ORGANIC CHEMISTRY I



Sridhar Budhi
Indiana Institute of Technology

LibreTexts™

Chemistry 2300 (Budhi)

This text is disseminated via the Open Education Resource (OER) LibreTexts Project (https://LibreTexts.org) and like the thousands of other texts available within this powerful platform, it is freely available for reading, printing, and "consuming."

The LibreTexts mission is to bring together students, faculty, and scholars in a collaborative effort to provide an accessible, and comprehensive platform that empowers our community to develop, curate, adapt, and adopt openly licensed resources and technologies; through these efforts we can reduce the financial burden born from traditional educational resource costs, ensuring education is more accessible for students and communities worldwide.

Most, but not all, pages in the library have licenses that may allow individuals to make changes, save, and print this book. Carefully consult the applicable license(s) before pursuing such effects. Instructors can adopt existing LibreTexts texts or Remix them to quickly build course-specific resources to meet the needs of their students. Unlike traditional textbooks, LibreTexts' web based origins allow powerful integration of advanced features and new technologies to support learning.



LibreTexts is the adaptable, user-friendly non-profit open education resource platform that educators trust for creating, customizing, and sharing accessible, interactive textbooks, adaptive homework, and ancillary materials. We collaborate with individuals and organizations to champion open education initiatives, support institutional publishing programs, drive curriculum development projects, and more.

The LibreTexts libraries are Powered by NICE CXone Expert and was supported by the Department of Education Open Textbook Pilot Project, the California Education Learning Lab, the UC Davis Office of the Provost, the UC Davis Library, the California State University Affordable Learning Solutions Program, and Merlot. This material is based upon work supported by the National Science Foundation under Grant No. 1246120, 1525057, and 1413739.

Any opinions, findings, and conclusions or recommendations expressed in this material are those of the author(s) and do not necessarily reflect the views of the National Science Foundation nor the US Department of Education.

Have questions or comments? For information about adoptions or adaptions contact info@LibreTexts.org or visit our main website at https://LibreTexts.org.

This text was compiled on 01/12/2026

TABLE OF CONTENTS

Licensing

1: Electronic Structure and Covalent Bonding

- 1.1: The Structure of an Atom
- 1.2: How Electrons in an Atom are Distributed
- 1.3: Ionic and Covalent Bonds
- 1.4: How the Structure of a Compound is Represented
- 1.5: Atomic Orbitals
- 1.6: How atoms form Covalent Bonds
- 1.7: How Single Bonds Are Formed in Organic Compounds
- 1.8: How a Double Bond is Formed- The Bonds in Ethene
- 1.9: How a Triple Bond is Formed- The Bonds in Ethyne
- 1.10: Bonding in the Methyl Cation, the Methyl Radical, and the Methyl Anion
- 1.11: The Bonds in Water
- 1.12: The Bonds in Ammonia and in the Ammonium Ion
- 1.13: The Bond in a Hydrogen Halide
- 1.14: Summary- Hybridization, Bond Lengths, Bond Strengths, and Bond Angles
- 1.15: The Dipole Moments of Molecules
- 1.16: An Introduction to Acids and Bases
- 1.17: pka and pH
- 1.18: 1.18 Organic Acids and Bases
- 1.19: How to Predict the Outcome of an Acid-Base Reaction
- 1.20: How to Determine the Position of Equilibrium
- 1.21: How the Structure of an Acid Affects its pka Value
- 1.22: How Substituents Affect the Strength of an Acid
- 1.23: An Introduction to Delocalized Electrons
- 1.24: A Summary of the Factors that Determine Acid Strength
- 1.25: How pH Affects the Structure of an Organic Compound
- 1.26: Buffer Solutions
- 1.27: Lewis Acids and Bases

2: Acids and Bases

- 2.1: An Introduction to Acids and Bases
- 2.2: pka and pH
- 2.3: Organic Acids and Bases
- 2.4: How to Predict the Outcome of an Acid-Base Reaction
- 2.5: How to Determine the Position of Equilibrium
- 2.6: How the Structure of an Acid Affects its pka Value
- 2.7: How pH Affects the Structure of an Organic Compound
- 2.8: Buffer Solutions
- 2.9: Lewis Acids and Bases

3: An Introduction to Organic Compounds- Nomenclature, Physical Properties, and Representation of Structure

- 3.1: How Alkyl Substituents Are Named
- 3.2: The Nomenclature of Alkanes
- 3.3: The Nomenclature of Cycloalkanes • Skeletal Structures
- 3.4: The Nomenclature of Alkyl Halides
- 3.5: The Structures of Alkyl Halides, Alcohols, Ethers, and Amines
- 3.6: The Physical Properties of Alkanes, Alkyl Halides, Alcohols, Ethers, and Amines
- 3.7: Rotation Occurs About Carbon-Carbon Single Bonds
- 3.8: Some Cycloalkanes Have Angle Strain
- 3.9: Conformers of Cyclohexane
- 3.10: Conformers of Monosubstituted Cyclohexanes
- 3.11: Conformers of Disubstituted Cyclohexanes
- 3.12: Fused Cyclohexane Rings

4: Alkenes- Structure, Nomenclature, and an Introduction to Reactivity

- 4.1: Molecular Formulas and the Degree of Unsaturation
- 4.2: The Nomenclature of Alkenes
- 4.3: The Structures of Alkenes
- 4.4: Alkenes Can Have Cis and Trans Isomers
- 4.5: Naming Alkenes Using the E Z System
- 4.6: How Alkenes React (Curved Arrows Show the Flow of Electrons)
- 4.7: A Reaction Coordinate Diagram Describes the Energy Changes That Take Place During a Reaction

5: The Reactions of Alkenes and Alkynes- An Introduction to Multistep Synthesis

- 5.1: The Addition of a Hydrogen Halide to an Alkene
- 5.2: Carbocation Stability Depends on the Number of Alkyl Groups Attached to the Positively Charged Carbon
- 5.3: Electrophilic Addition Reactions Are Regioselective
- 5.4: The Addition of Water to an Alkene
- 5.5: The Addition of an Alcohol to an Alkene
- 5.6: The Nomenclature of Alkynes
- 5.7: The Structure of Alkynes
- 5.8: The Physical Properties of Unsaturated Hydrocarbons
- 5.9: The Addition of Hydrogen Halides and Addition of Halogens to an Alkyne
- 5.10: The Addition of Hydrogen to Alkenes and Alkynes
- 5.11: A Hydrogen Bonded to an sp Carbon is “Acidic”
- 5.12: Synthesis Using Acetylide Ions
- 5.13: An Introduction to Multistep Synthesis

