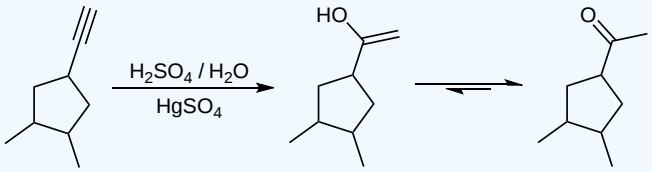
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Exercise 12.6.4

What alkyne would you start with to gain the following product?

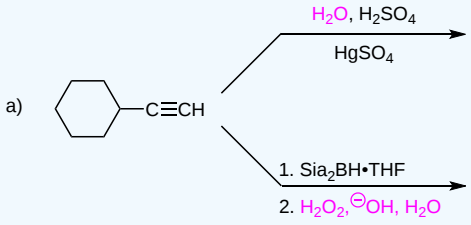


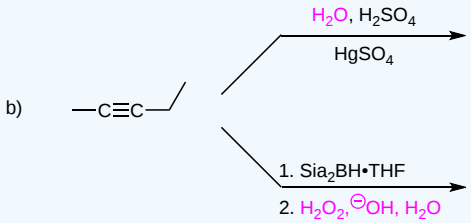
Answer



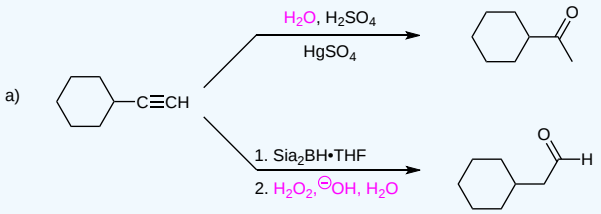
Exercise 12.6.5

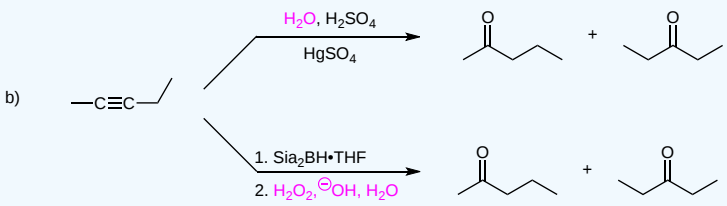
Draw the product(s) of the following reactions:





Answer





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For internal alkynes, there is no difference in the reaction products.

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12.7: Reduction of Alkynes

Objectives

After completing this section, you should be able to

1. write equations for the catalytic hydrogenation of alkynes to alkanes and cis alkenes.
2. identify the reagent and catalyst required to produce a given alkane or *cis* alkene from a given alkyne.
3. identify the product formed from the reaction of a given alkyne with hydrogen and a specified catalyst.
4. identify the alkyne that must be used to produce a given alkane or *cis* alkene by catalytic hydrogenation.
5. write the equation for the reduction of an alkyne with an alkali metal and liquid ammonia.
6. predict the structure of the product formed when a given alkyne is reduced with an alkali metal and liquid ammonia.
7. identify the alkyne that must be used to produce a given alkene by reduction with an alkali metal and ammonia.

Key Terms

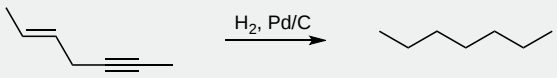
Make certain that you can define, and use in context, the key terms below.

- anion radical
- Lindlar catalyst

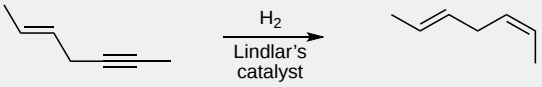
Study Notes

The Lindlar catalyst allows a chemist to reduce a triple bond in the presence of a double bond.

