CHEM106 INTRODUCTION TO ORGANIC CHEMISTRY



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CHEM106

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1: INTRODUCTION TO ORGANIC STRUCTURES AND FUNCTIONAL GROUPS

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1.1: What is organic chemistry?

Learning Objectives

- Recognize organic compounds from their formula.
- Understand some logical reason for why nature has selected C and H as the main constituent of organic compounds.

What are organic compounds?

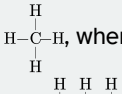
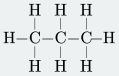
The compounds usually synthesized in living things are called organic compounds. The organic compounds are primarily composed of carbon (C) and hydrogen (H). For example, methane (CH_4) produced by decaying plant materials is composed of one C and four H's. Often one or more atoms of elements other than C and H are also present in organic compounds, like oxygen (O), nitrogen (N), phosphorous (P), sulfur (S), etc. For example, O atoms are present in glucose ($C_6H_{12}O_6$). The atoms other than C and H, e.g., O in $C_6H_{12}O_6$, are called **heteroatoms**. Figure 1.1.1 illustrates fruits and vegetables composed of organic compounds.

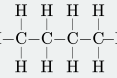
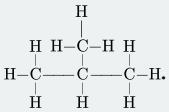


Figure 1.1.1: Fruits and vegetables comprise organic compounds. (Copyright; oy, CC BY 2.0, via Wikimedia Commons)

Why has nature chosen C and H as primary constituents of organic compounds?

Nature has chosen C and H as primary constituents composing the organic compounds because of several reasons, some of which are the following.

- C is a member of the second-row elements in the periodic table that usually make stronger and more stable bonds than the elements in the higher rows.
- C makes four bonds in neutral molecules, which is higher than any other element of the second row can make. For example, C has four bonds in a methane molecule represent as: , where each line represents a bond.
- C can make chains and rings, e.g., ethane: , and a propane:  are chains of two and three C's. The ability of C to make a chain of atoms is called **catenation**.

- A C atom can make bonds with more than two $\mathrm{C}'\mathrm{s}$ resulting in branched compounds that increases the number of compounds possible, e.g. four $\mathrm{C}'\mathrm{s}$ molecule can be in a straight chain as in n-butane:  or in a branched chain as in isobutane: .
- Two $\mathrm{C}'\mathrm{s}$ can make single, double, or triple bonds with each other, allowing more variations. For example, ethane () has all single bonds; ethene () as double bond; and acetylene ($\mathrm{H-C{\equiv}C-H}$) has a triple bond between $\mathrm{C}'\mathrm{s}$.
- H is the lightest monovalent atom that can occupy the valencies of C' not used in C to C bonds.
- H bonded with a strongly electronegative atom like O or N can interact with a O or N atom of a neighboring molecule through hydrogen bonding that plays a vital role in the functioning of organic molecules in living things.
- C or H in an organic compound can be replaced with a heteroatom that tremendously increases the variety of organic compounds available to living things.

Some other elements have the desired characteristics of C and H but are associated with significant disadvantages. For example, silicon (Si), like C, makes i) four bonds, ii) straight and branched chains, and iii) a single bond with hydrogen. The drawbacks of Si are i) it is two times heavier than C, ii) it makes weaker unstable $\mathrm{Si{-}Si}$, and $\mathrm{Si{-}H}$ bonds compared to $\mathrm{C{-}C}$ and $\mathrm{C{-}H}$ bonds, and iii) its oxidation product is solid silicon dioxide ($\mathrm{SiO_2}$) which is insoluble in water and would have been difficult to excrete than the gaseous $\mathrm{CO_2}$ from the C compounds which are easier to exhale. Similarly, halogens are monovalent like hydrogen, but halogens are significantly heavier than H and make weaker bonds with C than $\mathrm{C{-}H}$ bonds.

What is organic chemistry?

Organic chemistry is the study of the properties and reactions of organic compounds.

The following section describes chemical bonding that determines the compound's physical properties and chemical reactivity.

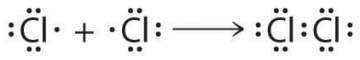
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1.2: Lewis Structures

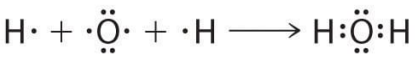
Using Lewis Dot Symbols to Describe Covalent Bonding

This sharing of electrons allowing atoms to "stick" together is the basis of covalent bonding. There is some intermediate distant, generally a bit longer than 0.1 nm, or if you prefer 100 pm, at which the attractive forces significantly outweigh the repulsive forces and a bond will be formed if both atoms can achieve a completen s^2np^6 configuration. It is this behavior that Lewis captured in his octet rule. The valence electron configurations of the constituent atoms of a covalent compound are important factors in determining its structure, stoichiometry, and properties. For example, chlorine, with seven valence electrons, is one electron short of an octet. If two chlorine atoms share their unpaired electrons by making a covalent bond and forming Cl_2, they can each complete their valence shell:



Each chlorine atom now has an octet. The electron pair being shared by the atoms is called a bonding pair A pair of electrons in a Lewis structure that is shared by two atoms, thus forming a covalent bond.; the other three pairs of electrons on each chlorine atom are called lone pairs A pair of electrons in a Lewis structure that is not involved in covalent bonding. Lone pairs are not involved in covalent bonding.

We can illustrate the formation of a water molecule from two hydrogen atoms and an oxygen atom using Lewis dot symbols:



The structure on the right is the *Lewis electron structure*, or *Lewis structure*, for H_2O. With two bonding pairs and two lone pairs, the oxygen atom has now completed its octet. Moreover, by sharing a bonding pair with oxygen, each hydrogen atom now has a full valence shell of two electrons. Chemists usually indicate a bonding pair by a single line, as shown here for our two examples:



The following procedure can be used to construct Lewis electron structures for more complex molecules and ions:

1. **Arrange the atoms to show specific connections.** When there is a central atom, it is usually the least electronegative element in the compound. Chemists usually list this central atom first in the chemical formula (as in CCl_4 and CO_3^{2-}, which both have C as the central atom), which is another clue to the compound's structure. Hydrogen and the halogens are almost always connected to only one other atom, so they are usually *terminal* rather than central.

Note the Pattern

The central atom is usually the least electronegative element in the molecule or ion; hydrogen and the halogens are usually terminal.

2. **Determine the total number of valence electrons in the molecule or ion.** Add together the valence electrons from each atom. (Recall that the number of valence electrons is indicated by the position of the element in the periodic table.) If the species is a polyatomic ion, remember to add or subtract the number of electrons necessary to give the total charge on the ion. For CO_3^{2-}, for example, we add two electrons to the total because of the –2 charge.

3. **Place a bonding pair of electrons between each pair of adjacent atoms to give a single bond.** In H_2O, for example, there is a bonding pair of electrons between oxygen and each hydrogen.

4. **Beginning with the terminal atoms, add enough electrons to each atom to give each atom an octet (two for hydrogen).**

These electrons will usually be lone pairs.

5. **If any electrons are left over, place them on the central atom.**

6. **If the central atom has fewer electrons than an octet, use lone pairs from terminal atoms to form multiple (double or triple) bonds to the central atom to achieve an octet.** This will not change the number of electrons on the terminal atoms.

Now let's apply this procedure to some particular compounds, beginning with one we have already discussed.

H_2O

1. Because H atoms are almost always terminal, the arrangement within the molecule must be HOH.

2. Each H atom (group 1) has 1 valence electron, and the O atom (group 16) has 6 valence electrons, for a total of 8 valence electrons.

3. Placing one bonding pair of electrons between the O atom and each H atom gives H:O:H, with 4 electrons left over.

4. Each H atom has a full valence shell of 2 electrons.

5. Adding the remaining 4 electrons to the oxygen (as two lone pairs) gives the following structure:



This is the Lewis structure we drew earlier. Because it gives oxygen an octet and each hydrogen two electrons, we do not need to use step 6.

OCl^-

1. With only two atoms in the molecule, there is no central atom.

2. Oxygen (group 16) has 6 valence electrons, and chlorine (group 17) has 7 valence electrons; we must add one more for the negative charge on the ion, giving a total of 14 valence electrons.

3. Placing a bonding pair of electrons between O and Cl gives O:Cl, with 12 electrons left over.

4. If we place six electrons (as three lone pairs) on each atom, we obtain the following structure:



Each atom now has an octet of electrons, so steps 5 and 6 are not needed. The Lewis electron structure is drawn within brackets as is customary for an ion, with the overall charge indicated outside the brackets, and the bonding pair of electrons is indicated by a solid line. OCl^- is the hypochlorite ion, the active ingredient in chlorine laundry bleach and swimming pool disinfectant.

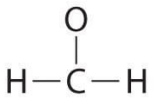
CH_2O

1. Because carbon is less electronegative than oxygen and hydrogen is normally terminal, C must be the central atom. One possible arrangement is as follows:



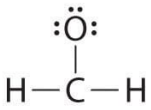
2. Each hydrogen atom (group 1) has one valence electron, carbon (group 14) has 4 valence electrons, and oxygen (group 16) has 6 valence electrons, for a total of [(2)(1) + 4 + 6] = 12 valence electrons.

3. Placing a bonding pair of electrons between each pair of bonded atoms gives the following:



Six electrons are used, and 6 are left over.

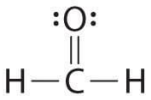
4. Adding all 6 remaining electrons to oxygen (as three lone pairs) gives the following:



Although oxygen now has an octet and each hydrogen has 2 electrons, carbon has only 6 electrons.

5. There are no electrons left to place on the central atom.

6. To give carbon an octet of electrons, we use one of the lone pairs of electrons on oxygen to form a carbon–oxygen double bond:



Both the oxygen and the carbon now have an octet of electrons, so this is an acceptable Lewis electron structure. The O has two bonding pairs and two lone pairs, and C has four bonding pairs. This is the structure of formaldehyde, which is used in embalming fluid.

An alternative structure can be drawn with one H bonded to O. *Formal charges*, discussed later in this section, suggest that such a structure is less stable than that shown previously.

Example

Write the Lewis electron structure for each species.

1. NCl_3
2. S_2^{2-}
3. NOCl

Given: chemical species

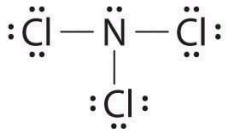
Asked for: Lewis electron structures

Strategy:

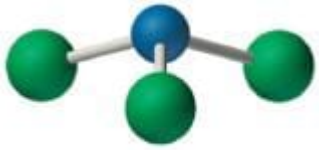
Use the six-step procedure to write the Lewis electron structure for each species.

Solution:

1. Nitrogen is less electronegative than chlorine, and halogen atoms are usually terminal, so nitrogen is the central atom. The nitrogen atom (group 15) has 5 valence electrons and each chlorine atom (group 17) has 7 valence electrons, for a total of 26 valence electrons. Using 2 electrons for each N–Cl bond and adding three lone pairs to each Cl account for (3 × 2) + (3 × 2 × 3) = 24 electrons. Rule 5 leads us to place the remaining 2 electrons on the central N:

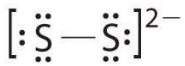


Nitrogen trichloride is an unstable oily liquid once used to bleach flour; this use is now prohibited in the United States.

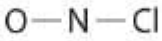


Nitrogen trichloride

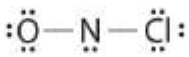
2. In a diatomic molecule or ion, we do not need to worry about a central atom. Each sulfur atom (group 16) contains 6 valence electrons, and we need to add 2 electrons for the –2 charge, giving a total of 14 valence electrons. Using 2 electrons for the S–S bond, we arrange the remaining 12 electrons as three lone pairs on each sulfur, giving each S atom an octet of electrons:



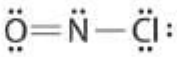
3. Because nitrogen is less electronegative than oxygen or chlorine, it is the central atom. The N atom (group 15) has 5 valence electrons, the O atom (group 16) has 6 valence electrons, and the Cl atom (group 17) has 7 valence electrons, giving a total of 18 valence electrons. Placing one bonding pair of electrons between each pair of bonded atoms uses 4 electrons and gives the following:



Adding three lone pairs each to oxygen and to chlorine uses 12 more electrons, leaving 2 electrons to place as a lone pair on nitrogen:



Because this Lewis structure has only 6 electrons around the central nitrogen, a lone pair of electrons on a terminal atom must be used to form a bonding pair. We could use a lone pair on either O or Cl. Because we have seen many structures in which O forms a double bond but none with a double bond to Cl, it is reasonable to select a lone pair from O to give the following:



All atoms now have octet configurations. This is the Lewis electron structure of nitrosyl chloride, a highly corrosive, reddish-orange gas.

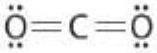


Nitrosyl chloride

Exercise

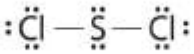
Write Lewis electron structures for CO_2 and SCl_2, a vile-smelling, unstable red liquid that is used in the manufacture of rubber.

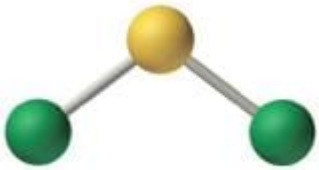
Answer:

1. 



Carbon dioxide

1. 



Sulfur dichloride

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1.3: Formal Charge

Formal Charges

It is sometimes possible to write more than one Lewis structure for a substance that does not violate the octet rule, as we saw for CH_2O, but not every Lewis structure may be equally reasonable. In these situations, we can choose the most stable Lewis structure by considering the formal charge. The difference between the number of valence electrons in a free atom and the number of electrons assigned to it in a particular Lewis electron structure. on the atoms, which is the difference between the number of valence electrons in the free atom and the number assigned to it in the Lewis electron structure. The formal charge is a way of computing the charge distribution within a Lewis structure; the sum of the formal charges on the atoms within a molecule or an ion must equal the overall charge on the molecule or ion. A formal charge does *not* represent a true charge on an atom in a covalent bond but is simply used to predict the most likely structure when a compound has more than one valid Lewis structure.

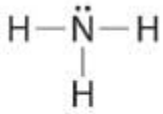
To calculate formal charges, we assign electrons in the molecule to individual atoms according to these rules:

- Nonbonding electrons are assigned to the atom on which they are located.
- Bonding electrons are divided equally between the bonded atoms.

For each atom, we then compute a formal charge:

$$formal\ charge = \underset{(free\ atom)}{valence\ e^-} - \underset{(atom\ in\ Lewis\ structure)}{\left(non-bonding\ e^- + \frac{bonding\ e^-}{2}\right)}$$

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



Ammonia

A neutral nitrogen atom has five valence electrons (it is in group 15). From its Lewis electron structure, the nitrogen atom in ammonia has one lone pair and shares three bonding pairs with hydrogen atoms, so nitrogen itself is assigned a total of five electrons [2 nonbonding e^- + (6 bonding e^-/2)]. Substituting into the equation, we obtain

$$formal\ \ charge\,(N) = 5\ \ valence\ \ e^- - \left(2\ non-bonding\ e^- + \frac{6\ bonding\ e^-}{2}\right) = 0$$

A neutral hydrogen atom has one valence electron. Each hydrogen atom in the molecule shares one pair of bonding electrons and is therefore assigned one electron [0 nonbonding e^- + (2 bonding e^-/2)]. Using the equation to calculate the formal charge on hydrogen, we obtain

$$formal\ \ charge\,(H) = 1\ \ valence\ \ e^- - \left(0\ non-bonding\ e^- + \frac{2\ bonding\ e^-}{2}\right) = 0$$

The hydrogen atoms in ammonia have the same number of electrons as neutral hydrogen atoms, and so their formal charge is also zero. Adding together the formal charges should give us the overall charge on 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 charge on the NH_3 molecule.

Typically, the structure with the most charges on the atoms closest to zero is the more stable Lewis structure. In cases where there are positive or negative formal charges on various atoms, 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.

Example

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

Given: chemical species

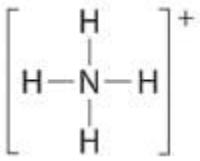
Asked for: formal charges

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 nonbonding electrons associated with each atom and then use the equation to calculate the formal charge on each atom.

Solution:

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



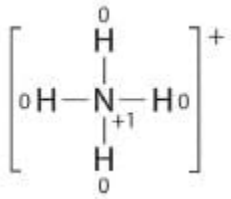
The nitrogen atom shares four bonding pairs of electrons, and a neutral nitrogen atom has five valence electrons. Using the equation the formal charge on the nitrogen atom is therefore

$$formal\ \ charge\,(N) = 5 - \left(0 + \frac{8}{2}\right) = 0$$

Each hydrogen atom in has one bonding pair. The formal charge on each hydrogen atom is therefore

$$formal\ \ charge\,(H) = 1 - \left(0 + \frac{2}{2}\right) = 0$$

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

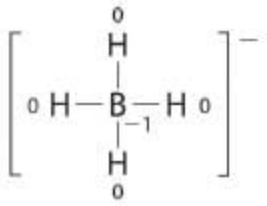


Adding together the formal charges on the atoms should give us the total charge on the molecule or ion. In this case, the sum of the formal charges is 0 + 1 + 0 + 0 + 0 = +1.

Exercise

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

Answer:



If an atom in a molecule or ion has the number of bonds that is typical for that atom (e.g., four bonds for carbon), its formal charge is zero.

Note the Pattern

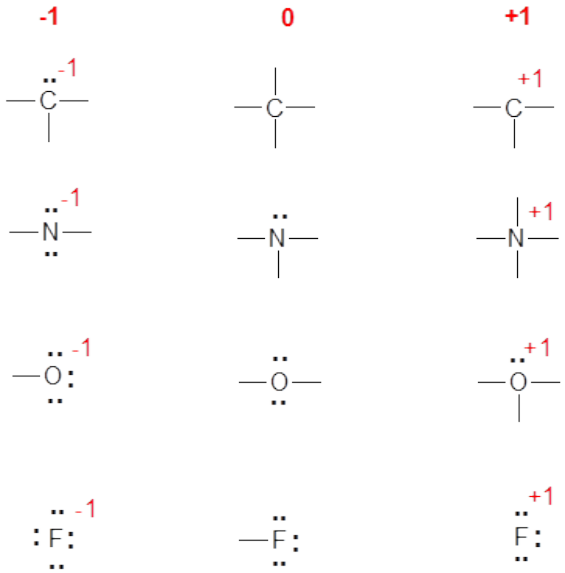
An atom, molecule, or ion has a formal charge of zero if it has the number of bonds that is typical for that species.

Intuitive Method

The intuitive method relies on experience and the understanding of common, known neutral structures. To do this you need to know the common bonding patterns for H, C, N, O, and the halides:

- H: 1 bond;
- C: 4 bonds;
- N: 3 bonds, 1 lone pair;
- O: 2 bonds, 2 lone pairs;
- F: 1 bond, 3 lone pairs (or any other halide).

Once mastered, this is much easier and quicker. The diagram below shows the common bonding situations for C, N, O, and F. The central column is the neutral atom, in the left most column the atom has gained an electron by having a bonding pair converted to a lone pair of electrons. The right most column has a formal charge of +1 due to either: a) using a lone pair of electrons as a bonding pair (N and O), b) losing a bonding pair of electrons (C), or c) losing a lone pair of electrons (F).



Example

Calculate the formal charges on each atom in the CO_3^- ion.

Given: chemical species

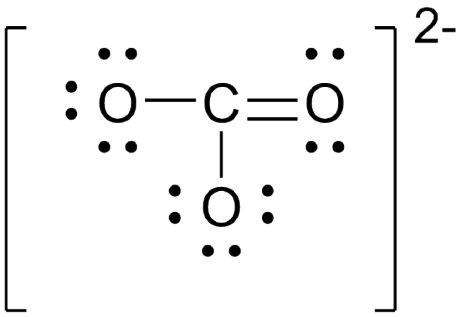
Asked for: formal charges

Strategy:

For each atom in the Lewis Structure compare the number of bonds and lone pair present to the number of each present in the known neutral structures and determine formal charges based on how they compare to those structures.

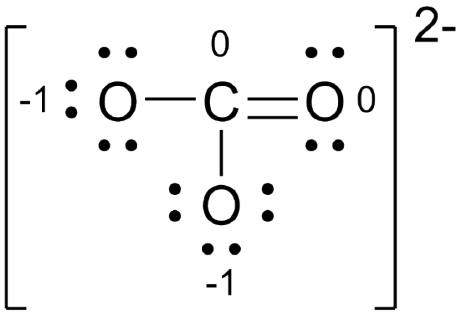
Solution:

The Lewis electron structure for the CO_3^- ion is as follows:



Starting with comparing oxygens to their known neutral structures. The left and bottom oxygens both have one bond and three lone pairs compared to the known neutral structure with two bonds and two lone pairs so the formal charges on both would be -1. For the oxygen on the right it has the same number of bonds and lone pairs as the known neutral structure so the formal charge would be 0. For the carbon it has four bonds and no lone pairs, which matches the known neutral structure and would also have a formal charge of 0.

The formal charges on the atoms in the CO_3^- 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 -1 + -1 + 0 + 0 = -2.

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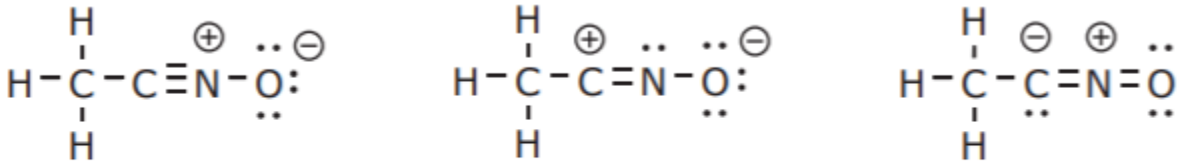
- Formal Charges by Richard Spinney is licensed CC BY-NC-SA 4.0. Original source: https://cbc-uged.asc.ohio-state.edu/.

1.4: Resonance Structures

RESONANCE STRUCTURES AND SOME LIMITATIONS OF LEWIS FORMULAS:

Lewis formulas are misleading in the sense that atoms and electrons are shown as being static. By being essentially two-dimensional representations they also fail to give an accurate idea of the three-dimensional features of the molecule, such as actual bond angles and topography of the molecular frame.

Furthermore, a given compound can have several valid Lewis formulas. For example CH_3CNO can be represented by at least three different but valid Lewis structures called **resonance forms, or resonance structures**, shown below.



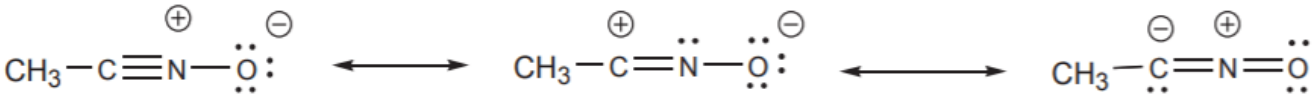
I II III

However, a stable compound such as the above does not exist in multiple states represented by structures I, or II, or III. The compound exists in a single state called a **hybrid** of all three structures. That is, it contains **contributions** of all three resonance forms, much like a person might have physical features inherited from each parent to varying degrees.

In the resonance forms shown above the atoms remain in one place. The basic bonding pattern, or **connectivity**, is the same in all structures, but some electrons have changed locations. This means that there are certain rules for electron mobility that enable us to "push" electrons around to arrive from one resonance structure to another. These rules will be examined in detail in a later paper.

ALL RESONANCE STRUCTURES MUST BE VALID LEWIS FORMULAS:

By convention, we use double-headed arrows to indicate that several resonance structures contribute to the same hybrid. Continuing with the example we've been using, the resonance structures for CH_3CNO should be written in this way if we want to emphasize that they represent the same hybrid.



I II III

Do not confuse double-headed arrows with double arrows. A double arrow indicates that two or more species are in equilibrium with each other and therefore have a separate existence. Double-headed arrows indicate resonance structures that do not exist by themselves. They simply represent features that the actual molecule, the hybrid, possesses to one extent or another.

When writing resonance structures keep in mind that THEY ALL MUST BE VALID LEWIS FORMULAS. The factors that make up valid Lewis formulas are as follows.

1. Observe the rules of covalent bonding, including common patterns as discussed previously. Make sure to show all single, double, and triple bonds.

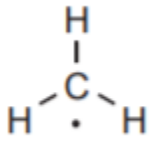
2. Account for the total number of valence electrons being shared (from all the elements), including bonding and nonbonding

electrons. Make sure to show these nonbonding electrons.

3. Account for the net charge of the molecule or species, showing formal charges where they belong.

4. Observe the octet rule as much as possible, but also understand that there are instances where some atoms may not fulfill this rule.

5. Avoid having unpaired electrons (single electrons with no partners) unless the total number of valence electrons for all elements is an odd number. This is not a very frequent occurrence, but the following example shows a species that could exist as a reaction intermediate in some high energy environments.

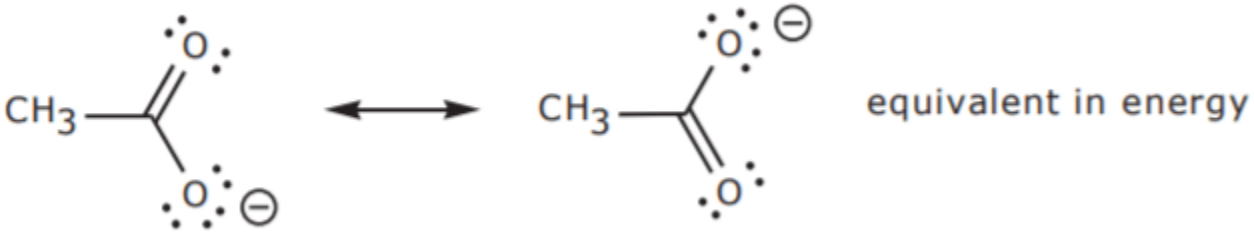


The total number of valence electrons being shared for all atoms is 4 from carbon and 3 from the three hydrogens, for a total of 7. Because it is an odd number, it is impossible to have all these electrons paired. Therefore the presence of a single electron cannot be avoided. Notice that there is no formal charge on carbon, since it has no surplus or deficit of valence electrons.

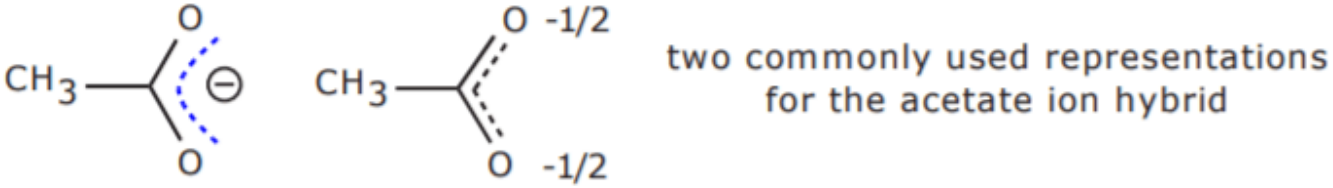
RELATIVE ENERGIES OF RESONANCE STRUCTURES.

From the examples given so far it can be seen that some resonance forms are structurally equivalent and others are not. **The potential energy associated with equivalent Lewis structures is the same**. If the Lewis structures are not equivalent, then the potential energy associated with them is most likely different. This means that equivalent resonance structures are also equivalent in stability and nonequivalent structures have different stabilities. This in turn means that equivalent structures contribute equally to the hybrid and nonequivalent structures do not contribute equally to the hybrid.

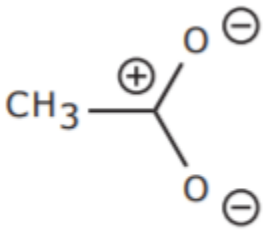
In the example below, the two structures are equivalent. Therefore they make equal contributions to the hybrid.



It is very difficult to accurately represent the hybrid with drawings because it is a composite of all the resonance contributors. Some representations such as the first one shown below are sometimes given. In this case the broken line represents the electrons and the negative charge which are spread over three atoms (O-C-O). Another commonly used representation of the hybrid is given on the right, showing that each oxygen atom shares a -1/2 charge. However, none of them accurately conveys the true picture. For convenience, the unshared electrons are sometimes omitted from some representations, just like it's done with hydrogen atoms. This must be kept in mind when examining the different structures.

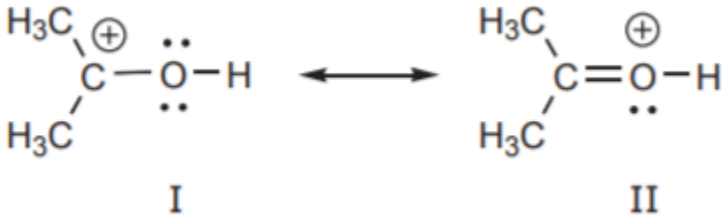


There is a third resonance form that can be drawn for the acetate ion hybrid. The structure shown below is structurally different from the ones shown above. This means that it is of different energy and therefore does not contribute to the hybrid to the same extent as the others. In this case, it happens to be less stable than the other two and therefore does not make a significant contribution to the hybrid.

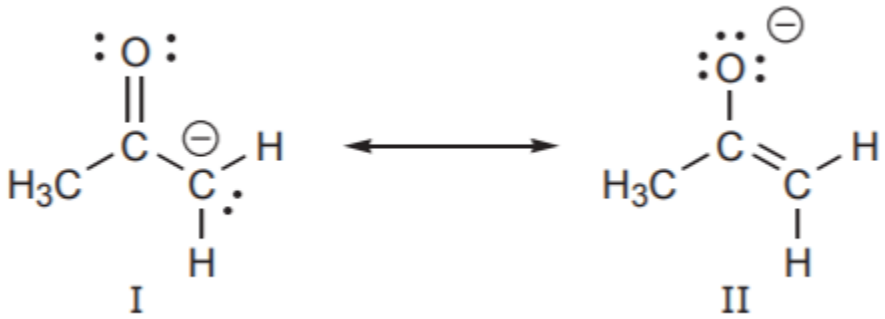


What factors dictate the relative stabilities of different resonance structures? **Charge separation** is an important one. In the example just given there are too many charges present in the structure (even though the net charge is still the same). This results in a structure with higher potential energy than others with fewer or no formal charges. This structure is less stable and its contribution to the hybrid is probably minor.

Another important factor that increases potential energy (lowers stability) is the presence of atoms with an **incomplete octet**. In the example below structure I has a carbon atom with a positive charge and therefore an incomplete octet. Based on this criterion, this structure is less stable than structure II and makes a less significant contribution to the hybrid.

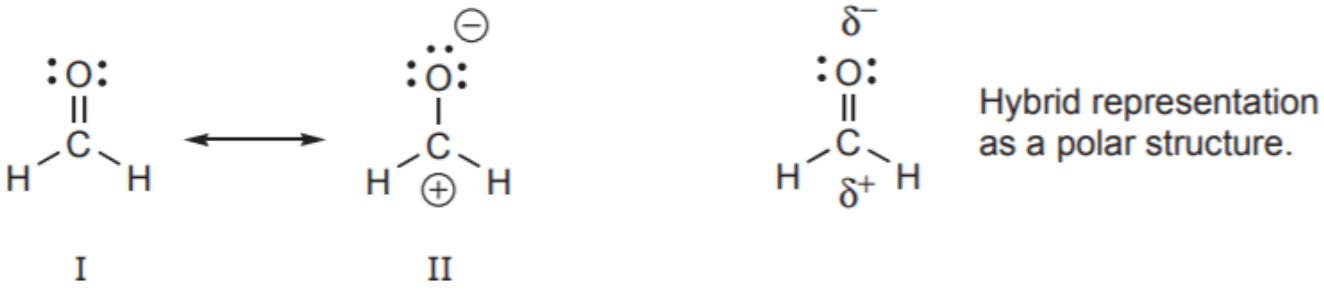


Finally, another factor that comes into play when determining the relative energies of resonance structures is the **relative electronegativities of atoms that bear charges.** More electronegative atoms are more comfortable with negative charges. Less electronegative atoms are more comfortable with positive charges. In the example below, structure I is less stable than II. The negative charge is on carbon, which is less electronegative than oxygen. Therefore structure II makes a larger contribution to the hybrid.

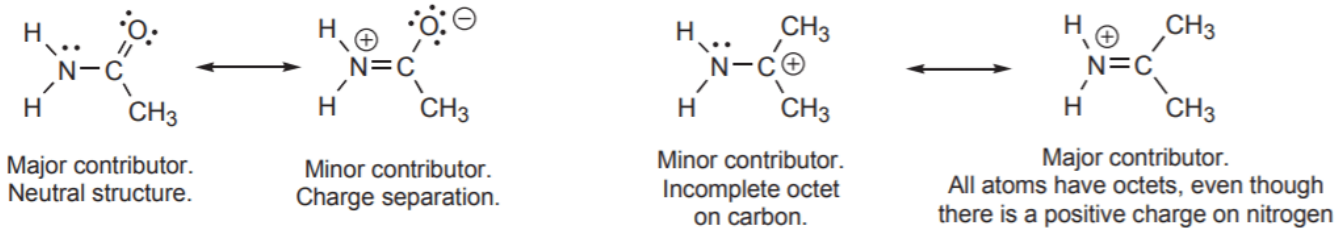


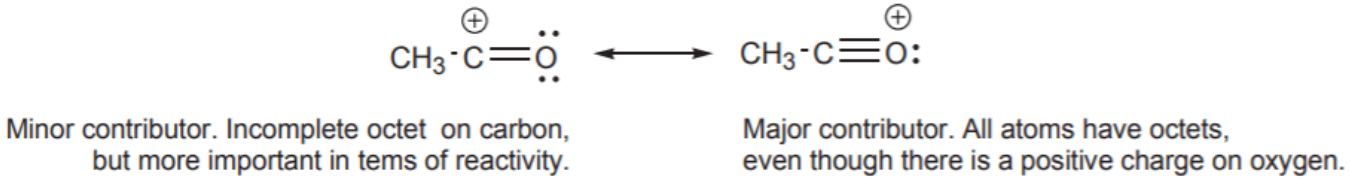
Some texts refer to the different contributors as “important” or “unimportant.” This can be misleading, because “importance” is context-dependent. In the example above, structure I is less important in terms of its contribution to the hybrid, but in terms of reactivity, it is very important. It will be seen later that this structure provides a better indication of how this species reacts with electrophiles in certain types of reactions.

Based on the charge separation criterion, structure II below might be labeled “unimportant,” or “less important” because it is less stable than I. But if we are trying to assess the polarity of this molecule, structure II becomes very important because it reveals that the carbon atom has positive character and the oxygen has negative character. The hybrid representation on the right then portrays the molecule as a polar molecule, which structure I alone does not give much indication of.



The following additional examples further illustrate the relative importance of the factors that contribute to structural energy and stability.

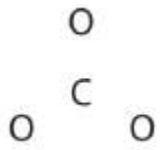




Example CO_3^{2-}

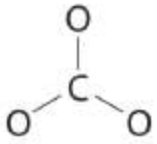
The electronic structure of the carbonate ion cannot be described by a single Lewis electron structure. Unlike O_3, though, the Lewis structures describing CO_3^{2-} has *three* equivalent representations.

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

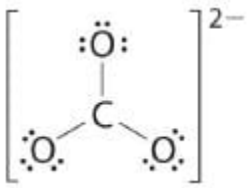


2. Carbon has 4 valence electrons, each oxygen has 6 valence electrons, and there are 2 more for the –2 charge. This gives 4 + (3 × 6) + 2 = 24 valence electrons.

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

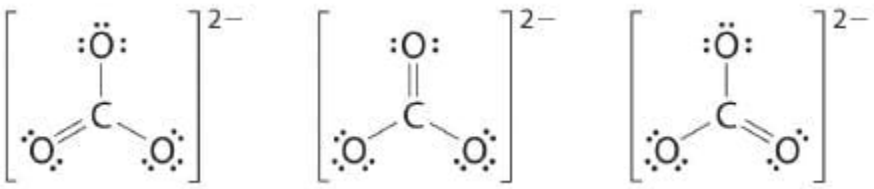


4. We divide the remaining 18 electrons equally among the three oxygen atoms by placing three lone pairs on each and indicating the –2 charge:

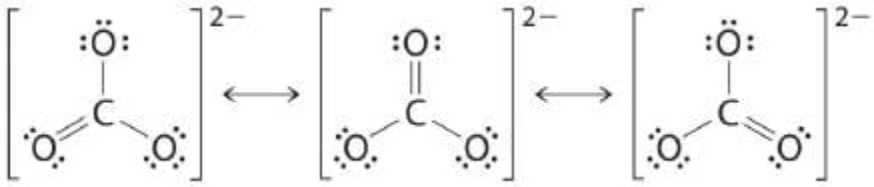


5. No electrons are left for the central atom.

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 ozone, 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 ozone, 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

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:

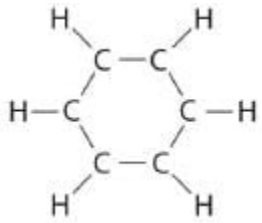
A Draw a structure for benzene illustrating the bonded atoms. Then calculate the number of valence electrons used in this drawing.

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.

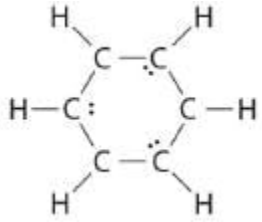
Solution:

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:



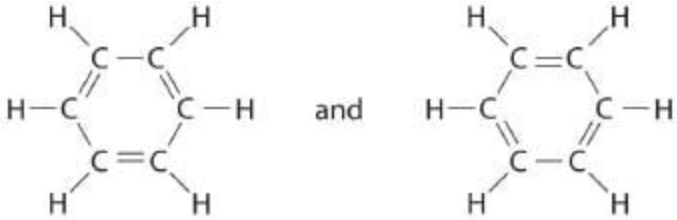
Each carbon atom in this structure has only 6 electrons and has a formal charge of +1, but we have used only 24 of the 30 valence electrons.

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

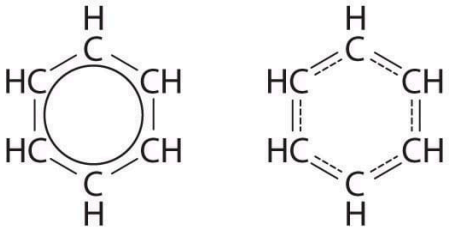


Three carbon atoms now have an octet configuration and a formal charge of –1, while three carbon atoms have only 6 electrons and a formal charge of +1. We can convert each lone pair to a bonding electron pair, which gives each atom an octet of electrons and a formal charge of 0, by making three C=C double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

Exercise

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

Answer:



Resonance structures are particularly common in oxoanions of the *p*-block elements, such as sulfate and phosphate, and in aromatic hydrocarbons, such as benzene and naphthalene.

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1.5: Using Formal Charge to Distinguish Between Lewis Structures

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.

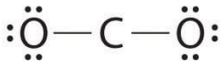
CO_2

1. C is less electronegative than O, 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 CO_2 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 Pattern

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

Example 5

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:

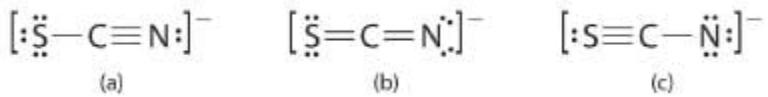
A Use the step-by-step procedure to write two plausible Lewis electron structures for SCN^-.

B Calculate the formal charge on each atom.

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:


(a) (b) (c)

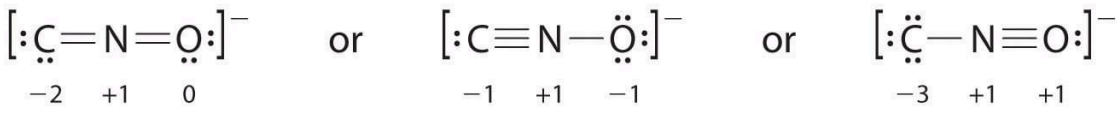
B We must calculate the formal charges on each atom to identify the more stable structure. If we begin with carbon, we notice that the carbon atom in each of these structures shares four bonding pairs, the number of bonds typical for carbon, so it has a formal charge of zero. Continuing with sulfur, 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 $6 - \left(6 + \frac{2}{2}\right) = -1.5 - \left(4 + \frac{4}{2}\right) = -1$ In (c), nitrogen 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

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:


−2 +1 0 or −1 +1 −1 or −3 +1 +1

The second structure is predicted to be more stable.

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1.6: Intermolecular forces

Learning Objective

- To describe the intermolecular forces in liquids.

The properties of liquids are intermediate between those of gases and solids but are more similar to solids. In contrast to *intra*molecular forces, such as the covalent bonds that hold atoms together in molecules and polyatomic ions, *inter*molecular forces hold molecules together in a liquid or solid. Intermolecular forces are generally much weaker than covalent bonds. For example, it requires 927 kJ to overcome the intramolecular forces and break both O–H bonds in 1 mol of water, but it takes only about 41 kJ to overcome the intermolecular attractions and convert 1 mol of liquid water to water vapor at 100°C. (Despite this seemingly low value, the intermolecular forces in liquid water are among the strongest such forces known!) Given the large difference in the strengths of intra- and intermolecular forces, changes between the solid, liquid, and gaseous states almost invariably occur for molecular substances *without breaking covalent bonds*.

Note the Pattern

The properties of liquids are intermediate between those of gases and solids but are more similar to solids.

Intermolecular forces determine bulk properties such as the melting points of solids and the boiling points of liquids. Liquids boil when the molecules have enough thermal energy to overcome the intermolecular attractive forces that hold them together, thereby forming bubbles of vapor within the liquid. Similarly, solids melt when the molecules acquire enough thermal energy to overcome the intermolecular forces that lock them into place in the solid.

Intermolecular forces are electrostatic in nature; that is, they arise from the interaction between positively and negatively charged species. Like covalent and ionic bonds, intermolecular interactions are the sum of both attractive and repulsive components. Because electrostatic interactions fall off rapidly with increasing distance between molecules, intermolecular interactions are most important for solids and liquids, where the molecules are close together. These interactions become important for gases only at very high pressures, where they are responsible for the observed deviations from the ideal gas law at high pressures.

In this section, we explicitly consider three kinds of intermolecular interactions:There are two additional types of electrostatic interaction that you are already familiar with: the ion–ion interactions that are responsible for ionic bonding and the ion–dipole interactions that occur when ionic substances dissolve in a polar substance such as water. The intermolecular forces between neutral molecules are *dipole–dipole interactions*, *London dispersion forces*, and *hydrogen bonds*. The first two are often described collectively as van der Waals forcesThe intermolecular forces known as dipole–dipole interactions and London dispersion forces..

Dipole–Dipole Interactions

Recall that polar covalent bonds behave as if the bonded atoms have localized fractional charges that are equal but opposite (i.e., the two bonded atoms generate a *dipole*). If the structure of a molecule is such that the individual bond dipoles do not cancel one another, then the molecule has a net dipole moment. Molecules with net dipole moments tend to align themselves so that the positive end of one dipole is near the negative end of another and vice versa, as shown in part (a) in Figure 12.7.1 . These arrangements are more stable than arrangements in which two positive or two negative ends are adjacent (part (c) in Figure 12.7.1). Hence dipole–dipole interactionsA kind of intermolecular interaction (force) that results between molecules with net dipole moments., such as those in part (b) in Figure 12.7.1 , are *attractive intermolecular interactions*, whereas those in part (d) in Figure 12.7.1 are *repulsive intermolecular interactions*. Because molecules in a liquid move freely and continuously, molecules always experience both attractive and repulsive dipole–dipole interactions simultaneously, as shown in Figure 12.7.2 . On average, however, the attractive interactions dominate.

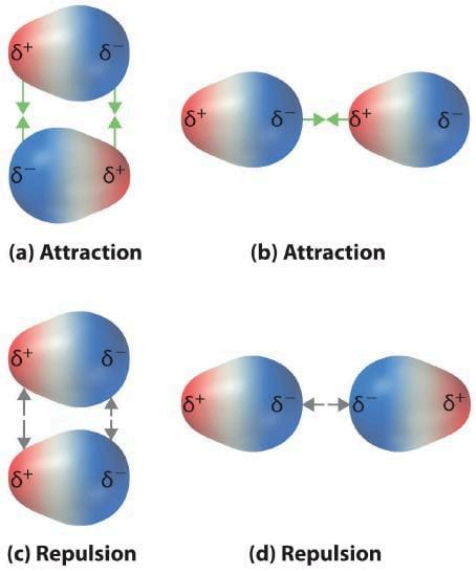


Figure 12.7.1 Attractive and Repulsive Dipole–Dipole Interactions *(a and b) Molecular orientations in which the positive end of one dipole (δ^+) is near the negative end of another (δ^-) (and vice versa) produce attractive interactions. (c and d) Molecular orientations that juxtapose the positive or negative ends of the dipoles on adjacent molecules produce repulsive interactions.*

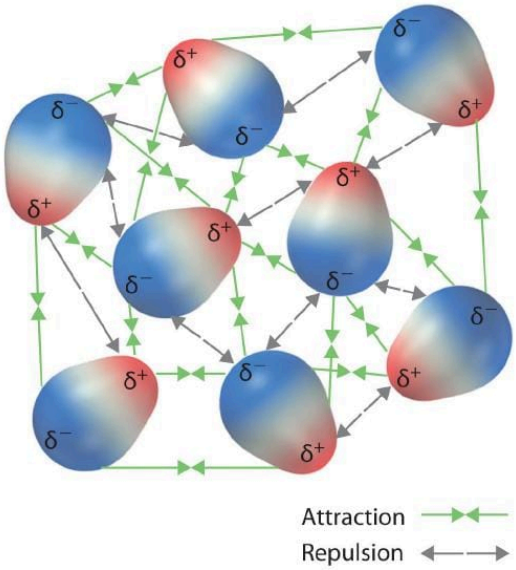


Figure 12.7.2 Both Attractive and Repulsive Dipole–Dipole Interactions Occur in a Liquid Sample with Many Molecules

Because each end of a dipole possesses only a fraction of the charge of an electron, dipole–dipole interactions are substantially weaker than the interactions between two ions, each of which has a charge of at least ±1, or between a dipole and an ion, in which one of the species has at least a full positive or negative charge. In addition, the attractive interaction between dipoles falls off much more rapidly with increasing distance than do ion–ion interactions. The attractive energy between two ions is proportional to $1/r$, where r is the distance between the ions. Doubling the distance ($r \rightarrow 2r$) decreases the attractive energy by one-half. In contrast, the energy of the interaction of two dipoles is proportional to $1/r^6$, so doubling the distance between the dipoles decreases the strength of the interaction by 2^6, or 64-fold. Thus a substance such as HCl, which is partially held together by dipole–dipole interactions, is a gas at room temperature and 1 atm pressure, whereas NaCl, which is held together by interionic interactions, is a high-melting-point solid. Within a series of compounds of similar molar mass, the strength of the intermolecular interactions increases as the dipole moment of the molecules increases, as shown in Table 12.7.1. Using what we learned previously about predicting relative bond polarities from the electronegativities of the bonded atoms, we can make educated guesses about the relative boiling points of similar molecules.

Table 12.7.1 Relationships between the Dipole Moment and the Boiling Point for Organic Compounds of Similar Molar Mass

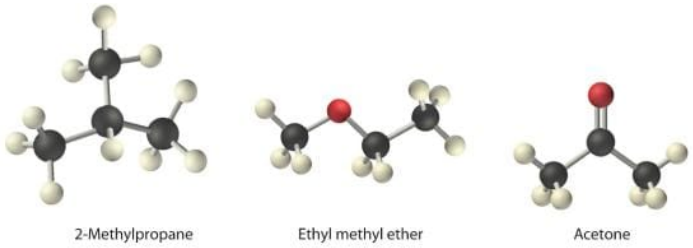
Compound	Molar Mass (g/mol)	Dipole Moment (D)	Boiling Point (K)
C_3H_6 (cyclopropane)	42	0	240
CH_3OCH_3 (dimethyl ether)	46	1.30	248
CH_3CN (acetonitrile)	41	3.9	355

Note the Pattern

The attractive energy between two ions is proportional to $1/r$, whereas the attractive energy between two dipoles is proportional to $1/r^6$.

Example 12.7.1

Arrange ethyl methyl ether ($CH_3OCH_2CH_3$), 2-methylpropane [isobutane, $(CH_3)_2CHCH_3$], and acetone (CH_3COCH_3) in order of increasing boiling points. Their structures are as follows:



Given: compounds

Asked for: order of increasing boiling points

Strategy:

Compare the molar masses and the polarities of the compounds. Compounds with higher molar masses and that are polar will have the highest boiling points.

Solution:

The three compounds have essentially the same molar mass (58–60 g/mol), so we must look at differences in polarity to predict the strength of the intermolecular dipole–dipole interactions and thus the boiling points of the compounds. The first compound, 2-methylpropane, contains only C–H bonds, which are not very polar because C and H have similar electronegativities. It should therefore have a very small (but nonzero) dipole moment and a very low boiling point. Ethyl methyl ether has a structure similar to H_2O; it contains two polar C–O single bonds oriented at about a 109° angle to each other, in addition to relatively nonpolar C–H bonds. As a result, the C–O bond dipoles partially reinforce one another and generate a significant dipole moment that should give a moderately high boiling point. Acetone contains a polar C=O double bond oriented at about 120° to two methyl groups with nonpolar C–H bonds. The C–O bond dipole therefore corresponds to the molecular dipole, which should result in both a rather large dipole moment and a high boiling point. Thus we predict the following order of boiling points: 2-methylpropane < ethyl methyl ether < acetone. This result is in good agreement with the actual data: 2-methylpropane, boiling point = –11.7°C, and the dipole moment (μ) = 0.13 D; methyl ethyl ether, boiling point = 7.4°C and μ = 1.17 D; acetone, boiling point = 56.1°C and μ = 2.88 D.

Exercise

Arrange carbon tetrafluoride (CF_4), ethyl methyl sulfide ($CH_3SC_2H_5$), dimethyl sulfoxide [$(CH_3)_2S{=}O$], and 2-methylbutane [isopentane, $(CH_3)_2CHCH_2CH_3$] in order of decreasing boiling points.

Answer: dimethyl sulfoxide (boiling point = 189.9°C) > ethyl methyl sulfide (boiling point = 67°C) > 2-methylbutane (boiling point = 27.8°C) > carbon tetrafluoride (boiling point = –128°C)

London Dispersion Forces

Thus far we have considered only interactions between polar molecules, but other factors must be considered to explain why many nonpolar molecules, such as bromine, benzene, and hexane, are liquids at room temperature, and others, such as iodine and naphthalene, are solids. Even the noble gases can be liquefied or solidified at low temperatures, high pressures, or both (Table 12.7.2)

What kind of attractive forces can exist between nonpolar molecules or atoms? This question was answered by Fritz London (1900–1954), a German physicist who later worked in the United States. In 1930, London proposed that temporary fluctuations in the electron distributions within atoms and nonpolar molecules could result in the formation of short-lived instantaneous dipole momentsThe short-lived dipole moment in atoms and nonpolar molecules caused by the constant motion of their electrons, which results in an asymmetrical distribution of charge at any given instant., which produce attractive forces called London dispersion forcesA kind of intermolecular interaction (force) that results from temporary fluctuations in the electron distribution within atoms and nonpolar molecules. between otherwise nonpolar substances.

Table 12.7.2 Normal Melting and Boiling Points of Some Elements and Nonpolar Compounds

Substance	Molar Mass (g/mol)	Melting Point (°C)	Boiling Point (°C)
Ar	40	–189.4	–185.9
Xe	131	–111.8	–108.1
N_2	28	–210	–195.8
O_2	32	–218.8	–183.0
F_2	38	–219.7	–188.1
I_2	254	113.7	184.4
CH_4	16	–182.5	–161.5

Consider a pair of adjacent He atoms, for example. On average, the two electrons in each He atom are uniformly distributed around the nucleus. Because the electrons are in constant motion, however, their distribution in one atom is likely to be asymmetrical at any given instant, resulting in an instantaneous dipole moment. As shown in part (a) in Figure 12.7.3, the instantaneous dipole moment on one atom can interact with the electrons in an adjacent atom, pulling them toward the positive end of the instantaneous dipole or repelling them from the negative end. The net effect is that the first atom causes the temporary formation of a dipole, called an induced dipoleA short-lived dipole moment that is created in atoms and nonpolar molecules adjacent to atoms or molecules with an instantaneous dipole moment., in the second. Interactions between these temporary dipoles cause atoms to be attracted to one another. These attractive interactions are weak and fall off rapidly with increasing distance. London was able to show with quantum mechanics that the attractive energy between molecules due to temporary dipole–induced dipole interactions falls off as $1/r^6$. Doubling the distance therefore decreases the attractive energy by 2^6, or 64-fold.

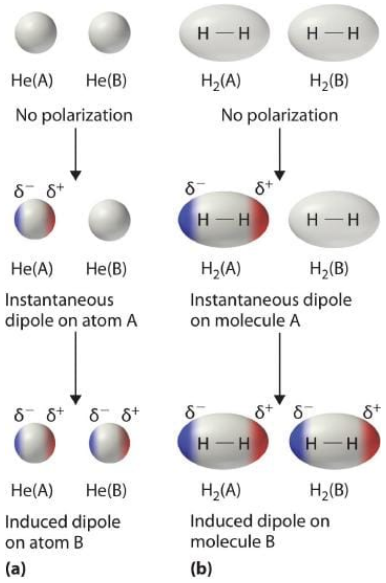


Figure 12.7.3 Instantaneous Dipole Moments *The formation of an instantaneous dipole moment on one He atom (a) or an H_2 molecule (b) results in the formation of an induced dipole on an adjacent atom or molecule.*

Instantaneous dipole–induced dipole interactions between nonpolar molecules can produce intermolecular attractions just as they produce interatomic attractions in monatomic substances like Xe. This effect, illustrated for two H_2 molecules in part (b) in Figure 12.7.3 tends to become more pronounced as atomic and molecular masses increase (Table 12.7.2). For example, Xe boils at −108.1°C, whereas He boils at −269°C. The reason for this trend is that the strength of London dispersion forces is related to the ease with which the electron distribution in a given atom can be perturbed. In small atoms such as He, the two 1s electrons are held close to the nucleus in a very small volume, and electron–electron repulsions are strong enough to prevent significant asymmetry in their distribution. In larger atoms such as Xe, however, the outer electrons are much less strongly attracted to the nucleus because of filled intervening shells. As a result, it is relatively easy to temporarily deform the electron distribution to generate an instantaneous or induced dipole. The ease of deformation of the electron distribution in an atom or molecule is called its polarizability. Because the electron distribution is more easily perturbed in large, heavy species than in small, light species, we say that heavier substances tend to be much more *polarizable* than lighter ones.

Note the Pattern

For similar substances, London dispersion forces get stronger with increasing molecular size.

The polarizability of a substance also determines how it interacts with ions and species that possess permanent dipoles. Thus London dispersion forces are responsible for the general trend toward higher boiling points with increased molecular mass and greater surface area in a homologous series of compounds, such as the alkanes (part (a) in Figure 12.7.4). The strengths of London dispersion forces also depend significantly on molecular shape because shape determines how much of one molecule can interact with its neighboring molecules at any given time. For example, part (b) in Figure 12.7.4 shows 2,2-dimethylpropane (neopentane) and *n*-pentane, both of which have the empirical formula C_5H_{12}. Neopentane is almost spherical, with a small surface area for intermolecular interactions, whereas *n*-pentane has an extended conformation that enables it to come into close contact with other *n*-pentane molecules. As a result, the boiling point of neopentane (9.5°C) is more than 25°C lower than the boiling point of *n*-pentane (36.1°C).

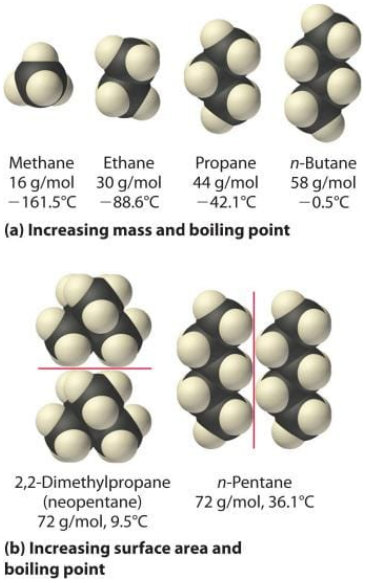


Figure 12.7.4 Mass and Surface Area Affect the Strength of London Dispersion Forces *(a) In this series of four simple alkanes, larger molecules have stronger London forces between them than smaller molecules and consequently higher boiling points. (b) Linear n-pentane molecules have a larger surface area and stronger intermolecular forces than spherical neopentane molecules. As a result, neopentane is a gas at room temperature, whereas n-pentane is a volatile liquid.*

All molecules, whether polar or nonpolar, are attracted to one another by London dispersion forces in addition to any other attractive forces that may be present. In general, however, dipole–dipole interactions in small polar molecules are significantly stronger than London dispersion forces, so the former predominate.

Example 12.7.2

Arrange *n*-butane, propane, 2-methylpropane [isobutene, $(CH_3)_2CHCH_3$], and *n*-pentane in order of increasing boiling points.

Given: compounds

Asked for: order of increasing boiling points

Strategy:

Determine the intermolecular forces in the compounds and then arrange the compounds according to the strength of those forces. The substance with the weakest forces will have the lowest boiling point.

Solution:

The four compounds are alkanes and nonpolar, so London dispersion forces are the only important intermolecular forces. These forces are generally stronger with increasing molecular mass, so propane should have the lowest boiling point and *n*-pentane should have the highest, with the two butane isomers falling in between. Of the two butane isomers, 2-methylpropane is more compact, and *n*-butane has the more extended shape. Consequently, we expect intermolecular interactions for *n*-butane to be stronger due to its larger surface area, resulting in a higher boiling point. The overall order is thus as follows, with actual boiling points in parentheses: propane (–42.1°C) < 2-methylpropane (–11.7°C) < *n*-butane (–0.5°C) < *n*-pentane (36.1°C).

Exercise

Arrange GeH_4, $SiCl_4$, SiH_4, CH_4, and $GeCl_4$ in order of decreasing boiling points.

Answer: $GeCl_4$ (87°C) > $SiCl_4$ (57.6°C) > GeH_4 (–88.5°C) > SiH_4 (–111.8°C) > CH_4 (–161°C)

Hydrogen Bonds

Molecules with hydrogen atoms bonded to electronegative atoms such as O, N, and F (and to a much lesser extent Cl and S) tend to exhibit unusually strong intermolecular interactions. These result in much higher boiling points than are observed for substances in which London dispersion forces dominate, as illustrated for the covalent hydrides of elements of groups 14–17 in Figure 12.7.5 . Methane and its heavier congeners in group 14 form a series whose boiling points increase smoothly with increasing molar mass. This is the expected trend in nonpolar molecules, for which London dispersion forces are the exclusive intermolecular forces. In contrast, the hydrides of the lightest members of groups 15–17 have boiling points that are more than 100°C greater than predicted on the basis of their molar masses. The effect is most dramatic for water: if we extend the straight line connecting the points for H_2Te and H_2Se to the line for period 2, we obtain an estimated boiling point of –130°C for water! Imagine the implications for life on Earth if water boiled at –130°C rather than 100°C.

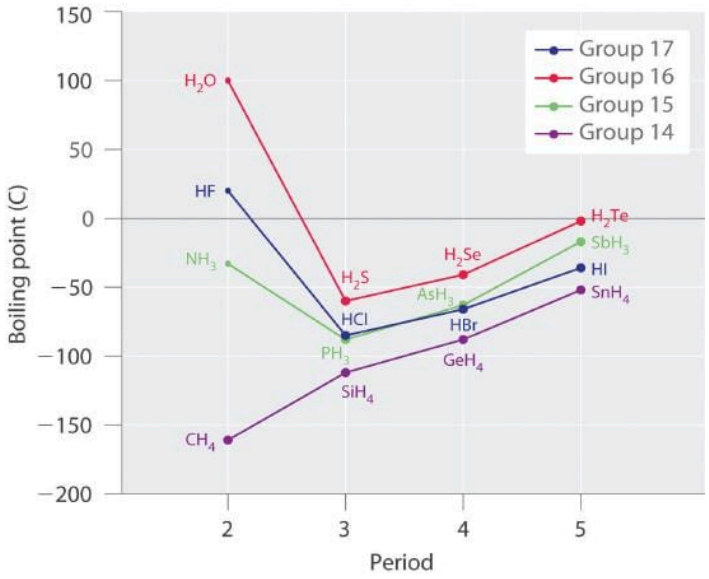


Figure 12.7.5 The Effects of Hydrogen Bonding on Boiling Points *These plots of the boiling points of the covalent hydrides of the elements of groups 14–17 show that the boiling points of the lightest members of each series for which hydrogen bonding is possible (HF, NH_3, and H_2O) are anomalously high for compounds with such low molecular masses.*

Why do strong intermolecular forces produce such anomalously high boiling points and other unusual properties, such as high enthalpies of vaporization and high melting points? The answer lies in the highly polar nature of the bonds between hydrogen and very electronegative elements such as O, N, and F. The large difference in electronegativity results in a large partial positive charge on hydrogen and a correspondingly large partial negative charge on the O, N, or F atom. Consequently, H–O, H–N, and H–F bonds have very large bond dipoles that can interact strongly with one another. Because a hydrogen atom is so small, these dipoles can also approach one another more closely than most other dipoles. The combination of large bond dipoles and short dipole–dipole distances results in very strong dipole–dipole interactions called hydrogen bondsAn unusually strong dipole-dipole interaction (intermolecular force) that results when hydrogen is bonded to very electronegative elements, such as O, N, and F., as shown for ice in Figure 12.7.6 . A hydrogen bond is usually indicated by a dotted line between the hydrogen atom attached to O, N, or F (the *hydrogen bond donor*) and the atom that has the lone pair of electrons (the *hydrogen bond acceptor*). Because each water molecule contains two hydrogen atoms and two lone pairs, a tetrahedral arrangement maximizes the number of hydrogen bonds that can be formed. In the structure of ice, each oxygen atom is surrounded by a distorted tetrahedron of hydrogen atoms that form bridges to the oxygen atoms of adjacent water molecules. The bridging hydrogen atoms are *not* equidistant from the two oxygen atoms they connect, however. Instead, each hydrogen atom is 101 pm from one oxygen and 174 pm from the other. In contrast, each oxygen atom is bonded to two H atoms at the shorter distance and two at the longer distance, corresponding to two O–H covalent bonds and two O · H hydrogen bonds from adjacent water molecules, respectively. The resulting open, cagelike structure of ice means that the solid is actually slightly less dense than the liquid, which explains why ice floats on water rather than sinks. Remember that the hydrogens in one water molecule point towards one of the lone pairs of tetrahedal sp^3 orbitals of the oxygen atom on another water molecule.

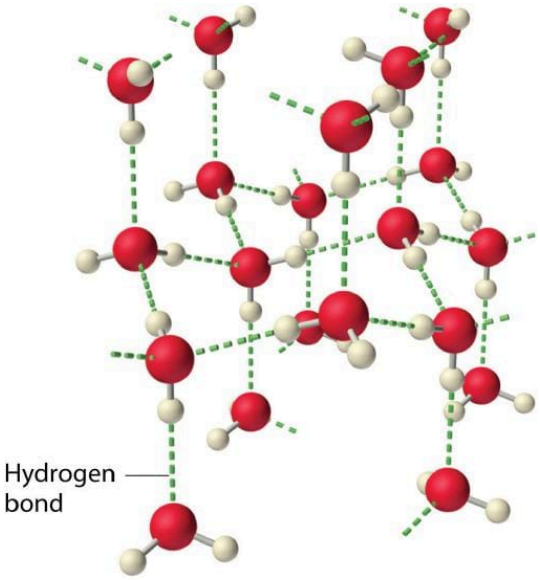


Figure 12.7.6 The Hydrogen-Bonded Structure of Ice *Each water molecule accepts two hydrogen bonds from two other water molecules and donates two hydrogen atoms to form hydrogen bonds with two more water molecules, producing an open, cagelike structure. The structure of liquid water is very similar, but in the liquid, the hydrogen bonds are continually broken and formed because of rapid molecular motion.*

Note the Pattern

Hydrogen bond formation requires *both* a hydrogen bond donor *and* a hydrogen bond acceptor.

Because ice is less dense than liquid water, rivers, lakes, and oceans freeze from the top down. In fact, the ice forms a protective surface layer that insulates the rest of the water, allowing fish and other organisms to survive in the lower levels of a frozen lake or sea. If ice were denser than the liquid, the ice formed at the surface in cold weather would sink as fast as it formed. Bodies of water would freeze from the bottom up, which would be lethal for most aquatic creatures. The expansion of water when freezing also explains why automobile or boat engines must be protected by “antifreeze” and why unprotected pipes in houses break if they are allowed to freeze.

Although hydrogen bonds are significantly weaker than covalent bonds, with typical dissociation energies of only 15–25 kJ/mol, they have a significant influence on the physical properties of a compound. Compounds such as HF can form only two hydrogen bonds at a time as can, on average, pure liquid NH_3. Consequently, even though their molecular masses are similar to that of water, their boiling points are significantly lower than the boiling point of water, which forms *four* hydrogen bonds at a time.

Example 12.7.3

Considering CH_3OH, C_2H_6, Xe, and $(CH_3)_3N$, which can form hydrogen bonds with themselves? Draw the hydrogen-bonded structures.

Given: compounds

Asked for: formation of hydrogen bonds and structure

Strategy:

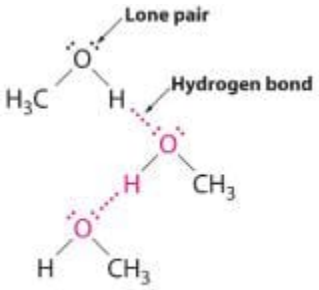
A Identify the compounds with a hydrogen atom attached to O, N, or F. These are likely to be able to act as hydrogen bond donors.

B Of the compounds that can act as hydrogen bond donors, identify those that also contain lone pairs of electrons, which allow them to be hydrogen bond acceptors. If a substance is both a hydrogen donor and a hydrogen bond acceptor, draw a structure showing the hydrogen bonding.

Solution:

A Of the species listed, xenon (Xe), ethane (C_2H_6), and trimethylamine [$(CH_3)_3N$] do not contain a hydrogen atom attached to O, N, or F; hence they cannot act as hydrogen bond donors.

B The one compound that can act as a hydrogen bond donor, methanol (CH_3OH), contains both a hydrogen atom attached to O (making it a hydrogen bond donor) and two lone pairs of electrons on O (making it a hydrogen bond acceptor); methanol can thus form hydrogen bonds by acting as either a hydrogen bond donor or a hydrogen bond acceptor. The hydrogen-bonded structure of methanol is as follows:

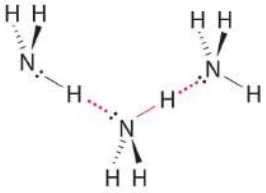


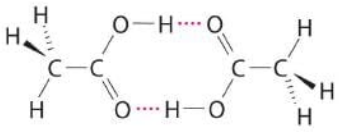
Hydrogen bonding in methanol

Exercise

Considering CH_3CO_2H, $(CH_3)_3N$, NH_3, and CH_3F, which can form hydrogen bonds with themselves? Draw the hydrogen-bonded structures.

Answer: CH_3CO_2H and NH_3;


Hydrogen bonding in ammonia


Hydrogen bonding in acetic acid

Example 12.7.4

Arrange C_{60} (buckminsterfullerene, which has a cage structure), NaCl, He, Ar, and N_2O in order of increasing boiling points.

Given: compounds

Asked for: order of increasing boiling points

Strategy:

Identify the intermolecular forces in each compound and then arrange the compounds according to the strength of those forces. The substance with the weakest forces will have the lowest boiling point.

Solution:

Electrostatic interactions are strongest for an ionic compound, so we expect NaCl to have the highest boiling point. To predict the relative boiling points of the other compounds, we must consider their polarity (for dipole–dipole interactions), their ability to form hydrogen bonds, and their molar mass (for London dispersion forces). Helium is nonpolar and by far the lightest, so it should have the lowest boiling point. Argon and N_2O have very similar molar masses (40 and 44 g/mol, respectively), but N_2O is polar while Ar is not. Consequently, N_2O should have a higher boiling point. A C_{60} molecule is nonpolar, but its molar mass is 720 g/mol, much greater than that of Ar or N_2O. Because the boiling points of nonpolar substances increase rapidly with molecular

mass, C_{60} should boil at a higher temperature than the other nonionic substances. The predicted order is thus as follows, with actual boiling points in parentheses: He (–269°C) < Ar (–185.7°C) < N_2O (–88.5°C) < C_{60} (>280°C) < NaCl (1465°C).

Exercise

Arrange 2,4-dimethylheptane, Ne, CS_2, Cl_2, and KBr in order of decreasing boiling points.

Answer: KBr (1435°C) > 2,4-dimethylheptane (132.9°C) > CS_2 (46.6°C) > Cl_2 (–34.6°C) > Ne (–246°C)

Summary

Molecules in liquids are held to other molecules by intermolecular interactions, which are weaker than the intramolecular interactions that hold the atoms together within molecules and polyatomic ions. Transitions between the solid and liquid or the liquid and gas phases are due to changes in intermolecular interactions but do not affect intramolecular interactions. The three major types of intermolecular interactions are dipole–dipole interactions, London dispersion forces (these two are often referred to collectively as **van der Waals forces**), and hydrogen bonds. **Dipole–dipole interactions** arise from the electrostatic interactions of the positive and negative ends of molecules with permanent dipole moments; their strength is proportional to the magnitude of the dipole moment and to $1/r^6$, where r is the distance between dipoles. **London dispersion forces** are due to the formation of **instantaneous dipole moments** in polar or nonpolar molecules as a result of short-lived fluctuations of electron charge distribution, which in turn cause the temporary formation of an **induced dipole** in adjacent molecules. Like dipole–dipole interactions, their energy falls off as $1/r^6$. Larger atoms tend to be more **polarizable** than smaller ones because their outer electrons are less tightly bound and are therefore more easily perturbed. **Hydrogen bonds** are especially strong dipole–dipole interactions between molecules that have hydrogen bonded to a highly electronegative atom, such as O, N, or F. The resulting partially positively charged H atom on one molecule (the *hydrogen bond donor*) can interact strongly with a lone pair of electrons of a partially negatively charged O, N, or F atom on adjacent molecules (the *hydrogen bond acceptor*). Because of strong O · H> hydrogen bonding between water molecules, water has an unusually high boiling point, and ice has an open, cagelike structure that is less dense than liquid water.

Key Takeaway

- Intermolecular forces are electrostatic in nature and include van der Waals forces and hydrogen bonds.

Conceptual Problems

1. What is the main difference between intramolecular interactions and intermolecular interactions? Which is typically stronger? How are changes of state affected by these different kinds of interactions?

2. Describe the three major kinds of intermolecular interactions discussed in this chapter and their major features. The hydrogen bond is actually an example of one of the other two types of interaction. Identify the kind of interaction that includes hydrogen bonds and explain why hydrogen bonds fall into this category.

3. Which are stronger—dipole–dipole interactions or London dispersion forces? Which are likely to be more important in a molecule with heavy atoms? Explain your answers.

4. Explain why hydrogen bonds are unusually strong compared to other dipole–dipole interactions. How does the strength of hydrogen bonds compare with the strength of covalent bonds?

5. Liquid water is essential for life as we know it, but based on its molecular mass, water should be a gas under standard conditions. Why is water a liquid rather than a gas under standard conditions?

6. Describe the effect of polarity, molecular mass, and hydrogen bonding on the melting point and boiling point of a substance.

7. Why are intermolecular interactions more important for liquids and solids than for gases? Under what conditions must these interactions be considered for gases?

8. Using acetic acid as an example, illustrate both attractive and repulsive intermolecular interactions. How does the boiling point of a substance depend on the magnitude of the repulsive intermolecular interactions?

9. In group 17, elemental fluorine and chlorine are gases, whereas bromine is a liquid and iodine is a solid. Why?

10. The boiling points of the anhydrous hydrogen halides are as follows: HF, 19°C; HCl, −85°C; HBr, −67°C; and HI, −34°C. Explain any trends in the data, as well as any deviations from that trend.

11. Identify the most important intermolecular interaction in each of the following.

    1. SO_2
    2. HF
    3. CO_2
    4. CCl_4
    5. CH_2Cl_2

12. Identify the most important intermolecular interaction in each of the following.

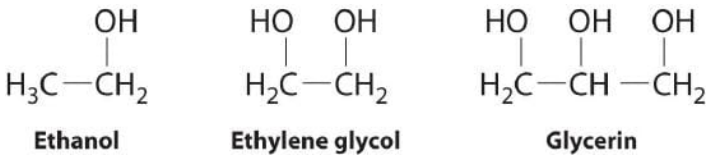
    1. LiF
    2. I_2
    3. ICl
    4. NH_3
    5. NH_2Cl

13. Would you expect London dispersion forces to be more important for Xe or Ne? Why? (The atomic radius of Ne is 38 pm, whereas that of Xe is 108 pm.)

14. Arrange Kr, Cl_2, H_2, N_2, Ne, and O_2 in order of increasing polarizability. Explain your reasoning.

15. Both water and methanol have anomalously high boiling points due to hydrogen bonding, but the boiling point of water is greater than that of methanol despite its lower molecular mass. Why? Draw the structures of these two compounds, including any lone pairs, and indicate potential hydrogen bonds.

16. The structures of ethanol, ethylene glycol, and glycerin are as follows:



Ethanol **Ethylene glycol** **Glycerin**

    Arrange these compounds in order of increasing boiling point. Explain your rationale.

17. Do you expect the boiling point of H_2S to be higher or lower than that of H_2O? Justify your answer.

18. Ammonia (NH_3), methylamine (CH_3NH_2), and ethylamine ($CH_3CH_2NH_2$) are gases at room temperature, while propylamine ($CH_3CH_2CH_2NH_2$) is a liquid at room temperature. Explain these observations.

19. Why is it not advisable to freeze a sealed glass bottle that is completely filled with water? Use both macroscopic and microscopic models to explain your answer. Is a similar consideration required for a bottle containing pure ethanol? Why or why not?

20. Which compound in the following pairs will have the higher boiling point? Explain your reasoning.

    1. NH_3 or PH_3
    2. ethylene glycol ($HOCH_2CH_2OH$) or ethanol
    3. 2,2-dimethylpropanol [$CH_3C(CH_3)_2CH_2OH$] or *n*-butanol ($CH_3CH_2CH_2CH_2OH$)

21. Some recipes call for vigorous boiling, while others call for gentle simmering. What is the difference in the temperature of the cooking liquid between boiling and simmering? What is the difference in energy input?

22. Use the melting of a metal such as lead to explain the process of melting in terms of what is happening at the molecular level.

As a piece of lead melts, the temperature of the metal remains constant, even though energy is being added continuously. Why?

23. How does the O–H distance in a hydrogen bond in liquid water compare with the O–H distance in the covalent O–H bond in the H_2O molecule? What effect does this have on the structure and density of ice?

24. 1. Explain why the hydrogen bonds in liquid HF are stronger than the corresponding intermolecular <math display="inline" xml:id="av_1.0-ch11_m0003"><semantics><mrow><mtext>H</mtext><mo>⋅</mo><mo>⋅</mo><mo>⋅</mo><mtext>I</
    interactions in liquid HI.
    2. In which substance are the individual hydrogen bonds stronger: HF or H_2O? Explain your reasoning.
    3. For which substance will hydrogen bonding have the greater effect on the boiling point: HF or H_2O? Explain your reasoning.

Answers

1.
2.
3.
4.

5. Water is a liquid under standard conditions because of its unique ability to form four strong hydrogen bonds per molecule.

6.
7.
8.

9. As the atomic mass of the halogens increases, so does the number of electrons and the average distance of those electrons from the nucleus. Larger atoms with more electrons are more easily polarized than smaller atoms, and the increase in polarizability with atomic number increases the strength of London dispersion forces. These intermolecular interactions are strong enough to favor the condensed states for bromine and iodine under normal conditions of temperature and pressure.

10.
11. 1. The V-shaped SO_2 molecule has a large dipole moment due to the polar S=O bonds, so dipole–dipole interactions will be most important.
    2. The H–F bond is highly polar, and the fluorine atom has three lone pairs of electrons to act as hydrogen bond acceptors; hydrogen bonding will be most important.
    3. Although the C=O bonds are polar, this linear molecule has no net dipole moment; hence, London dispersion forces are most important.
    4. This is a symmetrical molecule that has no net dipole moment, and the Cl atoms are relatively polarizable; thus, London dispersion forces will dominate.
    5. This molecule has a small dipole moment, as well as polarizable Cl atoms. In such a case, dipole–dipole interactions and London dispersion forces are often comparable in magnitude.
12.
13.
14.

15. Water has two polar O–H bonds with H atoms that can act as hydrogen bond donors, plus two lone pairs of electrons that can act as hydrogen bond acceptors, giving a net of *four* hydrogen bonds per H_2O molecule. Although methanol also has two lone pairs of electrons on oxygen that can act as hydrogen bond acceptors, it only has one O–H bond with an H atom that can act as a hydrogen bond donor. Consequently, methanol can only form *two* hydrogen bonds per molecule on average, versus four for water. Hydrogen bonding therefore has a much greater effect on the boiling point of water.

16.
17.
18.
19.
20.

21. Vigorous boiling causes more water molecule to escape into the vapor phase, but does not affect the temperature of the liquid. Vigorous boiling requires a higher energy input than does gentle simmering.

22.
23.
24.

Contributors

- Anonymous

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1.7: The Shapes of Molecules

Learning Objectives

- Predict the structures of small molecules using valence shell electron pair repulsion (VSEPR) theory.

The Lewis electron-pair approach can be used to predict the number and types of bonds between the atoms in a substance, and it indicates which atoms have lone pairs of electrons. This approach gives no information about the actual arrangement of atoms in space, however. We continue our discussion of structure and bonding by introducing the **valence-shell electron-pair repulsion** (VSEPR) model (pronounced "vesper"), which can be used to predict the shapes of many molecules and polyatomic ions. Keep in mind, however, that the VSEPR model, like any model, is a limited representation of reality; the model provides no information about bond lengths or the presence of multiple bonds.

The VSEPR Model

The VSEPR model can predict the structure of nearly any molecule or polyatomic ion in which the central atom is a nonmetal, as well as the structures of many molecules and polyatomic ions with a central metal atom. The premise of the VSEPR theory is that electron pairs located in bonds and lone pairs repel each other and will therefore adopt the geometry that places electron pairs as far apart from each other as possible. This theory is very simplistic and does not account for the subtleties of orbital interactions that influence molecular shapes; however, the simple VSEPR counting procedure accurately predicts the three-dimensional structures of a large number of compounds, which cannot be predicted using the Lewis electron-pair approach.

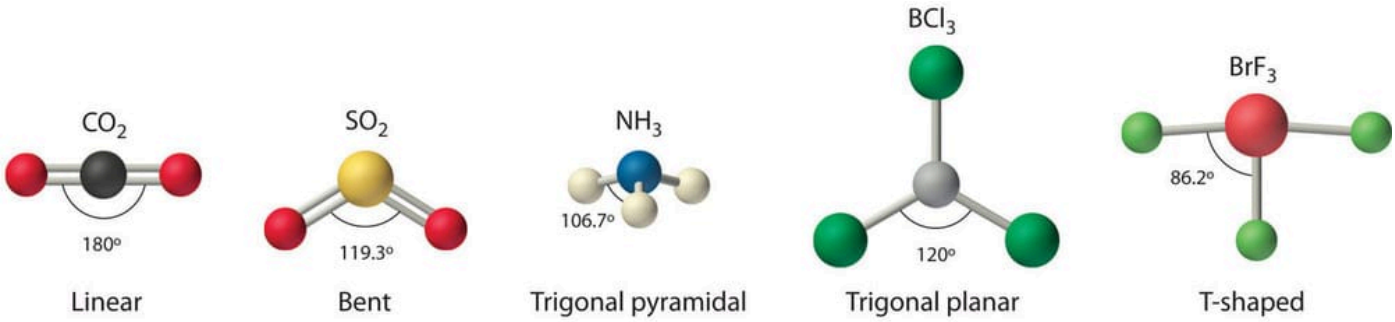


Figure 1.7.1: Common Structures for Molecules and Polyatomic Ions That Consist of a Central Atom Bonded to Two or Three Other Atoms. (CC BY-NC-SA; anonymous)

We can use the VSEPR model to predict the geometry of most polyatomic molecules and ions by focusing only on the number of electron pairs around the *central atom*, ignoring all other valence electrons present. According to this model, valence electrons in the Lewis structure form **electron groups** (regions of electron density), which may consist of a single bond, a double bond, a triple bond, a lone pair of electrons, or even a single unpaired electron, which in the VSEPR model is counted as a lone pair. Because electrons repel each other electrostatically, the most stable arrangement of electron groups (i.e., the one with the lowest energy) is the one that minimizes repulsions. Groups are positioned around the central atom in a way that produces the molecular structure with the lowest energy, as illustrated in Figure 1.7.1.

It is important to note that electron group geometry around a central atom is *not* the same thing as its molecular structure. Electron group geometries describe ***all*** regions where electrons are located, bonds as well as lone pairs. Molecular structure describes the location of the *atoms* alone, not including the lone pair electrons.

We differentiate between these two situations by naming the geometry that includes *all* electron pairs the **electron group geometry**. The structure that includes only the placement of the atoms in the molecule is called the **molecular structure** (or molecular shape). The electron group geometries will be the *same* as the molecular structures when there are no lone electron

pairs around the central atom, but they will be *different* when there are lone pairs present on the central atom.

Predicting Electron Group Geometry and Molecular Structure

The following procedure uses VSEPR theory to determine electron group geometry and molecular structures (molecular shape):

1. Draw the Lewis structure of the molecule or polyatomic ion.
2. Count the number of electron groups or regions of electron density (lone pairs and bonds) around the central atom. A single, double, or triple bond counts as one electron group.
3. Determine the electron group geometry by placing the groups as far apart as possible.
4. Determine the molecular structure (looking at the bonded groups only).

Table 1.7.1 summarizes the shapes of molecules based on the number of electron groups and surrounding atoms.

Table 1.7.1: Summary of Electron Group Geometries and Molecular Structures

Number of Electron Groups on Central Atom	Number of Bonding Groups	Number of Lone Pairs	Electron Group Geometry	Molecular Structure
2	2	0	linear	linear
3	3	0	trigonal planar	trigonal planar
3	2	1	trigonal planar	bent 120°
4	4	0	tetrahedral	tetrahedral
4	3	1	tetrahedral	trigonal pyramidal
4	2	2	tetrahedral	bent 109°

Two Electron Groups

Any molecule with only two atoms is **linear**. A molecule whose central atom contains only two electron groups orients those two groups as far apart from each other as possible, which is 180° apart. When the two electron groups are 180° apart, the atoms attached to those electron groups are also 180° apart, so the overall molecular structure is linear. Examples include BeH_2 and CO_2:



Figure 1.7.2: Beryllium hydride and carbon dioxide bonding.

Three Electron Groups

A molecule with three electron groups orients the three groups as far apart as possible. They adopt the positions of an equilateral triangle, 120° apart and in a plane. The shape of such molecules is **trigonal planar**. An example is BF_3:

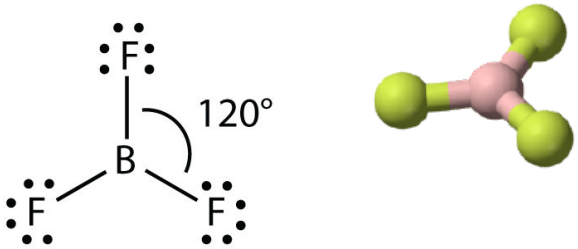


Figure 1.7.3: Boron trifluoride bonding. (CK12 Licence)

Some substances have a trigonal planar electron group distribution but have atoms bonded to only two of the three electron groups. An example is GeF_2:

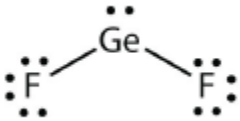


Figure 1.7.4: Germanium difluoride bonding.

From an electron group geometry perspective, GeF_2 has a trigonal planar shape, but its real shape is dictated by the positions of the atoms. This molecular structure is called **bent 120°** or angular.

Four Electron Groups

A molecule with four electron groups about the central atom orients the four groups in the direction of a tetrahedron with bond angles of approximately 109.5°. If there are four atoms attached to these electron groups, then the molecular structure is also **tetrahedral**. Methane (CH_4) is an example.

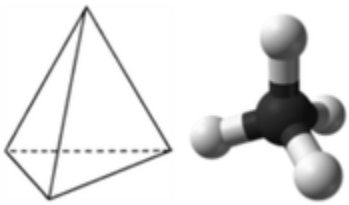


Figure 1.7.5: Tetrahedral structure of methane. (CK12 Licence)

This diagram of CH_4 illustrates the standard convention of displaying a three-dimensional molecule on a two-dimensional surface. The straight lines are in the plane of the page, the solid wedged line is coming out of the plane toward the reader, and the dashed wedged line is going out of the plane away from the reader.

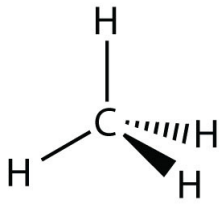


Figure 1.7.6: Methane bonding. (CK12 Licence)

NH_3 is an example of a molecule whose central atom has four electron groups, but only three of them are bonded to surrounding atoms.

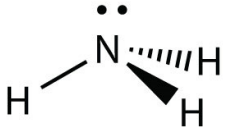


Figure 1.7.7: Ammonia bonding. (CK12 Licence)

Although the electron groups are oriented in the shape of a *tetrahedron*, from a molecular geometry perspective, the shape of NH_3 is **trigonal pyramidal**.

H_2O is an example of a molecule whose central atom has four electron groups, but only two of them are bonded to surrounding atoms.



Figure 1.7.8: Water bonding.

Although the electron groups are oriented in the shape of a tetrahedron, the shape of the molecule is **bent 109°** or angular. A molecule with four electron groups about the central atom, but only one electron group bonded to another atom, is linear because there are only two atoms in the molecule.

Shapes of Molecules with Double or Triple Bonds

Double or triple bonds count as a single electron group. The Lewis electron dot diagram of formaldehyde (CH_2O) is shown in Figure 1.7.9.



Figure 1.7.9: Lewis Electron Dot Diagram of Formaldehyde.

The central C atom has three electron groups around it because the double bond counts as one electron group. The three electron groups repel each other to adopt a *trigonal planar shape*.

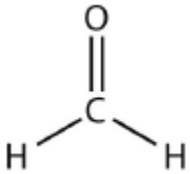


Figure 1.7.10: Formaldehyde bonding.

(The lone electron pairs on the O atom are omitted for clarity.) The molecule will not be a perfect equilateral triangle because the C–O double bond is different from the two C–H bonds, but both planar and triangular describe the appropriate approximate shape of this molecule.

Example 1.7.1

What is the approximate shape of each molecule?

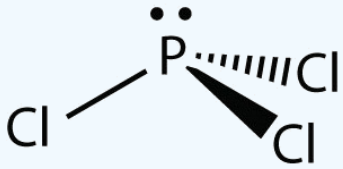
a. PCl_3

b. NOF

Solution

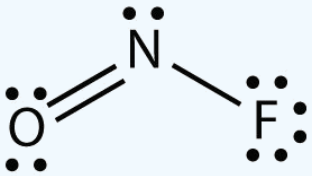
The first step is to draw the Lewis structure of the molecule.

For $\mathrm{PCl_3}$, the electron dot diagram is as follows:



The lone electron pairs on the Cl atoms are omitted for clarity. The P atom has four electron groups with three of them bonded to surrounding atoms, so the molecular shape is trigonal pyramidal.

The electron dot diagram for NOF is as follows:



The N atom has three electron groups on it, two of which are bonded to other atoms. The molecular shape is bent.

Exercise 1.7.1

What is the approximate molecular shape of $\mathrm{CH_2Cl_2}$?

Answer available at the end of this section.

Exercise 1.7.2

Ethylene ($\mathrm{C_2H_4}$) has two central atoms. Determine the geometry around each central atom and the shape of the overall molecule. (Hint: hydrogen is a terminal atom.)

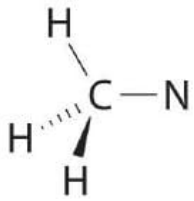
Answer available at the end of this section.

Answer available at the end of this section.

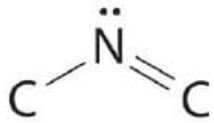
Molecules With Multiple Central Atoms

The VSEPR model can be used to predict the structure of somewhat more complex molecules with more than one central atom by using VSEPR as described above for each central atom individually. We will demonstrate with methyl isocyanate (CH_3–N=C=O), a volatile and highly toxic molecule that is used to produce the pesticide Sevin.

Start by looking at the electron groups around the first carbon atom at the left, which is connected to three H atoms and one N atom by single bonds. There are four groups or electrons or four bonds around the carbon. We can therefore predict the CH_3–N portion of the molecule to be roughly *tetrahedral*, similar to methane:



The nitrogen atom is connected to one carbon by a single bond and to the other carbon by a double bond, producing a total of three bonds, C–N=C. For nitrogen to have an octet of electrons, it must also have a lone pair:



One carbon bonded to nitrogen and another carbon double bonded to the nitrogen. The nitrogen has one lone pair.

Because multiple bonds are not shown in the VSEPR model, the nitrogen is effectively surrounded by three electron groups. Thus according to the VSEPR model, the C–N=C fragment should be *bent* with an angle ~120°.

The carbon in the –N=C=O fragment is doubly bonded to both nitrogen and oxygen, which in the VSEPR model gives carbon a total of two electron pairs. The N=C=O angle should therefore be 180°, or linear. The three fragments combine to give the following structure:

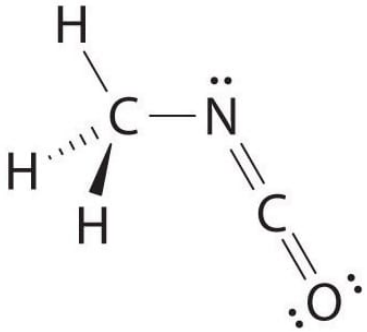


Figure 1.7.11). The Lewis Structure of Methyl Isocyanate

Three hydrogens are bonded to a carbon. The carbon is also bonded to a nitrogen. The nitrogen is double bonded to another carbon. The second carbon is double bonded to an oxygen. The nitrogen has one lone pair. The oxygen has two lone pairs.

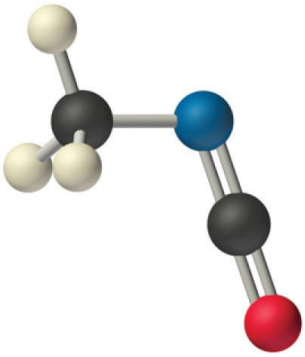


Figure 1.7.12: The Experimentally Determined Structure of Methyl Isocyanate

Certain patterns are seen in the structures of moderately complex molecules. For example, carbon atoms with four bonds (such as the carbon on the left in methyl isocyanate) are generally tetrahedral. Similarly, the carbon atom on the right has two double bonds that are similar to those in CO_2, so its geometry, like that of CO_2, is linear. Recognizing similarities to simpler molecules

will help you predict the molecular geometries of more complex molecules.

Example 1.7.3

Use the VSEPR model to predict the molecular geometry of propyne ($H_3C–C≡CH$), a gas with some anesthetic properties.

Given: chemical compound

Asked for: molecular geometry

Strategy:

Count the number of electron groups around each carbon, recognizing that in the VSEPR model, a multiple bond counts as a single group. Use Figure 1.7.3 to determine the molecular geometry around each carbon atom and then deduce the structure of the molecule as a whole.

Solution:

Because the carbon atom on the left is bonded to four other atoms, we know that it is approximately tetrahedral. The next two carbon atoms share a triple bond, and each has an additional single bond. Because a multiple bond is counted as a single bond in the VSEPR model, each carbon atom behaves as if it had two electron groups. This means that both of these carbons are linear, with C–C≡C and C≡C–H angles of 180°.

Exercise 1.7.3

Predict the geometry of allene ($H_2C=C=CH_2$), a compound with narcotic properties that is used to make more complex organic molecules.

Answer available at the end of this section.

Answers

Exercise 1.7.1

Tetrahedral

Exercise 1.7.2

Exercise 1.7.2

Trigonal planar about both central C atoms.

Exercise 1.7.3

The terminal carbon atoms are trigonal planar, the central carbon is linear, and the C–C–C angle is 180°.

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1.8: The Nature of Organic Molecules

Learning Objectives

- Describe the basic structural properties of simple organic molecules.

Organic chemistry is the study of the chemistry of carbon-containing compounds. Carbon is singled out because it has a chemical diversity unrivaled by any other chemical element. Its diversity is based on the following:

- Carbon atoms bond reasonably strongly with other carbon atoms.
- Carbon atoms bond reasonably strongly with atoms of other elements.
- Carbon atoms make a large number of covalent bonds (four).

Curiously, elemental carbon is not particularly abundant. It does not even appear in the list of the most common elements in Earth's crust. Nevertheless, all living things consist of organic compounds. Most organic chemicals are covalent compounds, which is why we introduce organic chemistry here. By convention, compounds containing carbonate ions and bicarbonate ions, as well as carbon dioxide and carbon monoxide, are not considered part of organic chemistry, even though they contain carbon.

Structural Properties of Carbon Compounds

A carbon atom has four valence electrons, it is **tetravalent**. Carbon can form four *covalent* bonds, or *share electrons with* up to four atoms in order to gain a complete octet. The simplest carbon compounds contain only carbon and hydrogen and are called **hydrocarbons**. Methane, the simplest hydrocarbon, contains a single carbon with four covalently bonded hydrogen atoms. Recalling what you have learned about molecular structures and VSEPR, we know that methane is **tetrahedral** (four electron groups and no lone pairs).

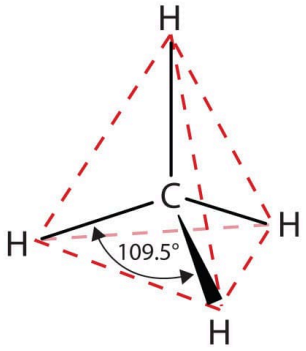


Figure 1.8.1: The Tetrahedral Methane Molecule

Carbon can also form **double bonds** by sharing *four electrons* with a neighboring carbon atom or **triple bonds** by sharing *six electrons* with a neighboring carbon atom. As shown in Figure 1.8.2 below, carbon with three electron groups attached will be **trigonal planar**, and carbon with two electron groups attached will be **linear**.

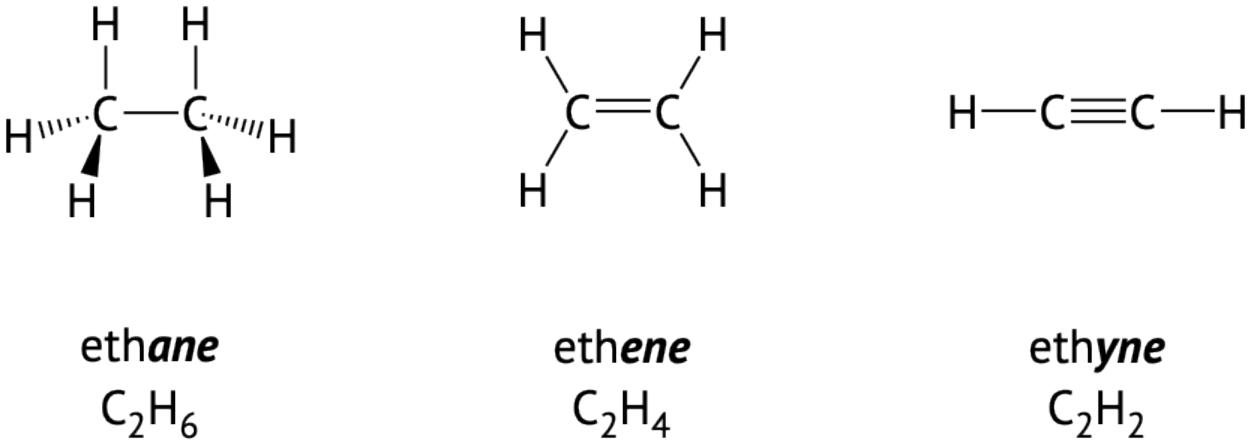


Figure 1.8.2: Two carbons can be attached together in single bond, a double bond, or a triple bond. Notice, in each example carbon makes four total bonds. The number of hydrogen atoms in each molecule decreases as the number of carbon–carbon bonds increase.

Simple hydrocarbon compounds are *nonpolar* due to the shape and the small electronegativity difference between carbon and hydrogen atoms. When carbon is bonded to a halogen or oxygen atom, the resulting bond is *polar*. It may be useful to review the section on electronegativity and polarity of bonds and molecules to be able to describe the properties of different organic compounds, specifically how they react and interact with other molecules.

Comparing Organic and Inorganic Compounds

Organic compounds, like inorganic compounds, obey all the natural laws. Often there is no clear distinction in the chemical or physical properties among organic and inorganic molecules. Nevertheless, it is useful to compare typical members of each class, as in Table 1.8.1. Keep in mind, however, that there are exceptions to every category in this table.

Table 1.8.1: Contrasting Properties and Examples of Organic and Inorganic Compounds

Organic Properties	Example: Hexane	Inorganic Properties	Example: NaCl
low melting points	−95°C	high melting points	801°C
low boiling points	69°C	high boiling points	1,413°C
low solubility in water; high solubility in nonpolar solvents	insoluble in water; soluble in gasoline	greater solubility in water; low solubility in nonpolar solvents	soluble in water; insoluble in gasoline
flammable	highly flammable	nonflammable	nonflammable
aqueous solutions do not conduct electricity	nonconductive	aqueous solutions conduct electricity	conductive in aqueous solution
exhibit covalent bonding	covalent bonds	exhibit ionic bonding	ionic bonds

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1.9: Representing organic compounds

Learning Objectives

- Read and draw molecular, Lewis, condensed, and structural formulae of simple organic compounds.
- Understand the mixed versions of and slight variations in drawing the formulae of simple organic compounds.

The molecular formula, Lewis formula, condensed formula, skeletal formula, or a combination of these can represent an organic compound. These ways of representing organic compound and what they mean is described below.

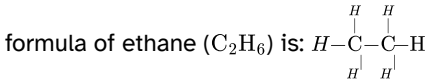
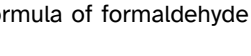
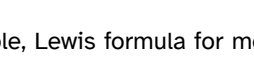
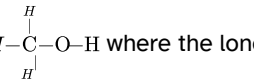
Molecular formula

The **molecular formula** tells the symbols of the elements that compose the compound, and the subscript to the element symbol denotes how many atoms of that element are in the molecule.

For example, (CH_4) is a molecule formula of methane which means there is one carbon and four hydrogen atoms in a methane molecule. C_2H_6 is a molecule formula of ethane, which means the ethane molecule has two carbon and six hydrogen atoms. Molecular formulas do not tell about the molecule's bonds and shapes.

Lewis formula

The **Lewis structure** or Lewis formula shows all the bonding electron pairs as lines (bonds) and lone pairs (non-bonding electron pairs) as pairs of dots around each atom in a molecule.

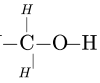
For example, Lewis formula of ethane (C_2H_6) is:  that shows each carbon is bonded with one C and three $H's$ by single bonds. Similarly, Lewis formula of formaldehyde (CH_2O) is:  that shows C is bonded with two $H's$ by single bonds and with one O by a double bond and O has two lone pairs on it. The lone pairs are usually omitted from Lewis structures except when needed to emphasize their presence. For example, Lewis formula for methanol (CH_4O) with lone pairs is: , but it can also be shown as  where the lone pairs are not shown on O but it is understood that two lone pairs are there.

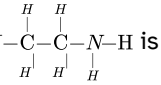
Condensed formula

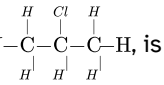
The Lewis formulas become complicated and time-consuming for larger organic compounds.

Condensed formula simplifies the Lewis formula by writing each C followed by $H's$ attached with it. Subscripts are used to show more than one $H's$. If there is a heteroatom, i.e., any atom other than C or H in the chain, it is condensed like C, except for halogens which are condensed like H.

For example, the Lewis formula of ethane  is condensed as CH_3CH_3.

The Lewis formula for methanol  is condensed as CH_3OH.

The Lewis formula for ethanamine  is condensed as $CH_3CH_2NH_2$.

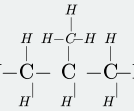
The Lewis formula for 2-chloropropane , is condensed as $CH_3CHClCH_3$.

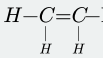
Line Bond or Line Angle Formulas

The Lewis and condensed formulas do not show the geometry of the organic compounds. Further, the Lewis and condensed formulas become complicated and time-consuming for large organic compounds.

Line Bond or line-angle formulas overcome these drawbacks by simplifying the representation of organic compounds by omitting $C's$ and $H's$ in the formula and showing only the skeleton of the compound by C-to-C bonds as lines in a geometry that is closer to the actual geometry. Any heteroatom and $H's$ attached to the heteroatom are shown in the skeletal formula.

Some terms related to the primary classification of organic compounds

- Before learning line bond formulas, it is essential to understand the following terms related to the primary type of organic compounds.
- Organic compounds containing only $C's$ and $H's$ are called **hydrocarbons**. For example, ethane (CH_3CH_3), ethene (CH_2CH_2), and ethyne ($CHCH$) described in previous sections are hydrocarbons.
- The hydrocarbons contain only σ-bonds are called **alkanes**. For example, methane (CH_4) and ethane (CH_3CH_3) are alkanes.
  - Alkanes containing a chain of $C's$ where $C's$ are connected with either one or two $C's$ are called **straight chain alkanes** or normal-chain alkanes (**n-alkanes**). For example, n-alkane having four carbons is n-butane (($CH_3CH_2CH_2CH_3$), five carbons is n-pentane ($CH_3CH_2CH_2CH_2CH_3$), six carbons is n-hexane ($CH_3CH_2CH_2CH_2CH_2CH_3$), and so on.
- Alkanes in which at least on C connected with three or four other $C's$ are called **branched-chain alkanes**. For example, isopropane  is a branched-chain alkane
- The hydrocarbons containing at least one double bond, i.e., a σ-bond and a π-bond together, are called **alkenes**. For example, ethene

   is an alkene.
- The hydrocarbons containing at least one triple-bond, i.e., a σ-bond and two π-bonds together, are called alkynes. For example, ethyne $H-C\equiv C-H$ is an alkyne.
- The hydrocarbons with a planer cyclic structure having alternating odd numbers of double bonds are a special class of hydrocarbons called **aromatic hydrocarbons** that will be described later.
- Organic compounds containing at least one heteroatom, i.e., O, N, S, P, etc. are not hydrocarbons. For example, methanol CH_3OH is not a hydrocarbon. Several classes of organic compounds are not hydrocarbons, which will be described later.

Line Bond formulas of n-alkanes

Methane (CH_4) is the simplest alkane that has a tetrahedral geometry around its C, as illustrated in Figure 1.9.1a. Gray lines in Figure 1.9.1a show the outline of the tetrahedron shape, and the black lines show C–H bonds. The plane defined by C, H on the top, and H on the right is in the plane of the paper in this perspective drawing (Figure 1.9.1a). The H on the hashed wedge is going below, and the H on the solid wedge is coming above the plane of the paper. The plane of the paper cuts through the middle of two H's on the left of the drawing. The point of view is slightly above C towards the top-right corner.

Figure 1.9.1b shows the same structure without the tetrahedron layout drawing. All bonds are equal, and all bond angles are 109.5°. Figure 1.9.1c shows the model of CH_4 molecule from approximately the same view. Note that the geometry of CH_4 molecule is two V's of 109.5° internal angle, placed perpendicular to each other, and joined at the vertex. Figure 1.9.1d shows the same structure rotated such that the two H's in the plane of the paper are on a straight line at the bottom of the drawing. Figure 1.9.1e shows the model rotated in the same orientation as the perspective drawing in Figure 1.9.1d.

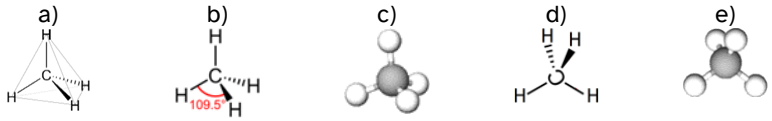


Figure 1.9.1: a) Perspective drawing of methane (CH_4) with the outlines of the tetrahedron drawing with gray lines. The plane of the paper (or the screen) is along the plane of C and two H's to the right and cuts through the middle of the two H's on the left (angel of view is slightly below the top-right corner) b) perspective drawing of CH_4 in the same view without drawing of the outlines of the tetrahedron, c) model of CH_4 from the same view, d) perspective drawing of CH_4 rotated to bring the two H's in the plane of the page at the base making an inverted bigger V-shape, and e) model of CH_4 in the same view as the perspective drawing in d. (Copyright; Public domain)

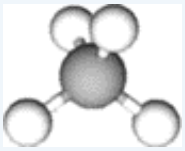
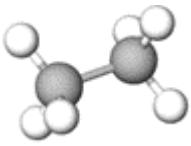
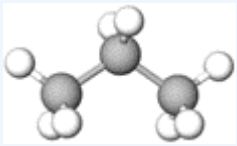
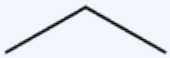
Replacing any H with another C results in ethane (CH_3CH_3) as shown in row two of Table 1. A line drawn to represent C–C bond in ethane is the skeletal formula of ethane, as shown in row two of Table 1. When 2nd H of methane is also replaced with C, it results in propane ($CH_3CH_2CH_3$), as shown in row three of Table 1. Two H's of methane in the plane of the page have been replaced with C's in this case resulting in C–C–C bonds in an inverted V-shape in the plane of the page. The skeletal formula representing a propane molecule is two lines connected in an inverted V-shape, as shown in row three of Table 1.

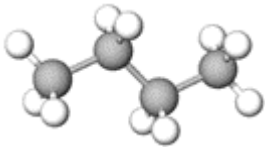
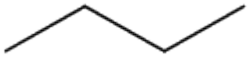
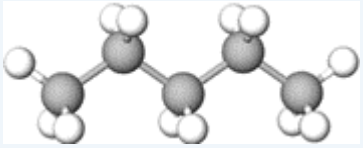
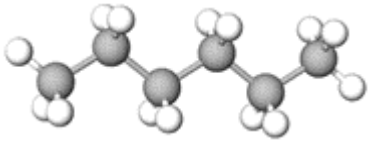
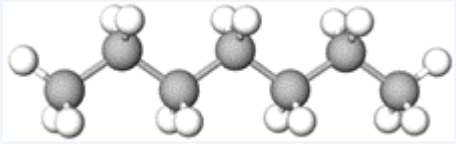
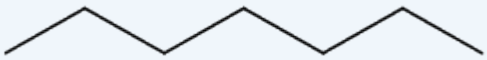
Replacing any H of a terminal C of a propane with another C results in butane ($CH_3CH_2CH_2CH_3$) as shown in 4th row of Table 1. Remember rotation around C–C single bond happens. Therefore, the 4th C of butane can be placed at any angle relative to the plane defined by the other three C's. However, placing all four C's of butane in the same plane is the most stable arrangement because the terminal C's, which are the bulkiest groups attached to the internal C's, are farthest apart in this arrangement. Three lines connected by zigzag is the skeletal formula representing butane, as shown in row 4th of Table 1. The zigzag lines representing a chain of 4 C's can be extended to represent a chain of 5 C's, by adding one line to represent a chain of 6 C's by adding two lines, and so on, as shown in Table 1 for the cases of n-alkanes having a chain of 2 to 12 C's.

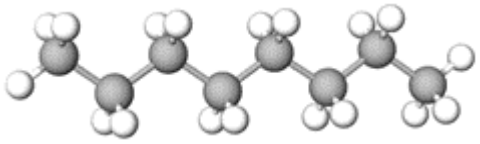
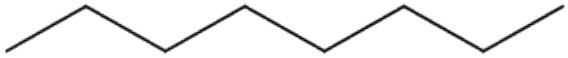
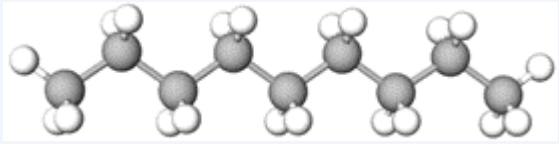
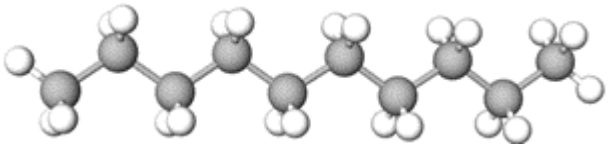
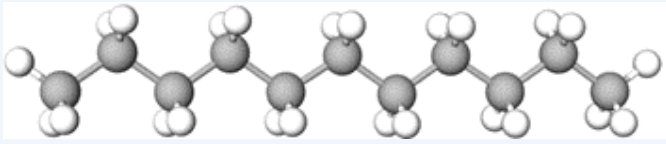
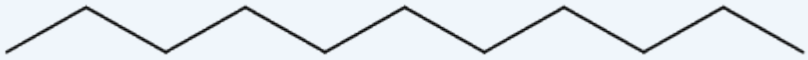
> In summary, the **skeletal formula** of n-alkane is a line or lines connected zigzag representing C–C bonds. It is understood that:
>
> - the terminals (end) and corners (bends) of the lines are C's, and
> - each C has four bonds, so the bonds which are not shown by the lines are the bonds to H's.

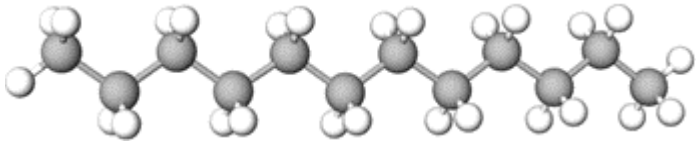
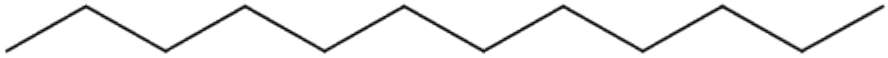
With this knowledge, it is clear that a line or lines connected zigzag way are the structural formulas that represent structures of n-alkanes without showing C's and H's in the formula.

Table 1: Names, molecular formulas, condensed formulas, models, and skeletal formulas of n-alkanes containing 2 to 12 $\mathrm{C's}$ in a chain. (Note: Methane has no structural formula as it has no $\mathrm{C-C}$ bond. The $\mathrm{C's}$ are black and $\mathrm{H's}$ are white color in the models))

# of $\mathrm{C's}$	Name	Molecular formula	Model, Condensed formula, and Structural formula
1	Methane	$\mathrm{CH_4}$	 $\mathrm{CH_4}$
2	Ethane	$\mathrm{C_2H_6}$	 $\mathrm{CH_3CH_3}$ 
3	Propane	$\mathrm{C_3H_8}$	 $\mathrm{CH_3CH_2CH_3}$ 

4	Butane	C_4H_{10}	 $CH_3CH_2CH_2CH_3$ 
5	Pentane	C_5H_{12}	 $CH_3CH_2CH_2CH_2CH_3$ 
6	Hexane	C_6H_{14}	 $CH_3CH_2CH_2CH_2CH_2CH_3$ 
7	Heptane	C_7H_{16}	 $CH_3CH_2CH_2CH_2CH_2CH_2CH_3$ 

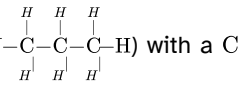
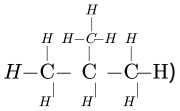
8	Octane	C_8H_{18}	 $CH_3CH_2CH_2CH_2CH_2CH_2CH_2CH_3$ 
9	Nonane	C_9H_{20}	 $CH_3CH_2CH_2CH_2CH_2CH_2CH_2CH_2CH_3$ 
10	Decane	$C_{10}H_{22}$	 $CH_3CH_2CH_2CH_2CH_2CH_2CH_2CH_2CH_2CH_3$ 
11	Undecane	$C_{11}H_{24}$	 $CH_3CH_2CH_2CH_2CH_2CH_2CH_2CH_2CH_2CH_2CH_3$ 

12	Dodecane	$C_{12}H_{26}$	 $CH_3CH_2CH_2CH_2CH_2CH_2CH_2CH_2CH_2CH_2CH_2CH_3$ 

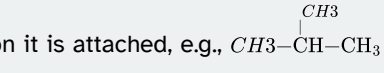
Stem names of organic compounds

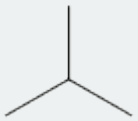
Names of n-alkanes without the last syllable, i.e., without -ane, are the **stem names** that represent the number of $C's$ in the organic compound. For example, meth- from methane represents one C, eth- from ethane represents two $C's$, prop- from propane represents three $C's$, and so on. These stem names will be described later in reference to name organic compounds.

Condensed and line bond formulas of branched-alkanes

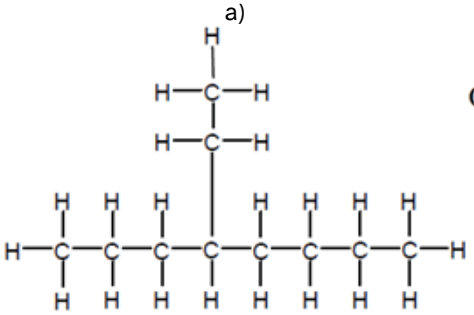
Replacing one or both $H's$ of a non-terminal carbon of straight chain alkane (n-alkane) with a C or a C chain results in a branched-alkane. Replacing hydrogen on the middle carbon of propane () with a C results in isopropane () which is a branched chain alkane.

There are two ways to show the condensed formula of the branched alkane:

- show the condensed formula of the branch within small brackets next to the carbon it is attached to, e.g., $CH_3CH(CH_3)CH_3$ is the condensed formula of isopropane;
- show the condensed formula of the branch hanging above or below the carbon it is attached, e.g.,  is the condensed formula of isopropane.

The skeletal formula of the branched alkane shows the skeletal formula of the branch with the terminal connected to the carbon in the main branch to which it is attached. For example,  is the skeletal formula of isopropane. Figure $1.9.3$ shows another example of branched alkane and its condensed and skeletal formulas.

a)



b)

$$CH_3CH_2CH_2\underset{\displaystyle CH_2CH_3}{\underset{|}{C}}HCH_2CH_2CH_2CH_3$$

or

c)

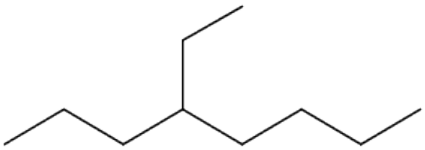


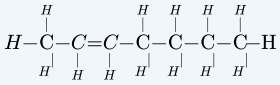
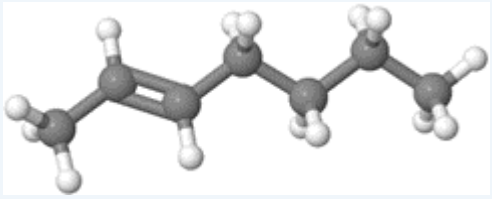
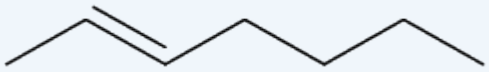
Figure 1.9.3: 4-Ethyloctane -a branched alkane: a) Lewis formula, b) two ways of writing condensed formulas, and c) its skeletal formula. (Copyright; Public domain).

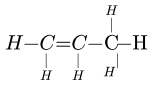
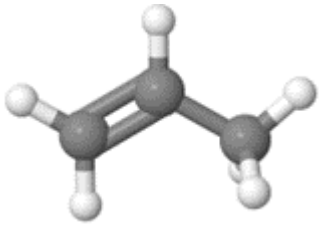
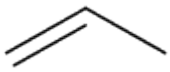
Skeletal formulas of alkenes

Hydrocarbons containing at least one double bond ($C{=}C$ bond) are called alkene.

Table 2 shows the names, Lewis structures, models, condensed formulas, and skeletal formulas of two alkene examples. Their nomenclature will be explained later.

Table 2: Names, Lewis structures, models, condensed formulas, and skeletal formulas of some alkene examples. (Note: $C's$ are black and $H's$ are white color in the models)

Name	Lewis structure	Model, Condensed formula, and Structural formula
Hept-2-ene		 $CH_3CHCHCH_2CH_2CH_2CH_3$ 

Propene		 CH_2CHCH_3 

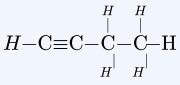
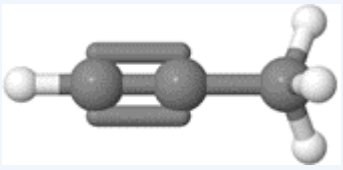
Skeletal formulas of alkynes

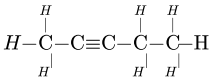
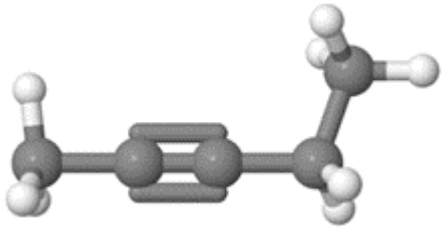
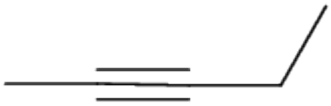
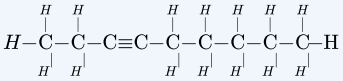
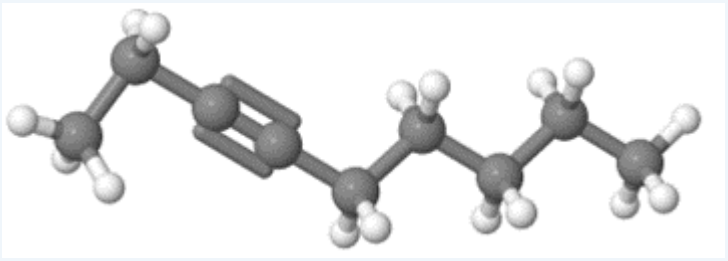
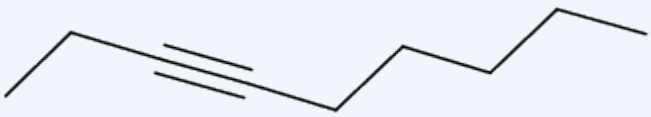
Hydrocarbons containing at least one triple bond ($C{\equiv}C$) bond are called alkyne.

> Since the two $C's$ at the triple-bond have linear geometry, three lines show the triple bond and the two single bonds to the other atoms attached to them are drawn in line with the triple bond. The zigzag skeletal structure shows the rest of the structure as usual.

Table 3 shows some alkyne examples' names, Lewis structures, models, condensed formulas, and skeletal formulas. Their nomenclature will be explained later.

Table 3: Names, Lewis structures, models, condensed formulas, and skeletal formulas of some alkyne examples. (Note: $C's$ are black and $H's$ are white color in the models)

Name	Lewis structure	Model, Condensed formula, and Structural formula
Propyne		 $CHCCH_3$ 

Pent-2-yne		 $CH_3CCCH_2CCH_3$ 
Non-3-yne		 $CH_3CH_2CCCH_2CH_2CH_2CH_2CH_3$ 

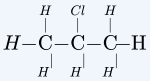
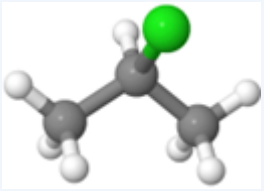
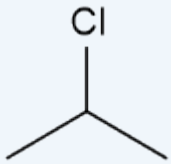
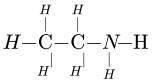
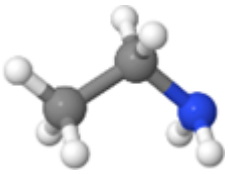
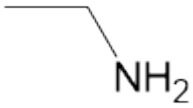
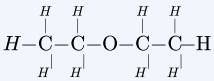
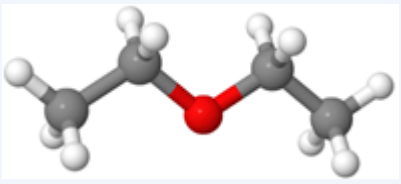
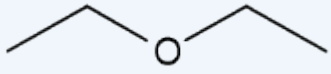
Skeletal formulas of organic compounds containing heteroatoms

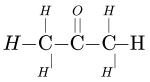
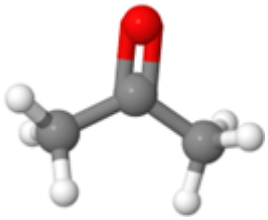
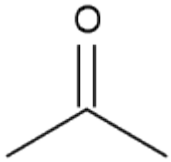
If any heteroatom, i.e., an atom other than C or H, is present in an organic compound:

- its symbol in the skeletal formula shows it and
- any H present on the heteroatom is also shown next to the heteroatom as in the condensed formulas.

The skeletal structure shows the rest of the structure as usual. Table 4 shows the names, Lewis structures, models, condensed formulas, and skeletal formulas of some example organic compounds containing heteroatoms. Their nomenclature will be explained later.

Table 4: Names, Lewis structures, models, condensed formulas, and skeletal formulas of some organic compounds containing heteroatoms. (Note: C′s are black, H′s are white, and heteroatom are in other colors in the models)

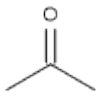
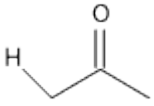
Name	Lewis structure	Model, Condensed formula, and Structural formula
2-Chloropropane		 $CH_3CHClCH_3$ 
Ethanamine		 $CH_3CH_2NH_2$ 
Diethyl ether		 $CH_3CH_2OCH_2CH_3$ 

Acetone		 CH_3COCH_3 or $CH3\overset{O}{\overset{\|}{C}}CH3$ 

Variations in the formulas representing organic compounds

The condensed and the skeletal formulas are usually presented in organic chemistry, as described in the previous sections. However, they may be varied slightly according to the need.

> If needed, mixed Lewis, condensed, and skeletal structures emphasize a particular part of the molecule.

For example, the $\mathrm{H's}$ are usually written to the right of C or to the right of heteroatoms in the condensed formula, but sometimes this order may be reversed. For example, Lewis formula for methanol $H-\overset{H}{\overset{\|}{\mathrm{C}}}-\mathrm{O}-\mathrm{H}$ is presented in condensed form as $\mathrm{CH_3OH}$, but it may be condensed as $\mathrm{H_3COH}$, or as $\mathrm{H_3C-OH}$ to emphasize the $\mathrm{C-O}$-bond. Similarly, Lewis formula of acetone $H-\overset{H}{\underset{H}{\mathrm{C}}}-\overset{O}{\overset{\|}{\mathrm{C}}}-\overset{H}{\underset{H}{\mathrm{C}}}-\mathrm{H}$ is changed to skeletal formula as , but it may also be shown as  to emphasize the $\mathrm{C-H}$ bond.

Sometimes the formula is further condensed by placing the repeating units within a bracket and subscript outside the bract to show the number of repeat units. For example, the condensed formula of isopropane is $CH3-\overset{CH3}{\underset{|}{\mathrm{CH}}}-\mathrm{CH_3}$ that has three $\mathrm{CH_3}$ units attached to the central C. It can be further condensed as $(\mathrm{CH_3})_3\mathrm{CH}$. Similarly, the condensed formula of decane $\mathrm{CH_3CH_2CH_2CH_2CH_2CH_2CH_2CH_2CH_2CH_3}$ contains eight $\mathrm{CH_2}$ units and can be condensed further as $\mathrm{CH_3(CH_2)_8CH_3}$.

Examples of drawing Lewis, condensed, and skeletal formulae

Example 1.9.1

Draw molecular, Lewis, condensed, and skeletal formulas of butane.

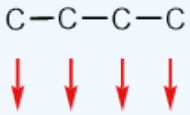
Solution

But- in butane means four $C's$ and -ane means it is an alkane. Substituting n = 4 in the general formula of alkanes ($C_nH_{n\times2+2}$) gives:

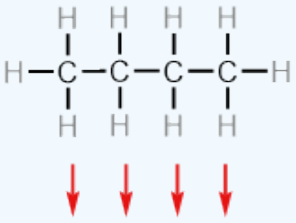
molecular formula = $(C_4H_{4\times2+2} = C_4H_{10}$.

For Lewis, condensed, and skeletal formulas follow the steps shown in the figure below.

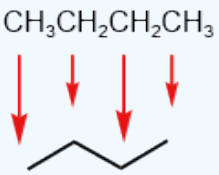
Step 1: Draw the C chain connected by bonds



Step 2: C has four bonds. Draw the missing bonds to H's
This is **Lewis formula**, aslo called **Expanded formula**.



Step 3: Condense H's to the left of the C's with subscript telling the numbers.
This is is the **condensed formula**.



Step 4: Draw a zigzag line representing C's as ends and corners (bends).
This is **skeletal formula** with ends and bends as C's and
H's on each C = 4- number of bonds shown on the C.

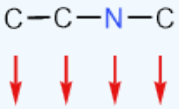
Example 1.9.2

Draw Lewis, condensed, and skeletal formulas for methylethylamine

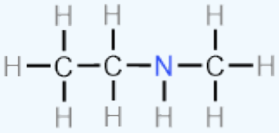
Solution

Meth- means one C, eth-means two $C's$, and aminie indicates a N two which the carbon chains are attached. With this information, follow the steps shown in the figure below.

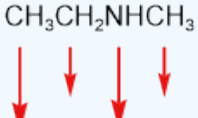
Step 1: Draw the C chain, with the heteroatom in it, connected by bonds



Step 2: C has four bonds and N has three. Draw the missing bonds to H's
This is **Lewis formula**, aslo called **Expanded formula**.



Step 3: Condense H's to the left of the C's and the heteroatom
with subscript telling the numbers.
This is is the **condensed formula**.



Step 4: Draw a zigzag line representing C's as ends and corners (bends).
Heteroatom is shown with its H's as in the condensed formula.
This is **skeletal formula** with ends and bends as C's and
H's on each C = 4- number of bonds shown on the C.

Example 1.9.3

Draw Lewis, condensed, and skeletal formula of 1-chlorobutane

Solution

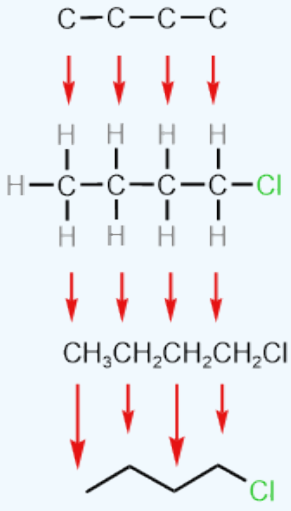
But- means four C's chain and 1-chloro- means there is chlorine at the terminal C. The nomenclature will be explained later. With this information, follow the steps shown in the figure below.

Step 1: Draw the C chain, with the heteroatom in it, connected by bonds

Step 2: C has four bonds. Draw the missing bonds to H's.
Terminal C has one missing bond with Cl, add one Cl.
This is **Lewis formula**, aslo called **Expanded formula**.

Step 3: Condense H's to the left of the C's and trad Cl as H.
with subscript telling the numbers.
This is is the **condensed formula**.

Step 4: Draw a zigzag line representing C's as ends and corners (bends).
Heteroatom is shown with its H's (if any) as in the condensed formula.
This is **skeletal formula** with ends and bends as C's and
H's on each C = 4- number of bonds shown on the C.



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1.10: Functional Groups

Objectives

After completing this section, you should be able to

1. explain why the properties of a given organic compound are largely dependent on the functional group or groups present in the compound.
2. identify the functional groups present in each of the following compound types: alkenes, alkynes, arenes, (alkyl and aryl) halides, alcohols, ethers, aldehydes, ketones, esters, carboxylic acids, (carboxylic) acid chlorides, amides, amines, nitriles, nitro compounds, sulfides and sulfoxides.
3. identify the functional groups present in an organic compound, given its structure.
4. Given the structure of an organic compound containing a single functional group, identify which of the compound types listed under Objective 2, above, it belongs to.
5. draw the structure of a simple example of each of the compound types listed in Objective 2.

Key Terms

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

- functional group

Study Notes

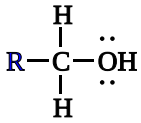
The concept of functional groups is a very important one. We expect that you will need to refer back to tables at the end of Section 3.1 quite frequently at first, as it is not really feasible to learn the names and structures of all the functional groups and compound types at one sitting. Gradually they will become familiar, and eventually you will recognize them automatically.

Functional groups are small groups of atoms that exhibit a characteristic reactivity. A particular functional group will almost always display its distinctive chemical behavior when it is present in a compound. Because of their importance in understanding organic chemistry, functional groups have specific names that often carry over in the naming of individual compounds incorporating the groups.

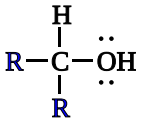
As we progress in our study of organic chemistry, it will become extremely important to be able to quickly recognize the most common functional groups, because they are the key structural elements that define how organic molecules react. For now, we will only worry about drawing and recognizing each functional group, as depicted by Lewis and line structures. Much of the remainder of your study of organic chemistry will be taken up with learning about how the different functional groups tend to behave in organic reactions.

Drawing abbreviated organic structures

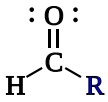
Often when drawing organic structures, chemists find it convenient to use the letter 'R' to designate part of a molecule outside of the region of interest. If we just want to refer in general to a functional group without drawing a specific molecule, for example, we can use 'R groups' to focus attention on the group of interest:



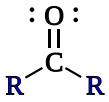
a primary alcohol



a secondary alcohol



an aldehyde



a ketone

The 'R' group is a convenient way to abbreviate the structures of large biological molecules, especially when we are interested in something that is occurring specifically at one location on the molecule.

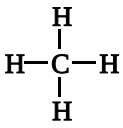
Common Functional Groups

In the following sections, many of the common functional groups found in organic chemistry will be described. Tables of these functional groups can be found at the bottom of the page.

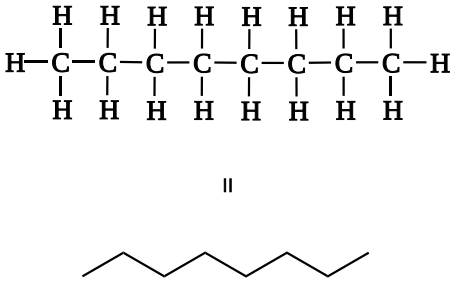
Hydrocarbons

The simplest functional group in organic chemistry (which is often ignored when listing functional groups) is called an **alkane**, characterized by single bonds between two carbons and between carbon and hydrogen. Some examples of alkanes include methane, CH_4, is the natural gas you may burn in your furnace or on a stove. Octane, C_8H_{18}, is a component of gasoline.

Alkanes



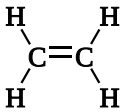
methane



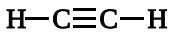
octane

Alkenes (sometimes called **olefins**) have carbon-carbon double bonds, and **alkynes** have carbon-carbon triple bonds. Ethene, the simplest alkene example, is a gas that serves as a cellular signal in fruits to stimulate ripening. (If you want bananas to ripen quickly, put them in a paper bag along with an apple - the apple emits ethene gas, setting off the ripening process in the bananas). Ethyne, commonly called acetylene, is used as a fuel in welding blow torches.

Alkenes and alkynes

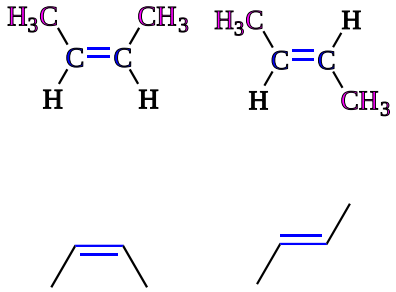


ethene (an alkene)



ethyne (an alkyne)

Alkenes have trigonal planar electron geometry (due to sp^2 hybrid orbitals at the alkene carbons) while alkynes have linear geometry (due to sp hybrid orbitals at the alkyne carbons). Furthermore, many alkenes can take two geometric forms: ***cis*** or ***trans*** *(or Z and E which will be explained in detail in Chapter 7)*. The *cis* and *trans* forms of a given alkene are different molecules with different physical properties there is a very high energy barrier to rotation about a double bond. In the example below, the difference between *cis* and *trans* alkenes is readily apparent.



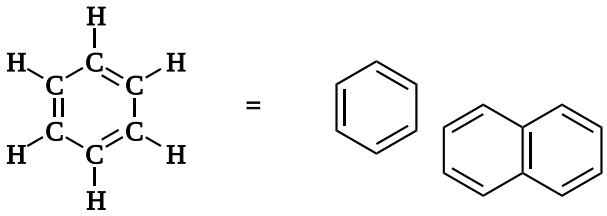
cis-alkene
CH_3 groups on the same side

trans-alkene
CH_3 groups on opposite sides

Alkanes, alkenes, and alkynes are all classified as **hydrocarbons**, because they are composed solely of carbon and hydrogen atoms. Alkanes are said to be **saturated hydrocarbons**, because the carbons are bonded to the maximum possible number of hydrogens - in other words, they are *saturated* with hydrogen atoms. The double and triple-bonded carbons in alkenes and alkynes have fewer hydrogen atoms bonded to them - they are thus referred to as **unsaturated hydrocarbons**. As we will see in Chapter 7, hydrogen can be added to double and triple bonds, in a type of reaction called 'hydrogenation'.

The **aromatic** group is exemplified by benzene (which used to be a commonly used solvent on the organic lab, but which was shown to be carcinogenic), and naphthalene, a compound with a distinctive 'mothball' smell. Aromatic groups are planar (flat) ring structures, and are widespread in nature. We will learn more about the structure and reactions of aromatic groups in Chapter 15.

Aromatics

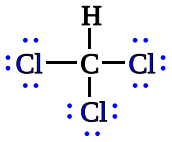


benzene naphthalene

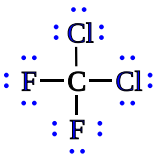
Functional Groups with Carbon Single Bonds to other Atoms

Halides

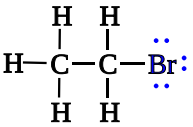
When the carbon of an alkane is bonded to one or more halogens, the group is referred to as a **alkyl halide** or **haloalkane**. The presence of a halogen atom (F, Cl, Br, or I), is often represented by X due to the similar chemistry of halogens. Chloroform is a useful solvent in the laboratory, and was one of the earlier anesthetic drugs used in surgery. Chlorodifluoromethane was used as a refrigerant and in aerosol sprays until the late twentieth century, but its use was discontinued after it was found to have harmful effects on the ozone layer. Bromoethane is a simple alkyl halide often used in organic synthesis. Alkyl halides groups are quite rare in biomolecules.



trichloromethane
(chloroform)



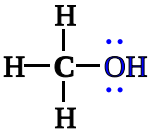
dichlorodifluoromethane
(Freon-12)



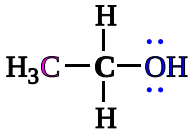
bromoethane

Alcohols and Thiols

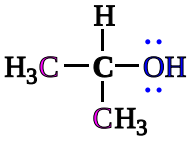
In the **alcohol** functional group, a carbon is single-bonded to an OH group (the OH group, by itself, is referred to as a **hydroxyl**). Except for methanol, all alcohols can be classified as primary, secondary, or tertiary. In a **primary alcohol**, the carbon bonded to the OH group is also bonded to only one other carbon. In a **secondary alcohol** and **tertiary alcohol,** the carbon is bonded to two or three other carbons, respectively. When the hydroxyl group is *directly* attached to an aromatic ring, the resulting group is called a **phenol**.



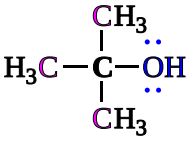
methanol



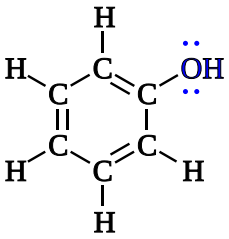
a primary
alcohol



a secondary
alcohol

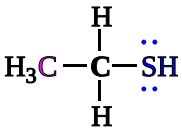


a tertiary
alcohol

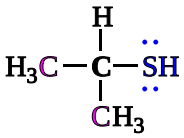


a phenol

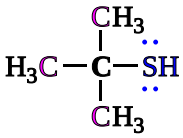
The sulfur analog of an alcohol is called a **thiol** (the prefix *thio*, derived from the Greek, refers to sulfur).



a primary
thiol



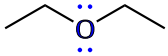
a secondary
thiol

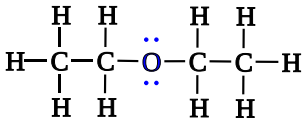


a tertiary
thiol

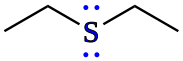
Ethers and sulfides

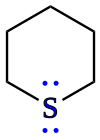
In an **ether** functional group, a central oxygen is bonded to two carbons. Below are the line and Lewis structures of diethyl ether, a common laboratory solvent and also one of the first medical anaesthesia agents.





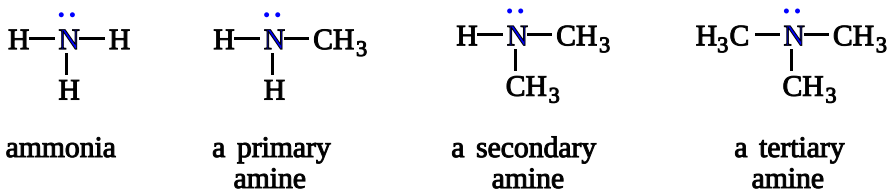
In **sulfides**, the oxygen atom of an ether has been replaced by a sulfur atom.



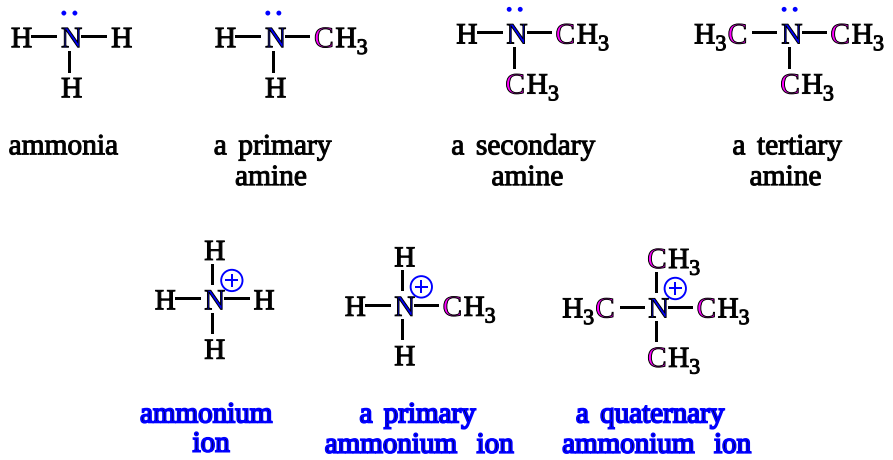


Amines

Amines are characterized by nitrogen atoms with single bonds to hydrogen and carbon. Just as there are primary, secondary, and tertiary alcohols, there are primary, secondary, and tertiary amines. Ammonia is a special case with no carbon atoms.

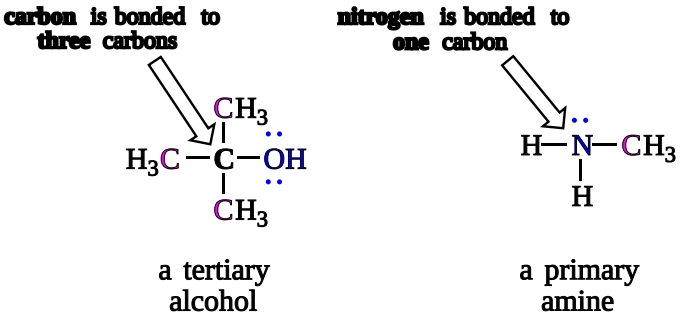


One of the most important properties of amines is that they are basic, and are readily protonated to form **ammonium** cations. In the case where a nitrogen has four bonds to carbon (which is somewhat unusual in biomolecules), it is called a quaternary ammonium ion.



Caution

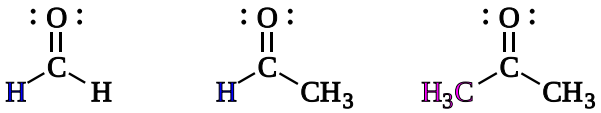
Do not be confused by how the terms 'primary', 'secondary', and 'tertiary' are applied to alcohols and amines - the definitions are different. In alcohols, what matters is how many other carbons the alcohol *carbon* is bonded to, while in amines, what matters is how many carbons the *nitrogen* is bonded to.



Carbonyl Containing Functional Groups

Aldehydes and Ketones

There are a number of functional groups that contain a carbon-oxygen double bond, which is commonly referred to as a **carbonyl**. **Ketones** and **aldehydes** are two closely related carbonyl-based functional groups that react in very similar ways. In a ketone, the carbon atom of a carbonyl is bonded to two other carbons. In an aldehyde, the carbonyl carbon is bonded on one side to a hydrogen, and on the other side to a carbon. The exception to this definition is formaldehyde, in which the carbonyl carbon has bonds to two hydrogens.



formaldehyde | an aldehyde | a ketone

Carboxylic acids and acid derivatives

If a carbonyl carbon is bonded on one side to a carbon (or hydrogen) and on the other side to a **heteroatom** (in organic chemistry, this term generally refers to oxygen, nitrogen, sulfur, or one of the halogens), the functional group is considered to be one of the '**carboxylic acid derivatives'**, a designation that describes a grouping of several functional groups. The eponymous member of this grouping is the **carboxylic acid** functional group, in which the carbonyl is bonded to a hydroxyl (OH) group.



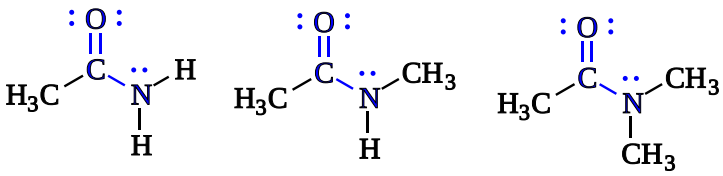
formic acid | acetic acid (vinegar)

As the name implies, carboxylic acids are acidic, meaning that they are readily deprotonated to form the conjugate base form, called a **carboxylate** (much more about carboxylic acids in Chapter 20).

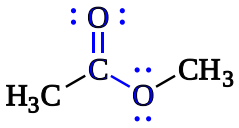


formate | acetate

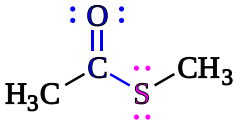
In **amides**, the carbonyl carbon is bonded to a nitrogen. The nitrogen in an amide can be bonded either to hydrogens, to carbons, or to both. Another way of thinking of an amide is that it is a carbonyl bonded to an amine. Recall when naming that it is how many carbons the nitrogen is bonded to that will determine if it is a primary, secondary or tertiary amide.



In **esters**, the carbonyl carbon is bonded to an oxygen which is itself bonded to another carbon. Another way of thinking of an ester is that it is a carbonyl bonded to an alcohol. **Thioesters** are similar to esters, except a sulfur is in place of the oxygen.

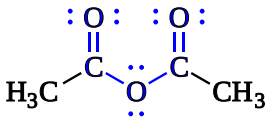


an ester



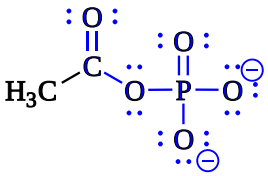
a thioester

In an **acid anhydride**, there are two carbonyl carbons with an oxygen in between. An acid anhydride is formed from combination of two carboxylic acids with the loss of water (anhydride).

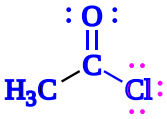


an anhydride

In an **acyl phosphate**, the carbonyl carbon is bonded to the oxygen of a phosphate, and in an **acid chloride**, the carbonyl carbon is bonded to a chlorine.



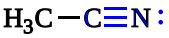
an acyl phosphate



an acid chloride

Nitriles and Imines

In a **nitrile** group, a carbon is triple-bonded to a nitrogen. Nitriles are also often referred to as **cyano** groups.



a nitrile

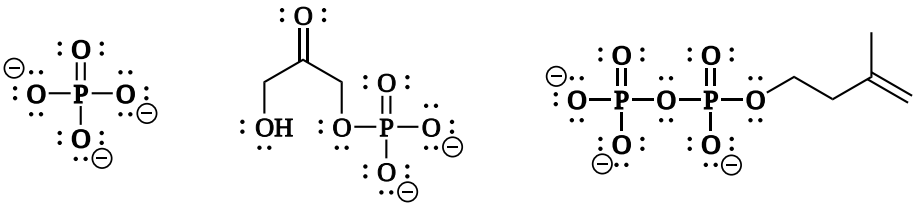
Molecules with carbon-nitrogen double bonds are called **imines**, or **Schiff bases**.



imines

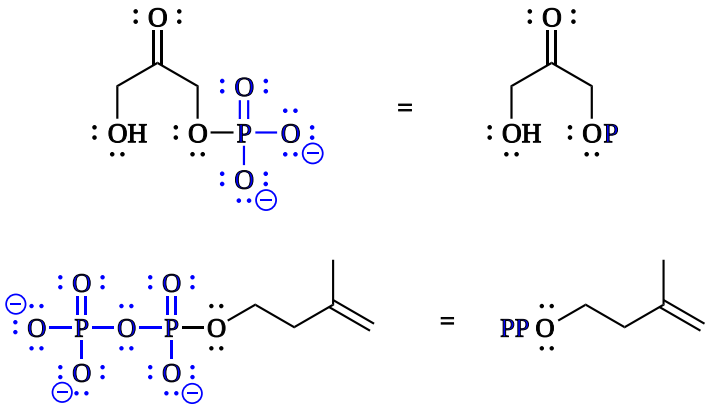
Phosphates

Phosphorus is a very important element in biological organic chemistry, and is found as the central atom in the **phosphate** group. Many biological organic molecules contain phosphate, diphosphate, and triphosphate groups, which are linked to a carbon atom by the **phosphate ester** functionality.



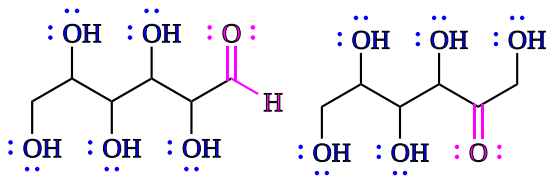
inorganic phosphate | an organic phosphate ester | an organic diphosphate ester

Because phosphates are so abundant in biological organic chemistry, it is convenient to depict them with the abbreviation 'P'. Notice that this 'P' abbreviation includes the oxygen atoms and negative charges associated with the phosphate groups.



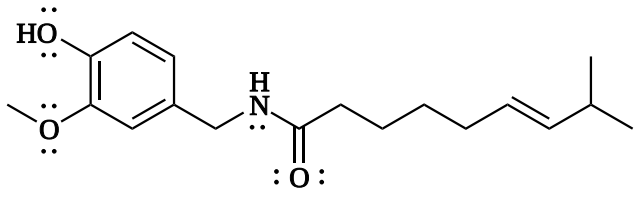
Molecules with Multiple Functional Groups

A single compound may contain several different functional groups. The six-carbon sugar molecules glucose and fructose, for example, contain aldehyde and ketone groups, respectively, and both contain five alcohol groups (a compound with several alcohol groups is often referred to as a '**polyol**').



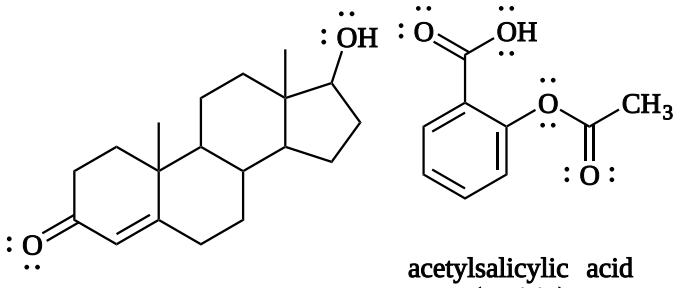
glucose | fructose

Capsaicin, the compound responsible for the heat in hot peppers, contains phenol, ether, amide, and alkene functional groups.



capsaicin

The male sex hormone testosterone contains ketone, alkene, and secondary alcohol groups, while acetylsalicylic acid (aspirin) contains aromatic, carboxylic acid, and ester groups.



testosterone

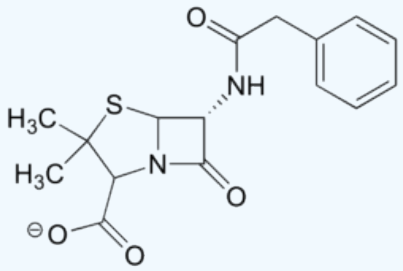
acetylsalicylic acid (aspirin)

While not in any way a complete list, this section has covered most of the important functional groups that we will encounter in biological and laboratory organic chemistry. The table found below provides a summary of all of the groups listed in this section, plus a few more that will be introduced later in the text.

Exercise 1.10.1

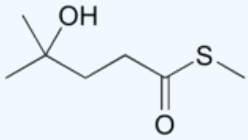
Identify the functional groups in the following organic compounds. State whether alcohols and amines are primary, secondary, or tertiary.

a)

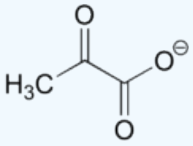


penicillin

b)

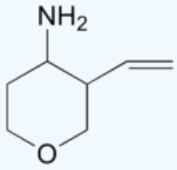


c)



pyruvate

d)



Answer available at the end of this section.

2: Draw one example each (there are many possible correct answers) of compounds fitting the descriptions below, using line structures. Be sure to designate the location of all non-zero formal charges. All atoms should have complete octets (phosphorus may exceed the octet rule).

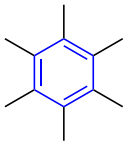
a) a compound with molecular formula $C_6H_{11}NO$ that includes alkene, secondary amine, and primary alcohol functional groups

b) an ion with molecular formula $C_3H_5O_6P^{2-}$ that includes aldehyde, secondary alcohol, and phosphate functional groups.

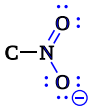
c) A compound with molecular formula C_6H_9NO that has an amide functional group, and does *not* have an alkene group.

Functional Group Tables

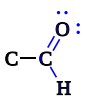
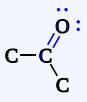
Exclusively Carbon Functional Groups

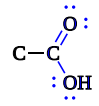
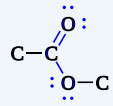
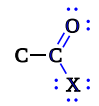
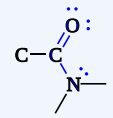
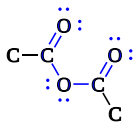
Group Formula	Class Name	Specific Example	IUPAC Name	Common Name
	alkene	$H_2C{=}CH_2$	ethene	ethylene
	alkyne	HC≡CH	ethyne	acetylene
	arene	C_6H_6	benzene	benzene

Functional Groups with Single Bonds to Heteroatoms

Group Formula	Class Name	Specific Example	IUPAC Name	Common Name
	halide	H_3C-I	iodomethane	methyl iodide
	alcohol	CH_3CH_2OH	ethanol	ethyl alcohol
	ether	$CH_3CH_2OCH_2CH_3$	diethyl ether	ether
	amine	H_3C-NH_2	aminomethane	methylamine
	nitro compound	H_3C-NO_2	nitromethane	
	thiol	H_3C-SH	methanethiol	methyl mercaptan
	sulfide	H_3C-S-CH_3	dimethyl sulfide	

Functional Groups with Multiple Bonds to Heteroatoms

Group Formula	Class Name	Specific Example	IUPAC Name	Common Name
	nitrile	H_3C-CN	ethanenitrile	acetonitrile
	aldehyde	H_3CCHO	ethanal	acetaldehyde
	ketone	H_3CCOCH_3	propanone	acetone

	carboxylic acid	H_3CCO_2H	ethanoic Acid	acetic acid
	ester	$H_3CCO_2CH_2CH_3$	ethyl ethanoate	ethyl acetate
	acid halide	H_3CCOCl	ethanoyl chloride	acetyl chloride
	amide	$H_3CCON(CH_3)_2$	N,N-dimethylethanamide	N,N-dimethylacetamide
	acid Anhydride	$(H_3CCO)_2O$	ethanoic anhydride	acetic anhydride

Exercises

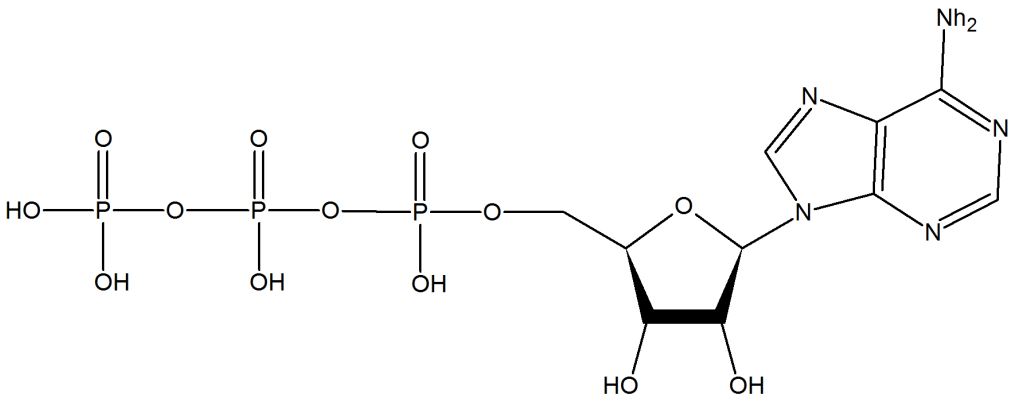
3.1 Functional Groups

3.1 Exercises

Questions

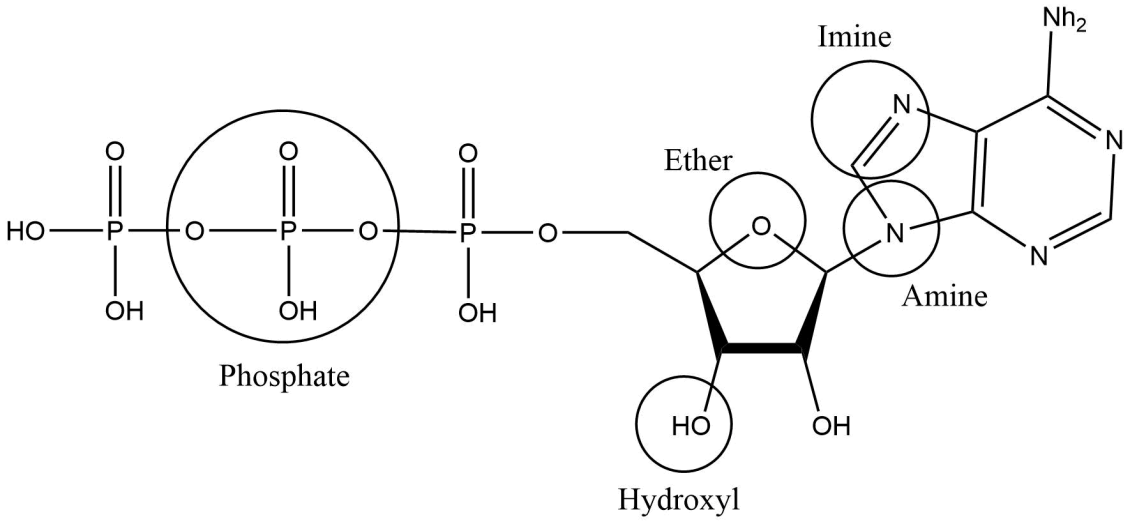
Q3.1.1

The following is the molecule for ATP, or the molecule responsible for energy in human cells. Identify the functional groups for ATP.



Solutions

S3.1.1



Answers

Exercise 1.10.1

a) carboxylate, sulfide, aromatic, two amide groups (one of which is cyclic)

b) tertiary alcohol, thioester

c) carboxylate, ketone

d) ether, primary amine, alkene

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1.11: Organic Reactions

Learning Outcomes

- Identify and describe substitution, elimination, addition, hydrolysis, and condensation reactions.
- Predict products of each reaction type.
- Predict products of hydration reactions based on Markovnikov's rule.
- Explain why condensation reactions are also called dehydration reactions.
- Define "polymer".

Organic reactions require the breaking of strong covalent bonds, which takes a considerable input of energy. In order for relatively stable organic molecules to react at a reasonable rate, they often must be modified with the use of highly reactive materials or in the presence of a catalyst. In this lesson, you will learn about several general categories of organic reactions.

Substitution Reactions

A **substitution reaction**, which is the same as a single replacement reaction in inorganic reactions, *is a reaction in which one or more atoms in a molecule are replaced with another atom or group of atoms.* Alkyl halides are formed by the substitution of a halogen atom for a hydrogen atom. When methane reacts with chlorine gas, ultraviolet light can act as a catalyst for the reaction.

$$\mathrm{CH_4\,(g) + Cl_2\,(g) \overset{\text{UV light}}{\rightarrow} CH_3Cl\,(g) + HCl\,(g)} \tag{1.11.1}$$

The reaction produces chloromethane and hydrogen chloride. When the mixture is allowed to react for longer periods of time, further substitution reactions may occur.

$$\mathrm{CH_3Cl\,(g) + Cl_2\,(g) \overset{\text{UV light}}{\rightarrow} CH_2Cl_2\,(g) + HCl\,(g)} \tag{1.11.2}$$

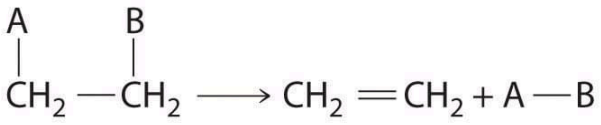
The product above is dichloromethane. Further substitution products trichloromethane and tetrachloromethane, commonly called carbon tetrachloride. A mixture of products occurs in the reaction, with the relative amounts dependent upon the time that the reaction is allowed to proceed. Chlorofluorocarbons are produced by reacting chloroalkanes with HF, because the fluorine atom makes a stronger bond to the carbon atom than chlorine does.

$$\mathrm{CCl_4\,(g) + HF\,(g) \overset{SbF_5}{\rightarrow} CCl_3F\,(g) + HCl\,(g)} \tag{1.11.3}$$

The fluorine atom substitutes for a chlorine atom in the reaction.

Elimination Reactions

An **elimination reaction** involves the removal of adjacent atoms from a molecule. This results in the formation of a multiple bond and the release of a small molecule, so they are called elimination reactions. They have the general form



A typical example is the conversion of ethyl chloride to ethylene:

$$CH_3CH_2Cl \rightarrow CH_2 = CH_2 + HCl \tag{1.11.4}$$

Much of the approximately 26 million tons of ethylene produced per year in the United States is used to synthesize plastics, such as polyethylene. In the above reaction, the A–B molecule eliminated is HCl, whose components are eliminated as H^+ from the carbon atom on the left and Cl^- from the carbon on the right. When an acid is produced, as occurs here, the reaction is generally carried out in the presence of a base (such as NaOH) to neutralize the acid. Other elimination reactions will produce H_2, X_2 (where X = halogen), or H_2O. These reactions are often referred to by more descriptive terms such as dehydrogenation (removing hydrogen) or dechlorination (removing chlorine).

Addition Reactions

An **addition reaction** *is a reaction in which an atom or molecule is added to an unsaturated molecule, making a single product.* An addition reaction can often be thought of as adding a molecule across the double bond of an alkene or across the triple bond of an alkyne. Knowing that "ation" means to add, the specific names of these reactions, such as hydrogenation, hydration, or chlorination, should make sense. Note that hydrogenation (adding H_2) and hydration (adding H_2O) are very different processes.

One type of addition reaction is called hydrogenation. **Hydrogenation** *is a reaction that occurs when molecular hydrogen is added to an alkene to produce an alkane* or *hydrogen is added to an alkyne to produce an alkene or alkane*. The reaction is typically performed with the use of a transition metal catalyst. For example, ethene reacts with hydrogen to form ethane.

$$\mathrm{CH_2{=}CH_2\,(g) + H_2\,(g) \overset{Pt}{\rightarrow} CH_3CH_3\,(g)} \tag{1.11.5}$$

Note that the hydrogenation reaction is also a redox reaction. Ethene is reduced, because the oxidation numbers of the carbon atoms change from -2 to -3 as a result of the reaction.

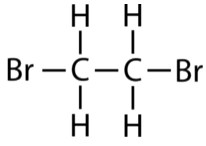
Vegetable oils consist of long carbon chains with carboxyl groups on the end; these molecules are referred to as fatty acids. The carbon chains of the fatty acids in vegetable oils are unsaturated, usually containing multiple double bonds. When hydrogen gas is blown through a sample of the oil, hydrogen atoms add across the double bonds. This conversion changes the substance from a liquid oil into a solid fat. The "hydrogenated" on a food product is an indication that oil (liquid) has been converted into fat (solid) by this process. Margarine is manufactured from unsaturated vegetable oil in this way by hydrogenating some of the double bonds making it a "partially hydrogenated vegetable oil".

Addition reactions are also useful ways to introduce a new functional group into an organic molecule. Alkyl halides can be produced from an alkene by the addition of either the elemental halogen or the hydrogen halide. A monosubstituted alkyl halide can be produced by the addition of a hydrogen halide to an alkene. Shown below is the formation of chloroethane.

$$\mathrm{CH_2{=}CH_2\,(g) + HCl\,(g) \rightarrow CH_3CH_2Cl\,(g)} \tag{1.11.6}$$

When the reactant is the diatomic halogen, the product is a disubstituted alkyl halide as in the addition of bromine to ethene.

$$\mathrm{CH_2{=}CH_2\,(g) + Br_2\,(l) \rightarrow CH_2BrCH_2Br\,(g)} \tag{1.11.7}$$



1,2-dibromoethane

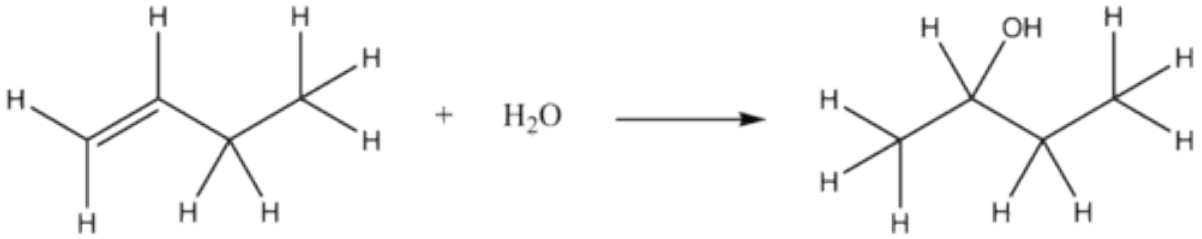
The addition of bromine to an unknown organic compound can be used as a test for unsaturation in the compound. Bromine has a distinctive brownish-orange color, while most bromoalkanes are colorless. When bromine is slowly added to a solution of the compound, the orange color will fade if it undergoes an addition reaction to produce an alkyl halide. If the orange color remains, then the original compound was already saturated, and no reaction occurred.

A **hydration reaction** *is a reaction in which water is added to an alkene*. Hydration reactions can take place when the alkene and water are heated to near $100^{\circ}\mathrm{C}$ in the presence of a strong acid, which acts as a catalyst. Shown below is the hydration of ethene to produce ethanol.

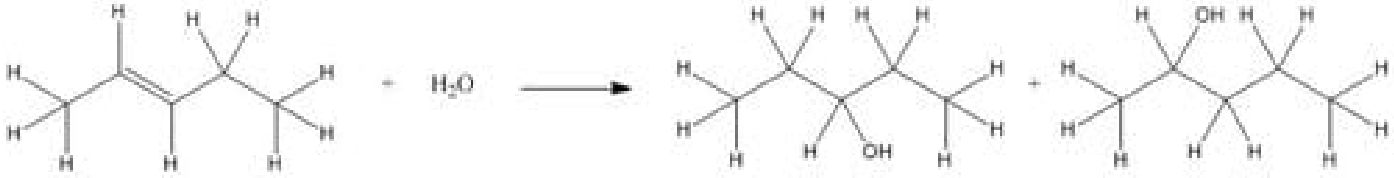
$$\mathrm{CH_2{=}CH_2\,(g) + H_2O\,(l) \rightarrow CH_3CH_2OH\,(g)} \tag{1.11.8}$$

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Unlike addition reactions involving H_2 or Br_2, the addition of water can have two possible products because an $-H$ and an $-OH$ are being added to the carbons in the double bond. **Markovnikov's rule** helps predict the main product in a hydration reaction. The rule states that the hydrogen atom from water will add to the carbon that originally had more hydrogen atoms. For example, look at the hydration of 1-butene.



Note that the first carbon in 1-butene started with two hydrogen atoms and the second carbon started with one hydrogen. Therefore, the hydrogen from water adds to the first carbon and the $-OH$ group adds to the second carbon. When there are equal numbers of hydrogen atoms on both carbons in a double bond then the two products will form in approximately equal amounts. For example, the hydration of 2-pentene results in two products. In the first product, the $-OH$ group is on the third carbon and in the second product, the $-OH$ group is on the second carbon. While these two molecules will have similar properties, there will be differences.



Condensation Reactions

A **condensation reaction** *is a reaction in which two molecules combine to form a single molecule.* A small molecule, often water, is usually removed during a condensation reaction. Amino acids are important biological molecules that have an amine functional group on one end of the molecule and a carboxylic acid functional group on the other end. When two amino acids combine in a condensation reaction, a covalent bond forms between the amine nitrogen of one amino acid and the carboxyl carbon of the second amino acid. A molecule of water is then removed as a second product (see figure below).

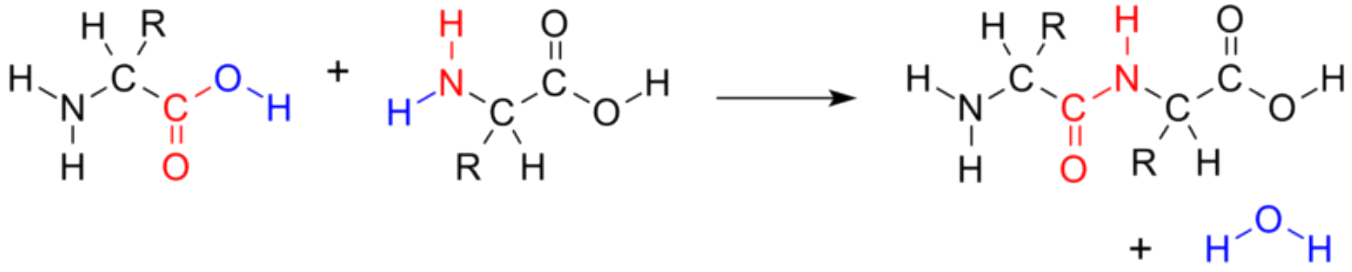
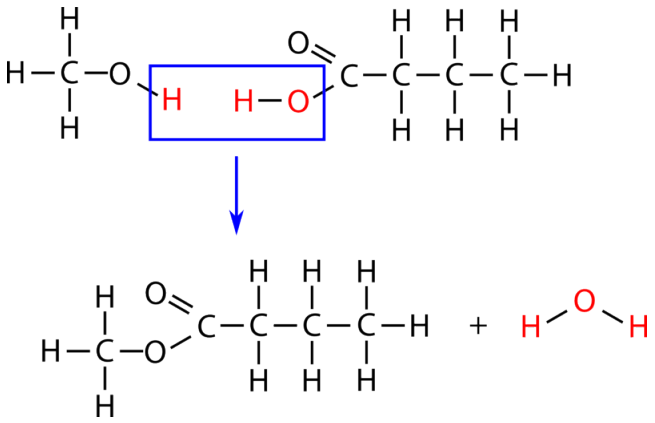


Figure 1.11.1: Amino acids join together to form a molecule called a dipeptide. The $-OH$ from the carboxyl group of one amino acid combines with a hydrogen atom from the amine group of the other amino group to produce water (blue).

This reaction forms a molecule called a dipeptide, and the resulting carbon-nitrogen covalent bond is often called a peptide bond. When repeated numerous times, a long molecule called a protein is eventually produced.

An **esterification** *is a condensation reaction in which an ester is formed from an alcohol and a carboxylic acid.* Esterification is a subcategory of condensation reactions because a water molecule is produced in the reaction. The reaction can be catalyzed by a strong acid, usually sulfuric acid. When the carboxylic acid, butanoic acid, is heated with an excess of methanol and a few drops of sulfuric acid, the ester methyl butanoate is produced. Methyl butanoate has the scent of pineapples. The reaction is shown below with both molecular and structural formulas. Esterification reactions are reversible.

$$\mathrm{CH_3CH_2CH_2COOH + HOCH_3 \overset{H_2SO_4}{\rightarrow} CH_3CH_2CH_2COOCH_3 + H_2O} \tag{1.11.9}$$

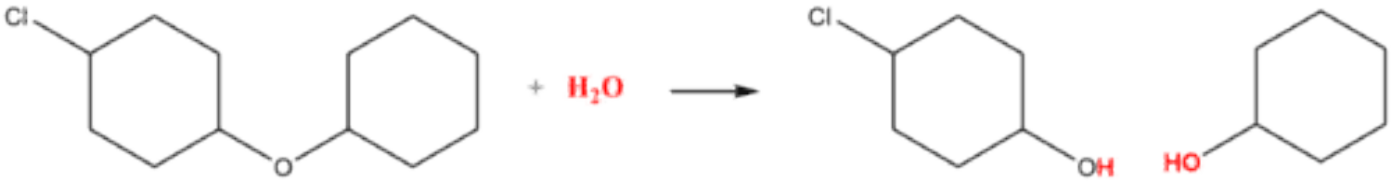


Saponification *describes the alkaline hydrolysis reaction of an ester*. The term saponification originally described the hydrolysis of long-chain esters called fatty acid esters to produce soap molecules, which are the salts of fatty acids. One such soap molecule is sodium stearate, formed from the hydrolysis of ethyl stearate.

$$\underset{\text{ethyl stearate}}{\mathrm{C_{17}H_{35}COOC_2H_5}} + \mathrm{NaOH} \rightarrow \underset{\text{sodium stearate (soap)}}{\mathrm{C_{17}H_{35}COO^-Na^+}} + \mathrm{C_2H_5OH} \tag{1.11.10}$$

Hydrolysis Reactions

Hydrolysis is the reverse of condensation. "Hydro" indicates that water is involved and "lysis" means to break apart. In a hydrolysis reaction, water is added and the molecule breaks apart, usually at a $\mathrm{C{-}O{-}C}$ linkage.



Polymerization

Polymers are very different than the other kinds of organic molecules that you have seen so far. Whereas other compounds are of relatively low molar mass, polymers are giant molecules of very high molar mass. Polymers are the primary components of all sorts of plastics and related compounds. A **polymer** *is a large molecule formed of many smaller molecules covalently bonded to one another in a repeating pattern*. The *small molecules that make up the polymer are called* **monomers**. Polymers are generally formed by either addition or condensation reactions. Teflon (see figure below) is a non-reactive, non-stick coating used on cookware as well as in containers and pipes for reactive or corrosive chemicals.

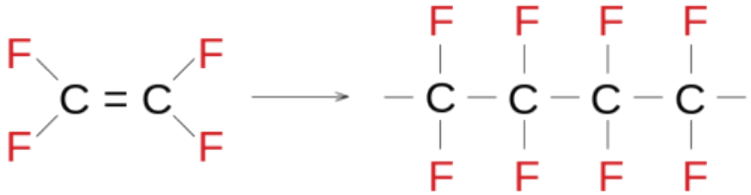


Figure 1.11.2: Polytetrafluoroethylene (also known as Teflon) is formed from the polymerization of tetrafluoroethylene.

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1.12: ADDITIONAL PRACTICE

The following pages are intended to provide refreshers and practice problems related to the previous sections.

1.9.1: Lewis and Formal Charge (WorkSheet)

1.9.2: Line drawings

1.9.3: The need for resonance structures

1.9.4: Three dimensional drawings

1.9.5: Organic functional groups

1.9.6: Solutions to Selected (IM) Problems

1.11.7: London Attractions

1.11.8: Dipole-dipole attractions

1.11.9: Hydrogen Bonding

1.11.10: Solutions to selected (SP) problems

1.12.1: Lewis and Formal Charge (WorkSheet)

1.12.2: Line drawings

1.12.3: The need for resonance structures

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1.12.5: Organic functional groups

1.12.6: Solutions to Selected (IM) Problems

1.12.7: London Attractions

1.12.8: Dipole-dipole attractions

1.12.9: Hydrogen Bonding

1.12.10: Solutions to selected (SP) problems

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1.12.1: Lewis and Formal Charge (WorkSheet)

Looking at the structure of a molecule can help us to understand or to predict the behaviour of that compound. One of the tools that we will eventually use to understand reactivity is formal charge. That is because reactivity has to do with the reorganization of electrons between atoms. New chemical bonds are formed by sharing electrons. Old chemical bonds are broken when one atom takes the bonding electrons away from another atom.

- chemical reactions occur via attraction and donation of electrons

Formal charge can help us to understand the behaviour of carbon monoxide, CO. When exposed to transition metal cations such as the iron in hemoglobin (Fe2+), the carbon is attracted to and binds to the metal. In the case of hemoglobin, because the carbon monoxide binds very strongly to the iron, the CO blocks the position where oxygen would normally be bound and carbon monoxide poisoning results.

- formal charge can help us predict how a molecule behaves
- atoms with positive formal charges often attract electrons
- atoms with negative formal charges often donate electrons

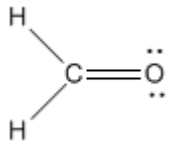
Why does the molecule behave in this way? There are actually a number of reasons. However, the fact that the carbon is attracted to a metal cation begs the question: Is the carbon an anion? Yes, in a sense. In a Lewis structure of the compound, the carbon has a formal negative charge. You will see why below.

Formal charges are an important book-keeping device that we use in Lewis structures. They tell us if one atom is donating extra electrons to another to give it an octet. If an atom needs to donate more electrons than normal in order for everyone to get an octet, it will have a positive formal charge. If an atom donates fewer electrons than normal and everyone still has an octet, it must be getting extra electrons from somewhere else. It will have a negative formal charge.

- formal charge is often present if the atom does not have its usual number of bonds
- valence rules can act as flags to alert you that formal charges are present

To help us think about formal charges, let's look at a few small molecules that all contain carbon-oxygen multiple bonds but that are slightly different from each other. Formaldehyde (CH_2O) is a chemical that is used to preserve tissues; you may be familiar with its odour from anatomy lab. Carbon monoxide results from burning fossil fuels; it is also an important industrial chemical used in manufacturing detergents. Carbonate is an anion that is found in many forms. Calcium carbonate is found in limestone and chalk, for instance.

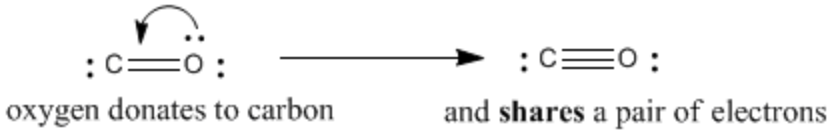
Look at the structure of formaldehyde. Oxygen has a normal valence of two, and it has two bonds in formaldehyde, so there is no formal charge on the oxygen. Carbon has a normal valence of four, and it has four bonds here. There is no formal charge on carbon. There are no formal charges on the hydrogens either.

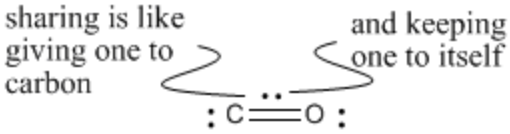


Carbon monoxide has a structure that is very similar to formaldehyde. It does not have any hydrogens, though. With ten electrons total, the only way to get an octet on both atoms is to make three bonds between carbon and oxygen.



Oxygen has normal valence two, but here it is making three bonds. It is sharing an extra pair of its electrons with carbon to make that third bond. If it is sharing a pair of electrons, we can think of it keeping one for itself and giving the other to carbon. Since it gives one of its electrons to carbon, it has formal charge +1.





Carbon has normal valence four, but here it is only making three bonds, even though it has an octet. How did it get an octet with only three bonds? It got an extra electron from somewhere (the oxygen). It has formal charge -1.



Notice that overall the carbon monoxide molecule is neutral. Oxygen has a plus charge and carbon has a minus charge. These charges cancel to give an overall neutral molecule.

What we are really doing when we assign formal charge is comparing how many electrons the atom brought with it from the periodic table to how many it has now. If the atom brought four electrons of its own and it is now sharing eight, things are even. It brought four to share and got four from its neighbours in an even trade. If it only brought three of its own and is now sharing eight, it got more electrons than it gave, and it will have a negative charge.

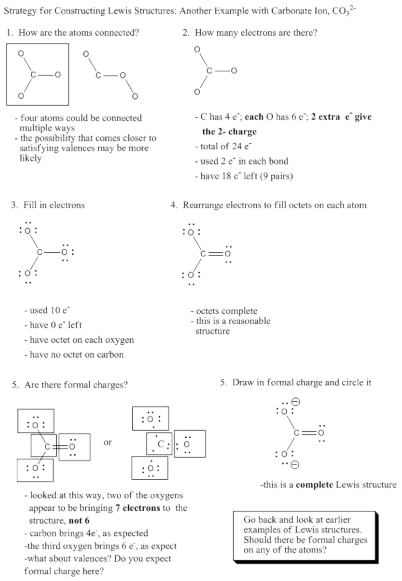
To determine formal charge:

- check the number of electrons on the atom in the periodic table
- check the number of electrons entirely owned by the atom in the molecule; *this is different than looking for an octet*
- "entirely owned" electrons include any electrons in lone pairs, since they belong completely to one atom
- "entirely owned" electrons also include half of the electrons in the bonds to the atom, since it is sharing each of those pairs with other atoms.

Compare the number of entirely owned valence electrons in the periodic table to those entirely owned by the atom in the molecule.

- if the number of entirely owned electrons on the atom in the molecule is higher than in the periodic table, the atom has a negative charge
- if the number of entirely owned electrons on the atom in the molecule is lower than in the periodic table, the atom has a positive charge
- the formal charge is additive: if the atom has two extra electrons in the molecule, it has a two minus charge. If it is two short, it has a two plus charge.

Remember, electron counting to determine an octet counts all of the bonding and nonbonding electrons equally. It is done simply to determine whether the atom has a noble gas configuration right now. Electron counting to determine formal charge is done to keep track of who has given electrons to whom when making the molecule. If, in getting to an octet, atoms have received more electrons than they have given, their electron/proton ratio has changed, and they become charged.



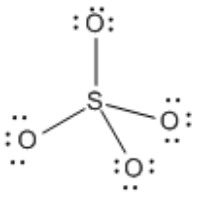
Problem IM5.1

Draw Lewis or Kekule structures for the following molecules, remembering to include formal charges, if any (and notice that some of these molecules are ions):

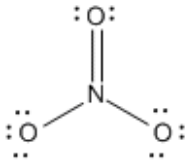
a) NO^+ b) CN^- c) CH_3O^- d) CH_3^+ e) HNO_3 f) $CH_3CO_2^-$

Problem IM5.2.

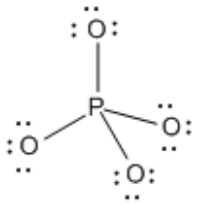
Given the structures below, assign any missing formal charges.



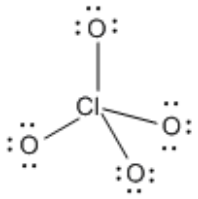
sulfate



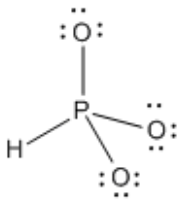
nitrate



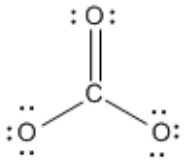
phosphate



perchlorate



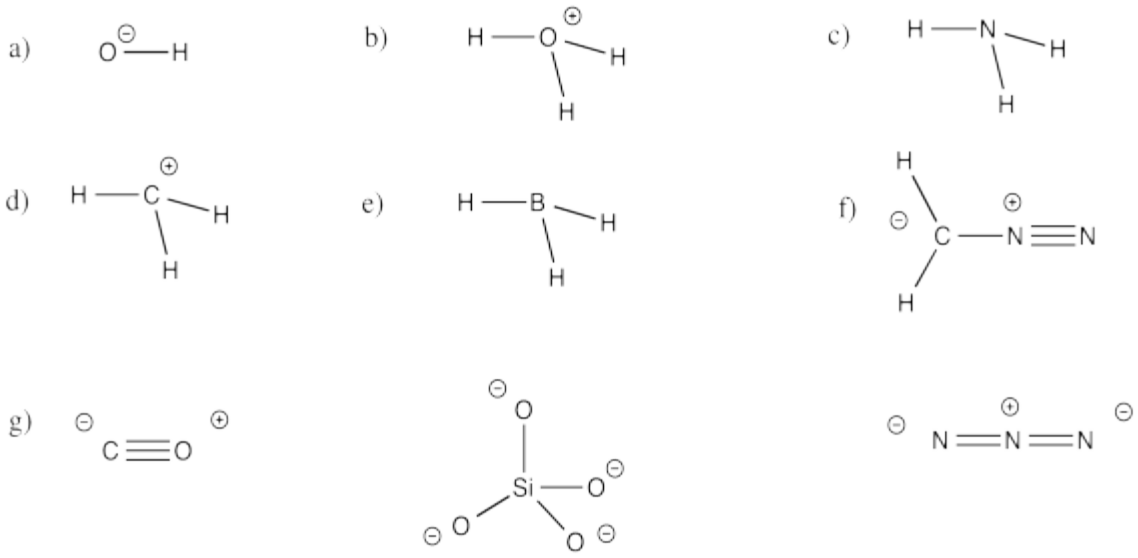
phosphite



carbonate

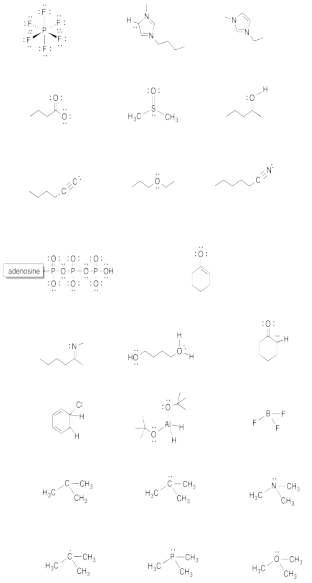
Problem IM5.3.

Given the structures below, draw in the missing electrons, if any.



Problem IM5.4.

Label all atoms in the following compounds with the correct non-zero formal charge.



Problem IM5.5.

Provide structures for the following oxoanions (anions with oxygens attached to another atom) of chlorine:

a) hypochlorite, ClO^- b) chlorite, ClO_2^- c) chlorate, ClO_3^- d) perchlorate, ClO_4^-

Problem IM5.6.

Provide structures for the following oxoanions of sulfur:

a) sulfite, SO_3^{2-} b) sulfate, SO_4^{2-} c) thiosulfate, $S_2O_3^{2-}$ d) disulfate, $S_2O_7^{2-}$ e) persulfate or peroxomonosulfate, SO_5^{2-}

Problem IM5.6.

Provide structures for the following oxoanions of phosphorus:

a) phosphate, PO_4^{3-} b) phosphite, HPO_3^{2-} c) hypophosphite, $H_2PO_2^-$

Note that hydrogen atoms in some phosphorus oxoanions are attached to the phosphorus atom.

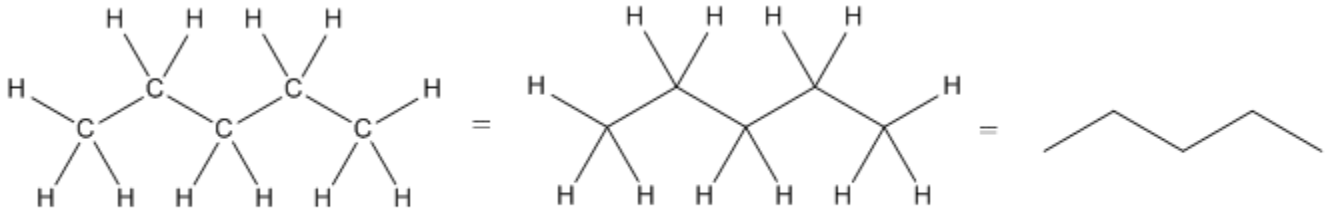
This page titled 1.12.1: Lewis and Formal Charge (WorkSheet) is shared under a CC BY-NC-SA 4.0 license and was authored, remixed, and/or curated by Matthew Davis.

1.12.2: Line drawings

Line drawings

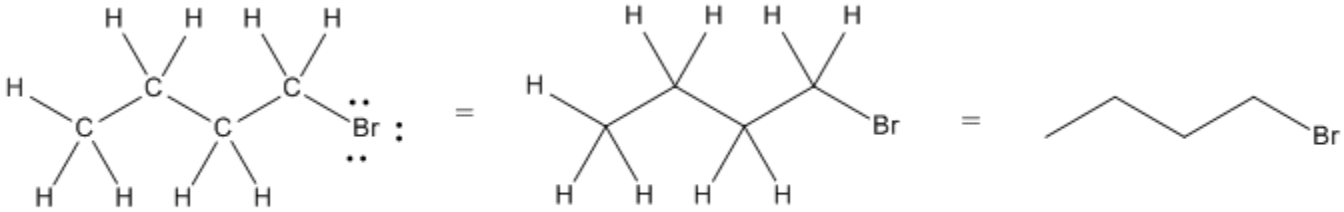
Lewis structures can tell us a lot about how atoms come together to make molecules. They can also be cumbersome, especially if we are dealing with very large molecules. Drawing a line instead of a pair of dots for bonding pairs of electrons makes it easier to draw structures. There are other abbreviations that are helpful in some situations.

Because organic chemistry is based on the compounds of carbon, we would have to draw the letter C over and over again unless we had a shortcut. In line structures, we drop the label "C" for the carbon atoms. Anytime there is a joint between two bonds (drawn as a vertex in a zig-zag line), the atom attached to that bond is assumed to be a carbon unless written otherwise.



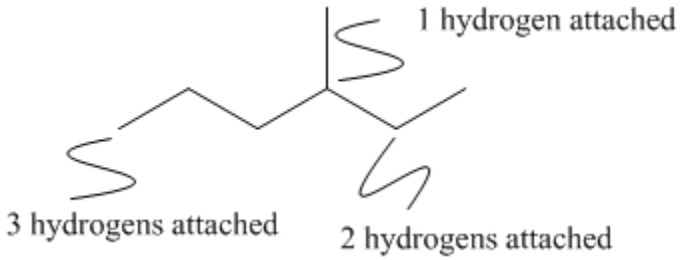
pentane

The atom at the end of a zig-zag line would also be a carbon, unless it is explicitly written as another atom.

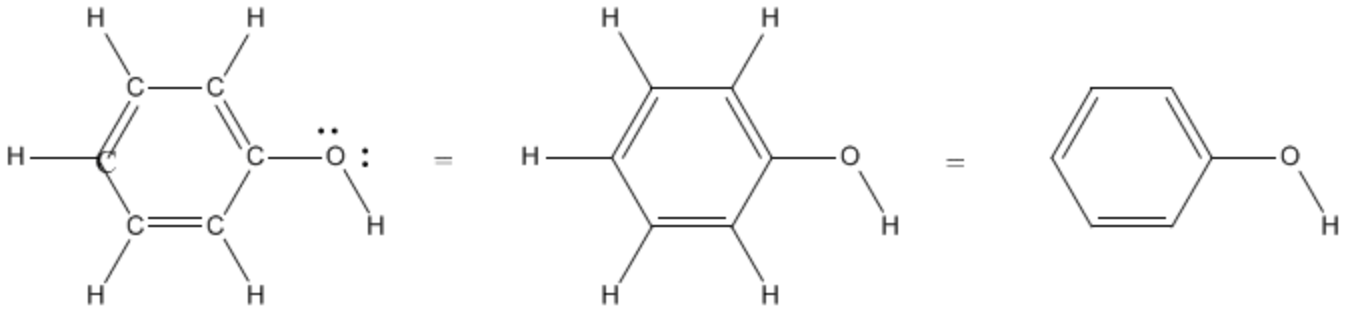


1-bromobutane

Taken even further, we will omit the hydrogens from our structures, since the compounds of carbon almost always contain hydrogen as well. Since we know carbon has a valence of four, we always know how many hydrogen atoms are attached to each carbon in order to reach that valence. A carbon with two bonds drawn in must have two hydrogens on it. A carbon with only one bond drawn to it must have three hydrogens.



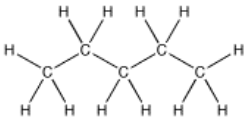
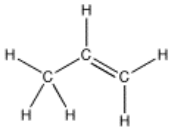
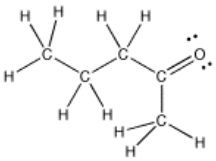
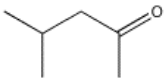
Note that the hydrogens are not normally omitted if they are attached to heteroatoms (atoms other than carbon, such as oxygen or nitrogen).



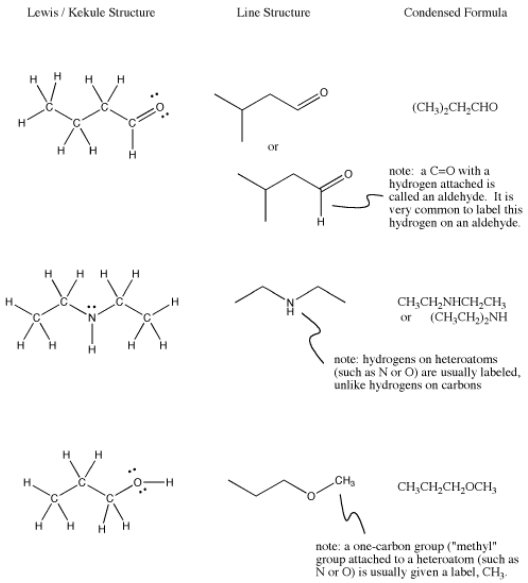
phenol

You will also note that lone pairs are frequently left out when we use line structures, so you will have to add them back in to think about Lewis structures. Adding the lone pairs back to the heteroatoms in line structures is a good habit to get into, because later in the course we will be very concerned with keeping track of where all the electrons are.

Below is a summary, showing the relationship between Lewis/Kekule structures, line structures and condensed formulae for a few different compounds.

Lewis / Kekule Structure	Line Structure	Condensed Formula
		$CH_3CH_2CH_2CH_2CH_3$ or $CH_3(CH_2)_3CH_3$
		CH_3CHCH_2
		$(CH_3)_2CH_2COCH_3$

Remember, in phenol, the hydrogen attached to oxygen was labeled in the line structure. Sometimes there are exceptions in line structures, in which atoms that you might not think about labeling usually do get labels. The most common exceptions are shown below.



Problem IM8.1.

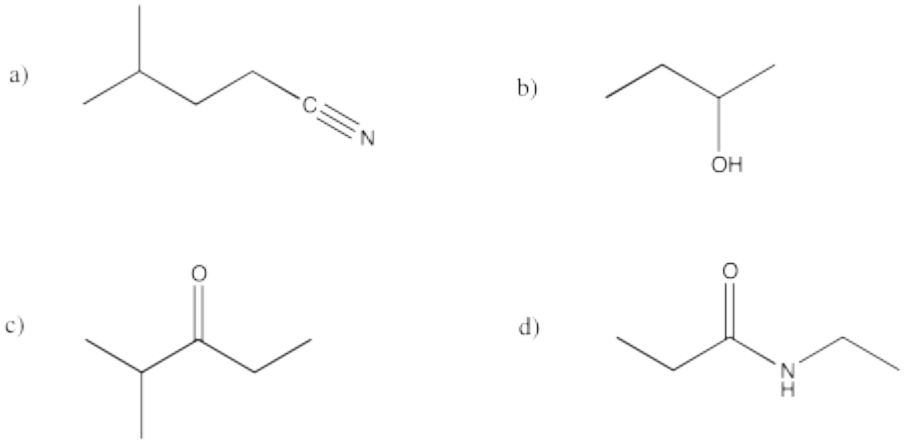
Translate the following condensed formulae into line drawings.

a) $CH_3CH_2NHCH_2CH_3$ b) $CH_3CHFCH_2CH_2CH_2Cl$

c) $CH_2CHOCH_2CH_3$ d) $CH_3CHClCH_2SCH_2CH_3$

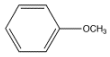
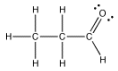
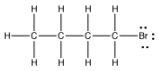
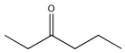
Problem IM8.2.

Translate the following structures into condensed formula.



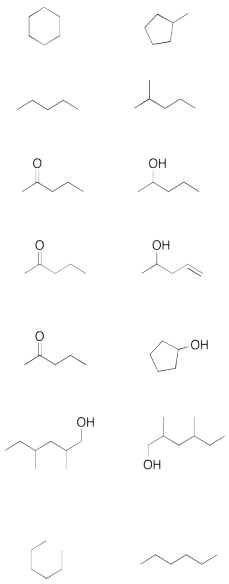
Problem IM8.3.

Try filling in the missing line drawing, Lewis / Kekule structures or condensed formulae in each line of the table below.

Lewis - Kekule Structure	Line structure	Condensed Formula
		$CH_3CH(CH_3)CH_2NH_2$
		
		$CH_3CH_2CO_2CH_3$
		
		$CH_3CO_2CH_2CH_3$
		
		$C_6H_5CH_2OH$
		

Problem IM8.4.

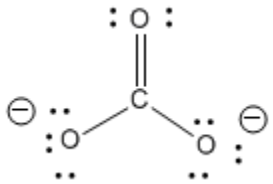
Look at the following pairs of compounds. Are the compounds constitutional isomers? (Hint: You may need to add in all hydrogens)



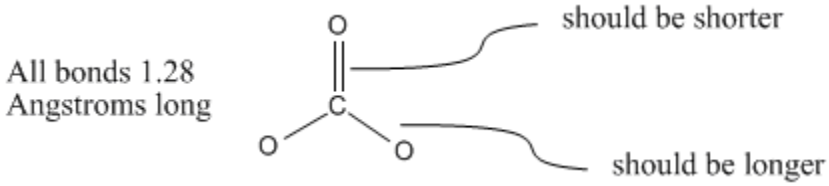
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1.12.3: The need for resonance structures

The carbonate anion shown below has one double bond and two single bonds. Normally, the number of bonds between two atoms in the Lewis structure can tell you how closely the two atoms are held. That means there is one C-O bond in the molecule that is shorter than the other two.

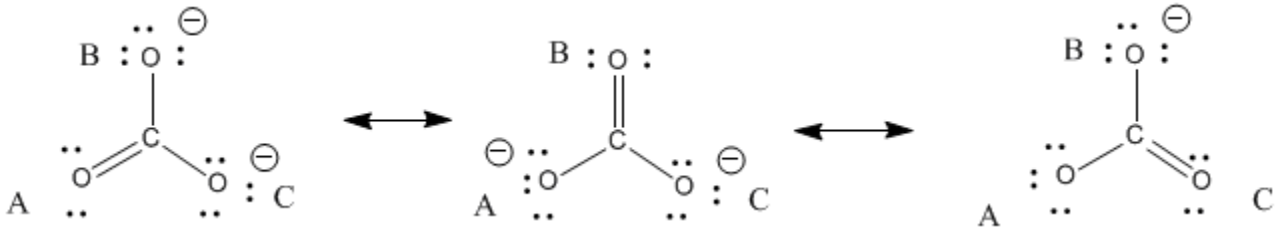


However, carbonate ion is an exception to the rule. In fact, carbonate ion is a symmetric, trigonal planar molecule. All three carbon-oxygen bond distances are about 1.28 Angstroms long.



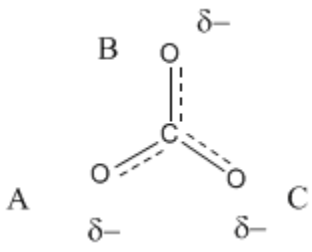
You cannot draw a Lewis structure that would suggest all three bonds are the same length. Instead, you can use resonance structures to understand this fact. Resonance structures are just alternate Lewis structures that take into account different possible arrangements of lone pairs and multiple bonds for a given skeletal structure. In carbonate, there are three ways to arrange these extra electrons.

If you label the oxygen atoms A, B and C, as shown below, then A has a double bond in 1/3 of the structures you could draw, but it would have a single bond in the other 2/3 of the ways in which you could draw the structure. The same is true for the atoms B and C.