6: Isomers and Stereochemistry

- 6.1: Cis-Trans Isomers Result from Restricted Rotation
- 6.2: A Chiral Object Has a Nonsuperimposable Mirror Image
- 6.3: An Asymmetric Center Is a Cause of Chirality in a Molecule
- 6.4: Isomers with One Asymmetric Center
- 6.5: Asymmetric Centers and Stereocenters
- 6.6: How to Draw Enantiomers

- 6.7: Naming Enantiomers by the R,S System
- 6.8: Chiral Compounds Are Optically Active
- 6.9: How Specific Rotation is Measured
- 6.10: Enantiomeric Excess
- 6.11: Isomers with More than One Asymmetric Center
- 6.12: Meso Compounds Have Asymmetric Centers but Are Optically Inactive
- 6.13: How to Name Isomers with More than One Asymmetric Center
- 6.14: Reactions of Compounds that Contain an Asymmetric Center
- 6.15: Using Reactions that Do Not Break Bonds to an Asymmetric Center to Determine Relative Configurations
- 6.16: How Enantiomers Can Be Separated
- 6.17: Nitrogen and Phosphorus Atoms Can Be Asymmetric Centers
- 6.18: Stereochemistry of Reactions- Regioselective, Stereoselective, and Stereospecific Reactions
- 6.19: The Stereochemistry of Electrophilic addition Reactions of Alkenes
- 6.20: The Stereochemistry of Enzyme-Catalyzed Reactions
- 6.21: Enantiomers Can Be Distinguished by Biological Molecules

7: Delocalized Electrons and Their Effect on Stability, Reactivity, and pKa (Ultraviolet and Visible Spectroscopy)

- 7.1: Delocalized Electrons Explain Benzene's Structure
- 7.2: The Bonding in Benzene
- 7.3: Resonance Contributors and the Resonance Hybrid
- 7.4: How to Draw Resonance Contributors
- 7.5: The Predicted Stabilities of Resonance Contributors
- 7.6: Delocalized Energy Is the Additional Stability Delocalized Electrons Give to a Compound
- 7.7: Examples That Show How Delocalized Electrons Affect Stability
- 7.8: A Molecular Orbital Description of Stability
- 7.9: How Delocalized Electrons Affect pKa Values
- 7.10: Delocalized Electrons Can Affect the Product of a Reaction
- 7.11: Thermodynamic Versus Kinetic Control of Reactions
- 7.12: The Diels-Adler Reaction Is a 1,4-Addition Reaction

8: Aromaticity- Reactions of Benzene and Substituted Benzenes

- 8.1: The Two Criteria for Aromaticity
- 8.2: Applying the Criteria for Aromaticity
- 8.3: Aromatic Heterocyclic Compounds
- 8.4: The Nomenclature of Monosubstituted Benzenes
- 8.5: How Benzene Reacts
- 8.6: The General Mechanism for Electrophilic Aromatic Substitution Reactions
- 8.7: Halogenation of Benzene
- 8.8: Nitration of Benzene
- 8.9: Sulfonation of Benzene
- 8.10: The Friedel-Crafts Acylation of Benzene
- 8.11: The Friedel-Crafts Alkylation of Benzene
- 8.12: The Nomenclature of Disubstituted and Polysubstituted Benzenes
- 8.13: The Effect of Substituents on Reactivity
- 8.14: The Effect of Substituents on Orientation
- 8.15: The Effect of Substituents on pKa

9: Substitution and Elimination Reactions of Alkyl Halides

- 9.1: How Alkyl Halides React
- 9.2: The Mechanism For an S_N2 Reaction
- 9.3: Factors That Affect S_N2 Reactions
- 9.4: The Mechanism for an S_N1 Reaction
- 9.5: Factors That Affect S_N1 Reactions
- 9.6: Comparing the S_N2 and S_N1 Reactions of Alkyl Halides
- 9.7: Elimination Reaction of Alkyl Halides
- 9.8: Products of Elimination Reactions
- 9.9: Comparing the E2 and E1 Reactions of Alkyl Halides
- 9.10: Does an Alkyl Halide Undergo SN2, E2 Reactions or SN1 Reactions?
- 9.11: Does an Alkyl Halide Undergo SN2/E2 Reactions or SN1/E1 Reactions?
- 9.12: Solvent Effects
- 9.13: Using Substitution Reactions to Synthesize Organic Compounds
- 9.14: Biological Methylating Reagents

10: Reactions of Alcohols, Amines, Ethers, and Epoxides

- 10.1: Nomenclature of Alcohols
- 10.2: Substitution Reactions of Alcohols
- 10.3: Elimination Reactions of Alcohols- Dehydration
- 10.4: Oxidation of Alcohols
- 10.5: Amines Do Not Undergo Substitution or Elimination Reactions
- 10.6: Nomenclature of Ethers
- 10.7: Nucleophilic Substitution Reactions of Ethers
- 10.8: Nucleophilic Substitution Reactions of Epoxides
- 10.9: Using Carbocation Stability to Determine the Carcinogenicity of an Arene Oxide

11: Carbonyl Compounds I- Reactions of Carboxylic Acids and Carboxylic Derivatives

- 11.1: The Nomenclature of Carboxylic Acids and Carboxylic Acid Derivatives
- 11.2: The Structures of Carboxylic Acids and Carboxylic Acid Derivatives
- 11.3: The Physical Properties of Carbonyl Compounds
- 11.4: Carboxylic Acids and Carboxylic Acid Derivatives found in Nature
- 11.5: How Carboxylic Acids and Carboxylic Acids Compounds React
- 11.6: Relative Reactivities of Carboxylic Acids and Carboxylic Acid Derivatives
- 11.7: Reactions of Acyl Halides
- 11.8: Reactions of Esters
- 11.9: Acid-Catalyzed Ester Hydrolysis
- 11.10: Soaps, Detergents, and Micelles
- 11.11: Reactions of Carboxylic Acids
- 11.12: Reactions of Amides
- 11.13: Acid-Catalyzed Amide Hydrolysis
- 11.14: The Synthesis of Carboxylic Acid Derivatives
- 11.15: Nitriles