Thus

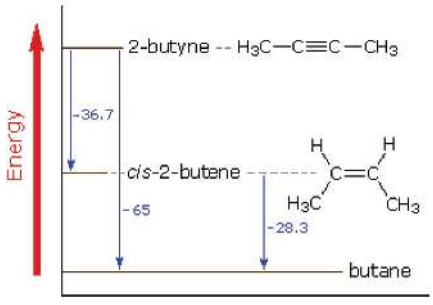


but



Hydrogenation and the Relative Stability of Hydrocarbons

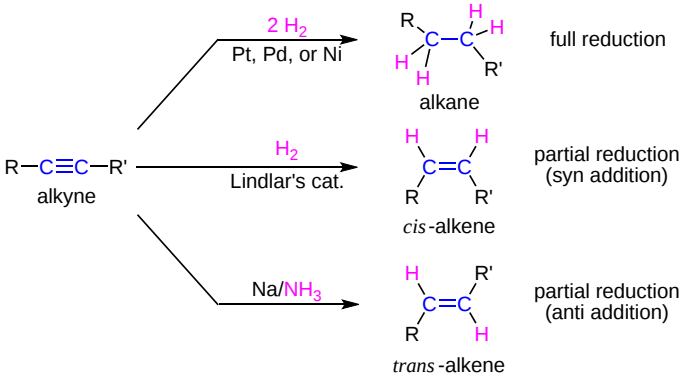
Like alkenes, alkynes readily undergo catalytic hydrogenation partially to *cis*-alkenes or fully to alkanes depending on the reaction employed.



The catalytic addition of hydrogen to 2-butyne provides heat of reaction data that reflect the relative thermodynamic stabilities of these hydrocarbons, as shown above. From the heats of hydrogenation, shown in blue in units of kcal/mole, it would appear that alkynes are thermodynamically less stable than alkenes to a greater degree than alkenes are less stable than alkanes. The standard bond energies for carbon-carbon bonds confirm this conclusion. Thus, a double bond is stronger than a single bond, but not twice

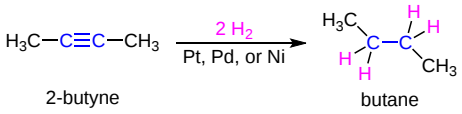
as strong. The difference (63 kcal/mole) may be regarded as the strength of the π-bond component. Similarly, a triple bond is stronger than a double bond, but not 50% stronger. Here the difference (54 kcal/mole) may be taken as the strength of the second π-bond. The 9 kcal/mole weakening of this second π-bond is reflected in the heat of hydrogenation numbers (36.7 - 28.3 = 8.4).

Alkynes can undergo reductive hydrogenation reactions similar to alkenes. Due to the presence of two pi bonds within alkynes, reductive hydrogenation reactions can be partial to form an alkene or complete to form an alkane. Since partial reductive hydrogenation of an alkyne produces an alkene, the stereochemistry provided by the reaction's mechanism determines whether a *cis*- or *trans*- alkene is formed. The three most significant alkyne reduction reactions are summarized below:

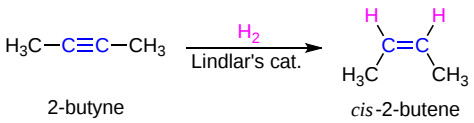


Catalytic Hydrogenation of an Alkyne

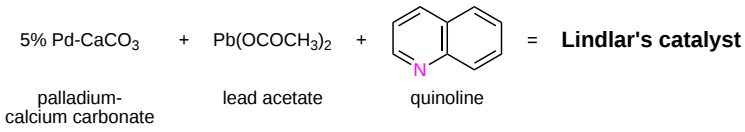
Much like alkenes, alkynes can be fully hydrogenated into alkanes with the help of a platinum, palladium, or nickel catalyst. Because the reaction is catalyzed on the surface of the metal, it is common for these catalysts to be dispersed on carbon (Pd/C) or finely dispersed, such as Raney-Ni. The presence of two pi bonds in the alkyne causes two equivalents of H_2 to be added during the reaction. An alkene intermediate is formed during the reaction but is not isolated.



For catalytic hydrogenation, the Pt, Pd, or Ni catalysts are so effective in promoting the addition of hydrogen to carbon-carbon triple bonds that the alkene intermediate formed cannot be isolated. A less efficient **Lindlar's catalyst**, permits alkynes to be converted to alkenes without further reduction to an alkane. Lindlar's Catalyst transforms an alkyne to a *cis*-alkene because both hydrogen atoms are added to the same side of the alkyne (syn) as shown in the in the previous chapter.