In fact, carbonate really has about 1-1/3 bonds between each carbon and oxygen. Furthermore, there is not a full negative charge on any of the oxygens but about two-thirds of a negative charge on each of the three oxygens.

Occasionally we might draw a structure that shows partial bonds between atoms as dashed lines to suggest, in this case, 1-1/3 bonds instead of either one bond or two. We might also write ⛛⛛ ("delta minus") to denote a partial negative charge.



The limitation of this type of drawing is that it fails to show us exactly how many electrons we are dealing with. Later in the course, it will be very important to keep track of all the electrons in molecules as they undergo chemical reactions. Consequently, we almost always draw out different possible Lewis structures and keep in mind that the structure is something like a combination of all of them.

When we have structures that differ only in the way their electrons are arranged, but have exactly the same connectivity between the atoms, we refer to the set of structures as *resonance structures*. The double ended arrows between the resonance structures is the symbol we use to say that we have two or more different ways of drawing the same structure, and that we need to take all of the structures into account to understand how the molecule really behaves.

There is a subtlety here. The compound is not one structure or the other, and it is not an equilibrium where the structure changes back and forth rapidly. It is a superposition, in which a single molecule can behave like all three structures at the same time.

Problem IM6.1

Draw sets of resonance structures for the following compounds.

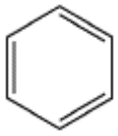
a) cyanate ion, NCO^- (a linear structure) b) formate ion, HCO_2^-

c) ozone, O_3 (a bent or "boomerang" structure) d) nitrate ion, NO_3^-

e) azide ion, NNN^- f) diazomethane, CH_2NN g) enolate ion, CH_2CHO^-

Problem IM6.2

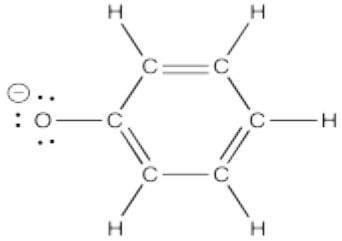
All of the bonds in benzene (below) are the same bond distance (1.39 A). Show why this is true.



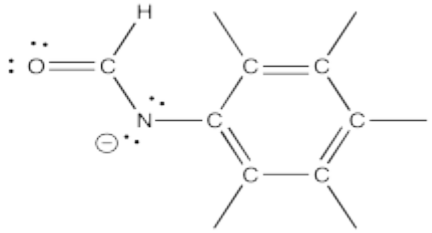
Problem IM6.3.

There are several resonance structures for each of the following ions. Show at least three for each.

a)



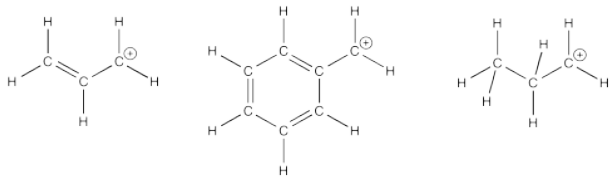
b)



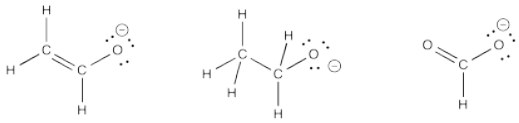
Problem IM6.4.

Ions can be greatly stabilized by delocalization. That is, if a charge can be spread out over several atoms by resonance, the charge is more stable. Use this idea to predict the relative stabilities of the following ions (rank them from most stable to least stable).

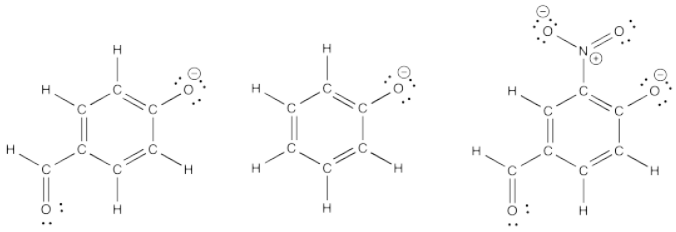
a)



b)

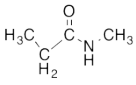


c)

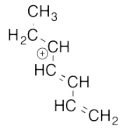


Problem IM6.5.

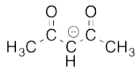
A.



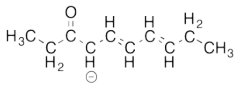
B.



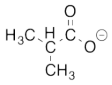
C.



D.



E.



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1.12.4: Three dimensional drawings

What is the three-dimensional shape of the molecule?

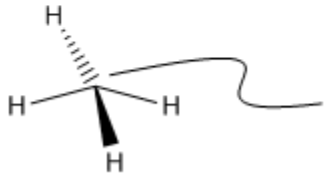
Our purpose in this chapter is to be able to represent the structure of a molecule. When we draw the Lewis structure for methane, it is only a 2-dimensional representation, but really the compound has a three-dimensional shape. The central carbon in methane is tetrahedral, with the four hydrogens at the alternate corners of a cube.

We can draw a tetrahedron by making a vertex between two lines, then attaching a wedged line and a hatched line to the outside of the corner. The black, wedged line is read as "this atom is towards us". The hatched line is read as "this atom is farther away from us". Although the drawing is flat, the hatched and wedged lines is a shorthand notation for 3-dimensionality.



methane

but not

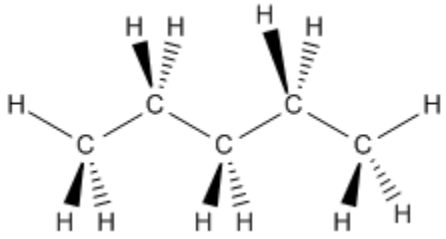


a highly distorted methane!

Representing the three-dimensional shape of a molecule can be done on paper, but only if we are very careful about drawing conventions such as wedge-dash drawings.

Carbons that have bonds to four *different* neighbors are always tetrahedral. The neighbors arranged around a tetrahedral carbon are around 109° apart. Sometimes, for reasons we won't go into here, tetrahedral carbons are called sp3 carbons.

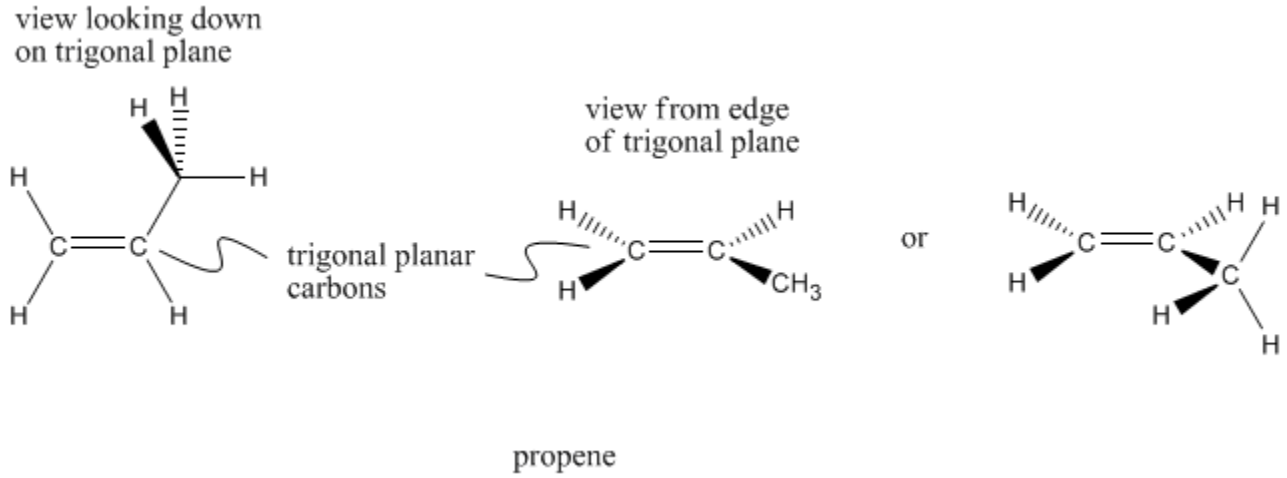
Pentane is a compound that contains four tetrahedral carbons in a row. Each tetrahedral carbon could be shown with wedge - dash projections.



It is also very common to use computer drawing programs to show the shapes of molecules. You can view the three-dimensional structure of pentane in many different ways. Three of the most common ways are shown here. Ball & Stick is an easy way to see where all the atoms are and how they are connected. Wireframe allows you to see connections without having your view obscured by atoms. Space-filling models are meant to most closely show you the shape of the molecule, although the atoms involved get obscured in this view.

Go to **Animation IM9.1.** A three-dimensional model of pentane.

Carbons double bonded to one neighbor, and consequently bonded to three different neighbors overall, are trigonal planar. The neighbors are all in the same plane and are about 120° apart. Trigonal planar carbons are sometimes described as sp2 carbons.



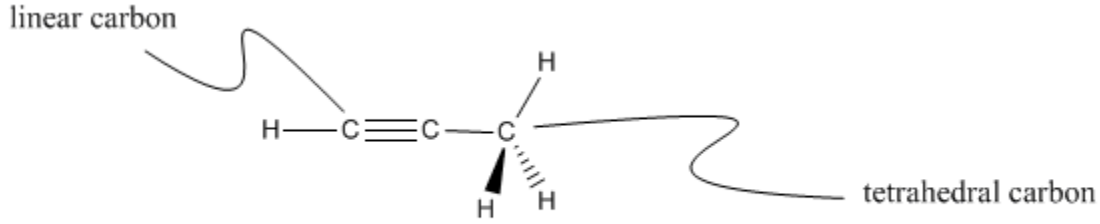
propene

Propene has two trigonal planar carbons as well as one tetrahedral carbon. Notice that a trigonal planar carbon is flat if viewed from one direction, but not if viewed from the other. Sometimes you will see trigonal carbons drawn differently, if the drawer wants you to look at the molecule from one direction or the other.

See if you can find both kinds of carbon on the model below.

Go to **Animation IM9.2.** A three-dimensional model of propene.

Carbons that have only two different neighbors are linear; each neighbor is 180° apart from the other. Linear carbons are sometimes called sp carbons.



propyne

Propyne has two linear carbons as well as one tetrahedral carbon. See if you can find both kinds of carbon on the model below.

Go to **Animation IM9.3.** A three-dimensional model of propyne.

Saying a carbon is sp or sp2 is only giving the shape of one atom within a molecule. The molecule itself may have a particular shape which is determined by the geometries of it constituent atoms, but which can't be described simply in words as "tetrahedral" or "linear".

Pentane is roughly a zig-zag shape. In a space-filling model, it resembles a fat caterpillar inching along. Propene is almost boomerang-shaped. Propyne is shaped like a dart; it has a pointed end and a feathered end.

Other molecules have more complicated shapes. The shape of ginkgolide B (a natural product isolated from the medicinally interesting *ginkgo biloba* tree) is hard to describe. However, it is clear that individual carbons in ginkgolide B are mostly tetrahedral, with just a couple of trigonal planar ones.

Go to **Animation IM9.4.** A three-dimensional model of ginkgolide B.

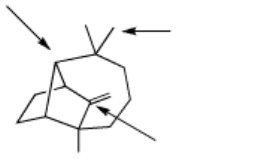
Understanding the overall shape of a molecule is particularly important in various aspects of biochemistry. For example, the effect of any drug in the body is strongly influenced by the shape of the drug and how that shape can interact with specific receptors.

Problem IM9.1. Cis and trans cyclic isomers have two substituents attached to a ring. The cis isomer has both substituents on the same face of the ring. The trans isomer has substituents on opposite faces of the ring. Use wedge-dash projections to draw the shapes of the following molecules:

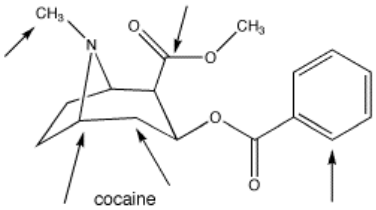
a) *cis*-1,2-dichlorocyclopropane, $C_3H_4Cl_2$ (the numbers mean there is a chlorine on the first carbon and a chlorin on the second carbon)

b) *trans*-1,2-dichlorocyclopropane, $C_3H_4Cl_2$ c) *cis*-1,3-dibromocyclobutane, $C_4H_6Br_2$ d) *trans*-1,3-dibromocyclobutane, $C_4H_6Br_2$

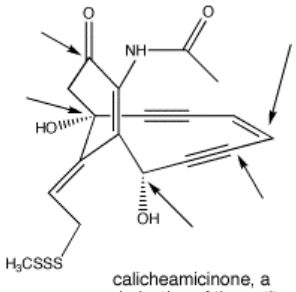
Problem IM9.2. Identify the geometry at the indicated carbons in the following molecules:



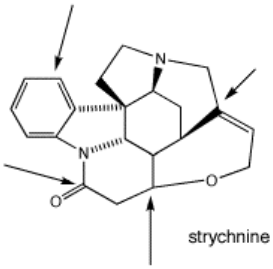
longifolene, a component of terpentine



cocaine



calicheamicinone, a derivative of the antitumour compound, calicheamicin



strychnine

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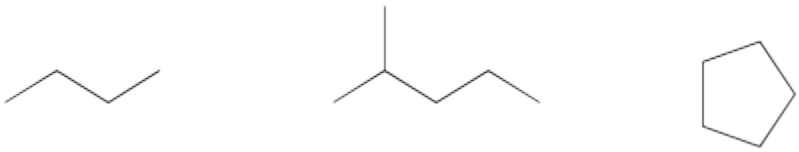
1.12.5: Organic functional groups

Organic compounds are very common in chemistry and biology. Some familiarity with some common types of compounds based on carbon and a few other elements will help you to understand organic chemistry and related fields.

The most common structural piece in organic chemistry is the carbon-carbon bond. Most organic compounds are filled with carbon-carbon bonds. Very often, a network of carbon atoms are single-bonded to each other, and to hydrogen atoms, to build up a complicated structure.

Other pieces, called functional groups, are attached to this framework. Functional groups are specific collections of atoms bonded together in a certain way. These collections of atoms are seen over and over in organic chemistry, and so they are given specific names. This appendix is meant to help you learn to recognize these functional groups. It will also help you learn how to talk about them.

Before looking at functional groups, let's look at simpler compounds that have no functional groups. Alkanes are compounds that contain only carbon and hydrogen, and that contain no double or triple bonds.



Problem IM12.1.

Translate the above structures into Lewis - Kekule structures..

Specific alkanes are given names that say something about their structures. Their names end in "ane"; that means they contain only single bonds, not double or triple bonds. A compound that contains no double or triple bonds is sometimes called "saturated". They are sometimes called "paraffinic" hydrocarbons, which means the same thing as saturated hydrocarbons.

The name also contains a part that tells how many carbons are found connected in the chain. These prefixes are used throughout organic chemistry to name other kinds of compounds, so you need to memorize them.

prefix	# carbons
meth	1
eth	2
prop	3
but	4
pent	5
hex	6
hept	7
oct	8
non	9
dec	10

Problem IM12.2.

Provide names for the following alkanes.

a)  b)  c) 

The chain of carbons in an alkane is called an alkyl chain. Sometimes there are smaller alkyl chains attached to the main chain of an alkane. The same prefixes can be used to tell how many carbons are in these smaller branches.

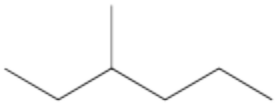
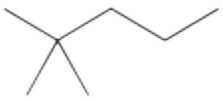
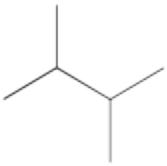
Numbers are used to count how far along the chain these branches occur. You need to start on the end of the chain and count the carbons until you get to the place where the branch occurs. If there are two different possible chains, choose the longest chain as the base name. If there are two different directions possible, start at the one that gives the lowest numbers for the branches.

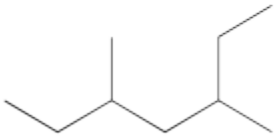
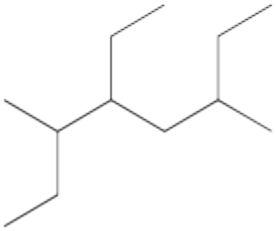
If there are two different branches of the same size on a chain, you need to say so. A different prefix is used to say how many of the same piece are present.

prefix	# of groups
di	2
tri	3
tetra	4
penta	5

Problem IM12.3.

Provide names for the following branched alkanes.

a)  b)  c) 

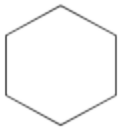
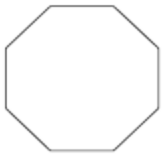
d)  e)  f) 

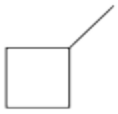
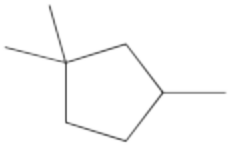
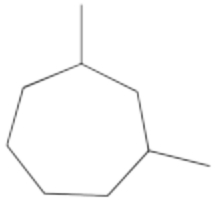
"Aliphatic hydrocarbons" specifically refers to branched chains of saturated hydrocarbons. "Alicyclic hydrocarbons" are very similar but they contain rings of carbons. If a chain of carbons wraps around to form a ring, the prefix "cyclo" is used.

All these elements will be used in naming other compounds as well.

Problem IM12.4.

Provide names for the following cyclic alkanes.

a)  b)  c) 

d)  e)  f) 

Homoatomic functional groups

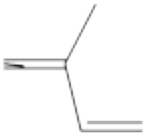
Any feature other than an alkyl chain is called a "functional group". A functional group is also just a place where reactions take place.

Homoatomic functional groups contain only carbon and hydrogen. They differ from alkyl groups only in having multiple C-C bonding.

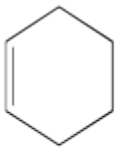
The C=C functional group is called an alkene. Simple compounds that contain C=C double bonds are also called alkenes. The term "olefin" also means alkene, and "unsaturated" or "olefinic" hydrocarbons contain double bonds.



propene
used in making plastics & textiles



isoprene
produced by oaks & poplars

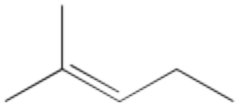


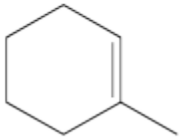
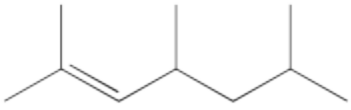
cyclohexene
used to make nylon

In naming alkenes, the suffix "ene" is used instead of "ane". The base name of the alkene describes the length of the chain containing the double bond. A number says how far the double bond is from the nearest end of the chain.

Problem IM12.5.

Provide names for the following alkenes.

a)  b) 

c)  d) 

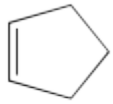
The C-C triple bond is called an alkyne. "Acetylenic" hydrocarbons or alkynes are compounds that contain C-C triple bonds. These compounds are also examples of "unsaturated hydrocarbons".

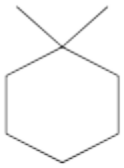


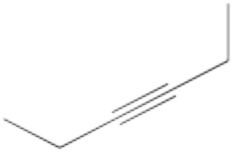
acetylene or ethyne

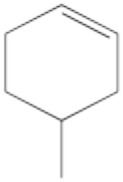
Problem IM12.6.

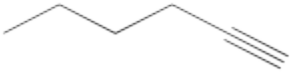
Provide names for the following hydrocarbons.

a) 

b) 

c) 

d) 

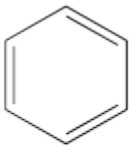
e) 

Problem 12.7.

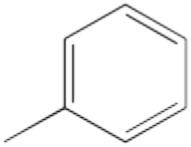
Describe the geometries of the following carbons:

a) any carbon in pentane. b) the second carbon in 2-butene. c) the first carbon in 1-hexyne.

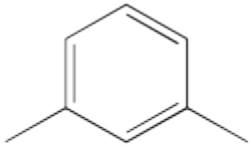
Aromatic compounds appear to contain C-C double bonds but they are very different from alkenes. The most common aromatic is benzene. Because benzene is a very common structural piece, you should be familiar with some of the language associated with it.



benzene



toluene
(tall-you-een)



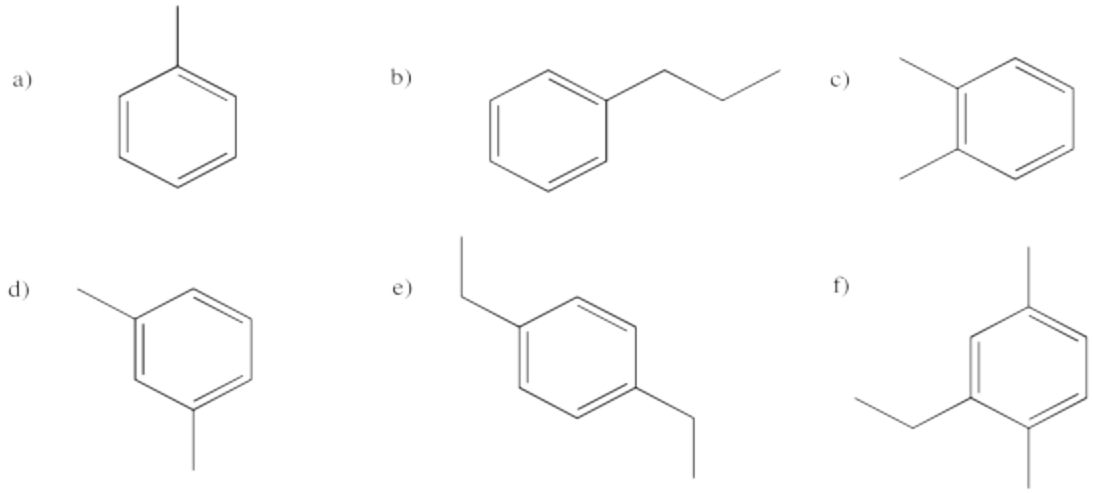
xylene
(zeye-leen)

Benzene rings with two groups attached are common enough that different terms are used to describe their isomers. The terms *ortho-*, *meta-* and *para-* are used only to describe the relationship between two groups around benzene, and not any other compounds. These terms are sometimes abbreviated to *o-*, *m-* or *p-*. Alternatively, two groups attached to a benzene can simply be numbered in order to make it clear where they are. If more than two groups are attached, numbering is used; terms such as "ortho" no longer apply.

Note that a benzene group is sometimes called a phenyl group. It is not called a benzyl group, nor a benzoyl group. Those two groups both contain a phenyl ring but they are not exactly the same.

Problem IM12.8.

Provide names for the following aromatics.



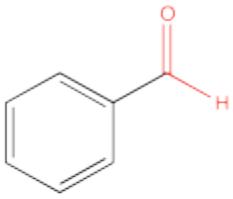
Heteroatomic Functional Groups: Carbonyls

Heteroatomic functional groups contain atoms other than carbon and hydrogen.

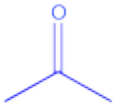
Probably the most important set of heteroatomic functional groups is the set that contains carbon-oxygen double bonds. The C=O group is called a carbonyl (carbon-EEL). Carbonyl compounds all contain the carbonyl group.

There are two subsets of carbonyl compounds: regular carbonyls and heteroatom-substituted carbonyls. In regular carbonyls, the carbon in the C=O group is attached only to carbon or hydrogen. It is not attached to additional heteroatoms such as nitrogen or oxygens.

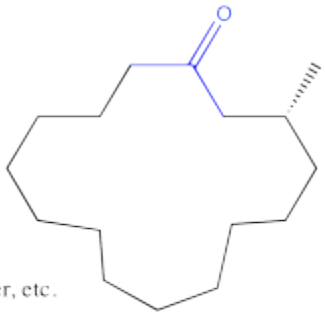
There are two kinds of regular carbonyls. In ketones, the carbonyl carbon is attached only to other carbons. In aldehydes, the carbonyl carbon is attached to a hydrogen atom as well as a carbon.



an aldehyde:
benzaldehyde
part of the odour of almonds and cherries



a ketone:
acetone or 2-propanone
a solvent in nail polish remover, etc.



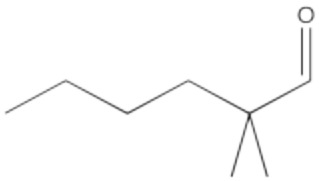
a ketone:
muscone
primary component of musk

Aldehydes and ketones have specific naming conventions. The suffix for the name of an aldehyde is "-al"; whereas the suffix for the name of a ketone is "-one". In the case of a ketone, the location of the carbonyl along the chain can be described with a number. Otherwise, the names of aldehydes and ketones follow the rules we have seen for other organic compounds.

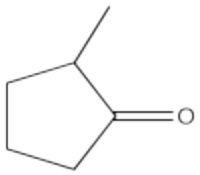
Problem IM12.9.

Provide names for the following compounds.

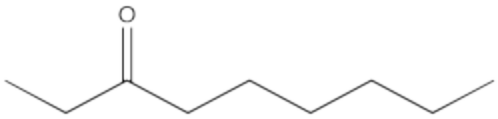
a)



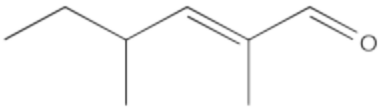
b)



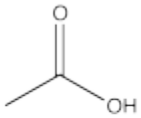
c)



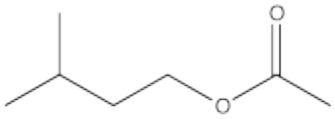
d)



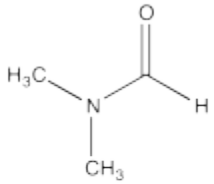
Heteroatom-substituted carbonyls all have a heteroatom attached to the carbonyl carbon. A heteroatom is an atom other than hydrogen or carbon, such as nitrogen, oxygen or chlorine. Heteroatom-substituted carbonyls are often called "carboxylic acid derivatives" or sometimes "carboxyloids".



a carboxylic acid:
acetic acid or ethanoic acid
active ingredient in vinegar



an ester:
isoamyl acetate or 3-methylbutyl ethanoate
has an aroma like bananas



an amide:
DMF or
N,N-dimethylformamide or
N,N-dimethylethanamide

In carboxylic acids, the carbonyl carbon is attached to an OH group. The OH group is often called a hydroxyl group. Fatty acids and amino acids are examples of biological compounds that contain carboxylic acids.

Two biologically important carboxyloids are amides and esters

In esters, the carbonyl carbon is attached to an oxygen, like in a carboxylic acid. However, the oxygen is not attached to a hydrogen. The oxygen is attached to a carbon. The properties of esters differ enough from carboxylic acids that they are given a different name. Glycerides are biological compounds that contain ester groups. Glycerides are found in fats.

In amides, the carbonyl carbon is attached to a nitrogen. Unlike esters and carboxylic acids, it doesn't matter whether the nitrogen is attached to a hydrogen or to another carbon. The presence of a hydrogen on the nitrogen changes the properties of the amide less dramatically than in esters and carboxylic acids.

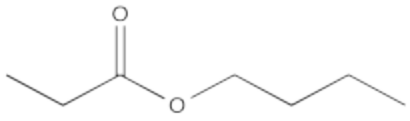
Because the amide does change subtly if there is a hydrogen attached to the nitrogen, there is a way to describe the presence ar absence of hydrogens. An amide with two hydrogens on the nitrogen is called a primary amide. The nitrogen is connected to only one (Latin for first: primus) carbon: the carbonyl carbon.

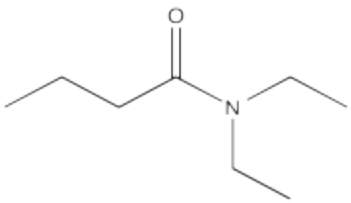
An amide with two carbons connected to the nitrogen is called a secondary amide (Latin for second: secondus). An amide with three carbons connected to the nitrogen is called a tertiary amide (Latin for third: tertius).

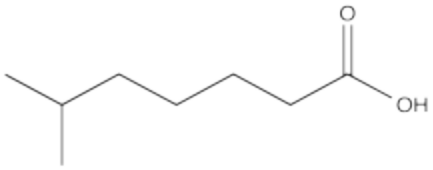
Naming simple examples of these compounds, as before, involves a change in the suffix of the name. The suffix for a carboxylic acid is "-oic acid". Esters really have a two-part name. The first part describes the group attached to the enchained oxygen atom of the ester, with the suffix "-yl". The second part describes the portion that contains the carbonyl, with the suffix "-oate". For an amide, the suffix is "amide". However, other groups attached to the nitrogen are usually prefixed with "*N*-"; this is a little like numbering the position of a group in previous examples, but this time it underscores that the group is attached to a nitrogen.

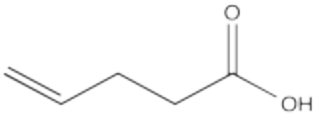
Problem 12.10.

Provide names for the following carboxyloids.

a) 

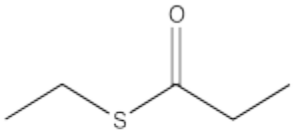
b) 

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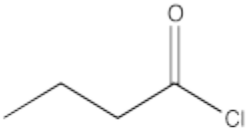
d) 

A third biologically important carboxylic acid derivative contains a sulfur attached to the carbonyl carbon. Usually the sulfur is attached to another carbon as well. Because sulfur is in the same group in the periodic table as oxygen, this functional group is similar to an ester. It is called a thioester. It is much less common than amides and esters. A biological example of a thioester is acetyl conezyme A, which plays an important role in many biological reactions. In fact, the thioester plays the key role in the reactions of acetyl coenzyme A.

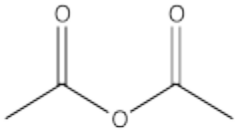
Naming thioesters is just like naming other esters, except that the prefix "thio-" is inserted into the second part of the name.



a thioester:
ethyl thiopropanoate



an acid chloride:
butanoyl chloride



an acid anhydride:
acetic anhysride or
ethanoic anhydride

Two other important carboxylic acid derivatives are not normally seen in biology. They are important because they are used synthetically or industrially to make the other carboxylic acid derivatives.

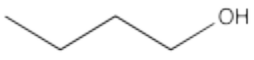
Acid anhydrides are prepared by heating carboxylic acids at high temperatures until water is lost. Acid anhydrides contain two carbonyl units, connected by an oxygen. Usually those two units are the same as each other. The name for an anhydride indicates the number of carbons in just one of those pieces (since the other one is the same) with the suffix "-oic (space) anhydride".

Acid chlorides have a chlorine atom attached to the carbonyl carbon. The name for an acid chloride contains the suffix "-oyl (space) chloride". Other acid halides (such as acid fluorides) are known, but they are less common than acid chlorides.

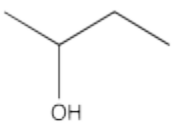
Simple Heteroatomic Functional Groups (No Carbonyls)

There are several heteroatomic functional groups that do not contain carbonyls.

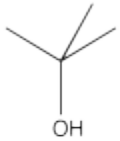
Alcohols contain an OH or hydroxyl group, but the hydroxyl is not attached to a carbonyl.



a "primary" alcohol:
butanol or *n*-butanol



a "secondary" alcohol:
2-butanol or *sec*-butanol



a "tertiary" alcohol:
2-methyl-2-propanol or *tert*-butanol

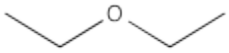
Sometimes alcohols are classed into sub-groups, as "primary", "secondary" or "tertiary". Those words just describe the carbon attached to the OH group. How many carbons are attached, in turn, to that carbon? Are there two, three, or just one? Those

classifications have some influence on how reactive the alcohol will be under different conditions.

The suffix in the name of an alcohol is "ol". It doesn't matter whether the alcohol is described as a primary, secondary or tertiary one They are still named according to the same rule.

Phenols are alcohols in which the hydroxyl group is directly attached to a phenyl group, or benzene ring. Their behaviour is different enough from other alcohols that they are sometimes thought of as a separate group. For one thing, they are somewhat acidic. Coming into contact with phenols, whether they are found in pine resin or, in a much more extreme case, poison ivy, can cause severe itching in the skin. Regular alcohols are much less likely to cause that reaction.

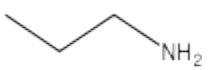
Ethers are kind of like alcohols in that they contain oxygen atoms. Ethers contain a C-O-C group, but neither carbon is part of a carbonyl. Generally, to name an ether, we list the two parts attached to the oxygen atom, and follow those two names with "ether".



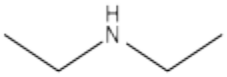
an ether: diethyl ether

Amines contain nitrogen atoms connected to three different atoms, but not connected to a carbonyl. If the nitrogen is attached only to one carbon, the functional group is a primary amine. If it is attached to two carbons, it is a secondary amine. If it is attached to three carbons, it is a tertiary amine. This classification system is a little bit different from the one used with alcohols, in that it refers to the number of things attached to the nitrogen itself. In oxygen compounds, the number of things attached to the oxygen determined whether we called it an alcohol or an ether.

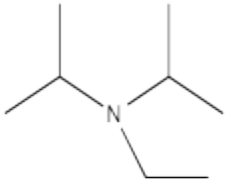
Naming amines is a little like naming ethers. We list the groups attached to the nitrogen, followed by "amine". Usually these groups are listed in alphabetical order. Sometimes, as with amides, the idea that a group is attached to the nitrogen is usually reinforced with the prefix "*N*-".



a "primary" amine:
propylamine



a "secondary" amine:
diethylamine

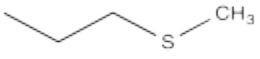


a "tertiary" amine:
N,*N*-diisopropylethylamine or
ethyldiisopropylamine

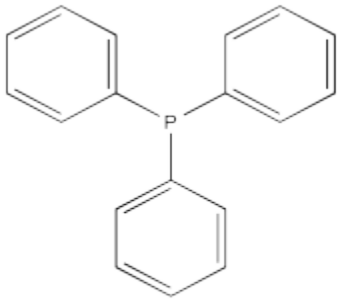
Thiols and thioethers are the sulfur analogues of alcohols and ethers. Phosphines are the phosphorus analogues of amines. None of these groups are as common as alcohols, ethers and amines. The sulfur-containing compounds are named in a similar way to their oxygen analogues, but with the suffix "-thioether" or "-thiol" used instead of "-ether" or "-ol". Similarly, phosphines have the suffix "-phosphine" instead of "-amine".



a thiol:
butanethiol

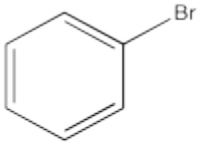


a thioether:
methyl propyl thioether



a phosphine:
triphenylphosphine

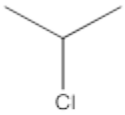
Alkyl halides, or haloalkanes, are compounds that contain a halogen that is not attached to a carbonyl. These compounds are not common biologically, but they are important industrially. Usually halogens are treated like alkyl groups in terms of naming compounds that contain them. A halogen is described as a prefix ending in "-o", rather than the prefix ending in "-yl" that is used with alkyl groups. For example, an alkyl bromide is named as a bromoalkane, such as bromoethane or bromohexane.



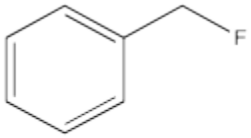
bromobenzene



1-iodopropane or propyl iodide

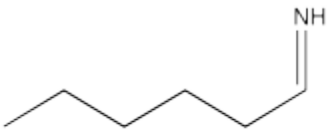


2-chloropropane or isopropyl chloride

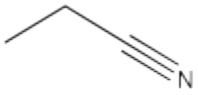


benzyl fluoride

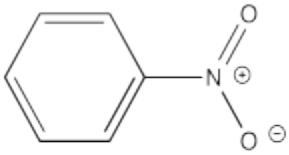
There are a few other functional groups that contain multiple bonds to nitrogen. An imine is the nitrogen analogue of an aldehyde. An imine contains a carbon-nitrogen double bond. The carbon almost always has a hydrogen attached as well. The word "imine" is just appended to the name of the related aldehyde to describe a specific imine.



an imine: hexanal imine



a nitrile: propanenitrile



a nitro compound: nitrobenzene

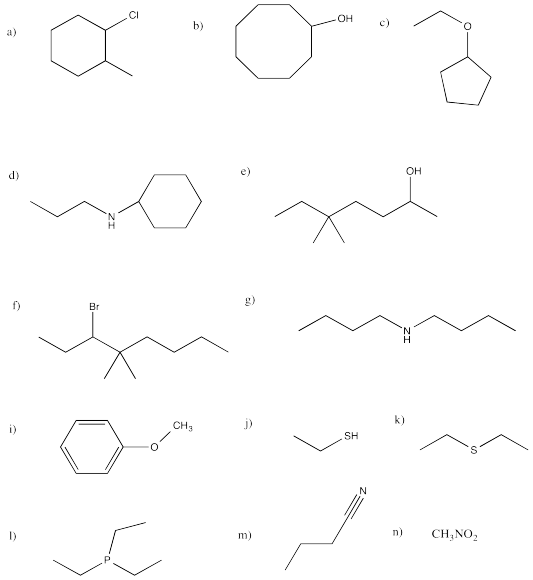
A nitrile contains a carbon-nitrogen triple bond. The suffix for a nitrile is just "-nitrile".

A nitro group contains the NO_2 unit. "Nitro-" is usually added as a prefix to signal the presence of this group in a compound.

fun group	suffix
none	ane
alkene	ene
alkyne	yne
ketone	one
aldehyde	al
carboxylic acid	oic acid
ester	-yl ...-oate
amide	amide
thioester	

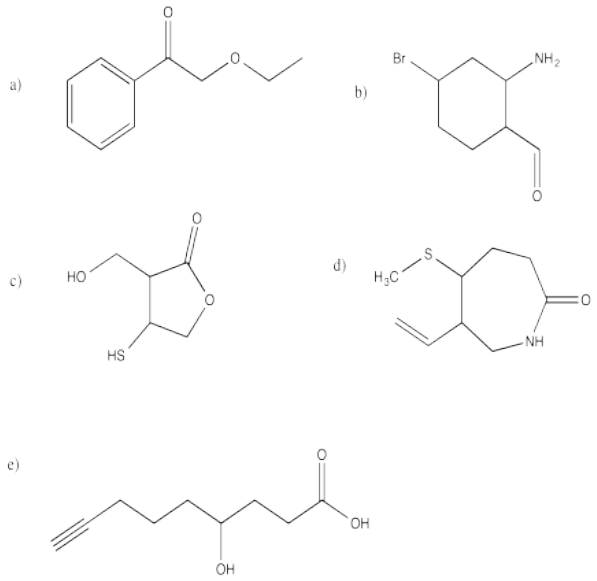
Problem IM12.11.

Provide names for each of the following compounds.



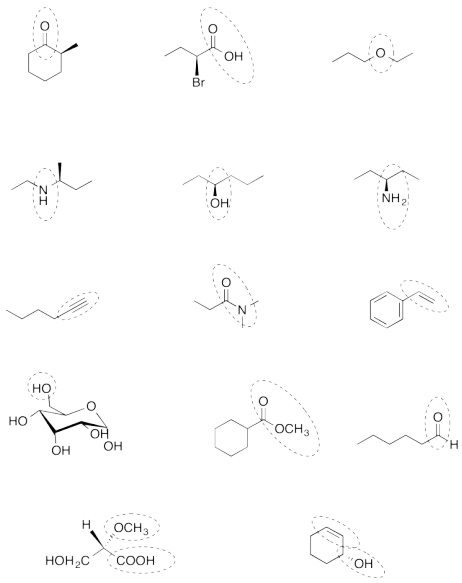
Problem IM12.12.

Each of the following compounds contains three functional groups. Identify them.



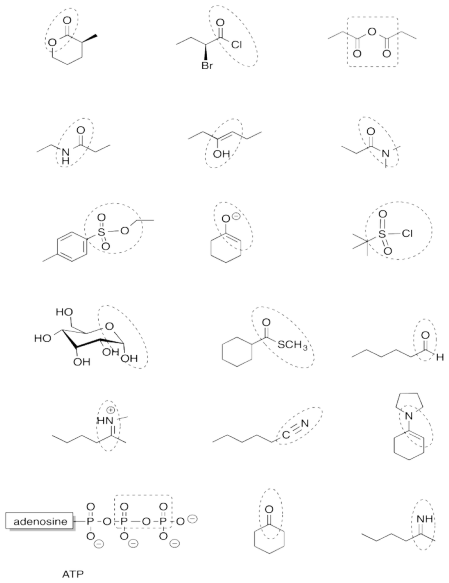
Problem IM12.13

Identify the circled functional groups.



Problem IM12.14

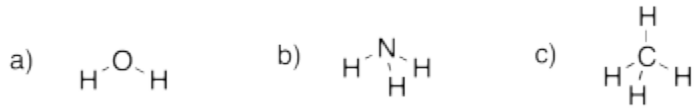
Identify the circled functional groups (more advanced level).



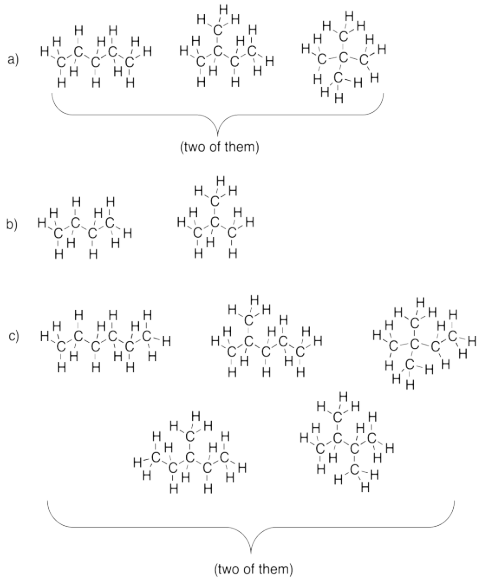
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1.12.6: Solutions to Selected (IM) Problems

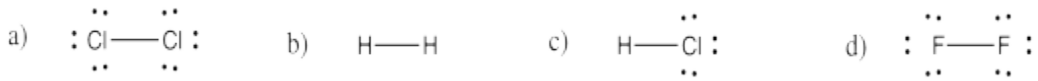
Problem IM1.1.



Problem IM1.2.



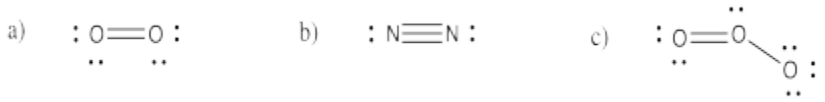
Problem IM2.1.



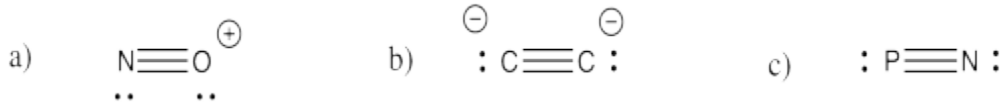
Problem IM2.2.



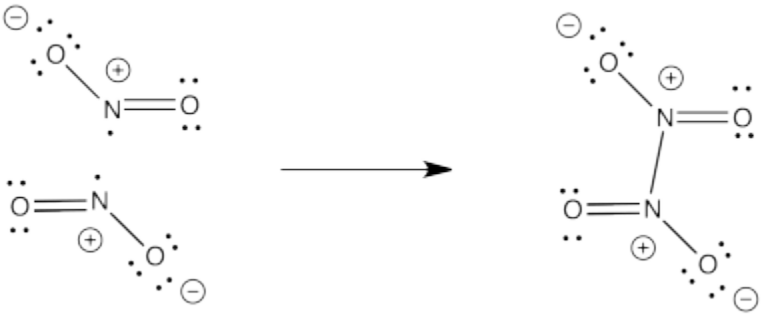
Problem IM3.1.



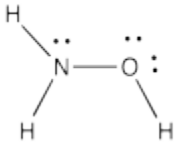
Problem IM3.2.

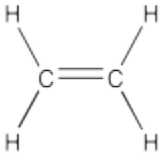


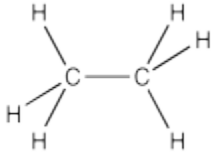
Problem IM3.3.



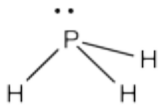
Problem IM4.1.

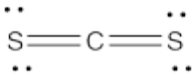
a) 

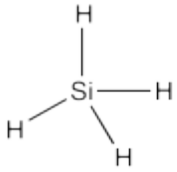
b) 

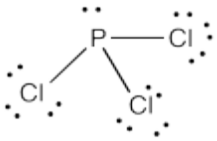
c) 

Problem IM4.2.

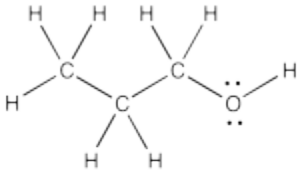
a) 

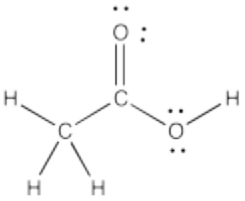
b) 

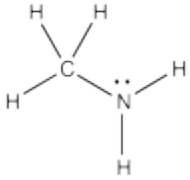
c) 

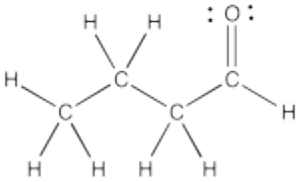
d) 

Problem IM4.3.

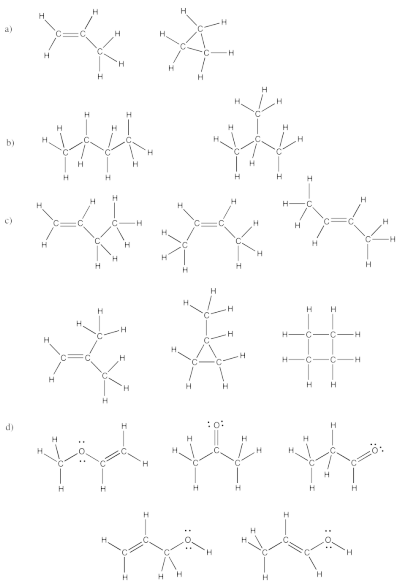
a) 

b) 

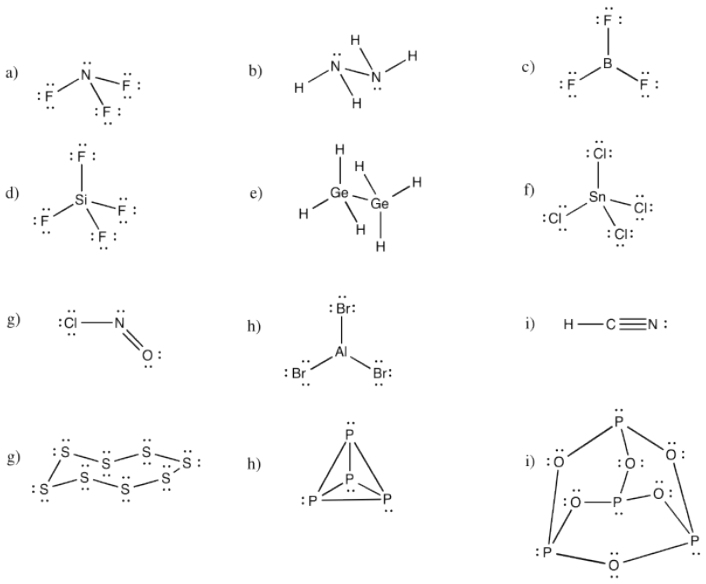
c) 

d) 

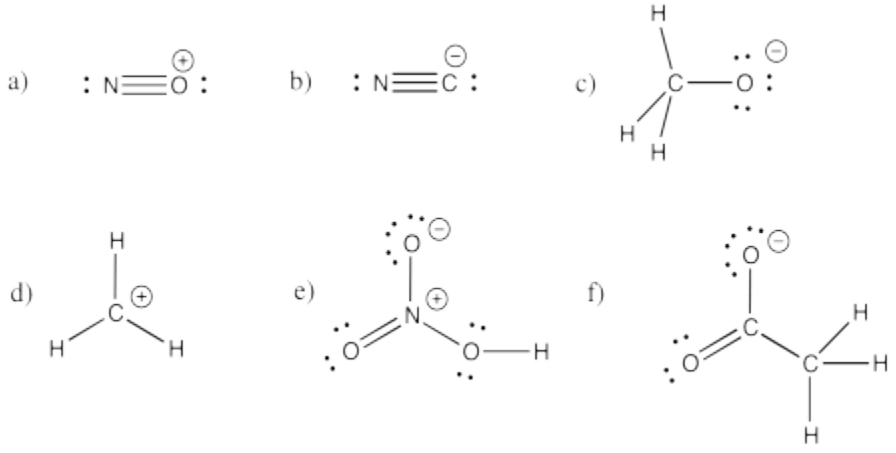
Problem IM4.4.



Problem IM4.5.

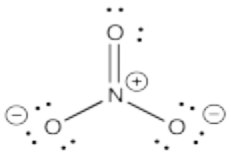


Problem IM5.1.

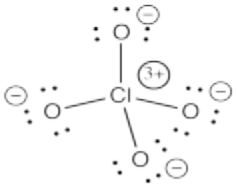


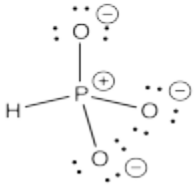
Problem IM5.2.

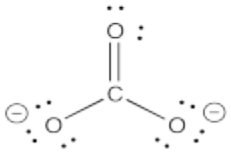
a) 

b) 

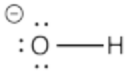
c) 

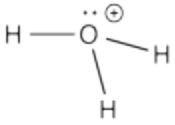
d) 

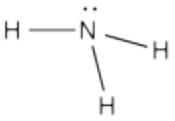
e) 

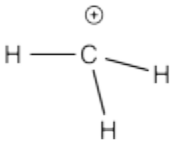
f) 

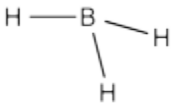
Problem IM5.3.

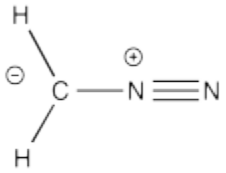
a) 

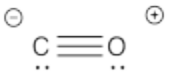
b) 

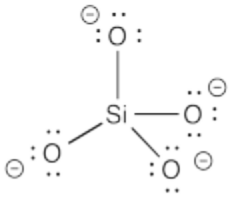
c) 

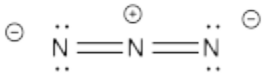
d) 

e) 

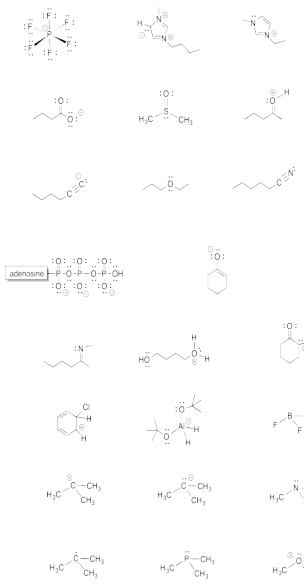
f) 

g) 

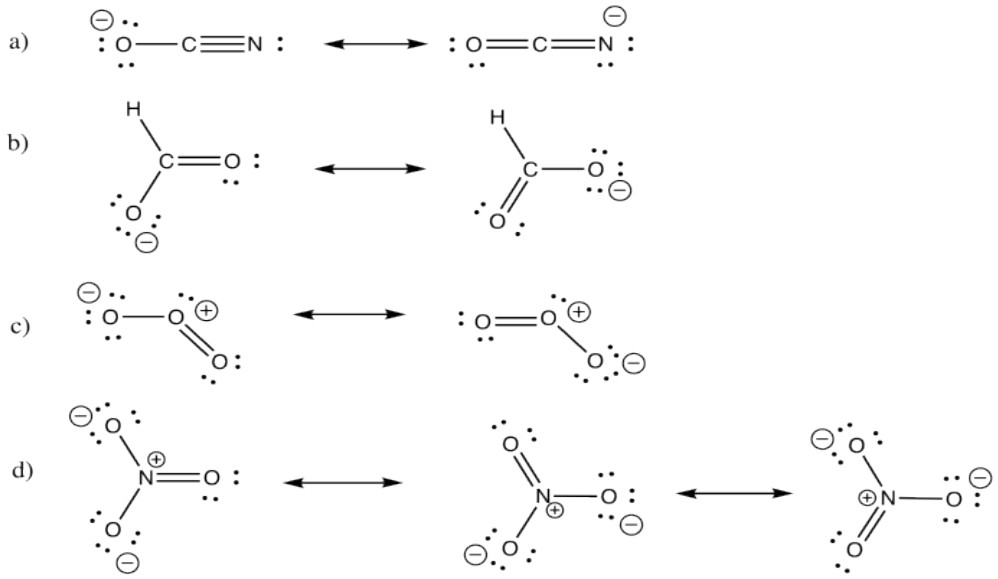




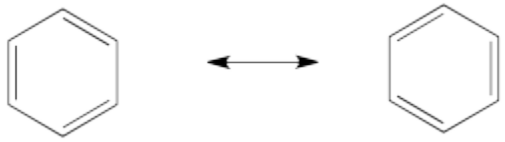
Problem IM5.4.



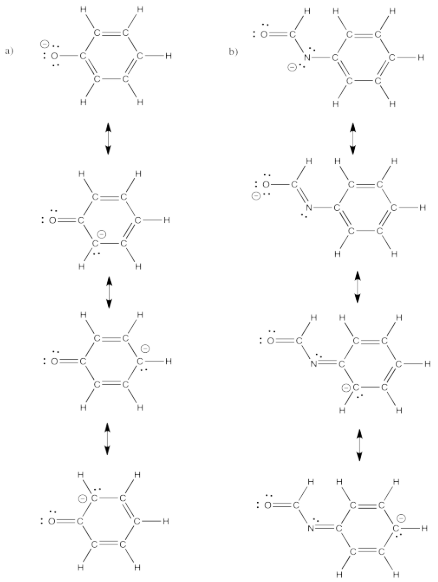
Problem IM6.1.



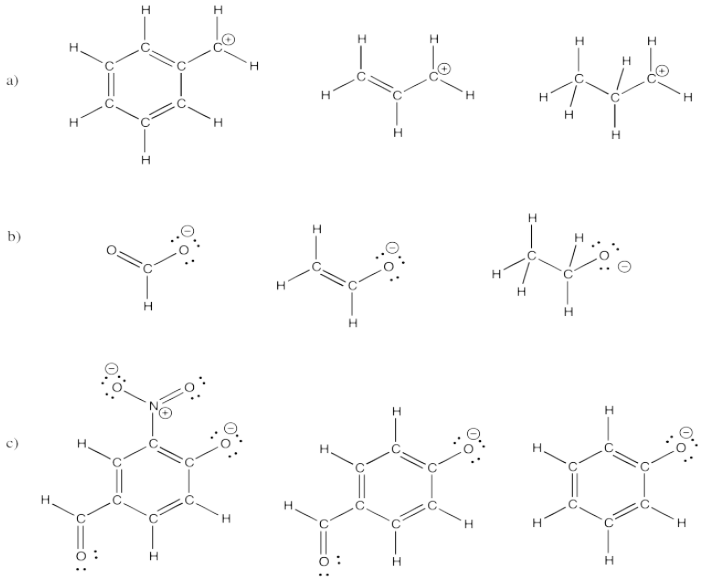
Problem IM6.2.



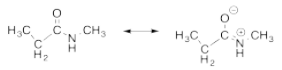
Problem IM6.3.

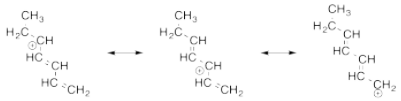


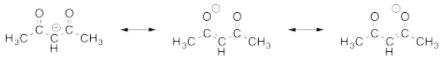
Problem IM6.4.

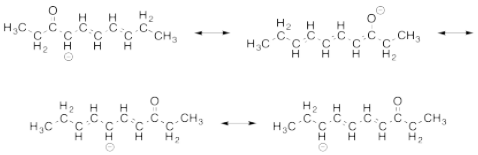


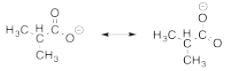
Problem IM6.5.

A. 

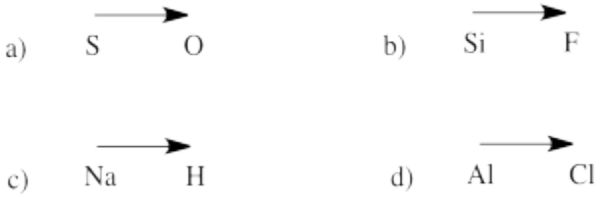
B. 

C. 

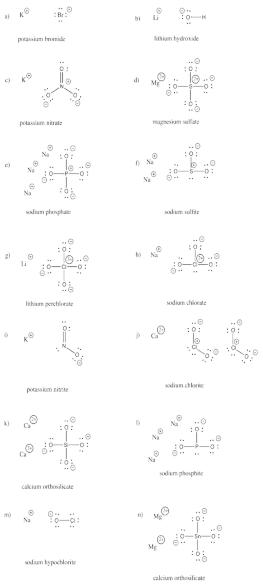
D. 

E. 

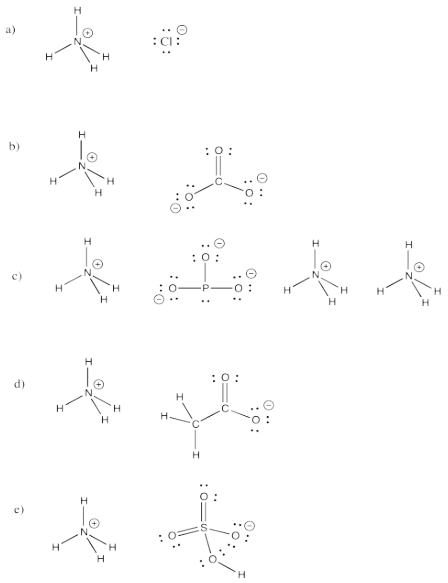
Problem IM7.1.



Problem IM7.2.



Problem IM7.3.



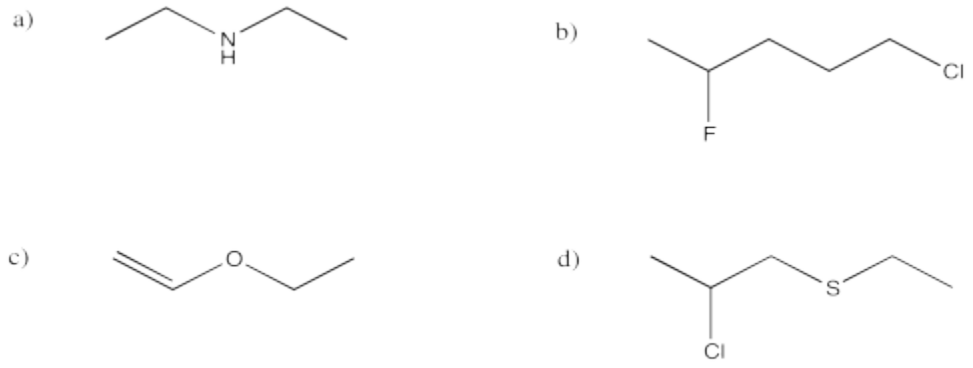
Problem IM7.4.

a) bromide b) oxide c) fluoride d) carbonate e) nitrate f) nitrite

g) sulfide h) sulfate i) sulfite j) persulfate k) carbide l) nitride m) arsenide

n) phosphate o) phosphite p) iodide q) iodate r) periodate

Problem IM8.1.

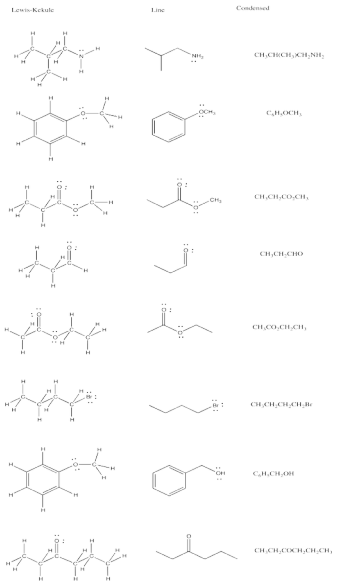


Problem IM8.2.

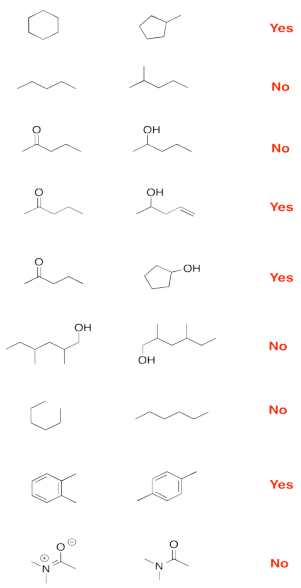
a) $(CH_3)_2CHCH_2CH_2CN$ b) $CH_3CH_2CH(OH)CH_3$

c) $(CH_3)_2CHCOCH_2CH_3$ d) $CH_3CH_2CONHCH_2CH_3$

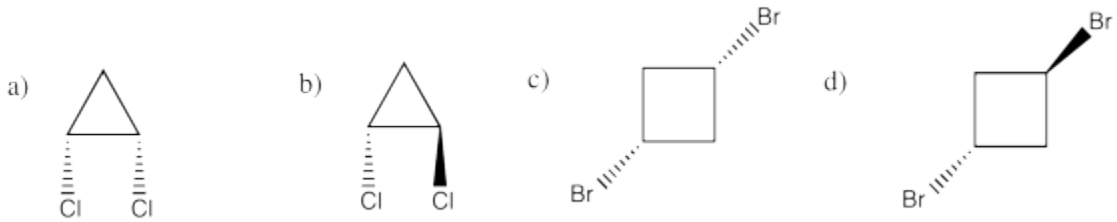
Problem IM8.3.



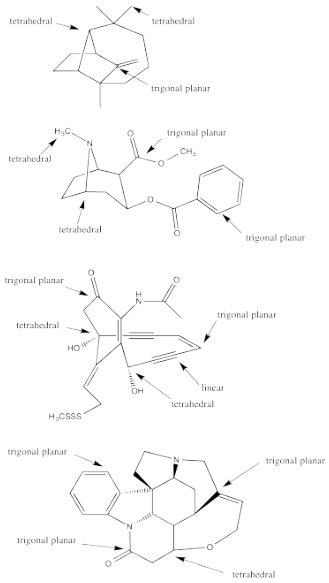
Problem IM8.4.



Problem IM9.1.



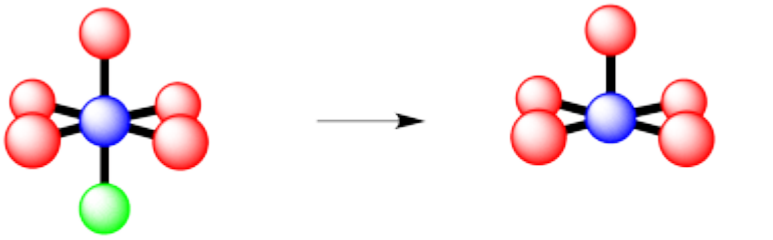
Problem IM9.2.



Problem IM10.1.

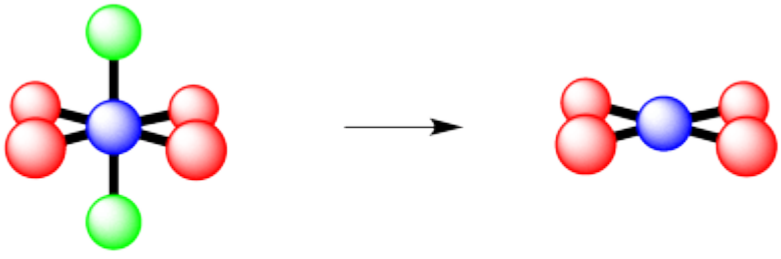
a) octahedral.

b)



octahedral square pyramidal

c)



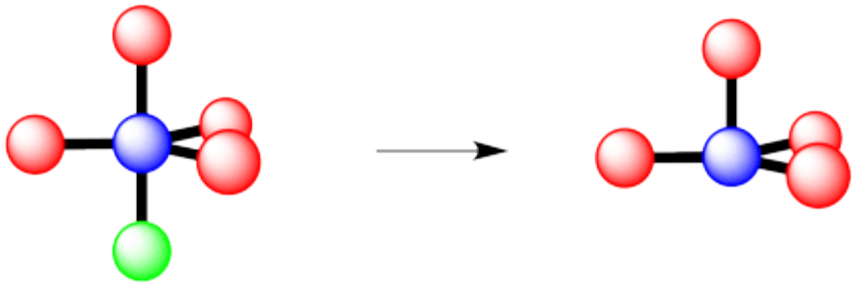
octahedral square planar

Problem 10.2.

a) trigonal bipyramidal

b) This time there could be two different answers.

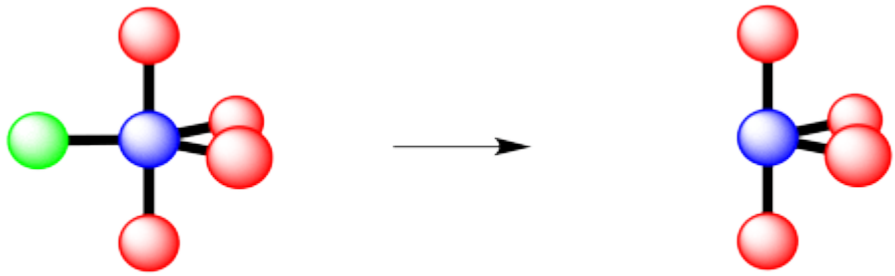
If the lone pair occupies one of the axial positions, it would be pretty close to three other atoms



trigonal bipyramidal

trigonal pyramidal

If the lone pairs occupies one of the equatorial positions, it would be pretty close to only two other atoms. The other equatorial atoms are pretty far away.

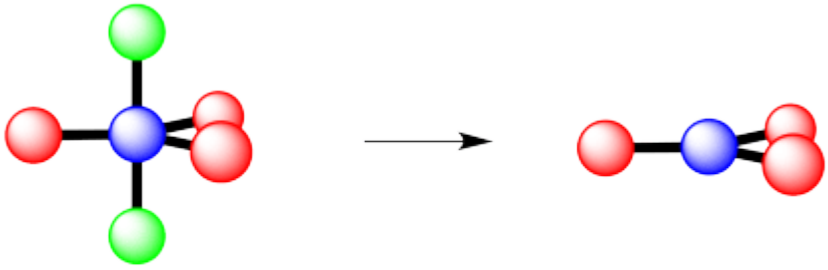


trigonal bipyramidal

see saw

The rule is that the lone pair goes in the less crowded position, so this molecule would be see-saw shaped.

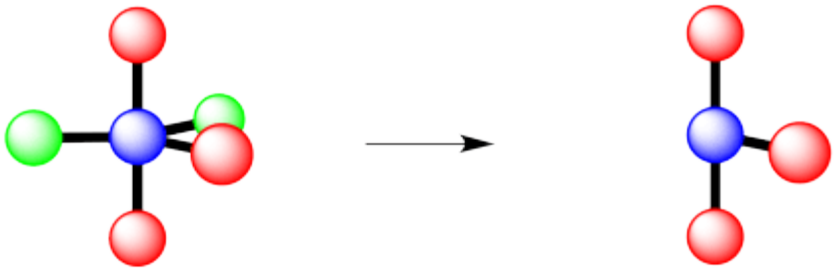
c) Again, there are two possible geometries. One of them would be trigonal planar, a pretty common geometry.



trigonal bipyramidal

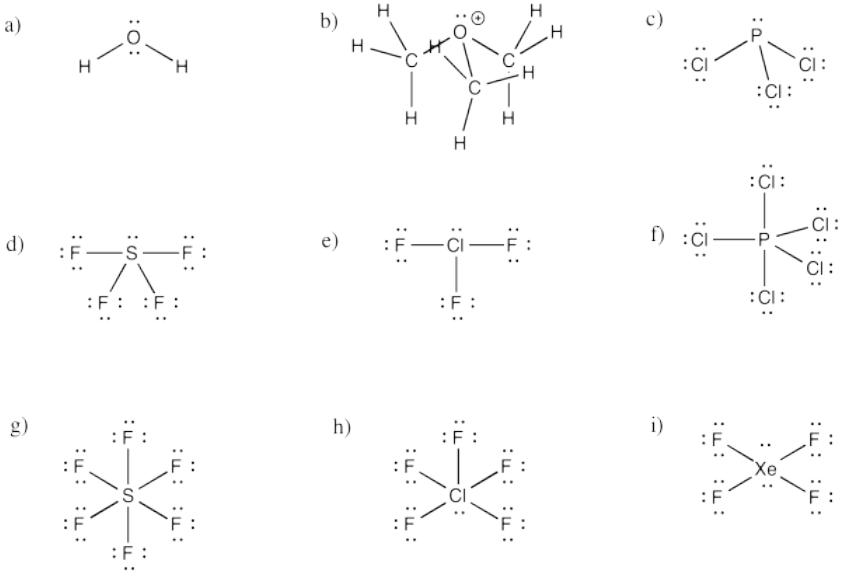
trigonal planar

However, that places the lone pairs in the more crowded positions. Instead, the molecule is going to be tee shaped.



trigonal bipyramidal tee

Problem IM10.3.



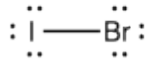
Problem IM10.4.

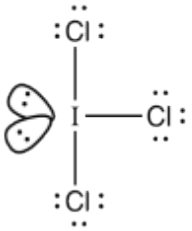
a) bent b) pyramidal at O, although tetrahedral at C c) pyramidal

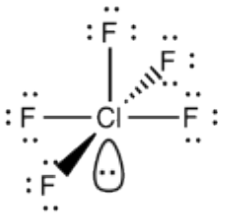
d) see-saw e) tee f) trigonal bipyramidal

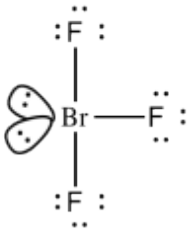
g) octahedral h) square pyramidal i) square planar

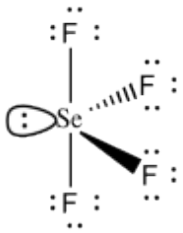
Problem IM10.5.

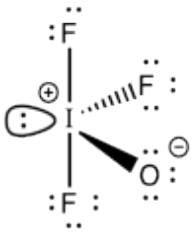
a) 

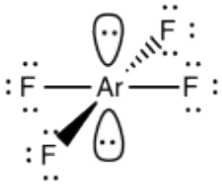
b) 

c) 

d) 

e) 

f) 

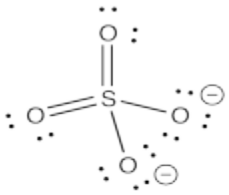
g) 

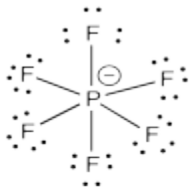
(probably; it hasn't been made before)

Problem IM10.6.

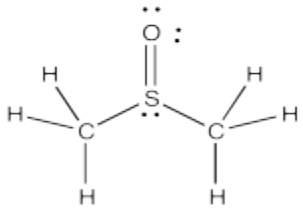
You may be able to imagine some other possibilites for this number of neighbours, but IF_7 adopts a pentagonal bipyramid shape.

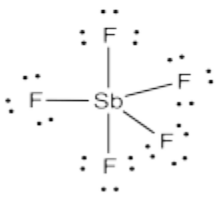
Problem IM11.1.

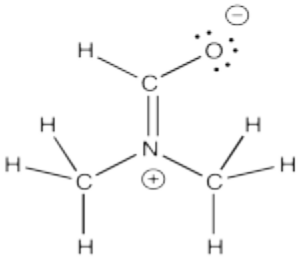
a) 

b) 

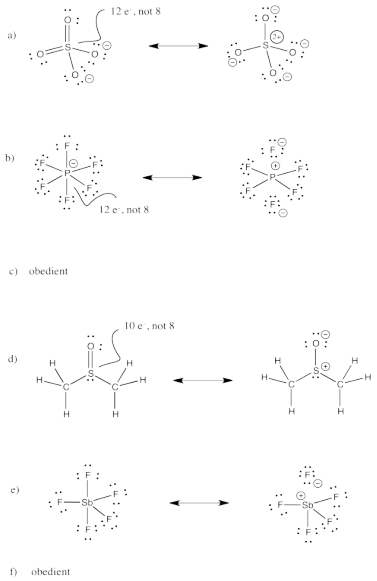
c) 

d) 

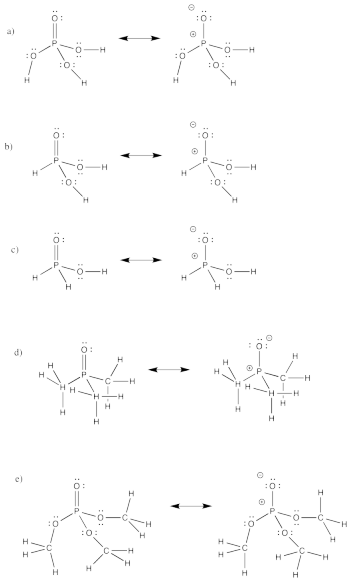
e) 

f) 

Problem IM11.2.



Problem IM11.3.



Problem IM12.2.

a) propane b) pentane c) hexane

Problem IM12.3.

a) 3-methylhexane b) 2,2-dimethylpentane c) 2,3-dimethylbutane

d) 2,2,3,3-tetramethylpentane e) 3,5-dimethylheptane f) 4-ethyl-3,6-dimethyloctane

Problem IM12.4.

a) cyclopentane b) cyclohexane c) cyclooctane

d) methylcyclobutane e) 1,1,3-trimethylcyclopentane f) 1,3-dimethylcycloheptane

Problem IM12.5.

a) 1-hexene b) 2-methyl-2-pentene c) 1-methylcyclohexene d) 2,4,6-trimethyl-2-heptene

Problem IM12.6.

a) cyclopentene b) 1,1-dimethylcyclohexane c) 3-hexyne

d) 4-methylcyclohexene e) 1-hexyne

Problem IM12.7.

a) tetrahedral b) trigonal planar c) linear

Problem IM12.8.

a) methylbenzene b) propylbenzene c) 1,2-dimethylbenzene or *o*-dimethylbenzene (also *o*-xylene)

d) 1,3-dimethylbenzene or *m*-dimethylbenzene (also *m*-xylene) e) 1,4-diethylbenzene or *p*-diethylbenzene

f) 2-ethyl-1,4-dimethylbenzene

Problem IM12.9.

a) 2,2-dimethylhexanal b) 2-methylcyclopentanone

c) 3-nonanone d) 2,4-dimethyl-2-hexenal

Problem IM12.10.

a) butyl propanoate b) *N,N*-diethylbutanamide

c) 6-methylheptanoic acid d) 4-pentenoic acid

Problem IM12.11.

a) 1-chloro-2-methylcyclohexane b) cyclooctanol c) ethyl cyclopentyl ether

d) *N*-propylcyclohexylamine e), 5,5-dimethylheptan-2-ol f) 3-bromo-4,4-dimethyloctane

g) dibutylamine i) methyl phenyl ether (or anisole) j) ethane thiol k) diethyl thioether

l) triethylphosphine m) butanenitrile n) nitromethane

Note that sometimes a number is located directly in front of the suffix for the group to which it refers.

Problem IM12.12

a) benzene (or aromatic), ketone and ether

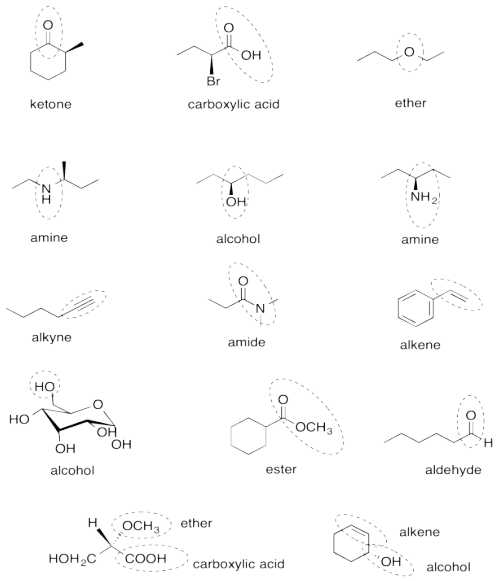
b) bromide, amine and aldehyde

c) alcohol, thiol and ester

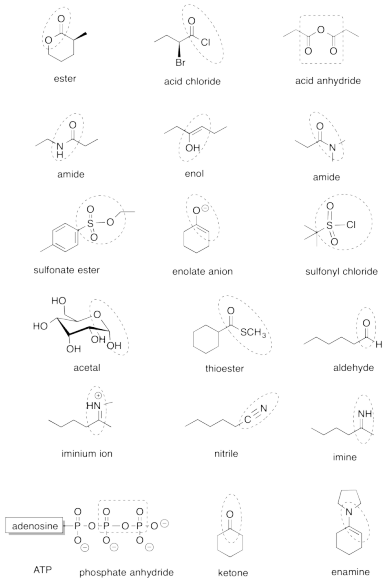
d) thioether, amide and alkene

e) alkyne, alcohol and carboxylic acid

Problem IM12.13.

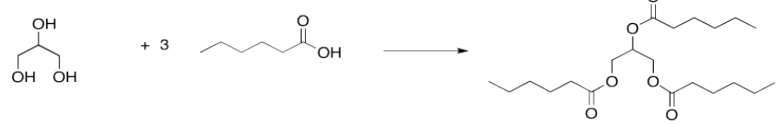


Problem IM12.14.

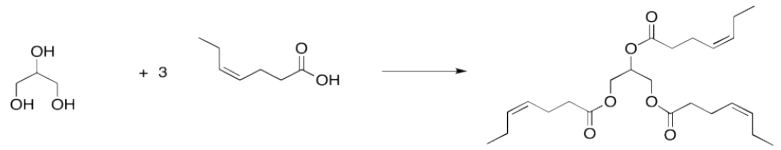


Problem IM13.1.

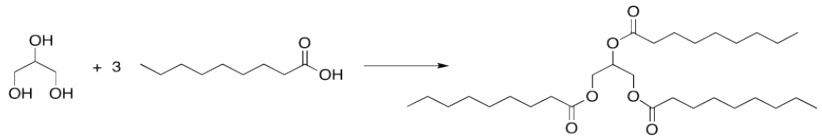
a)



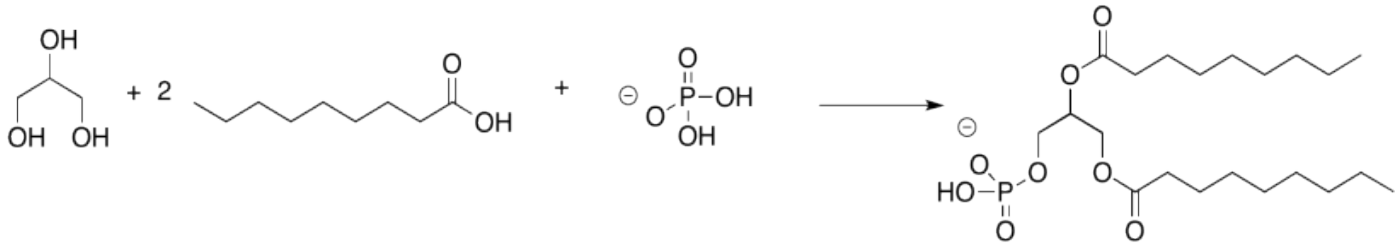
b)



c)

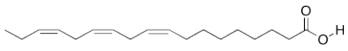


Problem IM13.2.

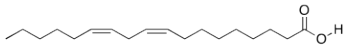


Problem IM13.3.

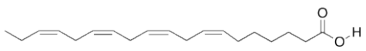
a)



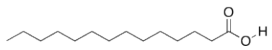
b)



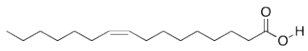
c)



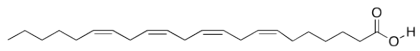
d)



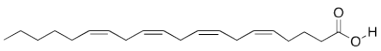
e)



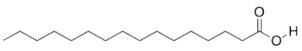
f)



g)

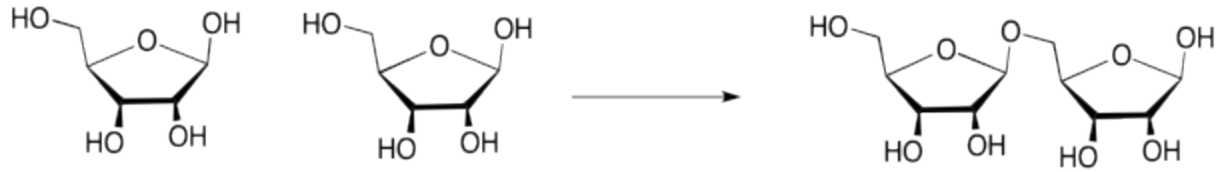


h)



Problem IM13.4.

a)



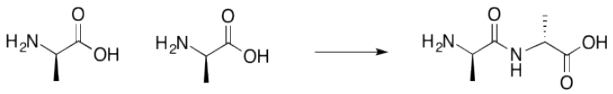
b)



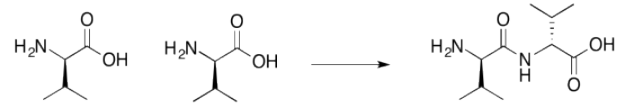
Problem IM13.5.

If you don't know what the wedged and dashed lines in the drawing mean, don't worry about it. They just represent different orientations in space. You will learn about these representations in a later topic called "stereochemistry".

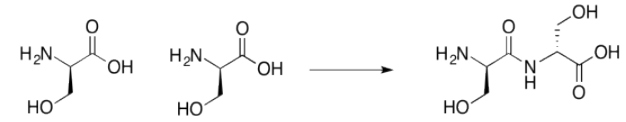
a)



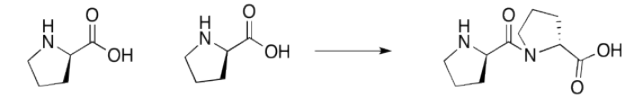
b)



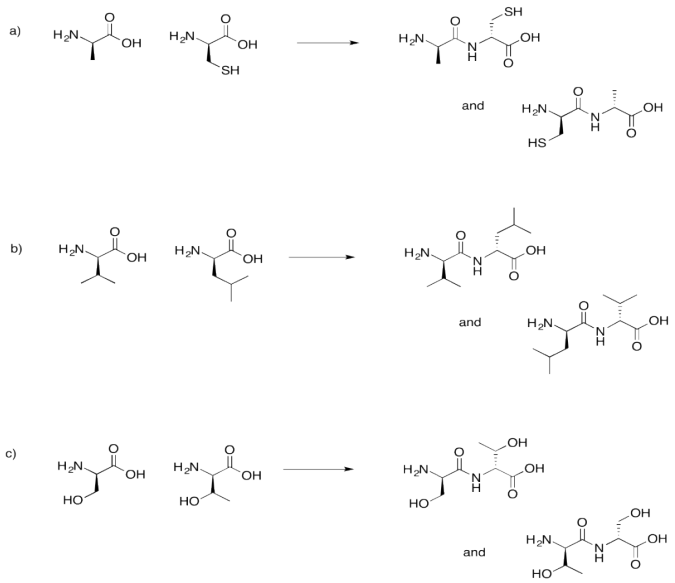
c)



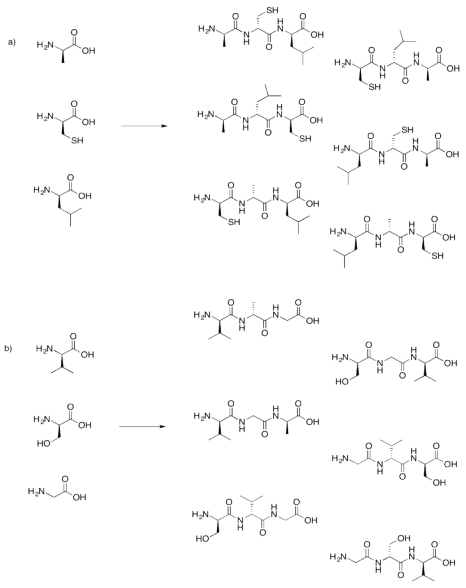
d)



Problem IM13.6.

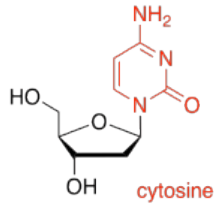


Problem IM13.7.



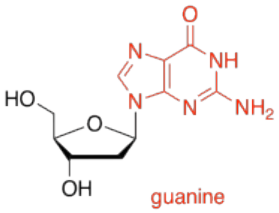
Problem IM13.8.

a)



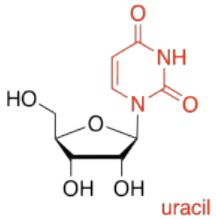
cytosine

b)



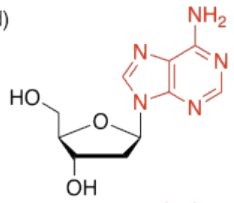
guanine

c)



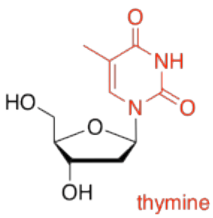
uracil

d)



adenine

e)



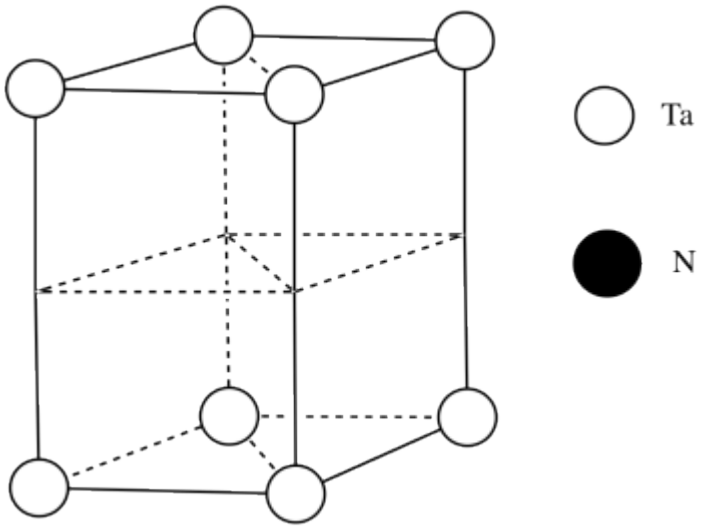
thymine

Problem IM15.1.

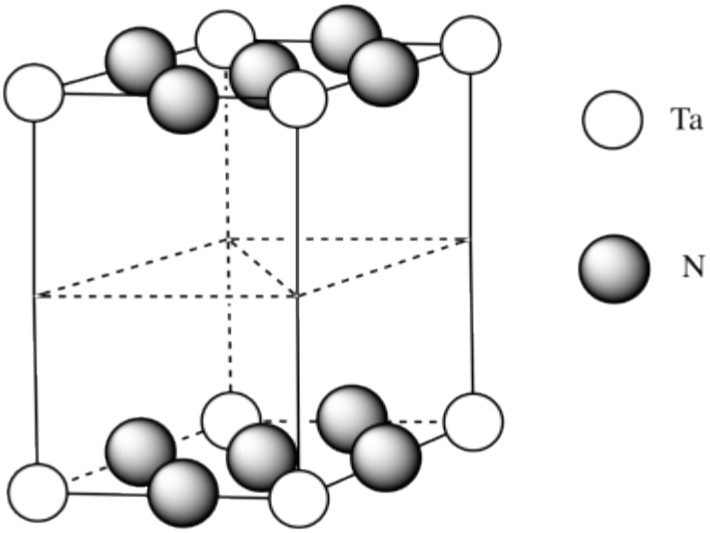
a) N^{3-} would get to a noble gas configuration.

b) Ta^{3+} would balance the charge in TaN.

c)



d)

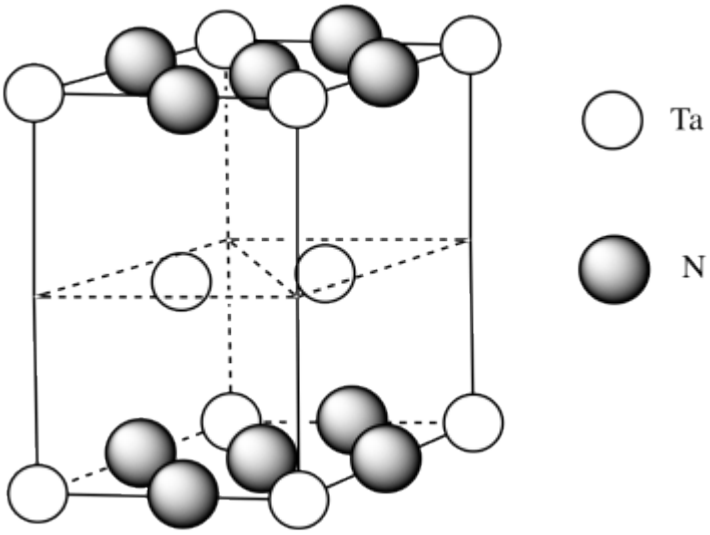


e) #Ta = (1/6)(1/2)(4) for the acute corners and (1/3)(1/2)(4) for the obtuse corners = 4/12 + 4/6 = 4/12 + 8/12 = 1

(note that it's the same outcome as the corners of a cube)

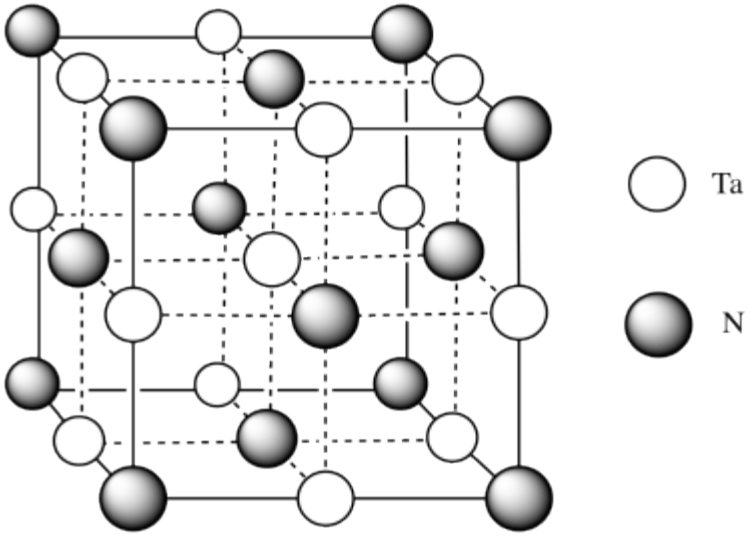
f) #N = (1/4)(8) for the edges and (1/2)(2) for the faces = 2 + 1 = 3

g) Need 2 more Ta.

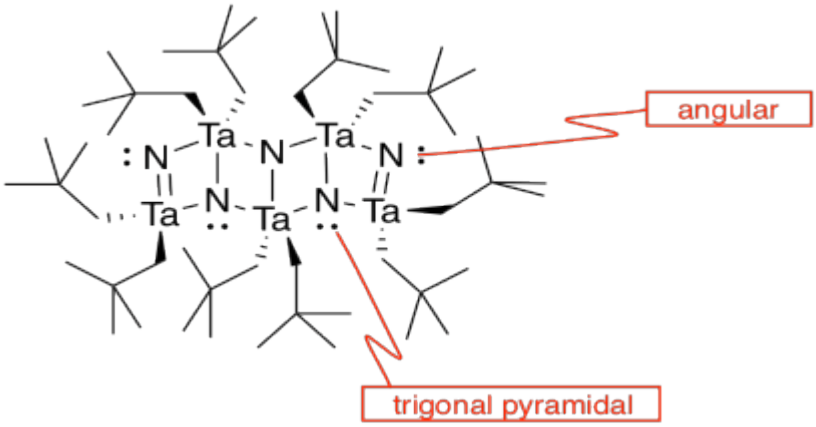


h) Each tantalum has three nitrogens above and three below it. It's almost octahedral, but the top layer of nitrogens is lined up above the bottom layer rather than being twisted 120 degrees to form an octahedron. The geometry is a trigonal prism.

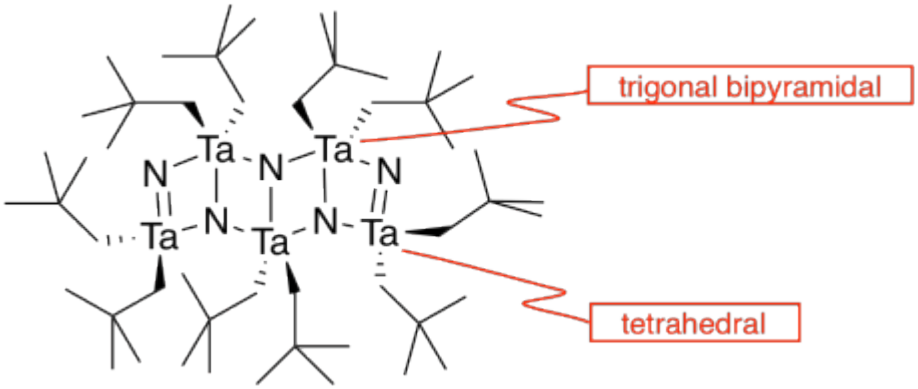
i)



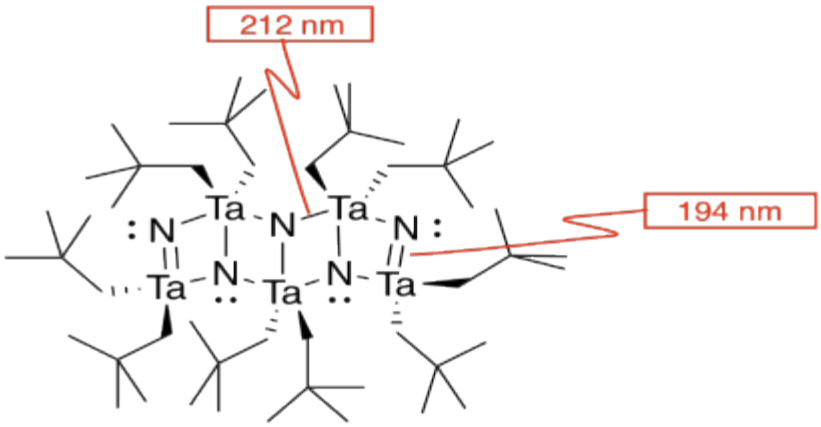
j)



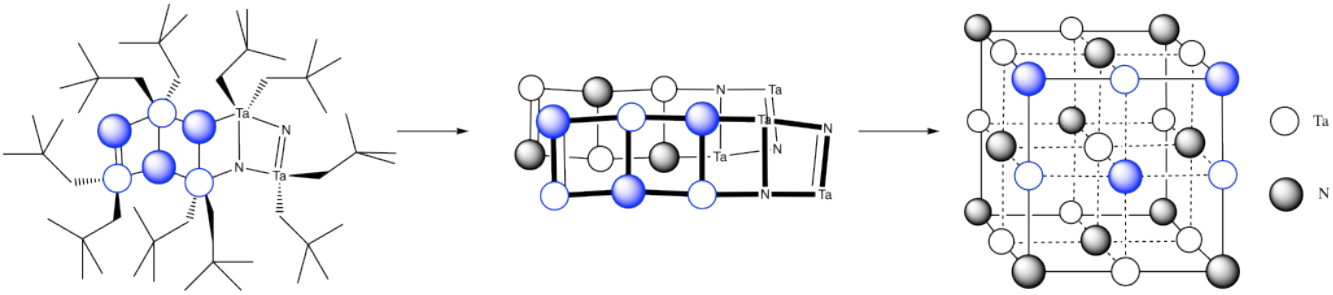
k)



l) The double bonds hold the atoms more closely together than the single bonds.



m) You can imagine the molecules stacking together to make a cubic array of TaN.

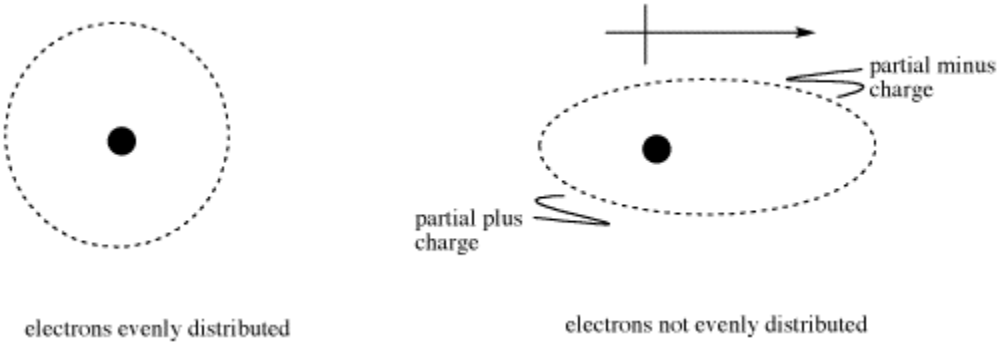


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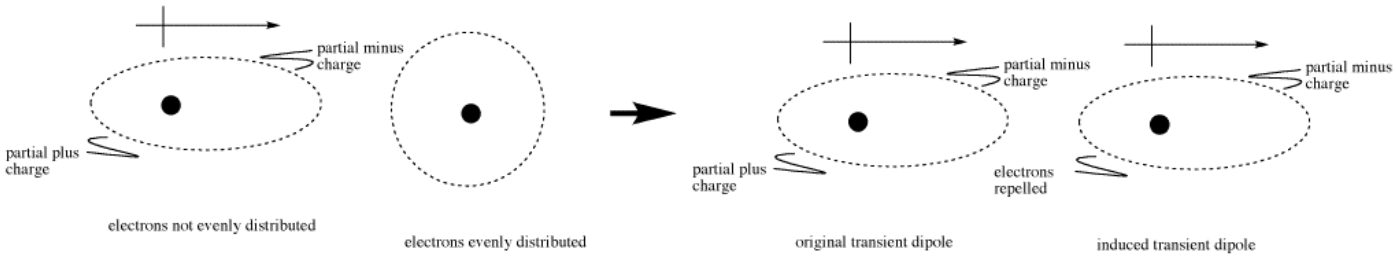
1.12.7: London Attractions

All molecules can experience London interactions or dispersion forces (sometimes called *van der Waals interactions*, although many people use this term to describe any kind of intermolecular attraction). These interactions are temporary electrostatic attractions caused by the random movement of electrons around a molecule. If at one moment more of the electrons are found on one side of the molecule than the other, then the molecule will develop a dipole.

A dipole is a separation of charge. If electrons slosh over to one side of the molecule, that end of the molecule becomes negatively charged, because electrons are negative. The other end of the molecule, however, becomes positively charged, because the negatively charged electrons that should be balancing the positive charge of the nucleus have drifted to the other end of the molecule. We symbolize this charge separation with a dipole arrow. One end of the arrow looks like a plus sign; that's the more positive end. The pointy end of the arrow represents the negative end.



This dipole is transient, meaning it does not last very long. However, in its short lifetime it could actually induce another dipole in a neighboring molecule. The electrons gathering on one side of one molecule could repel the electrons on the near side of the next molecule. This situation would leave the more negative end of one molecule next to the more positive end of its neighbor, and a weak attraction would result.



In most molecules, and especially relatively non-polar ones, these kinds of interactions last for tiny fractions of seconds. That means that if molecules rely entirely on London interactions to stick together, they probably don't stick together very well.

However, there are a couple of factors that can make these small interactions add up until they are pretty significant. First, molecules with many, loosely-held electrons would experience more London interactions than molecules with fewer, more tightly-held electrons. That's because the more electrons there are, and the more freely they are moving, the more likely they are to create that initial transient dipole. This factor is pretty significant when comparing the halogens, since fluorine has nine tightly-held electrons while iodine has fifty three, and most of them are so far from the nucleus that they are hard to keep track of.

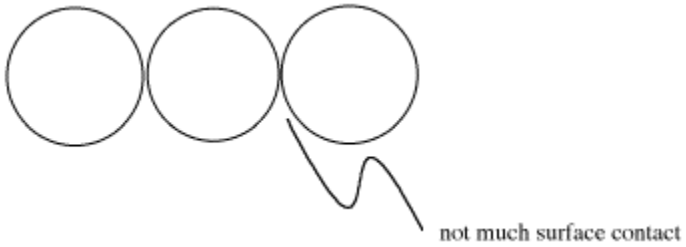
In addition, this type of attraction does not work very well between two molecules that are far away from each other. Because it is such a weak attraction, it works best when the two molecules are very close to each other. The more contact there is between the surfaces of the two molecules, the more likely it is that one molecule can induce a dipole in its neighbor, and the stronger the attraction will be.

It's all a matter of surface area. The more surface contact between two molecules or two materials, the more likely they are to interact with each other. In fact, this sort of phenomenon can lead to some surprising results if taken to the extreme. Many

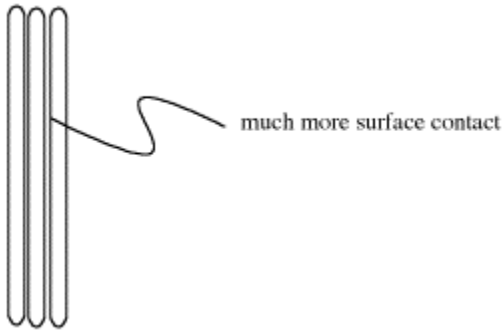
researchers believe that the ability of geckos to walk on walls and ceilings, even if the surface is very smooth, is entirely due to van der Waals forces. Millions of tiny fibers (or setae) cover the bottoms of the lizard's feet, and each of these fibers is covered in hundreds of tinier pads (or spatulae). These structures ensure that there is enough surface contact for many, many weak interactions to add up to one strong grip. Some companies are even trying to use this idea to make very strong but removable adhesives based on this gecko model.

Now consider the difference between the attractive forces that would be found in two different shapes of molecules. In one case, the molecules are small and round, like ping-pong balls. In the other case, the molecules are long, and linear, like ribbons of spaghetti or lasagna.

You can arrange ping pong balls in any way you like (without squashing them flat), and they will never be able to do more than barely touch their neighbors.



Lasagna noodles stack very easily on top of each other, and have a good deal of contact with the other lasagna noodles.



If London interactions rely on temporary dipoles that are induced only if molecules can get very close to each other; it would be best if the two molecules could almost touch each other.

This factor results from the physical law that electric forces fall off very quickly with increasing distance. The farther apart the molecules, the less strongly they can have an effect on each other.

So, the long, ribbon-like molecules, having more surface area in contact with their neighbors, are more likely to induce dipoles in their neighbors, and are more likely to stick together. The spherical molecules, with less surface area in contact, will attract each other more weakly.

What sort of molecules are shaped like ping pong balls and spaghetti? Two very similar molecules, both with the formula C_5H_{12}, can serve as examples.



normal pentane
or n-pentane



neopentane
or 2,2-dimethylpropane

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Wire Frame

Ball & Stick

Spacefilling

Normal pentane, or n-pentane, is a molecule in which all five carbons are arranged in a string, with the hydrogens completing the valence of each carbon. Neopentane, or 2,2-dimethylpropane, is a molecule in which one central carbon is bonded to each of the four other carbons, and each of those four carbons has three hydrogens on it. On paper, one might imagine pentane is spaghetti shaped, but neopentane looks more like a cross. You need to look at a space-filling model to see that neopentane is very much like a ball.

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Wire Frame

Ball & Stick

Spacefilling

It turns out that pentane has a boiling point of 35 ^{o}C, while neopentane, with the exact same molecular formula, has a boiling point of -9 ^{o}C. That means that, at comfortable room temperature, pentane is a liquid, while neopentane is a gas even on a pretty cold day. The pentane molecules stick together more because there is more contact between them; the neopentane molecules don't, and they each go their own way, forming a gas.

Pentane and neopentane are isomers. They have the same formula but different structures. Isomers is from the Greek, meaning "same things", referring to their identical content. However, isomers often have very different physical and biological properties.

Problem SP4.1

Compare London forces in the following pairs of molecules, and predict the relative melting points of the two compounds.

a) $CH_3(CH_2)_6CH_3$ and $CH_3(CH_2)_{100}CH_3$ b) $CH_3(CH_2)_6CH_3$ and $CH_3(CH_2)_3C(CH_3)_3$ c) CH_3Br and CH_3Cl

Problem SP4.2.

Predict the relative boiling points of 3,4-dibromohexane and 3,3-dimethylhexane.

Problem SP4.3.

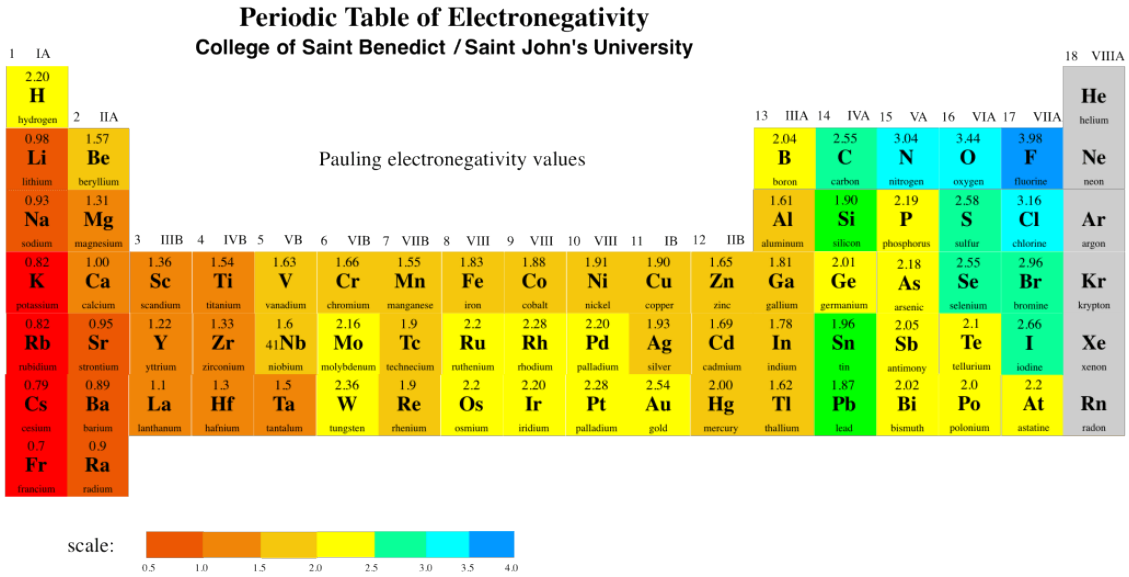
What would you predict about the relative melting points of dibenzyl ether and bis(cyclohexylmethyl) ether. (Note: "bis" is often used instead of "di" as a prefix for more complicated groups.)

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1.12.8: Dipole-dipole attractions

When two different kinds of atoms are connected to each other, the electrons between them are typically not shared evenly. That's because in most cases, two different atoms would have two different electronegativity values. One atom would be more electronegative than the other. It would have a stronger attraction for the electrons in the shared bond, and the electrons would be a little bit more attracted to that atom than the other.

Remember, electronegativity is a periodic trend. As we move to the right in the periodic table, more and more protons are added to the nucleus, and so atoms on the right attract electrons more strongly that do the atoms on the left. Also, as we move from top to bottom of the periodic table, the valence shells of the atoms become larger; that means valence electrons are getting farther from the nucleus, so they are less tightly held. Those two factors, distance and amount of charge, control the strength of interaction between charged particles.



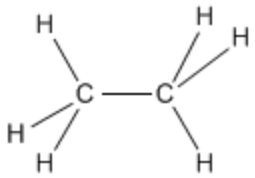
The periodic table above shows Pauling electronegativity values. There are different ways to calculate electronegativity, but the Pauling scale is very commonly used. Calculating the Pauling scale depends on being able to observe compounds, so the noble gases are not usually given a value in this scale, because they normally don't form any compounds.

For example, when a carbon atom is bonded to a fluorine atom, there is an electronegativity difference between the two atoms. There is a difference in electronegativity values of almost 1.5 units between these two atoms. Fluorine is more electronegative than carbon because it has more protons in the nucleus than carbon. The electrons are pulled closer to the fluorine than to the carbon. A carbon-fluorine bond is polarized towards the fluorine. A molecule like fluoromethane, CH_3F, has a permanent dipole.

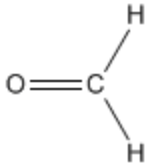
Note that there are also dipoles in C-H bonds, but they are so much smaller than the ones in the C-F bond that they do not matter. The overall dipole has a buildup of negative charge on the fluorine.

You can imagine that molecules with permanent dipoles would interact with each other much more strongly than molecules that rely on temporary dipoles in order to stick together. Molecules with no natural dipole will stick only loosely together, but molecules with permanent dipoles will stick to each other easily.

Ethane, C_2H_6 (sometimes written CH_3CH_3, suggesting two carbons are each connected to three hydrogens, and also to each other), and formaldehyde, CH_2O, have different formulae but the same molecular weight. Based on weight alone, it would take about the same amount of energy to move an ethane molecule and a molecule of formaldehyde.



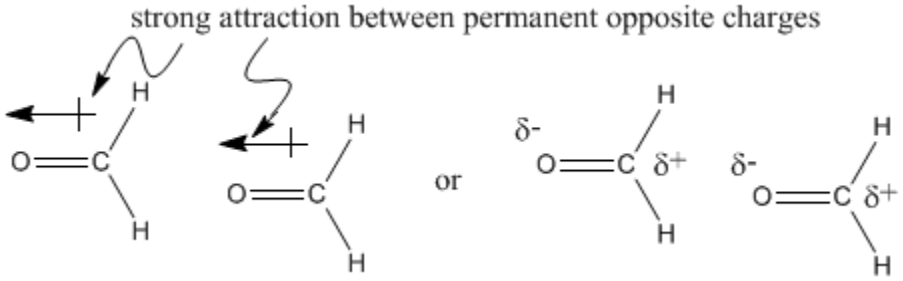
ethane



formaldehyde or methanal

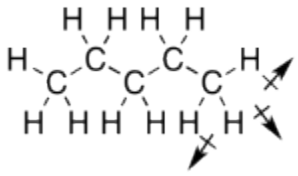
The two molecules also have somewhat similar shapes, unlike neopentane and pentane. At room temperature, ethane and formaldehyde are both gases. Nevertheless the two compounds have very different boiling points; formaldehyde becomes liquid around -20 ^{o}C, which would be a very cold winter day in, say, Chicago. Ethane does not become liquid unless it is cooled to around -90 ^{o}C, a cold winter day on Neptune, at which point formaldehyde is just about ready to freeze solid.

The difference between these two molecules must be due to the oxygen atom in formaldehyde. Oxygen, the second most electronegative element in the periodic table, can form some very polar bonds. The difference between carbon and oxygen is 0.89 units, almost a full electronegativity unit. The permanent dipole that results between the oxygen and carbon makes the formaldehyde molecules much stickier than the ethane molecules, which depend on fleeting London interactions if they are going to hold on to each other.



In contrast, the difference in electronegativity between carbon and hydrogen is actually pretty small (about 0.35 units, based on the Pauling scale). The tiny dipole in the C-H bond is so much smaller than the one in the C=O bond that it really isn't a factor here.

Taking that story a little further, hydrocarbons (molecules made up of hydrogen and carbon) are the most common example of non-polar compounds, because their bonds are either completely nonpolar C-C bonds or else C-H bonds with very low polarity. There is a tiny dipole in a C-H bond, but it isn't enough to make the molecules attract each other very well. Furthermore, there tend to be a lot of C-H bonds in a hydrocarbon pointing in all sorts of directions; an approaching molecule would be unlikely to encounter either a fully positive end or a fully negative end of the molecule. In the end, all those little dipoles in all those C-H bonds end up cancelling each other out.



There are other variations on dipole interactions that are pretty common. For example, you could imagine that a dipolar molecule would interact pretty strongly with an ion. We will take a look at that situation shortly when we think about how mixtures of different compounds interact with each other. However, perhaps the most important variation in organic chemistry is hydrogen bonding.

Problem SP5.1.

Comment on dipole moments in the following compounds and predict their relative boiling points.

a) 1-chlorobutane vs. pentane b) triethylamine vs. 3-ethylpentane c) diethyl ether vs. pentane

Sometimes a molecule that contains polar bonds is not really polar overall. Carbon dioxide is a good example. Polar molecules strongly attract each other because the more negative end of one molecule is attracted to the more positive end of the next molecule via electrostatics. Opposites attract. In carbon dioxide, however, both ends of the molecule are more negative. How can they attract each other?

There's more to it. Dipoles are "vector quantities". That means it isn't just the amount of charge separation that matters; it's also the direction of separation. In carbon dioxide, a linear molecule, there are two polar bonds. Those polar bonds point directly away from each other. The dipole of one bond balances out the dipole of the other bond. Overall, the molecule does not have a dipole.

Water, on the other hand, is a different case. Like carbon dioxide, water has two polar bonds. However, the bonds in water do not lie in a straight line like the ones in carbon dioxide. They are at an angle to each other instead. That means their dipoles are not quite pointing in opposite directions. As a result, water has an overall dipole moment.

At the extreme, a polar bond can get to the point that one atom is pulling the electrons so strongly toward itself that it pulls them completely away from the other atom. The first atom becomes an anion, and the second atom becomes a cation. At this point, we have an ionic bond, rather than a covalent one. How different must the electronegativity values be in order to have an ionic bond? The usual rule of thumb is a difference of about 1.6 electronegativity units. So, for example, all of the blue atoms in the periodic table above would form ionic bonds with all of the red atoms. The green atoms would form ionic bonds with most of the dark red atoms, but not with the light red ones.

Problem SP5.2.

> The dipole moment of a molecule (essentially the size of its dipole) can be calculated from the dielectric constant of a material, which can be measured experimentally on a bulk quantity of the compound. The dipole moment of chloromethane, 12.9 D, is higher than that of dichloromethane, 9.08 D, even though dichloromethane has a greater number of polar bonds than chloromethane. Explain why.

Problem SP5.3.

> Dichloromethane nonetheless has a higher boiling point (39 °C) than chloromethane (-24 °C). Explain why.

Problem SP5.4.

> Comment on dipole moments in the following compounds and predict their relative boiling points.
>
> a) butane and ethyl methyl ether
>
> b) ethyl methyl ether and 2-propanone
>
> c) trimethylamine and propanenitrile
>
> d) 2-propanone and 2-chloropropane

Problem SP5.5.

> a) Draw the Lewis structure for each molecule with the correct electronic geometry.
>
> b) Draw in dipole moments.
>
> c) Decide if the molecule is polar.

CBr_4

$CH_3(CO)CH_3$

CO_2

$CH_3CH_2CH_2CH_3$

BF_3

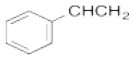
CH_3OH

$CH_3CH_2OCH_2CH_3$

$(CH_3CH_2)_3N$

XeF_6

CH_3CH_2CN

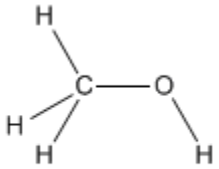


CH_3Cl

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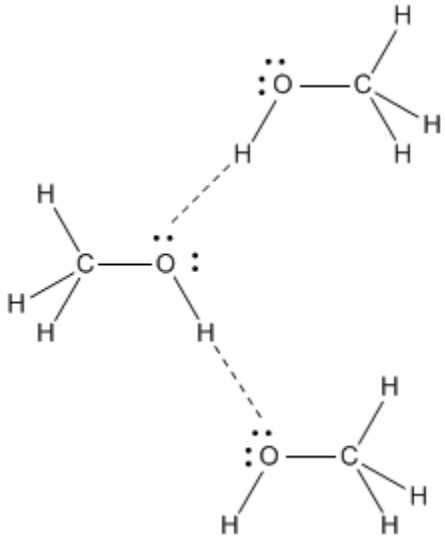
1.12.9: Hydrogen Bonding

Methanol, CH_4O (or CH_3OH, a CH_3 group attached to an OH), is another example of a molecule with a similar molecular weight to ethane. Like formaldehyde, methanol freezes somewhere around-90 ^{0}C, but it does not become a gas until it is heated to 65 ^{0}C. Methanol is certainly similar to formaldehyde in some ways. It contains oxygen and is very polar. The huge difference in their boiling points is due to the very strong hydrogen bonds in methanol.

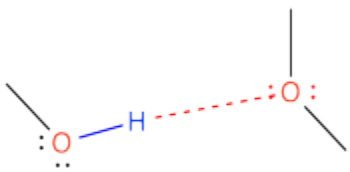


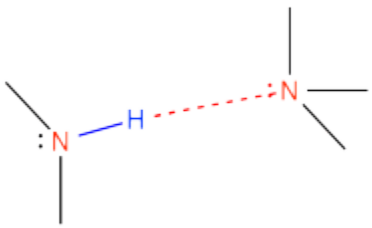
methanol

Hydrogen bonding occurs when there is a significant amount of positive charge building up on a hydrogen atom. That happens because the hydrogen is attached to an atom that is much more electronegative than the hydrogen. As a result of that positive charge, a lone pair on another molecule strongly interacts with the hydrogen.



Hydrogen bonds occur only when a hydrogen is attached to one of the few most electronegative elements in the periodic table: fluorine, oxygen or nitrogen. It is these strong hydrogen bonds that are responsible for the relatively high boiling point of methanol; there is so much positive charge on the hydrogen of the OH group that it can essentially form a real bond with the lone pair on another methanol molecule.





Water is an even better example of a hydrogen bonding compound; in fact, water molecules are so tightly bound to each other that this very small molecule freezes at 0 ^{0}C and does not boil until 100 ^{0}C (way, way hotter than an August day in Las Vegas). Water

molecules are much less able to move around freely than are ethane molecules, even though ethane molecules weigh almost twice as much.

For practical purposes, hydrogen bonding usually involves compounds that contain N-H and O-H bonds. That's because oxygen and nitrogen are the second- and third-most electronegative elements in the periodic table, respectively. There are many, many examples of compounds like that. It also occurs in HF, of course, because fluorine is usually considered the most electronegative element, but there is really only one example of a compound with that bond, so you are much less likely to have to worry about that example. Slightly weaker hydrogen bonds have also been shown to occur involving other species, such as S-H bonds, but the most significant ones involve N-H and O-H bonds.

Problem SP6.1.

Which of the following molecules are capable of strong hydrogen bonding?

a) ethanal, CH_3CHO b) ethylamine, $CH_3CH_2NH_2$ c) acetic or ethanoic acid, CH_3CO_2H d) dimethyl peroxide, CH_3OOCH_3

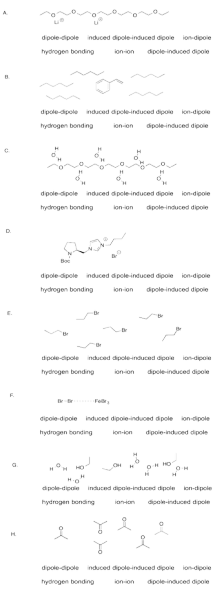
Problem SP6.2.

Predict the relative order of melting points in the following amines:

hexylamine, $CH_3(CH_2)_4CH_2NH_2$; triethylamine, $(CH_3CH_2)_3N$; dipropylamine, $(CH_3CH_2CH_2)NH$

Problem SP6.3.

Identify the strongest IMF in each case.



Biological Molecules and IMFs

Because compounds containing oxygen and nitrogen are so common in biology, hydrogen bonding is a fairly common feature in organic and biological chemistry.

Carbohydrates are one of the major classes of biomolecules. Carbohydrates are compounds that contain lots of OH groups, so they have lots of potential to form hydrogen bonds.

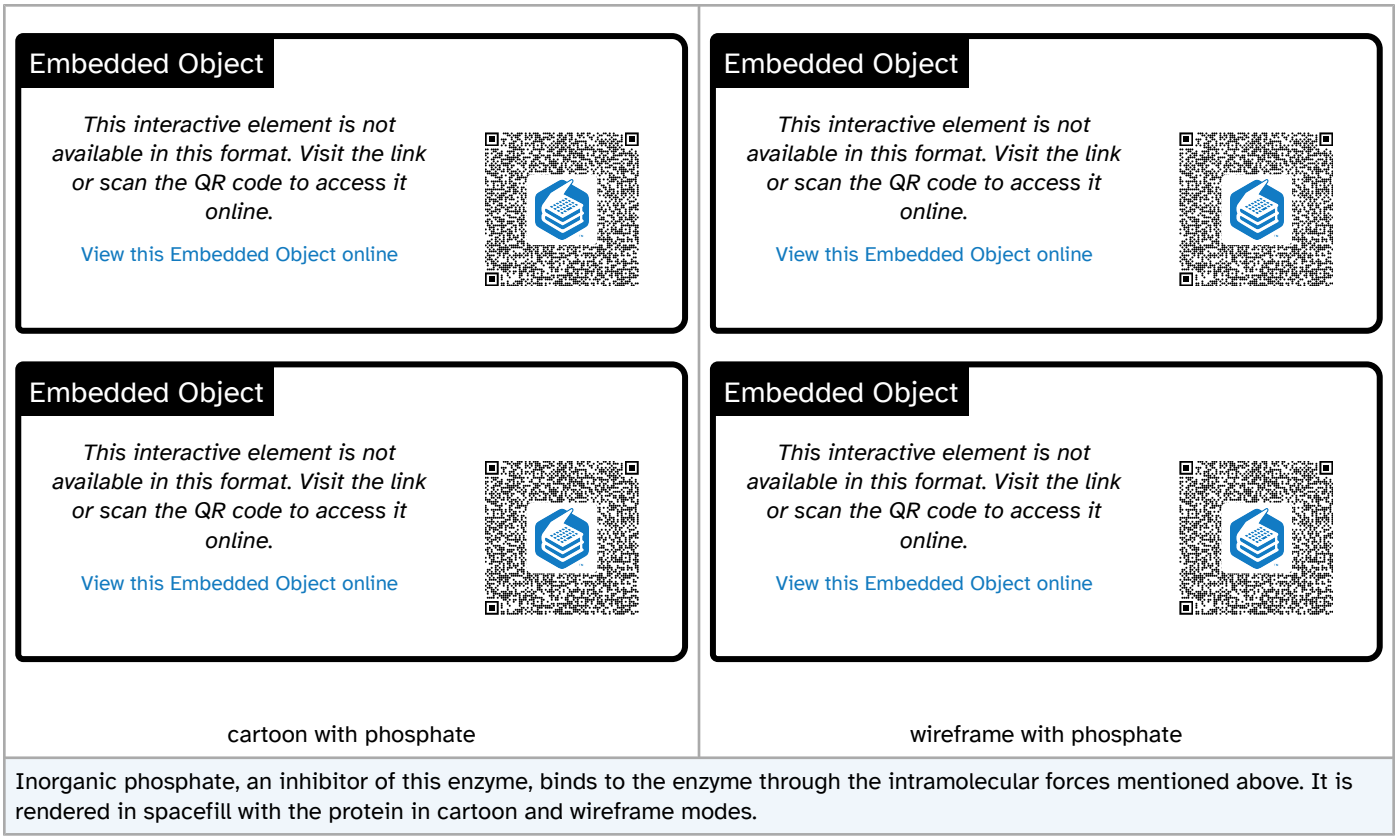
Proteins and peptides contain amide groups. Amides contain N-H bonds; hydrogen bonds involving amides are crucial influences in the structure of proteins.

Large biological molecules like proteins consists of 1000s of atoms, which interact through "intramolecular" ion-ion, London dispersion, dipole-dipole, and hydrogen bonding to create a unique 3D structure. Other molecules, both small and large, can bind

to biological macromolecule using the same intermolecular interactions. An example of a protein, bovine low molecular weight protein tyrosyl phosphate, binding to inorganic phosphate, is shown below. Select the radio buttons below to alter the rendering of the molecular and obtain a better understanding of the structure/activity relationships of the protein:

Embedded Object *This interactive element is not available in this format. Visit the link or scan the QR code to access it online.* View this Embedded Object online Embedded Object *This interactive element is not available in this format. Visit the link or scan the QR code to access it online.* View this Embedded Object online	Embedded Object *This interactive element is not available in this format. Visit the link or scan the QR code to access it online.* View this Embedded Object online Embedded Object *This interactive element is not available in this format. Visit the link or scan the QR code to access it online.* View this Embedded Object online	Embedded Object *This interactive element is not available in this format. Visit the link or scan the QR code to access it online.* View this Embedded Object online Embedded Object *This interactive element is not available in this format. Visit the link or scan the QR code to access it online.* View this Embedded Object online
spacefill	wireframe	cartoon

The displays above show three different ways to render the LMW-PTPase. You will recognize the spacefill and wireframe models, but note their complexity compared to the smaller molecules you have studied thus far. The cartoon molecules removes much of the detail by stripping away atoms and bonds, and replacing them with lines, ribbons (representing alpha helices) and block arrows (representing beta structure).



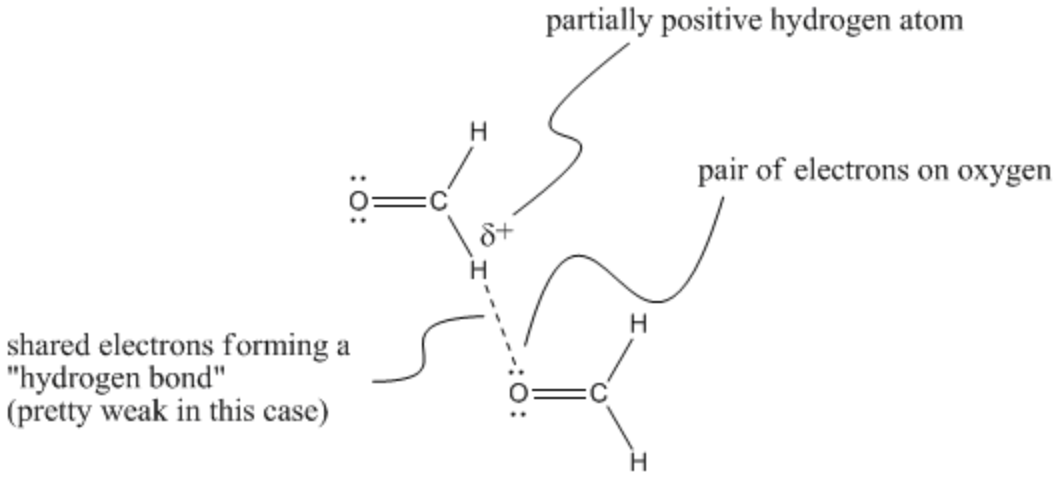
Inorganic phosphate, an inhibitor of this enzyme, binds to the enzyme through the intramolecular forces mentioned above. It is rendered in spacefill with the protein in cartoon and wireframe modes.

DNA may be the most well-known example of a compound that displays hydrogen bonding. In DNA, complementary "base pairs" hydrogen bond to each other to held two strands of DNA together.

Weak, "Secondary" Hydrogen Bonds

Hydrogen bonding is really a special case of dipole forces. It occurs under very particular circumstances: in the presence of O-H or N-H bonds, which provide both a very positive hydrogen and a lone pair, the two features necessary for a hydrogen bonding interaction.

In general, we think of a hydrogen bond as the electrostatic interaction between an electron pair on one atom and a hydrogen atom that has built up a partial positive charge. There are some examples where that might be happenning, but that we would rather keep separate from the general idea of a hydrogen bond. For example, a lone pair on an oxygen atom in formaldehyde might be attracted to a hydrogen on another formaldehyde, which would be at the more positive end of the molecule. There is evidence from x-ray crystallography that such weak "hydrogen bonds" occur in the solid state in molecules containing aldehyde groups, similar to the one in formaldehyde.



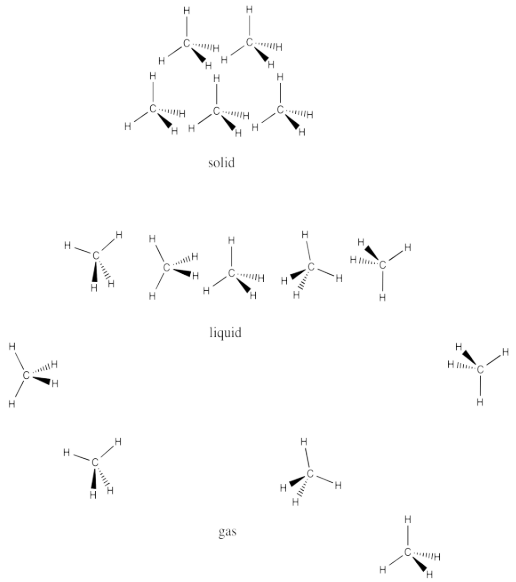
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1.12.10: Solutions to selected (SP) problems

Problem SP1.1.

One difference between water and these other molecules is that water is polar: there is a significant electronegativity difference between the oxygen and the hydrogen. The charges in one water molecule may be interacting with charges in other water molecules.

Problem SP2.1.



Problem SP3.1.

As far as we can tell from these data, the melting point of nitrogen and oxygen would be somewhere around -220°C, whereas the boiling point would be around -180°C. We would expect these numbers to be similar to fluorine, which has a similar mass. In fact, the melting and boiling points of oxygen are about -219°C and -183°C, respectively. The melting and boiling points of nitrogen are about -210°C and -196°C, respectively.

Problem SP4.1.

a) A chain that is 8 carbons long would have much lower London interactions than a chain that is 102 atoms long. The greater the contact between molecules, the greater the chance for weak attractions due to small charges arising from random electron movement. The molecule with the longer chain would have the higher melting point, because more energy would have to be added in order to overcome those attractions and get the molecules moving.

b) The first chain is more linear whereas the second chain is more branched. The more linear molecules will pack together more easily, allowing greater surface contact for increased London interactions. The straighter chain would have a higher melting point.

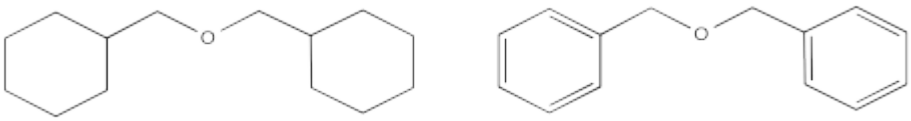
c) Bromomethane has a lot more electrons than chloromethane. Based on London interactions alone, we would expect bromomethane to have a higher melting point. In fact, the melting point of bromomethane is about -94°C, compared to about -97°C for chloromethane; there must be another factor that compensates for the difference in numbers of electrons and makes these values so close.

Problem SP4.2.

Because of the large numbers of electrons in bromine, we would expect a higher boiling point in 3,4-dibromohexane.

Problem SP4.3.

Remember benzyl refers to the group $C_6H_5CH_2$ (below right); cyclohexylmethyl suggests the superficially similar $C_6H_{12}CH_2$ (below left).



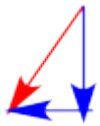
The benzyl group contains trigonal planar carbons, whereas the cyclohexylmethyl group contains only tetrahedral carbons. The benzyl groups,being flatter, could pack more easily together and interact more strongly. We would expect dibenzyl ether to have a higher melting point.

Problem SP5.1.

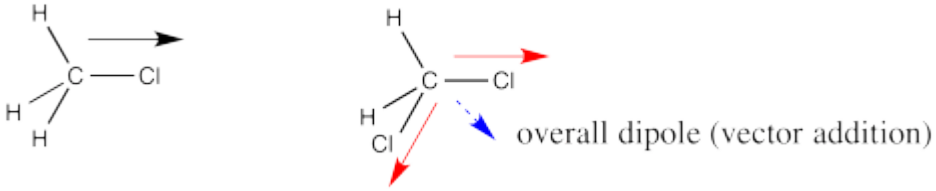
These compounds all contains lots of non-polar C-C and C-H bonds, which would not have appreciable dipoles. However, in each pair, there is a compound that contains more polar bonds as well: C-Cl, C-N and C-O.

Problem SP5.2.

Dipoles are vectors. If we have two polar bonds, they will add together using vector addition. Any vector can be shown as the sum of two other vectors. Below, the red arrow points down and to the left. How far down and how far to the left? We can show how far using the blue arrows. The blue arrow down and the blue arrow to the left add up to give the red arrow that goes down and to the left.

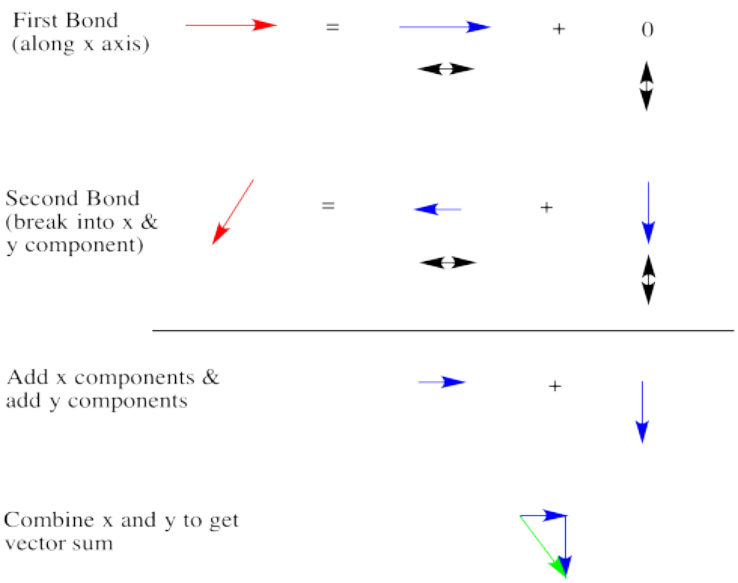


In dichloromethane, there are two polar bonds. Both bonds are polarized towards the more electronegative chlorine. As drawn below, one bond has a dipole straight to the right. The other bond has a dipole that goes down and to the left. If the molecule has an *overall* dipole, with a positive end of the whole molecule and a negative end of the whole molecule, which end would be positive and which would be negative?



It seems reasonable that the positive end would be somewhere over on the hydrogen side and the negative end would be somewhere over on the chlorine side. The overall dipole, as opposed to the individual bond dipoles, would point somewhere in the direction of the blue, dashed arrow. But how big would it be? Surely it's bigger than either of the two individual dipoles, because they are adding together, right?

Let's take a very qualitative look. The first red arrow is just to the right. We'll break the second arrow into a smaller arrow down and an even smaller arrow to the left. The sum of the left/right arrows is a very small arrow to the right.



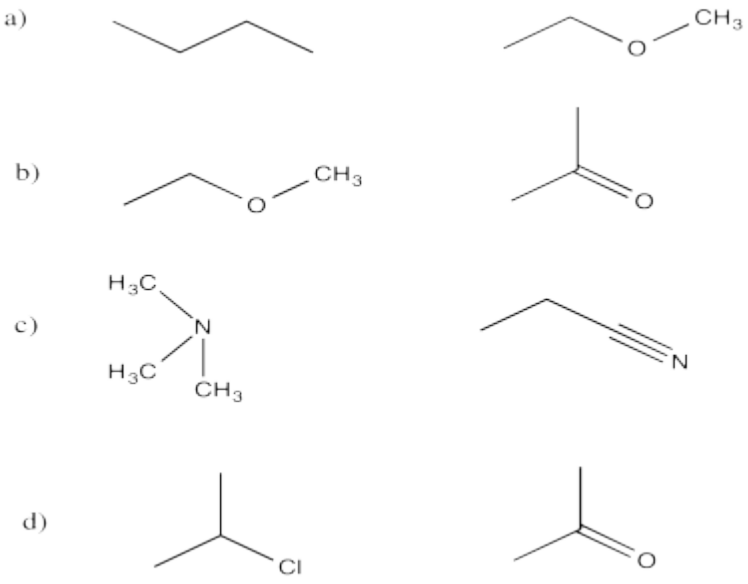
The sum of the up/down arrows is just a small arrow down. Overall, the sum is a green arrow going down and to the right. The result doesn't really seem any bigger than an individual bond dipole.

Problem SP5.3.

Despite the relatively similar dipole moments, dichloromethane's boiling point is much higher than chloromethane's. The difference probably lies in the much greater mass of dichloromethane.

Problem SP5.4.

In each case, the one on the right has a larger dipole and a higher melting point.



Problem SP6.1.

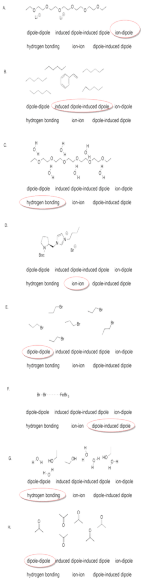
Only ethylamine and ethanoic acid have the N-H or O-H bonds that are polar enough for hydrogen bonding.

Problem SP6.2.

hexylamine > dipropylamine > triethylamine

The one with the greatest potential for hydrogen bonding will have the highest melting point.

Problem SP6.3.



Problem SP8.1.

The hydrogen bonding between 2-propanol molecules is a stronger interaction and is more difficult to overcome than the dipole-dipole interactions between 2-propanone molecules. Thus, 2-propanone molecules can more easily escape into the vapour phase.

Problem SP8.2.

There is hydrogen bonding between molecules of *N*-methylethylamine, but not between molecules of triethylamine, which are held together by relatively weak dipoles. Trimethylamine molecules are not held together as tightly as the *N*-methylethylamine molecules, which therefore pack more densely. On the other hand, *n*-propylamine contains two N-H bond, compared to only one in *N*-methylethylamine. Consequently, *n*-propylamine has a greater propensity to form hydrogen bonds, and it packs together even more densley than the *N*-methylethylamine..

Problem SP8.3.

Temperature is a measure of how much energy is available in the environment. As temperature increases, molecules obtain more energy and they transfer that energy into a variety of molecular motions. As they move around more, they are less able to remain densely packed. The density decreases as the temperature goes up. Conversely, things tend to shrink as they cool, because molecules slow down and begin to pack more tightly. They become more dense.

Problem SP8.4.

a) Acetic acid posesses hydrogen bonding capability, whereas 2-propanone has the ability to form only dipole-dipole interactions. Thus, 2-propanone molecules are not held in the liquid phase as strongly as acetic acid, and the former compound has a higher vapour pressure.

b) The C=O bond of ethyl acetate has a substantial dipole, but the dipoles in ether don't add up to very much; they are smaller to begin with and they partially cancel out via vectorial addition. Ether molecules can escape the liquid more easily, resulting in a higher vapour pressure.

c) Both molecules are limited to relatively weak London dispersion interactions. Because heptane forms a longer chain than pentane, there will be a slightly greater interaction between heptane molecules than between pentane molecules. Pentane thus has the higher vapour pressure.

Problem SP8.5.

a) The C=O bond 2-butanone has a substantial dipole, but the dipoles in ether don't add up to very much; they are smaller to begin with and they partially cancel out via vectorial addition. The 2-butanone molecules cling together more strongly, resulting in a higher viscosity.

b) Both molecules are limited to relatively weak London dispersion interactions. Because decane forms a longer chain than hexane, there will be a slightly greater interaction between decane molecules than between hexane molecules. Decane thus has the higher viscosity. Later, if you study macromolecules, you will see that in very, very long chains, "entanglement" becomes a factor as well. Just as the name implies, really long chains get tangled up together and have a difficult time moving past each other; that's why materials like cooking oil and motor oil are so viscous.

c) The 1-butanol can hydrogen bond together, but the ether only has weak dipole-dipole interactions. The 1-butanol is therefore more viscous.

Problem SP7.6.

a) The 1-butanol can hydrogen bond together, but the ether only has weak dipole-dipole interactions. The 1-butanol therefore has greater surface tension.

b) The 1-butanol can hydrogen bond together, but the 1,3-butanediol has two OH groups and can form even more hydrogen bonds than 1-butanol can. The 1,3-butanediol therefore has greater surface tension.

c) The formamide has N-H bonds and so it is capable of hydrogen bonding. Despite having a pretty darned big dipole, the nitromethane can't really hydrogen bond together. The formamide therefore has greater surface tension.

Problem SP8.7.

a) 2-propenol. It has hydrogen bonding capability but propanal does not.

b) heptanoic acid. It has hydrogen bonding capability but ethyl pentanoate does not.

c) 1-hexen-3-one. Its dipole is greater than that in the ether, because it comes from a C=O bond rather than C-O bonds.

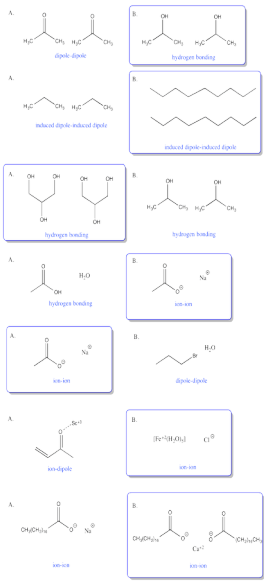
Problem SP8.8.

a) 2-butanone. Its dipole is greater than that in the ether, because it comes from a C=O bond rather than C-O bonds.

b) octane. It has greater London dispersion interactions that pentane because of the greater surface contact area in octane.

c) 1,3-butanediol. It has hydrogen bonding but the DME does not.

Problem SP8.9.



Problem SP9.1.

Hydrogen bonding.

Problem SP9.2.

a) dipole interactions b) London interactions c) dipole interactions d) hydrogen bonding

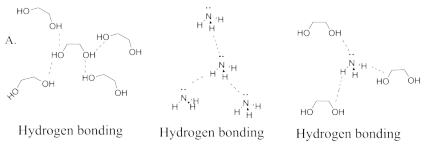
Problem SP9.3.

Water molecules interact with each other mainly through hydrogen bonding, whereas octane molecules interact with each other via London interactions. The main problem here is the strong hydrogen bonding between the water molecules. All molecules, in principle, could interact with each other via London interactions. However, if octane molecules were introduced among the water molecules, they would take up space. Some of the water molecules would not be able to get close enough to each other to hydrogen bond anymore. The loss of that very stabilizing interaction would be too costly.

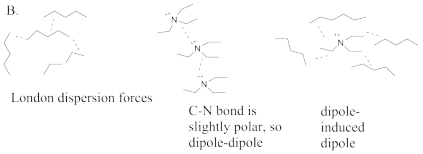
Problem SP9.4.

This problem is similar to the previous one, but in this case the attraction between the strong dipoles of the nitrile groups would be too much to overcome.

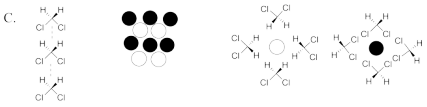
Problem SP9.5.



IMF's comparable; therefore solute is likely soluble.



Even though forces are different, the dipole in the amine is weak and there would also be significant LDF's between the pentane and the ethyl groups, so likely miscible.



Given that the dipole in CH_2Cl_2 is weak, NaCl will likely not dissolve.

Problem SP9.6.

a) dipole / induced dipole b) dipole / dipole c) hydrogen bonding d) dipole / induced dipole

Problem SP10.1.

The predicted order, from most soluble to least, would be LiCl > $MgSO_4$ > $AlPO_4$ because the ions increase in charge from 1+/- to 2+/- to 3+/-

Problem SP10.2.

The predicted order, from most soluble to least, would be dimethylsulfoxide > acetonitrile > pyridine > dichloromethane > triethylamine.

Problem SP11.1.

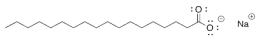
a) H-bond acceptor b) H-bond acceptor c) fully H-bonding d) H-bond acceptor e) fully H-bonding f) neither

Problem SP12.1.

SP11

1. The structure of soap is shown below.

a. Calculate the formal charge on the oxygens and the sodium.



b. The 'tail' of the soap is circled. Is it polar or non-polar?



tail is nonpolar& hydrophobic

head is polar & hydrophilic

c. What type of IMF would you predict for:

tail-tail of 2 soap molecules: _____ induced dipole - induced dipole
head-tail of 2 soap molecules: _____ ion - induced dipole
water-tail of a soap molecule: _____ dipole-induced dipole
water-head of a soap molecule: _____ ion-dipole

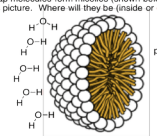
d. Would you expect the tails to be soluble in water?

No The dipole-induced dipole is too weak to overcome hydrogen bonding between waters.

e. Which IMF interactions would be strongest?

Ion-dipole between water and the hydrophilic head of the soap.

f. Soap molecules form micelles (shown below) in water. Draw several water molecules in this picture. Where will they be (inside or outside) this micelle structure.



picture from wikipedia: http://en.wikipedia.org/wiki/Soap

f. Explain why soap forms this micelle structure in the presence of water. Use IMF.

Water is attracted to the hydrophilic heads to form this strong ion-dipole interaction whereas the tails cannot overcome the strong hydrogen bonding of water-water interactions.

g. Dirt is usually non-polar fats or other non-polar organic structures. Where would dirt be in this picture above?

Hydrophobic dirt & grease will prefer to interact with the hydrophobic tails (inside micelle).

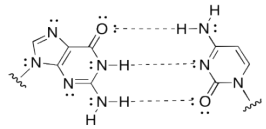
h. How does soap clean dirt/grease off your hands?

The grease will be encapsulated in the micelle and washed away in water.

Problem SP13.1.

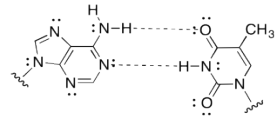
Note that the last example is actually found in RNA, not DNA. RNA is found as a single strand, rather than a pair of strands. It hydrogen bonds to itself in a particular shape, not unlike the way a protein adopts a specific shape.

a)



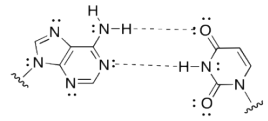
guanine cytosine

b)



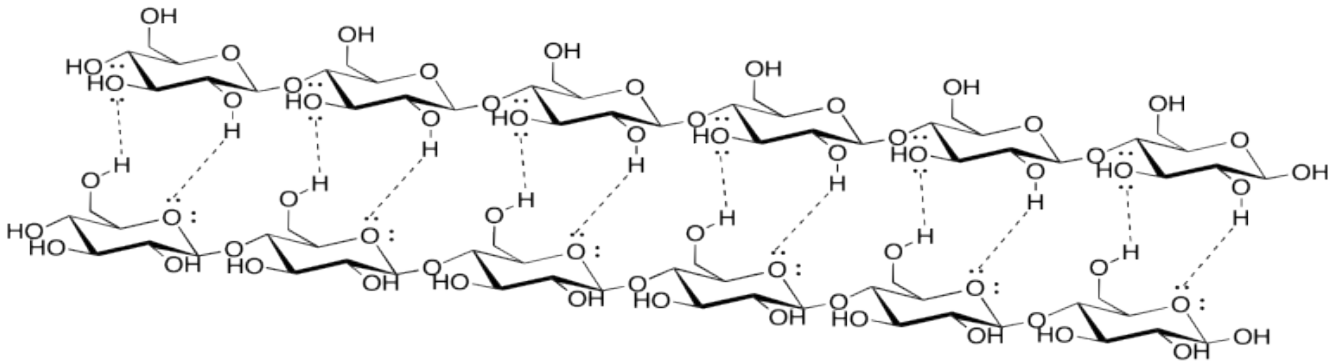
adenine thymine

c)



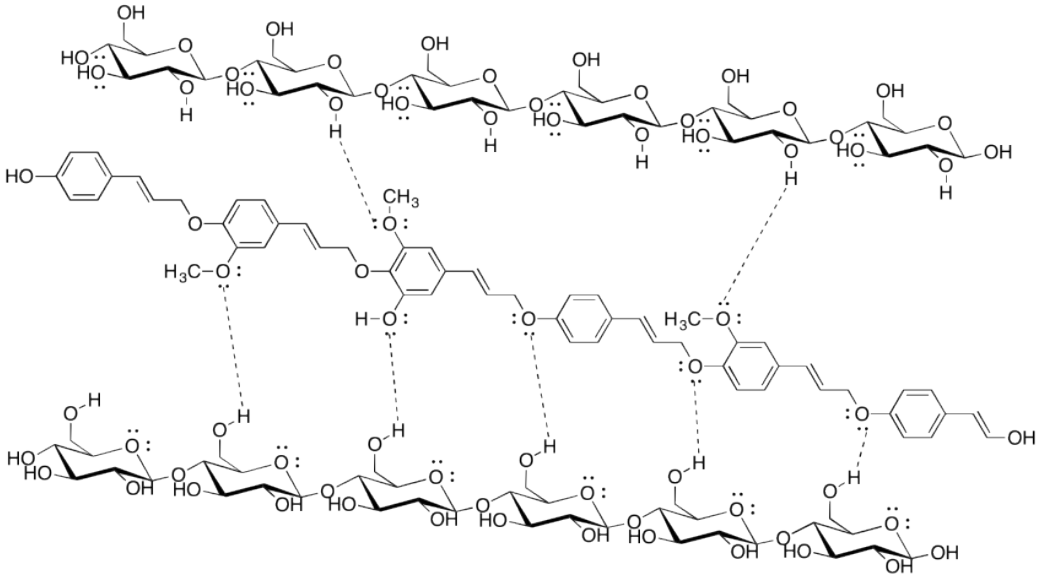
adenine uracil

Problem SP13.2.



Problem SP13.3.

Although lignin is capable of some hydrogen bonding, it cannot make nearly as many hydrogen bonds as cellulose can. Paper containing lignin would be much weaker, and more likely to tear or to fall apart when it gets wet, because the cellulose molecules would not be able to bind each other as tightly with lignin mixed in. In fact, brown paper bags from the grocery store are made from *kraft*, which has not had lignin removed; they are much weaker than most paper, especially if they get wet.



Problem SP13.4.

The dominant intermolecular attraction here is just London dispersion (or induced dipole only). London dispersion is very weak, so it depends strongly on lots of contact area between molecules in order to build up appreciable interaction. The stearic acid-containing triglycerides will be able to pack much more closely together than the more jumbled oleic acid-containing ones, so they will have much more surface contact and much stronger attractions. they will hold together into a solid.

Problem SP13.5.

a) alpha helix b) beta sheet c) alpha helix d) beta sheet e) beta sheet

f) alpha helix g) alpha helix h) beta sheet i) alpha helix j) alpha helix

Problem SP14.1.

a)

	water	**water**
ionic	no	no
H-bond acceptor	yes	yes
H-bond donor	yes	yes
dipole	yes	yes
induced dipole	yes	yes

Water hydrogen bonds with water.

b)

	goof	**goof**
ionic	no	no
H-bond acceptor	no	no
H-bond donor	no	no

dipole	no	no
induced dipole	yes	yes

Goof-off forms induced dipole/induced dipole interactions (London dispersion forces) with itself.

c)

	goof	**grease**
ionic	no	no
H-bond acceptor	no	no
H-bond donor	no	no
dipole	no	no
induced dipole	yes	yes

Goof-off forms induced dipole/induced dipole interactions (London dispersion forces) with grease.

d)

	grease	**water**
ionic	no	no
H-bond acceptor	no	yes
H-bond donor	no	yes
dipole	no	yes
induced dipole	yes	yes

Water forms dipole/induced dipole interactions with grease.

The key to why goof-off works is that it engages in the same London dispersion interactions with the grease as the grease does itself. Water is good at dissolvng many things, but not grease. That's mostly because the water would have to give up some of the strong hydrogen bonds with other water molecules in order to fit grease molecules among the water molecules.

Problem SP14.2.

a)

	octane	**octane**
ionic	no	no
H-bond acceptor	no	no
H-bond donor	no	no
dipole	no	no
induced dipole	yes	yes

That's going to be induced dipole-induced dipole interactions in octane.

b)

	isopropanol	**isopropanol**

ionic	no	no
H-bond acceptor	yes	yes
H-bond donor	yes	yes
dipole	yes	yes
induced dipole	yes	yes

Hydrogen bonding in isopropanol.

c)

i)

	isopropanol	**water**
ionic	no	no
H-bond acceptor	yes	yes
H-bond donor	yes	yes
dipole	yes	yes
induced dipole	yes	yes

Hydrogen bonding between isopropanol and water.

ii)

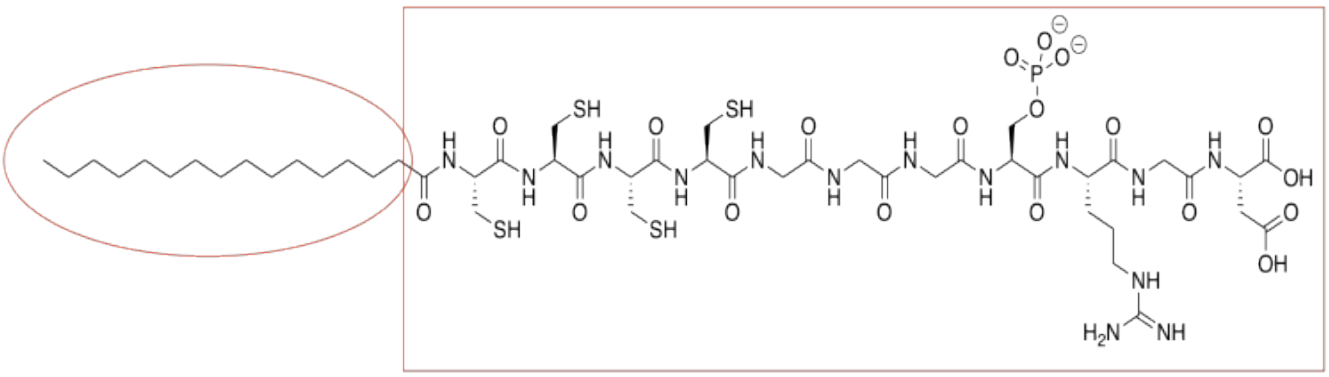
	octane	**isopropanol**
ionic	no	no
H-bond acceptor	no	yes
H-bond donor	no	yes
dipole	no	yes
induced dipole	yes	yes

Dipole-induced dipole interactions between octane and isopropanol.

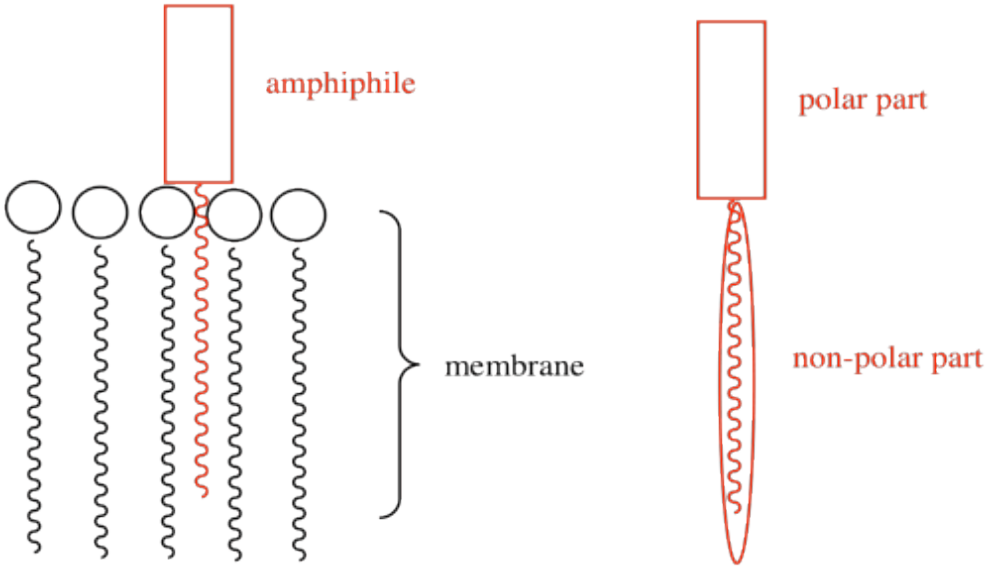
d)

e) No, the ethanol should do the same thing that the HEET does.

Problem SP14.3.



b) The amphiphile inserts into the cell membrane. Draw a cartoon of a portion of a cell membrane. Add a cartoon of the synthetic amphiphile to the membrane. What is the IMF through which it interacts with the membrane?

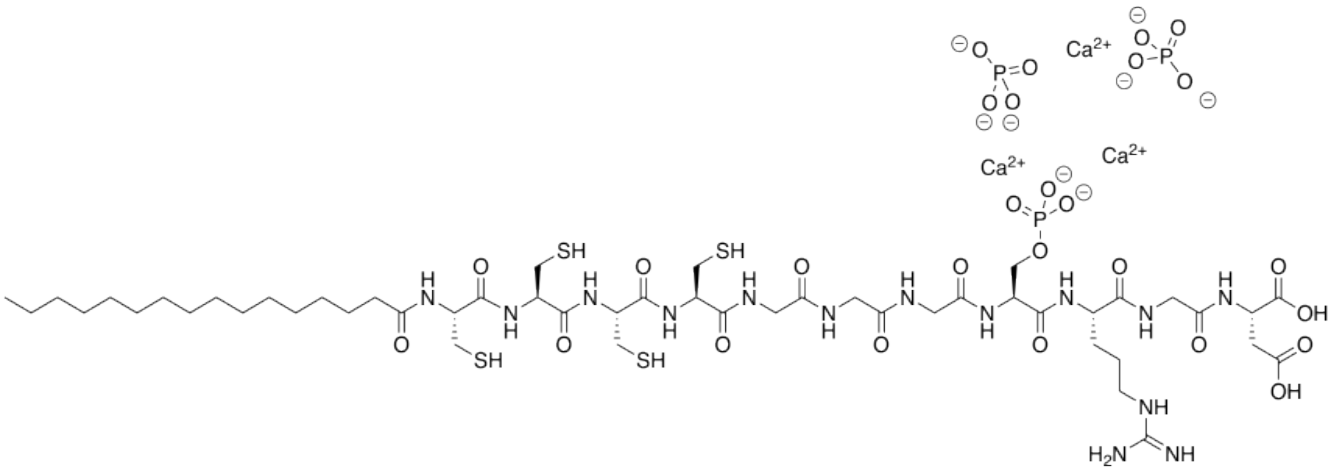


c) Ca^{2+} (two atoms from the left edge).

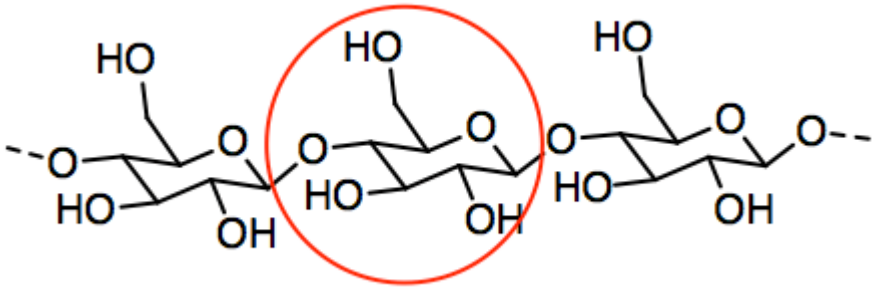
d) PO_4^{3-} because 3 x (2^+) + 2 x (3^-) = 0; neutral charge overall.

e) These high charges ($2^+/3^-$) bind much more tightly than the low charges ($1^+/1^-$) in sodium chloride.

f)



Problem SP14.4.



e) The carboxylic acid group provides sites for hydrogen bonding, including both a hydrogen bond donor in the OH group and an additional hydrogen bond acceptor in the C=O group.

f) It introduces a "hydrophobic" part in which the major intermolecular force with water would be a dipole-induced dipole interaction. If the water molecules keep to themselves, they will be able to maximize the amount of hydrogen bonding they can do with each other. The water is better off not mixing in with the paper.

g) All proteins have polar backbones formed by their amide bonds or peptide linkages (-NH-C=O). These portions can hydrogen bond with the cellulose in the paper. In addition, there may be polar side chains such as serine or threonine, for example, containing OH groups that can hydrogen bond with the paper.

h) Hydrophobic residues would add water resistance, for the same reason as the hydrophobic part of the abietic acid in rosin.

i) Ti^{4+} would have the same electronic configuration as argon. O^{2-} would have the same electronic configuration as neon.

j) The formula is TiO_2, so that the positive charges (4^+) and the negative charges ($2 \times 2^- = 4^-$) are balanced.

k) The 4^+ and 2^- charges are pretty large. Highly charged ions are difficult to dissolve, because the ion-dipole attraction of the ion with the water cannot compete with the very strong ionic attractions between the ions.

l) Ion-dipole. You can imagine the partially negative oxygen atoms of cellulose interacting with the titanium cations and the partially positive hydrogens of the OH groups in the cellulose interacting with the oxide anions.

m) Ti: one full atom in the center and eight in the corners, so 1 + 8x(1/8) = 2 Ti atoms.

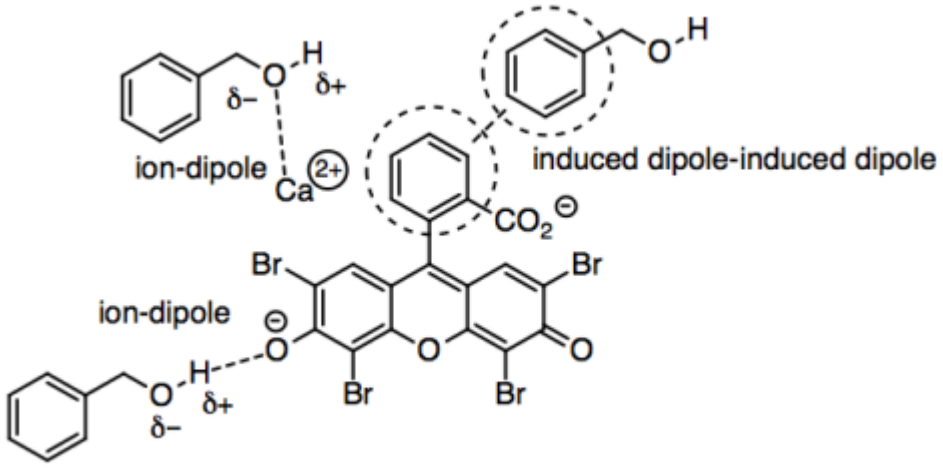
O: two full atoms (towards the left and right ends of the picture) plus four half atoms (on the upper and lower faces of the

cell), so 2 + 4x(1/2) = 4 O atoms.

ratio: 1 Ti : 2 O or TiO_2 in formula notation.

n) The Ti are packed in a cell that resembles a body-centered cubic cell. However, the cell is not really cubic, because it is stretched out a little. Sometimes we call that shape "tetragonal".

o) The benzyl alcohol could interact with the eosin in a number of ways, because eosin is a fairly large, complicated molecule (at least at this stage in your studies). We could imagine ion-dipole interactions, in which the partially positive hydrogens on the OH groups in the benzyl alcohol interact with the anionic oxygens of the eosin, or the partially negative oxygens in the benzyl alcohol interact with the positive calcium ion.



However, the polar part of benzyl alcohol is really the smaller part of the molecule. The bigger part of the molecules is the benzene, a six-membered carbon ring with three double bonds. The carbons at the ends of those double bonds are trigonal planar, so because the benzene is built up from planar atoms, it is completely flat. C-C bonds are not polar, and C-H bonds are hardly polar at all, so the dominant IMF in this part of the molecule is London dispersion or induced dipole-induced dipole interaction. That's a pretty weak interaction generally, but it can get a little stronger between large molecules, or between flat ones, because two flat molecules can have more surface area in contact with each other. That means the benzenes in benzyl alcohol and the benzenes in eosin have appreciable London forces that allow them to interact with each other.

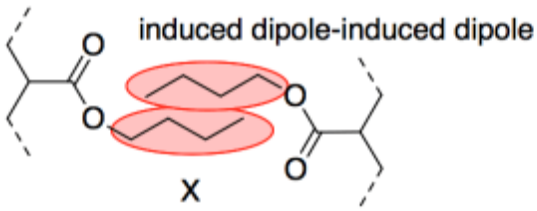
p) With the cellulose, covered in OH groups, the polar interactions outlined above will become more prominent.

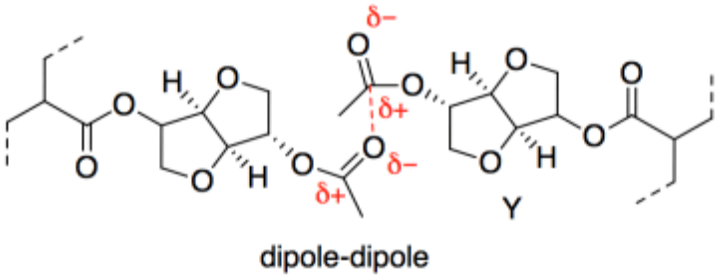
Problem SP14.5.

a) OAc is an ester.

b) AAI has three chiral centres; GATA has five.

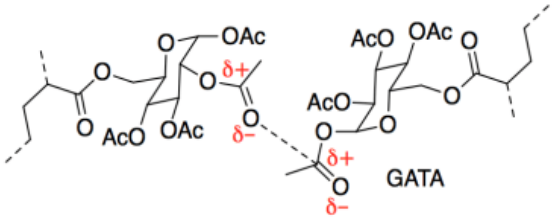
c) The chains in the adhesive would stick to each other via intermolecular attractions. Dipole-dipole attractions would be the strongest. However, induced dipole-induced dipole or London dispersion forces would actually be significant because there would be hundreds of such interactions along the chains.

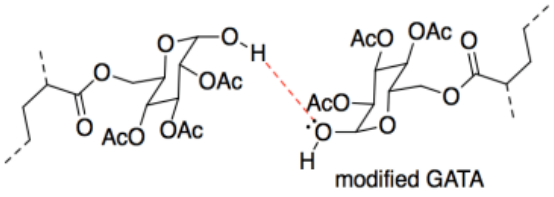




d) The most significant interaction with the paper would be hydrogen bonding. The cellulose in the paper would provide hydrogen bond donors (the OH groups) and the side groups in the adhesive chains would provide hydrogen bond acceptors (all those oxygens). However, if the paper contains a lot of sizing, induced dipole-induced dipole or London dispersion forces may form a significant part of the interaction. As with cohesion, this would not be a significant factor except that there are so many alkyl chains involved, so these tiny attractions would add up.

e)





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2: ALKANES AND ALKYL HALIDES

2.1: Alkanes and Alkane Isomers

2.2: Naming Alkanes

2.3: Naming Cycloalkanes

2.4: Properties of Alkanes

2.5: Reactions of Alkanes

2.6: Preparing Alkyl Halides from Alkanes - Radical Halogenation

2.7: Names and Properties of Alkyl Halides

2.8: Organic Chemistry- Alkanes and Halogenated Hydrocarbons (Exercises)

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2.1: 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.

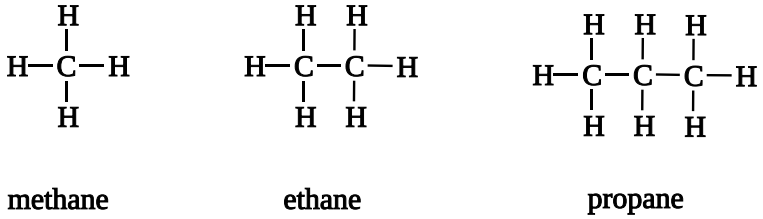
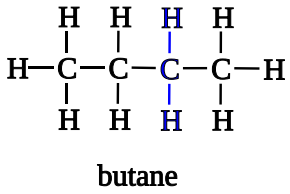


Figure 25.3.1 : The Three Simplest Alkanes

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.



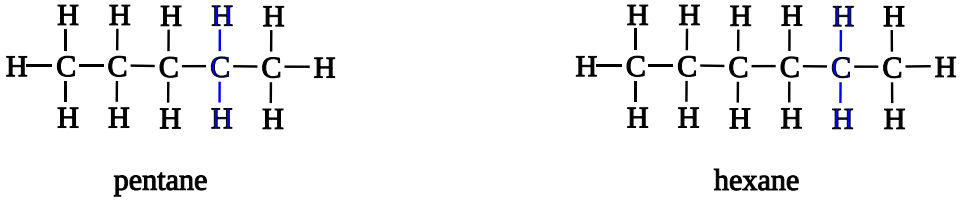


Figure 25.3.2: Members of a Homologous Series. Each succeeding formula incorporates one carbon atom and two hydrogen atoms more than the previous formula.

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:

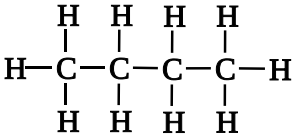
Table 2.1.1**: Molecular formulas for small alkanes**

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

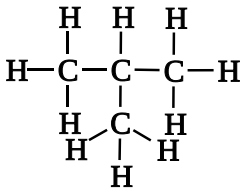
You can work out the formula of any of the alkanes using the general formula C_nH_{2n+2}

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.

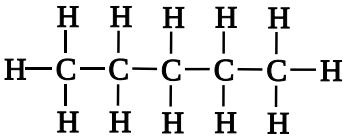


butane

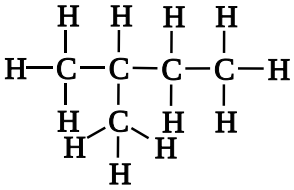


isobutane

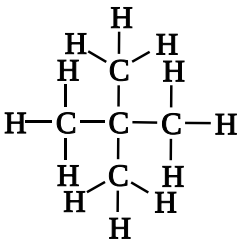
Likewise the molecular formula: C_5H_{12} has three possible isomer. The compound at the far left is pentane because it has all five carbon atoms in a continuous chain. The compound in the middle is isopentane; like isobutane, it has a one CH_3 branch off the second carbon atom of the continuous chain. 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

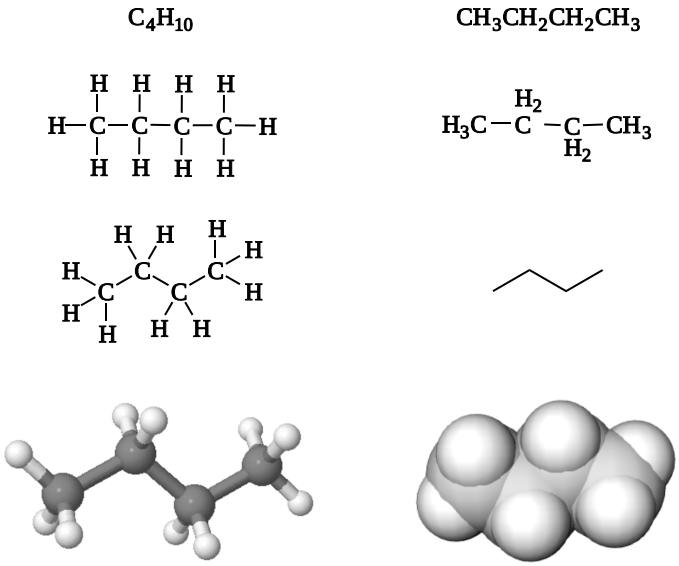
Of the structures show above, butane and pentane are called **normal alkanes** or **straight-chain alkanes**, indicating that all contain a single continuous chain of carbon atoms and can be represented by a projection formula whose carbon atoms are in a straight line. The other structures, isobutane, 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 2.1.2: Number of isomers for hydrocarbons

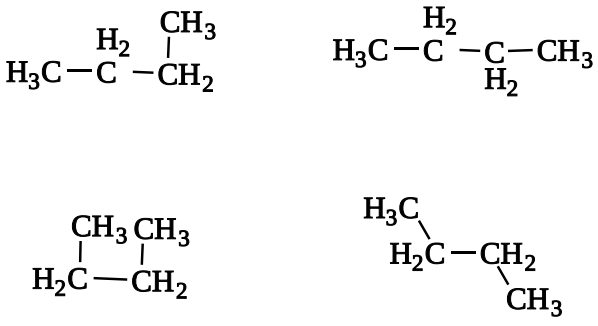
Molecular Formula	Number of Structural Isomers
CH_4	1
C_2H_6	1
C_3H_8	1
C_4H_{10}	2
C_5H_{12}	3
C_6H_{14}	5
C_7H_{16}	9
C_8H_{18}	18

Molecular Formula	Number of Structural Isomers
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.

9.2.1

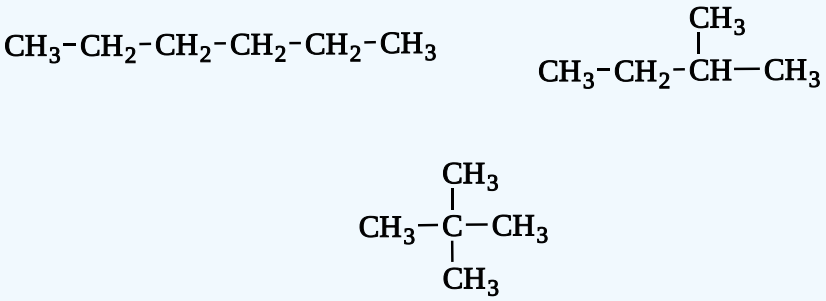
" role="presentation" style="position:relative;" tabindex="0">

Table 2.1.3: 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 2.1.1: 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 2.1.1

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

Answer available at the end of this section.

Exercise 2.1.2

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

Answer available at the end of this section.

Exercise 2.1.3

Draw all possible isomers for C_3H_8O.

Answer available at the end of this section.

Exercise 2.1.4

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

Answer available at the end of this section.

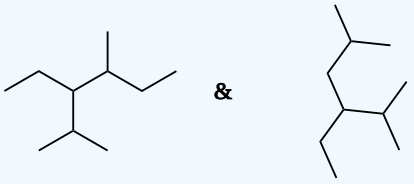
Exercise 2.1.5

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

Answer available at the end of this section.

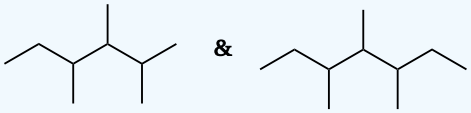
Exercise 2.1.6

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

a) 

b) 

c) 

d) 

Answer available at the end of this section.

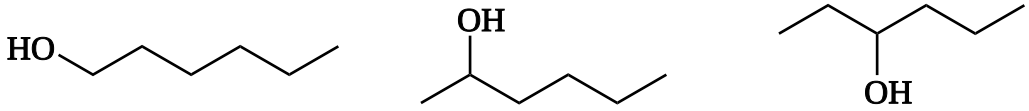
Exercise 2.1.7

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.

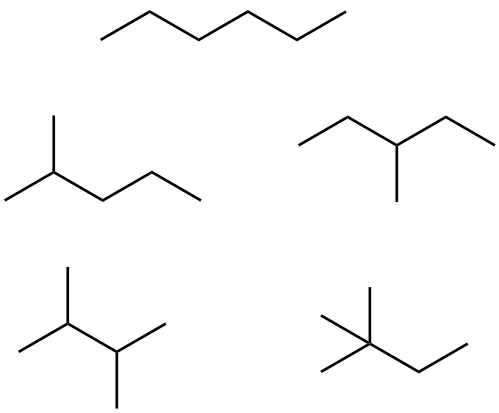
Answer available at the end of this section.

Answers

Exercise 2.1.1



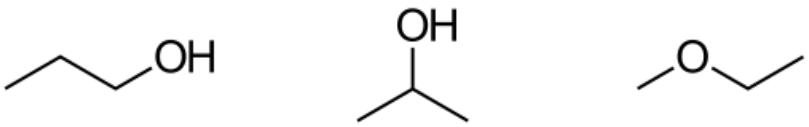
Exercise 2.1.2



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.

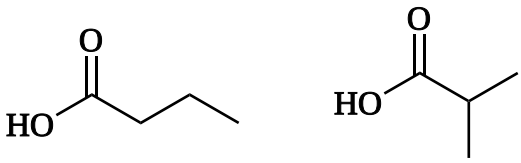
Exercise 2.1.3

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_8O.

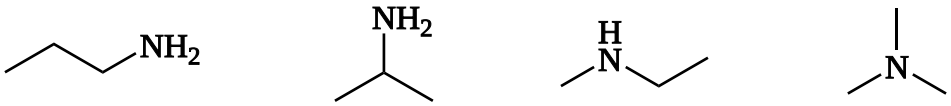


Exercise 2.1.4

There are only 2 possibilities.



Exercise 2.1.5



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

Exercise 2.1.6

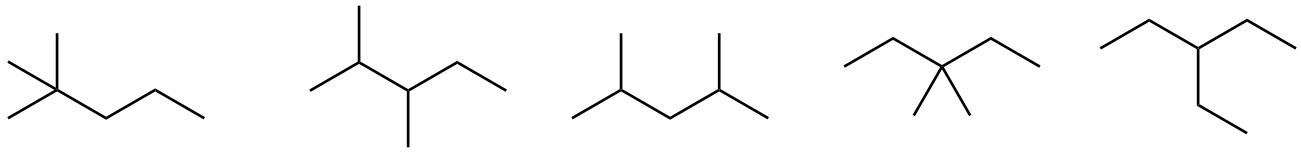
a) Both structures have formulas of $C_{10}H_{22}$ and have different connectivity which makes these **constitutional isomers**.

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**.

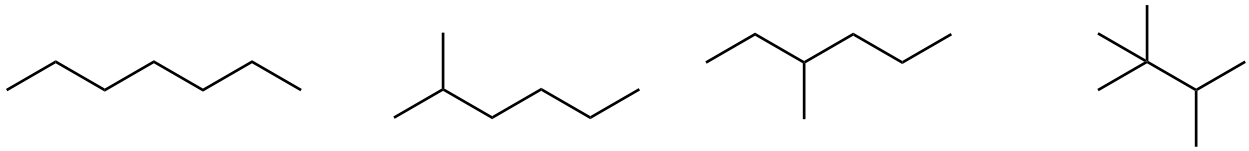
d) The structure on the left has a formula of C_9H_{20} and the structure on the right has a formula of $C_{10}H_{22}$ so these are **different compounds**.

Exercise 2.1.7



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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2.2: 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.

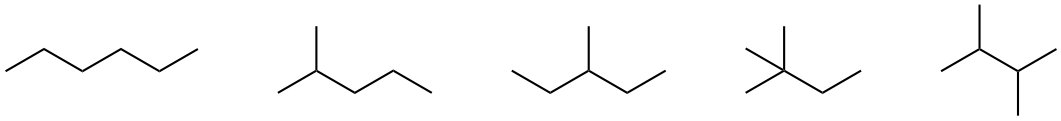
Table 7.5.1.1 : Simple Unbranched Alkanes

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**):



A **B** **C** **D** **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.

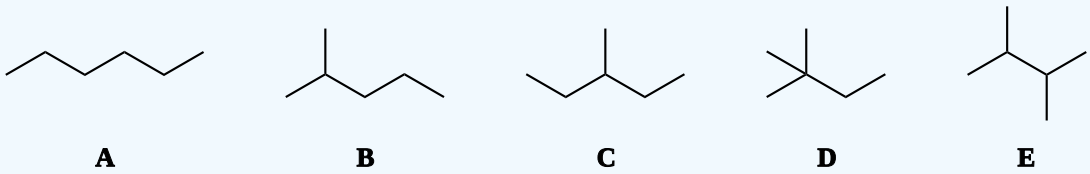
Table 7.5.1.2 : Alkyl Groups Names

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 7.5.1.1 : 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

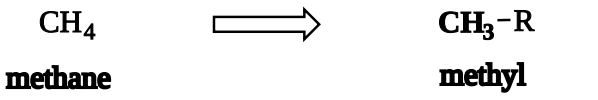
Halogen substituents are easily accommodated, using the names: fluoro (F-), chloro (Cl-), bromo (Br-) and iodo (I-).

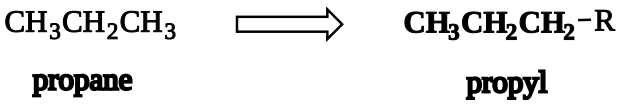
Example 7.5.1.2 : Halogen Substitution

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}	$CH_3(CH_2)_5CH_3$

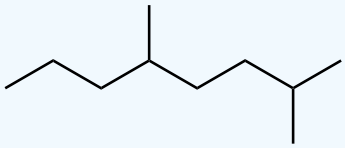
Name	Molecular Formula	Condensed Structural Formula
Octane	C_8H_{18}	$CH_3(CH_2)_6CH_3$
Nonane	C_9H_{20}	$CH_3(CH_2)_7CH_3$
Decane	$C_{10}H_{22}$	$CH_3(CH_2)_8CH_3$
Undecane	$C_{11}H_{24}$	$CH_3(CH_2)_9CH_3$
Dodecane	$C_{12}H_{26}$	$CH_3(CH_2)_{10}CH_3$
Tridecane	$C_{13}H_{28}$	$CH_3(CH_2)_{11}CH_3$
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.

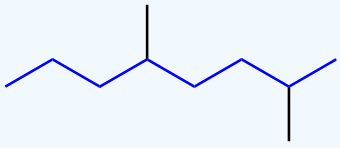
Example 7.5.1.3

What is the name of the follow molecule?

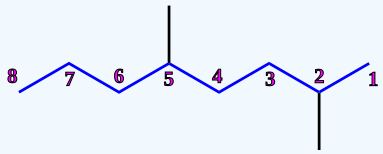


Solution

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.

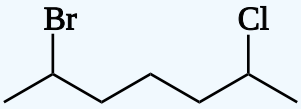


Rule 3: In this example, there is no need to utilize the third rule. Because the two substitutes are identical, neither takes alphabetical precedence with respect to numbering the carbons. This concept will become clearer in the following examples.

The name of this molecule is **2,5-dimethyloctane**

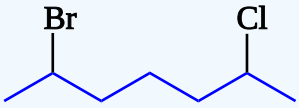
Example 7.5.1.4

What is the name of the follow molecule?



Solution

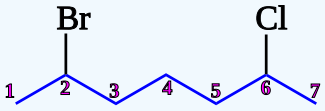
Rule #1: Choose the longest, most substituted carbon chain containing a functional group. This example contains two functional groups, bromine and chlorine. The longest carbon chain has been highlighted in blue and consists of seven carbons.



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.



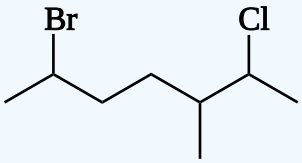
Rule #3: After applying the first two rules, take the alphabetical order into consideration. Alphabetically, bromine comes before chlorine. Therefore, bromine is assigned the second carbon position, and chlorine is assigned the sixth carbon position.



The name of this molecule is: **2-bromo-6-chloroheptane**

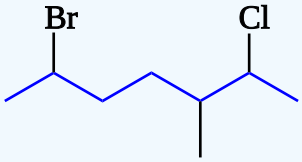
Example 7.5.1.5

What is the name of the follow molecule?

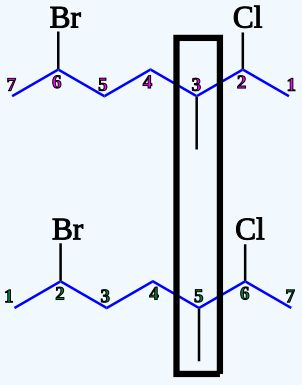


Solution

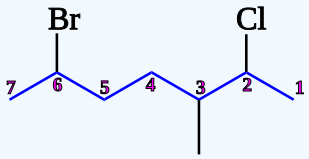
Rule #1: Choose the longest, most substituted carbon chain containing a functional group. This example contains two functional groups, bromine and chlorine, and one substitute, the methyl group. The longest carbon chain has been highlighted in blue and consists of seven carbons.



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

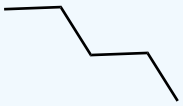
The name of this molecule is: **6-bromo-2-chloro-3-methylheptane**

Exercises

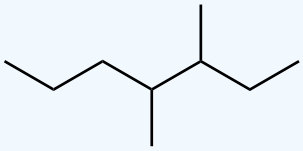
Exercise 7.5.1.1

Give the proper IUPAC names of the following compounds.

a)



b)



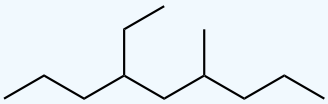
c)

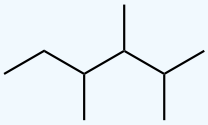


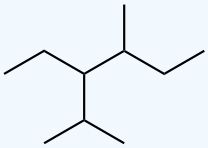
Answer available at the end of this section.

Exercise 7.5.1.2

Give the proper IUPAC names of the following compounds.

a) 

b) 

c) 

Answer available at the end of this section.

Exercise 7.5.1.3

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 available at the end of this section.

Exercise 7.5.1.4

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

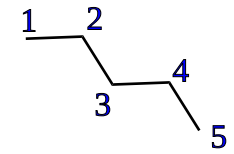
Answer available at the end of this section.

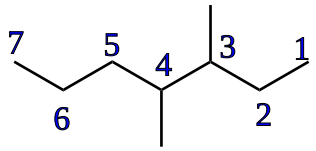
Answers

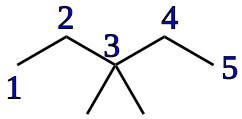
a) Since this structure is an unbranched alkane (all single bonds) with a 5 carbon chain length, its name would be **pentane**.

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) 

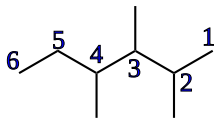
c) 

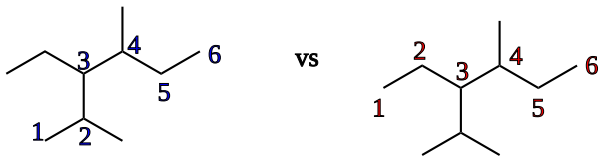
a) This alkane has a 9 carbon longest continuous chain length that we number from left to right (structure on left numbered in blue) to make the ethyl substituent be number 4. For the structure on the right (numbered in red) going from right to left, the methyl substituent is number 4. Since ethyl is 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**.

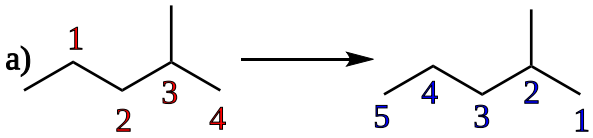
c) This 6 carbon alkane can be numbered along different chains (see below) as well as in the opposite directions. This shows the two different chains that can be drawn (making the first substituent in that chain the lowest number). The structure on the left (numbered in blue) is the correct choice since 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.)

a) 

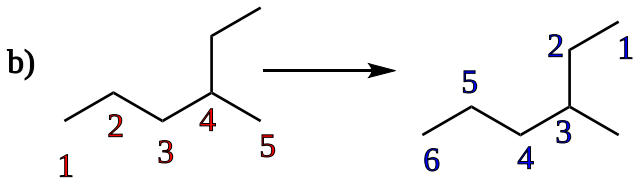
b) 

c) 

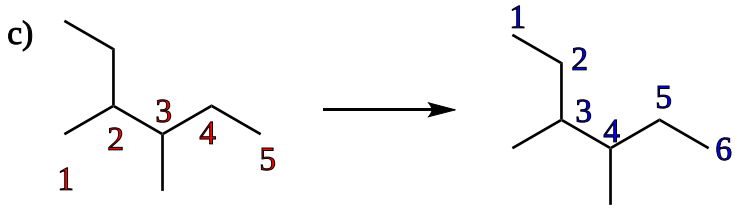
a) The structure that can be drawn for the improper name is shown below on the left. When you renumber it properly (structure on the right), the correct name should be **2-methylpentane**.



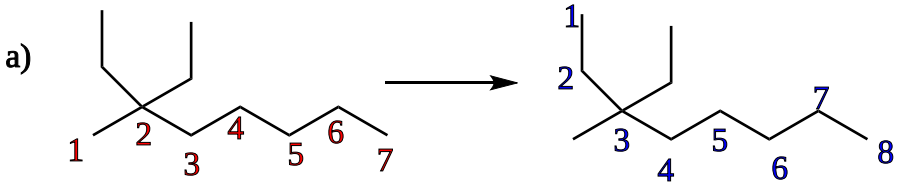
b) The structure that can be drawn for the improper name is shown below on the left. When you renumber it properly (structure on the right), notice that the longest chain is 6 C's and we start the numbering on the end to the right to make the methyl substituent come off at C-3 (instead of beong at C-4 if we numbered it the opposite direction) the correct name should be **3-methyl hexane**.



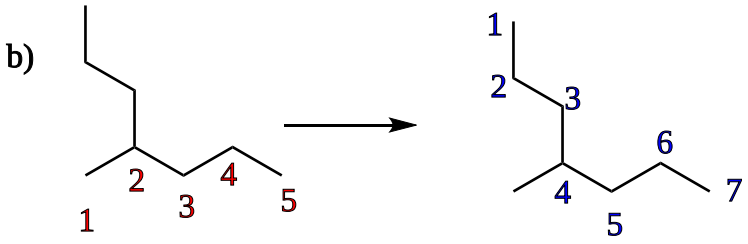
c) The structure that can be drawn for the improper name is shown below on the left. When you renumber it properly (structure on the right), notice that the longest chain is 6 C's and since this molecule is symmetrical (between carbon 3 & 4), you can start the numbers from either end. In this case, we have methyl substituents coming off of carbons 3 & 4 so the proper name is **3,4-dimethyl hexane**.



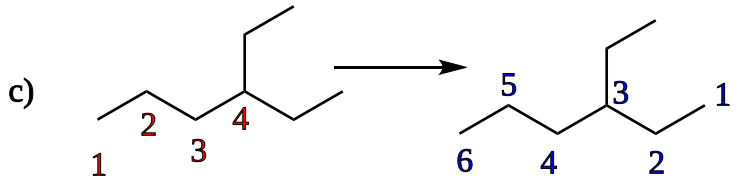
a) The structure that can be drawn for the improper name is shown below on the left. When you renumber it properly (structure on the right), notice that the longest chain is now 8 C's and you have an ethyl substituent at C-3 and a methyl substituent also at C-3 so the proper name is **3- ethyl-3-methyloctane**.



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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2.3: Naming Cycloalkanes

Objectives

After completing this section, you should be able to

1. name a substituted or unsubstituted cycloalkane, given its Kekulé structure, shorthand structure or condensed structure.
2. 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.

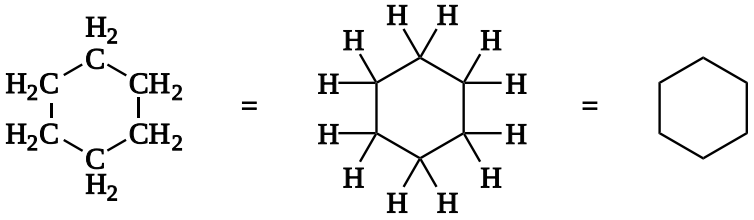
- cycloalkane

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.

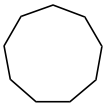
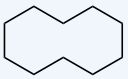
Like alkanes, cycloalkane molecules are often drawn as skeletal structures in which each intersection between two lines is assumed to have a carbon atom with its corresponding number of hydrogens. Cyclohexane, one of the most common cycloalkanes is shown below as an example.



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 $\mathbf{C_nH_{2n}}$, and not $\mathbf{C_nH_{2n+2}}$ 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 2.3.1: Examples of Simple Cycloalkanes

Cycloalkane	Molecular Formula	Skeleton Structure
Cyclopropane	C_3H_6	
Cyclobutane	C_4H_8	
Cyclopentane	C_5H_{10}	

Cycloalkane	Molecular Formula	Skeleton Structure
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

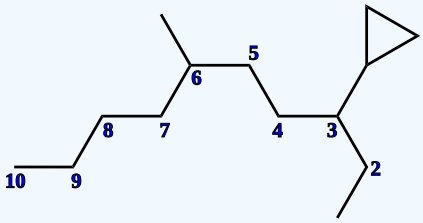
The naming of substituted cycloalkanes follows the same basic steps used in naming alkanes.

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.

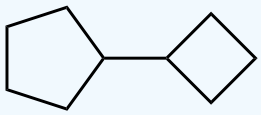
Example 2.3.1



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 2.3.2

Name the cycloalkane structure.

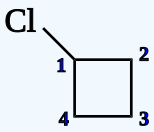
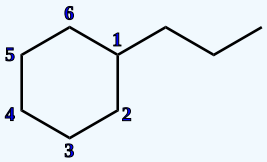


Solution

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.

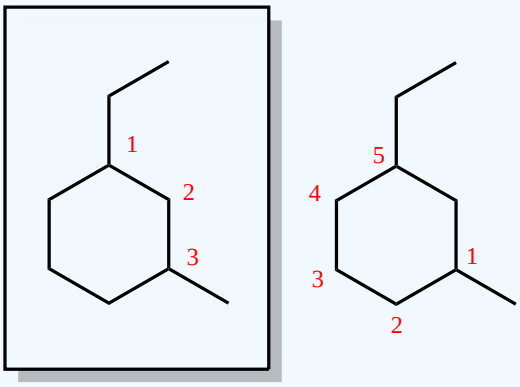
Example 2.3.3

	
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.

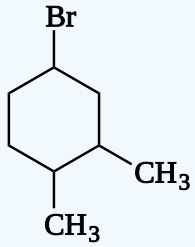
Example 2.3.4



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 2.3.5

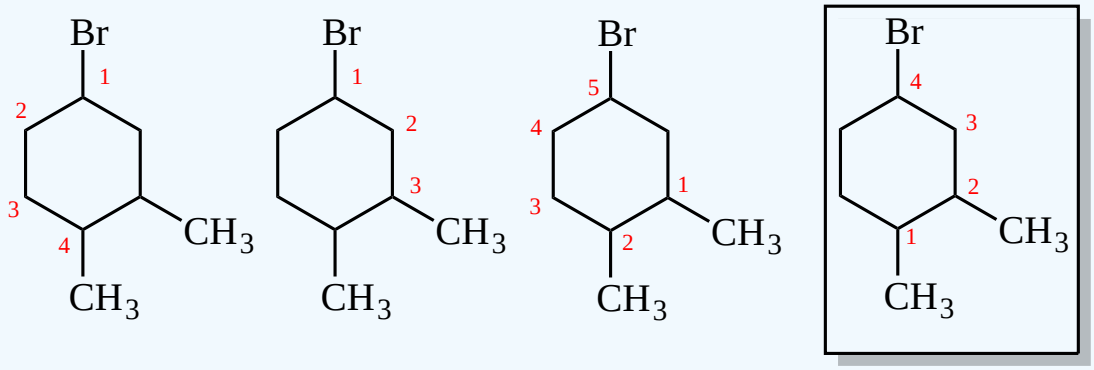
Name the following structure using IUPAC rules.



Solution

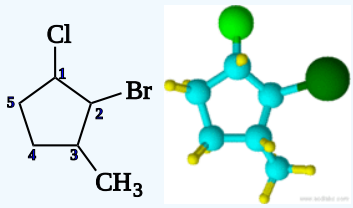
Remember when dealing with cycloalkanes with more than two substituents, finding the lowest possible 2nd substituent numbering takes precedence. Consider a numbering system with each substituent attachment point as being carbon one. Compare them and whichever produces the lowest first point of difference 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.

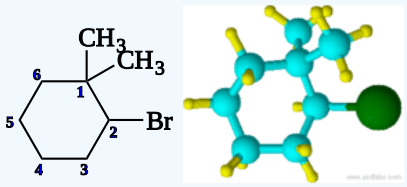
Example 2.3.6



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.

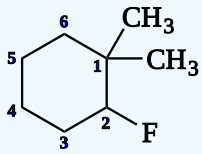
Example 2.3.7



(2-bromo-1,1-dimethylcyclohexane)

Although "di" alphabetically precedes "f", "di" is not used in determining the alphabetical order.

Example 2.3.8



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)

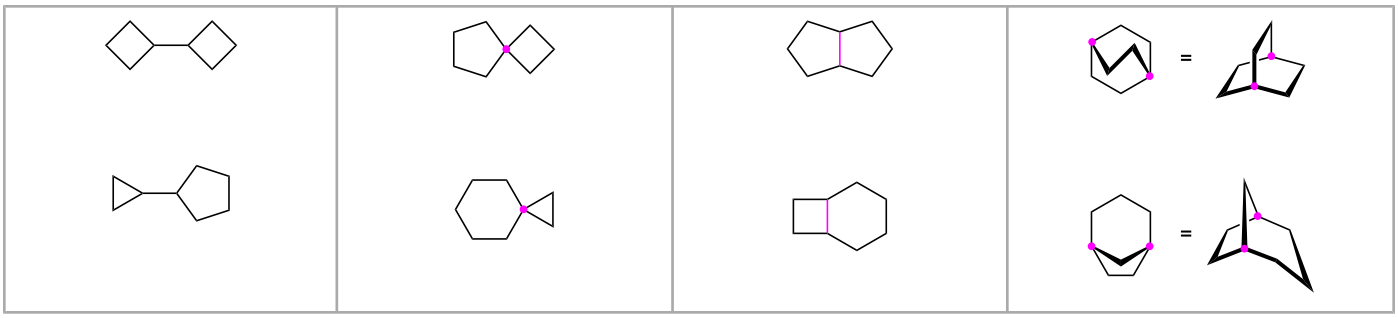
Although "di" alphabetically precedes "f", "di" is not used in determining the alphabetical order of the substituents. Notice that the attachment point of the two methyl groups is assigned carbon 1 despite the fact that fluorine comes first alphabetically. This is because this assignment allows for a lower overall numbering of substituents, so assigning alphabetical priority is not necessary.