12: Carbonyl Compounds II- Reactions of Aldehydes and Ketones • More Reactions of Carboxylic Acid Derivatives

- 12.1: The Nomenclature of Aldehydes and Ketones
- 12.2: The Relative Reactivities of Carbonyl Compounds
- 12.3: How Aldehydes and Ketones React
- 12.4: Gringard Reagents
- 12.5: Reactions of Carbonyl Compounds with Hydride Ion
- 12.6: Reactions of Aldehydes and Ketones with Amines
- 12.7: Reactions of Aldehydes and Ketones with Water
- 12.8: Reactions of Aldehydes and Ketones with Alcohols
- 12.9: Nucleophilic Addition to α, β- Unsaturated Carboxylic Acid Derivatives
- 12.10: Nucleophilic Addition to α, β- Unsaturated Carbonyl Compounds
- 12.11: Protecting Groups
- 12.12: Addition of Sulfur Nucleophiles
- 12.13: The Wittig Reaction Forms an Alkene
- 12.14: Stereochemistry of Nucleophilic Addition Reactions- Re and Si Faces
- 12.15: Designing a Synthesis VI- Disconnections, Synthons, and Synthetic Equivalents
- 12.16: Enzyme-Catalyzed Additions to α, β- Unsaturated Carbonyl Compounds

13: Carbonyl Compounds III- Reactions at the α- Carbon

- 13.1: Alkylation and Acylation of the α-Carbon Using an Enamine Intermediate
- 13.2: Alkylation of the β-Carbon- The Michael Reaction
- 13.3: An Aldol Addition Forms β-Hydroxaldehydes or β-Hydroxyketones
- 13.4: Dehydration of Aldol Addition Products Form α, β-Unsaturated Aldehydes and Ketones
- 13.5: The Crossed Aldol Addition
- 13.6: A Claisen Condensation Forms a β-Keto Ester
- 13.7: Other Crossen Condensations
- 13.8: Intramolecular Condensation and Addition Reactions
- 13.9: The Robinson Annulation
- 13.10: Carboxylic Acids with a Carbonyl Group at the 3-Position can be Decarboxylated
- 13.11: The Acidity of an α- Hydrogen
- 13.12: The Malonic Ester Synthesis- A Way to Synthesize a Carboxylic Acid
- 13.13: The Acetoacetic Ester Synthesis- A Way to Synthesize a Methyl Ketone
- 13.14: Designing a Synthesis VII- Making New Carbon-Carbon Bonds
- 13.15: Reactions at the α-Carbon in Biological Systems
- 13.16: Keto-Enol Tautomers
- 13.17: Keto-Enol Interconversion
- 13.18: How Enolate Ions and Enols React
- 13.19: Halogenation of the α- Carbon and Aldehydes and Ketones
- 13.20: Halogenation of the α- Carbon of Carboxylic Acids- The Hell-Volhard-Zelinski Reaction
- 13.21: α- Halogenated Carbonyl Compounds Are Useful in Synthesis
- 13.22: Using LDA to Form an Enolate Ion
- 13.23: Alkylating the α-Carbon of Carbonyl Compounds

14: Determing the Structure of Organic Compounds

15: The Organic Chemistry of Carbohydrates

- 15.1: Classification of Carbohydrates
- 15.2: The D and L Notation
- 15.3: The Configurations of Aldoses
- 15.4: The Configurations of Ketoses
- 15.5: The Reactions of Monosaccharides in Basic Solutions
- 15.6: The Oxidation-Reduction Reactions of Monosaccharides
- 15.7: Monosaccharides form Crystalline Osazones
- 15.8: Lengthening the Chain- The Kiliani-Fischer Synthesis
- 15.9: Shortening the Chain- The Wohl Degradation
- 15.10: The Stereochemistry of Glucose- The Fischer Proof
- 15.11: Monosaccharides Form Cyclic Hemiacetals
- 15.12: Glucose is the Most Stable Aldohexose
- 15.13: Formation of Glycosides
- 15.14: The Anomeric Effect
- 15.15: Reducing and Nonreducing Sugars
- 15.16: Disaccharides
- 15.17: Polysaccharides
- 15.18: Some Naturally Occurring Products Derived from Carbohydrates
- 15.19: Carbohydrates on Cell Surfaces
- 15.20: Synthetic Sweeteners

Index

Glossary

Detailed Licensing

Licensing

*A detailed breakdown of this resource's licensing can be found in **Back Matter/Detailed Licensing**.*

CHAPTER OVERVIEW

1: Electronic Structure and Covalent Bonding

1.1: The Structure of an Atom
1.2: How Electrons in an Atom are Distributed
1.3: Ionic and Covalent Bonds
1.4: How the Structure of a Compound is Represented
1.5: Atomic Orbitals
1.6: How atoms form Covalent Bonds
1.7: How Single Bonds Are Formed in Organic Compounds
1.8: How a Double Bond is Formed- The Bonds in Ethene
1.9: How a Triple Bond is Formed- The Bonds in Ethyne
1.10: Bonding in the Methyl Cation, the Methyl Radical, and the Methyl Anion
1.11: The Bonds in Water
1.12: The Bonds in Ammonia and in the Ammonium Ion
1.13: The Bond in a Hydrogen Halide
1.14: Summary- Hybridization, Bond Lengths, Bond Strengths, and Bond Angles
1.15: The Dipole Moments of Molecules
1.16: An Introduction to Acids and Bases
1.17: pka and pH
1.18: 1.18 Organic Acids and Bases
1.19: How to Predict the Outcome of an Acid-Base Reaction
1.20: How to Determine the Position of Equilibrium
1.21: How the Structure of an Acid Affects its pka Value
1.22: How Substituents Affect the Strength of an Acid
1.23: An Introduction to Delocalized Electrons
1.24: A Summary of the Factors that Determine Acid Strength
1.25: How pH Affects the Structure of an Organic Compound
1.26: Buffer Solutions
1.27: Lewis Acids and Bases

1: Electronic Structure and Covalent Bonding is shared under a not declared license and was authored, remixed, and/or curated by LibreTexts.