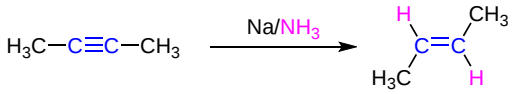


Lindlar's catalyst is prepared by deactivating (or poisoning) a conventional palladium catalyst. Lindlar's catalyst has three components: palladium-calcium carbonate, lead acetate, and quinoline. The quinoline serves to prevent complete hydrogenation of the alkyne to an alkane.



Hydrogenation of an Alkyne to a *Trans*-Alkene

The anti-addition of hydrogen to an alkyne pi bond occurs through reaction with sodium or lithium metal dissolved in ammonia. This reaction, also called a **dissolving metal reduction**, involves a radical mechanism, and produces a *trans*-alkene product.

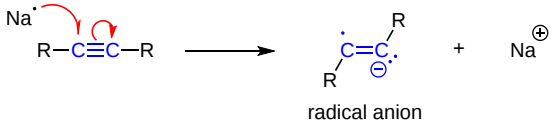


2-Butyne **_Trans_-2-Butene**

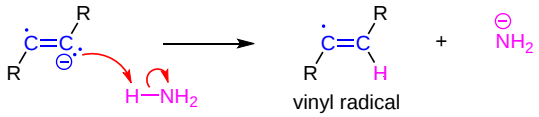
Mechanism

Sodium metal is a powerful reducing agent due to the presence of a $3s^1$ electron in its valence shell. Sodium metal easily gives up this electron to become Na^+. The mechanism start with a sodium atom donating an electron to the alkyne to create an intermediate with a negative charge and an unpaired electron called a radical anion. Next the amine solvent protonates the anion to create a vinyl radical. A second sodium atom then donates an electron to pair the radical to form a vinyl anion. This vinyl anion intermediate rapid interconverts between *cis* and *trans* conformations and determines the stereochemistry of the reaction. The *trans*-vinyl anion is more stable due to reduced steric crowding and is preferentially formed. Finally, the protonation of the *trans*-vinyl anion creates the *trans*-alkene product.

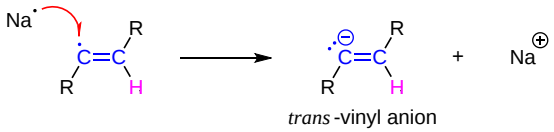
Step 1: Electron Donation



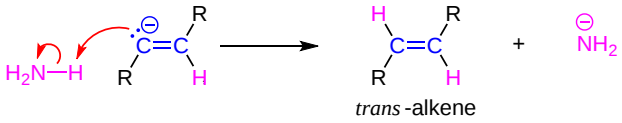
Step 2: Protonation



Step 3: Electron Donation



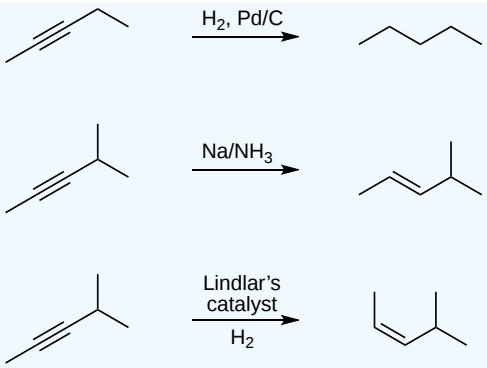
Step 4: Protonation



? Exercise 12.7.1

Using any alkyne how would you prepare the following compounds: pentane, *trans*-4-methyl-2-pentene, *cis*-4-methyl-2-pentene.

Answer



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12.8: Oxidative Cleavage of Alkynes

Objectives

After completing this section, you should be able to

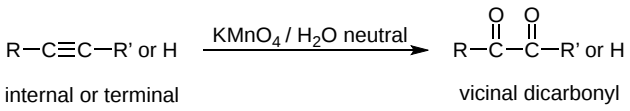
- write an equation to represent the oxidative cleavage of an alkyne with potassium permanganate or ozone.
- identify the products that result from the oxidative cleavage of a given alkyne.
- identify the reagents needed to carry out the oxidative cleavage of an alkyne.
- use the results of an oxidative cleavage to determine the identity of an alkyne of unknown structure.

Study Notes

Compare the oxidative cleavage of alkynes with the oxidative cleavage of alkenes, discussed in Section 8.8.