Polycyclic Compounds

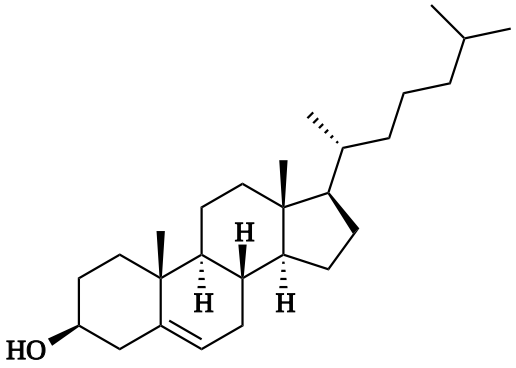
Hydrocarbons having more than one ring are common, and are referred to as **bicyclic** (two rings), **tricyclic** (three rings) and in general, **polycyclic compounds**. The molecular formulas of such compounds have H/C ratios that decrease with the number of rings. In general, for a hydrocarbon composed of n carbon atoms associated with m rings the formula is: $\mathrm{C}_n\mathrm{H}_{2n+2-2m}$. 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 2.3.2: Examples of Isomeric $\mathrm{C}_8\mathrm{H}_{14}$ Bicycloalkanes

Isolated Rings	Spiro Rings	Fused Rings	Bridged Rings
No common atoms	One common atom	One common bond	Two common atoms



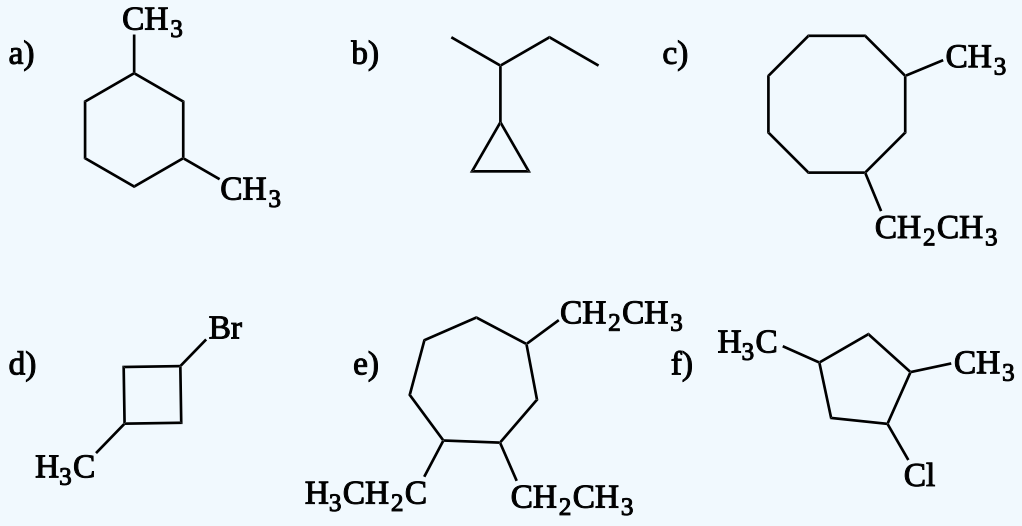
Polycyclic compounds, like cholesterol shown below, are biologically important and typically have common names accepted by IUPAC. However, the common names do not generally follow the basic IUPAC nomenclature rules, and will not be covered here.



Cholesterol (polycyclic)

Exercise 2.3.1

Give the IUPAC names for the following cycloalkane structures.



Answer available at the end of this section.

Exercise 2.3.2

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-propylcyclodecane

Answer available at the end of this section.

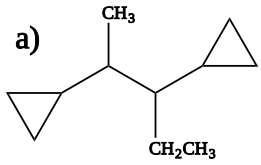
Answers

Exercise 2.3.1

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

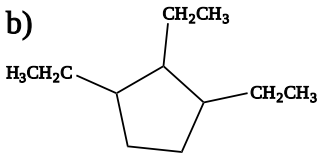
Exercise 2.3.2

a)



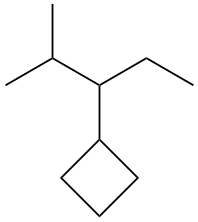
2,3-dicyclopropylpentane

b)



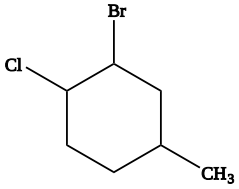
1,2,3-triethylcyclopentane

c)



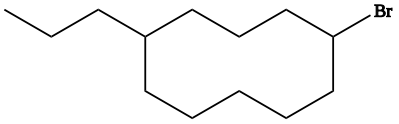
3-cyclobutyl-2-methylhexane

d)



2-bromo-1-chloro-4-methylcyclohexane

e)



1-bromo-5-propylcyclodecane

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2.4: Properties of Alkanes

Learning Objectives

- To identify the physical properties of alkanes and describe trends in these properties.

Because alkanes have relatively predictable physical properties and undergo relatively few chemical reactions other than combustion, they serve as a basis of comparison for the properties of many other organic compound families. Let's consider their physical properties first.

Table 2.4.1 describes some of the properties of some of the first 10 straight-chain alkanes. Because alkane molecules are nonpolar, they are insoluble in water, which is a polar solvent, but are soluble in nonpolar and slightly polar solvents. Consequently, alkanes themselves are commonly used as solvents for organic substances of low polarity, such as fats, oils, and waxes. Nearly all alkanes have densities less than 1.0 g/mL and are therefore less dense than water (the density of H_2O is 1.00 g/mL at 20°C). These properties explain why oil and grease do not mix with water but rather float on its surface.

Table 2.4.1: 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.**					

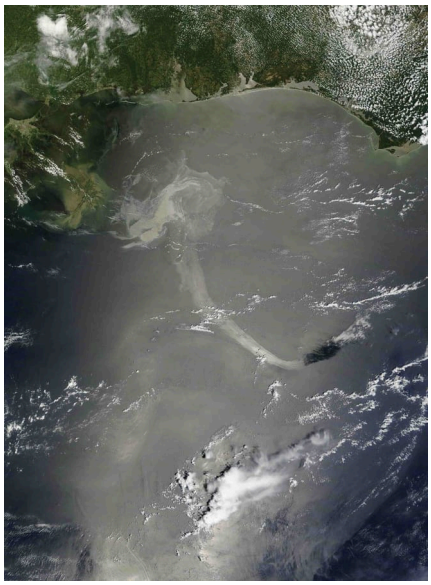


Figure 2.4.1: Oil Spills. Crude oil coats the water's surface in the Gulf of Mexico after the *Deepwater Horizon* oil rig sank following an explosion. The leak was a mile below the surface, making it difficult to estimate the size of the spill. One liter of oil can create a slick 2.5 hectares (6.3 acres) in size. This and similar spills provide a reminder that hydrocarbons and water don't mix. Source: Photo courtesy of NASA Goddard / MODIS Rapid Response Team, NASA.gov, Topics, Earth Features, Oil Spill(opens in new window) [www.nasa.gov].

Looking Closer: Gas Densities and Fire Hazards

Table 2.4.1 indicates that the first four members of the alkane series are gases at ordinary temperatures. Natural gas is composed chiefly of methane, which has a density of about 0.67 g/L. The density of air is about 1.29 g/L. Because natural gas is less dense than air, it rises. When a natural-gas leak is detected and shut off in a room, the gas can be removed by opening an upper window. On the other hand, bottled gas can be either propane (density 1.88 g/L) or butanes (a mixture of butane and isobutane; density about 2.5 g/L). Both are much heavier than air (density 1.2 g/L). If bottled gas escapes into a building, it collects near the floor. This presents a much more serious fire hazard than a natural-gas leak because it is more difficult to rid the room of the heavier gas.

Also shown in Table 2.4.1 are the boiling points of the straight-chain alkanes increase with increasing molar mass. This general rule holds true for the straight-chain homologs of all organic compound families. Larger molecules have greater surface areas and consequently interact more strongly; more energy is therefore required to separate them. For a given molar mass, the boiling points of alkanes are relatively low because these nonpolar molecules have only weak dispersion forces to hold them together in the liquid state.

Looking Closer: An Alkane Basis for Properties of Other Compounds

An understanding of the physical properties of the alkanes is important in that 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 fatlike 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.

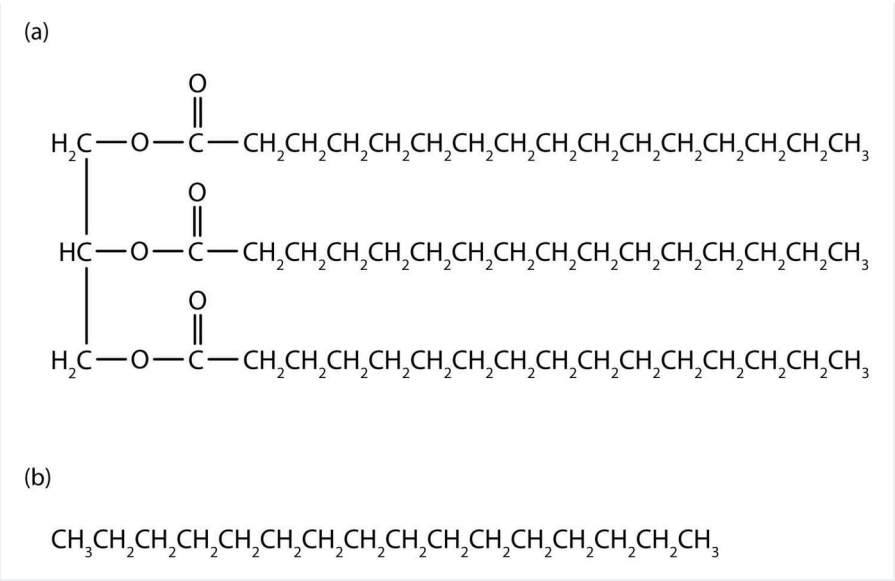


Figure 2.4.2: Tripalmitin (a), a typical fat molecule, has long hydrocarbon chains typical of most lipids. Compare these chains to hexadecane (b), an alkane with 16 carbon atoms

Key Takeaway

- Alkanes are nonpolar compounds that are low boiling and insoluble in water.

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2.5: Reactions of Alkanes

Learning Objectives

- Understand the reactions of alkanes: combustion and halogenation.

Alkanes are relatively stable, nonpolar molecules, that will not react with acids, bases, or oxidizing or reducing reagents. Alkanes undergo so few reactions that they are sometimes called *paraffins*, from the Latin *parum affinis*, meaning “little affinity.”

However, heat or light can initiate the breaking of C–H or C–C single bonds in reactions called **combustion** and **halogenation**.

Combustion

Nothing happens when alkanes are merely mixed with oxygen (O_2) at room temperature, but when a flame or spark provides the activation energy, a highly exothermic combustion reaction proceeds vigorously. For methane (CH_4), the **combustion** reaction is as follows:

$$CH_4 + 2O_2 \rightarrow CO_2 + 2H_2O + \text{heat} \tag{2.5.1}$$

As a consequence, alkanes are excellent fuels. For example, methane, CH_4, is the principal component of natural gas. Butane, C_4H_{10}, used in camping stoves and lighters is an alkane. Gasoline is a liquid mixture of straight- and branched-chain alkanes, each containing from five to nine carbon atoms, plus various additives to improve its performance as a fuel. Kerosene, diesel oil, and fuel oil are primarily mixtures of alkanes with higher molecular masses. The main source of these liquid alkane fuels is crude oil, a complex mixture that is separated by fractional distillation. Fractional distillation takes advantage of differences in the boiling points of the components of the mixture (Figure 2.5.1). You may recall that boiling point is a function of intermolecular interactions, which was discussed in an earlier chapter.

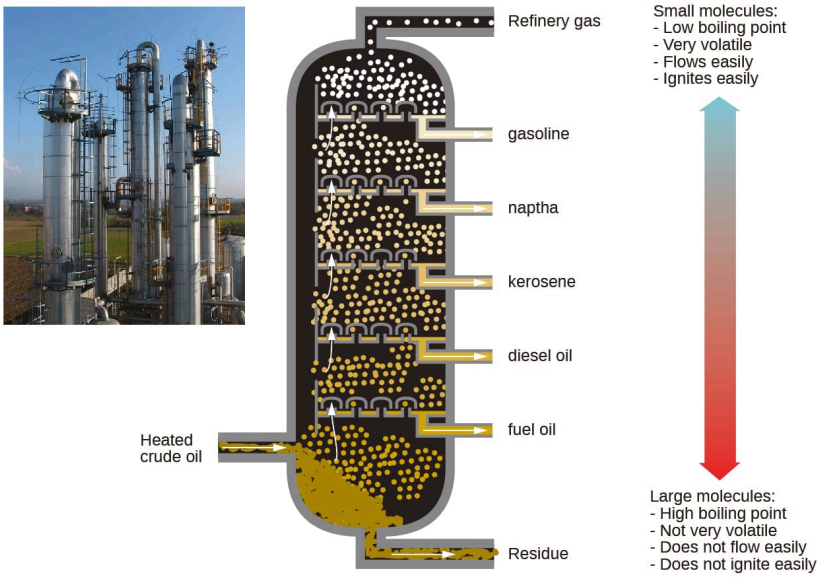


Figure 2.5.1:In a column for the fractional distillation of crude oil, oil heated to about 425 °C in the furnace vaporizes when it enters the base of the tower. The vapors rise through bubble caps in a series of trays in the tower. As the vapors gradually cool, fractions of higher, then of lower, boiling points condense to liquids and are drawn off. (credit left: modification of work by Luigi Chiesa)

If the reactants of combustion reactions are adequately mixed, and there is sufficient oxygen, the only products are carbon dioxide (CO_2), water (H_2O), and energy—heat for cooking foods, heating homes, and drying clothes. Because conditions are rarely ideal, other unwanted by-products are frequently formed. When the oxygen supply is limited, carbon monoxide (CO) is a by-product:

$$2CH_4 + 3O_2 \rightarrow 2CO + 4H_2O \tag{2.5.2}$$

This reaction is responsible for dozens of deaths each year from unventilated or improperly adjusted gas heaters. (Similar reactions with similar results occur with kerosene heaters.)

Halogenation

In **halogenation** reactions, alkanes react with the halogens chlorine (Cl_2) and bromine (Br_2) in the presence of ultraviolet light or at high temperatures to yield chlorinated and brominated alkanes. For example, chlorine reacts with excess methane (CH_4) to give methyl chloride (CH_3Cl).

$$CH_4 + Cl_2 \rightarrow CH_3Cl + HCl \tag{2.5.3}$$

With more chlorine, a mixture of products is obtained: CH_3Cl, CH_2Cl_2, $CHCl_3$, and CCl_4. Fluorine (F_2), the lightest halogen, combines explosively with most hydrocarbons. Iodine (I_2) is relatively unreactive. Fluorinated and iodinated alkanes are produced by indirect methods.

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 2.5.1, along with some of their uses.

Table 2.5.1: 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

Note 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.

Note To Your Health: Chlorofluorocarbons and The Ozone Layer

Alkanes substituted with both fluorine (F) and chlorine (Cl) atoms have been used as the dispersing gases in aerosol cans, as foaming agents for plastics, and as refrigerants. Two of the best known of these chlorofluorocarbons (CFCs) are listed in Table 2.5.2.

Chlorofluorocarbons contribute to the greenhouse effect in the lower atmosphere. They also diffuse into the stratosphere, where they are broken down by ultraviolet (UV) radiation to release Cl atoms. These in turn break down the ozone (O_3) molecules that protect Earth from harmful UV radiation. Worldwide action has reduced the use of CFCs and related compounds. The CFCs and other Cl- or bromine (Br)-containing ozone-destroying compounds are being replaced with more benign substances. Hydrofluorocarbons (HFCs), such as CH_2FCF_3, which have no Cl or Br to form radicals, are one alternative. Another is hydrochlorofluorocarbons (HCFCs), such as $CHCl_2CF_3$. HCFC molecules break down more readily in the troposphere, and fewer ozone-destroying molecules reach the stratosphere.

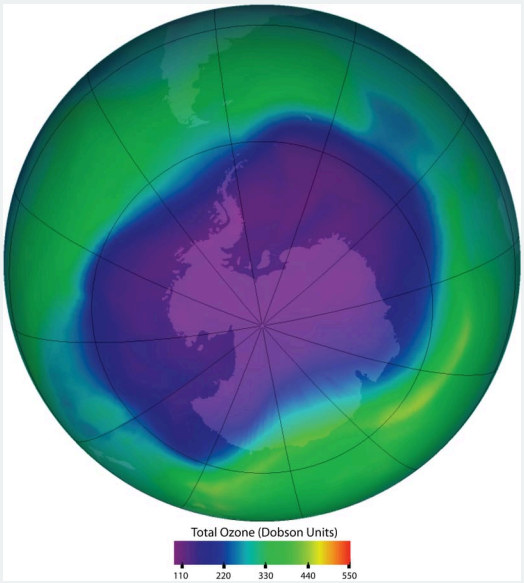


Figure 2.5.2: Ozone in the upper atmosphere shields Earth's surface from UV radiation from the sun, which can cause skin cancer in humans and is also harmful to other animals and to some plants. Ozone "holes" in the upper atmosphere (the gray, pink, and purple areas at the center) are large areas of substantial ozone depletion. They occur mainly over Antarctica from late August through early October and fill in about mid-November. Ozone depletion has also been noted over the Arctic regions. The largest ozone hole ever observed occurred on 24 September 2006. Source: Image courtesy of NASA, http://ozonewatch.gsfc.nasa.gov/daily.php?date=2006-09-24.

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2.6: Preparing Alkyl Halides from Alkanes - Radical Halogenation

As we saw briefly in Section 6.7, simple alkyl halides can sometimes be prepared by the radical reaction of an alkane with Cl_2 or Br_2 in the presence of ultraviolet light. The detailed mechanism is shown in Figure 2.6.1 for chlorination.

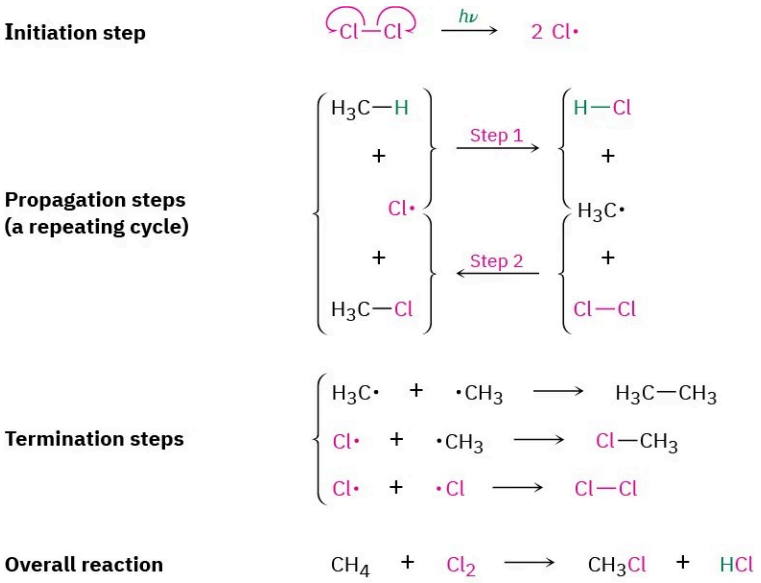
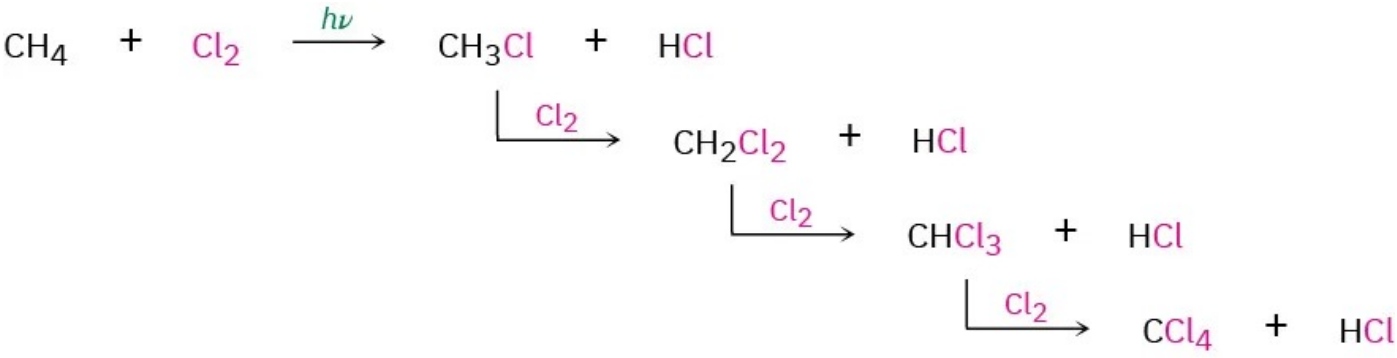


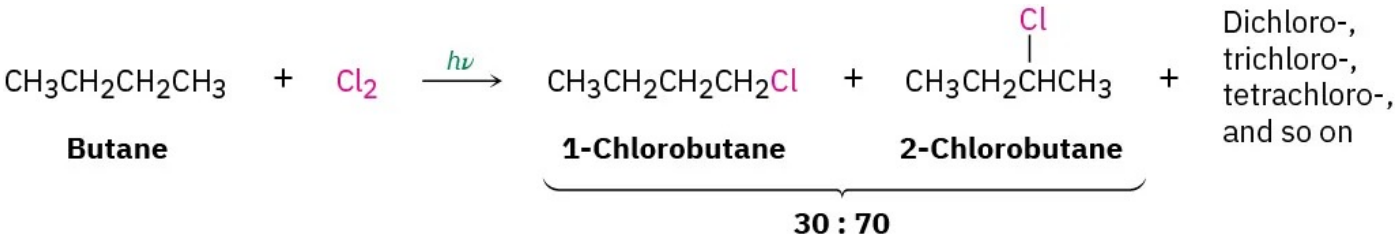
Figure 2.6.1: Mechanism of the radical chlorination of methane. Three kinds of steps are required in radical substitution reactions: initiation, propagation, and termination. The propagation steps are a repeating cycle, with Cl• a reactant in step 1 and a product in step 2, and with •CH_3 a product in step 1 and a reactant in step 2. The symbol *hν* shown in the initiation step is the standard way of indicating irradiation with light (*ν* is the lowercase Greek letter nu).

Radical substitution reactions require three kinds of steps: *initiation, propagation*, and *termination*. Once an initiation step has started the process by producing radicals, the reaction continues in a self-sustaining cycle. The cycle requires two repeating propagation steps in which a radical, the halogen, and the alkane yield alkyl halide product plus more radical to carry on the chain. The chain is occasionally terminated by the combination of two radicals.

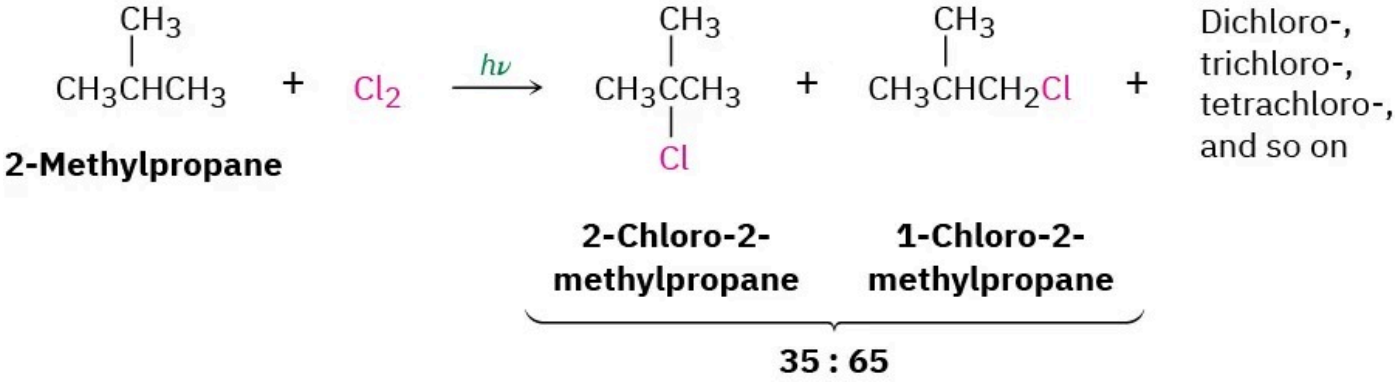
Unfortunately, alkane halogenation is a poor synthetic method for preparing alkyl halides because mixtures of products invariably result. For example, chlorination of methane does not stop cleanly at the monochlorinated stage but continues to give a mixture of dichloro, trichloro, and even tetrachloro products.



The situation is even worse for chlorination of alkanes that have more than one kind of hydrogen. Chlorination of butane, for instance, gives two monochlorinated products in a 30:70 ratio in addition to multiply chlorinated products such as dichlorobutane, trichlorobutane, and so on.

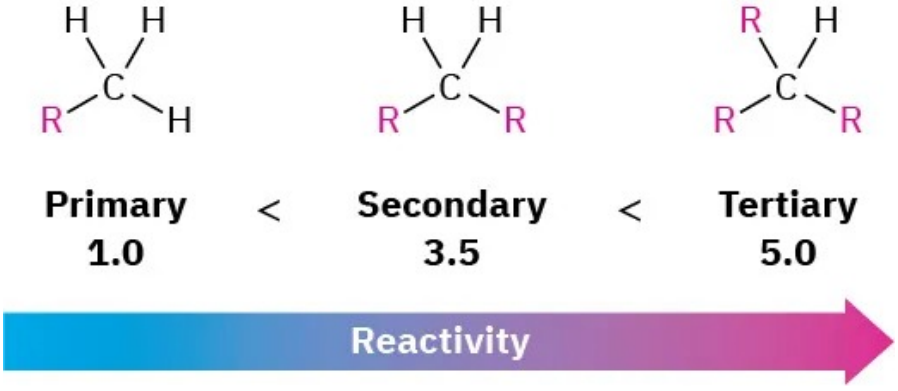


As another example, 2-methylpropane yields 2-chloro-2-methylpropane and 1-chloro-2-methylpropane in a 35 : 65 ratio, along with more highly chlorinated products.

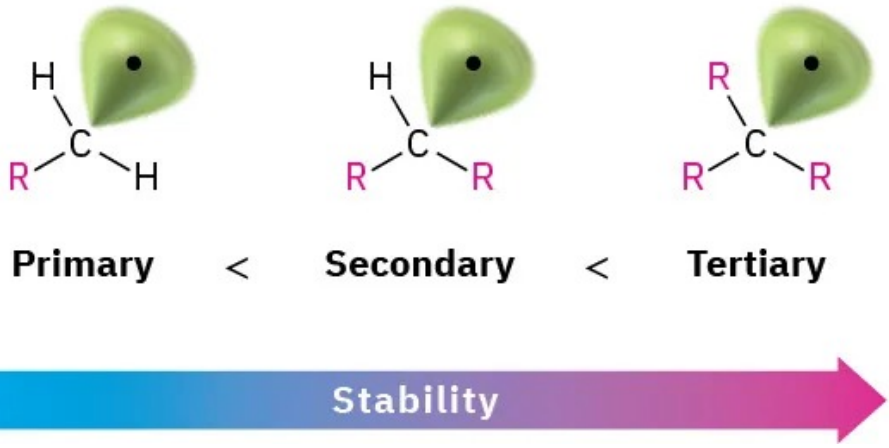


From these and similar reactions, it's possible to calculate a reactivity order toward chlorination for different kinds of hydrogen atoms in a molecule. Take the butane chlorination, for instance. Butane has six equivalent primary hydrogens ($-CH_3$) and four equivalent secondary hydrogens ($-CH_2-$). The fact that butane yields 30% of 1-chlorobutane product means that each one of the six primary hydrogens is responsible for 30% ÷ 6 = 5% of the product. Similarly, the fact that 70% of 2-chlorobutane is formed means that each of the four secondary hydrogens is responsible for 70% ÷ 4 = 17.5% of the product. Thus, a secondary hydrogen reacts 17.5% ÷ 5% = 3.5 times as often as a primary hydrogen.

A similar calculation for the chlorination of 2-methylpropane indicates that each of the nine primary hydrogens accounts for 65% ÷ 9 = 7.2% of the product, while the single tertiary hydrogen (R_3CH) accounts for 35% of the product. Thus, a tertiary hydrogen is 35% ÷ 7.2% = 5 times as reactive as a primary hydrogen toward chlorination.



The observed reactivity order of alkane hydrogens toward radical chlorination can be explained by looking at the bond dissociation energies given previously in Table 6.3. The data show that a tertiary C–H bond (400 kJ/mol; 96 kcal/mol) is weaker than a secondary C–H bond (410 kJ/mol; 98 kcal/mol), which is in turn weaker than a primary C–H bond (421 kJ/mol; 101 kcal/mol). Since less energy is needed to break a tertiary C–H bond than to break a primary or secondary C–H bond, the resultant tertiary radical is more stable than a primary or secondary radical.



Exercise 2.6.1

Draw and name all monochloro products you would expect to obtain from radical chlorination of 2-methylpentane. Which, if any, are chiral?

Answer available at the end of this section.

Exercise 2.6.2

Taking the relative reactivities of primary, secondary, and tertiary hydrogens atoms into account:

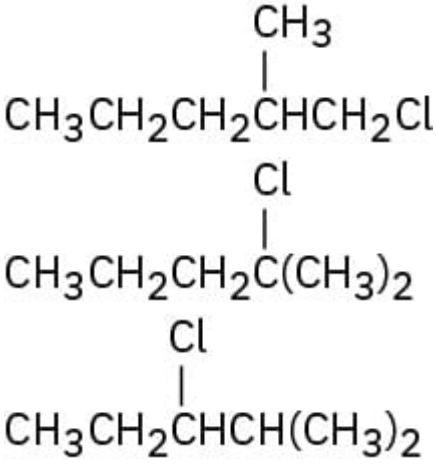
a. what product(S) would you expect to obtain from monochloration of 2-methylbutane**?**
b. What would the approximate percentage of each product be? (don't forget to take into account the number of each kind of hydrogen)

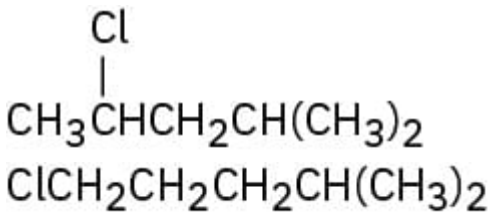
Answer available at the end of this section.

Answers

Exercise 2.6.1

Chiral: 1-chloro-2-methylpentane, 3-chloro-2-methylpentane, 2-chloro-4-methylpentane Achiral: 2-chloro-2-methylpentane, 1-chloro-4-methylpentane





Exercise 2.6.2

1-Chloro-2-methylbutane (29%), 1-chloro-3-methylbutane (14%), 2-chloro-2-methylbutane (24%), 2-chloro-3-methylbutane (33%)

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2.7: Names and Properties of Alkyl Halides

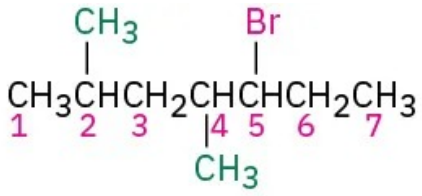
Although commonly called *alkyl halides*, halogen-substituted alkanes are named systematically as *haloalkanes* (Section 3.5), treating the halogen as a substituent on a parent alkane chain. There are three steps:

STEP 1

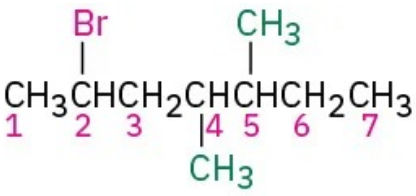
Find the longest chain, and name it as the parent. If a double or triple bond is present, the parent chain must contain it.

STEP 2

Number the carbons of the parent chain beginning at the end nearer the first substituent, whether alkyl or halo. Assign each substituent a number according to its position on the chain.

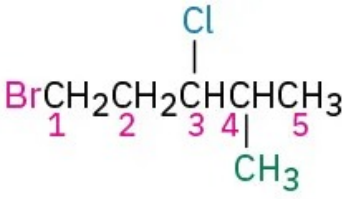


5-Bromo-2,4-dimethylheptane



2-Bromo-4,5-dimethylheptane

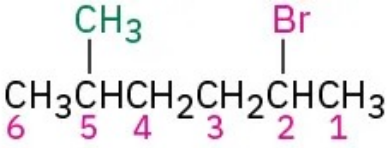
If different halogens are present, number each one and list them in alphabetical order when writing the name.



1-Bromo-3-chloro-4-methylpentane

STEP 3

If the parent chain can be properly numbered from either end by step 2, begin at the end nearer the substituent that has alphabetical precedence.



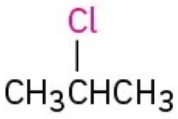
2-Bromo-5-methylhexane
(*Not* 5-bromo-2-methylhexane)

In addition to their systematic names, many simple alkyl halides are also named by identifying first the alkyl group and then the halogen. For example, CH_3I can be called either iodomethane or methyl iodide. Such names are well entrenched in the chemical

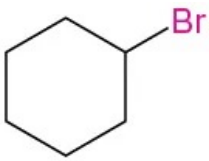
literature and in daily usage, but they won't be used in this book.



Iodomethane (or methyl iodide)



2-Chloropropane (or isopropyl chloride)



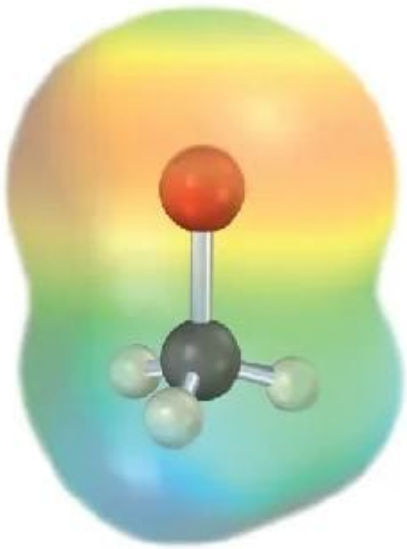
Bromocyclohexane (or cyclohexyl bromide)

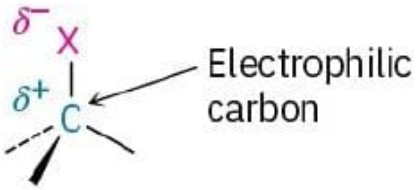
Halogens increase in size going down the periodic table, so the lengths of the corresponding carbon–halogen bonds increase accordingly (Table 2.7.1). In addition, C–X bond strengths decrease going down the periodic table. As we've been doing thus far, we'll continue using an X to represent any of the halogens F, Cl, Br, or I.

Table 2.7.1: A Comparison of the Halomethanes

Halomethane	Bond length (pm)	Bond strength		Dipole moment (*D*)
		(kJ/mol)	(kcal/mol)	
CH_3F	139	460	110	1.85
CH_3Cl	178	350	84	1.87
CH_3Br	193	294	70	1.81
CH_3I	214	239	57	1.62

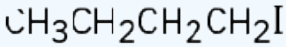
In our discussion of bond polarity in functional groups in Section 6.4, we noted that halogens are more electronegative than carbon. The C–X bond is therefore polar, with the carbon atom bearing a slight positive charge (δ+) and the halogen a slight negative charge (δ–). This polarity results in a dipole moment for all the halomethanes (Table 10.1) and implies that the alkyl halide C–X carbon atom should behave as an electrophile in polar reactions. We'll soon see that this is indeed the case.

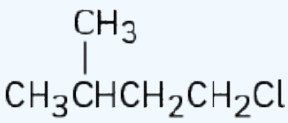


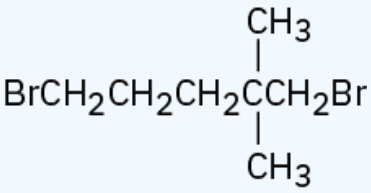


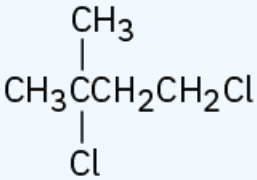
Exercise 2.7.1

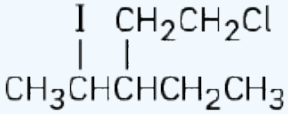
Give IUPAC names for the following alkyl halides:

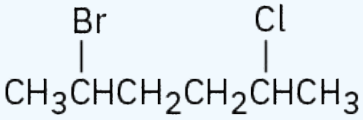
a. 

b. 

c. 

d. 

e. 

f. 

Answer available at the end of this section.

Exercise 2.7.1

Draw structures corresponding to the following IUPAC names:

a. 2-Chloro-3,3-dimethylhexane
b. 3,3-Dichloro-2-methylhexane
c. 3-Bromo-3-ethylpentane
d. 1,1-Dibromo-4-isopropylcyclohexane
e. 4-*sec*-Butyl-2-chlorononane
f. 1,1-Dibromo-4-*tert*-butylcyclohexane

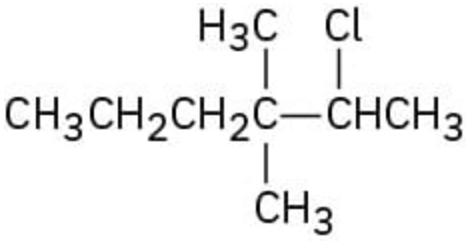
Answer available at the end of this section.

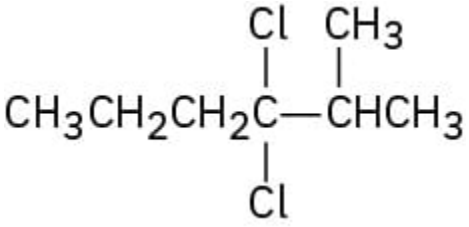
Answers

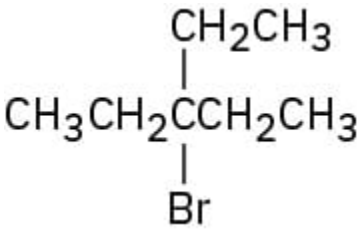
Exercise 2.7.1

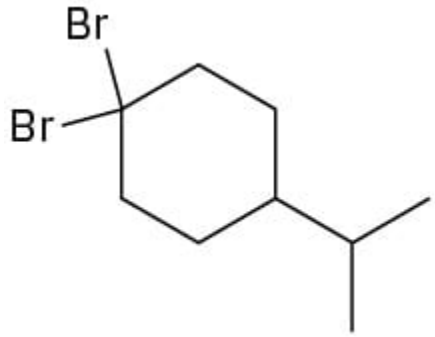
a. 1-Iodobutane
b. 1-Chloro-3-methylbutane
c. 1,5-Dibromo-2,2-dimethylpentane
d. 1,3-Dichloro-3-methylbutane
e. 1-Chloro-3-ethyl-4-iodopentane
f. 2-Bromo-5-chlorohexane

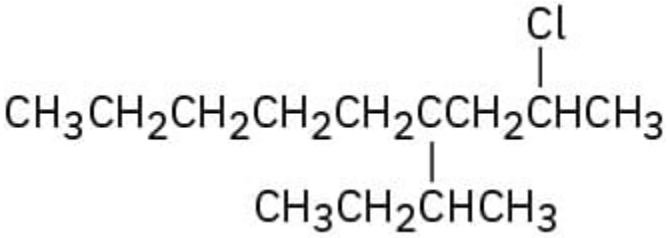
Exercise 2.7.1

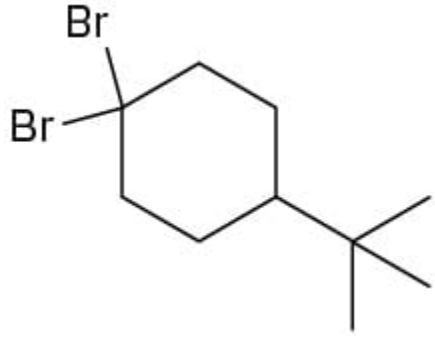
a. 

b. 

c. 

d. 

e. 

f. 

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2.8: Organic Chemistry- Alkanes and Halogenated Hydrocarbons (Exercises)

12.1: Organic Chemistry

Concept Review Exercises

1. Classify each compound as organic or inorganic.

    a. C_3H_8O
    b. $CaCl_2$
    c. $Cr(NH_3)_3Cl_3$
    d. $C_{30}H_{48}O_3N$

2. Which compound is likely organic and which is likely inorganic?

    a. a flammable compound that boils at 80°C and is insoluble in water
    b. a compound that does not burn, melts at 630°C, and is soluble in water

Answers

1. a. organic
    b. inorganic
    c. inorganic
    d. organic
2. a. organic
    b. inorganic

1. Classify each compound as organic or inorganic.

    a. C_6H_{10}
    b. $CoCl_2$
    c. $C_{12}H_{22}O_{11}$

2. Classify each compound as organic or inorganic.

    a. CH_3NH_2
    b. $NaNH_2$
    c. $Cu(NH_3)_6Cl_2$

3. Which member of each pair has a higher melting point?

    a. CH_3OH and NaOH
    b. CH_3Cl and KCl

4. Which member of each pair has a higher melting point?

    a. C_2H_6 and $CoCl_2$
    b. CH_4 and LiH

Answers

1. a. organic

b. inorganic
c. organic

3. a. NaOH
   b. KCl

12.2: Structures and Names of Alkanes

Concept Review Exercises

1. In the homologous series of alkanes, what is the molecular formula for the member just above C_8H_{18}?
2. Use the general formula for alkanes to write the molecular formula of the alkane with 12 carbon atoms.

Answers

1. C_9H_{20}
2. $C_{12}H_{26}$

Exercises

1. What compounds contain fewer carbon atoms than C_3H_8 and are its homologs?
2. What compounds contain five to eight carbon atoms and are homologs of C_4H_{10}?

Answer

1. CH_4 and C_2H_6

12.3: Branched-Chain Alkanes

Concept Review Exercises

1. In alkanes, can there be a two-carbon branch off the second carbon atom of a four-carbon chain? Explain.
2. A student is asked to write structural formulas for two different hydrocarbons having the molecular formula C_5H_{12}. She writes one formula with all five carbon atoms in a horizontal line and the other with four carbon atoms in a line, with a CH_3 group extending down from the first attached to the third carbon atom. Do these structural formulas represent different molecular formulas? Explain why or why not.

Answers

1. No; the branch would make the longest continuous chain of five carbon atoms.
2. No; both are five-carbon continuous chains.

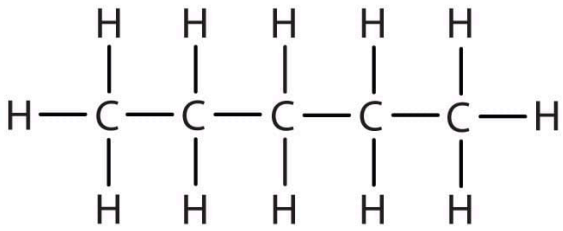
Key Takeaway

- Alkanes with four or more carbon atoms can exist in isomeric forms.

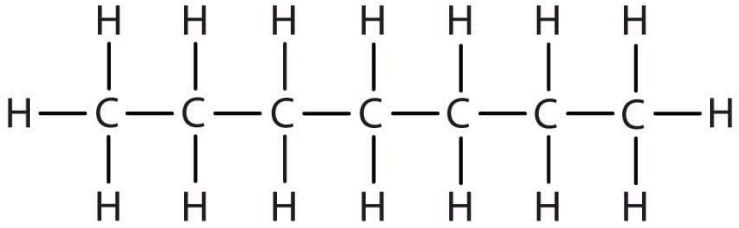
Exercises

1. Briefly identify the important distinctions between a straight-chain alkane and a branched-chain alkane.
2. How are butane and isobutane related? How do they differ?
3. Name each compound.

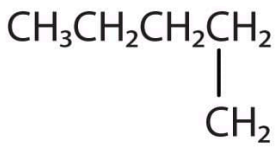
a.



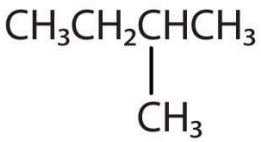
b.



4. Write the structural formula for each compound.
    a. hexane
    b. octane
5. Indicate whether the structures in each set represent the same compound or isomers.
    a. $CH_3CH_2CH_2CH_3$ and



    b. $CH_3CH_2CH_2CH_2CH_3$ and



Answers

1. Straight-chain alkanes and branched-chain alkanes have different properties as well as different structures.

3. a. pentane

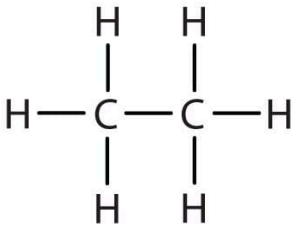
b. heptane

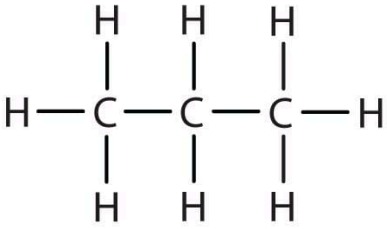
5. a. no
   b. yes

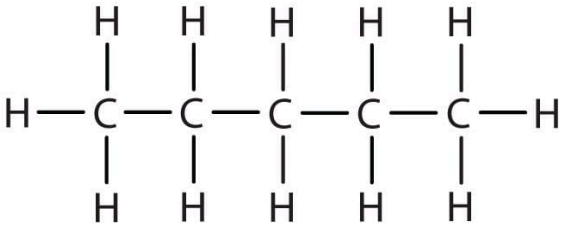
12.4: Condensed Structural and Line-Angle Formulas

Exercises

1. Write the condensed structural formula for each structural formula.

   a. 

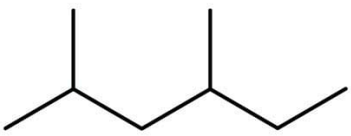
   b. 

   c. 

2. A condensed structural formula for isohexane can be written as $(CH_3)_2CHCH_2CH_2CH_3$. Draw the line-angle formula for isohexane.

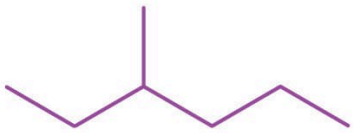
3. Draw a line-angle formula for the compound $CH_3CH_2CH(CH_3)CH_2CH_2CH_3$.

4. Give the structural formula for the compound represented by this line-angle formula:



Answers

1. a. CH_3CH_3
   b. $CH_3CH_2CH_3$
   c. $CH_3CH_2CH_2CH_2CH_3$

3. 

12.5: IUPAC Nomenclature

Concept Review Exercises

1. What is a CH_3 group called when it is attached to a chain of carbon atoms—a substituent or a functional group?
2. Which type of name uses numbers to locate substituents—common names or IUPAC names?

Answers

1. substituent

2. IUPAC names

Exercises

1. Briefly identify the important distinctions between an alkane and an alkyl group.

2. How many carbon atoms are present in each molecule?

   a. 2-methylbutane
   b. 3-ethylpentane

3. How many carbon atoms are present in each molecule?

   a. 2,3-dimethylbutane
   b. 3-ethyl-2-methylheptane

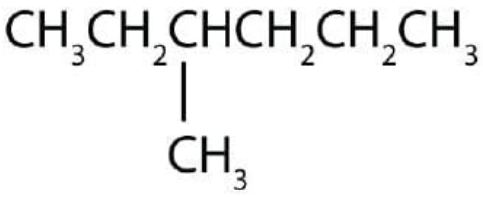
4. Draw the structure for each compound.

   a. 3-methylpentane
   b. 2,2,5-trimethylhexane
   c. 4-ethyl-3-methyloctane

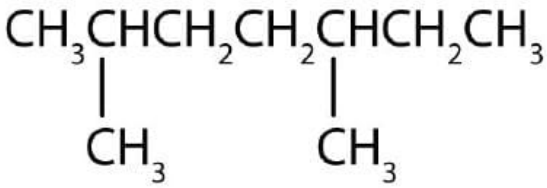
5. Draw the structure for each compound.

   a. 2-methylpentane
   b. 4-ethyl-2-methylhexane
   c. 2,2,3,3-tetramethylbutane

6. Name each compound according to the IUPAC system.

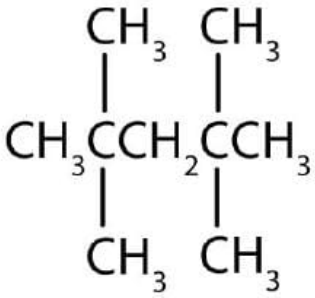


a.

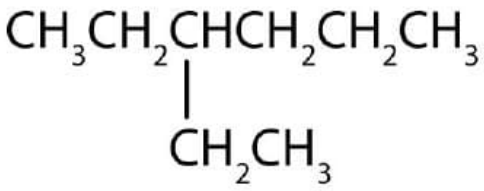


b.

7. Name each compound according to the IUPAC system.



a.



b.

8. What is a substituent? How is the location of a substituent indicated in the IUPAC system?

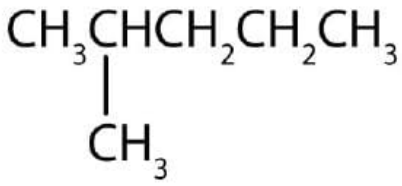
9. Briefly identify the important distinctions between a common name and an IUPAC name.

Answers

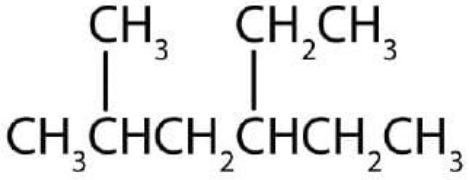
1. An alkane is a molecule; an alkyl group is not an independent molecule but rather a part of a molecule that we consider as a unit.

3. a. 6
   b. 10

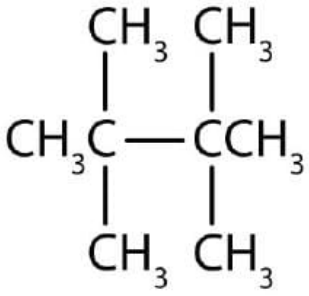
5. a.



b.



c.



7. a. 2,2,4,4-tetramethylpentane
   b. 3-ethylhexane

9. Common names are widely used but not very systematic; IUPAC names identify a parent compound and name other groups as substituents.

12.6: Physical Properties of Alkanes

Concept Review Exercises

1. Without referring to a table, predict which has a higher boiling point—hexane or octane. Explain.
2. If 25 mL of hexane were added to 100 mL of water in a beaker, which of the following would you expect to happen? Explain.
   a. Hexane would dissolve in water.
   b. Hexane would not dissolve in water and would float on top.
   c. Hexane would not dissolve in water and would sink to the bottom of the container.

Answers

1. octane because of its greater molar mass
2. b; hexane is insoluble in water and less dense than water.

Exercises

1. Without referring to a table or other reference, predict which member of each pair has the higher boiling point.
   a. pentane or butane
   b. heptane or nonane
2. For which member of each pair is hexane a good solvent?
   a. pentane or water
   b. sodium chloride or soybean oil

Answer

1. a. pentane
   b. nonane

12.7: Chemical Properties of Alkanes

Concept Review Exercises

1. Why are alkanes sometimes called paraffins?
2. Which halogen reacts most readily with alkanes? Which reacts least readily?

Answers

1. Alkanes do not react with many common chemicals. They are sometimes called paraffins, from the Latin parum affinis, meaning “little affinity.”
2. most readily: F_2; least readily: I_2

Exercises

1. Why do alkanes usually not react with ionic compounds such as most laboratory acids, bases, oxidizing agents, or reducing agents?
2. Write an equation for the complete combustion of methane (CH_4), the main component of natural gas).
3. What is the most important reaction of alkanes?
4. Name some substances other than oxygen that react readily with alkanes.

Answers

1. Alkanes are nonpolar; they do not attract ions.

12.8: Halogenated Hydrocarbons

Concept Review Exercises

1. What is the IUPAC name for the HFC that has the formula CH_2FCF_3? (Hint: you must use a number to indicate the location of each substituent F atom.)
2. What is the IUPAC name for the HCFC that has the formula $CHCl_2CF_3$?

Answers

1. 1,1,1,2-tetrafluoroethane
2. 1,1,1-trifluoro-2,2-dichloroethane

Exercises

1. Write the condensed structural formula for each compound.
   a. methyl chloride
   b. chloroform
2. Write the condensed structural formula for each compound.
   a. ethyl bromide
   b. carbon tetrachloride
3. Write the condensed structural formulas for the two isomers that have the molecular formula C_3H_7Br. Give the common name and the IUPAC name of each.
4. Write the condensed structural formulas for the four isomers that have the molecular formula C_4H_9Br. Give the IUPAC name of each.
5. What is a CFC? How are CFCs involved in the destruction of the ozone layer?
6. Explain why each compound is less destructive to the ozone layer than are CFCs.
   a. fluorocarbons
   b. HCFCs

Answers

1. a. CH_3Cl
   b. $CHCl_3$

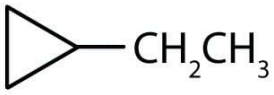
3. $CH_3CH_2CH_2Br$, propyl bromide, 1-bromopropane; $CH_3CHBrCH_3$, isopropyl bromide, 2-bromopropane

5. compounds containing Cl, F, and C; by releasing Cl atoms in the stratosphere

12.9: Cycloalkanes

Concept Review Exercises

1. What is the molecular formula of cyclooctane?
2. What is the IUPAC name for this compound?



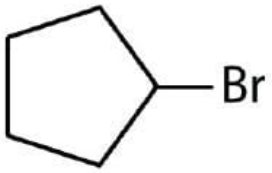
Answers

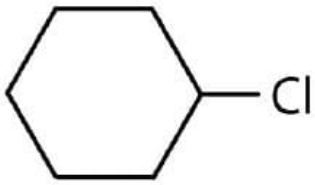
1. C_8H_{16}
2. ethylcyclopropane

Exercises

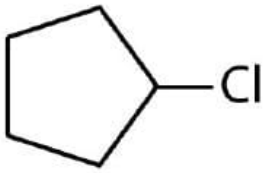
1. Draw the structure for each compound.
   a. ethylcyclobutane
   b. propylcyclopropane

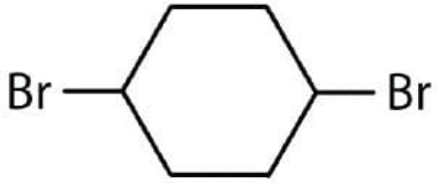
2. Draw the structure for each compound.
   a. methylcyclohexane
   b. butylcyclobutane
3. Cycloalkyl groups can be derived from cycloalkanes in the same way that alkyl groups are derived from alkanes. These groups are named as cyclopropyl, cyclobutyl, and so on. Name each cycloalkyl halide.

   a. 

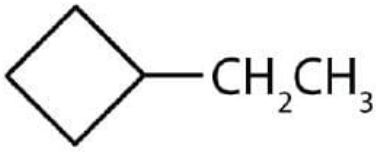
   b. 

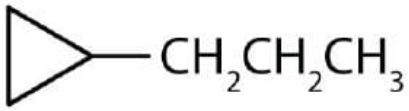
4. Halogenated cycloalkanes can be named by the IUPAC system. As with alkyl derivatives, monosubstituted derivatives need no number to indicate the position of the halogen. To name disubstituted derivatives, the carbon atoms are numbered starting at the position of one substituent (C1) and proceeding to the second substituted atom by the shortest route. Name each compound.

   a. 

   b. 

Answers

1. a. 

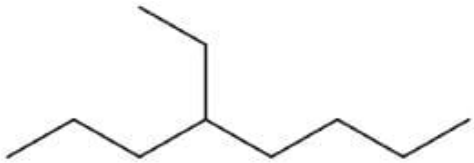
   b. 

3. a. cyclopentyl bromide
   b. cyclohexyl chloride

12.10: Chapter Summary

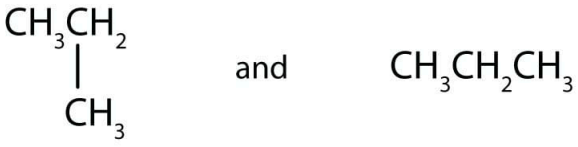
Additional Exercises

1. You find an unlabeled jar containing a solid that melts at 48°C. It ignites readily and burns readily. The substance is insoluble in water and floats on the surface. Is the substance likely to be organic or inorganic?
2. Give the molecular formulas for methylcyclopentane, 2-methylpentane, and cyclohexane. Which are isomers?
3. What is wrong with each name? (Hint: first write the structure *as if* it were correct.) Give the correct name for each compound.
   a. 2-dimethylpropane
   b. 2,3,3-trimethylbutane
   c. 2,4-diethylpentane
   d. 3,4-dimethyl-5-propylhexane
4. What is the danger in swallowing a liquid alkane?
5. Distinguish between lighter and heavier liquid alkanes in terms of their effects on the skin.
6. Following is the line formula for an alkane. Draw its structure and give its name.

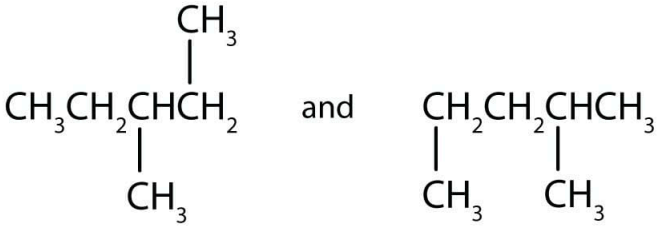


7. Write equations for the complete combustion of each compound.
   a. propane (a bottled gas fuel)
   b. octane (a typical hydrocarbon in gasoline).
8. The density of a gasoline sample is 0.690 g/mL. On the basis of the complete combustion of octane, calculate the amount in grams of carbon dioxide (CO_2) and water (H_2O) formed per gallon (3.78 L) of the gasoline when used in an automobile.
9. Draw the structures for the five isomeric hexanes (C_6H_{14}). Name each by the IUPAC system.
10. Indicate whether the structures in each set represent the same compound or isomers.

a.



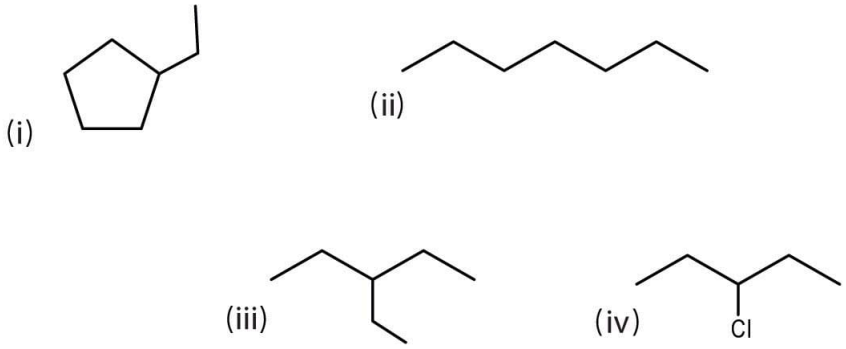
b.





c.

11. Consider the line-angle formulas shown here and answer the questions.



a. Which pair of formulas represents isomers? Draw each structure.
b. Which formula represents an alkyl halide? Name the compound and write its condensed structural formula.
c. Which formula represents a cyclic alkane? Name the compound and draw its structure.
d. What is the molecular formula of the compound represented by (i)?

Answers

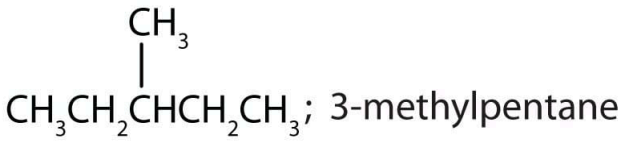
1. organic

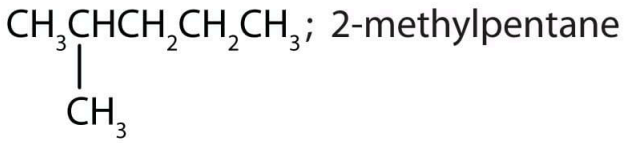
3. a. Two numbers are needed to indicate two substituents; 2,2-dimethylpropane.
   b. The lowest possible numbers were not used; 2,2,3-trimethylbutane.
   c. An ethyl substituent is not possible on the second carbon atom; 3,5-dimethylheptane.
   d. A propyl substituent is not possible on the fifth carbon atom; 3,4,5-trimethyloctane.

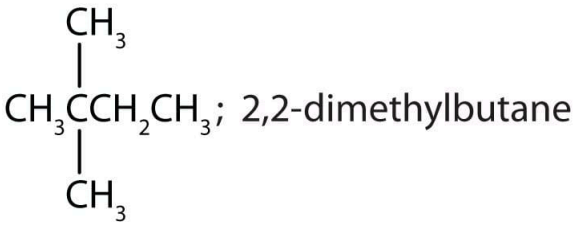
5. Lighter alkanes wash away protective skin oils; heavier alkanes form a protective layer.

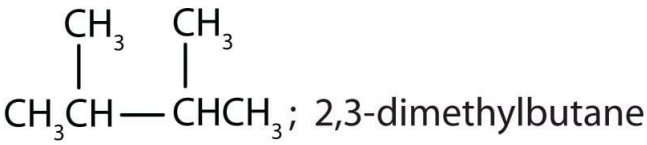
7. a. $C_3H_8 + 5O_2 \rightarrow 3CO_2 + 4H_2O$
   b. $2C_8H_{18} + 25O_2 \rightarrow 16CO_2 + 18H_2O$

9. $CH_3CH_2CH_2CH_2CH_2CH_3$; hexane

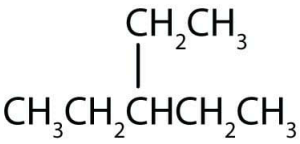






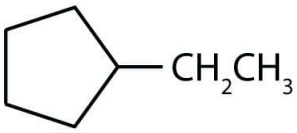


11. a. ii and iii; $CH_3CH_2CH_2CH_2CH_2CH_2CH_3$ and



b. iv; 3-chloropentane; $CH_3CH_2CHClCH_2CH_3$

c. i; ethylcyclopentane;



d. C_7H_{14}

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3: UNSATURATED HYDROCARBONS

3.1: Alkenes and Alkynes

3.2: Naming Alkenes and Alkynes

3.3: The Structure of Alkenes- Cis-Trans Isomerism

3.4: Types of Isomers

3.5: Properties of Alkenes and Alkynes

3.6: Addition Reactions of Alkenes

3.7: Markovnikov's Rule

3.8: Aromatic Compounds- Benzene and Its Relatives

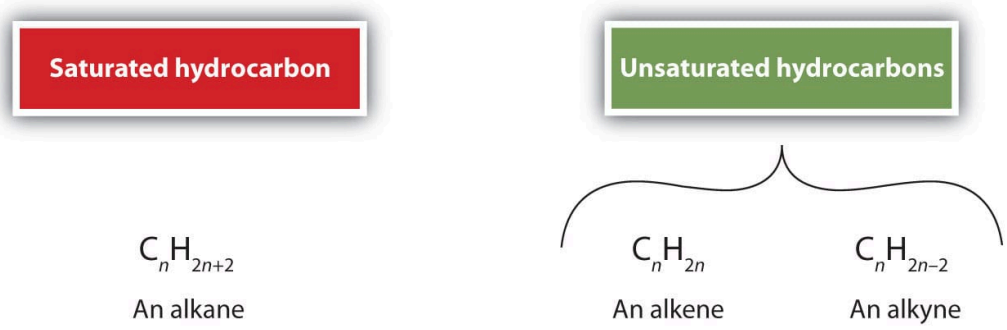
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3.1: Alkenes and Alkynes

Learning Objectives

- Identify the difference between saturated and unsaturated hydrocarbons.
- Describe the functional groups, alkenes and alkynes.

As noted before, **alkenes** are hydrocarbons with carbon-to-carbon double bonds ($R_2C{=}CR_2$) and **alkynes** are hydrocarbons with carbon-to-carbon triple bonds (R–C≡C–R). Collectively, they are called **unsaturated** hydrocarbons because they have fewer hydrogen atoms than does an alkane with the same number of carbon atoms, as is indicated in the following general formulas:



You have likely heard of *unsaturated fats*. These are complex organic molecules with long chains of carbon atoms, which contain at least one double bond between carbon atoms. Double and triple bonds give rise to a different geometry around the carbon atom that participates in them, leading to important differences in molecular shape and properties. The differing geometries are responsible for the different properties of unsaturated versus saturated fats.

Alkenes

Ethene, C_2H_4, is the simplest alkene. Each carbon atom in ethene, commonly called ethylene, has a trigonal planar structure. The second member of the series is propene (propylene) (Figure 3.1.1); the butene isomers follow in the series. Four carbon atoms in the chain of butene allows for the formation of isomers based on the position of the double bond, as well as a new form of isomerism.

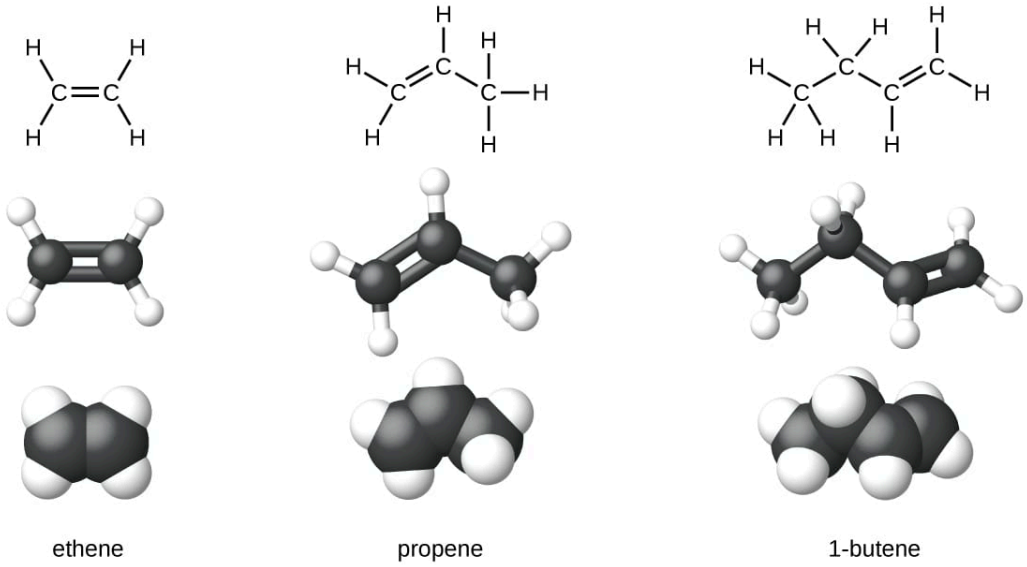


Figure 3.1.6: Expanded structures, ball-and-stick structures, and space-filling models for the alkenes ethene, propene, and 1-butene are shown.

Ethylene (the common industrial name for ethene) is a basic raw material in the production of polyethylene and other important compounds. Over 135 million tons of ethylene were produced worldwide in 2010 for use in the polymer, petrochemical, and plastic industries. Ethylene is produced industrially in a process called cracking, in which the long hydrocarbon chains in a petroleum mixture are broken into smaller molecules.

Alkynes

Hydrocarbon molecules with one or more triple bonds are called **alkynes**; they make up another series of unsaturated hydrocarbons. Two carbon atoms joined by a triple bond have bond angles of 180°, giving these types of bonds a linear shape.

The simplest member of the alkyne series is ethyne, C_2H_2, commonly called acetylene. The Lewis structure for ethyne, a linear molecule, is:



> Acetylene is used in oxyacetylene torches for cutting and welding metals. The flame from such a torch can be very hot. Most acetylene, however, is converted to chemical intermediates that are used to make vinyl and acrylic plastics, fibers, resins, and a variety of other products.

Alkynes are similar to alkenes in both physical and chemical properties. For example, alkynes undergo many of the typical addition reactions of alkenes. The International Union of Pure and Applied Chemistry (IUPAC) names for alkynes parallel those of alkenes, except that the family ending is *-yne* rather than *-ene*.

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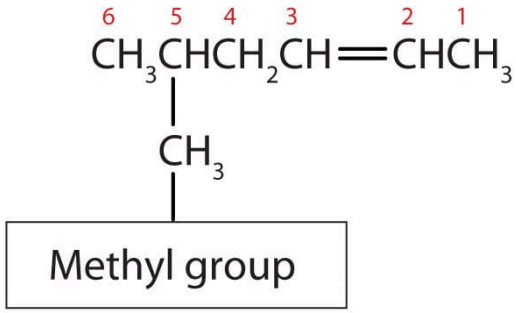
3.2: Naming Alkenes and Alkynes

Learning Objectives

- Objective 1
- Objective 2

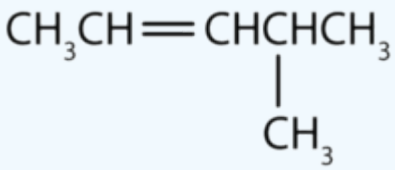
Here are some basic rules for naming alkenes from the International Union of Pure and Applied Chemistry (IUPAC):

1. The longest chain of carbon atoms *containing the double bond* is considered the parent chain. It is named using the same stem as the alkane having the same number of carbon atoms but ends in *-ene* to identify it as an alkene. Thus the compound CH_2=$CHCH_3$ is *propene*.
2. If there are four or more carbon atoms in a chain, we must indicate the position of the double bond. The carbons atoms are numbered so that the first of the two that are doubly bonded is given the lower of the two possible numbers.The compound CH_3CH=$CHCH_2CH_3$, for example, has the double bond between the second and third carbon atoms. Its name is 2-pentene (not 3-pentene).
3. Substituent groups are named as with alkanes, and their position is indicated by a number. Thus, the structure below is 5-methyl-2-hexene. Note that the numbering of the parent chain is always done in such a way as to give the double bond the lowest number, even if that causes a substituent to have a higher number. *The double bond always has priority in numbering.*

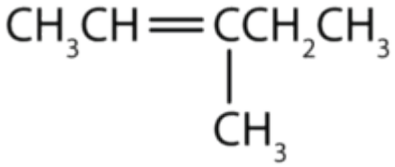


Example 3.2.1

Name each compound.



a.



b.

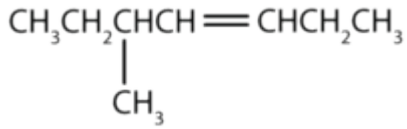
Solution

a. The longest chain containing the double bond has five carbon atoms, so the compound is a *pentene* (rule 1). To give the first carbon atom of the double bond the lowest number (rule 2), we number from the left, so the compound is a 2-pentene. There is a methyl group on the fourth carbon atom (rule 3), so the compound's name is 4-methyl-2-pentene.
b. The longest chain containing the double bond has five carbon atoms, so the parent compound is a *pentene* (rule 1). To give the first carbon atom of the double bond the lowest number (rule 2), we number from the left, so the compound is a 2-pentene. There is a methyl group on the third carbon atom (rule 3), so the compound's name is 3-methyl-2-pentene.

Exercise 3.2.1

Name each compound.

1. $CH_3CH_2CH_2CH_2CH_2CH{=}CHCH_3$



Just as there are cycloalkanes, there are *cycloalkenes*. These compounds are named like alkenes, but with the prefix *cyclo-* attached to the beginning of the parent alkene name.

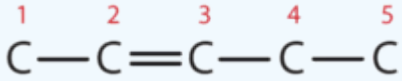
Example 3.2.2

Draw the structure for each compound.

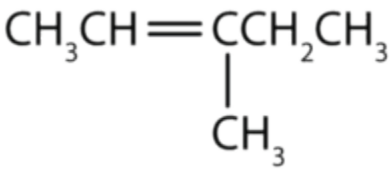
1. 3-methyl-2-pentene
2. cyclohexene

Solution

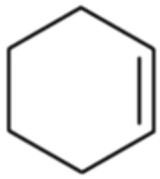
1. First write the parent chain of five carbon atoms: C–C–C–C–C. Then add the double bond between the second and third carbon atoms:



Now place the methyl group on the third carbon atom and add enough hydrogen atoms to give each carbon atom a total of four bonds.



- First, consider what each of the three parts of the name means. *Cyclo* means a ring compound, *hex* means 6 carbon atoms, and *-ene* means a double bond.



Exercise 3.2.2

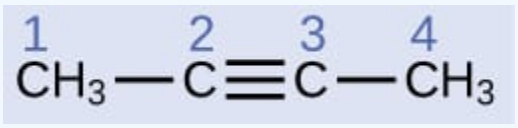
Draw the structure for each compound.

a. 2-ethyl-1-hexene
b. cyclopentene

The IUPAC nomenclature for alkynes is similar to that for alkenes except that the suffix *-yne* is used to indicate a triple bond in the chain. For example, $\mathrm{CH_3CH_2C \equiv CH}$ is called 1-butyne.

Example 3.2.6: Structure of Alkynes

Describe the geometry and hybridization of the carbon atoms in the following molecule:

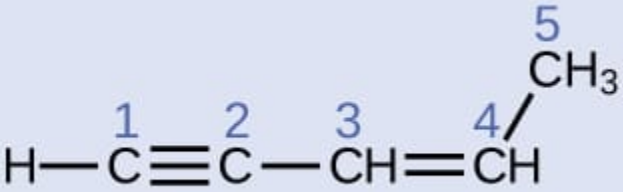


Solution

Carbon atoms 1 and 4 have four single bonds and are thus tetrahedral with sp^3 hybridization. Carbon atoms 2 and 3 are involved in the triple bond, so they have linear geometries and would be classified as *sp* hybrids.

Exercise 3.2.6

Identify the hybridization and bond angles at the carbon atoms in the molecule shown:



Answer available at the end of this section.

Answers

Exercise 3.2.6

carbon 1: *sp*, 180°; carbon 2: *sp*, 180°; carbon 3: sp^2, 120°; carbon 4: sp^2, 120°; carbon 5: sp^3, 109.5°

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3.3: The Structure of Alkenes- Cis-Trans Isomerism

Learning Objectives

- Recognize that alkenes that can exist as cis-trans isomers.
- Classify isomers as cis or trans.
- Draw structures for cis-trans isomers given their names.

There is free rotation about the carbon-to-carbon single bonds (C–C) in alkanes. In contrast, the structure of alkenes requires that the carbon atoms of a double bond and the two atoms bonded to each carbon atom all lie in a single plane, and that each doubly bonded carbon atom lies in the center of a triangle. This part of the molecule's structure is rigid; rotation about doubly bonded carbon atoms is *not* possible without rupturing the bond. Look at the two chlorinated hydrocarbons in Figure 3.3.1.

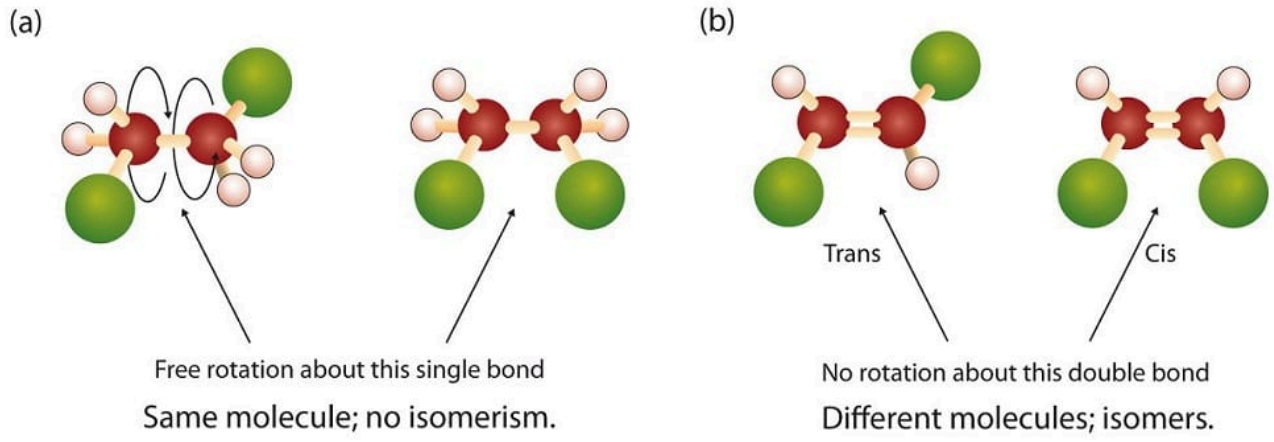


Figure 3.3.1*: Rotation about Bonds. In 1,2-dichloroethane (a), free rotation about the C–C bond allows the two structures to be interconverted by a twist of one end relative to the other. In 1,2-dichloroethene (b), restricted rotation about the double bond means that the relative positions of substituent groups above or below the double bond are significant.*

In 1,2-dichloroethane (part (a) of Figure 3.3.1), there is free rotation about the C–C bond. The two models shown represent exactly the same molecule; they are *not* isomers. You can draw structural formulas that look different, but if you bear in mind the possibility of this free rotation about single bonds, you should recognize that these two structures represent the same molecule:



In 1,2-dichloroethene (Figure 3.3.1*b*), however, 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. The isomer in which the two chlorine (Cl) atoms lie on the same side of the molecule is called the cis isomer (Latin *cis*, meaning "on this side") and is named cis-1,2-dichloroethene. The isomer with the two Cl atoms on opposite sides of the molecule is the trans isomer (Latin *trans*, meaning "across") and is named *trans*-1,2-dichloroethene. 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.

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; the double bond results in cis-trans isomerism (Figure 3.3.2).

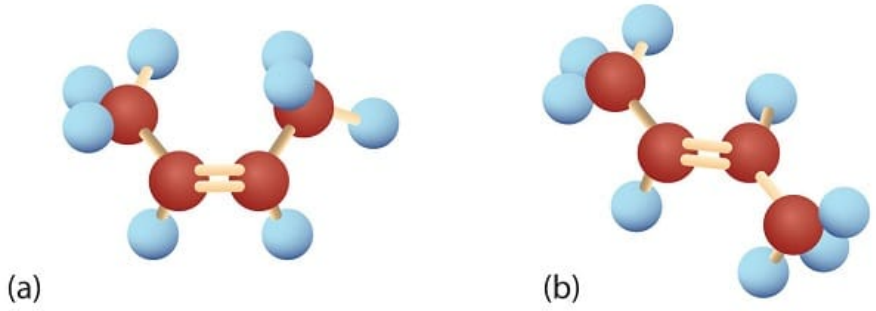


Figure 3.3.2: Ball-and-Spring Models of (a) Cis-2-Butene and (b) Trans-2-Butene. Cis-trans isomers have different physical, chemical, and physiological properties.

Cis-2-butene has both methyl groups on the same side of the molecule. *Trans*-2-butene has the methyl groups on opposite sides of the molecule. Their structural formulas are as follows:



Figure 3.3.3*: Models of (left) Cis-2-Butene and (right) Trans-2-Butene.*

Note, however, that the presence of a double bond does **not** necessarily lead to cis-trans isomerism (Figure 3.3.4). We can draw two s*eemingly* different propenes:



Figure 3.3.4*: Different views of the propene molecule (flip vertically). These are not isomers.*

However, these two structures are not really different from each other. If you could pick up either molecule from the page and flip it over top to bottom, you would see that the two formulas are identical. Thus there are two requirements for cis-trans isomerism:

1. Rotation must be restricted in the molecule.
2. There must be **two nonidentical groups** on **each** doubly bonded carbon atom.

In these propene structures, the second requirement for cis-trans isomerism is not fulfilled. One of the doubly bonded carbon atoms does have two different groups attached, but the rules require that *both* carbon atoms have two different groups. In general, the following statements hold true in cis-trans isomerism:

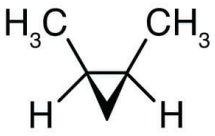
- Alkenes with a $C=CH_2$ unit do not exist as cis-trans isomers.
- Alkenes with a $C=CR_2$ unit, where the two R groups are the same, do not exist as cis-trans isomers.
- Alkenes of the type R–CH=CH–R can exist as cis and trans isomers; cis if the two R groups are on the same side of the

carbon-to-carbon double bond, and trans if the two R groups are on opposite sides of the carbon-to-carbon double bond.

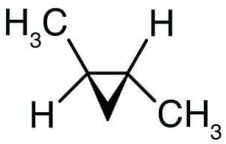
Advanced Note: E/Z Isomerization

If a molecule has a C=C bond with one non-hydrogen group attached to each of the carbons, cis/trans nomenclature descried above is enough to describe it. However, if you have three different groups (or four), then the cis/trans approach is insufficient to describe the different isomers, since we do not know which two of the three groups are being described. For example, if you have a C=C bond, with a methyl group and a bromine on one carbon , and an ethyl group on the other, it is neither trans nor cis, since it is not clear whether the ethyl group is trans to the bromine or the methyl. This is addressed with a more advanced E/Z nomenclature discussed elsewhere.

Cis-trans isomerism also occurs in cyclic compounds. In ring structures, groups are unable to rotate about any of the ring carbon–carbon bonds. Therefore, groups can be either on the same side of the ring (cis) or on opposite sides of the ring (trans). For our purposes here, we represent all cycloalkanes as planar structures, and we indicate the positions of the groups, either above or below the plane of the ring.



Cis-1,2-dimethylcyclopropane



Trans-1,2-dimethylcyclopropane

Example 3.3.1

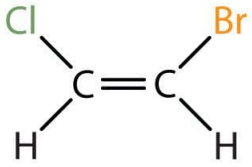
Which compounds can exist as cis-trans (geometric) isomers? Draw them.

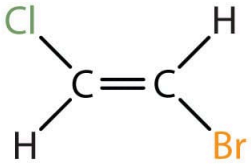
1. CHCl=CHBr
2. CH_2=$CBrCH_3$
3. $(CH_3)_2C$=$CHCH_2CH_3$
4. CH_3CH=$CHCH_2CH_3$

Solution

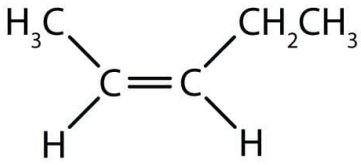
All four structures have a double bond and thus meet rule 1 for cis-trans isomerism.

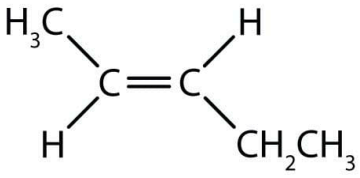
1. This compound meets rule 2; it has two nonidentical groups on *each* carbon atom (H and Cl on one and H and Br on the other). It exists as both cis and trans isomers:





- This compound has two hydrogen atoms on one of its doubly bonded carbon atoms; it fails rule 2 and does not exist as cis and trans isomers.
- This compound has two methyl (CH_3) groups on one of its doubly bonded carbon atoms. It fails rule 2 and does not exist as cis and trans isomers.
- This compound meets rule 2; it has two nonidentical groups on *each* carbon atom and exists as both cis and trans isomers:

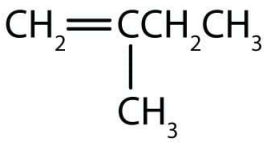


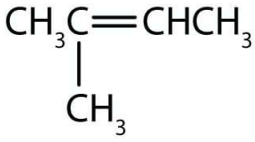


Exercise 3.3.1

Which compounds can exist as cis-trans isomers? Draw them.

a. $CH_2=CHCH_2CH_2CH_3$
b. $CH_3CH=CHCH_2CH_3$
c. $CH_3CH_2CH=CHCH_2CH_3$
d.

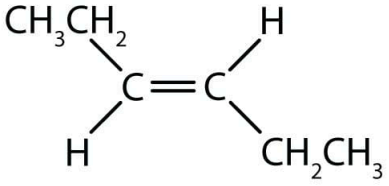


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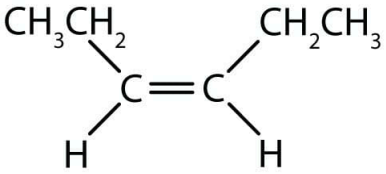
Concept Review Exercises

1. What are cis-trans (geometric) isomers? What two types of compounds can exhibit cis-trans isomerism?
2. Classify each compound as a cis isomer, a trans isomer, or neither.

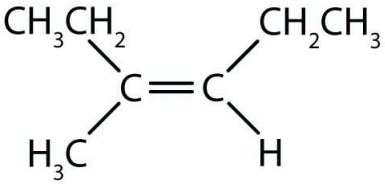
a.

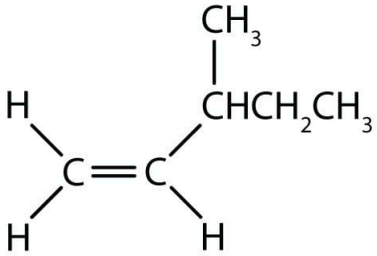


b.



c.



d. 

Answers

1. Cis-trans isomers are compounds that have different configurations (groups permanently in different places in space) because of the presence of a rigid structure in their molecule. Alkenes and cyclic compounds can exhibit cis-trans isomerism.

2. a. trans (the two hydrogen atoms are on opposite sides)
   b. cis (the two hydrogen atoms are on the same side, as are the two ethyl groups)
   c. cis (the two ethyl groups are on the same side)
   d. neither (fliping the bond does not change the molecule. There are no isomers for this molecule)

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- 13.2: Cis-Trans Isomers (Geometric Isomers) by Staff is licensed CC BY-NC-SA 3.0. Original source: https://2012books.lardbucket.org/books/introduction-to-chemistry-general-organic-and-biological.

3.4: Types of Isomers

Objective

After completing this section, you should be able to explain the differences among constitutional (structural) isomers and stereoisomers (geometric isomers).

Key Terms

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

- constitutional
- (structural) isomers
- stereoisomers

The following flow chart can be used to identify the relationship of two compounds with respect to isomerization:

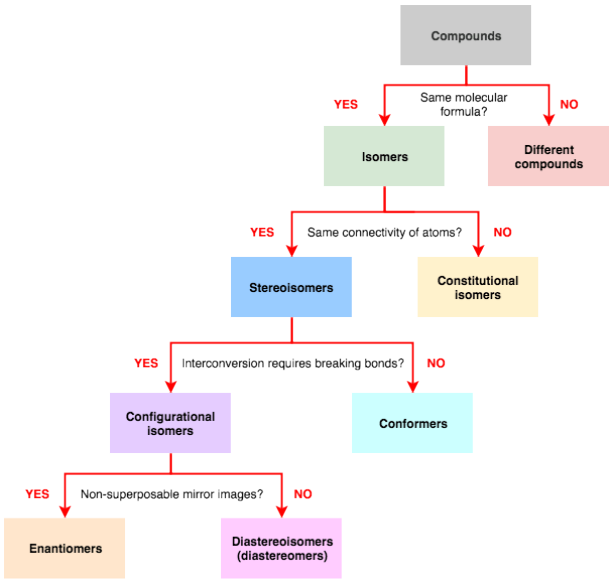
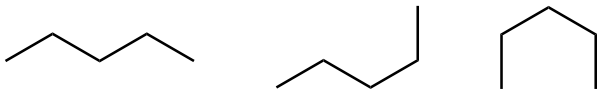


Figure 3.4.1: Different types of isomers. When using the flow chart, it is really important to remember that each decision on the flow chart is related to comparing two molecules, ie. it doesn't make sense to ask "what is compound A", but it does make sense to ask "how are compounds A and B related"? A molecule may be the enantiomer of another molecule, but a diastereomer of another. (CC-BY-SA 4.0; Mark Coster via StackExchange)

Conformational Isomers

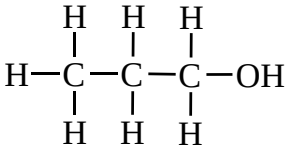
The C–C single bonds in ethane, propane, and other alkanes are formed by the overlap of an sp^3 hybrid orbital on one carbon atom with an sp^3 hybrid orbital on another carbon atom, forming a σ bond. Each sp^3 hybrid orbital is cylindrically symmetrical (all cross-sections are circles), resulting in a carbon–carbon single bond that is also cylindrically symmetrical about the C–C axis. Because rotation about the carbon–carbon single bond can occur without changing the overlap of the sp^3 hybrid orbitals, there is no significant electronic energy barrier to rotation. Consequently, many different arrangements of the atoms are possible, each corresponding to different degrees of rotation. Differences in three-dimensional structure resulting from rotation about a σ bond are called differences in conformation, and each different arrangement is called a conformational isomer (or conformer).



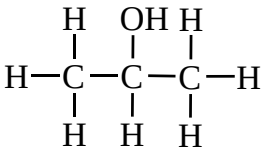
Conformational Isomers of Pentane

Structural Isomers

Unlike conformational isomers, which do not differ in connectivity, structural isomers differ in connectivity, as illustrated here for 1-propanol and 2-propanol. Although these two alcohols have the same molecular formula (C_3H_8O), the position of the –OH group differs, which leads to differences in their physical and chemical properties.

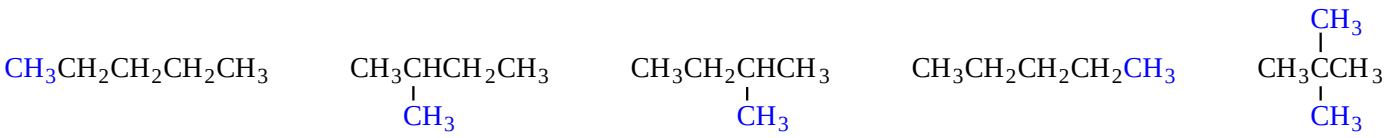


1-propanol (*n*-propanol)



2-propanol (isopropanol)

In the conversion of one structural isomer to another, at least one bond must be broken and reformed at a different position in the molecule. Consider, for example, the following five structures represented by the formula C_5H_{12}:



(a) (b) (c) (d) (e)

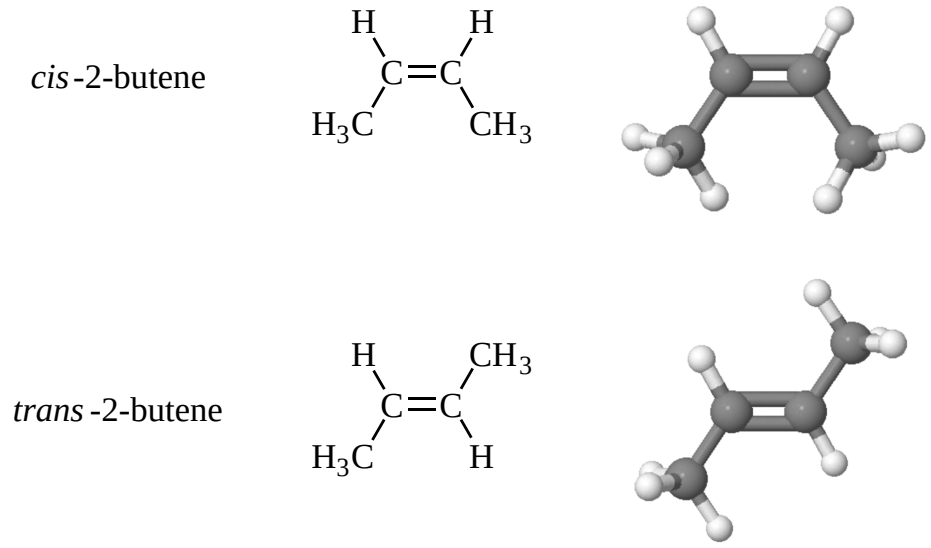
Of these structures, (a) and (d) represent the same compound, as do (b) and (c). No bonds have been broken and reformed; the molecules are simply rotated about a 180° vertical axis. Only three—n-pentane (a) and (d), 2-methylbutane (b) and (c), and 2,2-dimethylpropane (e)—are structural isomers. Because no bonds are broken in going from (a) to (d) or from (b) to (c), these alternative representations are not structural isomers. The three structural isomers—either (a) or (d), either (b) or (c), and (e)—have distinct physical and chemical properties.

Stereoisomers

Stereoisomers have the same connectivity in their atoms but a different arrangement in three-dimensional space. There are different classifications of stereoisomers depending on how the arrangements differ from one another. Notice that in the structural isomers, there was some difference in the connection of atoms. For example, 1-butene has a double bond followed by two single bonds while 2-butene has a single bond, then a double bond, then a single bond. A stereoisomer will have the same connectivity among all atoms in the molecule.

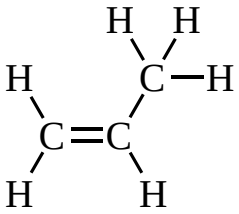
Geometric Isomers

With a molecule such as 2-butene, a different type of isomerism called geometric isomerism can be observed. **Geometric isomers** are isomers in which the order of atom bonding is the same but the arrangement of atoms in space is different. The double bond in an alkene is not free to rotate because of the nature of the bond. Therefore, there are two different ways to construct the 2-butene molecule (see figure below). The image below shows the two geometric isomers, called *cis*-2-butene and *trans*-2-butene.



Geometric Isomers of 2-Butene

The *cis* isomer has the two single hydrogen atoms on the same side of the molecule, while the *trans* isomer has them on opposite sides of the molecule. In both molecules, the bonding order of the atoms is the same. In order for geometric isomers to exist, there must be a rigid structure in the molecule to prevent free rotation around a bond. This occurs with a double bond or a ring. In addition, the two carbon atoms must each have two different groups attached in order for there to be geometric isomers. Propene (see figure below) has no geometric isomers because one of the carbon atoms (the one on the far left) involved in the double bond has two single hydrogens bonded to it.

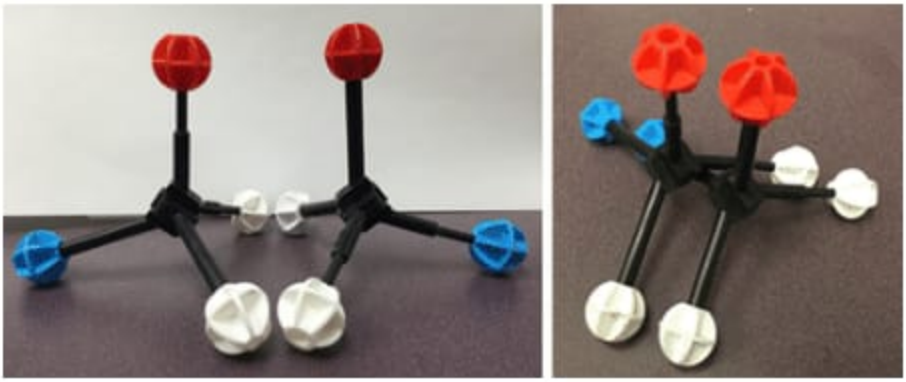


Physical and chemical properties of geometric isomers are generally different. As with alkenes, alkynes display structural isomerism beginning with 1-butyne and 2-butyne. However, there are no geometric isomers with alkynes because there is only one other group bonded to the carbon atoms that are involved in the triple bond.

Optical Isomers

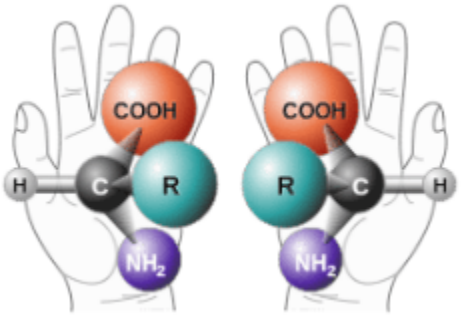
Stereoisomers that are not geometric isomers are known as optical isomers. Optical isomers differ in the placement of substituted groups around one or more atoms of the molecule. They were given their name because of their interactions with plane-polarized light. Optical isomers are labeled enantiomers or diastereomers.

Enantiomers are non-superimposable mirror images. A common example of a pair of enantiomers is your hands. Your hands are mirror images of one another but no matter how you turn, twist, or rotate your hands, they are not superimposable.



Two models that are mirror images and superimposable.

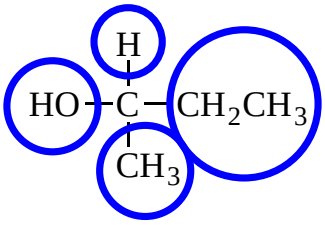
Since they are superimposable, they are the same molecule and are not isomers.



Your hands and some molecules are mirror images but are not superimposable.

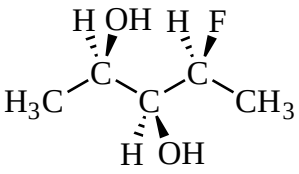
These pairs of molecules are called enantiomers.

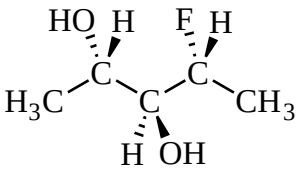
Objects that have non-superimposable mirror images are called **chiral**. When examining a molecule, carbon atoms with four unique groups attached are considered chiral. Look at the figure below to see an example of a chiral molecule. Note that we have to look beyond the first atom attached to the central carbon atom. The four circles indicate the four unique groups attached to the central carbon atom, which is chiral.



A chiral carbon has four unique groups attached to it

Another type of optical isomer are **diastereomers**, which are non-mirror image optical isomers. Diastereomers have a different arrangement around one or more atoms while some of the atoms have the same arrangement. As shown in the figure below, note that the orientation of groups on the first and third carbons are different but the second one remains the same so they are not the same molecule. The solid wedge indicates a group coming out of the page/screen towards you and the dashed line indicates that a group is going away from you "behind" the page/screen.

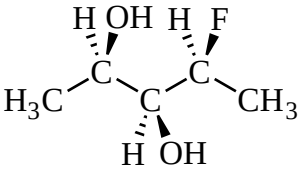


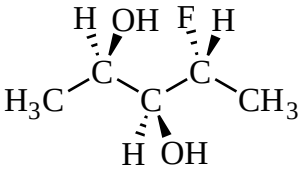


Diastereomers differ at one or more atom. These molecules are not mirror images and they are not superimposable.

They are optical isomers because they have the same connectivity between atoms but a different arrangement of substituent groups.

Epimers are a sub-group of diastereomers that differ at only one location. All epimers are diastereomers but not all diastereomers are epimers.





Epimers have a different arrangement around one atom, while arrangements around the other atoms are the same

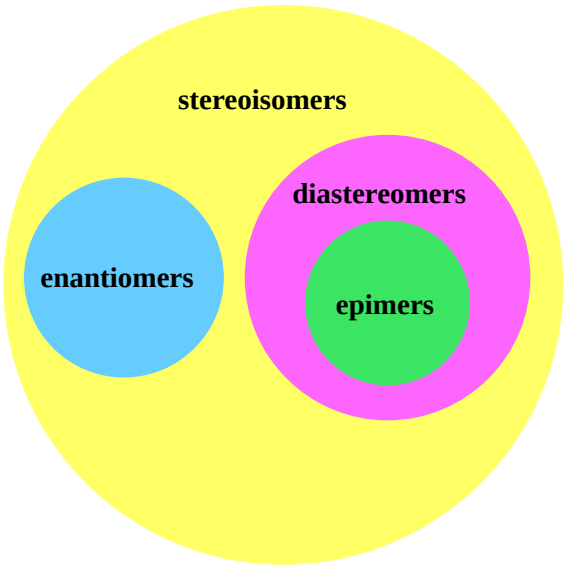
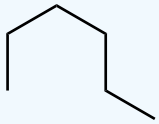
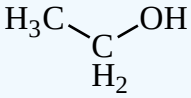
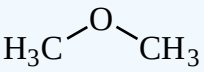


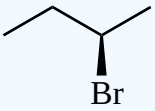
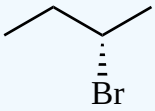
Diagram showing the division of stereoisomers (also known as optical isomers)

Exercise 3.4.1

What kind of isomers are the following pairs?

a)  and 

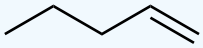
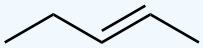
b)  and 

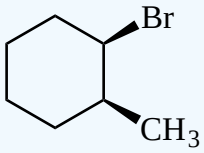
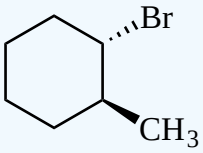
c)  and 

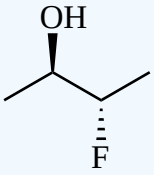
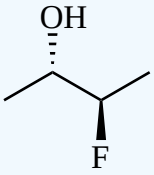
Answer available at the end of this section.

Exercise 3.4.2

What kind of isomers are the following pairs?

a)  and 

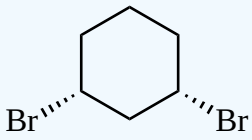
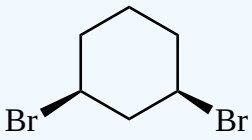
b)  and 

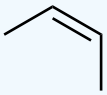
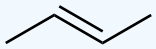
c)  and 

Answer available at the end of this section.

Exercise 3.4.3

What is the relationship between the following pairs?

a)  and 

b)  and 

c) (*R*) – 2 chlorohexane & 1-chlorohexane

d) (2*R*, 3*R*) dichlorohexane & (2*S*, 3*R*) dichlorohexane

Answer available at the end of this section.

Answers

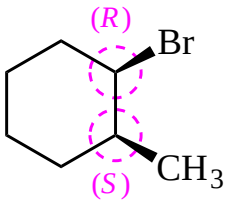
Exercise 3.4.1

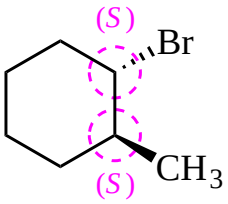
a. Since both structures have the same formula (C_6H_{12}) and they have the same connectivity, but are in a different arrangement of the atoms in space, they are conformational isomers.
b. Since both structures have the same formula (C_2H_6O) but different connectivity, they are structural isomers.
c. Since both structures have the same formula (C_3H_9Br) and the same connectivity but the structure on the left has *R* stereochemistry and the structure on the right has S stereochemistry, they are stereoisomers called enantiomers.

Exercise 3.4.2

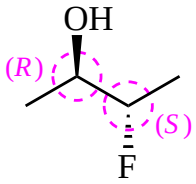
a) Since both structures have the same formula (C_2H_6O) but different connectivity of where the double bond is, they are structural isomers.

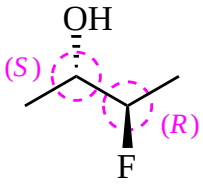
b) Both structures have the same formula and the same connectivity but the structure on the left has (*R*,S) stereochemistry and the structure on the right has (S,S) stereochemistry, they are stereoisomers that are diastereomers.





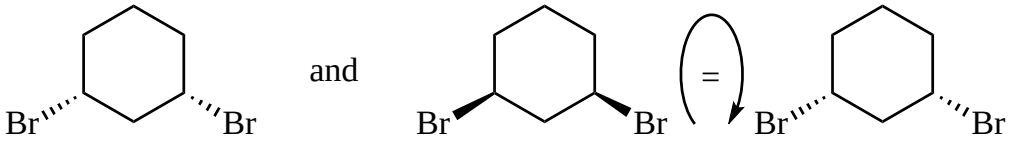
c) Both structures and have the same connectivity but their stereochemistry differs so they are stereoisomers. Since the one on the left is (R,S) and the one on the right is (S,R), they are non-super imposable mirror images of each other and enantiomers.



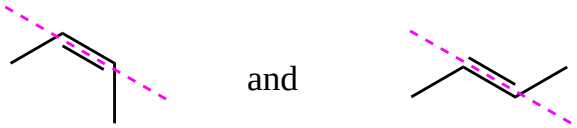


Exercise 3.4.3

a) Both structures have the same connectivity and same chemical formula and when you rotate the structure on the right you can see that these are the same compound both with (R,S) stereochemistry.



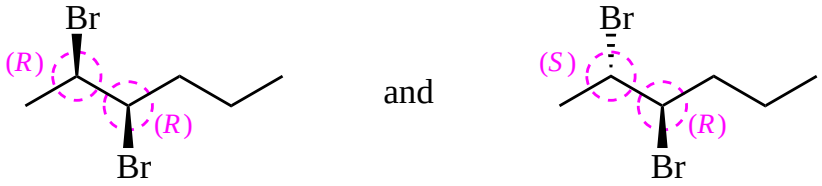
b)) Since both structures have the same formula (C_4H_8) and the same connectivity they are stereoisomers since they differ in what is known as cis/trans isomerism (covered more in Ch 7).Due to the pi bond between carbons 2 & 3, there is not free rotation between the C2-C3 bond so the structure on the left has the carbon chains on the same side of the double bond (cis) and the structure on the right has the carbon chains on opposite sides of the double bond (trans).



c) Looking at the structures below, you can see that they have the same formula ($C_6H_{13}Cl$) and different connectivity, so they are structural isomers.



d) Looking at the structures below, you can see that they have the same formula ($C_6H_{12}Br_2$) and the same connectivity, but the structure on the left is (*R*,*R*) and the structure on the right is (*S*,*R*) so since they differ by only one stereocenter, they are stereoisomers that are diastereomers (& epimers in this case).



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3.5: Properties of Alkenes and Alkynes

Learning Objectives

- To identify the physical properties of alkenes and describe trends in these properties.

The physical properties of alkenes are similar to those of the alkanes. The table at the start of the chapter shows that the boiling points of straight-chain alkenes increase with increasing molar mass, just as with alkanes. For molecules with the same number of carbon atoms and the same general shape, the boiling points usually differ only slightly, just as we would expect for substances whose molar mass differs by only 2 u (equivalent to two hydrogen atoms). Like other hydrocarbons, the alkenes are insoluble in water but soluble in organic solvents.

Looking Closer: Environmental Note

Alkenes occur widely in nature. Ripening fruits and vegetables give off ethylene, which triggers further ripening. Fruit processors artificially introduce ethylene to hasten the ripening process; exposure to as little as 0.1 mg of ethylene for 24 h can ripen 1 kg of tomatoes. Unfortunately, this process does not exactly duplicate the ripening process, and tomatoes picked green and treated this way don't taste much like vine-ripened tomatoes fresh from the garden.



The bright red color of tomatoes is due to lycopene—a polyene.

Other alkenes that occur in nature include 1-octene, a constituent of lemon oil, and octadecene ($C_{18}H_{36}$) found in fish liver. Dienes (two double bonds) and polyenes (three or more double bonds) are also common. Butadiene (CH_2=$CHCH$=CH_2) is found in coffee. Lycopene and the carotenes are isomeric polyenes ($C_{40}H_{56}$) that give the attractive red, orange, and yellow colors to watermelons, tomatoes, carrots, and other fruits and vegetables. Vitamin A, essential to good vision, is derived from a carotene. The world would be a much less colorful place without alkenes.

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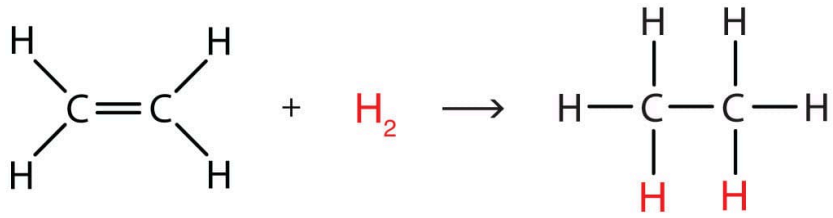
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3.6: Addition Reactions of Alkenes

Learning Objectives

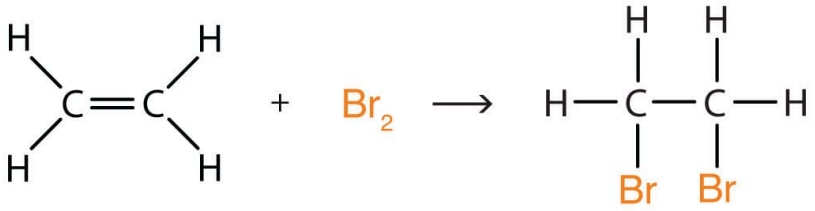
- To write equations for the addition reactions of alkenes with hydrogen, halogens, and water

Alkenes are valued mainly for addition reactions, in which one of the bonds in the double bond is broken. Each of the carbon atoms in the bond can then attach another atom or group while remaining joined to each other by a single bond. Perhaps the simplest addition reaction is hydrogenation—a reaction with hydrogen (H_2) in the presence of a catalyst such as nickel (Ni) or platinum (Pt).

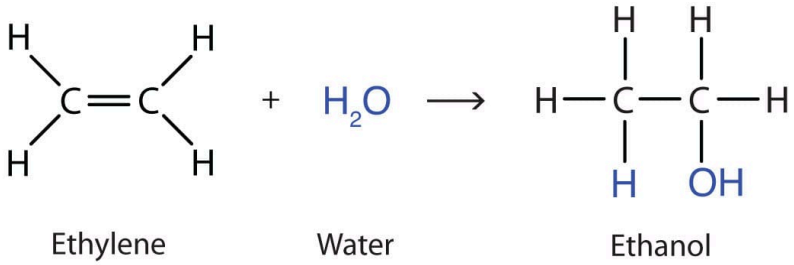


The product is an alkane having the same carbon skeleton as the alkene.

Alkenes also readily undergo halogenation—the addition of halogens. Indeed, the reaction with bromine (Br_2) can be used to test for alkenes. Bromine solutions are brownish red. When we add a Br_2 solution to an alkene, the color of the solution disappears because the alkene reacts with the bromine:



Another important addition reaction is that between an alkene and water to form an alcohol. This reaction, called hydration, requires a catalyst—usually a strong acid, such as sulfuric acid (H_2SO_4):



The hydration reaction is discussed later, where we deal with this reaction in the synthesis of alcohols.

Example 3.6.1

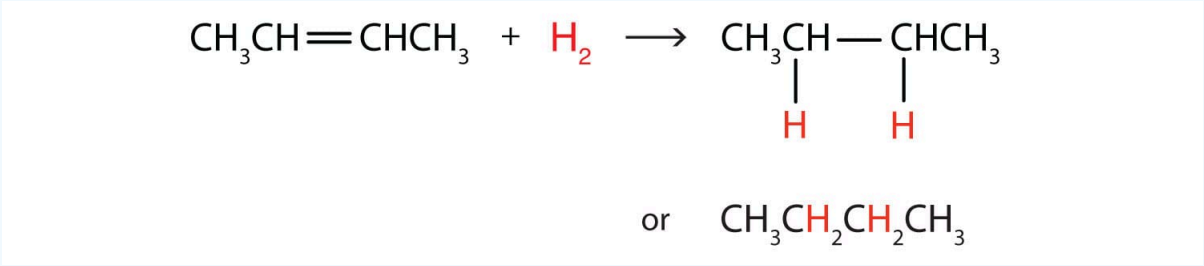
Write the equation for the reaction between $CH_3CH{=}CHCH_3$ and each substance.

a. H_2 (Ni catalyst)
b. Br_2
c. H_2O (H_2SO_4 catalyst)

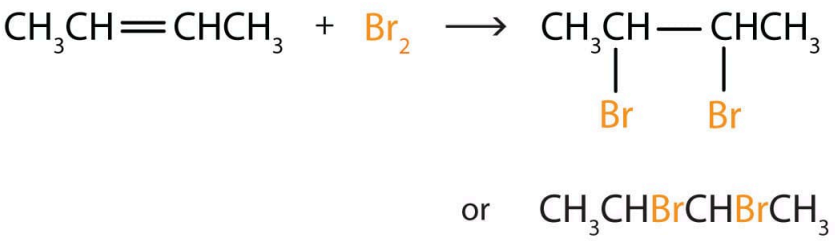
Solution

In each reaction, the reagent adds across the double bond.

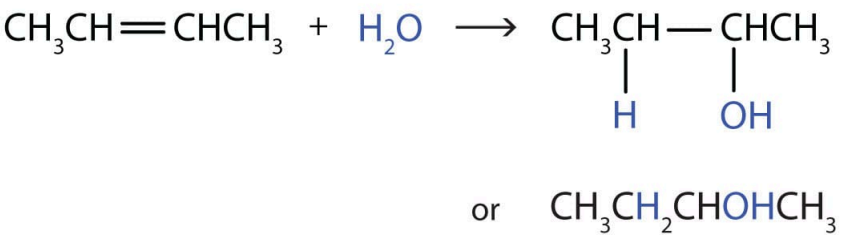
a.



-



-



Exercise 3.6.1

Write the equation for each reaction.

a. $CH_3CH_2CH{=}CH_2$ with H_2 (Ni catalyst)
b. $CH_3CH{=}CH_2$ with Cl_2
c. $CH_3CH_2CH{=}CHCH_2CH_3$ with H_2O (H_2SO_4 catalyst)

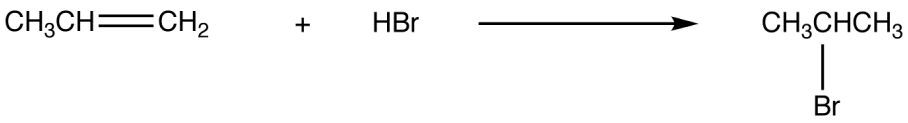
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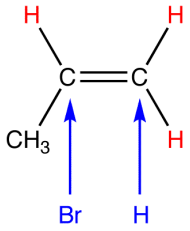
3.7: Markovnikov's Rule

Markovnikov's rule is an empirical rule used to predict regioselectivity of electrophilic addition reactions of alkenes and alkynes. It states that, in hydrohalogenation of an unsymmetrical alkene, the hydrogen atom in the hydrogen halide forms a bond with the doubly bonded carbon atom in the alkene, bearing the greater number of hydrogen atoms. (Morrison and Boyd in the fifth edition of *Organic Chemistry* quotes the King James Bible as a metaphor to Markovnikov's rule: Unto everyone that hath shall be given. In simpler language, the rich get richer.)

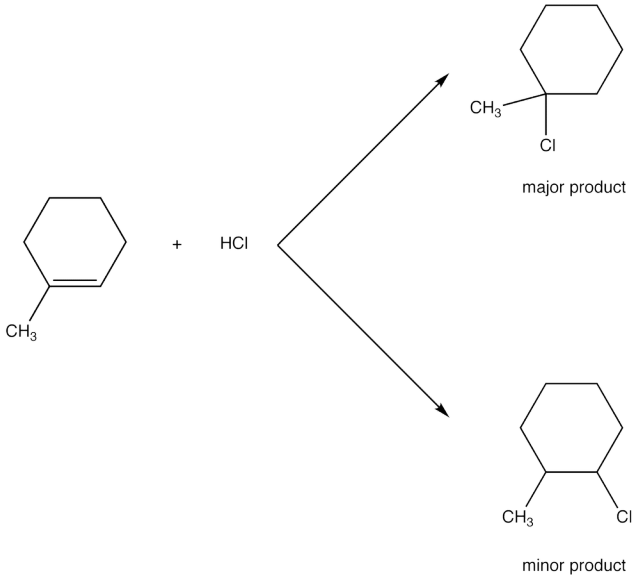
eg. 1:



To afford the observed product, the net reaction is addition of the hydrogen atom in HBr to the doubly bonded carbon atom in the alkene, bearing the greater number of hydrogen atoms.

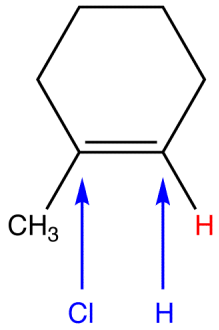


eg. 2:



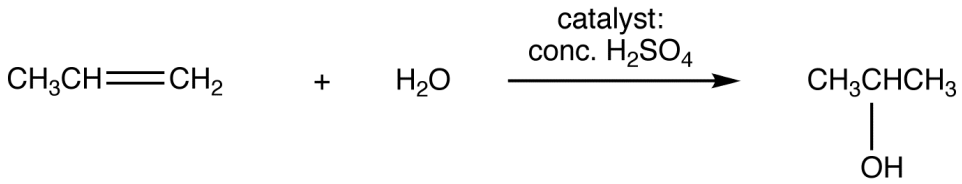
To afford the observed major product, the net reaction is addition of the hydrogen atom in HCl to the doubly bonded carbon atom in the alkene, bearing the greater number of hydrogen atoms.

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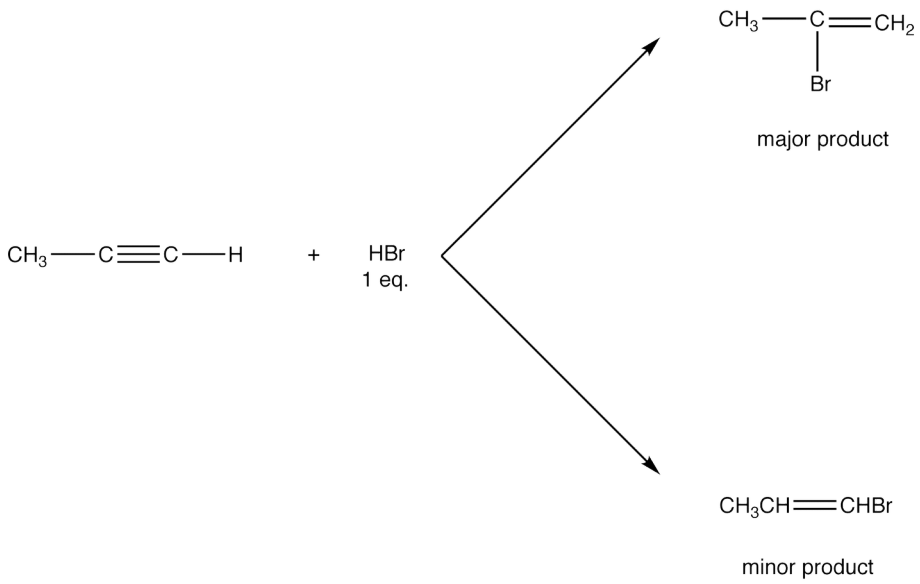


Although originally stated in relation to hydrohalogenation of unsymmetrical alkenes, Markovnikov's rule applies to some other electrophilic addition reactions of unsymmetrical alkenes (eg. 3) and to some electrophilic addition reactions of unsymmetrical alkynes (eg. 4).

eg. 3:



eg. 4:



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3.8: Aromatic Compounds- Benzene and Its Relatives

Learning Objective

- Name and identify aromatic compounds.

Benzene is the parent compound of the large family of organic compounds known as aromatic compounds. Unlike cyclohexane, benzene only contains six hydrogen atoms, giving the impression that the ring is unsaturated and each carbon atom participates in one double bond. Two different structures with alternating single and double bonds around the ring can be written for benzene.

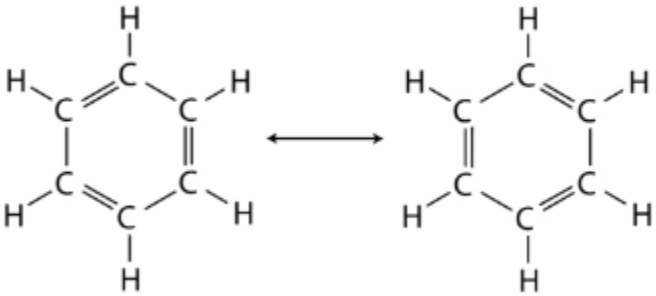


Figure 3.8.1 benzene

In benzene, the true bonding between carbon atoms is neither a single nor a double bond. Rather, all of the bonds are a hybrid of a single and double bond. In benzene, the pi bonding electrons are free to move completely around the ring. **Delocalized electrons** are electrons that are not confined to the bond between two atoms, but are instead allowed to move between three or more. The delocalization of the electrons in benzene can best be shown by showing benzene with a ring inside the hexagon, with the hydrogen atoms understood.

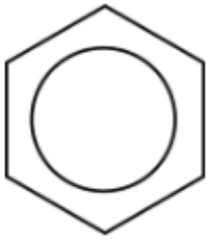


Figure 3.8.2 Delocalized electrons

Delocalization of the electrons makes for a more stable molecule than a similar molecule that does not have delocalized electrons. Benzene is a more stable and less reactive compound than straight-chain hexenes. The sp^2 hybridization of the carbon atoms results in a planar molecule as opposed to the puckered structure of cyclohexane.

There are many derivatives of benzene. The hydrogen atoms can be replaced by many different substituents. Aromatic compounds more readily undergo substitution reactions than addition reactions; replacement of one of the hydrogen atoms with another substituent will leave the delocalized double bonds intact. The following are typical examples of substituted benzene derivatives:

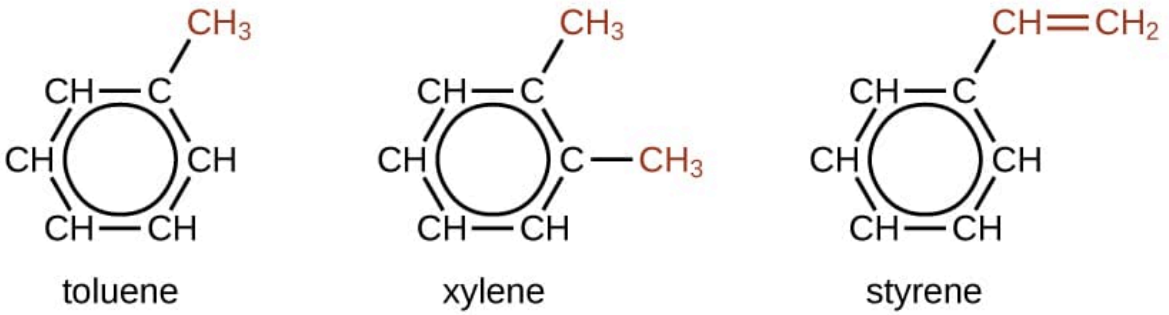


Figure 3.8.3 Three structural formulas are shown. The first is labeled toluene. This molecule has a six carbon hydrocarbon ring in which five of the C atoms are each bonded to only one H atom. At the upper right of the ring, the C atom that does not have a bonded H atom has a red C H subscript 3 group attached. A circle is at the center of the ring. The second is labeled xylene. This molecule has a six carbon hydrocarbon ring in which four of the C atoms are each bonded to only one H atom. At the upper right and right of the ring, the two C atoms that do not have bonded H atoms have C H subscript 3 groups attached. These C H subscript 3 groups appear in red. A circle is at the center of the ring. The third is labeled styrene. This molecule has a six carbon hydrocarbon ring in which five of the carbon atoms are each bonded to only one H atom. At the upper right of the ring, the carbon that does not have a bonded H atom has a red C H double bond C H subscript 2 group attached. A circle is at the center of the ring.

Toluene and xylene are important solvents and raw materials in the chemical industry. Styrene is used to produce the polymer polystyrene. The figure below shows the structural formulas for vanilla and naphthalene. Naphthalene is a chemical which is commonly used in mothballs. The vanilla molecule is extracted from vanilla beans.

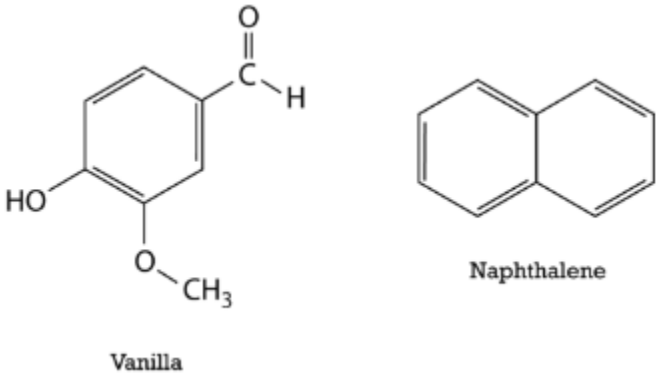


Figure 3.8.4 (left) vanilla molecule ; (right) naphthalene

Nomenclature of Aromatic Compounds

The simplest aromatic compounds are benzene rings with one substituent replacing one of the hydrogen atoms. If this substituent is an alkyl group, it is named first, followed in one word with "benzene". The molecule shown below is therefore called ethylbenzene.

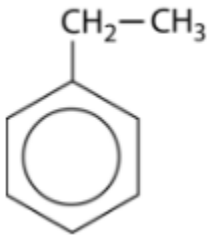


Figure 3.8.5 ethylbenzene

Substituents can be groups other than alkyl groups. If a chlorine atom were substituted for a hydrogen, the name becomes chlorobenzene. An $-NH_2$ group is called an amino group, so the corresponding molecule is called aminobenzene, often referred to as an aniline. An $-NO_2$ group is called a nitro group and so the third example below is nitrobenzene.

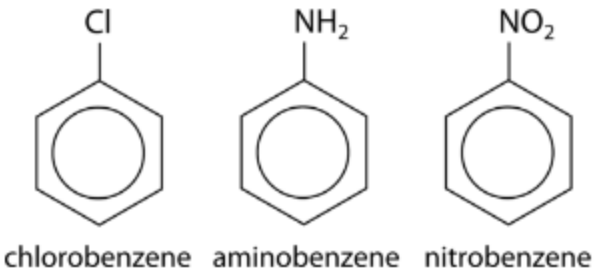


Figure 3.8.6 from left to right: chlorobenzene; aminobenzene; nitrobenzene

If more than one substituent is present, their location relative to each other can be indicated by numbering the positions on the benzene ring.

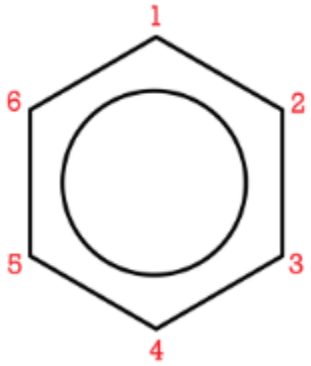


Figure 3.8.7 substituent locations relative to each other can be indicated by numbering the positions on the benzene ring

The number of the carbon location then precedes the name of the substituent in the overall name, with the numbers separated by a comma. As with branched alkanes, the system requires that the numbers be the lowest possible and that prefixes be used for more than one of the same substituent. If there are different substituents, the first in alphabetical order is given the lower number and listed first. The structures below are called 1,2-dimethylbenzene and 1-ethyl-4-methylbenzene.

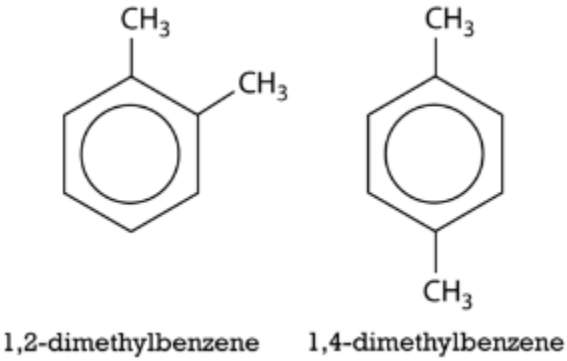


Figure 3.8.8 1,2-dimethylbenzene (left); 1-ethyl-4-methylbenzene (right)

An alternate system for naming di-substituted benzene rings uses three different prefixes: *ortho*, *meta*, and *para*. If two groups are in the **ortho** position, they are on adjacent carbon atoms. The **meta** positioning refers to being in a 1,3 arrangement. The **para** positioning refers to being in a 1,4 arrangement. Shown below are the three possibilities for dimethylbenzene, also called xylene.

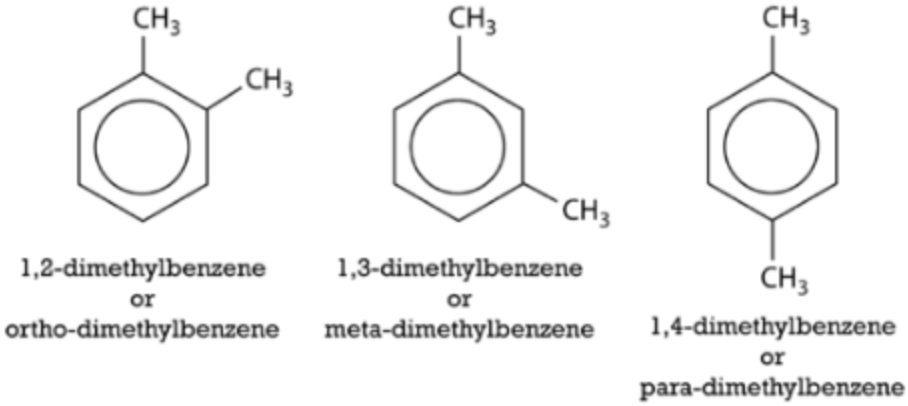


Figure 3.8.9 from left to right: ortho-dimethylbenzene; meta-dimethylbenzene ; para-dimethylbenzene

Lastly, a benzene ring missing one hydrogen atom $(-C_6H_5)$ can itself be considered the substituent on a longer chain of carbon atoms. That group is called a *phenyl* group and so the molecule below is called 2-phenylbutane.

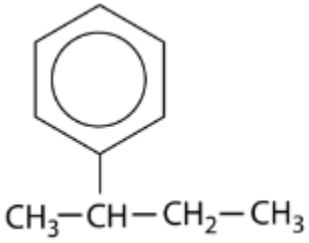


Figure 3.8.10 2-phenylbutane

Summary

- Aromatic hydrocarbons contain ring structures with delocalized π electron systems.
- Benzene is the parent compound of the large family of organic compounds known as aromatic compounds.
- Naming of aromatic compound i.e. benzene rings with different substituents is described.

Contributors and Attributions

-

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4: ORGANIC COMPOUNDS THAT CONTAIN OXYGEN, HALOGENS, OR SULFUR

4.1: Physical Properties of Ether

4.2: Ethers

4.3: Thiols and Disulfides

4.4: Background

4.5: Uses of Alcohols

4.6: Acidities of Alcohols

4.7: Nomenclature of Alcohols

4.8: Elimination Reactions of Alcohols

4.9: Oxidation of Alcohols

4.10: Oxidation by PCC (pyridinium chlorochromate)

4.11: Replacing the OH Group by Halogen Atoms

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4.1: Physical Properties of Ether

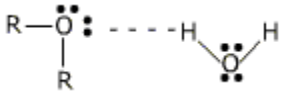
Dimethylether and ethyl methyl ether are gases at ordinary temperature. The other lower homologues are colorless, pleasant smelling, volatile liquids with typical ether smell.

Boiling points

The C - O bonds in ether are polar and thus ethers have a net dipole moment. The weak polarity of ethers do not appreciably affect their boiling points which are comparable to those of the alkenes of comparable molecular mass. Ethers have much lower boiling points as compared to isomeric alcohols. This is because alcohols molecules are associated by hydrogen bonds while ether molecules are not.

Solubility

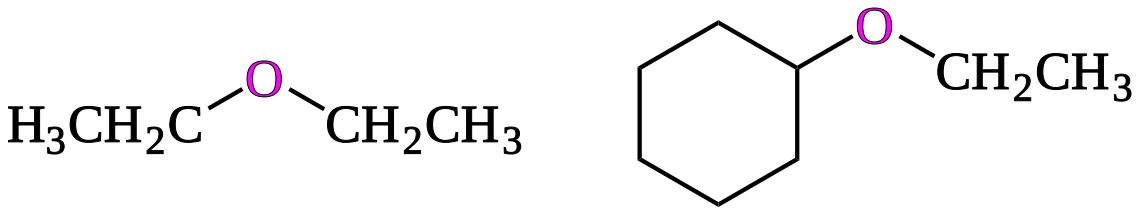
Ethers containing up to 3 carbon atoms are soluble in water, due to their hydrogen bond formation with water molecules.



The solubility decreases with increase in the number of carbon atoms. The relative increase in the hydrocarbon portion of the molecule decreases the tendency of H-bond formation. Ethers are appreciably soluble in organic solvents like alcohol, benzene, acetone etc.

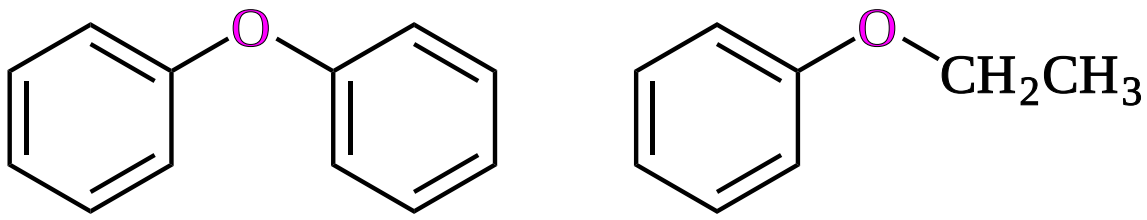
Structure of EthersEdit section

Ethers are a class of organic compounds that contain an sp^3 hybridized oxygen between two alkyl groups and have the formula R-O-R'. these compounds are used in dyes, perfumes, oils, waxes and other industrial uses. Aliphatic ethers have no aryl groups directly attached to the ether oxygen.



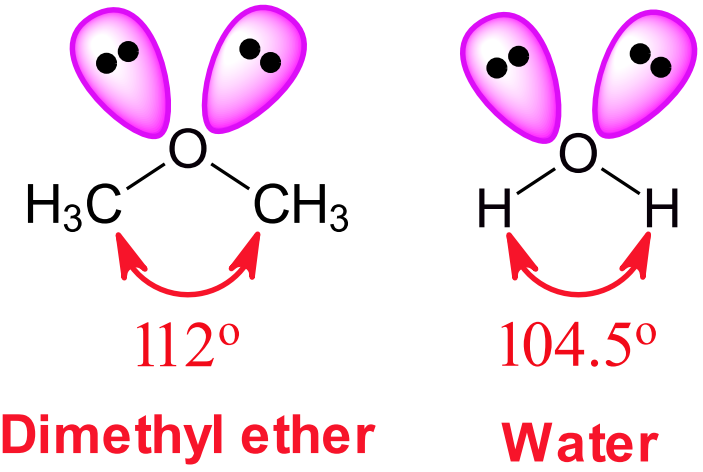
Examples of Aliphatic Ethers

Aromatic ethers have at least one aryl ring directly attached to the ether oxygen. In aryl ethers, the lone pair elections on oxygen are conjugated with the aromatic ring which significantly changes the properties of the ether.

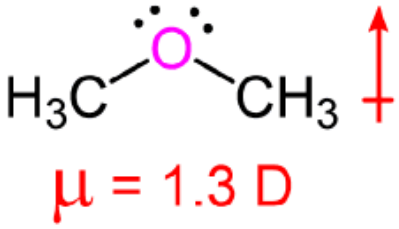


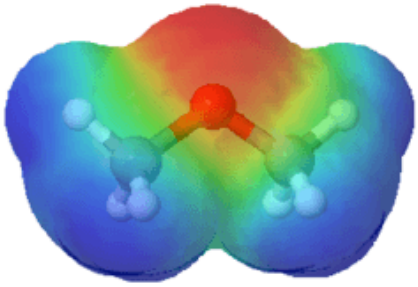
Example of Aromatic Ethers

The sp^3 hybridization of oxygen gives ethers roughly the same geometry as alcohols and water. The R-O-R' bond angle is close to what is expected in a tetrahedral geometry. The bond angle of dimethyl ether is 112^o which is larger than the H-O-H bond angle in water (104.5^o) due to the steric repulsion of the methyl groups.



The presence of an electronegative oxygen atom gives ethers a small dipole moment.





Comparisons of Physical Properties of Alcohols and Ethers

Ethers, unlike alcohols, have no hydrogen atom on the oxygen atom (that is, no OH group). Therefore, there is no intermolecular hydrogen bonding between ether molecules, which makes their boiling points much lower than an alcohol with similar mass. Despite the presence of a small dipole moment, ethers have boiling points that about the same alkanes of comparable molar mass. (Table 18.1.2).

Table 18.1.2 Comparison of Boiling Points of Alkanes, Alcohols, and Ethers

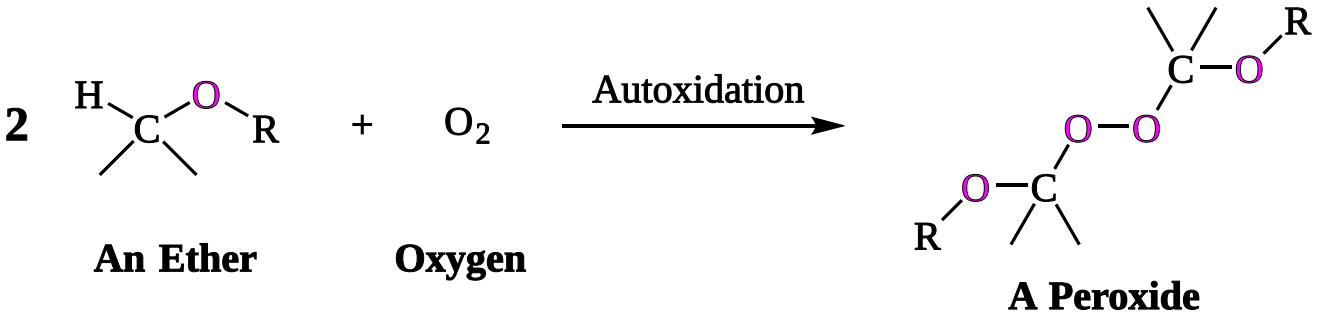
Condensed Structural Formula	Name	Molar Mass	Boiling Point (°C)	Intermolecular Hydrogen Bonding in Pure Liquid?
$CH_3CH_2CH_3$	propane	44	–42	no
CH_3OCH_3	dimethyl ether	46	–25	no
CH_3CH_2OH	ethyl alcohol	46	78	yes
$CH_3CH_2CH_2CH_2CH_3$	pentane	72	36	no
$CH_3CH_2OCH_2CH_3$	diethyl ether	74	35	no

Condensed Structural Formula	Name	Molar Mass	Boiling Point (°C)	Intermolecular Hydrogen Bonding in Pure Liquid?
$CH_3CH_2CH_2CH_2OH$	butyl alcohol	74	117	yes

Ether molecules do have an oxygen atom, however, and engage in hydrogen bonding with water molecules. Consequently, an ether has about the same solubility in water as the alcohol that is isomeric with it. For example, dimethyl ether and ethanol (both having the molecular formula C_2H_6O) are completely soluble in water, whereas diethyl ether and 1-butanol (both $C_4H_{10}O$) are barely soluble in water (8 g/100 mL of water).

Peroxide Formation

Many ethers can react with oxygen to form explosive peroxide compounds n a free radical process called autoxidation. For this reason ethers should not be stored for long periods of time and should not be stored in glass bottles. The danger is particularly acute when ether solutions are distilled to near dryness. The hydroperoxides can become more concentrated during a distillation because they tend to have a slightly higher boiling point than the corresponding ether. Before performing an ether distillation great care should be taken to test for the presence of peroxides.



Contributors

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4.2: Ethers

Learning Objectives

- Describe the structural difference between an alcohol and an ether that affects physical characteristics and reactivity of each.
- Name simple ethers.
- Describe the structure and uses of some ethers.

With the general formula ROR′, an ether may be considered a derivative of water in which both hydrogen atoms are replaced by alkyl or aryl groups. It may also be considered a derivative of an alcohol (ROH) in which the hydrogen atom of the OH group is been replaced by a second alkyl or aryl group:

$$\mathrm{HOH} \xrightarrow[\text{H atoms}]{\text{replace both}} \mathrm{ROR'} \xleftarrow[\text{of OH group}]{\text{replace H atom}} \mathrm{ROH}$$

Simple ethers have simple common names, formed from the names of the groups attached to oxygen atom, followed by the generic name *ether*. For example, CH_3–O–$CH_2CH_2CH_3$ is methyl propyl ether. If both groups are the same, the group name should be preceded by the prefix *di-*, as in dimethyl ether (CH_3–O–CH_3) and diethyl ether CH_3CH_2–O–CH_2CH_3.

Ether molecules have no hydrogen atom on the oxygen atom (that is, no OH group). Therefore there is no intermolecular hydrogen bonding between ether molecules, and ethers therefore have quite low boiling points for a given molar mass. Indeed, ethers have boiling points about the same as those of alkanes of comparable molar mass and much lower than those of the corresponding alcohols (Table 4.2.1).

Table 4.2.1: Comparison of Boiling Points of Alkanes, Alcohols, and Ethers

Condensed Structural Formula	Name	Molar Mass	Boiling Point (°C)	Intermolecular Hydrogen Bonding in Pure Liquid?
$CH_3CH_2CH_3$	propane	44	–42	no
CH_3OCH_3	dimethyl ether	46	–25	no
CH_3CH_2OH	ethyl alcohol	46	78	yes
$CH_3CH_2CH_2CH_2CH_3$	pentane	72	36	no
$CH_3CH_2OCH_2CH_3$	diethyl ether	74	35	no

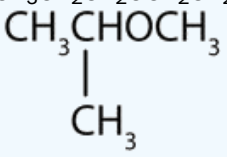
Condensed Structural Formula	Name	Molar Mass	Boiling Point (°C)	Intermolecular Hydrogen Bonding in Pure Liquid?
$CH_3CH_2CH_2CH_2OH$	butyl alcohol	74	117	yes

Ether molecules do have an oxygen atom, however, and engage in hydrogen bonding with water molecules. Consequently, an ether has about the same solubility in water as the alcohol that is isomeric with it. For example, dimethyl ether and ethanol (both having the molecular formula C_2H_6O) are completely soluble in water, whereas diethyl ether and 1-butanol (both $C_4H_{10}O$) are barely soluble in water (8 g/100 mL of water).

Example 4.2.1

What is the common name for each ether?

a. $CH_3CH_2CH_2OCH_2CH_2CH_3$

b. 

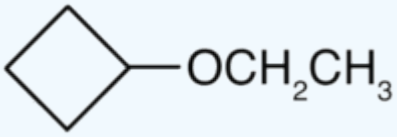
Solution

a. The carbon groups on either side of the oxygen atom are propyl ($CH_3CH_2CH_2$) groups, so the compound is dipropyl ether.
b. The three-carbon group is attached by the middle carbon atom, so it is an isopropyl group. The one-carbon group is a methyl group. The compound is isopropyl methyl ether.

Exercise 4.2.1

What is the common name for each ether?

a. $CH_3CH_2CH_2CH_2OCH_2CH_2CH_2CH_3$

b. 

IUPAC Naming Rules for Ethers

1. **Identify the Longest Carbon Chain**: Determine the longest carbon chain attached to the oxygen atom. This chain will serve as the parent hydrocarbon.
2. **Name the Alkoxy Group**: The shorter carbon chain attached to the oxygen atom is named as an alkoxy group. This is done by replacing the "-yl" suffix of the alkyl group with "-oxy." For example, a methyl group (CH_3) becomes methoxy (CH_3O-).
3. **Combine the Names**: Place the name of the alkoxy group before the name of the parent hydrocarbon. The position of the alkoxy group is indicated by a number, if necessary, to show its location on the parent chain.

Examples:

- **Methoxyethane**: $CH_3OCH_2CH_3$
  - The longest chain is ethane (2 carbons).
  - The methoxy group (CH_3O-) is attached to the first carbon.
- **1-Ethoxypropane**: $CH_3CH_2OCH_2CH_2CH_3$
  - The longest chain is propane (3 carbons).
  - The ethoxy group (CH_3CH_2O-) is attached to the first carbon.
- **1-Methoxybutane**: $CH_3OCH_2CH_2CH_2CH_3$
  - The longest chain is butane (4 carbons).
  - The methoxy group (CH_3O-) is attached to the first carbon.
- **1-Methoxy-2-methylpropane**: $CH_3OCH_2CH(CH_3)_2$
  - The longest chain is propane (3 carbons).
  - The methoxy group (CH_3O-) is attached to the first carbon, and there is a methyl group on the second carbon.
- **1-Butoxybutane**: $CH_3CH_2CH_2CH_2OCH_2CH_2CH_2CH_3$
  - The longest chain is butane (4 carbons).
  - The butoxy group ($CH_3CH_2CH_2CH_2O$-) is attached to the first carbon.

These rules help in systematically naming ethers, ensuring clarity and consistency in chemical nomenclature.

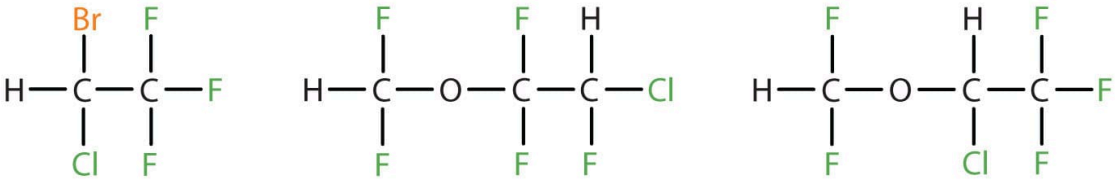
To Your Health: Ethers as General Anesthetics

A *general anesthetic* acts on the brain to produce unconsciousness and a general insensitivity to feeling or pain. Diethyl ether ($CH_3CH_2OCH_2CH_3$) was the first general anesthetic to be used.



William Morton, a Boston dentist, introduced diethyl ether into surgical practice in 1846. This painting shows an operation in Boston in 1846 in which diethyl ether was used as an anesthetic. Inhalation of ether vapor produces unconsciousness by depressing the activity of the central nervous system. Source: Painting of William Morton by Ernest Board.

Diethyl ether is relatively safe because there is a fairly wide gap between the dose that produces an effective level of anesthesia and the lethal dose. However, because it is highly flammable and has the added disadvantage of causing nausea, it has been replaced by newer inhalant anesthetics, including the fluorine-containing compounds halothane, enflurane, and isoflurane. Unfortunately, the safety of these compounds for operating room personnel has been questioned. For example, female operating room workers exposed to halothane suffer a higher rate of miscarriages than women in the general population.



Halothane Enflurane Isoflurane

These three modern, inhalant, halogen-containing, anesthetic compounds are less flammable than diethyl ether.

YouTube Video

This interactive element is not available in this format. Visit the link or scan the QR code to access it online.

View this YouTube Video online

Summary

To give ethers common names, simply name the groups attached to the oxygen atom, followed by the generic name *ether*. If both groups are the same, the group name should be preceded by the prefix *di-*. To give ethers IUPAC names, place the name of the alkoxy group before the name of the parent hydrocarbon. The position of the alkoxy group is indicated by a number, if necessary, to show its location on the parent chain. Ether molecules have no OH group and thus no intermolecular hydrogen bonding. Ethers therefore have quite low boiling points for a given molar mass. Ether molecules have an oxygen atom and can engage in hydrogen bonding with water molecules. An ether molecule has about the same solubility in water as the alcohol that is isomeric with it.

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4.3: Thiols and Disulfides

Learning Objectives

- Identify thiols (mercaptans) by the presence of an SH group.
- The mild oxidation of thiols gives disulfides.

Because sulfur is in the same group (6A) of the periodic table as oxygen, the two elements have some similar properties. We might expect sulfur to form organic compounds related to those of oxygen, and indeed it does. Thiols (also called mercaptans), which are sulfur analogs of alcohols, have the general formula RSH. Methanethiol (also called methyl mercaptan), has the formula CH_3SH. Ethanethiol (ethyl mercaptan) is the most common odorant for liquid propane (LP) gas.

The mild oxidation of thiols gives compounds called disulfides.

$$2\mathrm{RSH} \xrightarrow{[O]} \mathrm{RSSR}$$

The amino acids cysteine [$HSCH_2CH(NH_2)COOH$] and methionine [$CH_3SCH_2CH_2CH(NH_2)COOH$] contain sulfur atoms, as do all proteins that contain these amino acids. Disulfide linkages (–S–S–) between protein chains are extremely important in protein structure.

Thioethers, which are sulfur analogs of ethers, have the form general formula RSR′. An example is dimethylsulfide (CH_3SCH_3), which is responsible for the sometimes unpleasant odor of cooking cabbage and related vegetables. Note that methionine has a thioether functional group.

Career Focus: Paramedic

Paramedics are highly trained experts at providing emergency medical treatment. Their critical duties often include rescue work and emergency medical procedures in a wide variety of settings, sometimes under extremely harsh and difficult conditions. Like other science-based professions, their work requires knowledge, ingenuity, and complex thinking, as well as a great deal of technical skill. The recommended courses for preparation in this field include anatomy, physiology, medical terminology, and—not surprisingly—chemistry. An understanding of basic principles of organic chemistry, for example, is useful when paramedics have to deal with such traumas as burns from fuel (hydrocarbons) or solvent (alcohols, ethers, esters, and so on) fires and alcohol and drug overdoses.

To become a paramedic requires 2–4 y of training and usually includes a stint as an emergency medical technician (EMT). An EMT provides basic care, can administer certain medications and treatments, such as oxygen for respiratory problems and epinephrine (adrenalin) for allergic reactions, and has some knowledge of common medical conditions. A paramedic, in contrast, must have extensive knowledge of common medical problems and be trained to administer a wide variety of emergency drugs.

Paramedics usually work under the direction of a medical doctor with a title such as “medical director.” Some paramedics are employed by fire departments and may work from a fire engine that carries medical equipment as well as fire-fighting gear. Some work from hospital-sponsored ambulances and continue to care for their patients after reaching the hospital emergency room. Still other paramedics work for a government department responsible for emergency health care in a specific geographical area. Finally, some work for private companies that contract to provide service for a government body.

An experienced paramedic has a broad range of employment options, including training for mountain or ocean rescue, working with police department special weapons and tactics (SWAT) teams, or working in isolated settings such as on oil rigs. With their expertise at treating and stabilizing patients before quickly moving them to a hospital, paramedics often provide the first critical steps in saving an endangered life. The following quotation, inscribed on the Arlington National Cemetery headstone of Army Lieutenant R. Adams Cowley, who is often called the “father” of shock trauma medicine, serves as the motto for many paramedic units: “Next to creating a life the finest thing a man can do is save one.” —Abraham Lincoln

Summary

Thiols, thioethers, and disulfides are common in biological compounds.

Concept Review Exercises

1. What is the functional group of a thiol? Write the condensed structural formula for ethanethiol (ethyl mercaptan).
2. What is the functional group of a disulfide? Write the condensed structural formula for dipropyl disulfide.

Answers

1. SH; CH_3CH_2SH
2. –S–S–; $CH_3CH_2CH_2SSCH_2CH_2CH_3$

Exercises

1. A common natural gas odorant is *tert*-butyl mercaptan. What is its condensed structural formula?
2. Write the equation for the oxidation of ethanethiol to diethyl disulfide.

Answer

1. $(CH_3)_3CSH$

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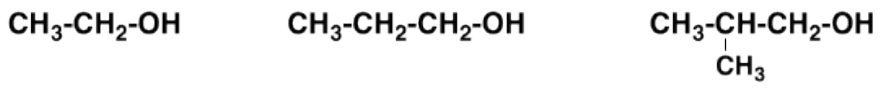
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4.4: Background

This page defines an alcohol, and explains the differences between primary, secondary and tertiary alcohols. It examines in some detail their simple physical properties such as solubility and boiling points. Alcohols are compounds in which one or more hydrogen atoms in an alkane have been replaced by an -OH group. Alcohols fall into different classes depending on how the -OH group is positioned on the chain of carbon atoms. There are some chemical differences between the various types.

Primary alcohols

In a primary (1°) alcohol, the carbon atom that carries the -OH group is only attached to one alkyl group. Some examples of primary alcohols are shown below:

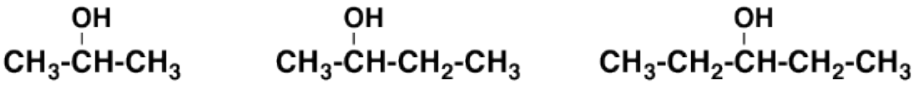


ethanol propan-1-ol 2-methylpropan-1-ol

Notice that the complexity of the attached alkyl group is irrelevant. In each case there is only one linkage to an alkyl group from the CH_2 group holding the -OH group. There is an exception to this. Methanol, CH_3OH, is counted as a primary alcohol even though there are no alkyl groups attached to the the -OH carbon atom.

Secondary alcohols

In a secondary (2°) alcohol, the carbon atom with the -OH group attached is joined directly to two alkyl groups, which may be the same or different. Examples include the following:



propan-2-ol butan-2-ol pent-3-ol

Tertiary alcohols

In a tertiary (3°) alcohol, the carbon atom holding the -OH group is attached directly to three alkyl groups, which may be any combination of the same or different groups. Examples of tertiary alcohols are given below:



2-methylpropan-2-ol 2-methylbutan-2-ol

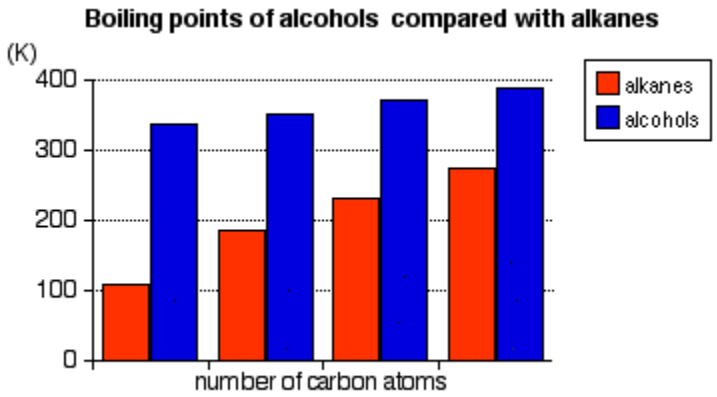
Physical properties of alcohols

Boiling Points

The chart below shows the boiling points of the following simple primary alcohols with up to 4 carbon atoms:

CH_3OH	CH_3CH_2OH	$CH_3CH_2CH_2OH$	$CH_3CH_2CH_2CH_2OH$
methanol	ethanol	propan-1-ol	butan-1-ol

These boiling points are compared with those of the equivalent alkanes (methane to butane) with the same number of carbon atoms.



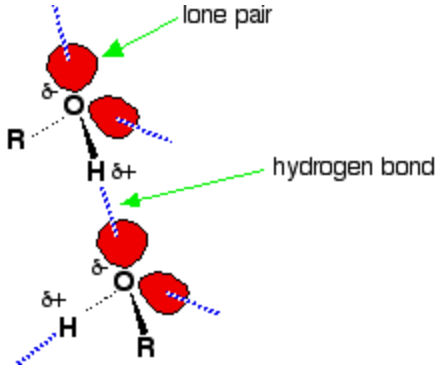
Notice that:

- The boiling point of an alcohol is always significantly higher than that of the analogous alkane.
- The boiling points of the alcohols increase as the number of carbon atoms increases.

The patterns in boiling point reflect the patterns in intermolecular attractions.

Hydrogen bonding

Hydrogen bonding occurs between molecules in which a hydrogen atom is attached to a strongly electronegative element: fluorine, oxygen or nitrogen. In the case of alcohols, hydrogen bonds occur between the partially-positive hydrogen atoms and lone pairs on oxygen atoms of other molecules.



The hydrogen atoms are slightly positive because the bonding electrons are pulled toward the very electronegative oxygen atoms. In alkanes, the only intermolecular forces are van der Waals dispersion forces. Hydrogen bonds are much stronger than these; therefore, more energy is required to separate alcohol molecules than to separate alkane molecules. This is the main reason for higher boiling points in alcohols.

Physical Properties of Alchols and Selected Analogous Haloalkanes and Alkanes

Compound	IUPAC Name	Common Name	Melting Poing (°C)	Boiling Point (°C)	Solubility in H_2O at 23°C
CH_3OH	Methanol	Methyl alcohol	-97.8	65.0	Infinite
CH_3Cl	Chloromethane	Methyl chloride	-97.7	-24.2	0.74 g/100 mL
CH_4	Methane		-182.5	-161.7	3.5 mL (gas)/ 100 mL
CH_3CH_2OH	Ethanol	Ethyl alcohol	-114.7	78.5	Infinite
CH_3CH_2Cl	Chloroethane	Ethyl chloride	-136.4	12.3	0.447 g/100 mL
CH_3CH_3	Ethane		-183.3	-88.6	4.7 mL (gas)/ 100 mL
$CH_3CH_2CH_2OH$	1-Propanol	Propyl alcohol	-126.5	97.4	Infinite
$CH_3CH_2CH_3$	Propane		-187.7	-42.1	6.5 mL (gas)/ 100 mL
$CH_3CH_2CH_2CH_2OH$	1-Butanol	Butyl alcohol	-89.5	117.3	8.0 g/100 mL
$CH_3(CH_2)_4OH$	1-Pentanol	Pentyl alcohol	-79	138	2.2 g/100 mL

This table shows that alcohols (in red) have higher boiling points and greater solubility in H_2O than haloalkanes and alkanes with the same number of carbons. It also shows that the boiling point of alcohols increase with the number of carbon atoms.

The effect of van der Waals forces

- **Boiling points of alcohols**: Hydrogen bonding is not the only intermolecular force alcohols experience. They also experience van der Waals dispersion forces and dipole-dipole interactions. The hydrogen bonding and dipole-dipole interactions are similar for all alcohols, but dispersion forces increase as the size of the alcohols increase. These attractions become stronger as the molecules lengthen and contain more electrons. This increases the sizes of the temporary dipoles formed. This is why the boiling points increase as the number of carbon atoms in the chains increases. It takes more energy to overcome the dispersion forces; thus, the boiling points rise.
- **Comparison between alkanes and alcohols**: Even without any hydrogen bonding or dipole-dipole interactions, the boiling point of the alcohol would be higher than the corresponding alkane with the same number of carbon atoms.

Compare ethane and ethanol:

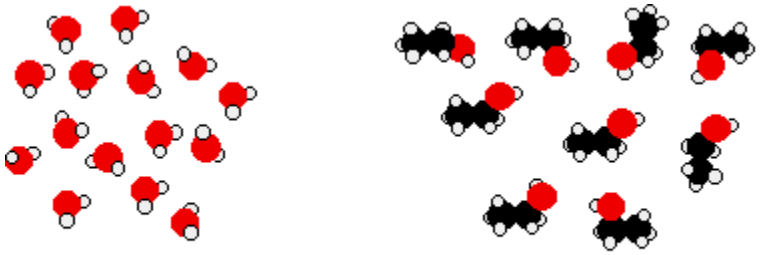


Ethanol is a longer molecule, and the oxygen atom brings with it an extra 8 electrons. Both of these increase the size of the van der Waals dispersion forces, and subsequently the boiling point. A more accurate measurement of the effect of the hydrogen bonding on boiling point would be a comparison of ethanol with propane rather than ethane. The lengths of the two molecules are more similar, and the number of electrons is exactly the same.

Solubility of alcohols in water

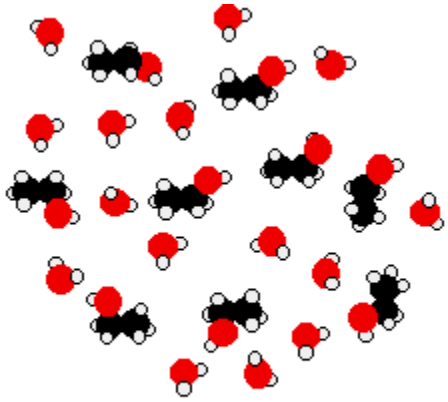
Small alcohols are completely soluble in water; mixing the two in any proportion generates a single solution. However, solubility decreases as the length of the hydrocarbon chain in the alcohol increases. At four carbon atoms and beyond, the decrease in solubility is noticeable; a two-layered substance may appear in a test tube when the two are mixed.

Consider ethanol as a typical small alcohol. In both pure water and pure ethanol the main intermolecular attractions are hydrogen bonds.



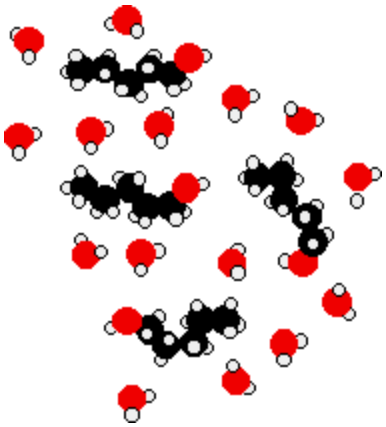
Both of these are held together mainly by hydrogen bonding.

In order to mix the two, the hydrogen bonds between water molecules and the hydrogen bonds between ethanol molecules must be broken. Energy is required for both of these processes. However, when the molecules are mixed, new hydrogen bonds are formed between water molecules and ethanol molecules.



New hydrogen bonds are set up between ethanol and water molecules.

The energy released when these new hydrogen bonds form approximately compensates for the energy needed to break the original interactions. In addition, there is an increase in the disorder of the system, an increase in entropy. This is another factor in deciding whether chemical processes occur. Consider a hypothetical situation involving 5-carbon alcohol molecules.



The hydrocarbon chains are forced between water molecules, breaking hydrogen bonds between those water molecules. The -OH ends of the alcohol molecules can form new hydrogen bonds with water molecules, but the hydrocarbon "tail" does not form hydrogen bonds. This means that many of the original hydrogen bonds being broken are never replaced by new ones.

In place of those original hydrogen bonds are merely van der Waals dispersion forces between the water and the hydrocarbon "tails." These attractions are much weaker, and unable to furnish enough energy to compensate for the broken hydrogen bonds. Even allowing for the increase in disorder, the process becomes less feasible. As the length of the alcohol increases, this situation becomes more pronounced, and thus the solubility decreases.

Contributors

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4.5: Uses of Alcohols

This page briefly discusses some of the important uses of simple alcohols, such as methanol, ethanol and propan-2-ol.

Alcoholic Drinks

The word "alcohol" in alcoholic drinks refers to ethanol (CH_3CH_2OH).

Industrial methylated spirits

Ethanol is usually sold as industrial methylated spirits, which is ethanol with a small quantity of methanol and possibly some color added. Because methanol is poisonous, industrial methylated spirits are unfit to drink, allowing purchasers to avoid the high taxes levied on alcoholic drinks.

Use of ethanol as a fuel

Ethanol burns to produce carbon dioxide and water, as shown in the equation below, and can be used as a fuel in its own right or in mixtures with petrol (gasoline). "Gasohol" is a petrol/ethanol mixture containing approximately 10–20% ethanol. Because ethanol can be produced by fermentation, this is a useful method for countries without an oil industry to reduce the amount of petrol imports.

$$CH_3CH_2OH + 3O_2 \rightarrow 2CO_2 + 3H_2O \tag{4.5.1}$$

Ethanol as a solvent

Ethanol is widely used as a solvent. It is relatively safe and can be used to dissolve many organic compounds that are insoluble in water. It is used, for example, in many perfumes and cosmetics.

Methanol as a fuel

Methanol also burns to form carbon dioxide and water:

$$2CH_3OH + 3O_2 \rightarrow 2CO_2 + 4H_2O \tag{4.5.2}$$

It can be used a a petrol additive to improve combustion, and its use as a fuel in its own right is under investigation.

Methanol as an industrial feedstock

Most methanol is used to make other compounds, for example, methanal (formaldehyde), ethanoic acid, and methyl esters of various acids. In most cases, these are then converted into further products.

Contributors

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4.6: Acidities of Alcohols

Alcohols are very weak Brønsted acids with pK_a values generally in the range of 15 - 20. Because the hydroxyl proton is the most electrophilic site, proton transfer is the most important reaction to consider with nucleophiles. There are small differences in the acidities of aliphatic alcohols in aqueous solution, which are due to differences in structure and, more importantly, solvation.

General Assessment of Acidities

When considering alcohols as organic reagents, pK_as are often used because they reflect reactivity in aqueous solution. In general, alcohols in aqueous solution are slightly less acidic than water. However, the differences among the pK_as of the alcohols are not large. This is not surprising because all alcohols are oxy-acids (OH), and the differences in acidities are due to the effect of substituents in the 1-position removed from the acidic site. Moreover, the more highly substituted alcohols vary only in the structure two positions removed from the acidic site. The marginal effects of additional substituents at the carbon tow positions removed from the acidic site are even evident in the gas-phase enthalpies of reaction for the reaction

$$ROH \rightarrow RO^- + H^+ \tag{1}$$

The pK_as and gas-phase enthalpies of reaction for various alcohols, ROH, with various substituents (R) are shown in Table 1 below.

Table 1: *pK_as and gas-phase enthalpies of reaction*

R	Name	pKa1	ΔH_{acid} kJ/mol^2
H	water	14.0	1633.1
CH_3	methanol	15.5	1597 ± 6
CH_3CH_2	ethanol	15.9	1587 ± 4
$(CH_3)_2CH$	propan-2-ol (isopropyl alcohol)	16.5	1569 ± 4
$(CH_3)_3C$	2-methylpropan-2-ol (t-butanol)	17	1568 ± 4
C_6H_5 (phenyl)	phenol	9.95	1462 ± 10

Interpretation of the Relative Acidities of Alcohols

There are many sites on the internet with explanations of the relative ordering of alcohol acidities **in aqueous solution**. The general explanation is that the larger substituents are better electron donors, which destabilize the resulting alkoxide anions. Because hydrogen is least donating of the substituents, water is the strongest acid. Unfortunately, although this belief persists, it is incomplete because it does not account for the gas-phase results. The problem with the electron donation explanation is that it suggests that the order of acidity is due solely to the intrinsic electronic effects of the substituents. However, if that were the case, the electron donating effect should also be evident in the gas-phase data. However, the relative acidities in the gas phase are opposite to those in aqueous solution. Consequently, any interpretation of the acidities of alcohols must take the gas phase data into account.

The inversion of the acidities of alcohols between the gas phase and aqueous solution was pointed out by Brauman and Blair in 1968.[3] They proposed that the ordering of acidities of alcohols **in solution** is predominantly due to the combination of a) polarizibility and b) solvation, and that the electron donating ability of the substituent does not play a significant role.[4]

Polarizibility almost completely accounts for the trend in gas-phase acidities. As the size of the substituent increases, the acid becomes stronger due to the ability for the charge to be distributed over a larger volume, thereby reducing the charge density and, consequently, the Coulombic repulsion. Therefore, in the gas-phase, t-butanol is the most acidic alcohol, more acidic than isopropanol, followed by ethanol and methanol. In the gas phase, water is much less acidic than methanol, which is consistent with the difference in polarizibility between a proton and a methyl group. As before, the fact that water is less acidic than methanol in the gas phase is not consistent with the expected electronic donating capabilities of the two substituents. Given the absence

of a solvent, the gas-phase properties reflect the instrinsic effects on the acidities.

In solution, however, the ions can be stabilized by solvation, and this is what leads to the inversion of acidity ordering. Brauman and Blair[3] showed that smaller ions are better stabilized by solvation, which is consistent with the Born equation. Therefore, methanol is more acidic than t-butanol because the smaller methoxide ion has a shorter radius of solvation, leading to a larger solvation energy, which overcomes the stabilization that results from polarization of the charge. Because the solvation energy of hydroxide is even larger than that of methoxide, water is more acidic than methanol.

Note: Phenol

Discussions of acidities of alcohols usually include phenol in which the enhanced acidity is generally attributed to stabilization of the phenoxide ion by resonance delocalization. In this case, the gas-phase results agree with the solution trend that phenol is a much stronger acid than the aliphatic alcohols, and the difference is certainly due to electronic effects. However, this commonly encountered explanation is incomplete because it ignores the role that inductive effects have on acidities of oxy-acids. However, it is true that the acidity of phenol is much more a result of resonance stabilization than, for example, the acidities of carboxylic acids.

Practical Considerations

With pK_a values in the 15.5 - 20.0 range, useful concentrations of alkoxides cannot be formed by proton transfer with hydroxide:

$$ROH + OH^- \rightarrow RO^- + H_2O \tag{2}$$

The equilibrium constant for the proton transfer reaction is on the order of 10^{-2}-10^{-5}. Phenoxide can be formed almost completely by reaction with aqueous alkaline base because the value of the equilibrium constant is roughly 10^4. The acidity of alcohols also indicates that it will react by proton transfer with any base more basic than hydroxide, which includes most organic bases, such as acetylide ions, cyanide, and vinyl/phenyl/alkyl anions. Therefore, alcohols will protonate most organic nucleophiles and effectively destroy most organometallic reagents, including Grignard or organolithium reagents.

Formation of alkoxide ions

Alkoxide ions can be formed by deprotonating alcohols with an extremely strong base such as an amide ion, NH_2^-. However, this method is rarely used. Alkoxides are more often formed by reaction of an alkali metal such as sodium with the pure alcohol:

$$2ROH + 2Na \rightarrow 2RO^- + 2Na^+ + H_2 \tag{3}$$

Conclusions

Relative acidities of all acids depend on many factors, including intrinsic electronic factors such as electronegativity, inductive and resonance effects, and polarizibility, as well as extrinsic factors such as solvation. For aliphatic alcohols, the most important effects are polarizibility and solvation, not electronic donation, as is generally assumed. In systems where the intrinsic factors are large, their effects are manifested in the overall properties, regardless of the medium.

References

1. http://research.chem.psu.edu/brpgrou...ompilation.pdf with correction for pK_a of water
2. http://webbook.nist.gov/chemistry/ accessing Reaction Thermochemistry Data for each compound
3. Brauman,J.I.; Blair,L.K. *J. Am. Chem. Soc.* **1968**, *90*, 6561.
4. Brauman,J.I.; Blair,L.K. *J. Am. Chem. Soc.* **1970**, *92*, 5986.

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4.7: Nomenclature of Alcohols

Alcohols are one of the most important functional groups in organic chemistry. Alcohols are a good source of reagents for synthesis reactions. The ability to identify alcohols is important especially when looking at IR and NMR spectra. The alcohol signal is very easy to spot on IR graphs, because they have a strong signal near the 3200 cm^{-1} region.

Introduction

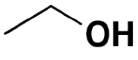
The following is list of some common primary alcohols based on the IUPAC naming system.

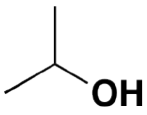
Name	Molecular Formula
Methanol (methyl alcohol)	CH_3OH
Ethanol (ethyl alcohol)	C_2H_5OH
Propanol	C_3H_7OH
Butanol	C_4H_9OH
Pentanol	$C_5H_{11}OH$
Hexanol	$C_6H_{13}OH$
Heptanol	$C_7H_{15}OH$
Octanol	$C_8H_{17}OH$

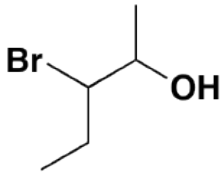
Rules for naming the alcohols

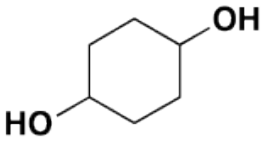
1. Find the longest chain containing the hydroxy group (OH). If there is a chain with more carbons than the one containing the OH group it will be named as a subsitutent.
2. Place the OH on the lowest possible number for the chain. With the exception of carbonyl groups such as ketones and aldehydes, the alcohol or hydroxy groups have first priority for naming.
3. When naming a cyclic structure, the -OH is assumed to be on the first carbon unless the carbonyl group is present, in which case the later will get priority at the first carbon.
4. When multiple -OH groups are on the cyclic structure, number the carbons on which the -OH groups reside.
5. Remove the final **e** from the parent alkane chain and add -**ol**. When multiple alcohols are present use **di, tri,** et.c before the **ol,** after the parent name. ex. 2,3-hexan**diol.** If a carbonyl group is present, the -OH group is named with the prefix "hydroxy," with the carbonyl group attached to the parent chain name so that it ends with -**al** or -**one.**

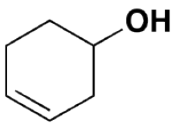
Examples

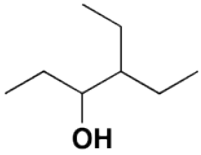
Ethan**e**: CH_3CH_3 ----->Ethan**ol**:  (the alcohol found in beer, wine and other consumed sprits)

Secondary alcohol:  2-propanol

Other functional groups on an alcohol:  3-bromo-2-pentanol

Cyclic alcohol (two -OH groups):  cyclohexan-1,4-diol

Other functional group on the cyclic structure:  3-hex**ene**ol (the alkene is in **bold** and indicated by numbering the carbon closest to the alcohol)

A complex alcohol:  4-ethyl-3hexanol (the parent chain is in red and the substituent is in blue)

Outside Links

- http://en.Wikipedia.org/wiki/Alcohol#Simple_alcohols

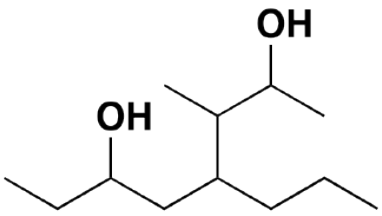
References

- Thurlow, K.J.. Chemical Nomenclature. Netherlands: Kluwer Academic Publishers, 1998.

Problems

Name the following alchols:

1.



3-methyl-4-propyl-octane-2,6-diol

Contributors

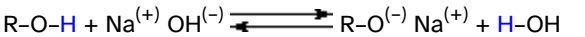
- Abhiram Kondajji (UCD)

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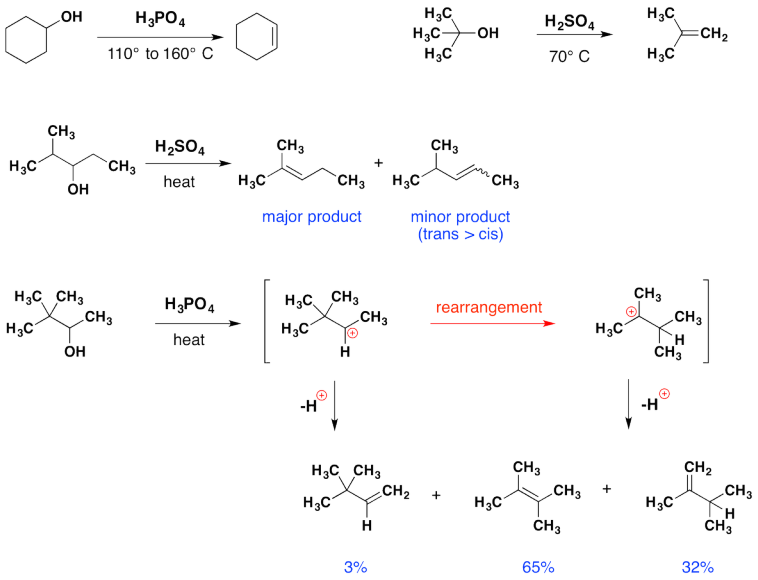
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4.8: Elimination Reactions of Alcohols

The discussion of alkyl halide reactions noted that 2° and 3°-alkyl halides experience rapid E2 elimination when treated with strong bases such as hydroxide and alkoxides. Alcohols do not undergo such base-induced elimination reactions and are, in fact, often used as solvents for such reactions. This is yet another example of how leaving-group stability influences the rate of a reaction. When an alcohol is treated with sodium hydroxide, the following acid-base equilibrium occurs. Most alcohols are slightly weaker acids than water, so the left side is favored.

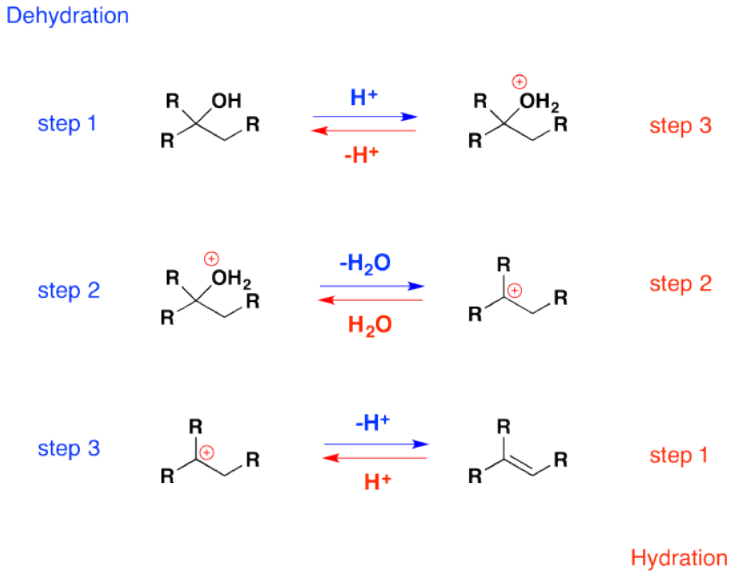


The elimination of water from an alcohol is called **dehydration**. Recalling that water is a much better leaving group than hydroxide ion, it is sensible to use acid-catalysis rather than base-catalysis in such reactions. Four examples of this useful technique are shown below. Note that hydrohalic acids (HX) are not normally used as catalysts because their conjugate bases are good nucleophiles and may create substitution products. The conjugate bases of sulfuric and phosphoric acids are not good nucleophiles, and do not participate in substitution under typical conditions.



The first two examples (in the top row) are typical, and the more facile elimination of the 3°-alcohol suggests the predominant E1 character for the reaction. This agrees with the tendency of branched 1° and 2°-alcohols to yield rearrangement products, as shown in the last example. The last two reactions also demonstrate that the Zaitsev rule applies to alcohol dehydrations, as well as to alkyl halide eliminations. Therefore, the more highly-substituted double bond isomer is favored among the products.

It should be noted that the acid-catalyzed dehydrations discussed here are the reverse of the acid-catalyzed hydration reactions of alkenes. Indeed, for these types of reversible reactions, the laws of thermodynamics require that the mechanism in both directions proceed by the same reaction path. This is known as **the principle of microscopic reversibility**. To illustrate, the following diagram lists the three steps in each transformation. The dehydration reaction is shown by the blue arrows; the hydration reaction by magenta arrows. The intermediates in these reactions are common to both, and common transition states are involved. This can be seen clearly in the energy diagrams depicted by clicking the button beneath the equations.



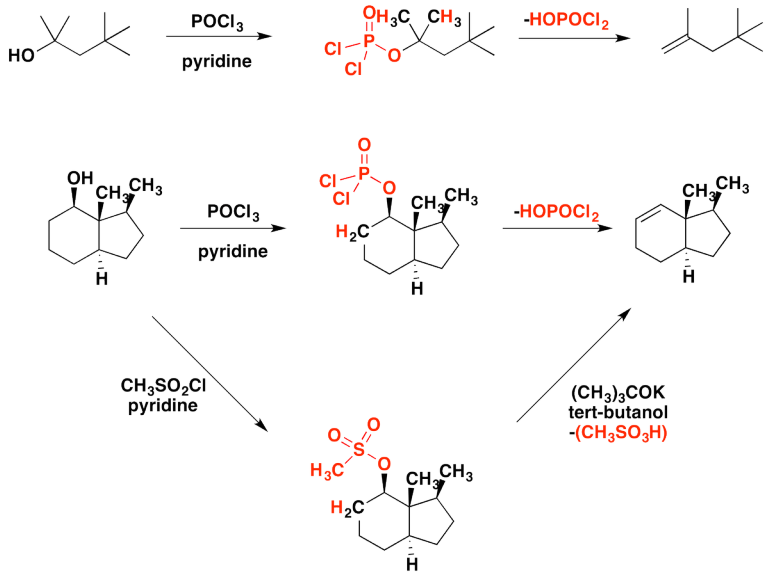
Energy Profile

Base-induced E2 eliminations of alcohols may be achieved from sulfonate ester derivatives. This has the advantage of avoiding strong acids, which may cause molecular rearrangement or double bond migration in some cases. Because 3°-sulfonate derivatives are sometimes unstable, this procedure is best used with 1° and 2°-mesylates or tosylates. Application of this reaction sequence is shown here for 2-butanol. The Zaitsev rule favors the formation of 2-butene (cis + trans) over 1-butene.

$CH_3CH_2CH(CH_3)–OH$	CH_3SO_2Cl →	$CH_3CH_2CH(CH_3)–OSO_2CH_3$	$C_2H_5O^{(-)}Na^{(+)}$ →

$CH_3CH{=}CHCH_3 + CH_3CH_2CH{=}CH_2 + CH_3SO_2O^{(-)}\ Na^{(+)} + C_2H_5OH$

The E2 elimination of 3°-alcohols under relatively non-acidic conditions may be accomplished by treatment with phosphorous oxychloride ($POCl_3$) in pyridine. This procedure is also effective with hindered 2°-alcohols, but for unhindered and 1°-alcohols, an S_N2 chloride ion substitution of the chlorophosphate intermediate competes with elimination. Examples of these and related reactions are given in the following figure. The first equation shows the dehydration of a 3°-alcohol. The predominance of the non-Zaitsev product (less substituted double bond) is presumed due to steric hindrance of the methylene group hydrogen atoms, which interferes with the approach of the base at that site. The second example shows two elimination procedures applied to the same 2°-alcohol. The first uses the single step $POCl_3$ method, which works well in this case because S_N2 substitution is impeded by steric hindrance. The second method is another example in which an intermediate sulfonate ester confers halogen-like reactivity on an alcohol. In every case, the anionic leaving group is the conjugate base of a strong acid.



Pyrolytic syn-Eliminations

Ester derivatives of alcohols may undergo unimolecular syn-elimination upon heating. To see examples of these, Click Here.

Contributors

- William Reusch, Professor Emeritus (Michigan State U.), Virtual Textbook of Organic Chemistry

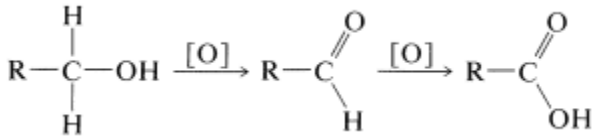
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4.9: Oxidation of Alcohols

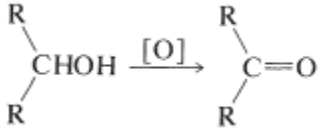
According to the scale of oxidation levels established for carbon (see Table 11-1), primary alcohols $(\mathrm{RCH_2OH})$ are at a lower oxidation level than either aldehydes (RCHO) or carboxylic acids $(\mathrm{RCO_2H})$. With suitable oxidizing agents, primary alcohols in fact can be oxidized first to aldehydes and then to carboxylic acids.

primary alcohols

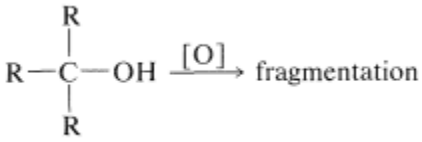


Unlike the reactions discussed previously in this chapter, oxidation of alcohols involves the alkyl portion of the molecule, or more specifically, the $\mathrm{C{-}H}$ bonds of the hydroxyl-bearing carbon (the α carbon). Secondary alcohols, which have only one such $\mathrm{C{-}H}$ bond, are oxidized to ketones, whereas tertiary alcohols, which have no $\mathrm{C{-}H}$ bonds to the hydroxylic carbon, are oxidized only with accompanying degradation into smaller fragments by cleavage of carbon-carbon bonds.

secondary alcohols



tertiary alcohols



Industrial Oxidation of Alcohols

Conversion of ethanol to ethanal is carried out on a commercial scale by passing gaseous ethanol over a copper catalyst at 300°:

$$\mathrm{CH_3CH_2OH} \xrightarrow[300^{\circ}]{\mathrm{Cu}} \mathrm{CH_3CH{=}O + H_2} \qquad \Delta H^{0}(25^{\circ}) = +15 \text{ kcal}$$

At room temperature this reaction is endothermic with an equilibrium constant of about 10^{22}. At 300° conversions of 20%-50% per pass can be realized and, by recycling the unreacted alcohol, the yield can be greater than 90%.

Another commercial process uses a silver catalyst and oxygen to combine with the hydrogen, which makes the net reaction substantially exothermic:

$$\mathrm{CH_3CH_2OH + \tfrac{1}{2}O_2} \xrightarrow{\mathrm{Ag}} \mathrm{CH_3CH{=}O + H_2O} \qquad \Delta H^{0} = -43 \text{ kcal}$$

In effect, this is a partial combustion reaction and requires very careful control to prevent overoxidation. In fact, by modifying the reaction conditions (alcohol-to-oxygen ratio, temperature, pressure, and reaction time), the oxidation proceeds smoothly to

ethanoic acid:

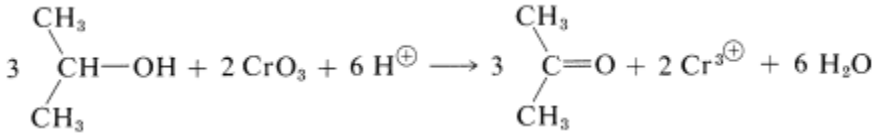
$$CH_3CH_2OH + O_2 \xrightarrow[550°]{Ag} CH_3CO_2H + H_2O$$

Reactions of this type are particularly suitable as industrial processes because they generally can be run in continuous-flow reactors, and can utilize a cheap oxidizing agent, usually supplied directly as air.

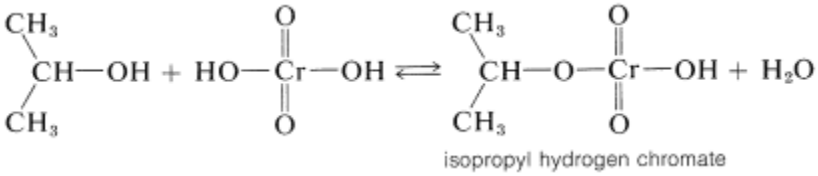
Oxidation of Alcohols

Chromic Acid Oxidation

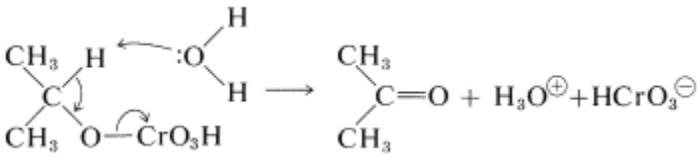
Laboratory oxidation of alcohols most often is carried out with chromic acid (H_2CrO_4), which usually is prepared as required from chromic oxide (CrO_3) or from sodium dichromate $(Na_2Cr_2O_7)$ in combination with sulfuric acid. Ethanoic (acetic) acid is a useful solvent for such reactions:



The mechanism of the chromic acid oxidation of 2-propanol to 2-propanone (acetone) has been investigated very thoroughly. It is a highly interesting reaction in that it reveals how changes of oxidation state can occur in a reaction involving a typical inorganic and a typical organic compound. The initial step is reversible formation of an isopropyl ester of chromic acid. This ester is unstable and is not isolated:



The subsequent step is the slowest in the sequence and appears to involve attack of a base (water) at the alpha hydrogen of the chromate ester concurrent with elimination of the $HCrO_3^-$ group. There is an obvious analogy between this step and an $E2$ reaction (Section 8-8A):



The transformation of chromic acid (H_2CrO_4) to H_2CrO_3 amounts to the reduction of chromium from an oxidation state of $+6$ to $+4$. Disproportionation of Cr(IV) occurs rapidly to give compounds of Cr(III) and Cr(VI):

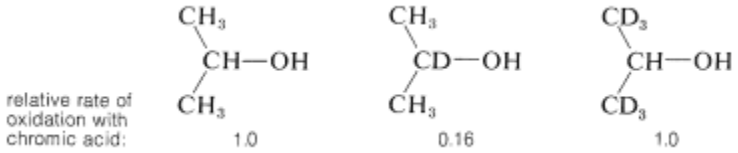
$$3Cr(IV) \longrightarrow Cr(VI) + 2Cr(III)$$

or

$$3H_2CrO_3 + 6H^{\oplus} \longrightarrow CrO_3 + 2Cr^{3\oplus} + 6H_2O$$

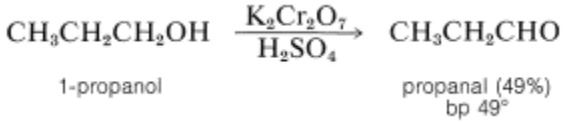
The $E2$ character of the ketone-forming step has been demonstrated in two ways. First, the rate of decomposition of isopropyl

hydrogen chromate to 2-propanone and H_2CrO_3 is strongly accelerated by efficient proton-removing substances. Second, the hydrogen on the α carbon clearly is removed in a slow reaction because *the overall oxidation rate is diminished sevenfold by having a deuterium in place of the α hydrogen*. No significant slowing of oxidation is noted for 2-propanol having deuterium in the methyl groups:

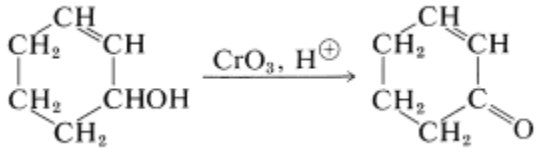


Carbon-deuterium bonds normally are broken more slowly than carbon-hydrogen bonds. This so-called **kinetic isotope effect** provides a general method for determining whether particular carbon-hydrogen bonds are broken in slow reaction steps.

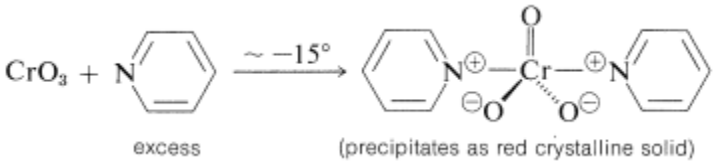
Primary alcohols are oxidized by chromic acid in sulfuric acid solution to aldehydes, but to stop the reaction at the aldehyde stage, it usually is necessary to remove the aldehyde from the reaction mixture as it forms. This can be done by distillation if the aldehyde is reasonably volatile:



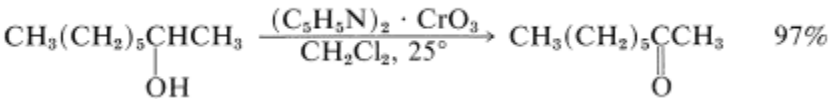
Unsaturated alcohols can be oxidized to unsaturated ketones by chromic acid, because chromic acid usually attacks double bonds relatively slowly:



However, complications are to be expected when the double bond of an unsaturated alcohol is particularly reactive or when the alcohol rearranges readily under strongly acidic conditions. It is possible to avoid the use of strong acid through the combination of chromic oxide with the weak base azabenzene (pyridine). A crystalline solid of composition $(C_5H_5N)_2 \cdot CrO_3$ is formed when CrO_3 is added to excess pyridine at low temperatures. (Addition of pyridine to CrO_3 is likely to give an uncontrollable reaction resulting in a fire.)



The pyridine-CrO_3 reagent is soluble in chlorinated solvents such as dichloromethane, and the resulting solutions rapidly oxidize  to  at ordinary temperatures:

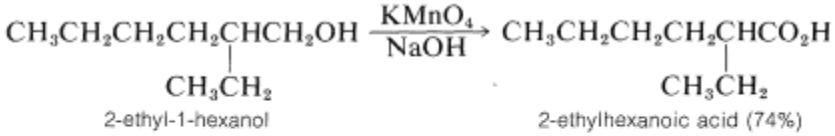


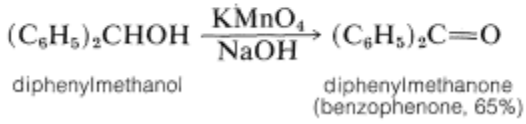
The yields usually are good, partly because the absence of strong acid minimizes degradation and rearrangement, and partly because the product can be isolated easily. The inorganic products are insoluble and can be separated by filtration, thereby

leaving the oxidized product in dichloromethane from which it can be easily recovered.

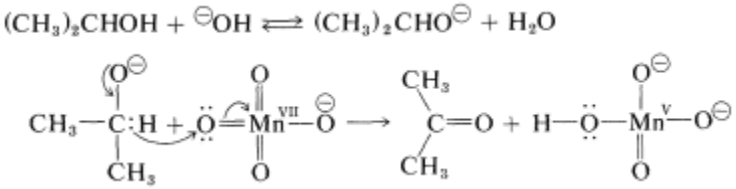
Permanganate Oxidation

Permanganate ion, MnO_4^-, oxidizes both primary and secondary alcohols in either basic or acidic solution. With primary alcohols the product normally is the carboxylic acid because the intermediate aldehyde is oxidized rapidly by permanganate:

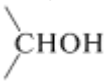
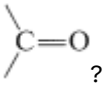


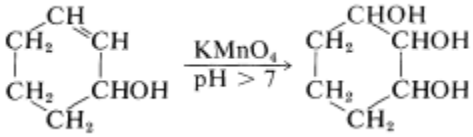


Oxidation under *basic* conditions evidently involves the alkoxide ion rather than the neutral alcohol. The oxidizing agent, MnO_4^-, abstracts the alpha hydrogen from the alkoxide ion either as an atom (one-electron transfer) or as hydride, $H^\ominus$ (two-electron transfer). The steps for the two-electron sequence are:



In the second step, permanganate ion is reduced from Mn(VII) to Mn(V). However, the stable oxidation states of manganese are $+2$, $+4$, and $+7$; thus the Mn(V) ion formed disproportionates to Mn(VII) and Mn(IV). The normal manganese end product from oxidations in basic solution is manganese dioxide, MnO_2, in which Mn has an oxidation state of $+4$ corresponding to Mn(IV).

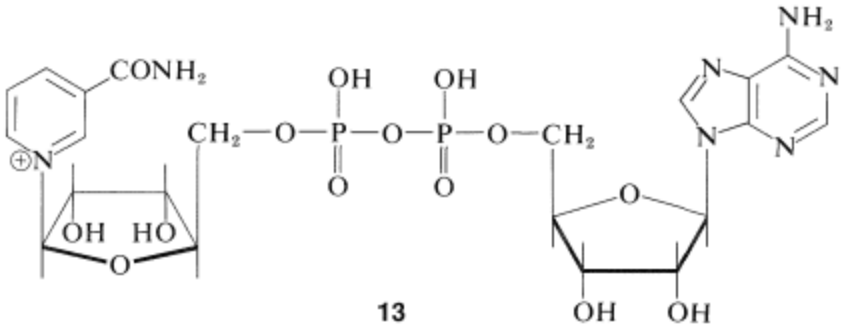
In Section 11-7C we described the use of permanganate for the oxidation of alkenes to 1,2-diols. How is it possible to control this reaction so that it will stop at the diol stage when permanganate also can oxidize  to  ? Overoxidation with permanganate is always a problem, but the relative reaction rates are very much a function of the pH of the reaction mixture and, in basic solution, potassium permanganate oxidizes unsaturated groups more rapidly than it oxidizes alcohols:



Biological Oxidations

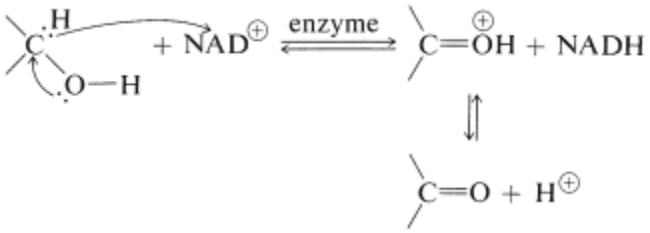
There are many biological oxidations that convert a primary or secondary alcohol to a carbonyl compound. These reactions cannot possibly involve the extreme pH conditions and vigorous inorganic oxidants used in typical laboratory oxidations. Rather, they occur at nearly neutral pH values and they all require enzymes as catalysts, which for these reactions usually are called *dehydrogenases*.