1.1: The Structure of an Atom

Additional Resources

Michigan State Virtual Textbook of Organic Chemistry

Electron Configurations of Atoms

MasterOrganicChemistry

From General Chemistry to Organic

The Atom

Electrons and Orbitals

Effective Nuclear Charge

Carey 4th Edition On-Line Activity

Atoms, Electrons and Orbitals

Khan Academy

Elements and Atoms

Introduction to the Atom

Atomic Orbitals

Orbitals and Electron Configurations

Electron Configurations

Electron Configurations Part 2

Valence Electrons

Leah4Sci

Sub-Atomic Particles and Atomic Structure

Periodic Table and Trends

Atomic Orbitals and Shapes

Electron Configuration Part 1

Electron Configuration Part 2

Intro to Organic Chemistry 1

Intro to Organic Chemistry 2

Cliffs Notes

Principles of Atomic Structure

Slide Presentations

Web Pages

Electron Configurations

Electron Configurations and Orbital Diagrams

Visualizing Atomic Orbitals

**Very complete introduction to the electronic structure of atoms

Atomic orbitals

Videos

Electron Configurations and Orbital Diagrams

Atomic Orbital Video

electron configuration video

Tutorial

Chemistry is Easy! Electron Configurations

1.1: The Structure of an Atom is shared under a not declared license and was authored, remixed, and/or curated by LibreTexts.

1.2: How Electrons in an Atom are Distributed

Additional Resources

Michigan State Virtual Textbook of Organic Chemistry

Electron Configurations of Atoms

MasterOrganicChemistry

From General Chemistry to Organic

The Atom

Electrons and Orbitals

Effective Nuclear Charge

Carey 4th Edition On-Line Activity

Atoms, Electrons and Orbitals

Khan Academy

Elements and Atoms

Introduction to the Atom

Atomic Orbitals

Orbitals and Electron Configurations

Electron Configurations

Electron Configurations Part 2

Valence Electrons

Leah4Sci

Sub-Atomic Particles and Atomic Structure

Periodic Table and Trends

Atomic Orbitals and Shapes

Electron Configuration Part 1

Electron Configuration Part 2

Intro to Organic Chemistry 1

Intro to Organic Chemistry 2

Cliffs Notes

Principles of Atomic Structure

Slide Presentations

Web Pages

Electron Configurations

Electron Configurations and Orbital Diagrams

Visualizing Atomic Orbitals

**Very complete introduction to the electronic structure of atoms

Atomic orbitals

Videos

Electron Configurations and Orbital Diagrams

Atomic Orbital Video

electron configuration video

Tutorial

Chemistry is Easy! Electron Configurations

1.2: How Electrons in an Atom are Distributed is shared under a not declared license and was authored, remixed, and/or curated by LibreTexts.

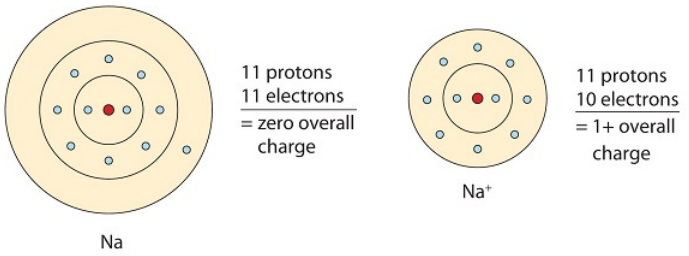
1.3: Ionic and Covalent Bonds

There are many types of chemical bonds and forces that bind molecules together. The two most basic types of bonds are characterized as either ionic or covalent. In ionic bonding, atoms transfer electrons to each other. Ionic bonds require at least one electron donor and one electron acceptor. In contrast, atoms with the same electronegativity share electrons in covalent bonds, because neither atom preferentially attracts or repels the shared electrons.

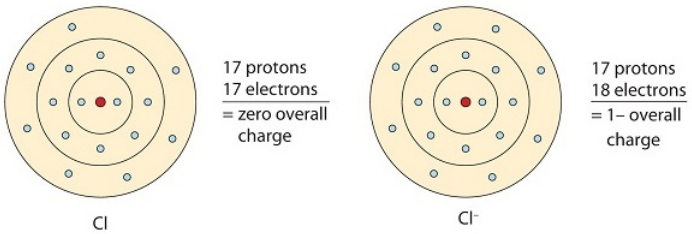
Introduction

Ionic bonding is the complete transfer of valence electron(s) between atoms. It is a type of chemical bond that generates two oppositely charged ions. In ionic bonds, the metal loses electrons to become a positively charged cation, whereas the nonmetal accepts those electrons to become a negatively charged anion. Ionic bonds require an electron donor, often a metal, and an electron acceptor, a nonmetal.

Ionic bonding is observed because metals have few electrons in their outer-most orbitals. By losing those electrons, these metals can achieve noble gas configuration and satisfy the octet rule. Similarly, nonmetals that have close to 8 electrons in their valence shells tend to readily accept electrons to achieve noble gas configuration. In ionic bonding, more than 1 electron can be donated or received to satisfy the octet rule. The charges on the anion and cation correspond to the number of electrons donated or received. In ionic bonds, the net charge of the compound must be zero.



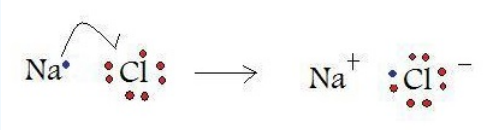
This sodium molecule donates the lone electron in its valence orbital in order to achieve octet configuration. This creates a positively charged cation due to the loss of electron.



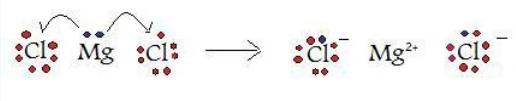
This chlorine atom receives one electron to achieve its octet configuration, which creates a negatively charged anion.

The predicted overall energy of the ionic bonding process, which includes the ionization energy of the metal and electron affinity of the nonmetal, is usually positive, indicating that the reaction is endothermic and unfavorable. However, this reaction is highly favorable because of the electrostatic attraction between the particles. At the ideal interatomic distance, attraction between these particles releases enough energy to facilitate the reaction. Most ionic compounds tend to dissociate in polar solvents because they are often polar. This phenomenon is due to the opposite charges on each ion.

Example 1.3.1: Chloride Salts



In this example, the sodium atom is donating its 1 valence electron to the chlorine atom. This creates a sodium cation and a chlorine anion. Notice that the net charge of the resulting compound is 0.