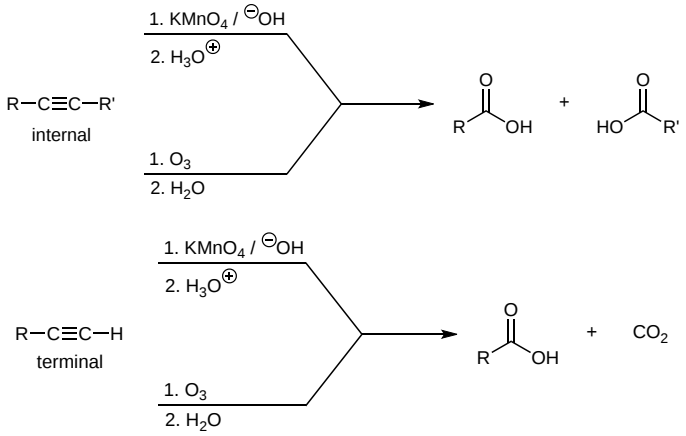
Alkynes, similar to alkenes, can be oxidized gently or strongly depending on the reaction environment. Since alkynes are less stable than alkenes, the reaction conditions can be gentler. For example, alkynes form vicinal dicarbonyls in neutral permanganate solution.

Gentle Alkyne Oxidation



Strong Alkyne Oxidation - Oxidative Cleavage

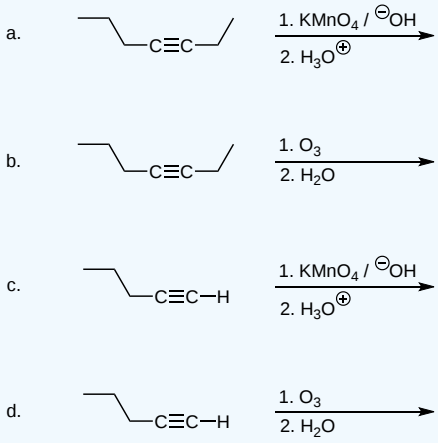
During strong oxidation with ozone or basic potassium permanganate, the alkyne is cleaved into two products. Because at least one of the reaction products is a carboxylic acid, it is important to consider the acid-base chemistry of the product in the reaction solution. Carboxylic acids are deprotonated in basic solutions to carboxylates. A second reaction step is required to protonate the carboxylate to the neutral form of the carboxylic acid.



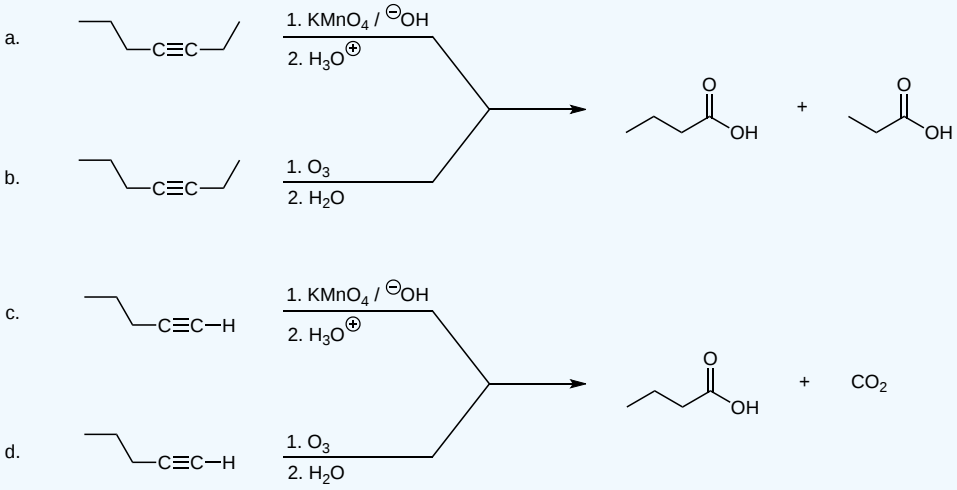
Exercise 12.8.1

Draw the bond-line structures for the product(s) of the following reactions.

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Answer



Oxidative cleavage of alkynes produces carboxylic acids and/or carbon dioxide. Aldehydes are not produced.

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12.9: An Introduction to Organic Synthesis

Objective

After completing this section, you should be able to design a multistep synthesis to prepare a given product from a given starting material, using any of the reactions introduced in the textbook up to this point.