An important group of biological oxidizing agents includes the pyridine nucleotides, of which nicotinamide adenine dinucleotide ($NAD^\oplus$, 13) is an example:

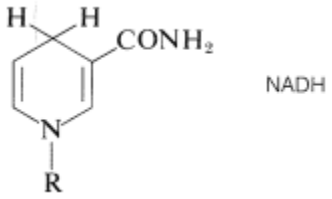


13

This very complex molecule functions to accept hydride $(H^{\ominus})$ or the equivalent $(H^{\oplus} + 2e^{-})$ from the α carbon of an alcohol:

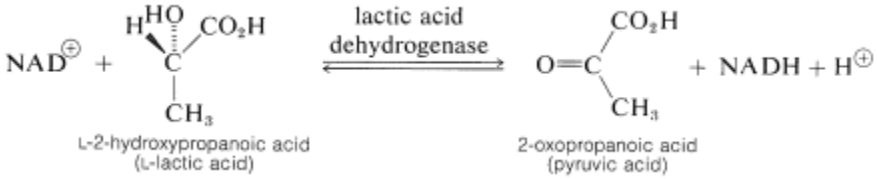


The reduced form of $NAD^{\oplus}$ is abbreviated as $NADH$ and the $H^{\ominus}$ is added at the 4-position of the pyridine ring:



NADH

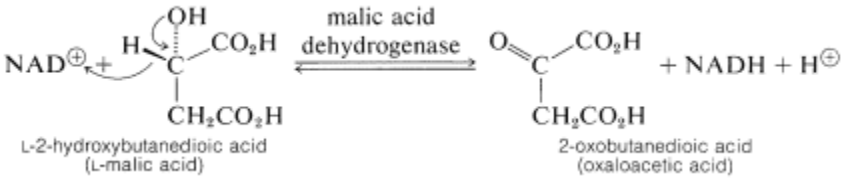
Some examples follow that illustrate the remarkable specificity of this kind of redox system. One of the last steps in the metabolic breakdown of glucose (glycolysis; Section 20-10A) is the reduction of 2-oxopropanoic (pyruvic) acid to L-2-hydroxypropanoic (lactic) acid. The reverse process is oxidation of L-lactic acid. The enzyme *lactic acid dehydrogenase* catalyses this reaction, and it functions only with the L-enantiomer of lactic acid:



L-2-hydroxypropanoic acid (L-lactic acid)

2-oxopropanoic acid (pyruvic acid)

A second example, provided by one of the steps in metabolism by way of the Krebs citric acid cycle (see Section 20-10B), is the oxidation of L-2-hydroxy-butanedioic (L-malic) acid to 2-oxobutanedioic (oxaloacetic) acid. This enzyme functions only with L -malic acid:

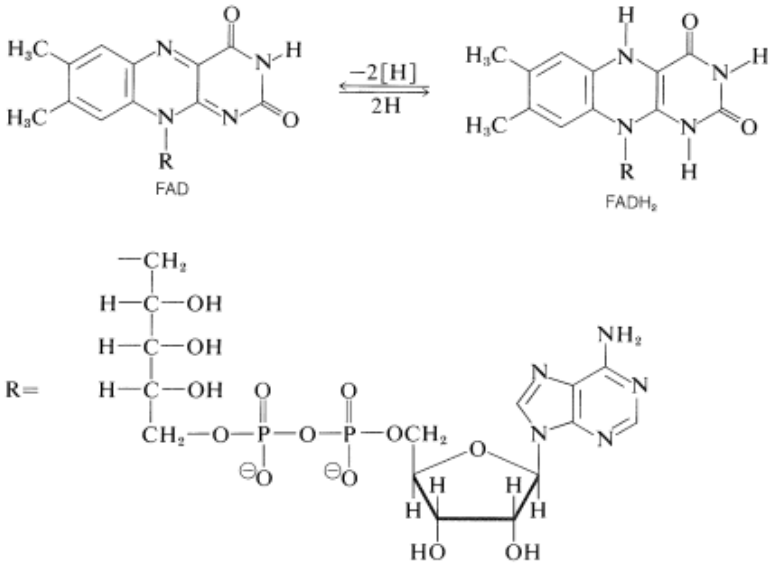


L-2-hydroxybutanedioic acid (L-malic acid)

2-oxobutanedioic acid (oxaloacetic acid)

All of these reactions release energy. In biological oxidations much of the energy is utilized to form ATP from ADP and inorganic phosphate (Section 15-5F). That is to say, electron-transfer reactions are coupled with ATP formation. The overall process is called **oxidative phosphorylation**.

Another important oxidizing agent in biological systems is flavin adenine dinucleotide, FAD. Like $\mathrm{NAD}^{\oplus}$, it is a two-electron acceptor, but unlike $\mathrm{NAD}^{\oplus}$, it accepts two electrons as $2\mathrm{H}\cdot$ rather than as $\mathrm{H}^{\ominus}$. The reduced form, FADH_2, has the hydrogens at ring nitrogens:



Contributors

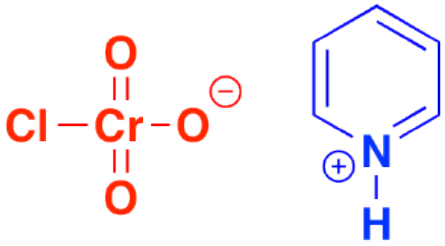
John D. Robert and Marjorie C. Caserio (1977) *Basic Principles of Organic Chemistry, second edition*. W. A. Benjamin, Inc. , Menlo Park, CA. ISBN 0-8053-8329-8. This content is copyrighted under the following conditions, "You are granted permission for individual, educational, research and non-commercial reproduction, distribution, display and performance of this work in any format."

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4.10: Oxidation by PCC (pyridinium chlorochromate)

Pyridinium chlorochromate (PCC) is a milder version of chromic acid.

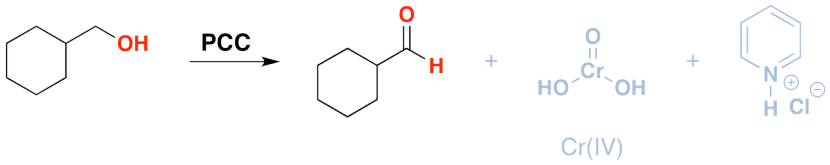


PCC (Pyridinium Chlorochromate)

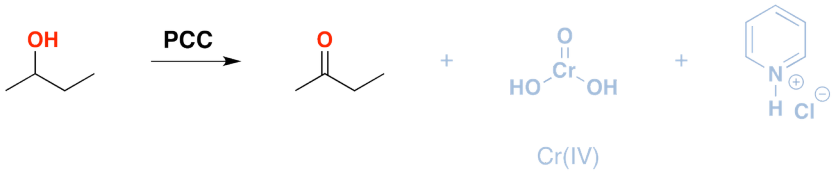
PCC oxidizes alcohols one rung up the oxidation ladder, from primary alcohols to aldehydes and from secondary alcohols to ketones. In contrast to chromic acid, PCC will not oxidize aldehydes to carboxylic acids. Similar to or the same as: CrO_3 and pyridine (the Collins reagent) will also oxidize primary alcohols to aldehydes. Here are two examples of PCC in action.

- If you add one equivalent of PCC to either of these alcohols, the oxidized version will be produced. The byproducts (featured in grey) are Cr(IV) as well as pyridinium hydrochloride.
- One has to be careful with the amount of water present in the reaction. If water is present, it can add to the aldehyde to create the hydrate, which could be further oxidized by a second equivalent of PCC if it is present. This is not a concern with ketones because there is no H directly bonded to C.

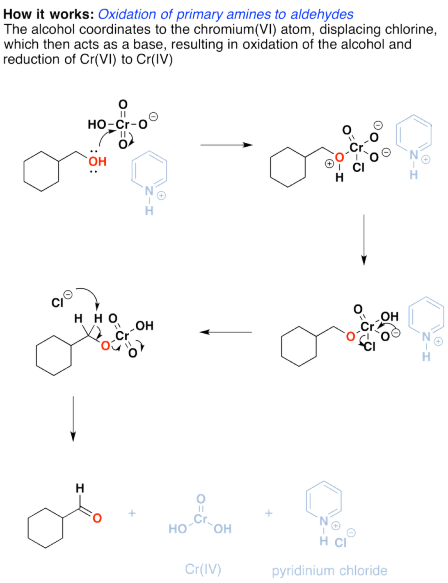
Example 1: Oxidation of primary alcohols to aldehydes



Example 2: Oxidation of primary alcohols to aldehydes



How does it work? Oxidation reactions of this sort are actually a type of elimination reaction. The reaction starts with a carbon-oxygen single bond and results in a carbon-oxygen double bond. The elimination reaction can occur because of the good leaving group on the oxygen, namely the chromium, which will be displaced when the neighboring C-H bond is broken with a base.



The first step is attack of oxygen on the chromium to form the Cr-O bond. Secondly, a proton on the (now positive) OH is transferred to one of the oxygens of the chromium, possibly through the intermediacy of the pyridinium salt. A chloride ion is then displaced in a reaction reminiscent of a 1,2 elimination reaction to form what is known as a chromate ester.

The C-O double bond is formed when a base removes the proton on the carbon adjacent to the oxygen. [aside: I've drawn the base as Cl(-) although there are certainly other species which could also act as bases here (such as an alcohol). It is also possible for pyridine to be used as the base here, although only very low concentrations of the deprotonated form will be present under these acidic conditions.] The electrons from the C-H bond move to form the C-O bond, and in the process, the O-Cr bond is broken, and Cr(VI) becomes Cr(IV) (drawn here as $O=Cr(OH)_2$).

Real life notes: If you end up using PCC in the lab, do not forget to add molecular sieves or Celite or some other solid to the bottom of the flask because otherwise you get a nasty brown tar that is difficult to clean up. The toxicity and mess associated with chromium has spurred the development of other alternatives, such as TPAP, IBX, DMP, and a host of other reagents you generally do not typically learn about until grad school.

Contributors

- **James Ashenhurst** (MasterOrganicChemistry.com)

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4.11: Replacing the OH Group by Halogen Atoms

This page looks at reactions in which the -OH group in an alcohol is replaced by a halogen such as chlorine or bromine. It includes a simple test for an -OH group using phosphorus(V) chloride. The general reaction looks like this:

$$ROH + HX \rightarrow RX + H_2O \tag{4.11.1}$$

Reaction with hydrogen chloride

Tertiary alcohols react reasonably rapidly with concentrated hydrochloric acid, but for primary or secondary alcohols the reaction rates are too slow for the reaction to be of much importance. A tertiary alcohol reacts if it is shaken with with concentrated hydrochloric acid at room temperature. A tertiary halogenoalkane (haloalkane or alkyl halide) is formed.



Replacing -OH by bromine

Rather than using hydrobromic acid,the alcohol is typically treated with a mixture of sodium or potassium bromide and concentrated sulfuric acid. This produces hydrogen bromide, which reacts with the alcohol. The mixture is warmed to distil off the bromoalkane.

$$CH_3CH_2OH + HBr \rightarrow CH_3CH_2Br + H_2O \tag{4.11.2}$$

Replacing -OH by iodine

In this case, the alcohol is reacted with a mixture of sodium or potassium iodide and concentrated phosphoric(V) acid, H_3PO_4, and the iodoalkane is distilled off. The mixture of the iodide and phosphoric(V) acid produces hydrogen iodide, which reacts with the alcohol.

$$CH_3CH_2OH + HI \rightarrow CH_3CH_2I + H_2O \tag{4.11.3}$$

Phosphoric(V) acid is used instead of concentrated sulfuric acid because sulfuric acid oxidizes iodide ions to iodine and produces hardly any hydrogen iodide. A similar phenomenon occurs to some extent with bromide ions in the preparation of bromoalkanes but not enough to interfere with the main reaction. There is no reason why you could not use phosphoric(V) acid in the bromide case instead of sulfuric acid if desired.

Reacting Alcohols with Phosphorus Halides

Alcohols react with liquid phosphorus(III) chloride (also called phosphorus trichloride) to yield chloroalkanes.

$$3CH_3CH_2CH_2OH + PCl_3 \rightarrow 3CH_3CH_2CH_2Cl + H_3PO_3 \tag{4.11.4}$$

Alcohols also violently react with solid phosphorus(V) chloride (phosphorus pentachloride) at room temperature, producing clouds of hydrogen chloride gas. While it is not a good approach to make chloroalkanes, it is a good test for the presence of -OH groups. To show that a substance was an alcohol, you would first have to eliminate all the other groups that also react with phosphorus(V) chloride. For example, carboxylic acids (containing the -COOH group) also react with it (because of the -OH in -COOH) as does water (H-OH).

If you have a neutral liquid not contaminated with water, and clouds of hydrogen chloride are produced when you add phosphorus(V) chloride, then you have an alcohol group present.

$$CH_3CH_2CH_2OH + PCl_5 \rightarrow CH_3CH_2CH_2Cl + POCl_3 + HCl \tag{4.11.5}$$

There are also side reactions involving the $POCl_3$ reacting with the alcohol.

Other reactions involving phosphorus halides

Instead of using phosphorus(III) bromide or iodide, the alcohol is usually heated under reflux with a mixture of red phosphorus and either bromine or iodine. The phosphorus first reacts with the bromine or iodine to give the phosphorus(III) halide.

$$2P_{(s)} + 3Br_2 \rightarrow 2PBr_3 \tag{4.11.6}$$

$$2P_{(s)} + 3I_2 \rightarrow 2PI_3 \tag{4.11.7}$$

These then react with the alcohol to give the corresponding halogenoalkane, which can be distilled off.

$$3CH_3CH_2CH_2OH + PBr_3 \rightarrow 3CH_3CH_2CH_2Br + H_3PO_3 \tag{4.11.8}$$

$$3CH_3CH_2CH_2OH + PI_3 \rightarrow 3CH_3CH_2CH_2I + H_3PO_3 \tag{4.11.9}$$

Reacting alcohols with Thionyl Chloride

Sulfur dichloride oxide (thionyl chloride) has the formula $SOCl_2$. Traditionally, the formula is written as shown, despite the fact that the modern name writes the chlorine before the oxygen (alphabetical order). The sulfur dichloride oxide reacts with alcohols at room temperature to produce a chloroalkane. Sulfur dioxide and hydrogen chloride are given off. Care would have to be taken because both of these are poisonous.

$$CH_3CH_2CH_2OH + SOCl_2 \rightarrow CH_3CH_2CH_2Cl + SO_2 + HCl \tag{4.11.10}$$

The advantage that this reaction has over the use of either of the phosphorus chlorides is that the two other products of the reaction (sulfur dioxide and HCl) are both gases. That means that they separate themselves from the reaction mixture.

Contributors

- Jim Clark (Chemguide.co.uk)

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5: ALDEHYDES AND KETONES

5.1: The Carbonyl Group
5.2: Properties of Aldehydes and Ketones
5.3: Some Common Aldehydes and Ketones
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5.5: Preparation of Aldehydes and Ketones
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5.7: Addition of Alcohols to form Hemiacetals and Acetals

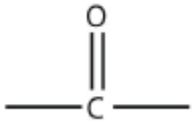
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5.1: The Carbonyl Group

Learning Objective

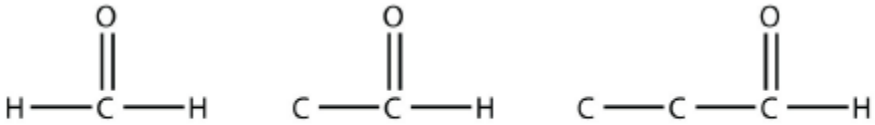
- Identify the aldehyde and ketone functional groups.

There are other functional groups that contain O atoms. Before we introduce them, we define the **carbonyl group**, which is formed when an O atom and a C atom are joined by a double bond:



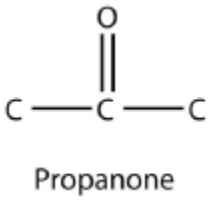
The other two bonds on the C atom are attached to other atoms. It is the identities of these other atoms that define what specific type of compound an organic molecule is.

If one bond of the carbonyl group is made to an H atom, then the molecule is classified as an **aldehyde** (If there are two H atoms, there is only 1 C atom). When naming aldehydes, the main chain of C atoms must include the carbon in the carbonyl group, which is numbered as position 1 in the carbon chain. The parent name of the hydrocarbon is used, but the suffix *-al* is appended. (Do not confuse *-al* with *-ol*, which is the suffix used for alcohols.) So we have

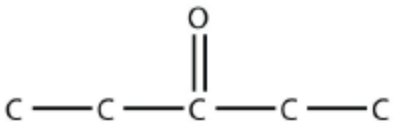


Methanal has a common name with which you may be familiar: formaldehyde. The main thing to note about aldehydes is that the carbonyl group is at the *end* of a carbon chain.

A carbonyl group in the middle of a carbon chain implies that both remaining bonds of the carbonyl group are made to C atoms. This type of molecule is called a **ketone.** Despite the fact that aldehydes and ketones have the same carbonyl group, they have different chemical and physical properties and are properly grouped as two different types of compounds. The smallest ketone has three C atoms in it. When naming a ketone, we take the name of the parent hydrocarbon and change the suffix to *-one*:



The common name for propanone is acetone. With larger ketones, we must use a number to indicate the position of the carbonyl group, much like a number is used with alkenes and alkynes:



3-Pentanone

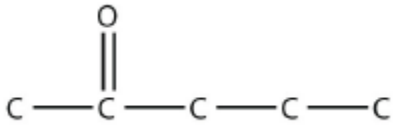
There is another way to name ketones: name the alkyl groups that are attached to the carbonyl group and add the word *ketone* to the name. So propanone can also be called dimethyl ketone, while 2-butanone is called methyl ethyl ketone.

Example 5.1.1

Draw the structure of 2-pentanone.

Solution

This molecule has five C atoms in a chain, with the carbonyl group on the second C atom. Its structure is as follows:



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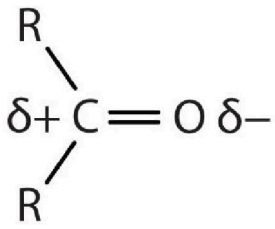
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5.2: Properties of Aldehydes and Ketones

Learning Objectives

- Explain why the boiling points of aldehydes and ketones are higher than those of ethers and alkanes of similar molar masses but lower than those of comparable alcohols.
- Compare the solubilities in water of aldehydes and ketones of four or fewer carbon atoms with the solubilities of comparable alkanes and alcohols.
- Name the typical reactions take place with aldehydes and ketones.
- Describe some of the uses of common aldehydes and ketones.

The carbon-to-oxygen double bond is quite polar, more polar than a carbon-to-oxygen single bond. The electronegative oxygen atom has a much greater attraction for the bonding electron pairs than does the carbon atom. The carbon atom has a partial positive charge, and the oxygen atom has a partial negative charge:



In aldehydes and ketones, this charge separation leads to dipole-dipole interactions that are great enough to significantly affect the boiling points. Table 5.2.1 shows that the polar single bonds in ethers have little such effect, whereas hydrogen bonding between alcohol molecules is even stronger.

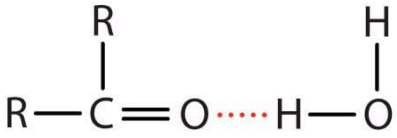
Table 5.2.1: Boiling Points of Compounds Having Similar Molar Masses but Different Types of Intermolecular Forces

Compound	Family	Molar Mass	Type of Intermolecular Forces	Boiling Point (°C)
$CH_3CH_2CH_2CH_3$	alkane	58	dispersion only	–1
$CH_3OCH_2CH_3$	ether	60	weak dipole	6
CH_3CH_2CHO	aldehyde	58	strong dipole	49
$CH_3CH_2CH_2OH$	alcohol	60	hydrogen bonding	97

Formaldehyde is a gas at room temperature. Acetaldehyde boils at 20°C; in an open vessel, it boils away in a warm room. Most other common aldehydes are liquids at room temperature.

Although the lower members of the homologous series have pungent odors, many higher aldehydes have pleasant odors and are used in perfumes and artificial flavorings. As for the ketones, acetone has a pleasant odor, but most of the higher homologs have rather bland odors.

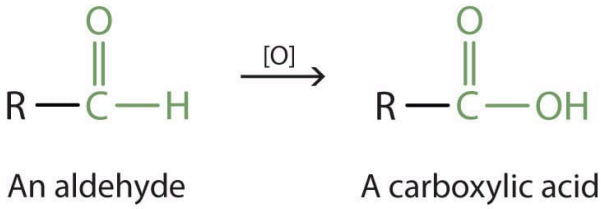
The oxygen atom of the carbonyl group engages in hydrogen bonding with a water molecule.

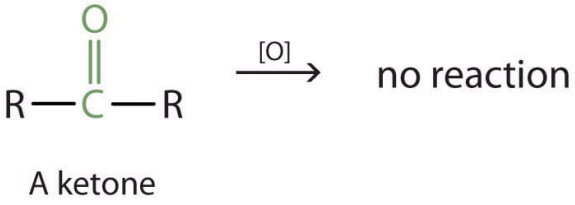


The solubility of aldehydes is therefore about the same as that of alcohols and ethers. Formaldehyde, acetaldehyde, and acetone are soluble in water. As the carbon chain increases in length, solubility in water decreases. The borderline of solubility occurs at about four carbon atoms per oxygen atom. All aldehydes and ketones are soluble in organic solvents and, in general, are less dense than water.

Oxidation of Aldehydes and Ketones

Aldehydes and ketones are much alike in many of their reactions, owing to the presence of the carbonyl functional group in both. They differ greatly, however, in one most important type of reaction: oxidation. Aldehydes are readily oxidized to carboxylic acids, whereas ketones resist oxidation.





The aldehydes are, in fact, among the most easily oxidized of organic compounds. They are oxidized by oxygen (O_2) in air to carboxylic acids.

$$2RCHO + O_2 \rightarrow 2RCOOH \tag{5.2.1}$$

The ease of oxidation helps chemists identify aldehydes. A sufficiently mild oxidizing agent can distinguish aldehydes not only from ketones but also from alcohols. Tollens' reagent, for example, is an alkaline solution of silver (Ag^+) ion complexed with ammonia (NH_3), which keeps the Ag^+ ion in solution.

$$H_3N—Ag^+—NH_3 \tag{5.2.2}$$

When Tollens' reagent oxidizes an aldehyde, the Ag^+ ion is reduced to free silver (Ag).

$$RCHO(aq) + 2Ag(NH_3)_2^+(aq) + 3OH^-(aq) \longrightarrow$$

An aldehyde

$$RCOO^-(aq) + 2Ag(s) + 4\,NH_3(aq) + 2H_2O$$

Free silver

Deposited on a clean glass surface, the silver produces a mirror (Figure 5.2.1). Ordinary ketones do not react with Tollens' reagent.



Figure 5.2.1: Aldehyde Reactions. A reaction related to the Tollens' reaction is often used to silver mirrors. These ornaments were silvered by such a reaction. Glucose, a simple sugar with an aldehyde functional group, is used as the reducing agent. Source: Photo courtesy of Krebs Glas Lauscha, commons.wikimedia.org/wiki/File:Silvering.jpg.

Although ketones resist oxidation by ordinary laboratory oxidizing agents, they undergo combustion, as do aldehydes.

Summary

The polar carbon-to-oxygen double bond causes aldehydes and ketones to have higher boiling points than those of ethers and alkanes of similar molar masses but lower than those of comparable alcohols that engage in intermolecular hydrogen bonding. Aldehydes are readily oxidized to carboxylic acids, whereas ketones resist oxidation.

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5.3: Some Common Aldehydes and Ketones

Learning Objectives

- Objective 1
- Objective 2

Formaldehyde has an irritating odor. Because of its reactivity, it is difficult to handle in the gaseous state. For many uses, it is therefore dissolved in water and sold as a 37% to 40% aqueous solution called *formalin*. Formaldehyde denatures proteins, rendering them insoluble in water and resistant to bacterial decay. For this reason, formalin is used in embalming solutions and in preserving biological specimens.

Aldehydes are the active components in many other familiar substances. Large quantities of formaldehyde are used to make phenol-formaldehyde resins for gluing the wood sheets in plywood and as adhesives in other building materials. Sometimes the formaldehyde escapes from the materials and causes health problems in some people. While some people seem unaffected, others experience coughing, wheezing, eye irritation, and other symptoms.

> The odor of green leaves is due in part to a carbonyl compound, cis-3-hexenal, which with related compounds is used to impart a “green” herbal odor to shampoos and other products.

Acetaldehyde is an extremely volatile, colorless liquid. It is a starting material for the preparation of many other organic compounds. Acetaldehyde is formed as a metabolite in the fermentation of sugars and in the detoxification of alcohol in the liver. Aldehydes are the active components of many other familiar materials (Figure 5.3.2).

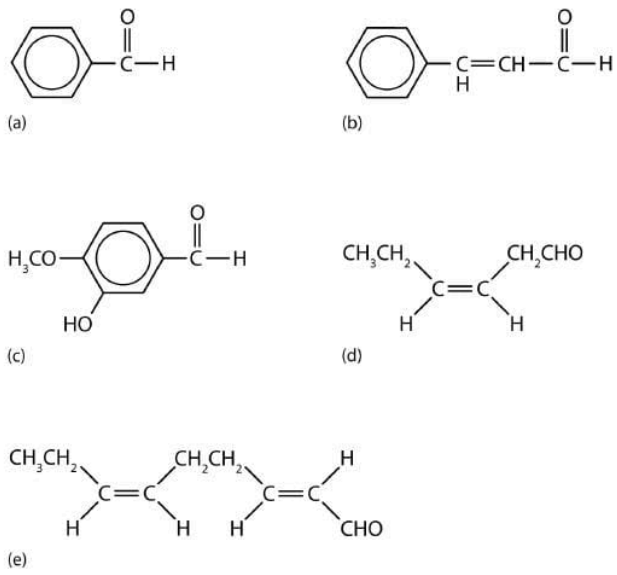


Figure 5.3.2 Some Interesting Aldehydes. (a) Benzaldehyde is an oil found in almonds; (b) cinnamaldehyde is oil of cinnamon; (c) vanillin gives vanilla its flavor; (d) *cis*-3-hexenal provides an herbal odor; and (e) *trans*-2-*cis*-6-nonadienal gives a cucumber odor.

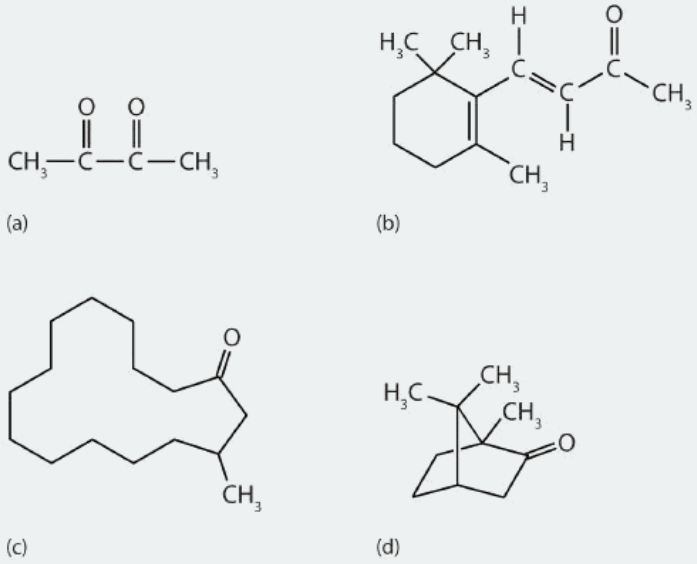
Acetone is the simplest and most important ketone. Because it is miscible with water as well as with most organic solvents, its chief use is as an industrial solvent (for example, for paints and lacquers). It is also the chief ingredient in some brands of nail

polish remover.

To Your Health: Acetone in Blood, Urine, and Breath

Acetone is formed in the human body as a by-product of lipid metabolism. Normally, acetone does not accumulate to an appreciable extent because it is oxidized to carbon dioxide and water. The normal concentration of acetone in the human body is less than 1 mg/100 mL of blood. In certain disease states, such as uncontrolled diabetes mellitus, the acetone concentration rises to higher levels. It is then excreted in the urine, where it is easily detected. In severe cases, its odor can be noted on the breath.

Ketones are also the active components of other familiar substances, some of which are noted in the accompanying figure.



Some ketones have interesting properties: (a) Butter flavoring comes from 2,3-butanedione; (b) β-ionone is responsible for the odor of violets; (c) muscone is musk oil, an ingredient in perfumes; and (d) camphor is used in some insect repellents.

Certain steroid hormones have the ketone functional group as a part of their structure. Two examples are progesterone, a hormone secreted by the ovaries that stimulates the growth of cells in the uterine wall and prepares it for attachment of a fertilized egg, and testosterone, the main male sex hormone. These and other sex hormones affect our development and our lives in fundamental ways.

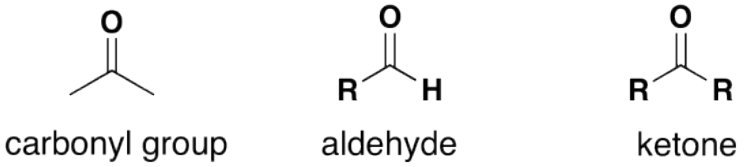
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5.4: Nomenclature of Aldehydes and Ketones

Aldehydes and ketones contain the carbonyl group. Aldehydes are considered the most important functional group. They are often called the formyl or methanoyl group. Aldehydes derive their name from the *dehydr*ation of *al*cohols. Aldehydes contain the carbonyl group bonded to at least one hydrogen atom. Ketones contain the carbonyl group bonded to two carbon atoms.

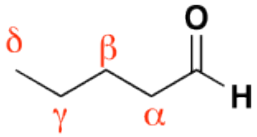
Aldehydes and ketones are organic compounds which incorporate a **carbonyl functional group**, C=O. The carbon atom of this group has two remaining bonds that may be occupied by hydrogen, alkyl or aryl substituents. If at least one of these substituents is hydrogen, the compound is an **aldehyde**. If neither is hydrogen, the compound is a **ketone**.

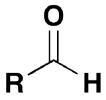


Naming Aldehydes

The IUPAC system of nomenclature assigns a characteristic suffix ***-al*** to aldehydes. For example, $H_2C{=}O$ is methan**al**, more commonly called formaldehyde. Since an aldehyde carbonyl group must always lie at the end of a carbon chain, it is always is given the #1 location position in numbering and it is not necessary to include it in the name. There are several simple carbonyl containing compounds which have common names which are retained by IUPAC.

Also, there is a common method for naming aldehydes and ketones. For aldehydes common parent chain names, similar to those used for carboxylic acids, are used and the suffix ***–aldehyde*** is added to the end. In common names of aldehydes, carbon atoms near the carbonyl group are often designated by Greek letters. The atom adjacent to the carbonyl function is alpha, the next removed is beta and so on.



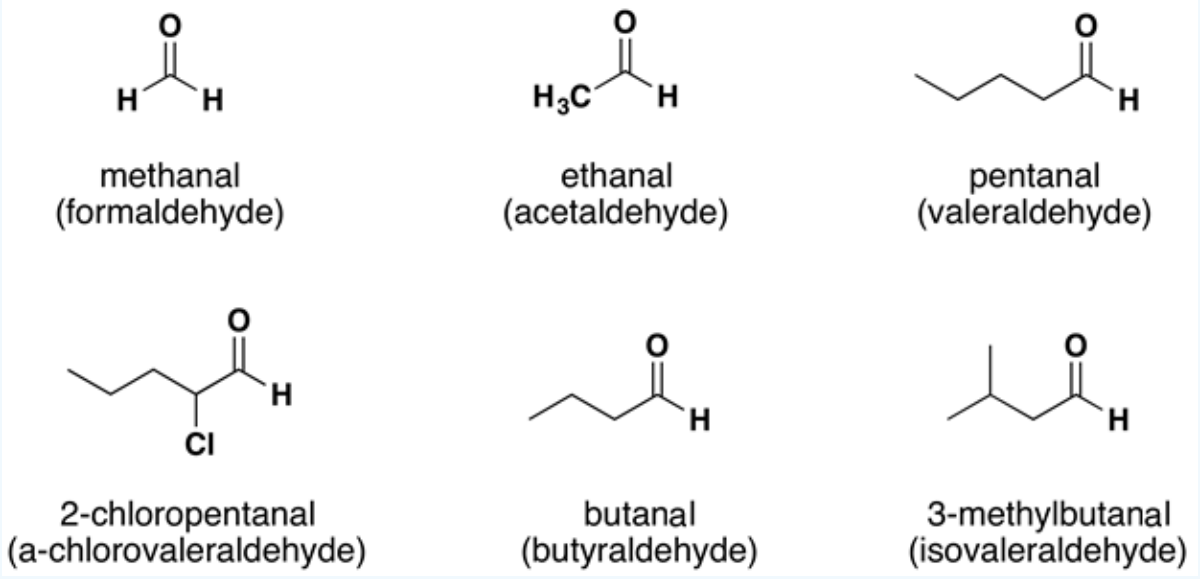
If the aldehyde moiety  (-CHO) is attached to a ring the suffix ***–carbaldehyde*** is added to the name of the ring. The carbon attached to this moiety will get the #1 location number in naming the ring.

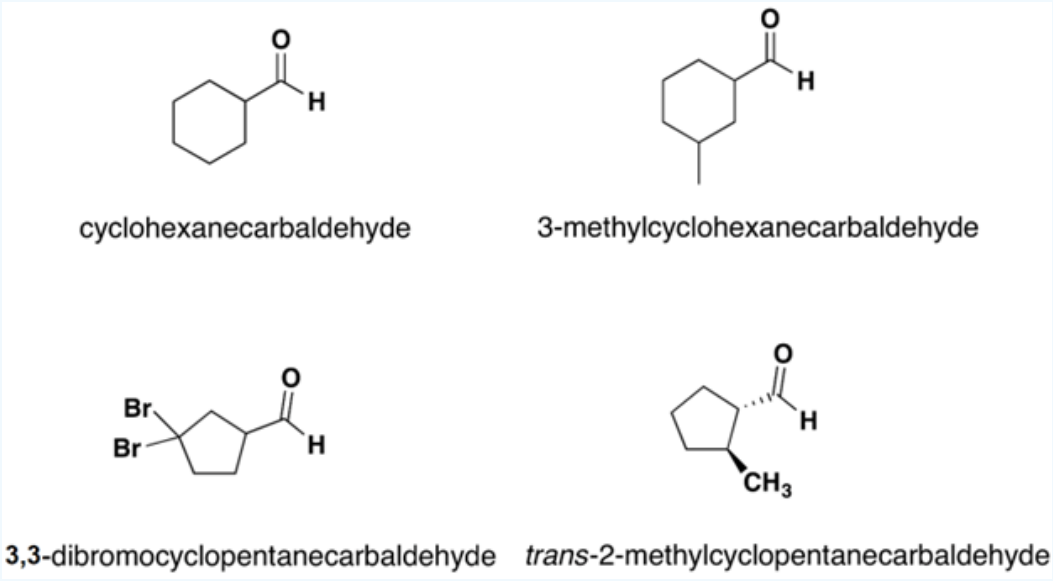
Summary of Aldehyde Nomenclature rules

1. Aldehydes take their name from their parent alkane chains. The ***-e*** is removed from the end and is replaced with ***-al***.
2. The aldehyde funtional group is given the #1 numbering location and this number is not included in the name.
3. For the common name of aldehydes start with the common parent chain name and add the suffix ***-aldehyde***. Substituent positions are shown with Greek letters.
4. When the -CHO functional group is attached to a ring the suffix ***-carbaldehyde*** is added, and the carbon attached to that group is C1.

Example 1

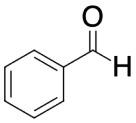
The IUPAC system names are given on top while the common name is given on the bottom in parentheses.





Aldehyde Common Names to Memorize

There are some common names that are still used and need to be memorized. Recognizing the patterns can be helpful.

Structure	IUPAC (root names from alkanes)		Common (root names from common names of related carboxylic acids)	
	root	methane	root	formic acid
	aldehyde name	methanal	aldehyde name	formaldehyde
	root	ethane	root	acetic acid
	aldehyde name	ethanal	aldehyde name	acetaldehyde
	root	benzenecarboxylic acid	root	benzoic acid
	aldehyde name	benzenecarbaldehyde	aldehyde name	benzaldehyde

Naming Ketones

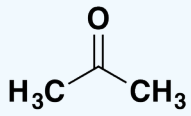
The IUPAC system of nomenclature assigns a characteristic suffix of -**one** to ketones. A ketone carbonyl function may be located anywhere within a chain or ring, and its position is usually given by a location number. Chain numbering normally starts from the end nearest the carbonyl group. Very simple ketones, such as propanone and phenylethanone do not require a locator number, since there is only one possible site for a ketone carbonyl function. The common names for ketones are formed by naming both alkyl groups attached to the carbonyl then adding the suffix -**ketone**. The attached alkyl groups are arranged in the name alphabetically.

Summary of Ketone Nomenclature rules

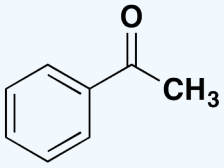
1. Ketones take their name from their parent alkane chains. The ending ***-e*** is removed and replaced with ***-one***.
2. The common name for ketones are simply the **substituent groups listed alphabetically + *ketone*.**
3. Some common ketones are known by their generic names. Such as the fact that *propanone* is commonly referred to as *acetone*.

Example 2

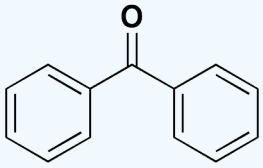
The IUPAC system names are given on top while the common name is given on the bottom in parentheses.



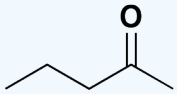
propanone
(acetone)



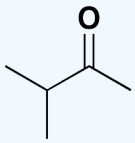
acetophenone
(methyl phenyl ketone)



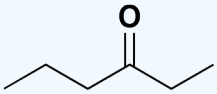
benzophenone
(diphenyl ketone)



2-pentanone
(methyl propyl ketone)



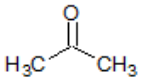
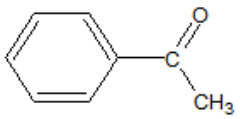
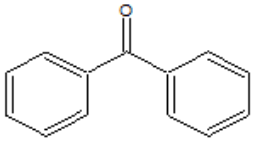
3-methyl-2-butanone
(methyl isopropyl ketone)



3-hexanone
(ethyl propyl ketone)

Ketone Common Names to Memorize

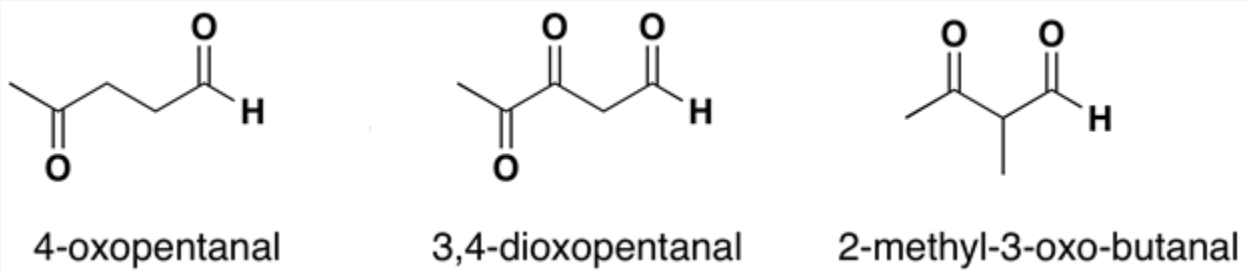
There are some common names that are still used and need to be memorized. Recognizing the patterns can be helpful.

Compound	Systematic	Common
	propane → propanone	acetone or dimethyl ketone
	1-phenylethane → 1-phenylethanone	acetophenone or methyl phenyl ketone
	benzophenone	diphenyl ketone

Naming Aldehydes and Ketones in the Same Molecule

As with many molecules with two or more functional groups, one is given priority while the other is named as a substituent. Because aldehydes have a higher priority than ketones, molecules which contain both functional groups are named as aldehydes and the ketone is named as an **"oxo"** substituent. It is not necessary to give the aldehyde functional group a location number, however, it is usually necessary to give a location number to the ketone.

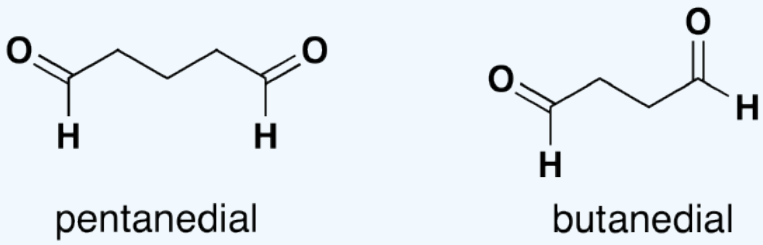
Example 3



Naming Dialdehydes and Diketones

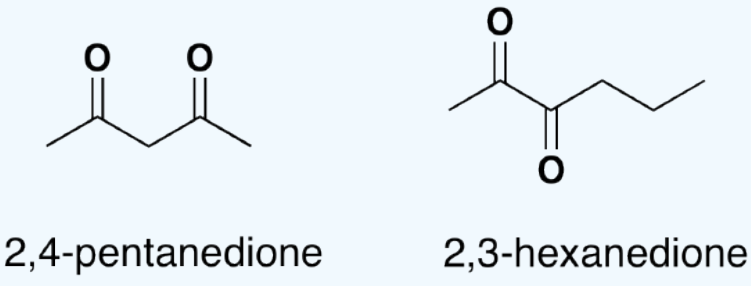
For dialdehydes the location numbers for both carbonyls are omitted because the aldehyde functional groups are expected to occupy the ends of the parent chain. The ending **–dial** is added to the end of the parent chain name.

Example 4



For diketones both carbonyls require a location number. The ending **-dione** or **-dial** is added to the end of the parent chain.

Example 5



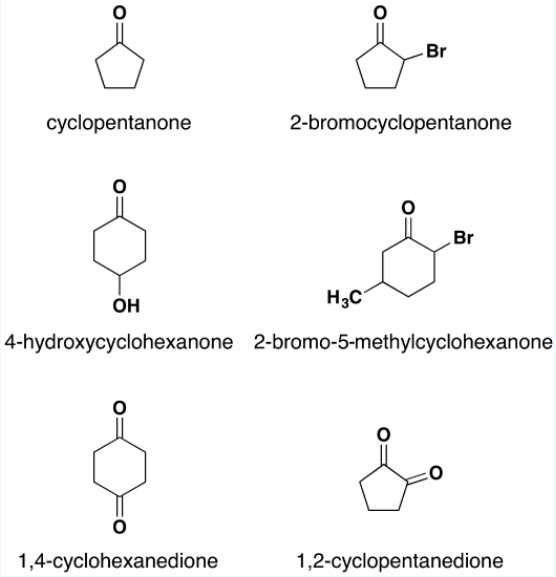
Naming Cyclic Ketones and Diketones

In cyclic ketones the carbonyl group is assigned location position #1, and this number is not included in the name, unless more than one carbonyl group is present. The rest of the ring is numbered to give substituents the lowest possible location numbers. Remember the prefix **cyclo** is included before the parent chain name to indicate that it is in a ring. As with other ketones the **–e** ending is replaced with the **–one** to indicate the presence of a ketone.

With cycloalkanes which contain two ketones both carbonyls need to be given a location numbers. Also, an **–e** is not removed

from the end, but the suffix **–dione** is added.

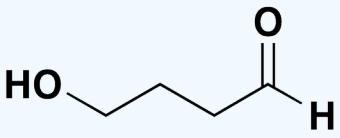
Example 6



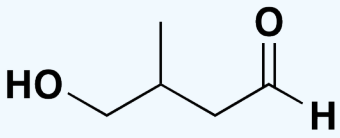
Naming Carbonyls and Hydroxyls in the Same Molecule

When and aldehyde or ketone is present in a molecule which also contains an alcohol functional group the carbonyl is given nomenclature priority by the IUPAC system. This means that the carbonyl is given the lowest possible location number and the appropriate nomenclature suffix is included. In the case of alcohols the **OH** is named as a **hydroxyl** substituent. However, the **l** in hydroxyl is generally removed.

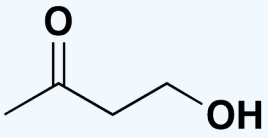
Example 7



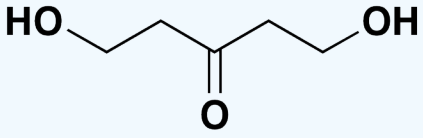
4-hydroxybutanal



4-hydroxy-3-methylbutanal



4-hydroxy-2-butanone



1,5-dihydroxy-3-pentanone

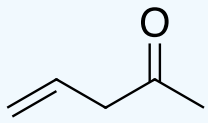
Naming Carbonyls and **Alkenes** in the Same Molecule

When and aldehyde or ketone is present in a molecule which also contains analkene functional group the carbonyl is given nomenclature priority by the IUPAC system. This means that the carbonyl is given the lowest possible location number and the appropriate nomenclature suffix is included. When carbonyls are included with an alkene the following order is followed:

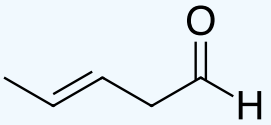
*(Location number of the alkene)-(Prefix name for the longest carbon chain minus the **-ane** ending)-(an **-en** ending to indicate the presence of an alkene)-(the location number of the carbonyl if a ketone is present)-(either an **–one** or and **-anal** ending).*

Remember that the carbonyl has priority so it should get the lowest possible location number. Also, remember that cis/tran or E/Z nomenclature for the alkene needs to be included if necessary.

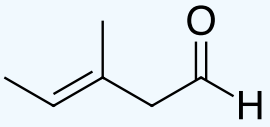
Example 8



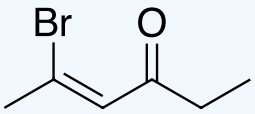
4-penten-2-one



trans-3-pentenal
or (E)-3-pentenal



(E)-3-methyl-3-pentenal

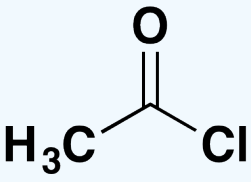


(Z)-5-bromo-4-hexen-3-one

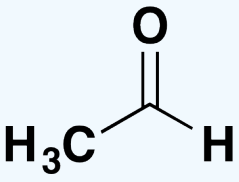
Aldehydes and Ketones as Fragments

- *Alkanoyl* is the common name of the R-C=O- fragment, though the older naming, *acyl*, is still widely used.
- *Formyl* is the common name of the H-C=O- fragment.
- *Acety* is the common name of the CH_3-C=O- fragment.

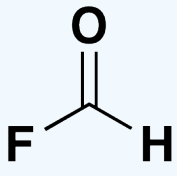
Example 9



acetyl chloride



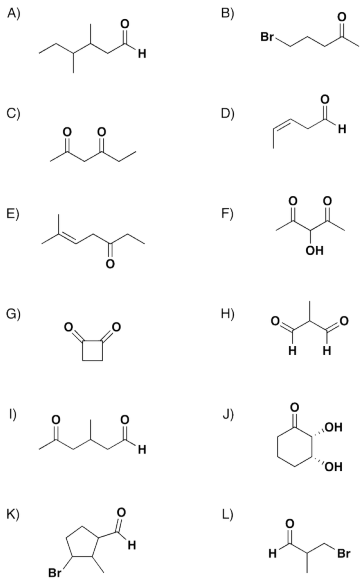
acetylaldehyde



formyl fluoride

Additional Examples of Carbonyl Nomenclature

1) Please give the IUPAC name for each compound:



Answers for Question 1

A. 3,4-dimethylhexanal
B. 5-bromo-2-pentanone
C. 2,4-hexanedione
D. cis-3-pentenal (or (*Z*)-3-pentenal)
E. 6-methyl-5-hepten-3-one
F. 3-hydroxy-2,4-pentanedione
G. 1,2-cyclobutanedione
H. 2-methyl-propanedial
I. 3-methyl-5-oxo-hexanal
J. cis-2,3-dihydroxycyclohexanone
K. 3-bromo-2-methylcyclopentanecarboaldehyde
L. 3-bromo-2-methylpropanal

2) Please give the structure corresponding to each name:

A) butanal

B) 2-hydroxycyclopentanone

C) 2,3-pentanedione

D) 1,3-cyclohexanedione

E) 4-hydoxy-3-methyl-2-butanone

F) (*E*) 3-methyl-2-hepten-4-one

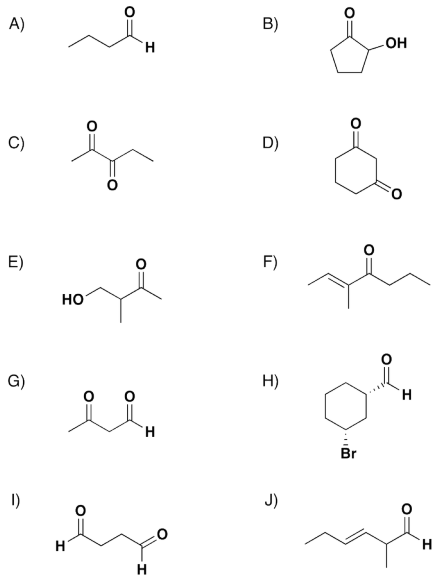
G) 3-oxobutanal

H) *cis*-3-bromocyclohexanecarboaldehyde

I) butanedial

J) *trans*-2-methyl-3-hexenal

Answers to question 2:



References

1. Vollhardt, K. Peter C., and Neil E. Schore. Organic Chemistry. 5th ed. New York: W.H. Freeman, 2007.
2. Zumdahl, Steven S., and Susan A. Zumdahl. Chemistry. 6th ed. Boston: Houghton Mifflin College Division, 2002.

Contributors

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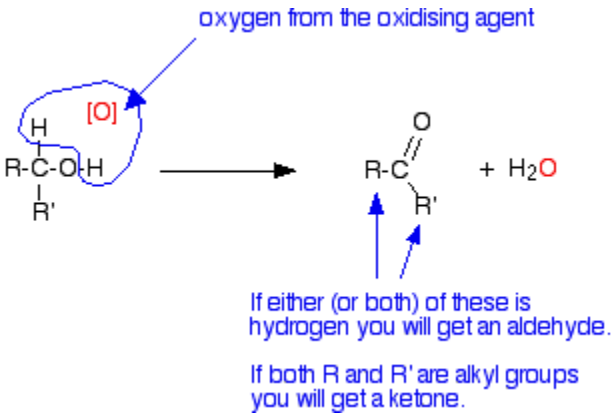
5.5: Preparation of Aldehydes and Ketones

This page explains how aldehydes and ketones are made in the lab by the oxidation of primary and secondary alcohols.

Oxidizing alcohols to make aldehydes and ketones

The oxidizing agent used in these reactions is normally a solution of sodium or potassium dichromate(VI) acidified with dilute sulfuric acid. If oxidation occurs, the orange solution containing the dichromate(VI) ions is reduced to a green solution containing chromium(III) ions.

The net effect is that an oxygen atom from the oxidizing agent removes a hydrogen from the -OH group of the alcohol and one from the carbon to which it is attached.



[O] is often used to represent oxygen coming from an oxidising agent.

R and R' are alkyl groups or hydrogen. They could also be groups containing a benzene ring, but I'm ignoring these to keep things simple.

If at least one of these groups is a hydrogen atom, then you will get an aldehyde. If they are both alkyl groups then you get a ketone. If you now think about where they are coming from, you will get an aldehyde if your starting molecule looks like this:



In other words, if you start from a primary alcohol, you will get an aldehyde. You will get a ketone if your starting molecule looks like this:



. . . where R and R' are both alkyl groups. Secondary alcohols oxidize to give ketones.

Making aldehydes

Aldehydes are made by oxidising primary alcohols. There is, however, a problem.

The aldehyde produced can be oxidised further to a carboxylic acid by the acidified potassium dichromate(VI) solution used as the oxidising agent. In order to stop at the aldehyde, you have to prevent this from happening.

To stop the oxidation at the aldehyde, you . . .

- use an excess of the alcohol. That means that there isn't enough oxidizing agent present to carry out the second stage and oxidize the aldehyde formed to a carboxylic acid.
- distil off the aldehyde as soon as it forms. Removing the aldehyde as soon as it is formed means that it doesn't stay in the mixture to be oxidized further.

If you used ethanol as a typical primary alcohol, you would produce the aldehyde ethanal, CH_3CHO. The full equation for this reaction is fairly complicated, and you need to understand about electron-half-equations in order to work it out.

$$3CH_3CH_2OH + Cr_2O_7^{2-} + 8H^+ \longrightarrow 3CH_3CHO + 2Cr^{3+} + 7H_2O$$

In organic chemistry, simplified versions are often used which concentrate on what is happening to the organic substances. To do that, oxygen from an oxidising agent is represented as [O]. That would produce the much simpler equation:

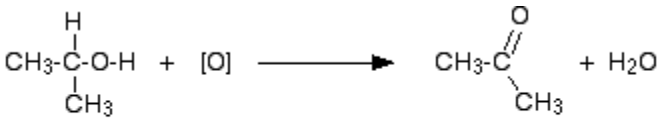
$$CH_3CH_2OH + [O] \longrightarrow CH_3CHO + H_2O$$

This means "oxygen from an oxidising agent".

Secondary alcohols

Secondary alcohols are oxidised to ketones. There is no further reaction which might complicate things. For example, if you heat the secondary alcohol propan-2-ol with sodium or potassium dichromate(VI) solution acidified with dilute sulphuric acid, you get propanone formed.

Playing around with the reaction conditions makes no difference whatsoever to the product. Using the simple version of the equation:



propan-2-ol propanone

Contributors

Jim Clark (Chemguide.co.uk)

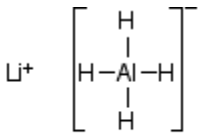
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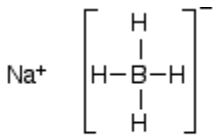
5.6: Reduction of Aldehydes and Ketones

Despite the fearsome names, the structures of the two reducing agents are very simple. In each case, there are four hydrogens ("tetrahydido") around either aluminium or boron in a negative ion (shown by the "ate" ending). The "(III)" shows the oxidation state of the aluminium or boron, and is often left out because these elements only ever show the +3 oxidation state in their compounds.

The formulae of the two compounds are $LiAlH_4$ and $NaBH_4$. Their structures are:



lithium tetrahydridoaluminate

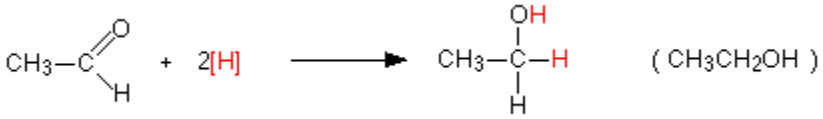


sodium tetrahydridoborate

In each of the negative ions, one of the bonds is a co-ordinate covalent (dative covalent) bond using the lone pair on a hydride ion (H-) to form a bond with an empty orbital on the aluminium or boron.

The reduction of an aldehyde

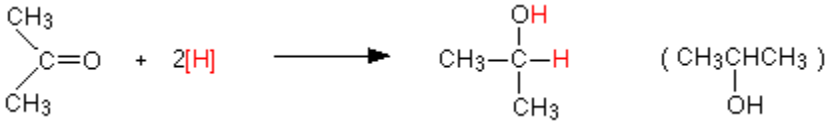
You get exactly the same organic product whether you use lithium tetrahydridoaluminate or sodium tetrahydridoborate. For example, with ethanal you get ethanol:



Notice that this is a simplified equation where [H] means "hydrogen from a reducing agent". In general terms, reduction of an aldehyde leads to a primary alcohol.

The reduction of a Ketone

Again the product is the same whichever of the two reducing agents you use. For example, with propanone you get propan-2-ol:

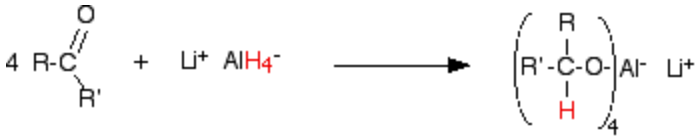


Reduction of a ketone leads to a secondary alcohol.

Using lithium tetrahydridoaluminate (lithium aluminium hydride)

Lithium tetrahydridoaluminate is much more reactive than sodium tetrahydridoborate. It reacts violently with water and alcohols, and so any reaction must exclude these common solvents. The reactions are usually carried out in solution in a carefully dried ether such as ethoxyethane (diethyl ether). The reaction happens at room temperature, and takes place in two separate stages.

In the first stage, a salt is formed containing a complex aluminium ion. The following equations show what happens if you start with a general aldehyde or ketone. R and R' can be any combination of hydrogen or alkyl groups.



The product is then treated with a dilute acid (such as dilute sulfuric acid or dilute hydrochloric acid) to release the alcohol from the complex ion.

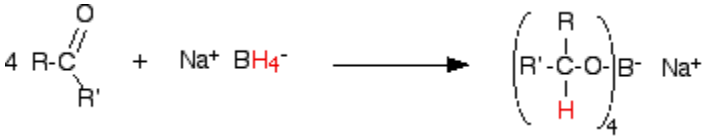


The alcohol formed can be recovered from the mixture by fractional distillation.

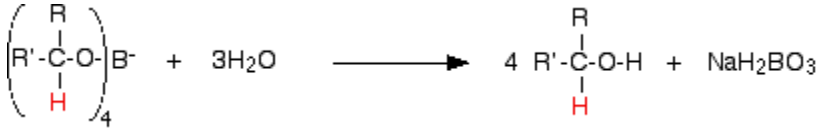
Using sodium tetrahydridoborate (sodium borohydride)

Sodium tetrahydridoborate is a more gentle (and therefore safer) reagent than lithium tetrahydridoaluminate. It can be used in solution in alcohols or even solution in water - provided the solution is alkaline. Solid sodium tetrahydridoborate is added to a solution of the aldehyde or ketone in an alcohol such as methanol, ethanol or propan-2-ol. Depending on which recipe you read, it is either heated under reflux or left for some time around room temperature. This almost certainly varies depending on the nature of the aldehyde or ketone.

At the end of this time, a complex similar to the previous one is formed.



In the second stage of the reaction, water is added and the mixture is boiled to release the alcohol from the complex.



Again, the alcohol formed can be recovered from the mixture by fractional distillation.

Contributors

- Jim Clark (Chemguide.co.uk)

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5.7: Addition of Alcohols to form Hemiacetals and Acetals

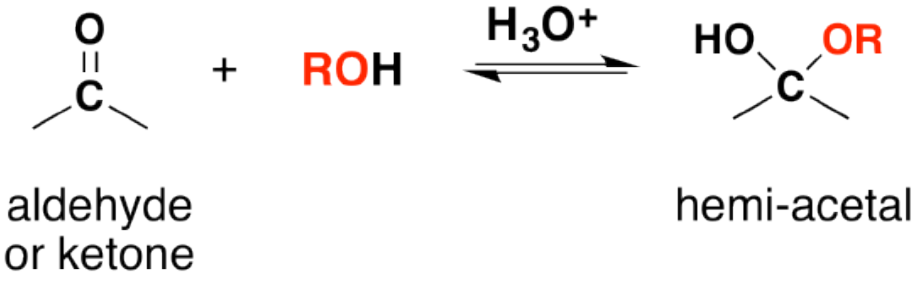
In this organic chemistry topic, we shall see how alcohols (R-OH) add to carbonyl groups. Carbonyl groups are characterized by a carbon-oxygen double bond. The two main functional groups that consist of this carbon-oxygen double bond are Aldehydes and Ketones.

Introduction

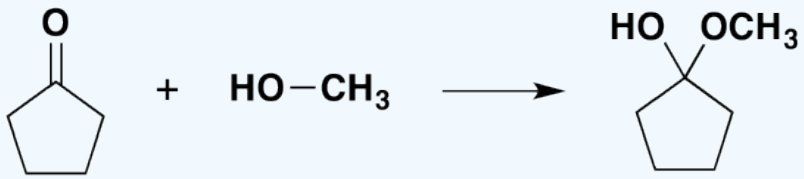
It has been demonstrated that water adds rapidly to the carbonyl function of aldehydes and ketones to form geminal-diol. In a similar reaction alcohols add reversibly to aldehydes and ketones to form hemiacetals (h*emi,* Greek, half). This reaction can continue by adding another alcohol to form an acetal. Hemiacetals and acetals are important functional groups because they appear in sugars.

To achieve effective hemiacetal or acetal formation, two additional features must be implemented. First, an acid catalyst must be used because alcohol is a weak nucleophile; and second, the water produced with the acetal must be removed from the reaction by a process such as a molecular sieves or a **Dean-Stark trap**. The latter is important, since acetal formation is reversible. Indeed, once pure hemiacetal or acetals are obtained they may be hydrolyzed back to their starting components by treatment with aqueous acid and an excess of water.

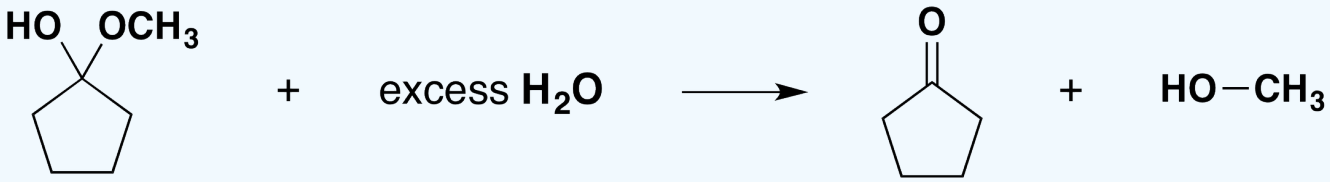
Formation of Hemiacetals



Example 1: Formation of Hemiacetals

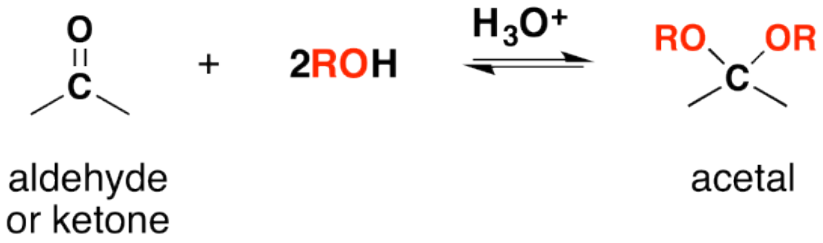


Example 2: Hemiacetal Reversibility

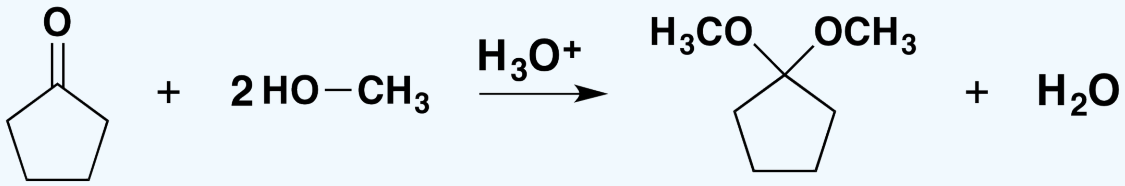


Formation of Acetals

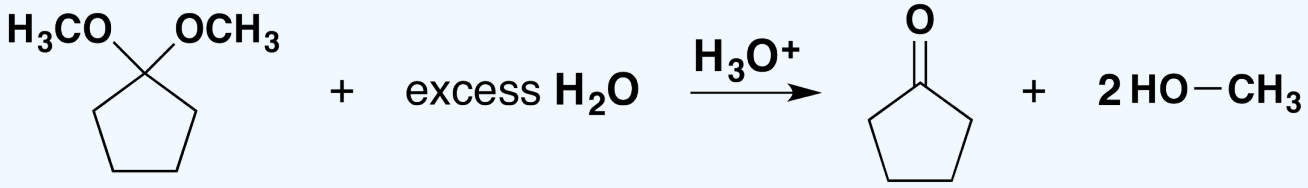
Acetals are geminal-diether derivatives of aldehydes or ketones, formed by reaction with two equivalents (or an excess amount) of an alcohol and elimination of water. Ketone derivatives of this kind were once called ketals, but modern usage has dropped that term. It is important to note that a hemiacetal is formed as an intermediate during the formation of an acetal.



Example 3: Formation of Acetals



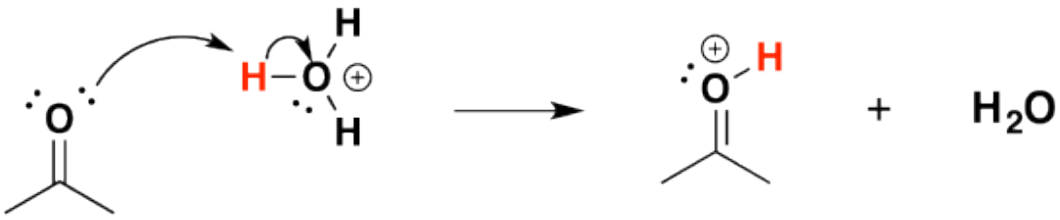
Example 4: Acetal Reversibility



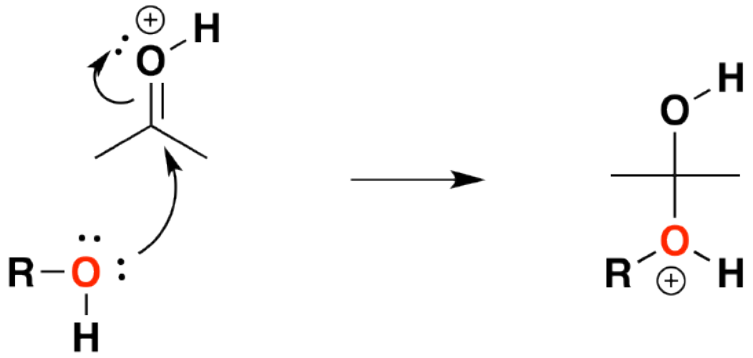
Mechanism for Hemiacetal and Acetal Formation

The mechanism shown here applies to both acetal and hemiacetal formation

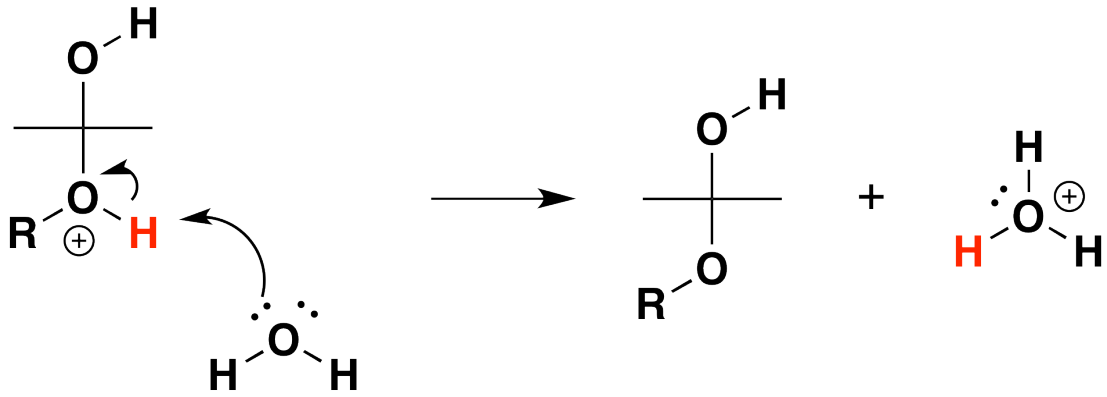
1) Protonation of the carbonyl



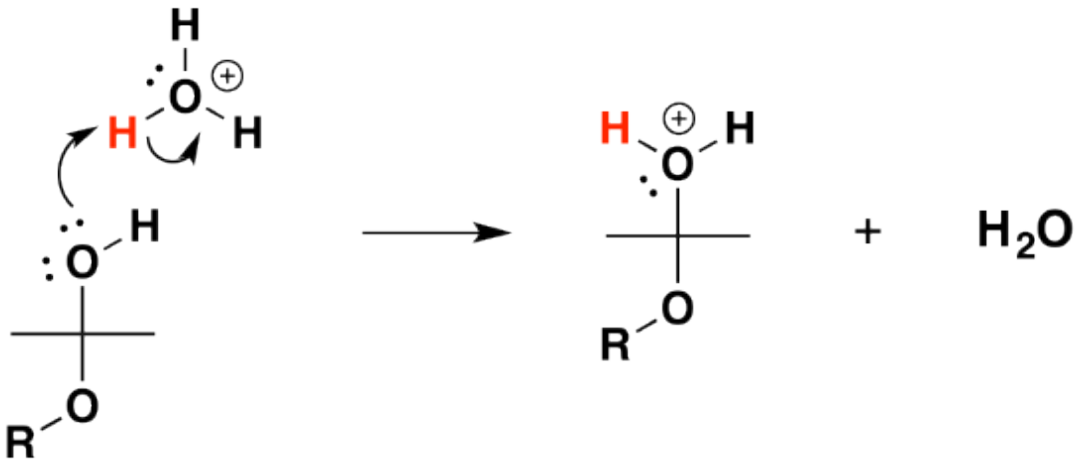
2) Nucleophilic attack by the alcohol



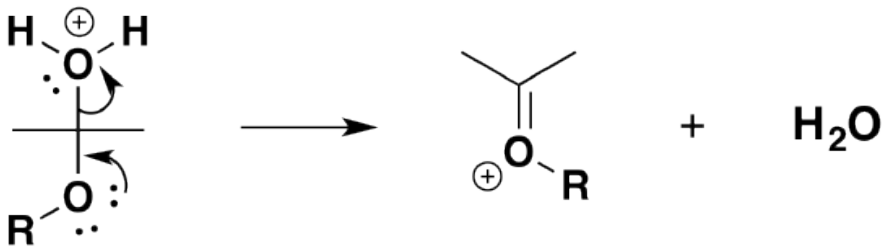
3) Deprotonation to form a hemiacetal



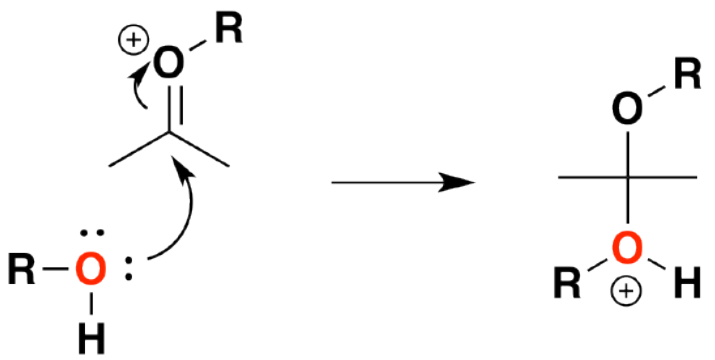
4) Protonation of the alcohol



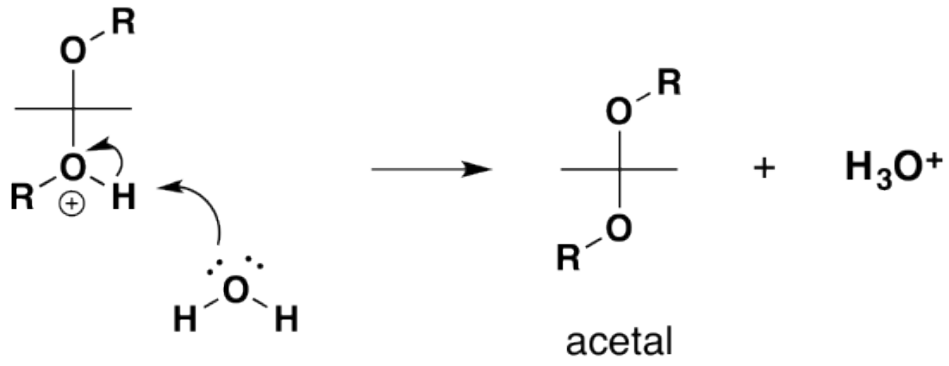
5) Removal of water



6) Nucleophilic attack by the alcohol

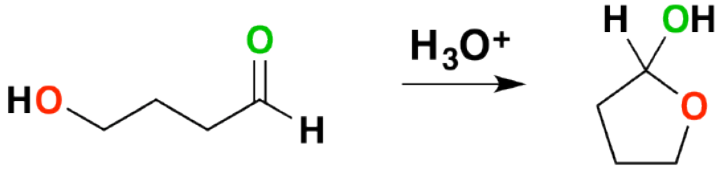


7) Deprotonation by water

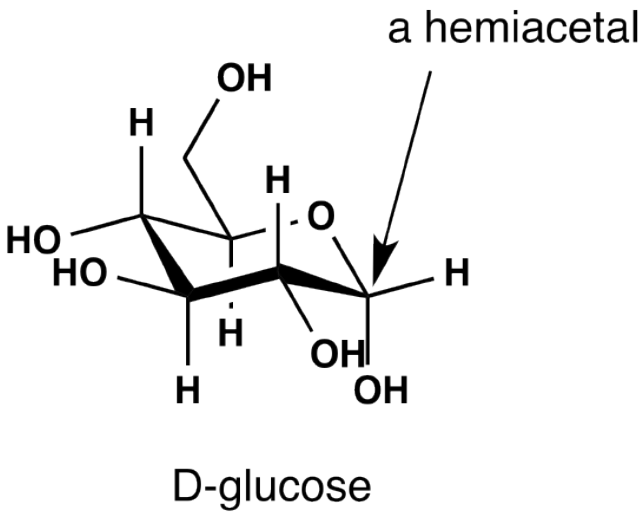


Formation of Cyclic Hemiacetal and Acetals

Molecules which have an alcohol and a carbonyl can undergo an intramolecular reaction to form a cyclic hemiacetal.

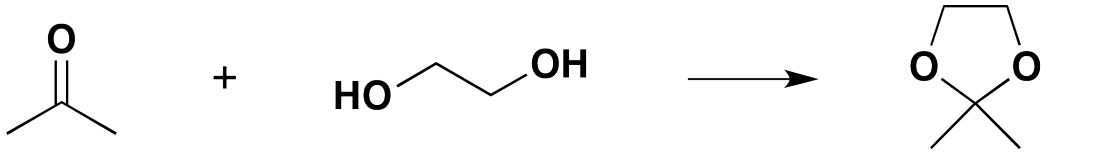


Intramolecular Hemiacetal formation is common in sugar chemistry. For example, the common sugar glucose exists in the cylcic manner more than 99% of the time in a mixture of aqueous solution.



D-glucose

Carbonyls reacting with diol produce a cyclic acetal. A common diol used to form cyclic acetals is ethylene glycol.

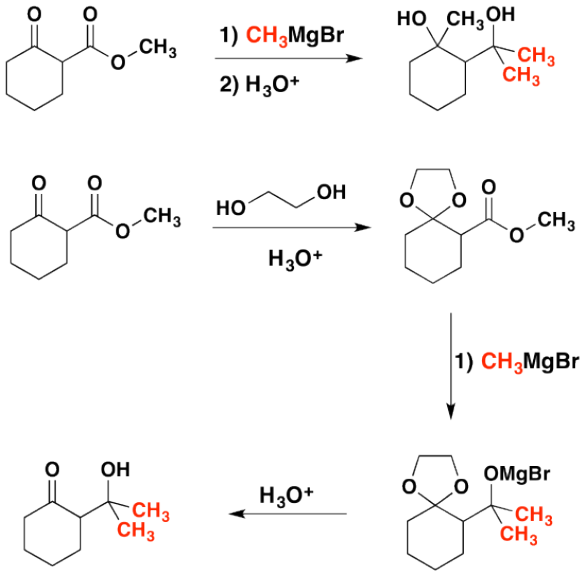


ethylene glycol cyclic acetal

Acetals as Protecting Groups

The importance of acetals as carbonyl derivatives lies chiefly in their stability and lack of reactivity in neutral to strongly basic environments. As long as they are not treated by acids, especially aqueous acid, acetals exhibit all the lack of reactivity associated with ethers in general. Among the most useful and characteristic reactions of aldehydes and ketones is their reactivity toward strongly nucleophilic (and basic) metallo-hydride, alkyl and aryl reagents. If the carbonyl functional group is converted to an acetal these powerful reagents have no effect; thus, acetals are excellent protective groups, when these irreversible addition reactions must be prevented.

In the following example we would like a Grignard reagent to react with the ester and not the ketone. This cannot be done without a protecting group because Grignard reagents react with esters and ketones.



References

1. Vollhardt, K. Peter C., and Neil E. Schore. Organic Chemistry: Structure and Function. New York: W.H. Freeman and Company, 2007
2. Carey, Francis. Advanced Organic Chemistry. 5th ed. Springer, 2007.

Outside Links

- http://en.Wikipedia.org/wiki/Acetal
- http://en.Wikipedia.org/wiki/Hemiacetal

Contributors

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- Ekram Alexander and Ahmed Rahim (UCD)

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6: THE THREE-DIMENSIONAL SHAPE OF MOLECULES

6.1: Why This Chapter?

6.2: The Reason for Handedness in Molecules - Chirality

6.3: Enantiomers and the Tetrahedral Carbon

6.4: Pasteur's Discovery of Enantiomers

6.5: Optical Activity

6.6: Chirality in Nature and Chiral Environments

6.7: Chemistry Matters—Chiral Drugs

6.8: Sequence Rules for Specifying Configuration

6.9: Depicting Carbohydrate Stereochemistry - Fischer Projections

6.10: Diastereomers

6.11: Meso Compounds

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6.1: Why This Chapter?

Understanding the causes and consequences of molecular handedness is crucial to understanding organic and biological chemistry. The subject can be a bit complex at first, but the material covered in this chapter nevertheless forms the basis for much of the remainder of the book.

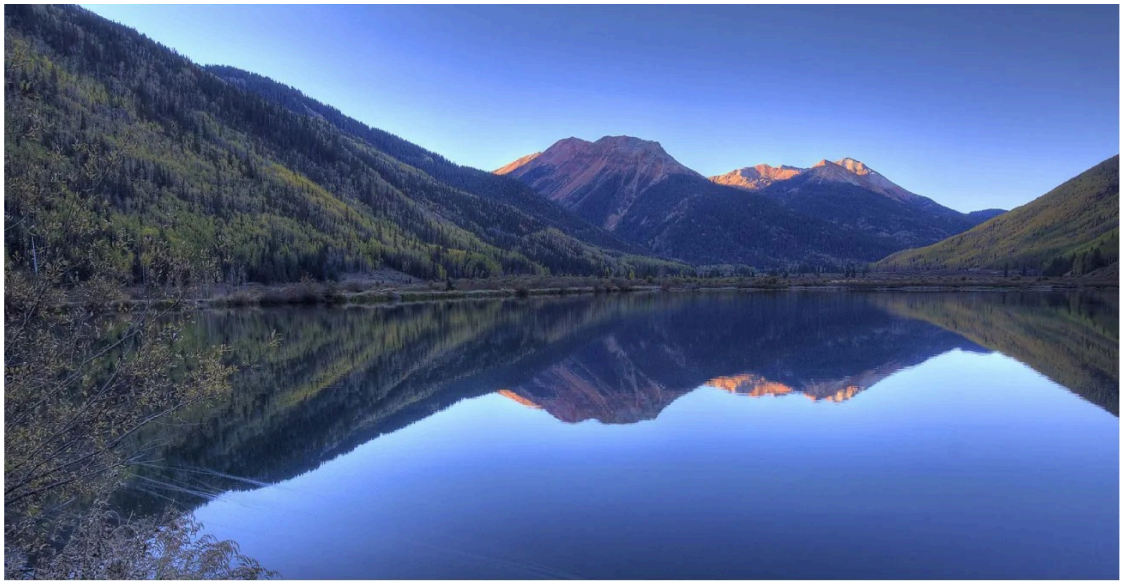


Figure 6.1.1: Like the mountain whose image is reflected in a lake, many organic molecules also have mirror-image counterparts. (credit: modification of work “Crystal Lake sunrise reflection” by Sandy Horvath-Dori/Wikimedia Commons, CC BY 2.0)

Are you right-handed or left-handed? You may not spend much time thinking about it, but handedness plays a surprisingly large role in your daily activities. Many musical instruments, such as oboes and clarinets, have a handedness to them; the last available softball glove always fits the wrong hand. The reason for these difficulties is that our hands aren’t identical; rather, they’re *mirror images*. When you hold a left hand up to a mirror, the image you see looks like a right hand. Try it.



Handedness is also important in organic and biological chemistry, where it arises primarily as a consequence of the tetrahedral stereochemistry of sp^3-hybridized carbon atoms. Many drugs and almost all the molecules in our bodies—amino acids, carbohydrates, nucleic acids, and many more—have a handedness. Furthermore, molecular handedness enables the precise

interactions between enzymes and their substrates that are involved in the hundreds of thousands of chemical reactions on which life is based.

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6.2: The Reason for Handedness in Molecules - Chirality

A molecule that is not identical to its mirror image is said to be chiral (**ky**-ral, from the Greek *cheir,* meaning “hand”). You can’t take a chiral molecule and its enantiomer and place one on the other so that all atoms coincide.

How can you predict whether a given molecule is or is not chiral? A molecule is not chiral if it has a plane of symmetry. A plane of symmetry is a plane that cuts through the middle of a molecule (or any object) in such a way that one half of the molecule or object is a mirror image of the other half. A coffee mug, for example, has a plane of symmetry. If you were to cut the coffee mug in half from top to bottom, one half would be a mirror image of the other half. A hand, however, does not have a plane of symmetry. One “half” of a hand is not a mirror image of the other half (Figure 6.2.1).

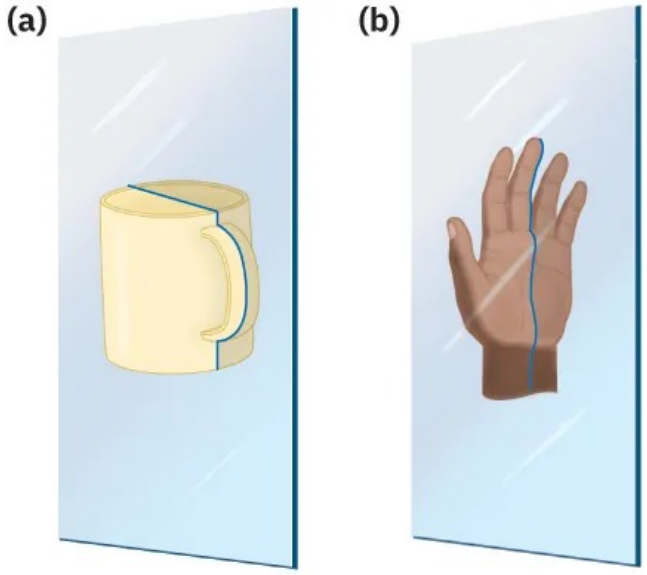


Figure 6.2.1: The meaning of symmetry plane. **(a)** An object like the coffee mug has a symmetry plane cutting through it so that right and left halves are mirror images. **(b)** An object like a hand has no symmetry plane; the right “half” of a hand is not a mirror image of the left half.

A molecule that has a plane of symmetry in any conformation must be identical to its mirror image and must be nonchiral, or achiral. Thus, propanoic acid, $CH_3CH_2CO_2H$, has a plane of symmetry when lined up as shown in Figure 6.2.2 and is achiral, while lactic acid, $CH_3CH(OH)CO_2H$, has no plane of symmetry in any conformation and is chiral.

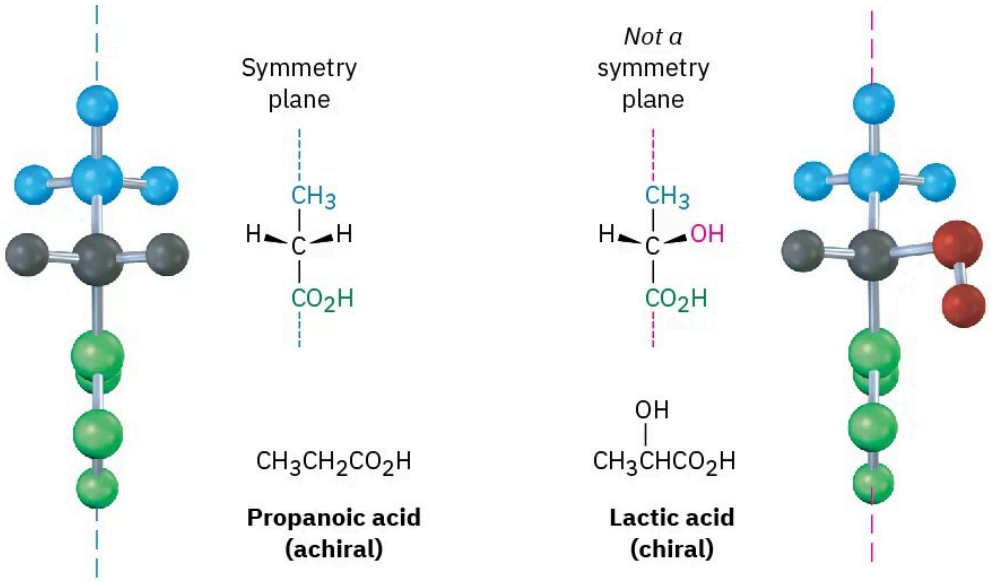
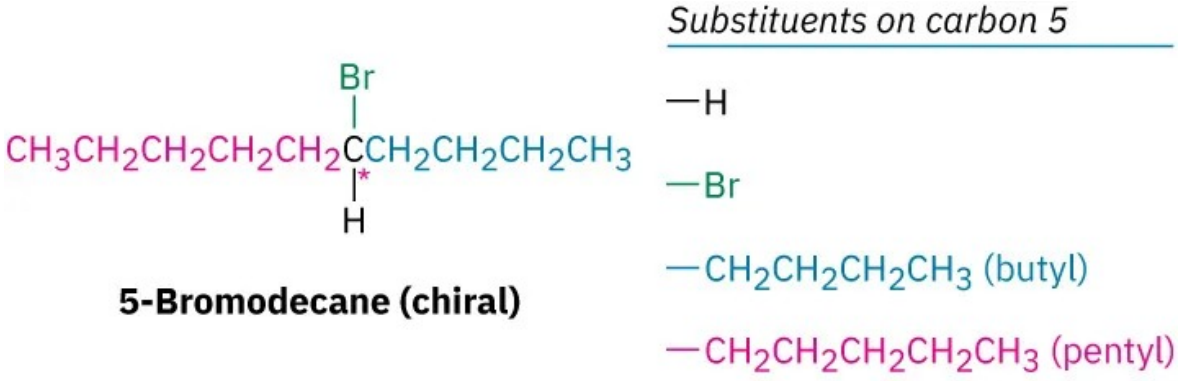


Figure 6.2.2: The achiral propanoic acid molecule versus the chiral lactic acid molecule. Propanoic acid has a plane of symmetry that makes one side of the molecule a mirror image of the other. Lactic acid has no such symmetry plane.

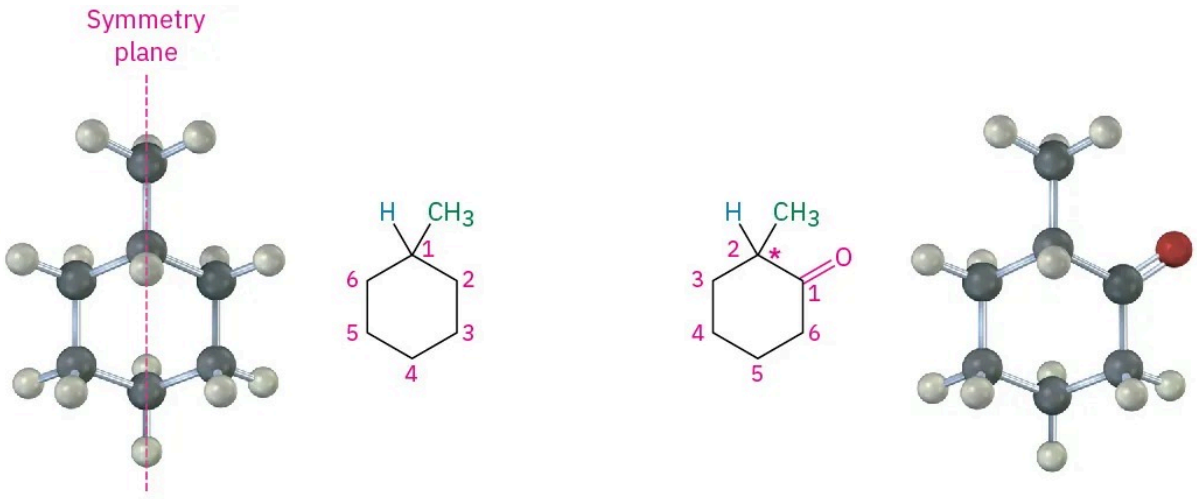
The most common, although not the only, cause of chirality in organic molecules is the presence of a tetrahedral carbon atom bonded to four different groups—for example, the central carbon atom in lactic acid. Such carbons are referred to as chirality centers, although other terms such as stereocenter, asymmetric center, and stereogenic center have also been used. Note that *chirality* is a property of the entire molecule, whereas a chirality *center* is the *cause* of chirality.

Detecting a chirality center in a complex molecule takes practice because it's not always immediately apparent whether four different groups are bonded to a given carbon. The differences don't necessarily appear right next to the chirality center. For example, 5-bromodecane is a chiral molecule because four different groups are bonded to C5, the chirality center (marked with an asterisk). A butyl substituent is similar to a pentyl substituent, but it isn't identical. The difference isn't apparent until looking four carbon atoms away from the chirality center, but there's still a difference.



As other possible examples, look at methylcyclohexane and 2-methylcyclohexanone. Methylcyclohexane is achiral because no carbon atom in the molecule is bonded to four different groups. You can immediately eliminate all $-CH_2-$ carbons and the $-CH_3$ carbon from consideration, but what about C1 on the ring? The C1 carbon atom is bonded to a $-CH_3$ group, to an –H atom, and to C2 and C6 of the ring. Carbons 2 and 6 are equivalent, however, as are carbons 3 and 5. Thus, the C6–C5–C4 "substituent" is equivalent to the C2–C3–C4 substituent, and methylcyclohexane is achiral. Another way of reaching the same conclusion is to realize that methylcyclohexane has a symmetry plane, which passes through the methyl group and through C1 and C4 of the ring.

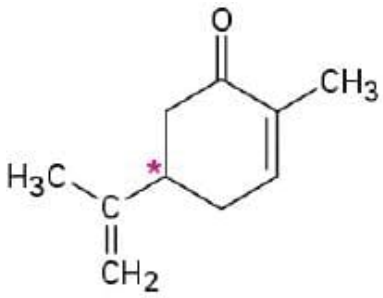
The situation is different for 2-methylcyclohexanone. 2-Methylcyclohexanone has no symmetry plane and is chiral because its C2 is bonded to four different groups: a $-CH_3$ group, an –H atom, a $-COCH_2-$ ring bond (C1), and a $-CH_2CH_2-$ ring bond (C3).



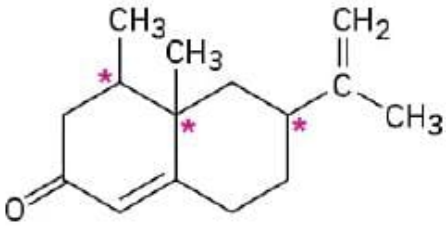
Methylcyclohexane (achiral)

2-Methylcyclohexanone (chiral)

Several more examples of chiral molecules are shown below. Check for yourself that the labeled carbons are chirality centers. You might note that carbons in $-CH_2-$, $-CH_3$, C=O, C=C, and C≡C groups can't be chirality centers. (Why not?)



Carvone (spearmint oil)



Nootkatone (grapefruit oil)

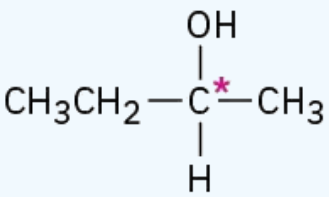
Worked Example 6.2.1: Drawing the Three-Dimensional Structure of a Chiral Molecule

Draw the structure of a chiral alcohol.

Strategy

An alcohol is a compound that contains the –OH functional group. To make an alcohol chiral, we need to have four different groups bonded to a single carbon atom, say –H, –OH, $-CH_3$, and $-CH_2CH_3$.

Solution



2-Butanol (chiral)

Exercise 6.2.1

Which of the following objects are chiral?

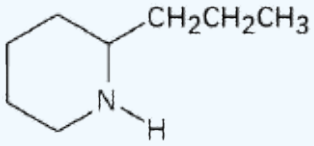
a. Soda can
b. Screwdriver
c. Screw
d. Shoe

Answer available at the end of this section.

Exercise 6.2.2

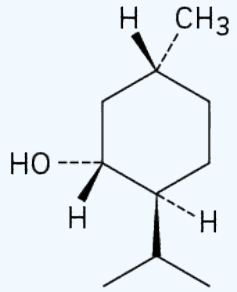
Which of the following molecules are chiral? Identify the chirality center(s) in each.

a.



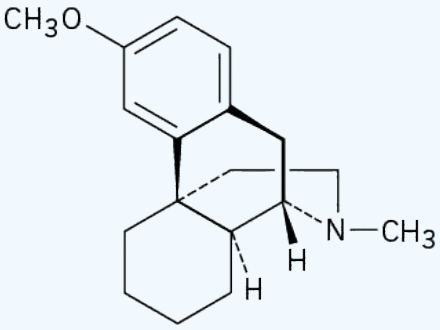
Coniine
(poison hemlock)

b.



Menthol
(flavoring agent)

c.

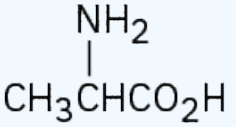


Dextromethorphan
(cough suppressant)

Answer available at the end of this section.

Exercise 6.2.3

Alanine, an amino acid found in proteins, is chiral. Draw the two enantiomers of alanine using the standard convention of solid, wedged, and dashed lines.

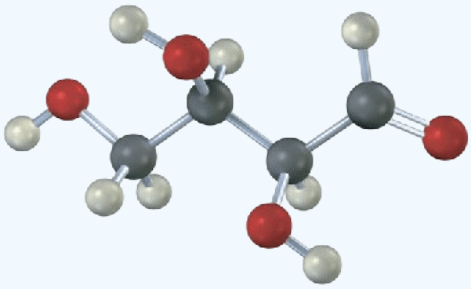


Alanine

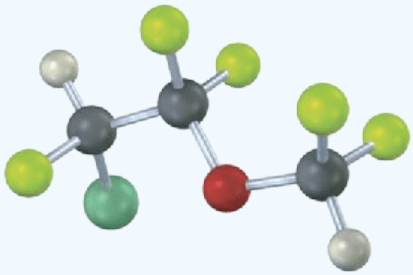
Answer available at the end of this section.

Exercise 6.2.4

Identify the chirality centers in the following molecules (gray = H, black = C, red = O, green = Cl, yellow-green = F):



a.



b.

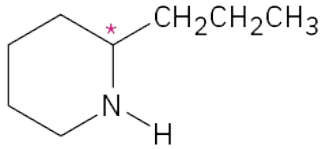
Answer available at the end of this section.

Answers

Exercise 6.2.1

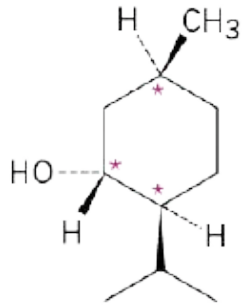
Chiral: screw, shoe

Exercise 6.2.2

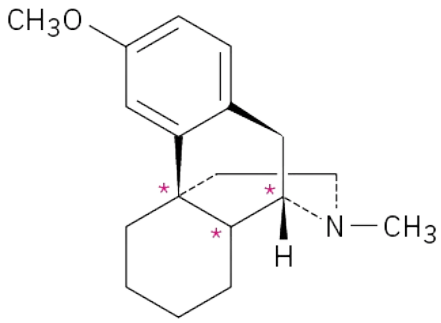


a.

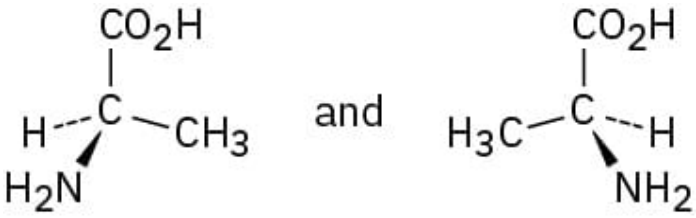
b.



c.

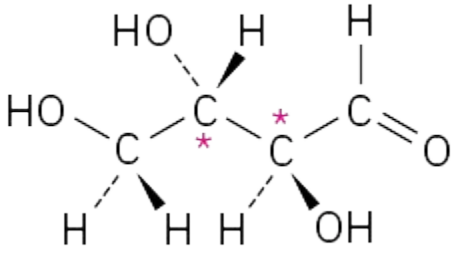


Exercise 6.2.3

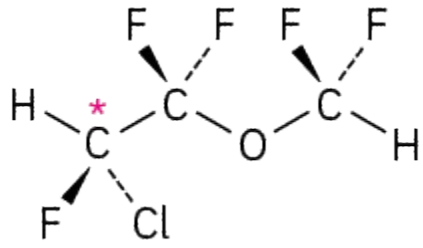


Exercise 6.2.4

a.



b.



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6.3: Enantiomers and the Tetrahedral Carbon

What causes molecular handedness? Look at generalized molecules of the type CH_3X, CH_2XY, and CHXYZ shown in Figure 6.3.1 . On the left are three molecules, and on the right are their images reflected in a mirror. The CH_3X and CH_2XY molecules are identical to their mirror images and thus are not handed. If you make a molecular model of each molecule and its mirror image, you find that you can superimpose one on the other so that all atoms coincide. The CHXYZ molecule, by contrast, is not identical to its mirror image. You can't superimpose a model of this molecule on a model of its mirror image for the same reason that you can't superimpose a left hand on a right hand: they simply aren't the same.

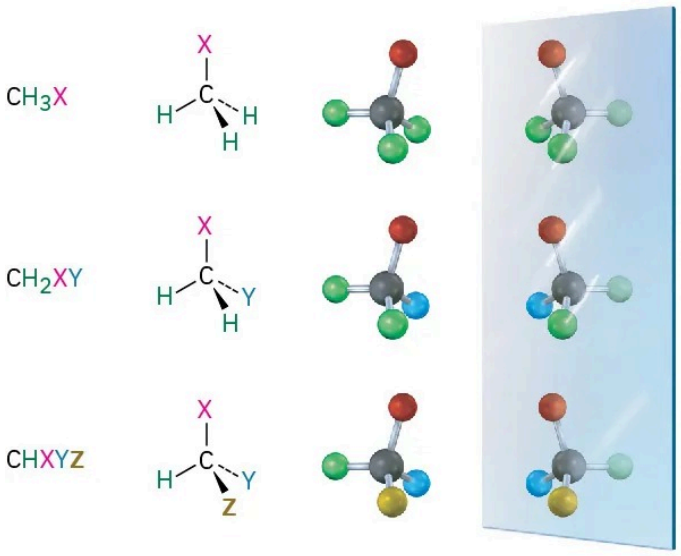
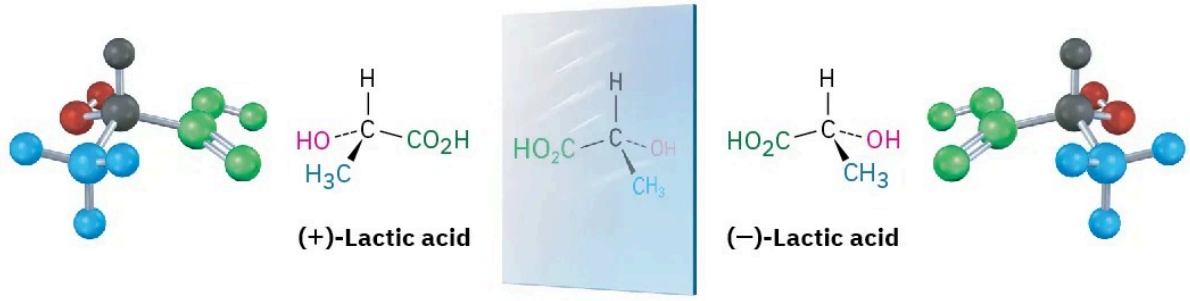


Figure 6.3.1: Tetrahedral carbon atoms and their mirror images. Molecules of the type CH_3X and CH_2XY are identical to their mirror images, but a molecule of the type CHXYZ is not. A CHXYZ molecule is related to its mirror image in the same way a right hand is related to a left hand.

A molecule that is not identical to its mirror image is a kind of stereoisomer (Section 4.3) called an enantiomer (e-**nan**-tee-oh-mer, from the Greek enantio, meaning "opposite"). Enantiomers are related to each other as a right hand is related to a left hand and result whenever a tetrahedral carbon is bonded to four different substituents (one need not be H). For example, lactic acid (2-hydroxypropanoic acid) exists as a pair of enantiomers because there are four different groups (–H, –OH, $–CH_3$, $–CO_2H$) bonded to the central carbon atom. The enantiomers are called (+)-lactic acid and (–)-lactic acid. Both are found in sour milk, but only the (+) enantiomer occurs in muscle tissue.



Lactic acid: a molecule of the general formula CHXYZ



No matter how hard you try, you can't superimpose a molecule of (+)-lactic acid on a molecule of (−)-lactic acid. If any two groups match up, say –H and $-CO_2H$, the remaining two groups don't match (Figure 6.3.2).

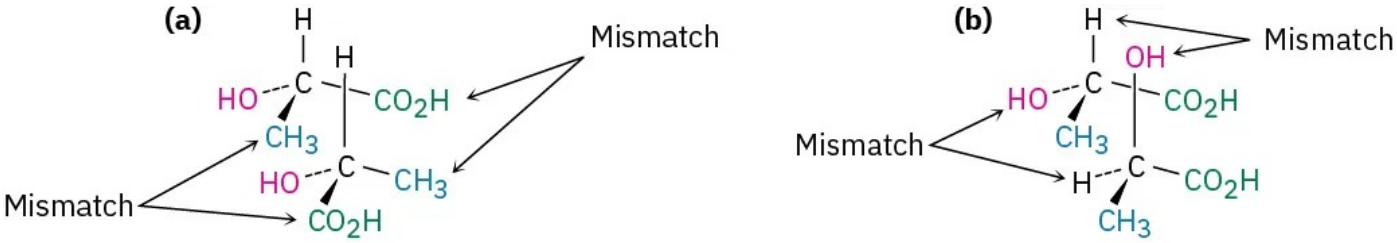


Figure 6.3.2: Attempts at superimposing the mirror-image forms of lactic acid. **(a)** When the –H and –OH substituents match up, the $-CO_2H$ and $-CH_3$ substituents don't; **(b)** when $-CO_2H$ and $-CH_3$ match up, –H and –OH don't. Regardless of how the molecules are oriented, they aren't identical.

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6.4: Pasteur's Discovery of Enantiomers

Little was done to build on Biot's discovery of optical activity until 1848, when Louis Pasteur began work on a study of crystalline tartaric acid salts derived from wine. On crystallizing a concentrated solution of sodium ammonium tartrate below 28 °C, Pasteur made the surprising observation that two distinct kinds of crystals were obtained. Furthermore, the two kinds of crystals were nonsuperimposable mirror images and were related in the same way that a right hand is related to a left hand.

Working carefully with tweezers, Pasteur was able to separate the crystals into two piles, one of "right-handed" crystals and one of "left-handed" crystals, like those shown in Figure 6.4.1. Although the original sample, a 50:50 mixture of right and left, was optically inactive, solutions of the crystals from each of the sorted piles were optically active and their specific rotations were equal in magnitude but opposite in sign.

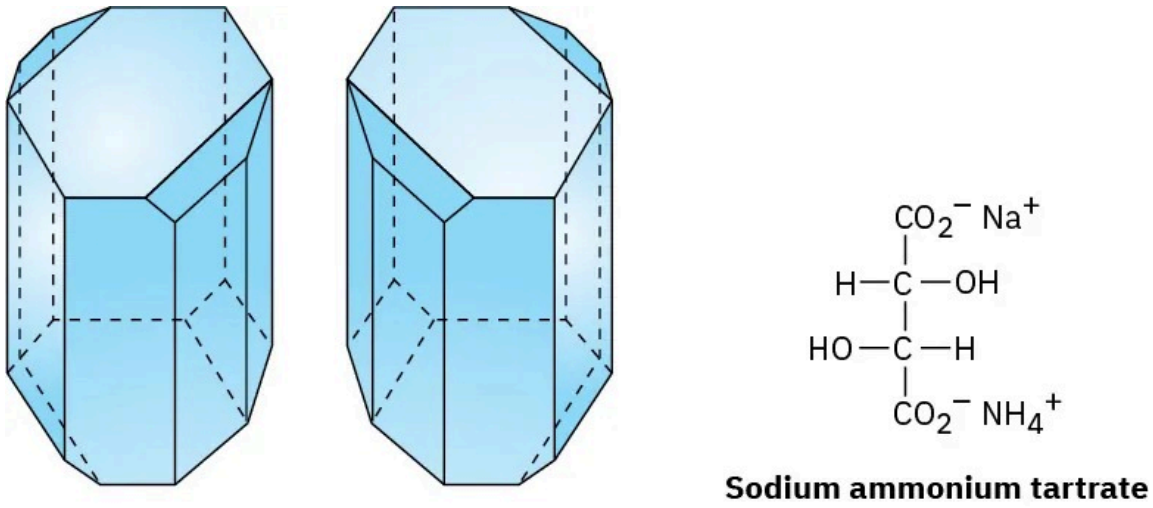


Figure 6.4.1: Drawings of sodium ammonium tartrate crystals taken from Pasteur's original sketches. One of the crystals is dextrorotatory in solution, and the other is levorotatory.

Pasteur was far ahead of his time. Although the structural theory of Kekulé had not yet been proposed, Pasteur explained his results by speaking of the molecules themselves, saying, "There is no doubt that [in the *dextro* tartaric acid] there exists an asymmetric arrangement having a nonsuperimposable image. It is no less certain that the atoms of the *levo* acid have precisely the inverse asymmetric arrangement." Pasteur's vision was extraordinary, for it was not until 25 years later that his ideas regarding asymmetric carbon atoms were confirmed.

Today, we would describe Pasteur's work by saying that he had discovered enantiomers. **Enantiomers**, also called **optical isomers**, have identical physical properties, such as melting point and boiling point, but differ in the direction in which their solutions rotate plane-polarized light.

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6.5: Optical Activity

The study of chirality originated in the early 19th century during investigations by the French physicist Jean-Baptiste Biot into the nature of *plane-polarized light*. A beam of ordinary light consists of electromagnetic waves that oscillate in an infinite number of planes at right angles to its direction of travel. When a beam of ordinary light passes through a device called a polarizer, however, only the light waves oscillating in a single plane pass through and the light is said to be plane-polarized. Light waves in all other planes are blocked out.

Biot made the remarkable observation that when a beam of plane-polarized light passes through a solution of certain organic molecules, such as sugar or camphor, the plane of polarization is rotated through an angle, α. Not all organic substances exhibit this property, but those that do are said to be optically active.

The angle of rotation can be measured with an instrument called a polarimeter, represented in Figure 6.5.1. A solution of optically active organic molecules is placed in a sample tube, plane-polarized light is passed through the tube, and rotation of the polarization plane occurs. The light then goes through a second polarizer called the analyzer. By rotating the analyzer until the light passes through *it*, we can find the new plane of polarization and can tell to what extent rotation has occurred.

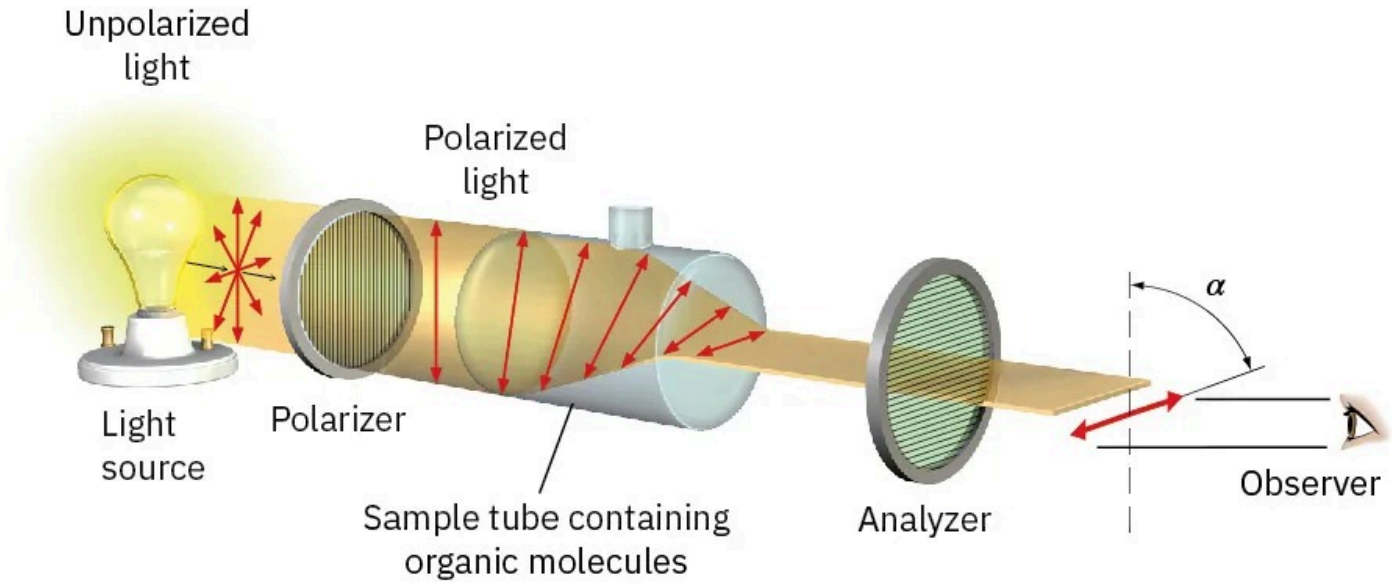


Figure 6.5.1: Schematic representation of a polarimeter. Plane-polarized light passes through a solution of optically active molecules, which rotate the plane of polarization.

In addition to determining the extent of rotation, we can also find the direction. From the vantage point of the observer looking directly at the analyzer, some optically active molecules rotate polarized light to the left (counterclockwise) and are said to be **levorotatory**, whereas others rotate polarized light to the right (clockwise) and are said to be **dextrorotatory**. By convention, rotation to the left is given a minus sign (–) and rotation to the right is given a plus sign (+). (–)-Morphine, for example, is levorotatory, and (+)-sucrose is dextrorotatory.

The extent of rotation observed in a polarimetry experiment depends on the number of optically active molecules encountered by the light beam. This number, in turn, depends on sample concentration and sample pathlength. If the concentration of the sample is doubled, the observed rotation doubles. If the concentration is kept constant but the length of the sample tube is doubled, the observed rotation doubles. It also happens that the angle of rotation depends on the wavelength of the light used.

To express optical rotations in a meaningful way so that comparisons can be made, we have to choose standard conditions. The **specific rotation**, $[\alpha]_D$, of a compound is defined as the observed rotation when light of 589.6 nanometer (nm; 1 nm = 10^{-9} m) wavelength is used with a sample pathlength l of 1 decimeter (dm; 1 dm = 10 cm) and a sample concentration c of 1 g/cm^3. (Light of 589.6 nm, the so-called sodium D line, is the yellow light emitted from common sodium street lamps.)

$$[\alpha]_D = \frac{\text{Observed rotation (degrees)}}{\text{Pathlength, } l(\text{dm}) \times \text{ Concentration, } c(\text{ g/cm}^3)} = \frac{\alpha}{l \times c}$$

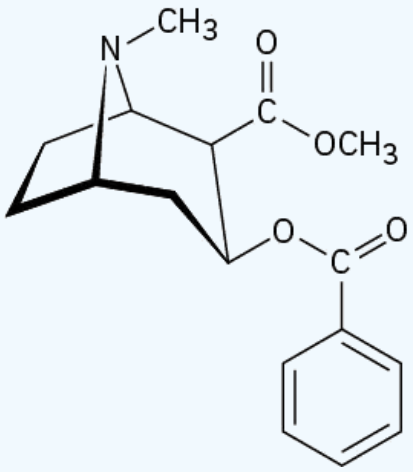
When optical rotations are expressed in this standard way, the specific rotation, $[\alpha]_D$, is a physical constant characteristic of a given optically active compound. For example, (+)-lactic acid has $[\alpha]_D = +3.82$, and (−)-lactic acid has $[\alpha]_D = -3.82$. That is, the two enantiomers rotate plane-polarized light to exactly the same extent but in opposite directions. Note that the units of specific rotation are [(deg • cm^2)/g] but the values are usually expressed without units. Some additional examples are listed in Table 6.5.1.

Table 6.5.1 Specific Rotations of Some Organic Molecules

Compound	$[\alpha]_D$	Compound	$[\alpha]_D$
Penicillin V	+233	Cholesterol	−31.5
Sucrose	+66.47	Morphine	−132
Camphor	+44.26	Cocaine	−16
Chloroform	0	Acetic acid	0

Worked Example 6.5.1: Calculating an Optical Rotation

A 1.200 g sample of cocaine, $[\alpha]_D = -16$, was dissolved in 7.500 mL of chloroform and placed in a sample tube having a pathlength of 5.000 cm. What was the observed rotation?



Cocaine

Strategy

Since

$$\alpha]_D = \frac{\alpha}{l \times c}$$

Then

$$\alpha = l \times c \times [\alpha]_D$$

where $[\alpha]_D = -16; l = 5.00 \text{ cm} = 0.500\text{dm}; c = 1.20 \text{ g}/7.50 \text{ cm}^3 = 0.160 \text{ g/cm}^3$

Solution

$$\alpha = (-16)(0.500)(0.160) = -1.3^\circ.$$

Exercise 6.5.1

Is cocaine (Worked Example 6.5.1) dextrorotatory or levorotatory?

Answer available at the end of this section.

Exercise 6.5.2

A 1.50 g sample of coniine, the toxic extract of poison hemlock, was dissolved in 10.0 mL of ethanol and placed in a sample cell with a 5.00 cm pathlength. The observed rotation at the sodium D line was +1.21°. Calculate $[\alpha]_D$ for coniine.

Answer available at the end of this section.

Answers

Exercise 6.5.1

Levorotatory

Exercise 6.5.2

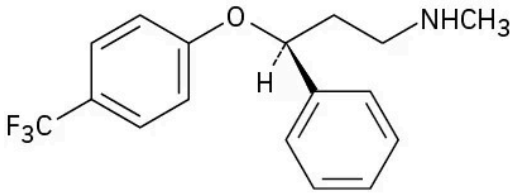
+16.1°

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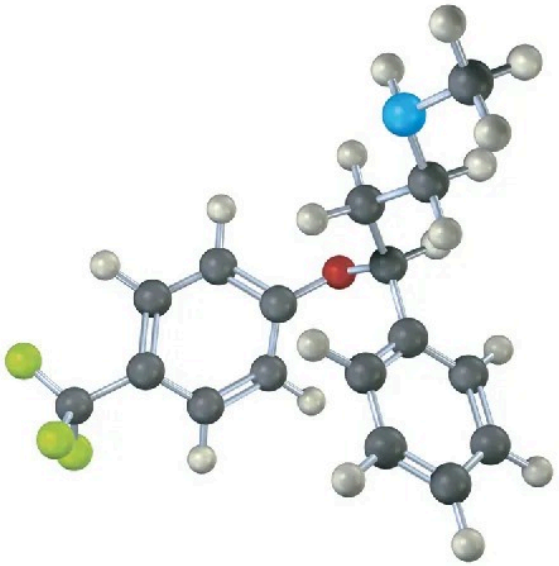
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6.6: Chirality in Nature and Chiral Environments

Although the different enantiomers of a chiral molecule have the same physical properties, they usually have different biological properties. For example, a change in chirality can affect the biological properties of many drugs, such as fluoxetine, a heavily prescribed medication sold under the trade name Prozac. Racemic fluoxetine is an effective antidepressant but has no activity against migraine. The pure S enantiomer, however, works remarkably well in preventing migraine. Other examples of how chirality affects biological properties are given in the Chapter 5 *Chemistry Matters* at the end of this chapter.



(*S*)-Fluoxetine
(prevents migraine)



Why do different enantiomers have different biological properties? To have a biological effect, a substance typically must fit into an appropriate receptor that has a complementary shape. But because biological receptors are chiral, only one enantiomer of a chiral substrate can fit, just as only a right hand can fit into a right-handed glove. The mirror-image enantiomer will be a misfit, like a left hand in a right-handed glove. A representation of the interaction between a chiral molecule and a chiral biological receptor is shown in Figure 6.6.1: one enantiomer fits the receptor perfectly, but the other does not.

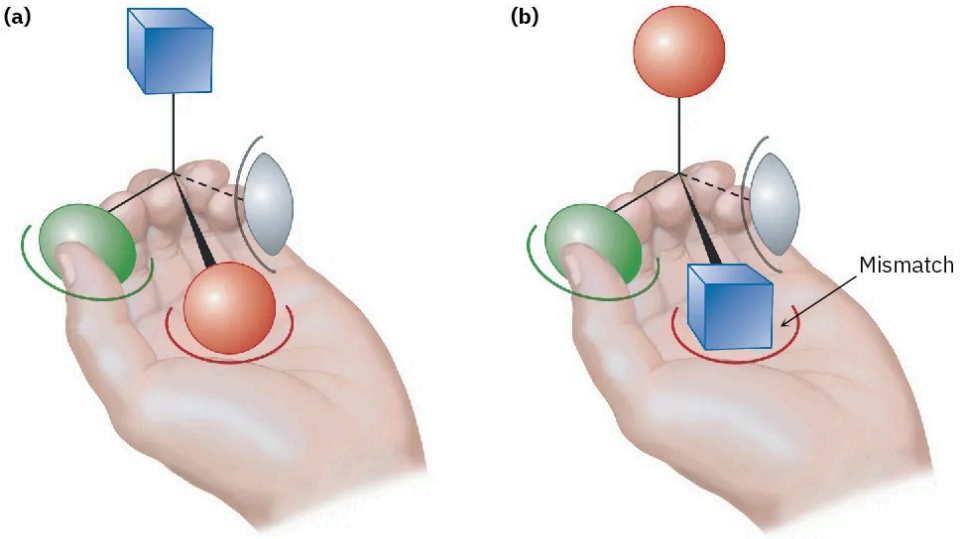
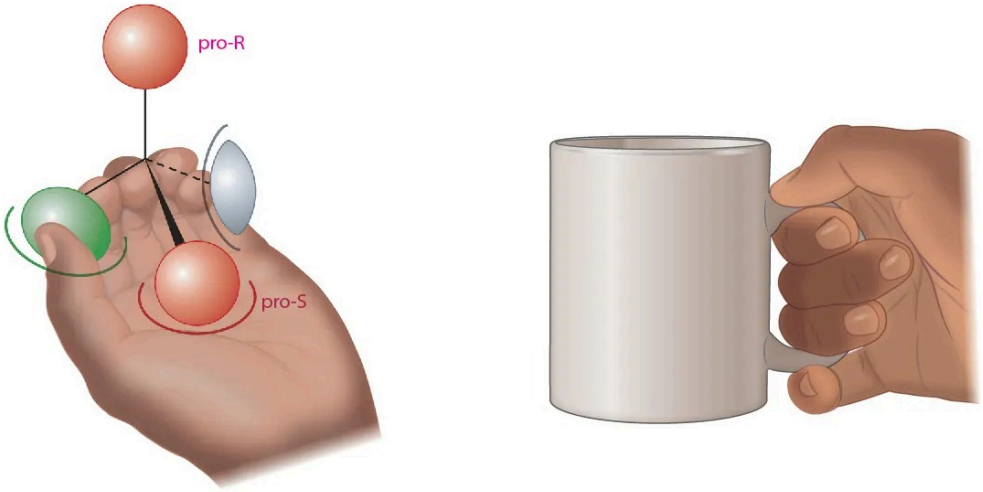


Figure 6.6.1: Interaction of a chiral object with a chiral receptor. A left hand interacts with a chiral object, much as a biological receptor interacts with a chiral molecule. **(a)** One enantiomer fits into the hand perfectly: **green thumb**, **red palm**, and **gray pinkie finger**, with the **blue substituent exposed**. **(b)** The other enantiomer, however, can't fit into the hand. When the green thumb and gray pinkie finger interact appropriately, the palm holds a blue substituent rather than a red one, with the **red substituent exposed**.

The hand-in-glove fit of a chiral substrate into a chiral receptor is relatively straightforward, but it's less obvious how a prochiral substrate can undergo a selective reaction. Take the reaction of ethanol with NAD^+ catalyzed by yeast alcohol dehydrogenase. As we saw at the end of Section 5.12, this reaction occurs with exclusive removal of the pro-*R* hydrogen from ethanol and with addition only to the Re face of the NAD^+ carbon.

We can understand this result by imagining that the chiral enzyme receptor again has three binding sites, as in Figure 6.6.1. When green and gray substituents of a prochiral substrate are held appropriately, however, only one of the two red substituents—say, the pro-S one—is also held while the other, pro-*R,* substituent is exposed for reaction.

We describe the situation by saying that the receptor provides a chiral environment for the substrate. In the absence of a **chiral environment**, the two red substituents are chemically identical, but in the presence of a chiral environment, they are chemically distinctive (Figure 6.6.2*a*). The situation is similar to what happens when you pick up a coffee mug. By itself, the mug has a plane of symmetry and is achiral. When you pick up the mug, however, your hand provides a chiral environment so that one side becomes much more accessible and easier to drink from than the other (Figure 6.6.2*b*).



(a) (b)

Figure 6.6.2: (a) When a prochiral molecule is held in a chiral environment, the **two seemingly identical substituents** are **distinguishable.** **(b)** Similarly, when an achiral coffee mug is held in the chiral environment of your hand, it's much easier to drink from one side than the other because the two sides of the mug are now distinguishable.

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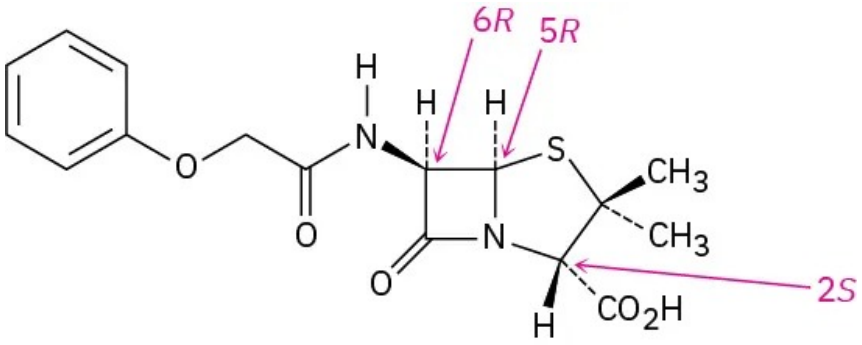
6.7: Chemistry Matters—Chiral Drugs

The many hundreds of different pharmaceutical agents approved for use by the U.S. Food and Drug Administration come from many sources. Many drugs are isolated directly from plants or bacteria, and others are made by chemical modification of naturally occurring compounds. An estimated 33%, however, are made entirely in the laboratory and have no relatives in nature.



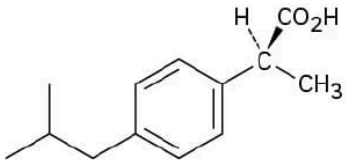
Figure 6.7.1: The S enantiomer of ibuprofen soothes the aches and pains of athletic injuries much more effectively than the *R* enantiomer. (credit: "World Athletic Championships 2007 in Osaka" by Eckhard Pecher/Wikimedia Commons, CC BY 2.5)

Those drugs that come from natural sources, either directly or after laboratory modification, are usually chiral and are generally found only as a single enantiomer rather than as a racemate. Penicillin V, for example, an antibiotic isolated from the *Penicillium* mold, has the 2*S*,5*R*,6*R* configuration. Its enantiomer, which does not occur naturally but can be made in the laboratory, has no antibiotic activity.

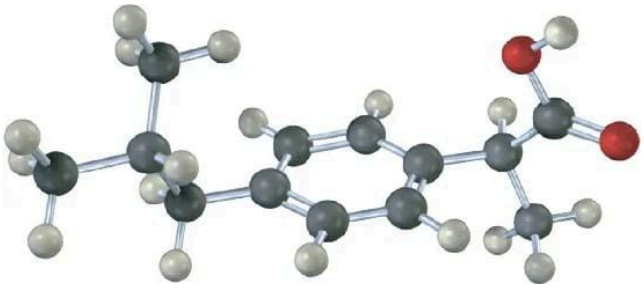


Penicillin V (2*S*,5*R*,6*R* configuration)

In contrast to drugs from natural sources, drugs that are made entirely in the laboratory are either achiral or, if chiral, are often produced and sold as racemates. Ibuprofen, for example, has one chirality center and is sold commercially under such trade names as Advil, Nuprin, and Motrin as a 50 : 50 mixture of *R* and S. It turns out, however, that only the S enantiomer is active as an analgesic and anti-inflammatory agent. The *R* enantiomer of ibuprofen is inactive, although it is slowly converted in the body to the active S form.



(*S*)-Ibuprofen
(an active analgesic agent)



Not only is it chemically wasteful to synthesize and administer an enantiomer that does not serve the intended purpose, many instances are now known where the presence of the "wrong" enantiomer in a racemic mixture either affects the body's ability to utilize the "right" enantiomer or has unintended pharmacological effects of its own. The presence of (*R*)-ibuprofen in the racemic mixture, for instance, slows the rate at which the S enantiomer takes effect in the body, from 12 minutes to 38 minutes.

To get around this problem, pharmaceutical companies attempt to devise methods of *enantioselective* synthesis, which allow them to prepare only a single enantiomer rather than a racemic mixture. Viable methods have been developed for the preparation of (*S*)-ibuprofen, which is marketed in Europe. We'll look further into enantioselective synthesis in the Chapter 19 *Chemistry Matters*.

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6.8: Sequence Rules for Specifying Configuration

Structural drawings provide a visual representation of stereochemistry, but a written method for indicating the three-dimensional arrangement, or configuration, of substituents at a chirality center is also needed. The method used a set of **sequence rules** to rank the four groups attached to the chirality center and then looks at the handedness with which those groups are attached. Called the **Cahn–Ingold–Prelog rules** after the chemists who proposed them, the sequence rules are as follows:

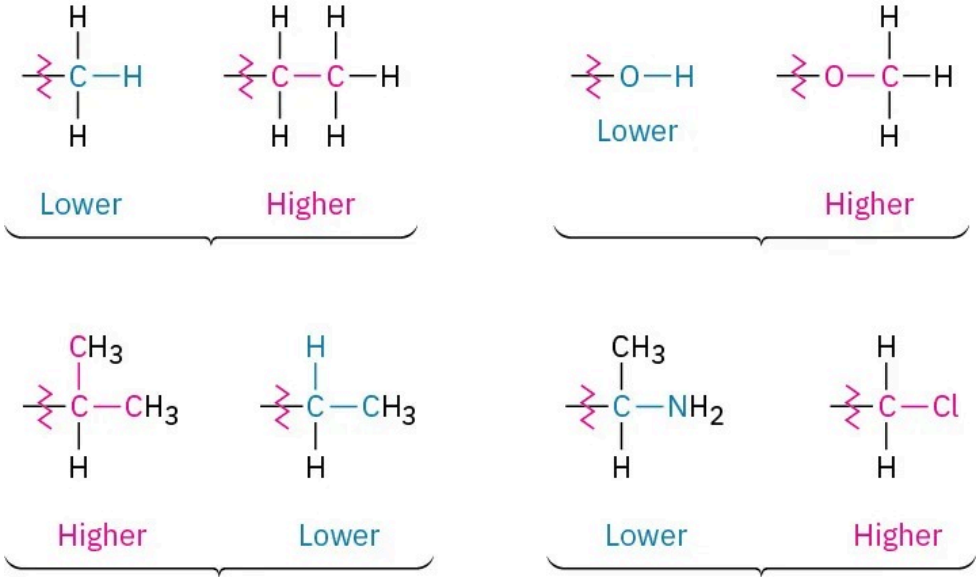
RULE 1

Look at the four atoms directly attached to the chirality center, and rank them according to atomic number. The atom with the highest atomic number has the highest ranking (first), and the atom with the lowest atomic number (usually hydrogen) has the lowest ranking (fourth). When different isotopes of the same element are compared, such as deuterium (^2H) and protium (^1H), the heavier isotope ranks higher than the lighter isotope. Thus, atoms commonly found in organic compounds have the following order.

Atomic number	35	17	16	15	8	7	6	(2)	(1)	
Higher rank	Br	> Cl	> S	> P	> O	> N	> C	> ^2H	> ^1H	Lower rank

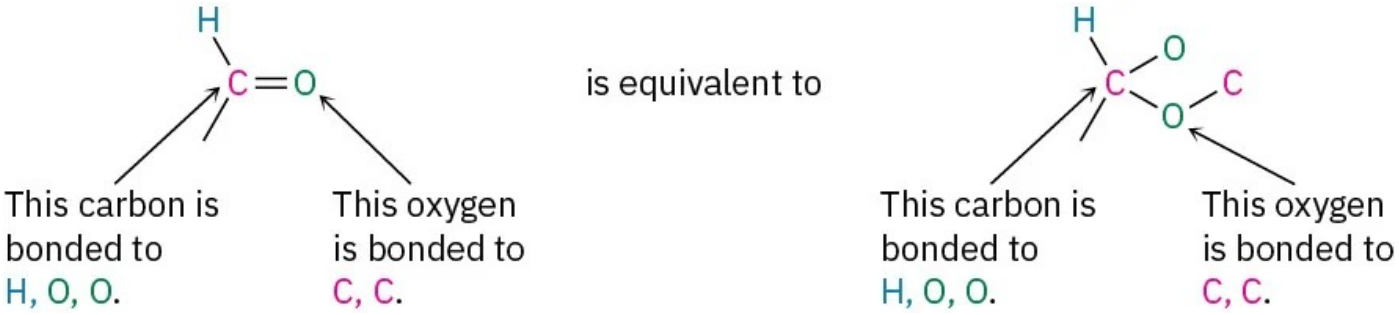
RULE 2

If a decision can't be reached by ranking the first atoms in the substituent, look at the second, third, or fourth atoms away from the chirality center until the first difference is found. A $–CH_2CH_3$ substituent and a $–CH_3$ substituent are equivalent by rule 1 because both have carbon as the first atom. By rule 2, however, ethyl ranks higher than methyl because ethyl has a carbon as its highest second atom, while methyl has only hydrogen as its second atom. Look at the following pairs of examples to see how the rule works:

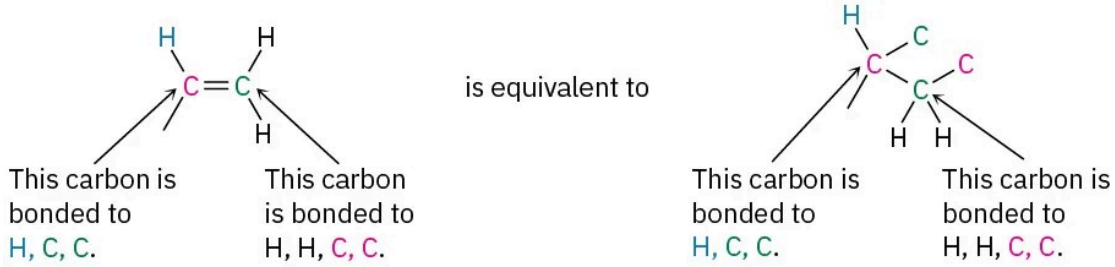


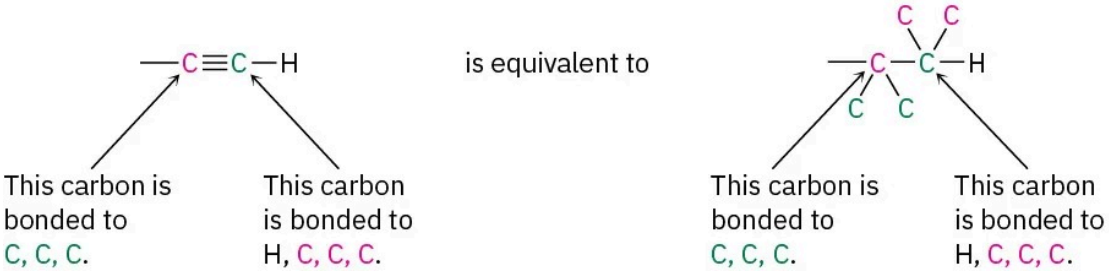
RULE 3

Multiple-bonded atoms are equivalent to the same number of single-bonded atoms. For example, an aldehyde substituent ($–CH=O$), which has a carbon atom *doubly* bonded to *one* oxygen, is equivalent to a substituent having a carbon atom *singly* bonded to *two* oxygens:



As further examples, the following pairs are equivalent:





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) points directly away from us. We then look at the three remaining substituents, which now appear to radiate toward us like the spokes on a steering wheel (Figure 6.8.1). If a curved arrow drawn from the highest to second-highest to third-highest ranked substituent (1 → 2 → 3) is clockwise, we say that the chirality center has the *R* configuration (S for the Latin *rectus,* meaning “right”). If an arrow from 1 → 2 → 3 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 *R*ight (clockwise) turn.

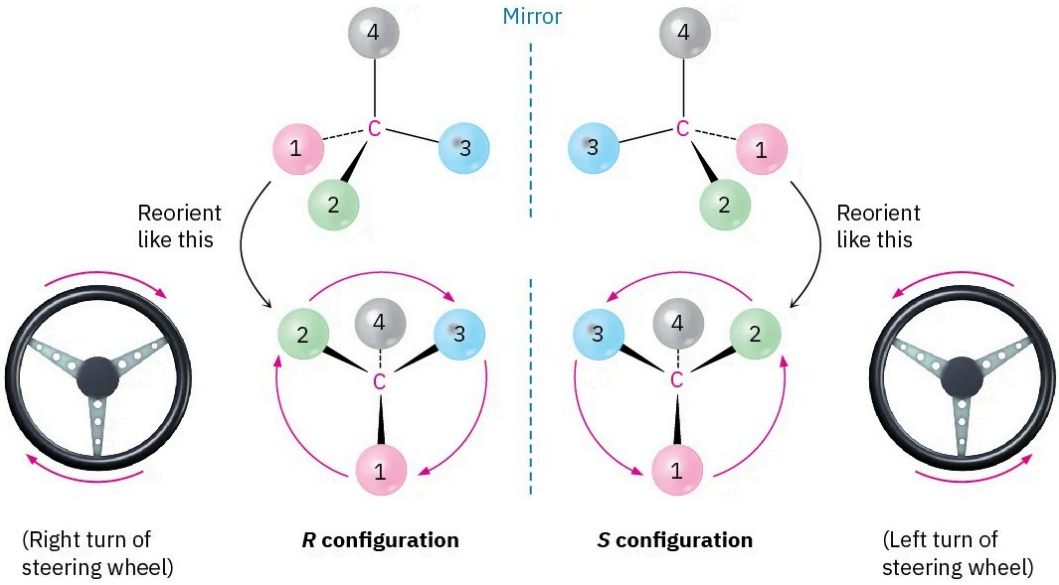


Figure 6.8.1: Assigning *R* and S configurations to chirality centers. When the molecule is oriented so that the lowest-ranked group (**4**) is toward the rear, the remaining three groups radiate toward the viewer like the spokes of a steering wheel. If the direction of travel 1 → 2 → 3 is clockwise (right turn), the center has the *R* configuration. If the direction of travel 1 → 2 → 3 is counterclockwise (left turn), the center is S.

Look at (–)-lactic acid in Figure 6.8.2 for an example of how to assign configuration. Sequence rule 1 says that –OH is ranked 1 and –H is ranked 4, but it doesn't allow us to distinguish between $-CH_3$ and $-CO_2H$ because both groups have carbon as their first atom. Sequence rule 2, however, says that $-CO_2H$ ranks higher than $-CH_3$ because O (the highest second atom in $-CO_2H$) outranks H (the highest second atom in $-CH_3$). Now, turn the molecule so that the fourth-ranked group (–H) is oriented toward the rear, away from the observer. Since a curved arrow from 1 (–OH) to 2 ($-CO_2H$) to 3 ($-CH_3$) is clockwise (right turn of the steering wheel), (–)-lactic acid has the *R* configuration. Applying the same procedure to (+)-lactic acid leads to the opposite assignment.

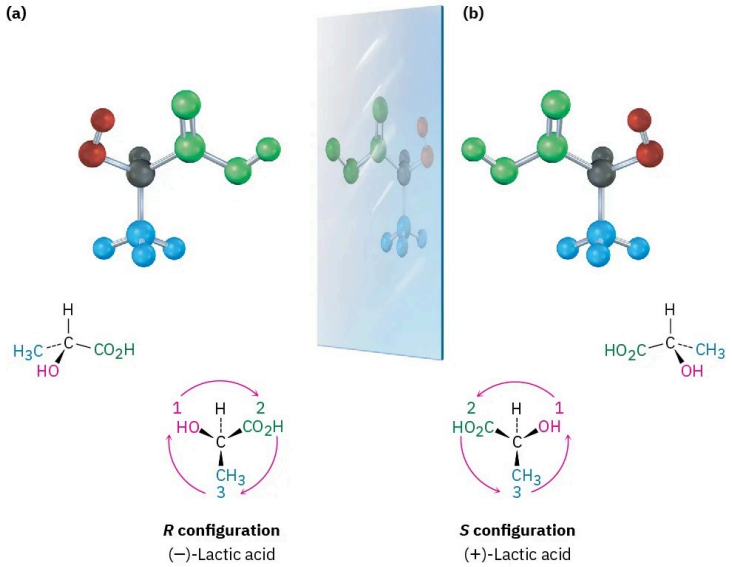


Figure 6.8.2: Assigning configuration to **(a)** (*R*)-(–)-lactic acid and **(b)** (S)-(+)-lactic acid.

Further examples are provided by naturally occurring (–)-glyceraldehyde and (+)-alanine, which both have the *S* configuration as shown in Figure 6.8.3. Note that the sign of optical rotation, (+) or (–), is not related to the *R,S* designation. (*S*)-Glyceraldehyde happens to be levorotatory (–), and (S)-alanine happens to be dextrorotatory (+). There is no simple correlation between *R,S* configuration and direction or magnitude of optical rotation.

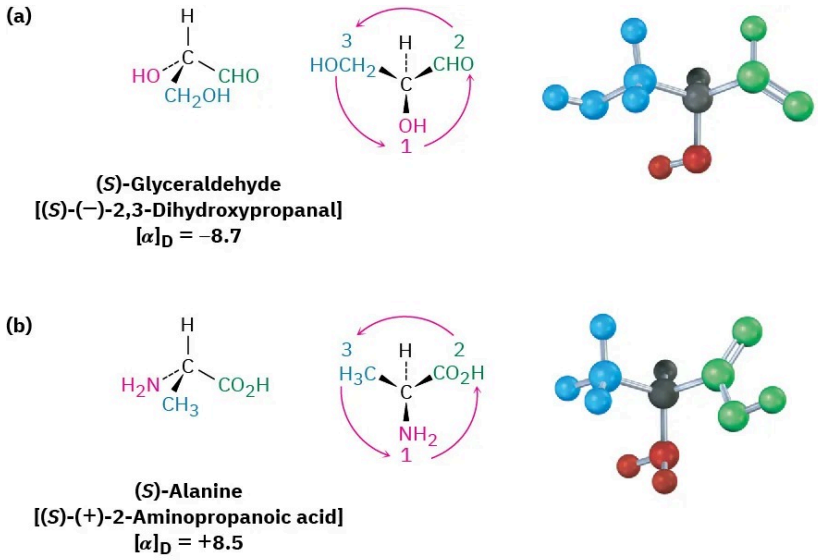
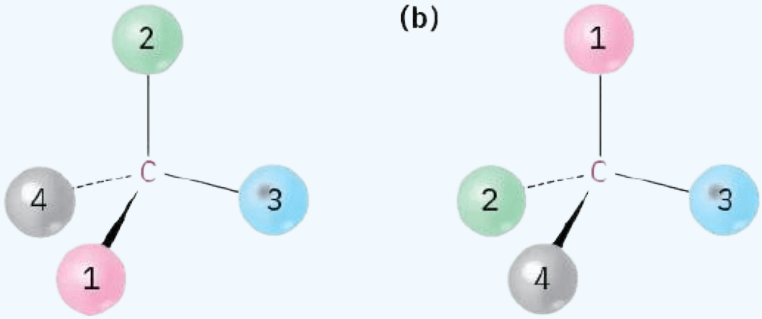


Figure 6.8.3: Assigning configuration to **(a)** (−)-glyceraldehyde. **(b)** (+)-alanine. Both happen to have the S configuration, although one is levorotatory and the other is dextrorotatory.

One additional point needs to be mentioned—the matter of absolute configuration. How do we know that the assignments of *R* and S configuration are correct in an absolute sense, rather than a relative, sense? Since there is no correlation between the *R,S* configuration and the direction or magnitude of optical rotation, how do we know that the *R* configuration belongs to the levorotatory enantiomer of lactic acid? This difficult question was finally solved in 1951, when an X-ray diffraction method was found for determining the absolute spatial arrangement of atoms in a molecule. Based on those results, we can say with certainty that the *R,S* conventions are correct.

Worked Example 6.8.1: Assigning Configuration to Chirality Centers

Orient each of the following drawings so that the lowest-ranked group is toward the rear, and then assign *R* or S configuration to each:

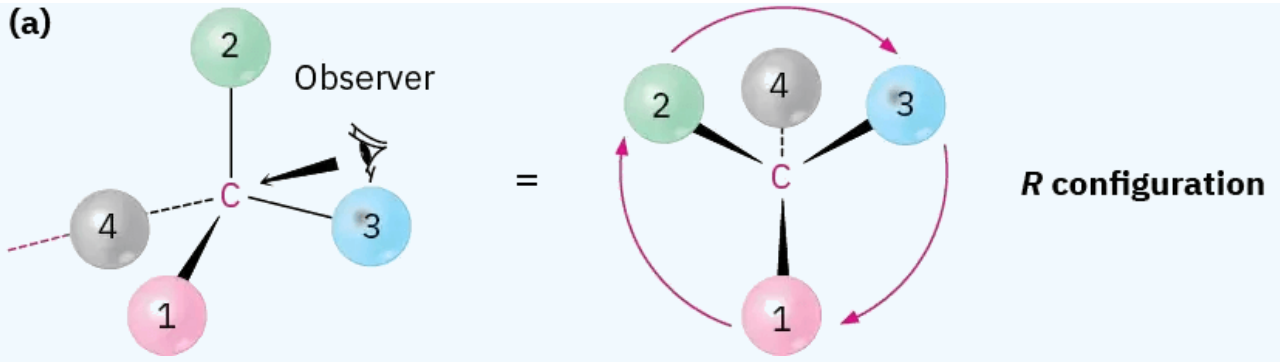


Strategy

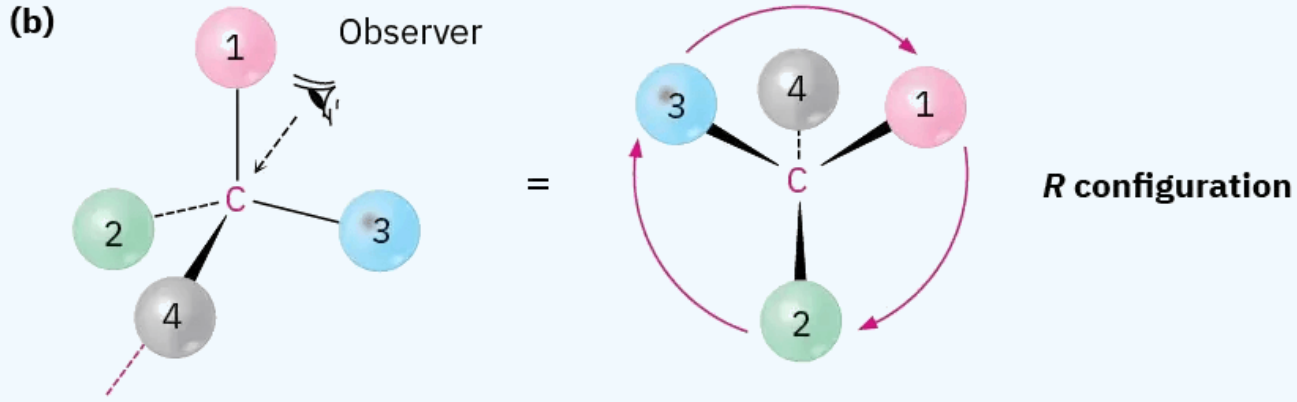
It takes practice to be able to visualize and orient a chirality center in three dimensions. You might start by indicating where the observer must be located—180° opposite the lowest-ranked group. Then imagine yourself in the position of the observer, and redraw what you would see.

Solution

In **(a)**, you would be located in front of the page toward the top right of the molecule, and you would see group 2 to your left, group 3 to your right, and group 1 below you. This corresponds to an *R* configuration.



In **(b)**, you would be located behind the page toward the top left of the molecule from your point of view, and you would see group 3 to your left, group 1 to your right, and group 2 below you. This also corresponds to an *R* configuration.



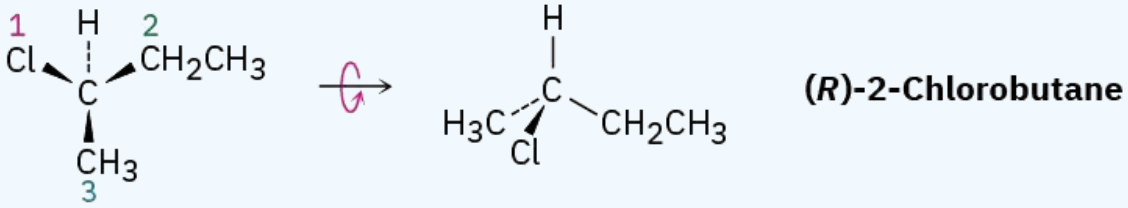
Worked Example 6.8.2: Drawing the Three-Dimensional Structure of a Specific Enantiomer

Draw a tetrahedral representation of (*R*)-2-chlorobutane.

Strategy

Begin by ranking the four substituents bonded to the chirality center: (1) –Cl, (2) $-CH_2CH_3$, (3) $-CH_3$, (4) –H. To draw a tetrahedral representation of the molecule, orient the lowest-ranked group (–H) away from you and imagine that the other three groups are coming out of the page toward you. Then, place the remaining three substituents such that the direction of travel 1 → 2 → 3 is clockwise (right turn), and tilt the molecule toward you to bring the rear hydrogen into view. Using molecular models is a real help in working problems of this sort.

Solution



Exercise 6.8.1

Which member in each of the following sets ranks higher?

a. –H or –Br
b. –Cl or –Br

c. $-CH_3$ or $-CH_2CH_3$
d. $-NH_2$ or $-OH$
e. $-CH_2OH$ or $-CH_3$
f. $-CH_2OH$ or $-CH{=}O$

Answer available at the end of this section.

Exercise 6.8.2

Rank each of the following sets of substituents:

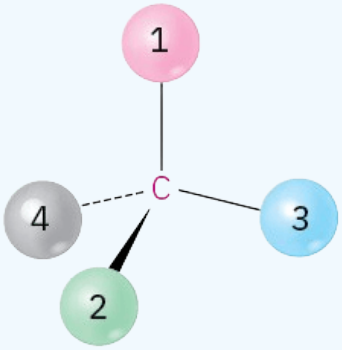
a. $-H$, $-OH$, $-CH_2CH_3$, $-CH_2CH_2OH$
b. $-CO_2H$, $-CO_2CH_3$, $-CH_2OH$, $-OH$
c. $-CN$, $-CH_2NH_2$, $-CH_2NHCH_3$, $-NH_2$
d. $-SH$, $-CH_2SCH_3$, $-CH_3$, $-SSCH_3$

Answer available at the end of this section.

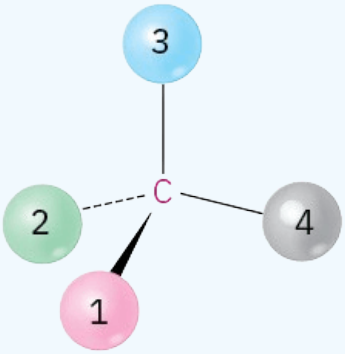
Exercise 6.8.1

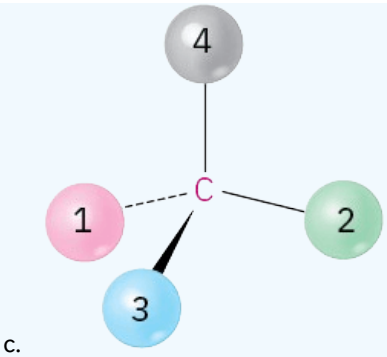
Orient each of the following drawings so that the lowest-ranked group is toward the rear, and then assign *R* or *S* configuration:

a.



b.



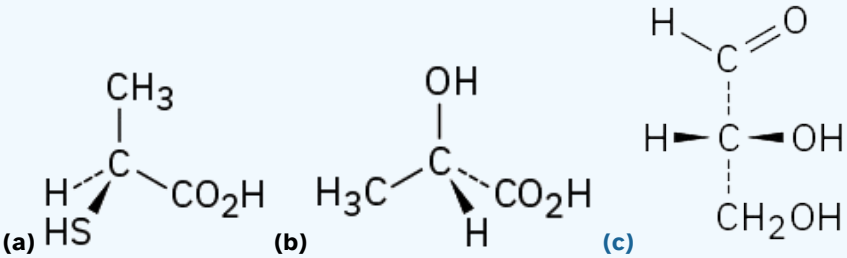


c.

Answer available at the end of this section.

Exercise 6.8.4

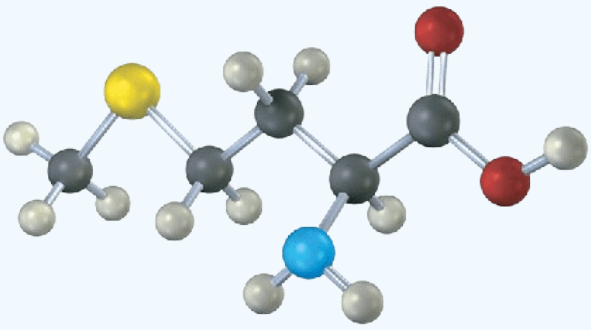
Assign *R* or *S* configuration to the chirality center in each of the following molecules:



Answer available at the end of this section.

Exercise 6.8.5

Assign *R* or *S* configuration to the chirality center in the following molecular model of the amino acid methionine (blue = N, yellow = S):



Answer available at the end of this section.

Answers

Exercise 6.8.1

a. –Br
b. –Br
c. $-CH_2CH_3$
d. –OH

e. $-CH_2OH$
f. $-CH{=}O$

Exercise 6.8.2

a. $-OH$, $-CH_2CH_2OH$, $-CH_2CH_3$, $-H$
b. $-OH$, $-CO_2CH_3$, $-CO_2H$, $-CH_2OH$
c. $-NH_2$, $-CN$, $-CH_2NHCH_3$, $-CH_2NH_2$
d. $-SSCH_3$, $-SH$, $-CH_2SCH_3$, $-CH_3$

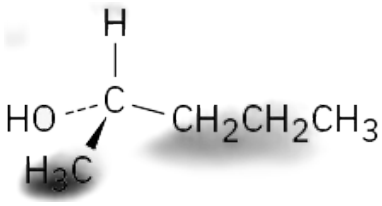
Exercise 6.8.1

a. S
b. *R*
c. S

Exercise 6.8.4

(a) S **(b)** S **(c)** *R*

Exercise 6.8.5



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6.9: Depicting Carbohydrate Stereochemistry - Fischer Projections

Objectives

After completing this section, you should be able to

1. draw the Fischer projection of a monosaccharide, given its wedge and dash structure or a molecular model.
2. draw the wedge and dash structure of a monosaccharide, given its Fischer projection or a molecular model.
3. construct a molecular model of a monosaccharide, given its Fischer projection or wedge and dash structure.

Key Terms

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

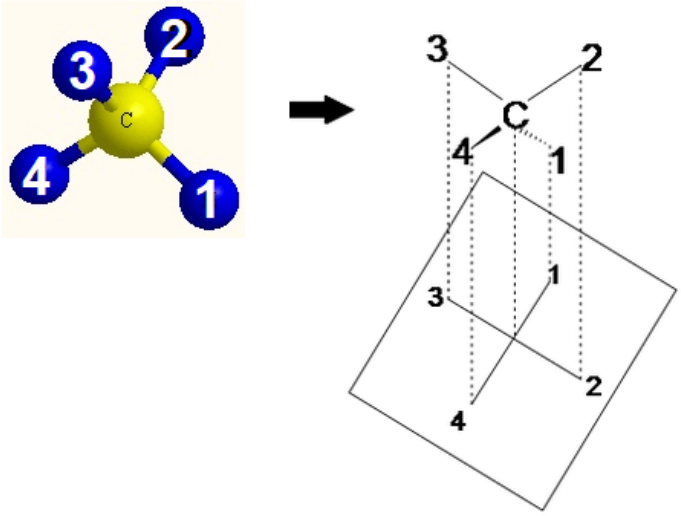
- Fischer projection

Study Notes

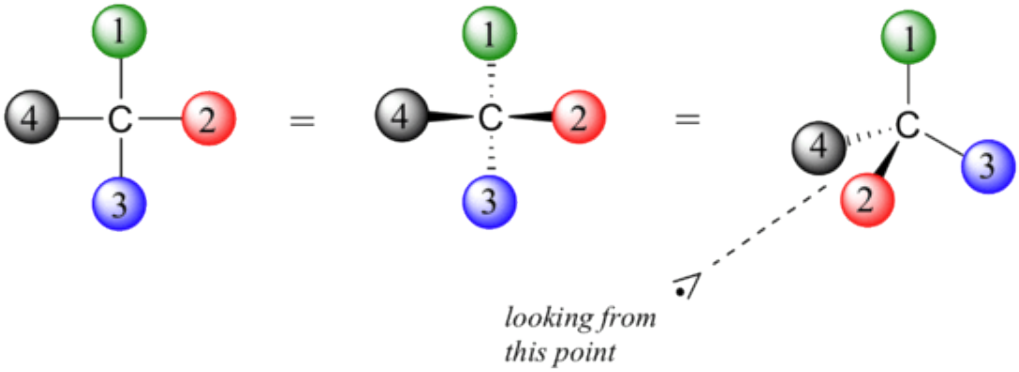
When studying this section, use your molecular model set to assist you in visualizing the structures of the compounds that are discussed. It is important that you be able to determine whether two apparently different Fischer projections represent two different structures or one single structure. Often the simplest way to check is to construct a molecular model corresponding to each projection formula, and then compare the two models.

Drawing Representations of 3D Structures

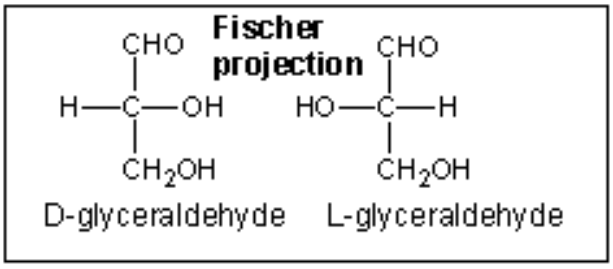
The problem of drawing three-dimensional configurations on a two-dimensional surface, such as a piece of paper, has been a long-standing concern of chemists. The wedge and dash notations we have been using are effective, but can be troublesome when applied to compounds having many chiral centers. As part of his Nobel Prize-winning research on carbohydrates, the great German chemist Emil Fischer, devised a simple notation that is still widely used. Fischer Projections allow us to represent 3D molecular structures in a 2D environment without changing their properties and/or structural integrity.

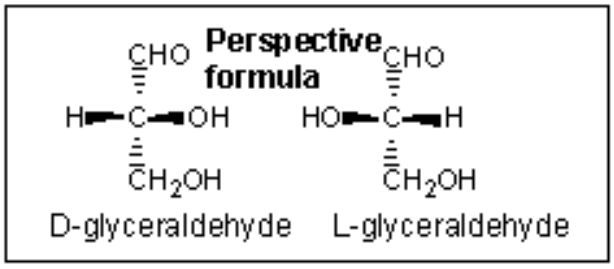


Fisher projections show sugars in their open chain form. In a Fischer projection, the carbon atoms of a sugar molecule are connected vertically by solid lines, while carbon-oxygen and carbon-hydrogen bonds are shown horizontally. Stereochemical information is conveyed by a simple rule: vertical bonds point into the plane of the page, while horizontal bonds point out of the page.

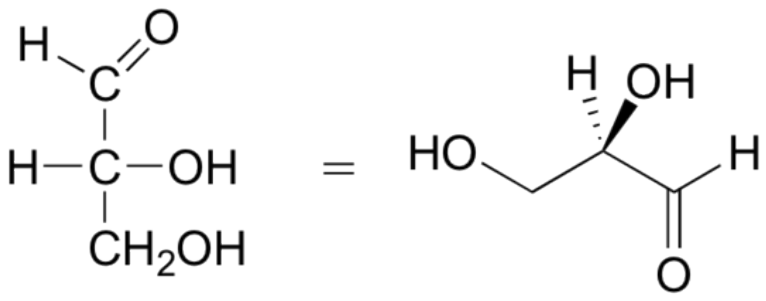


Sugars can be drawn in the straight chain form as either Fisher projections or perspective structural formulas. When drawing Fischer projections, the aldehyde group is written at the top, and the H and OH groups that are attached to each chiral carbon are written to the right or left. The arrangement of the atoms distinguishes one stereoisomer from the other.



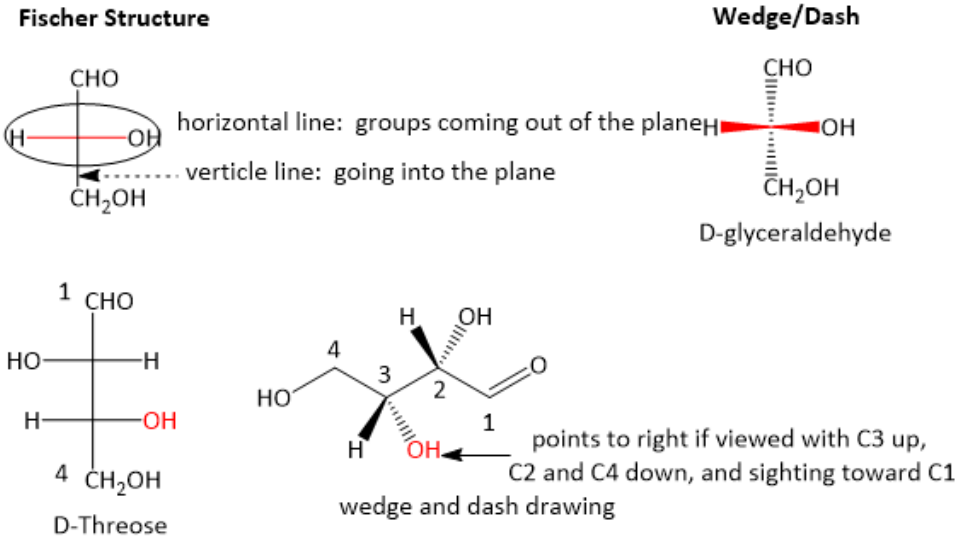


Below are two different representations of (R)-glyceraldehyde, the smallest sugar molecule (also called D-glyceraldehyde in the stereochemical nomenclature used for sugars):

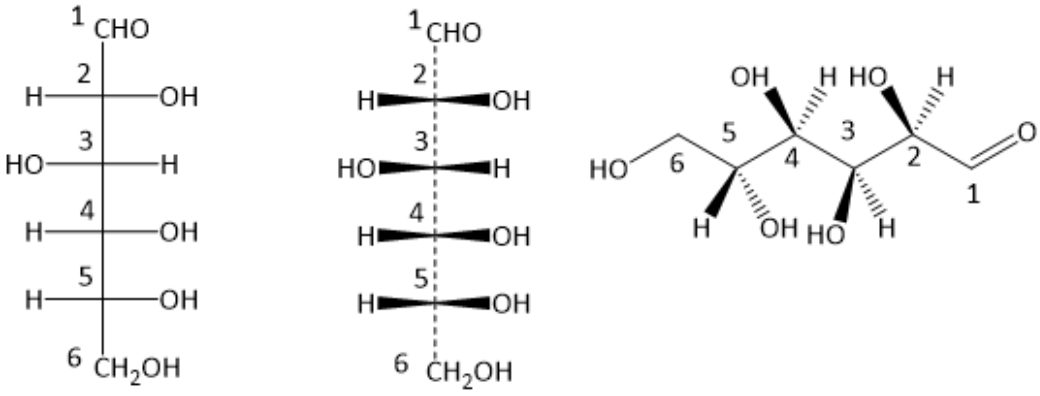


(R)-glyceraldehyde
(D-glyceraldehyde)

In the Fisher projection, the vertical bonds point down into the plane of the paper. That's easy to visualize for 3C molecules. but more complicated for bigger molecules. For those draw a wedge and dash line drawing of the molecule. When determining the orientation of the hydroxides on each C, orient the wedge and dash drawing in your mind so that the C atoms adjacent to the one of interest are pointing down. Sighting towards the carbonyl C, if the OH is pointing to the right in the Fisher project, it should be pointing to the right in the wedge and dash drawing, as shown below for D-erthyrose and D-glucose.

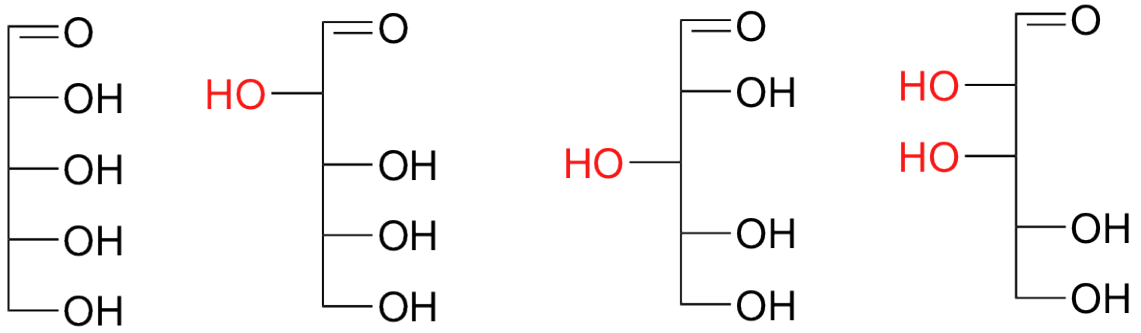


Below are three representations of the open chain form of D-glucose: in the conventional Fischer projection, a wedge/dash version of a Fischer projection, and finally in the 'zigzag' style that is preferred by many organic chemists.



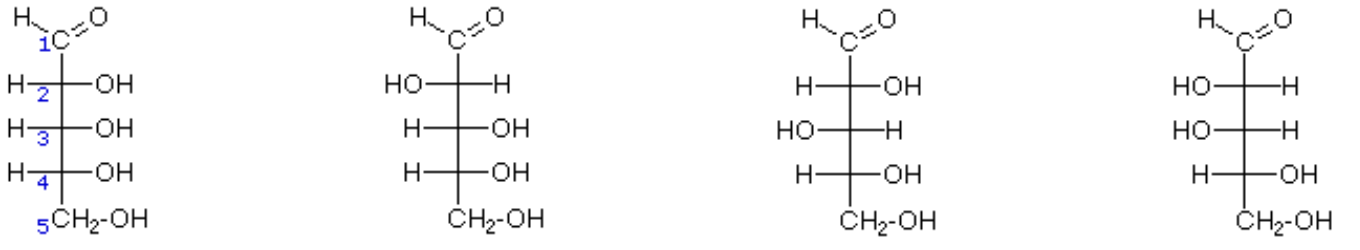
D-Glucose

Fischer projections are useful when looking at many different diastereomeric sugar structures, because the eye can quickly pick out stereochemical differences according to whether a hydroxyl group is on the left or right side of the structure.



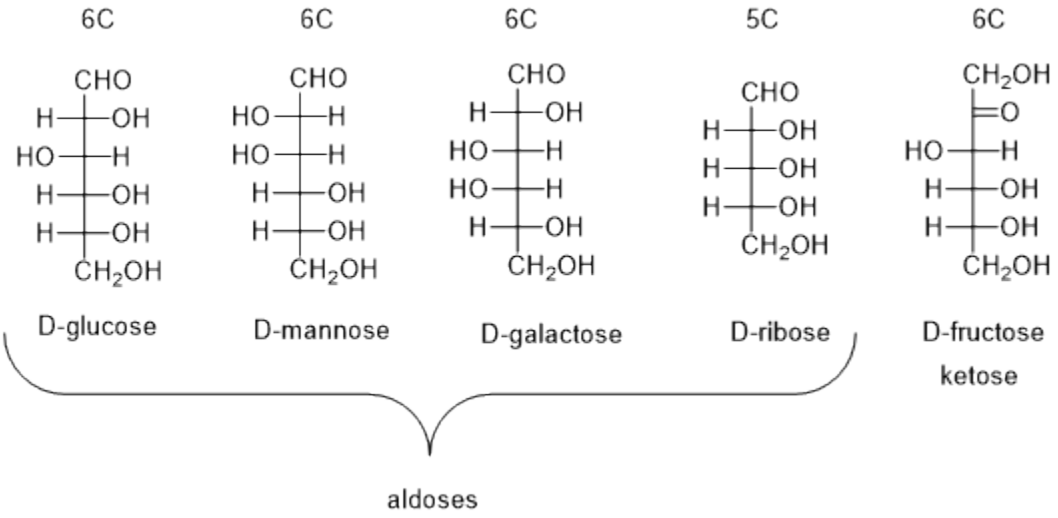
The usefulness of this notation to Fischer, in his carbohydrate studies, is evident in the following diagram. There are eight stereoisomers of 2,3,4,5-tetrahydroxypentanal, a group of compounds referred to as the aldopentoses (aldo- since the oxidized carbon is an aldehyde and -pentose since the molecules contain 5 carbons). Since there are three chiral centers in this constitution, we should expect a maximum of 2^3 stereoisomers. These eight stereoisomers consist of four sets of enantiomers. If the configuration at C-4 is kept constant (*R* in the examples shown here), the four stereoisomers that result will be **diastereomers**.

Four Diastereomeric $C_5H_{10}O_5$ Aldopentoses



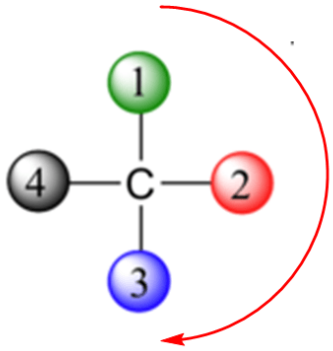
The aldopentose structures drawn above are all diastereomers. A more selective term, **epimer**, is used to designate diastereomers that differ in configuration at only one chiral center. Thus, ribose and arabinose are epimers at C-2, and arabinose and lyxose are epimers at C-3. However, arabinose and xylose are not epimers, since their configurations differ at both C-2 and C-3.

The Fisher structures of the most common monosaccharides (other than glyceraldehyde and dihydroxyacetone), which you will encounter most frequently are shown below.



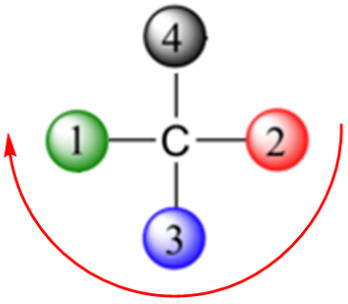
Determining R and S in Fischer Projections

Determining whether a chiral carbon is R or S may seem difficult when using Fischer projections, but it is actually quite simple. If the lowest priority group (often a hydrogen) is on a vertical bond, the configuration is given directly from the relative positions of the three higher-ranked substituents. If the lowest priority group is on a horizontal bond, the positions of the remaining groups give the wrong answer (you are in looking at the configuration from the wrong side), so you simply reverse it.



Lowest Priority is on a horizontal bond so answer is reversed

Substiuents 1-3 are clockwise so the carbon is S

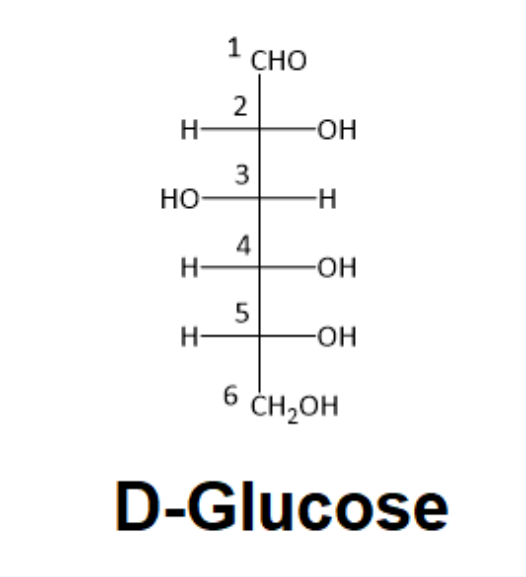


Lowest Priority is on a vertical bond so answer is correct

Substiuents 1-3 are clockwise so the carbon is R

Worked Example 6.9.1

Determine if carbon #2 in D-glucose is R or S.



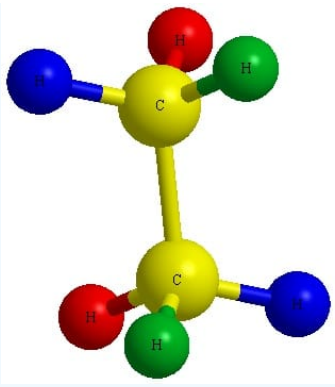
Answer available at the end of this section.

How to make Fischer Projections

To make a Fischer Projection, it is easier to show through examples than through words. Lets start with the first example, turning a 3D structure of ethane into a 2D Fischer Projection.

Exercise 6.9.1

Start by mentally converting a 3D structure into a Dashed-Wedged Line Structure. Remember, the atoms that are pointed toward the viewer would be designated with a wedged lines and the ones pointed away from the viewer are designated with dashed lines.



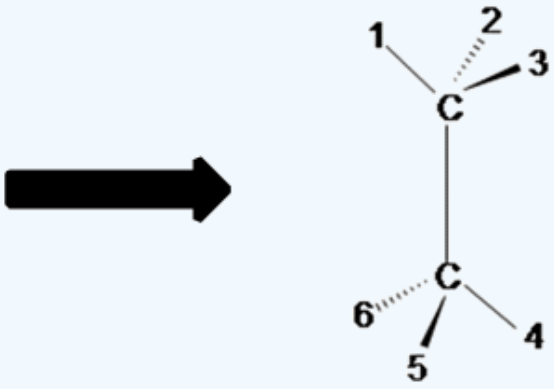


Figure B

Notice the red balls (atoms) in Figure A above are pointed away from the screen. These atoms will be designated with dashed lines like those in Figure B by number 2 and 6. The green balls (atoms) are pointed toward the screen. These atoms will be designated with wedged lines like those in Figure B by number 3 and 5. The blue atoms are in the plane of the screen so they are designated with straight lines.

Now that we have our Dashed- Wedged Line Structure, we can convert it to a Fischer Projection. However, before we can convert this Dashed-Wedged Line Structure into a Fischer Projection, we must first convert it to a "flat" Dashed-Wedged Line Structure. Then from there we can draw our Fischer Projection. Lets start with a more simpler example. Instead of using the ethane shown in Figure A and B, we will start with a methane. The reason being is that it allows us to only focus on one central carbon, which make things a little bit easier.

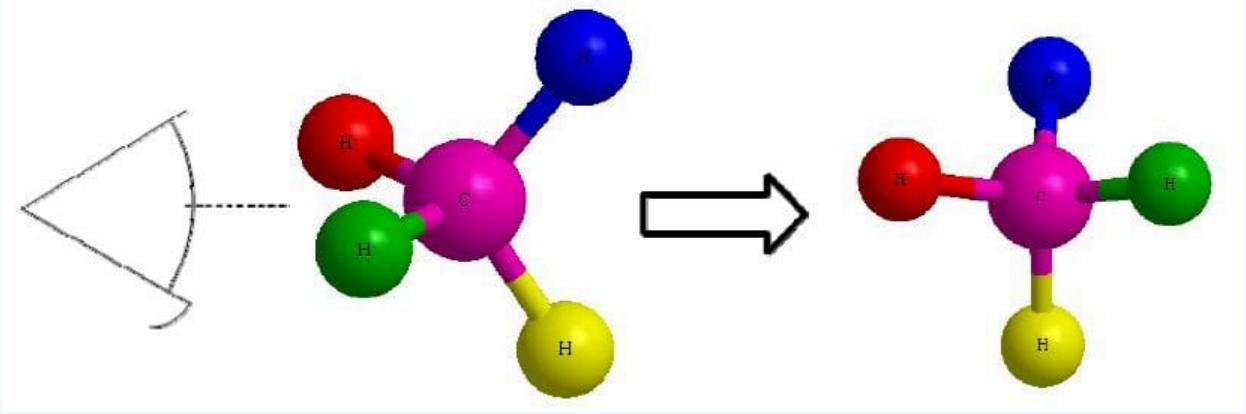
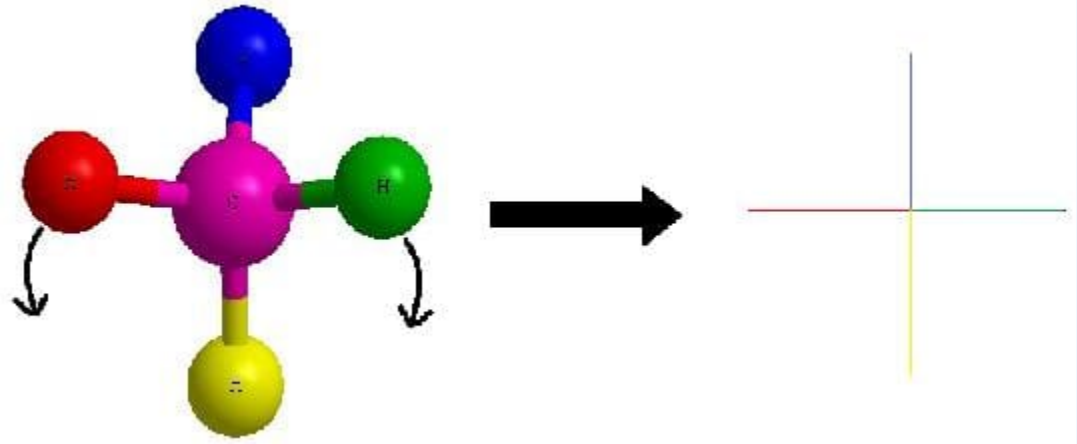


Figure D

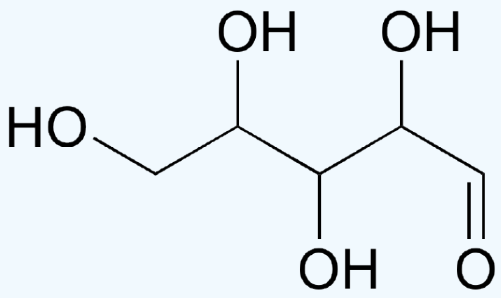
Lets start with this 3D image and work our way to a dashed-wedged image. Start by imagining yourself looking directly at the central carbon from the left side as shown in Figure C. It should look something like Figure D. Now take this Figure D and flatten it out on the surface of the paper and you should get an image of a cross.



As a reminder, the horizontal line represents atoms that are coming out of the paper and the vertical line represents atoms that are going into the paper. The cross image to the right of the arrow is a Fischer projection.

Exercise 6.9.1

Draw 'zigzag' structures (using the solid/dash wedge convention to show stereochemistry) for the four sugars in the figure below. Label all stereocenters *R* or S.

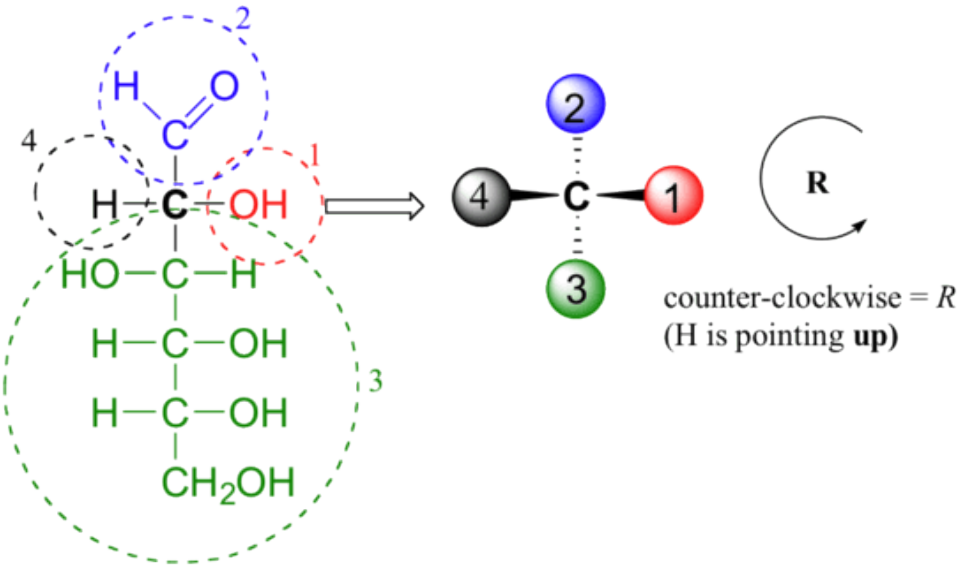


Answer available at the end of this section.

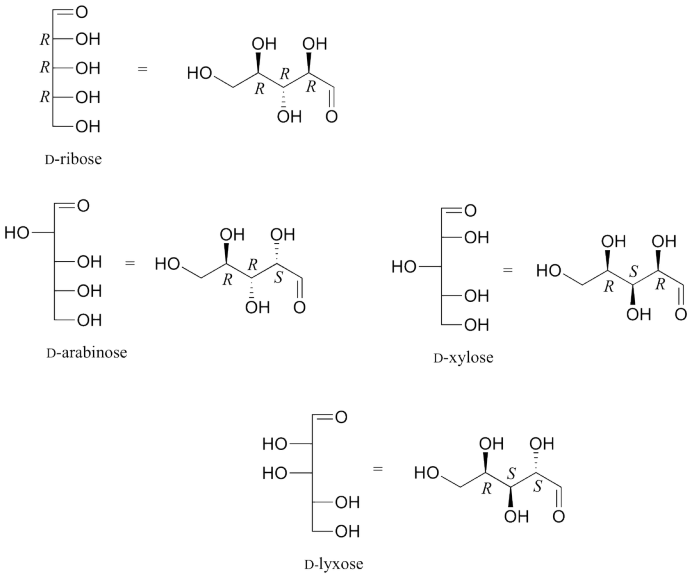
Answers

Worked Example 6.9.1

When deciding whether a stereocenter in a Fischer projection is *R* or S, realize that the hydrogen, in a horizontal bond. Therefore, the orientation of the three remaining substituents is reversed to create the correct answer or a counterclockwise circle means *R*, and a clockwise circle means S. For carbon #2 in D-Glucose substituent 1, 2, and 3 form a counterclockwise circle so the carbon is R.



Exercise 6.9.1



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6.10: Diastereomers

Molecules like lactic acid, alanine, and glyceraldehyde are relatively simple because each has only one chirality center and thus only two stereoisomers. The situation becomes more complex, however, with molecules that have more than one chirality center. As a general rule, a molecule with *n* chirality centers can have up to 2^n stereoisomers (although it may have fewer, as we'll see below). Take the amino acid threonine (2-amino-3-hydroxybutanoic acid), for example. Since threonine has two chirality centers (C2 and C3), there are four possible stereoisomers, as shown in Figure 6.10.1. Check for yourself that the *R*,S configurations of all stereoisomers are correct.

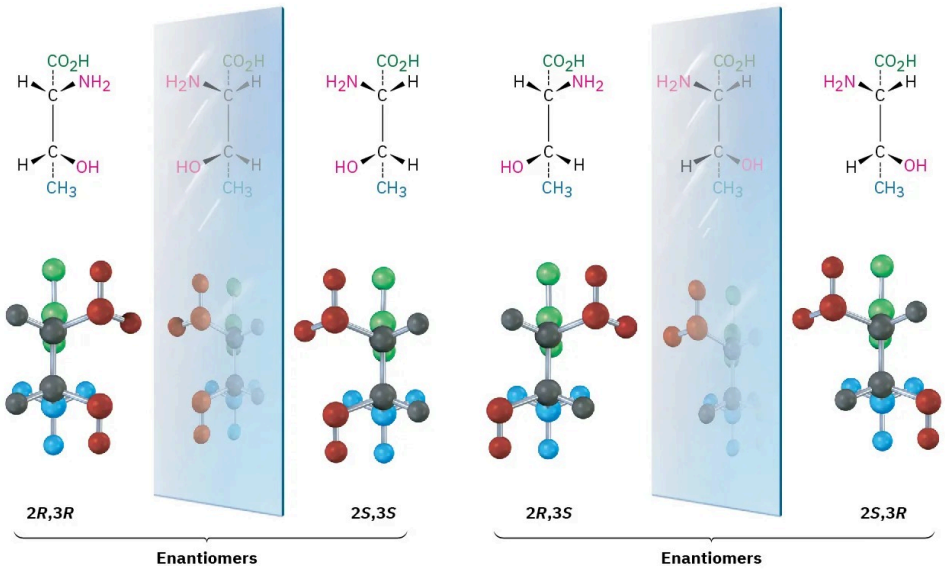


Figure 6.10.1: The four stereoisomers of 2-amino-3-hydroxybutanoic acid.

The four stereoisomers of 2-amino-3-hydroxybutanoic acid can be grouped into two pairs of enantiomers. The 2*R*,3*R* stereoisomer is the mirror image of 2*S*,3*S*, and the 2*R*,3*S* stereoisomer is the mirror image of 2*S*,3*R*. But what is the relationship between any two molecules that are not mirror images? What, for instance, is the relationship between the 2*R*,3*R* isomer and the 2*R*,3*S* isomer? They are stereoisomers, yet they aren't enantiomers. To describe such a relationship, we need a new term: *diastereomer*.

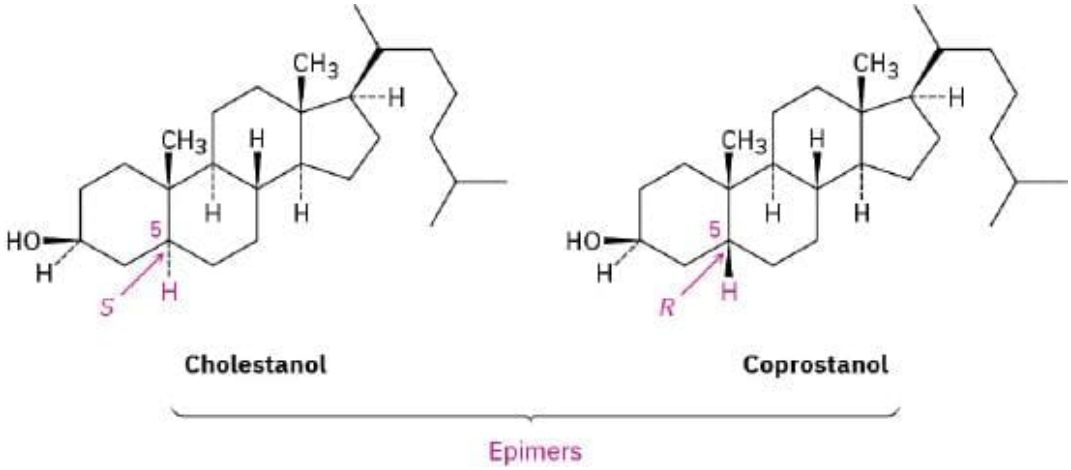
Diastereomers are stereoisomers that are not mirror images. Since we used the right-hand/left-hand analogy to describe the relationship between two enantiomers, we might extend the analogy by saying that the relationship between diastereomers is like that of hands from different people. Your hand and your friend's hand look similar, but they aren't identical and they aren't mirror images. The same is true of diastereomers: they're similar, but they aren't identical, and they aren't mirror images.

Note carefully the difference between enantiomers and diastereomers: enantiomers have opposite configurations at *all* chirality centers, whereas diastereomers have opposite configurations at *some* (one or more) chirality centers but the same configuration at others. A full description of the four stereoisomers of threonine is given in Table 6.10.1. Of the four, only the 2*S*,3*R* isomer, $[\alpha]_D = -28.3$, occurs naturally in plants and animals and is an essential nutrient for humans. This result is typical: most biological molecules are chiral, and usually only one stereoisomer is found in nature.

Table 6.10.1 Relationships among the Four Stereoisomers of Threonine

Stereoisomer	Enantiomer	Diastereomer
2*R*,3*R*	2*S*,3*S*	2*R*,3*S* and 2*S*,3*R*
2*S*,3*S*	2*R*,3*R*	2*R*,3*S* and 2*S*,3*R*
2*R*,3*S*	2*S*,3*R*	2*R*,3*R* and 2*S*,3*S*
2*S*,3*R*	2*R*,3*S*	2*R*,3*R* and 2*S*,3*S*

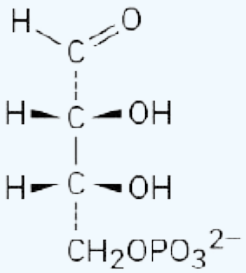
In the special case where two diastereomers differ at only one chirality center but are the same at all others, we say that the compounds are **epimers**. Cholestanol and coprostanol, for instance, are both found in human feces, and both have nine chirality centers. Eight of the nine are identical, but the one at C5 is different. Thus, cholestanol and coprostanol are *epimeric* at C5.



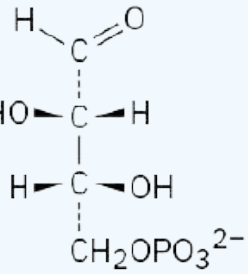
Exercise 6.10.1

One of the following molecules **(a)**–**(d)** is D-erythrose 4-phosphate, an intermediate in the Calvin photosynthetic cycle by which plants incorporate CO_2 into carbohydrates. If D-erythrose 4-phosphate has *R* stereochemistry at both chirality centers, which of the structures is it? Which of the remaining three structures is the enantiomer of D-erythrose 4-phosphate, and which are diastereomers?

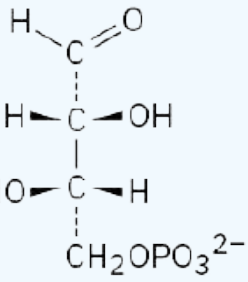
a.



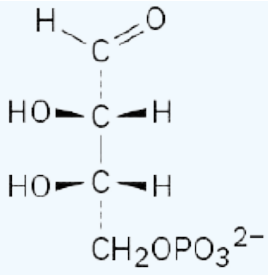
b.



c.



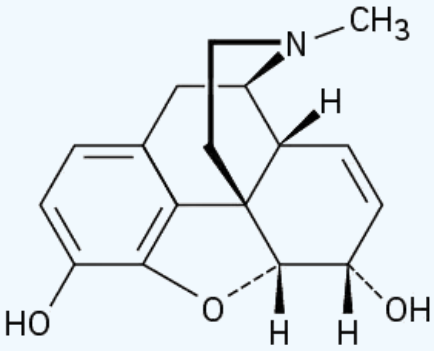
d.



Answer available at the end of this section.

Exercise 6.10.2

How many chirality centers does morphine have? How many stereoisomers of morphine are possible in principle?

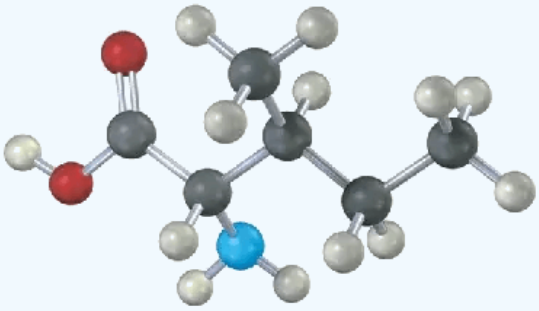


Morphine

Answer available at the end of this section.

Exercise 6.10.3

Assign *R* or *S* configuration to each chirality center in the following molecular model of the amino acid isoleucine (blue = N):



Answer available at the end of this section.

Answers

Exercise 6.10.1

Compound **(a)** is D-erythrose 4-phosphate, **(d)** is its enantiomer, and **(b)** and **(c)** are diastereomers.

Exercise 6.10.2

Five chirality centers and 2^5 = 32 stereoisomers

Exercise 6.10.3

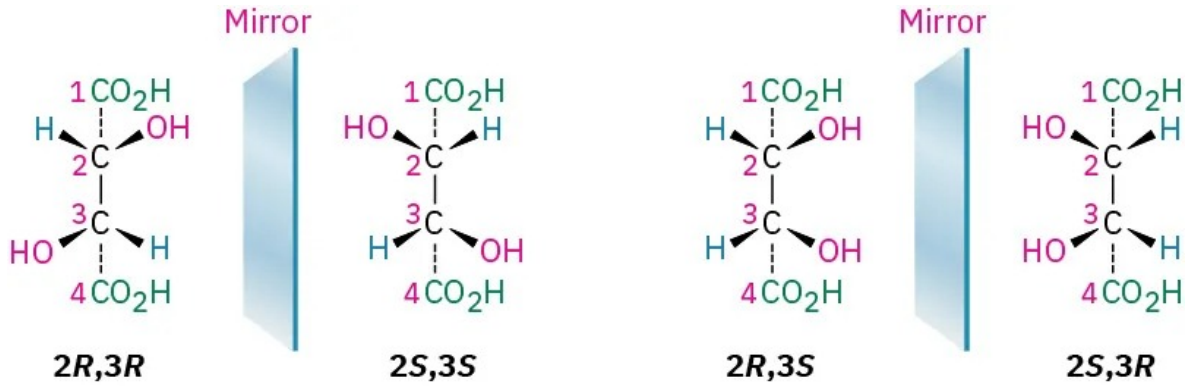
S,S

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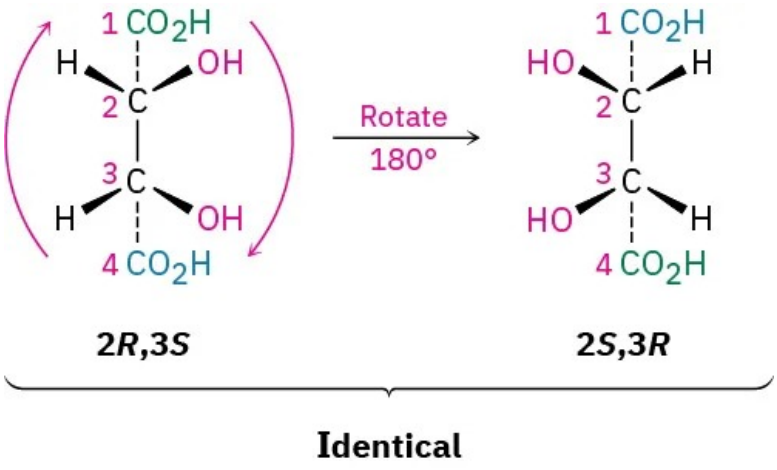
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6.11: Meso Compounds

Let's look at another example (Section 5.5) of a compound with more than one chirality center: the tartaric acid used by Pasteur. The four stereoisomers can be drawn as follows:



The 2*R*,3*R* and 2S,3S structures are nonsuperimposable mirror images and therefore represent a pair of enantiomers. A close look at the 2*R*,3S and 2S,3*R* structures, however, shows that they *are* superimposable, and thus identical, as can be seen by rotating one structure 180°.



The 2*R*,3S and 2S,3*R* structures are identical because the molecule has a plane of symmetry and is therefore achiral. The symmetry plane cuts through the C2–C3 bond, making one half of the molecule a mirror image of the other half (Figure 6.11.1). Because of the plane of symmetry, the molecule is achiral, despite the fact that it has two chirality centers. Such compounds, which are achiral, yet contain chirality centers, are called **meso compounds (me-zo)**. Thus, tartaric acid exists in three stereoisomeric forms: two enantiomers and one meso form.

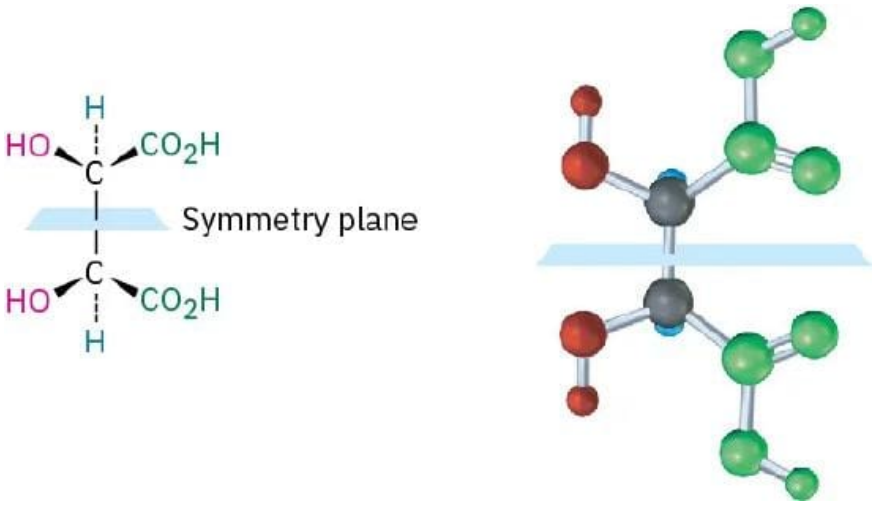


Figure 6.11.1: A symmetry plane through the C2–C3 bond of *meso*-tartaric acid makes the molecule achiral.

Some physical properties of the three stereoisomers are listed in Table 6.11.1. The (+)- and (–)-tartaric acids have identical melting points, solubilities, and densities, but they differ in the sign of their rotation of plane-polarized light. The meso isomer, by contrast, is diastereomeric with the (+) and (–) forms. It has no mirror-image relationship to (+)- and (–)-tartaric acids, is a different compound altogether, and thus has different physical properties.

Table 6.11.1 Some Properties of the Stereoisomers of Tartaric Acid Some Properties of the Stereoisomers of Tartaric Acid

Stereoisomer	Melting point (°C)	$[\alpha]_D$	Density (g/cm^3)	Solubility at 20 °C (g/100 mL H_2O)
(+)	168–170	+12	1.7598	139.0
(–)	168–170	–12	1.7598	139.0
Meso	146–148	0	1.6660	125.0

Worked Example 6.11.1: Distinguishing Chiral Compounds from Meso Compounds

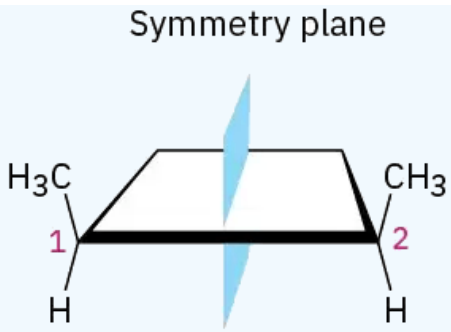
Does *cis*-1,2-dimethylcyclobutane have any chirality centers? Is it chiral?

Strategy

To see whether a chirality center is present, look for a carbon atom bonded to four different groups. To see whether the molecule is chiral, look for the presence or absence of a symmetry plane. Not all molecules with chirality centers are chiral overall—meso compounds are an exception.

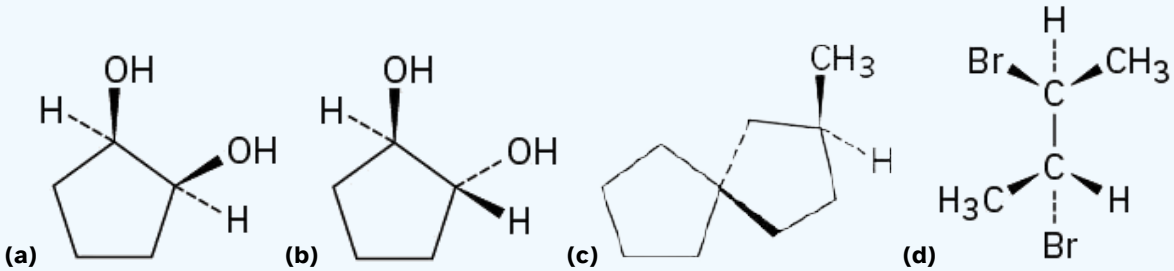
Solution

A look at the structure of *cis*-1,2-dimethylcyclobutane shows that both methyl-bearing ring carbons (C1 and C2) are chirality centers. Overall, though, the compound is achiral because there is a symmetry plane bisecting the ring between C1 and C2. Thus, the molecule is a meso compound.



Exercise 6.11.1

Which of the following structures represent meso compounds?



Answer available at the end of this section.

Exercise 6.11.2

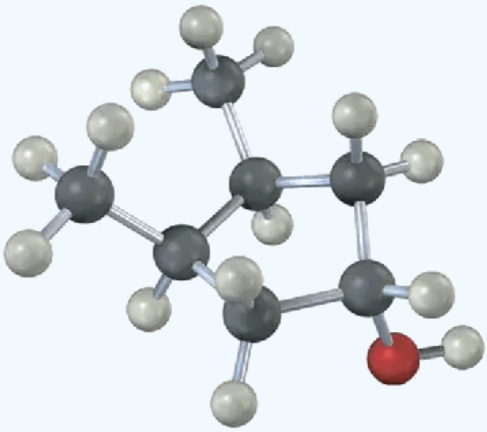
Which of the following have a meso form? (Recall that the *-ol* suffix refers to an alcohol, ROH.)

a. 2,3-Butanediol
b. 2,3-Pentanediol
c. 2,4-Pentanediol

Answer available at the end of this section.