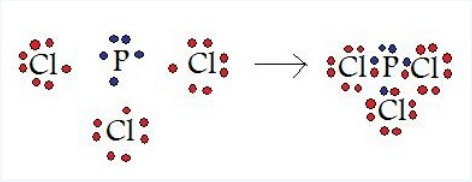
In this example, the magnesium atom is donating both of its valence electrons to chlorine atoms. Each chlorine atom can only accept 1 electron before it can achieve its noble gas configuration; therefore, 2 atoms of chlorine are required to accept the 2 electrons donated by the magnesium. Notice that the net charge of the compound is 0.

Covalent Bonding

Covalent bonding is the sharing of electrons between atoms. This type of bonding occurs between two atoms of the same element or of elements close to each other in the periodic table. This bonding occurs primarily between nonmetals; however, it can also be observed between nonmetals and metals.

If atoms have similar electronegativities (the same affinity for electrons), covalent bonds are most likely to occur. Because both atoms have the same affinity for electrons and neither has a tendency to donate them, they share electrons in order to achieve octet configuration and become more stable. In addition, the ionization energy of the atom is too large and the electron affinity of the atom is too small for ionic bonding to occur. For example: carbon does not form ionic bonds because it has 4 valence electrons, half of an octet. To form ionic bonds, Carbon molecules must either gain or lose 4 electrons. This is highly unfavorable; therefore, carbon molecules share their 4 valence electrons through single, double, and triple bonds so that each atom can achieve noble gas configurations. Covalent bonds include interactions of the sigma and pi orbitals; therefore, covalent bonds lead to formation of single, double, triple, and quadruple bonds.

✔ Example 1.3.2: PCl_3



In this example, a phosphorous atom is sharing its three unpaired electrons with three chlorine atoms. In the end product, all four of these molecules have 8 valence electrons and satisfy the octet rule.

Bonding in Organic Chemistry

Ionic and covalent bonds are the two extremes of bonding. Polar covalent is the intermediate type of bonding between the two extremes. Some ionic bonds contain covalent characteristics and some covalent bonds are partially ionic. For example, most carbon-based compounds are covalently bonded but can also be partially ionic. Polarity is a measure of the separation of charge in a compound. A compound's polarity is dependent on the symmetry of the compound and on differences in electronegativity between atoms. Polarity occurs when the electron pushing elements, found on the left side of the periodic table, exchanges electrons with the electron pulling elements, on the right side of the table. This creates a spectrum of polarity, with ionic (polar) at one extreme, covalent (nonpolar) at another, and polar covalent in the middle.

Both of these bonds are important in organic chemistry. Ionic bonds are important because they allow the synthesis of specific organic compounds. Scientists can manipulate ionic properties and these interactions in order to form desired products. Covalent bonds are especially important since most carbon molecules interact primarily through covalent bonding. Covalent bonding allows molecules to share electrons with other molecules, creating long chains of compounds and allowing more complexity in life.

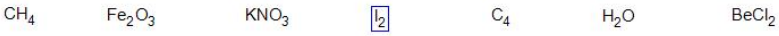
References

1. Vollhardt, K. Peter C., and Neil E. Schore. Organic Chemistry Structure and Function. New York: W. H. Freeman, 2007.
2. Petrucci, Ralph H. General Chemistry: Principles and Modern Applications. Upper Saddle River, NJ: Pearson Education, 2007.

3. Brown, Theodore L., Eugene H. Lemay, and Bruce E. Bursten. Chemistry: The Central Science. 6th ed. Englewood Cliffs, NJ: Prentice Hall, 1994.

Problems

1. Are these compounds ionic or covalent?

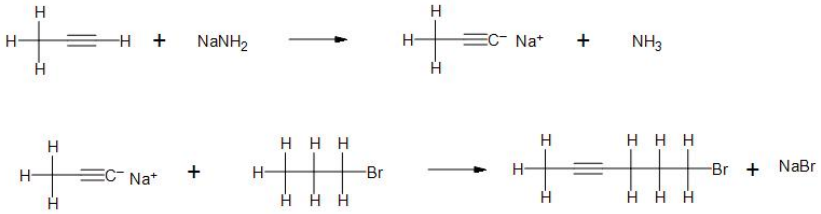


2. In the following reactions, indicate whether the reactants and products are ionic or covalently bonded.

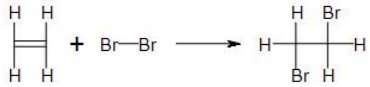
a)



b) Clarification: What is the nature of the bond between sodium and amide? What kind of bond forms between the anion carbon chain and sodium?



c)



Solutions

- 1) From left to right: Covalent, Ionic, Ionic, Covalent, Covalent, Covalent, Ionic.
- 2a) All products and reactants are ionic.
- 2b) From left to right: Covalent, Ionic, Ionic, Covalent, Ionic, Covalent, Covalent, Ionic.
- 2c) All products and reactants are covalent.

1.3: Ionic and Covalent Bonds is shared under a not declared license and was authored, remixed, and/or curated by LibreTexts.

- **Ionic and Covalent Bonds** is licensed CC BY-NC-SA 4.0.

1.4: How the Structure of a Compound is Represented

Molecular orbitals

1.4: How the Structure of a Compound is Represented is shared under a not declared license and was authored, remixed, and/or curated by LibreTexts.

1.5: Atomic Orbitals

Objectives

After completing this section, you should be able to

1. describe the physical significance of an orbital.
2. list the atomic orbitals from 1*s* to 3*d* in order of increasing energy.
3. sketch the shapes of *s* and *p* orbitals.

Key Terms

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

- nodal plane
- node
- orbital
- quantum mechanics
- wave function

Atomic Orbitals

An orbital is the quantum mechanical refinement of Bohr's orbit. In contrast to his concept of a simple circular orbit with a fixed radius, orbitals are mathematically derived regions of space with different *probabilities* of having an electron. One way of representing electron probability distributions is Ψ^2. Because Ψ^2 gives the probability of finding an electron in a given volume of space (such as a cubic picometer), a plot of Ψ^2 versus distance from the nucleus (r) is a plot of the **probability density**. For example, the 1*s* orbital is spherically symmetrical, so the probability of finding a 1*s* electron at any given point depends *only* on its distance from the nucleus. The probability density is greatest at $r = 0$ (at the nucleus) and decreases steadily with increasing distance. At very large values of *r*, the electron probability density is very small but *not* zero.