Study Notes

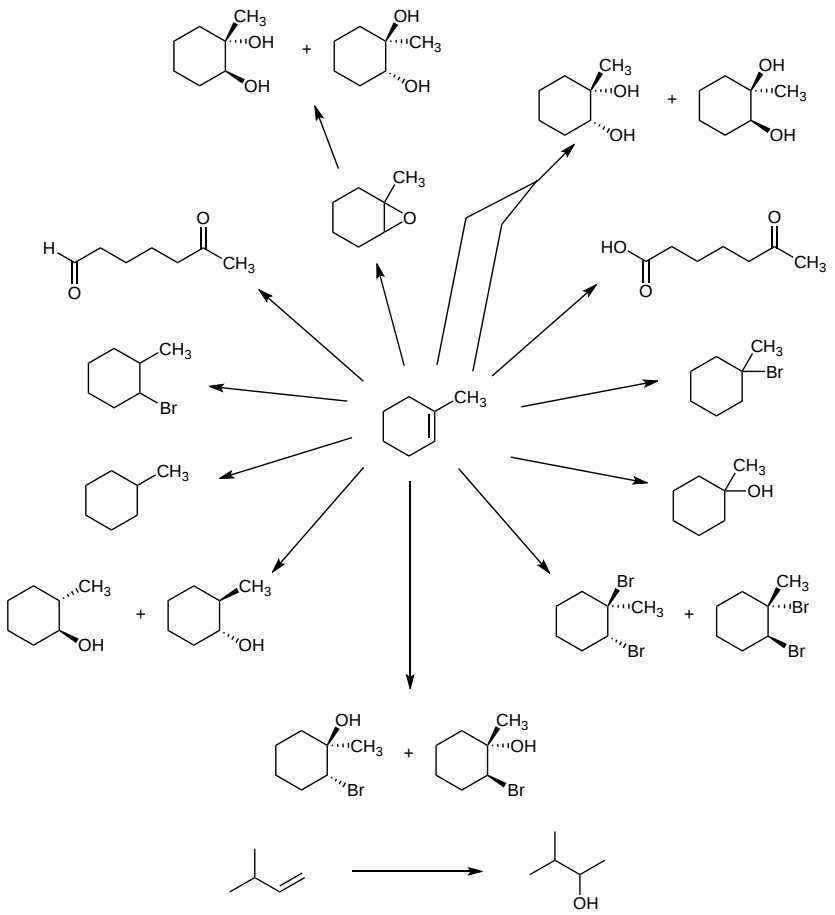
You should have noticed that some of the assigned problems have required that you string together a number of organic reactions to convert one organic compound to another when there is no single reaction to achieve this goal. Such a string of reactions is called an “organic synthesis.” One of the major objectives of this course is to assist you in designing such syntheses. To achieve this objective, you will need to have all of the reactions described in the course available in your memory. You will need to recall some reactions much more frequently than others, and the only way to master this objective is to practise. The examples given in this chapter will be relatively simple, but you will soon see that you can devise some quite sophisticated syntheses using a limited number of basic reactions.

Introduction

The study of organic chemistry introduces students to a wide range of interrelated reactions. Alkenes, for example, may be converted to structurally similar alkanes, alcohols, alkyl halides, epoxides, glycols and boranes; cleaved to smaller aldehydes, ketones and carboxylic acids; and enlarged by carbocation and radical additions as well as cycloadditions. Most of these reactions are shown in the Alkene Reaction Map below. All of these products may be subsequently transformed into a host of new compounds incorporating a wide variety of functional groups. Consequently, the logical conception of a multi-step synthesis for the construction of a designated compound from a specified starting material becomes one of the most challenging problems that may be posed. Functional group reaction maps like the one below for alkenes can be helpful in designing multi-step syntheses. It can be helpful to build and design your own reaction maps for each functional group studied.

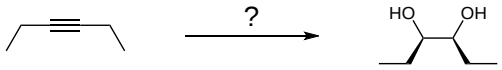
Alkene Reaction Map

Please note: The reagents for each chemical transformation have been intentionally omitted so that this map can be used as a study tool. The answers are provided at the end of this section as part of the exercises.