Exercise 6.11.3

Does the following structure represent a meso compound? If so, indicate the symmetry plane.



Answer available at the end of this section.

Answers

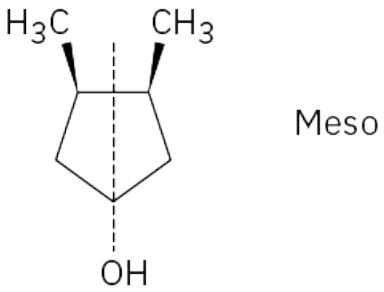
Exercise 6.11.1

Compounds **(a)** and **(d)** are meso.

Exercise 6.11.2

Compounds **(a)** and **(c)** have meso forms.

Exercise 6.11.3



Meso

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7: CARBOHYDRATES

7.1: What are carbohydrates
7.2: General class names and Common names of monosaccharides
7.3: Cyclic structures of monosaccharides
7.4: Haworth Formula
7.5: Reactions of monosaccharides
7.6: Disaccharides
7.7: Oligosaccharides
7.8: Polysaccharides

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7.1: What are carbohydrates

Learning Objectives

- Define carbohydrates, monosaccharides, polysaccharides, and write their general formulas.
- Draw and interpret fisher projections of monosaccharides.

What are carbohydrates

Carbohydrates are primary energy storage compounds, e.g., glucose ($C_6H_{12}O_6$) synthesized by using carbon dioxide (CO_2) from the air, water (H_2O) from the soil, and energy from sunlight, along with the release of oxygen (O_2), as illustrated in Figure 7.1.1.

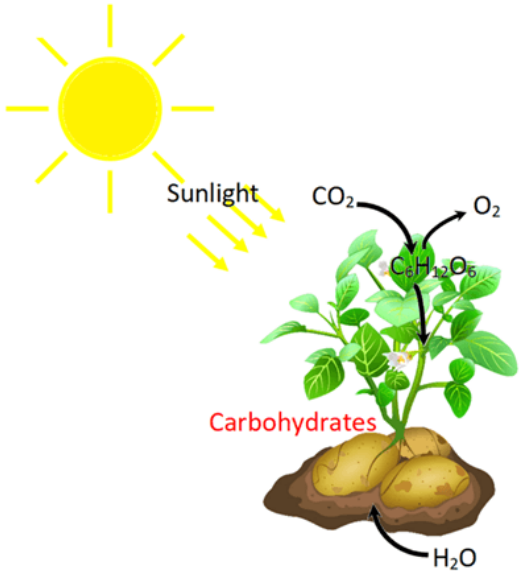


Figure 7.1.1: Illustration of photosynthesis by plants. (Copyright; Public domain)

Oxidation of carbohydrates, e.g., the reverse of the photosynthesis reaction, release energy that plant and animals use for activities. Carbohydrates are the support structure material in plants, e.g., cell-wall and wood, shell material of crustaceans, and connective tissues in animals.

Glucose is a polyhydroxy aldehyde, and fructose, i.e., another carbohydrate found in honey, is a polyhydroxy ketone, as illustrated in Figure 7.1.2.

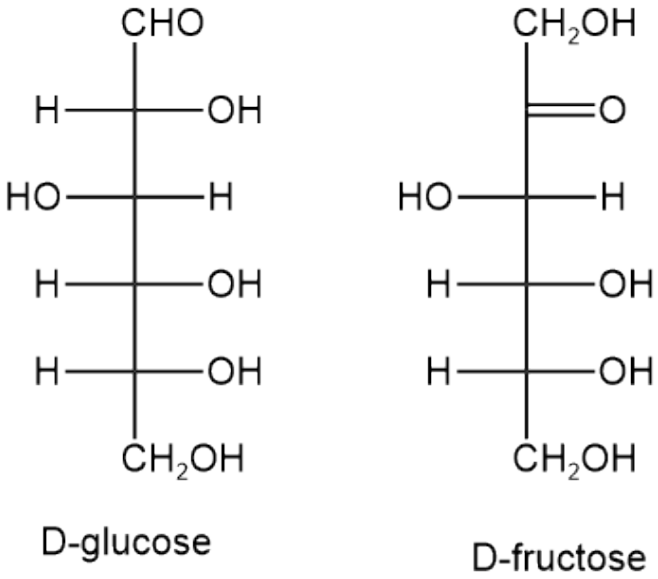


Figure 7.1.2: Fisher projections of D-glucose and D-fructose. (Copyright; Public domain)

Carbohydrates

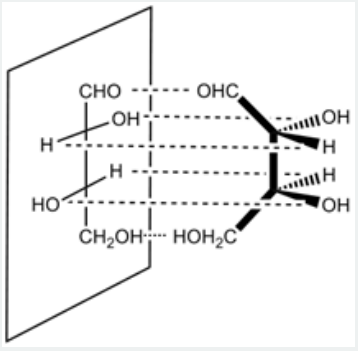
Carbohydrates are polyhydroxy aldehydes, polyhydroxy ketones, or other compounds that hydrolyze to polyhydroxy aldehydes or polyhydroxy ketones.

The general formula of simple carbohydrates is $\mathrm{C}_n\mathrm{H}_{2n}\mathrm{O}_n$, which can also be written as $\mathrm{C}_n \cdot (\mathrm{H}_2\mathrm{O})_n$ which is the origin of the name carbohydrates, i.e., hydrates of carbon.

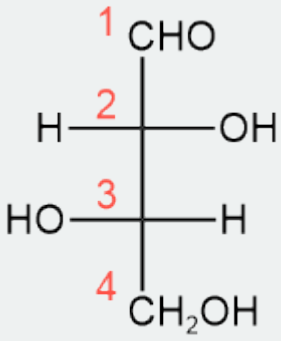
Fisher projections

Fisher projections are two-dimensional representations of molecules for showing the configuration of chiral centers:

- the chiral center is in the plane of the page,
- horizontal lines represent bonds projecting toward the viewers,
- and vertical lines represent bonds projecting away from the viewer.
- The parent C chain is placed on the vertical line, with the most oxidized C, i.e., the $\mathrm{C}{=}\mathrm{O}$ in carbohydrates, at the top or near the top end, and the numbering starts from the top most C, as illustrated in Figure $7.1.2$.



(a)



D-threose

(b)

Figure 7.1.2: Illustration of creating a Fisher projection (a) and numbering the C chain of carbohydrates using D-threose as an example. (Copyright: (a) Olion17, Public domain, via Wikimedia Commons, (b) Public domain)

Monosaccharides and polysaccharides

Monosaccharides

Simple carbohydrates that can not be hydrolyzed to more simple ones are called **monosaccharides**. For example, D-glucose, D-fructose, and D-threose shown in previous figures are monosaccharides.

Polysaccharides

Linear or branched chain polymers comprised of monosaccharide repeat units (monomers) are called **polysaccharides**. For example, starch is a polysaccharide with a D-glucose monomer, illustrated in Figure 7.1.3.

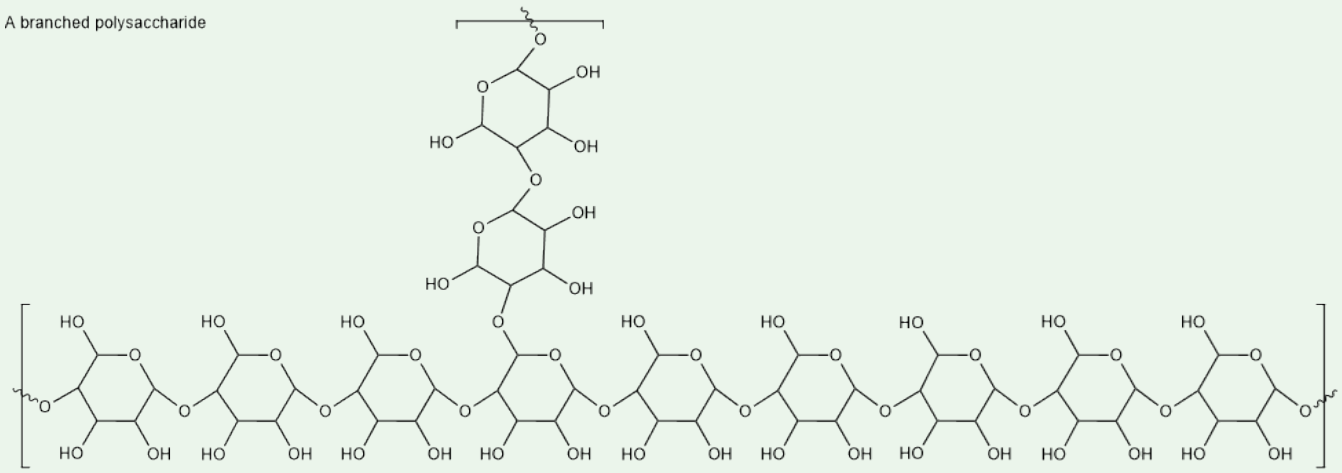
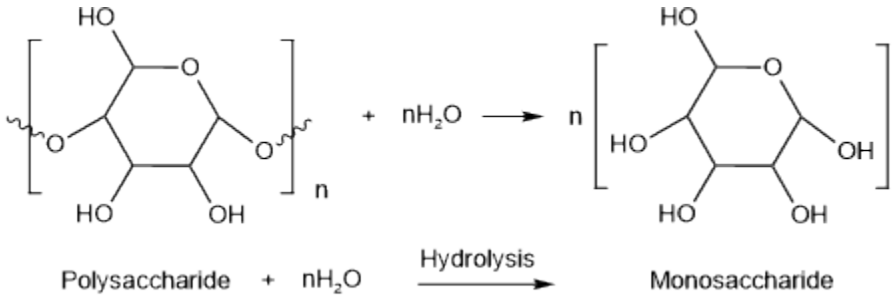


Figure 7.1.3: General structural formula of a starch -a polysaccharide D-glucose. (Copyright; Public domain)

Polysaccharides hydrolyze to monosaccharides, as illustrated in the following general hydrolysis reaction.



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7.2: General class names and Common names of monosaccharides

Learning Objectives

- Assign and interpret class names of monosaccharides.
- Assign D/L stereodescriptors to the common names and define epimers.
- Draw structure from the name and vice versa for important monosaccharides, including D-ribose, D-glucose, D-mannose, and D-galactose.

General class names of monosaccharides

Monosaccharides are either polyhydroxy aldehydes that take *aldo* as prefixes or polyhydroxy ketones that take *keto* as prefixes in their general name. The general formula of monosaccharides is $\mathrm{C}_n\mathrm{H}_{2n}\mathrm{O}_n$ where n can be 3, 4, 5, 6, 7, or 8 representing triose, tetrose, pentose, hexose, heptose, or octose, respectively, in the general name. For example, D-glucose belongs to aldohexose, where the aldo- prefix tells it is an aldehyde, -hex- in the middle of the name tells it has six $\mathrm{C}'\mathrm{s}$, and -ose suffix denotes it is a carbohydrate. D-fructose belongs to ketohexose, i.e., it is a monosaccharide with a ketone group and six $\mathrm{C}'\mathrm{s}$. D-glyceraldehyde is an aldotriose, i.e., a monosaccharide with an aldehyde group and three $\mathrm{C}'\mathrm{s}$.

Common names of monosaccharides

Common names are specific for each monosaccharide. All $\mathrm{C}'\mathrm{s}$ in a monosaccharide are chiral centers except the two terminal $\mathrm{C}'\mathrm{s}$ and the C of ketone group if it is a ketose. The absolute configuration of the **penultimate** C, i.e., the second-last C, is explicitly expressed by D- or L-stereochemical descriptors and the absolute configuration of all other chiral centers is implicit in the common name of the monosaccharide. There is one set of common names for all D-isomers, and their mirror images (enantiomers) have the same common name with D- replaced with L-. For example, D-glyceraldehyde and L-glyceraldehyde, D-glucose, and L-glucose are enantiomer pairs shown in Figure $7.2.1$.

D/L Stereochemical descriptors

If the $-\mathrm{OH}$ group on the second-last carbon (penultimate C or the second C from the bottom end) in Fisher projection of a monosaccharide is on the right side, it is assigned D- and if it is on the left side, it is assigned L-configuration. Monosaccharides that are enantiomer pairs have the same common name, but D- is replaced with L- or vice versa. For example, D-glyceraldehyde and L-glyceraldehyde, D-glucose and L-glucose enantiomer pairs are shown in Figure $7.2.1$. with the penultimate C defining D- or L-configuration shown in red color.

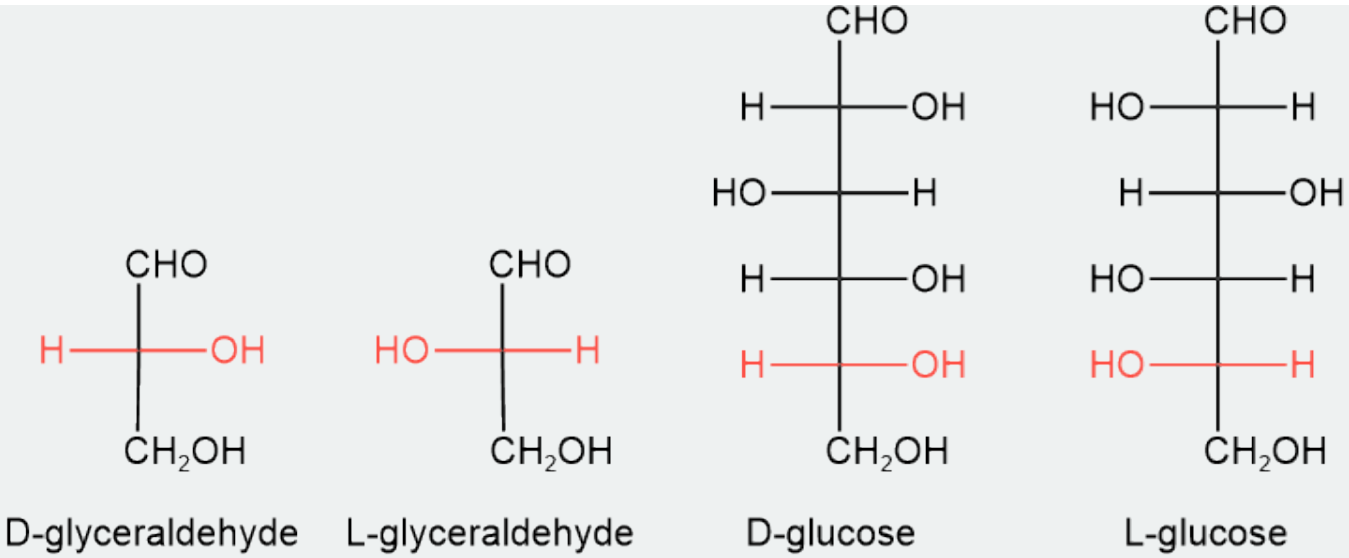


Figure 7.2.1: Assigning D- or L-configuration based on orientation of $-\mathrm{OH}$ on penultimate C in Fisher projection. (Copyright; Public domain)

D-configuration of monosaccharides is commonly found in nature. The D/L stereodescriptors do not indicate the rotation of the plane polarized light, i.e., the enantiomer's dextro/levo rotatory nature. However, if one enantiomer is dextro (d-), the other is levo (l-) to the same degree, and vice versa.

The structures as Fisher projections and common names of D-aldoses are shown in Figure 7.2.2. and those of D-ketoses are shown in Figure 7.2.3. These are the most common monosaccharides found in nature.

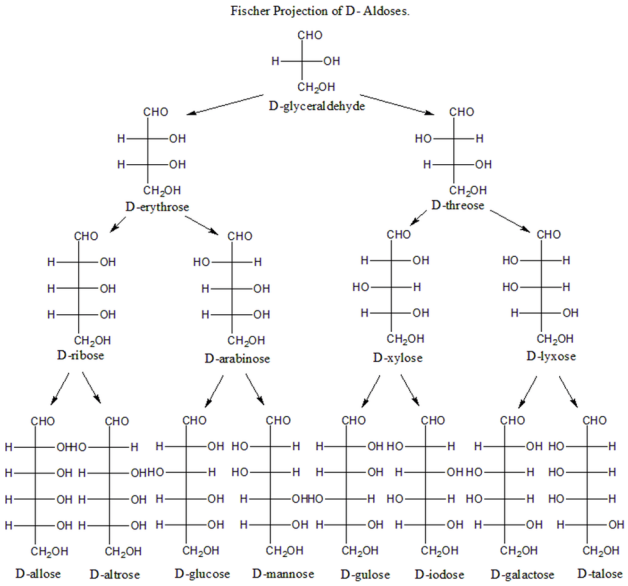


Figure 7.2.2: Fisher projections and common names of D-aldoses. (Copyright; Dineshts, Public domain, via Wikimedia Commons)

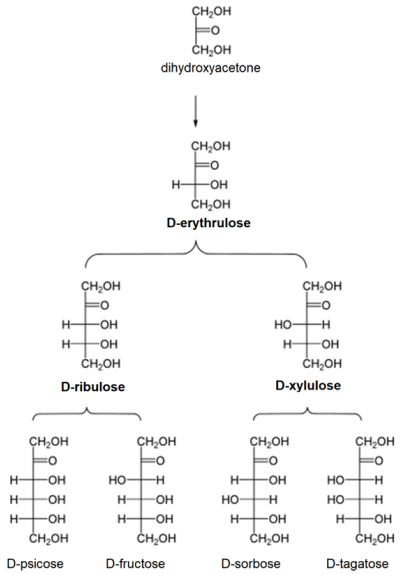


Figure 7.2.3: Fisher projections and common names of D-ketoses. (Copyright;modified from: Yikrazuul, Public domain, via Wikimedia Commons)

Some important monosaccharides

D-Glucose is the most abundant monosaccharide in nature. Plants produce it in a photosynthesis process. D-Galactose and D-mannose are two important diastereomers of D-glucose that differ from D-glucose in the configuration of only one chiral center.

Epimers

Epimers are diastereomers that differ in absolute configuration of only one chiral center. For example, D-galactose configuration is different from D-glucose only at C#4, i.e., D-galactose is a $\mathrm{C}4$-epimer of D-glucose. Similarly, D-mannose is $\mathrm{C}2$-epimer of D-glucose.

D-Fructose is another important monosaccharide that differs at C#1 and C#2 from glucose. That is, the $\mathrm{C}{=}\mathrm{O}$ is an aldehyde group at C#1 in D-glucose, but it is a ketone at C#2 in D-fructose. Fisher projections of D-glucose, D-galactose, D-mannose, and D-fructose are shown in Figure $7.2.4$. with the differences from D-glucose highlighted by red-color fonts. D-ribose is another important monosaccharide present in RNA.

Drawing structures of important monosaccharides

D-ribose is aldopentose, i.e., an aldehyde with five $\mathrm{C}'\mathrm{s}$. All chiral $\mathrm{C}'\mathrm{s}$ have $-\mathrm{OH}$ groups oriented towards the right in the Fisher projection. D-allose is aldohexose with the same structural features as D-ribose, i.e., all chiral $\mathrm{C}'\mathrm{s}$ have $-\mathrm{OH}$ groups oriented towards the right in the Fisher projection. D-glucose is $\mathrm{C}3$ epimer of D-allose. The other three important monosaccharides can be drawn by relating them to D-glucose, i.e., D-galactose is a $\mathrm{C}4$ epimer, D-mannose is a $\mathrm{C}2$ epimer of D-glucose, and D-fructose has a ketone group at $\mathrm{C}2$ in the place of aldehyde group of D-glucose at $\mathrm{C}1$.

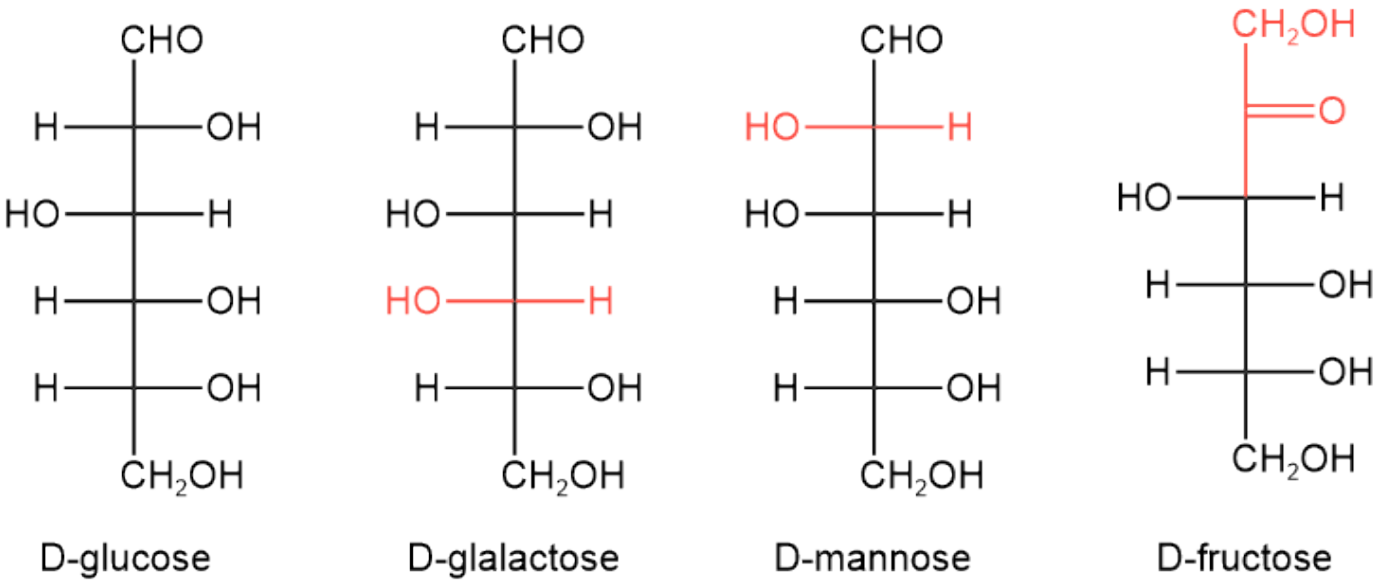


Figure 7.2.4: Fisher projections of four important monosaccharides with their differences from D-glucose highlighted by red-color fonts. (Copyright; Public domain)

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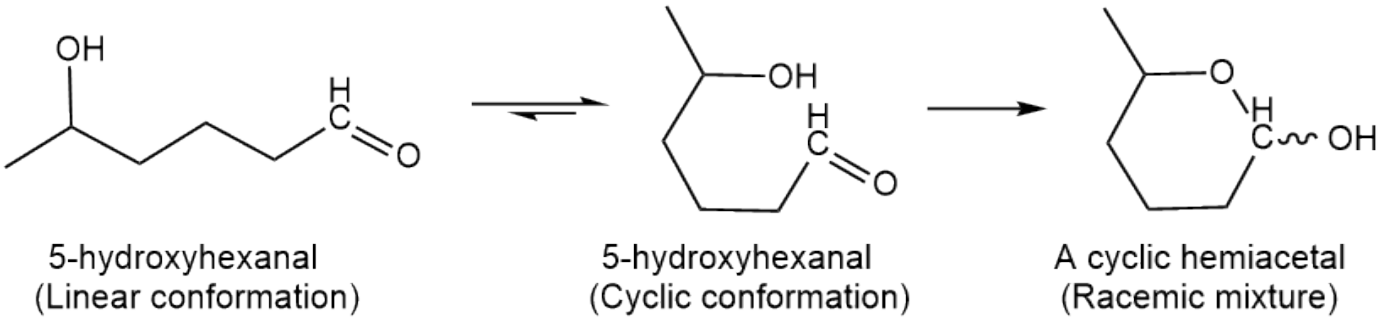
7.3: Cyclic structures of monosaccharides

Learning Objectives

- Draw and inter-convert open-chain and cyclic hemiacetal forms of compounds containing carbonyl and alcohol groups in the same molecule.
- Convert Fisher projections to Howarth projections and to chair conformation in the cases of pyranose forms of monosaccharides.
- Define Howarth projection, anomeric carbon, α and β configuration of the anomeric carbon, furanose, and pyranose forms, and mutarotation of monosaccharides.

Cyclic hemiacetal

Alcohol ($\mathrm{R-OH}$) and a carbonyl ($\mathrm{C=O}$) groups react with each other and form a hemiacetal group. The hemiacetals are usually unstable and revert to the reactants. However, suppose the alcohol and the carbonyl groups are on the same molecule and can react to form a five- or six-member cyclic hemiacetal. The product is more stable than the reactants, as shown in the following example reaction.



5-hydroxyhexanal (Linear conformation) | 5-hydroxyhexanal (Cyclic conformation) | A cyclic hemiacetal (Racemic mixture)

Note that the hemiacetal C is a new chiral center that is produced as a racemic mixture, which is represented by a wavy line in the $-\mathrm{OH}$ group. Monosaccharides are polyhydroxy aldehydes or polyhydroxy ketones that often exist as hemiacetal as the dominant form in equilibrium with the open-chain form, as described in the next section.

Fisher projections to Haworth projections

Fisher projections represent the open-chain forms of monosaccharides where the C-chain is a vertical line. Hemiacetals are five or six-member ring structures represented by pentagon or hexagon shapes.

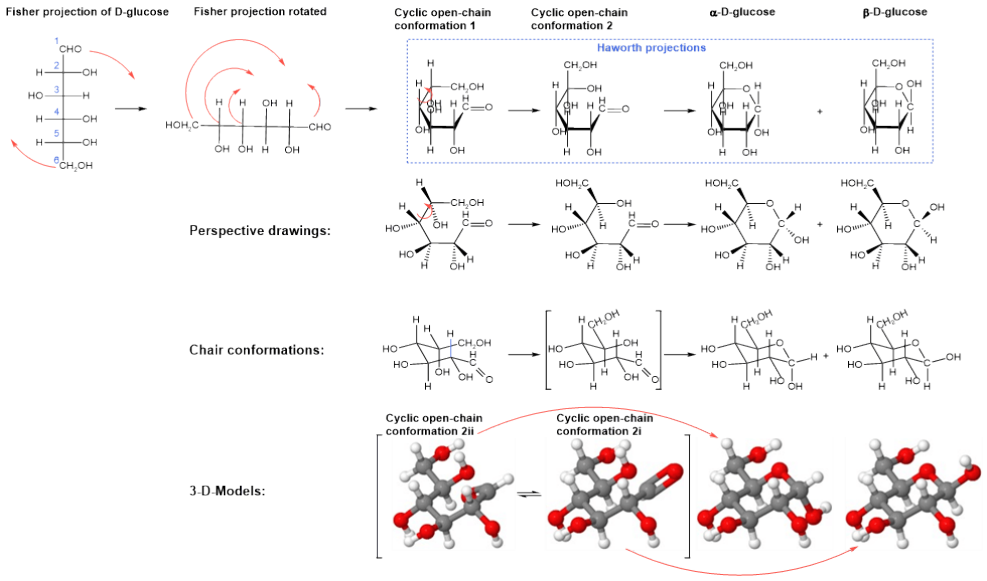
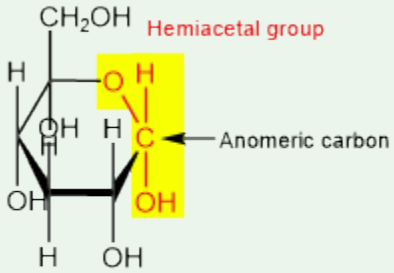


Figure 7.3.1: Fisher projections to Haworth projections explained. Follow the movement of atoms or rotations around single bonds, represented by curvy arrows in red color (Copyright; Public domain)

Figure 7.3.1 explains the steps to re-draw Fisher projection in cyclic conformation.

1. Rotate the Fisher projection by 90^{o} clockwise from vertical to horizontal orientation. The groups on the left of Fisher's projection end up above, and those to the right end below in the horizontal orientation.
2. Move C′s#1, 4, 5, and 6 up by 60^{o} each to arrive at the cyclic open-chain conformation#1.
3. Rotate the C4-C5 bond by 60^{o} counterclock wise to bring the C#5$-$OH group in the cycle of C′s and C#6 pointing above, i.e., cyclic conformation#1 in Figure 7.3.1.
4. C#5$-$OH and a carbonyl (C$=$O) of C#1 react to produce the hemiacetal group with the new $-$OH group on C#1 either pointing away from the hemiacetal O, i.e., α- or point towards the hemiacetal O, i.e., β-orientation in the cyclic hemiacetal.

Anomeric C

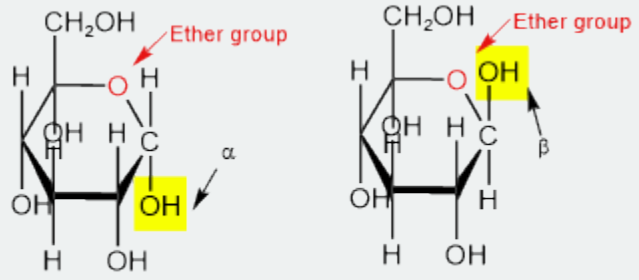


Howeverth projetion of α-D-glucose **Anomeric** C is the C of carbonyl (C$=$O) group in the open chain conformation that becomes the C of the hemiacetal group in the cyclic structure of a monosaccharide. For example, C#1 of D-glucose is the anomeric C, as highlighted in the figure on the right.

Haworth projection

Haworth projection is five or six-membered cyclic hemiacetals of monosaccharides, presented as pentagon or hexagon shape. It is viewed through its edge perpendicular to the plane of the page, such that the anomeric C s the right corner in the plane of the page and ether group (R$-$O$-$R) is the top right corner in the rear, as shown in the figure on the right. Bold lines usually show the ring bonds toward the viewer (above the page) and those below the page (away from the viewer) as solid lines. Bonds outside the ring are shown as solid lines pointing above or below it.

Assigning α- or β- to the cyclic structures of monosaccharides



α-D-glucose **β-D-glucose**

Conversion of monosaccharides from open chain to cyclic hemiacetal produced a new chiral center at the anomeric C. It is a mixture of two conformations: the $-\mathrm{OH}$ group on anomeric C going away from the ether $(\mathrm{R-O-R})$ group is α- and towards it is β-configuration, as illustrated in the figure on the right with the help of D-glucose example.

D-Fructose exists in five-membered and six-membered hemiacetal forms, as shown in Figure $7.3.2$.

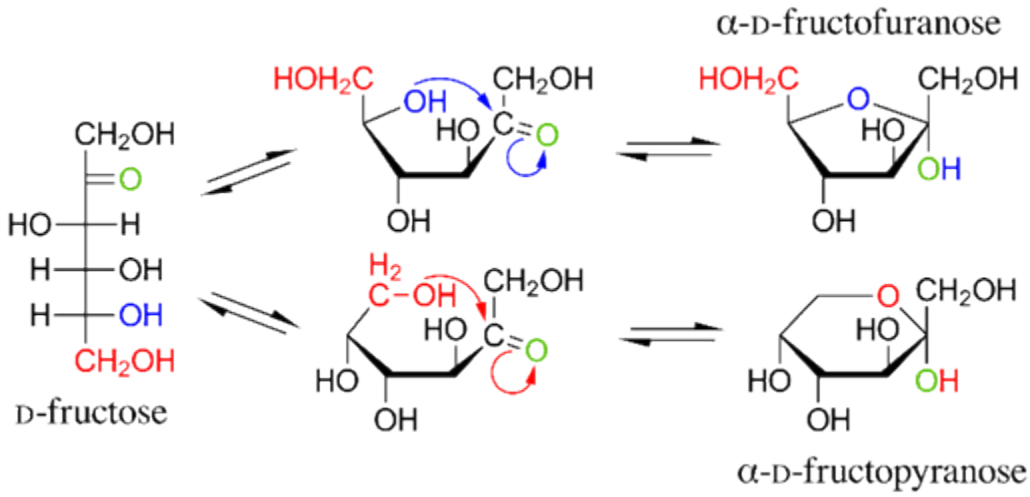
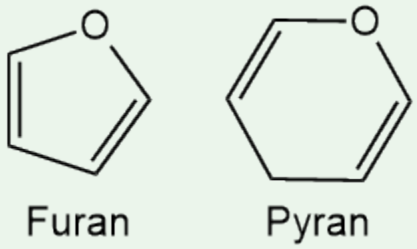


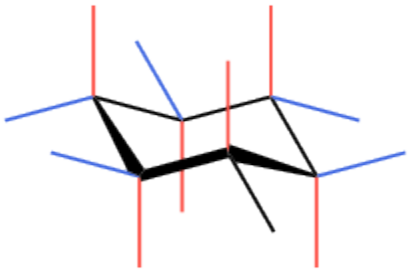
Figure $7.3.2$: Equilibrium reaction between the acyclic and the cyclic hemiketal forms of D-fructose (note: hemiacetal group from a ketone is called hemiketal. α-forms of the hemiketal are shown and the corresponding β-forms are not shown in this figure). (Copyright; Vaccinationist, Public domain, via Wikimedia Commons)

Furanose and pyranose forms of monosaccharides

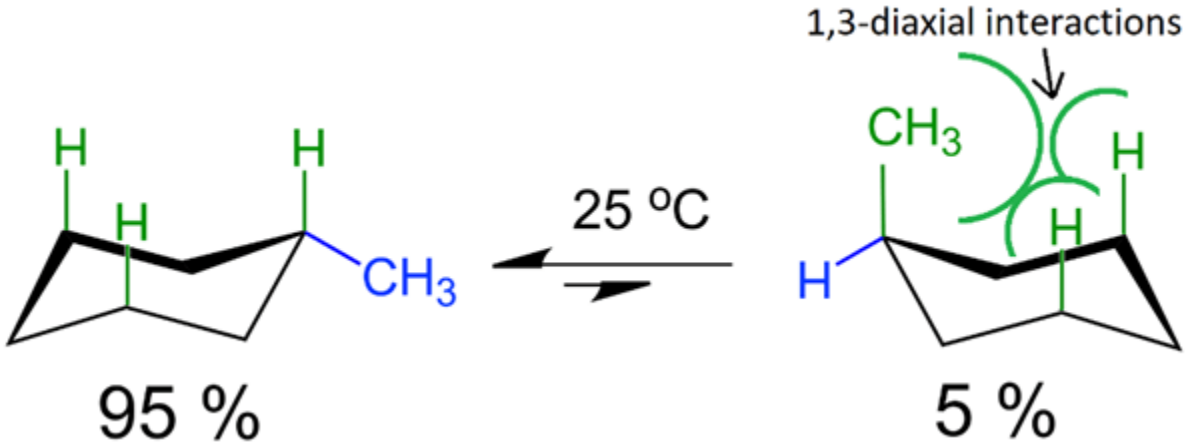


Furanose is a five-membered, and **pyranose** is a six-membered cyclic hemiacetal of monosaccharide. These names originate from the names of cyclic ethers, furan, and pyran, shown in the figure on the right. Based on this nomenclature, the class name of α-D-Glucose is α-D-glucopyranose and of β-D-glucose is β-D-glucopyranose. D-Fructose exists in pyranose and furanose forms, as shown in Figure $7.3.2$.

Chair conformations of pyranose forms



Haworth projections assume a flat ring structure. It is close to the structure of furanose forms (five-membered rings), but pyranose forms (six-membered rings) exist in chair conformations. The figure on the right shows a chair conformation of a six-membered cyclic structure. The points to note are the following.



1. Each C has two bonds (shown in black) in the cycle, one axial bond (shown in red) pointing along the axis of the cycle and one equatorial bond (shown in blue) pointing approximately along the equator of the cycle.
2. The axial bonds point in opposite directions, up and down, on neighboring C'. The same applies to equatorial bonds.
3. Bulky group, i.e., any group other than $-\mathrm{H}$, is more stable at the equatorial than axial position because of steric strain (push away) from the other two axial positions on the same face of the ring., as illustrated in the figure on the left.

How to draw chair conformations of monosaccharides

> Alpha (α) and axial start with the letter *a*. Remember α- means an axial $-\mathrm{OH}$ at anomeric C in the case of pyranose chair conformation.

Since $\alpha-\mathrm{OH}$ is axial, $\beta-\mathrm{OH}$ is equatorial at anomeric C. The Howarth projection of β-D-glucose in the figure on the right shows that the bulky groups alternate between up and down positions on C#1 to C#5. It means all of them are either axial or equatorial. Since $\beta-\mathrm{OH}$ is equatorial, all bulky groups in β-D-glucose are equatorial, as shown in Figure $7.3.3$.

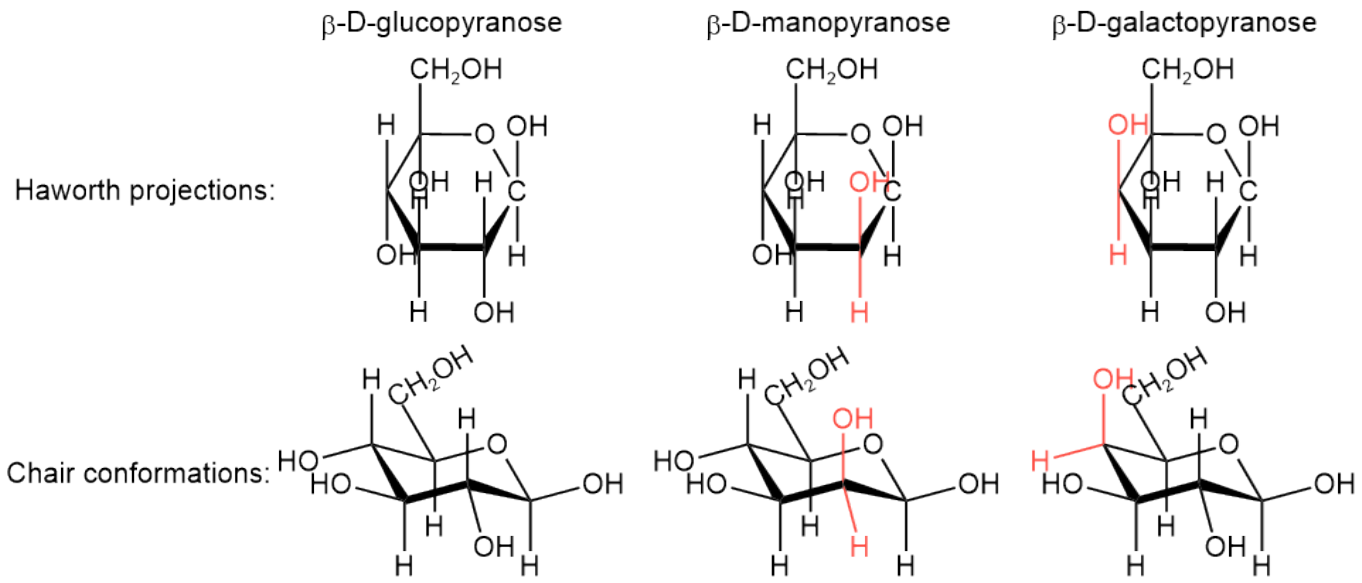


Figure 7.3.3: Haworth projections and the corresponding chair conformations of β-D-glucopyranose, β-D-manopyranose, and β-D-galactopyranose with the differences form β-D-glucopyranose shown in red color. The corresponding α forms (not shown) have $ce{-OH}$ on C#1 (right-most) on axial positions . (Copyright; Public domain)

After learning how to draw β-D-glucopyranose, the other monosaccharides can be drawn easily based on the knowledge of the difference from β-D-glucopyranose. For example, β-D-manopyranose is C#2 epimer, β-D-galactopyranose is C#4 epimer, and their α forms have an axial $-\mathrm{OH}$ at anomeric C, as shown in Figure 7.3.3.

Mutarotation

D-Glucose is a chiral compound. A freshly prepared aqueous solution of β-D-glucopyranose has a specific rotation of +112.2. A freshly prepared solution of α-D-glucopyranose has a specific rotation of +18.7. However, the specific rotation of β-D-glucopyranose and α-D-glucopyranose gradually changes to +52.5. This is because the open chain and the two cyclic forms establish equilibrium in the solution, as illustrated in Figure 7.3.4.

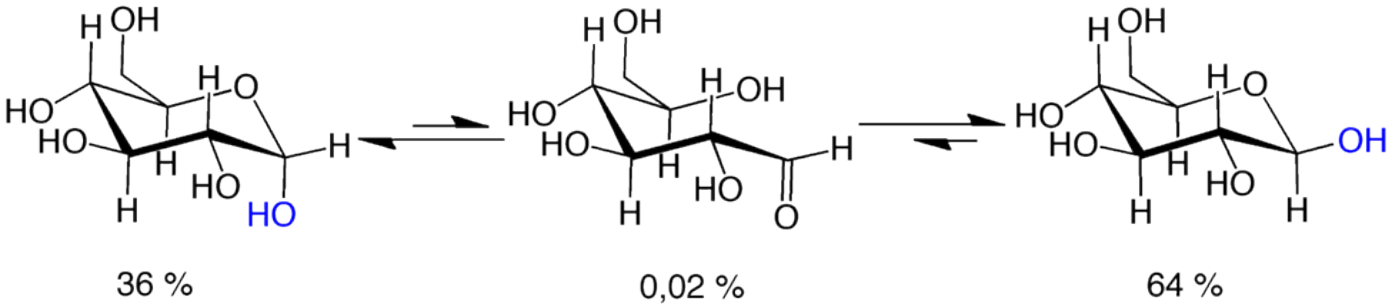


Figure 7.3.4: Equilibrium between three forms of D-glucose: open-chain D-glucose in the middle, β-D-glucopyranose on the right, and α-D-glucopyranose on the left side, with their % ratios shown below the structure. (Copyright; Jü, CC0, via Wikimedia Commons)

Open chain and the two cyclic forms of D-glucose exist in equilibrium in solution where β-D-glucose has all bulky group in equatorial position is the most stable, α-D-glucose with one bulky group in axial position is the second most stable and, and open chain for is the least stable, as reflected by their proportions at equilibrium shown in Figure 7.3.4.

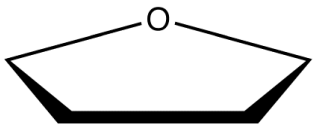
> Mutarotation is the change in the optical rotation of carbohydrate solution over time due to the change in the composition of different compound forms to achieve equilibrium composition.

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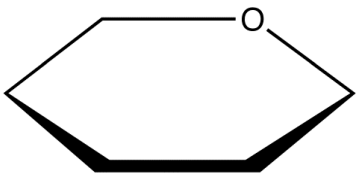
- 5.3: Cyclic structures of monosaccharides by Muhammad Arif Malik is licensed Public Domain.

7.4: Haworth Formula

Traditionally, in carbohydrate chemistry, the furanose rings and the pyranose rings in carbohydrate molecules are shown in the planar conformation, placed on the plane perpendicular to the plane of the paper.

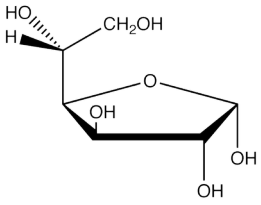


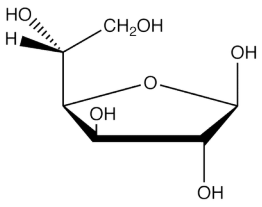
furanose ring

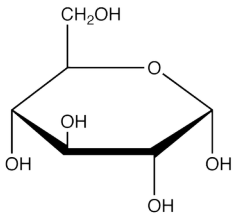


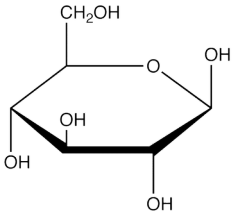
pyranose ring

This representation of rings is known as the *Haworth formula*. eg: cyclic forms of D-glucose



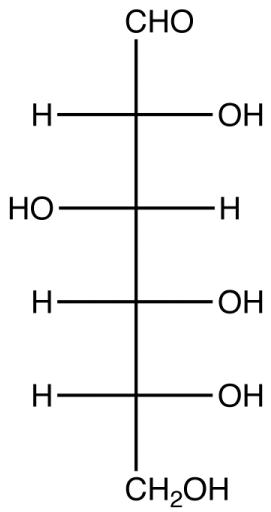






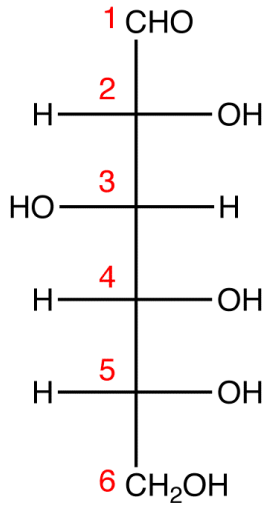
To generate the Haworth formulas of the cyclic forms of a monosaccharide, use the following procedure, explained using the pyranoses of D-glucose.

Step 1: Draw the Fischer projection of the acyclic form of D-glucose. (See D,L convention)



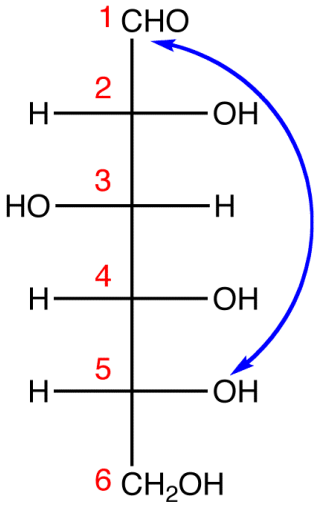
1

Step 2: Number the carbon chain in 1 starting at the top.



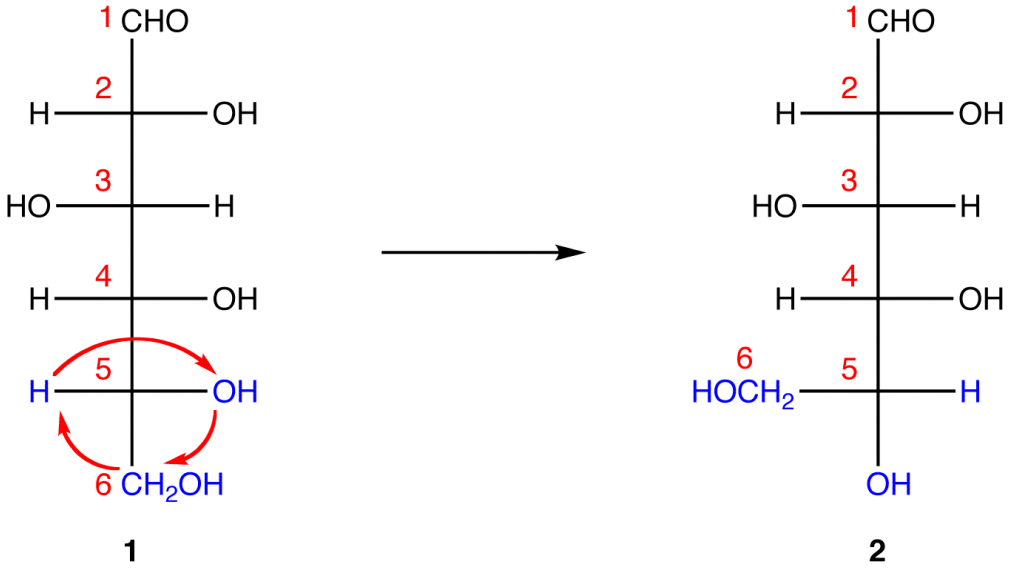
1

Step 3: To generate the pyranose ring, the oxygen atom on C-5 in 1 needs to be attached to C-1 by a single bond.



1

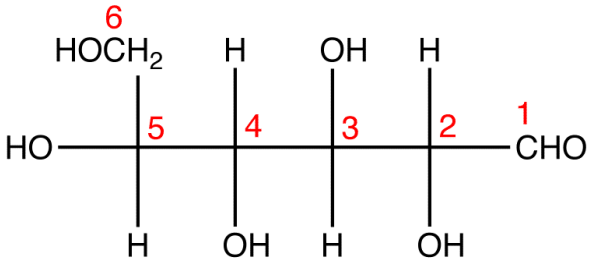
In 1, C-1 is behind the plane of the paper and the hydroxy group on C-5 is in front. For the pyranose ring to be planar, both C-1 and the hydroxy group on C-5 have to be either behind or in front of the plane of the paper. C-5 is a chiral center. In order to bring the hydroxy group on C-5 to the site occupied by the CH_2OH group without changing the absolute configuration at C-5, rotate the three ligands H, OH, and CH2OH on C-5 in 1 clockwise without moving the fourth ligand. (See Fischer projection)



1 **2**

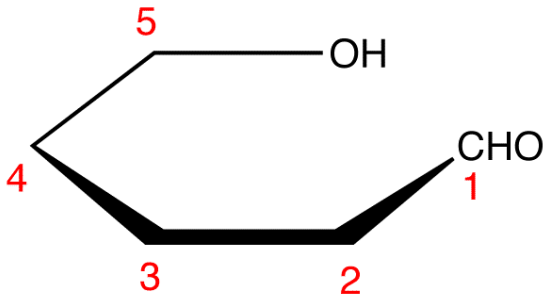
1 and 2 both represent D-glucose, but, in 2, unlike in 1, C-1 and the hydroxy group on C-5 are on the same side of the plane of the paper.

Step 4: Ignore that 2 is a Fischer projection and rotate it clockwise by 90°.



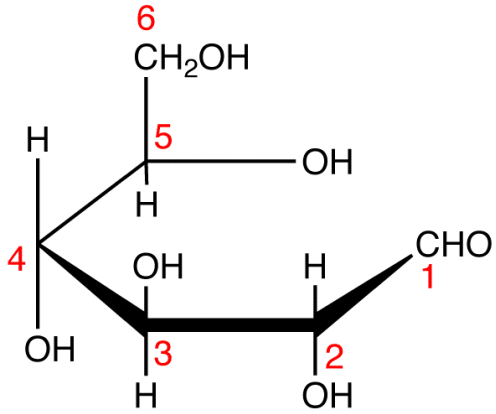
3

Step 5: Redraw the atom chain along the horizontal axis as follows.



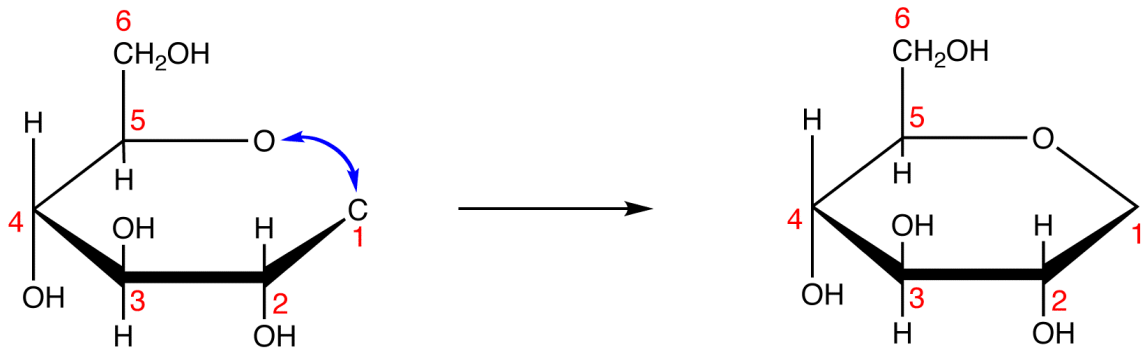
4

Step 6: Add the ligands on C-2 through C-5 in 4. The ligands pointing up in 3 are pointing up in 4; those pointing down in 3 are pointing down in 4.



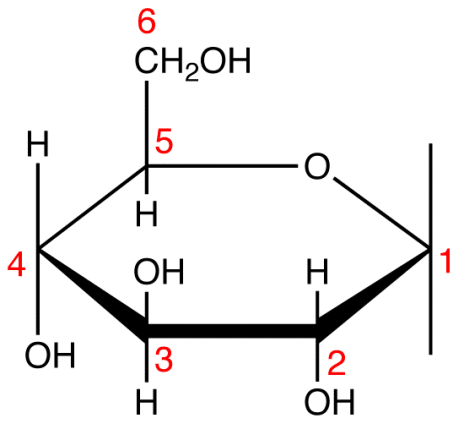
5

Step 7: Remove the hydrogen atom and the oxygen atom on C-1 and the hydrogen atom in the hydroxy group on C-5 in 5 and connect the two atoms by a single bond.



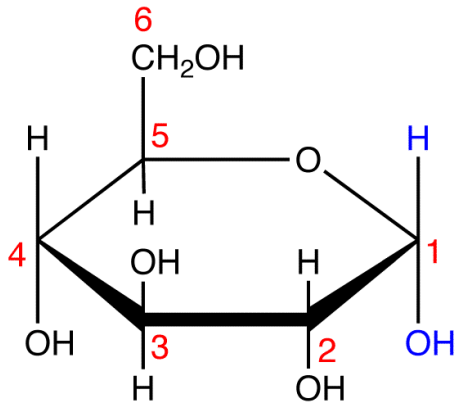
6

Step 8: Add the two remaining bonds to C-1 in 6.



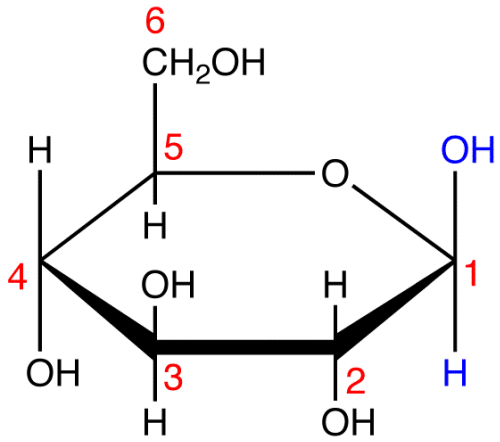
7

Step 9: Attach a hydrogen atom to the bond pointing up and a hydroxy group to the bond pointing down on C-1 in 7.



8

Step 10: Interchange the hydrogen atom and the hydroxy group on C-1 in 8.



9

8 and 9 are the Haworth formulas of the pyranoses of D-glucose. If, in the acyclic form of a monosaccharide, the hydroxy group that reacts with the carbonyl carbon is not on a chiral carbon (eg: D-fructose → pyranoses), skip step 3.

Contributors and Attributions

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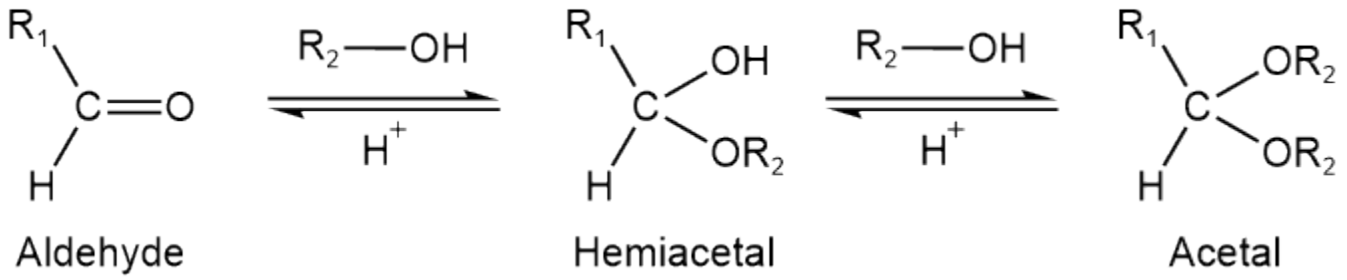
7.5: Reactions of monosaccharides

Learning Objectives

- Write and understand chemical reactions of monosaccharides, including conversion of cyclic hemiacetal to glycosides and N-glycosides, oxidation of open-chain aldehyde form to aldonic acids, and reduction to alditols.
- Define reducing sugars with the examples of D-glucose and D-fructose.

Glycosidic bond formation

Aldehydes and ketones react with alcohols to form hemiacetals. If the alcohol reagent is in excess, a second molecule of the alcohol reacts and converts hemiacetal to acetal. Acetals can be isolated. Acetals convert to alcohol and the aldehyde or ketone when their aqueous solution is acidified, as shown in the general reaction below.



Cyclic (pyranose and furanose) forms of monosaccharides are hemiacetals that react with alcohols to form acetals.

Glycosides are the acetals of monosaccharides. The glucose formed by a reaction with alcohol is also called **O-glycoside**.

For example, β-D-glucopyranose reacts with methanol to form glycosides, shown in Figure $7.5.1$.

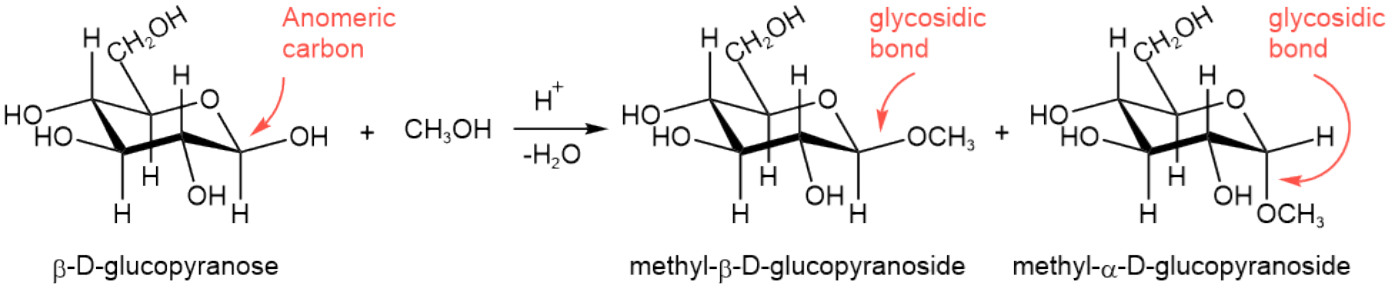


Figure $7.5.1$: Conversion of β-D-glucopyranose to its methyl glycosides. Mixture of α and β glycosides is produced, irrespective of whether the reactant is α or β form of the carbohydrate.(Copyright; Public domain)

Glycoside and glycosidic bond

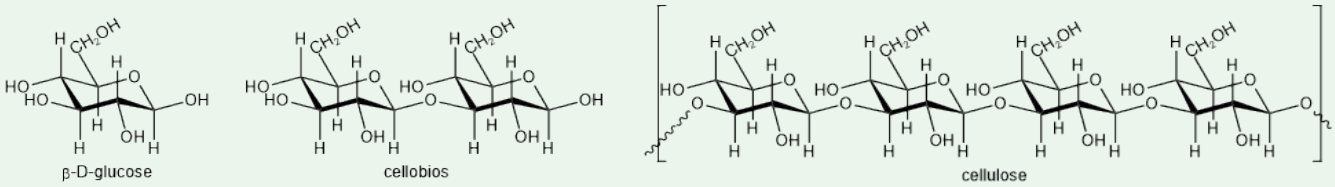
An acetal of a monosaccharide is a glycoside. The bond between anomeric C to the new ether $-\mathrm{OR}$ group in the glycoside is called the glycosidic bond. Anomeric C and glycosidic bonds are indicated by red arrows in Figure $7.5.1$.

Glycoside is named by replacing the last e of the carbohydrate name with ide and adding the name of the alkyl part of the new ether $-\mathrm{OR}$ group as a prefix separated by a hyphen. other For example, β-D-glucopyranose reacts with methanol to form methyl-β-D-glucopyranoside and methyl-α-D-glucopyranoside, as shown in Figure $7.5.1$.

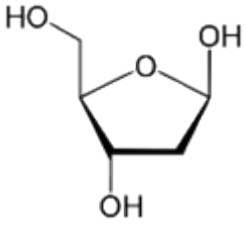
Since monosaccharides have many alcohol groups, two monosaccharides can react with each to form a glycoside, called a **disaccharide**, three can form a **trisaccharide**, and many can form a **polysaccharide**. The di-, tri-, and polysaccharides can be hydrolyzed to monosaccharides in an acidic aqueous solution.

Monosaccharide, disaccharide, oligosaccharide, and polysaccharide

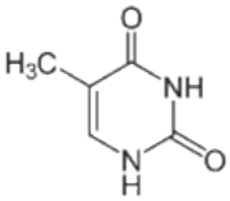
A carbohydrate that can not be hydrolyzed to a simpler carbohydrate is a **monosaccharide**, e.g., D-glucose. A glycoside of two monosaccharides is a **disaccharide**, e.g., cellobiose. A glycoside of three to ten monosaccharides is an **oligosaccharide**, e.g., a fragment of cellulose. A glycoside of more than ten monosaccharides is a **polysaccharide**, e.g., cellulose. The figure below illustrates the structures of D-glucose -a monosaccharide; cellobiose -a disaccharide; and cellulose, -a polysaccharide.



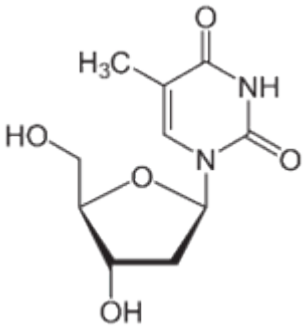
Amines react with hemiacetals forms of monosaccharides the same way as alcohols and produce N-glycosides. For example, β -D-2-deoxyribose reacts with thymine and produced an N-glycoside called deoxythymidine, a part of a monomer of DNA molecule, as shown in the figure below.



-D-2-Deoxyribose (a monosaccharide)



Thymine (an amine)



Doxythymidine (an N-glycoside)

Exceptions to the general formula of carbohydrates

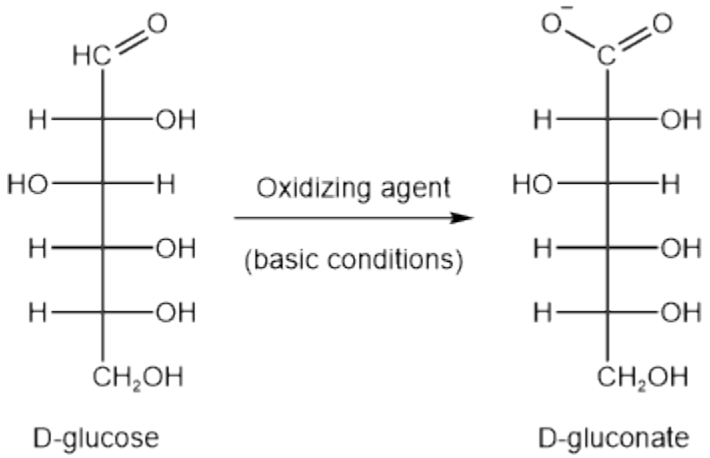
The general formula of carbohydrates is $\mathrm{C}_m(\mathrm{H}_2\mathrm{O})_n$, and usually for monosaccharides m is equal to n, i.e., $\mathrm{C}\cdot{}_n(\mathrm{H}_2\mathrm{O})_n$ or $\mathrm{C}_n\mathrm{H}_{2n}\mathrm{O}_n$. However, there are exceptions.

- Carbohydrates do not necessarily conform to this formula. For example, β-D-2-Deoxyribose $\mathrm{C}_5\mathrm{H}_{10}\mathrm{O}_4$ has less $\mathrm{O}'\mathrm{s}$ than what is dictated by the general formula.
- Compounds following this general formula are not necessarily always carbohydrates. For example, acetic acid $\mathrm{C}_2\mathrm{H}_4\mathrm{O}_2$ follows the general formula, but it is not a carbohydrate.

Oxidation to aldonic acids

Aldehydes are oxidized by a variety of reagents to carboxylic acids. Similarly, the aldehyde group $(-\mathrm{CHO})$ of the open-chain

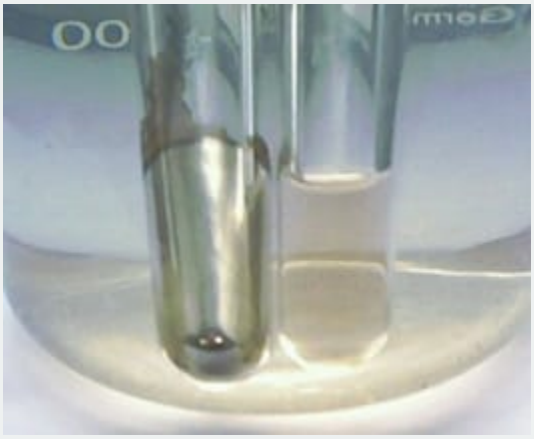
form of aldoses is oxidized to a carboxylic acid ($-\mathrm{COOH}$) group by oxygen $\mathrm{O_2}$ in the presence of enzymes called oxidases. The acid is named by replacing the suffix -ose of the class name aldose with -onic acid. For example, D-glucose is oxidized to D-gluconic acid. Since, $-\mathrm{COOH}$ exists in ionized ($-\mathrm{COO^-}$) form, the suffix -onic acid is replaced with -onate for the ionized form. For example, D-glucose is oxidized to D-gluconate, as shown in the figure below.



Reducing sugars

A carbohydrate that reacts with a mild oxidizing agent under alkaline conditions to form an aldonic acid (or aldonate anion in physiological conditions) is called a reducing sugar. For example, D-glucose is a reducing sugar, as shown in the figure above. The carbohydrate reduces the oxidizing agent.

Common reagents used to test the presence of a reducing sugar include Tollen's reagent in which $\mathrm{Ag^+}$ is reduced to Ag that forms a silver mirror on the glass, and Benedict's reagent in which $\mathrm{Cu^{2+}}$ is reduced to $\mathrm{Cu^+}$ that forms red color precipitate $\mathrm{Cu_2O}$, as shown in Figure $7.5.2$.



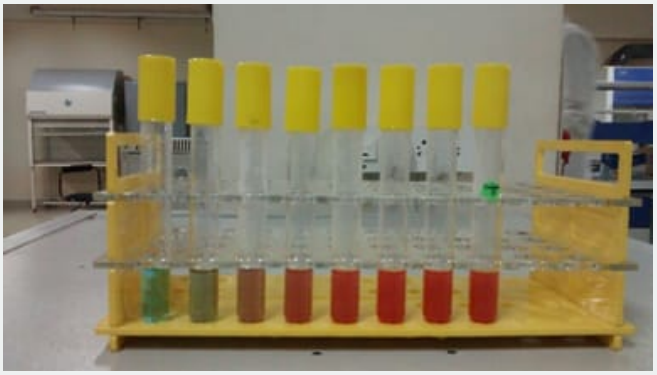
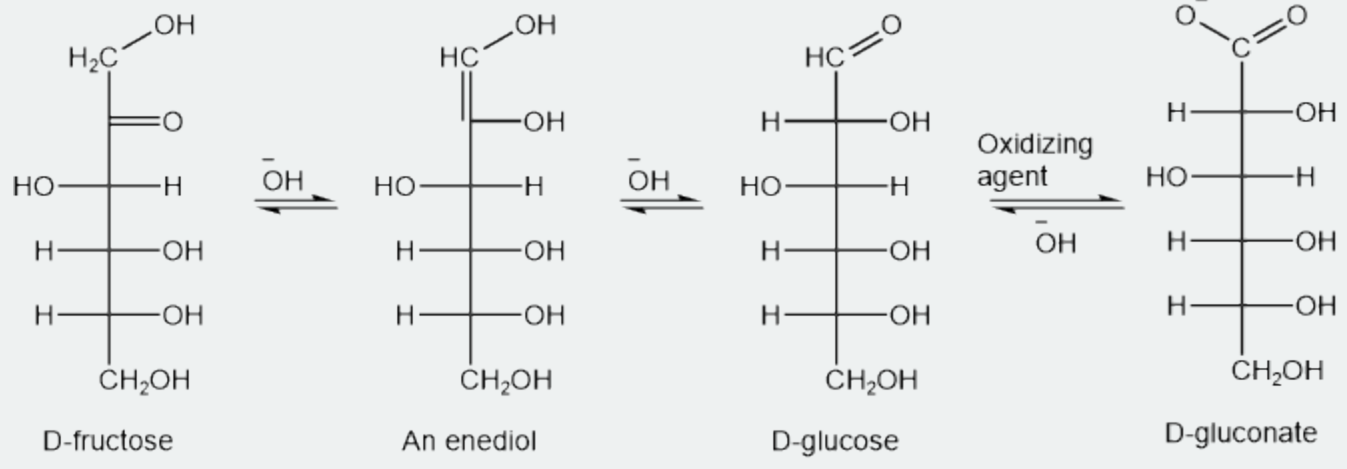


Figure $7.5.2$: Tests for reducing sugars: silver mirror test forming silver mirror as a positive test (left) and Benedict's test forming red color precipitate as a positive test (right). (Copyright; silver mirror test: K1954, Public domain, via Wikimedia Commons, Benedict's test: Psgs123xyz at English Wikipedia, CC0, via Wikimedia Commons)

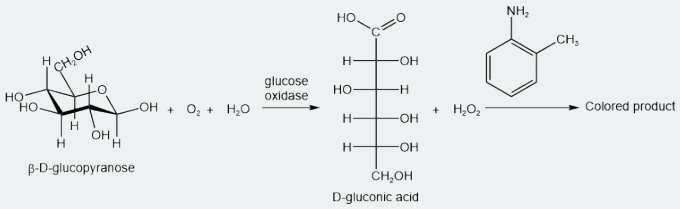
Although open-chain form is in small concentration at equilibrium, it is continuously formed from the hemiacetal forms as the oxidation reaction removes it. The 2-ketoses are also reducing sugars. This is because 2-ketoses exist in equilibrium with the corresponding aldoses under the basic conditions. The aldose form is the actual reducing agent in this mixture. For example, D-fructose is a reducing sugar. D-fructose exists in equilibrium with D-glucose in basic conditions, where D-glucose is the reducing agent, as illustrated in the figure below.

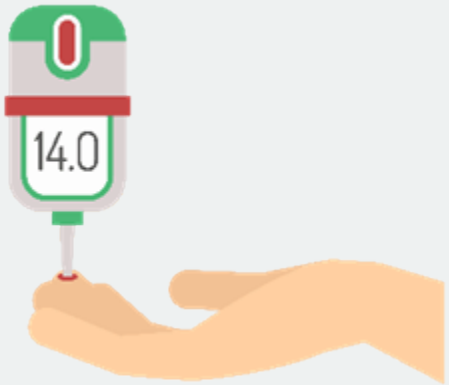


Diabetes and blood-sugar test

D-Glucose is also called blood sugar, as it is normally present in blood at about 70 mg/dL to 130 mg/dL. It may rise up to 140 mg/dL after eating food, but it returns to the normal range in healthy persons. Enzyme insulin controls blood sugar. If blood glucose control is not functioning properly, the blood glucose may stay higher than normal -a condition called hyperglycemia or diabetes; or it may stay below the normal level -a condition called hypoglycemia.

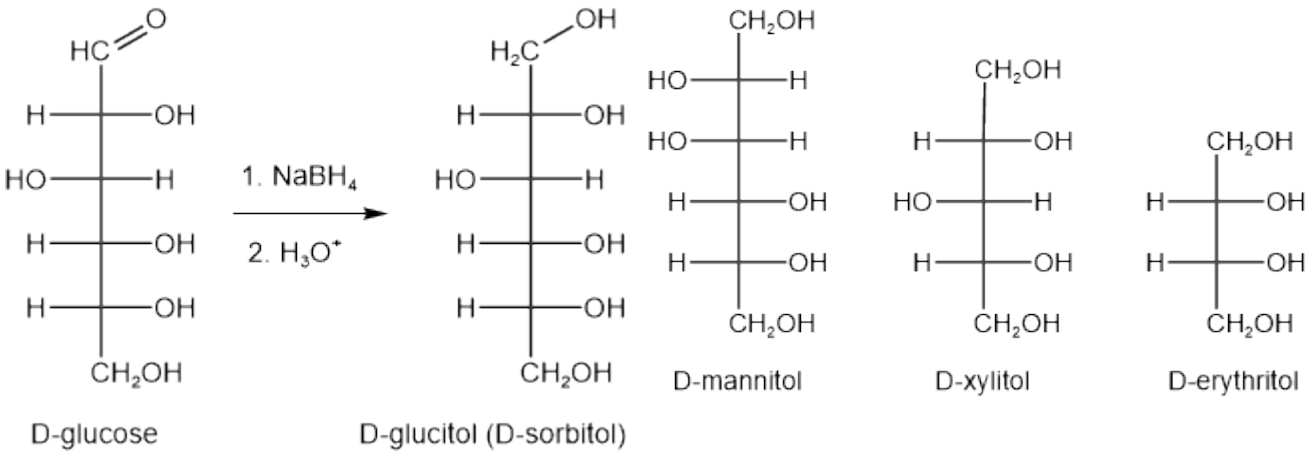
Blood glucose is usually tested based on enzyme-catalyzed reactions. Glucose oxidase enzyme oxidizes β-D-glucose using O_2 to D-gluconate and hydrogen peroxide H_2O_2. α-D-glucose does not react directly, but it converts to β-D-glucose as the latter is consumed. A second enzyme, peroxidase, causes H_2O_2 to react with 2-methylaniline and produces a colored product that is monitored to measure blood glucose, as illustrated in the figure below.





Reduction to alditols

Aldehydes are reduced to alcohols by a variety of reducing agents. Aldoses in the open-chain form are reduced by reducing agents like sodium borohydride ($NaBH_4$), H_2 in the presence of Pt, Pd, or Ni. Oxidases enzymes are reducing agents in biochemical systems. Although open-chain aldehyde form is in small concentration in the equilibrium mixture, cyclic hemiacetal forms convert to open-chain form as the latter is consumed. The product alcohol is named by replacing -ose suffix of the aldose name with -itol. For example, D-glucose is reduced to D-glucitol, as shown below.



D-glucitol is found in berries, cherries, plums, pears, seaweed, and algae. It is commonly known as D-sorbitol and is a sugar substitute for diabetes. Other alditol examples include D-erythritol, D-mannitol, and D-xylitol. D-xylitol is used in cereals, sugarless candies, and gums.

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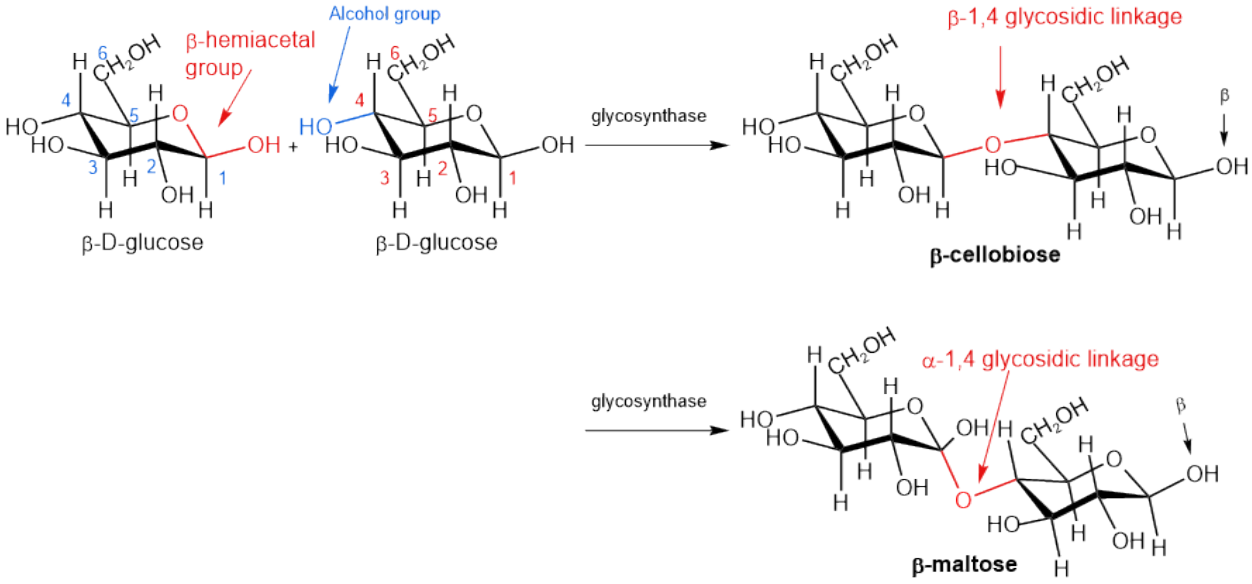
7.6: Disaccharides

Learning Objectives

- Be able to draw and name the glycosidic linkage in disaccharides.
- Know common disaccharides' structures, sources, and properties, including maltose, cellobiose, lactose, and sucrose.

Nomenclature of glycosidic linkage

Disaccharides are glycosides of two monosaccharides. Glycosidic linkage is formed by a reaction between the hemiacetal group of one monosaccharide and an alcohol group of the other, as illustrated in the figure below.

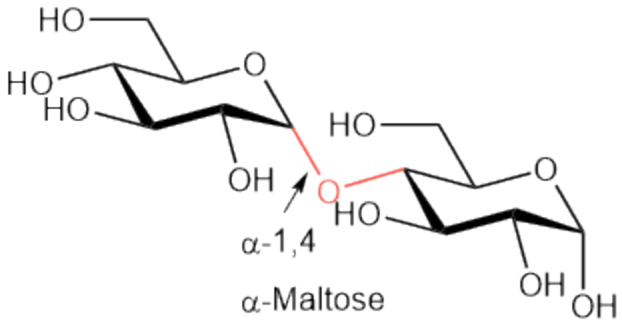


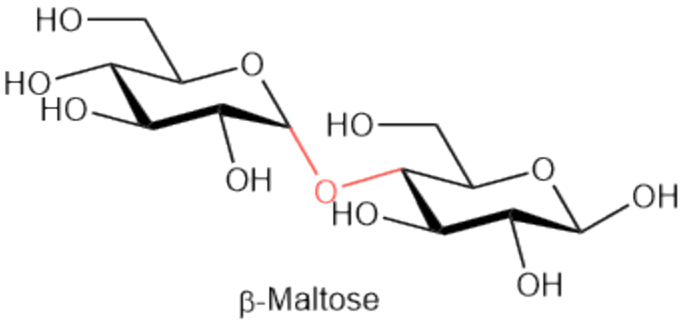
The glycosidic linkage is named by listing the number of the $\mathrm{C's}$ linked, separated by a comma. In the case of an anomeric carbon, α/β orientation is also indicated, separated by a hyphen from the number of the anomeric carbon. For example, β-cellobiose is linked by β-1,4 glycosidic linkage and β-maltose by α-1,4 glycosidic linkage. The β in the name β-cellobiose and β-maltose indicates the orientation of the free hemiacetal group in the second saccharide unit. It is not related to the orientation of the glycosidic linkage, as indicated by the black arrow in the figure. β-Cellobiose and β-maltose are configurational isomers having different physical and chemical properties.

Examples of disaccharides include maltose, cellobiose, lactose, and sucrose, described next.

Maltose

Maltose is a disaccharide of two D-glucose units connected through α-1,4-glycosidic linkage, as shown below.

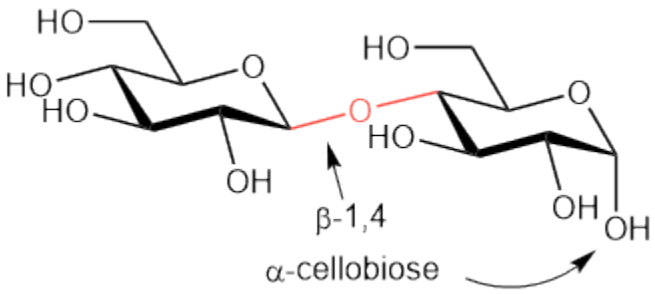


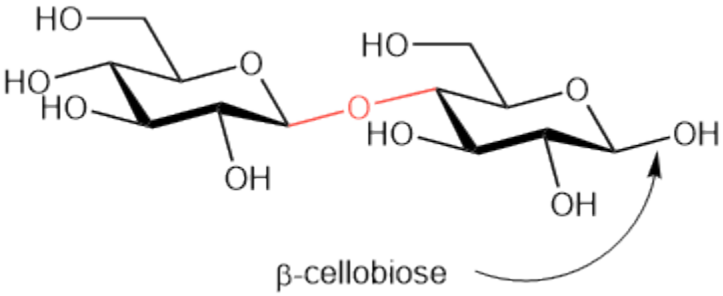


The second D-glucose unit with free hemiacetal group can be either in α- or β-configuration, as indicated by α/β prefix to the name. An aqueous solution exists in equilibrium between α, β, and open-chain aldose forms. Since common oxidizing agents can reduce the open-chain aldose form, maltose is a reducing sugar. Maltose is found in the juice of sprouted barley grains and other grains.

Cellobiose

Cellobiose is a disaccharide of two D-glucose units connected by β-1,4-glycosidic linkage, as shown below. Hemiacetal forms of cellobiose are shown below.

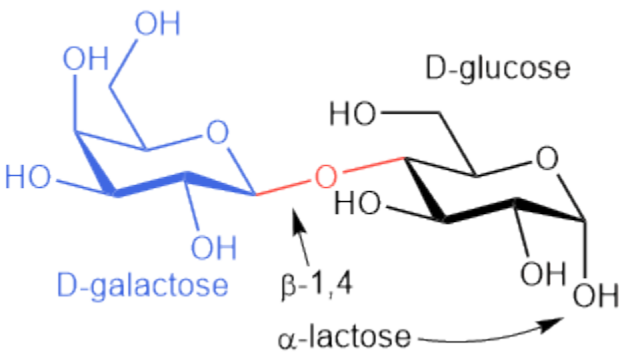


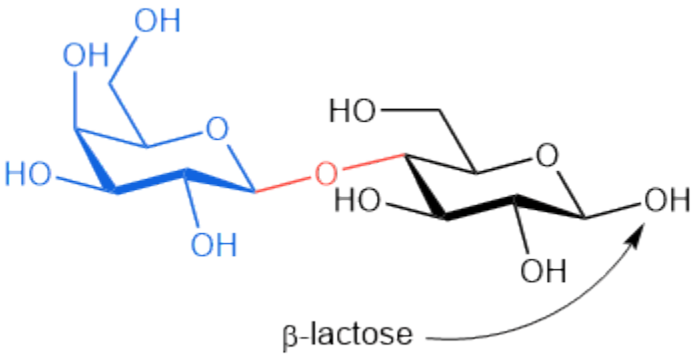


Cellulobiose is a reducing sugar because, like maltose, the D-glucose unit with free hemiacetal group can exist in α, β, or open-chain aldose forms in solution. Cellobiose is obtained by hydrolysis of cellulose.

Lactose

Lactose is a disaccharide of D-galactose joined by β-1,4-glycosidic linkage with D-glucose, as shown below.

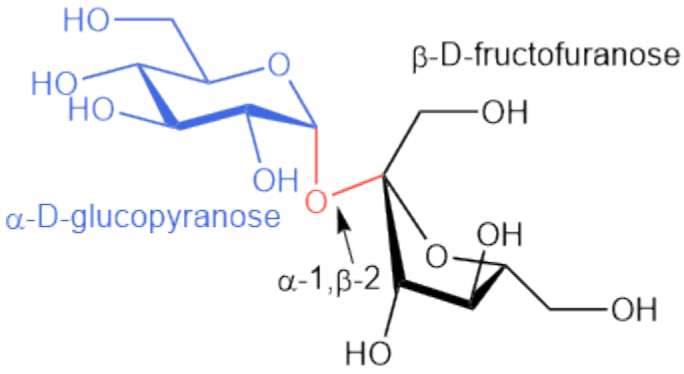




Lactose is a reducing sugar because, like maltose, the D-glucose unit with free hemiacetal group can exist in α, β, or open-chain aldose forms in solution. Lactose is present in milk, up to 5% to 8% in human milk and 4% to 6% in cow milk. Lactase is the enzyme that hydrolysis lactose in the digestion process. Many adults develop lactose intolerance due to a lack of or insufficient lactase production. Without lactase, lactose enters the colon undigested and is fermented by bacteria causing bloating and abdominal cramps. Therefore, some products that use lactose also add lactase to avoid the problem.

Sucrose

Sucrose is a disaccharide of D-glucose (in pyranose form) and D-fructose (in furanose form) joined by α-1,β-2-glycosidic linkage, as shown below.



Sucrose

Both anomeric $\mathrm{C,s}$ in the glycosidic linkage can not exist in open-chain aldose or ketose forms. Therefore, sucrose is a non-reducing sugar. Sucrose is commonly used as table sugar. It is the most abundant disaccharide found in sugar cane and sugar beats.

Relative sweetness

Monosaccharides and disaccharides are sweet, but sweetness varies. Fructose is the sweetest monosaccharide, and lactose is the least sweet, as shown in Table 1. Honey is a mixture of fructose and glucose and has a sweetness about the same as table sugar (sucrose). Relative sweetness in the table is based on the results of a group of people tasting and ranking them in order of taste relative to sucrose (table sugar), rated 1. Some artificial sweeteners listed in the table are commonly used as sugar-substitute in diet foods.

Table 1: Relative sweetness of some carbohydrates and artificial sweeteners (Based on the results of a group of people tasting and ranking them in order of taste relative to sucrose (table sugar) rated 1 as reference).

Carbohydrates	Sweetness relative to sucrose	Sugar alcohols	Sweetness relative to sucrose	Artificial sweeteners	Sweetness relative to sucrose
Fructose	1.74	Xylitol	1.00	Advantame	2,000
Sucrose (table sugar)	1.00	Maltitol	0.80	Saccharin	450
Honey	0.97	Sorbitol	0.60	Acesulfame-K	200
Glucose	0.74			Aspartame	180
Maltose	0.33			Stevia	150
Galactose	0.65			Sucralose	60
Lactose	0.16				

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7.7: Oligosaccharides

Learning Objectives

- Differentiate between blood types based on the oligosaccharides attached to the red blood cell surface and blood compatibility related to the blood type.

Oligosaccharides are polymers containing a small number, typically three to ten of monosaccharides. Oligosaccharides include dextrins which are microbial breakdown products of long polysaccharides like starch or cellulose and other glycans linked to lipids or proteins through N- or O-glycosidic bonds. The primary role of the last class is cell recognition and cell adhesion. For example, oligosaccharides attached to red-blood cells define the blood type A, B, AB, or O, depending on the linked oligosaccharides, as described next.

A, B, AB, or O blood types

The membrane of animal plasma cells typically has oligosaccharides comprising 4 to 17 monosaccharides attached to them. Their purpose is cell recognition, i.e., if there is a foreign cell or an object in the biochemical system, it is identified through the surface oligosaccharides and either destroyed or flagged for destruction by the body's immune system. For example, red blood cells have different types based on the oligosaccharides attached to their cell membrane, as shown in Figure 7.7.1.

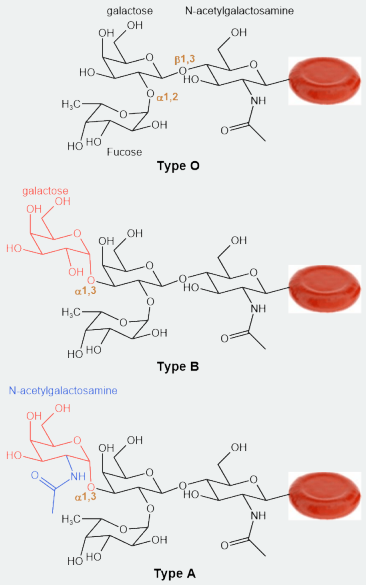


Figure 7.7.1: Oligosaccharide structures of blood type O, type B, and type A. Type AB has type A + type B in it. (Copyright; Public domain)

Blood type O has a combination of N-acetylgalactoseamine-galactose-Fucose. This combination is present in all other blood types also. So, Blood type O is not recognized as foreign in any blood type. A person with blood type O can donate blood to every type, i.e., type O is a universal donor. Any class other than type O has some additional monosaccharide attached which is recognized as foreign by blood type O. So, a person with blood type O can accept only type O blood.

Blood type B has an additional monosaccharide, i.e., galactose attached to galactose of type O oligosaccharide. Type B can receive blood from type O or type B and donate to type B or type AB, as shown in Figure 7.7.2.

Blood type A has an additional monosaccharide, N-acetyl galactosamine, attached to galactose of type O oligosaccharide. Type A can receive blood from type O or type A and can donate to type A or type A.B

Blood type AB has a mix of type A and type B. Type AB can accept all types, i.e., it is a universal recipient but can donate only to type AB.

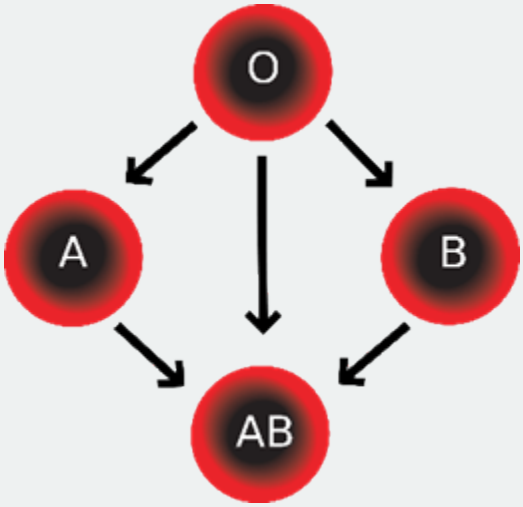


Figure 7.7.2: Diagram showing the blood group compatibility for transfusion purposes. (Copyright; InvictaHOG, Public domain, via Wikimedia Commons)

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7.8: Polysaccharides

Learning Objectives

- Learn the structures and some characteristics of polysaccharides, including starches, cellulose, and chitin.

Polysaccharides are long polymers from ten to thousands of monosaccharides joined by glycosidic linkages. The most abundant polysaccharides are starch, glycogen, cellulose, and chitin. Except for chitin, all others are composed of D-glucose. Chitin is composed of a modified form of glucose. These are described next.

Starch

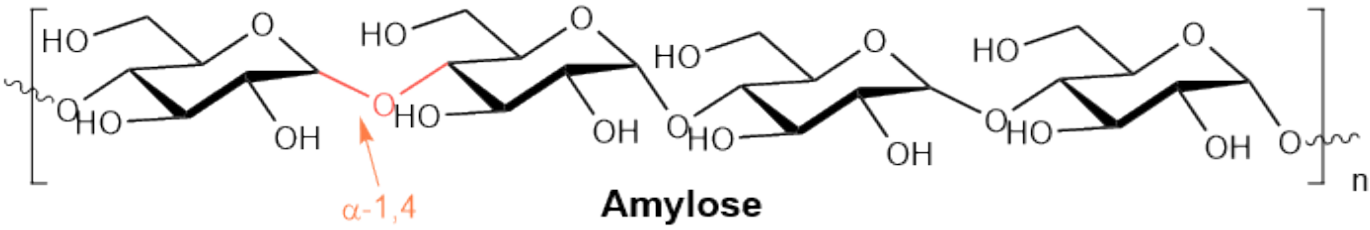
Starch is a storage form of D-glucose in plants. It is found in potatoes, beans, rice, wheat, and other grains and roots, as illustrated in Figure 7.8.1. Starch is a mixture of two forms, 20% to 25% amylose and 75 to 80% amylopectin.



Figure 7.8.1: Starch food: Sindhi Biryani is a delicious Dish of Sindh. (Copyright; Miansari66, Public domain, via Wikimedia Commons)

Amylose

Amylose is an unbranched chain of up to 4,000 D-glucose units joined by α-1,4-glycosidic linkage, as shown below.



Amylose

The orientation of bonds with α-1,4-glycosidic linkage makes the amylose chain exist in a helical structure, as shown in Figure 7.8.2, that allows water molecules to access and establish hydrogen bonds with $-\mathrm{OH}$ groups. Starch is a water-soluble polymer. It can dissolve in water due to extensive hydrogen bonding with the water molecules when mixed with water.

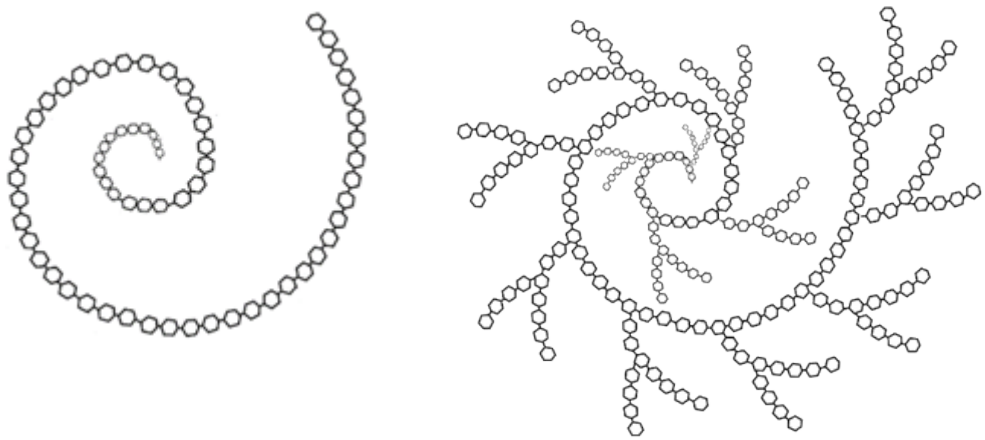
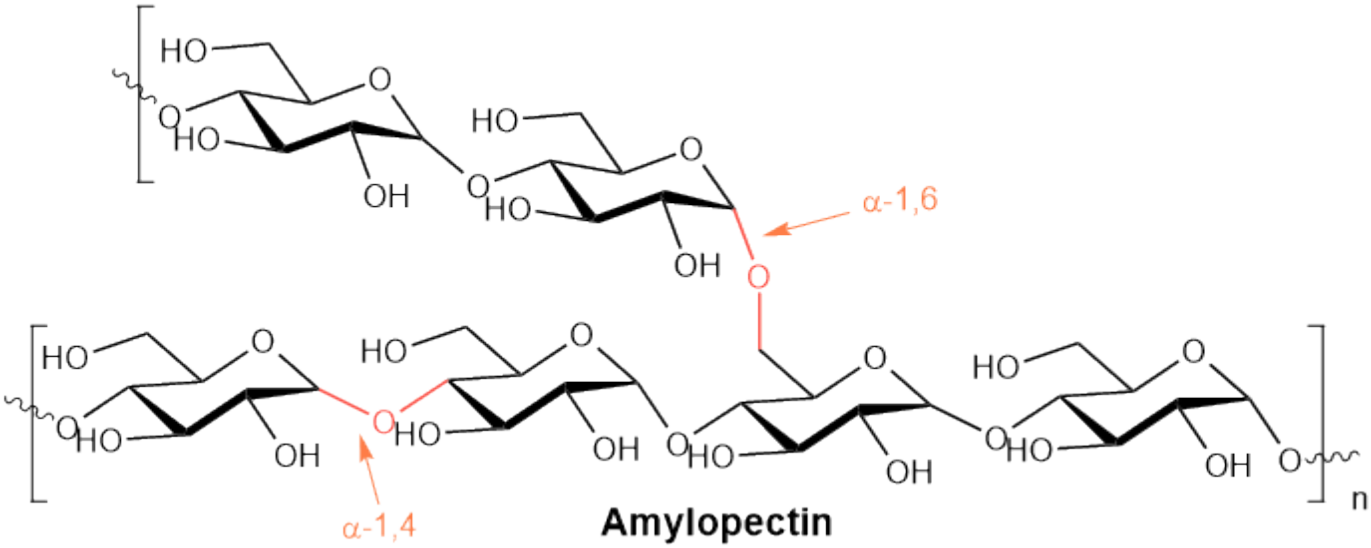


Figure 7.8.2: Illustration of a spiral structure of amylose (left) and branched helical structure of amylopectin (right). (Copyright; modified the free download from: https://www.hiclipart.com/free-trans...lumuh/download)

Amylopectin

Amylopectin is a branched chain polymer of D-glucose, as shown below.



The main chain comprises 10,000 D-glucose units joined by α-1,4-glycosidic linkage. The main chain exists in the form of a helix. Branches originate at every 24 to 30 unit intervals on the main chain connected to the main chain by a α-1,6-glycosidic linkage, as shown in Figure 7.8.2. This helix with branches going outwards makes amylopectin more accessible to water for hydrogen bonding and easier to digest.

Glycogen

Glycogen is an energy-storage polysaccharide in animals with the same structure as amylopectin. it has up to 10^6 D-glucose units joined by α-1,4-glycosidic linkages and branching through α-1,6-glycosidic linkages. The main difference from amylopectin is that glycogen has more frequent branching at 10 to 15 D-glucose units interval, as illustrated in Figure 7.8.3. More branching makes it more soluble in water and easier to hydrolyze multiple D-glucose units from the ends of branches, when the body needs D-glucose.

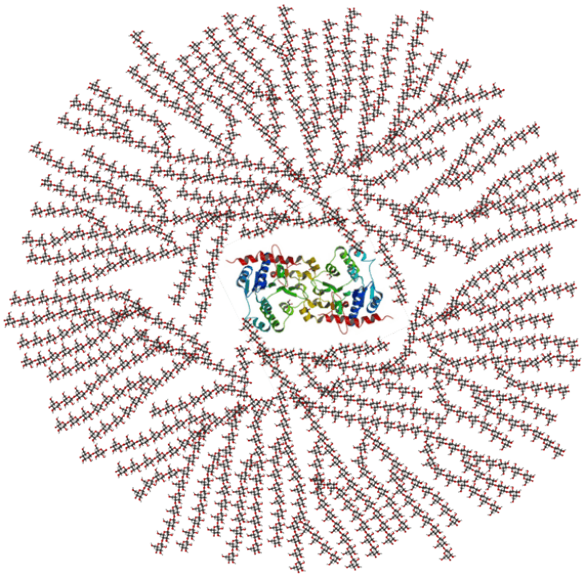


Figure 7.8.3: A 2-D cross-sectional view of glycogen -A core glycogen protein surrounded by branches of glucose units. (Copyright; Mikael Häggström. Public domain, via Wikimedia Commons)

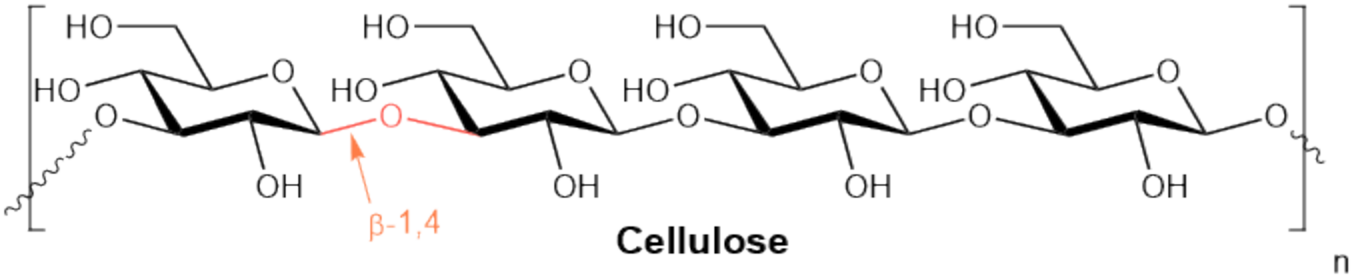
Cellulose

Cellulose is the most abundant polysaccharide in nature that makes up about 50% of the cell wall of plant cells. Cotton, shown in Figure 7.8.4, is almost pure cellulose.



Figure 7.8.4: Cellulse: Cotton is almost pure cellulose. (Copyright; United States Department of Agriculture, Public domain via Wikimedia Common)

Cellulose is a linear polysaccharide of about 2200 D-glucose units joined by β-1,4-glycosidic linkage, as shown below.



The β-1,4-glycosidic linkage allowes glucose units to adopt a linear structure with intra-molecule hydrogen bonding. The linear polymer packs nicely with inter-molecular hydrogen bonding and the London-dispersion forces, as shown in Figure 7.8.5. It gives cellulose its mechanical strength and makes it insoluble in water. Due to the extensive inter- and intra-molecular hydrogen bonding within cellulose, water can not establish enough hydrogen-bonds to dissolve it.

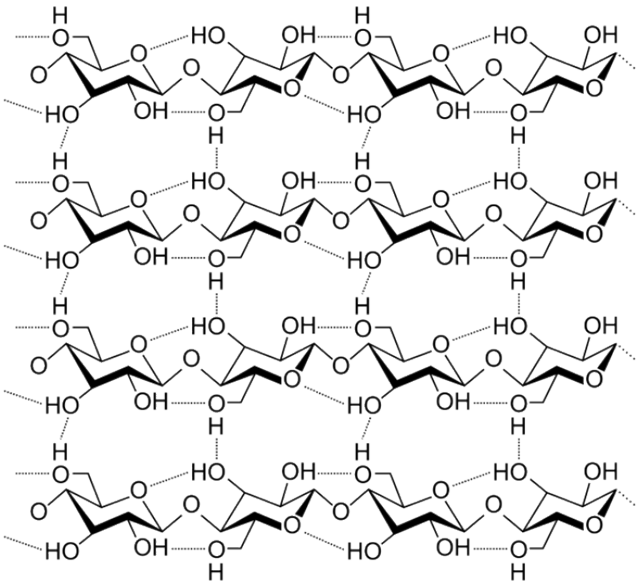


Figure 7.8.5: Illustration of linear chains of cellulose polymer with intra- and inter-molecular hydrogen bonding shown by dotted lines. (Copyright; Laghi.l, CC BY-SA 3.0, via Wikimedia Commons)

Animals have α-glucosidase enzymes that allow them to hydrolyze starch and glycogen to D-glucose, but they do not have β -glucosidase enzymes needed to hydrolyze cellulose. Grazing animals and termite host bacteria in their stomach that have the β -glucosidase enzymes. Therefore, grazing animals and termites can digest cellulose.

Chitin

Chitin is the second most abundant polysaccharide, second only to cellulose. It is found in the exoskeleton of crustaceans and insects, as shown in Figure 7.8.6.



Figure 7.8.6: Blue crab, an example of chitin in the exoskeleton of crustaceans and insets. (Copyright; Blue Crab. USEPA Environmental-Protection-Agency, Public domain, via Wikimedia Commons)

Chitin has the same structure as cellulose except that it is composed of N-acetylglucosamine, an amide derivative of D-glucose, in place of D-glucose in cellulose, as illustrated below Figure 7.8.7.

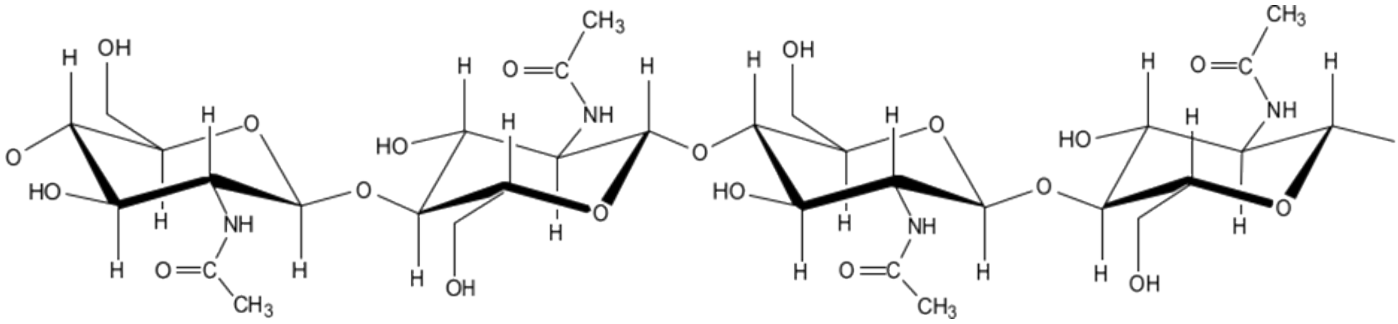


Figure 7.8.7: Structure of chitin. (Copyright; Ronny Flores, Public domain, via Wikimedia Commons)

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8: CARBOXYLIC ACIDS, ESTERS, AND AMIDES

8.1: Carboxylic Acids Background

8.2: Related Derivatives

8.3: Physical Properties of Carboxylic Acids

8.4: Acidity of Carboxylic Acids and Phenols

8.5: Esters

8.6: Physical Properties of Esters

8.7: Amides

8.8: Physical Properties of Amides

8.9: Nomenclature of Carboxylic Acids

8.10: Naming Carboxylic Acid Derivatives

8.11: Chemistry of Esters

8.12: Hydrolysis of Esters

8.13: Soap

8.14: Chemistry of Amides

8.15: Polyamides and Polyesters - Step-Growth Polymers

8.16: Esters of Phosphoric Acid

8.17: Carbonyl-Containing Compounds (Exercises)

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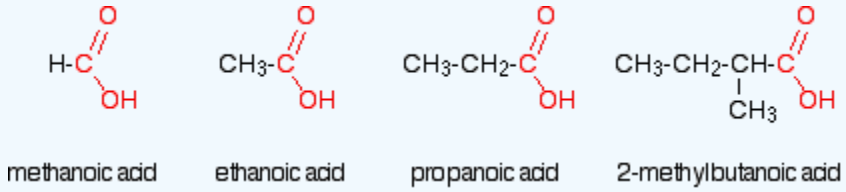
8.1: Carboxylic Acids Background

This page explains what carboxylic acids are, and looks at the ions that they form in their salts. It also considers their simple physical properties such as solubility and boiling points.

Carboxylic acids contain a -COOH group

Carboxylic acids are compounds which contain a -COOH group. For the purposes of this page we shall just look at compounds where the -COOH group is attached either to a hydrogen atom or to an alkyl group.

Example

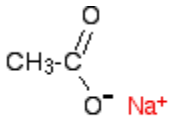


methanoic acid ethanoic acid propanoic acid 2-methylbutanoic acid

The name counts the total number of carbon atoms in the longest chain - including the one in the -COOH group. If you have side groups attached to the chain, notice that you always count from the carbon atom in the -COOH group as being number 1.

Salts of carboxylic acids

Carboxylic acids are acidic because of the hydrogen in the -COOH group. When the acids form salts, this is lost and replaced by a metal. Sodium ethanoate, for example, has the structure:



sodium ethanoate

Depending on whether or not you wanted to stress the ionic nature of the compound, this would be simplified to $CH_3COO^-\ Na^+$ or just CH_3COONa. Notice:

- The bond between the sodium and the ethanoate is ionic. Do not draw a line between the two (implying a covalent bond). That is absolutely wrong!
- Although the name is written with the sodium first, the formula is always written in one of the ways shown. This is something you just have to get used to.

Physical properties of carboxylic acids

The physical properties (for example, boiling point and solubility) of the carboxylic acids are governed by their ability to form hydrogen bonds.

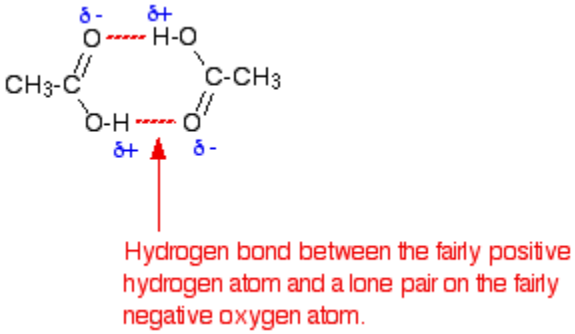
Boiling points

Before we look at carboxylic acids, a reminder about alcohols: The boiling points of alcohols are higher than those of alkanes of similar size because the alcohols can form hydrogen bonds with each other as well as van der Waals dispersion forces and

dipole-dipole interactions. The boiling points of carboxylic acids of similar size are higher still. For example:

propan-1-ol	$CH_3CH_2CH_2OH$	97.2°C
ethanoic acid	CH_3COOH	118°C

These are chosen for comparison because they have identical relative molecular masses and almost the same number of electrons (which affects van der Waals dispersion forces). The higher boiling points of the carboxylic acids are still caused by hydrogen bonding, but operating in a different way. In a pure carboxylic acid, hydrogen bonding can occur between two molecules of acid to produce a dimer.



This immediately doubles the size of the molecule and so increases the van der Waals dispersion forces between one of these dimers and its neighbors - resulting in a high boiling point.

Solubility in water

In the presence of water, the carboxylic acids do not dimerize. Instead, hydrogen bonds are formed between water molecules and individual molecules of acid. The carboxylic acids with up to four carbon atoms will mix with water in any proportion. When you mix the two together, the energy released when the new hydrogen bonds form is much the same as is needed to break the hydrogen bonds in the pure liquids.

The solubility of the bigger acids decreases very rapidly with size. This is because the longer hydrocarbon "tails" of the molecules get between water molecules and break hydrogen bonds. In this case, these broken hydrogen bonds are only replaced by much weaker van der Waals dispersion forces. The energetics of dissolving carboxylic acids in water is made more complicated because some of the acid molecules actually react with the water rather than just dissolving in it.

Contributors

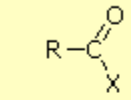
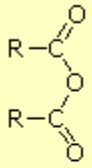
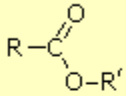
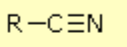
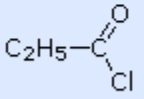
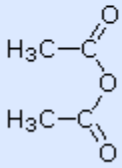
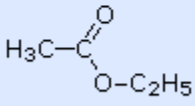
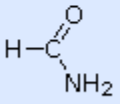
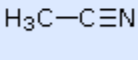
Jim Clark (Chemguide.co.uk)

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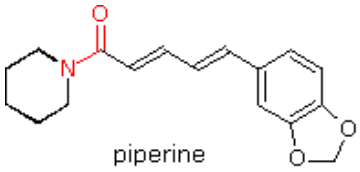
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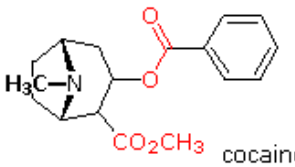
8.2: Related Derivatives

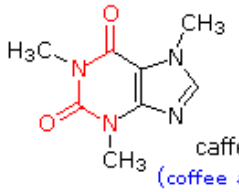
Other functional group combinations with the carbonyl group can be prepared from carboxylic acids, and are usually treated as related derivatives. Five common classes of these **carboxylic acid derivatives** are listed in the following table. Although nitriles do not have a carbonyl group, they are included here because the functional carbon atoms all have the same oxidation state. The top row (yellow shaded) shows the general formula for each class, and the bottom row (light blue) gives a specific example of each. As in the case of amines, amides are classified as 1°, 2° or 3°, depending on the number of alkyl groups bonded to the nitrogen.

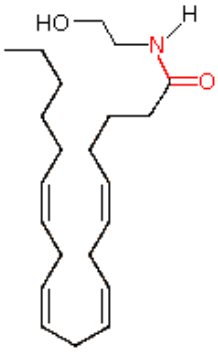
acyl halide	anhydride	ester	amide	nitrile
 X = F, Cl, Br or I			 R′ = H or alkyl	
 propanoyl chloride	 acetic anhydride	 ethyl acetate	 formamide	 acetonitrile

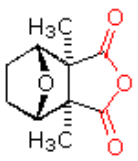
Functional groups of this kind are found in many kinds of natural products. Some examples are shown below with the functional group colored red. Most of the functions are amides or esters, cantharidin being a rare example of a natural anhydride. Cyclic esters are called **lactones**, and cyclic amides are referred to as **lactams**. Penicillin G has two amide functions, one of which is a β-lactam. The Greek letter locates the nitrogen relative to the carbonyl group of the amide.

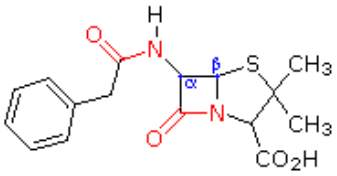

piperine
(from black pepper)

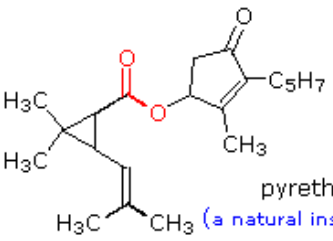

cocaine
(the coca bush)


caffeine
(coffee and tea)


anandamide
(from chocolate)


cantharidin
(blister beetle)


penicillin G
(an antibiotic)


pyrethrin
(a natural insecticide)

Contributors

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8.3: Physical Properties of Carboxylic Acids

Learning Objectives

- Compare the boiling points of carboxylic acids with alcohols of similar molar mass.
- Compare the solubilities of carboxylic acids in water with the solubilities of comparable alkanes and alcohols in water.

Many carboxylic acids are colorless liquids with disagreeable odors. The carboxylic acids with 5 to 10 carbon atoms all have "goaty" odors (explaining the odor of Limburger cheese). These acids are also produced by the action of skin bacteria on human sebum (skin oils), which accounts for the odor of poorly ventilated locker rooms. The acids with more than 10 carbon atoms are waxlike solids, and their odor diminishes with increasing molar mass and resultant decreasing volatility.

Carboxylic acids exhibit strong hydrogen bonding between molecules. They therefore have high boiling points compared to other substances of comparable molar mass.

The carboxyl group readily engages in hydrogen bonding with water molecules (Figure 8.3.1). The acids with one to four carbon atoms are completely miscible with water. Solubility decreases as the carbon chain length increases because dipole forces become less important and dispersion forces become more predominant. Hexanoic acid [$CH_3(CH_2)_4COOH$] is barely soluble in water (about 1.0 g/100 g of water). Palmitic acid [$CH_3(CH_2)_{14}COOH$], with its large nonpolar hydrocarbon component, is essentially insoluble in water. The carboxylic acids generally are soluble in such organic solvents as ethanol, toluene, and diethyl ether.

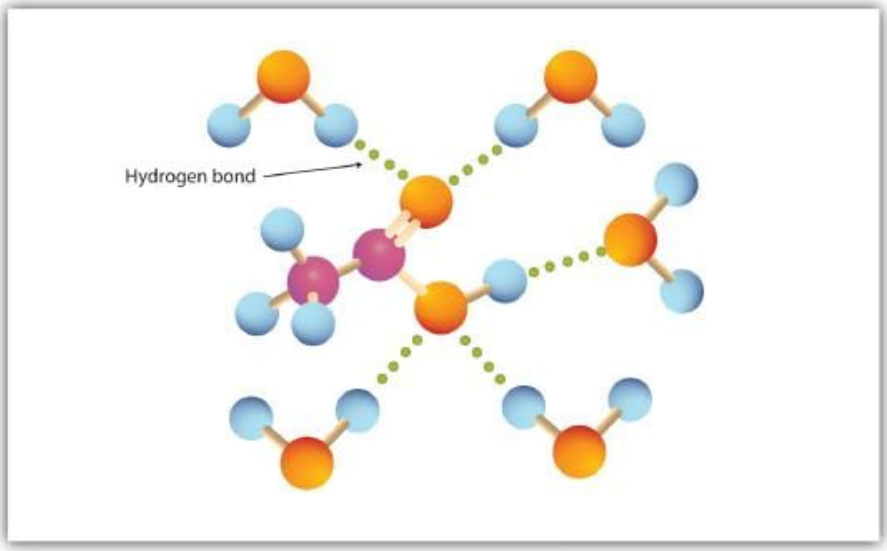


Figure 8.3.1: Hydrogen Bonding between an Acetic Acid Molecule and Water Molecules. Carboxylic acids of low molar mass are quite soluble in water.

Table 15.4.1 lists some physical properties for selected carboxylic acids. The first six are homologs. Notice that the boiling points increase with increasing molar mass, but the melting points show no regular pattern.

Table 8.3.1: Physical Constants of Carboxylic Acids

Condensed Structural Formula	Name of Acid	Melting Point (°C)	Boiling Point (°C)	Solubility (g/100 g of Water)
HCOOH	formic acid	8	100	miscible
CH_3COOH	acetic acid	17	118	miscible
CH_3CH_2COOH	propionic acid	–22	141	miscible

Condensed Structural Formula	Name of Acid	Melting Point (°C)	Boiling Point (°C)	Solubility (g/100 g of Water)
$CH_3(CH_2)_2COOH$	butyric acid	–5	163	miscible
$CH_3(CH_2)_3COOH$	valeric acid	–35	187	5
$CH_3(CH_2)_4COOH$	caproic acid	–3	205	1.1
C_6H_5COOH	benzoic acid	122	249	0.29

Key Takeaways

- Carboxylic acids have high boiling points compared to other substances of comparable molar mass. Boiling points increase with molar mass.
- Carboxylic acids having one to four carbon atoms are completely miscible with water. Solubility decreases with molar mass.

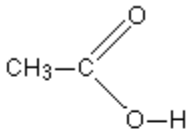
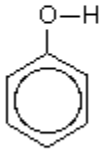
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8.4: Acidity of Carboxylic Acids and Phenols

Comparing the strengths of weak acids[Edit section]

The strengths of weak acids are measured on the pK_a scale. The smaller the number on this scale, the stronger the acid is. Three of the compounds we shall be looking at, together with their pK_a values are:

		pK_a
ethanoic acid		4.76
phenol		10.00
ethanol	$CH_3—CH_2—O—H$	about 16

Remember - the smaller the number the stronger the acid. Comparing the other two to ethanoic acid, you will see that phenol is very much weaker with a pK_a of 10.00, and ethanol is so weak with a pK_a of about 16 that it hardly counts as acidic at all!

Acidity of Carboxylic Acids

The pK_a 's of some typical carboxylic acids are listed in the following table. When we compare these values with those of comparable alcohols, such as ethanol (pK_a = 16) and 2-methyl-2-propanol (pK_a = 19), it is clear that carboxylic acids are stronger acids by over ten powers of ten! Furthermore, electronegative substituents near the carboxyl group act to increase the acidity.

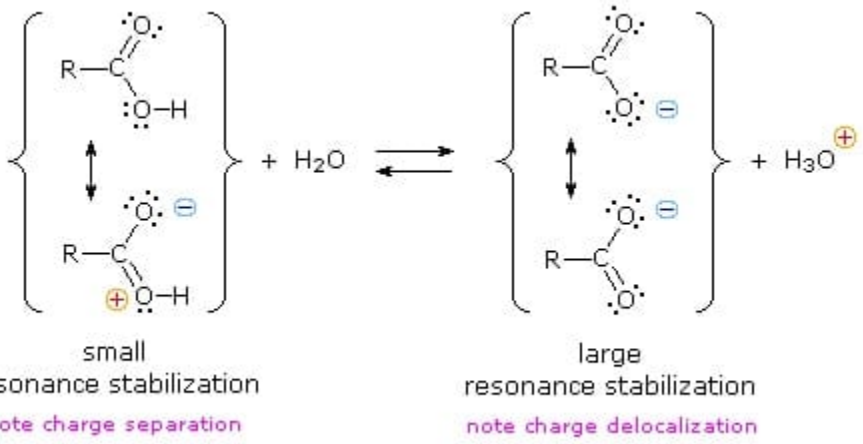
Compound	pK_a		Compound	pK_a
HCO_2H	3.75		$CH_3CH_2CH_2CO_2H$	4.82
CH_3CO_2H	4.74		$ClCH_2CH_2CH_2CO_2H$	4.53
FCH_2CO_2H	2.65		$CH_3CHClCH_2CO_2H$	4.05
$ClCH_2CO_2H$	2.85		$CH_3CH_2CHClCO_2H$	2.89
$BrCH_2CO_2H$	2.90		$C_6H_5CO_2H$	4.20
ICH_2CO_2H	3.10		p-$O_2NC_6H_4CO_2H$	3.45
Cl_3CCO_2H	0.77		p-$CH_3OC_6H_4CO_2H$	4.45

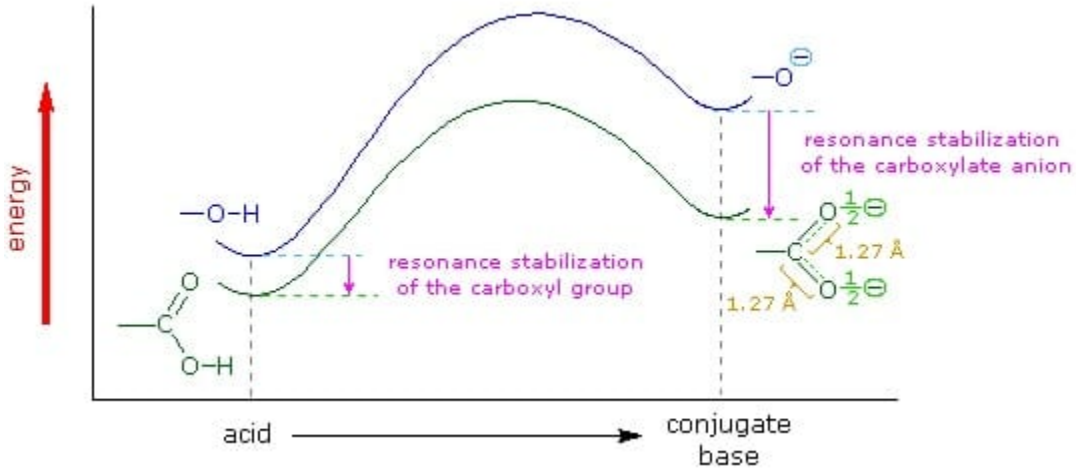
Why should the presence of a carbonyl group adjacent to a hydroxyl group have such a profound effect on the acidity of the hydroxyl proton? To answer this question we must return to the nature of acid-base equilibria and the definition of pK_a , illustrated by the general equations given below. These relationships were described in an previous section of this text.

$$H\text{–}A + H_2O \rightleftharpoons H_3O^{\oplus} + A:^{\ominus} \qquad K_{eq} = \frac{[H_3O^{\oplus}]\,[A:^{\ominus}]}{[HA]\,[H_2O]}$$

$$K_a = \frac{[H_3O^{\oplus}]\,[A:^{\ominus}]}{[HA]} \qquad pK_a = -\log K_a = \log\left(\frac{1}{K_a}\right)$$

We know that an equilibrium favors the thermodynamically more stable side, and that the magnitude of the equilibrium constant reflects the energy difference between the components of each side. In an acid base equilibrium the equilibrium always favors the weaker acid and base (these are the more stable components). Water is the standard base used for pK_a measurements; consequently, anything that stabilizes the conjugate base ($A:^{(-)}$) of an acid will necessarily make that acid (H–A) stronger and shift the equilibrium to the right. Both the carboxyl group and the carboxylate anion are stabilized by resonance, but the stabilization of the anion is much greater than that of the neutral function, as shown in the following diagram. In the carboxylate anion the two contributing structures have equal weight in the hybrid, and the C–O bonds are of equal length (between a double and a single bond). This stabilization leads to a markedly increased acidity, as illustrated by the energy diagram.





The pKa of ethanol is about 17, while the pKa of acetic acid is about 5: this is a 10^{12}-fold difference in the two acidity constants. In both compounds, the acidic proton is bonded to an oxygen atom. How can they be so different in terms of acidity? We begin by considering the conjugate bases.



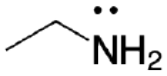
ethoxide acetate

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 localized on the second oxygen of the group. The two resonance forms for the conjugate base are equal in energy. 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 – it has nowhere else to go.

Recall the findamental idea that electrostatic charges, whether positive or negative, are more stable when they are 'spread out' than when they are confined to one atom. Here, a charge is being 'spread out' (in other words, delocalized) *by resonance*, rather than simply by the size of the atom involved.

The delocalization of charge by resonance has a very powerful effect on the reactivity of organic molecules, enough to account for the difference of over 12 pK_a units between ethanol and acetic acid. The acetate ion is that much more stable than the ethoxide ion, all due to the effects of resonance delocalization.

The resonance effect also explains why a nitrogen atom is much more basic when it is in an amine, but *not* significantly basic when it is part of an amide group. Recall that in an amide, there is significant double-bond character to the carbon-nitrogen bond, due to a second resonance contributor in which the nitrogen lone pair is part of a p bond.

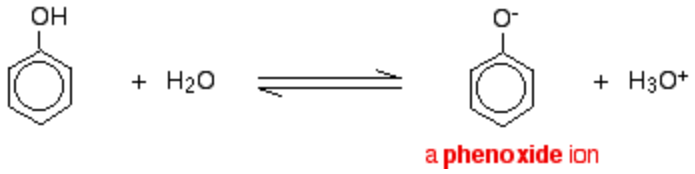
amine 

amide 

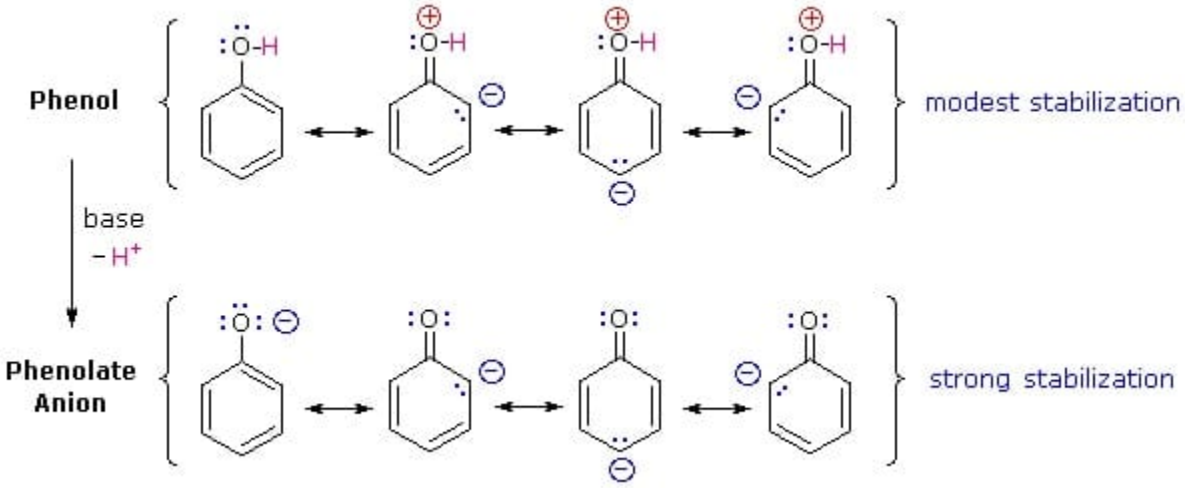
While the electron lone pair of an amine nitrogen is 'stuck' in one place, the lone pair on an amide nitrogen is delocalized by resonance. Notice that in this case, we are extending our central statement to say that electron density – in the form of a lone pair – is stabilized by resonance delocalization, even though there is not a negative charge involved. 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 'comfortable' being part of the delocalized pi-bonding system. The lone pair on an amine nitrogen, by contrast, is not part of a delocalized pi system, and is very ready to form a bond with any acidic proton that might be nearby.

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 solution in water:



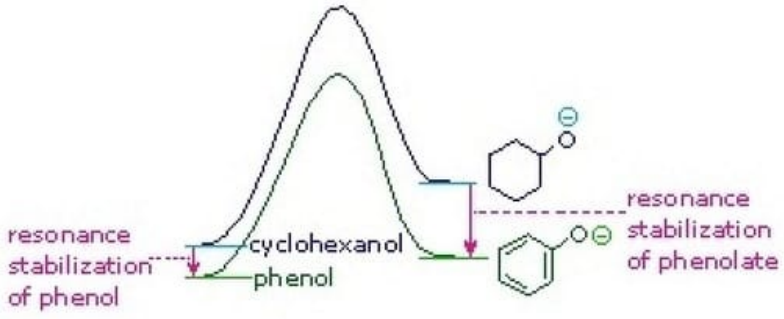
Phenol is a very weak acid and the position of equilibrium lies well to the left. Phenol can lose a hydrogen ion because the phenoxide ion formed is stabilised to some extent. The negative charge on the oxygen atom is delocalised around the ring. The more stable the ion is, the more likely it is to form. One of the lone pairs on the oxygen atom overlaps with the delocalised 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.

Why is phenol a much stronger acid than cyclohexanol? To answer this question we must evaluate the manner in which an oxygen substituent interacts with the benzene ring. As noted in our earlier treatment of electrophilic aromatic substitution reactions, an oxygen substituent enhances the reactivity of the ring and favors electrophile attack at ortho and para sites. It was proposed that resonance delocalization of an oxygen non-bonded electron pair into the pi-electron system of the aromatic ring was responsible for this substituent effect. A similar set of resonance structures for the phenolate anion conjugate base appears below the phenol structures.



The resonance stabilization in these two cases is very different. An important principle of resonance is that charge separation diminishes the importance of canonical contributors to the resonance hybrid and reduces the overall stabilization. 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.

Contributors

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8.5: Esters

Learning Objectives

- Identify the general structure for an ester.
- Use common names to name esters.
- Name esters according to the IUPAC system.

Esters are carboxylic acid derivatives formed by replacing the H in the hydroxyl group with a carbon group. Esters have the general formula RCOOR′, where R may be a hydrogen atom, an alkyl group, or an aryl group, and R′ may be an alkyl group or an aryl group but *not* a hydrogen atom (if it were a hydrogen atom, the compound would be a carboxylic acid). Figure 8.5.1 shows the general structure for an ester, with the functional group shown in red.

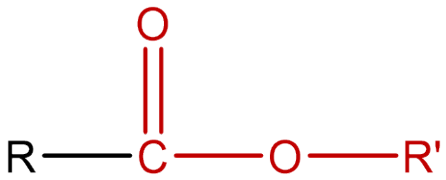


Figure 8.5.1: The structure of an ester. Esters feature a carbon-oxygen double bond that is also singly bonded to a second oxygen atom, which is then joined to an alkyl or an aryl group.

Esters occur widely in nature. Unlike carboxylic acids, esters generally have pleasant odors and are often responsible for the characteristic fragrances of fruits and flowers. Once a flower or fruit has been chemically analyzed, flavor chemists can attempt to duplicate the natural odor or taste. Both natural and synthetic esters are used in perfumes and as flavoring agents.

Fats and vegetable oils are esters of long-chain fatty acids and glycerol. Esters of phosphoric acid are of the utmost importance to life.

Naming Esters

Although esters are covalent compounds and salts are ionic, esters are named in a manner similar to that used for naming salts.

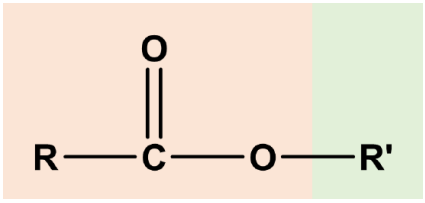
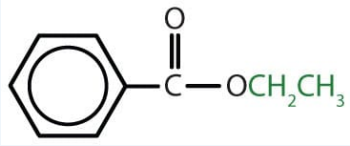


Figure 8.5.2: Guide for naming esters.

The common and International Union of Pure and Applied Chemistry (IUPAC) rules for naming esters are similar. In both systems, the identity of the R' carbon group (that replaced the hydrogen) is given and is followed by the name of the acid portion. Another similarity among the systems is that the *-ic acid* ending of the parent acid is replaced by the suffix *-ate* (Table 8.5.1).

If the ester molecule has substituents, as with carboxylic acids, the carbonyl carbon atom is always assigned to C1. It is unnecessary to designate this group by number.

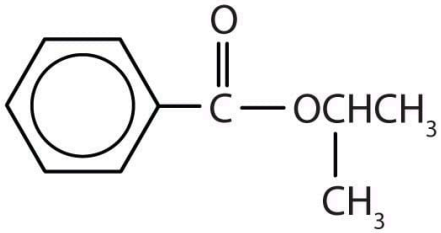
Table 8.5.1: Nomenclature of Esters

Condensed Structural Formula	Common Name	IUPAC Name
$HCOOCH_3$	methyl formate	methyl methanoate
CH_3COOCH_3	methyl acetate	methyl ethanoate
$CH_3COOCH_2CH_3$	ethyl acetate	ethyl ethanoate
$CH_3CH_2COOCH_2CH_3$	ethyl propionate	ethyl propanoate
$CH_3CH_2CH_2COOCH(CH_3)_2$	isopropyl butyrate	isopropyl butanoate
	ethyl benzoate	ethyl benzoate

Example 8.5.1

Give the common and IUPAC names for each compound.

a. 

b. 

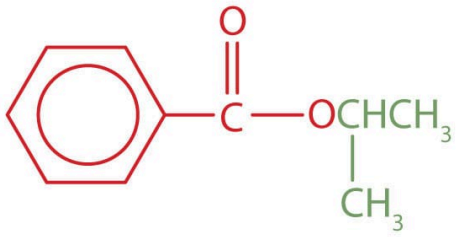
Solution

a. The alkyl group attached directly to the oxygen atom is a butyl group (in green).



The part of the molecule derived from the carboxylic acid (in red) has three carbon atoms. It is called propionate (common) or propanoate (IUPAC). The ester is therefore butyl propionate or butyl propanoate.

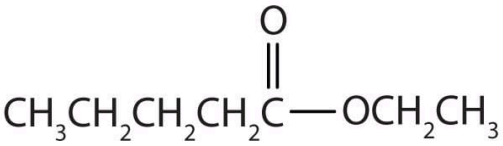
b. An alkyl group (in green) is attached directly to the oxygen atom by its middle carbon atom; it is an isopropyl group. The part derived from the acid (that is, the benzene ring and the carbonyl group, in red) is benzoate. The ester is therefore isopropyl benzoate (both the common name and the IUPAC name).



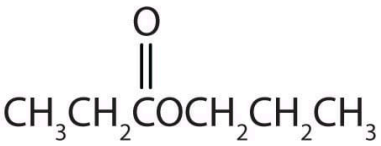
Exercise 8.5.1

Give the common and IUPAC names for each compound.

a.



b.

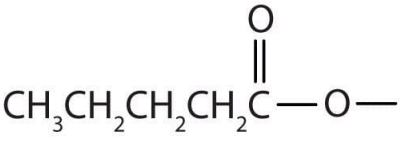


Example 8.5.2

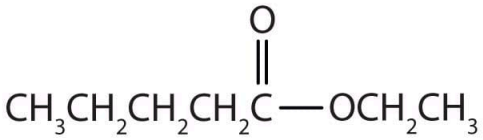
Draw the structure for ethyl pentanoate.

Solution

Start with the portion from the acid. Draw the pentanoate (five carbon atoms) group first; keeping in mind that the last carbon atom is a part of the carboxyl group.



Then attach the ethyl group to the bond that ordinarily holds the hydrogen atom in the carboxyl group.



Exercise 8.5.2

Draw the structure for phenyl pentanoate.

Key Takeaway

- An ester has an OR' group attached to the carbon atom of a carbonyl group.
- The R' cannot be H, because this will represent a carboxylic acid.
- The common and IUPAC names for esters identify the R' group that replaced the H followed by the name of the acid portion of the molecule.

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8.6: Physical Properties of Esters

Learning Objectives

- Compare the boiling points of esters with alcohols of similar molar mass.
- Compare the solubilities of esters in water with the solubilities of comparable alkanes and alcohols in water.

Ester molecules are polar but have no hydrogen atom attached directly to an oxygen atom. They are therefore incapable of engaging in intermolecular hydrogen bonding with one another and thus have considerably lower boiling points than their isomeric carboxylic acids counterparts. Because ester molecules can engage in hydrogen bonding with water molecules, however, esters of low molar mass are somewhat soluble in water. Borderline solubility occurs in those molecules that have three to five carbon atoms. Table 8.6.1 lists the physical properties of some common esters.

Esters are common solvents. Ethyl acetate is used to extract organic solutes from aqueous solutions—for example, to remove caffeine from coffee. It also is used to remove nail polish and paint. Cellulose nitrate is dissolved in ethyl acetate and butyl acetate to form lacquers. The solvent evaporates as the lacquer "dries," leaving a thin film on the surface. High boiling esters are used as softeners (plasticizers) for brittle plastics.

Table 8.6.1: Physical Properties of Some Esters

Condensed Structure	Name	Molar Mass (g/mol)	Melting Point (°C)	Boiling Point (°C)	Aroma
$HCOOCH_3$	methyl formate	60	−99	32	
$HCOOCH_2CH_3$	ethyl formate	74	−80	54	rum
CH_3COOCH_3	methyl acetate	74	−98	57	
$CH_3COOCH_2CH_3$	ethyl acetate	88	−84	77	
$CH_3CH_2CH_2COOCH_3$	methyl butyrate	102	−85	102	apple
$CH_3CH_2CH_2COOCH_2CH_3$	ethyl butyrate	116	−101	121	pineapple
$CH_3COO(CH_2)_4CH_3$	pentyl acetate	130	−71	148	pear
$CH_3COOCH_2CH_2CH(CH_3)_2$	isopentyl acetate	130	−79	142	banana
$CH_3COOCH_2C_6H_5$	benzyl acetate	150	−51	215	jasmine
$CH_3CH_2CH_2COO(CH_2)_4CH_3$	pentyl butyrate	158	−73	185	apricot
$CH_3COO(CH_2)_7CH_3$	octyl acetate	172	−39	210	orange

Example 8.6.1

a. Which compound has the higher boiling point—$CH_3CH_2CH_2CH_2OH$ or CH_3COOCH_3? Explain.
b. Which compound is more soluble in water—methyl butyrate or butyric acid? Explain.

Solution

a. $CH_3CH_2CH_2CH_2OH$ has the higher boiling point because there is hydrogen bonding and there is no hydrogen bonding in CH_3COOCH_3.

b. Butyric acid is more soluble in water because of hydrogen bonding with water.

Exercise 8.6.1

a. Which compound has the higher boiling point—$CH_3CH_2CH_2CH_2OH$ or CH_3COOCH_3? Explain.

b. Which compound is more soluble in water—methyl butyrate or butyric acid? Explain.

Summary

Esters have polar bonds but do not engage in hydrogen bonding and are therefore intermediate in boiling points between the nonpolar alkanes and the alcohols, which engage in hydrogen bonding. Ester molecules can engage in hydrogen bonding with water, so esters of low molar mass are therefore somewhat soluble in water.

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8.7: Amides

Learning Objectives

- Identify the general structure for an amide.
- Identify the functional group for an amide.
- Names amides with common names.
- Name amides according to the IUPAC system.

Amides are carboxylic acid derivatives that contain a functional group has an nitrogen atom attached to a carbonyl carbon atom. If the two remaining bonds on the nitrogen atom are attached to hydrogen atoms, the compound is a *simple amide*. If one or both of the two remaining bonds on the atom are attached to alkyl or aryl groups, the compound is a *substituted amide*.

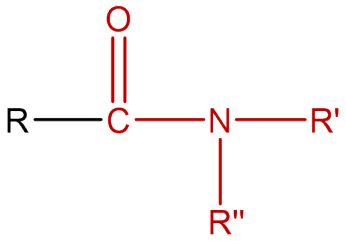


Figure 8.7.1: General structure of an amide. If R' and R" are both hydrogen atoms, the compound is a simple amide. If not, it is a substituted amide.

The carbonyl carbon-nitrogen bond is called an **amide linkage**. This bond is quite stable and is found in the repeating units of protein molecules, where it is called a *peptide linkage*.

Naming Amides

Simple amides are named as derivatives of carboxylic acids. The *-ic acid* ending of the common name or the *-oic acid* ending of the International Union of Pure and Applied Chemistry (IUPAC) name of the carboxylic acid is replaced with the suffix *-amide*.



Figure 8.7.2: Structures of a carboxylic acid (left) and amide (right) along with common (top) and IUPAC (bottom) names.

The names of substituted amides, include the identity of the R' or R" (of N–R) substituents. Instead of locator numbers, N– is used to indicate the location of these groups (Figure 8.7.3).

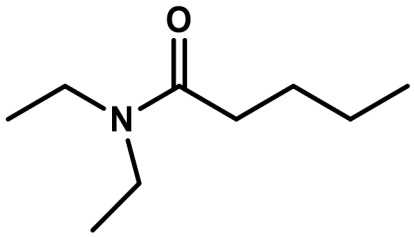
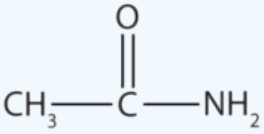
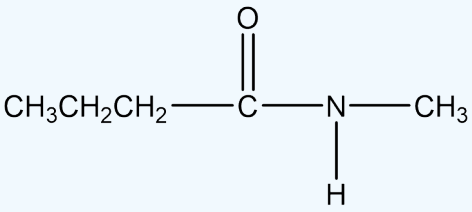


Figure 8.7.3: Skeletal structure of N,N-diethylpentanamide.

Example 8.7.1

Name each compound with the common name, the IUPAC name, or both.

a. 

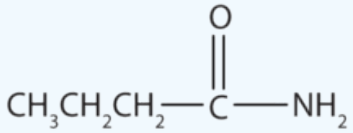
b. 

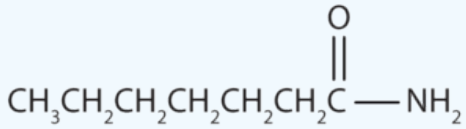
Solution

a. This amide has two carbon atoms and is thus derived from acetic acid. The OH of acetic acid is replaced by an NH_2 group. The *-ic acid* from *acetic acid* (or *-oic acid* from ethanoic acid) is dropped, and *-amide* is added to give *acetamide* (or ethanamide in the IUPAC system).
b. This is a substituted amide since there is a methyl group bonded to the nitrogen. The parent portion of the molecule is derived from butanoic acid. The *-oic acid* is dropped, and *-amide* is added to give butanamide. The methyl group is attached to the nitrogen (N) of the functional group, so the location is indicated as N-methyl. Therefore the name of the molecule is N-methylbutanamide.

Exercise 8.7.1

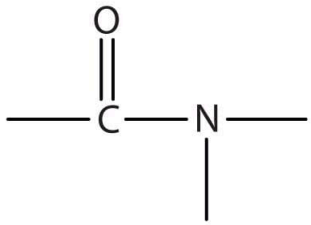
Name each compound with the common name, the IUPAC name, or both.

a. 

b. 

Key Takeaways

- Amides have a general structure in which a nitrogen atom is bonded to a carbonyl carbon atom.
- The functional group for an amide is as follows:



- In names for amides, the *-ic acid* of the common name or the *-oic acid* ending of the IUPAC for the corresponding carboxylic acid is replaced by *-amide*.

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8.8: Physical Properties of Amides

Learning Objectives

- Compare the boiling points of amides with alcohols of similar molar mass.
- Compare the solubilities in water of amides of five or fewer carbon atoms with the solubilities of comparable alkanes and alcohols in water.

With the exception of formamide ($HCONH_2$), which is a liquid, all simple amides are solids (Table 8.8.1). The lower members of the series are soluble in water, with borderline solubility occurring in those that have five or six carbon atoms. Like the esters, solutions of amides in water usually are neutral—neither acidic nor basic.

Table 8.8.1: Physical Constants of Some Unsubstituted Amides

Condensed Structure	Name	Melting Point (°C)	Boiling Point (°C)	Solubility in Water
$HCONH_2$	formamide	2	193	soluble
CH_3CONH_2	acetamide	82	222	soluble
$CH_3CH_2CONH_2$	propionamide	81	213	soluble
$CH_3CH_2CH_2CONH_2$	butyramide	115	216	soluble
$C_6H_5CONH_2$	benzamide	132	290	slightly soluble

The amides generally have high boiling points and melting points. These characteristics and their solubility in water result from the polar nature of the amide group and hydrogen bonding (Figure 8.8.1). Similar hydrogen bonding plays a critical role in determining the structure and properties of proteins, deoxyribonucleic acid (DNA), ribonucleic acid (RNA), and other giant molecules so important to life processes.

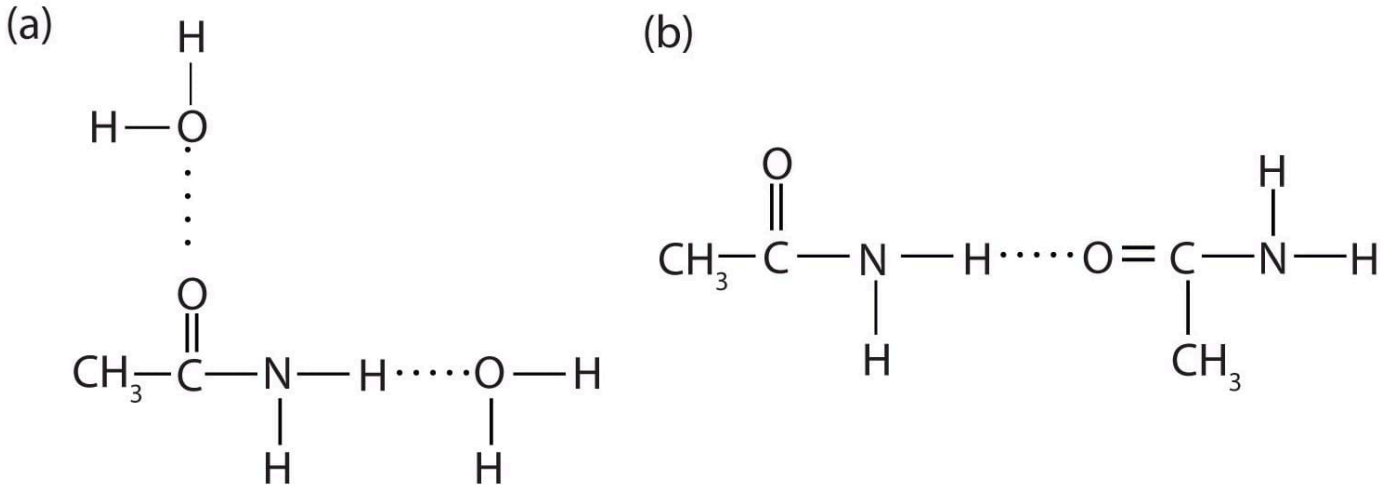


Figure 8.8.1: Hydrogen Bonding in Amides. Amide molecules can engage in hydrogen bonding with water molecules (a). Those amides with a hydrogen atom on the nitrogen atom can also engage in hydrogen bonding (b). Both hydrogen bonding networks extend in all directions.

Example 8.8.1

a. Which compound has the higher boiling point—pentanamide or propyl acetate? Explain.

b. Which compound is more soluble in water—propanamide or 1-pentene? Explain.

Solution

a. Pentanamide ($CH_3CH_2CH_2CH_2CONH_2$) has the higher boiling point because the nitrogen-hydrogen (N–H) and the carbon-oxygen double (C=O) bonds can engage in hydrogen bonding. Propyl acetate ($CH_3COOCH_2CH_2CH_3$) cannot engage in hydrogen bonding.
b. Propanamide ($CH_3CH_2CONH_2$) is more soluble in water because the N–H and C=O bonds can engage in hydrogen bonding with water. 1-pentene (CH_2=$CHCH_2CH_2CH_3$) cannot engage in hydrogen bonding with water

Exercise 8.8.1

a. Which compound has the higher boiling point—butyramide or dimethylacetamide [$CH_3CON(CH_3)_2$]? Explain.

b. Which compound is more soluble in water—acetamide (CH_3CONH_2) or 1-butene (CH_2=$CHCH_2CH_3$)? Explain.

Key Takeaways

- Most amides are solids at room temperature; the boiling points of amides are much higher than those of alcohols of similar molar mass.
- Amides of five or fewer carbon atoms are soluble in water.

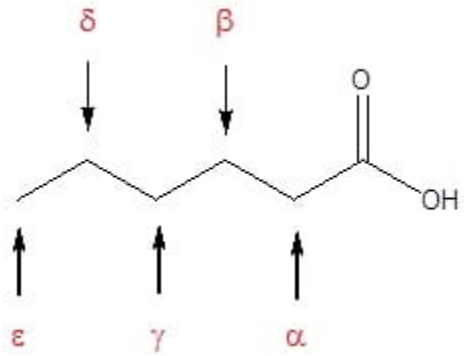
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8.9: Nomenclature of Carboxylic Acids

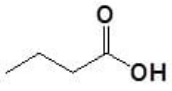
The IUPAC system of nomenclature assigns a characteristic suffix to these classes. The **–e** ending is removed from the name of the parent chain and is replaced **-anoic acid**. Since a carboxylic acid group must always lie at the end of a carbon chain, it is always is given the #1 location position in numbering and it is not necessary to include it in the name.

Many carboxylic acids are called by the common names. These names were chosen by chemists to usually describe a source of where the compound is found. In common names of aldehydes, carbon atoms near the carboxyl group are often designated by Greek letters. The atom adjacent to the carbonyl function is alpha, the next removed is beta and so on.

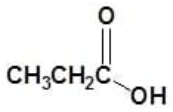


Formula	Common Name	Source	IUPAC Name	Melting Point	Boiling Point
HCO_2H	formic acid	ants (L. formica)	methanoic acid	8.4 °C	101 °C
CH_3CO_2H	acetic acid	vinegar (L. acetum)	ethanoic acid	16.6 °C	118 °C
$CH_3CH_2CO_2H$	propionic acid	milk (Gk. protus prion)	propanoic acid	-20.8 °C	141 °C
$CH_3(CH_2)_2CO_2H$	butyric acid	butter (L. butyrum)	butanoic acid	-5.5 °C	164 °C
$CH_3(CH_2)_3CO_2H$	valeric acid	valerian root	pentanoic acid	-34.5 °C	186 °C
$CH_3(CH_2)_4CO_2H$	caproic acid	goats (L. caper)	hexanoic acid	-4.0 °C	205 °C
$CH_3(CH_2)_5CO_2H$	enanthic acid	vines (Gk. oenanthe)	heptanoic acid	-7.5 °C	223 °C
$CH_3(CH_2)_6CO_2H$	caprylic acid	goats (L. caper)	octanoic acid	16.3 °C	239 °C
$CH_3(CH_2)_7CO_2H$	pelargonic acid	pelargonium (an herb)	nonanoic acid	12.0 °C	253 °C
$CH_3(CH_2)_8CO_2H$	capric acid	goats (L. caper)	decanoic acid	31.0 °C	219 °C

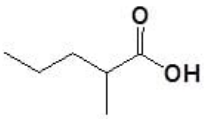
Example (Common Names Are in Red)



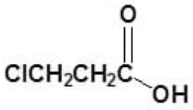
Butanoic acid
(Butyric Acid)



Propanoic acid
(Propionic Acid)



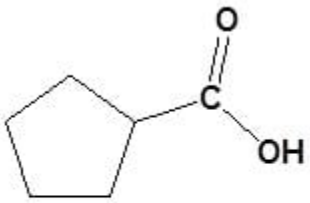
2-Methylpentanoic acid
(β-Methylvaleric acid)



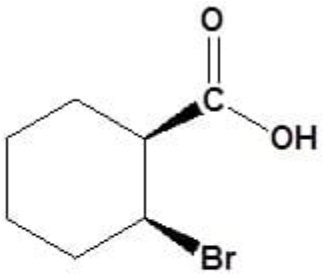
3-Chloropropanoic acid
(γ-Chloropropionic acid)

Naming carboxyl groups added to a ring

When a carboxyl group is added to a ring the suffix **-carboxylic acid** is added to the name of the cyclic compound. The ring carbon attached to the carboxyl group is given the #1 location number.



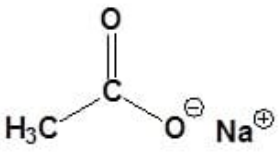
Cyclopentanecarboxylic acid



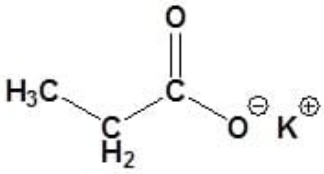
Cis-2-Bromocyclohexanecarboylic acid

Naming carboxylates

Salts of carboxylic acids are named by writing the name of the cation followed by the name of the acid with the **–ic acid** ending replaced by an **–ate** ending. This is true for both the IUPAC and Common nomenclature systems.



Sodium ethanoate
(Sodium Acetate)

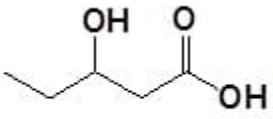


Potassium Propanoate
(Potassium propionate)

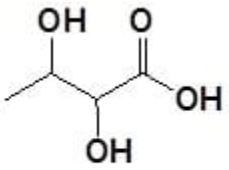
Naming carboxylic acids which contain other functional groups

Carboxylic acids are given the highest nomenclature priority by the IUPAC system. This means that the carboxyl group is given

the lowest possible location number and the appropriate nomenclature suffix is included. In the case of molecules containing carboxylic acid and alcohol functional groups the OH is named as a hydroxyl substituent. However, the **l** in hydroxyl is generally removed.

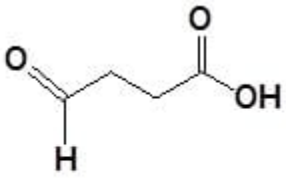


3-Hydroxypentanoic acid

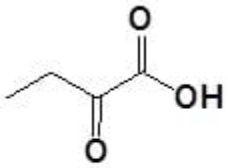


2,3-Dihydroxybutanoic acid

In the case of molecules containing a carboxylic acid and aldehydes and/or ketones functional groups the carbonyl is named as a "Oxo" substituent.

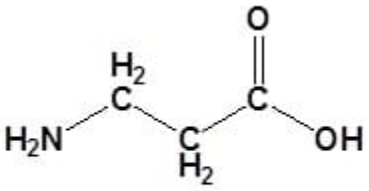


4-Oxobutanoic acid

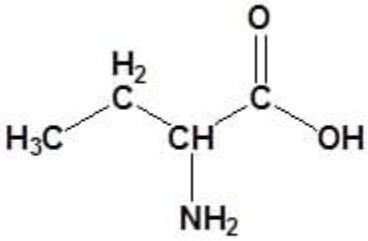


2-Oxobutanoic acid

In the case of molecules containing a carboxylic acid an amine functional group the amine is named as an "amino" substituent.



3-Aminopropanoic acid

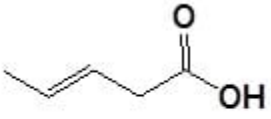


2-Aminobutanoic acid

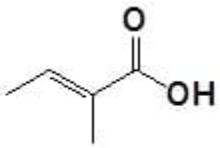
When carboxylic acids are included with an alkene the following order is followed:

(Location number of the alkene)-(Prefix name for the longest carbon chain minus the -ane ending)-(an –enoic acid ending to indicate the presence of an alkene and carboxylic acid)

Remember that the carboxylic acid has priority so it should get the lowest possible location number. Also, remember that cis/tran or E/Z nomenclature for the alkene needs to be included if necessary.



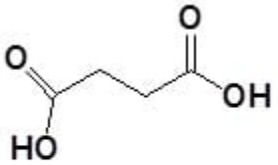
Trans-3-pentenoic acid



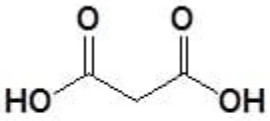
(E)-2-Methyl-2-butenoic acid

Naming dicarboxylic acids

For dicarboxylic acids the location numbers for both carboxyl groups are omitted because both functional groups are expected to occupy the ends of the parent chain. The ending **–dioic acid** is added to the end of the parent chain.



Butanedioic acid



Propanedioic acid

Contributors

Prof. Steven Farmer (Sonoma State University)

William Reusch, Professor Emeritus (Michigan State U.), Virtual Textbook of Organic Chemistry

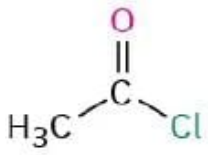
- Layne A. Morsch - University of Illinois Springfield

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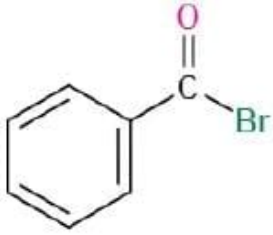
8.10: Naming Carboxylic Acid Derivatives

Acid Halides, RCOX

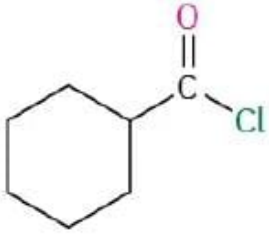
Acid halides are named by identifying first the acyl group and then the halide. As described in Section 20.1 and shown in Table 20.1, the acyl group name is derived from the carboxylic acid name by replacing the *-ic acid* or *-oic acid* ending with *-oyl,* or the *-carboxylic acid* ending with *-carbonyl*. To keep things interesting, however, IUPAC recognizes eight exceptions for which a *-yl* rather than an *-oyl* ending is used: formic (formyl), acetic (acetyl), propionic (propionyl), butyric (butyryl), oxalic (oxalyl), malonic (malonyl), succinic (succinyl), and glutaric (glutaryl).



Acetyl chloride



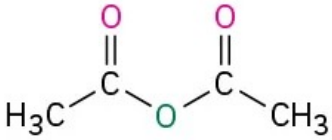
Benzoyl bromide



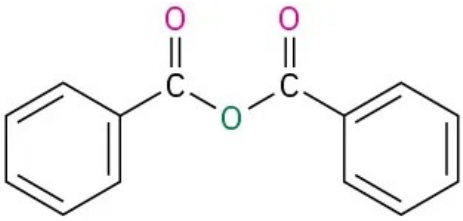
Cyclohexanecarbonyl chloride

Acid Anhydrides, RCO_2COR'

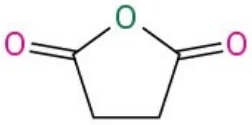
Symmetrical anhydrides of unsubstituted monocarboxylic acids and cyclic anhydrides of dicarboxylic acids are named by replacing the word *acid* with *anhydride*.



Acetic anhydride

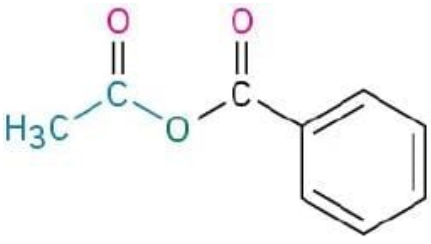


Benzoic anhydride



Succinic anhydride

Unsymmetrical anhydrides—those prepared from two different carboxylic acids—are named by listing the two acids alphabetically and then adding *anhydride*.

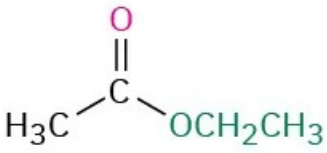


Acetic benzoic anhydride

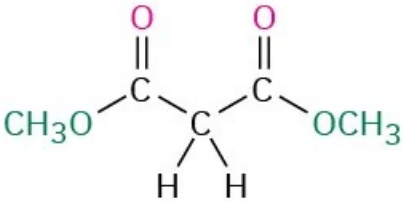
Esters, RCO_2R'

Esters are named by first identifying the alkyl group attached to oxygen and then the carboxylic acid, with the *-ic acid* ending

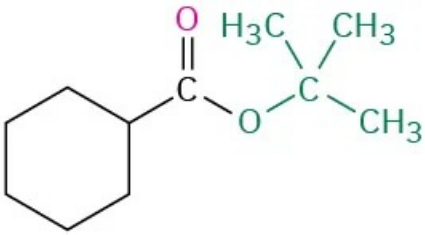
replaced by *-ate*.



Ethyl acetate



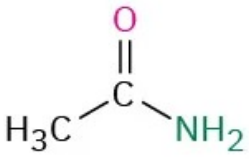
Dimethyl malonate



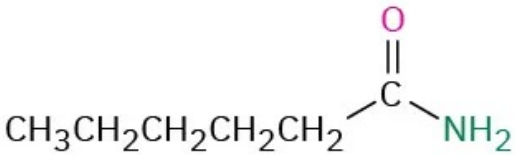
***tert*-Butyl cyclohexane-carboxylate**

Amides, $RCONH_2$

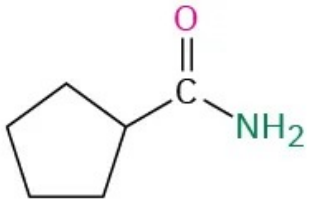
Amides with an unsubstituted $–NH_2$ group are named by replacing the *-oic acid* or *-ic acid* ending with *-amide,* or by replacing the *-carboxylic acid* ending with *-carboxamide*.



Acetamide

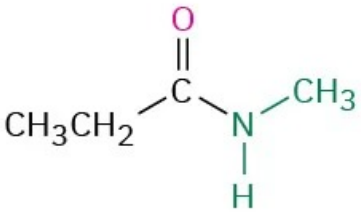


Hexanamide

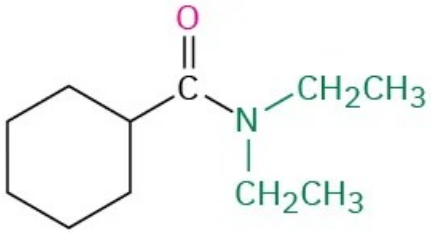


Cyclopentane-carboxamide

If the nitrogen atom is further substituted, the compound is named by first identifying the substituent groups and then the parent amide. The substituents are preceded by the letter *N* to identify them as being directly attached to nitrogen.



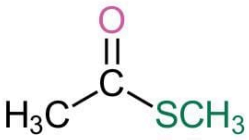
***N*-Methylpropanamide**



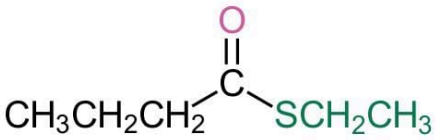
***N,N*-Diethylcyclohexanecarboxamide**

Thioesters, RCOSR′

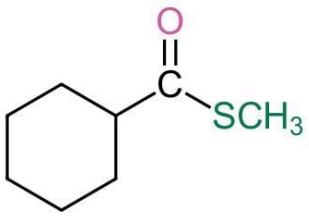
Thioesters are named like the corresponding esters. The name begins with the alkyl group attached to the sulfur preceded with the letter S. If the related ester has a common name, the prefix *thio-* is added to the name of the carboxylate: acetate becomes thioacetate, for instance. If the related ester has a systematic name, the *-oate* or *-carboxylate* ending is replaced by *-thioate* or *-carbothioate:* butanoate becomes butanethioate and cyclohexanecarboxylate becomes cyclohexanecarbothioate, for instance.



S-Methyl thioacetate



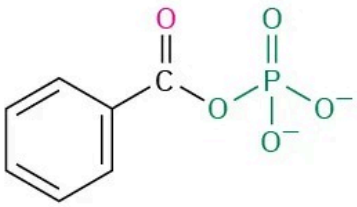
S-Ethyl butanethioate



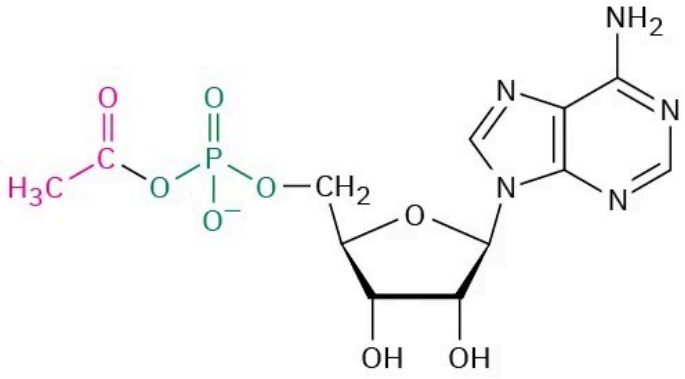
S-Methyl cyclohexane-carbothioate

Acyl Phosphates, $RCO_2PO_3^{2-}$ and $RCO_2PO_3R'^-$

Acyl phosphates are named by citing the acyl group and adding the word *phosphate*. If an alkyl group is attached to one of the phosphate oxygens, it is identified after the name of the acyl group. In biological chemistry, acyl adenosyl phosphates are particularly common.



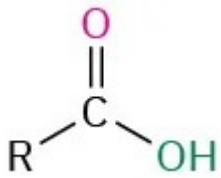
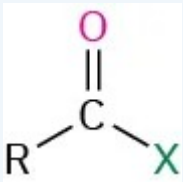
Benzoyl phosphate

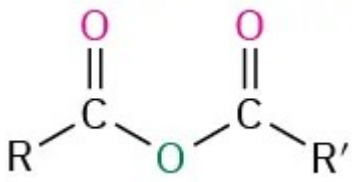
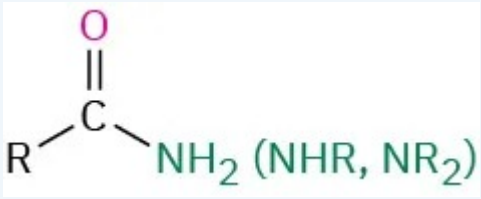
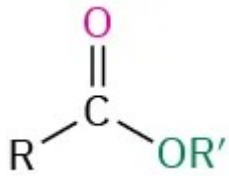
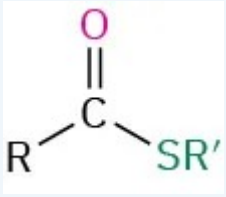
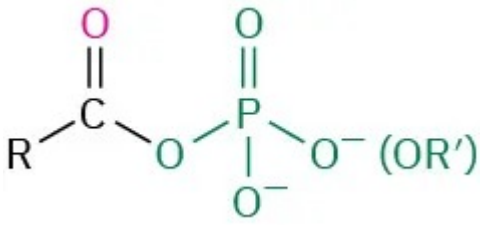


Acetyl adenosyl phosphate

A summary of nomenclature rules for carboxylic acid derivatives is given in Table 8.10.1.

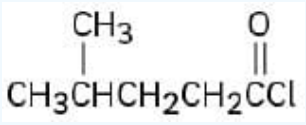
Table 8.10.1: Nomenclature of Carboxylic Acid Derivatives

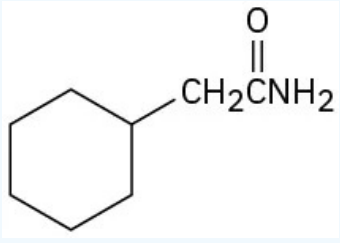
Functional group	Structure	Name ending
Carboxylic acid		*-ic acid (-carboxylic acid)*
Acid halide		*-oyl halide (-carbonyl halide)*

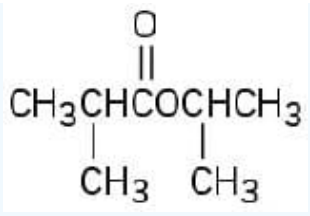
Functional group	Structure	Name ending
Acid anhydride		*anhydride*
Amide		*-amide (-carboxamide)*
Ester		*-oate (-carboxylate)*
Thioester		*-thioate (-carbothioate)*
Acyl phosphate		*-oyl phosphate*

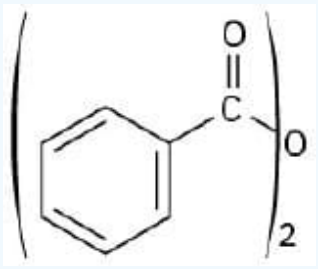
Exercise 8.10.1

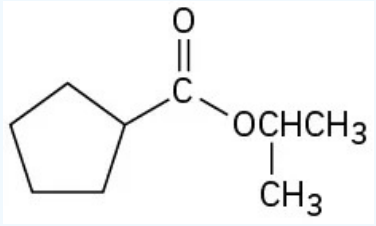
Give IUPAC names for the following substances:

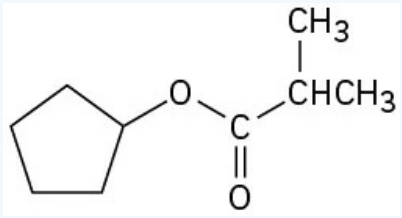
a. 

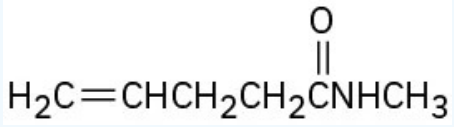
b. 

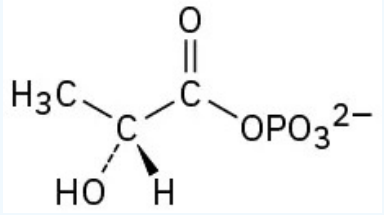
c. 

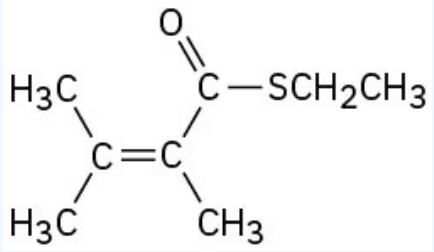
d. 

e. 

f. 

g. 

h. 

i. 

Answer available at the end of this section.

Exercise 8.10.2

Draw structures corresponding to the following names:

a. Phenyl benzoate
b. N-Ethyl-N-methylbutanamide
c. 2,4-Dimethylpentanoyl chloride
d. Methyl 1-methylcyclohexanecarboxylate
e. Ethyl 3-oxopentanoate
f. Methyl p-bromobenzenethioate
g. Formic propanoic anhydride
h. cis-2-Methylcyclopentanecarbonyl bromide

Answer available at the end of this section.

Answers

Exercise 8.10.1

a. 4-Methylpentanoyl chloride
b. Cyclohexylacetamide
c. Isopropyl 2-methylpropanoate
d. Benzoic anhydride
e. Isopropyl cyclopentanecarboxylate
f. Cyclopentyl 2-methylpropanoate
g. N-Methyl-4-pentenamide
h. (R)-2-Hydroxypropanoyl phosphate
i. Ethyl 2,3-dimethyl-2-butenethioate

Exercise 8.10.2

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8.11: Chemistry of Esters

Objectives

After completing this section, you should be able to

1. discuss the wide occurrence of esters in nature, and their important commercial uses, giving one example of an ester linkage in nature, and one example of a commercially important ester.
2. write an equation to describe the hydrolysis of an ester under acidic or basic conditions.
3. identify the products formed from the hydrolysis of an given ester.
4. identify the reagents that can be used to bring about ester hydrolysis.
5. identify the structure of an unknown ester, given the products of its hydrolysis.
6. write the mechanism of alkaline ester hydrolysis.
7. write the mechanism of acidic ester hydrolysis.
8. write an equation to describe the reduction of an ester with lithium aluminum hydride.
9. identify the product formed from the reduction of a given ester (or lactone) with lithium aluminum hydride.
10. identify the ester, the reagents, or both, that should be used to prepare a given primary alcohol.
11. write a detailed mechanism for the reduction of an ester by lithium aluminum hydride.
12. identify diisobutylaluminum hydride as a reagent for reducing an ester to an aldehyde, and write an equation for such a reaction.
13. write an equation to describe the reaction of an ester with a Grignard reagent.
14. identify the product formed from the reaction of a given ester with a given Grignard reagent.
15. identify the ester, the Grignard reagent, or both, needed to prepare a given tertiary alcohol.
16. write a detailed mechanism for the reaction of an ester with a Grignard reagent.

Key Terms

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

- lactone
- saponification

Study Notes

Many esters have characteristic aromas and flavours. Some examples are listed below.

Basic structure:

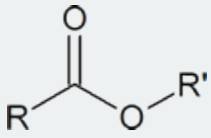
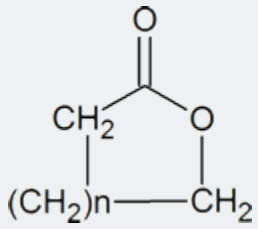


Table 21.1 Structures and characteristic odours of selected esters

IUPAC name	R	R′	Aroma
octyl ethanoate	CH_3	$CH_3(CH_2)_6CH_2$	orange
propyl ethanoate	CH_3	$CH_3CH_2\ CH_2$	pear
2-methylpropyl propanoate	CH_3CH_2	$(CH_3)_2CHCH_2$	rum

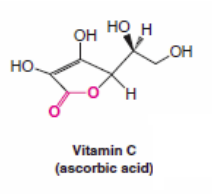
IUPAC name	R	R′	Aroma
methyl butanoate	$CH_3CH_2CH_2$	CH_3	apple
ethyl butanoate	$CH_3CH_2CH_2$	CH_3CH_2	pineapple

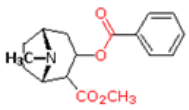
A “lactone” is a cyclic ester and has the general structure

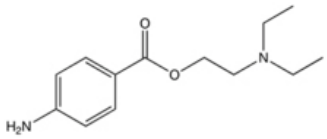


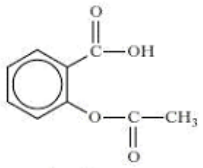
By recognizing that the steps in the acidic hydrolysis of an ester are exactly the same as those in a Fischer esterification (but in the reverse order!), you can again minimize the amount of memorization that you must undertake. The details of both mechanisms can be deduced from the knowledge that both reactions are acid-catalyzed nucleophilic acyl substitutions.

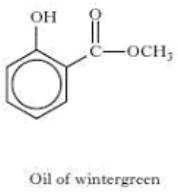
Esters are present in a many biologically important molecules, which have a wide range of effects including fats, waxes, Vitamin C, Cocaine, Novacaine, oil of wintergreen, and aspirin.

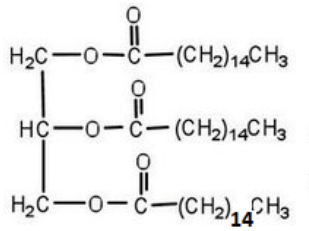




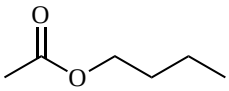




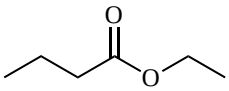




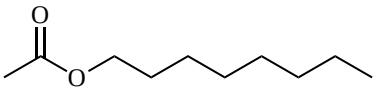
Esters compounds are often the source of the pleasant aromas of many fruits.



apple
butyl acetate



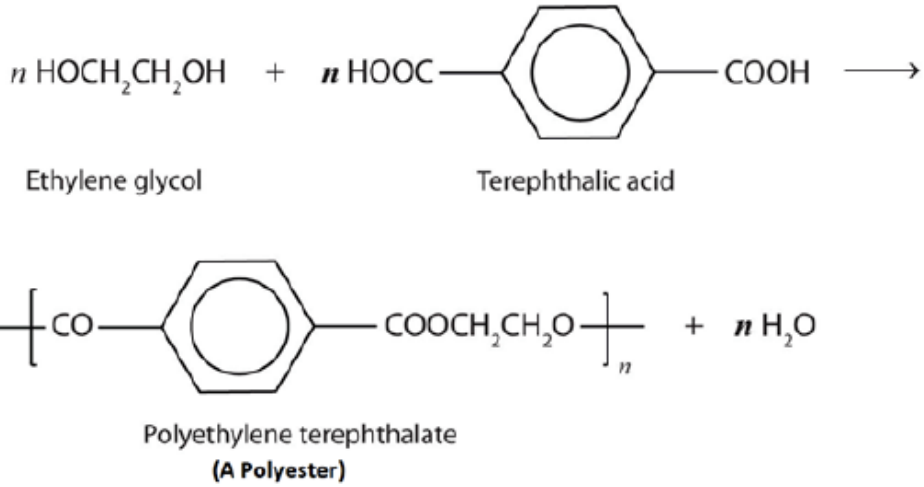
pineapple
ethyl butanoate



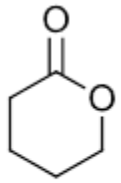
orange
octyl acetate

Esters are also present in a number of important commercial and synthetic application. For example, polyester molecules make excellent fibers and are used in many fabrics. A knitted polyester tube, which is biologically inert, can be used in surgery to repair or replace diseased sections of blood vessels. The most important polyester, polyethylene terephthalate (PET), is made from terephthalic acid and ethylene glycol monomers. PET is used to make bottles for water and other beverages. It is also formed into

films called Mylar which is used in balloons. Synthetic arteries can be made from PET, polytetrafluoroethylene (PTFE), and other polymers.



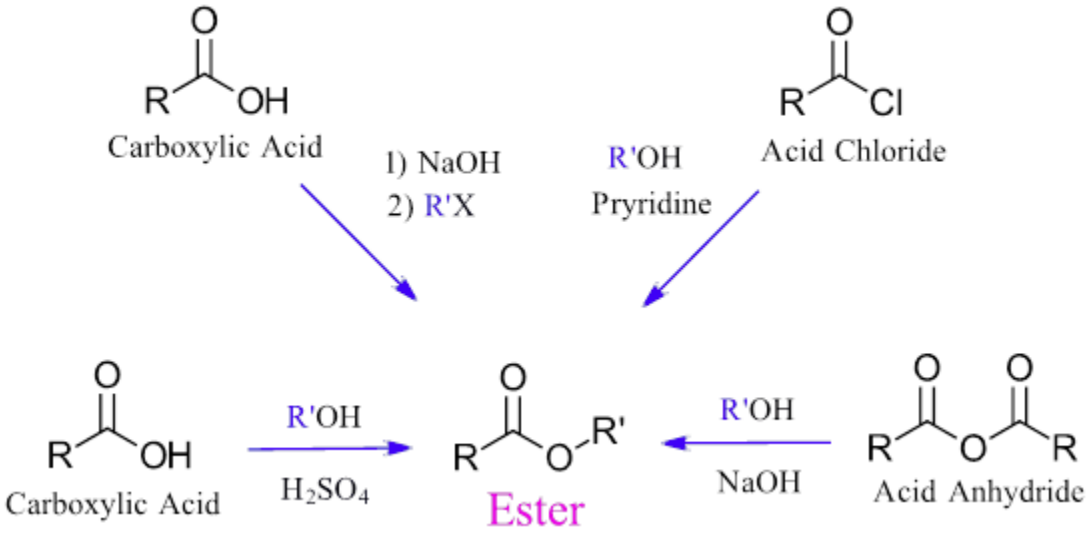
Lactones, cyclic esters, have similar reactivity as acyclic esters.



Lactone
(Cyclic Ester)

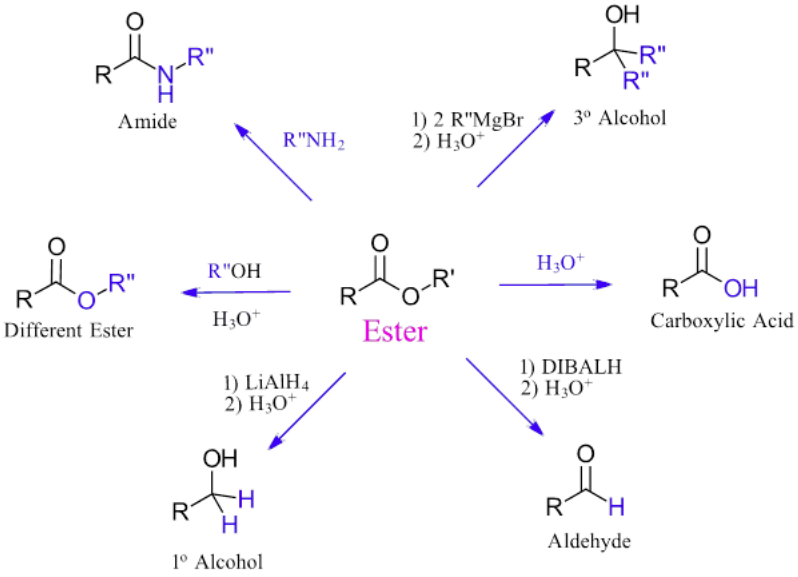
Preparation of Esters

The most versatile method for the preparations of esters is the nucleophilic acyl substitution of of an acid chloride with an alcohol. Acid ahydrides and carboxylic acids can also react with alcohols to form esters but both reactions are limited to formation of simple esters. Esters can also be formed by deprotonating a carboxylic acid to form a carboxylate and then reacting it with a primary alkyl halide using an S_N2 reaction.



Reactions of Esters

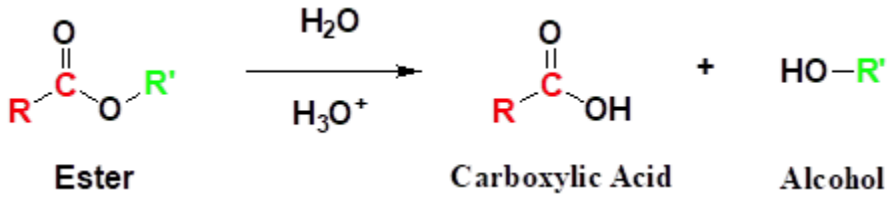
Esters are one of the more useful functional groups. Their low reactivity makes the easy to work with and they are stable enough to be used as a solvent in organic reactions (ex. ethyl acetate). Esters are still reactive enough to undergo hydrolysis to form carboxylic acids, alcoholysis, to form different esters, and aminolysis to form amides. Also, they can react with Grignard reagents to form 3^{o} alcohols and hydride reagents to form 1^{o} alcohols or aldehydes.



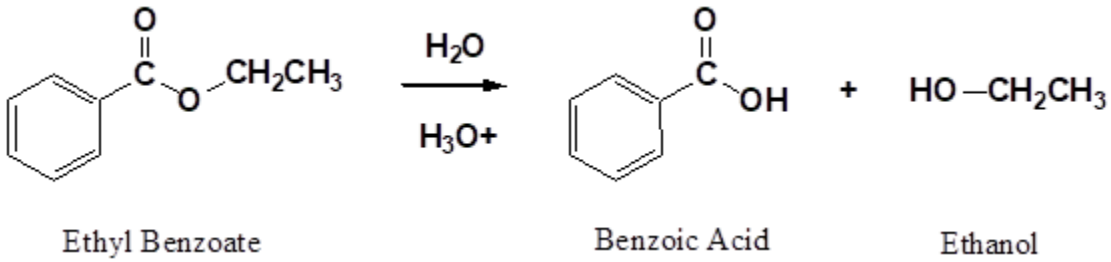
Conversion of Esters to Carboxylic Acids: Hydrolysis

Esters can be cleaved back into a carboxylic acid and an alcohol through reaction with water and a catalytic amount of strong acid. This reaction represents the reverse of the acid catalyzed esterification of a carboxylic acid and an alcohol discussed in Section 21.3. Both the ester formation and cleavage reactions are part of an equilibrium which can be manipulated using Le Chatelier's principle. For ester hydrolysis, the equilibrium is shifted toward carboxylic acid formation by using a large excess of water in the reaction.

General Reaction



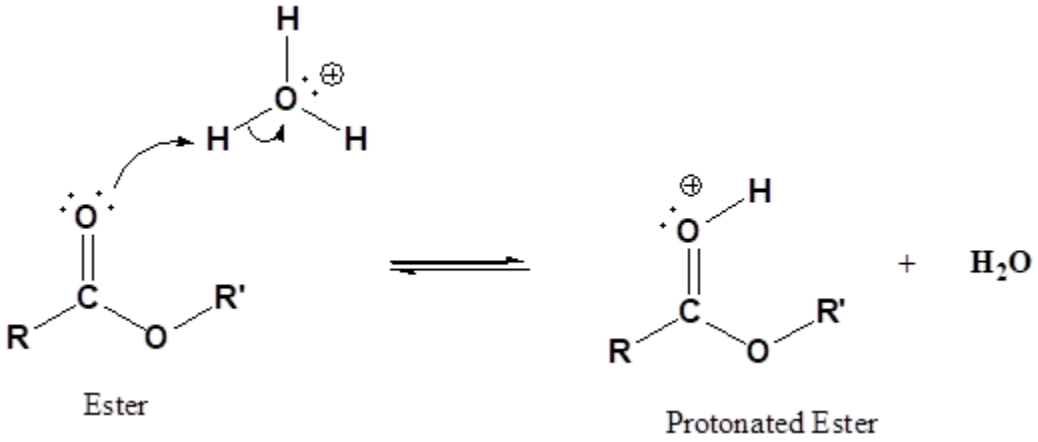
Example



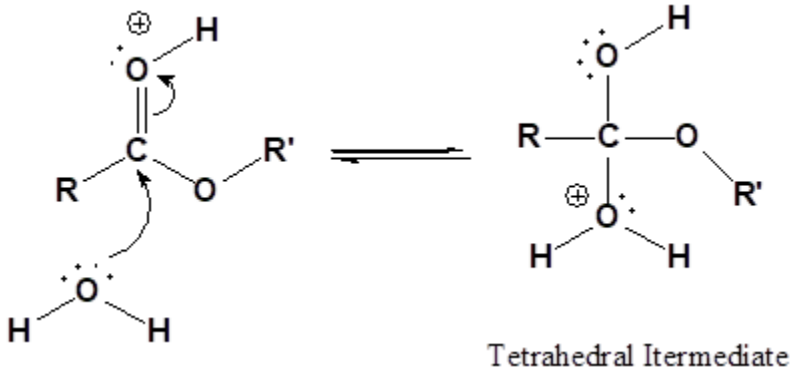
Mechanism

Acid catalysis is required during ester hydrolysis due to water being a weak nucleophile. Protonation of the ester carbonyl increases the partial positive charge on the carbonyl carbon increasing its electrophilicity. After protonation, water adds to the carbonyl carbon causing the formation of a tetrahedral alkoxide intermediate. Then a proton transfers to the –OR group, increasing its ability to act as a leaving group. Reforming the carbonyl double bond causes the elimination of an alcohol (HOR) as a leaving group, creating a protonated carboxylic acid. In the last step of the mechanism, water acts as a base, removing a hydrogen, to form a carboxylic acid and regenerating the acid catalyst.

1) Protonation of the carbonyl



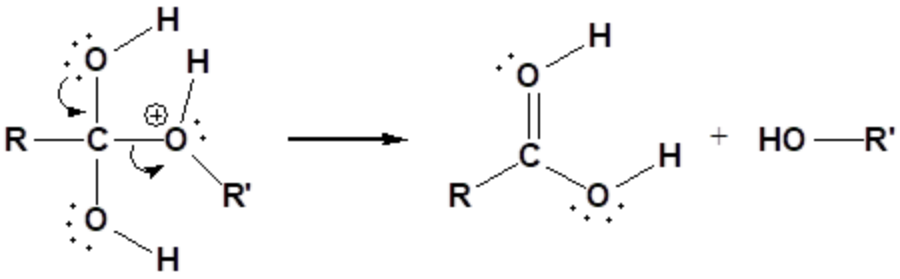
2) Nucleophilic attack by water



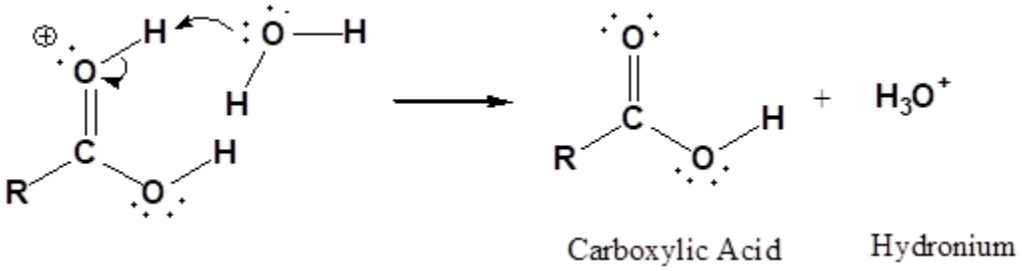
3) Proton transfer



4) Leaving group removal

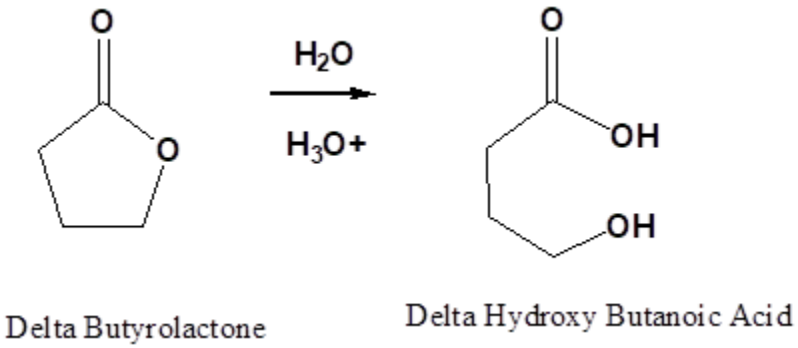


5) Deprotonation



Hydrolysis of Lactones

Lactones (Cyclic esters) undergo typical reactions of esters including hydrolysis. Hydrolysis of the lactone under acidic conditions creates a hydroxyacid.

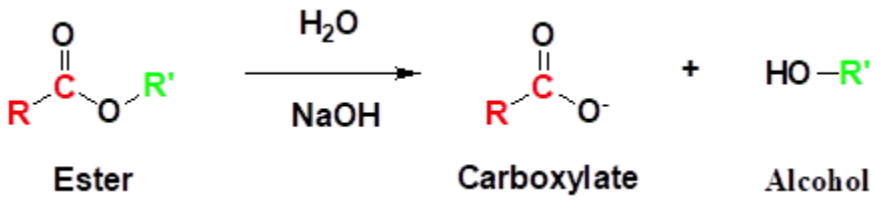


Conversion of Esters to Carboxylic Acids: Saponification

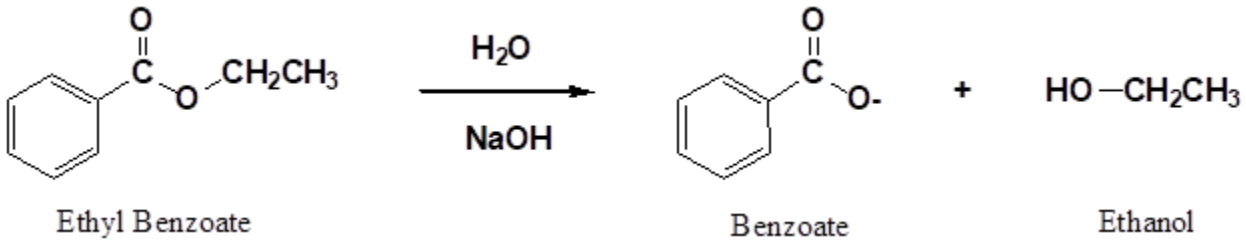
Esters can also be cleaved into a carboxylate and an alcohol through reaction with water and a base. The reaction is commonly called a saponification from the Latin sapo which means soap. This name comes from the fact that soap used to me made by the ester hydrolysis of fats.

Saponification reaction utilize a better nucleophile (hydroxide) and are typically faster than an acid catalyzed hydrolysis. The carboxylation ions produced by saponification are negatively charged and very unreactive toward further nucleophilic substitution which makes the reaction irreversible.

General Reaction



Example

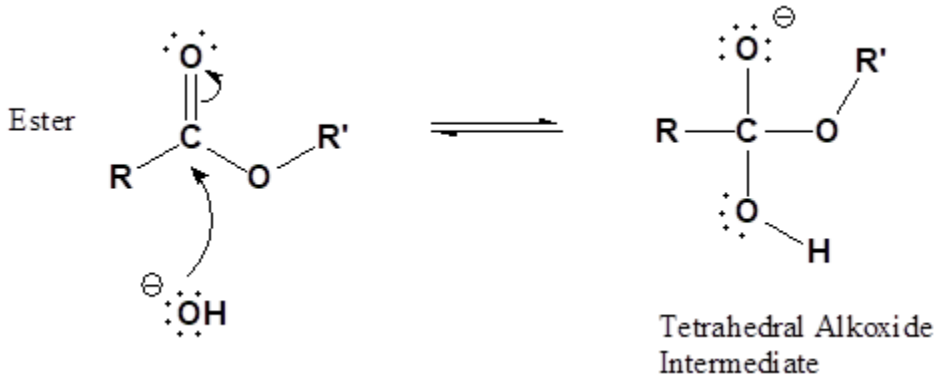


Mechanism

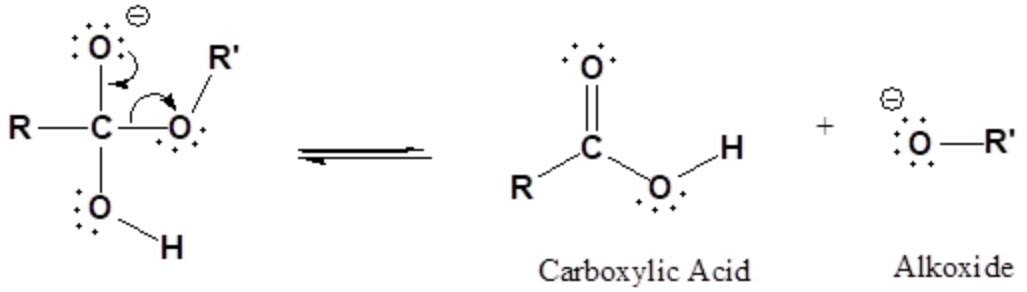
The base-promoted hydrolysis of an ester follows the typical nucleophilic acyl substitution mechanism. A full equivalent of hydroxide anion is used, so the reaction is called base-promoted and not base catalyzed. The mechanism of ester saponification begins with the nucleophilic addition of a hydroxide ion at the carbonyl carbon to give a tetrahedral alkoxide intermediate. The carbonyl bond is reformed along with the elimination of an alkoxide (-OR) leaving group yielding a carboxylic acid. The alkoxide base deprotonates the carboxylic acid to for a carboxylate salt and an alcohol as products.

The last deprotonation step essentially removes the carboxylic acid from the equilibrium which drives the saponification towards completion. Because the carboxylic acid is no longer part of the equilibrium the reaction is effectively irreversible.

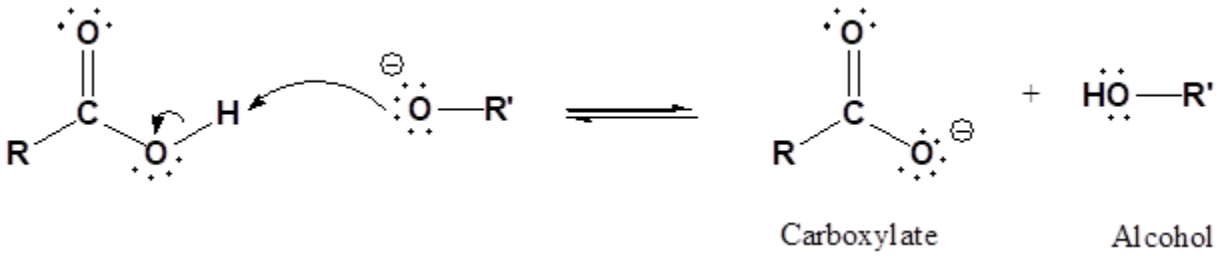
1) Nucleophilic attack by hydroxide



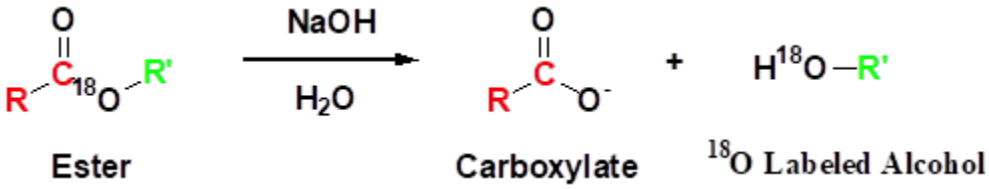
2) Leaving group removal



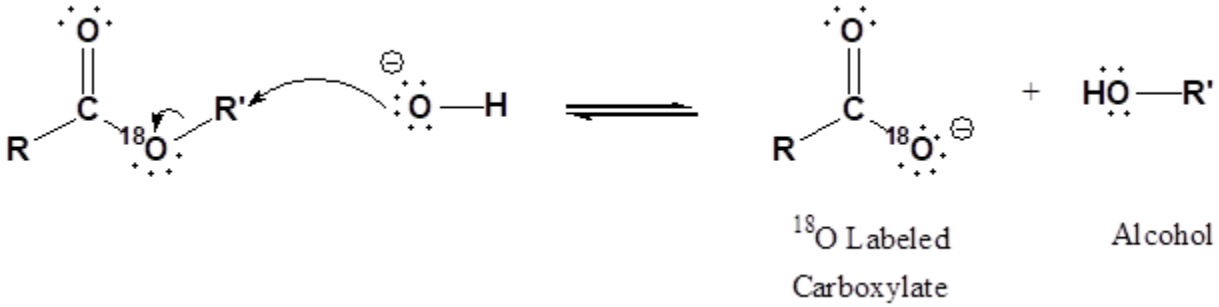
3) Deprotonation



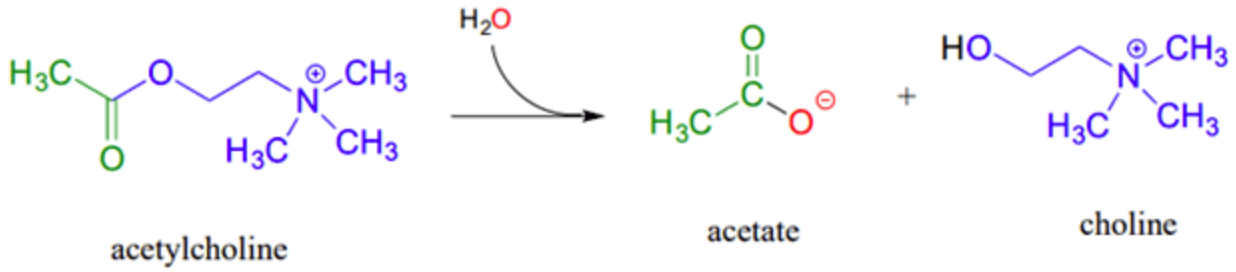
This mechanism is supported by experiments performed using isotopically labeled esters. When the ether-type oxygen of the ester was labeled with ^{18}O, the labeled oxygen showed up in the alcohol product after hydrolysis.