We can calculate the **radial probability** (the probability of finding a 1*s* electron at a distance *r* from the nucleus) by adding together the probabilities of an electron being at all points on a series of *x* spherical shells of radius r_1, r_2, r_3,…, r_{x-1}, r_x. In effect, we are dividing the atom into very thin concentric shells, much like the layers of an onion (part (a) in Figure **1.5.1**), and calculating the probability of finding an electron on each spherical shell. Recall that the electron probability density is greatest at $r = 0$ (part (b) in Figure **1.5.1**), so the density of dots is greatest for the smallest spherical shells in part (a) in Figure **1.5.1**. In contrast, the surface area of each spherical shell is equal to $4\pi r^2$, which increases very rapidly with increasing *r* (part (c) in Figure **1.5.1**). Because the surface area of the spherical shells increases more rapidly with increasing *r* than the electron probability density decreases, the plot of radial probability has a maximum at a particular distance (part (d) in Figure **1.5.1**). Most important, when *r* is very small, the surface area of a spherical shell is so small that the *total* probability of finding an electron close to the nucleus is very low; at the nucleus, the electron probability vanishes (part (d) in Figure **1.5.1**).

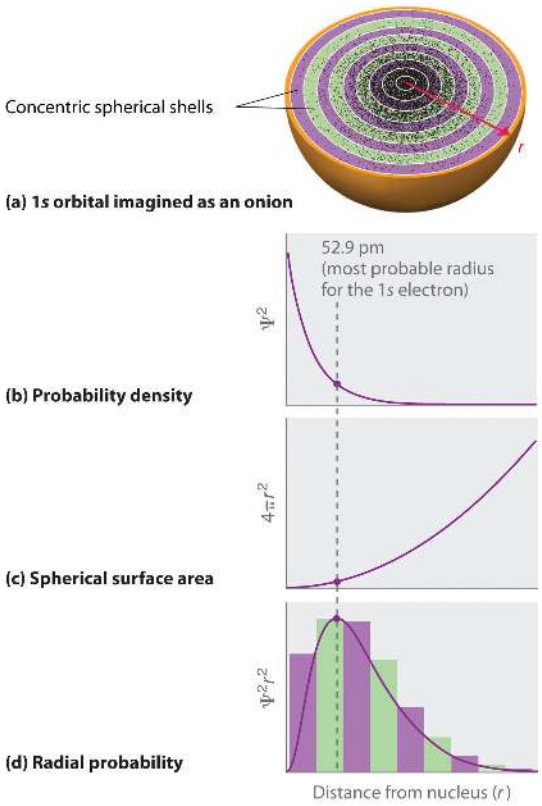


Figure **1.5.1**: Most Probable Radius for the Electron in the Ground State of the Hydrogen Atom. (a) Imagine dividing the atom's total volume into very thin concentric shells as shown in the onion drawing. (b) A plot of electron probability density Ψ^2 versus r shows that the electron probability density is greatest at $r = 0$ and falls off smoothly with increasing r. The density of the dots is therefore greatest in the innermost shells of the onion. (c) The surface area of each shell, given by $4\pi r^2$, increases rapidly with increasing r. (d) If we count the number of dots in each spherical shell, we obtain the total probability of finding the electron at a given value of r. Because the surface area of each shell increases more rapidly with increasing r than the electron probability density decreases, a plot of electron probability versus r (the *radial probability*) shows a peak. This peak corresponds to the most probable radius for the electron, 52.9 pm, which is exactly the radius predicted by Bohr's model of the hydrogen atom. (CC BY-NC-SA 3.0; Anonymous via LibreTexts)

For the hydrogen atom, the peak in the radial probability plot occurs at $r = 0.529$ Å (52.9 pm), which is exactly the radius calculated by Bohr for the $n = 1$ orbit. Thus the *most probable radius* obtained from quantum mechanics is identical to the radius calculated by classical mechanics. In Bohr's model, however, the electron was assumed to be at this distance 100% of the time, whereas in the quantum mechanical Schrödinger model, it is at this distance only some of the time. The difference between the two models is attributable to the wavelike behavior of the electron and the Heisenberg uncertainty principle.

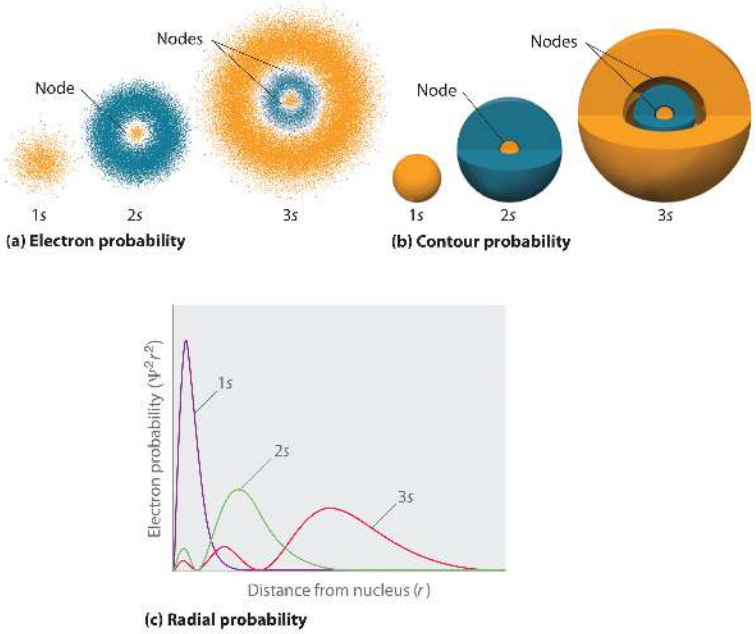


Figure **1.5.2**: Probability Densities for the 1*s*, 2*s*, and 3*s* Orbitals of the Hydrogen Atom. (a) The electron probability density in any plane that contains the nucleus is shown. Note the presence of circular regions, or nodes, where the probability density is zero. (b) Contour surfaces enclose 90% of the electron probability, which illustrates the different sizes of the 1*s*, 2*s*, and 3*s* orbitals. The cutaway drawings give partial views of the internal spherical nodes. The orange color corresponds to regions of space where the phase of the wave function is positive, and the blue color corresponds to regions of space where the phase of the wave function is negative. (c) In these plots of electron probability as a function of distance from the nucleus (*r*) in all directions (radial probability), the most probable radius increases as *n* increases, but the 2*s* and 3*s* orbitals have regions of significant electron probability at small values of *r*. (CC BY-NC-SA 3.0; Anonymous via LibreTexts)