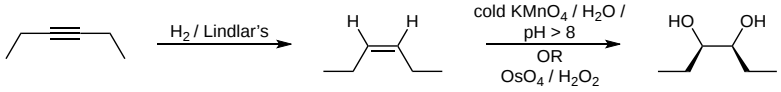


Simple Multi-Step Syntheses

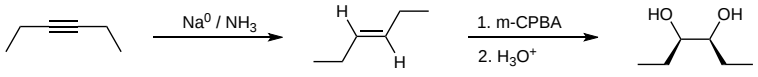
A one or two step sequence of simple reactions is not that difficult to deduce. For example, the synthesis of meso-3,4-hexanediol from 3-hexyne can occur by more than one multi-step pathway.



One approach would be to reduce the alkyne to cis or trans-3-hexene before undertaking glycol formation. Permanaganate or osmium tetroxide hydroxylation of cis-3-hexene would form the desired meso isomer.



From trans-3-hexene, it would be necessary to first epoxidize the alkene with a peracid followed by ring opening with acidic or basic hydrolysis.

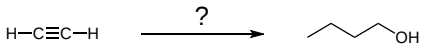


Longer multi-step syntheses require careful analysis and thought, since many options need to be considered. Like an expert chess player evaluating the long range pros and cons of potential moves, the chemist must appraise the potential success of various possible reaction paths, focusing on the scope and limitations constraining each of the individual reactions being employed. The skill is acquired by practice, experience, and often trial and error.

Thinking it Through with 3 Examples

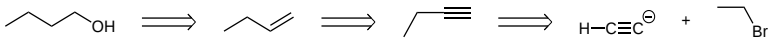
The following three examples illustrate strategies for developing multi-step syntheses from the reactions studied in the first ten chapters of this text. It is helpful to systematically look for structural changes beginning with the carbon chain and brainstorm relevant functional group conversion reactions. Retro-synthesis is the approach of working backwards from the product to the starting material.

In the first example, we are asked to synthesize 1-butanol from acetylene.

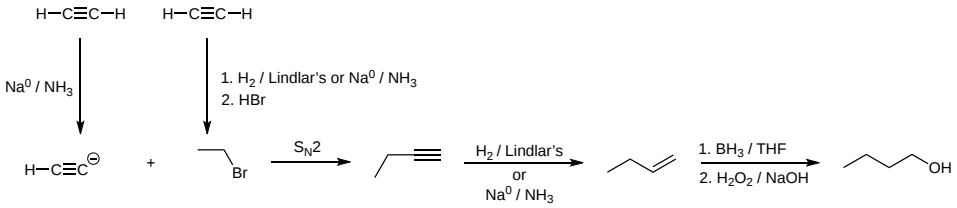


The carbon chain doubles in size indicating an acetylide S_N2 reaction with an alkyl halide. Primary alcohol formation from an anti-Markovnikov alkene hydration reaction (hydroboration-oxidation) is more likely than a substitution reaction. Applying retro-synthesis, we work backwards from the alcohol to the alkene to the alkyne from an acetylide reaction that initially builds the carbon chain.

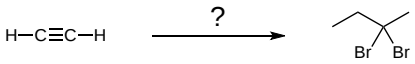
Retro-Synthesis



Working forwards, we specify the reagents needed for each transformation identified from the retro-synthesis. The ethylbromide must also be derived from acetylene so multiple reaction pathways are combined as shown below.

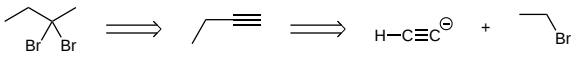


In the second example, we are asked to synthesize 1,2-dibromobutane from acetylene.