An alternative mechanism would be if the hydroxide participated in an S_N2 reaction to create the carboxylate product. If this were to happen the alcohol reaction product would not contain the labeled oxygen.



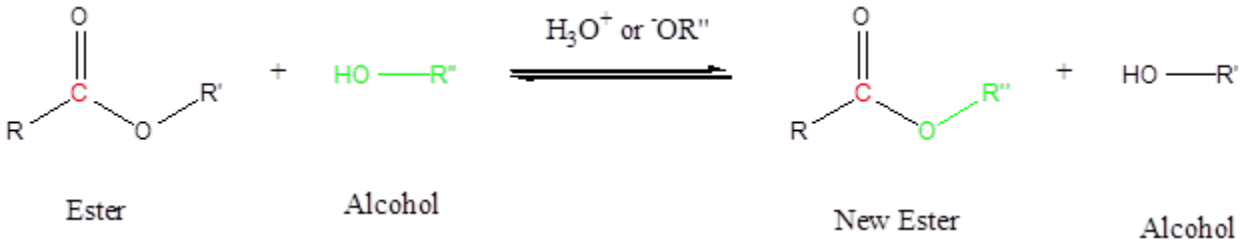
Ester saponification in biological systems, called hydrolytic acyl substitution reactions, are common. In particular, acetylcholinesterase, an enzyme present in the synapse, catalyzes hydrolysis of the ester group in acetylcholine which is a neurotransmitter that triggers muscle contraction. Like many other hydrolytic enzymes, the acetylcholinesterase reaction proceeds in two phases: first, a covalent enzyme-substrate intermediate is formed when the acyl group of acetylcholine is transferred to an active-site serine on the enzyme (a transesterification reaction). A water nucleophile then attacks this ester, driving off acetate and completing the hydrolysis



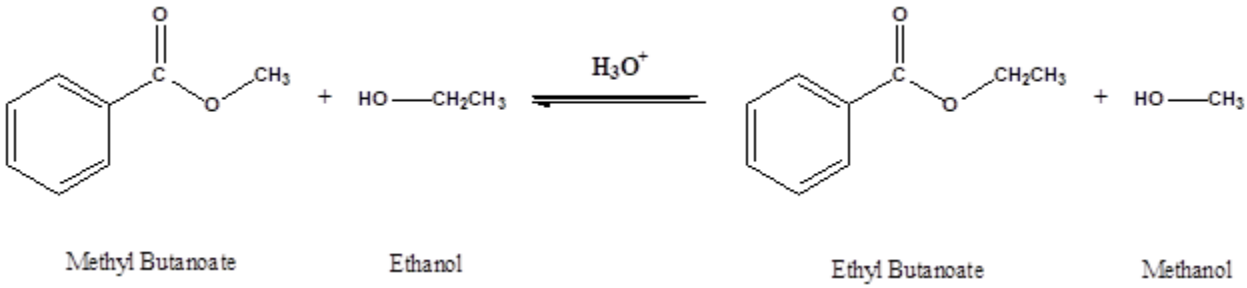
Conversion of Esters to Different Esters: Transesterification

Transesterification is a reaction where an ester is converted to a different ester through reaction with an alcohol. Because there is typically very little difference in stability between both esters, the equilibrium constant of this reaction is usually near one. Using a large excess of the reactant alcohol or removing the alcohol side-product can push the reaction equilibrium towards the products by Le Chatelier's principal. Transesterifications also shows that great care should be taken when an ester containing compound is used in a reaction involving an alcohol.

General Reaction



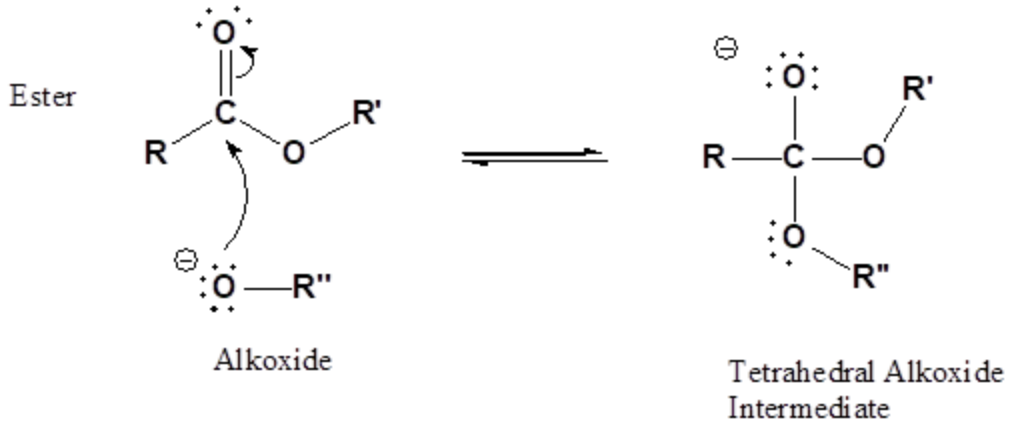
Example



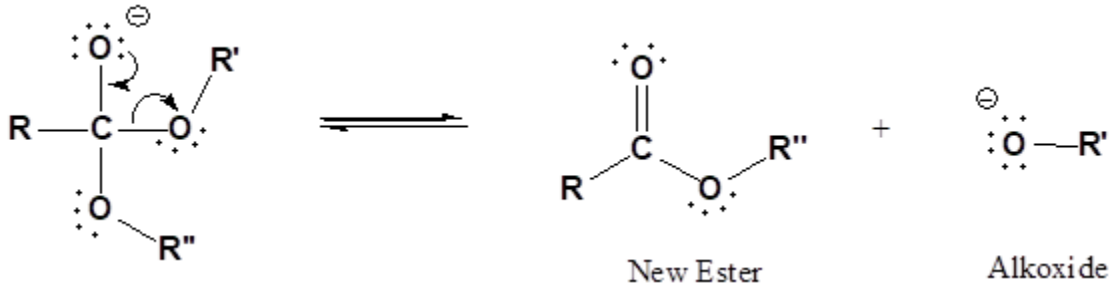
Mechanism in Basic Conditions

The reaction follows the basic mechanism of a nucleophilic acyl substitution. The alkoxide leaving group of the ester is replace by an incoming alkoxide nucleophile creating a different ester.

1) Nucleophilic attack by an alkoxide



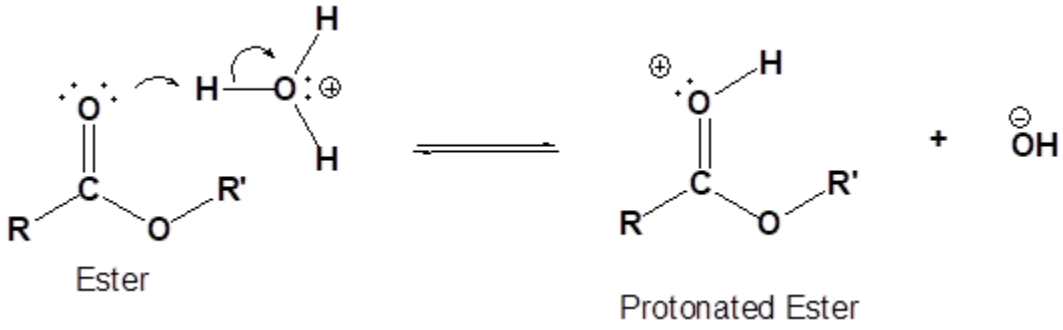
2) Leaving group removal



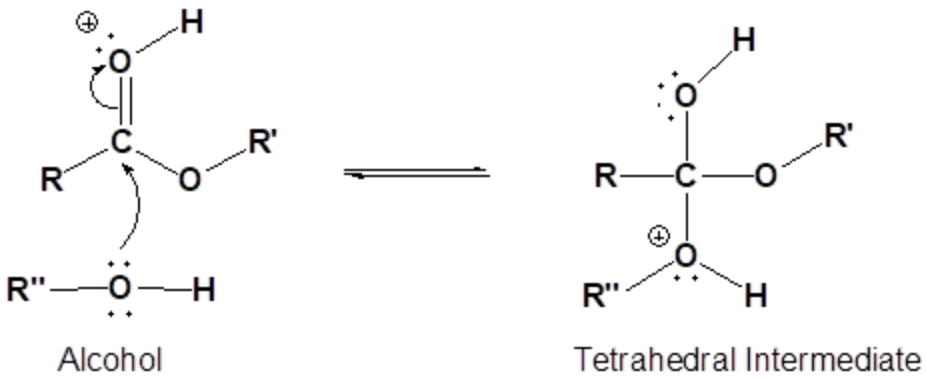
Mechanism in Acidic Conditions

Protonation allows the alcohol reactant to add to the ester carbonyl. Proton transfer to the ester's alkoxy group increases it ability to act as a leaving group. Reforming the C=O carbonyl bond removes the leaving group and subsequent deprotonation by water forms the ester product.

1) Protonation of the carbonyl



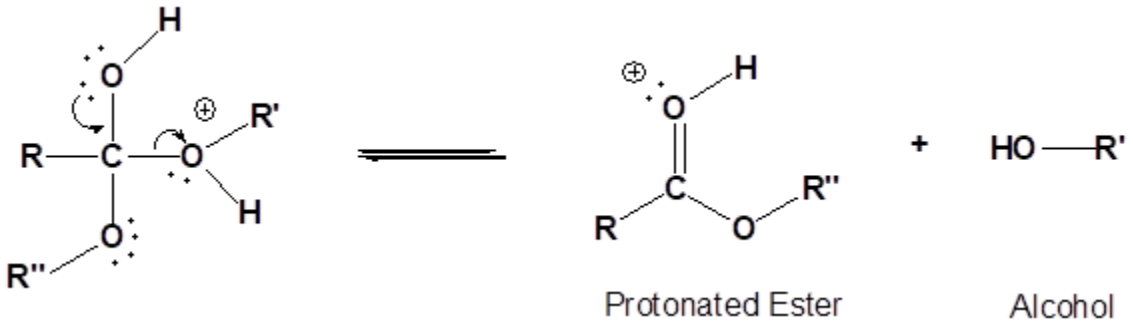
2) Nucleophilic attack on the carbonyl



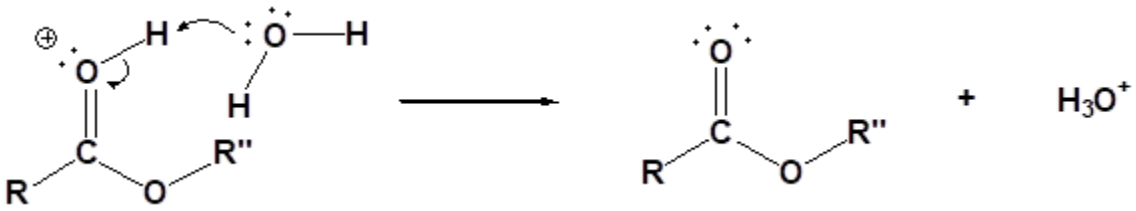
3) Proton transfer



4) Removal of the leaving group

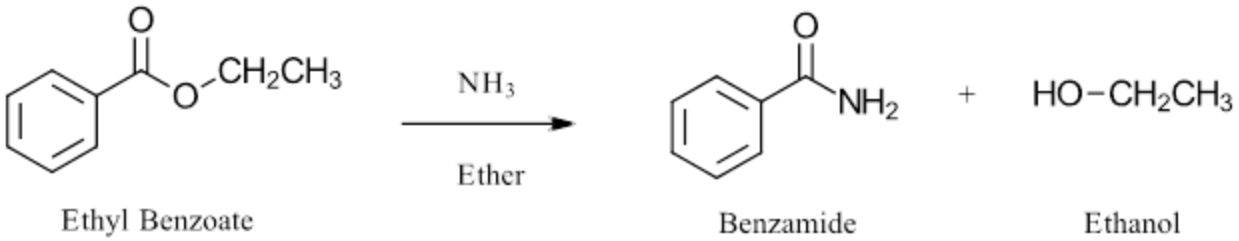


5) Deprotonation



Conversion of Ester to Amides: Aminolysis

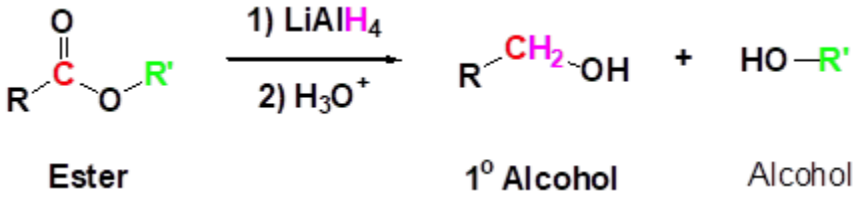
It is possible to convert esters to amides through direct reaction with ammonia or amines. However, these reactions are not commonly used because the formation of an amide using an acid chloride is a much simpler reaction.



Conversion of Esters to 1° Alcohols: Hydride Reduction

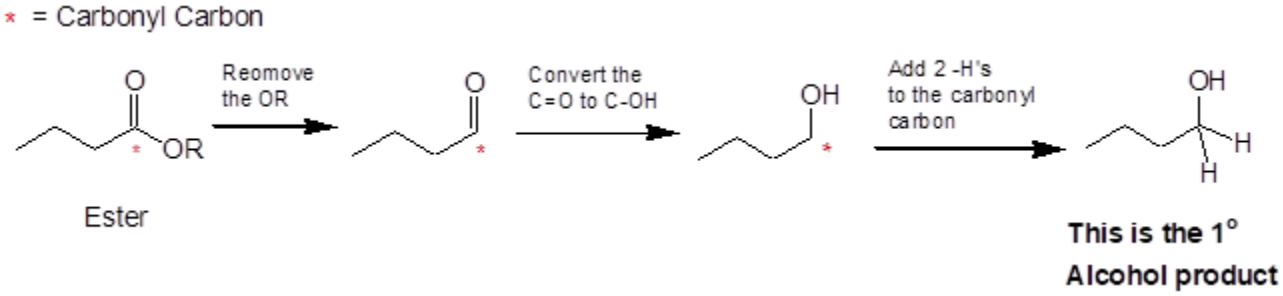
Esters can undergo hydride reduction with $LiAlH_4$ to form two alcohols. The alcohol derived from the acyl group of the ester will be 1° and is typically considered the main product of the reaction. The other alcohol is derived from the ester's alkoxy group and is typically considered a side-product of the reaction. Note! Sodium borohydride ($NaBH_4$) is not a reactive enough hydride agent to reduce esters or carboxylic acids. In fact, $NaBH_4$ can selectively reduce aldehydes and ketones in the presence of ester functional groups.

General Reaction

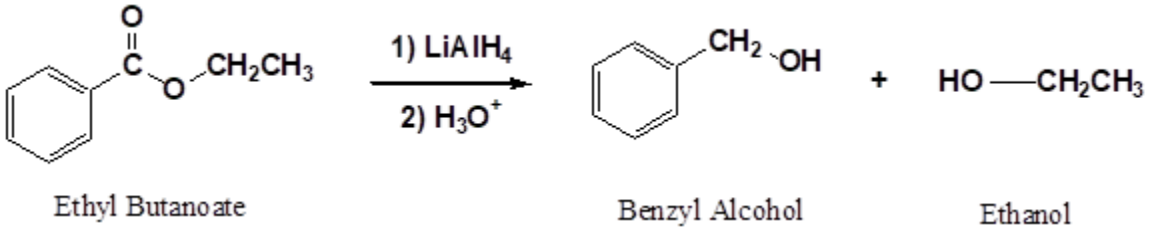


Predicting the Products of a Hydride Reduction

There are three major changes in bonding during this reaction: 1) The –OR leaving group is removed from the ester. 2) The C=O carbonyl bond is converted to a C-O-H, an alcohol. 3) Two C-H bonds are formed as two of the hydride nucleophiles are added to the original carbonyl carbon of the ester.



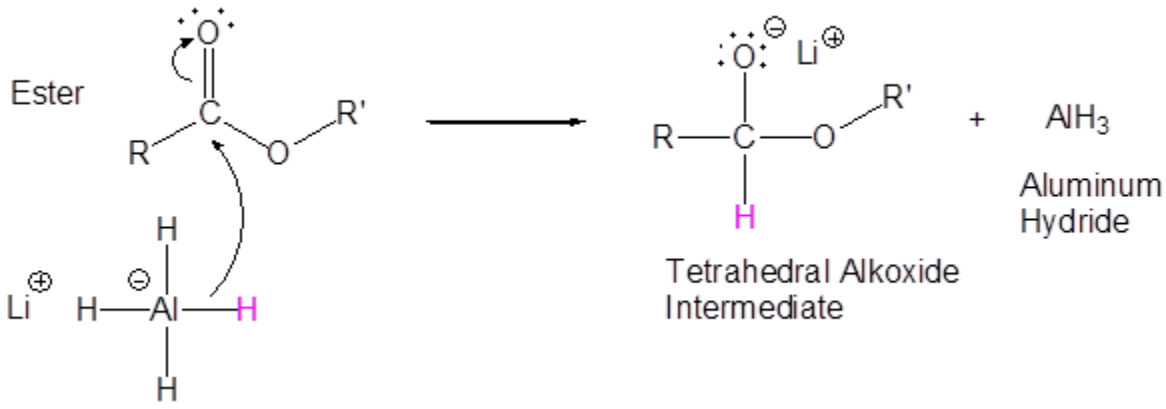
Example



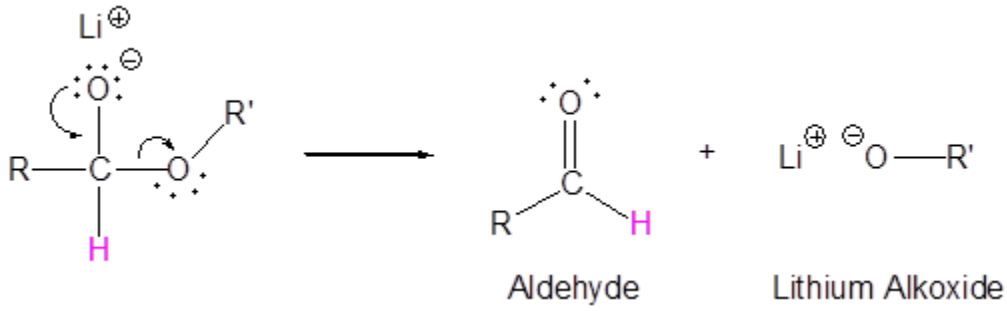
Mechanism

The mechanisms for the hydride reduction of esters is analogous to the hydride reduction of carboxylic acids. Nucleophilic acyl substitution replaces the –OR leaving group in ester with a hydride nucleophile to form an aldehyde intermediate. Because aldehydes are more reactive than esters, they rapidly undergo a second nucleophilic hydride addition to form a tetrahedral alkoxide intermediate. An acid work-up protonates the alkoxide to create a 1^{o} alcohol.

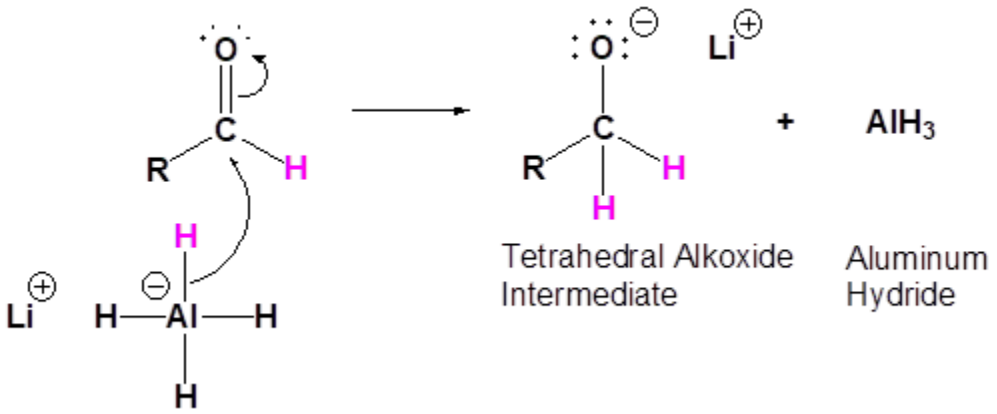
1) Nucleophilic attack by the hydride



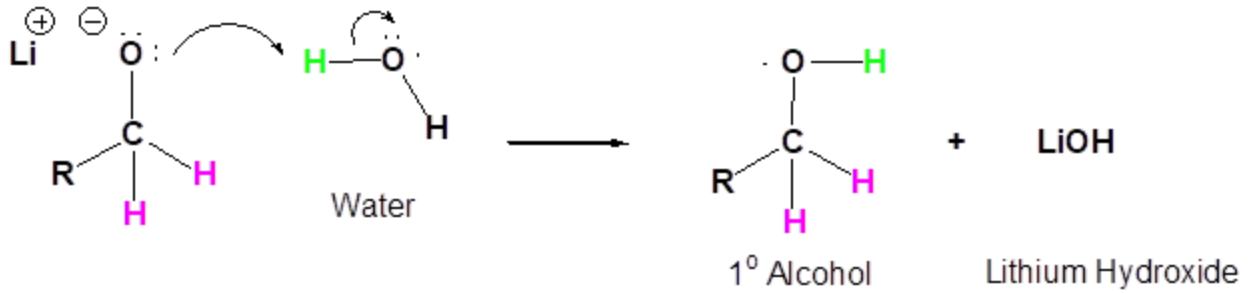
2) Leaving Group Removal



3) Nucleopilic attack by the hydride anion



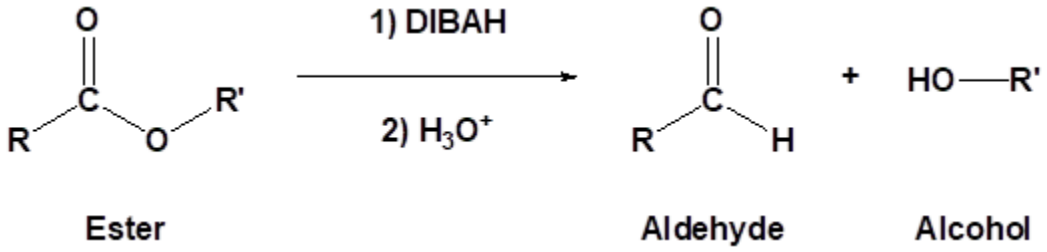
4) The alkoxide is protonated



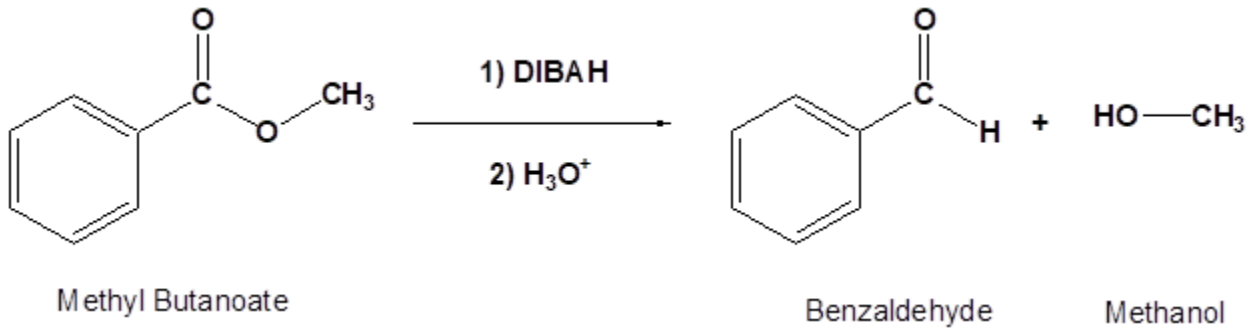
Conversion of Esters to Aldehydes: Hydride Reduction

Much like acid chlorides, esters can be converted to aldehydes using the weaker reducing reagent diisobutylaluminum hydride (DIBALH). As shown above, an aldehyde intermediate is produced after an ester undergoes nucleophilic acyl substitution with a hydride. When DIBALH is used as the hydride source, the aldehyde does not react further and is isolated as the product of the reaction. The reaction is usually carried out at -78 ^{o}C to help isolate the aldehyde product.

General Reaction



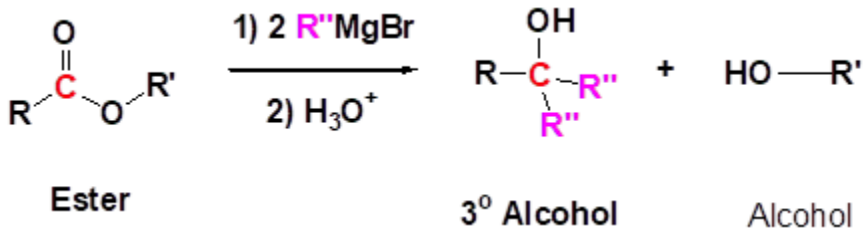
Example



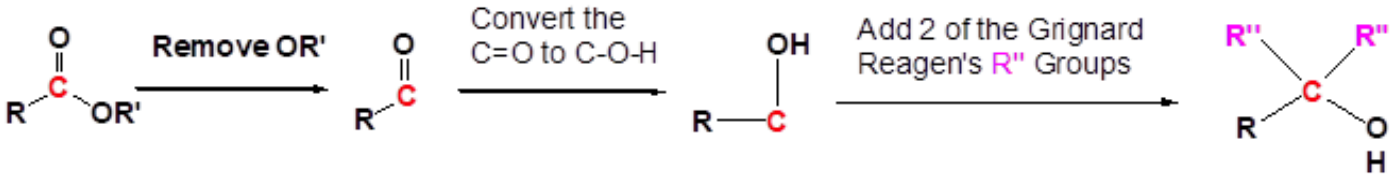
Conversion of Esters to 3^{o} Alcohols: Grignard Reagents

Addition of Grignard reagents converts esters to two alcohols, one 3^{o} alcohols (main product) and one 1^{o} alcohol (considered a side product). The Grignard reagent adds to the ester twice, once during a nucleophilic acyl substitution to form a ketone intermediate then again during a nucleophilic addition to form the 3^{o} alcohol product. Overall, during this reaction two C-C bonds are formed on the ester's original carbonyl carbon.

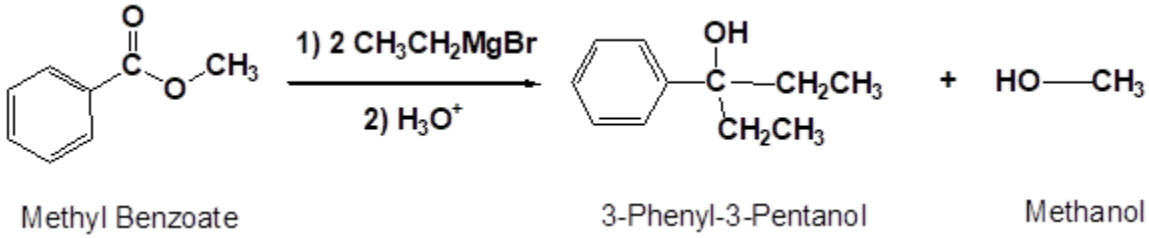
General Reaction



Predicting the Products of a Grignard Reaction



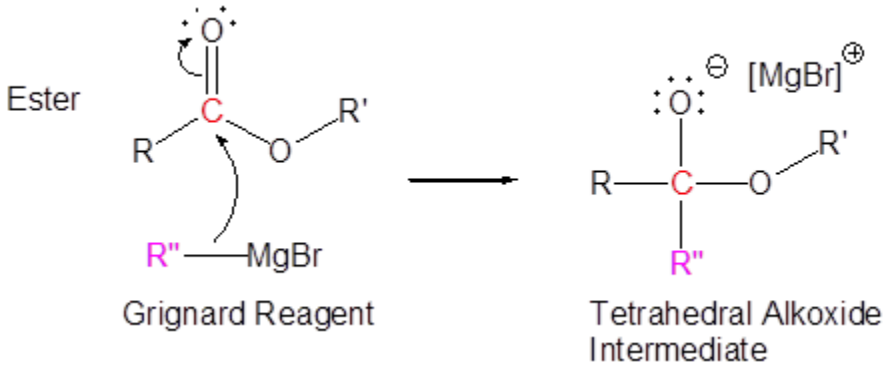
Example



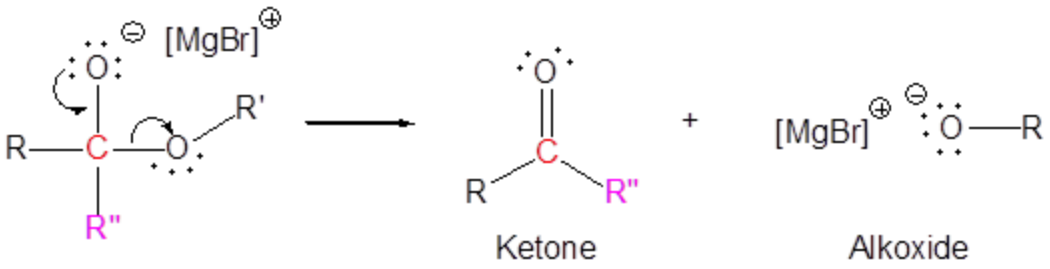
Mechanism

In the first two steps of the mechanism, the OR leaving group from the ester is replaced by the R group from the Grignard reagent through a nucleophilic acyl substitution. This forms a ketone intermediate which is not isolated because ketones, which are more reactive than esters, rapidly undergo nucleophilic addition with a second equivalent of the Grignard reagent to form an alkoxide intermediate. An acid work-up protonates the alkoxide to form the 3° alcohol product.

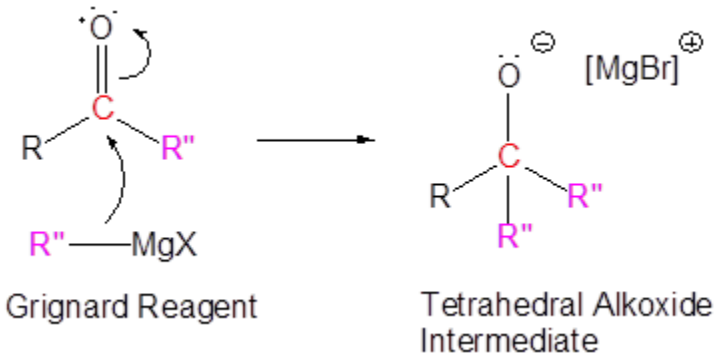
1) Nucleophilic Attack



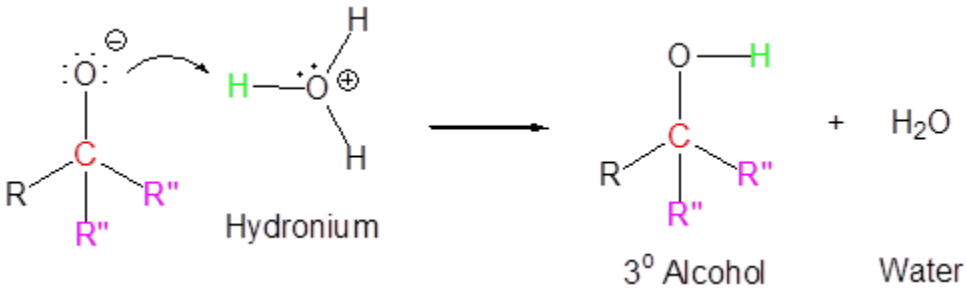
2) Leaving group removal



3) Nucleophilic attack

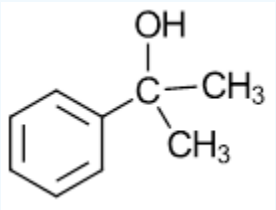


4) Protonation



Example 8.11.1

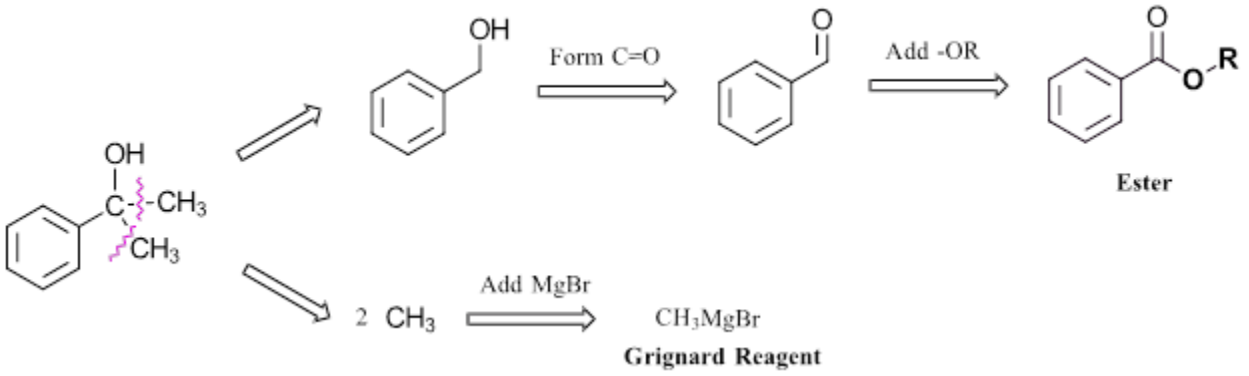
How could the following molecule be made using a Grignard reagent and an ester?

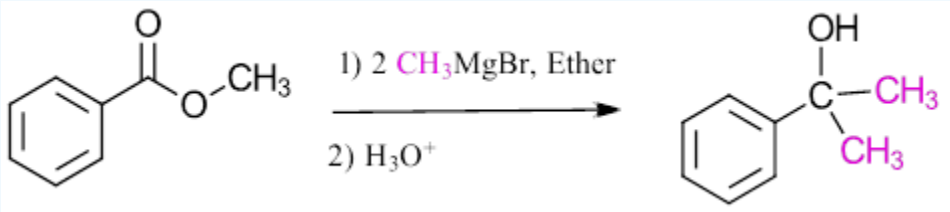


Solution

The key bond breaks for this example are two C-C sigma bonds between the carbonyl carbon and two alpha carbons. Reactions with esters involve a double addition of the Grignard reagent so the fragments removed must be the same. In this example, the C-C bonds involving the two methyl groups are broken. Breaking these bonds separate the target molecule into the required starting materials. The fragment which contains the alcohol carbon forms a C=O carbonyl bond and gains an

–OR to become an ester. The R group of the ester is largely unimportant to the overall reaction and is typically a methyl or ethyl group. The alkyl fragments gain MgBr to form a Grignard reagent. Remember that the Grignard reagent only contains one alkyl fragment.

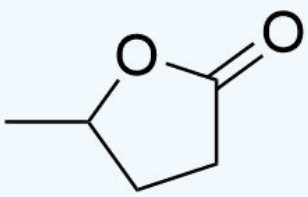




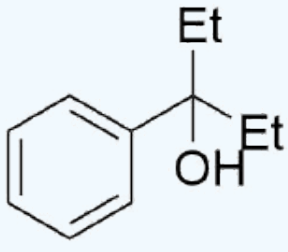
Exercises 8.11.1

1) Why is the alkaline hydrolysis of an ester not a reversible process? Why doesn't the reaction with a hydroxide ion and a carboxylic acid produce an ester?

2) Draw the product of the reaction between the following molecule and $LiAlH_4$, and the product of the reaction between the following molecule and DIBAL.

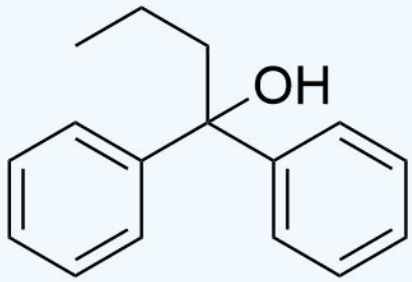


3) How might you Prepare the following molecules from esters and Grignard reagents?

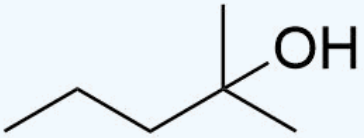


(a)

(b)



(c)

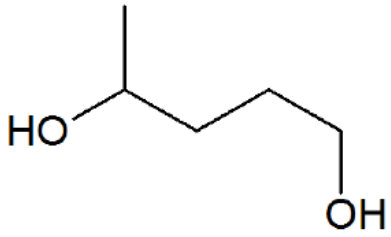


Answers available at the end of this section.

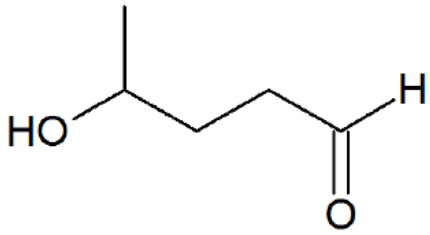
Answers

1) The reaction between a carboxylic acid and a hydroxide ion is an acid base reaction, which produces water and a carboxylate anion.

2)



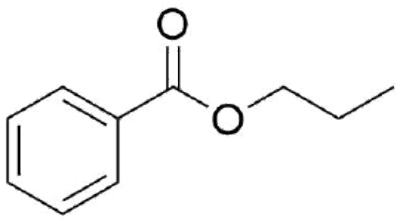
$(LiAlH_4)$



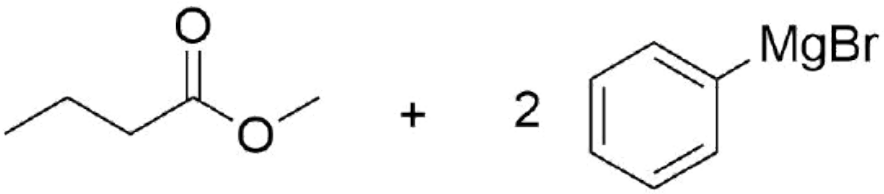
(DIBAH)

3)

(a)



\+ 2 EtMgBr



(b)
(c)

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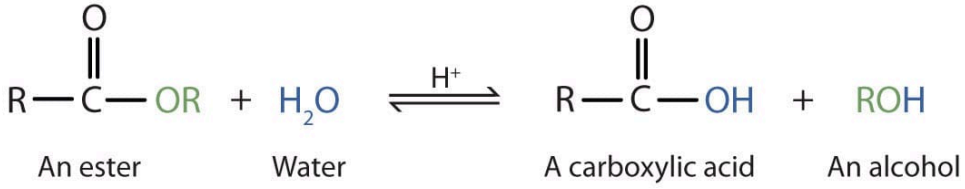
8.12: Hydrolysis of Esters

Learning Objectives

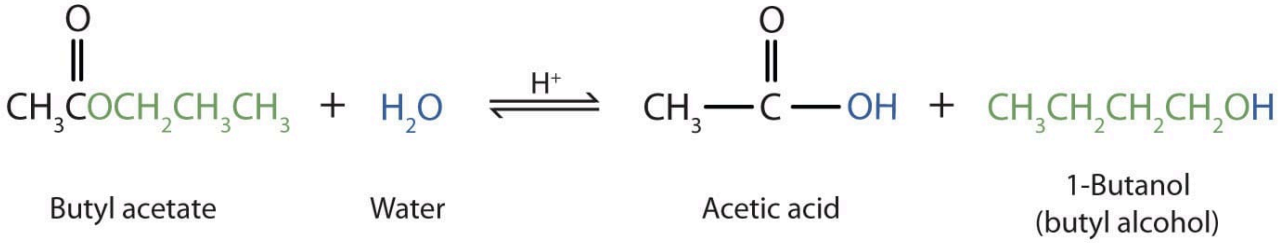
- Describe the typical reaction that takes place with esters.
- Identify the products of an acidic hydrolysis of an ester.
- Identify the products of a basic hydrolysis of an ester.

Esters are neutral compounds, unlike the acids from which they are formed. In typical reactions, the alkoxy (OR′) group of an ester is replaced by another group. One such reaction is hydrolysis, literally “splitting with water.” The hydrolysis of esters is catalyzed by either an acid or a base.

Acidic hydrolysis is simply the reverse of esterification. The ester is heated with a large excess of water containing a strong-acid catalyst. Like esterification, the reaction is reversible and does not go to completion.



As a specific example, butyl acetate and water react to form acetic acid and 1-butanol. The reaction is reversible and does not go to completion.

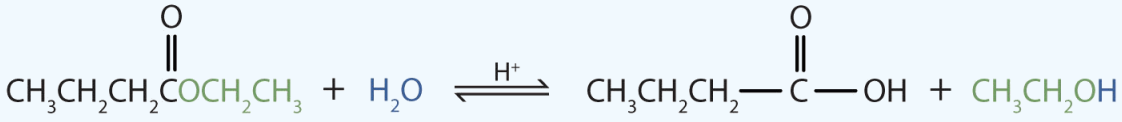


Example 8.12.1

Write an equation for the acidic hydrolysis of ethyl butyrate ($CH_3CH_2CH_2COOCH_2CH_3$) and name the products.

Solution

Remember that in acidic hydrolysis, water (HOH) splits the ester bond. The H of HOH joins to the oxygen atom in the OR part of the original ester, and the OH of HOH joins to the carbonyl carbon atom:

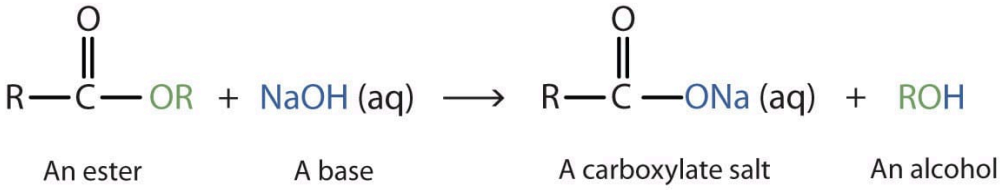


The products are butyric acid (butanoic acid) and ethanol.

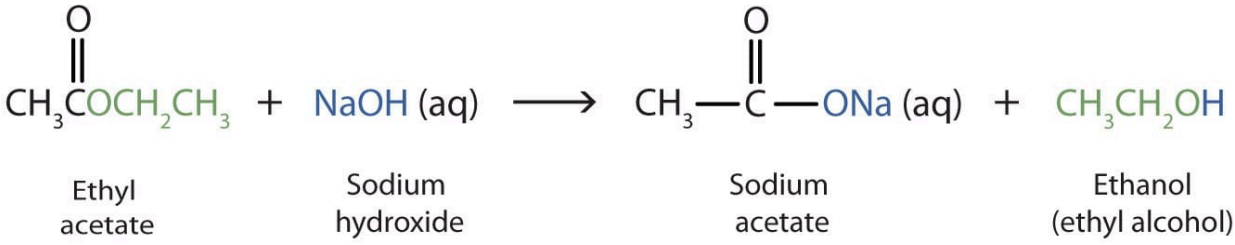
Exercise 8.12.1

Write an equation for the acidic hydrolysis of methyl butanoate and name the products.

When a base (such as sodium hydroxide [NaOH] or potassium hydroxide [KOH]) is used to hydrolyze an ester, the products are a carboxylate salt and an alcohol. Because soaps are prepared by the alkaline hydrolysis of fats and oils, alkaline hydrolysis of esters is called saponification (Latin *sapon*, meaning "soap," and *facere*, meaning "to make"). In a saponification reaction, the base is a reactant, not simply a catalyst. The reaction goes to completion:



As a specific example, ethyl acetate and NaOH react to form sodium acetate and ethanol:

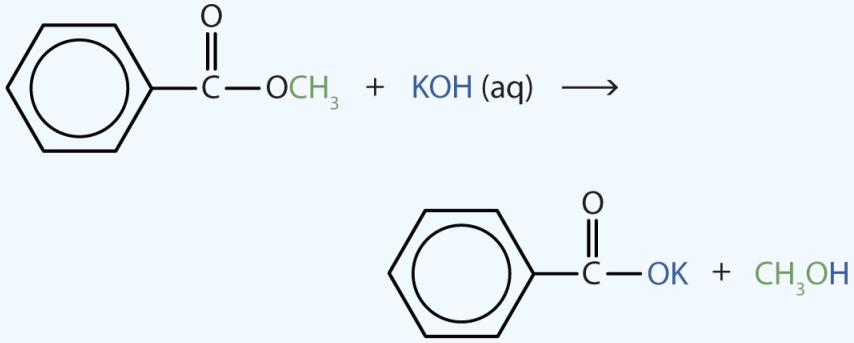


Example 8.12.2

Write an equation for the hydrolysis of methyl benzoate in a potassium hydroxide solution.

Solution

In basic hydrolysis, the molecule of the base splits the ester linkage. The acid portion of the ester ends up as the *salt* of the acid (in this case, the potassium salt). The alcohol portion of the ester ends up as the free alcohol.



Exercise 8.12.2

Write the equation for the hydrolysis of ethyl propanoate in a sodium hydroxide solution.

Summary

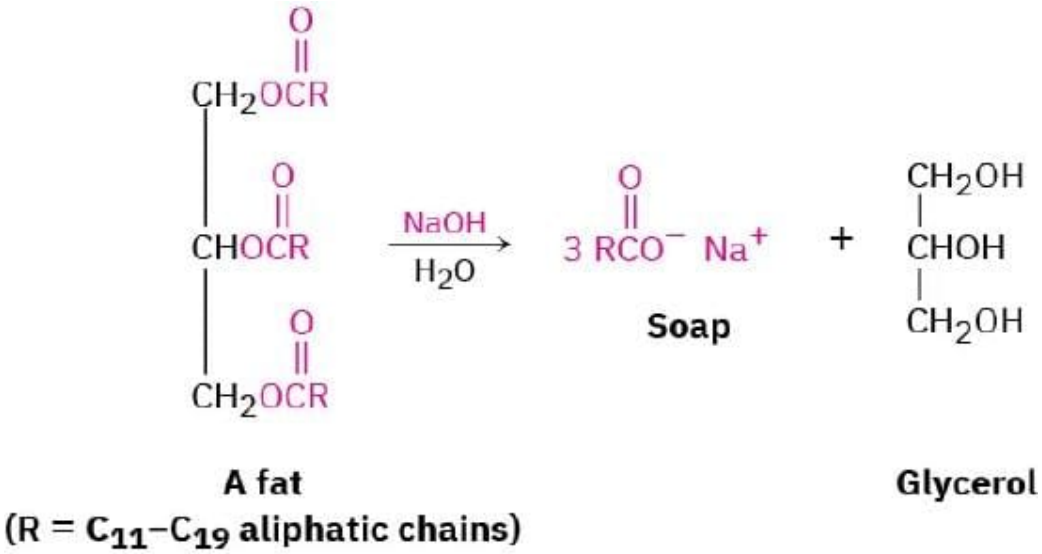
Hydrolysis is a most important reaction of esters. Acidic hydrolysis of an ester gives a carboxylic acid and an alcohol. Basic hydrolysis of an ester gives a carboxylate salt and an alcohol.

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8.13: Soap

Soap has been in use for nearly 5000 years. As early as 2800 BC, the Babylonians boiled fats with ashes to create a soap-like substance. Ancient Egyptian medical papyri dating from 1550 BC reveals that Egyptians bathed regularly with soap made from a mixture of animal fats, vegetable oils, and alkaline salts. Chemically, soap is a mixture of the sodium or potassium salts of the long-chain fatty acids produced by hydrolysis (saponification) of animal fat with alkali. Wood ash was used as a source of alkali until the early 1800s, when the LeBlanc process for making Na_2CO_3 by heating sodium sulfate with limestone became available.



Crude soap curds contain glycerol and excess alkali as well as soap but can be purified by boiling with water and adding NaCl or KCl to precipitate the pure carboxylate salts. The smooth soap that precipitates is dried, perfumed, and pressed into bars for household use. Dyes are added to make colored soaps, antiseptics are added for medicated soaps, pumice is added for scouring soaps, and air is blown in for soaps that float. Regardless of these extra treatments and regardless of price, though, all soaps are basically the same.

Soaps act as cleansers because the two ends of a soap molecule are so different. The carboxylate end of the long-chain molecule is ionic and therefore hydrophilic (Section 2.12), or attracted to water. The long hydrocarbon portion of the molecule, however, is nonpolar and hydrophobic, avoiding water and therefore more soluble in oils. The net effect of these two opposing tendencies is that soaps are attracted to both oils and water and are therefore useful as cleansers.

When soaps are dispersed in water, the long hydrocarbon tails cluster together on the inside of a tangled, hydrophobic ball, while the ionic heads on the surface of the cluster protrude into the water layer. These spherical clusters, called micelles, are shown schematically in Figure 8.13.1. Grease and oil droplets are solubilized in water when they are coated by the nonpolar, hydrophobic tails of soap molecules in the center of micelles. Once solubilized, the grease and dirt can be rinsed away.

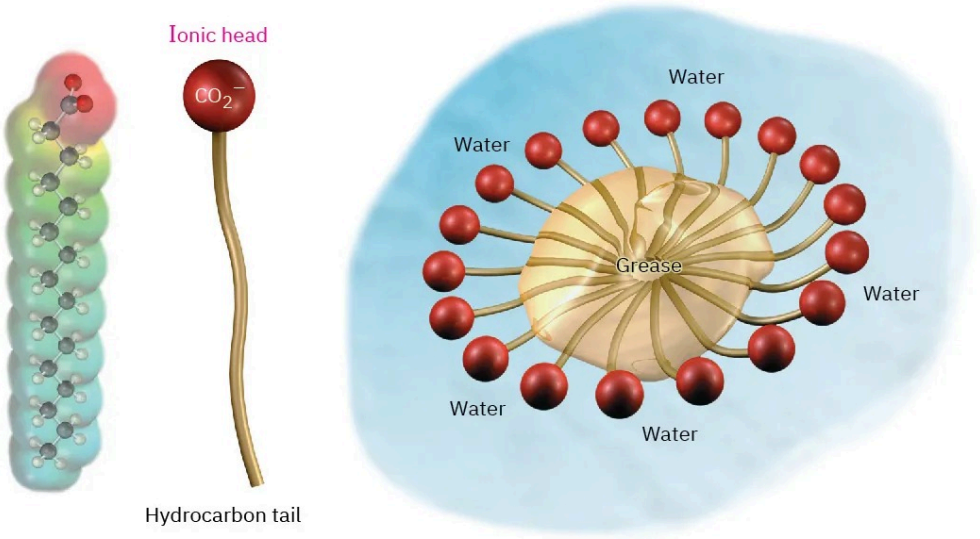
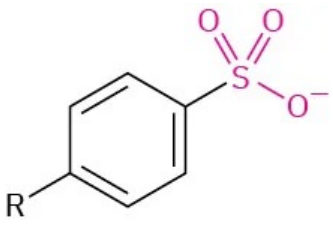


Figure 8.13.1: A soap micelle solubilizing a grease particle in water. An electrostatic potential map of a fatty acid carboxylate shows how the negative charge is located in the head group.

As useful as they are, soaps also have drawbacks. In hard water, which contains metal ions, soluble sodium carboxylates are converted into insoluble magnesium and calcium salts, leaving the familiar ring of scum around bathtubs and a gray tinge on white clothes. Chemists have circumvented this problem by synthesizing a class of synthetic detergents based on salts of long-chain alkylbenzenesulfonic acids. The mechanism of synthetic detergents is the same as that of soaps: the alkylbenzene end of the molecule is attracted to grease, while the anionic sulfonate end is attracted to water. Unlike soaps, though, sulfonate detergents don't form insoluble metal salts in hard water and don't leave an unpleasant scum.



A synthetic detergent
(R = various C_{12} chains)

Exercise 8.13.1

Draw the structure of magnesium oleate, a component of bathtub scum.

Answer available at the end of this section.

Exercise 8.13.2

Write the saponification reaction of glyceryl dioleate monopalmitate with aqueous NaOH.

Answer available at the end of this section.

Answers

Exercise 8.13.1

$$[CH_3(CH_2)_7CH{=}CH(CH_2)_7CO_2^-]_2\ Mg^{2+}$$

Exercise 8.13.2

Glyceryl dioleate monopalmitate → glycerol + 2 sodium oleate + sodium palmitate

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8.14: Chemistry of Amides

Objectives

After completing this section, you should be able to

1. write an equation to describe the preparation of an amide from an acid chloride.
2. identify the amide linkage as the basic unit from which all proteins are made, and hence recognize the importance of the amide linkage to biologists and biochemists.
3. write detailed mechanisms for the acidic and basic hydrolysis of amides.
4. write an equation to describe the reduction of an amide to an amine.
5. write a detailed mechanism for the reduction of an amide to an amine.
6. identify the product formed when a given amide is reduced with lithium aluminum hydride.
7. identify the amide, the reagents, or both, necessary to prepare a given amine by direct reduction.
8. identify lactams as being cyclic amides which undergo hydrolysis and reduction in a manner analogous to that of their acyclic counterparts.

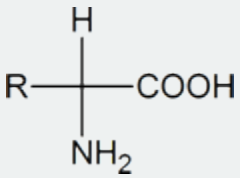
Key Terms

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

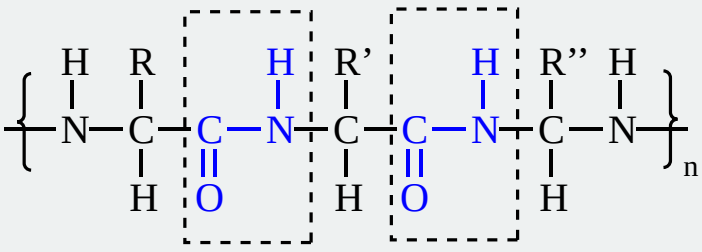
- lactam

Study Notes

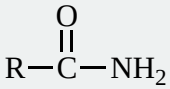
When we talk about amino acids, we are generally referring to *α*-amino acids; that is, compounds in which an amino (NH_2) group and a carboxyl group are attached to the same carbon atom:



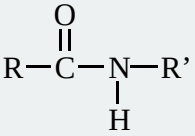
Notice that such compounds contain a chiral carbon atom (unless R = H, which is glycine). Proteins can be considered to consist of amino acid residues joined by amide (or peptide) links. These peptide links consist of exactly the same structural units that we find in *N*-substituted primary amides.



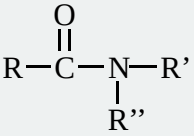
peptide (amide) links



primary amide

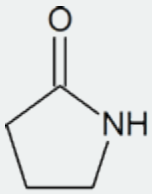


N—substituted primary amide

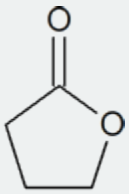


N, N—disubstituted primary amide

A lactam is a cyclic amide, in the same way that a lactone is a cyclic ester:

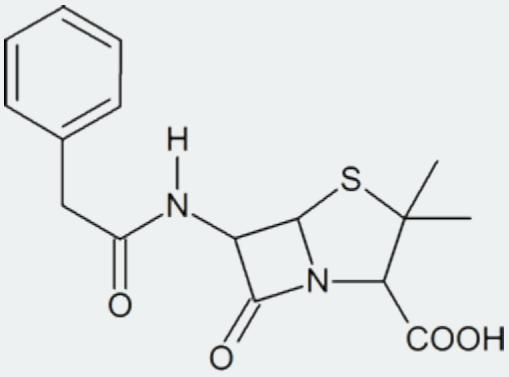


a lactam



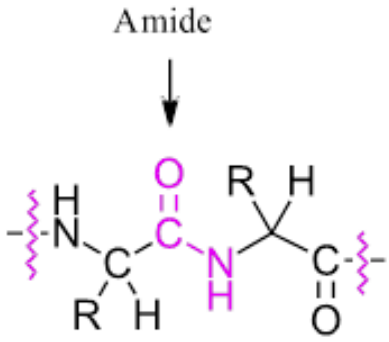
a lactone

Among the most important molecules that contain lactam rings are the penicillins:



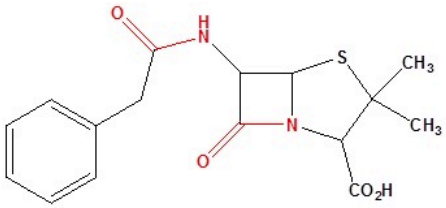
penicillin G (benzylpenicillin)

The amide functional group is extremely important for biological molecules because amides make up the backbone of proteins. Proteins are actually polymers of amino acids, linked by amide groups known as peptide bonds. Proteins (polymers of ~40 amino acids or more) and peptides (shorter polymers) are formed when the amino group of one amino acid monomer reacts with the carboxylate carbon of another amino acid to form an amide linkage, which in protein terminology is a **peptide bond**. The individual amino acids within a peptide or protein are called **amino acid residues**.

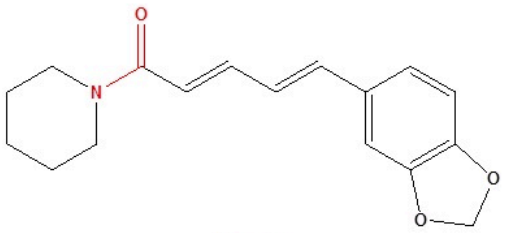


Protein Backbone

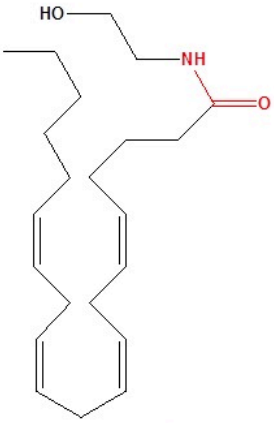
Compounds containing amides have a wide range of biological activity and include penicillin G an antibiotic, piperine which is responsible for the pungent flavor of black pepper, and anandamide which provides some of the pleasurable sensations gained from eating chocolate.



Penicillin G
(An Antibiotic)



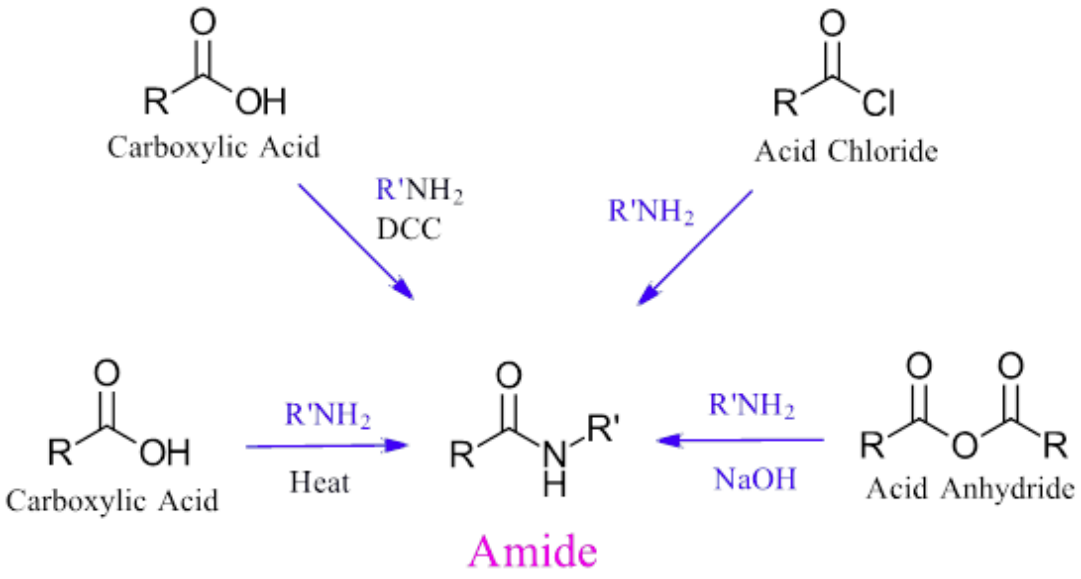
Piperine
(From Black Pepper)



Anandamide
(From Chocolate)

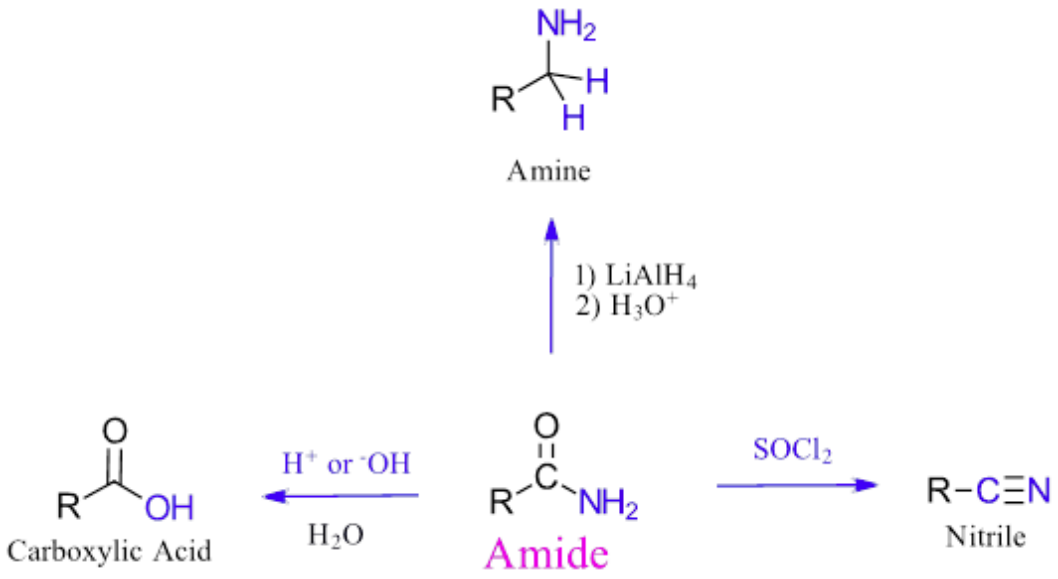
Preparation of Amides

Amides are most commonly prepared though the reaction of an acid chloride with ammonia, a 1^{o} amine, or 2^{o} amine. In an analogous reaction, an amide can be prepared through the reaction of a carboxylic acid and an amine using a coupling agent such as DCC. Simple amides can be prepared by reacting an acid anhydride with an amine. Lastly, amides can be formed through the direct reaction of a carboxylic acid and an amine. However, this reaction is rarely used because the conditions are relatively severe.

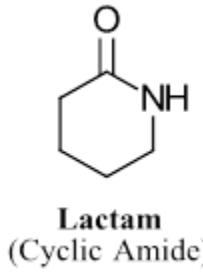


Reactions of Amides

Amides are relatively unreactive towards nucleophilic acyl substitutions due to the poor leaving group ability of its nitrogen containing Y group. Despite this, amides can react with water under acidic or basic conditions to create a carboxylic acid through nucleophilic acyl substitution. Reaction of primary amides with thionyl chloride ($SOCl_2$) creates nitriles. Hydride reduction using $LiAlH_4$ causes the carbonyl oxygen of the amide to eliminate as a leaving group creating the corresponding amine.



Lactams, cyclic amides, are affected by these reactions in the same fashion as acyclic amides.

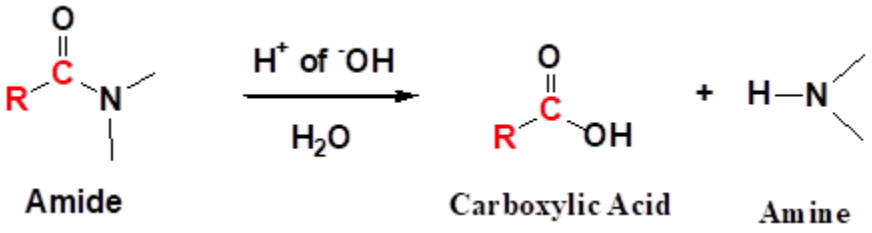


Lactam
(Cyclic Amide)

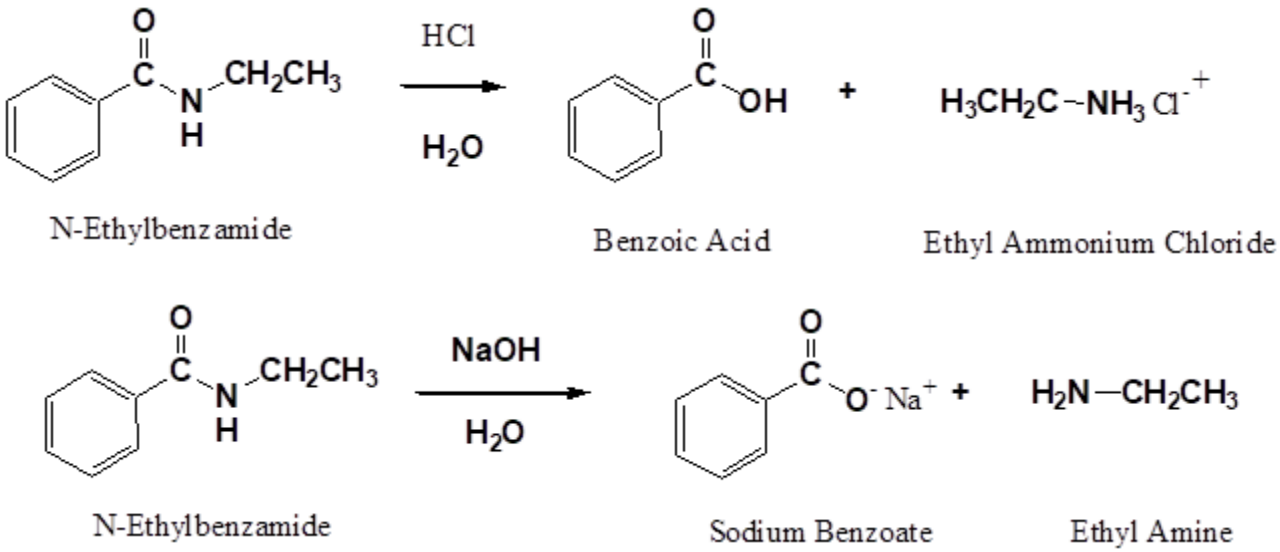
Conversion of Amides to Carboxylic Acids: Hydrolysis

Amides can be hydrolyzed into a carboxylic acid and ammonia or an amine by heating in an acidic or basic aqueous solution. In both cases, acid-base reactions occurring with the products make the overall reaction irreversible. Under acidic conditions the amine produced by the reaction is protonated to form a non-nucleophilic ammonium compound. Under basic conditions the carboxylic acid produced by the reaction is deprotonated to a non-electrophilic carboxylate.

General Reaction



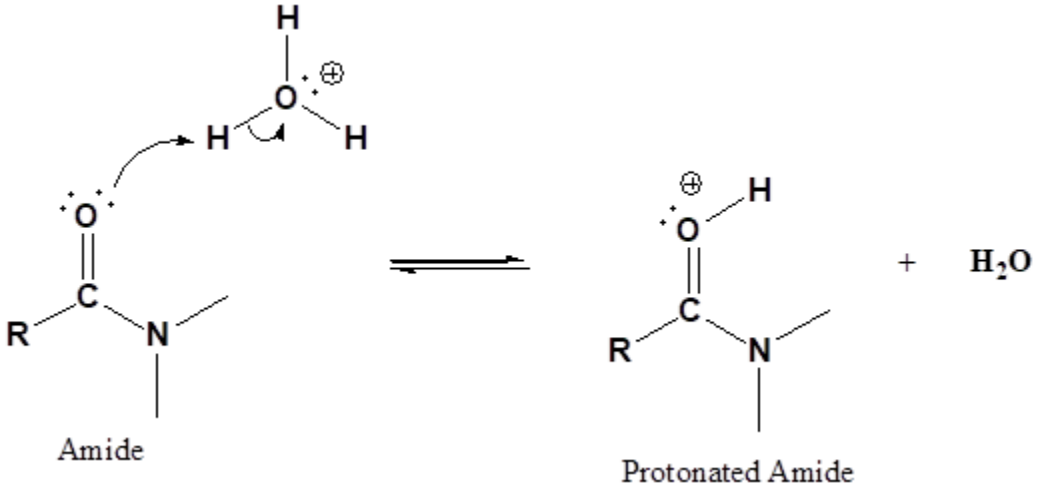
Examples



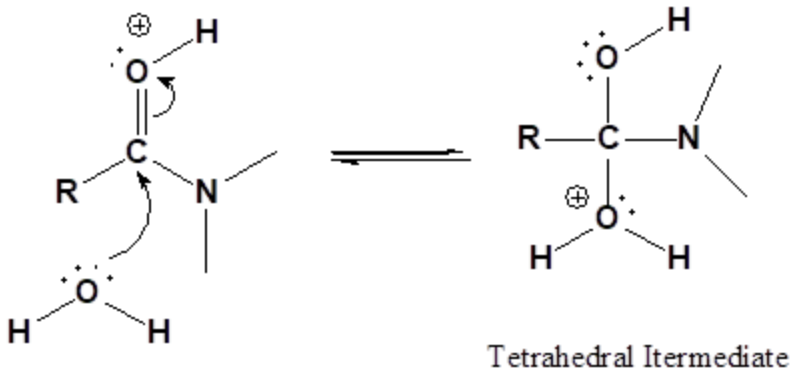
Mechanism Under Acidic Conditions

Protonation of the amide increases the electrophilicity of the carbonyl carbon allowing water to add causing formation of a tetrahedral oxonium intermediate. Next a proton is transferred to the amide nitrogen giving it a positive charge and increasing its ability to act as a leaving group. Reforming the carbonyl double bond causes the elimination of an amine as a leaving group, creating a protonated carboxylic acid. In the last step of the mechanism, the produced amine acts as a base, removing a hydrogen, to form a carboxylic acid and an ammonium compound. This final deprotonation step essentially removes the amine from the equilibrium which drives the reaction towards completion. Since the amine is no longer part of the equilibrium, the reaction is effectively irreversible.

1) Protonation of the carbonyl



2) Nucleophilic attack by water

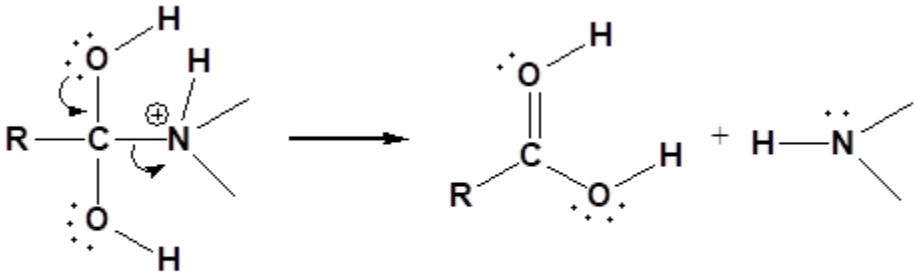


Tetrahedral Itermediate

3) Proton transfer



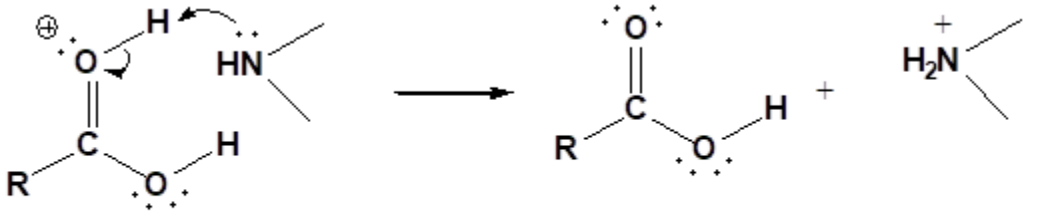
4) Leaving group removal



Protonated Carboxylic Acid

Amine

5) Deprotonation



Carboxylic Acid

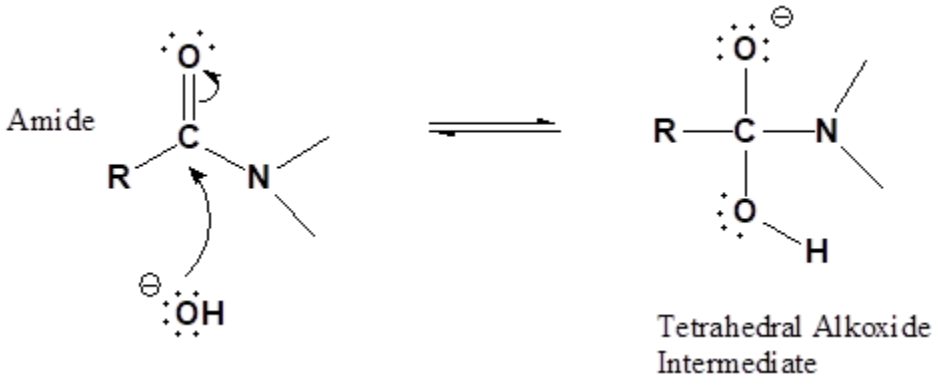
Ammonium Compound

Mechanism Under Basic Conditions

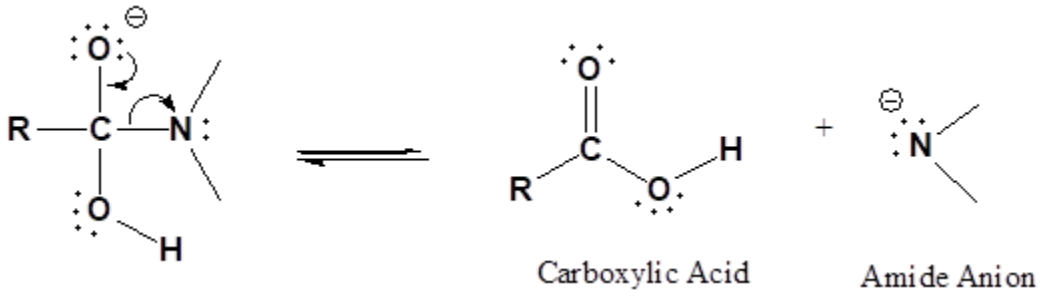
The base-promoted hydrolysis of an amide follows the typical nucleophilic acyl substitution mechanism. A full equivalent of hydroxide anion is used, so the reaction is called base-promoted and not base catalyzed. The mechanism of basic amide hydrolysis begins with the nucleophilic addition of a hydroxide ion at the carbonyl carbon creating a tetrahedral alkoxide

intermediate. The carbonyl bond is reformed along with the elimination of an amide ion (-NHR) leaving group (note this is a different use of the word amide meaning an amine anion), forming a carboxylic acid. In the last step, the amide ion deprotonates the carboxylic acid to form a carboxylate salt and an amine as products. This final deprotonation step essentially removes the carboxylic acid from the equilibrium which drives the reaction towards completion. Since the carboxylic acid is no longer part of the equilibrium, the reaction is effectively irreversible.

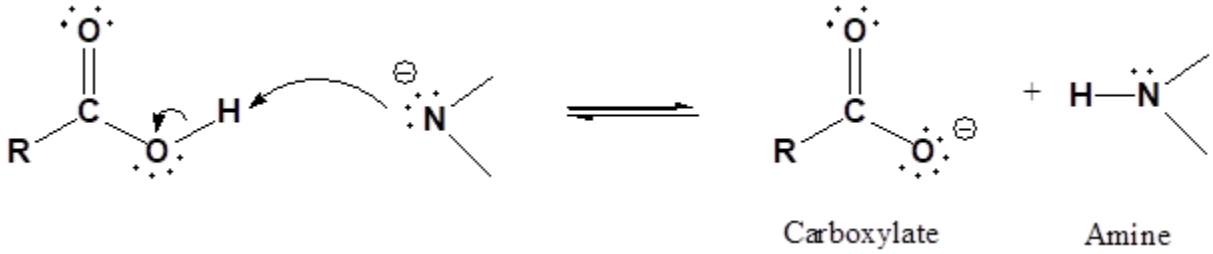
1) Nucleophilic attack by hydroxide



2) Leaving group removal

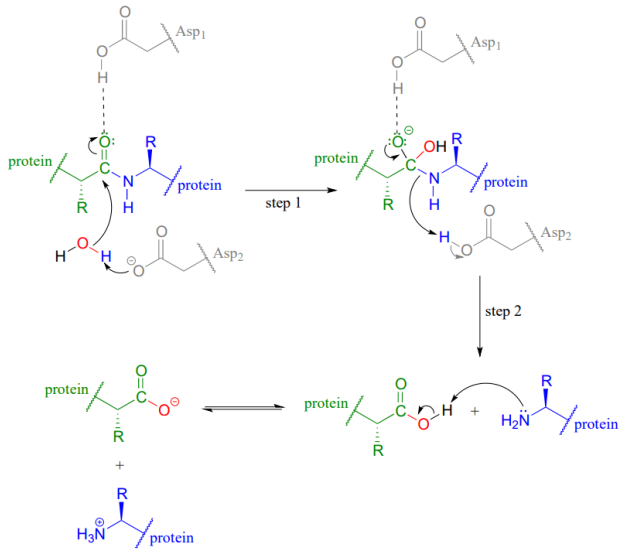


3) Deprotonation



Hydrolysis of Proteins

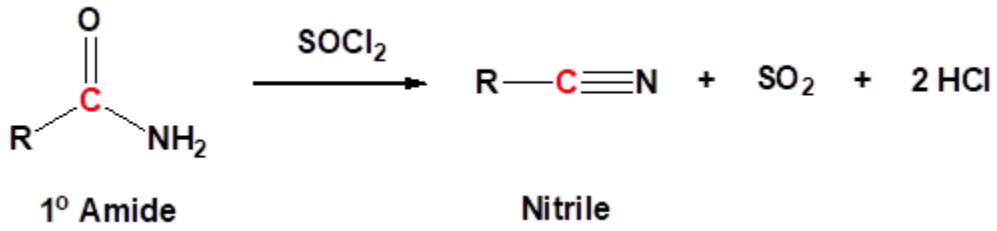
Hydrolysis of amide bonds is the first step in the metabolism of dietary proteins. Protein hydrolysis is catalyzed by protease enzymes (abbreviated Asp_1 and Asp_2 in the figure below). The mechanisms starts with the nucleophilic acyl substitution by water while breaking the amide C-N bond. This produces a protein fragment with an amine and another with a carboxylic acid. The amine fragment will deprotonate the carboxylic acid forming the carboxylate and ammonium fragments.



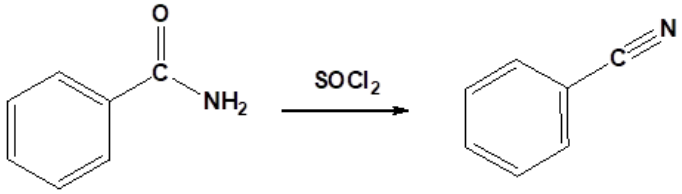
Conversion of 1° Amides to Nitriles: Dehydration

1° Amides can be converted into a nitrile through reaction with thionyl chloride ($SOCl_2$). Sulfurdioxide (SO_2) and hydrochloric acid are produced as byproducts.

General Reaction



1° Amide Nitrile

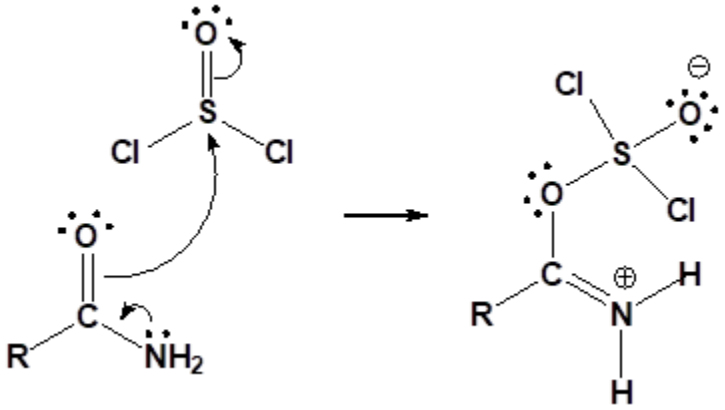


Benzamide Benzonitrile

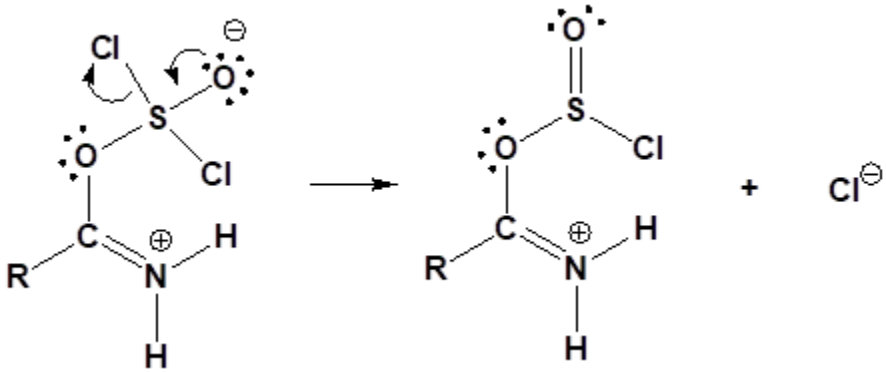
Mechanism for the Conversion of a 1° Amide to a Nitrile

During the first step of the mechanism, the amide acts as a nucleophile and attacks the electrophilic sulfur of thionyl chloride, pushing the pi electrons of the S=O bond onto oxygen. Removal of a chloride anion as a leaving group allows the sulfoxide S=O bond to reform creating a protonated imine chlorosulfite. Deprotonation forms an imine chlorosulfite intermediate. A second deprotonation eliminates the chlorosulfite leaving group as sulfur dioxide and a chloride anion and forms the C-N triple bond of the nitrile product.

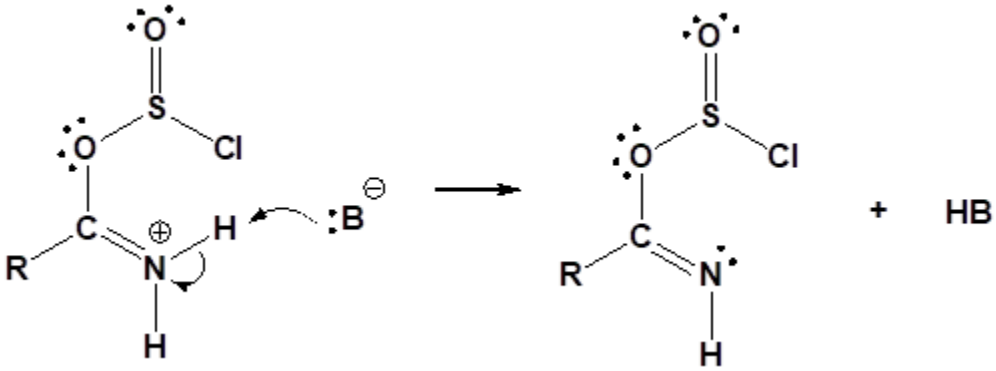
1) Nucleophilic attach on thionyl chloride



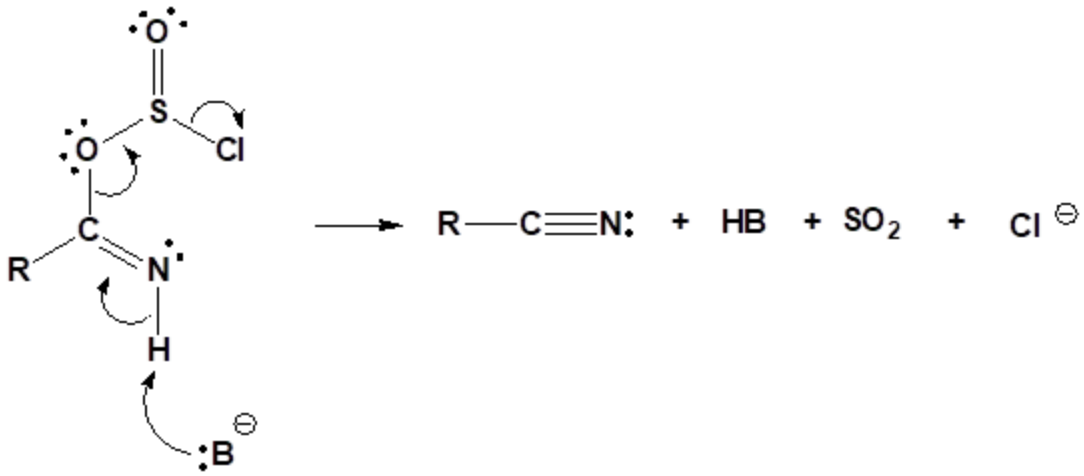
2) Leaving group removal



3) Deprotonation



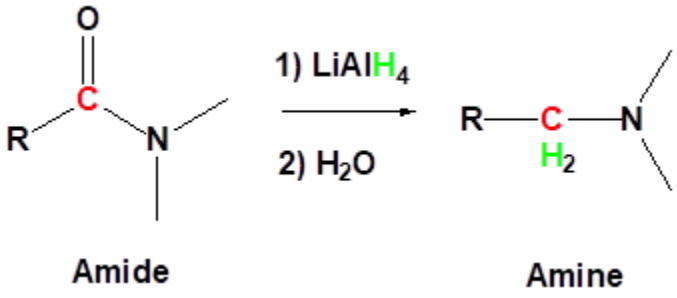
4) Leaving group removal



Conversion of Amides to 1°, 2° or 3° Amines: Hydride Reduction

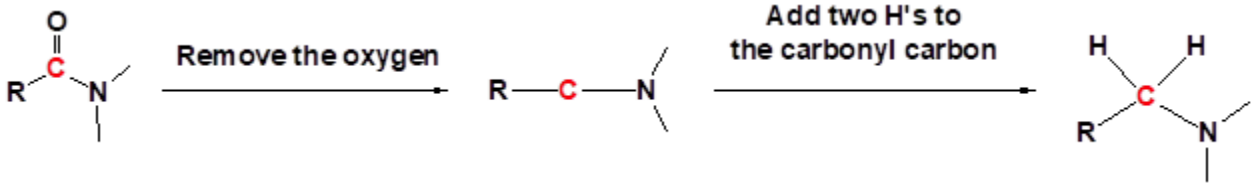
Amides are reduced to amines by treatment with $LiAlH_4$, and this has proven to be one of the most general methods for preparing all classes of amines (1°, 2° & 3°). Due to the nitrogen in the Y group of amides, the outcome of $LiAlH_4$ reductions is distinctly different than for esters since amide anions are poorer leaving groups than alkoxide anions. Furthermore, oxygen forms especially strong bonds to aluminum. During this reaction the carbonyl oxygen of the amide is removed as a leaving group and not the nitrogen containing Y group. Removal of the leaving group allows for a formation of a C=N iminium bond which can accept a second addition of a hydride nucleophile to form the amine.

General Reaction

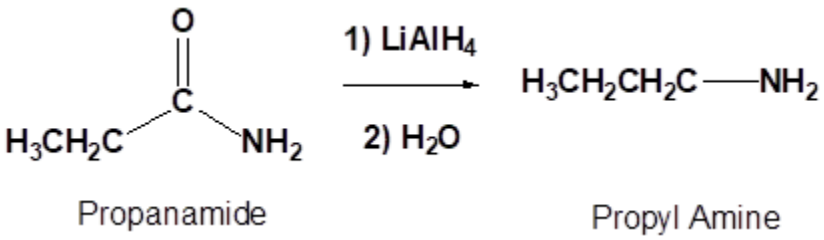


Predicting the Products of a Hydride Reduction

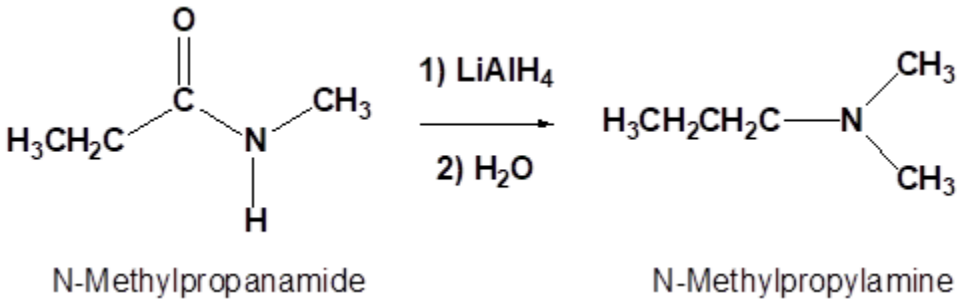
There are two major changes in bonding during this reaction: 1) The C=O carbonyl is removed from the starting material 2) Two hydride nucleophiles are added to what was the carbonyl carbon of the amide.

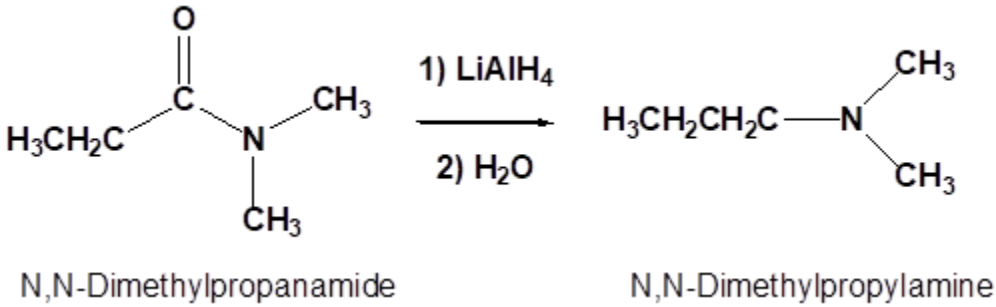


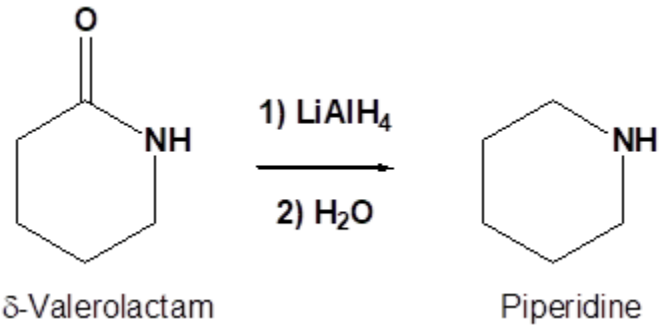
Example



Alkyl groups attached to the nitrogen do not affect the reaction.



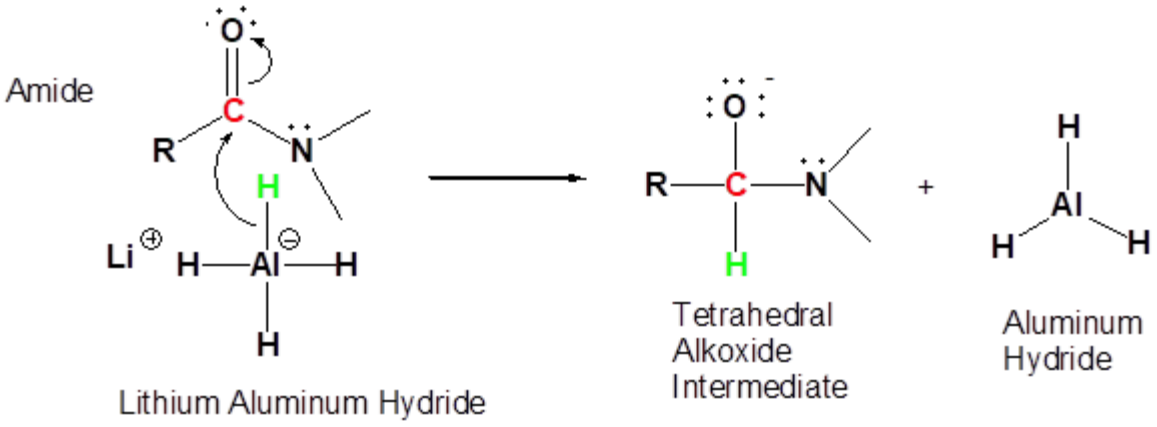




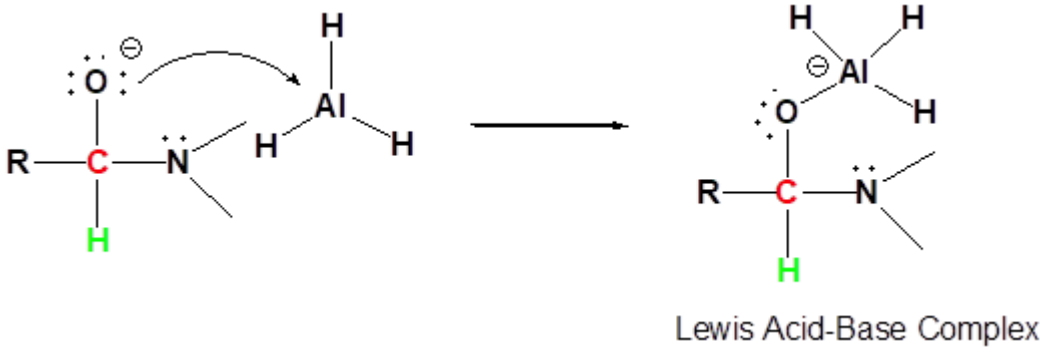
Mechanism for the Hydride Reduction of an Amide to Form an Amine

Addition of a hydride nucleophile to the carbonyl carbon of the amide produces a tetrahedral alkoxide intermediate. A Lewis acid-base interaction occurs between the alkoxide (Lewis Base) and AlH_3 (Lewis acid) forming a complex with an O-Al bond. The nitrogen lone pair forms a double bond with the previous carbonyl carbon ejecting a metal oxide species (e.g. $[H3Al–O]^{2-}$) as a leaving group, and while forming an iminium double bond. Addition of a second equivalent of hydride nucleophile to the iminium carbon produces an amine.

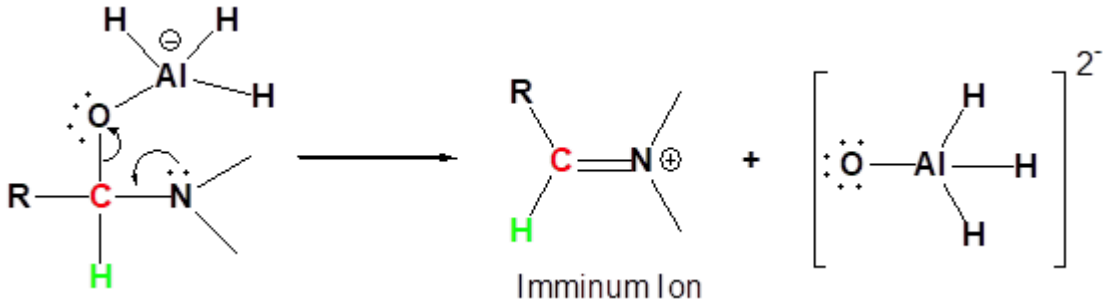
1) Nucleophilic attack by the hydride



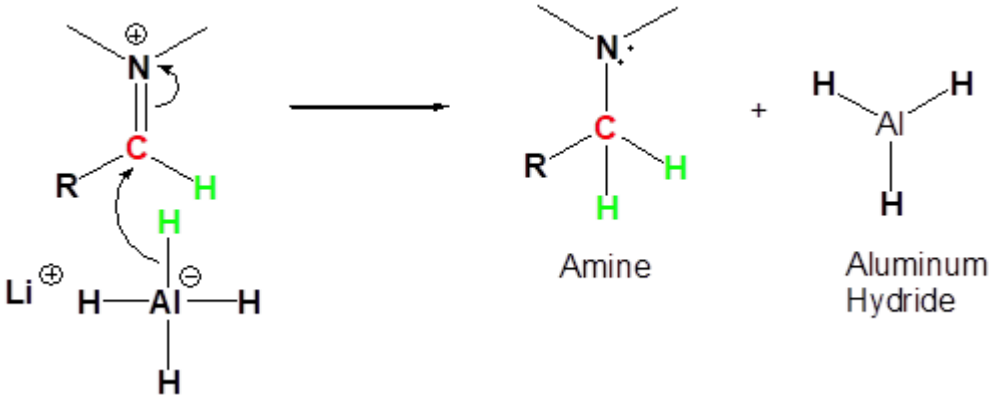
2) Complex formation



3) Leaving group removal

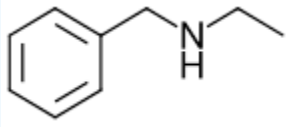


4) Nucleophilic attach by the hydride



Example 8.14.1

How could the following molecule be synthesized using an aminolysis of an acid chloride?

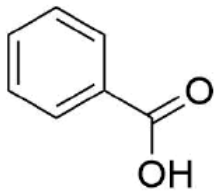


Answer available at the end of this section.

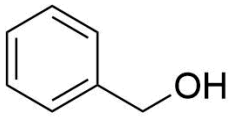
Exercise 8.14.1

1) How would you prepare the following compounds from N-Propypl benzamide?

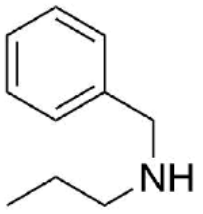
(a)



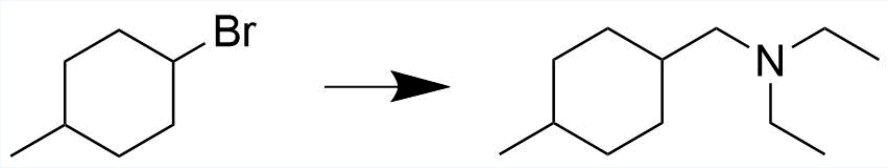
(b)



(c)



2) Propose a synthesis pathway for the following conversion:



Answer available at the end of this section.

Answers

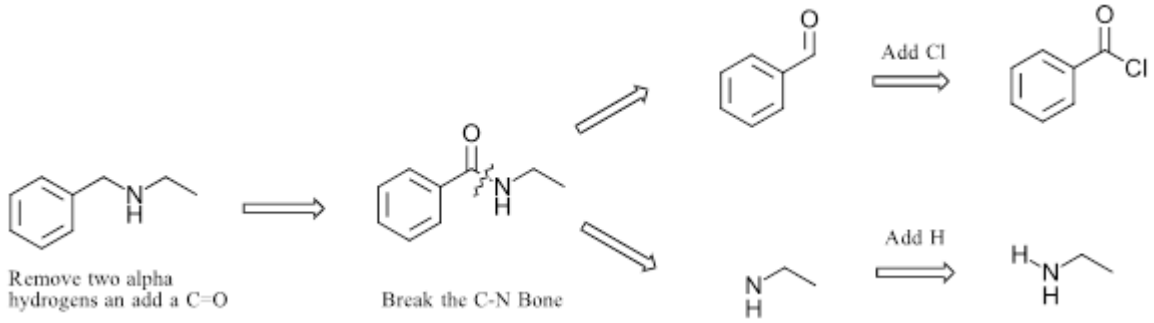
Example 8.14.1

One of the preferred methods for making amines is through a nucleophilic acyl substitution using an acid chloride and amine to form an amide. The amide is then reduced to the amine during a hydride reduction with $LiAlH_4$.

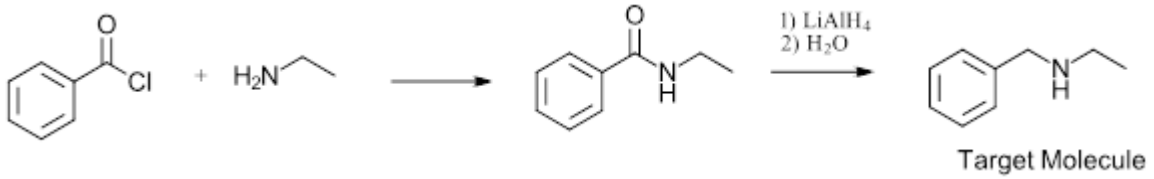
In the first step of retrosynthetic analysis, one of the carbons alpha to the amine nitrogen is converted to a carbonyl thus creating an amide intermediate. The key bond formed during this pathway is the C-N sigma bond between the carbonyl carbon and the nitrogen created during amide formation. Breaking this bond separated the target molecule into the two starting materials for the pathway. The carbonyl carbon gains a –Cl to become an acid chloride and the nitrogen fragment gains an H to become a 1^o amine. In the forward reaction pathway, the acid chloride and the 1^o amine are linked to from an amide in the first step of the reaction. Subsequent hydride reduction of the amide using $LiAlH_4$ produces the amine target molecule.

The target molecule has two alpha carbons which could possibly be converted to a carbonyl. This allows there to be two possible synthetic pathways.

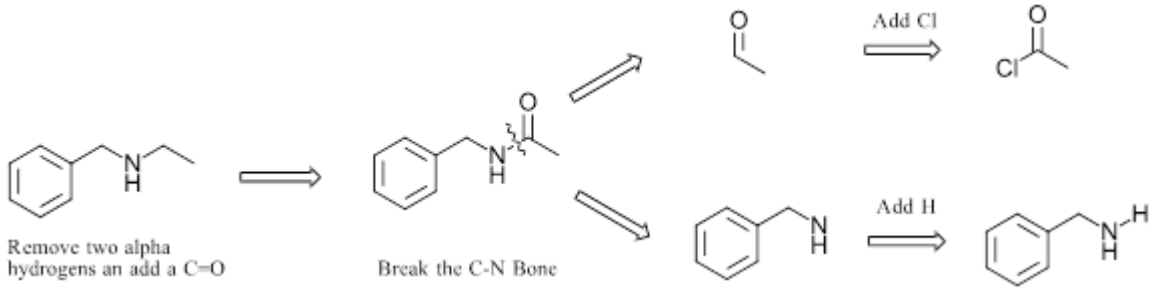
Pathway 1



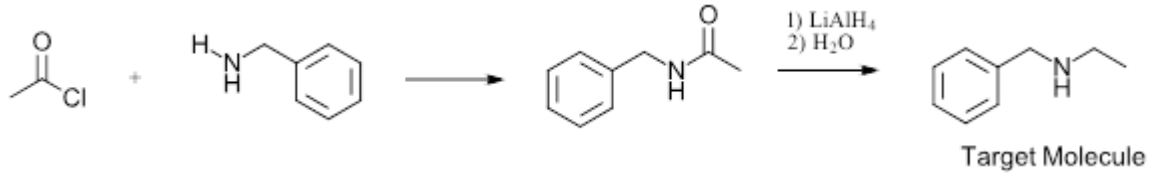
Solution 1



Pathway 2



Solution 2



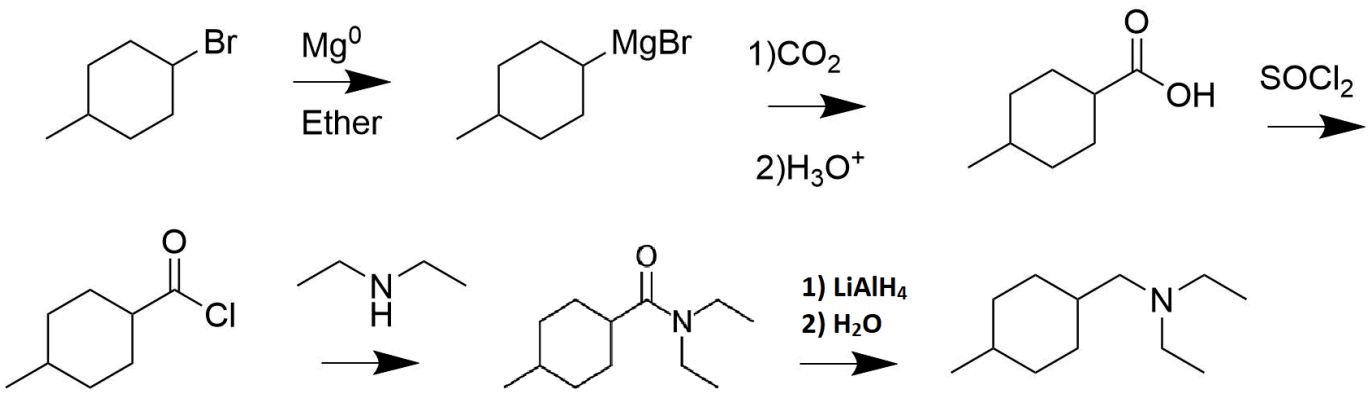
Exercise 8.14.1

1) (a) NaOH, H_2O

(b) NaOH, H_2O, then $LiAlH_4$

(c) $LiAlH_4$

2)



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8.15: Polyamides and Polyesters - Step-Growth Polymers

Objectives

After completing this section, you should be able to

1. write an equation to represent the formation of nylon 66 from adipic acid and hexamethylenediamine.
2. write an equation to represent the formation of nylon 6 from caprolactam.
3. predict the structure of the step-growth polymer formed from the reaction of two given monomers.
4. identify the monomers needed to prepare a step-growth polymer of a given structure.
5. write an equation to describe the formation of a polyester, such as poly(ethylene terephthalate), from a given diol and diester.
6. write an equation to describe the formation of a polycarbonate from a carbonate and a bisphenol.

Key Terms

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

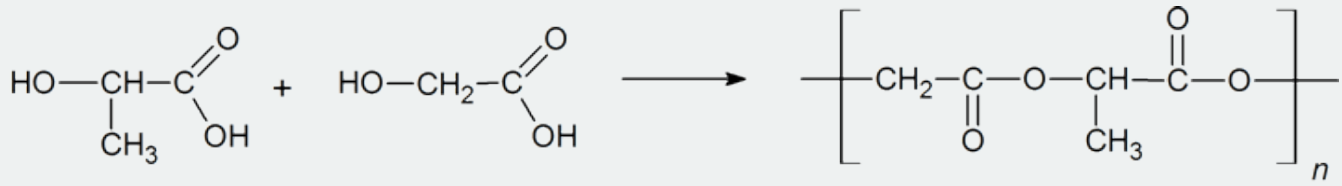
- chain-growth polymer
- polyamide
- polyester
- step-growth polymer

Study Notes

You may wish to review chain-growth polymerization in Section 8.10 and Section 14.6. In this section we discuss another important class of polymerization kknow as step-growth polymerization.

As you can see from the equation given in the discussion on forming condensation polymers, Dacron is formed from two monomers, one of which possesses two carboxylate groups and the other two hydroxyl groups.

It is also possible to form a polyester using two monomers that each possesse one carboxyl group and one hydroxyl group. An example is the polymer formed between lactic acid and glycolic acid. This polymer has been used to produce absorbable staples that provide surgeons with a convenient method of closing incisions made during operations on the bladder or intestines, or during hysterectomies. Two advantages of this polyester in such applications are, first, that it begins to hydrolyze in the body after six to eight weeks, and then, that the products of the hydrolysis are both compounds normally present in the body.

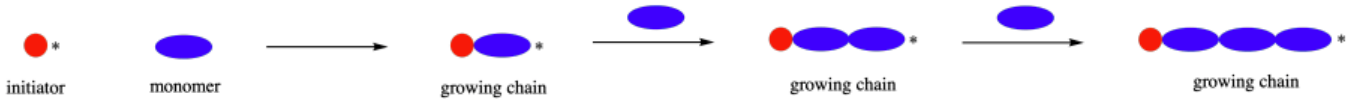


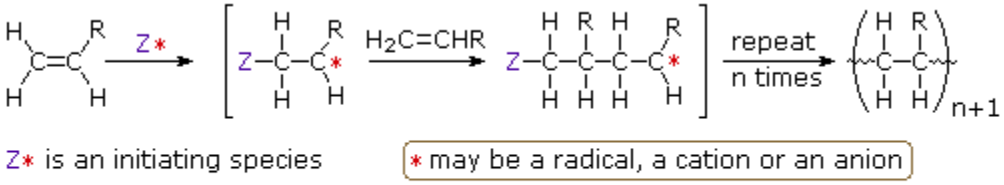
lactic acid
(2-hydroxypropanoic acid)

glycolic acid
(2-hydroxyethanoic acid)

Step-Growth Polymerizations

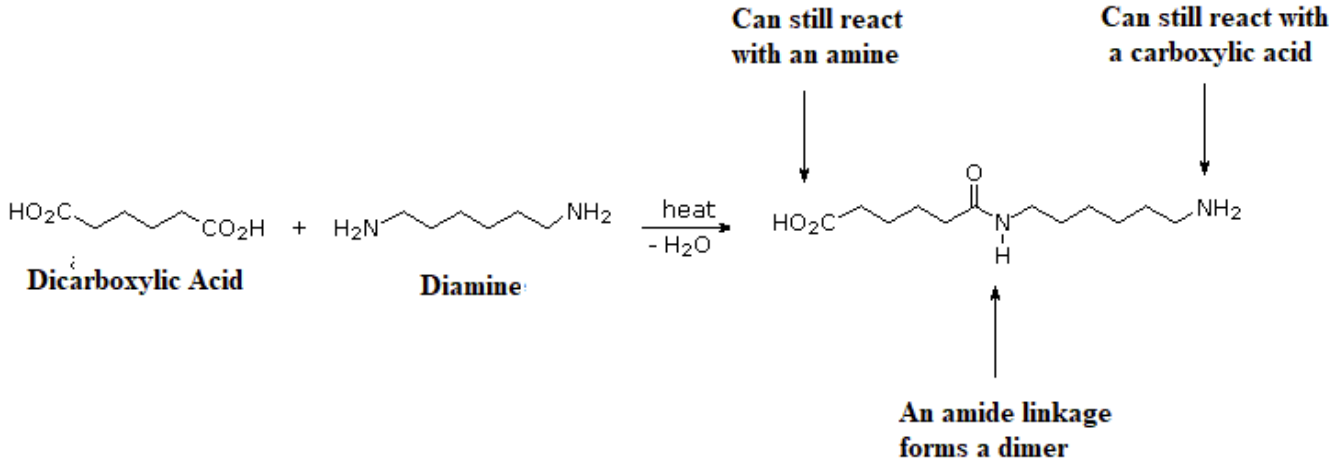
Step-growth and chain-growth are two broad classes of polymerization methods. Sections 8.11 and 14.7 discussed how chain-growth polymers usually start with a single alkene containing monomer, which is unreactive until an initiator is added. The initiator converts one monomer molecule into a reactive intermediate (radical, cation, anion) which is capable of reacting with another monomer forming a C-C bond and creating a new reactive intermediate. This reactive intermediate reacts with another monomer and the process is repeated as a chain reaction to form a polymer.



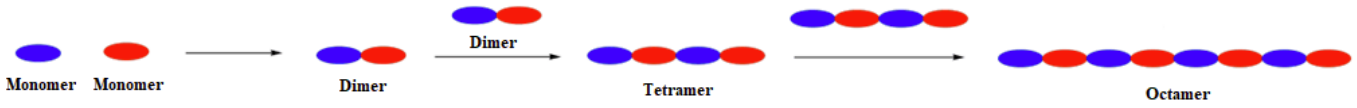


A Chain-Growth Polymerization

The process of step-growth polymerizations are fundamentally different than in chain-growth. In step-growth polymerizations, monomers are generally linked by a carbon-heteroatom bond (C-O & C-N) formed in non-sequential steps. Often, the reactions used to link these monomers include multiple nucleophilic acyl substitutions. Step-growth polymerizations usually use two different monomers, neither of which would undergo polymerization on its own. The two monomers are multifuntional and complementary to each other, such that each provides the other with a reactive partner. In this section, we will be focusing on monomers which are **difunctional**, meaning they contain two of the same reactive functional group. A step-growth polymerization starts with two complementary functional groups on different monomers reacting to form a dimer. Because both monomers were difunctional, each retains a reactive group and can react with additional complementary monomers.

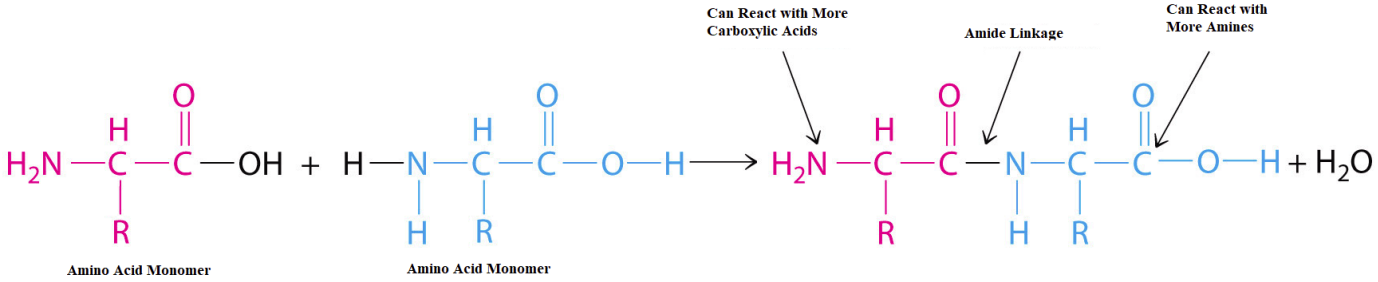


In fact the difuctionality of the monomers, allows step-growth polymers to grow in two directions at once. First, two complementary monomers react with each other to form a dimer. Assuming that monomers react at roughly similar rates, when one end of the dimer reacts again it will likely find another dimer and form a tetramer. Then when the tetramer goes to react again it will most likely find another tetramer and form an octamer. This process is repeated allowing the polymer to grow in two directions at the same time.



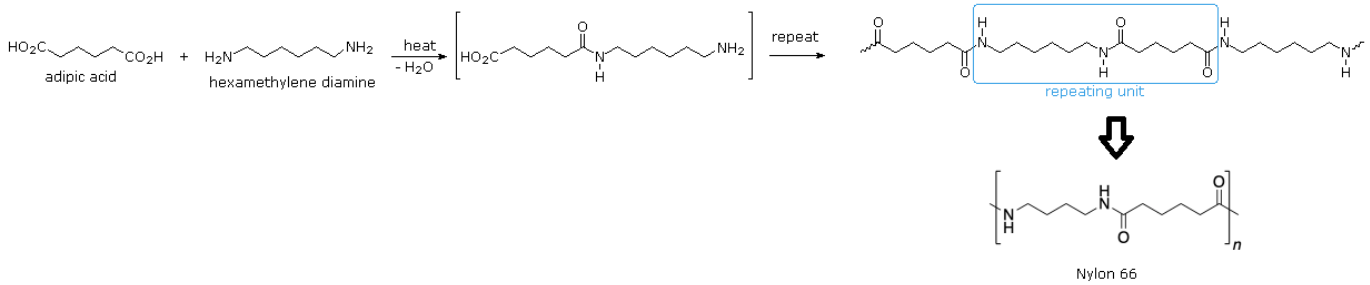
The Step-Growth Polymerization Process

Virtually all fibers are made from some form of polymer. In particular, silk and wool are composed of a naturally occurring protein polymer. The monomers of proteins are called **amino acid residues**. These residues are connected by amide linkages which are also called **peptide bonds**. Many of the early efforts of polymer chemistry were to artificially create fibers which mimicked the properties of silk and wool.

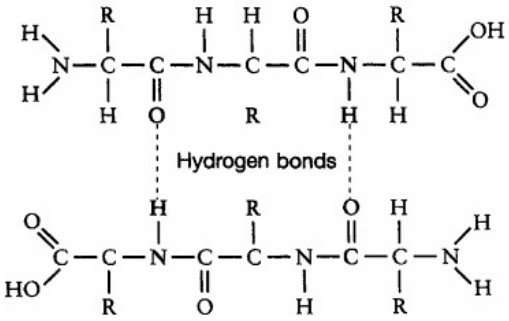


Polyamides

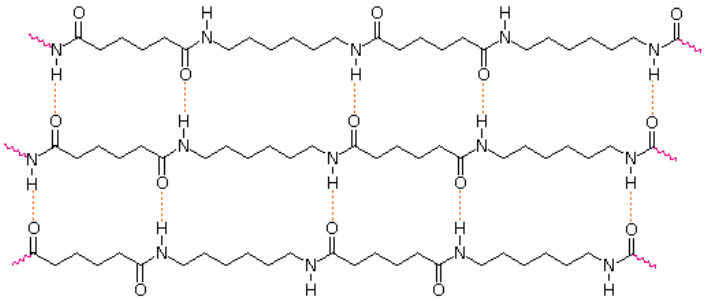
The first fully synthetic polymer fiber, nylon-6,6, was produced in 1938 by the company DuPont. The lead chemist of DuPont's work was Wallace H. Carothers, who reasoned that the properties of silk could be mimicked by constructing a polymer chain created with repeating amide bonds, just like the proteins in silk. Nylon-6,6 was created by first reacting 1,6-hexanedioic acid (adipic acid) and 1,6-hexanediamine to give a salt which was then heated creating multiple amide bonds through nucleophilic acyl substitution. The product of this particular reaction is a polyamide called nylon-6,6. The numbers of the name indicate how many carbons are contained in each monomer. The first “6” stands for the number of carbons in the diamine monomer while the second number indicated the number of carbons in the dicarboxylic acid. Simply by varying the number of carbons in each monomer, a wide variety of nylon polymers can be made.



Nylons are among the most widely used synthetic fibers—for example, they are used in ropes, sails, carpets, clothing, tires, brushes, and parachutes. Known for their high strength and abrasion resistance, nylons can be molded into blocks for use in electrical equipment, gears, bearings, and valves. The strength of nylon fibers comes, in part, from their ability to form strong hydrogen bonding intermolecular forces with each other in much the same fashion as proteins.



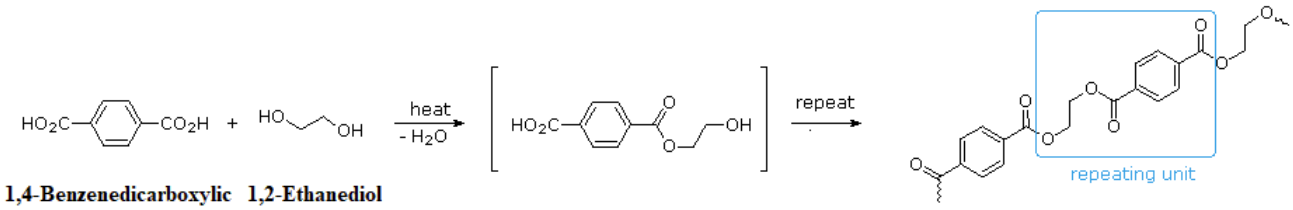
The Hydrogen Bonding between Proteins



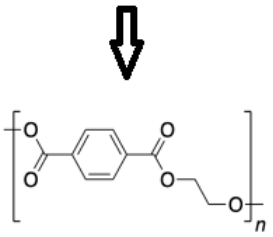
The Hydrogen Bonding between Nylon Polyamides

Polyesters

Esterfication, via nucleophilic acyl substitutions, can also be used to form the primary linkages in step-growth polymers. A polyester is typically produced when a dicarboxylic acid and a diol are reacted together. After the initial reaction, the ester product contains a free (unreacted) carboxyl group at one end and a free alcohol group at the other. Further esterification using a step-growth polymerization, produces a polyester. The most important polyester, polyethylene terephthalate (PET), is made from the reaction of 1,4-benzenedicarboxylic (terephthalic acid) and 1,2-ethanediol (ethylene glycol) monomers.



1,4-Benzenedicarboxylic 1,2-Ethanediol

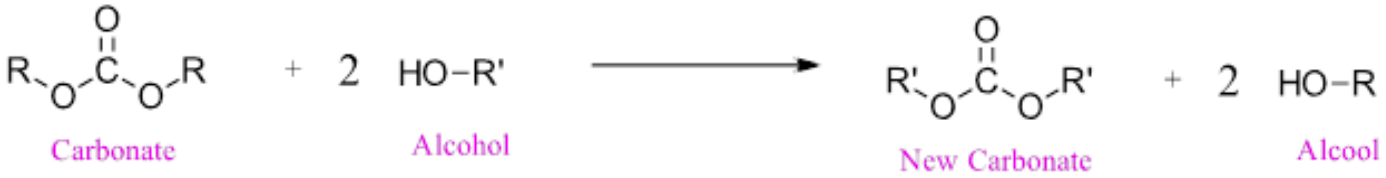


poly(ethyleneterephthalate)
(PET)
A Polyester

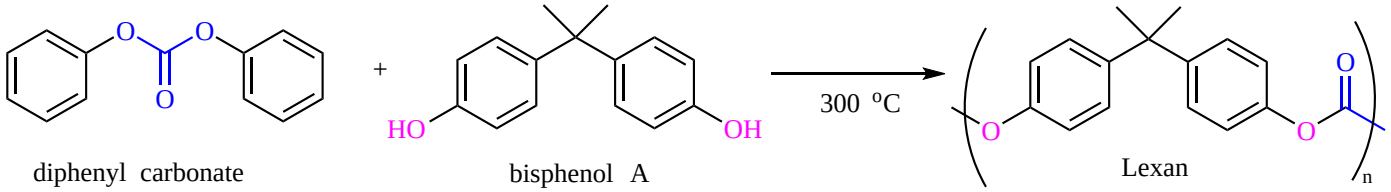
Polyester molecules make excellent fibers and are used in many fabrics. A knitted polyester tube, which is biologically inert, can be used in surgery to repair or replace diseased sections of blood vessels. PET is used to make bottles for soda and other beverages. It is also formed into films called Mylar. When magnetically coated, Mylar tape is used in audio- and videocassettes.

Polycarbonates

Beyond carboxylic acid derivatives, virtually any reaction which involves reactive species on two different molecules can be used to perform a step-growth polymerization. A variation involves using a monomer containing a carbonate functional group. A carbonate acts like a double ester and can undergo a type of double transesterification reaction with two alcohols to form a new carbonate containing compound.



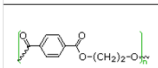
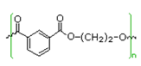
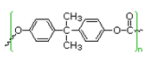
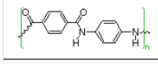
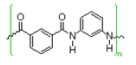
In effect, a carbonate is difunctional and can be reacted with a diol to form polymers containing repeated carbonate groups in their structure called polycarbonates. An example of a polycarbonate is the polymer, Lexan, which is created when diphenyl carbonate and bisphenol A (a diol) are reacted together.



diphenyl carbonate bisphenol A

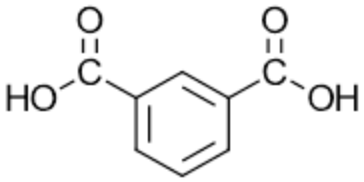
Polycarbonates used in engineering are strong, tough materials, and some grades are optically transparent. They are easily worked, molded, and thermoformed. Because of these properties, polycarbonates find many applications. One major application of polycarbonates is the production of compact discs, DVDs, and Blu-ray discs.

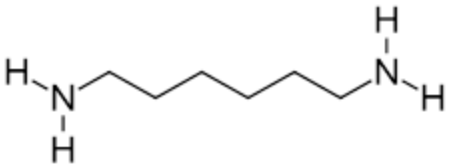
Bisphenol (BPA), primarily used to make polycarbonate, is one of the highest-volume chemicals produced in the world, with over six billion pounds made each year. Because polycarbonate is used to make plastic bottles, the lining for food cans, and the lining for beverage cans there has been much concern about trace amounts of BPA leaching from the containers and being ingested. A study conducted in 2003 and 2004 by the Center for Disease Control and Prevention found trace amounts BPA in the tissues of 93% of people in the United States. Consequently, this has led to many beverage companies switching to non-polycarbonate polymers.

Formula	Type	Components	T_g °C	T_m °C
~[CO(CH$_2$)$_4$CO-OCH$_2$CH$_2$O]$_n$~	polyester	HO$_2$C-(CH$_2$)$_4$-CO$_2$H HO-CH$_2$CH$_2$-OH	< 0	50
	polyester Dacron, Mylar	para HO$_2$C-C$_6$H$_4$-CO$_2$H HO-CH$_2$CH$_2$-OH	70	265
	polyester	meta HO$_2$C-C$_6$H$_4$-CO$_2$H HO-CH$_2$CH$_2$-OH	50	240
	polycarbonate Lexan	(HO-C$_6$H$_4$-)$_2$C(CH$_3$)$_2$ (Bisphenol A) X$_2$C=O (X = OCH$_3$ or Cl)	150	267
~[CO(CH$_2$)$_4$CO-NH(CH$_2$)$_6$NH]$_n$~	polyamide Nylon 66	HO$_2$C-(CH$_2$)$_4$-CO$_2$H H$_2$N-(CH$_2$)$_6$-NH$_2$	45	265
~[CO(CH$_2$)$_5$NH]$_n$~	polyamide Nylon 6 Perlon		53	223
	polyamide Kevlar	para HO$_2$C-C$_6$H$_4$-CO$_2$H para H$_2$N-C$_6$H$_4$-NH$_2$	---	500
	polyamide Nomex	meta HO$_2$C-C$_6$H$_4$-CO$_2$H meta H$_2$N-C$_6$H$_4$-NH$_2$	273	390

Example 8.15.1

Provide the structure of the polyamide made from the monomers as indicated. Please use bracketed notation.

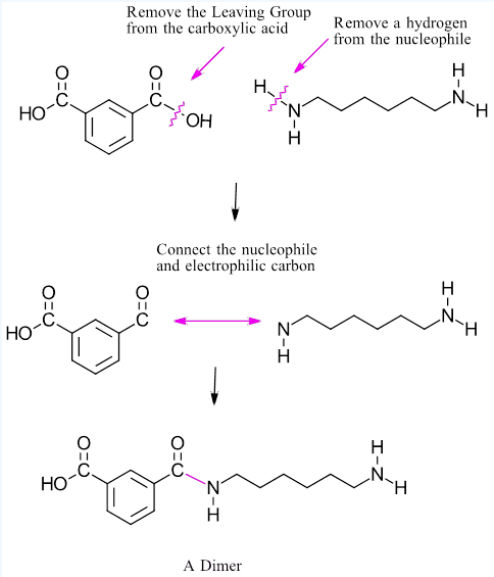




Solution

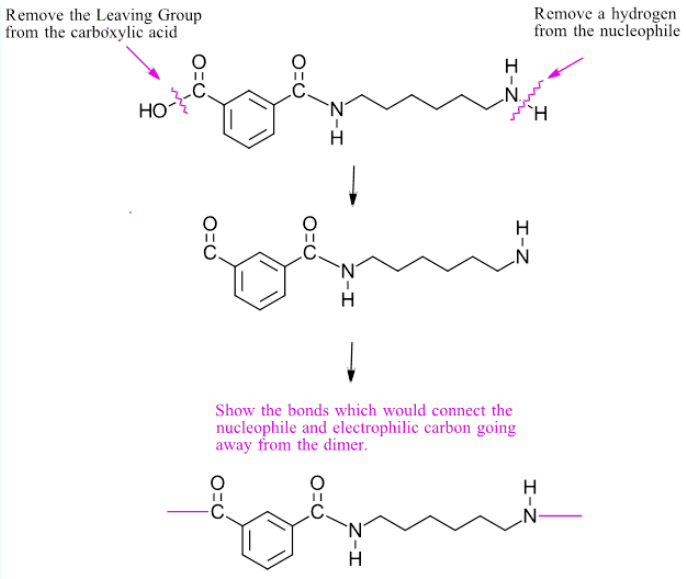
When drawing the polymer product of a step-growth polymerization, it is important to first identify the reaction which forms the repetitive linkage between monomers. In this case, the reaction is anucleophilic acyl substitution btween a carboxylic acid and an amine to form an amide. In total, the bracket structure of a polymer shows two versions of the linkage formation. The first is clearly shows connecting the monomers to form the dimer making up the repeating unit in the polymer. The second version involves bonds going out of the bracket and represents how the linkage repeats throughout the polymer.

1) The connect two monomers to make a dimer using the indicated reaction.

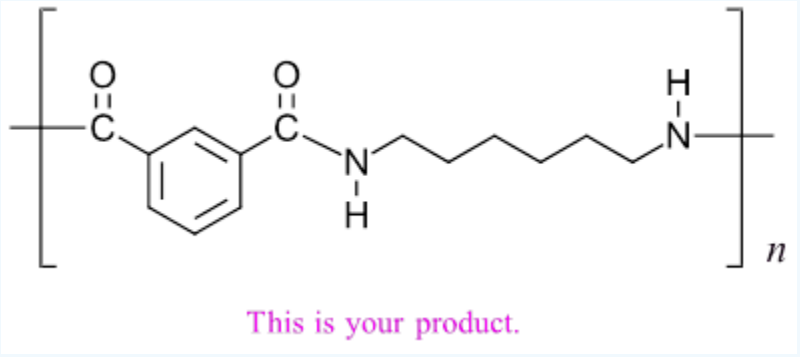


A Dimer

2) Beak the same bonds as before ecepptt the bonds for the final connection will be shown going away from the dimer.

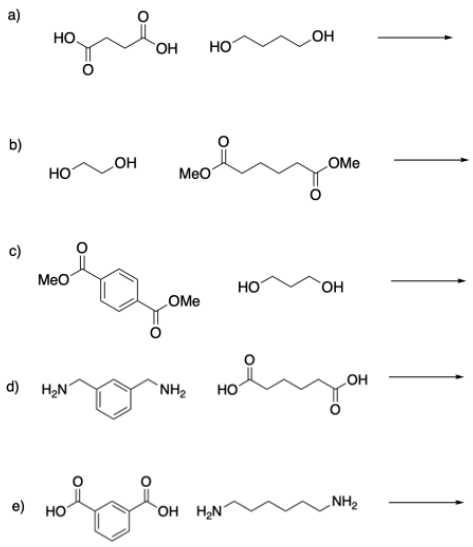


3) Place brackets around the dimer and put an italicized lower case "n" in the lower right.

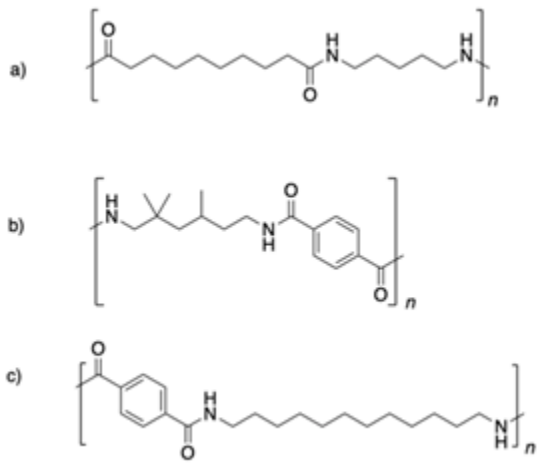


Exercises

1) Provide structures of the polyesters made from the monomers as indicated.

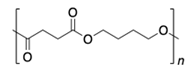


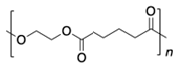
2) Identify the monomers that would be used to produce these polymers.

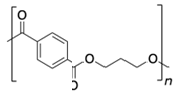


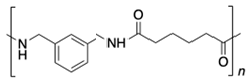
Solutions

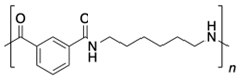
1)

a) 

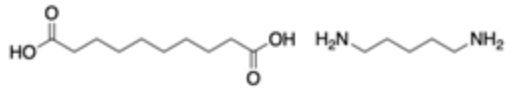
b) 

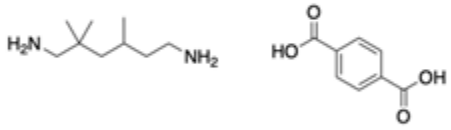
c) 

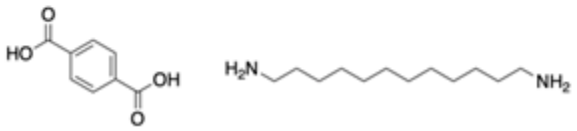
d) 

e) 

2)

a) 

b) 

c) 

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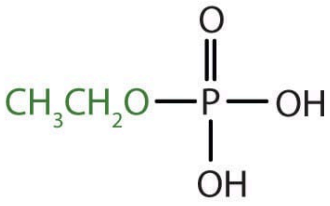
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8.16: Esters of Phosphoric Acid

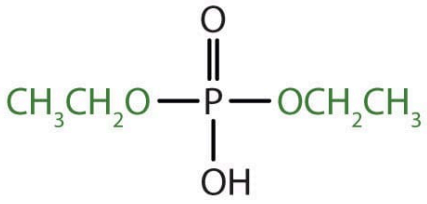
Learning Objectives

- Describe phosphate esters.
- Understand why phosphate esters are important in living cells.

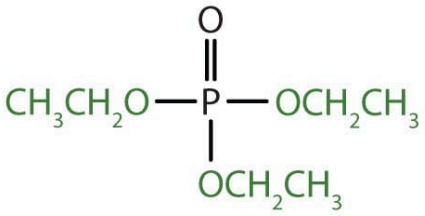
Just as carboxylic acids do, inorganic acids such as nitric acid (HNO_3), sulfuric acid (H_2SO_4), and phosphoric acid (H_3PO_4) also form esters. The esters of phosphoric acid are especially important in biochemistry. A phosphoric acid molecule can form a monoalkyl, a dialkyl, or a trialkyl ester by reaction with one, two, or three molecules of an alcohol.



Ethyl dihydrogen phosphate

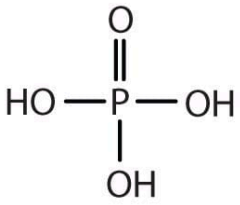


Diethyl hydrogen phosphate

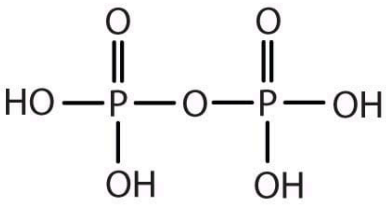


Triethyl phosphate

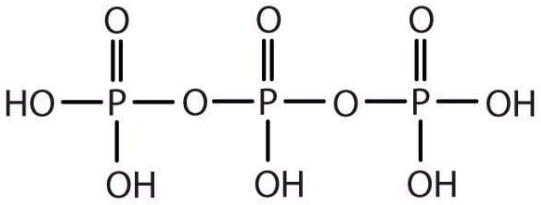
Esters of pyrophosphoric acid and triphosphoric acid are also important in biochemistry.



Phosphoric acid



Pyrophosphoric acid

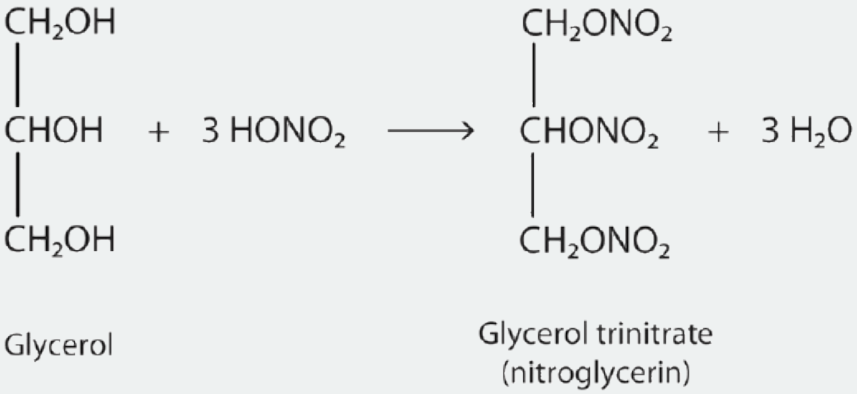


Triphosphoric acid

Esters of these acids are present in every plant and animal cell. They are biochemical intermediates in the transformation of food into usable energy. The bonds between phosphate units in adenosine triphosphate (ATP) are called **phosphoanhydride bonds**. These are high-energy bonds that store energy from the metabolism of foods. Hydrolysis of ATP releases energy as it is needed for biochemical processes (for instance, for muscle contraction). Phosphate esters are also important structural constituents of phospholipids and nucleic acids.

Nitroglycerin

The explosive nitroglycerin (glyceryl trinitrate) is an ester formed from glycerol and nitric acid. It is used in medicine to relieve chest pain in heart disease.



8.16.1Exe

What compounds combine to form phosphate esters?

Answer available at the end of this section.

Summary

Inorganic acids such as H_3PO_4 form esters. The esters of phosphoric acid are especially important in biochemistry.

Answers

phosphoric acids and alcohols

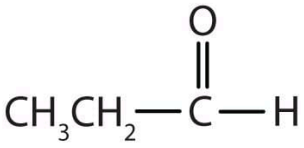
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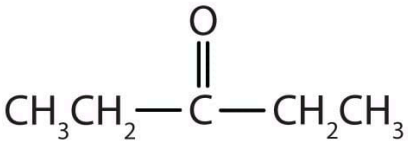
- 15.9: Esters of Phosphoric Acid by Staff is licensed CC BY-NC-SA 3.0. Original source: https://2012books.lardbucket.org/books/introduction-to-chemistry-general-organic-and-biological.

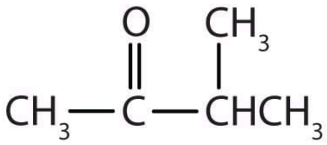
8.17: Carbonyl-Containing Compounds (Exercises)

Additional Exercises

1. Name each compound.

a. 

b. 

c. 

2. Draw the structure for each compound.
   a. butyraldehyde
   b. 2-hexanone
   c. *p*-nitrobenzaldehyde

3. Which compound in each pair has the higher boiling point?
   a. hexanal or 2-hexanol
   b. butane or 2-propanone

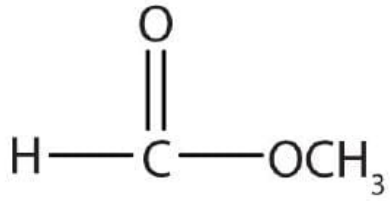
4. Draw the structure for each compound.
   a. *o*-nitrobenzoic acid
   b. *p*-chlorobenzoic acid
   c. 3-chloropentanoic acid
   d. α-chloropropionic acid

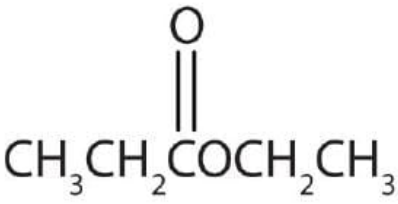
5. Name each compound with either the IUPAC name, the common name, or both.
   a. $(CH_3)_2CHCH_2COOH$
   b. $(CH_3)_3CCH(CH_3)CH_2COOH$
   c. $CH_2BrCH_2CH_2COOH$

6. Which compound has the higher boiling point: 1-pentanol or butanoic acid? Explain.

7. Which compound is more soluble in water: propanoic acid or hexanoic acid? Explain.

8. Name each compound with both the common name and the IUPAC name.

a. 

b. 

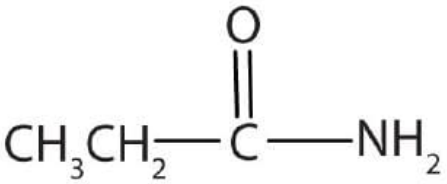
9. Draw the structure for each compound.
   a. ethyl hexanoate
   b. ethyl benzoate
   c. ethyl 3-methylhexanoate

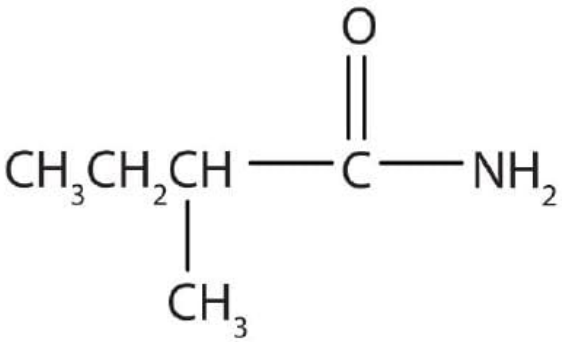
10. Which compound has the higher boiling point: 1-octanol or ethyl hexanoate? Explain.

11. Which compound is more soluble in water: methyl ethanoate or propanoic acid? Explain.

12. Draw the structure for each compound.
   a. propionamide
   b. butanamide

13. Name each compound with the common name, the IUPAC name, or both.

a. 

b. 

14. Which compound has the higher boiling point—butyramide or dimethylacetamide? Explain.

15. Which compound is more soluble in water: N-methylethanamide or 2-methylbutane? Explain.

Answers

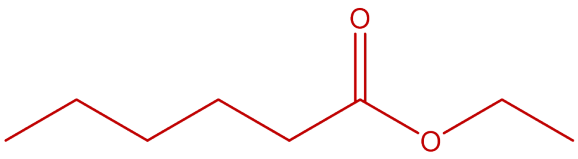
1. a. IUPAC: propanal; Common: propionaldehyde
   b. IUPAC: 3-pentanone; Common: diethyl ketone
   c. IUPAC: 3-methyl-2-butanone; Common: isopropyl methyl ketone

3. a. 2-hexanol
   b. 2-propanone

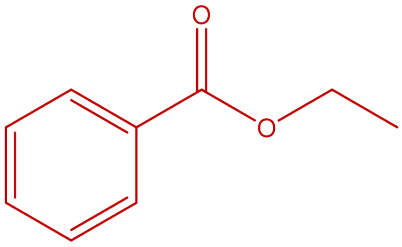
5. a. IUPAC: 3-methylbutanoic acid; Common: β-methylbutyric acid
   b. IUPAC: 3,4,4-trimethylpentanoic acid; no common name
   c. IUPAC: 4-bromobutanoic acid; Common: γ- bromobutyric acid

7. Propanoic acid because both molecules can form hydrogen bonds, but this compound is more polar. As the carbon chain length increases because dipole forces become less important and dispersion forces become more predominant.

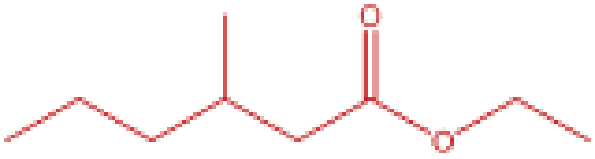
9. a.



b.



c.



11. Propanoic acid because it can form hydrogen bonds with water.

13. a. common: propionamide; IUPAC: propanamide
    b. common: α-methylbutyramide; IUPAC: 2-methylbutanamide

15. N-methylethanamide because it can form hydrogen bonds with water.

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9: LIPIDS

9.1: Prelude to Lipids

9.2: Fatty acyls

9.3: Glycerolipids

9.4: Membranes and Membrane Lipids

9.5: Cell membrane

9.6: Sterols

9.7: Lipid Soluble Vitamins

9.8: Prostaglandins and Other Eicosanoids

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9.1: Prelude to Lipids

Lipids

Fats and oils, found in many of the foods we eat, belong to a class of biomolecules known as lipids. Gram for gram, they pack more than twice the caloric content of carbohydrates: the oxidation of fats and oils supplies about 9 kcal of energy for every gram oxidized, whereas the oxidation of carbohydrates supplies only 4 kcal/g. Although the high caloric content of fats may be bad news for the dieter, it says something about the efficiency of nature's designs. Our bodies use carbohydrates, primarily in the form of glucose, for our *immediate* energy needs. Our capacity for storing carbohydrates for later use is limited to tucking away a bit of glycogen in the liver or in muscle tissue. We store our *reserve* energy in lipid form, which requires far less space than the same amount of energy stored in carbohydrate form. Lipids have other biological functions besides energy storage. They are a major component of the membranes of the 10 trillion cells in our bodies. They serve as protective padding and insulation for vital organs. Furthermore, without lipids in our diets, we would be deficient in the fat-soluble vitamins A, D, E, and K.

Lipids are not defined by the presence of specific functional groups, as carbohydrates are, but by a physical property—solubility. Compounds isolated from body tissues are classified as lipids if they are more soluble in organic solvents, such as dichloromethane, than in water. By this criterion, the lipid category includes not only fats and oils, which are esters of the trihydroxy alcohol glycerol and fatty acids, but also compounds that incorporate functional groups derived from phosphoric acid, carbohydrates, or amino alcohols, as well as steroid compounds such as cholesterol (Figure 9.1.1 presents one scheme for classifying the various kinds of lipids). We will discuss the various kinds of lipids by considering one subclass at a time and pointing out structural similarities and differences as we go.

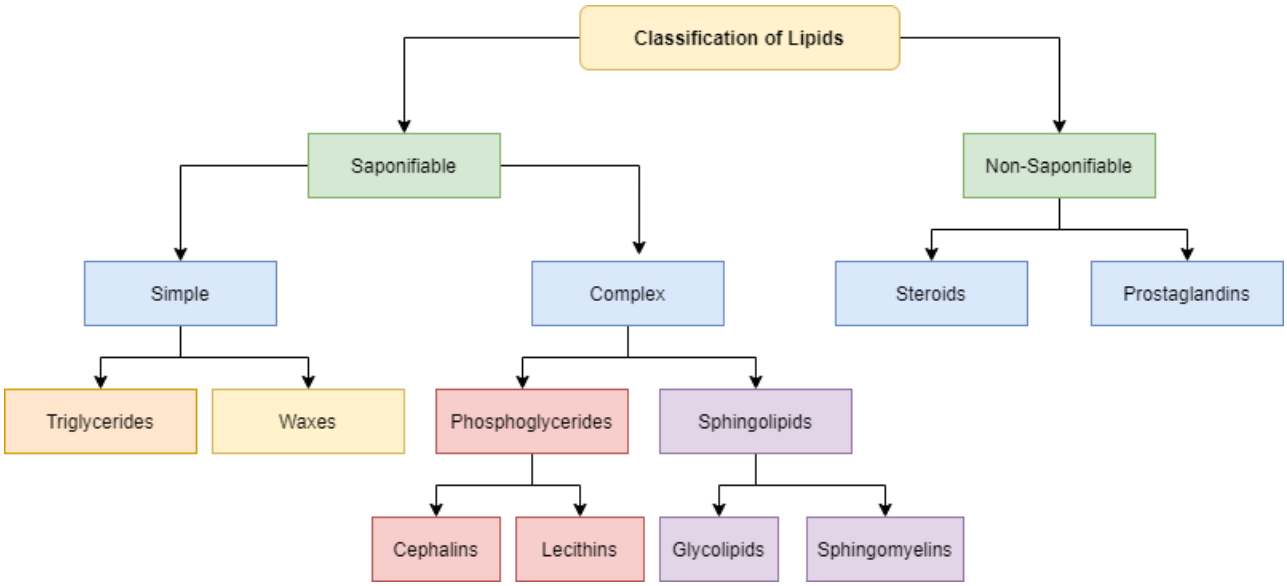


Figure 9.1.1: Lipid Organization Based on Structural Relationships

Sources

- Ball et al. The Basics of GOB Chemistry. LibreTexts adapted under CC BY-NC-SA 3.0 license.
- Seager, S. L., Hensen, M. S., & Slabaugh, M. R. (2018). *Chemistry for today: General, organic, and biochemistry* (9th ed.). Boston, MA, USA: Brooks/Cole, Cengage Learning.

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9.2: Fatty acyls

Learning Objectives

- Understand the basic structural features of fatty acids, the notations reflecting them, and their relationship to the melting points and health effects.
- Define essential fatty acids, omega fatty acids, and their importance.
- Understand the basic structure features, nomenclature, and functions of prostaglandins.
- Understand the structures and uses of important waxes.

Fatty acyls are a group of lipids that contain a fatty acid or its derivative.

Fatty acids

Fatty acids

Fatty acids are carboxylic acids with an alkyl chain that is usually unbranched and containing an even number of $\mathrm{C}'\mathrm{s}$, usually between 8 to 20 $\mathrm{C}'\mathrm{s}$.

Figure $9.2.1$ shows some examples of fatty acids that have 18 $\mathrm{C}'\mathrm{s}$ in the chain. Carboxylic acid group ($-\mathrm{COOH}$ is hydrophilic, and the alkyl chain is hydrophobic, making fatty acids amphiphilic. The hydrophobic property of the long alkyl chain dominates, making fatty acids insoluble in water.

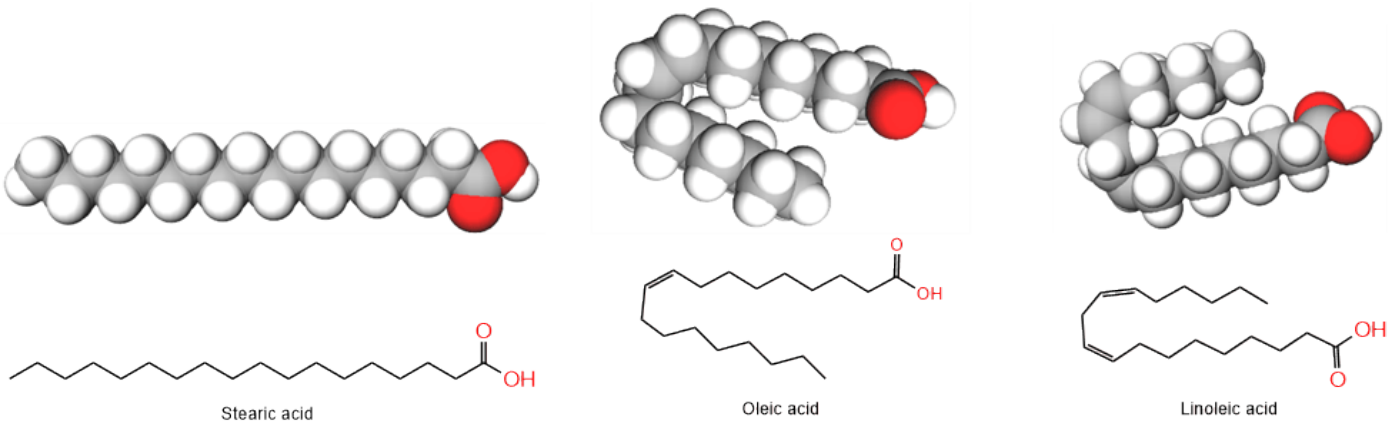


Figure $9.2.1$: Examples of fatty acids: a saturated steric acid (18:0), a monounsaturated oleic acid (18:1), and a polyunsaturated linoleic acid (18:2). Skeletal formulas are shown with the corresponding space-filling model shown on the top of each of the skeletal formula. (Copyright; Public domain)

Unsaturated, monounsaturated, and polyunsaturated fatty acids

- The alkyl chain can be saturated with all $\mathrm{C}-\mathrm{C}$ σ-bonds, called **saturated fatty acid (SFA)**, e.g., steric acid;
- or may contain some double bonds ($\mathrm{C}=\mathrm{C}$), called **unsaturated fatty acid (USFA)**., e.g., oleic acid and linoleic acid Figure $9.2.1$.
  - The unsaturated fatty acid may have one $\mathrm{C}=\mathrm{C}$ bond called **monounsaturated fatty acid (MUFA)**, e.g., oleic acid;
  - or more than one $\mathrm{C}=\mathrm{C}$ bonds called **polyunsaturated fatty acid (PUFA)**, e.g., linoleic acid.

Notations for and labelling $\mathrm{C}'\mathrm{s}$ in fatty acids

Short notations

Carboxylic acids are usually referred to by their trivial names. **Short notation** is used to indicate # of $\mathrm{C}'\mathrm{s}$:# of $\mathrm{C}{=}\mathrm{C}$ bonds, e.g., steric acid Figure $9.2.1$ is 18:0 meaning eighteen carbons and zero double bonds. Similarly, oleic acid is 18:1 meaning eighteen carbons and one double bond, and linoleic acid is 8:2 meaning eighteen carbons and two double bonds.

Labelling $\mathrm{C}'\mathrm{s}$

Systematic IUPAC nomenclature starts numbers from carbonyl-carbon ($\mathrm{C}{=}\mathrm{O}$) as shown in Figure $9.2.2$, red numbers. Trivial nomenclature uses Greek alphabets starting from C#2 as α, next one as β, than γ, and so on, as shown in Figure $9.2.2$, black numbers. **IUPAC short** notation shows the position labels of the double bonds' first $\mathrm{C}'\mathrm{s}$ in a bracket, separated by commas, next to the regular short notation. The numbering begins from ($-\mathrm{COOH}$ end. For example, steric acid 18:0, i.e., eighteen carbons and zero double bonds, oleic acid is 18:1(9), i.e., eighteen carbons and one double bond at C# 9, and linoleic acid is 18:2(9, 12), i.e., eighteen carbons and bonds, one at C# 9 and the other at C# 12.

Omega-minus (ω-#) labeling

In omega-minus (ω-#) labeling the last C, i.e., the $-\mathrm{CH_3}$ at the end opposite to carboxyl ($-\mathrm{COOH}$) group is labeled ω-1, the C next to it as ω-2, than ω-3 and so on, as as shown in Figure $9.2.2$, in blue fonts. Recall that ω is the last alphabet in Greek, so, ω-1 is the last carbon. **The "omega-#"** (ω-#) label is usually used to refer to the position of the first C of the first $\mathrm{C}{=}\mathrm{C}$ bond from the ω -end, i.e., from the $-\mathrm{CH_3}$ end, opposite to the $-\mathrm{COOH}$ end. For example, α-linolenic acid in Figure $9.2.2$ is an ω-3 fatty acid.

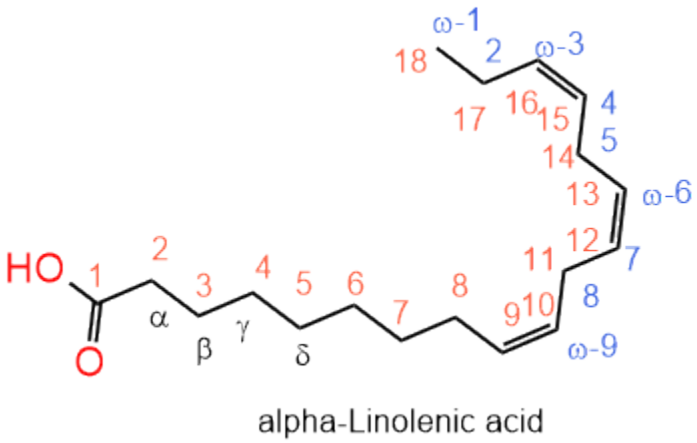


Figure $9.2.2$: Labelling of $\mathrm{C}'\mathrm{s}$ in fatty acids: systematic IUPAC numbers are in red, nonsystematic Greek letter labels are in black, and omega-minus (ω-#) are in blue. (Copyright; Public domain)

Table 1 lists common fatty acids with their IUPAC short notations, ω-#, and melting points.

Table 1: Some of the common fatty acids

Common name	Condensed formula	IUPAC notation*
Saturated fatty acids		
Caprylic acid	$\mathrm{CH_3(CH_2)_6COOH}$	8:0
Capric acid	$\mathrm{CH_3(CH_2)_8COOH}$	10:0
Lauric acid	$\mathrm{CH_3(CH_2)_{10}COOH}$	12:0
Myristic acid	$\mathrm{CH_3(CH_2)_{12}COOH}$	14:0

Common name	Condensed formula	IUPAC notation*
Palmitic acid	$CH_3(CH_2)_{14}COOH$	16:0
Stearic acid	$CH_3(CH_2)_{16}COOH$	18:0
Arachidic acid	$CH_3(CH_2)_{18}COOH$	20:0
Monounsaturated fatty acids		
Myristoleic acid	$CH_3(CH_2)_3$**CH=CH**$(CH_2)_7COOH$	14:1(9)
Oleic acid	$CH_3(CH_2)_7$**CH=CH**$(CH_2)_7COOH$	18:1(9)
Elaidic acid	$CH_3(CH_2)_7$**CH=CH**$(CH_2)_7COOH$	18:1(9t)
Erucic acid	$CH_3(CH_2)_7$**CH=CH**$(CH_2)_{11}COOH$	22:1(13)
Polyunsaturated fatty acids		
Linoleic acid	$CH_3(CH_2)_4$**CH=CH**CH_2**CH=CH**$(CH_2)_7COOH$	18:2(9,12)
α-Linolenic acid	CH_3CH_2**CH=CH**CH_2**CH=CH**CH_2**CH=CH**$(CH_2)_7COOH$	18:3(9,12,15)
Arachidonic acid	$CH_3(CH_2)_4$**CH=CH**CH_2**CH=CH**CH_2**CH=CH**CH_2**CH=CH**$(CH_2)_3COOH$	20:4(5,8,11,14)
Eicosapentaenoic acid	CH_3CH_2**CH=CH**CH_2**CH=CH**CH_2**CH=CH**CH_2**CH=CH**CH_2**CH=CH**$(CH_2)_3COOH$	20:5(5,8,11,14,17)
Docosahexaenoic acid	CH_3CH_3**CH=CH**CH_2**CH=CH**CH_2**CH=CH**CH_2**CH=CH**CH_2**CH=CH**CH_2**CH=CH**$(CH_2)_2COOH$	22:6(4,7,10,13,16,19)

* IUPAC notation shows Numbers of $C's$:number of double bonds(position of *cis*-double bond, except when there is symbol t for *tra*

Essential fatty acids

α-Linolenic acid (18:3(9,12,15)) -an ω–3 fatty acid, and linoleic acid (18:2(9,12)) - an ω–6 fatty acid are **essential fatty acids (EFAs)** because humans and other animals cannot synthesize them. They must be included in the diet as they are needed for good health. Although eicosapentaenoic acid (20:5(5,8,11,14,17)) and docosahexaenoic acid (22:6(4,7,10,13,16,19)),

called **long-chain unsaturated fatty acids**, can be synthesized from α-linolenic acid, the conversion efficiency is low, and it is recommended that these should also be included in the diet. Arachidonic acid (20:4(5,8,11,14)) is another long-chain unsaturated fatty acid that can be synthesized from linoleic acid.

Shapes and physical properties of fatty acids

Shapes

The saturated fatty acids are cylindrical that pack nicely in the solid state with a large contact area between the molecules. The double bonds in unsaturated fatty acids are usually in the *cis* configuration. A *cis*-$\mathrm{C{=}C}$ introduces a kink in the structure that does not let molecules pack with a large contact area between neighboring molecules, as illustrated in Figure $9.2.3$. Some unsaturated fatty acids have *trans*-double bonds and are cylindrical, like saturated fatty acids, but they are rare.

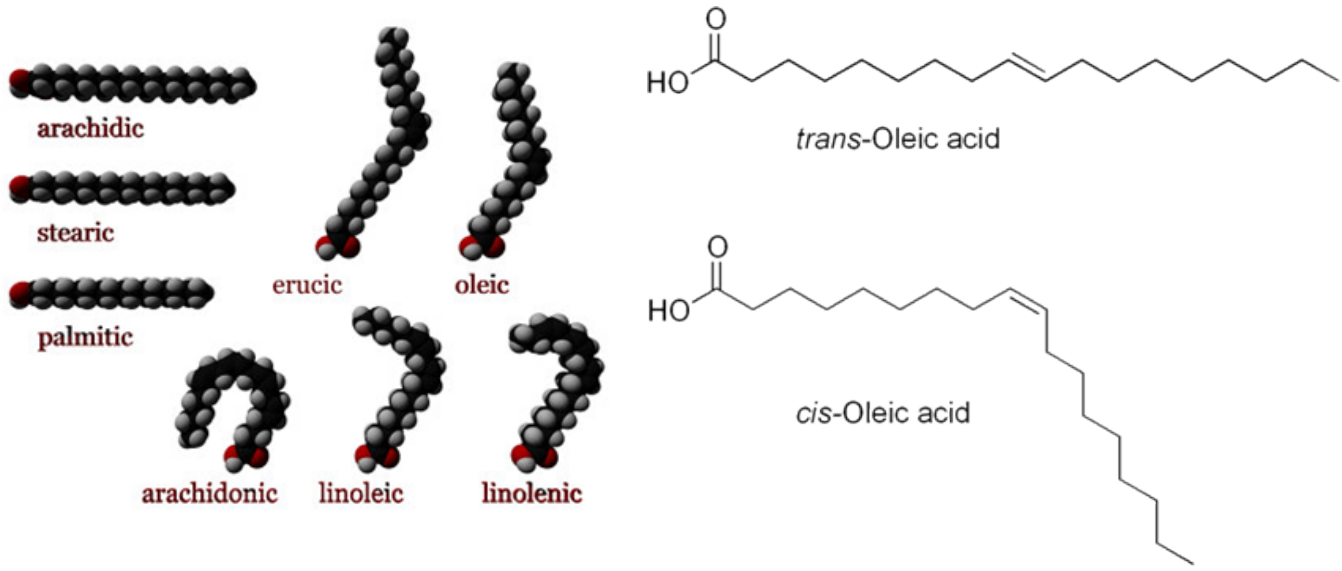


Figure $9.2.3$: Three-dimensional representations of several fatty acids. Saturated fatty acids (arachidic 20:0, steric acid 18:0. palmitic acid 16:0) are cylindrical. Unsaturated ones (erucic 21:1, oleic 18:1, arachidonic 20:4, linoleic 18:2, and linolenic (18:3) are typically bent unless they have a trans configuration (Copyright: Automated conversion, CC BY-SA 3.0, via Wikimedia Commons), right: Oleic acid and its trans isomer (Copyright: Edgar181, Public domain, via Wikimedia Commons)

Melting points

The melting point of fatty acids is affected by two factors, as shown in Table 1:

1. an increase in the number of $\mathrm{C's}$ increases the melting point because it increases London dispersion forces holding the molecules together, and
2. the presence of *cis*-$\mathrm{C{=}C}$ bond decreases the melting point due to the kink in the structure that reduces the contact area between molecules and, consequently, London dispersion forces are less.

Fats containing saturated fatty acids are considered unhealthy as they tend to deposit in arteries forming plaque, i.e., atherosclerosis. It can lead to high blood pressure, rupture of arteries, or heart attack. Saturated fatty acids are more common in animal fats, while unsaturated fatty acids, considered healthier, are more common in vegetable oils.

It has been observed that people from Alaska eat more unsaturated fats and have a low occurrence of atherosclerosis and heart attack. Fats in Alaskan food is primarily from fish, such as salmon, tuna, and herring, as shown in Figure $9.2.4$. Vegetable oils have higher contents of ω-6 fatty acids, such as linoleic acid and arachidonic acid. Fish oil mainly contains ω-3 fatty acids, such as linolenic acid, eicosapentaenoic acid, and docosahexaenoic acid.

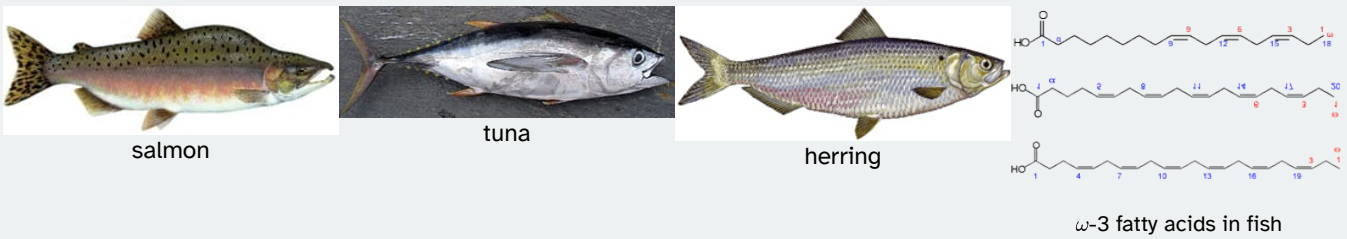


Figure 9.2.4: Three common fish in the diet of people of Alaska and three common ω-3 fatty acids found in the fish: linolenic acid (top), eicosapentaenoic acid (middle), and docosahexaenoic acid (bottom). (Copyright: Public domain).

Prostaglandins

Prostaglandins are lipids containing 20 $C's$ that are derived from arachidonic acid (20:4(5, 8, 11, 14)) and act like hormones. They are found in small concentrations in almost all body tissues and cells. Their activities include blood pressure regulation, blood clotting, inflammation, gastric secretions, kidney functions, and reproductive activities. They are usually short-lived and produced locally where they perform their function.

Prostaglandins synthesis

Prostaglandins synthesis starts from arachidonic acid using enzymes like cyclooxygenase (COX-1 and COX-2) and prostaglandin synthase, like PGE-synthase and PGF-synthase, as illustrated in Figure 9.2.5. The prostaglandins have a five-membered ring and two side chains. The prostaglandin PGG_2 is synthesized from arachidonate and quickly converts to PGH_2. PGH_2 regulates constriction and dilation of blood vessels and stimulates platelet aggregation. PGH_2 converts to PGE_2 and PGF_2 which induce labor by stimulating uterine contraction. PGF_2 also lowers blood pressure by relaxing smooth muscle cells in blood vessels. PGH_2 is also a precursor of several other Prostaglandins and related biomolecules.

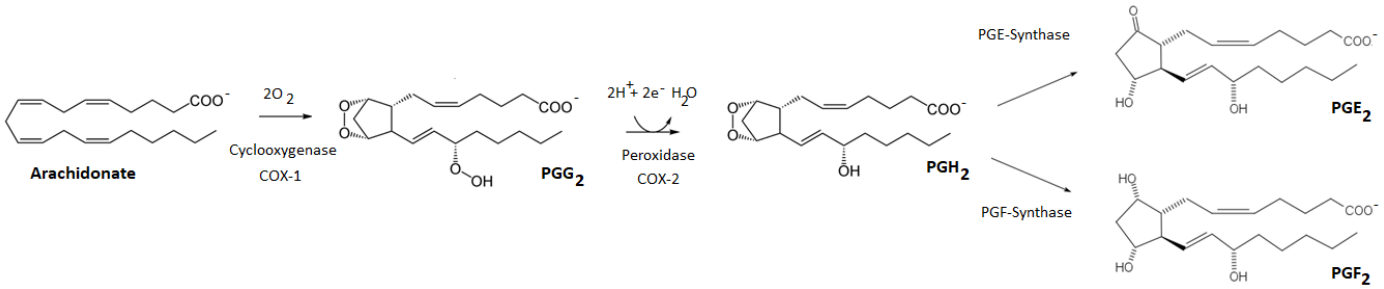


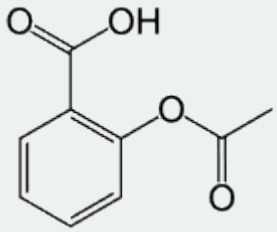
Figure 9.2.5: Synthesis of some prostaglandins from arachidonate. (Copyright; Public domain)

Prostaglandins names

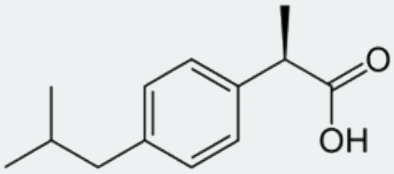
The names of prostaglandins are abbreviated as three letters followed by a subscript, where the first two letters, i.e., PG, stands for prostaglandin, the 3rd letter indicates the substitution pattern, and the subscript tells the number of $C{=}C$ bonds in the side chains. For example, the 3rd letter G has endoperoxide in the ring and a hydroperoxide group at $C's$ 15, H has endoperoxide in the ring, and a hydroxyl group at $C's$ 15, E has a β-hydroxyketone, and F has a 1,3-diol groups in the ring. The subscript 2 shows two $C{=}C$ bonds in the side chains. The letter E in PGE_2 also indicates that it is soluble in ether and F in PGF_2 indicates it is soluble in phosphate buffer.

Nonsteroidal anti-inflammatory drugs (NSAIDs) action on prostaglandin synthesis

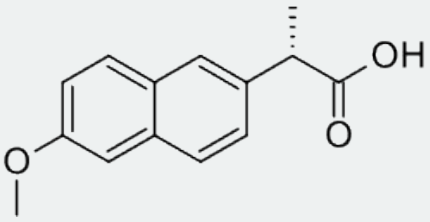
When tissues are injured, arachidonic acid is converted into prostaglandins that cause inflammation and pain. Nonsteroidal anti-inflammatory drugs, like aspirin, ibuprofen, and naproxen, shown below, inhibit the conversion of arachidonic acid into prostaglandins. Ibuprofen and naproxen inhibit the cyclooxygenase (COX) enzyme by binding with it. Aspirin deactivates the cyclooxygenase (COX) by transferring an acetyl group to the hydroxyl group of the active site of the cyclooxygenase. Care must be taken using NSAIDs as their long-term use can cause gastrointestinal, liver, or kidney damage.



aspirin



ibuprofen

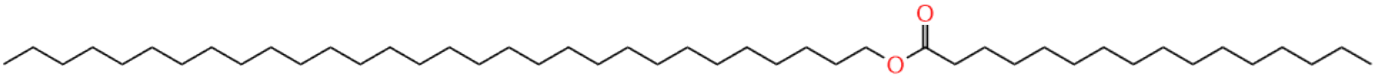


naproxen

Waxes

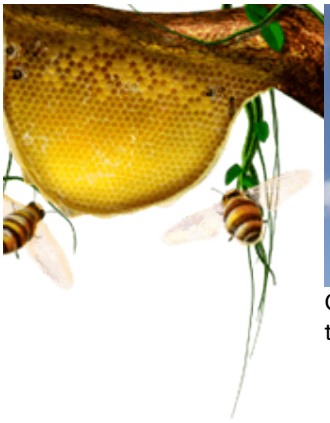
Lipid waxes are esters of one long-chain fatty acid with unbranched long-chain alcohol containing 14 to 30 $\mathrm{C's}$ per chain. For example, myricyl palmitate found in beeswax can be obtained by the esterification of palmitic acid and myricyl alcohol:

$$\mathrm{CH_3(CH_2)_{14}\text{-}\overset{\overset{\mathrm{O}}{\|}}{\mathrm{C}}\!-\!OH + HO\text{-}(CH_2)_{29}CH_3 \longrightarrow CH_3(CH_2)_{14}\text{-}\overset{\overset{\mathrm{O}}{\|}}{\mathrm{C}}\!-\!O\text{-}(CH_2)_{29}CH_3 + H_2O}$$



Functions of waxes

Waxes form a waterproof coating on plants' leaves, fruits, and stems to minimize water evaporation and protect against parasites. Examples include palm trees and jojoba wax from jojoba bushes. The wax coating on animals' skin, fur, and feathers protects water birds from water wetting and rainwater and shelters them from rainwater. Bees use wax to construct protection and housing for honey, as illustrated below. Sperm whales use spermaceti wax in their heads as a part of their eco analysis, i.e., navigation system.



neycomb made of beeswax:

$$_3(CH_2)_{14}\text{-}\overset{O}{\overset{||}{C}}\text{-O-}(CH_2)_{29}CH_3$$



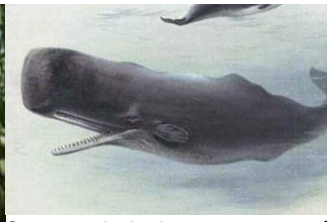
Carnauba wax coating on palm tree leaves:

$$CH_3(CH_2)_{24}\text{-}\overset{O}{\overset{||}{C}}\text{-O-}(CH_2)_{29}CH_3$$



Jojoba wax on leaves and fruits of jojoba bush:

$$CH_3(CH_2)_{18}\text{-}\overset{O}{\overset{||}{C}}\text{-O-}(CH_2)_{19}CH_3$$



Sperm whale has spermaceti in the head as a part of their analysis syterm:

$$CH_3(CH_2)_{14}\text{-}\overset{O}{\overset{||}{C}}\text{-O-}(CH_2)_{15}C$$

Figure 9.2.1: Examples of waxes, their uses, and formulas (Copyright: Public domain).

Beeswax and carnauba wax protective coatings on cars, furniture, floors, etc. Jojoba wax and spermaceti are used to make candles and cosmetics. A mixture of waxes obtained from wool is used in lotions for face and skin softening.

Petroleum waxes and earwax

Petroleum-derived waxes or paraffin are also called waxes, but they are not esters but mixtures of long-chain hydrocarbons. Earwax is a mixture of glycerol esters, cholesterol, phospholipids, etc., from dead skin and secretions of cerumen glands. Like other lipid waxes, it protects the ear canal against bacteria, fungi, and water. Excess earwax can cause blockage in the ear canal and hearing loss.

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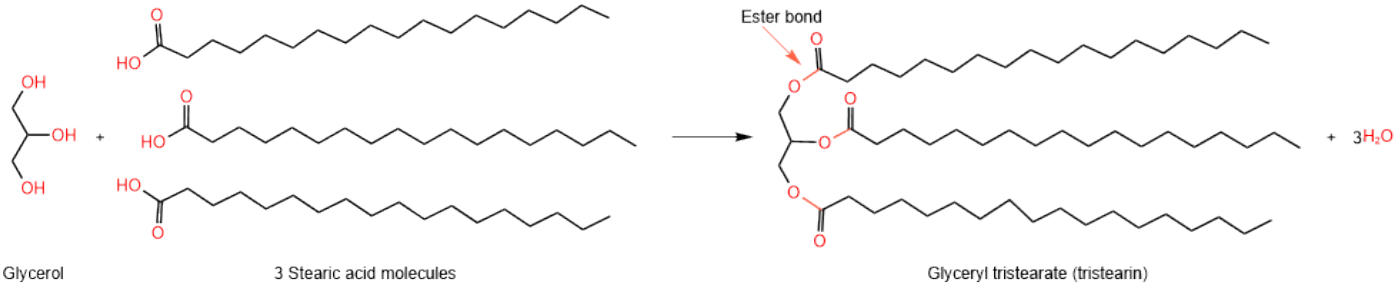
9.3: Glycerolipids

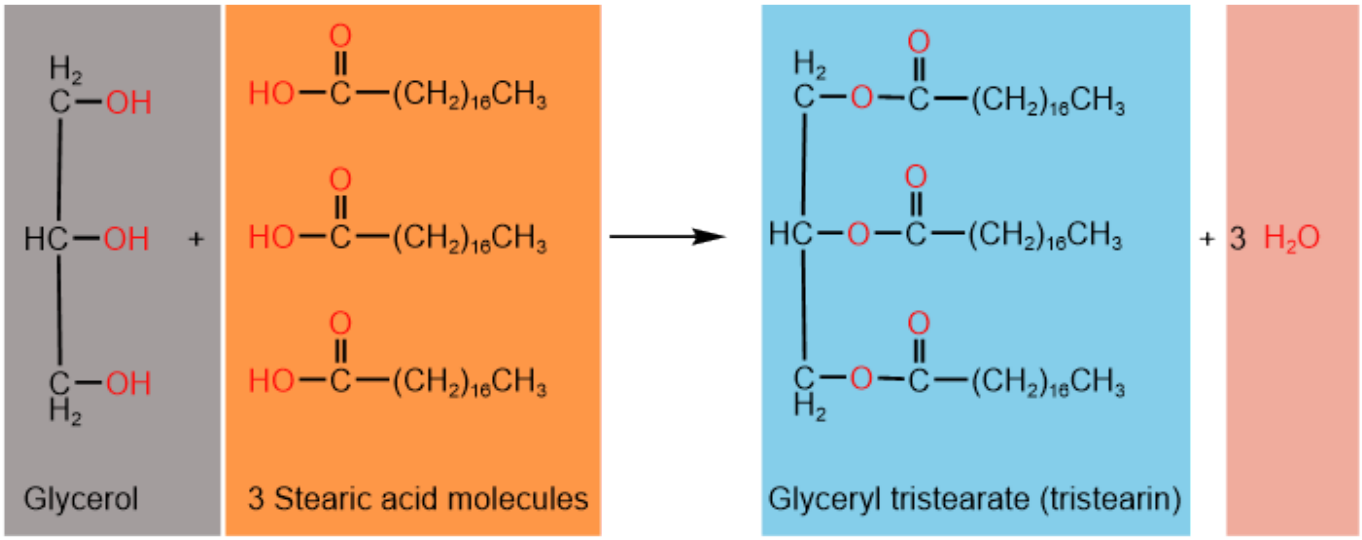
Learning Objectives

- Define glycerolipids and triglycerides and understand their structures.
- Understand the difference in composition and properties of fats and oils and their primary role as energy storage molecules.
- Understand the chemical properties of fats and oils, including hydrolysis, saponification, and partial or complete hydrogenation.

What is a glycerolipid?

Glycerolipids have two components: propane-1,2,3-triol, also called glycerol, and one, two, or three fatty acids. Recall that a condensation reaction between an alcohol and a carboxylic acid forms an ester by eliminating a water molecule. The following example shows the reaction of glycerol with three molecules of stearic acid, creating a triester.



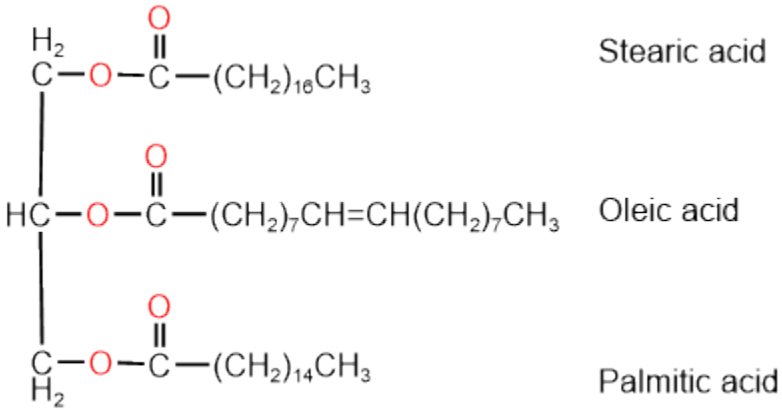


A mono-, di-, or tri-ester of glycerol is called glycerolipid.

The name of a glycerolipid begins with glyceryl and is followed by carboxylate. For example, the triester of glycerol shown above is glyceryl tristearate, which is commonly known as tristearin.

Glycerolipids that are triesters of glycerol with three fatty acids are called **triacylglycerol** or **triglycerides**. For example, glyceryl tristearate shown above is a triglyceride.

Triglycerides may be esters of three molecules of the same fatty acids, e.g., tristearin. Still, often the triglycerides found in nature are esters of two or three different fatty acids. Fatty acids usually found in fats and vegetable oils include lauric, myristic, palmitic, stearic, oleic, linoleic, and linolenic acids. An example of a mixed triglyceride of stearic, oleic, and palmitic acid is shown below.



A mixed triacylglycerol

Fats and oils

Fats and oils are triglycerides used as energy storage molecules in animals and plants.



Energy storage is essential for hibernating animals that live in icy environments. They have plenty of food available during summer but no food and below-freezing temperatures in winter. They eat plants, seeds, and nuts and accumulate fat that becomes their energy source when hibernating in winter. For example, the polar bear shown on the right can accumulate up to 14 kg of fat per week in summer when the food is plenty and uses it as an energy source when the animal hibernates for 4 to 7 months in winter.

Although glycogen is a quick energy source, fats and oils are more energy dense for two reasons:

- first, fats and oils are in a more reduced form than glycogen and release more energy per mass upon oxidation, and
- second, glycogen is hydrophilic and absorbs water, increasing its mass.

Physical properties of fats and oils

Pure fats and oils are colorless, odorless, and tasteless. The color, taste, and odor associated with butter -an animal fat, and olive oil -a vegetable oil, is due to a small number of other substances mixed with the triglycerides.

Fats come from animal sources, such as meat, whole milk, lard, butter, and cheese. Vegetable oils come from plant sources, e.g., soybeans, peanuts, sunflowers, etc.

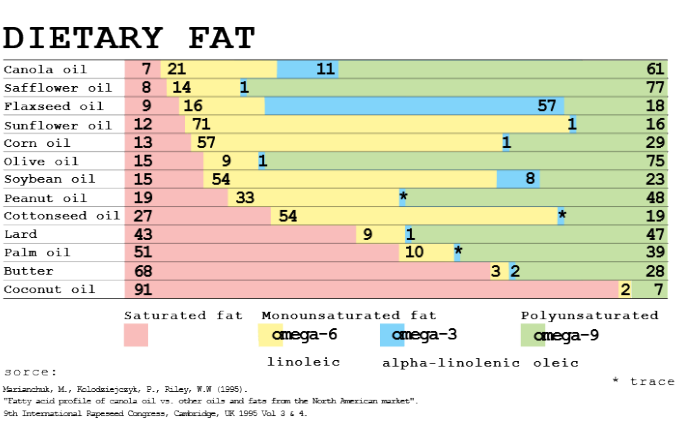
Fats are usually solid at room temperature because they have a higher proportion of long-chain unsaturated fatty acids with higher melting points, e.g., lard and butter shown in Figure 9.3.1. **Vegetable oils are usually liquid** at room temperature because they contain more unsaturated or short-chain saturated fatty acids.





Figure 9.3.1: Butter -a fat that is semisolid, and olive oil -a vegetable oil liquid at room temperature. (Copyright:Butter: Renee Comet (National Cancer Institute), Public domain, via Wikimedia Commons, Olive oil: Roberta Sorge robertina, CC0, via Wikimedia Commons)

For example, canola oil, safflower oil, flaxseed oil, sunflower oil, corn oil, olive oil, soyabean oil, peanut oil, and cottonseed oil are vegetable oils that are liquid at room temperature and have a higher proportion of unsaturated fatty acids as shown in Figure 9.3.2 . Palm and coconut oils are vegetable oils with a higher balance of saturated fatty acids. Still, they are liquid at room temperature because they have short-chain saturated fatty acids. For example, coconut mainly comprises lauric acid (12:0), a short-chain fatty acid.



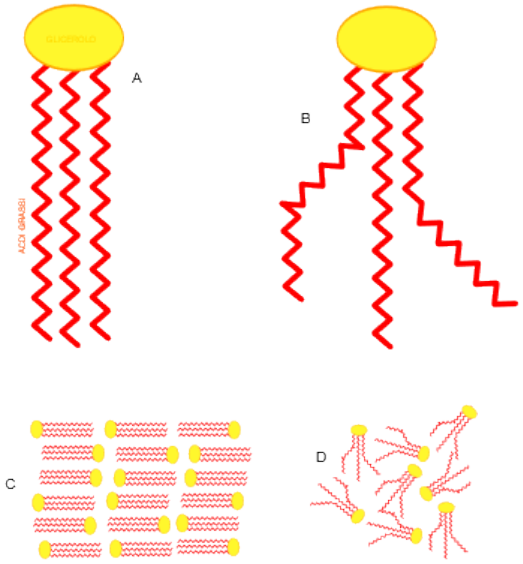


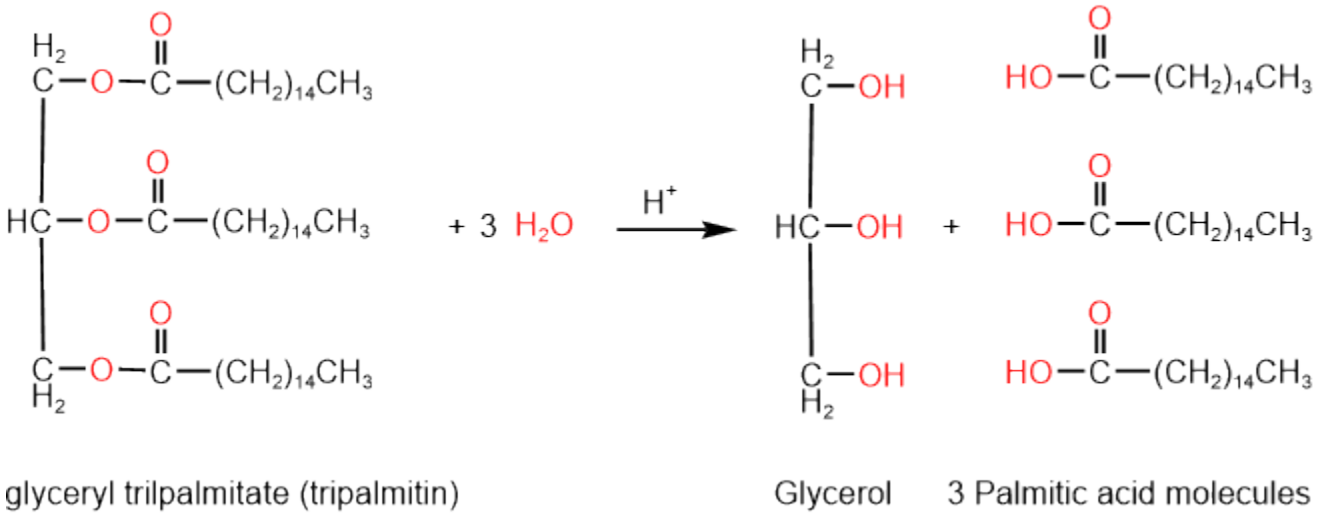
Figure 9.3.2: Right: Proportion of saturated, monounsaturated, and polyunsaturated fatty acids in fats (lard and butter) and vegetable oils. (Copyright; Diamboroid, CC BY-SA 4.0, via Wikimedia Commons). Left: Saturated triglyceride (top left) and unsaturated (top right). The drawing below shows how packing is easier in saturated triglycerides, so they tend to be solid at room temperature. (Copyright; AGeremia, CC BY 3.0, via Wikimedia Commons)

Chemical properties of fats and oils

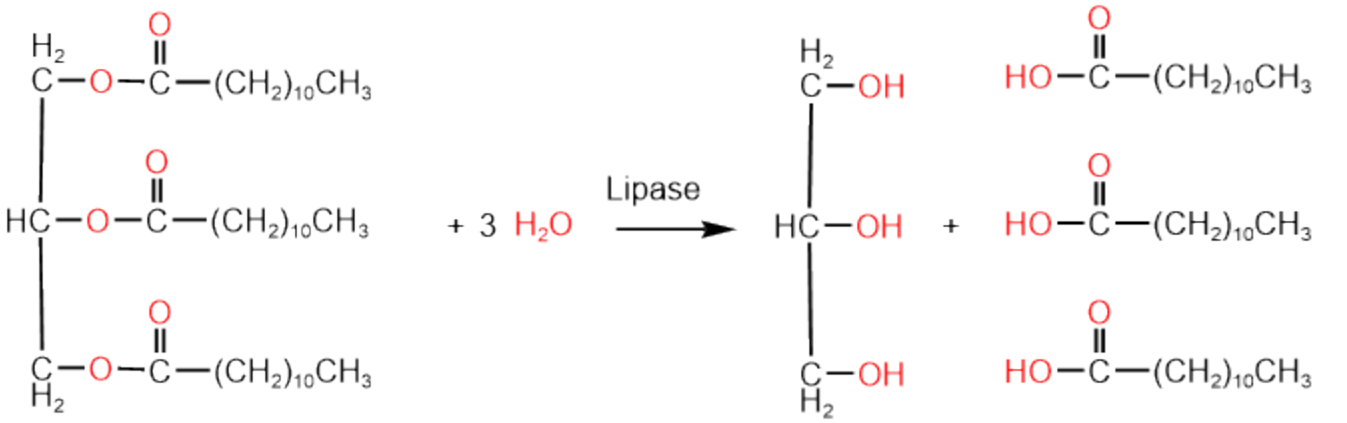
Three important reactions of triglycerides are hydrolysis by water in the presence of acid or lipase enzyme, saponification, i.e., base-promoted hydrolysis, and hydrogenation of double bonds in the fatty acids.

Hydrolysis

Easters are hydrolyzed (split) by water in the presence of an acid catalyst into alcohol and carboxylic acid. The same reaction happens with triglycerides, i.e., fats and vegetable oils—for example, tripalmitin hydrolyzes into glycerol and three palmitic acid molecules, as shown below.



Lipase enzymes do the same reaction during the digestion of triglycerides, e.g., trilaurin is hydrolyzed by lipase to glycerol and three molecules of lauric acid, as shown in the reaction below.

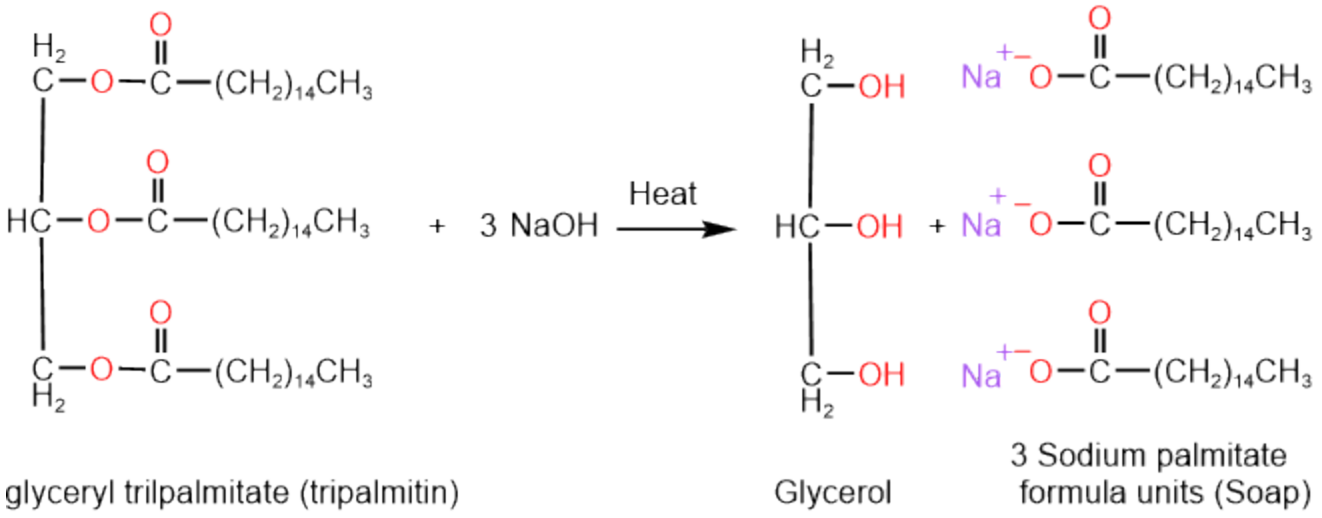


The digestion of lipids starts in the mouth with lingual lipases secreted by glands in the tongue and continues in the stomach with lingual and gastric lipases. Glycerol in the hydrolysis product is soluble in water, but fatty acids are not. Fatty acids are emulsified in the stomach and later mixed with bile and pancreatic juice to continue the process of digestion.

Saponification

Saponification is base-promoted hydrolysis of triglycerides that produces glycerol and salts of the fatty acids, a soap, as shown below for the case of saponification of tripalmitin.





Different varieties of soaps are shown in the figure on the right. Sodium salts of fatty acids make hard soaps, while potassium salts make soft soaps. Three of the most common soaps are sodium stearate, oleate, and linoleate. Salts of saturated fatty acids make rigid, and those of polyunsaturated fatty acids make soft soap. Perfumes are added for scent and dyes for color, sand is added in scouring soap, and the air is blown into the soap to make it float on water.

Hydrogenation

Alkenes add $\mathrm{H_2}$ and covert to alkane in the presence of Ni, Pt, or Pd catalyst. The same reaction happens with the $\mathrm{C{=}C}$ in unsaturated fatty acids found in triglycerides. The conversion of unsaturated fatty acids to saturated fatty acids increases the melting point of triglycerides. Therefore, vegetable oils with more unsaturated fatty acids become semisolid or solid after partial or complete hydrogenation, as illustrated by the reaction in Figure $9.3.3$. Hydrogenation of vegetable oils is a commercial process to convert vegetable oils to semisolid products like margarine and shortening.

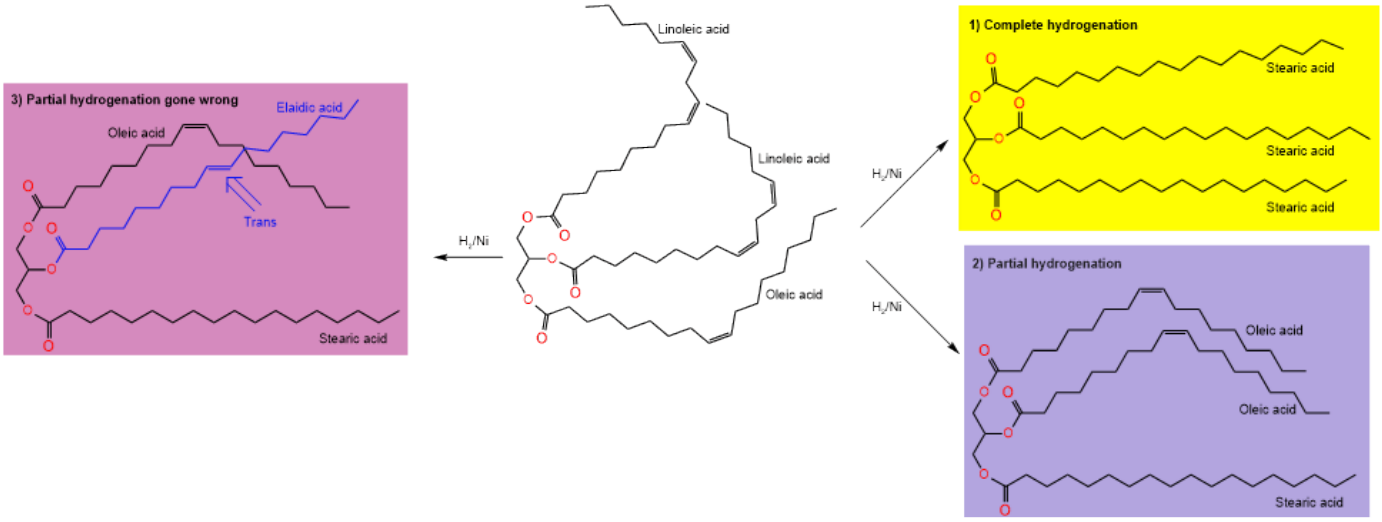


Figure $9.3.3$: Hydrogenation of unsaturated fatty acids in vegetable oils: 1) complete hydrogenation, 2) partial hydrogenation, 3) partial hydrogenation that results in conversion of some *cis*-$\mathrm{C{=}C}$ bonds to *trans*-$\mathrm{C{=}C}$ bonds that are undesirable. (Copyright; Public domain)

The driving force for the industrial process of hydrogenation of vegetable oils is that margarine or shortenings are used as cheaper alternatives to butter with a longer shelf-life. Complete hydrogenation of vegetable oils converts them into hard margarine. Often partial hydrogenation is performed as the partially hydrogenated product is semisolid and mimics butter better than hard shortening. Dyes and flavors are mixed with it to mimic butter's color, taste, and odor.

Unwanted trans-fatty acids are by-products of the hydrogenation of vegetable oils.

Like all other processed food products, hydrogenated vegetable oil products are associated with health problems. Partial hydrogenation converts some of the *cis*-$\mathrm{C{=}C}$ bonds to *trans*-$\mathrm{C{=}C}$ bonds, as illustrated in Figure $9.3.3$. *Trans*-$\mathrm{C{=}C}$ bonds are rare in some fatty acids. Research reports indicate that trans-fatty acids affect blood cholesterol like unsaturated fatty acids. Research reports also indicated that trans-fatty acids increase the level of low-density lipids (LDL), considered bad cholesterol, and decrease the level of high-density lipids (HDL), regarded as good cholesterol. Health organizations force the manufacturers to show the trans-fatty acid contents on the product labels. They are trying to educate the consumers about trans-fatty acids, as shown in Figure $9.3.4$ from U.S. Food and Drug Administration.



Figure $9.3.4$: A variety of processed foods—including the frozen, canned, and baked goods shown—contain *trans* fat. The amount per serving is listed on the Nutrition Facts label. Including partially hydrogenated oil in the list of ingredients is another indication that *trans* fat is present. (Copyright; The U.S. Food and Drug Administration, Public domain, via Wikimedia Commons)

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9.4: Membranes and Membrane Lipids

Learning Objectives

- Identify the distinguishing characteristics of membrane lipids.
- Describe membrane components and how they are arranged.

All living cells are surrounded by a cell membrane. Plant cells (Figure $9.4.1A$) and animal cells (Figure $9.4.1B$) contain a cell nucleus that is also surrounded by a membrane and holds the genetic information for the cell. Everything between the cell membrane and the nuclear membrane—including intracellular fluids and various subcellular components such as the mitochondria and ribosomes—is called the cytoplasm. The membranes of all cells have a fundamentally similar structure, but membrane function varies tremendously from one organism to another and even from one cell to another within a single organism. This diversity arises mainly from the presence of different proteins and lipids in the membrane.

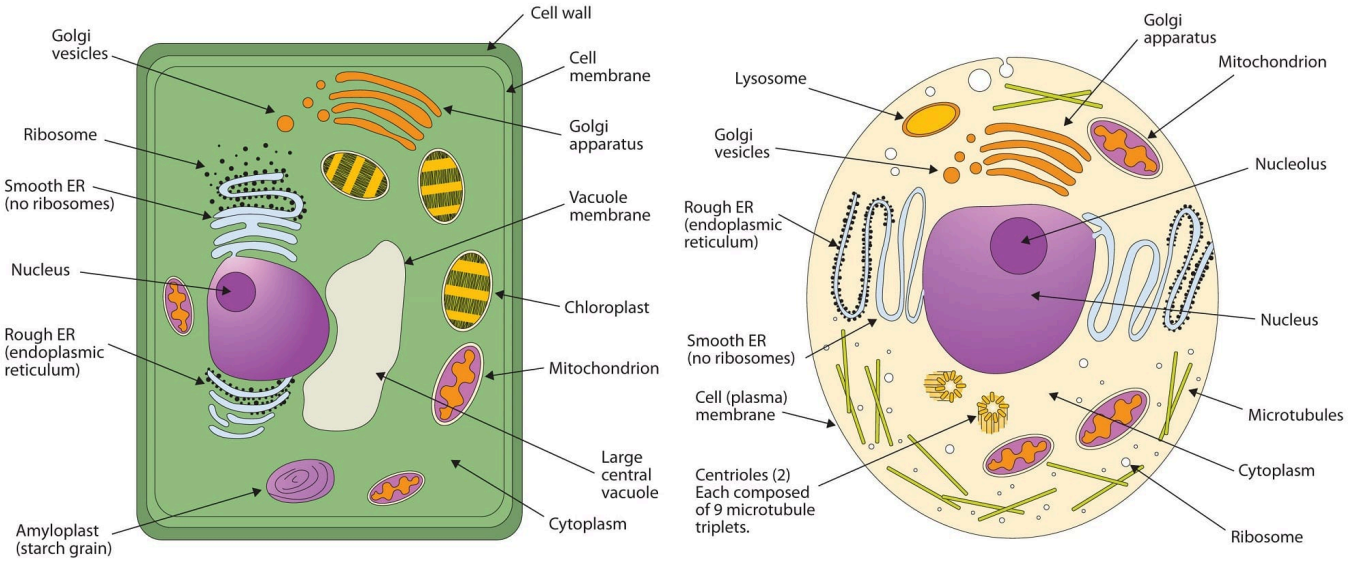


Figure $9.4.1$: (A) An Idealized Plant Cell. Not all the structures shown here occur in every type of plant cell. (B) An Idealized Animal Cell. The structures shown here will seldom all be found in a single animal cell.