Figure **1.5.2** compares the electron probability densities for the hydrogen 1*s*, 2*s*, and 3*s* orbitals. Note that all three are spherically symmetrical. For the 2*s* and 3*s* orbitals, however (and for all other *s* orbitals as well), the electron probability density does not fall off smoothly with increasing *r*. Instead, a series of minima and maxima are observed in the radial probability plots (part (c) in Figure **1.5.2**). The minima correspond to spherical nodes (regions of zero electron probability), which alternate with spherical regions of nonzero electron probability.

s Orbitals

Three things happen to *s* orbitals as *n* increases (Figure **1.5.2**):

1. They become larger, extending farther from the nucleus.
2. They contain more nodes. This is similar to a standing wave that has regions of significant amplitude separated by nodes, points with zero amplitude.
3. For a given atom, the *s* orbitals also become higher in energy as *n* increases because of their increased distance from the nucleus.

Orbitals are generally drawn as three-dimensional surfaces that enclose 90% of the electron density, as was shown for the hydrogen 1*s*, 2*s*, and 3*s* orbitals in part (b) in Figure **1.5.2**. Although such drawings show the relative sizes of the orbitals, they do not normally show the spherical nodes in the 2*s* and 3*s* orbitals because the spherical nodes lie inside the 90% surface. Fortunately, the positions of the spherical nodes are not important for chemical bonding.

p Orbitals

Only *s* orbitals are spherically symmetrical. As the value of *l* increases, the number of orbitals in a given subshell increases, and the shapes of the orbitals become more complex. Because the 2*p* subshell has $l = 1$, with three values of m_l (−1, 0, and +1), there are three 2*p* orbitals.

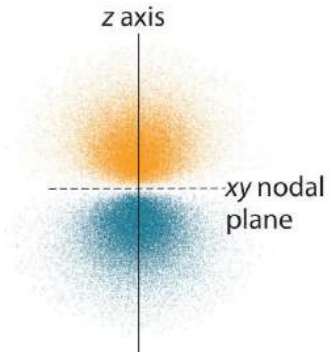


Figure **1.5.2**, the colors correspond to regions of space where the phase of the wave function is positive (orange) and negative (blue). (CC BY-NC-SA 3.0; Anonymous via LibreTexts)

The electron probability distribution for one of the hydrogen 2*p* orbitals is shown in Figure **1.5.3**. Because this orbital has two lobes of electron density arranged along the *z* axis, with an electron density of zero in the *xy* plane (i.e., the *xy* plane is a nodal plane), it is a $2p_z$ orbital. As shown in Figure **1.5.4**, the other two 2*p* orbitals have identical shapes, but they lie along the *x* axis ($2p_x$) and *y* axis ($2p_y$), respectively. Note that each *p* orbital has just one nodal plane. In each case, the phase of the wave function for each of the 2*p* orbitals is positive for the lobe that points along the positive axis and negative for the lobe that points along the negative axis. It is important to emphasize that these signs correspond to the *phase* of the wave that describes the electron motion, *not* to positive or negative charges.

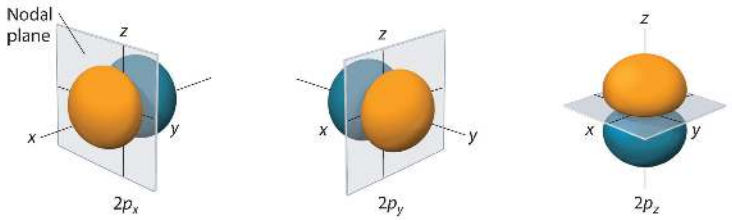


Figure **1.5.4** The Three Equivalent 2*p* Orbitals of the Hydrogen Atom. (CC BY-NC-SA 3.0; Anonymous via LibreTexts)

The surfaces shown enclose 90% of the total electron probability for the $2p_x$, $2p_y$, and $2p_z$ orbitals. Each orbital is oriented along the axis indicated by the subscript and a nodal plane that is perpendicular to that axis bisects each 2*p* orbital. The phase of the wave function is positive (orange) in the region of space where *x*, *y*, or *z* is positive and negative (blue) where *x*, *y*, or *z* is negative.

Just as with the *s* orbitals, the size and complexity of the *p* orbitals for any atom increase as the principal quantum number *n* increases. The shapes of the 90% probability surfaces of the 3*p*, 4*p*, and higher-energy *p* orbitals are, however, essentially the same as those shown in Figure **1.5.4**.

The electron configuration of an atom is the representation of the arrangement of electrons distributed among the orbital shells and subshells. Commonly, the electron configuration is used to describe the orbitals of an atom in its ground state, but it can also be used to represent an atom that has ionized into a cation or anion by compensating with the loss of or gain of electrons in their subsequent orbitals. Many of the physical and chemical properties of elements can be correlated to their unique electron configurations. The valence electrons, electrons in the outermost shell, are the determining factor for the unique chemistry of the element.

1.5: Atomic Orbitals is shared under a not declared license and was authored, remixed, and/or curated by LibreTexts.

- **1.2: Atomic Structure - Orbitals** by Dietmar Kennepohl, Steven Farmer is licensed CC BY-NC-SA 3.0.

1.6: How atoms form Covalent Bonds

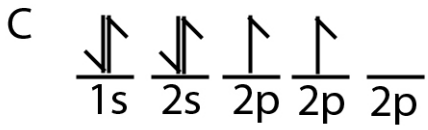
1.6: How atoms form Covalent Bonds is shared under a not declared license and was authored, remixed, and/or curated by LibreTexts.

1.7: How Single Bonds Are Formed in Organic Compounds

Hybridization was introduced to explain molecular structure when the valence bond theory failed to correctly predict them. It is experimentally observed that bond angles in organic compounds are close to 109°, 120°, or 180°. According to Valence Shell Electron Pair Repulsion (VSEPR) theory, electron pairs repel each other and the bonds and lone pairs around a central atom are generally separated by the largest possible angles.