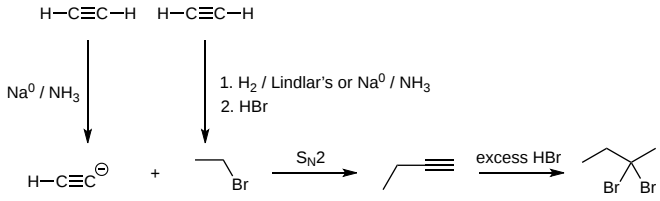


Once again there is an increase in the carbon chain length indicating an acetylide S_N2 reaction with an alkyl halide similar to the first example. The hydrohalogenation can be subtle to discern because the hydrogen atoms are not shown in bond-line structures. Comparing the chemical formulas of 1-butyne with 1,2-dibromobutane, there is a difference of two H atoms and two Br atoms indicating hydrohalogenation and not halogenation. The addition of both bromine atoms to the same carbon atom also supports the idea that hydrohalogenation occurs on an alkyne and not an alkene. The formation of the geminal dihalide also indicates hydrohalogenation instead of halogenation because halogenation produces vicinal dihalides. With this insight, the retro-synthesis indicates the following series of chemical transformations.

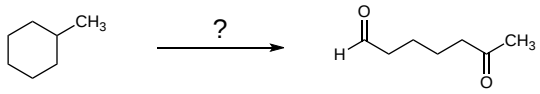
Retro-Synthesis



Working forwards, we specify the reagents needed for each transformation.

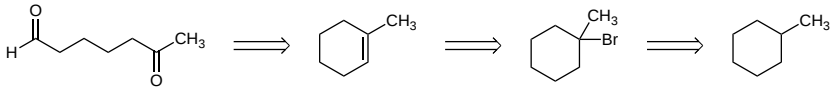


In the third example, we are asked to produce 6-oxoheptanal from methylcyclohexane.

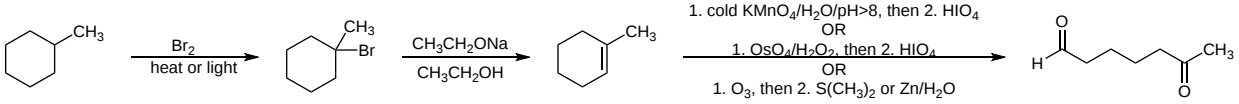


Counting the carbons, the starting material and product both contain seven carbon atoms and there is a cleavage reaction of an alkene under reductive conditions. One important missing aspect of this reaction is a good leaving group (LG). Alkanes are chemically quite boring. We can burn them as fuel or perform free-radical halogenation to create alkyl halides with excellent leaving groups. With these observations, the following retro-synthesis is reasonable.

Retro-Synthesis



Working forwards, we specify the reagents needed for each reaction. For the initial free-radical halogenation of the alkane, we have the option of chlorine (Cl_2) or bromine (Br_2). Because methylcyclohexane has several different classifications of carbons, the selectivity of Br_2 is more important than the faster reactivity of Cl_2. A strong base with heat can be used for the second step to follow an E2 mechanism and form 1-methylcyclohexene. The aldehyde group on the final product indicates gentle oxidative cleavage by any of several reaction pathways. These reactions can be combined in to the following multi-step synthesis.