The lipids in cell membranes are highly polar but have dual characteristics: part of the lipid is ionic and therefore dissolves in water, whereas the rest has a hydrocarbon structure and therefore dissolves in nonpolar substances. Often, the ionic part is referred to as hydrophilic, meaning “water loving,” and the nonpolar part as hydrophobic, meaning “water fearing” (repelled by water). When allowed to float freely in water, polar lipids spontaneously cluster together in any one of three arrangements: micelles, monolayers, and bilayers (Figure $9.4.2$).

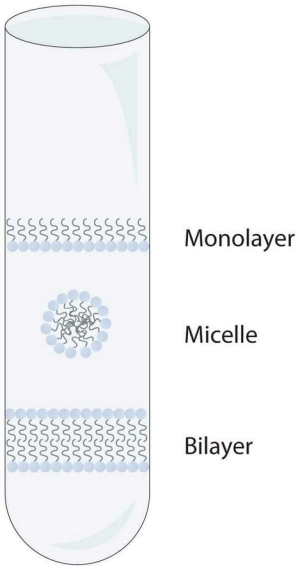


Figure 9.4.2: Spontaneously Formed Polar Lipid Structures in Water: Monolayer, Micelle, and Bilayer

Micelles are aggregations in which the lipids' hydrocarbon tails—being hydrophobic—are directed toward the center of the assemblage and away from the surrounding water while the hydrophilic heads are directed outward, in contact with the water. Each micelle may contain thousands of lipid molecules. Polar lipids may also form a monolayer, a layer one molecule thick on the surface of the water. The polar heads face into water, and the nonpolar tails stick up into the air. Bilayers are double layers of lipids arranged so that the hydrophobic tails are sandwiched between an inner surface and an outer surface consisting of hydrophilic heads. The hydrophilic heads are in contact with water on either side of the bilayer, whereas the tails, sequestered inside the bilayer, are prevented from having contact with the water. Bilayers like this make up every cell membrane (Figure 9.4.3).

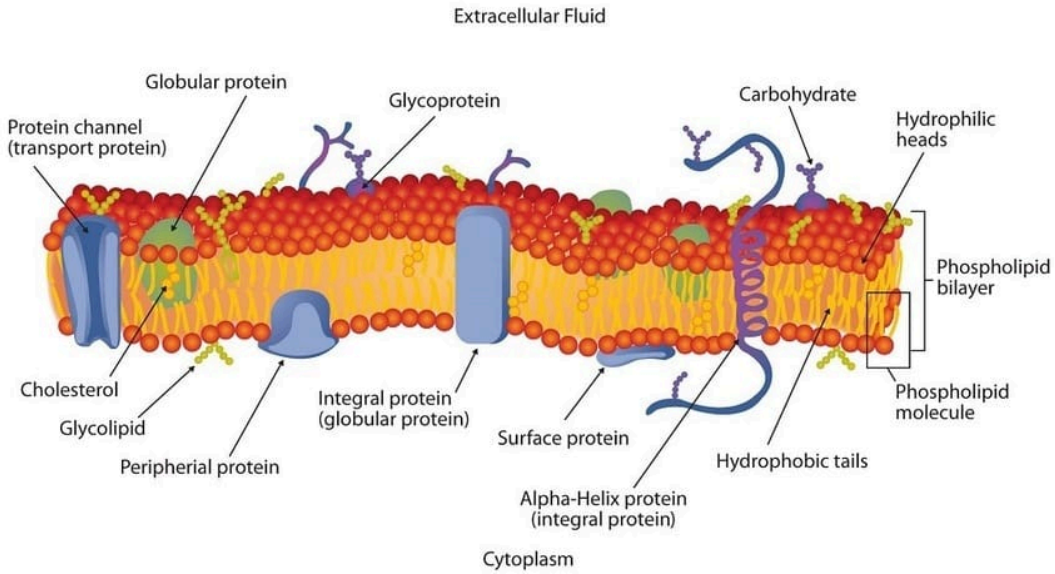


Figure 9.4.3: Schematic Diagram of a Cell Membrane. The membrane enclosing a typical animal cell is a phospholipid bilayer with embedded cholesterol and protein molecules. Short oligosaccharide chains are attached to the outer surface.

In the bilayer interior, the hydrophobic tails (that is, the fatty acid portions of lipid molecules) interact by means of dispersion forces. The interactions are weakened by the presence of unsaturated fatty acids. As a result, the membrane components are free to mill about to some extent, and the membrane is described as fluid.

The lipids found in cell membranes can be categorized in various ways. Phospholipids are lipids containing phosphorus. Glycolipids are sugar-containing lipids. The latter are found exclusively on the outer surface of the cell membrane, acting as distinguishing surface markers for the cell and thus serving in cellular recognition and cell-to-cell communication. Sphingolipids are phospholipids or glycolipids that contain the unsaturated amino alcohol sphingosine rather than glycerol. Diagrammatic

structures of representative membrane lipids are presented in Figure 9.4.4.

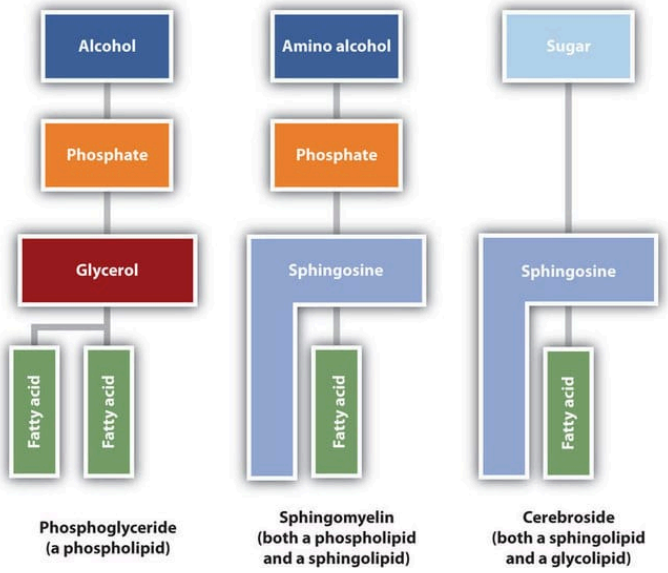


Figure 9.4.4: Component Structures of Some Important Membrane Lipids

Phosphoglyceride are composed of alcohol, phosphate, glycerol and 2 fatty acids. A sphingomyelin contains phosphate, sphingosine, and a fatty acid. A cerbroside contains sugar, sphingosine and a fatty acid.

Phosphoglycerides (also known as glycerophospholipids) are the most abundant phospholipids in cell membranes. They consist of a glycerol unit with fatty acids attached to the first two carbon atoms, while a phosphoric acid unit, esterified with an alcohol molecule (usually an amino alcohol, as in part (a) of Figure 9.4.5) is attached to the third carbon atom of glycerol (part (b) of Figure 9.4.5). Notice that the phosphoglyceride molecule is identical to a triglyceride up to the phosphoric acid unit (part (b) of Figure 9.4.5).

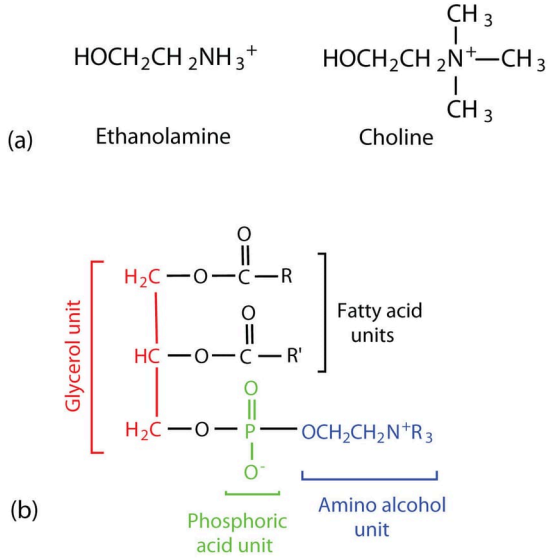
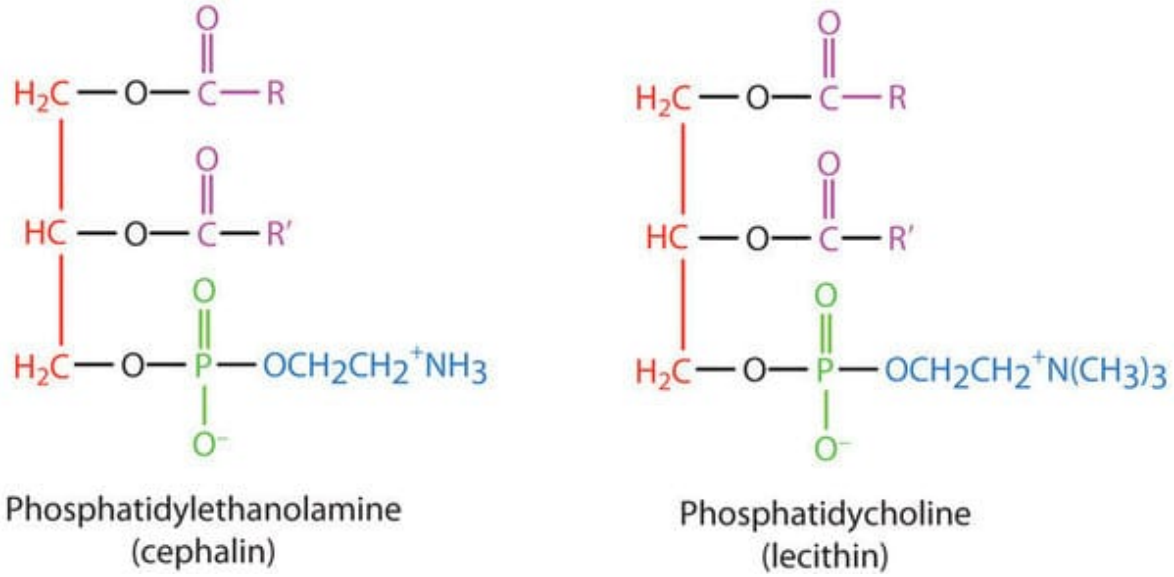


Figure 9.4.5: Phosphoglycerides. (a) Amino alcohols are commonly found in phosphoglycerides, which are evident in its structural formula (b). Structural formula of ethanolamine and choline are shown. The structural formula of a phosphoglyceride is shown with the glycerol unit, phosphoric unit, and amino alcohol unit highlighted in different colors.

There are two common types of phosphoglycerides. Phosphoglycerides containing ethanolamine as the amino alcohol are called *phosphatidylethanolamines* or *cephalins*. Cephalins are found in brain tissue and nerves and also have a role in blood clotting. Phosphoglycerides containing choline as the amino alcohol unit are called *phosphatidylcholines* or *lecithins*. Lecithins occur in all living organisms. Like cephalins, they are important constituents of nerve and brain tissue. Egg yolks are especially rich in lecithins. Commercial-grade lecithins isolated from soybeans are widely used in foods as emulsifying agents. An emulsifying

agent is used to stabilize an emulsion—a dispersion of two liquids that do not normally mix, such as oil and water. Many foods are emulsions. Milk is an emulsion of butterfat in water. The emulsifying agent in milk is a protein called *casein*. Mayonnaise is an emulsion of salad oil in water, stabilized by lecithins present in egg yolk.



Sphingomyelins, the simplest sphingolipids, each contain a fatty acid, a phosphoric acid, sphingosine, and choline (Figure 9.4.6). Because they contain phosphoric acid, they are also classified as phospholipids. Sphingomyelins are important constituents of the myelin sheath surrounding the axon of a nerve cell. Multiple sclerosis is one of several diseases resulting from damage to the myelin sheath.

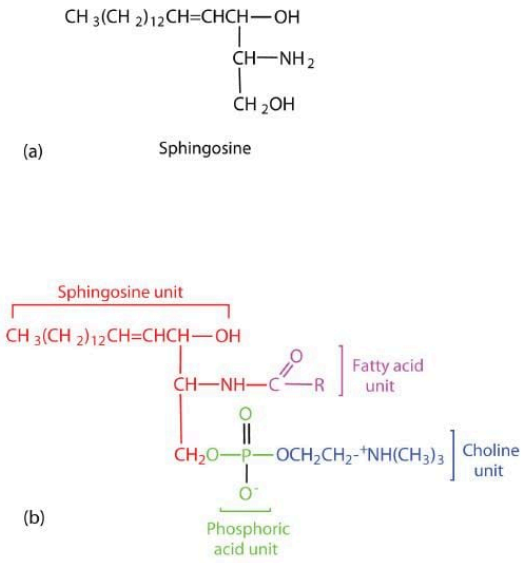


Figure 9.4.6: Sphingolipids. (a) Sphingosine, an amino alcohol, is found in all sphingolipids. (b) A sphingomyelin is also known as a phospholipid, as evidenced by the phosphoric acid unit in its structure.

Structural formula of sphingosine is shown. The general structure of a sphingolipid is shown with the sphingosine unit, fatty acid unit, phosphoric acid unit, and choline unit highlighted in different colors.

Most animal cells contain sphingolipids called cerebrosides (Figure 9.4.7). Cerebrosides are composed of sphingosine, a fatty acid, and galactose or glucose. They therefore resemble sphingomyelins but have a sugar unit in place of the choline phosphate group. Cerebrosides are important constituents of the membranes of nerve and brain cells.

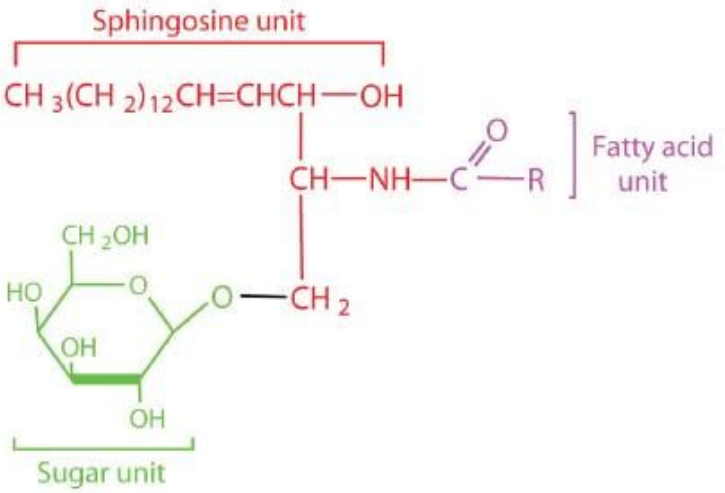


Figure 9.4.7: Cerebrosides. Cerebrosides are sphingolipids that contain a sugar unit.
General structure of a cerebroside with its sugar unit, sphingosine unit, and fatty acid unit highlighted in different colors.

The sphingolipids called gangliosides are more complex, usually containing a branched chain of three to eight monosaccharides and/or substituted sugars. Because of considerable variation in their sugar components, about 130 varieties of gangliosides have been identified. Most cell-to-cell recognition and communication processes (e.g., blood group antigens) depend on differences in the sequences of sugars in these compounds. Gangliosides are most prevalent in the outer membranes of nerve cells, although they also occur in smaller quantities in the outer membranes of most other cells. Because cerebrosides and gangliosides contain sugar groups, they are also classified as glycolipids.

Membrane Proteins

If membranes were composed only of lipids, very few ions or polar molecules could pass through their hydrophobic “sandwich filling” to enter or leave any cell. However, certain charged and polar species do cross the membrane, aided by proteins that move about in the lipid bilayer. The two major classes of proteins in the cell membrane are integral proteins, which span the hydrophobic interior of the bilayer, and peripheral proteins, which are more loosely associated with the surface of the lipid bilayer (Figure 9.4.3). Peripheral proteins may be attached to integral proteins, to the polar head groups of phospholipids, or to both by hydrogen bonding and electrostatic forces.

Small ions and molecules soluble in water enter and leave the cell by way of channels through the integral proteins. Some proteins, called *carrier proteins*, facilitate the passage of certain molecules, such as hormones and neurotransmitters, by specific interactions between the protein and the molecule being transported.

Summary

Lipids are important components of biological membranes. These lipids have dual characteristics: part of the molecule is hydrophilic, and part of the molecule is hydrophobic. Membrane lipids may be classified as phospholipids, glycolipids, and/or sphingolipids. Proteins are another important component of biological membranes. Integral proteins span the lipid bilayer, while peripheral proteins are more loosely associated with the surface of the membrane.

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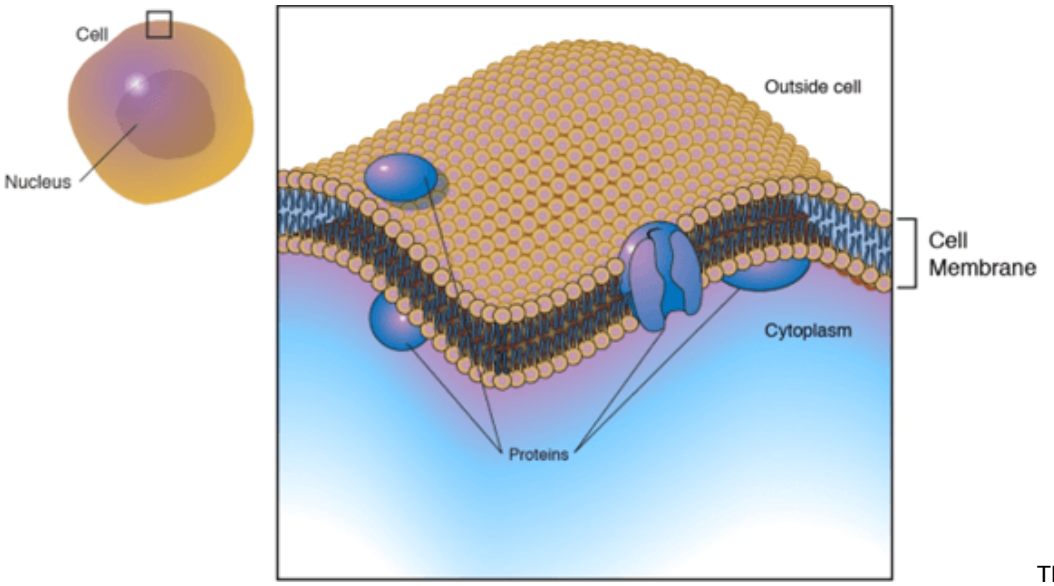
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9.5: Cell membrane

Learning Objectives

- Define and understand the composition of the cell membrane and how the composition adjusts the fluidity fo the membrane.
- Understand three modes of transport through the cell membrane: diffusion, facilitated transport, and active transport.

What is a cell membrane?



The cell membrane, also known as the plasma membrane, cytoplasmic membrane, and plasmalemma, is a lipid bilayer with proteins dispersed in it that separates the cell interior from the extracellular space, as illustrated in the figure on the right (*Copyright; National Human Genome Research Institute, Public domain*).

Composition of the cell membrane

A cell membrane is a complex structure with several components, as shown in Figure $9.5.1$. and described here.

- Phospholipid bilayer that has polar heads on the outside in contact with water and nonpolar tails inside the bilayer. Unsaturated fatty acids in the lipid hydrophobic tails increase the membrane fluidity -the more proportion of unsaturated fatty acids, the higher the fluidity.
- Cholesterol interspersed between phospholipids controls the rigidity of the membrane -the more the proportion of cholesterol, the more rigid the membrane.
- Two types of proteins: integral proteins that span the membrane and serve as transporters of species, and peripheral proteins that are loosely attached to the outer side of the membrane that act as enzymes to facilitate the interaction with the cell's environment.
- Glycoproteins and glycolipids have carbohydrate oligomers attached to the outer lipid layer and serve the purpose of cell-to-cell recognition.

The cell membrane controls the movement of substances in and out of the cells and organelles. It is selectively permeable to ions and organic molecules. It plays a role in cell adhesion, cell signaling, and attachment surface for the cytoskeleton to shape the cells and attach to the extracellular matrix to hold them together in tissues.

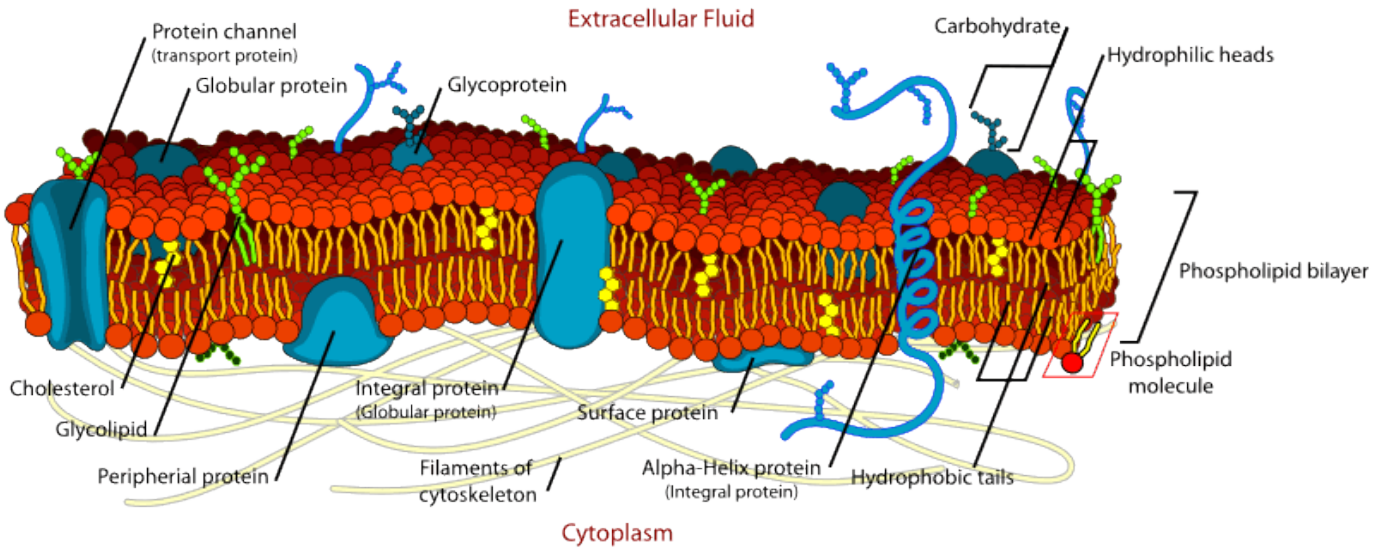


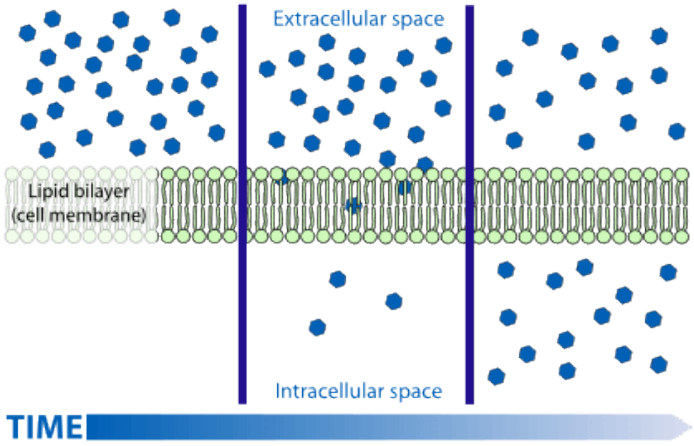
Figure 9.5.1: A detailed cell membrane structure. (Copyright; LadyofHats, Public domain, via Wikimedia Commons)

Transport through the cell membrane

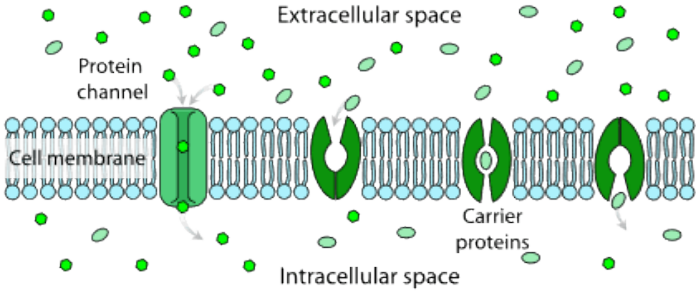
The cell membrane is a partition between intracellular and extracellular spaces. Still, some substances needed by the cell need to enter, and some products or wastes need to exit the cell. The cell membrane allows a selective movement of substances in and out of the cell in several ways.

Diffusion (passive) transport

The molecules in the lipid bilayer are vibrating due to thermal energy. Therefore, some molecules, such as O_2, CO_2, urea, water, etc., can move across the membrane from a higher concentration region to a lower concentration region through the process of diffusion, as illustrated in Figure 9.5.2 left.



Diffusion or passive transport



Facilitated transport through protein channels or carrier protein

Figure 9.5.2: Illustration of diffusion and facilitated transport across the cell membrane. (Copyright; LadyofHats, Public domain, via Wikimedia Commons)

Facilitated transport

Integral proteins form channels through which certain substances can diffuse more rapidly than by simple diffusion. The proteins have a channel size that matches the substance's size or changes the shape to adjust to the size of the substance that needs to be selectively transported through the facilitated transport, as illustrated in Figure 9.5.2 right. Particularly, water-soluble substances

such as chloride ion (Cl^-), bicarbonate ion HCO_3^-, and glucose molecules do not move fast enough through simple diffusion and are transported by the facilitate transport process to meet the need of the cells.

Active transport

Sometimes substances need to be moved against the concentration gradient. It takes place at the expense of energy in the form of ATP, just like pumping substances at the cost of electricity in everyday life. For example, K^+ concentration is greater inside the cell, and that of Na^+ is greater outside the cell. In the conduction of nerve impulses and contraction of muscles, K^+ moves into the cell, and Na^+ moves out of the cell by active transport process, as illustrated in Figure $9.5.3$.

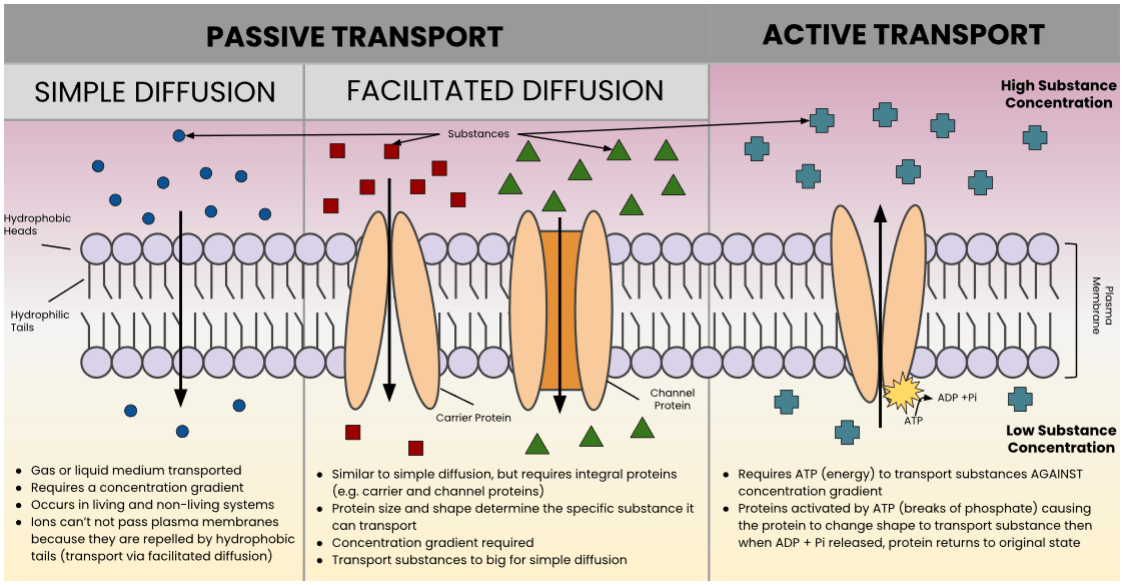


Figure $9.5.3$: Comparison of membrane transport methods: passive transport, which includes simple and facilitated diffusion, and active transport, which takes place at the expense of energy. (Copyright; LSumi, CC BY-SA 4.0, via Wikimedia Commons)

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- 6.8: Cell membrane by Muhammad Arif Malik is licensed Public Domain.

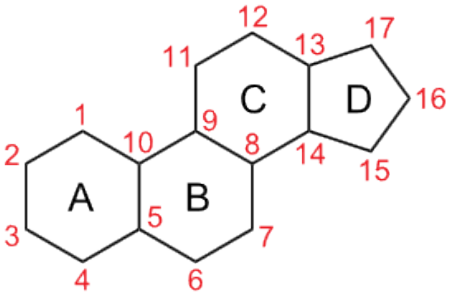
9.6: Sterols

Learning Objectives

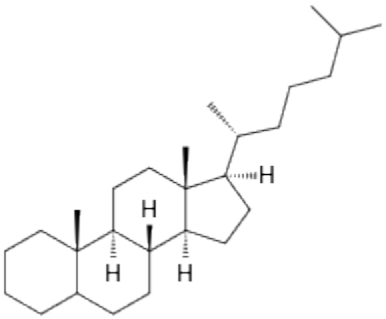
- Understand the core structure of steroids and sterols.
- Understand the structural features of cholesterol, its production, consumption, transport, and medical problems.
- Understand bile acids' structure features, their functions, and medical problems.
- Understand the structural features of steroid hormones, functions, abuses, and medical problems.

What are steroids?

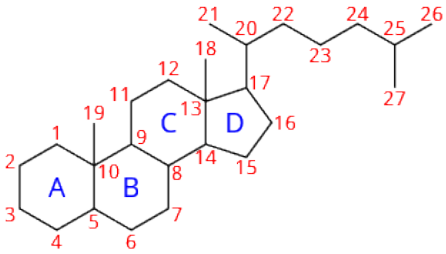
Steroids are biologically active compounds that have a core structure composed of four fused rings in a specific configuration: three six-membered rings designated A, B, and C and one five-membered ring D, as Figure $9.6.1$ right. Gonane has this core structure of steroids. Other steroids have gonane skeletons with some groups attached. For example, cholestane has methyl groups at positions 10 and 13 and an aliphatic chain at position 17. Cholesterol has the structure of cholestane. It is a biomarker found in rocks and petroleum deposits.



Gonane or sterane with numbered



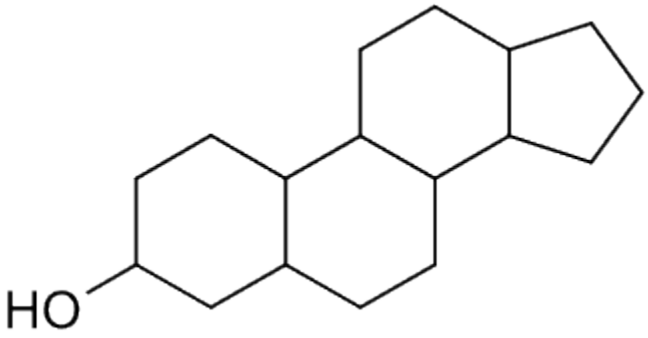
Cholestan with stereochemistry shown



cholestan with numbered

Figure $9.6.1$: Steroid core structure represented by gonane with C labels shown and cholestane that has the C skeleton of cholestrol with C labels. (Copyright; Public domain)

What are sterols?



Sterols are organic compounds derived from gonane with H #3 replaced with an alcohol ($-\mathrm{OH}$) group. The sterols are a sub-class of steroids. The simplest sterol is the alcohol gonane shown in the figure on the right. Other sterols have other groups attached to the gonane structure.

Cholesterol

Cholesterol is the most abundant sterol found in animals. It is a structural component of animal cell membranes, a precursor for steroid hormones, bile acids, and vitamin D. Cholesterol has the C skeleton of cholestane, with an $-\mathrm{OH}$ group at position #3 and a $\mathrm{C}{=}\mathrm{C}$ bond at position 5 and 6, as shown in Figure $9.6.2$.

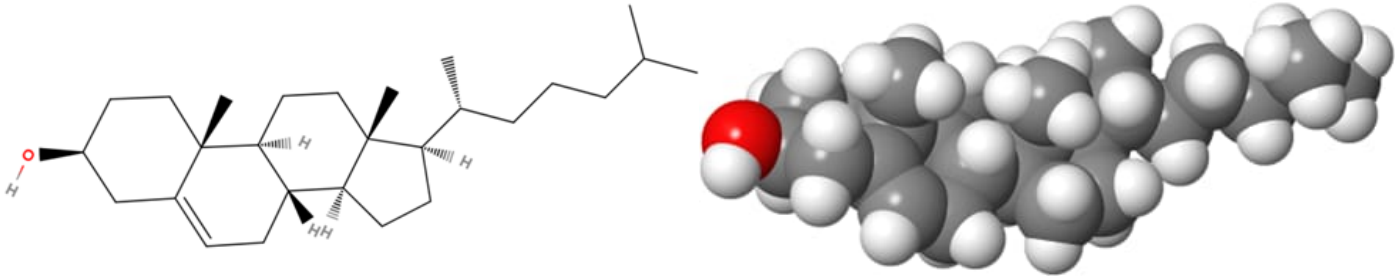


Figure $9.6.2$: Structure of cholesterol (left) and space-filling model of cholesterol: hydrophilic head, i.e., $-\mathrm{OH}$ group (O is read and H is white) and hydrophobic tail of tetracyclic rings and an alkyl side chain ($\mathrm{C}'\mathrm{s}$are gray and $\mathrm{H}'\mathrm{s}$ are white). (Copyright; Public domain)

Cholesterol sources and consumption

Cholesterol contents of foods

Foods	Cholesterol (mg/100 g)
Beef brain	3100
Egg yolk	1085
Egg	373
Lamb kidney	337
Pork liver	301
Butter	215
Lobster	200
Shrimp	125
Light whipping cream	111
Yellow cheese	108
Beef	90
Chicken	88
ChPork	80
Fish	70
Yogurt	13
Egg whites	0
Fruits	0
Grains	0
Nuts	0

Cholesterol is biosynthesized from lanosterol, which, in turn, is synthesized from squalene, as described in the previous section. Cholesterol is synthesized in the liver using fats, proteins, and carbohydrates as raw materials. An average human weighing 68 kg synthesizes about 1000 mg of cholesterol daily. Food is also a source of cholesterol intake, as shown in the figure on the right. Typically about 307 mg of cholesterol intake is through food per day in the US. The liver reduces cholesterol production to adjust for the intake from food sources.

Cholesterol is amphiphilic like phospholipids and sphingolipids, with $-\mathrm{OH}$ as a polar head and cholestane structure as a hydrophobic tail. The cholesterol molecule is stiff due to restricted movements around $\mathrm{C}{-}\mathrm{C}$ bonds locked in the cyclic structure.

> Cholesterol is used in the cell membrane to impart rigidity to the ring -the higher the proportion of cholesterol in the cell membrane, the more rigid the membrane.

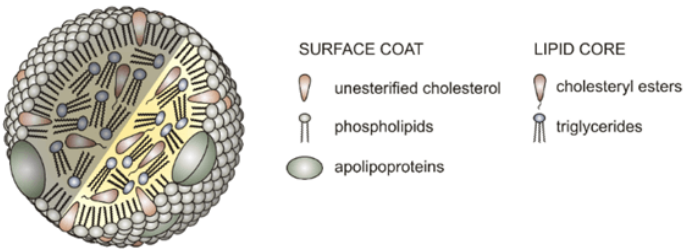
Usually, cholesterol is 30% of the cell membrane. It is involved in signaling and is found in the brain, plasma membrane, and myelin sheath of nerve cells. Cholesterol is a precursor to vitamin D and steroid hormones, including corticosteroids, such as cortisol and aldosterone, and sex hormones, such as progesterone, estrogens, and testosterone.

The liver recycles the excess cholesterol by converting it into bile acids stored in the gallbladder and excreted into the digestive

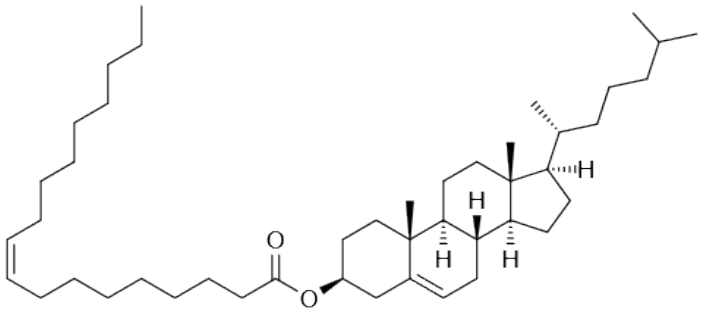
tract. Bile acids emulsify fats in the food, which helps digest the food. About 50% of the excreted cholesterol is re-absorbed into the bloodstream by the small intestine.

Transport of cholesterol

Cholesterol is insoluble in water like other lipids. It is transported by the blood, which is water rich medium. Like soap carries greases in water during washing, lipoprotein transport glycerolipids and cholesterol in the body. The lipoproteins exist as particles suspended in blood. Glycerides and cholesteryl esters are in the core, and phospholipids, proteins (apolipoprotein), and cholesterol form the outer layer having their hydrophobic parts oriented outwards in contact with water, as illustrated in Figure 9.6.3.

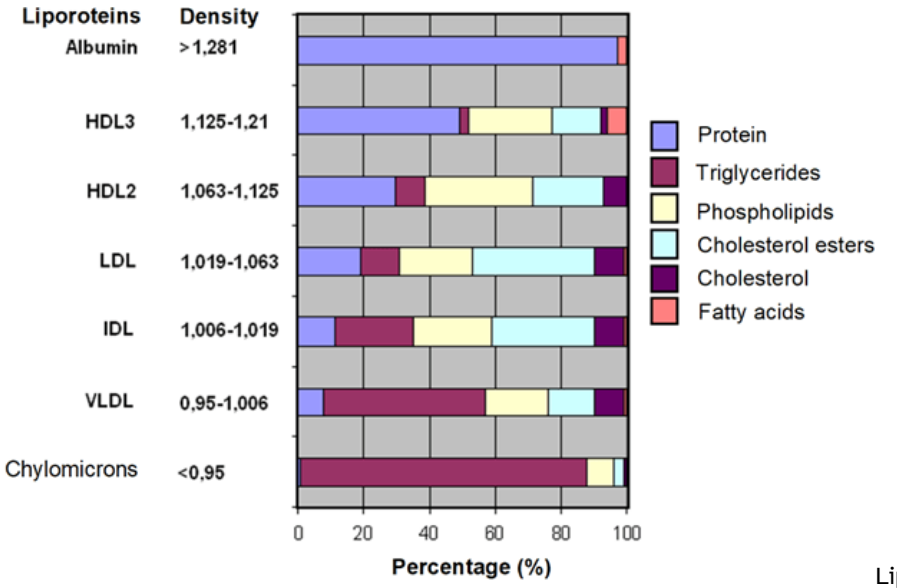


High-density lipoprotein (HDL)



Cholesterol oleate

Figure 9.6.3: High-density lipoprotein (HDL), as an example lipoprotein particles, are composed of a lipid core containing cholesteryl esters and triglycerides, and a surface coat of phospholipids, unesterified cholesterol, and apolipoprotein (left, copyright: AntiSense, CC BY-SA 3.0, via Wikimedia Commons) and cholesterol oleate as an example of cholesteryl ester (right, Public domain)



Lipoproteins are classified based on their density, as shown in the figure on the right (*Copyright: Modified from İnfoCan at Turkish Wikipedia., FAL, via Wikimedia Commons, Public domain*). Their density is based on the proportion of proteins in them -the higher the proportion of proteins, the higher the density. They also have roles in the transportation process of cholesterol and lipids:

- **Chylomicrons** – Transport triglycerides from the small intestine to the liver.
- **Very low-density lipoproteins** (VLDL) - transport newly synthesized triglycerides from the liver to the fatty tissues.
- **Intermediate-density lipoproteins** (IDL) are between VLDL and LDL in density. They are not usually seen in the blood.
- **Low-density lipoproteins** (LDL) - carry cholesterol from the liver to other tissues. They are also sometimes referred to as "**bad cholesterol**."
- **High-density lipoproteins** (HDL) - collect cholesterol from other tissues and return it to the liver. They are sometimes referred to as "**good cholesterol**."

Atherosclerosis and heart attack

Excessive fats and cholesterol in the body are associated with diabetes; cancers of the breast, pancreas, and colon; heart attack; and stroke. Lipoproteins transport cholesterol and fats in the body. LDLs transport cholesterol from the liver to the cells where they are needed, and HDLs transport surplus cholesterol back to the liver, where it is converted to other steroids and bile acids. If the LDL level is too high, some cholesterol is deposited in the artery as plagues, as shown in Figure $9.6.4$. That is why LDLs are sometimes called **bad cholesterol**. The plaque causes inflammation and death of the tissue in that area and restricts blood flow. It may lead to a heart attack if the blood flow to the heart is inadequate or a stroke if the blood flow to the brain is insufficient.

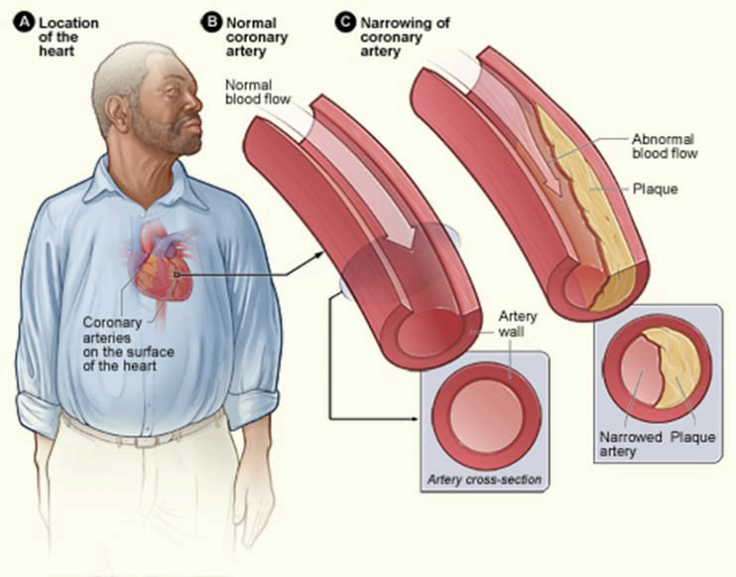


Figure $9.6.4$: Figure A shows the location of the heart in the body. Figure B shows a normal coronary artery with normal blood flow. The inset image shows a cross-section of a normal coronary artery. Figure C shows a coronary artery narrowed by plaque. The buildup of plaque limits the flow of oxygen-rich blood through the artery. The inset image shows a cross-section of the plaque-narrowed artery. (Copyright; National Heart Lung and Blood Insitute (NIH), Public domain, via Wikimedia Commons)

Since HDLs transport the surplus cholesterol back to the liver for recycling and avoid plaque formation, HDLs are also called good cholesterol. The HDL levels must be sufficiently high to prevent a heart attack. A lipid panel test is prescribed to assess the risk of a heart attack. It measures the levels of total cholesterol, LDLs, HDLs, and triglycerides in the blood. The normal levels are the following.

Total cholesterol	About 150 mg/dL, less is better
LDL ("bad") cholesterol	About 100 mg/dL, less is better
HDL ("good") cholesterol	At least 40 mg/dL in men and 50 mg/dL in women; higher is better
Triglycerides	Less than 150 mg/dL, less is better

Bile salts

Bile salts are synthesized from cholesterol in the liver. First, additional $-\mathrm{OH}$ groups are incorporated, and the alkyl side chain is shortened and oxidized to a carboxylic acid ($-\mathrm{COOH}$) group. Then the $-\mathrm{COOH}$ group is esterified with either glycine or taurine that imparts a negative charge group, as illustrated in Figure $9.6.5$.

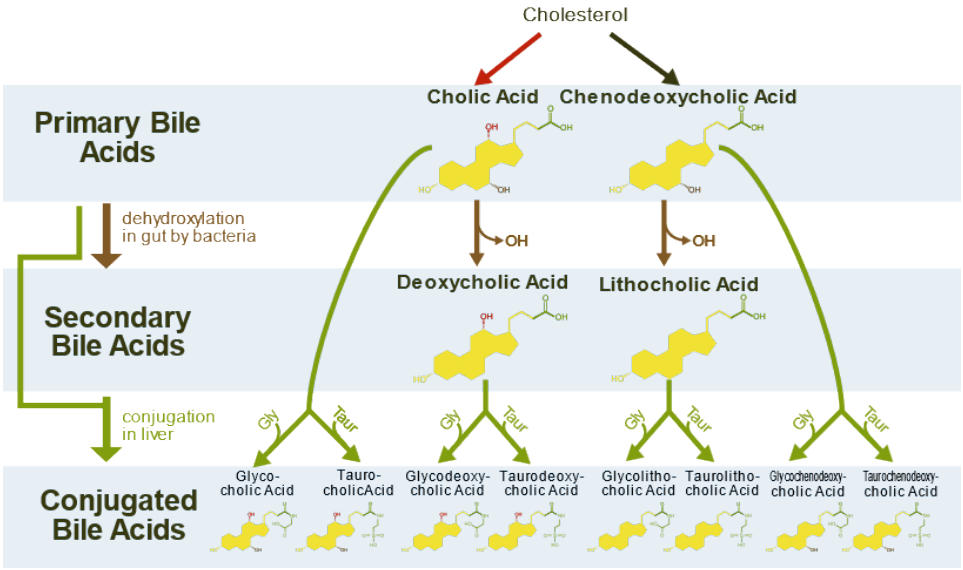


Figure 9.6.5: Synthesis of the 12 bile acids in human bile from cholesterol. (Copyright; Mcstrother, CC BY 3.0, via Wikimedia Commons)

Bile salts act like soaps with an ionic head and the remaining hydrophobic part. They are stored in the gallbladder and released into the small intestine, where they emulsify fats, i.e., convert the larger fat drops into smaller droplets, just like greases and dirt are emulsified by soaps. The smaller droplets have a larger surface area, increasing the fats' reaction rate with the pancreatic lipase enzymes, as illustrated in Figure 9.6.6.

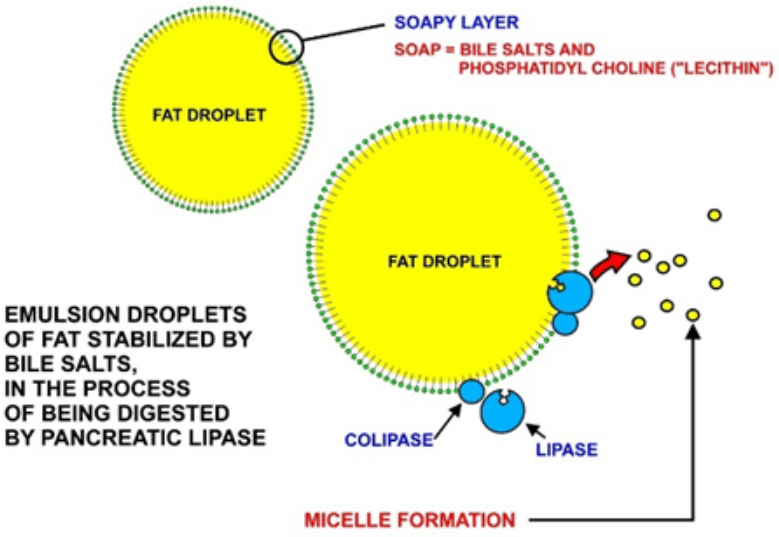


Figure 9.6.6: Dietary fats are emulsified in the duodenum by soaps in bile salts and phospholipids, which pancreatic lipase can attack. (Copyright; Cruithne9, CC BY-SA 4.0, via Wikimedia Commons)

Since bile salts are excreted with the feces, they remove cholesterol in two ways: 1) they are themselves the products of cholesterol, and 2) they dissolve cholesterol in the form of bile salt-cholesterol particles that are eliminated.

Gallstones and jaundice

When a large amount of cholesterol accumulates in the gallbladder, it turns into solid particles, i.e., gallstones. The gallstones are almost 100% cholesterol with a small amount of calcium salts, glycerophospholipids, and fatty acids. Small gallstones pass through the bile duct and enter the duodenum, i.e., the initial part of the small intestine, and are excreted. However, large gallstones may get stuck in the bile duct and cause pain, as illustrated in Figure 9.6.7. If a gallstone block the bile duct, the bile can not be excreted. Then the bile pigment, known as bilirubin, will back up into the liver and be passed via blood. It causes jaundice which gives a yellow color to the skin and whiteness to the eyes.

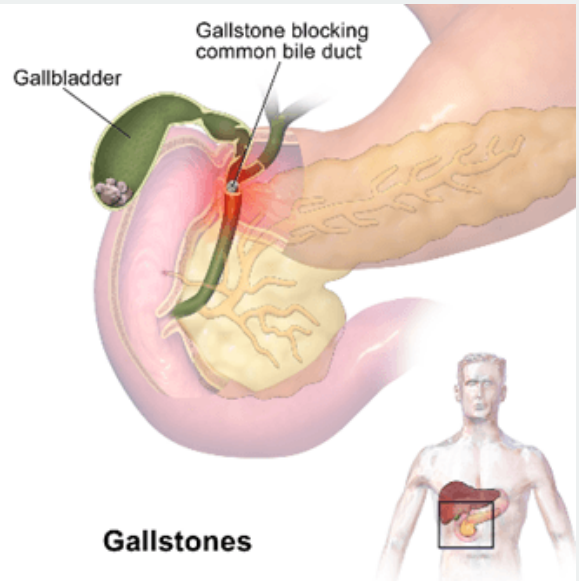


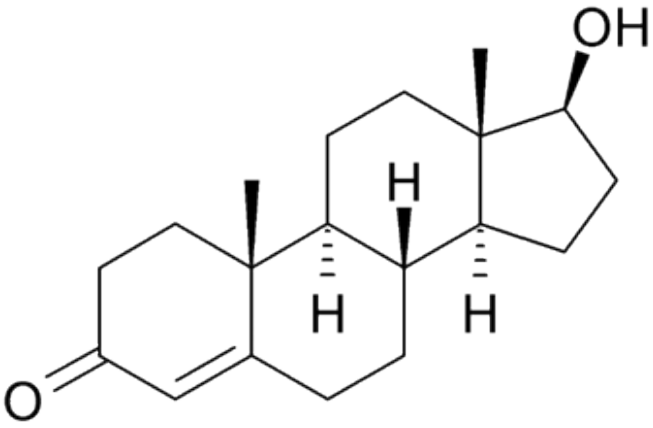
Figure 9.6.7: Illustration of gallstones blocking the bile duct that causes pain and jaundice. (Copyright; BruceBlaus, CC BY-SA 4.0, via Wikimedia Commons)

Steroid hormones

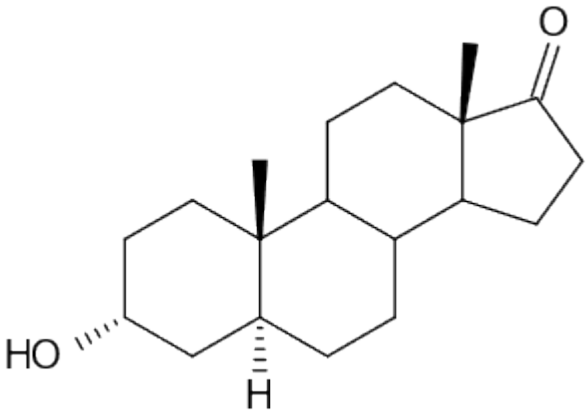
Steroid hormones have structural similarities with cholesterol and are derived from it. Two significant subclasses of steroid hormones are sex and adrenocortical hormones, described in the following sections.

Sex hormones

The male sex hormones are called androgens which include testosterone and androsterone. The female sex hormones are estrogens, e.g., estradiol and estrone, and progestins, e.g., progesterone. These five of the most essential sex hormones are shown in the figure below. All five are present in males and females, but androgens are produced more in males, and estrogens and progestins are produced more in females.

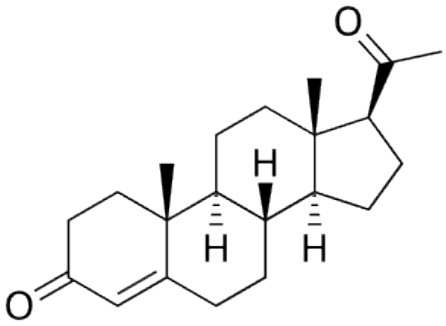


Testosterone

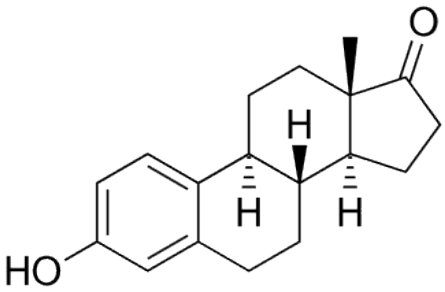


Androsterone

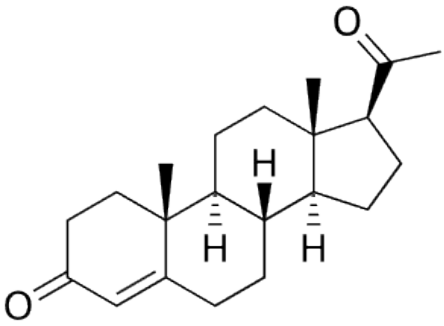
Male sex hormones (androgens)



Estradiol



Estrone



Progesterone

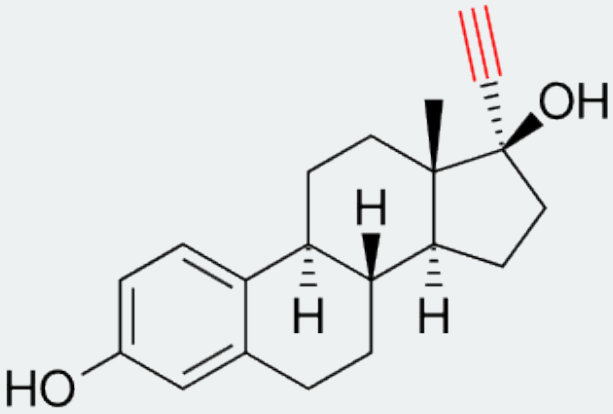
Female sex hormones

Functions of sex hormones

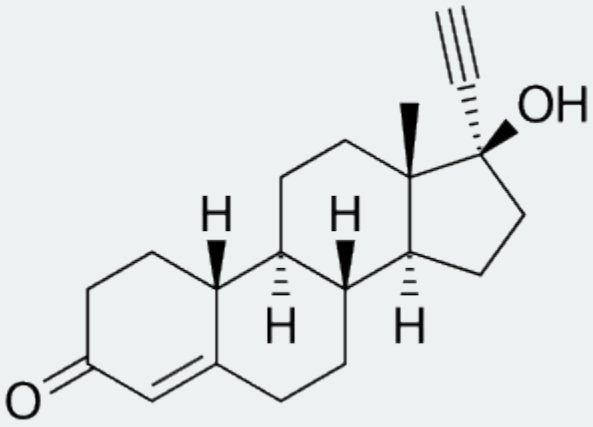
Testosterone and androsterone are the most potent male sex hormones. They control the development of male secondary sex characteristics, which include the growth of muscles, facial hair, maturation of sex organs, and sperms. Estrogens and progestins control the development of female secondary sex characteristics. Estrogens increase the size of the uterus, deposit fat in the breasts, and broaden the pelvis of females. Progestins prepare the uterus for nurturing the fertilized egg. If the egg is not fertilized, the levels of estrogens and progestins drop sharply, and menstruation begins.

Birth control

The release of estrogens and progestins during pregnancy prevents ovulation. This is mimicked by synthetic estrogens, such as ethynyl estradiol, and synthetic progestins, such as norethindrone, shown below, used in birth control formulations. As with the use of any steroid hormones, there are risks associated with synthetic hormones for birth control, including weight gain and a greater chance of forming blood clots.



Ethynyl estradiol

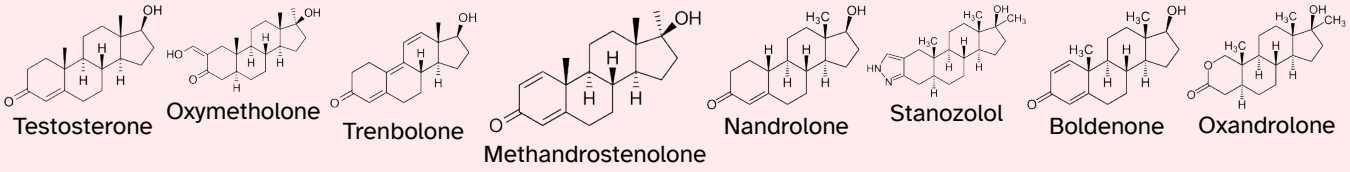


Norethindrone

Synthetic estrogens used in birth control

Anabolic steroids

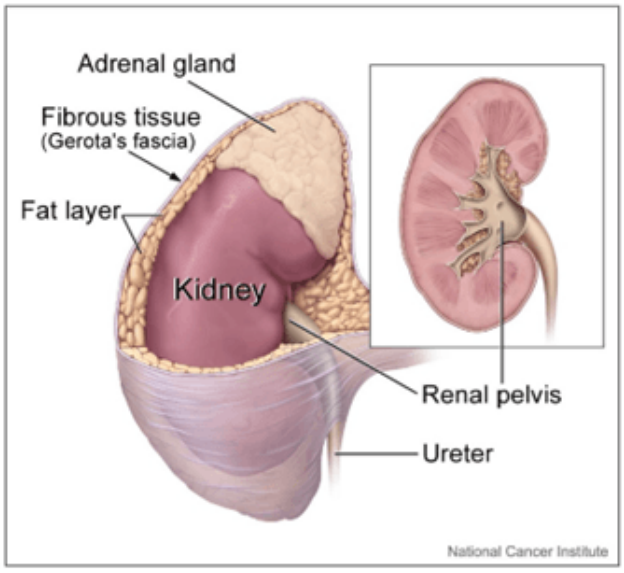
One physiological function of testosterone is increasing muscle mass and decreasing body fat. Several synthetic equivalents, called anabolic steroids, have been developed for use as **appearance and performance-enhancing drugs**, as shown in the figure below. Although there are some benefits of anabolic steroids, their harmful effects are numerous and outweigh their benefits. They may not produce a euphoric high but develop substance use disorder. They can cause early heart attacks, strokes, kidney failure, liver tumors, make pimples pop up, hair fallout, grow breasts, and reduced testicles in males, grow beards in females, and cause extreme mood changes that may lead to committing suicide. Some of these harmful effects are related to the changes in cholesterol levels, causing an increase in low-density lipoprotein (bad cholesterol), a decrease in high-density lipoprotein (good cholesterol), high blood pressure, and liver damage. The harmful effects are long-lasting and may be irreversible.



Testosterone | Oxymetholone | Trenbolone | Methandrostenolone | Nandrolone | Stanozolol | Boldenone | Oxandrolone

Anabolic steroids that are most commonly encountered by United States law enforcement

Adrenocortical hormones



Adrenocortical hormones are produced by adrenal glands on the top of the kidneys, as shown in the figure on the right (*Copyright; Alan Hoofring (Illustrator), Public domain, via Wikimedia Commons*). There are two major subclasses: **mineralocorticoids** which regulate Na^+ and K^+ ions, and **glucocorticoids** which control carbohydrate metabolism.

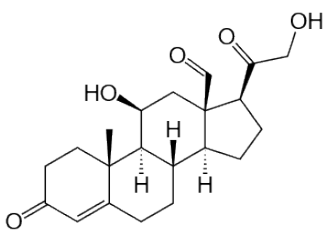
Mineralocorticoid

Aldosterone is an important mineralocorticoid that enhances the reabsorption of Na^+ and K^+ ions in the kidney tubules. The control of Na^+ and K^+ concentrations controls water absorption and swelling of tissues.

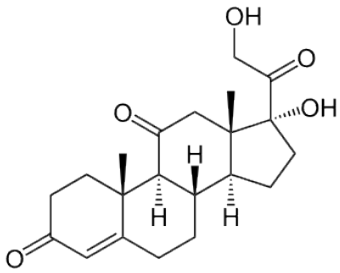
glucocorticoid

Cortisone is a glucocorticoid that increases blood glucose levels and glycogen synthesis in the liver. Cortisol is another glucocorticoid released under stress to increase blood glucose levels at the expense of the metabolism of carbohydrates, fats, and proteins.

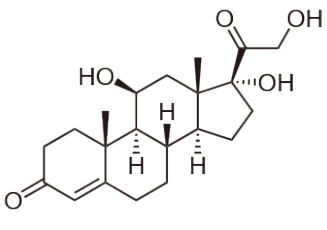
These hormones or their synthetic derivative, such as prednisone, shown below, are used to reduce inflammation, asthma, and arthritis. As with the use of steroids in general, health problems can result if these steroids are used for the long term.



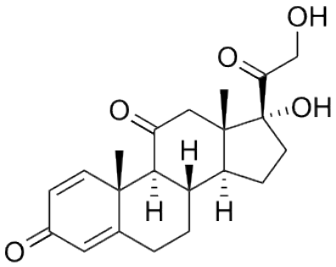
Aldosterone



Cortisone



Cortisol



Prednisone (a synthetic corticoid)

Adrenocortical hormones and their synthetic derivative

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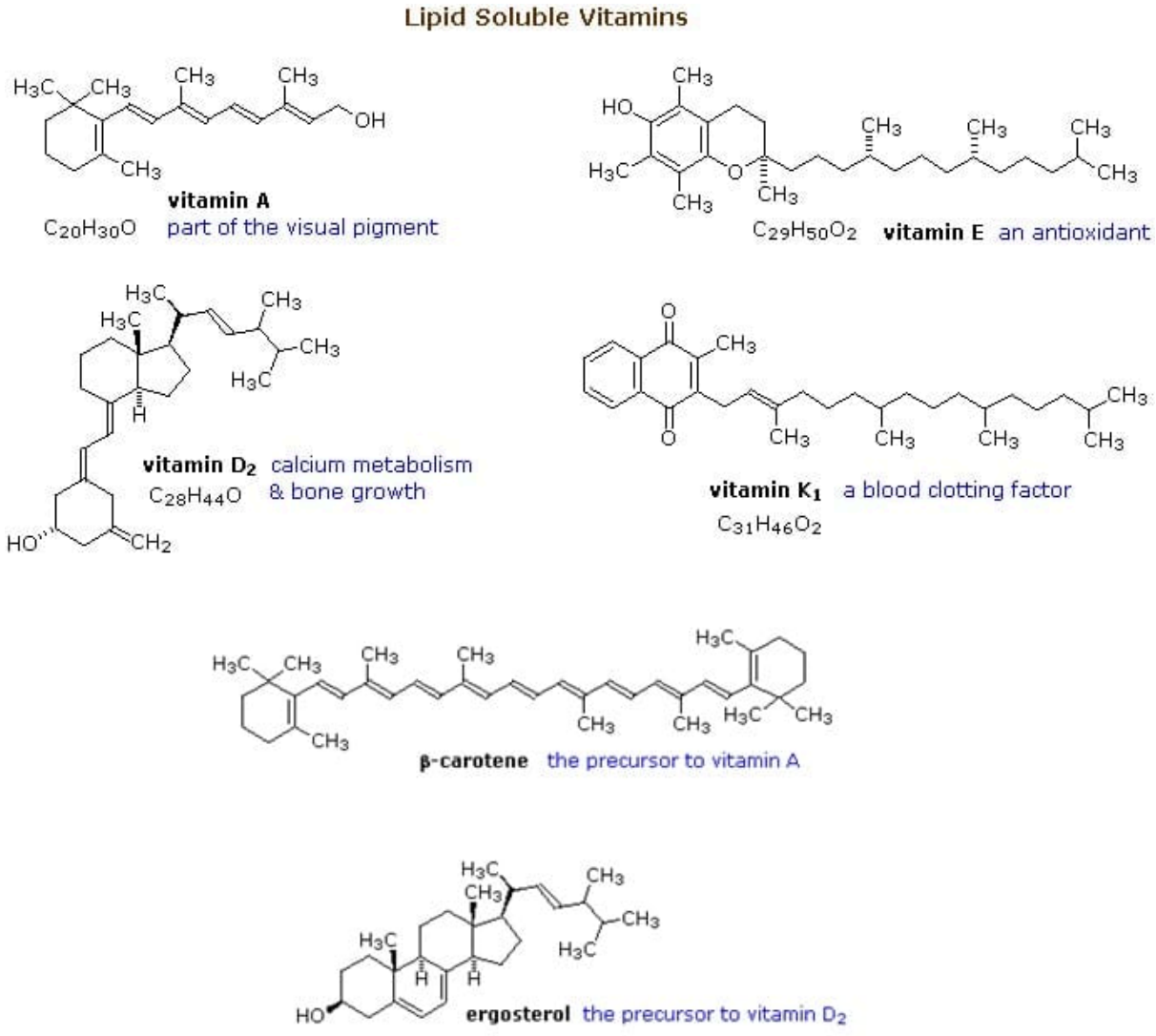
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9.7: Lipid Soluble Vitamins

The essential dietary substances called **vitamins** are commonly classified as "water soluble" or "fat soluble". Water soluble vitamins, such as vitamin C, are rapidly eliminated from the body and their dietary levels need to be relatively high. The recommended daily allotment (RDA) of vitamin C is 100 mg, and amounts as large as 2 to 3 g are taken by many people without adverse effects. The lipid soluble vitamins, shown in the diagram below, are not as easily eliminated and may accumulate to toxic levels if consumed in large quantity. The RDA for these vitamins are:

- Vitamin A 800 µg (upper limit ca. 3000 µg)
- Vitamin D 5 to 10 µg (upper limit ca. 2000 µg)
- Vitamin E 15 mg (upper limit ca. 1 g)
- Vitamin K 110 µg (upper limit not specified)

From this data it is clear that vitamins A and D, while essential to good health in proper amounts, can be very toxic. Vitamin D, for example, is used as a rat poison, and in equal weight is more than 100 times as poisonous as sodium cyanide.



From the structures shown here, it should be clear that these compounds have more than a solubility connection with lipids.

Vitamins A is a terpene, and vitamins E and K have long terpene chains attached to an aromatic moiety. The structure of vitamin D can be described as a steroid in which ring B is cut open and the remaining three rings remain unchanged. The precursors of vitamins A and D have been identified as the tetraterpene beta-carotene and the steroid ergosterol, respectively.

Contributors

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9.8: Prostaglandins and Other Eicosanoids

Prostaglandins are a group of C_{20} lipids that contain a five-membered ring with two long side chains. First isolated in the 1930s by Ulf von Euler at the Karolinska Institute in Sweden, much of the structural and chemical work on prostaglandins was carried out by Sune Bergström and Bengt Samuelsson. All three shared Nobel Prizes for their work. The name **prostaglandin** derives from the fact that the compounds were first isolated from sheep prostate glands, but they have subsequently been found to be present in small amounts in all body tissues and fluids.

The several dozen known prostaglandins have an extraordinarily wide range of biological effects. Among their many properties, they can lower blood pressure, affect blood platelet aggregation during clotting, lower gastric secretions, control inflammation, affect kidney function, affect reproductive systems, and stimulate uterine contractions during childbirth.

Prostaglandins, together with related compounds called thromboxanes and leukotrienes, make up a class of compounds called eicosanoids because they are derived biologically from 5,8,11,14-eicosatetraenoic acid, or arachidonic acid (Figure 9.8.1). Prostaglandins (PG) have a cyclopentane ring with two long side chains; thromboxanes (TX) have a six-membered, oxygen-containing ring; and leukotrienes (LT) are acyclic.

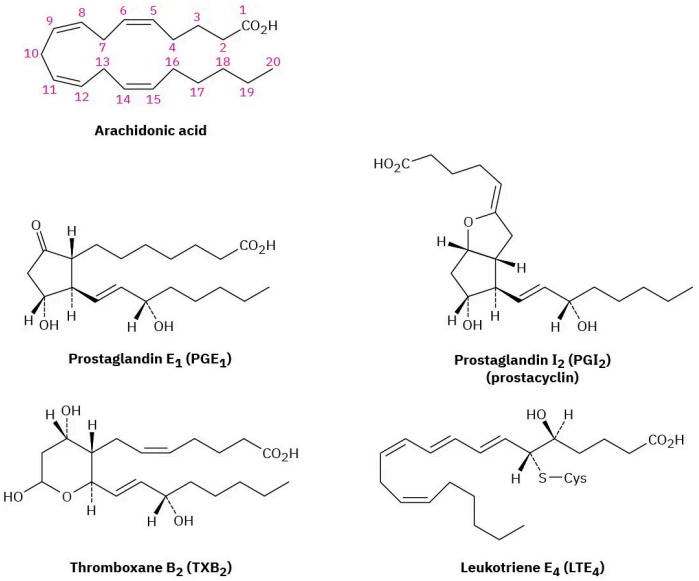


Figure 9.8.1: Structures of some representative eicosanoids. All are derived biologically from arachidonic acid.

Eicosanoids are named based on their ring system (PG, TX, or LT), substitution pattern, and number of double bonds. The various substitution patterns on the ring are indicated by letter as in Figure 9.8.2, and the number of double bonds is indicated by a subscript. Thus, PGE_1 is a prostaglandin with the "E" substitution pattern and one double bond. The numbering of the atoms in the various eicosanoids is the same as in arachidonic acid, starting with the $-CO_2H$ carbon as C1, continuing around the ring, and ending with the $-CH_3$ carbon at the other end of the chain as C20.

Eicosanoid biosynthesis begins with the conversion of arachidonic acid to PGH_2, catalyzed by the multifunctional PGH synthase (PGHS), also called cyclooxygenase (COX). There are two distinct enzymes, PGHS-1 and PGHS-2 (or COX-1 and COX-2), both of which accomplish the same reaction but appear to function independently. COX-1 carries out the normal physiological production of prostaglandins, and COX-2 produces additional prostaglandin in response to arthritis or other inflammatory conditions. Vioxx, Bextra, and several other drugs selectively inhibit the COX-2 enzyme but cause potentially serious heart and gastrointestinal problems in weakened patients. (See the Chapter 15 *Chemistry Matters*.)

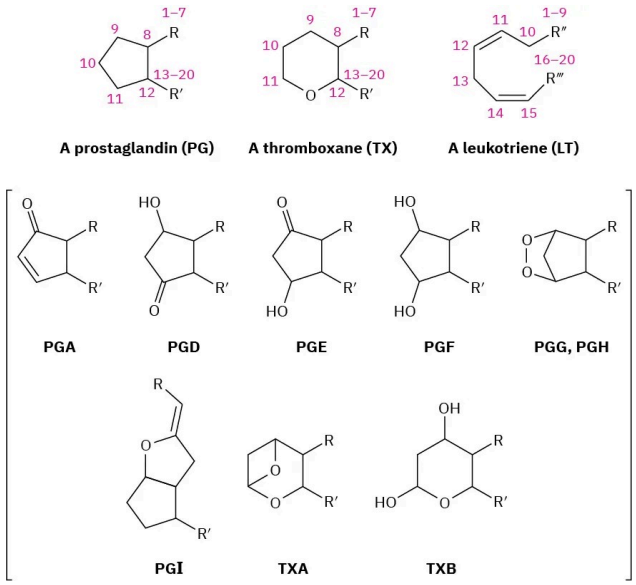


Figure 9.8.2: The naming system for eicosanoids.

PGHS accomplishes two transformations, an initial reaction of arachidonic acid with O_2 to yield PGG_2 and a subsequent reduction of the hydroperoxide group (–OOH) to the alcohol PGH_2. The sequence of steps involved in these transformations was shown in Figure 9.8.1.

Further processing of PGH_2 leads to other eicosanoids. PGE_2, for instance, arises by an isomerization of PGH_2 catalyzed by PGE synthase (PGES) (Figure 9.8.3).

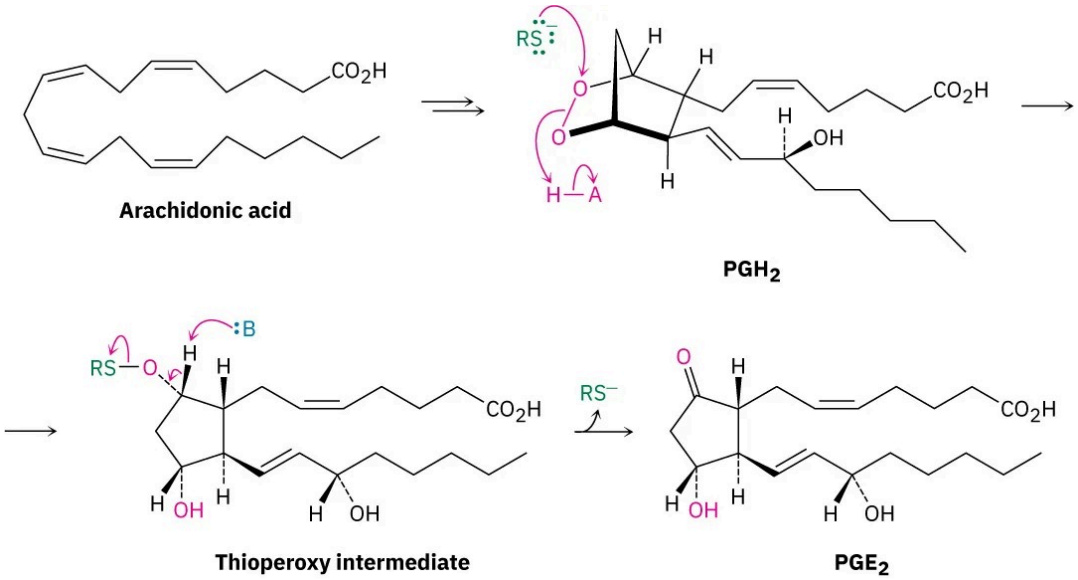


Figure 9.8.3: Mechanism of the conversion of PGH_2 into PGE_2.

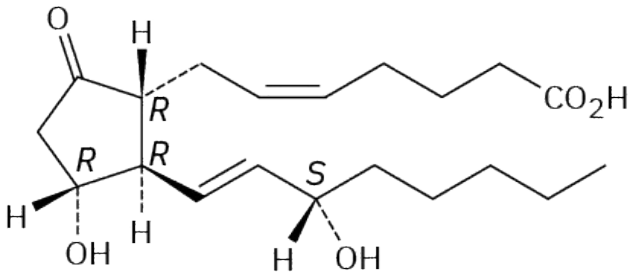
Exercise 9.8.1

Assign *R* or *S* configuration to each chirality center in prostaglandin E_2 (Figure 9.8.3), the most abundant and biologically potent of mammalian prostaglandins.

Answer available at the end of this section.

Answers

Exercise 9.8.1



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10: AMINES AND NEUROTRANSMITTERS

10.1: Why This Chapter?
10.2: Physical Properties of Amines
10.3: Chemical Properties of Amines. Bases and Salt Formation.
10.4: Naming Amines
10.5: Amines as Neurotransmitters
10.6: Neurotransmitters and Antidepressants

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10.1: Why This Chapter?

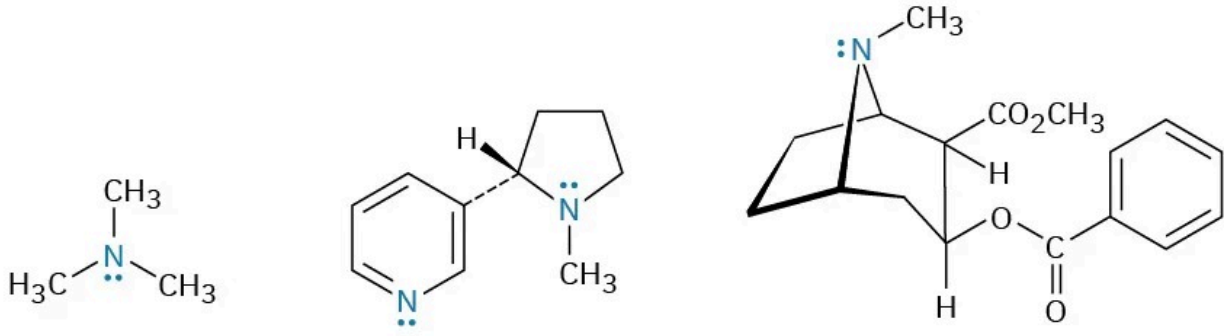
By the end of this chapter, we will have seen all the common functional groups. Of those groups, carbonyl compounds and amines are the most abundant and have the richest chemistry. In addition to proteins and nucleic acids, the majority of pharmaceutical agents contain amine functional groups, and many of the common coenzymes necessary for biological catalysis are amines.



Figure 10.1.1: The characteristic and unmistakable odor of fish is due to a mixture of simple alkylamines. (credit: modification of work “Pike Place” by Sharat Ganapati/Flickr, CC BY 2.0)

Amines are organic derivatives of ammonia in the same way that alcohols and ethers are organic derivatives of water. Like ammonia, amines contain a nitrogen atom with a lone pair of electrons, making amines both basic and nucleophilic. We’ll soon see, in fact, that most of the chemistry of amines depends on the presence of this lone pair of electrons.

Amines occur widely in all living organisms. Trimethylamine, for instance, occurs in animal tissues and is partially responsible for the distinctive odor of fish; nicotine is found in tobacco; and cocaine is a stimulant found in the leaves of the South American coca bush. In addition, amino acids are the building blocks from which all proteins are made, and cyclic amine bases are constituents of nucleic acids.



Trimethylamine **Nicotine** **Cocaine**

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10.2: Physical Properties of Amines

Learning Objectives

- Explain why the boiling points of primary and secondary amines are higher than those of alkanes or ethers of similar molar mass but are lower than those of alcohols.
- Compare the boiling points of tertiary amines with alcohols, alkanes, and ethers of similar molar mass.
- Compare the solubilities in water of amines of five or fewer carbon atoms with the solubilities of comparable alkanes and alcohols in water.

Primary and secondary amines have hydrogen atoms bonded to an nitrogen atom and are therefore capable of hydrogen bonding (part (a) of Figure 10.2.1), although not as strongly as alcohol molecules (which have hydrogen atoms bonded to an oxygen atom, which is more electronegative than nitrogen). These amines boil at higher temperatures than alkanes but at lower temperatures than alcohols of comparable molar mass. For example, compare the boiling point of methylamine (CH_3NH_2; –6°C) with those of ethane (CH_3CH_3; –89°C) and methanol (CH_3OH; 65°C). Tertiary amines have no hydrogen atom bonded to the nitrogen atom and so cannot participate in intermolecular hydrogen bonding. They have boiling points comparable to those of ethers (Table 10.2.1).

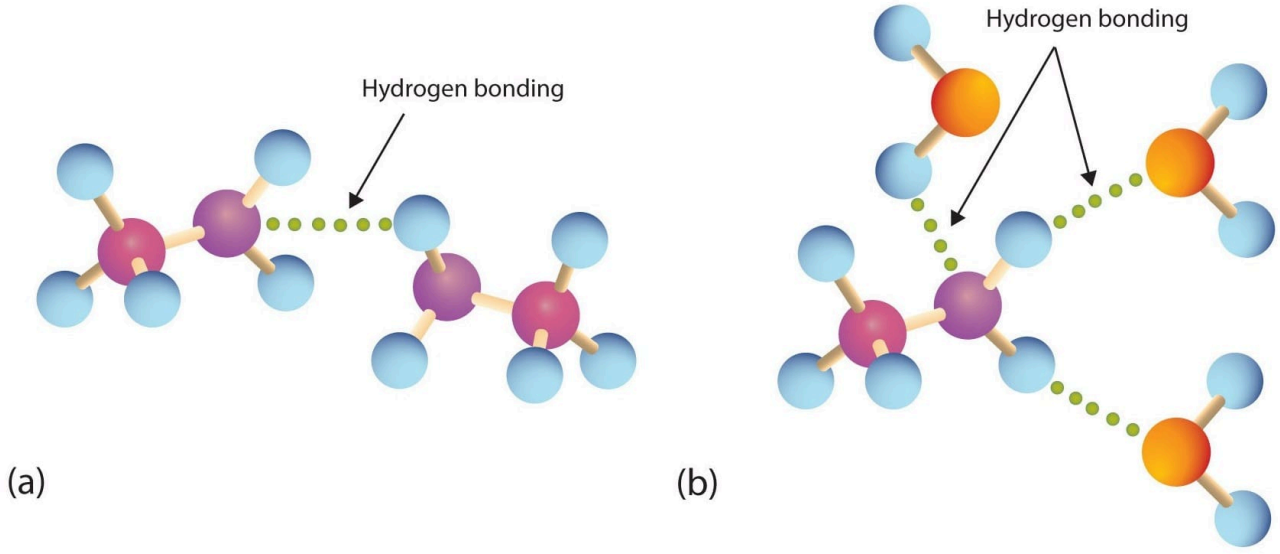


Figure 10.2.1: Hydrogen Bonding. (a) Amine molecules are associated through hydrogen bonding. (b) An amine molecule can form a hydrogen bond with water molecules.

Table 10.2.1: Physical Properties of Some Amines and Comparable Oxygen-Containing Compounds

Name	Condensed Structural Formula	Class	Molar Mass	Boiling Point (°C)	Solubility at 25°C (g/100 g Water)
butylamine	$CH_3CH_2CH_2CH_2NH_2$	1°	73	78	miscible
diethylamine	$(CH_3CH_2)_2NH$	2°	73	55	miscible
butyl alcohol	$CH_3CH_2CH_2CH_2OH$	—	74	118	8
dipropylamine	$(CH_3CH_2CH_2)_2NH$	2°	101	111	4
triethylamine	$(CH_3CH_2)_3N$	3°	101	90	14
dipropyl ether	$(CH_3CH_2CH_2)_2O$	—	102	91	0.25

All three classes of amines can engage in hydrogen bonding with water (Figure 10.2.1*b*). Amines of low molar mass are quite

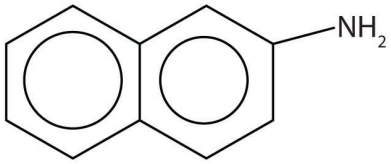
soluble in water; the borderline of solubility in water is at five or six carbon atoms.

To Your Health: Amines in Death and Life

Amines have “interesting” odors. The simple ones smell very much like ammonia. Higher aliphatic amines smell like decaying fish. Or perhaps we should put it the other way around: Decaying fish give off odorous amines. The stench of rotting fish is due in part to two diamines: putrescine and cadaverine. They arise from the decarboxylation of ornithine and lysine, respectively, amino acids that are found in animal cells.

$$HOCH_2CH_2OH$$

Aromatic amines generally are quite toxic. They are readily absorbed through the skin, and workers must exercise caution when handling these compounds. Several aromatic amines, including β-naphthylamine, are potent carcinogens.



Key Takeaways

- Primary and secondary amines have higher boiling points than those of alkanes or ethers of similar molar mass because they can engage in intermolecular hydrogen bonding. Their boiling points are lower than those of alcohols because alcohol molecules have hydrogen atoms bonded to an oxygen atom, which is more electronegative.
- The boiling points of tertiary amines, which cannot engage in hydrogen bonding because they have no hydrogen atom on the nitrogen atom, are comparable to those of alkanes and ethers of similar molar mass.
- Because all three classes of amines can engage in hydrogen bonding with water, amines of low molar mass are quite soluble in water.

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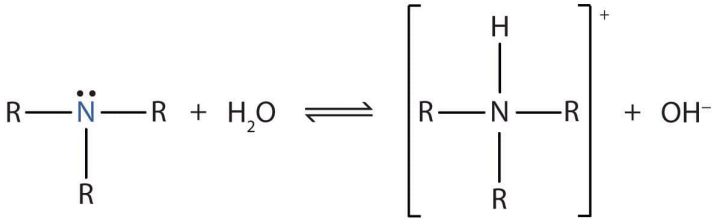
- 15.11: Physical Properties of Amines by Staff is licensed CC BY-NC-SA 3.0. Original source: https://2012books.lardbucket.org/books/introduction-to-chemistry-general-organic-and-biological.

10.3: Chemical Properties of Amines. Bases and Salt Formation.

Learning Objectives

- Name the typical reactions that take place with amines.
- Describe heterocyclic amines.

The main chemical property of amines is their ability to act as weak organic bases. Recall that ammonia (NH_3) acts as a base because the nitrogen atom has a lone pair of electrons that can accept a proton. Amines also have a lone electron pair on their nitrogen atoms and can accept a proton from water to form substituted ammonium (NH_4^+) ions and hydroxide (OH^-) ions:



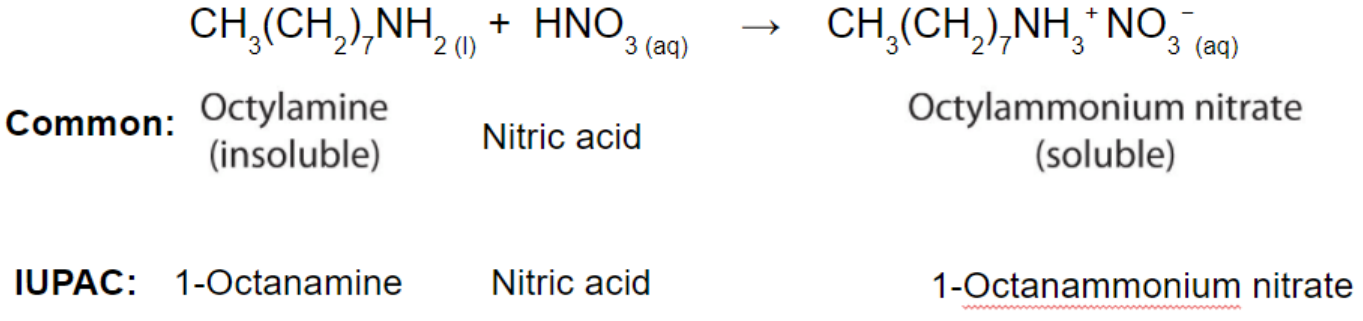
As a specific example, methylamine reacts with water to form the methylammonium ion and the OH^- ion.

$$CH_3NH_2(aq) + H_2O \rightleftharpoons CH_3NH_3^+(aq) + OH^-(aq)$$

Methylamine — Methylammonium ion

The K_b value for methylamine is 4.6×10^{-4}.

Since they are bases, amines will react with acids to form salts soluble in water, including those amines that are not very soluble in water:



Amine salts are named like other salts: the name of the cation is followed by the name of the anion. In the name for the cation, we change "**amine**" to "**ammonium**".

Example 10.3.1

What are the formulas of the acid and base that react to form $[CH_3NH_2CH_2CH_3]^+CH_3COO^-$? What is the name of the salt

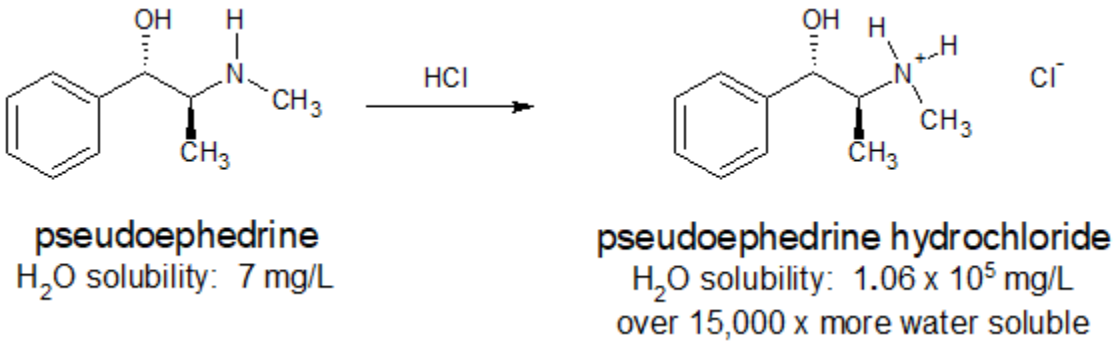
Solution

The cation has two groups—methyl and ethyl—attached to the nitrogen atom. It comes from ethylmethylamine ($CH_3NHCH_2CH_3$). The anion is the acetate ion. It comes from acetic acid (CH_3COOH).

The name of the salts is ehtylmethylammonium ethanoate (IUPAC name) or ehtylmethylammonium acetate (common name

Ammonium Salt Formation and Water Solubility

Many pharmaceuticals include amine functional groups. Sometimes the basicity of these amine groups is used to increase the water solubility of a drug so that it can be administered orally or intravenously. Ammonium salts are also thermally more stable and have less odor than their "free base" conjugates. The antihistamine, pseudoephedrine, reacts with hydrochloric acid to form the water-soluble ammonium salt as shown below.



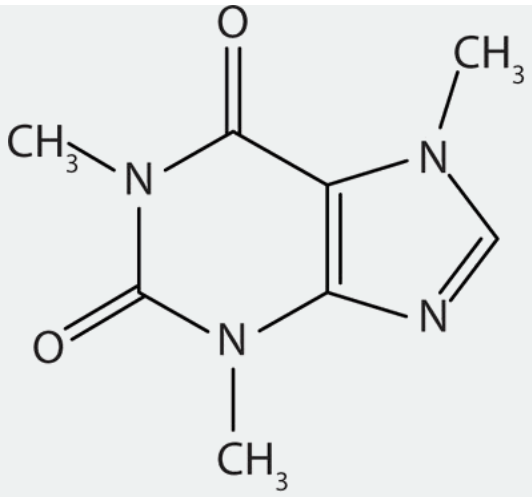
Heterocyclic Amines

Looking back at the various cyclic hydrocarbons discussed previously, we see that all the atoms in the rings of these compounds are carbon atoms. In other cyclic compounds, called **heterocyclic compounds** (Greek *heteros*, meaning “other”), nitrogen, oxygen, sulfur, or some other atom is incorporated in the ring. Many heterocyclic compounds are important in medicine and biochemistry. Some compose part of the structure of the nucleic acids, which in turn compose the genetic material of cells and direct protein synthesis.

Many heterocyclic amines occur naturally in plants. Like other amines, these compounds are basic. Such a compound is an **alkaloid**, a name that means “like alkalis.” Many alkaloids are physiologically active, including the familiar drugs caffeine, nicotine, and cocaine.

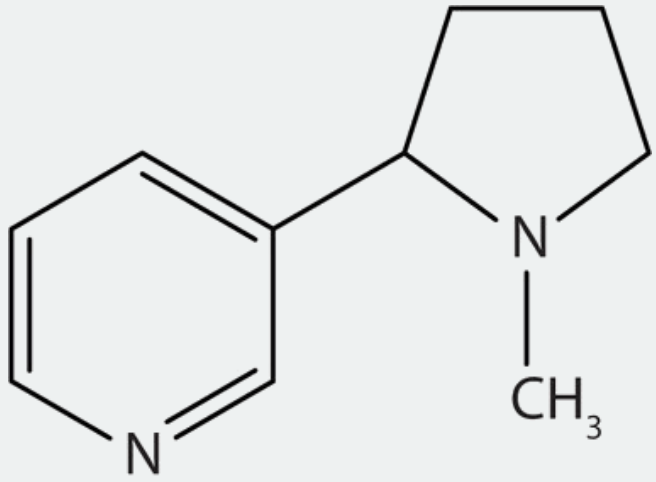
To Your Health: Three Well-Known Alkaloids

Caffeine is a stimulant found in coffee, tea, and some soft drinks. Its mechanism of action is not well understood, but it is thought to block the activity of adenosine, a heterocyclic base that acts as a neurotransmitter, a substance that carries messages across a tiny gap (synapse) from one nerve cell (neuron) to another cell. The effective dose of caffeine is about 200 mg, corresponding to about two cups of strong coffee or tea.



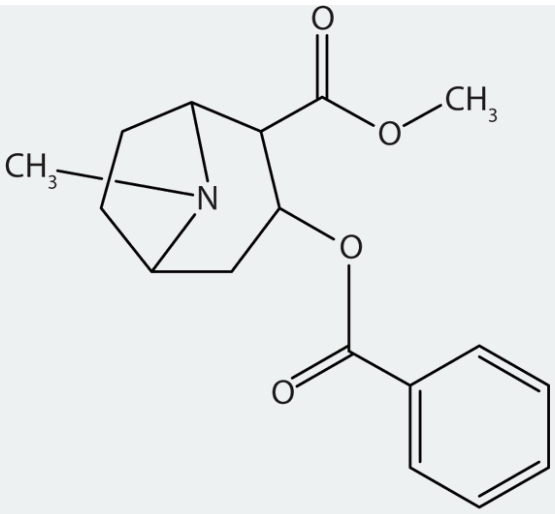
Caffeine

Nicotine acts as a stimulant by a different mechanism; it probably mimics the action of the neurotransmitter acetylcholine. People ingest this drug by smoking or chewing tobacco. Its stimulant effect seems transient, as this initial response is followed by depression. Nicotine is highly toxic to animals. It is especially deadly when injected; the lethal dose for a human is estimated to be about 50 mg. Nicotine has also been used in agriculture as a contact insecticide.



Nicotine

Cocaine acts as a stimulant by preventing nerve cells from taking up dopamine, another neurotransmitter, from the synapse. High levels of dopamine are therefore available to stimulate the pleasure centers of the brain. The enhancement of dopamine action is thought to be responsible for cocaine's "high" and its addictive properties. After the binge, dopamine is depleted in less than an hour. This leaves the user in a pleasureless state and (often) craving more cocaine.



Cocaine

Cocaine is used as the salt cocaine hydrochloride and in the form of broken lumps of the free (unneutralized) base, which is called *crack cocaine*.

$$C_{17}H_{21}O_4N + HCl \longrightarrow C_{17}H_{21}O_4NH^+Cl^-$$

Cocaine (freebase) → Cocaine hydrochloride

Because it is soluble in water, cocaine hydrochloride is readily absorbed through the watery mucous membranes of the nose when it is snorted. Crack cocaine is more volatile than cocaine hydrochloride. It vaporizes at the temperature of a burning cigarette. When smoked, cocaine reaches the brain in 15 s.

Summary

Amines are bases; they react with acids to form salts. Salts of aniline are properly named as *ammonium* compounds. Heterocyclic amines are cyclic compounds with one or more nitrogen atoms in the ring.

Concept Review Exercises

1. Explain the basicity of amines.
2. Contrast the physical properties of amines with those of alcohols and alkanes.
3. What is a cyclic amine?

Answers

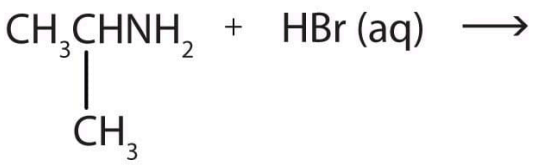
1. Amines have a lone pair of electrons on the nitrogen atom and can thus act as proton acceptors (bases).
2. The solubilities of amines are similar to those of alcohols; the boiling points of primary and secondary amines are similar to those of alcohols; the boiling points of tertiary amines, which cannot engage in hydrogen bonding because they do not have a hydrogen atom on the nitrogen atom, are comparable to those of alkanes.
3. Cyclic amines are ring compounds with nitrogen atoms in the ring.

Exercises

1. What salt is formed in each reaction? Write its condensed structural formula and its name.
   a. $CH_3NH_2(aq) + HBr(aq) \rightarrow$
   b. $CH_3NHCH_3(aq) + HNO_3(aq) \rightarrow$

2. What salt is formed in each reaction? Draw its structure.

a.



b.



Answer

1. a. $CH_3NH_3^+Br^-(aq)$ methylammonium bromide
   b. $[CH_3NH_2CH_3]^+NO_3^-(aq)$ dimethylammonium nitrate

Contributors and Attributions

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Amines as Bases. (2020, August 17). Retrieved May 23, 2021, from https://chem.libretexts.org/@go/page/16035

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10.4: Naming Amines

Objectives

After completing this section, you should be able to

1. classify a given amine as being primary, secondary or tertiary.
2. explain, briefly, the difference in meaning of the terms primary, secondary and tertiary when they are applied to the structures of amines and alcohols.
3. determine whether a given structure represents a quaternary ammonium cation.
4. provide an acceptable IUPAC name for an amine, given its Kekulé, condensed or shorthand structure.
5. draw the structure of an amine, given its IUPAC name.
6. give the name and structure of one typical heterocyclic amine (e.g., pyridine).

Key Terms

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

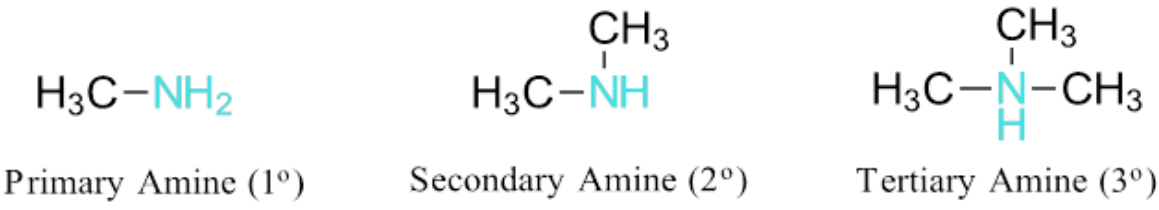
- amine
- primary amine
- secondary amine
- quaternary ammonium cation
- tertiary amine

Study Notes

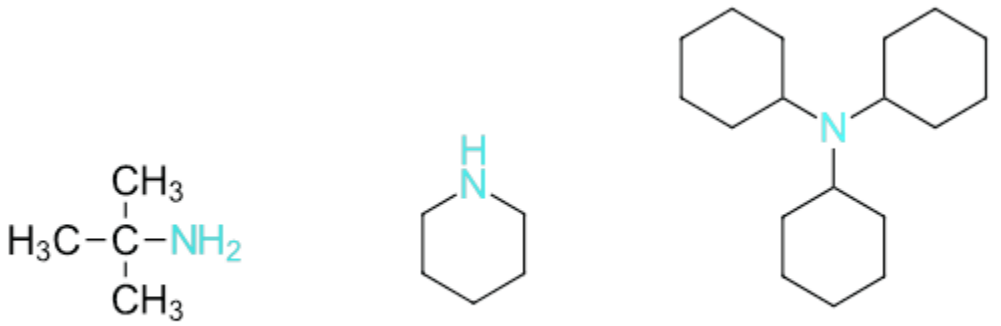
You should recognize that heterocyclic amines—compounds in which the nitrogen atom occurs as part of a ring—are very common in organic chemistry. Be prepared to meet such compounds throughout this, and subsequent chapters, but do not try to memorize all of the names and structures givenin the reading. You should, however, commit the structures of pyridine and pyrrole to memory.

Classification of Amines

Amines can be either alkyl-substituted (alkylamines) or aryl-substituted (arylamines). Although much of the chemistry of the two classes is similar, there are also substantial differences. Amines are classified as primary (RNH_2), secondary (R_2NH), or tertiary (R_3N), depending on the number of organic substituents attached to nitrogen. Thus, methylamine (CH_3NH_2) is a primary amine, dimethylamine [$(CH_3)_2NH$] is a secondary amine, and trimethylamine [$(CH_3)_3N$] is a tertiary amine.

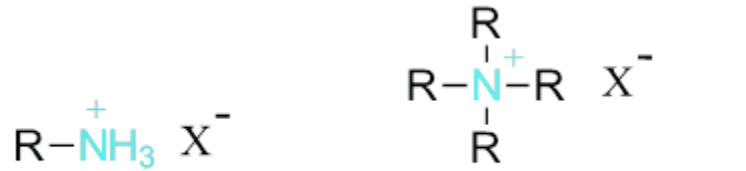


Example

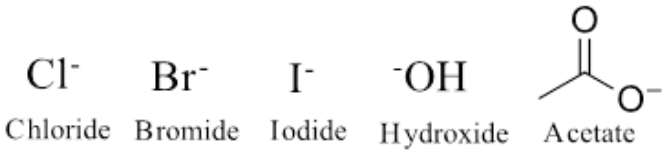


Primary Amine (1°) Secondary Amine (2°) Tertiary Amine (3°)

Amines attached to 4 substituents and at least one substituent is a hydrogen are called ammonium salts. Amines attached to 4 alkyl substituents are called quaternary ammonium salts. The nitrogen in ammonium salts lacks lone pair electrons and carries a formal positive charge. Ammonium salts are also require a negatively charged counter-ion which can vary in composition.

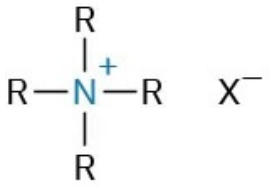


Ammonium Salt Quarternary Ammonium Salt



Chloride Bromide Iodide Hydroxide Acetate

Common Counterions of Ammonium Salts

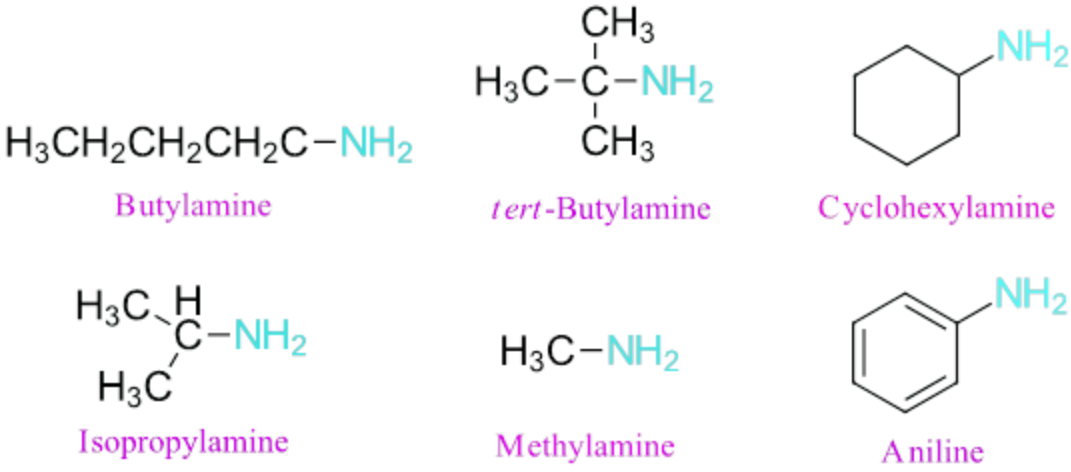


A quaternary ammonium salt

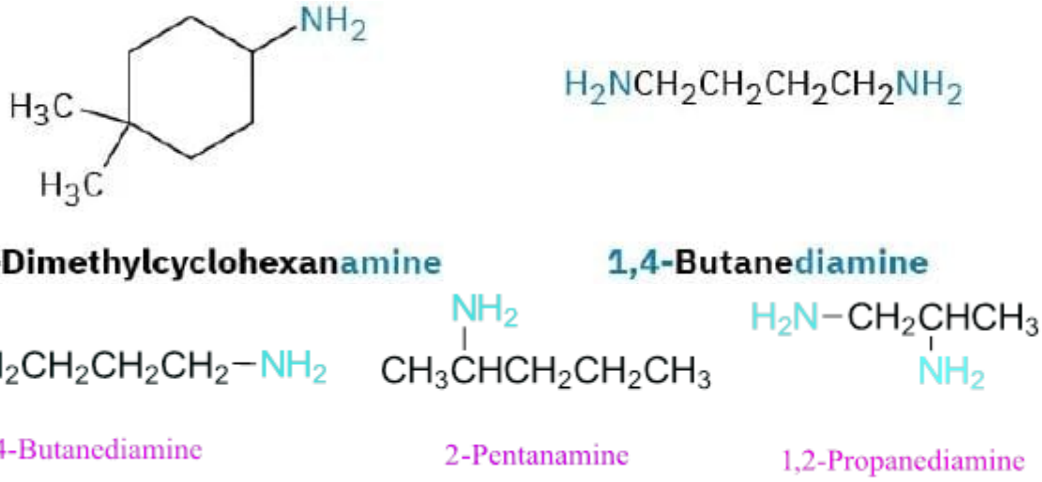
Nomenclature of Amines

Nomenclature of Primary Amines

Primary amines are named in two main ways using the IUPAC system. They can either be named as alkylamines or as alkanamines. Most 1^{o} amines which are attached to linear alkanes, cycloalkanes, and alkyl groups with common names (**Section 3.3**), tend to be named as alkylamines. The alkyl groups is named as a substituent (**prefix + yl**) then the suffix -amine is added. Many amines have common names that are used by IUPAC, for example the primary arylamine ($C_6H_5NH_2$) is called aniline.

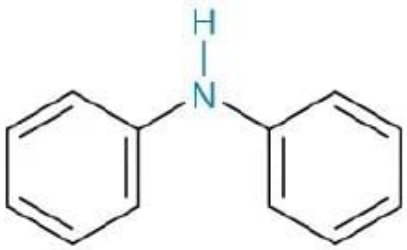


Other primary amines tend to be named as alkanamines. The alkyl group is named as an alkane (**prefix+ane**) and –e ending is replaced with the suffix **-amine**. The –e ending is not removed for diamines.

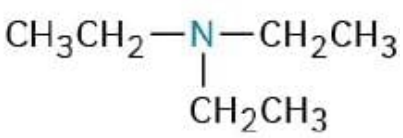


Nomenclature of Symmetrical Secondary and Tertiary Amines

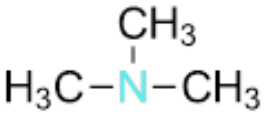
Symmetrical 2^{o} and 3^{o} amines (where all substituents are identical) are named as alkylamines and the prefix di- or tri -added to indicate the number of substituents.



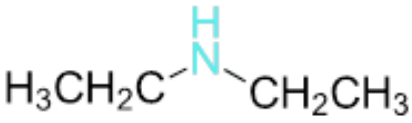
Diphenylamine



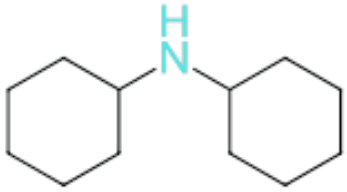
Triethylamine



Trimethylamine



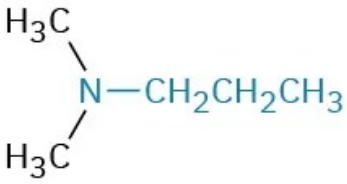
Diethylamine



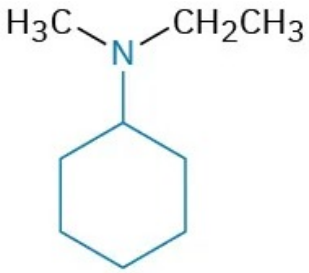
Dicyclohexylamine

Nomenclature of Unsymmetrical Secondary and Tertiary Amines

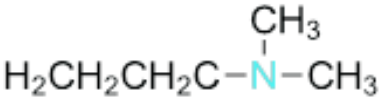
Unsymmetrical 2^{o} and 3^{o} amines are named with the largest chain being the base chain (**prefix+yl+amine**). The other alkyl groups are named as N-substituents. This notation is used to indicate that the substituent is attached to the amine nitrogen and not an alkyl carbon.



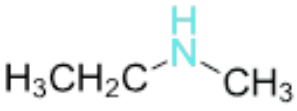
***N,N*-Dimethylpropylamine**



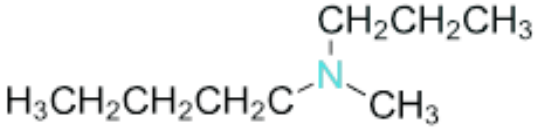
***N*-Ethyl-*N*-methylcyclohexylamine**



N,N-Dimethylpropylamine



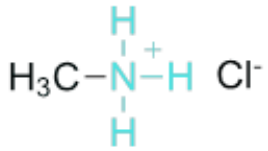
N-Methylethylamine



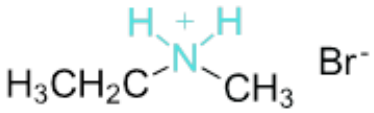
N-Methyl-N-propylbutylamine

Nomenclature of Ammonium Salts

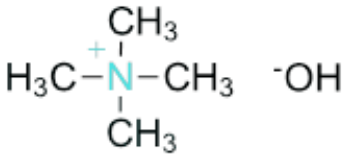
Ammonium salts and quaternary ammonium salts are named using the same rules as 2^{o} and 3^{o} amines except the –amine suffix is replaces with -ammonium + the name of the counter ion. The counter ion name is separated with a space.



Methylammonium Chloride



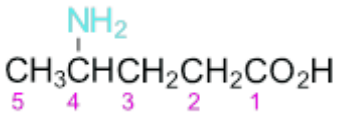
N-Methylethylammonium Bromide



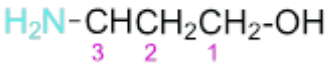
Tetramethylammonium Hydroxide

Amines as the lower functional group

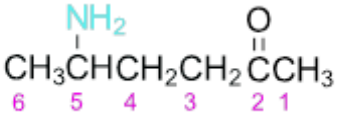
Amines have one of the lower functional group priorities in the IUPAC nomenclature system. When present in a compound with a functional group of higher priority, the amine group is named as a substituent called **“amino.”**



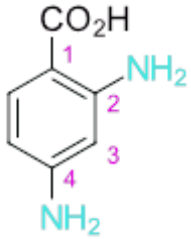
4-Aminopentanoic Acid



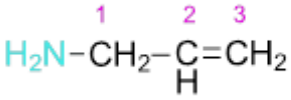
3-Amino-1-propanol



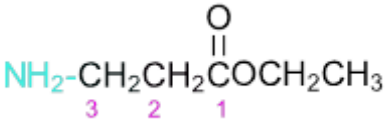
4-Amino-2-Butanone



2,4-Diaminobenzoic Acid



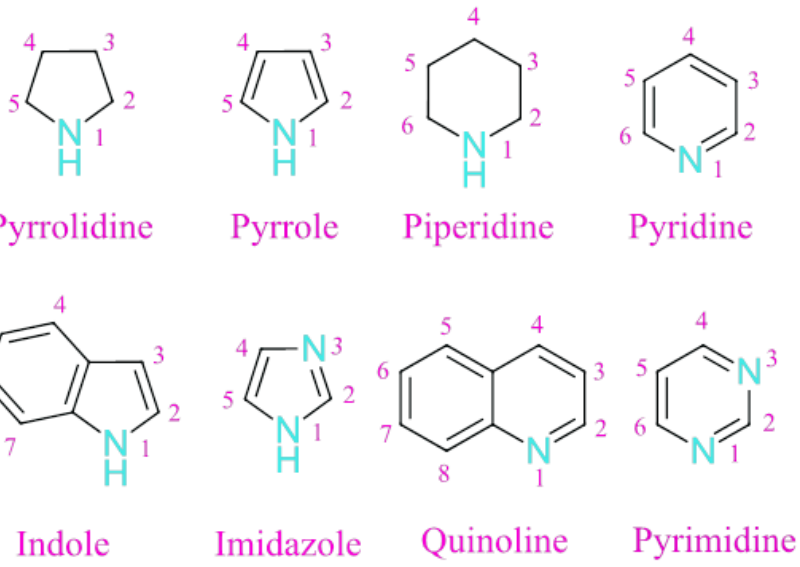
2-Propen-1-amine
(NH_2 Has Priority)



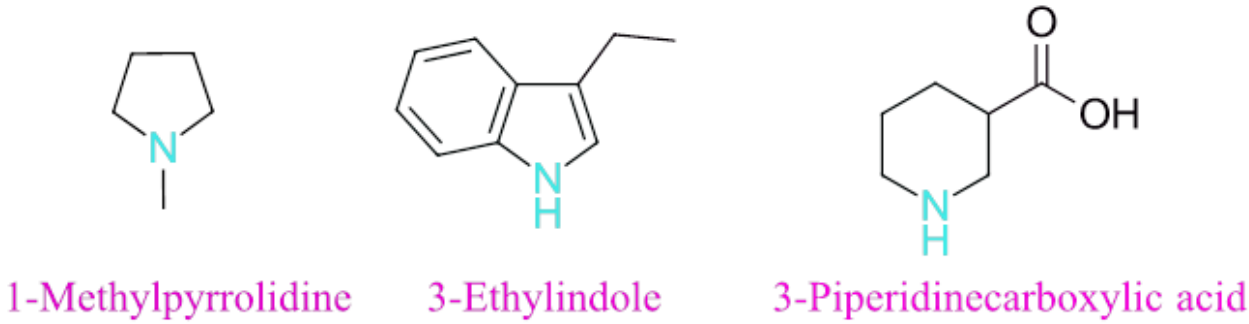
Ethyl 3-aminopropionate

Nomenclature of Heterocyclic Amines

Heterocyclic amines have one or more nitrogens as part of the ring and can be aliphatic or aromatic. Most heterocyclic amine ring systems have a common name and are numbered such that the heterocyclic nitrogen always gets position 1. An amine attached to a heterocyclic ring is named as an amino substituent.

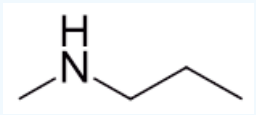


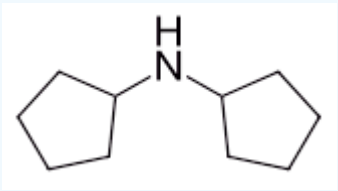
Examples:

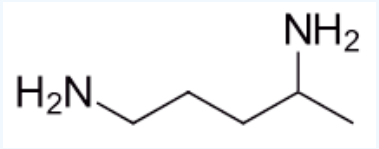


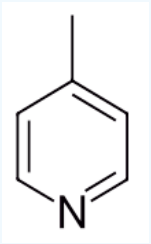
Exercises 10.4.1

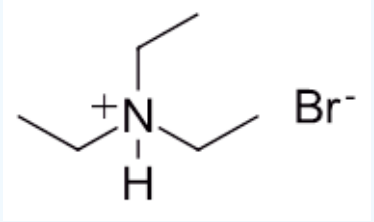
Name the following compounds:

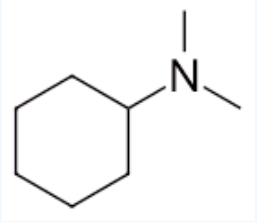
a) 

b) 

c) 

d) 

e) 

f) 

Answers available at the end of this section.

Exercise 10.4.2

Draw the structures corresponding to the following names:

a. 3-Bromo-pentan-2-amine
b. Cyclopentanamine
c. *Trans*-3-ethylcyclohexanamine
d. *Sec*-butyl-*tert*-butyl amine
e. N,N-Dimethyl-3-pentanamine
f. 4-Methyl-2-hexanamine
g. 6-Bromo-4-amino-2-heptanol

Answer available at the end of this section.

Exercise 10.4.3

Draw the structures of the following heterocyclic compounds:

a. 4-Methoxyindole
b. 1,4-Dimethylpyrrole
c. 3-(N,N-Dimethylamino)pyridine
d. 2-Aminopyrimidine

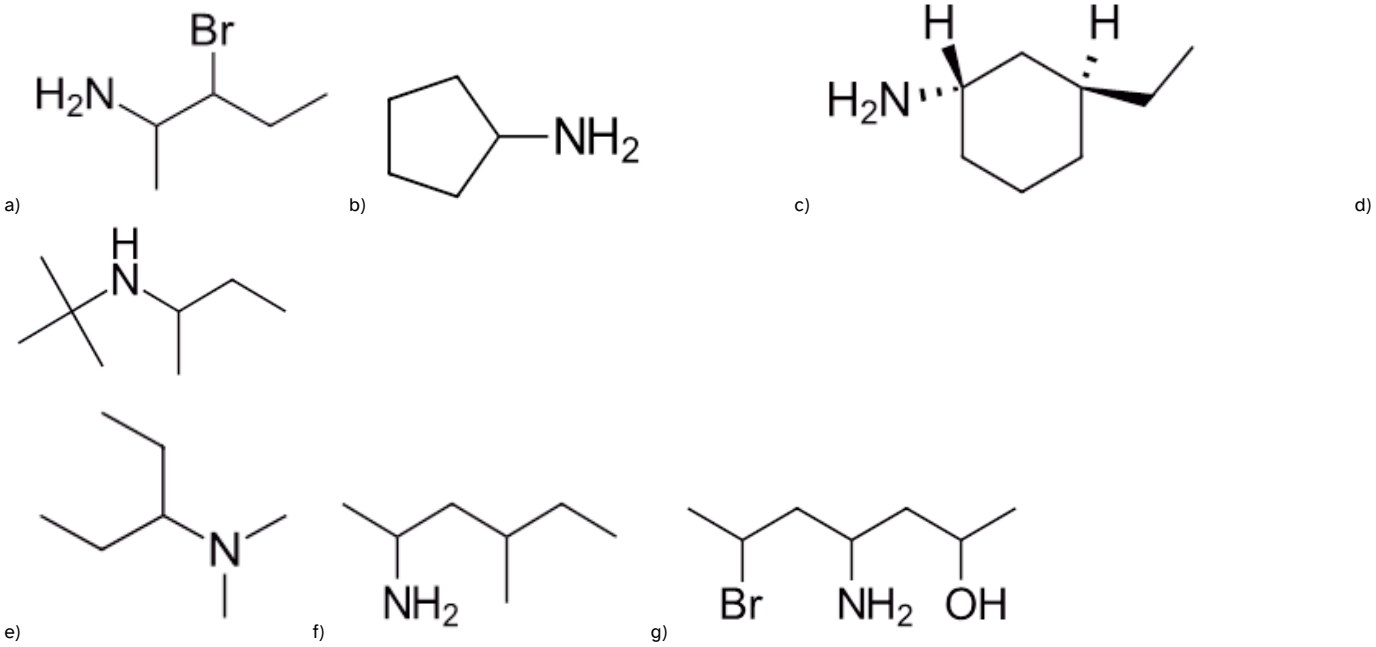
Answer available at the end of this section.

Answers

Exercises 10.4.1

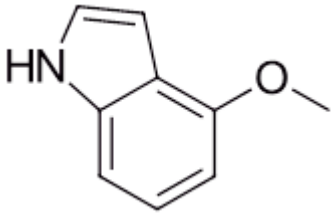
a. N-Methylpropylamine
b. Dicyclopentylamine
c. 1,4-Pentanediamine
d. 4-Methylpyridine
e. Triethylammonium Bromide
f. N,N-Dimethylcyclohexylamine

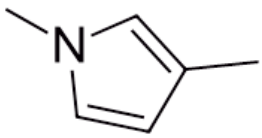
Exercise 10.4.2

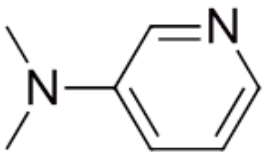


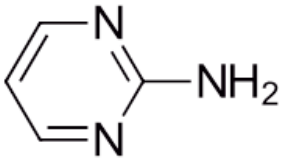
a) b) c) d) e) f) g)

Exercise 10.4.3

a) 

b) 

c) 

d) 

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10.5: Amines as Neurotransmitters

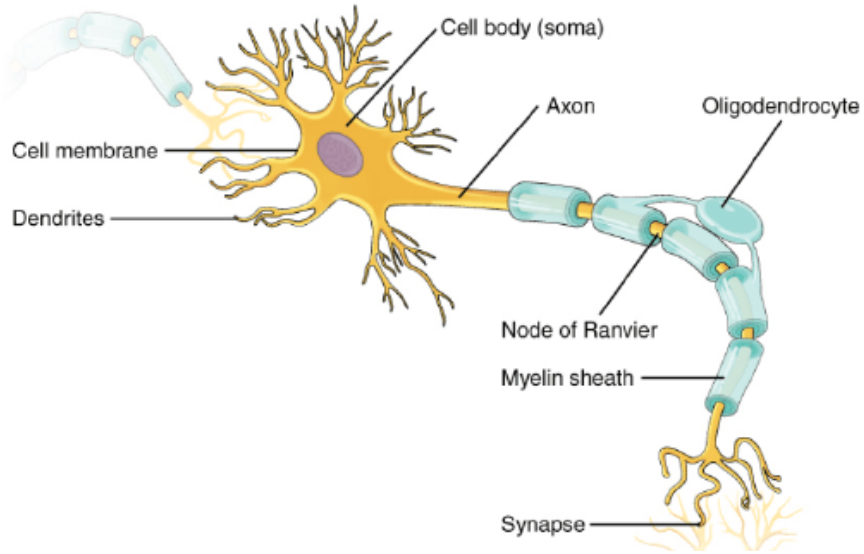
Learning Objectives

- Describe how neurotransmitters work.

Amines have powerful biological functions. Many amines act as neurotransmitter and psychoactive drugs. These molecules generally produce their effects by affecting brain chemistry, which in turn may cause changes in a person's mood, thinking, perception, and/or behavior. Each molecule tends to have a specific action on one or more neurotransmitters or neurotransmitter receptors in the brain. Generally, they act as either agonists or antagonists.

- **Agonists** are drugs that increase the activity of particular neurotransmitters. They might act by promoting the synthesis of the neurotransmitters, reducing their reuptake from synapses, or mimicking their action by binding to receptors for the neurotransmitters.
- **Antagonists** are drugs that decrease the activity of particular neurotransmitters. They might act by interfering with the synthesis of the neurotransmitters or by blocking their receptors so the neurotransmitters cannot bind to them.

Chemistry of the Nervous System



The brain and the rest of the nervous system are composed of many different types of cells, but the primary functional unit is a cell called the neuron (nerve cell) . All sensations, movements, thoughts, memories, and feelings are the result of signals that pass through neurons. Neurons consist of three parts (Figure

). The

cell body

contains the nucleus, where most of the molecules that the neuron needs to survive and function are manufactured.

Dendrites

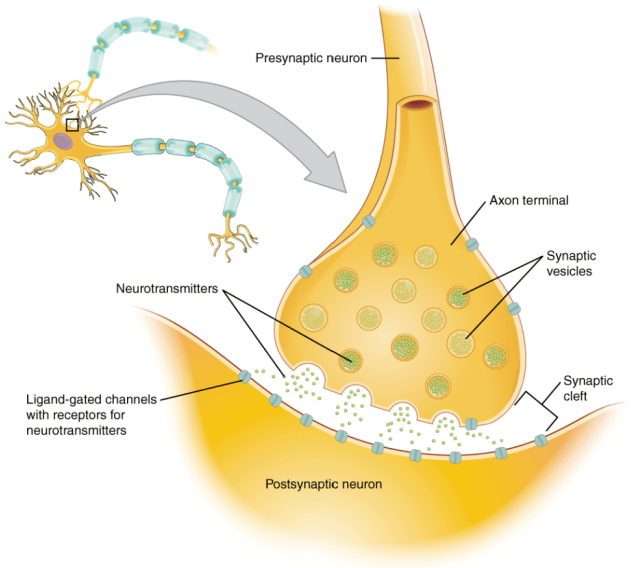
extend out from the cell body like the branches of a tree and receive messages from other nerve cells. Signals then pass from the dendrites through the cell body and may travel away from the cell body down an

axon

to another neuron, a muscle cell, or cells in some other organ.

Figure 10.5.2 *Parts of a neuron.*

Scientists have learned a great deal about neurons by studying the synapse—the place where a signal passes from the neuron



to another cell. When the signal reaches the end of the axon it stimulates the release of tiny **sacs**. These sacs release chemicals called neurotransmitters into the **synapse** (Figure 10.5.3) . The neurotransmitters cross the synapse and attach to **receptors** on the neighboring cell. These receptors can change the properties of the receiving cell. If the receiving cell is also a neuron, the signal can continue the transmission to the next cell.

> Neurotransmiters
>
> Neurotransmitters are that enable . It is a type of chemical messenger which transmits signals across a , such as a , from one (nerve cell) to another "target" neuron.

Figure 10.5.3 *The synapse.* The synapse is a connection between a neuron and its target cell (which is not necessarily a neuron).

Biochemical Theories of Brain Diseases

The only direct action of a neurotransmitter is to activate a receptor. Therefore, the effects of a neurotransmitter system depend on the connections of the neurons that use the transmitter, and the chemical properties of the receptors that the transmitter binds to. An understanding of the functions of neurotransmitters (Table 10.5.1) gives us a better idea of how an imbalance of these substances could contribute to certain brain disorders.

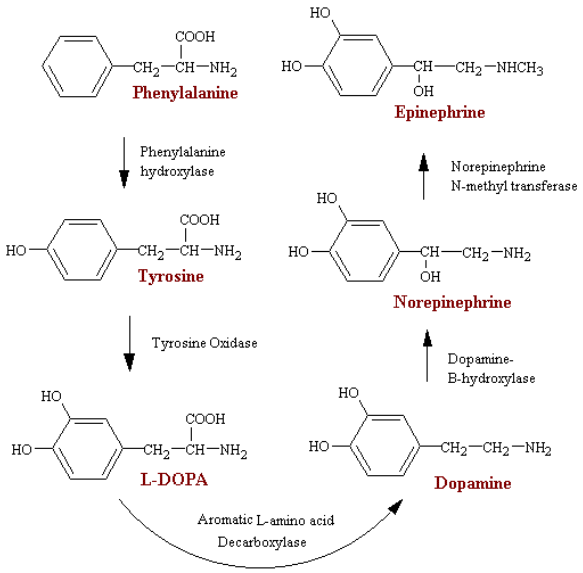
Strong imbalances or disruptions to neurotransmitter systems have been associated with many diseases and mental disorders. These include Parkinson's, depression, insomnia, Attention Deficit Hyperactivity Disorder (ADHD), anxiety, memory loss, dramatic changes in weight and addictions. Chronic physical or emotional stress can be a contributor to neurotransmitter system changes. Genetics also plays a role in neurotransmitter activities. Apart from recreational use, medications that directly and indirectly interact one or more transmitter or its receptor are commonly prescribed for psychiatric and psychological issues. Notably, drugs interacting with and are prescribed to patients with problems such as depression and anxiety—though the notion that there is much solid medical evidence to support such interventions has been widely criticized.

Monoamine Neurotransmitters: Serotonin, Dopamine, Epinephrine, and Norepinephrine

Monoamine neurotransmitters are and that contain one group connected to an ring by a two-carbon chain (such as -CH_2-CH_2-). Examples are , , norepinephrine and .

All monoamines are derived from aromatic like , , and by the action of . They are deactivated in the body by the enzymes known

as which clip off the amine group.



astrocytes, a chemical which maintains neuron integrity and provides neurons with trophic support.

Figures 10.5.4 and 10.5.5.

On top an L-tryptophan molecule with an arrow down to a 5-HTP molecule. Tryptophan hydroxylase catalyses this reaction with help of O2 and tetrahydrobiopterin, which becomes water and dihydrobiopterin. From the 5-HTP molecule goes an arrow down to a serotonin molecule. Aromatic L-amino acid decarboxylase or 5-Hydroxytryptophan decarboxylase catalyses this reaction with help of pyridoxal phosphate. From the serotonin molecule goes an arrow to a 5-HIAA molecule at the bottom. Monoamine oxidase catalyses this reaction, in the process O2 and water is consumed, and ammonia and hydrogen peroxide is produced.

Figure 10.5.4 The biosynthesis of dopamine, epinephrine, and norepinephrine.

Figure 10.5.5 *The biosynthesis of serotonin.*

Barbiturates

Barbiturates are CNS depressants and are similar, in many ways, to the depressant effects of alcohol. To date, there are about 2,500 derivatives of barbituric acid of which only 15 are used medically. The first barbiturate was synthesized from barbituric acid in 1864.

The original use of barbiturates was to replace drugs such as opiates, bromides, and alcohol to induce sleep. Barbiturates are effective as , , and , but have physical and psychological potential as well as potential among other possible adverse effects. They have largely been replaced by (discussed below) and ("Z-drugs") in routine medical practice, particularly in the treatment of

anxiety and insomnia, due to the significantly lower risk of addiction and and the lack of an for barbiturate overdose. Despite this, barbiturates are still in use for various purposes: in , , treatment of acute or , , , and .

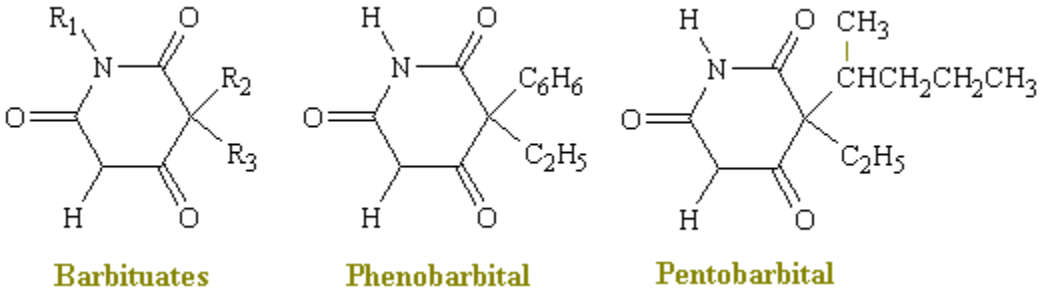


Figure 10.5.9 Barbitutrates.

Some symptoms of an overdose typically include sluggishness, incoordination, difficulty in thinking, slowness of speech, faulty judgement, drowsiness, shallow breathing, staggering, and, in severe cases, coma or death. The lethal dosage of barbiturates varies greatly with tolerance and from one individual to another.

Barbiturates in overdose with other CNS (central nervous system) depressants (e.g. alcohol, opiates, benzodiazepines) are even more dangerous due to additive CNS and respiratory depressant effects. In the case of benzodiazepines, not only do they have additive effects, barbiturates also increase the binding affinity of the benzodiazepine binding site, leading to exaggerated benzodiazepine effects. (ex. If a benzodiazepine increases the frequency of channel opening by 300%, and a barbiturate increases the duration of their opening by 300%, then the combined effects of the drugs increase the channels overall function by 900%, not 600%).

Anti-anxiety Agents

Anti-anxiety medications help reduce the symptoms of anxiety, such as panic attacks, or extreme fear and worry.

The most common anti-anxiety medications are called benzodiazepines. **Benzodiazepines** can treat generalized anxiety disorder. In the case of panic disorder or social phobia (social anxiety disorder), benzodiazepines are usually second-line treatments, behind SSRIs or other antidepressants. Benzodiazepines used to treat anxiety disorders include, clonazepam (Klonopin), alprazolam (Niravam), and lorazepam (Altivam and Lorazepam Intensol).

Short half-life (or short-acting) benzodiazepines (such as Lorazepam) and beta-blockers are used to treat the short-term symptoms of anxiety. Beta-blockers help manage physical symptoms of anxiety, such as trembling, rapid heartbeat, and sweating that people with phobias (an overwhelming and unreasonable fear of an object or situation, such as public speaking) experience in difficult situations. Taking these medications for a short period of time can help the person keep physical symptoms under control and can be used “as needed” to reduce acute anxiety.

Antipsychotic medicines are primarily used to manage psychosis. The word “psychosis” is used to describe conditions that affect the mind, and in which there has been some loss of contact with reality, often including delusions (false, fixed beliefs) or hallucinations (hearing or seeing things that are not really there). It can be a symptom of a physical condition such as drug abuse or a mental disorder such as schizophrenia, bipolar disorder, or very severe depression (also known as “psychotic depression”).

Antipsychotic medications are often used in combination with other medications to treat delirium, dementia, and mental health conditions, including:

- Attention-Deficit Hyperactivity Disorder (ADHD)
- Severe Depression
- Eating Disorders
- Post-traumatic Stress Disorder (PTSD)
- Obsessive Compulsive Disorder (OCD)
- Generalized Anxiety Disorder

Antipsychotic medicines do not cure these conditions. They are used to help relieve symptoms and improve quality of life.

Older or first-generation antipsychotic medications are also called conventional "typical" antipsychotics or “neuroleptics”. Some of the common typical antipsychotics include, chlorpromazine (Promapar and Thorazine), haloperidol (Haldol), perphenazine (Trilafon), and fluphenazine (Permitil and Prolixin). **Chlorpromazine** was discovered in 1950 and was the first antipsychotic. It is on the , the most effective and safe medicines needed in a . Its introduction has been labeled as one of the great advances in the .

Chlorpromazine (CPZ), is marketed under the **Thorazine** and **Largactil.** It is primarily used to treat such as . Other uses include the treatment of , , and , anxiety before surgery, and that do not improve following other measures. It can be given by mouth, by , or . Common side effects include , , dry mouth, , and increased weight. Serious side effects may include the potentially permanent movement disorder , , and . In older people with psychosis as a result of it may increase the risk of death. It is unclear if it is safe for use in . Chlorpromazine is in the class. Its mechanism of action is not entirely clear but believed to be related to its ability as a .

Newer or second generation medications are called **"atypical" antipsychotics**. The atypical antipsychotics (AAP; also known as second generation antipsychotics (SGAs)) are a group of drugs (antipsychotic drugs in general are also known as major and neuroleptics, although the latter is usually reserved for the) largely introduced after the 1970s and used to treat psychiatric conditions. Some atypical antipsychotics have received regulatory approval (e.g. by the of the , the of , the of the) for , , , and as an in .Some of the common atypical antipsychotics include risperidone (Risperdal), olanzapine (Zyprexa), quetiapine (Seroquel), ziprasidone (Geodon), aripiprazole (Abilify), paliperidone (Invega), and lurasidone (Latuda). The atypical antipsychotics have found favor among clinicians and are now considered to be for schizophrenia and are gradually replacing the .

According to a 2013 research review by the Agency for Healthcare Research and Quality, typical and atypical antipsychotics both work to treat symptoms of schizophrenia and the manic phase of bipolar disorder. Several atypical antipsychotics have a “broader spectrum” of action than the older medications, and are used for treating bipolar depression or depression that has not responded to an antidepressant medication alone.

Older antidepressant medications include tricyclics, tetracyclics, and monoamine oxidase inhibitors (MAOIs). All tricyclic antidepressants in current use in the U.S. potentiate the actions of biogenic amines in the CNS by blocking its re-uptake at nerve terminals. However, the potency and selectivity for the inhibition of the uptake of norepinephrine, serotonin, and dopamine vary greatly among the agents. For some people, tricyclics, tetracyclics, or MAOIs may be the best medications.

The most popular types of antidepressants are called **selective serotonin reuptake inhibitors (SSRIs)** seeexamples on Figure 10.5.10 . Examples of SSRIs include fluoxetine (Prozac), citalopram (Celexa), sertraline (Zoloft), paroxetine (Brisdelle, Paxil, Pexeva), and escitalopram (Lexapro). Prozac is the most famous drug in this class. In 2016 it was the 29th most prescribed medication in the United States with more than 23 million prescriptions. Clomiprimine, fluoxetine (Prozac), sertraline and paroxetine selectively block the reuptake of serotonin, thereby increasing the levels of serotonin in the central nervous system. Some of the newer, SSRIs (e.g., clomipramine) have been useful in the treatment of obsessive-compulsive disorders.

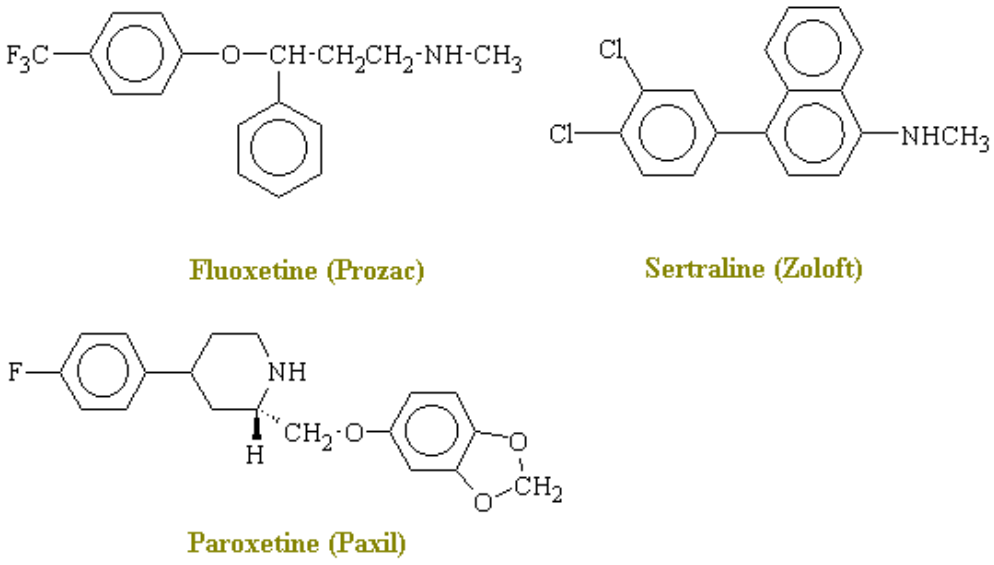


Figure 10.5.10 Examples of SSRIs.

Other types of antidepressants are **serotonin and norepinephrine reuptake inhibitors (SNRIs)**. SNRIs are similar to SSRIs and include venlafaxine (Effexor) and duloxetine (Cymbalta).

Another antidepressant that is commonly used is **bupropion** (Aplenzin, Wellbutrin, Wellbutrin SR, Wellbutrin XL) . Bupropion is a third type of antidepressant which works differently than either SSRIs or SNRIs. Bupropion is also used to treat seasonal affective disorder and to help people stop smoking.

SSRIs, SNRIs, and bupropion are popular because they do not cause as many side effects as older classes of antidepressants, and seem to help a broader group of depressive and anxiety disorders.

Cocaine, Caffeine, and Nicotine

Cocaine, also known as **coke**, is a strong most frequently used as a . It is commonly , inhaled as smoke, or dissolved and injected into a . Mental effects may include , an , or . Physical symptoms may include a , sweating, and .High doses can result in very or . Effects begin within seconds to minutes of use and last between five and ninety minutes. Cocaine has a small number of accepted medical uses such as and decreasing bleeding during nasal surgery.

Cocaine is due to its effect on the in the brain. After a short period of use, there is a high risk that will occur. Its use also increases the risk of , , lung problems in those who smoke it, , and . Cocaine sold on the street is commonly mixed with , cornstarch, , or sugar, which can result in additional toxicity. Following repeated doses a person may have and be very physically tired. Cocaine acts by

Caffeine is a (CNS) of the . Caffeine is a stimulant compound belonging to the class of chemicals naturally found in , , and (to a lesser degree) or . It is included in many , as well as a larger amount in . Caffeine is the world's most widely used psychoactive drug and by far the most common stimulant. In North America, 90% of adults consume caffeine daily. A few jurisdictions restrict its sale and use. Caffeine is also included in some medications, usually for the purpose of enhancing the effect of the primary ingredient, or reducing one of its side-effects (especially drowsiness). Tablets containing standardized doses of caffeine are also widely available.

Caffeine's mechanism of action differs from many stimulants, as it produces stimulant effects by inhibiting adenosine receptors. Adenosine receptors are thought to be a large driver of drowsiness and sleep, and their action increases with extended wakefulness. Caffeine (in coffee), theophylline (in tea) and theobromine (in choccolate) share in common several pharmacological actions of therapeutic interest. They stimulate the central nervous system, act on the kidney to produce diuresis, stimulate cardiac muscle, and relax smooth muscle, notably bronchial muscle. From the figure below, we can see that the methylxanthines have a structure which is very similar to adenine (the amino group in adenosine).

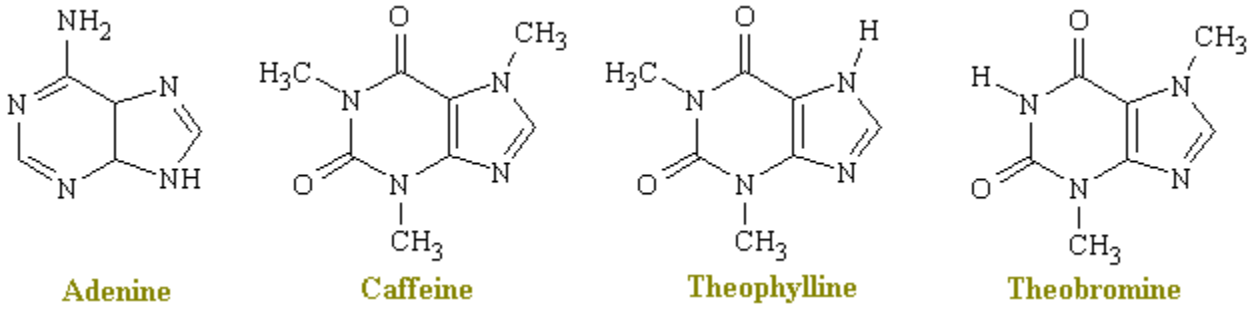


Figure 10.5.11 Adenine and other molecules with similar strucures.

is the active chemical constituent in , which is available in many forms, including , , , and aids such as , , and . Nicotine is used widely throughout the world for its stimulating and relaxing effects. Nicotine exerts its effects through the agonism of , resulting in multiple downstream effects such as increase in activity of dopaminergic neurons in the midbrain , as well as the decreased expression of in the brain. Nicotine is addictive and dependence forming.

Hallucinogens and Dissociative Drugs



feeling sensations that seem real but are not. While the exact mechanisms by which hallucinogens and dissociative drugs cause their effects are not yet clearly understood, research suggests that they work at least partially by temporarily disrupting communication between neurotransmitter systems throughout the brain and spinal cord that regulate mood, sensory perception, sleep, hunger, body temperature, sexual behavior, and muscle control.

Figure 10.5.12 Psilocybin mushrooms, LSD, and Salvia divinorum

are commonly used hallucinogenic and dissociative compounds.

Classic Hallucinogens

LSD (d-lysergic acid diethylamide)—also known as acid, blotter, doses, hits, microdots, sugar cubes, trips, tabs, or window panes—is one of the most potent moodand perception-altering hallucinogenic drugs. It is a clear or white, odorless, water-soluble material synthesized from lysergic acid, a compound derived from a rye fungus. LSD is initially produced in crystalline form, which can then be used to produce tablets known as “microdots” or thin squares of gelatin called “window panes.” It can also be diluted with water or alcohol and sold in liquid form. The most common form, however, is LSD-soaked paper punched into small individual squares, known as “blotters.”

Psilocybin (4-phosphoryloxyN, N-dimethyltryptamine)—also known as magic mushrooms, shrooms, boomers, or little smoke—is extracted from certain types of mushrooms found in tropical and subtropical regions of South America, Mexico, and the United States. In the past, psilocybin was ingested during religious ceremonies by indigenous cultures from Mexico and Central America. Psilocybin can either be dried or fresh and eaten raw, mixed with food, or brewed into a tea, and produces similar effects to LSD.

Peyote (Mescaline)— also known as buttons, cactus, and mesc— is a small, spineless cactus with mescaline as its main ingredient. It has been used by natives in northern Mexico and the southwestern United States as a part of religious ceremonies. The top, or “crown,” of the peyote cactus has disc-shaped buttons that are cut out, dried, and usually chewed or soaked in water to produce an intoxicating liquid. Because the extract is so bitter, some users prepare a tea by boiling the plant for several hours. Mescaline can also be produced through chemical synthesis.

DMT (Dimethyltryptamine)—also known as Dimitri—is a powerful hallucinogenic chemical found naturally occurring in some Amazonian plant species (see “Ayahuasca”) and also synthesized in the laboratory. Synthetic DMT usually takes the form of a white crystalline powder and is typically vaporized or smoked in a pipe. Ayahuasca—also known as hoasca, aya, and yagé—is a hallucinogenic brew made from one of several Amazonian plants containing DMT (the primary psychoactive ingredient) along with a vine containing a natural alkaloid that prevents the normal breakdown of DMT in the digestive tract. Ayahuasca tea has traditionally been used for healing and religious purposes in indigenous South American cultures, mainly in the Amazon region.

Dissociative Drugs

PCP (Phencyclidine)—also known as ozone, rocket fuel, love boat, hog, embalming fluid, or superweed—was originally developed in the 1950s as a general anesthetic for surgery. While it can be found in a variety of forms, including tablets or capsules, it is usually sold as a liquid or powder. PCP can be snorted, smoked, injected, or swallowed. It is sometimes smoked after being sprinkled on marijuana, tobacco, or parsley.

Ketamine—also known as K, Special K, or cat Valium—is a dissociative currently used as an anesthetic for humans as well as animals. Much of the ketamine sold on the street has been diverted from veterinary offices. Although it is manufactured as an injectable liquid, ketamine is generally evaporated to form a powder that is snorted or compressed into pills for illicit use. Because

ketamine is odorless and tasteless and has amnesia-inducing properties, it is sometimes added to drinks to facilitate sexual assault. 2 NIDA Research Report Series Common Hallucinogens and Dissociative Drugs *In this report, the term “hallucinogen” will refer to the classic hallucinogenic drugs LSD and Psilocybin.

DXM (Dextromethorphan)— also known as robo—is a cough suppressant and expectorant ingredient in some over-the-counter (OTC) cold and cough medications that are often abused by adolescents and young adults. The most common sources of abused DXM are “extra-strength” cough syrup, which typically contains around 15 milligrams of DXM per teaspoon, and pills and gel capsules, which typically contain 15 milligrams of DXM per pill. OTC medications that contain DXM often also contain antihistamines and decongestants.

Salvia divinorum—also known as diviner’s sage, Maria Pastora, Sally-D, or magic mint—is a psychoactive plant common to southern Mexico and Central and South America. Salvia is typically ingested by chewing fresh leaves or by drinking their extracted juices. The dried leaves of salvia can also be smoked or vaporized and inhaled.

Short-Term General Effects of Hallucinogens Sensory Effects

• Hallucinations, including seeing, hearing, touching, or smelling things in a distorted way or perceiving things that do not exist

• Intensified feelings and sensory experiences (brighter colors, sharper sounds)

• Mixed senses (“seeing” sounds or “hearing” colors)

• Changes in sense or perception of time (time goes by slowly) Physical Effects

• Increased energy and heart rate

• Nausea

Summary

- Neurotransmitters are that enable . It is a type of chemical messenger which transmits signals across a , such as a , from one (nerve cell) to another "target" neuron, , or .
- Strong imbalances or disruptions to neurotransmitter systems have been associated with many diseases and mental disorders.
- Psychoactive drugs are substances that change the function of the brain and result in alterations of mood, thinking, perception, and/or behavior. They include prescription medications such as opioid painkillers, legal substances such as nicotine and alcohol, and illegal drugs such as LSD and heroin.
- Psychoactive drugs are divided into different classes according to their pharmacological effects. They include stimulants, depressants, anxiolytics, euphoriants, hallucinogens, and empathogens. Many psychoactive drugs have multiple effects so they may be placed in more than one class.
- Psychoactive drugs generally produce their effects by affecting brain chemistry. Generally, they act either as agonists, which enhance the activity of particular neurotransmitters; or as antagonists, which decrease the activity of particular neurotransmitters.
- Psychoactive drugs are used for various purposes, including medical, ritual, and recreational purposes.
- Misuse of psychoactive drugs may lead to addiction, which is compulsive use of a drug despite negative consequences such use may entail. Sustained use of an addictive drug may produce physical or psychological dependence on the drug. Rehabilitation typically involves psychotherapy and sometimes the temporary use of other psychoactive drugs.

Sources

NIH National Institute of Neurological Disorder and Stroke (NIDS)

NIH National Institute of Mental Health

NIH National Institute on Drug Abuse

Wikipedia

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10.6: Neurotransmitters and Antidepressants

Neurotransmitters

The nervous system is made of nerve cells called neurons. These cells help with the transmissions of messages. Chemicals called neurotransmitters assist in the transmission of messages across gaps or synapses.

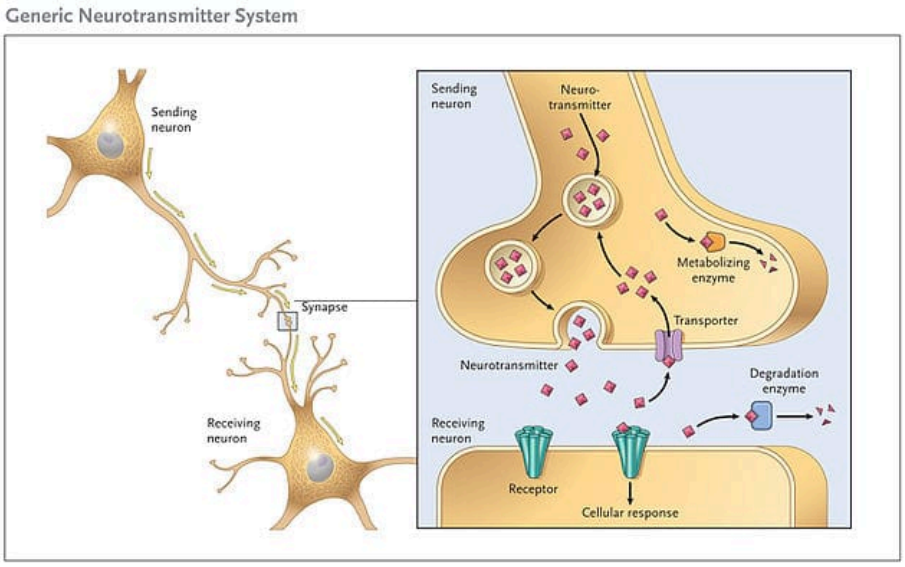


Figure 10.6.1: Generic Neurotransmitter System. (Copyright, NIDA(NIH)).

One theory that explains mental illness incorporates the various amounts of neurotransmitters. Using this theory, the lack or excess of specific neurotransmitters can be associated with depression, anxiety, bipolar disorder, or schizophrenia. Other disorders or health conditions, namely Attention Deficient Hyperactivity Disorder (ADHD) and Parkinson's Disease have also been linked with varying levels of neurotransmitters.

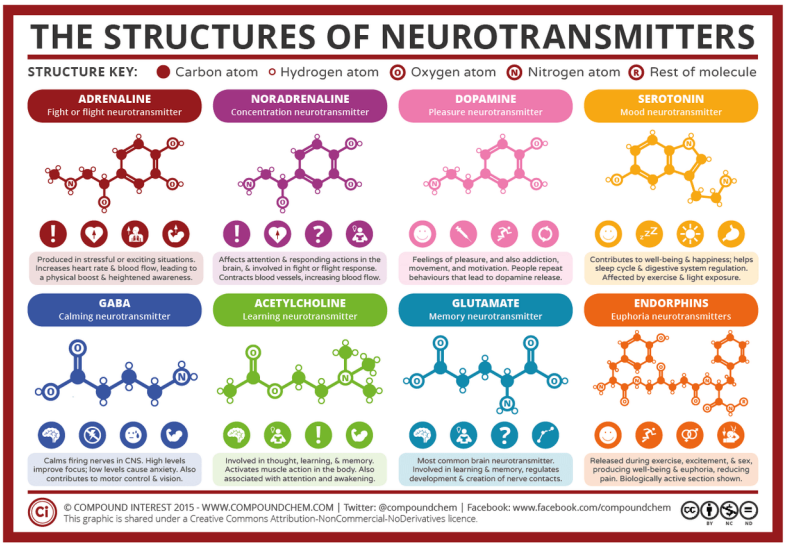


Figure 10.6.2: The Structures of Neurotransmitters.(CC BY-NC-ND; Andy Brunning)

The Noradrenaline neurotransmitter is also called norepinephrine. When evaluating antidepressants or other mental health medications, it is important to be aware of this terminology. For a brief overview of the correlation between neurotransmitters and mental health, watch the video below.

YouTube Video

This interactive element is not available in this format. Visit the link or scan the QR code to access it online.

View this YouTube Video online

Mental health conditions can result from a person's life experiences and/or genetics. Sometimes, drug usage or brain trauma can trigger mental illness. It is important to note all health conditions that are present in your family tree (biological). Also, recognizing emotional trauma and then seeking counseling/medical treatment is important for navigating a mental health condition.



Figure 10.6.3: Nason family picture circa 1905. Image courtesy of Elizabeth R. Gordon

Depression symptoms

Can be short or long-term. Experience-sadness, sleeping and eating issues, withdrawal, feelings of hopelessness, loss of interest/pleasure, lack of energy, feelings of worthlessness/guilt, slowed processing, trouble concentrating, frequent thought of suicide/death, anxiety, and unexplained health problems.

Treatments for depression

psychotherapy, brain stimulation, medication, exercise, light therapy. Discussions to have with dr: meds/vitamins you are on, self-medication is not answer, stopping antidepressants without assistance, and report problems with meds. Limit alcohol and refrain from illicit and scheduled drugs. FDA black-box warning for antidepressants in people under 25.

Antidepressant Medications

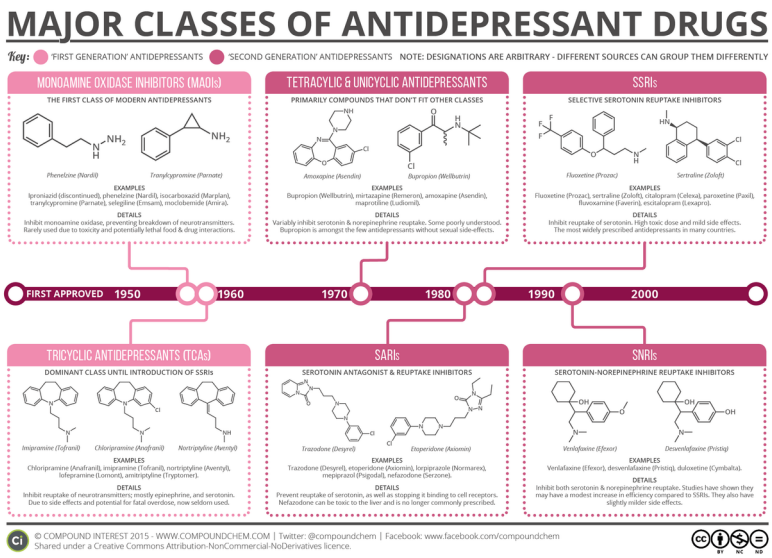


Figure 10.6.4: Major Classes of Antidepressant Drugs.(CC BY-NC-ND; Andy Brunning)

Finding the correct antidepressant

Trial and Error-take for six weeks, then wean, and start another. Since the early 2000's, Mayo Clinic has been researching gene technology. Test is now offered by Assurex Health and called Genesight.

https://genesight.com/gene-test-for-...surex%20Health

Common Side Effects of Antidepressants

This carry varies with the patient and type of medicine. Most common include weight gain, fatigue, dizziness, loss of sexual desire, nausea, dry mouth, blurred vision, agitation, insomnia, and constipation.

Support and information regarding mental health conditions.

National Alliance on Mental Illness

Figure 10.6.3: Official logo of the National Alliance on Mental Illness. (National Alliance on Mental Illness, http://www.nami.org/Template.cfm?Sec...ntentID=121014)

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11: AMINO ACIDS, PROTEINS, AND ENZYMES

11.1: Why This Chapter?

11.2: Nomenclature of Amino acids

11.3: Structures of Amino Acids

11.4: Peptides and Proteins

11.5: Peptides

11.6: Protein Structure

11.7: Enzymes

11.8: Enzyme Regulation- Allosteric Control and Feedback Inhibition

11.9: Amino Acids and Proteins (Exercises)

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11.1: Why This Chapter?

Continuing our look at the main classes of biomolecules, we'll focus in this chapter on amino acids, the fundamental building blocks from which up to 150,000 or so different proteins in our bodies are made. We'll then see how amino acids are incorporated into proteins and examine the structures of those proteins. Any understanding of biological chemistry would be impossible without this knowledge.



Figure 11.1.1: The building blocks of life that we call proteins are aptly named after Proteus, the early Greek sea-god whose name means "first" or "primordial." (credit: modification of work by Coyau/Wikimedia Commons, CC BY-SA 3.0)

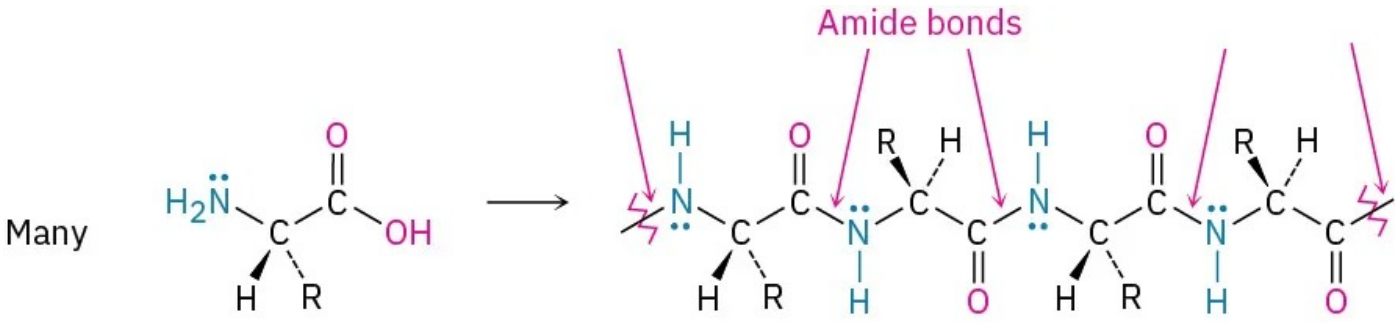
Proteins occur in every living organism, are of many different types, and have many different biological functions. The keratin of skin and fingernails, the fibroin of silk and spider webs, and the estimated 50,000 or so enzymes that catalyze the biological reactions in our bodies are all proteins. Regardless of their function, all proteins have a fundamentally similar structure and are made up of many *amino acids* linked together in a long chain.

Amino acids, as their name implies, are difunctional. They contain both a basic amino group and an acidic carboxyl group.



Alanine, an amino acid

Their value as building blocks to make proteins stems from the fact that amino acids can join together into long chains by forming amide bonds between the $-NH_2$ of one amino acid and the $-CO_2H$ of another. For classification purposes, chains with fewer than 50 amino acids are often called peptides, while the term protein is generally used for larger chains.



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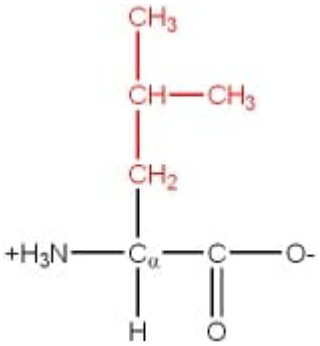
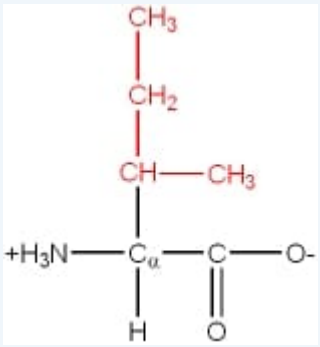
11.2: Nomenclature of Amino acids

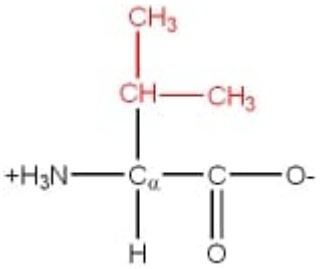
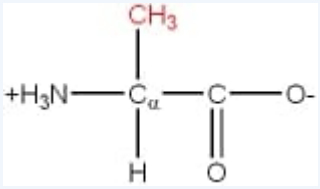
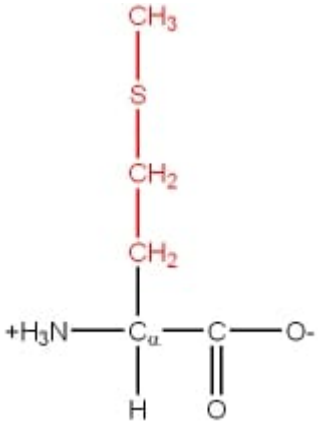
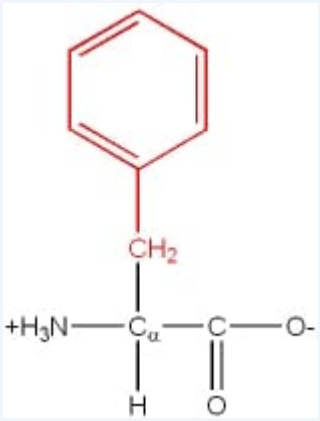
Common amino acids

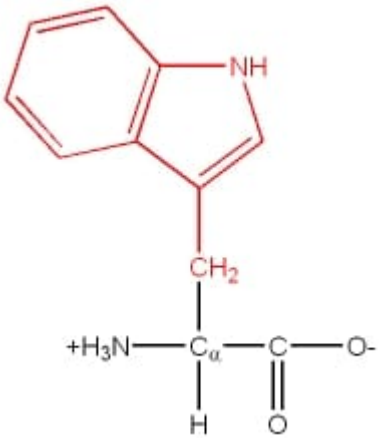
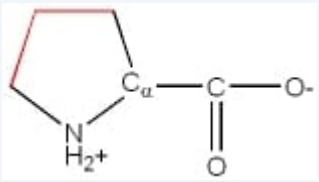
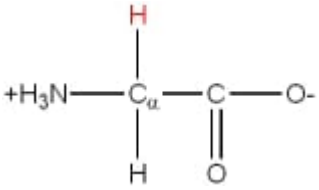
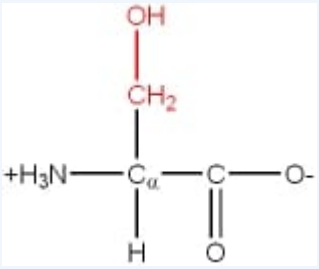
There are 20 common amino acids. They are composed of C, H, O, N and S atoms. They are structurally and chemically different, and also differ in size and volume. Some are branched structures, some are linear, some have ring structures. One of the 20 common amino acids is actually an imino acid. A typical grouping of their chemical nature is as follows:

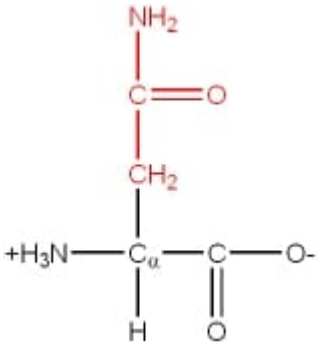
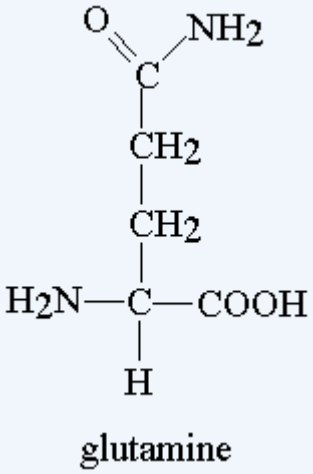
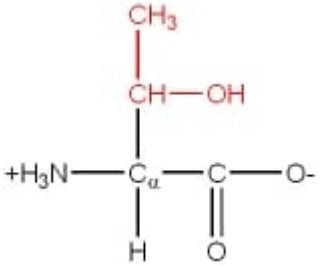
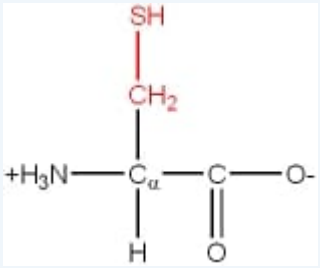
- Nonpolar (hydrocarbons and one sulfur-containing amino acid). Dispersion forces and hydrophobic effects predominate in their interactions. They cannot H-bond with water and these side chains have a characteristic hydrophobic effect in water.
- Polar uncharged. Contain functional groups that can H-bond with water and other amino acids. Include C, H, O, N and S atoms.
- Acidic. Contain a carboxylic acid functional group with a negative charge at neutral pH. Can H-bond with water, can form ionic interactions, and can also serve as nucleophiles or participate in acid-base chemistry.
- Basic. Nitrogen containing bases (e.g. guanidino, imidazole or amino groups) with a net positive charge at neutral pH. Can serve as proton donors in chemical reactions, and form ionic interactions.

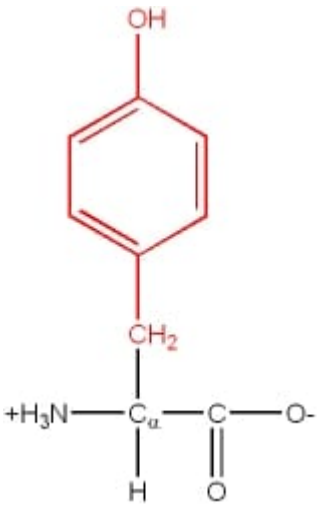
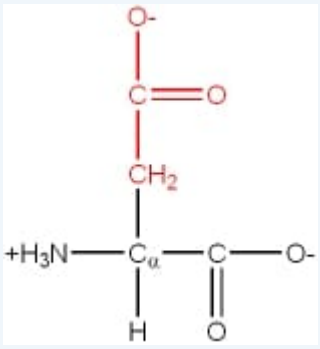
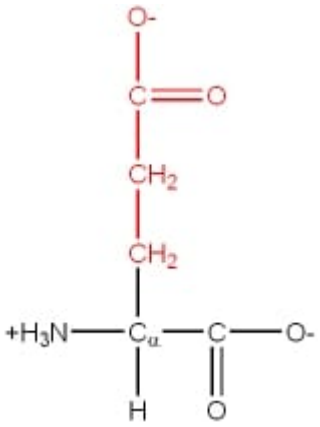
The amino acids have a name, as well as a three letter or single letter mnemonic code:

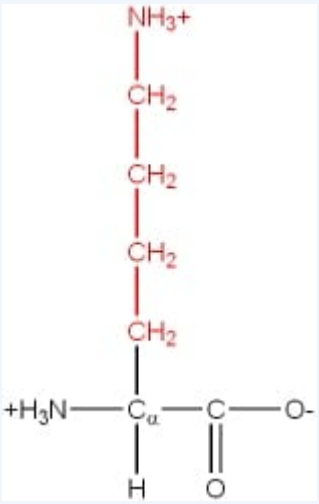
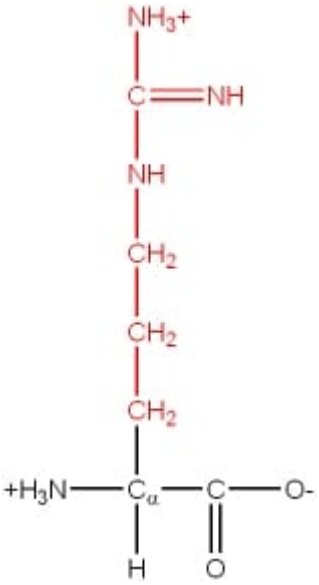
Type	Name	R-group Structure
Nonpolar	Leucine Leu, L	
	Isoleucine Ile, I	

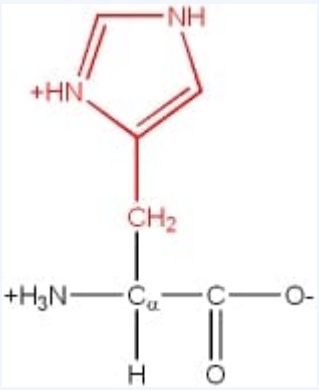
Type	Name	R-group Structure
	Valine Val, V	
	Alanine Ala, A	
	Methionine Met, M	
	Phenylalanine Phe, F	

Type	Name	R-group Structure
	Tryptophan Trp, W	
	Proline Pro, P	
	Glycine Gly, G (note: sometimes included in polar group)	
Polar, uncharged	Serine Ser, S	

Type	Name	R-group Structure
	Asparagine Asn, N	
	Glutamine Gln, Q	
	Threonine Thr, T	
	Cysteine Cys, C	

Type	Name	R-group Structure
	Tyrosine Tyr, Y	
Acidic	Aspartic acid Asp, D	
	Glutamic acid Glu, E	

Type	Name	R-group Structure
Basic	Lysine Lys, K	
	Arginine Arg, R	

Type	Name	R-group Structure
	Histidine His, H	

Uncommon amino acids

In addition to the 20 common amino acids, there are several uncommon ones found:

- Hydroxylysine and hydroxyproline. These are found in the protein collagen. Collagen is a fibrous protein made up of three polypeptides that form a stable assembly, but only if the proline and lysine residues are hydroxylated. (requires vitamin C for reduction of these amino acids to hydroxy form)
- Thyroxine, an iodinated derivative of tyrosine, found in thyroglobulin (produced by thyroid gland; requires iodine in diet)
- g-carboxyglutamic acid (i.e. glutamic acid with two carboxyl groups) found in certain blood clotting enzymes (requires vitamin K for production)
- N-methyl arginine and n-acetyl lysine. Found in some DNA binding proteins known as histones

Amino acid derivatives not found in proteins

Some amino acids are made that are not intended for incorporation into proteins, rather they have important functionalities on their own

- Serotonin (derivative of tryptophan) and g-amino butyric acid (a derivative of glutamic acid) are both neurotransmitters
- Histamine (derivative of histidine) involved in allergic response
- Adrenaline (derivative of tyrosine) a hormone
- Various antibiotics are amino acid derivatives (penicillin)

Contributors and Attributions

- Mike Blaber (Florida State University)

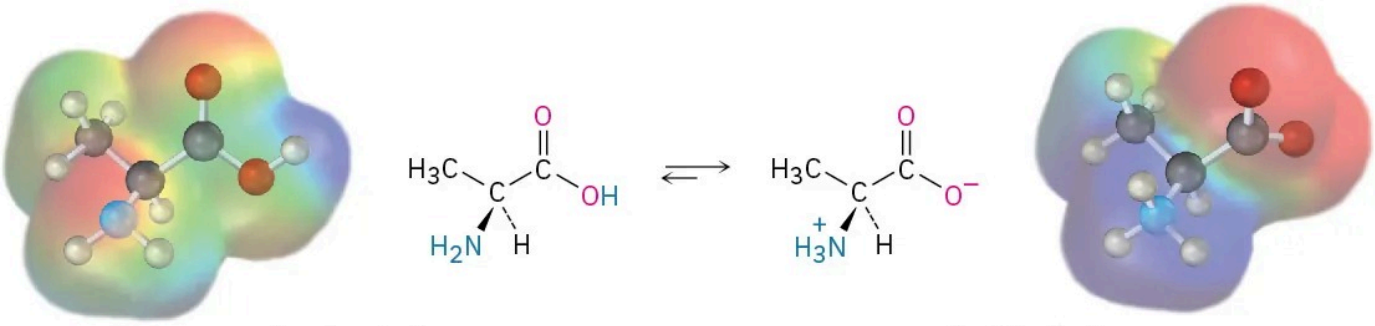
Thumbnail: 3D model of L-tryptophan. (Public Domain; Benjah-bmm27).

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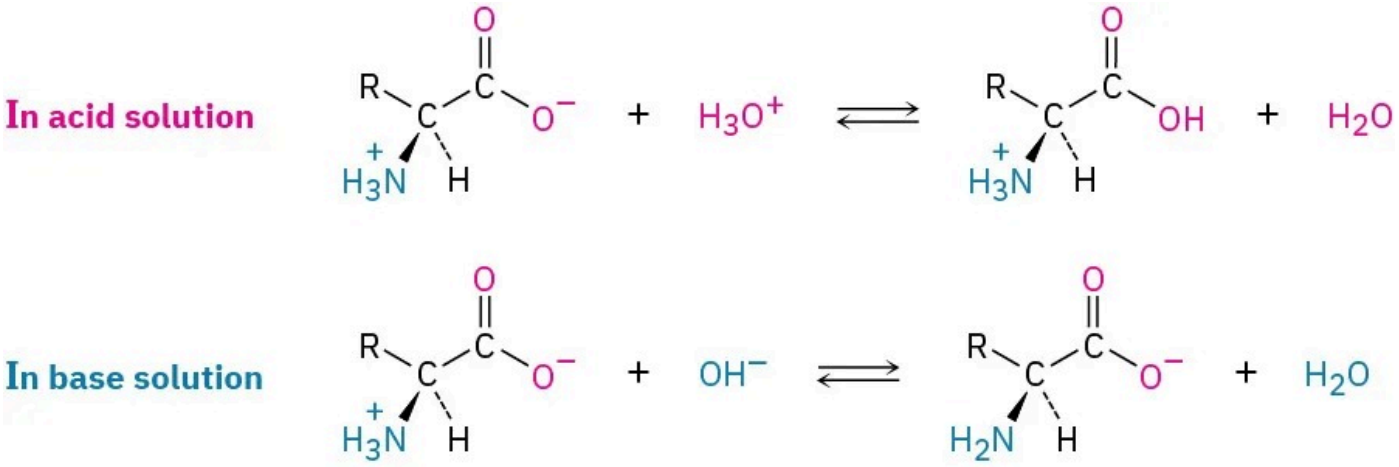
11.3: Structures of Amino Acids

We saw in Section 20.3 and Section 24.5 that a carboxyl group is deprotonated and exists as the carboxylate anion at a physiological pH of 7.3, while an amino group is protonated and exists as the ammonium cation. Thus, amino acids exist in aqueous solution primarily in the form of a dipolar ion, or zwitterion (from the German *zwitter,* meaning "hybrid").

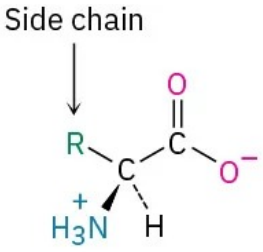


Alanine

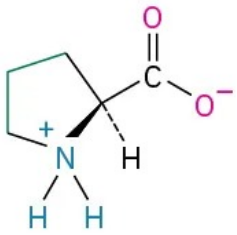
Amino acid zwitterions are internal salts and therefore have many of the physical properties associated with salts. They have large dipole moments, are relatively soluble in water but insoluble in hydrocarbons, and are crystalline with relatively high melting points. In addition, amino acids are **amphiprotic**; they can react either as acids or as bases, depending on the circumstances. In aqueous acid solution, an amino acid zwitterion is a base that accepts a proton onto its $-CO_2^-$ group to yield a cation. In aqueous base solution, the zwitterion is an acid that loses a proton from its $-NH_3^+$ group to form an anion.



The structures, abbreviations (both three- and one-letter), and pK_a values of the 20 amino acids commonly found in proteins are shown in Table 11.3.1. All are α-amino acids, meaning that the amino group in each is a substituent on the α carbon—the one next to the carbonyl group. Nineteen of the twenty amino acids are primary amines, RNH_2, and differ only in the nature of their side chain—the substituent attached to the α carbon. Proline is a secondary amine whose nitrogen and α carbon atoms are part of a five-membered pyrrolidine ring.

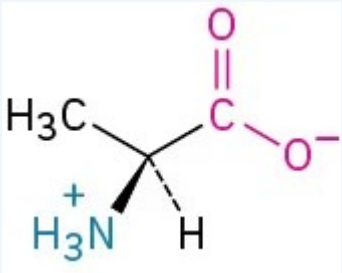
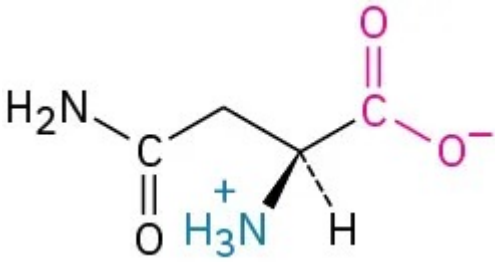
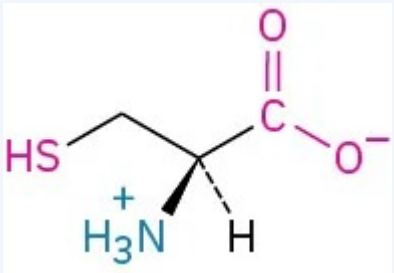
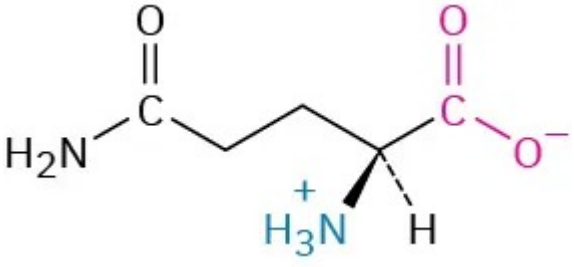


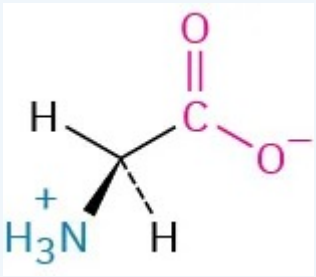
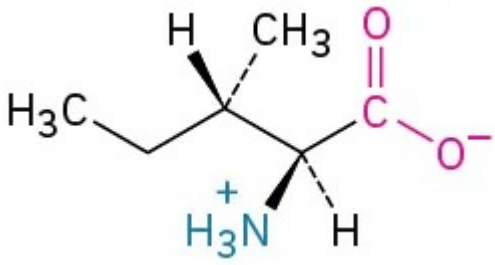
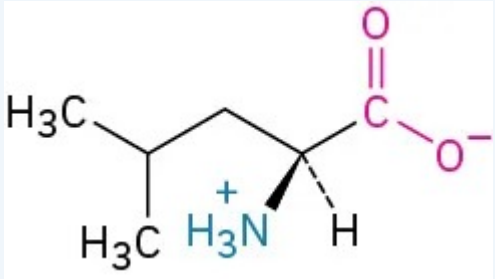
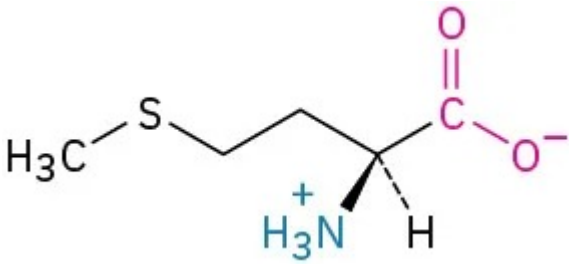
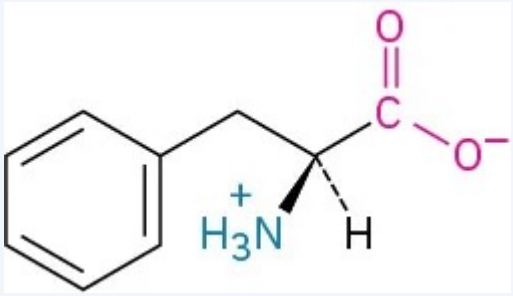
A primary α-amino acid

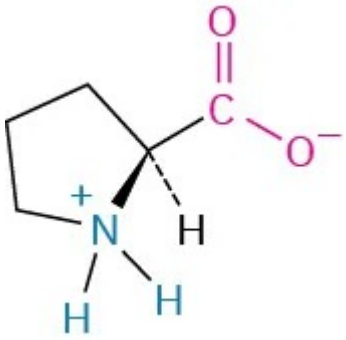
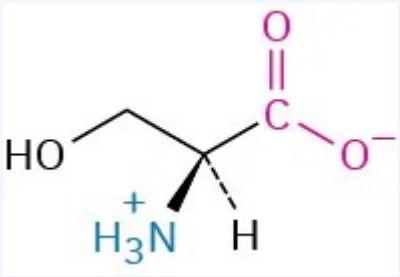
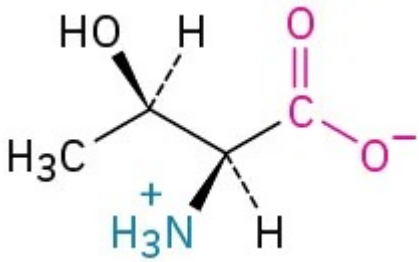
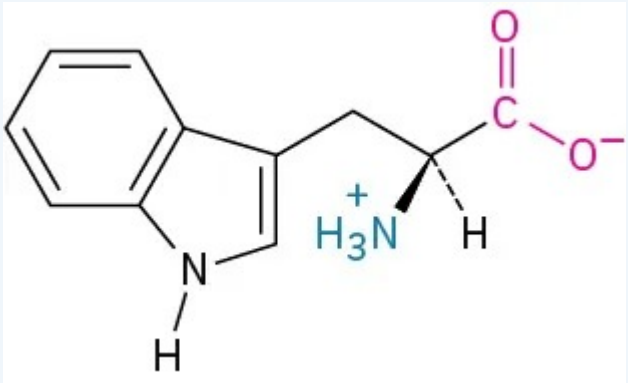


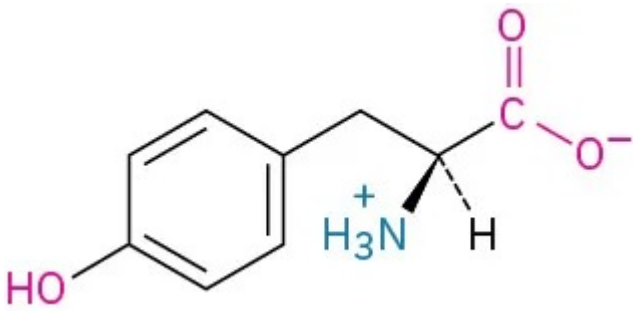
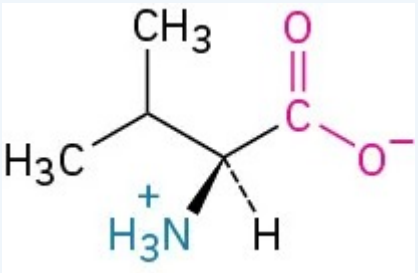
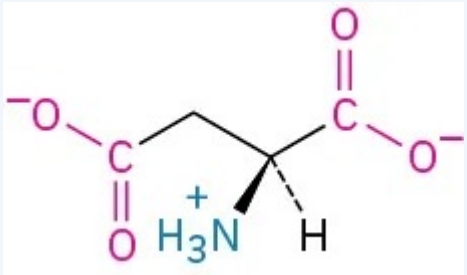
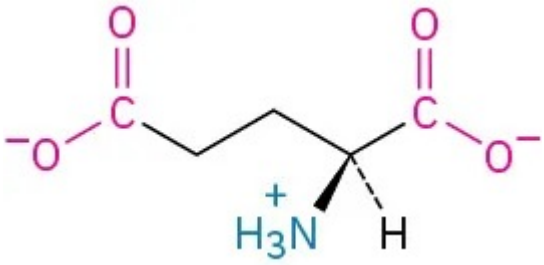
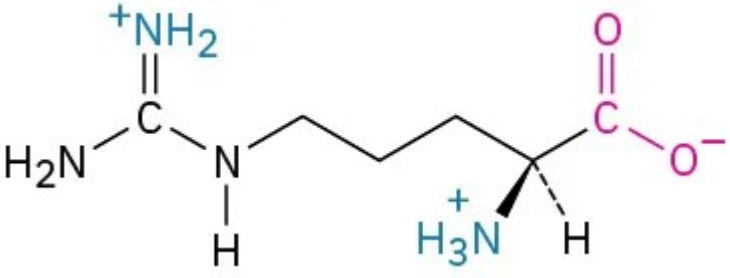
Proline, a secondary α-amino acid

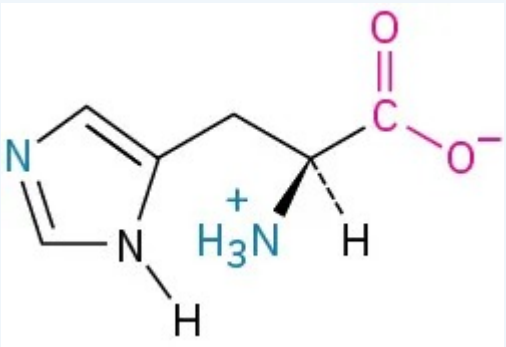
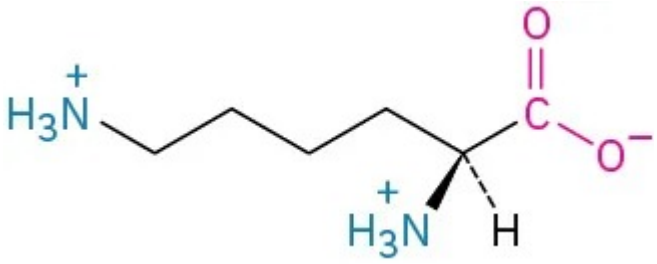
Table 11.3.1*: The 20 Common Amino Acids in Proteins*

Name	Abbreviations		MW	Structure	pK_a α-CO_2H	pK_a α-NH_3^+
Neutral Amino Acids						
Alanine	Ala	A	89		2.34	9.69
Asparagine	Asn	N	132		2.02	8.80
Cysteine	Cys	C	121		1.96	10.28
Glutamine	Gln	Q	146		2.17	9.13

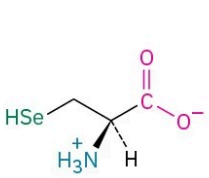
Name	Abbreviations		MW	Structure	pK_a α-CO_2H	pK_a α-NH_3^+
Glycine	Gly	G	75		2.34	9.60
Isoleucine	Ile	I	131		2.36	9.60
Leucine	Leu	L	131		2.36	9.60
Methionine	Met	M	149		2.28	9.21
Phenylalanine	Phe	F	165		1.83	9.13

Name	Abbreviations		MW	Structure	pK_a α-CO_2H	pK_a α-NH_3^+
Proline	Pro	P	115		1.99	10.60
Serine	Ser	S	105		2.21	9.15
Threonine	Thr	T	119		2.09	9.10
Tryptophan	Trp	W	204		2.83	9.39

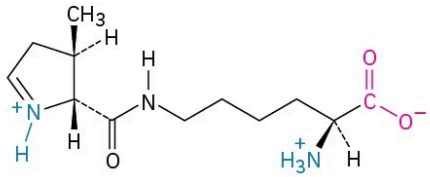
Name	Abbreviations		MW	Structure	pK_a α-CO_2H	pK_a α-NH_3^+
Tyrosine	Tyr	Y	181		2.20	9.11
Valine	Val	V	117		2.32	9.62
Acidic Amino Acids						
Aspartic acid	Asp	D	133		1.88	9.60
Glutamic acid	Glu	E	147		2.19	9.67
Basic Amino Acids						
Arginine	Arg	R	174		2.17	9.04

Name	Abbreviations		MW	Structure	pK_a α-CO_2H	pK_a α-NH_3^+
Histidine	His	H	155		1.82	9.17
Lysine	Lys	K	146		2.18	8.95

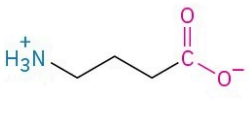
In addition to the 20 amino acids commonly found in proteins, 2 others—selenocysteine and pyrrolysine—are found in some organisms, and more than 700 nonprotein amino acids are also found in nature. γ-Aminobutyric acid (GABA), for instance, is found in the brain and acts as a neurotransmitter; homocysteine is found in blood and is linked to coronary heart disease; and thyroxine is found in the thyroid gland, where it acts as a hormone.



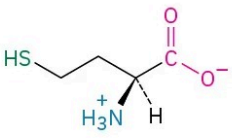
Selenocysteine



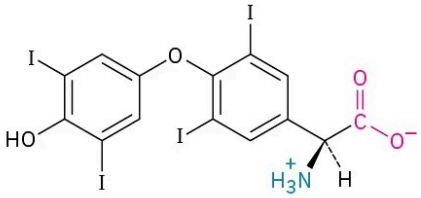
Pyrrolysine



γ-Aminobutyric acid

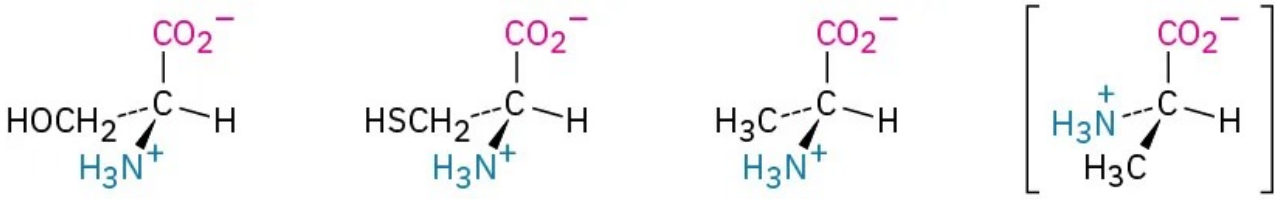


Homocysteine



Thyroxine

Except for glycine, $H_2NCH_2CO_2H$, the α carbons of amino acids are chirality centers. Two enantiomers of each are therefore possible, but nature uses only one to build proteins. In Fischer projections, naturally occurring amino acids are represented by placing the $-CO_2^-$ group at the top and pointing the side chain downwards, as if drawing a carbohydrate (Section 25.2) and then placing the $-NH_3^+$ group on the left. Because of their stereochemical similarity to L sugars (Section 25.3), the naturally occurring α-amino acids are often referred to as L amino acids. The nonnaturally occurring enantiomers are called D amino acids.



L-Serine
(*S*)-Serine

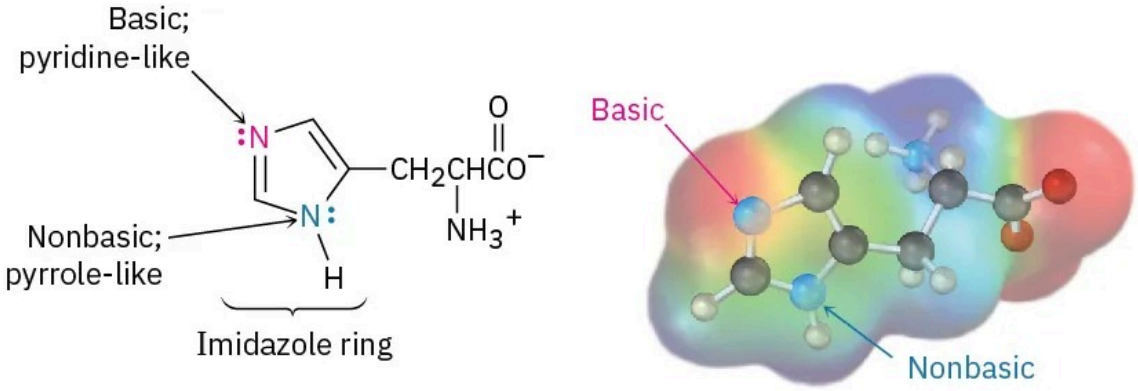
L-Cysteine
(*R*)-Cysteine

L-Alanine
(*S*)-Alanine

D-Alanine
(*R*)-Alanine

The 20 common amino acids can be further classified as neutral, acidic, or basic, depending on the structure of their side chains. Fifteen of the twenty have neutral side chains, two (aspartic acid and glutamic acid) have an extra carboxylic acid function in their side chains, and three (lysine, arginine, and histidine) have basic amino groups in their side chains. Note that both cysteine (a thiol) and tyrosine (a phenol), although usually classified as neutral amino acids, nevertheless have weakly acidic side chains that can be deprotonated in a sufficiently basic solution.

At the physiological pH of 7.3, the side-chain carboxyl groups of aspartic acid and glutamic acid are deprotonated and the basic side-chain nitrogens of lysine and arginine are protonated. Histidine, however, which contains a heterocyclic imidazole ring in its side chain, is not quite basic enough to be protonated at pH 7.3. Note that only the pyridine-like, doubly bonded nitrogen in histidine is basic. The pyrrole-like singly bonded nitrogen is nonbasic because its lone pair of electrons is part of the six-π-electron aromatic imidazole ring (Section 24.9).



Histidine

Humans are able to biosynthesize only 11 of the 20 protein amino acids, called nonessential amino acids. The other 9, called essential amino acids, are biosynthesized only in plants and microorganisms and must be obtained in our diet. The division between essential and nonessential amino acids is not clear-cut, however. Tyrosine, for instance, is sometimes considered nonessential because humans can produce it from phenylalanine, but phenylalanine itself is essential and must be obtained in the diet. Arginine can be synthesized by humans, but much of the arginine we need also comes from our diet.

Exercise 11.3.1

How many of the α-amino acids shown in Table 26.1 contain aromatic rings? How many contain sulfur? How many contain alcohol groups? How many contain hydrocarbon side chains?

Answer available at the end of this section.

Exercise 11.3.2

Of the 19 L amino acids, 18 have the S configuration at the α carbon. Cysteine is the only L amino acid that has an *R* configuration. Explain.

Answer available at the end of this section.

Exercise 11.3.3

The amino acid threonine, (2*S*,3*R*)-2-amino-3-hydroxybutanoic acid, has two chirality centers.

a. Draw threonine, using normal, wedged, and dashed lines to show dimensionality.
b. Draw a diastereomer of threonine, and label its chirality centers as *R* or S.

Answer available at the end of this section.

Answers

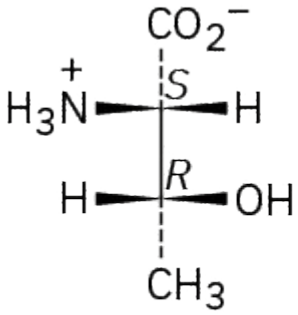
Exercise 11.3.1

Aromatic: Phe, Tyr, Trp, His; sulfur-containing: Cys, Met; alcohols: Ser, Thr; hydrocarbon side chains: Ala, Ile, Leu, Val, Phe

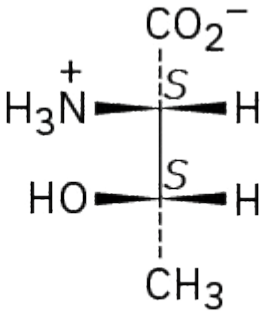
Exercise 11.3.2

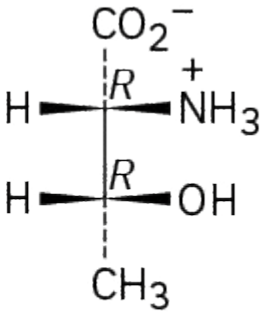
The sulfur atom in the $-CH_2SH$ group of cysteine makes the side chain higher in ranking than the $-CO_2H$ group.

Exercise 11.3.3



L-Threonine





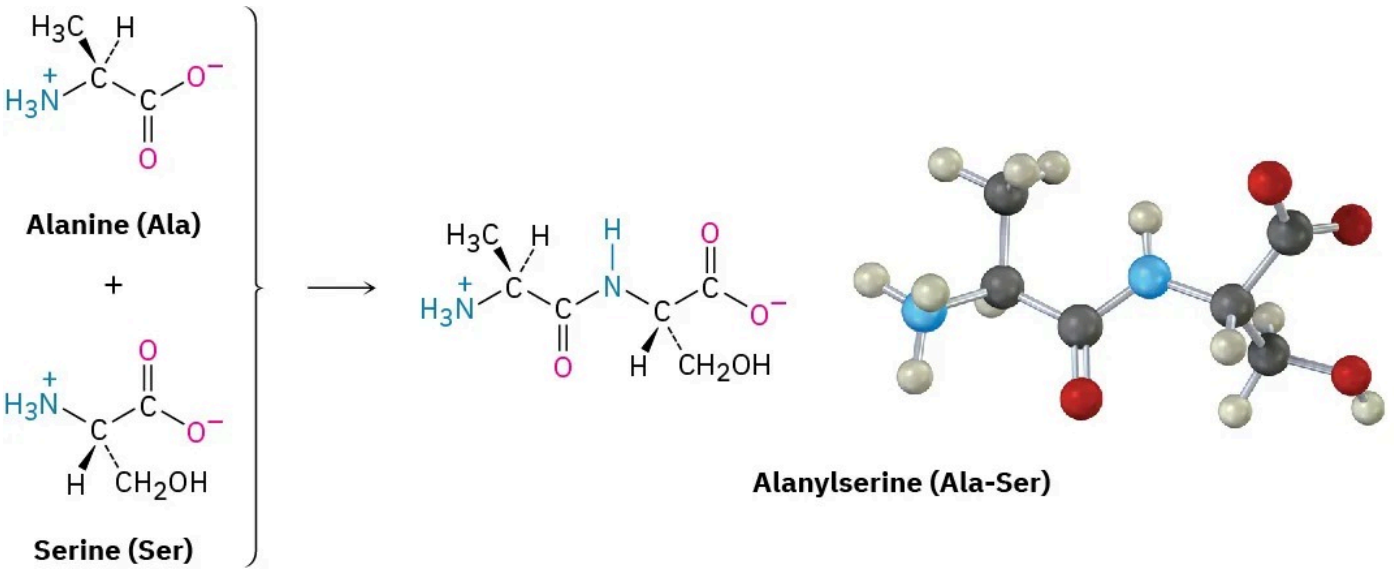
Diastereomers of L-threonine

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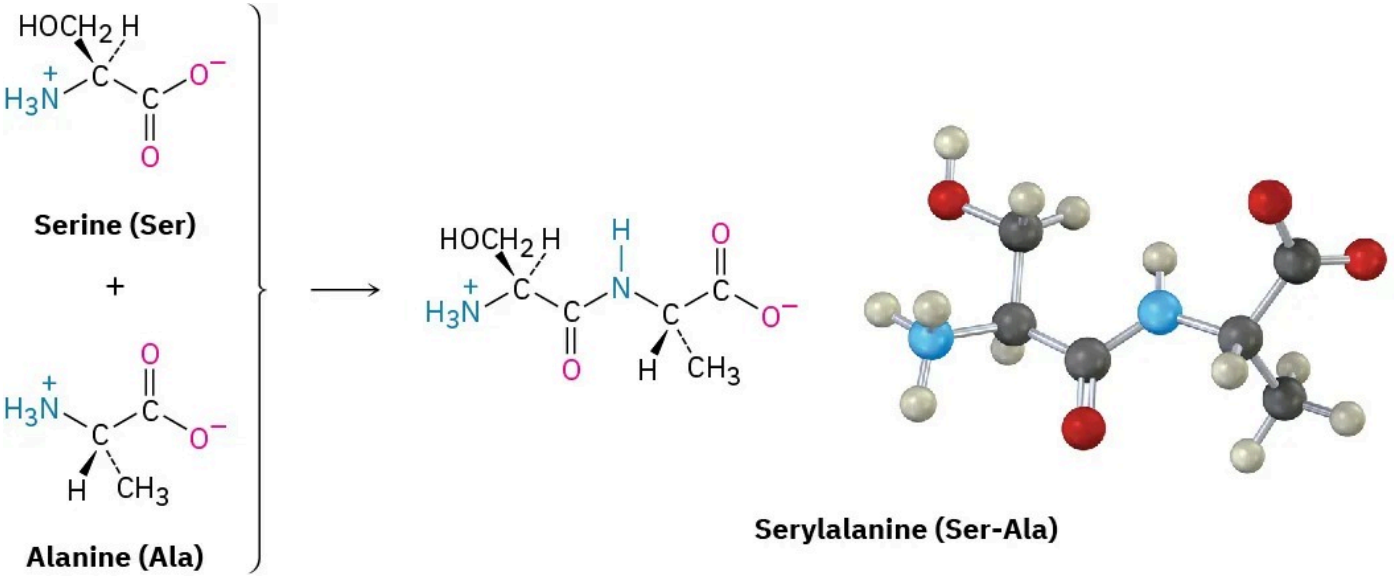
- 26.1: Structures of Amino Acids by OpenStax is licensed CC BY-NC-SA 4.0. Original source: https://openstax.org/details/books/organic-chemistry.

11.4: Peptides and Proteins

Proteins and peptides are amino acid polymers in which the individual amino acids, called residues, are linked together by amide bonds, or *peptide bonds*. An amino group from one residue forms an amide bond with the carboxyl of a second residue, the amino group of the second forms an amide bond with the carboxyl of a third, and so on. For example, alanylserine is the dipeptide that results when an amide bond forms between the alanine carboxyl and the serine amino group.

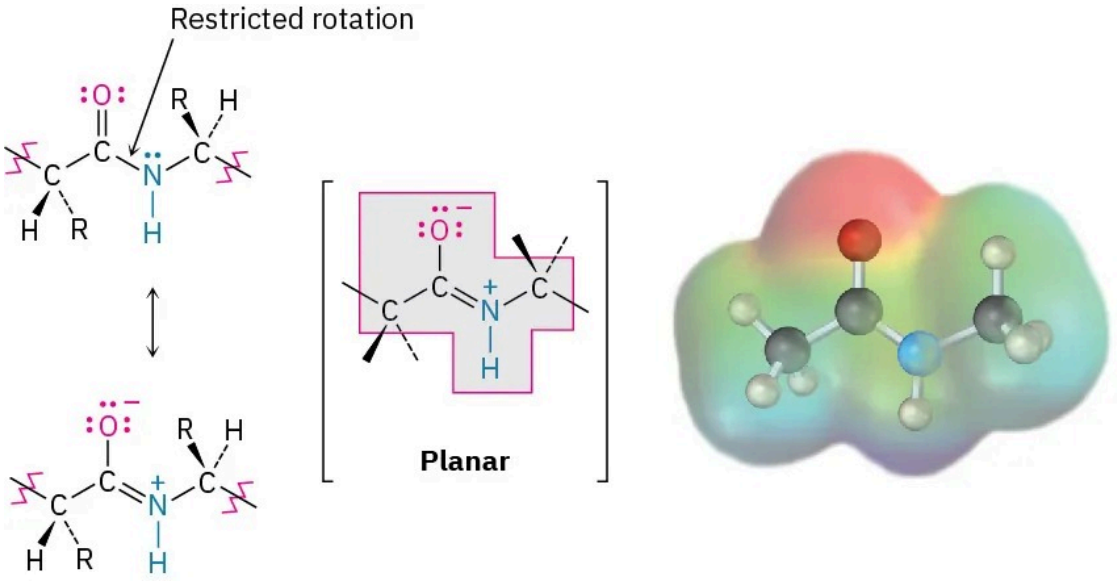


Note that two dipeptides can result from reaction between alanine and serine, depending on which carboxyl group reacts with which amino group. If the alanine amino group reacts with the serine carboxyl, serylalanine results.

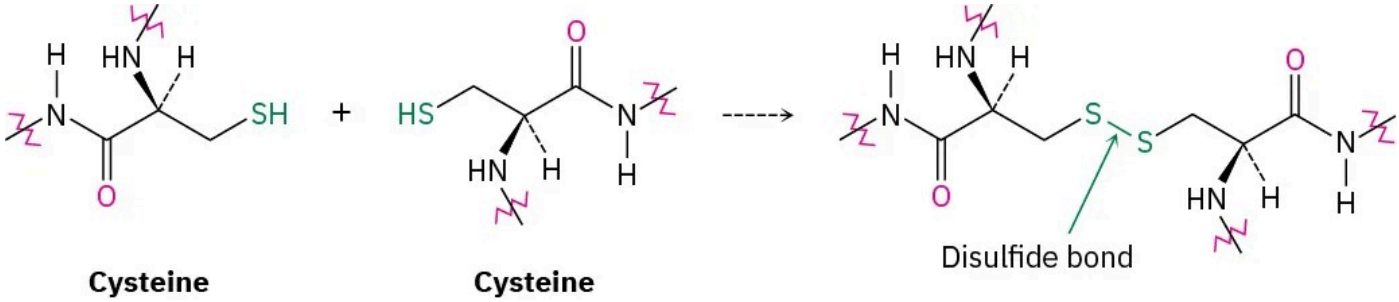


The long, repetitive sequence of –N–CH–CO– atoms that makes up a continuous chain is called the protein's backbone. By convention, peptides are written with the N-terminal amino acid (the one with the free $-NH_3^+$ group) on the left and the C-terminal amino acid (the one with the free $-CO_2^-$ group) on the right. The name of a peptide is denoted by the abbreviations listed in Table 26.1 for each amino acid. Thus, alanylserine is abbreviated Ala-Ser or A-S, and serylalanine is abbreviated Ser-Ala or S-A. The one-letter abbreviations are more convenient, though less immediately recognizable, than the three-letter abbreviations.

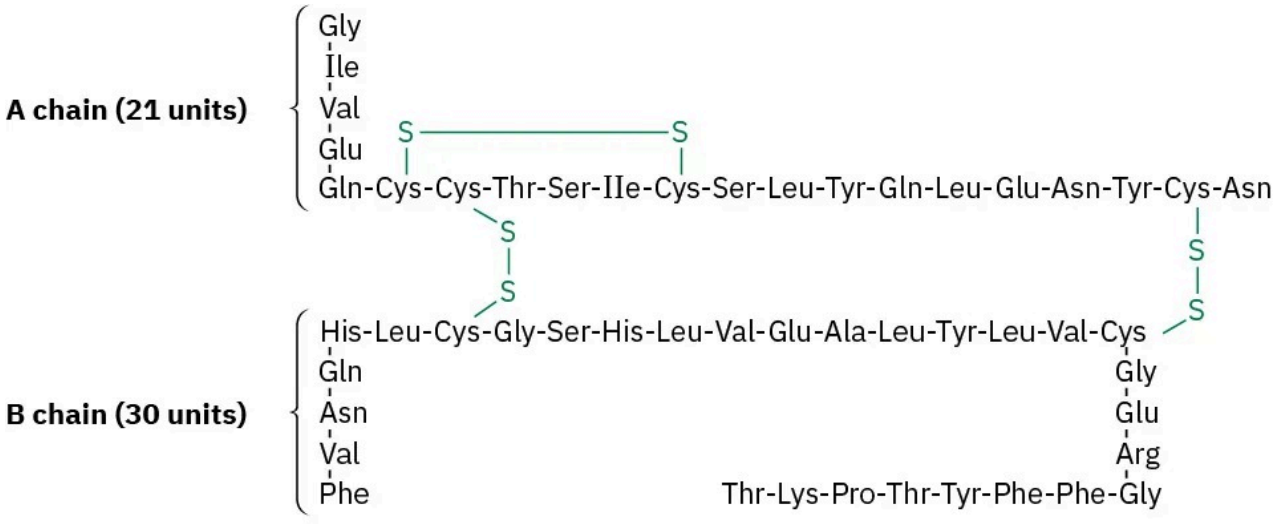
The amide bond that links amino acids together in peptides is no different from any other amide bond (Section 24.3). An amide nitrogen is nonbasic because its unshared electron pair is delocalized by resonance with the carbonyl group. This overlap of the nitrogen *p* orbital with the *p* orbitals of the carbonyl group imparts a certain amount of double-bond character to the C–N bond and restricts rotation around it. The amide bond is therefore planar, and the N–H is oriented 180° to the C=O.



A second kind of covalent bonding in peptides occurs when a disulfide linkage, RS–SR, is formed between two cysteine residues. As we saw in Section 18.7, a disulfide is formed by mild oxidation of a thiol, RSH, and is cleaved by mild reduction.



A disulfide bond between cysteine residues in different peptide chains links the otherwise separate chains together, whereas a disulfide bond between cysteine residues in the same chain forms a loop. Insulin, for instance, is composed of two chains that total 51 amino acids and are linked by two cysteine disulfide bridges.



Insulin

Exercise 11.4.1

Six isomeric tripeptides contain valine, tyrosine, and glycine. Name them using both three- and one-letter abbreviations.

Answer available at the end of this section.

Exercise 11.4.2

Draw the structure of M-P-V-G, and indicate its amide bonds.

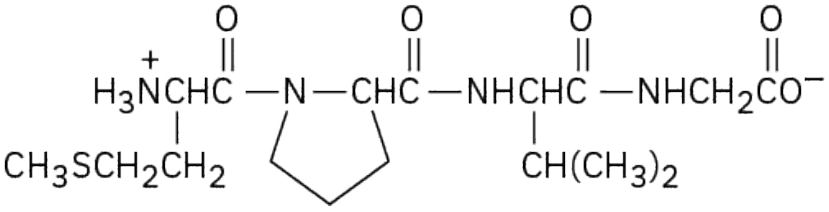
Answer available at the end of this section.

Answers

Exercise 11.4.1

Val-Tyr-Gly (VYG), Tyr-Gly-Val (YGV), Gly-Val-Tyr (GVY), Val-Gly-Tyr (VGY), Tyr-Val-Gly (YVG), Gly-Tyr-Val (GYV)

Exercise 11.4.2



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11.5: Peptides

Learning Outcomes

- Define polypeptide.
- Identify amide bond.
- Predict product of condensation of amino acids.
- Name polypeptides given the abbreviation of the amino acids.

Peptide cells in our bodies have an intricate mechanism for the manufacture of proteins. Humans have to use other techniques in order to synthesize the same proteins in a lab. The chemistry of peptide synthesis is complicated. Both active groups on an amino acid can react and the amino acid sequence must be a specific one in order for the protein to function. Robert Merrifield developed the first synthetic approach for making proteins in the lab, a manual approach which was lengthy and tedious (and, he won the Nobel Prize in Chemistry in 1984 for his work). Today, however, automated systems can crank out a peptide in a very short period of time.

Peptides

A **peptide** is a combination of amino acids in which the amine group of one amino acid has undergone a reaction with the carboxyl group of another amino acid. The reaction is a condensation reaction, forming an amide group $(\mathrm{CO{-}N})$, shown below.

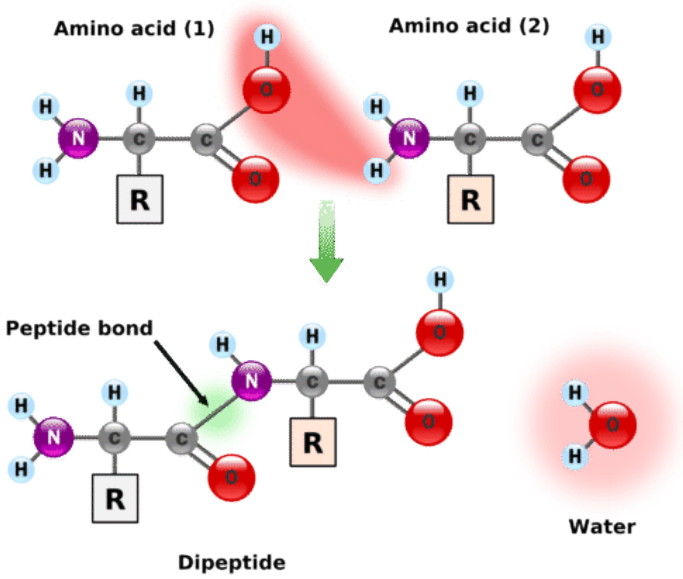
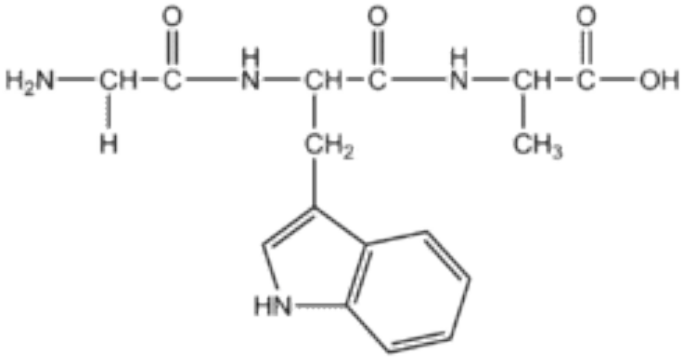


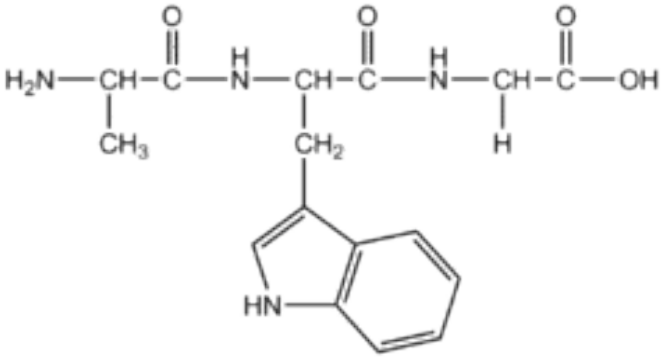
Figure $11.5.1$: Amino acids undergo condensation to form a molecule called a dipeptide. The $\mathrm{C{-}N}$ bond is called a peptide bond.

A **peptide bond** is the amide bond that occurs between the amine nitrogen of one amino acid and the carboxyl carbon of another amino acid. The resulting molecule is called a dipeptide. Notice that the particular side chains of each amino acid are irrelevant since the R groups are not involved in the peptide bond.

The dipeptide has a free amine group on one end of the molecule (known as the N-terminus) and a free carboxyl group on the other end (known as the C-terminus). Each is capable of extending the chain through the formation of another peptide bond. The particular sequence of amino acids in a longer chain is called an amino acid sequence. By convention, the amino acid sequence is listed in the order such that the free amine group is on the left end of the molecule and the free carboxyl group is on the right end of the molecule. For example, suppose that a sequence of the amino acids glycine, tryptophan, and alanine is formed with the free amine group as part of the glycine and the free carboxyl group as part of the alanine. The amino acid sequence can be easily written using the abbreviations as Gly-Trp-Ala. This is a different sequence from Ala-Trp-Gly because the free amine and carboxyl groups would be on different amino acids in that case.



Gly-Trp-Ala



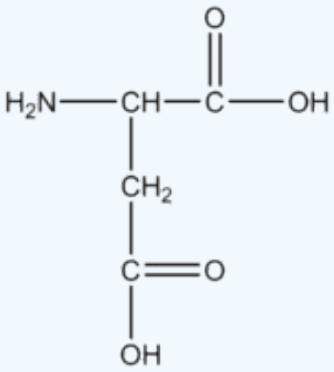
Ala-Trp-Gly

Example 11.5.1

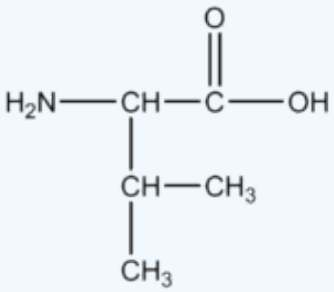
Draw the polypeptide Asp-Val-Ser.

Solution

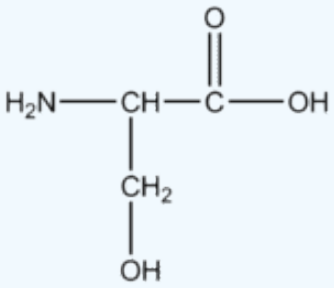
1. Identify the structures of each of the three given amino acids and draw them in the same order as given in the name.



Asp

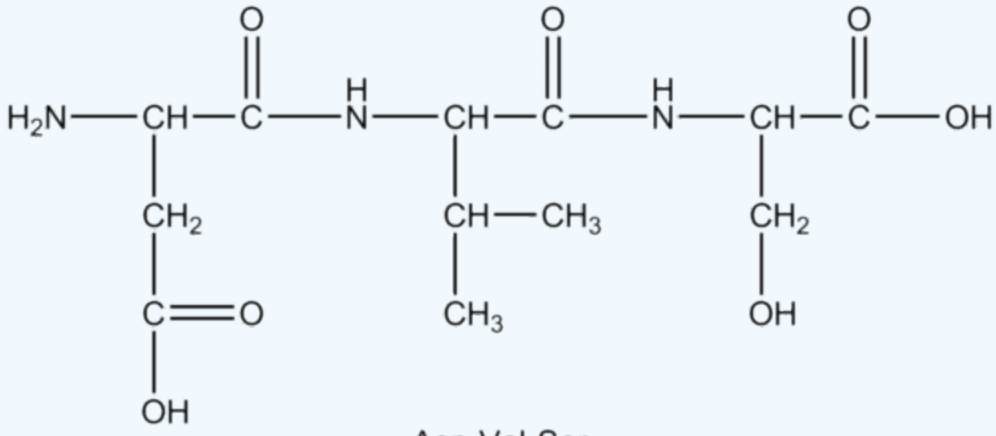


Val



Ser

2. Leaving the order the same, connect the amino acids to one another by forming peptide bonds. Note that the order given in the name is the same way the amino acids are connected in the molecule. The first one listed is always the N-terminus of the polypeptide.



Example 11.5.2

List all of the possible polypeptides that can be formed from cysteine (Cys), leucine (Leu), and arginine (Arg).

Solution

Although there are only three amino acids, the order in which they are bonded changes the identity, properties, and function of the resulting polypeptide. There are six possible polypeptides formed from these three amino acids.

Cys-Leu-Arg

Cys-Arg-Leu

Leu-Cys-Arg

Leu-Arg-Cys

Arg-Cys-Leu

Arg-Leu-Cys

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- Allison Soult, Ph.D. (Department of Chemistry, University of Kentucky)

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11.6: Protein Structure

Learning Outcomes

- Describe the four levels of protein structure.
- Identify the two types of secondary structure in proteins.
- Describe the interactive forces in each level of protein structure.
- Distinguish between globular and fibrous proteins.
- Define denaturation of proteins.
- Identify ways in which proteins are denatured.

Hemoglobin is a complex protein which has a quaternary structure and contains iron. There are four subunits in the hemoglobin molecule - two alpha subunits and two beta subunits. Each subunit contains one iron ion, whose oxidation state changes from $+2$ to $+3$ and back again, depending upon the environment around the iron. When oxygen binds to the iron, the three-dimensional shape of the molecule changes. Upon release of the oxygen to the cells, the shape changes again.

With hemoglobin of normal structure, this shift in conformation does not present any problems. However, individuals with hemoglobin S do experience serious complications. This hemoglobin has one amino acid in the two beta chains that is different from the amino acid at that point in the primary structure of normal hemoglobin. The result of this one structural change is aggregation of the individual protein molecules when oxygen is released. Adjacent hemoglobin molecules come in contact with one another and clump up, causing the red cells to deform and break.

This abnormality, known as sickle cell, is genetic in nature. A person may inherit the gene from one parent and have sickle cell trait (only some of the hemoglobin is hemoglobin S), which is usually not life-threatening. Inheriting the gene from both parents will result in sickle cell disease, a very serious condition.

Proteins

A **polypeptide** is a sequence of amino acids between ten and one hundred in length. A **protein** is a peptide that is greater than one hundred amino acids in length. Proteins are very prevalent in living organisms. Hair, skin, nails, muscles, and the hemoglobin in red blood cells are some of the important parts of your body that are made of different proteins. The wide array of chemical and physiological properties of proteins is a function of their amino acid sequences. Since proteins generally consist of one hundred or more amino acids, the number of amino acid sequences that are possible is virtually limitless.

The three-dimensional structure of a protein is very critical to its function. This structure can be broken down into four levels. The **primary structure** is the amino acid sequence of the protein. The amino acid sequence of a given protein is unique and defines the function of that protein. Peptide bonds form the connections between the amino acids.

The **secondary structure** is a highly irregular sub-structure of the protein. The two most common types of protein secondary structure are the alpha helix (see figure below) and the beta sheet (see figure below). An alpha helix consists of amino acids that adopt a spiral shape. A beta pleated sheet (like a fan-folded paper) is alternating rows of amino acids that line up in a side-by-side fashion. In both cases, the secondary structures are stabilized by extensive hydrogen bonding between the side chains. The interaction of the various side chains in the amino acid, specifically the hydrogen bonding, leads to the adoption of a particular secondary structure. The hydrogen bonding occurs between amino acids that are close to each other in the primary structure.

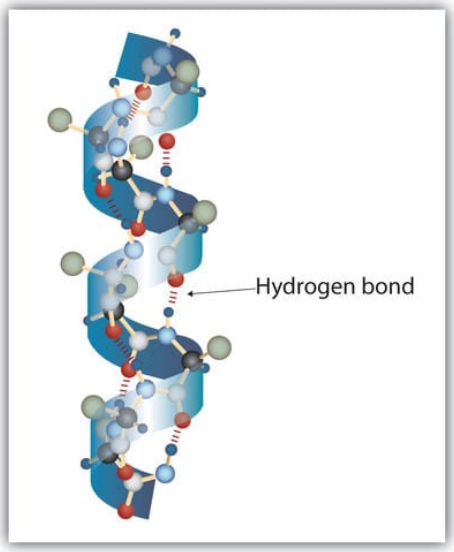


Figure 11.6.1: Alpha helix.

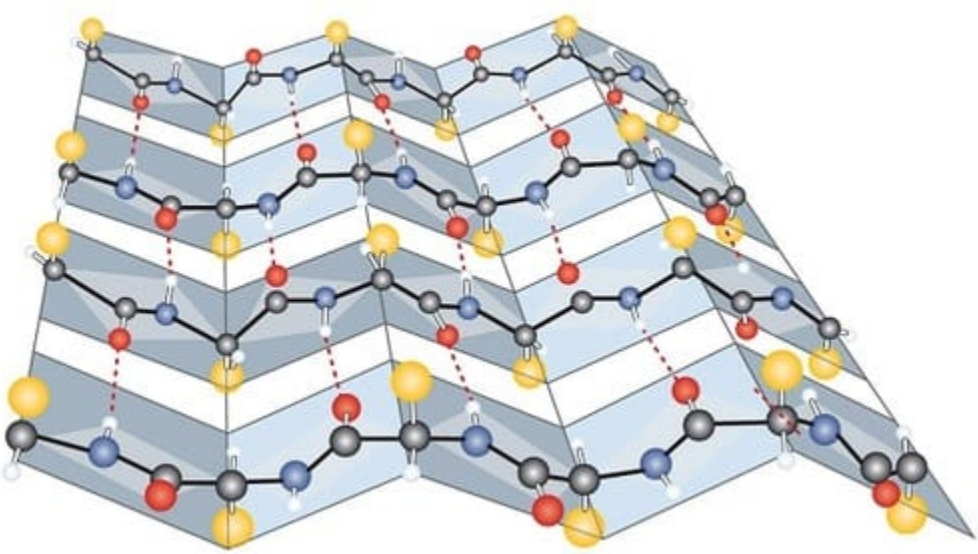
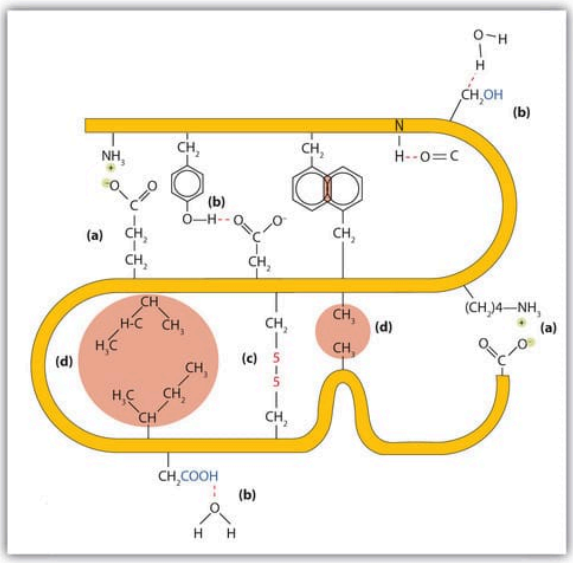


Figure 11.6.2: Beta pleated sheet.

The **tertiary structure** is the overall three-dimensional structure of the protein. A typical protein consists of several sections of a specific secondary structure (alpha helix or beta sheet) along with other areas in which a more random structure occurs. These areas combine to produce the tertiary structure. The tertiary structure is stabilized by forces similar to the intermolecular forces previously seen between molecules. These attractive forces include London dispersion forces (hydrophobic), hydrogen bonding, dipole-dipole forces, ion-dipole interactions, ionic salt bridges, and disulfide bonds (see figure below).



Some protein molecules consist of multiple protein subunits. The **quaternary structure** of a protein refers to the specific interaction and orientation of the subunits of that protein. The quaternary structure is a result of the same types of interactions as seen in tertiary structure but between different subunits. Quaternary structures can have different numbers of subunits. For example, hemoglobin contains four subunits while insulin contains two subunits.

Hemoglobin is a very large protein found in red blood cells and whose function is to bind and carry oxygen throughout the bloodstream. Hemoglobin consists of four subunits - two α subunits (yellow) and two β subunits (gray) - which then come together in a specific and defined way through interactions of the side chains (see figure below). Hemoglobin also contains four iron atoms, located in the middle of each of the four subunits. The iron atoms are part of a structure called a porphyrin, shown in red in the figure.

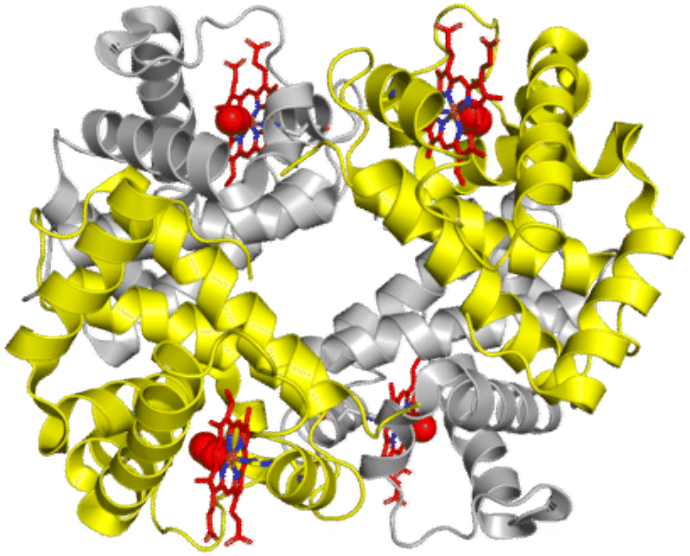


Figure 11.6.3: Hemoglobin.

Some proteins consist of only one subunit and thus do not have a quaternary structure. The figure below diagrams the interaction of the four levels of protein structure.

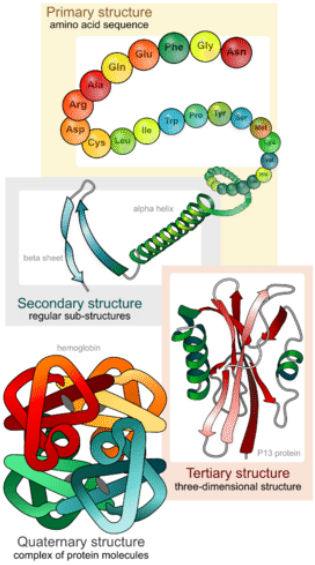


Figure 11.6.4: The four levels of protein structure.

Globular and Fibrous Proteins

Once proteins form and have developed all levels of their structure, they can be classified as either fibrous or globular. These classifications give the basic shape of the entire protein molecule. While many proteins are globular proteins (see figure below), keratin proteins are fibrous (see figure below) and make up the hair, nails, and the outer layer of skin.

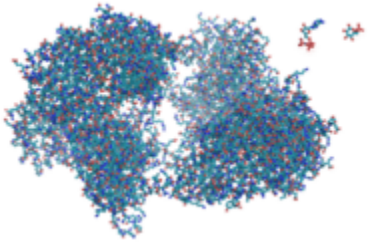


Figure 11.6.5: Globular protein.

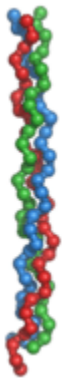


Figure 11.6.6: Fibrous protein.

Denaturation of Proteins

The highly organized structures of proteins are truly masterworks of chemical architecture. But highly organized structures tend to have a certain delicacy, and this is true of proteins. Denaturation is the term used for any change in the three-dimensional structure of a protein that renders it incapable of performing its assigned function. A denatured protein cannot do its job because there is a change in the secondary, tertiary, or quaternary structure (see figure below). A wide variety of reagents and conditions,

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such as heat, organic compounds, pH changes, and heavy metal ions can cause protein denaturation. Anyone who has fried an egg has observed denaturation. The clear egg white turns opaque as the albumin denatures and coagulates.

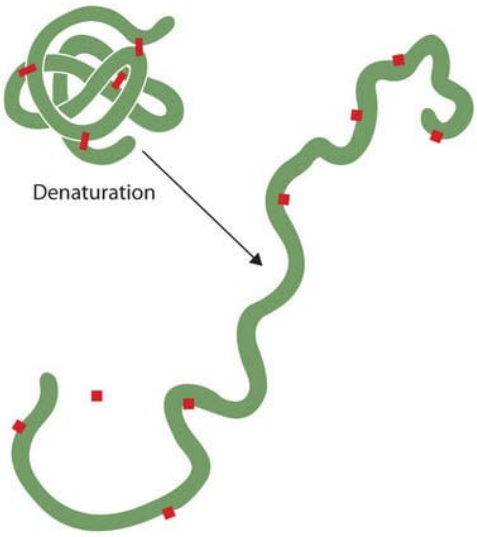


Figure 11.6.7: Denaturation of a protein.

The primary structures of proteins are quite sturdy. In general, fairly vigorous conditions are needed to hydrolyze peptide bonds. At the secondary through quaternary levels, however, proteins are quite vulnerable to attack, though they vary in their vulnerability to denaturation. The delicately folded globular proteins are much easier to denature than are the tough, fibrous proteins of hair and skin.

There are a variety of ways to denature proteins including those below.

- Heat above $50^{\circ}\mathrm{C}$
- Strong acids
- Strong bases
- Ionic compounds (i.e. NaCl)
- Reducing agents
- Detergents
- Heavy metal ions
- Agitation

If you have ever had a hair permanent or chemically straightened your hair, the process involved the denaturation of proteins. The reducing agent (usually an ammonium compound) breaks the disulfide bonds in the hair. The hair is then curled or straightened which aligns the amino acids in a different pattern. An oxidizing agent is applied and the disulfide bonds reform between different amino acids. The change is permanent for the hair that you have at the time but new hair growing in will have the structure of the original proteins and your hair is back to its normal state.

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11.7: Enzymes

Learning Objectives

- Understand enzyme-related terminology, nomenclature, and classification of enzymes.
- Understand the mode of action of enzymes, the factors that affect them, and the inhibitors that retard or damage the enzyme activity.

Enzymes and the related terminology

Three conditions are necessary for a chemical reaction to happen:

1. Reactants must collide -the more frequent the collisions faster the reaction,
2. the reactant must have proper orientation at the time of the collision -the higher the probability of proper orientation at the time of the collision, the faster the reaction, and
3. there must be enough energy at collision to surpass the energy barrier, i.e., the energy of activation for the reaction -the lower the activation energy, the faster the reaction.

Often chemical reactions are possible but so slow that they are practically useless. For example, a reaction between hydrogen $\mathrm{H_2}$ and nitrogen $\mathrm{N_2}$ producing ammonia $\mathrm{NH_3}$ is possible, but to make it practically useful, high-pressure, high-temperature, and catalysts are needed.

$$\mathrm{N_2\,(g) + H_2\,(g) \overset{\text{heat, pressure, catalyst}}{\rightleftharpoons} 2\,NH_3(g)} \quad -92.4\,\mathrm{kJ\ mol^{-1}}$$

Catalyst

A catalyst is a reagent that increases the rate of a chemical reaction without itself being altered in the process.

The catalysts usually increase the rate of chemical reactions by improving the last two factors, i.e., increasing the probability of proper orientation and providing an alternate route for the reaction with lower activation energy. There are more constraints for chemical reactions in living things, e.g., the reaction has to occur under physiological conditions of pH ~7.4 and body temperature ~37 ^{o}C. Special catalysts called enzymes are used to regulate chemical reactions in living things.

Enzyme

An **enzyme** is a substance that regulates the rate of chemical reaction in living things without itself being altered in the process. In other words, enzymes are biological catalysts.

Like other catalysts, the enzymes usually increase the rate of chemical reactions by improving the last two factors, i.e., increasing the probability of proper orientation and providing an alternate route for the reaction with lower activation energy. The enzymes achieve the appropriate orientation of the reactants by binding them in a specific region within the enzyme, which has the geometry of its interacting groups right for securing the reactant in a particular orientation.

Substrate

A reactant in an organic or biochemical reaction is a substrate.

Active site

The enzyme's active site is the region within an enzyme where the substrate binds for the reaction.

Enzymes are usually proteins having primary, secondary, and tertiary structures. The active site is usually a small region (10% to 20%) within the enzyme. A few side chains of amino acid residues within the active site participate in the catalytic action, as shown in Figure 11.7.1. The rest of the amino acid residues define and hold the secondary and tertiary structures.

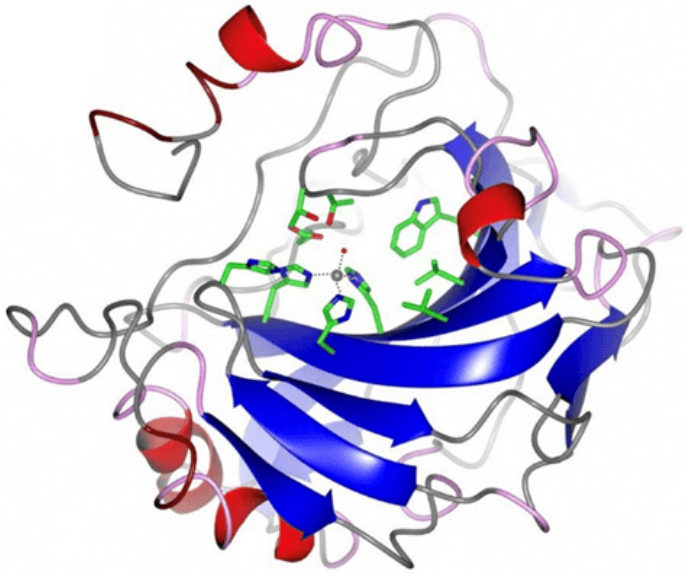


Figure 11.7.1: Human carbonic anhydrase II, CAII enzyme (PDB code: 1CA2) showing the secondary structures and the active site. The active site has a hydrophilic pocket comprising of three histidine residues (green ring with two blue nitrogen per ring) bonded to Zn^{2+} (gray dot), a water molecule (red dot) also connected to zinc and two threonine and one glutamic acid residues (green with red tips) above water. A hydrophobic pocket on the right side in the active site comprises two valine (gree Y-shapes) and a tryptophan (two fused rings, green). (Copyright; Eriksson, A.E., Jones, T.A., Liljas, A.(1988) Proteins 4: 274-282PubMed: 3151019 Search on PubMedDOI: 10.1002/prot.340040406, CC0, via Wikimedia Commons)

Some enzymes need a non-protein part to combine with them for their function.

Apoenzyme, cofactors, and coenzyme

The enzymes that need a non-protein portion to combine with them for their function are called **apoenzymes**. The non-protein portion of the enzymes is called the **cofactor**, as illustrated in Figure 11.7.2. The cofactor could be a metallic ion, .e.g., Zn^{2+} or Mg^{2+}, or an organic compound. Organic cofactor is called **coenzyme**. The apoenzyme and cofactors together are called holoenzymes, as illustrated in Figure 11.7.2.

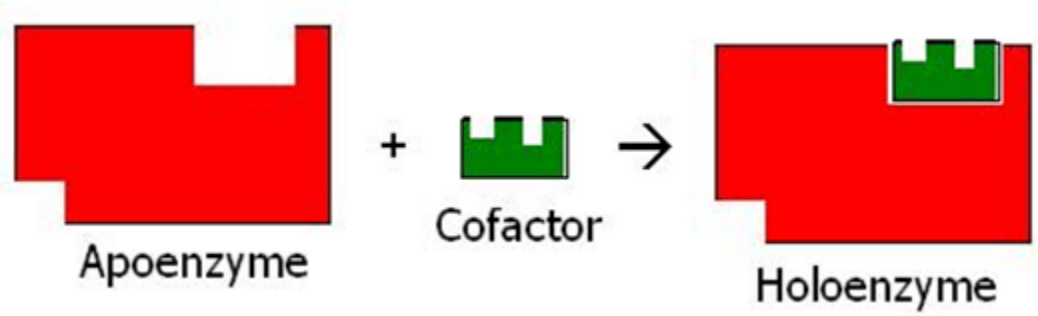
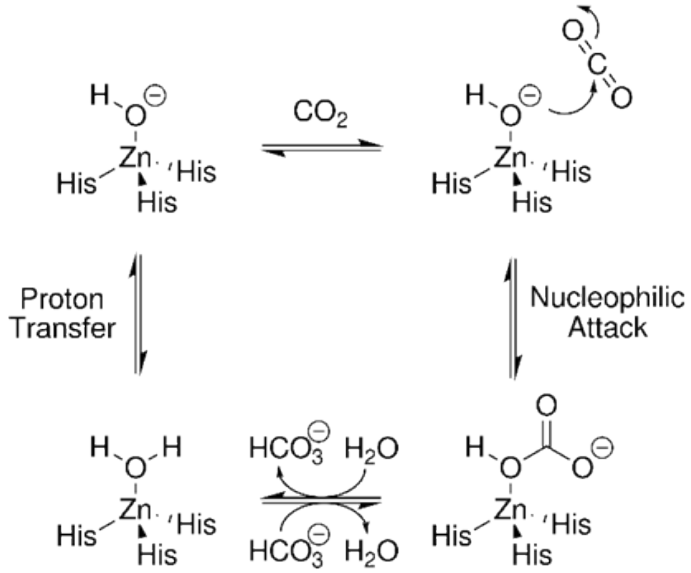


Figure 11.7.2: Apoenzyme, cofactor, and their combination, i.e., the holoenzyme illustrated. (Copyright; Moniquepena, Public domain, via Wikimedia Commons)

Enzymes usually make the reaction happen millions of times faster. For example, one molecule of carbonic anhydrase enzyme, shown in Figure 11.7.1, can catalyze about one million molecules in one second in human blood by the following reaction.



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Overall reaction: $\mathrm{CO_2 + H_2O \rightleftharpoons HCO_3^- + H^+}$

Selective

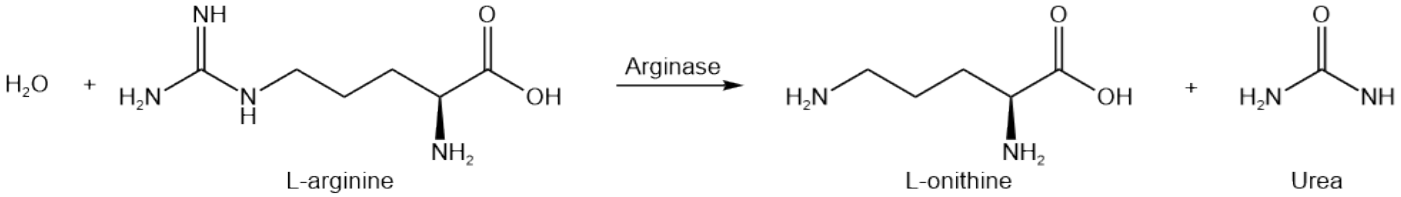
A catalyst or a reagent is selective if it produces one product preferentially or exclusively when more than one product is possibly formed.

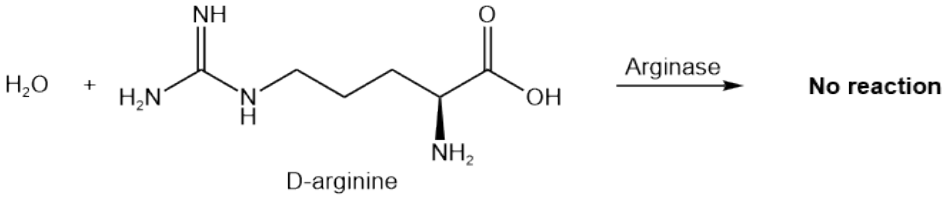
Enzymes are not only selective; they usually react with one compound or stereoisomer.

Stereospecific

Stereospecific catalysts or reagents are those that, when reacting with one stereoisomer, selectively produce a stereoisomer and either do not react with the isomers of the reactant or selectively produce other stereoisomers from them. Enzymes are usually stereospecific, i.e., they are selective among reactants and selective among products.

For example, the enzyme arginase is stereospecific, hydrolysis amino acid L-arginine to L-ornithine and urea, but does not react with D-arginine.

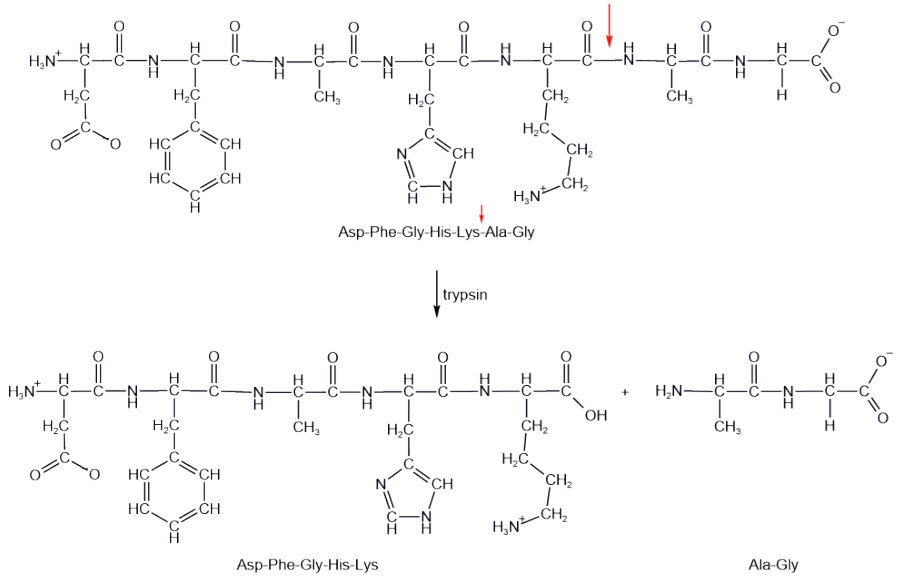




Usually, enzymes react with one compound or a specific bond of one compound. For example, enzyme ureas catalysis hydrolysis of urea ($(NH_2)_2C{=}O$) and does not hydrolyze any other amide.

$$(NH_2)_2C{=}O + H_2O \xrightarrow{\text{urease}} 2\,NH_3 + CO_2$$

Trypsin is a digestive enzyme that cleaves peptide bonds of proteins but not every peptide bond, only those on the C-side of lysine and arginine residue.



Some enzymes are specific for a class of compounds, e.g., lipases catalyzing triglyceride hydrolysis, but do not react with carbohydrates or proteins.

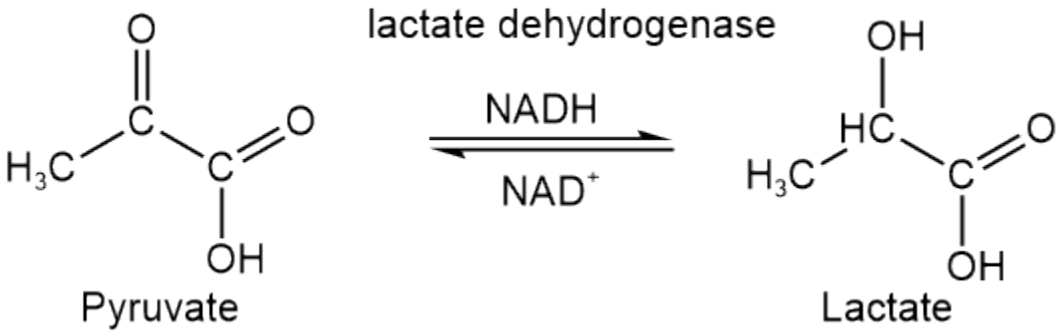
Names and classification of enzymes

Names of enzymes are derived by replacing the end of the name of a reactant or reaction with the suffix *ase*. For example, sucrase hydrolysis sucrose, lipase hydrolyzes lipids, oxidase catalyzes oxidation reactions, dehydrogenase removes hydrogen atoms, etc. Some old names of enzymes have the suffix *in*, e.g., digestive enzymes pepsin and trypsin. In the recent classification of enzymes, the name or the class name indicates the type of reaction it catalyzes. There are six major classes of enzymes, as described in the following.

Oxidoreductases

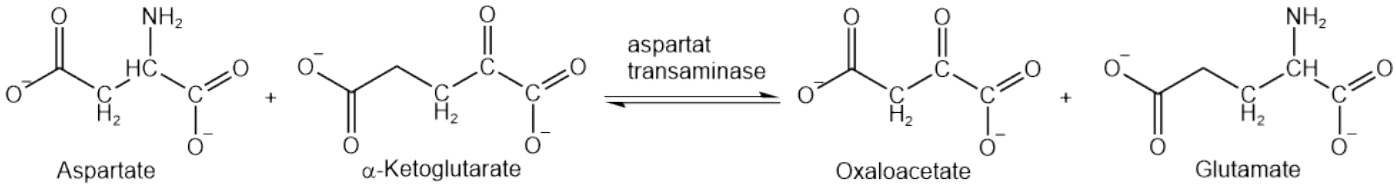
Oxidoreductases do oxidation-reduction reactions, i.e., **oxidases** oxidize a substance, **reductases** reduce a substance, and

dehydrogenases remove hydrogen. For example, lactate dehydrogenase reduces pyruvate and oxidizes lactate, as shown below.



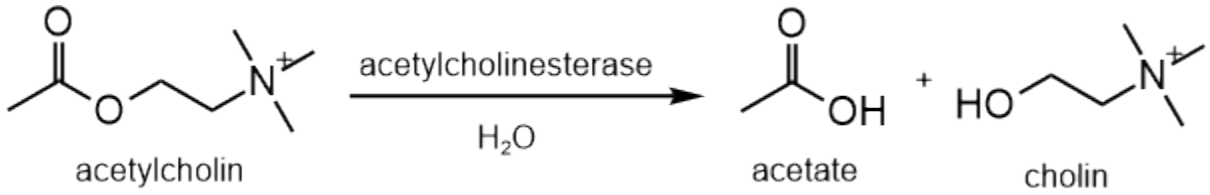
Transferases

Transferases transfer a group between two compounds. For example, kinases transfer phosphate groups, and transansaminases transfer amino groups, as shown below.



Hydrolases

Hydrolases do hydrolysis reactions: lipases hydrolyze lipids, carbohydrases hydrolyze carbohydrates, proteases hydrolyze proteins, phosphatases hydrolyze phosphate esters, and nucleases hydrolyze nucleic acids. For example, acetylcholinesterase hydrolysis acetylcholine, as shown below.



Lyases

Lyases add two groups to double bond or remove two groups from adjacent atoms to create a double bond or a ring structure by means other than hydrolysis and oxidation, e.g., carboxylases add or remove CO^2, and deaminases add or remove NH^3. For example, actonitase, shown in Figure 11.7.3, adds or removes water. double bond or add a new ring structure.

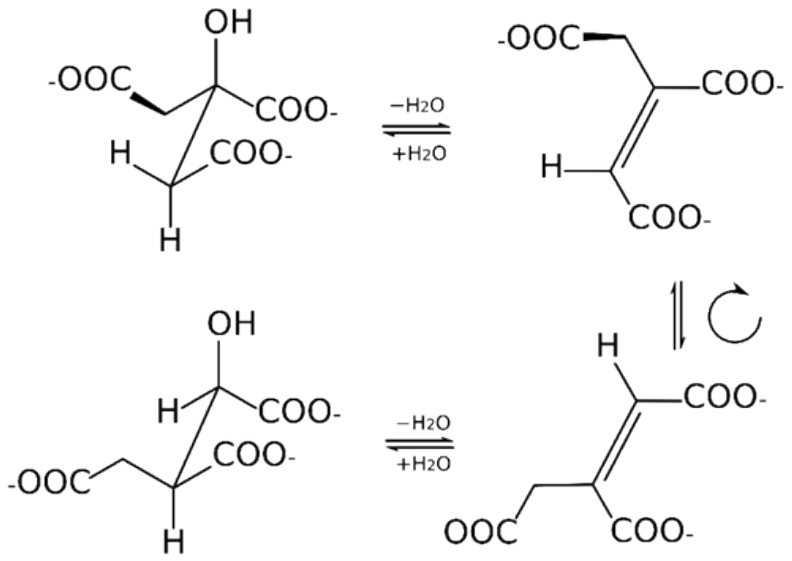
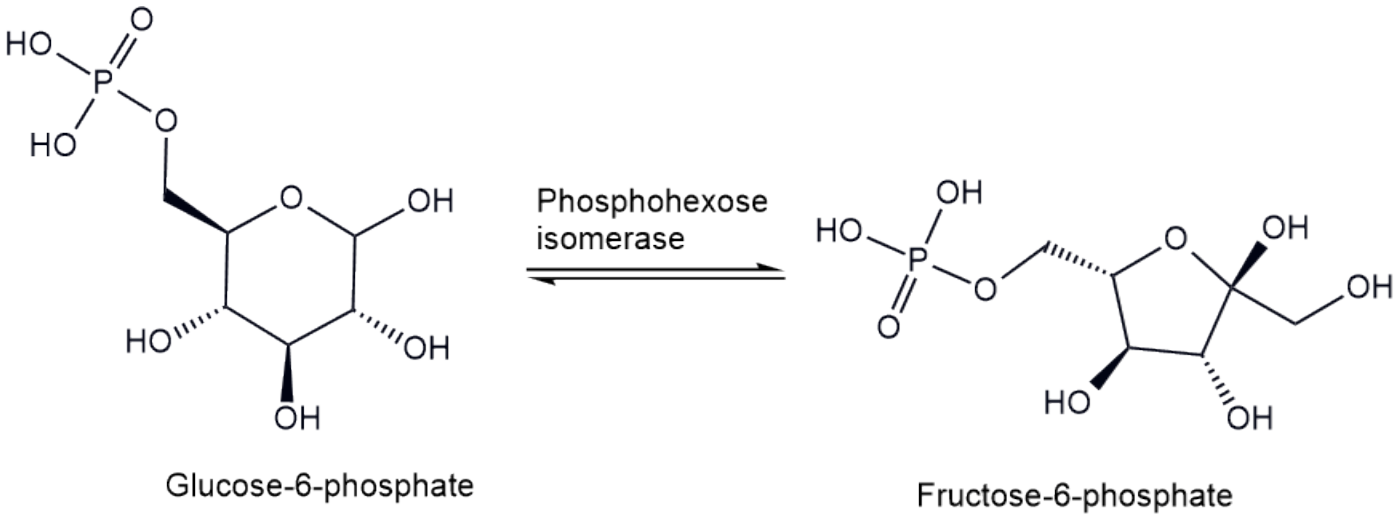


Figure 11.7.3: Reaction steps in the reaction catalyzed by aconitase, stereospecific view. Top left: Citrate. Bottom left: Isocitrate. Right: Aconitate. The aconitate has to flip by 180 degrees between the reactions. (Copyright; Ayacop, Public domain, via Wikimedia Commons

Isomerases

Isomerases rearrange atoms in a molecule: isomerases convert cis to trans or trans to cis isomer, and epimerases convert D to L or L to D streoisomers. Phosphohexose isomerizes shown below isomerizes glucose-6-phosphate to fructose-6-phosphate

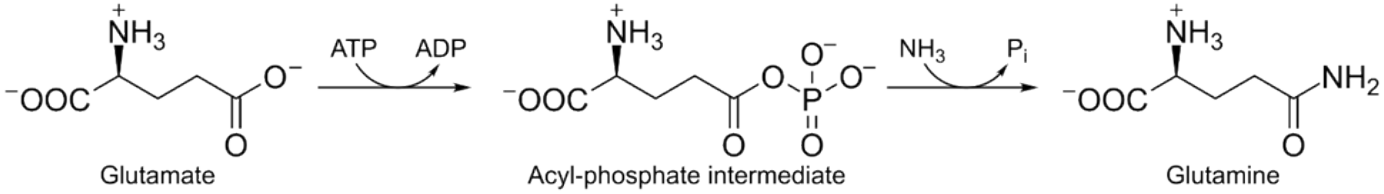


Glucose-6-phosphate

Fructose-6-phosphate

Ligases

Ligases or synthetases catalyze the joining of two molecules, e.g., glutamate to glutamine conversion by glutamine synthetase shown below.



Glutamate

Acyl-phosphate intermediate

Glutamine

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How do enzymes catalyze the reactions?

The chemical reactions that enzymes catalyze can occur without enzymes, but the reactions' rates are usually prolonged due to high activation energies. Enzymes provide alternate routes to the reactions with lower energy barriers (activation energies) and proper orientations of substrates that result in fast reactions, as illustrated in Figure $11.7.3$

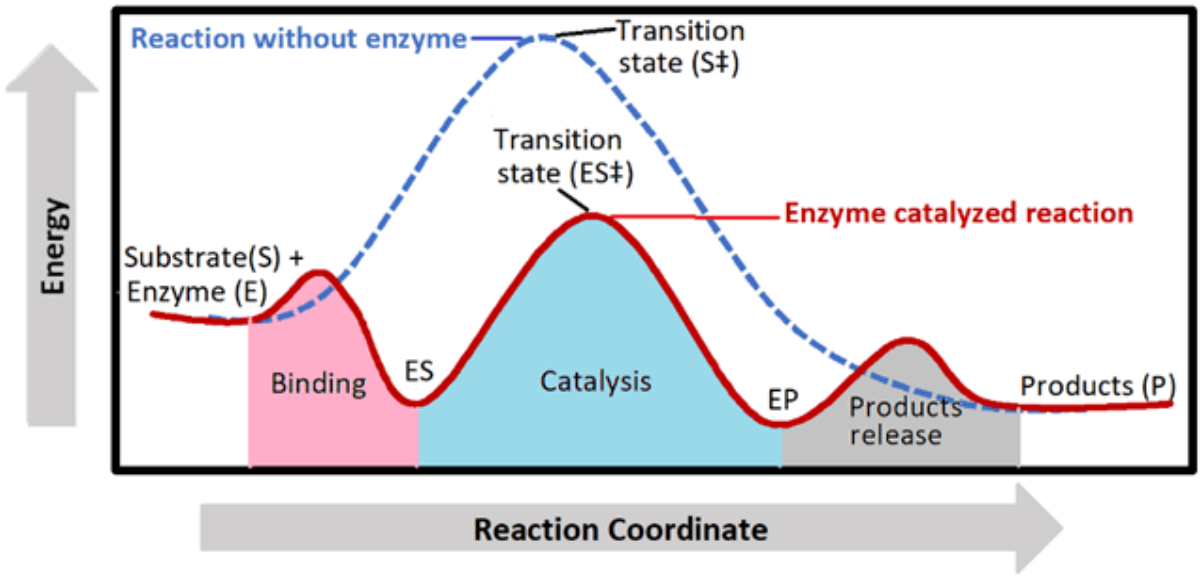


Figure $11.7.3$: Illustration of reaction coordinates of a biochemical reaction with and without enzyme. (Copyright; Public domain)

In a generalized enzyme-catalyzed reaction, enzyme (E) and substrate (S) bind to make an enzyme-substrate complex (ES). The intermolecular interactions between the enzyme and the substrate usually loosen the bonds of the substrate that need to be broken, resulting in a lower energy barrier for the catalyzed reaction that leads to the product (P) at a faster rate than otherwise. The product leaves the enzyme so it can bind with another substrate.

$$\mathrm{E + S \rightleftharpoons ES \longrightarrow E + P}$$

For example, carbonic anhydrase catalyzes the reaction of water ($\mathrm{H_2O}$) with carbon dioxide ($\mathrm{CO_2}$) in blood as illustrated in Figure $11.7.4$. The carbonic anhydrase enzyme is bound with cofactor $\mathrm{Zn^{2+}}$ through three histidine residues. The $\mathrm{Zn^{2+}}$ is also bound with $\mathrm{H_2O}$ that bond makes water ready for the proton transfer. After the proton transfer, a strong electrophile $-\bar{O}H$ is generated that attacks $\mathrm{CO_2}$, which is placed in the proper location in the hydrophobic pocket nearby. The product is displaced with another water molecule that repeats the process. One molecule of carbonic anhydrase can convert about million $\mathrm{CO_2}$ molecules per second in this reaction.

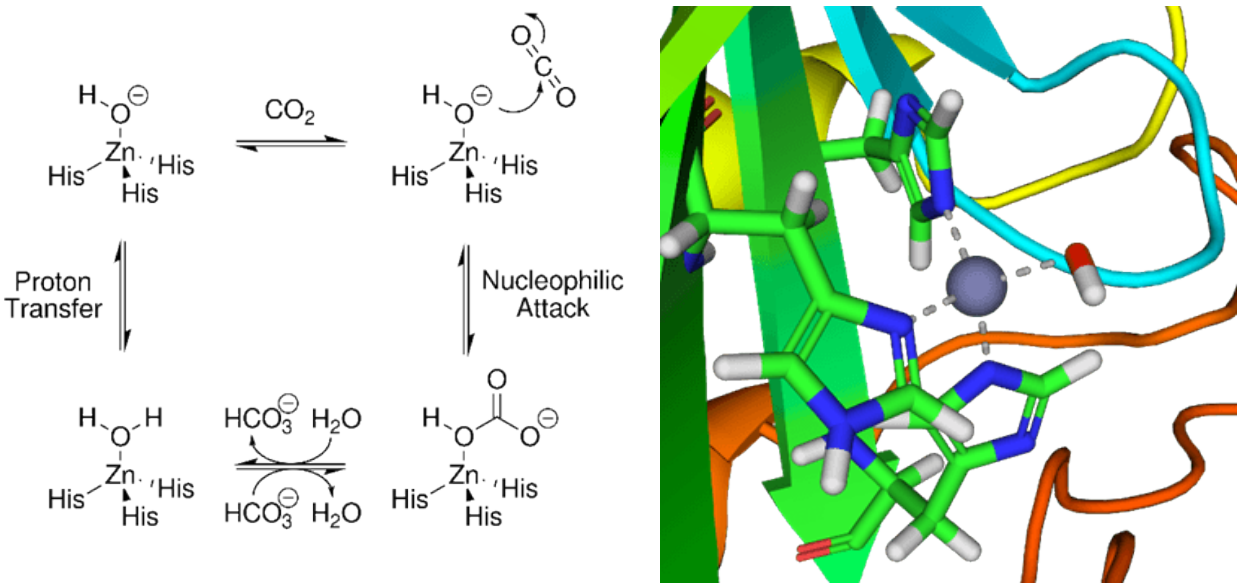
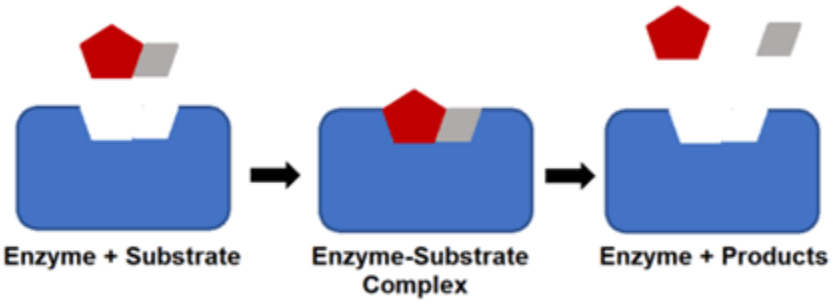


Figure 11.7.4: Mechanism of carbonic anhydrase catalyzed reaction of water with carbon dioxide in the blood (left) and a closeup of the active site of the enzyme showing Zn^{2+} (gray sphere) bonded with three histidine residue and $-\bar{O}H$ (red and white bar). There is a hydrophobic pocket near $-\bar{O}H$ that is shown in the full model in Figure 11.7.1. (Copyright; left: Own work, Public domain, via Wikimedia Commons, right: Own work, Public domain, via Wikimedia Commons)

Models of enzyme action

Enzymes are usually specific for a particular substrate or a class of reaction. This specificity was explained first by models of enzyme action explained below.

Lock-and-key model



Lock-and-key model of enzyme action illustrated.

The lock and key model assumes enzymes have a fixed shape with active sites similar to a lock in which a particular substrate with a fixed shape similar to a key can fit, as shown in the figure on the right.

This model explains the specificity of enzymes but ignores the dynamic nature of molecules. Further, according to this model, the products would be expected to be snug-fit in the active site and not easy to release. In reality, all the bonds in a molecule are vibrating and stretching, and the whole molecule is jiggling due to thermal energy, as illustrated in Figure 11.7.5.

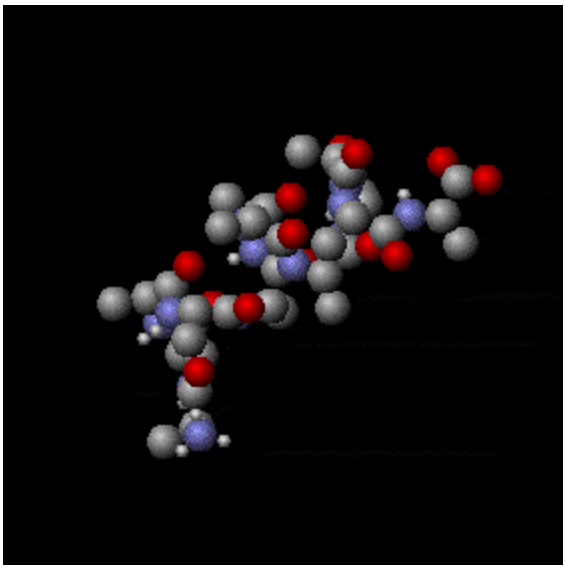


Figure 11.7.5: Illustration of thermal motion of a segment of protein alpha helix. These motions have various modes of vibrations, stretching, and rotations. In addition to these internal movements, molecules' external portions still move— like the jiggling of a water balloon. (Copyright; en:User:Greg L, CC BY-SA 3.0, via Wikimedia Commons)

Induced-fit model

The induced-fit model of enzyme action accounts for the flexibility of enzyme and substrate molecules. According to this model, the flexibility of the enzyme molecule allows the active site to adapt to the shape of the substrate and, at the same time, the substrate adopts the shape of the enzyme to acquire the best possible orientation for the reaction to occur, as illustrated in Figure 11.7.6. Then the active site shape re-adjusts to let the products be released to allow the next cycle of the enzyme action. The observation from experiments during the actual catalysis reaction supports the view that not only does the active site of the enzyme change shape, the backbone and the side chains of the enzyme molecule remain in constant motion during the enzyme action.

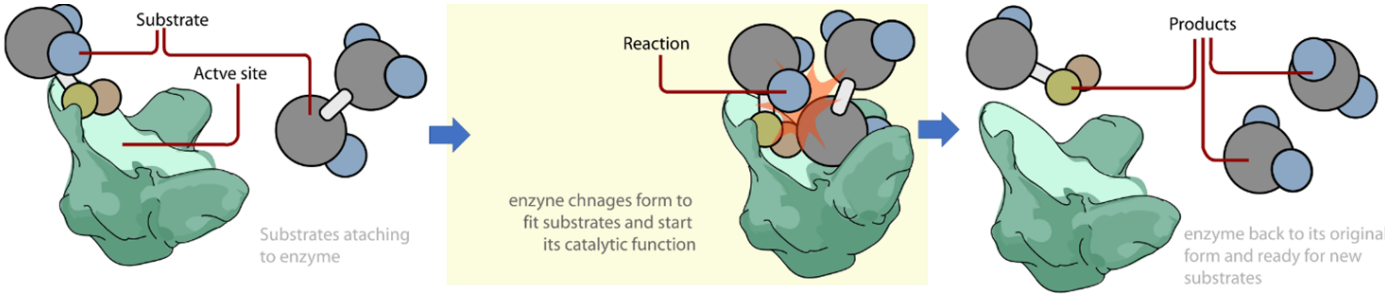


Figure 11.7.6: diagram showing the induced fit model of enzymes. (Copyright; Modified from LadyofHats, Public domain, via Wikimedia Commons)

Experimental data shows that the active site is usually a tiny portion (10% to 20%) of the enzyme. Within the active site, two or a few side chains of amino acid residues usually catalyze the reaction. Usually, the catalytically active residue is one of the following: His, Cys, Asp, Arg, and Glu. These amino acids have acidic or basic or thiol functional groups, which are not only capable of hydrogen bonding but also capable of acid, base, electrophile, or nucleophile catalysis. For example, the pepsin enzyme breaks peptide bonds by using histidine and cystine, as illustrated in Figure 11.7.7.

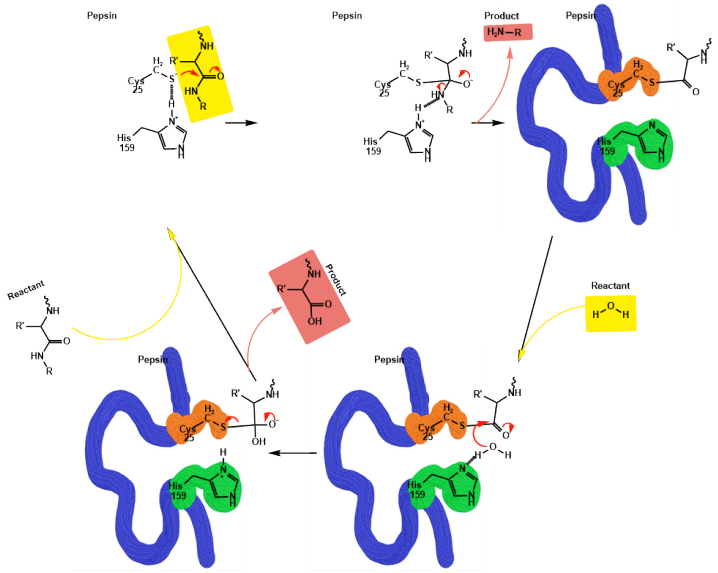


Figure 11.7.7: Illustration of the mechanism of peptide bond cleavage by pepsin enzyme: histidine removes a proton from $-\mathrm{SH}$ group of cystine making it a strong nucleophile $-\mathrm{S}^{-}$. The $-\mathrm{S}^{-}$ attacks a $\mathrm{C}{=}\mathrm{O}$ group of the peptide and breaks the peptide bond by nucleophilic acyl substitution mechanism. Then histidine brings in a $\mathrm{H_2O}$ at a suitable position for a second nucleophilic acyl substitution that breaks the $\mathrm{S}{-}\mathrm{C}$ bond. Products leave, and the enzyme repeats the cycle. (Copyright; Public domain)

The following video from RCSBProteinDataBank explains how enzymes work.

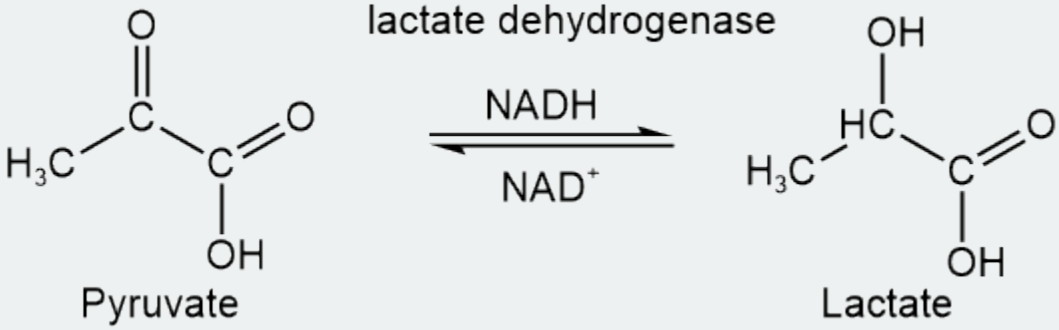
YouTube Video

This interactive element is not available in this format. Visit the link or scan the QR code to access it online.

View this YouTube Video online

Isoenzymes as a medical diagnostic tool

Isoenzymes are different enzymes that perform the same function in different body parts. They usually have a tertiary structure and differ in only a few amino acid residues. For example, lactate dehydrogenase (LDA) catalyzes the conversion between pyruvate and lactate, as shown below.



LDA is a tetramer made of two sub-units, the H-form, and the M-form, in five combinations found in different tissues, as shown in Table 1. Similarly, creatine phosphokinase (CPK) catalyzes the interconversion of phosphocreatine to creatine. CPK is a dimer in 3 isoenzyme forms shown in Table 2.

These isoenzymes usually function within cells. However, when some disease damages a tissue, the cells die, and the isoenzymes are released into the blood. Analysis of blood serum is used to diagnose the location of the damage. For example, an elevated level of LDH5 indicates liver damage and myocardial infarction (heart damage) is characterized by a high level of LDH1 isoenzyme. The heart damage will also elevate CK_2.

Table 1: Different forms of lactate dehydrogenase (LDA), their subunit composition the location in the body.

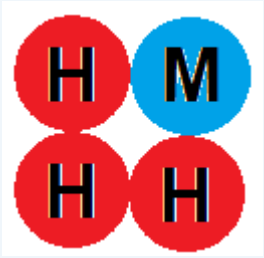
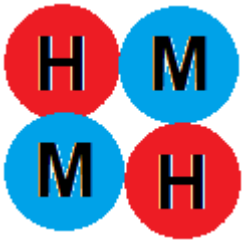
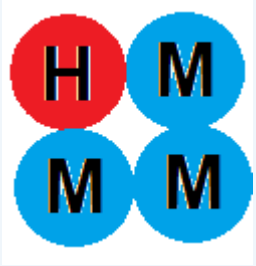
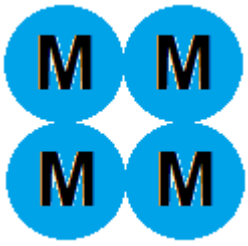
Type	Subunits	Illustration	Location
LDH_1	HHHH		Heart and Erythrocyte
LDH_2	HHHM		Heart and Erythrocyte
LDH_3	HHMM		Brain and Kidney
LDH_4	HMMM		Skeletal Muscle and Liver
LDH_5	MMMM		Skeletal Muscle and Liver

Table 2: Isoenzymes of creatine phosphokinase (CPK) dimer, composition, and location in the body.

Isoenzyme	Subunit	Illustration	Tissue of Origin
CPK_1	BB		Brain
CPK_2	MB		Heart
CPK_3	MM		Skeletal muscle

Factors that affect enzyme activity

The enzyme activity is related to how much it increases the reaction rate compared to the same reaction without the enzyme. The factors that affect enzyme activity include concentration, temperature, pH, and the presence of inhibitors.

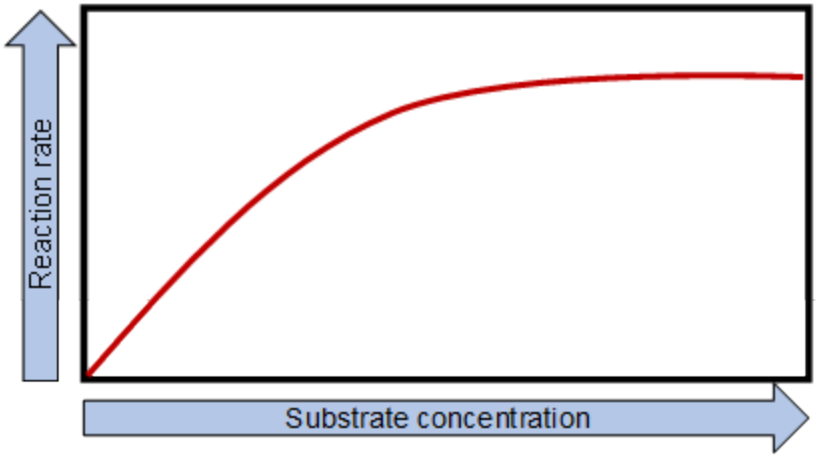
Concentration

Usually, the enzyme is in very low concentration relative to the concentration of the substrate. Therefore,



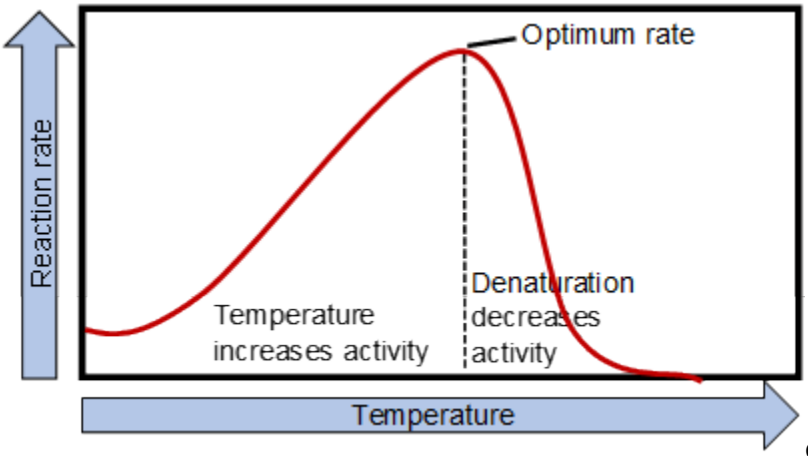
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an increase in the

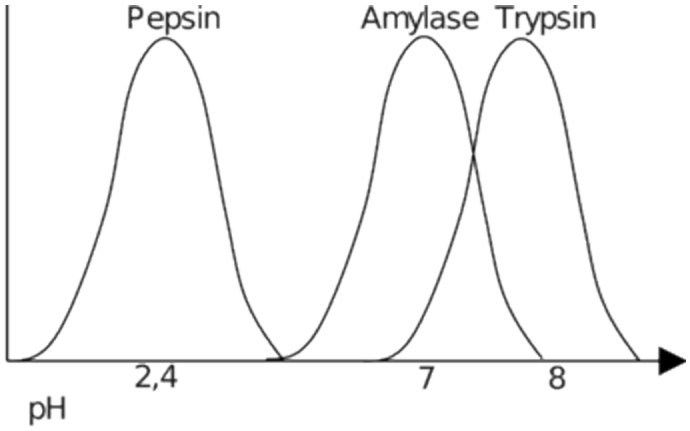


enzyme concentration increases the reaction rate linearly, i.e., doubling the enzyme concentration doubles the reaction rate, and tripling it triples the rate. An increase in the substrate concentration increases the reaction rate but not linearly; it follows a curvilinear curve. The rate increase reaches a saturation level and does not increase after that with a further increase in the substrate concentration, as illustrated in the figure on the left. This is because all the enzyme's active sites become occupied with the substrate at the saturation point, and the reaction proceeds at its maximum rate, as illustrated in the figure on the right.

Temperature



Generally, an increase in temperature increases the rate of a chemical reaction. This is because more molecules have energy than activation energy at higher temperatures. The same applies to enzyme-catalyzed reactions at lower temperature ranges. Still, the rate becomes optimum at around body temperature and then starts to fall off, as illustrated in the figure on the right. The enzymes have secondary, tertiary, and quaternary structures optimized to perform best at the body temperature of about 37 ^{o}C. Denaturation inactivates the enzymes. It is reversible if the temperature is slightly above body temperature, but enzymes are denatured beyond repair at a much higher temperature.



Copyright; Lanzi, GFDL, via Wikimedia Commons **pH**

The enzymes work best at the pH of the tissue or organ where they work. This is because the structure of enzymes is optimized for the pH at which they usually function. An increase or a decrease in pH from the optimum value disrupts the secondary, tertiary, and quaternary structures and causes a reduction in enzyme activity. The effect of a slight change in pH is reversible, but a significant difference in pH denatures the enzymes permanently.

The optimum pH for most enzymes is around the physiological pH of 7.4. Still, some enzymes have different optimum pH, depending on the pH in their natural environment, as illustrated in the figure on the left. For example, the optimum pH of the starch-splitting amylase is pH 7-7.5 in the mouth. Pepsin breaks down proteins at around pH 2 in the stomach. Trypsin breaks down proteins at pH 8 in the intestine.

Enzyme inhibition

Inhibitors are substances that make enzyme lose their catalytic activity. Inhibitors prevent the substrate from binding with the active site of the substrate. The inhibition may be reversible or irreversible. There are two subclasses of reversible inhibitors; competitive inhibitors and noncompetitive inhibitors.

Competitive inhibitor

The competitive inhibitor has a shape similar to the enzyme's natural substrate. So, they compete with the substrate for the active site but do not react, as illustrated in Figure 11.7.8. Since there is competition between the inhibitor and the substrate for the active site, increasing the concentration of the substrate wins by outnumbering the inhibitor in the completion, and the enzyme regains its activity.

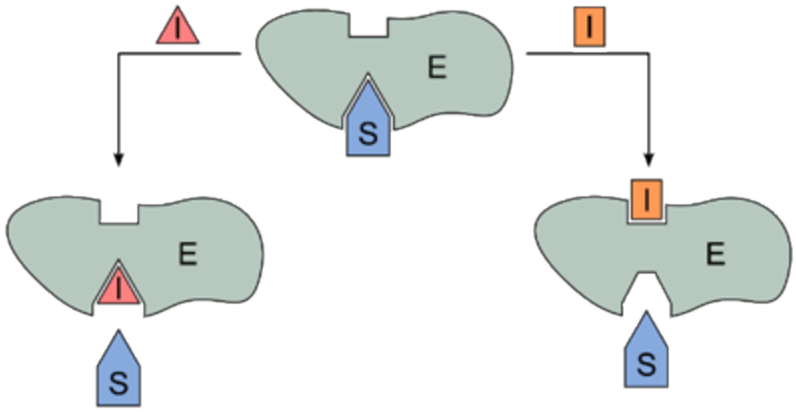


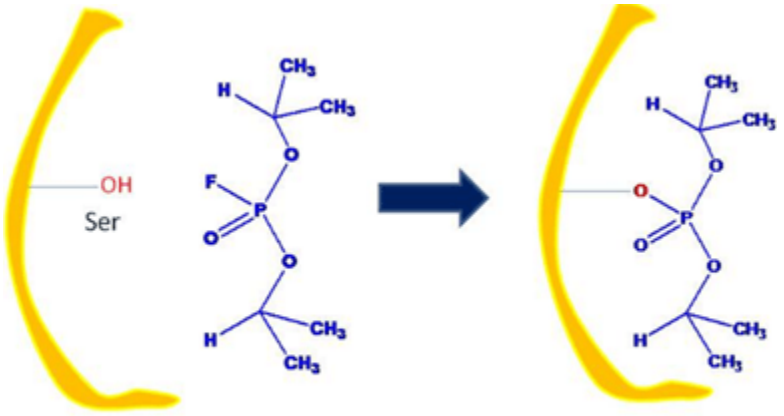
Figure 11.7.8: Illustration of an enzyme-substrate complex (top), competitive inhibitor inhibiting the enzyme activity by occupying the active site (bottom left), and a noncompetitive inhibitor binding to the enzyme outside the active area making the active site shape change such that the substrate can not fit in it properly (bottom right) (**E** enzyme, **I** inhibitor, **S** natural substrate). (Copyright; Sponk, Public domain, via Wikimedia Commons)

Noncompetitive inhibitor

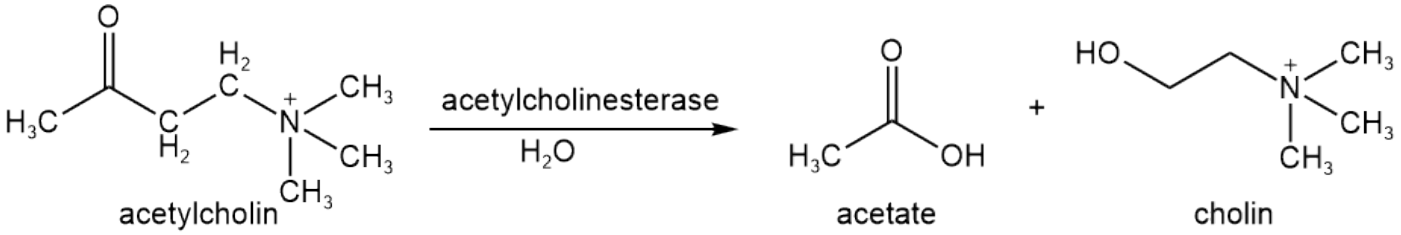
A noncompetitive inhibitor does not have a shape similar to the substrate and does not bind to the active site. It binds with the enzyme outside the active area but changes the folding patterns of the protein such that the active site can not acquire the proper shape. So, the substrate can not fit into the active site properly, as illustrated in Figure 11.7.8.

Examples of noncompetitive inhibitors are toxic metals, like $\mathrm{Pb^{2+}}$, $\mathrm{Hg^{2+}}$, and $\mathrm{Ag^{+}}$. Since the inhibitor does not compete with the substrate, increasing the substrate concentration does not recover the enzyme activity. However, some chemical agents can remove the inhibitor from the enzyme, and the catalytic activity can be recovered.

Irreversible inhibitor



Irreversible inhibitors bind with enzymes and destroy their catalytic activity permanently. They usually bind with enzymes by covalent bonds that are not easily broken. Irreversible inhibitors include antibiotics, insecticides, and never gases. For example, penicillin is an irreversible inhibitor of an enzyme needed to form cell walls in bacteria. The bacteria without a complete cell wall can not survive. It does not affect the cell membranes of humans. Similarly, a diisopropyl fluorophosphate (DIPF) which is an organophosphate insecticide, binds with the $-\mathrm{OH}$ of a serine residue in the enzyme acetylcholinesterase, as shown in the figure on the right. The enzyme-catalyzed reaction of acetylcholine, shown below, is needed for nerve impulse transmission. Inhibition of acetylcholinesterase blocks nerve impulses, causing paralysis.



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11.8: Enzyme Regulation- Allosteric Control and Feedback Inhibition

Learning Objectives

- Objective 1
- Objective 2

In the previous section you learned about the different types of enzyme inhibitors and how they can be used to *slow* or *stop* enzyme activity by binding to an enzyme or enzyme-substrate complex. All of these inhibitor types, except noncompetitive inhibitors, work by binding to enzyme active sites. Noncompetitive inhibitors, however, work by binding to an enzyme at a location other than the active site, an *allosteric site*. Inhibitors and other molecules, called activators, that bind to enzymes at allosteric sites are considered an important part of enzyme regulation called **allosteric control**. In this section, we will take a look at allosteric control and feedback control, two ways in which enzyme activity is regulated differently.

Allosteric Control

Allosteric enzymes have both a binding site, for substrate binding and catalysis, and an allosteric site, for regulation of enzyme activity. When a regulator molecule binds to the allosteric site of an enzyme, usually by noncovalent interactions, a conformational change occurs in the enzyme active site, which affects substrate binding and reaction rates. Allosteric regulation of enzyme activity can be either positive, increasing reaction rates, or negative, decreasing reaction rates.

When an enzyme binds a negative regulator (or inhibitor), it will undergo a change in the active site in a way that *prevents* substrate binding, thereby lowering the reaction rate. As illustrated in the left-hand panel in Figure 11.8.1, the active site changes (becomes smaller in this case) and the substrate can no longer bind. Positive regulators (activators) bind to allosteric sites and cause conformational changes that open up an active site to *promote* substrate binding, allowing catalysis or increasing the reaction rate. The right panel of Figure 11.8.1 shows an enzyme that will only bind substrate when the active site is formed after the allosteric activator binds.

Some enzymes will have more than one allosteric site that can interact with one another, which allows for highly-controlled or finely-tuned reaction rates.

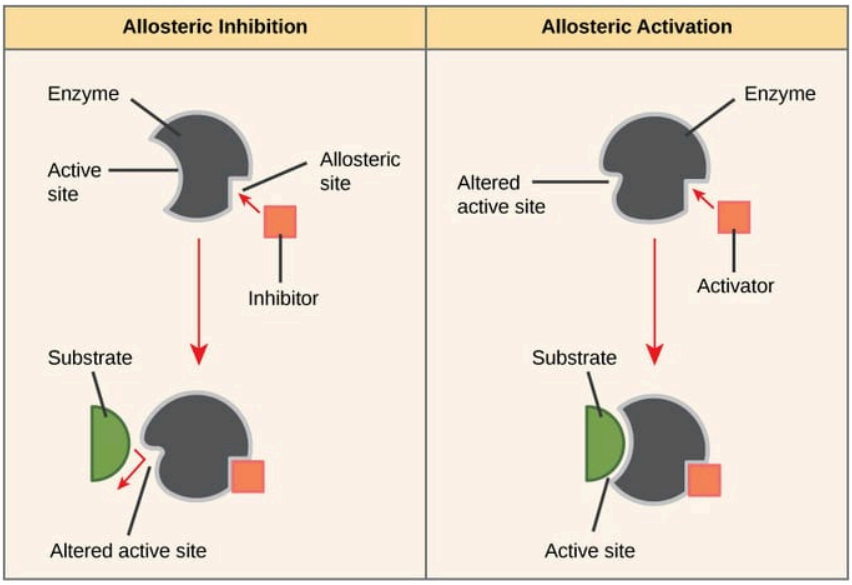


Figure 11.8.1: **Allosteric inhibitors and activators**: Allosteric inhibitors modify the active site of the enzyme so that substrate binding is reduced or prevented. In contrast, allosteric activators modify the active site of the enzyme so that the affinity for the substrate increases.

Feedback Control

Many biological processes involve the sequential action of multiple enzymes, a reaction pathway, in which the product of one reaction is the substrate for the next enzyme and so on until the final product is formed. Positive or negative regulation of these pathways often occurs by **feedback control**, where a product from one of the steps in the path *feedback* to an earlier step in the process to increase or decrease production. It may help to visualize a factory assembly line with each person responsible for one step (catalytic reaction) in making a perfect box of 12 donuts. If the last person in the line, who is responsible for putting 12 donuts in the box, falls behind, donuts will start to pile up. In order to not waste donuts or have less than full boxes at the end, it would be beneficial to signal to the other people to slow down or take a break. The process is similar in biochemical pathways: if too much product is being formed, the pathway needs to be turned off so energy and resources are not wasted.

Consider the pathway shown below in which substrate A is converted to product D through three enzymes and two intermediate products (B and C):

$$A \xrightarrow{Enzyme\ 1} B \xrightarrow{Enzyme\ 2} C \xrightarrow{Enzyme\ 3} D$$

If there is a lot of product D formed, there would be enough to bind to Enzyme 1, which would inhibit formation of products B, and subsequently product C, and D. This type of *feedback control* is useful to prevent waste of substrate A and any energy that is needed for the activity of Enzymes 1-3. As you will see in later chapters, there are many different types of feedback control that can both negatively and positively regulate pathways. Typically, feedback control occurs at points in pathways where it would be energetically unfavorable to proceede if the final product is not needed.

Feedback inhibition is used to regulate the synthesis of many amino acids. For example, bacteria synthesize isoleucine from threonine in a series of five enzyme-catalyzed steps. As the concentration of isoleucine increases, some of it binds as a noncompetitive inhibitor to the first enzyme of the series (threonine deaminase), thus bringing about a decrease in the amount of isoleucine being formed (Figure 11.8.2).

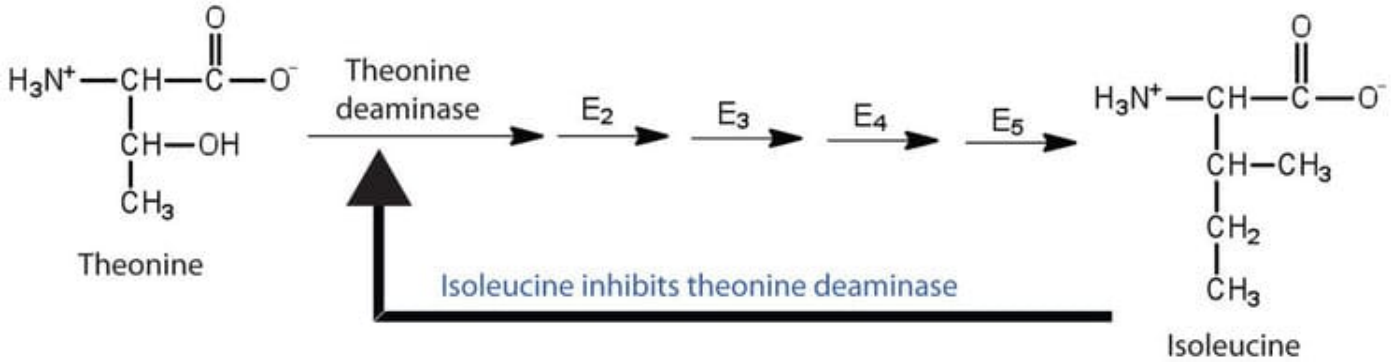


Figure 11.8.2: Feedback Inhibition of Threonine Deaminase by Isoleucine. Threonine deaminase is the first enzyme in the conversion of threonine to isoleucine. Isoleucine inhibits threonine deaminase through feedback inhibition.

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11.9: Amino Acids and Proteins (Exercises)

These are homework exercises to accompany Chapter 13 of the University of Kentucky's LibreText for CHE 103 - Chemistry for Allied Health.

Questions

13.1: Amino Acids

(click here for solutions)

Q13.1.1

Read the material at http://hyperphysics.phy-astr.gsu.edu/hbase/organic/essam.html and answer the following questions:

a. What are essential amino acids?
b. What are nonessential amino acids?
c. What happens if you are deficient in an amino acid?

Q13.1.2

Draw the functional groups present in all amino acids.

Q13.1.3

Complete the following for threonine, lysine, and tyrosine.

a. Draw the amino acid.
b. Circle the side chain.
c. Identify whether it is polar, nonpolar, acidic, or basic.
d. At what pH will it exist as a zwitterion?
e. What is the range of pH values when it will be positively charged?
f. What is the range of pH values when it will be negatively charged?

13.2: Peptides

(click here for solutions)

Q13.2.1

Draw the two dipeptides formed from each pair of amino acids.

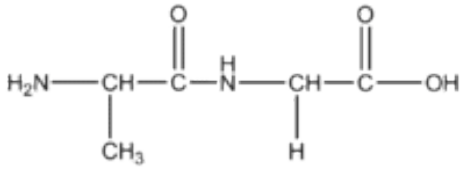
a. tyrosine and lysine
b. threonine and gluatmine
c. alanine and histidine

Q13.2.2

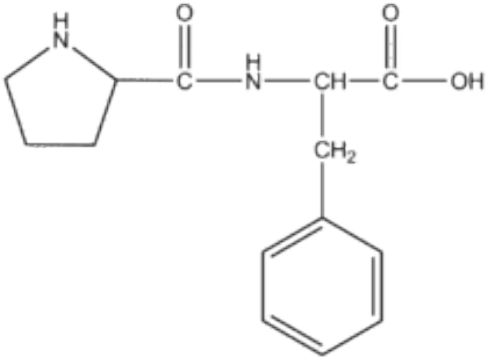
Draw and give the full names of the amino acids in the following dipeptides.

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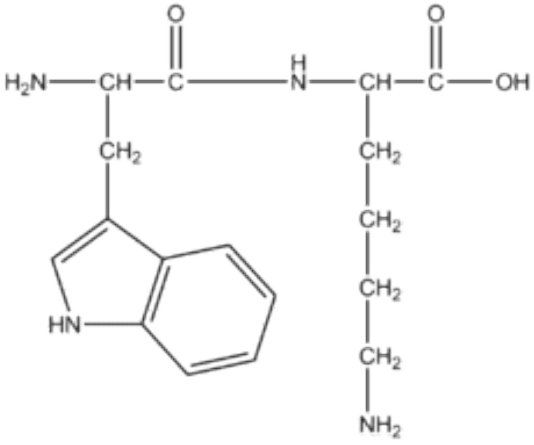
a.



b.



c.



Q13.2.3

List of all of the possible polypeptides that can be formed from threonine, alanine, and phenylalanine (use three character abbreviations for each amino acid).

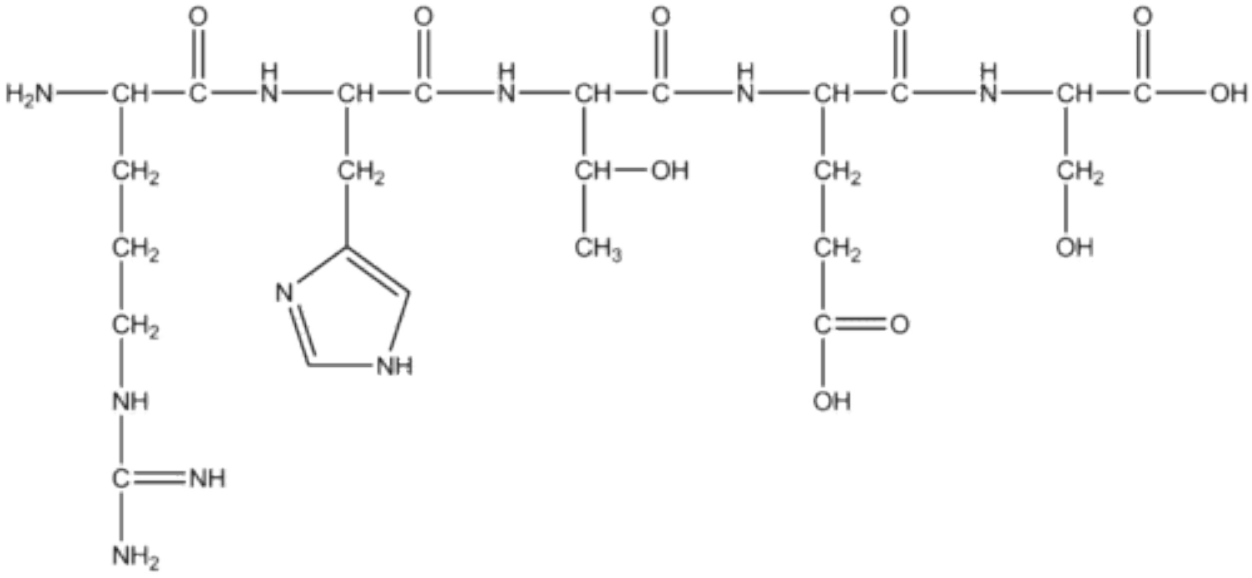
Q13.2.4

Draw the following polypeptides.

a. Ser-Tyr-Gln
b. Lys-Met-Gly

Q13.2.5

Identify each of the amino acids in the polypeptide and then name it using the three character abbreviations.



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13.3: Protein Structure

(click here for solutions)

Q13.3.1

Describe the four levels of protein structure.

Q13.3.2

What levels of structure involve hydrogen bonding?

Q13.3.3

What types of structure is the result of interactions between amino acids that are far apart in the primary structure?

Q13.3.4

What types of interactions hold the secondary structure together?

Q13.3.5

What types of interactions hold the tertiary structure together?

Q13.3.6

What levels of structure are affected by denaturation?

Q13.3.7

A protein has one subunit. Would it have a quaternary structure?

Answers

13.1: Amino Acids

Q13.1.1

a. Essential amino acids are those you get from your diet.
b. Nonessential amino acids are produced in the body.
c. Illness and/or degradation of body's proteins.

Q13.1.2

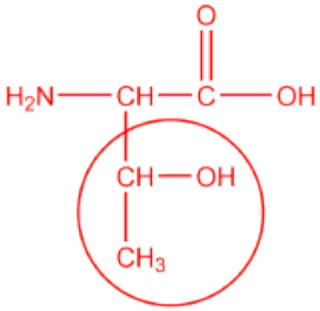


amine and carboxylic acid

Q13.1.3

Complete the following for threonine, lysine, and tyrosine.

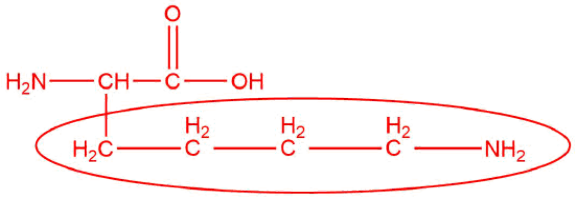
threonine
a.



b.
c. polar
d. 5.60
e. < 5.60
f. > 5.60

lysine

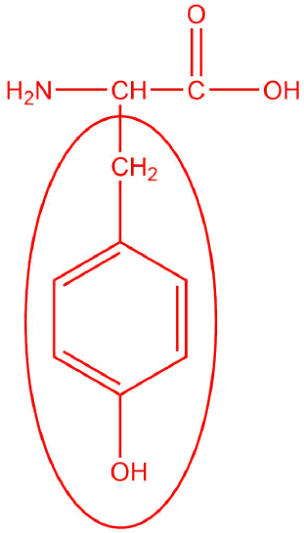
a.



b.
c. basic
d. 9.47
e. < 9.47
f. > 9.47

tyrosine

a.



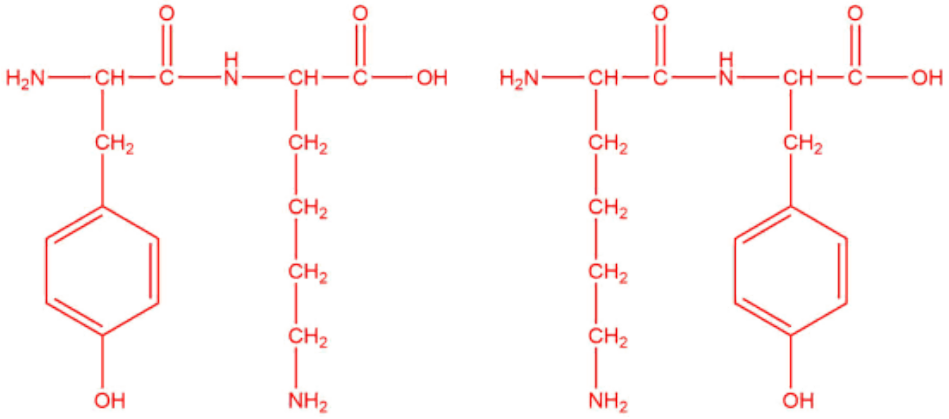
b.
c. polar
d. 5.63
e. < 5.63
f. > 5.63

13.2: Peptides

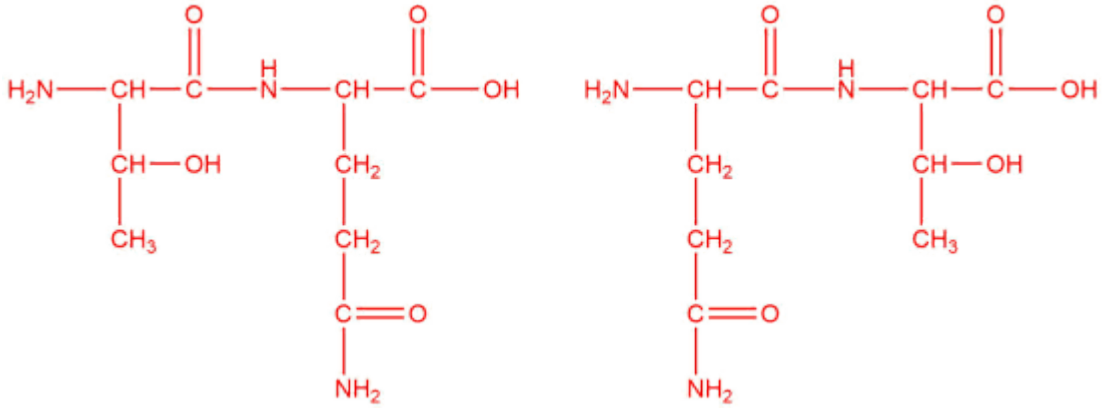
Q13.2.1

Draw the two dipeptides formed from each pair of amino acids.

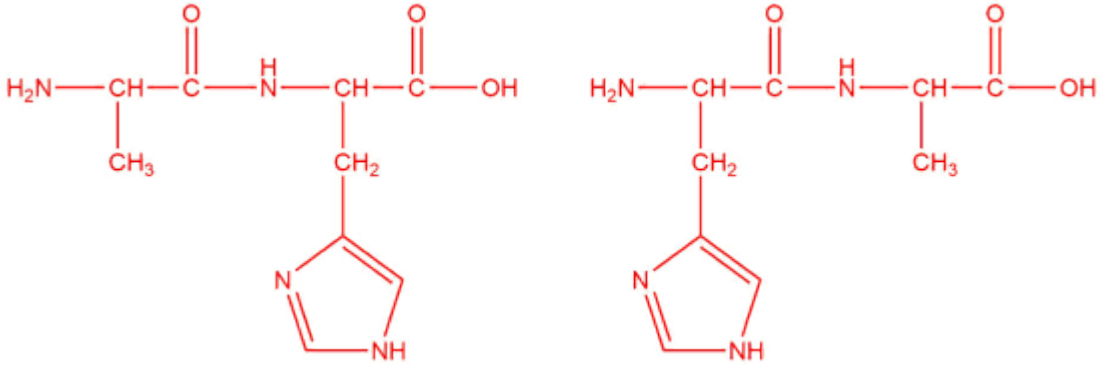
a.



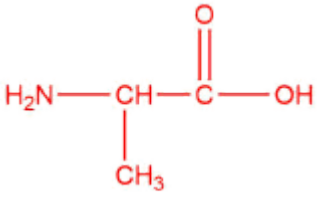
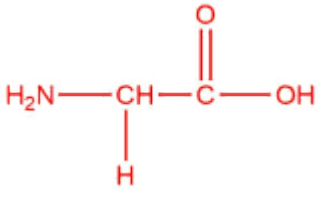
b.

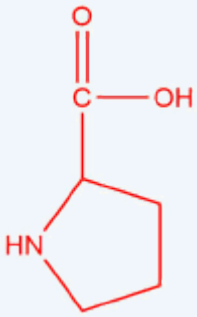
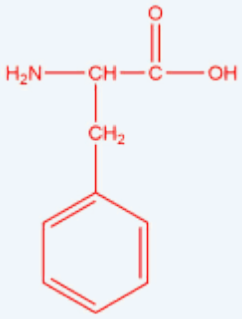
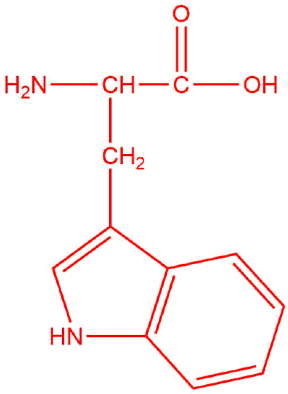
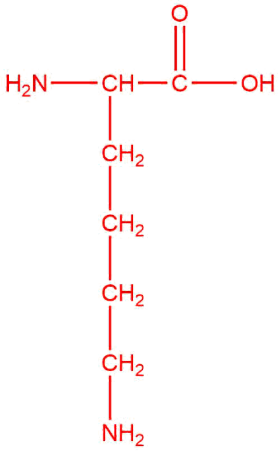


c.



Q13.2.2

a.	 alanine	 glycine

b.	 proline	 phenylalanine
c.	 tryptophan	 lysine

Q13.2.3

Thr-Ala-Phe

Thr-Phe-Ala

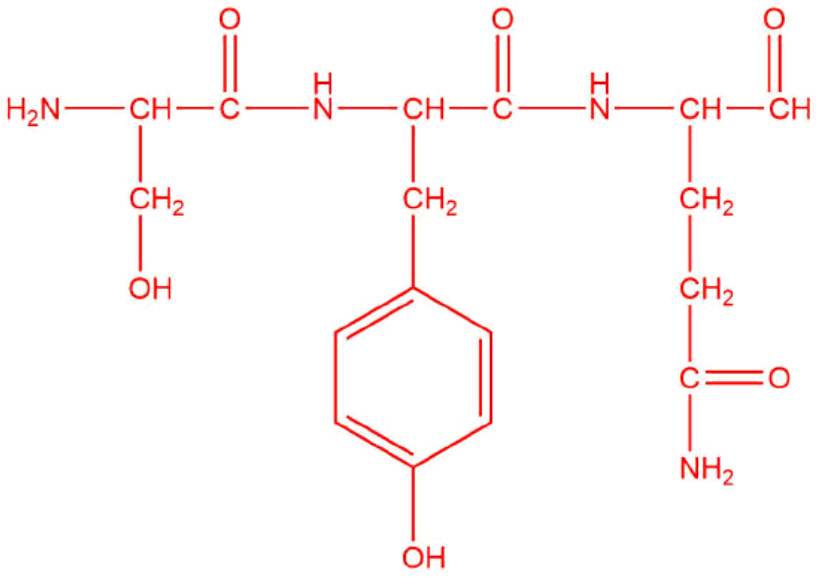
Ala-Thr-Phe

Ala-Phe-Thr

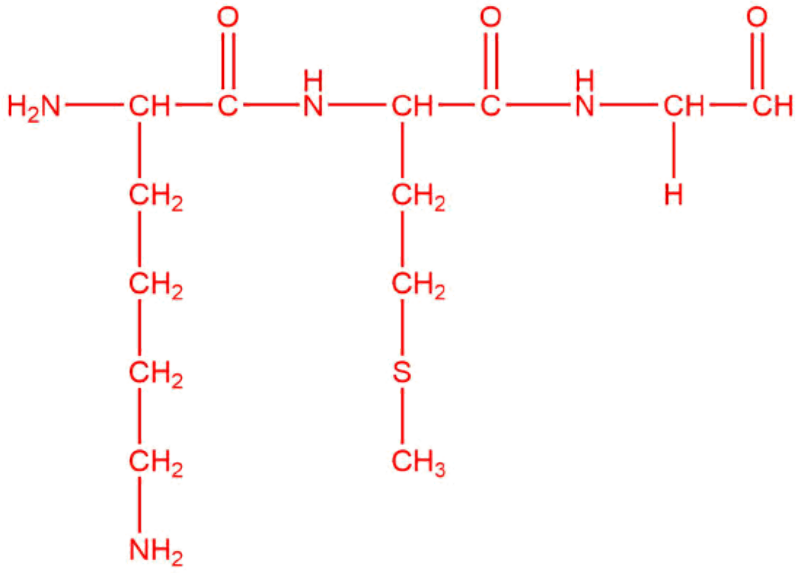
Phe-Ala-Thr

Phe-Thr-Ala

Q13.2.4

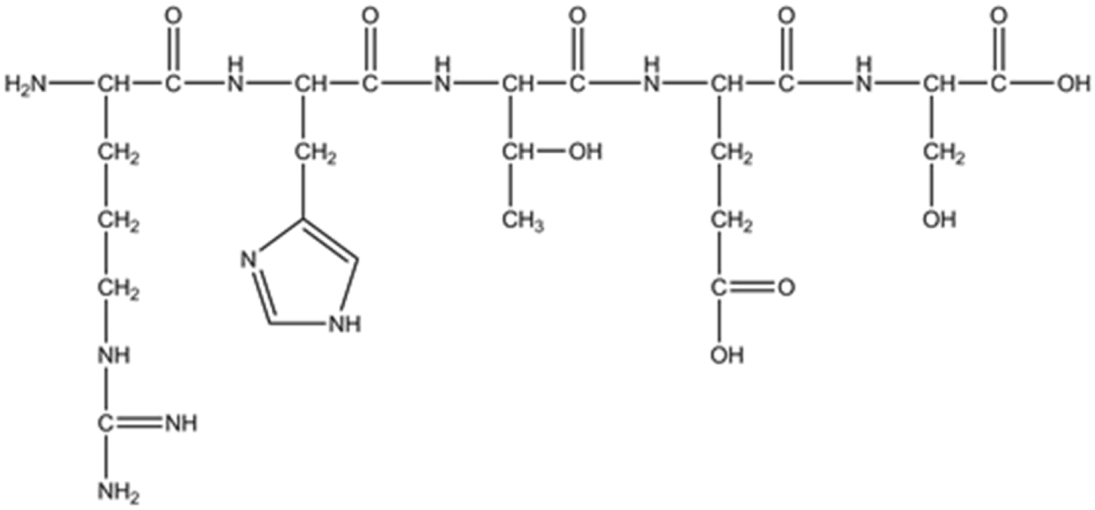


a.



b.

Q13.2.5



Arg-His-Thr-Glu-Ser

13.3: Protein Structure

Q13.3.1

Primary - sequence of amino acids

Secondary - alpha helix and Beta-pleated sheets held together by hydrogen bonds

Tertiary - third level of structure of protein often forming globular or fibrous structure, held together by variety of attractive forces

Quaternary - complex of multiple proteins held together to function as one, held together by variety of attractive forces (same as tertiary)

Q13.3.2

secondary, tertiary, and quaternary structures

Q13.3.3

tertiary structures

Q13.3.4

hydrogen bonds

Q13.3.5

London dispersion forces, hydrogen bonds, dipole-dipole forces, ion-dipole interactions, salt bridges, and disulfide bonds

Q13.3.6

secondary, tertiary, and quaternary

Q13.3.7

No, a quaternary structure must have multiple subunits.

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12: NUCLEIC ACIDS AND PROTEIN SYNTHESIS

12.1: Nucleotides -the building blocks of nucleic acids
12.2: Primary structure of deoxyribonucleic acid (DNA)
12.3: Secondary structure and replication of DNA
12.4: Ribonucleic acid (RNA) and transcription
12.5: Translation-Protein Synthesis
12.6: Mutations and Genetic Diseases

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12.1: Nucleotides -the building blocks of nucleic acids

Learning Objectives

- Understand the function of nucleic acids.
- Learn the structures and names of nucleotides -the building blocks of nucleic acids, and their constituents, including ribose, deoxyribose, nitrogen bases, and phosphate groups.

Nucleic acids are biopolymers that carry the codes for synthesizing proteins and pass them on from generation to generation, i.e., they are genetic materials. In other words, nucleic acids are the instruction manual for biochemical reactions in living things.

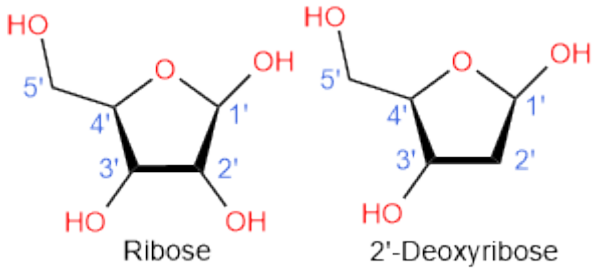
Nucleotides are the building blocks, i.e., the repeat units or monomers of nucleic acids.

Nucleotides are composed of three sub-units:

1. a 5-carbon carbohydrate,
2. a base that is an aromatic compound containing nitrogen, and
3. an anion of phosphoric acid, i.e., phosphate (PO_4^{3-}).

5-Carbon carbohydrate

Two 5-carbon carbohydrates, i.e., ribose and deoxyribose, are found in nucleic acids, as shown in the figure below. Both are D-sugars in five-membered cyclic form with hydroxyl ($-OH$) group at anomeric (C#1') pointing towards O in the ring, i.e., in a β configuration. The number labels have prime symbols, i.e., 1', 2', 3', etc., to distinguish them from regular numbers 1, 2, 3, etc., used for the nitrogen bases of the nucleic acids. The only difference between ribose and deoxyribose is that hydroxyl ($-OH$) group at C#2' is missing in the latter, which gives the deoxy- prefix to its name.

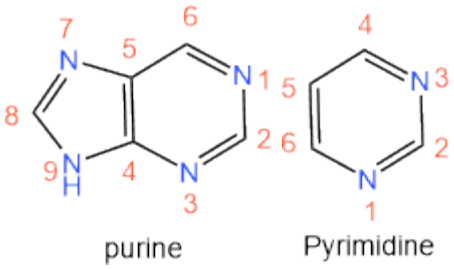


Types of nucleic acids

There are two types of nucleic acids: ribose in its nucleotides, called **ribonucleic acid** (**RNA**), and deoxyribose in its nucleotides, called **deoxyribonucleic acid** (**DNA**).

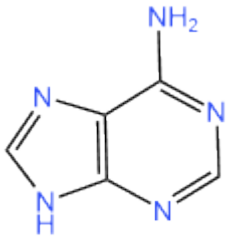
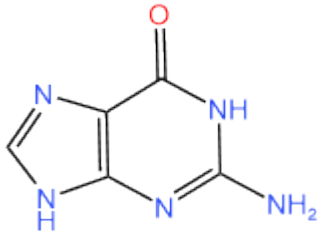
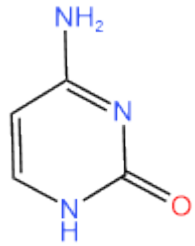
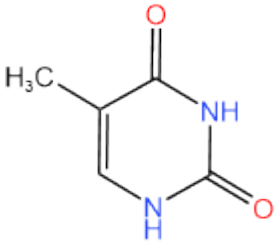
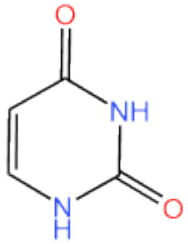
Nitrogen bases

Nitrogen bases in nucleic acids are derivatives of two aromatic compounds, purine and pyrimidine, shown below.



Cyclic compounds that contain atoms other than $\mathrm{C's}$ in the cycle are called heterocyclic compounds. Purine and pyrimidine are heterocyclic aromatic compounds because they contain $\mathrm{N's}$ in the cycles. Purine is bicyclic, containing a six-membered ring with two $\mathrm{N's}$ fused with a five-membered ring with two $\mathrm{N's}$. Pyrimidine is a six-membered cycle with two $\mathrm{N's}$. Both purine and pyrimidine are planer molecules like benzene.

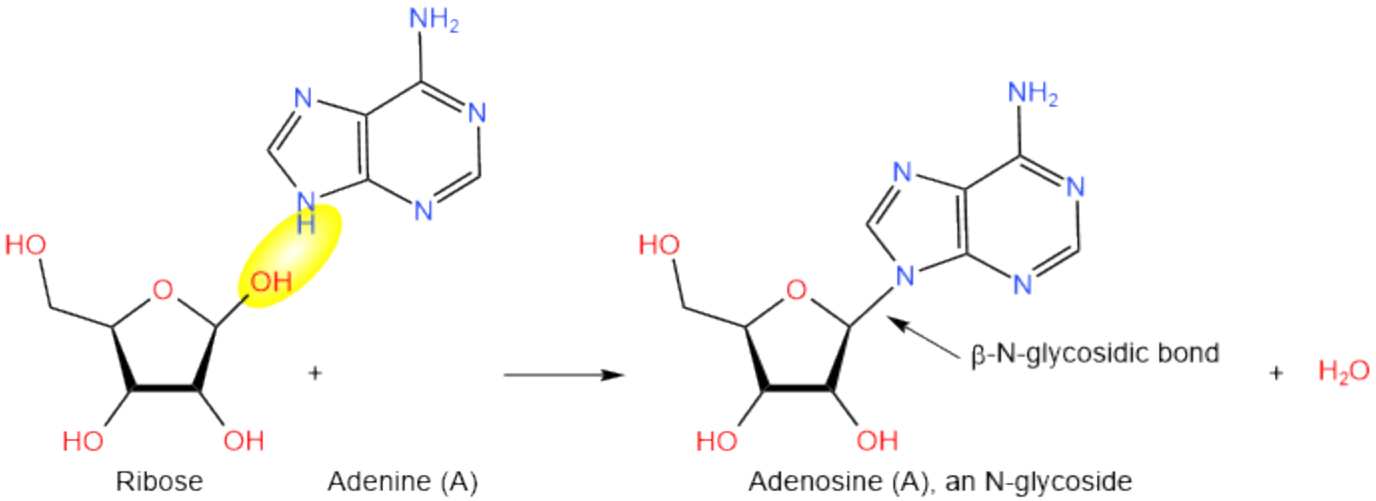
There are five nitrogen bases found in nucleic acids: two are purines, i.e., adenine (A) and guanine (G), and three are pyrimidines, i.e., cytosine (C), thymine (T), and uracil (U), as shown below. To remember what are pyrimidines, remember "cut pyramid" where 'c' is cytosine, 'u' for uracil, 't' for thymine, and 'pyramid' for pyrimidines

Purines		Pyrimidines		
 adenine	 guanine	 cytosine	 thymine	 uracil

DNA contains four nitrogen bases, i.e., adenine, guanine, cytosine, and thymine. RNA also has four nitrogen bases, i.e., adenine, guanine, cytosine, and uracil. Note that the first three, i.e., adenine, guanine, and cytosine, are common in DNA and RNA, but the fourth, i.e., ti.e.ine in DNA, is replaced with uracil in RNA.

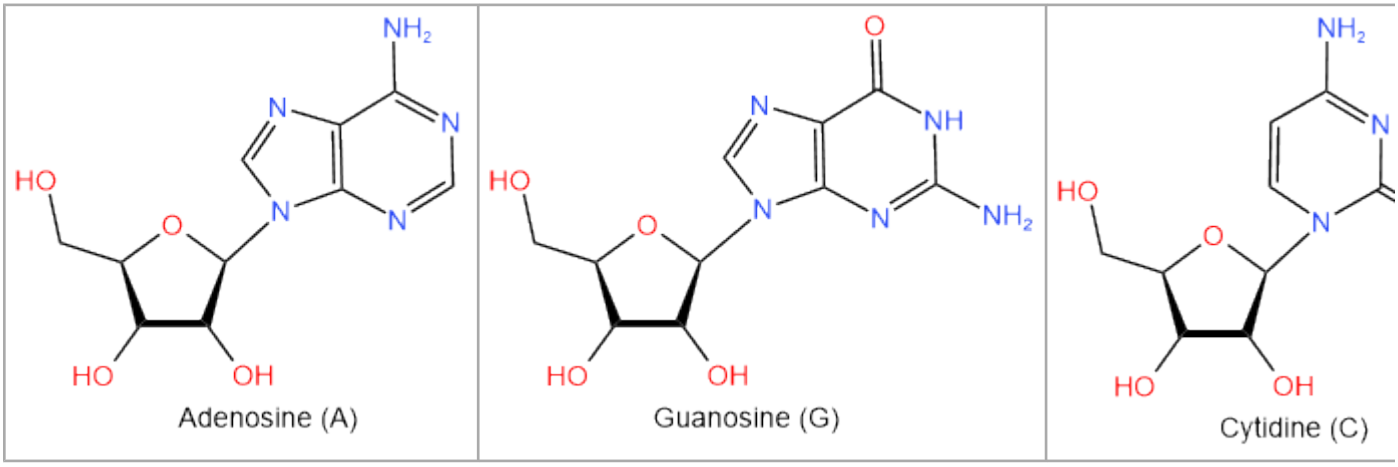
Nucleosides

When a monomer sugar like ribose or deoxyribose reacts with an amine, the $-\mathrm{OH}$ group at $\mathrm{C\#1'}$ is replaced with a N of the amine. The product is called N-glycoside, and the $\mathrm{C-N}$ bond in the N-glycoside is called an N-glycosidic bond, as shown in the following example.

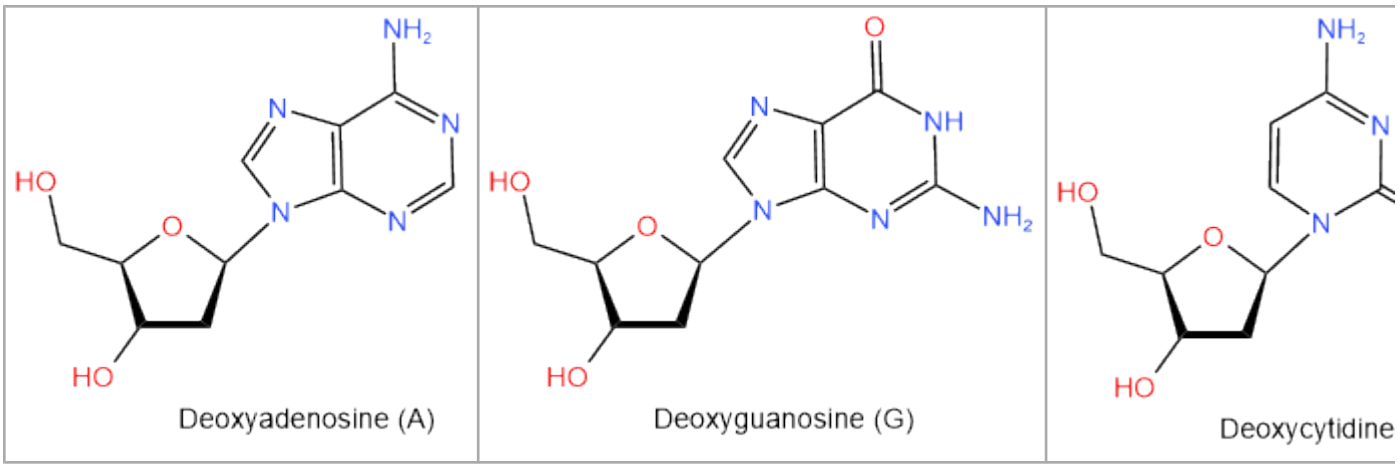


Purines connect through N#9 and pyrimidine through N#1 with anomeric carbon (C#1') of ribose or deoxyribose to form the N-glycoside.

The N-glycosides are named by using the name of purine but ending with -osine e.g., adenine becomes adenosine and guanine becomes gunosine, or by using the name of pyrimidine ending with -idine, e.g., cytosine becomes cytidine and uracil become uridine. One letter abbreviation of the nitrogen bases remains the same for the corresponding nucleoside, e.g., adenine (A) and adenosine (A). The four nucleosides found in RNA are shown below with their names and one-letter abbreviations.

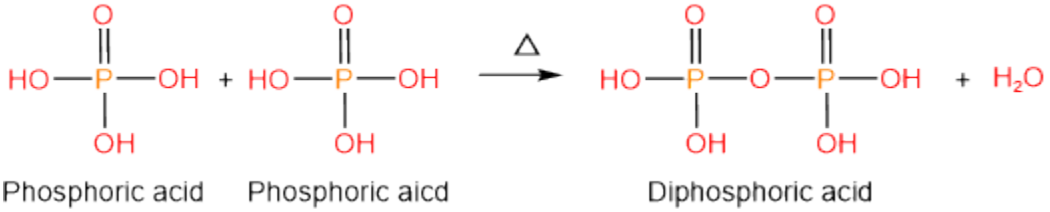


In DNA there is deoxyribose in place of ribose. So the names of nucleosides found in DNA begin with the deoxy- prefix. The four nucleosides found in DNA are shown below with their names and one-letter abbreviations.

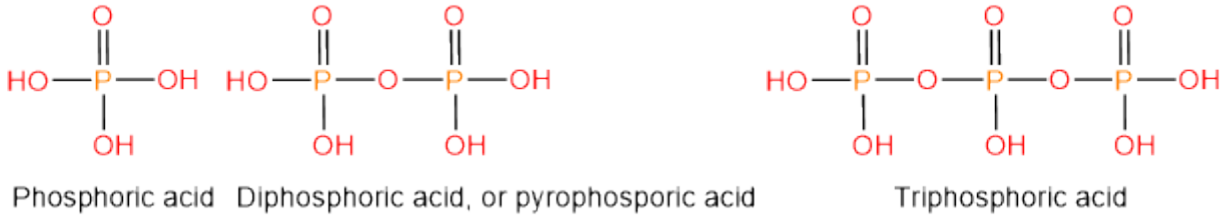


Phosphate

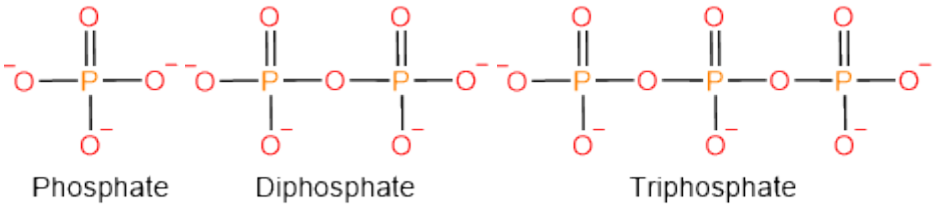
Phosphoric acid (H_3PO_4) is an oxyacid with three acidic protons, i.e., it is triprotic acid. Just as two carboxylic acids condense with each other and form a carboxylic acid anhydride with the elimination of water molecule, two phosphoric acids condense and form diphosphoric acid, also called pyrophosphoric acid, with the elimination of water.



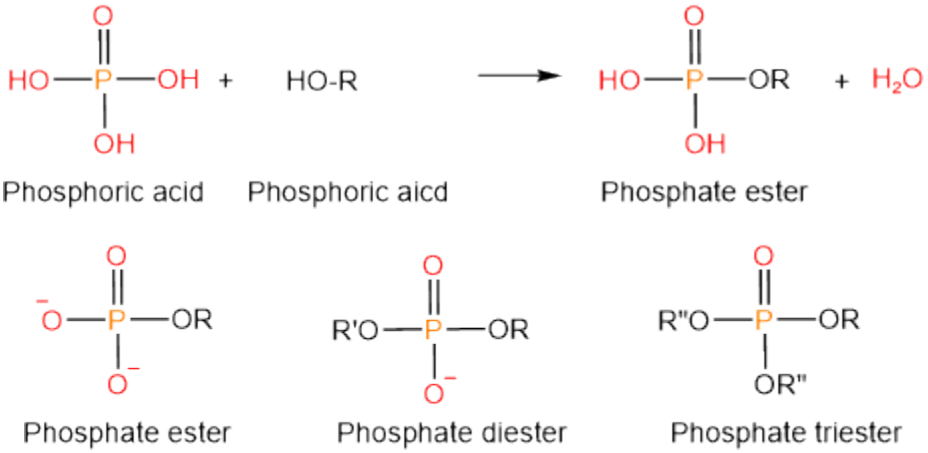
Similarly, three phosphoric acids can condense to form triphosphoric acid. Phosphoric acid, diphosphoric acid, and triphosphoric acid are shown below.



Under physiological conditions at pH ~7.4, the phosphoric acids lose proton and exist as phosphate anions, as shown below.

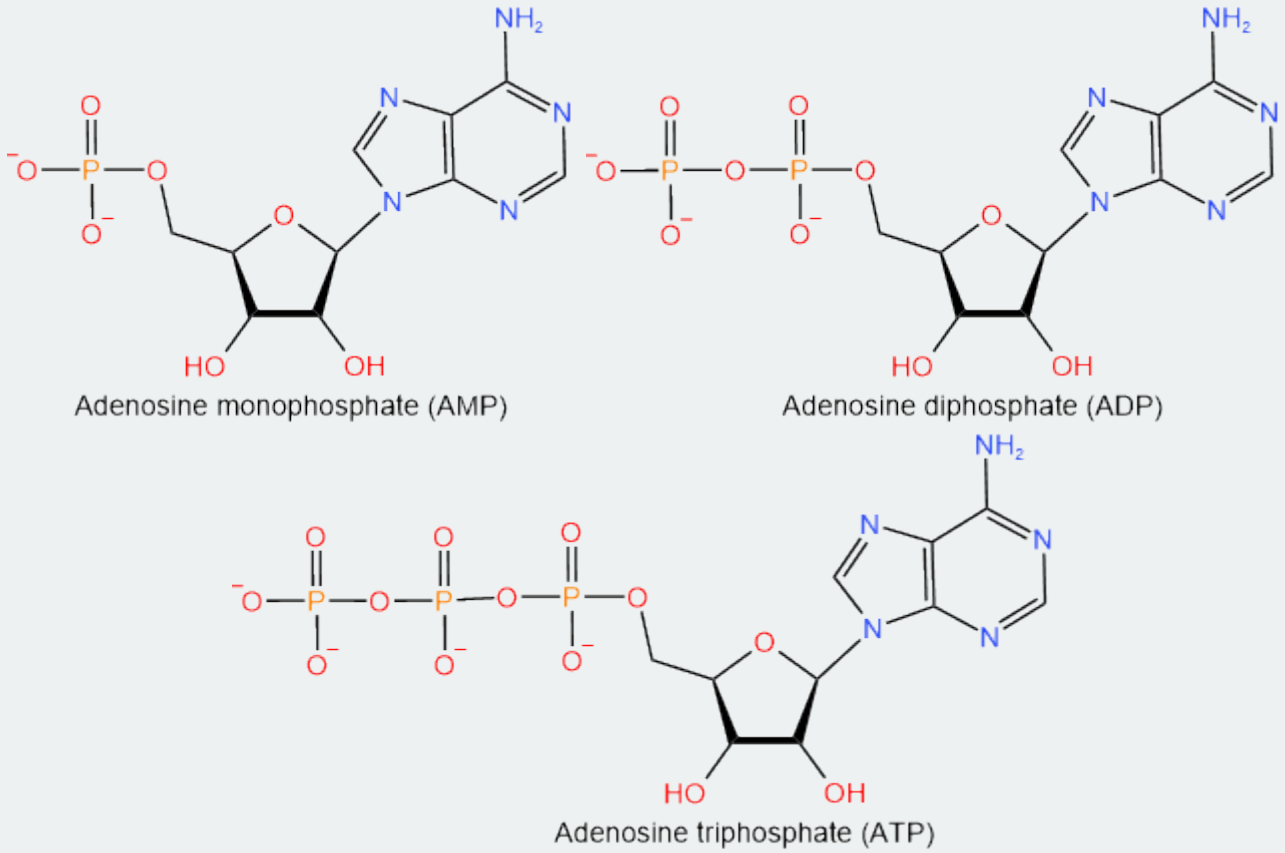


Phosphoric acids also condense with alcohols ($R-OH$) and form mono-, di-, or triesters, as illustrated below.



Nucleotide

Phosphate esters of nucleosides are called nucleotides. The nucleotides found in nucleic acids are formed when $-\mathrm{OH}$ group at C#5' of ribose or deoxyribose makes ester with a monophosphate, diphosphate, or triphosphate, as shown below.

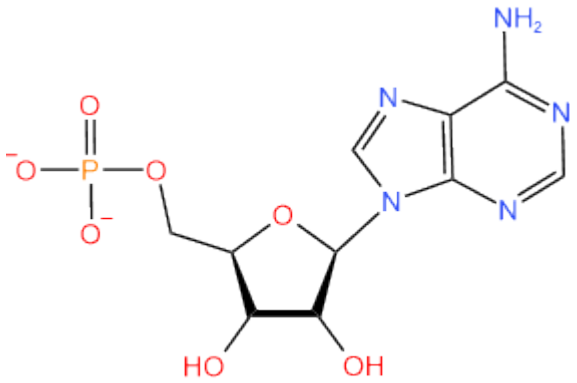


The names of the nucleotides are derived by using the name of the corresponding nucleoside with monophosphate, diphosphate, or triphosphate added at the end. Abbreviation of the nucleotide starts with the one-letter abbreviation of the nitrogen base followed by MP, DP, or TP depending on whether the phosphate group is monophosphate, diphosphate, or triphosphate, as shown in the example structures above.

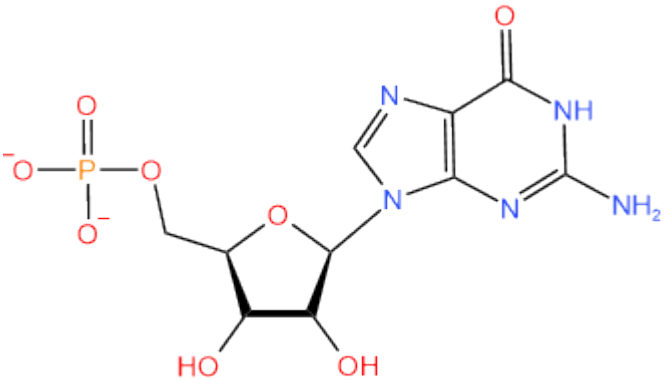
The nucleotides like ADP and ATP are high-energy molecules used as energy currency in biochemical systems. For example, when

ATP converts to ADP by releasing a phosphate, energy is released to do work or synthesize other compounds. Synthesis of nucleic acids begins with triphosphate esters that convert into monophosphate esters when incorporated in the nucleic acid polymer. The energy released in converting triphosphate to monophosphate drives the reaction forward.

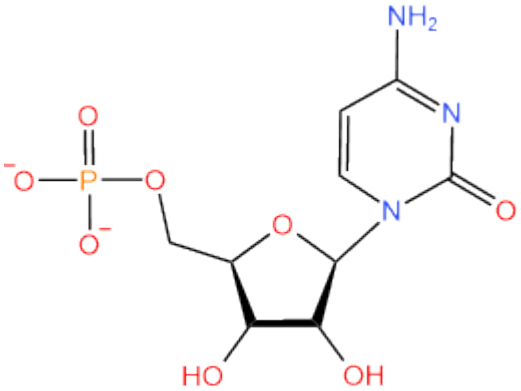
The four nucleotides found in RNA are shown below with their names and abbreviations.



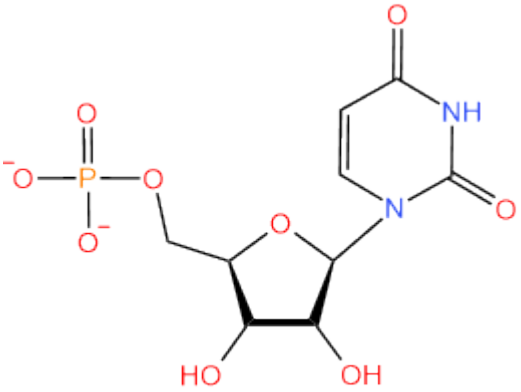
Adenosine monophosphate (AMP) ,



Guanosine monophosphate (GMP) ,

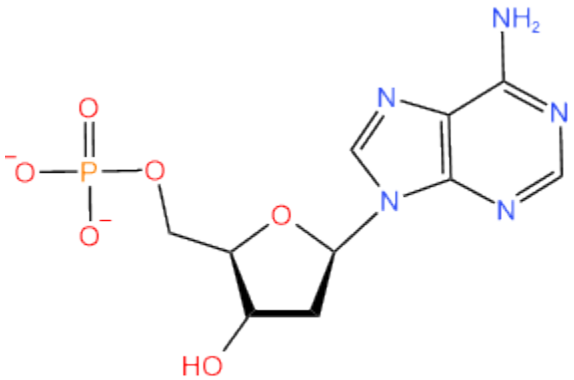


Cytidine monophosphate (CMP) , and

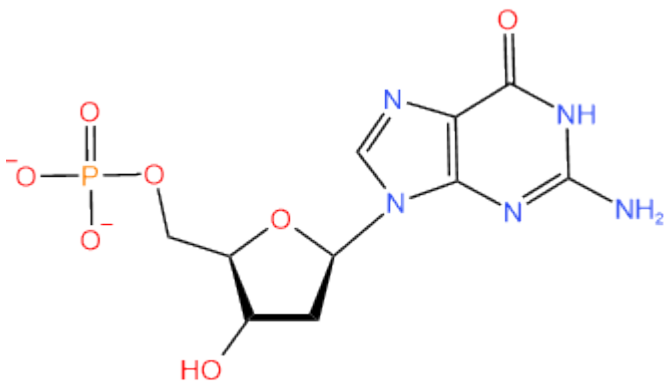


Uridine monophosphate (UMP) ,

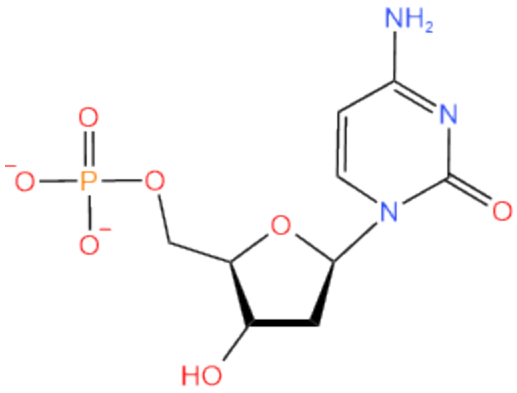
The nucleotides found in DNA are named similarly to those of RNA: start with the name of the corresponding nucleoside and end with monophosphate, diphosphate, or triphosphate. Remember that the names of DNA nucleosides begin with deoxy. The abbreviations of the nucleotides found in DNA start with a small alphabet *d* representing the deoxy- prefix of the nucleotides. The four nucleotides found in DNA are shown below with their names and abbreviations.



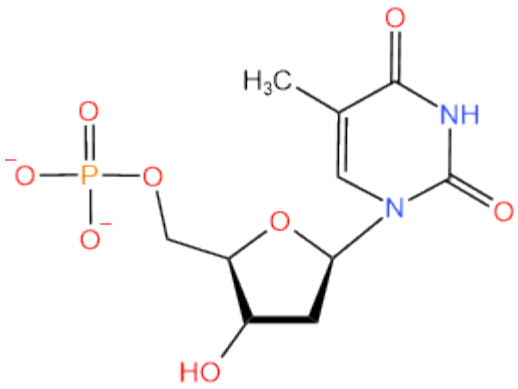
Deoxyadenosine monophosphate (dAMP) ,



Deoxyguanosine monophosphate (dGMP) ,



Deoxycytidine monophosphate (dCMP),



Doxythymidine monophosphate (dTMP)

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12.2: Primary structure of deoxyribonucleic acid (DNA)

Learning Objectives

- Define nucleic acids and understand the mechanism of nucleic acid synthesis and the related terminologies.
- Define and be able to write the primary structure of nucleic acids.

Nucleic acid

Nucleic acids are long unbranched strands (polymers) of nucleotide subunits (monomers) that primarily store and express genomic information in living things.

Nucleic acids are long unbranched strands (polymers) of nucleotide subunits (monomers). A nucleotide triphosphate is the starting material for nucleic acid synthesis. The synthesis of DNA is controlled by an enzyme called DNA polymerase. A nucleoside triphosphate containing adenine (A), guanine (G), cytosine (C), or thymine (T) uses $-\mathrm{OH}$ group at 3' position of deoxyribose to attack α-phosphorous of triphosphate group at 5' position of the next nucleoside in an SN_2 mechanism. It results in a **phosphodiester linkage** between the 3' position of the first and 5' position of the second nucleotide, and a pyrophosphate (diphosphate) is eliminated as shown in Figure 12.2.1. The pyrophosphate breaks down into two phosphate units which make the reaction irreversible.

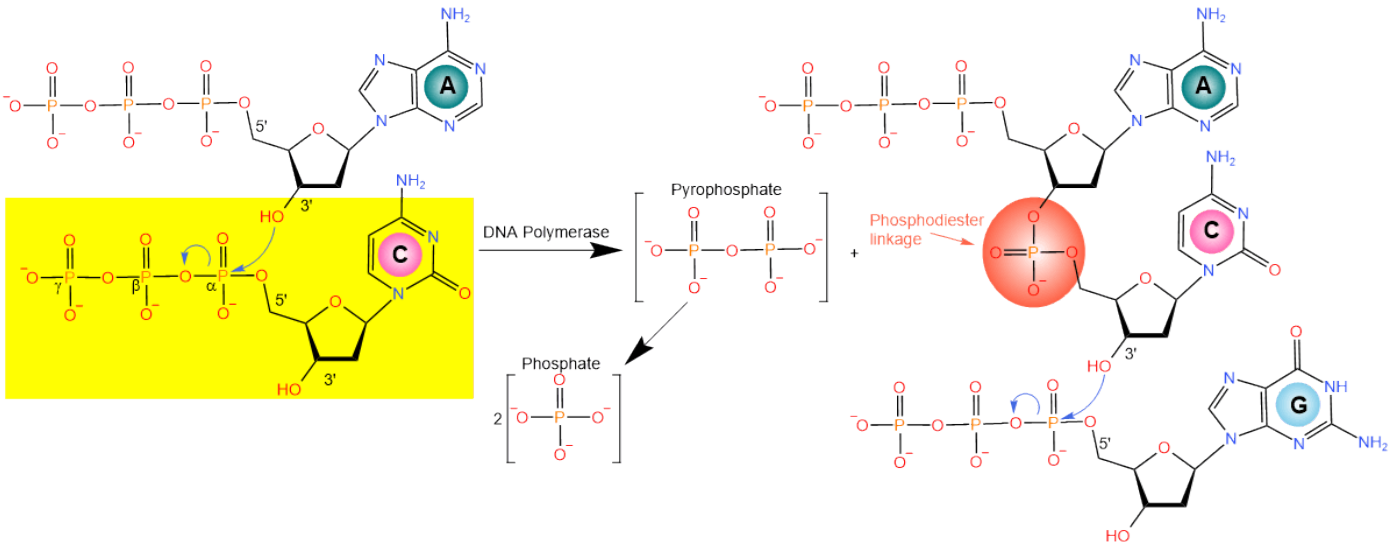


Figure 12.2.1: Chemical reaction mechanism for forming a phosphodiester linkage between nucleotides during DNA synthesis. (Copyright; Public domain)

Next, nucleotide triphosphate repeats the process and links at the 3' end of the growing strand; the cyclic process keeps repeating this way, as shown in Figure 12.2.1. The first nucleotide has unlinked triphosphate at the 5' position, called the **free 5' end**. The last nucleotide has an unlinked $-\mathrm{OH}$ group at the 3' position, and it is called the **free 3' end**. DNA synthesis occurs from 5' to 3' as shown in Figure 12.2.2. Deoxyribose and phosphodiester linkage alternate in the polymer's backbone, and the nitrogen bases hang on the side (1' position) of the deoxyribose units. Two nucleotides linked by a phosphodiester linkage are called a **dinucleotide**, 3 to 10 linked nucleotides are called an **oligonucleotide**, and many nucleotides linked are called a **polynucleotide**.

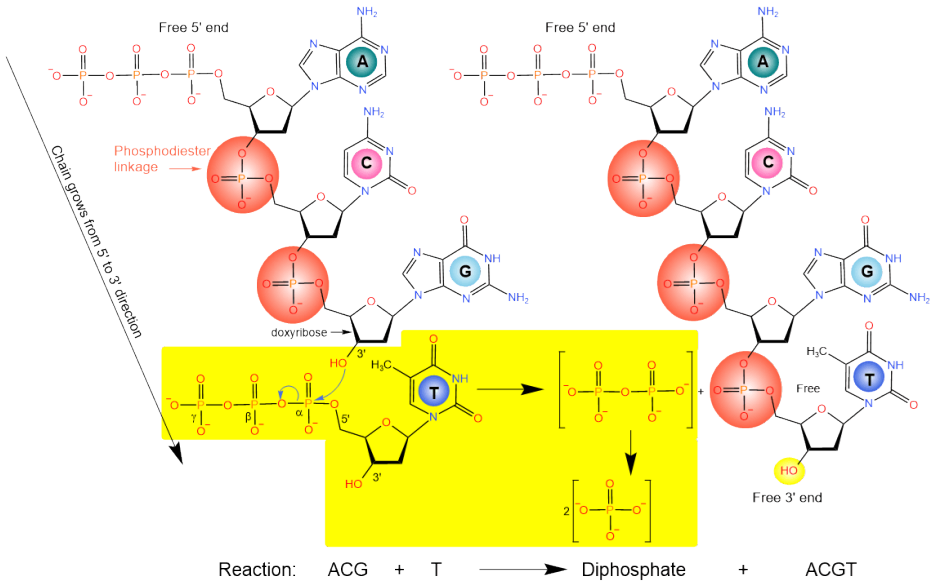


Figure 12.2.2: Synthesis of DNA illustrated. (Copyright; Public domain)

The synthesis of RNA takes place the same way as that of DNA, except for the following differences:

1. the enzyme carrying out the synthesis is RNA polymerase,
2. the sugar (5-carbon carbohydrate) is ribose, and
3. uracil (U) is used in place of thymine (T).

Primary structure of nucleic acid

The sequence of nucleotides in the nucleic acid is called the primary structure of nucleic acid.

The primary structure is written from the 5' to 3' direction, where the 5'-end is on the left end, and the one-letter abbreviation of the nitrogen base represents the nucleotides. For example, the primary structure of the oligonucleotide product shown in Figure 12.2.2 is ACGT. It is the sequence of nucleotides that carries the genetic information.

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12.3: Secondary structure and replication of DNA

Learning Objectives

- Understand the double helix model and the replication process of DNA.

Secondary structure of DNA

Double helix model of DNA

It was observed from experimental data that although the composition of DNA varies from specie to specie, the amount of adenine (A) is always equal to the amount of thymine (T), and the amount of guanine (G) is always equal to the amount of cytosine (C). In 1953, Watson and Crick proposed a model of DNA with the help of Franklin's X-ray analysis. The Model, illustrated in Figure 12.3.1, is:

1. a DNA molecule is made up of two strands wound around each other like a spiral stair ladder,
2. the two strands run antiparallel, i.e., one from a 5' to 3' and the other from a 3' to 5' direction,
3. each strand has a backbone of alternating deoxyribose and phosphate, groups like the rails of the stair ladder, and
4. the two strands are connected at each nucleotide through hydrogen bonds between nitrogen bases: adenine associated with thymine of the second strand, and guanine connected with cytosine of the second strand, or vice versa, like a closed zip.

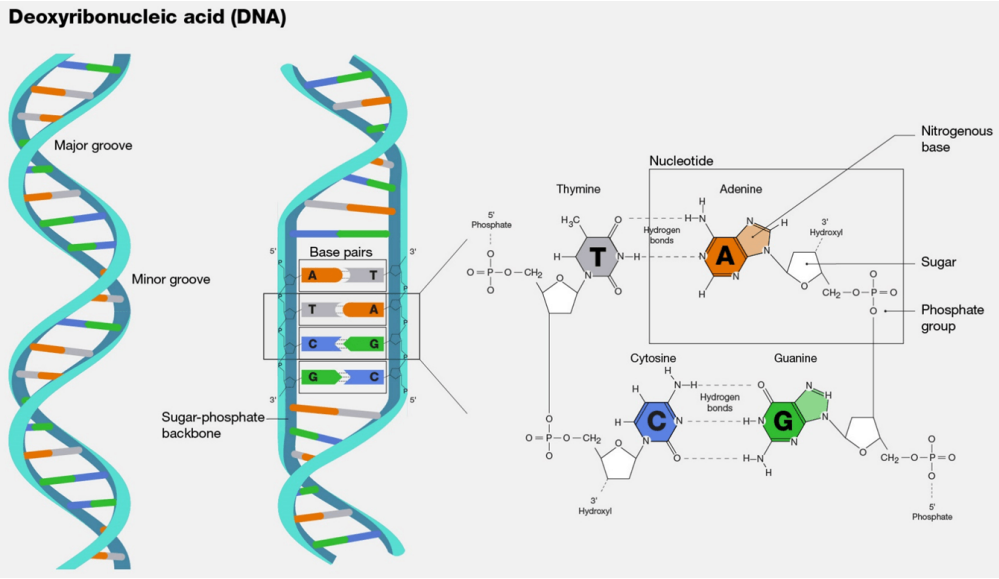


Figure 12.3.1: Double helix model of DNA (left), a section showing an overlay of alternating deoxyribose and phosphate backbone making the railing; adenine (A) paired with thymine (T) or guanine (G) paired with cytosine (C) making the steps of the double helix (middle); and a subsection enlarged to show the skeletal structure with T bonded with A by two hydrogen bonds and C connected with G by three hydrogen bonds (right). (Copyright; National Human Genome Research Institute, Public domain)

The logic of complementary base pairing

Two strands of DNA are complementary to each other as adenine (A) always faces thymine (T), and guanine (G) meets cytosine (C) in the other strand. The AT and GC are called complementary base pairs. The logic of this complementing is the following:

1. Purines, i.e., adenine (A) and guanine (G), are larger, and pyrimidines, i.e., cytosine (C) and thymine (T), are smaller. So, a purine in one strand pairs with a pyrimidine in the other strand to keep a nearly uniform gap between the two strands.
2. Adenine (A) makes two hydrogen bonds with thymine (T), and guanine (G) makes three hydrogen bonds with cytosine (C) in

the other strand. The other possible combinations of purine and pyrimidine are unstable: A can have no hydrogen bond with C, and G can have only one with T.

The base pairing, i.e., AT and GC, complements the two strands. The multiple hydrogen bonding between each nucleotide of DNA holds the two strands together like a closed zip.

Replication of DNA

When a cell divides into two, each daughter cell needs a complete set of genetic information from the parent cell. The genetic information is in the form of the sequence of nucleotides in the DNA.

> DNA replication is the process by which the DNA is copied in a cell at the time of cell division.

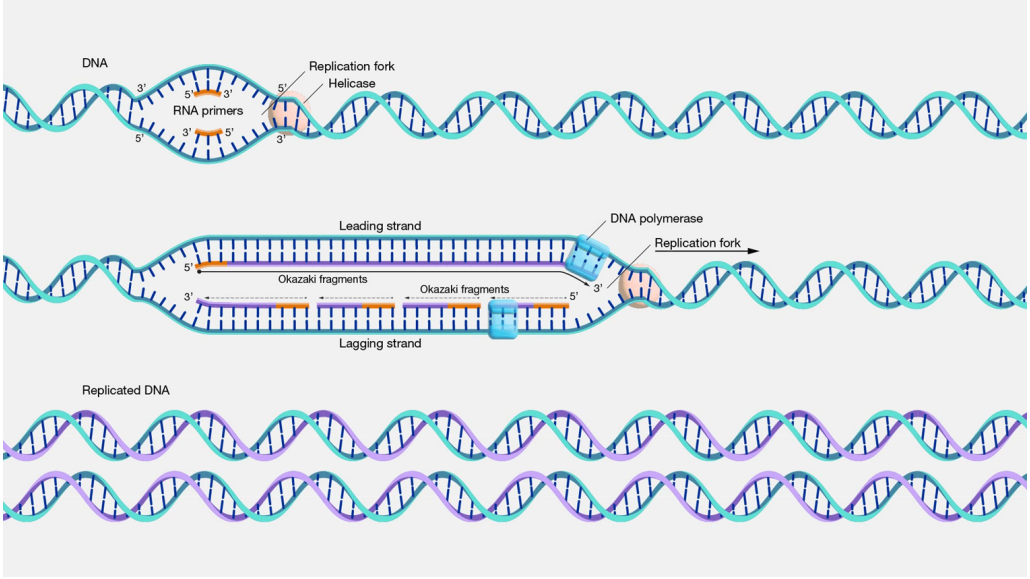


Figure 12.3.2: Illustration of DNA replication: Unzipping the double helix by enzyme helicase at the replication fork and initiation of the synthesis by RNA primers which are removed and replaced with DNA at the end (top), Continuous DNA strand synthesis in the leading strand and synthesis in fragments in the lagging strand from 5' to 3' directions (middle), and replicated DNA carrying one strand (blue) from the parent DNA and its complementary strand (purple) synthesized during the replication process. (Copyright; National Human Genome Research Institute, Public domain)

The process begins when an enzyme helicase catalyzes breaking hydrogen bonds, causing the DNA double helix to unzip, as illustrated by simulation in Figure 12.3.2 and explained in a video from yourgenome. Each strand acts as a temple for the synthesis of a new strand. As the complementary nucleotides come together, DNA polymerase joins the nucleotide by forming phosphodiester linkages from a 5' to 3' direction, as simulated in Figure 12.3.3. The leading strand is one strand of the initial DNA that unzips in a 3' to 5' direction. The leading strand's complementary strand is continually synthesized from the 5' to 3' direction. The other stand of the initial DNA that unzips in a 5' to 3' direction is called the lagging strand. The complementary strand of the lagging strand is synthesized in portions from 5' to 3' direction, called Okazaki fragments. An enzyme, called DNA ligase joins the fragments by forming phosphodiester linkages between them. This way, almost perfect copies of the entire DNA are synthesized. At this time, the cell can divide, and each daughter cell receives a replica of the parent DNA, which in many cases is identical to the DNA of the parent cell. The complementary base pairing in DNA ensures the correct placement of the nucleotides in the new DNA strands.

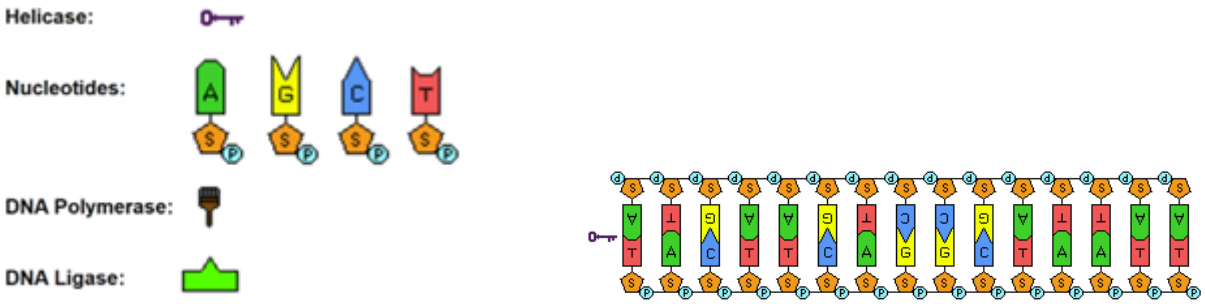


Figure 12.3.3: Simulation illustrating the DNA replication process. (Copyright: Steven Kuensting, CC BY-SA 4.0, via Wikimedia Commons)

YouTube Video

This interactive element is not available in this format. Visit the link or scan the QR code to access it online.

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12.4: Ribonucleic acid (RNA) and transcription

Learning Objectives

- Understand the basic structural features and functions of RNAs involved in protein synthesis, including mRNA, tRNA, and rRNA.
- Understand the transcription process, i.e., synthesis of mRNA from the DNA template, codons on DNA and mRNA, and anticodons on tRNA that specify amino acid to be incorporated in the protein.

Ribonucleic acid (RNA)

Ribonucleic acid (RNA) is a type of nucleic acid present in all cell types. It is structurally similar to DNA, as shown in Figure 12.4.1 , but differs from it concerning the following.

1. RNA is often single-stranded.
2. The backbone of RNA is made of ribose units (rather than deoxyribose in DNA) connected by phosphodiester linkages.
3. Three nitrogen bases in RNA, i.e., adenine (A), Guanine (G), and cytosine (C), are the same as in DNA, but the fourth one is uracil (U) in RNA in the place of thymine (T) in DNA.

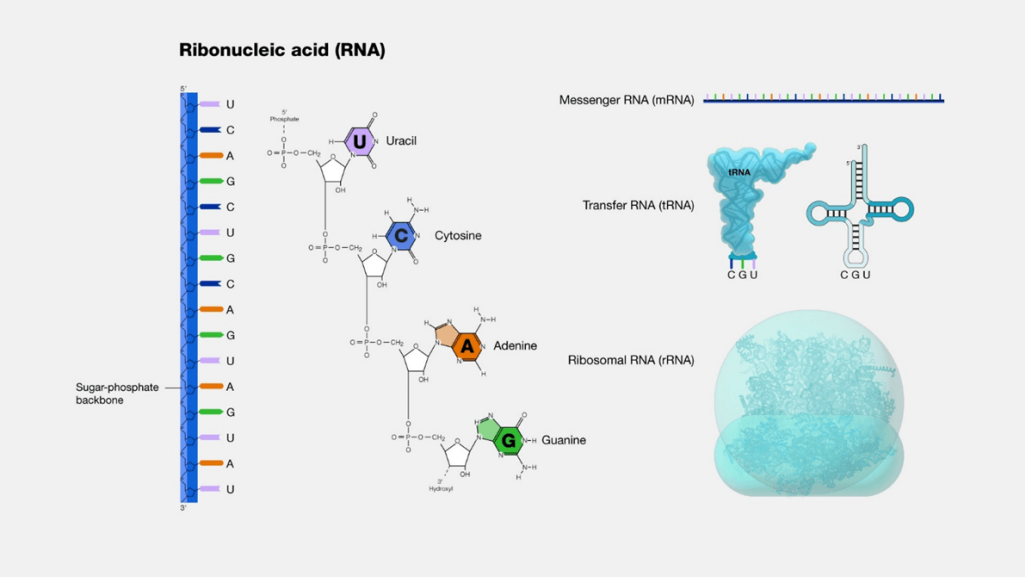


Figure 12.4.1: Illustration of a single-stranded ribonucleic acid (RNA) showing alternating phosphate-ribose backbone with nitrogen bases hanging out from ribose (left), the skeletal structure of a portion of an RNA (middle), and three types of RNA's involved in protein synthesis, i.e., messenger RNA (mRNA), transfer RNA (tRNA), and ribosomal RNA (rRNA) (right). (Copyright; National Human Genome Research Institute, Public domain)

Types of RNAs Involved in protein synthesis

Three types of RNA are involved in protein synthesis, i.e., messenger RNA (mRNA), transfer RNA (tRNA), and ribosomal RNA (rRNA), as illustrated in Figure 12.4.1. Some other RNAs have functions other than protein synthesis. Some viruses use RNA as genetic material rather than DNA.

Messenger RNA (mRNA)

Messenger RNA (mRNA) is a single-stranded RNas as illustrated in Figure 12.4.1. It is synthesized as a complementary strand

of a section of one of the two strands of DNA that carry information for synthesizing a protein cell needs. The message RNA is synthesized in the nucleus and travels to the cytoplasm (watery interior of the cell outside the nucleus), where protein-synthesis machinery, i.e., ribosomes, reads the information and synthesizes the protein.

Transfer RNA (tRNA)

The transfer RNA (tRNA) is a small RNA comprising 70 to 90 nucleotides. Its job is to bring an amino acid to the protein synthesis location and incorporate it at a specific place in the protein, dictated by the codons on the mRNA. Hydrogen bonding in some complimentary bases in the tRNA makes it fold, producing loops and double-stranded portions, as illustrated in Figure 12.4.2. The 3D shape of the tRNA is twisted, appearing like L-shape, but it is usually depicted as a cloverleaf-like shape in 2D presentation. The loops include a D loop, a T loop, an anticodon loop, a variable loop that is a slight bulge between the T loop and the anticodon loop, and a receptor stem that contains the 3' end and 5' end of the tRNA molecule. The anticodon makes the tRNA specific for one amino acid. The anticodon is complementary to the codon on the mRNA.

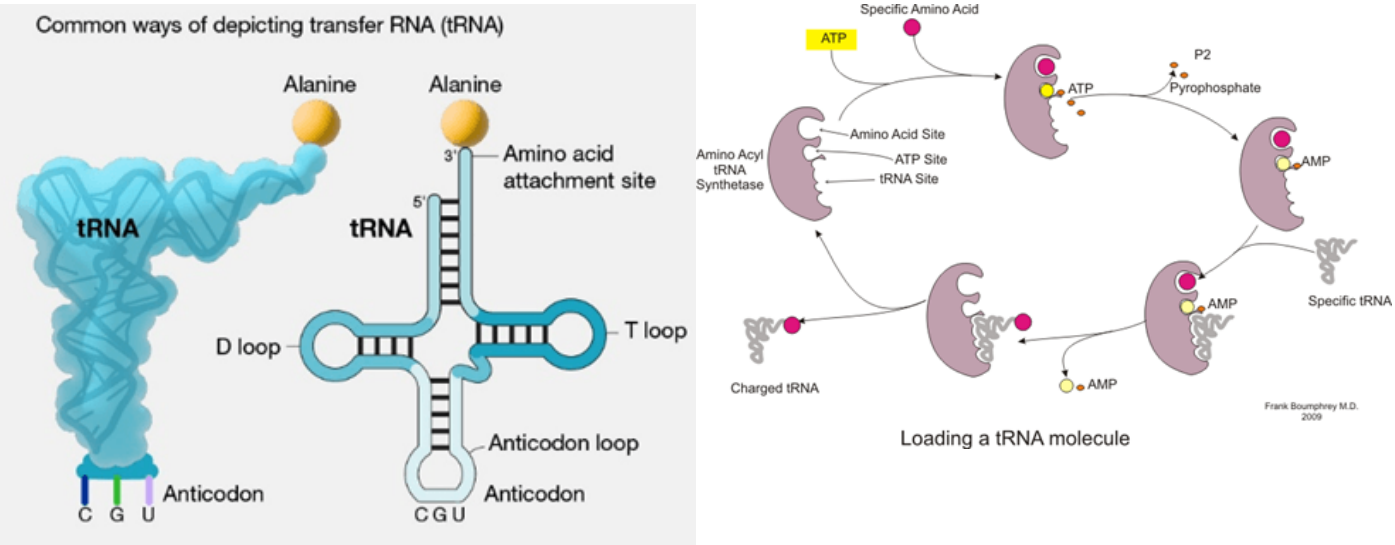
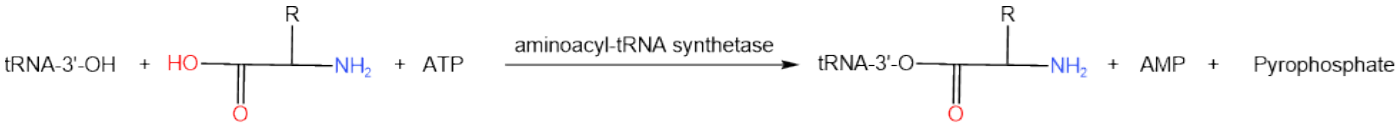


Figure 12.4.2: A 3D structure of a tRNA that is specific for amino acid alanine, its 2D depiction (left), and attachment of an amino acid to the free 3' $-\mathrm{OH}$ group of tRNA through an ester linkage using the energy released by ATP and catalyzed by enzyme aminoacyl tRNA synthetase (right). (Copyright; left: National Human Genome Research Institute, Public domain, right: Boumphreyfr, CC BY-SA 3.0, via Wikimedia Commons)

Activation of tRNA

Attaching an amino acid to tRNA is called activation of tRNA. The 3' end of tRNA always has adenosine (A) followed by two cytosines (C), i.e., ACC sequence. The free 3' $-\mathrm{OH}$ group of adenosine nucleotide makes an ester bond with an amino acid through the following reaction.



Anticodon

There is a different amino acyl-tRNA synthetase for each of the tRNA. Each tRNA is specific for one of the 20 amino acids. The particular shape of tRNA dictates this specificity. The tRNA and the amino acid corresponding to it fit in the active site of the corresponding amino acyl-tRNA synthetase, as illustrated in Figure 12.4.2. Each tRNA has a separate anticodon, a sequence of three nucleotides complementary to the corresponding codon on the mRNA, i.e., A pairs with U, G pairs with C, and vice versa. For example, mRNA codon GCA is complementary to the anticodon UGC on a tRNA shown in Figure 12.4.2 that specifies amino acid alanine in the protein.

Ribosomal RNA (rRNA)

Ribosomal RNA (rRNA) is the most abundant type of RNA that combines with proteins and makes ribosomes. Ribosome has two subunits, a large subunit, and a small subunit, as illustrated in Figure 12.4.1. Ribosome is the site for protein synthesis. There are many ribosomes in the cells.

Transcription

Gene is a section of DNA that is a basic unit of heredity passed from parent to child. Gene is a sequence of nucleotides in the DNA that encodes information for making specific proteins that lead to the expression of a particular physical character or trait, such as hair color or eye color, or some other specific function in the cell. Humans have about 20,000 protein-coding genes. Some genes encode the synthesis of RNAs that have functions other than protein synthesis.

Transcription is the process of mRNA synthesis using a protein synthesis gene portion of a DNA strand as a template, as illustrated in Figure 12.4.3.

The process begins when the gene portion of the DNA unwinds, and RNA polymerase catalyzes mRNA synthesis from a 3' to 5' direction, using a strand of the unwound DNA going from a 5' to 3' direction as a template. The unwound gene portion of the DNA is called the **transcription bubble**. The process stops when the RNA polymerase reaches the sequence of nucleotides on the template DNA that is a stop single. The mRNA is released from the DNA, and the unwound portion of the DNA returns to its regular double helix structure. The mRNA is processed further in the nucleus. Then it leaves from the nucleus to the cytoplasm (watery interior of the cell outside the nucleus), where protein-synthesis machinery, i.e., ribosomes, reads the information and synthesizes the protein in a process called **translation**.

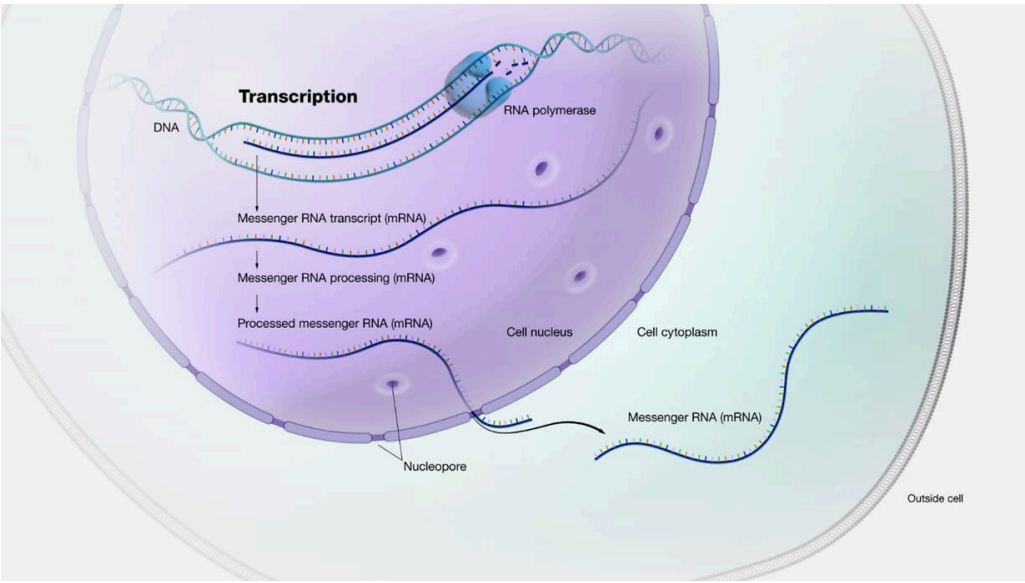


Figure 12.4.3: Illustration of the transcription process. (Copyright; National Human Genome Research Institute, Public domain)

The DNA strand used as a temple for mRNA synthesis s called the **template strand,** and the other is called the **information strand**. The mRNA complements the template strand, i.e., A in the template couples with U and G with C in the mRNA. The sequence of nucleotides in the mRNA is complementary to that of the template strand and the same as in the information strand, except that T in the information strand is replaced with U in the mRNA. Therefore, the primary structure of the information strand is shown as the primary structure of the DNA.

Codons

The gene encodes information about synthesizing a protein with the correct primary structure.

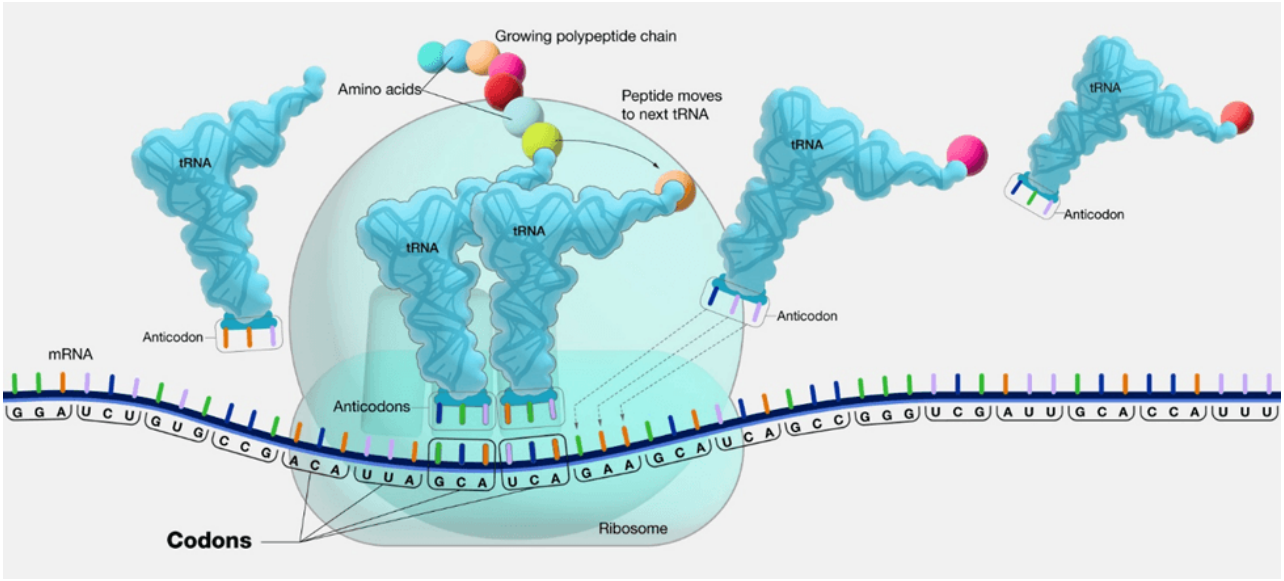


Figure 12.4.4: Illustration of codons on mRNA at the corresponding anticodons on tRNA for the synthesis of proteins. (Copyright; National Human Genome Research Institute, Public domain)

- A code called a **codon** is a sequence of three nucleotides (a trinucleotide) read from a 5' to 3' direction from mRNA, as illustrated in Figure 12.4.4.
- The codons:
  - start from the first appearance of AUG, i.e., adenine-uracil-guanine, reading from 5' to 3' direction on a mRNA,
  - are successive sets of frames of three nucleotides,
  - non-overlapping,
- Since there are four different nucleotides, there are 64 ways to spell out three-letter codons, as shown in Figure 12.4.5.
- Three codons, i.e., UGA, UAA, and UAG, are stop codons signaling the termination of protein synthesis. The remaining 61 specify amino acids.
- Since there are only 20 amino acids, amino acids have more than one codon, except tryptophan and methionine have one codon each. For example, four codons: GGU, GGC, GGA, and GGG, specify glycine.
- Codon AUG has two roles: i) in the middle of a series of codons, it specifies methionine, and ii) at the beginning of an mRNA, it signals the start of protein synthesis by bringing in methionine as the first amino acid, but the first methionine is usually removed later from the beginning (N-terminus) of the protein.

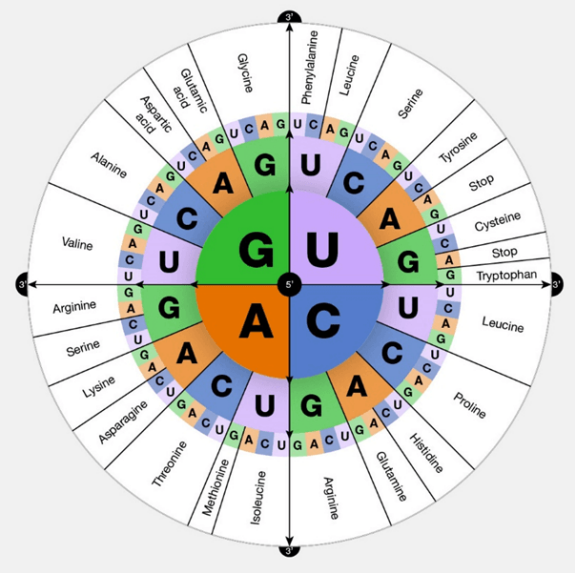


Figure 12.4.5: The 64 codons comprising three consecutive nucleotides in an mRNA read from 5' to 3' direction. The codon is read along the radius from the center to the periphery; e.g., UGG is a codon specifying tryptophan. (Copyright; National Human Genome Research Institute, Public domain)

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12.5: Translation-Protein Synthesis

Learning Objectives

- Define and understand the mechanism of biological translation.

Translation

Translation in biology is the process of protein synthesis using the information encoded in mRNA.

Translation process

The process starts when the ribosome binds to mRNA in the cytoplasm, as illustrated in Figure 12.5.1. The ribosome moves along the mRNA from 5' to 3" direction until it reaches the stats codon AUG. The AUG is also the codon for methionine. So, the methionine-tRNA (methionine-loaded aminoacyl-tRNA) with the complementary anticodon UAC arrives and aligns opposite the codon AUG. The aminoacyl-tRNA with a complementary anticodon to the codon next to AUG on the mRNA arrives and aligns opposite the codon.

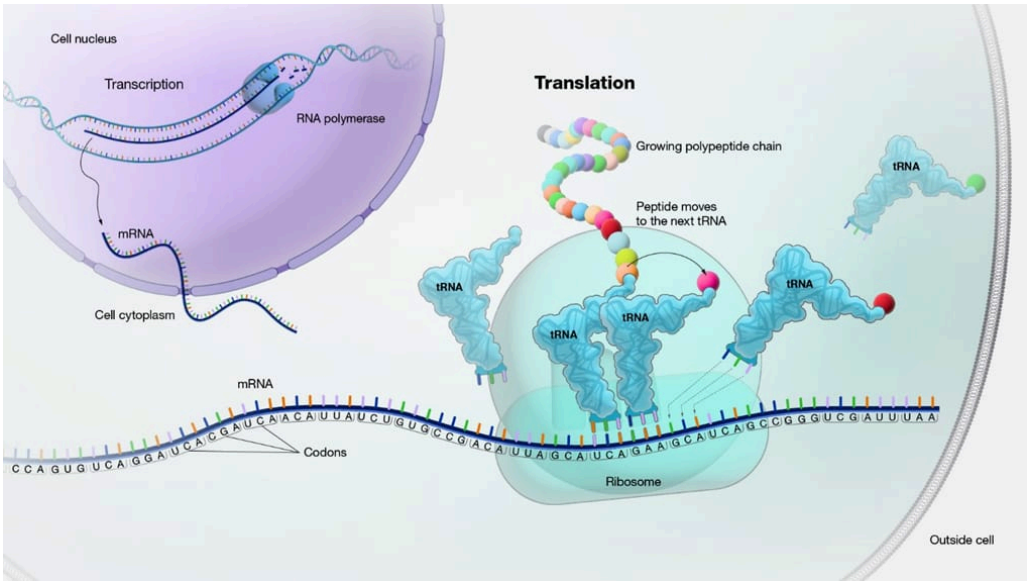


Figure 12.5.1: An illustration of the translation process. (Copyright; National Human Genome Research Institute, Public domain)

Ribosome catalyzes a peptide bond formation between $-\mathrm{NH}_2$ group of the amino acid on the second tRNA with the carboxylate group of the first by nucleophilic acyl substitution mechanism. The first tRNA becomes empty, and the second tRNA becomes peptidyl-tRNA. The ribosome moves on to the next codon -a process called **translocation**. The empty-tRNA leaves and a new aminoacyl-tRNA with a complementary anticodon to the third codon align on the mRNA and repeat the above process, as illustrated in Figure 12.5.2. The cycle repeats, and the peptide keeps elongating until the ribosome reaches a stop codon. The translation process stops at this point, and the newly formed peptide is released. The first methionine is usually removed from the peptide. The empty tRNA are re-loaded with the amino acid later on, as illustrated in Fig. 8.4.2. The hydrogen bonding and the other intramolecular interaction, like salt bridges, disulfide bonds, etc., make peptides acquire the secondary, tertiary, and sometimes quaternary structure. This is how functional proteins with the appropriate forms are synthesized.

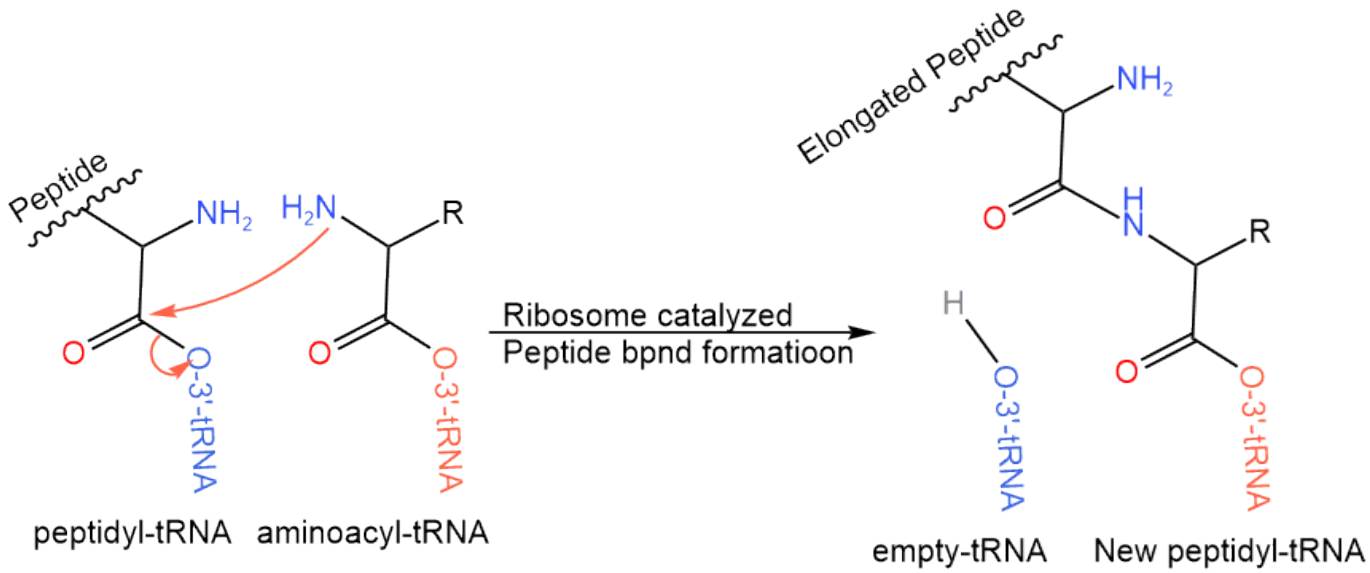


Figure 12.5.2: Illustration of the process of peptide elongation. (Copyright; author via source)

Figure 12.5.3 presents a simulation that summarizes the process of transcription and translation and the trinucleotide codons in DNA, mRNA, anticodons on tRNA, and the corresponding amino acids in the polypeptide that are shown in the simulation. Watch the DNA and RNA video summary by clicking this link or the video below.

YouTube Video

This interactive element is not available in this format. Visit the link or scan the QR code to access it online.

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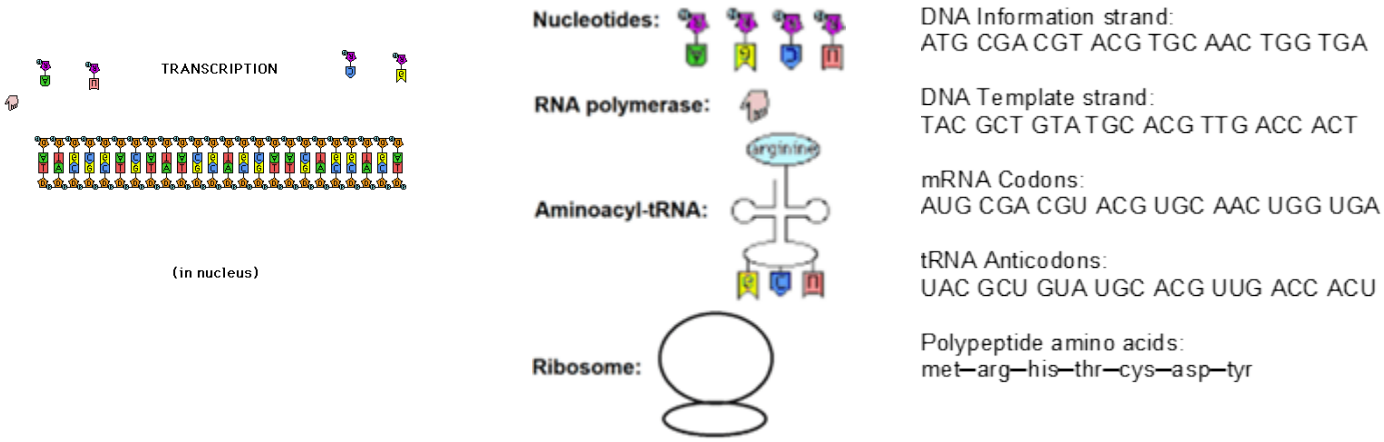


Figure 12.5.3: Simulation of the processes of transcription and translation (left), the corresponding ligands (middle), the corresponding codons, anticodon, and amino acids in DNA, mRNA, tRNA, and the polypeptide synthesized (rights). (Copyright; Steven Kuensting, CC BY-SA 4.0, via Wikimedia Commons)

Antibiotics that interrupt protein synthesis in bacteria

Antibiotics that interrupt protein synthesis in bacteria but not in humans are clinically useful. Some examples and their actions are shown in Table 1.

Table 1: Some antibiotics act by interrupting protein synthesis in bacteria but not in humans.

Antibiotic	Effect on protein synthesis in bacteria
Tetracycline	Prevents the aminoacyl-tRNA from binding to the ribosome
Erythromycin	Prevent the translocation of the ribosome along the mRNA
Streptomycin	Inhibits the initiation of protein synthesis
Chloramphenicol	Prevents the new peptide bond from being formed

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12.6: Mutations and Genetic Diseases

Learning Objectives

- Understand mutation, its causes, types, and effects, including genetic diseases and cancer.

What is mutation?

A **mutation** is any change in an organism's DNA nucleotide sequence. It may occur due to an error during DNA replication, exposure to mutagens, or a viral infection. A **mutagen** is a physical or chemical agent that can cause a permanent change in an organism's DNA. Physical mutagens include exposure to radioactivity, X-rays, UV light, etc. Chemical mutagens are chemical agents that react with and change the DNA, e.g., polycyclic aromatic hydrocarbons (PAH) found in smoke and barbecued foods. Some mutagens that may lead to cancer are called **carcinogens**. Mutations may be harmful, beneficial, or may have no effect. **Somatic mutations** in body cells affect daughter cells but are not passed on to the offspring. **Germline mutations** occur in eggs or sperm and are passed to the offspring. When a mutation alters proteins or enzymes severely, the cells may not survive, and the person may have a genetic disease.

Types of mutation

A mutation may be due to i) replacement, ii) deletion, or iii) insertion of one or more nucleotides, as illustrated in Figure 12.6.1 . There are many types of mutations. One subclass of mutation, i.e., related with change in one nucleotide is described here to introduce the basic terminologies related with mutaions.

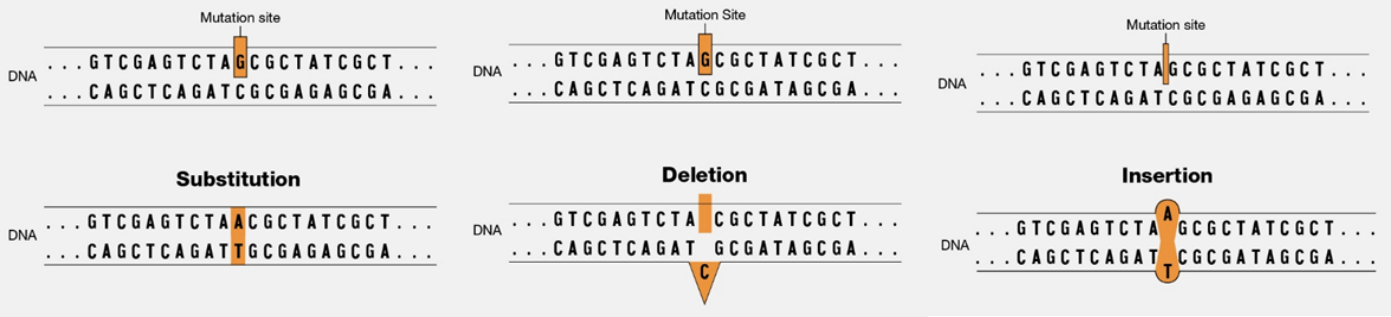


Figure 12.6.1: Illustration of three types of mutations, replacement or point mutation (left), deletion (middle), and insertion (right). (Copyright; National Human Genome Research Institute, Public domain)

Point mutation

Point mutation is the addition, deletion, or change (substitution) of one nucleotide with another. It changes the codon in which the nucleotide is located.

Substitution mutation

A replacement of one nucleotide with another in the DNA is substitution mutation. There are three sub-type of substitution mutations.

1. If the initial codon and the new codon represent the same amino acid, the mutation is called a **silent mutation**.
2. If a point mutation changes the codon to a different amino acid, it is called a **missense mutation**. If missense mutation

replaces an amino acid with significantly different properties, it may cause disease. For example, sickle cell disease is caused by a point mutation of codon GAG for glutamic acid (acidic) to GTG for valine (nonpolar) in the hemoglobin gene. On the other hand, if the new amino acid is similar to the previous one, there may be little or no change rendered in the proteins. For example, a change from AAA for lysine to AGA for arginine may not affect the protein as both amino acids are basic amino acids.

3. If a point mutation changes the codon for an amino acid to a stop codon, it is called a **nonsense mutation**. It results in premature termination of protein synthesis rendering nonfunctional protein. For example, β-thalassemia is caused by a change from CAG for glutamine to UAG, i.e., stop signal. The missense and nonsense mutations are illustrated in Figure 12.6.2

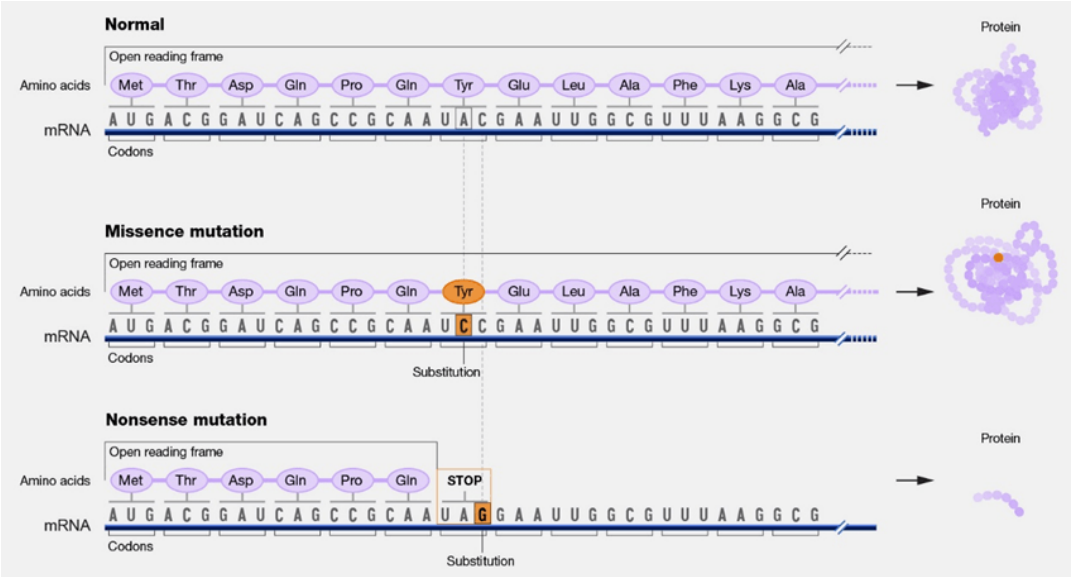


Figure 12.6.2: Misence and nonsense mutation illustrated. (Copyright; National Human Genome Research Institute, Public domain)

Deletion mutation

Deletion mutation is the loss of one or more nucleotides from a segment of DNA. Since the codon is three consecutive nucleotides, the loss of one nucleotide will not only change the codon from which the nucleotide is lost, but all the codons following it will be changed. Deletion mutation is related to a significant number of genetic diseases, e.g., two-thirds of cystic fibrosis cases are due to the loss of three nucleotides that results in the loss of amino acid phenylalanine in the protein involved, and cat cry syndrome is due to a partial chromosome deletion.

Insertion mutation

In insertion mutation, one or more nucleotides are inserted into the typical sequence of nucleotides in the DNA. So, the codon where insertion happens and all the codons following it are changed.

Effects of mutations

Some mutations do not cause a significant change in protein structures, allowing the protein to perform its function. Others may change an amino acid vital to the structure of the proteins with an amino acid of significantly different properties. It results in the proteins not being able to function correctly. For example, sickle cell disease is caused by replacing glutamic acid with a nonpolar valine that prevents the hemoglobin protein from working correctly. If the protein is an enzyme, it may no longer catalyze the reaction. In this situation, the reactants may accumulate and become poisonous, or the product may be vital for survival and not synthesized. For example, an enzyme required to metabolize galactose-1-phosphate is absent in galactosemia. It results in the accumulation of galactose-1-phosphate, which may cause cataracts and mental retardation.

Genetic disorder

Genetic disorders are health conditions caused by mutations in the genetic material. For example, phenylketonuria (PKU) results when DNA can not carry the correct codes for the synthesis of the enzyme phenylalanine hydroxylase that hydroxylates the phenyl ring of phenylalanine to convert it to tyrosine. When phenylalanine cumulates, other enzymes convert it to phenylpyruvate—cumulation of phenylalanine and phenylpyruvate cause mental retardation. If diagnosed early on, a diet can be prescribed to the child that avoids foods containing phenylalanine. It can prevent the buildup of phenylpyruvate.

Similarly, if the enzyme that converts tyrosine to melanin is not functioning, melanin is not produced, causing albinism. Melanin is a pigment that gives color to skin and hair. People with albinism do not have skin, eye, or hair pigments. This disease also happens in animals. When a genetic disorder is inherited from one or both parents, it is called a **hereditary disease**. A few more genetic diseases are listed below.

- **Cystic fibrosis** results from a defective gene. It affects the lungs and digestive system. People with this disease can not digest food properly and have repeated lung infections.
- **Down syndrome** is a genetic disease in which peoples have cognitive impairment that may be mild or severe.
- **Hemochromatosis** is an inherited condition where the body absorbs and stores so much iron that it can lead to organ damage.
- **Haemophilia** is a genetic disorder in which blood does not clot properly. It makes bleeding challenging to control.
- **Huntington's disease** is a genetic disorder that affects the nervous system, and the effect worsens over time.
- **Tay-Sachs disease** is a genetic disorder that causes brain damage.
- **Duchenne muscular dystrophy** is a condition that causes gradual loss of muscle function.
- **Thalassemia** is a genetic disorder that causes less hemoglobin to be produced, making the blood cells small and pale.
- **Tourette syndrome** is a genetic disorder related to neurological problems. Peoples with this disorder make involuntary vocal sounds and movements. Relaxation and exercise may reduce the symptoms.

Cancer

Cancer is a disease in which some of the body's cells grow and multiply uncontrolled. Mutation in a cell may cause this uncontrolled division of cells. The uncontrolled division and growth of cells appear as a tumor, as illustrated in Figure 12.6.3. It is benign if the tumor remains limited in growth without harming the neighboring tissue. However, the tumor is cancer if it invades other issues and interferes with their normal functions.

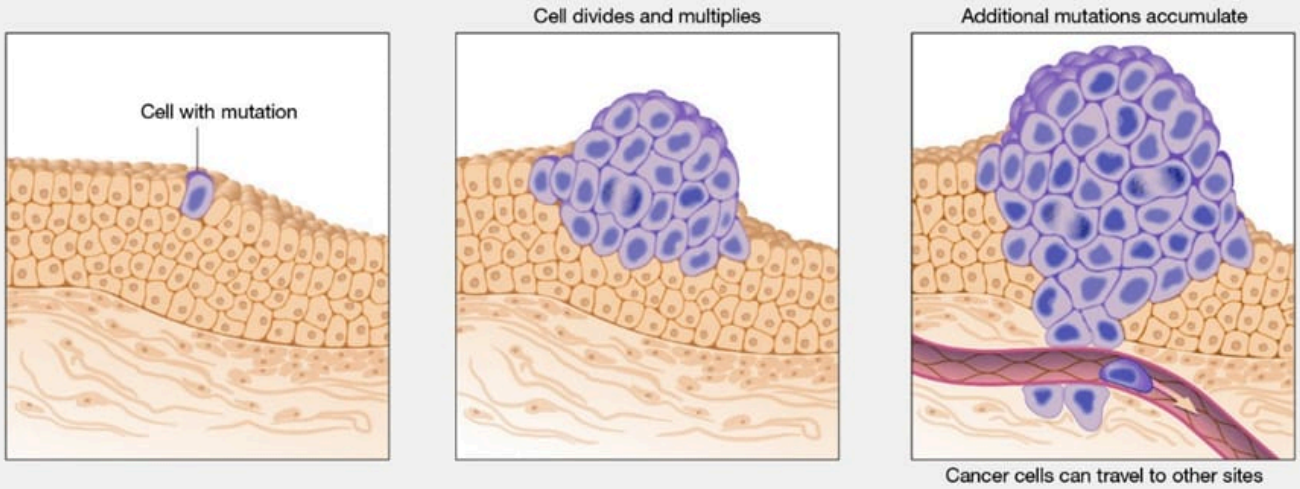


Figure 12.6.3: Illustration of tumor and cancer. (Copyright; National Human Genome Research Institute, Public domain)

The most common types of cancer are lung cancer, prostate cancer, breast cancer, colorectal cancer, stomach cancer, cervical cancer, and skin cancer. Melanoma and skin cancers account for about 40% of cancer cases. Cancer types common in children include acute lymphoblastic leukemia, brain tumors, and non-Hodgkin lymphoma.

The mutations causing cancers can result from errors during DNA replication or exposure to **carcinogens**, i.e., the substances or radiations that cause cancer. The **carcinogenic substances** include some compounds in tobacco smoke, automobile exhaust fumes, processed meat; asbestos; benzene; toxic metals like nickel, arsenic, beryllium, chromium, and cadmium and their compounds; nitrosamine; ethylene oxide, etc. About 22% of cancer-related deaths occur due to smoking. **Cancer-causing radiations** include radioactivity resulting in ionizing radiations, X-rays, and UV-radiations. About 15% of cancers are due to **cancer-causing viral infections** like HIV, hepatitis B, hepatitis C, Helicobacter pylori, Epstein-Bari virus, papillomavirus, etc. Sometimes inherited defects in genes are the cause of cancer. These factors cause or are at least partially involved in gene mutations that result in cancer.

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