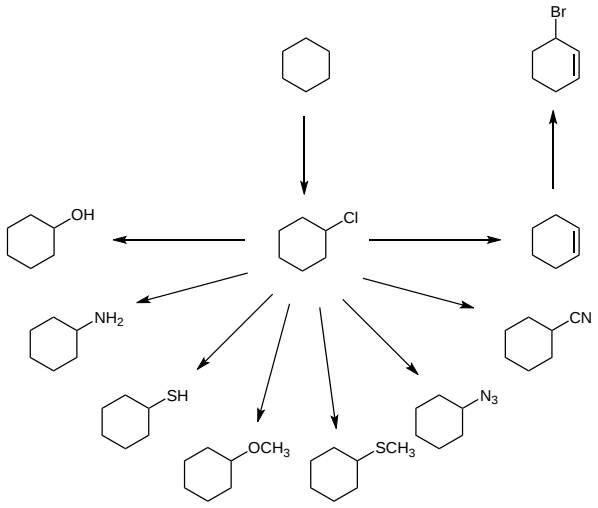


Reaction Maps to Build Functional Group Conversion Mastery

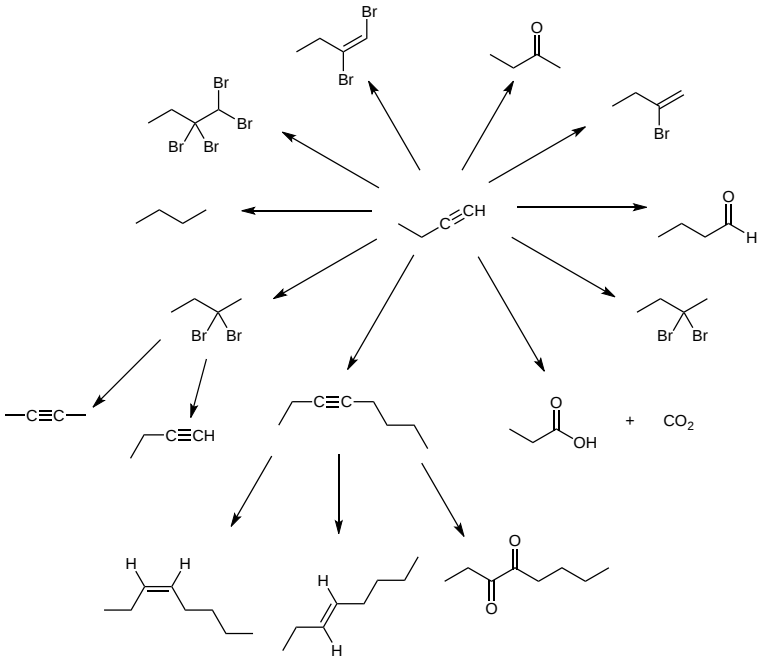
After working through the examples above, we can see how important it is to memorize all of the functional group reactions studied in the first ten chapters. We can apply the knowledge of these reactions to the wisdom of multi-step syntheses.

Please note: The reagents for each chemical transformation have been intentionally omitted so that these maps can be used as a study tools. The answers are provided at the end of this section as part of the exercises.

Alkane and Alkyl Halide Reaction Map



Alkyne Reaction Map



Exercise

1) Starting at 3-hexyne predict synthetic routes to achieve:

a) trans-3-hexene

b) 3,4-dibromohexane

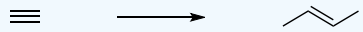
c) 3-hexanol.

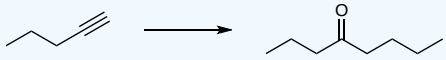
2) Starting with acetylene and any alkyl halides propose a synthesis to make

a) pentanal

b) hexane.

3) Show how you would accomplish the following synthetic transformations.

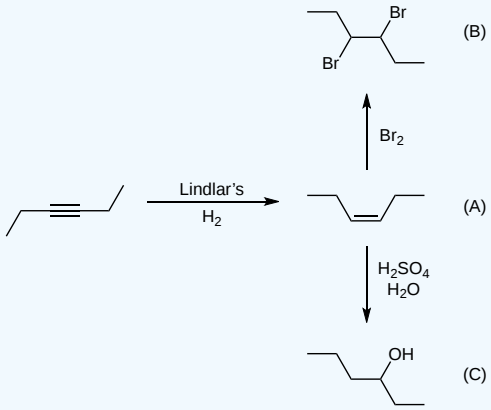
a) 

b) 

Answer

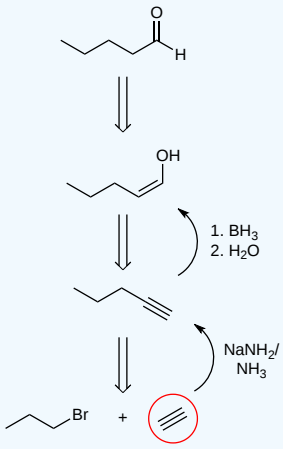
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1)

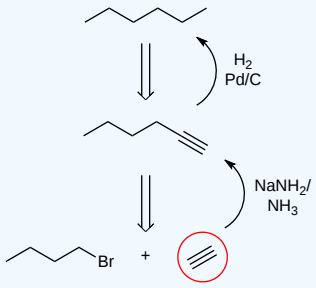


2)

a)

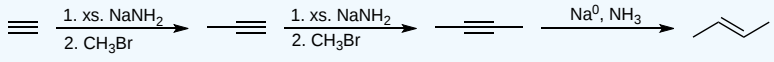


b)

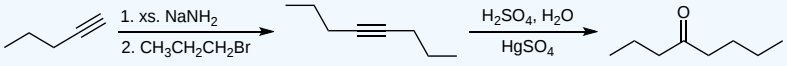


3)

a)



b)



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