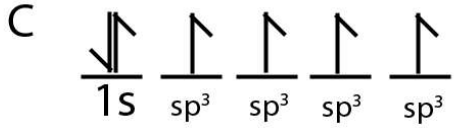
Introduction

Carbon is a perfect example showing the value of hybrid orbitals. Carbon's ground state configuration is:



According to Valence Bond Theory, carbon should form two covalent bonds, resulting in a CH_2, because it has two unpaired electrons in its electronic configuration.However, experiments have shown that $\boldsymbol{CH_2}$ is highly reactive and cannot exist outside of a reaction. Therefore, this does not explain how CH_4 can exist. To form **four** bonds the configuration of carbon must have **four** unpaired electrons.

One way CH_4 can be explained is, the 2s and the 3 2p orbitals combine to make four, equal energy sp^3 hybrid orbitals. That would give us the following configuration:



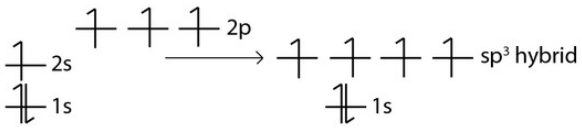
Now that carbon has four unpaired electrons it can have four equal energy bonds. The hybridization of orbitals is favored because hybridized orbitals are more directional which leads to greater overlap when forming bonds, therefore the bonds formed are stronger. This results in more stable compounds when hybridization occurs.

The next section will explain the various types of hybridization and how each type helps explain the structure of certain molecules.

sp^3 hybridization

sp^3 hybridization can explain the tetrahedral structure of molecules. In it, the 2s orbitals and all three of the 2p orbitals hybridize to form four sp^3 orbitals, each consisting of 75% p character and 25% s character. The frontal lobes align themselves in the manner shown below. In this structure, electron repulsion is minimized.

Energy changes occurring in hybridization

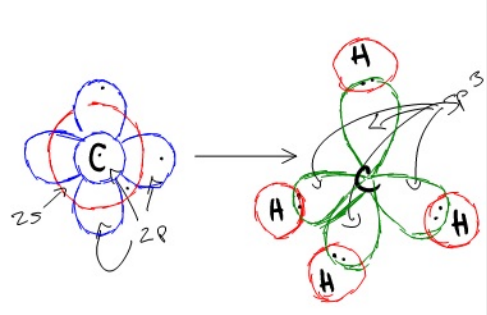


Hybridization of an s orbital with all three p orbitals (p_x , p_y, and p_z) results in four sp^3 hybrid orbitals. sp^3 hybrid orbitals are oriented at bond angle of 109.5° from each other. This 109.5° arrangement gives tetrahedral geometry (Figure 4).

Example: sp^3 Hybridization in Methane

Because carbon plays such a significant role in organic chemistry, we will be using it as an example here. Carbon's 2s and all three of its 2p orbitals hybridize to form four sp^3 orbitals. These orbitals then bond with four hydrogen atoms through sp^3-s orbital overlap, creating methane. The resulting shape is tetrahedral, since that minimizes electron repulsion.

Hybridization

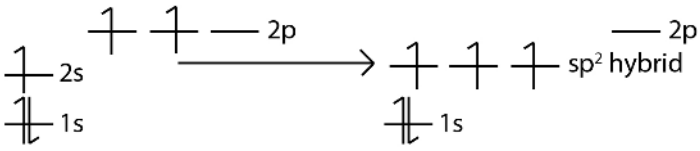


Lone Pairs: Remember to take into account lone pairs of electrons. These lone pairs cannot double bond so they are placed in their own hybrid orbital. This is why H_2O is tetrahedral. We can also build sp_3d and sp_3d_2 hybrid orbitals if we go beyond s and p subshells.

sp^2 hybridization

sp^2 hybridization can explain the trigonal planar structure of molecules. In it, the 2s orbitals and two of the 2p orbitals hybridize to form three sp orbitals, each consisting of 67% p and 33% s character. The frontal lobes align themselves in the trigonal planar structure, pointing to the corners of a triangle in order to minimize electron repulsion and to improve overlap. The remaining p orbital remains unchanged and is perpendicular to the plane of the three sp^2 orbitals.

Energy changes occurring in hybridization

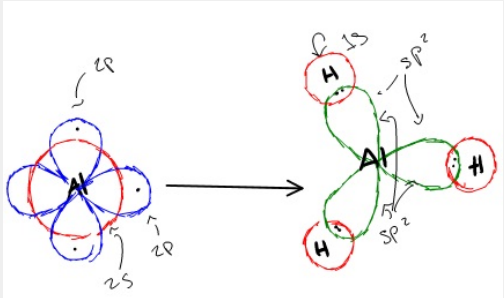


Hybridization of an s orbital with two p orbitals (p_x and p_y) results in three sp^2 hybrid orbitals that are oriented at 120° angle to each other (Figure 3). Sp^2 hybridization results in trigonal geometry.

figure3.gif

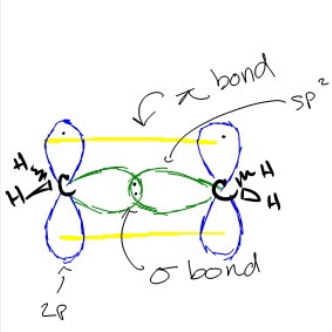
Example: sp^2 Hybridization in Aluminum Trihydride

In aluminum trihydride, one 2s orbital and two 2p orbitals hybridize to form three sp^2 orbitals that align themselves in the trigonal planar structure. The three Al sp^2 orbitals bond with with 1s orbitals from the three hydrogens through sp^2-s orbital overlap.



Example: sp^2 Hybridization in Ethene

Similar hybridization occurs in each carbon of ethene. For each carbon, one 2s orbital and two 2p orbitals hybridize to form three sp^2 orbitals. These hybridized orbitals align themselves in the trigonal planar structure. For each carbon, two of these sp orbitals bond with two 1s hydrogen orbitals through s-sp orbital overlap. The remaining sp^2 orbitals on each carbon are bonded with each other, forming a bond between each carbon through sp^2-sp^2 orbital overlap. This leaves us with the two p orbitals on each carbon that have a single carbon in them. These orbitals form a ? bonds through p-p orbital overlap, creating a double bond between the two carbons. Because a double bond was created, the overall structure of the ethene compound is linear. However, the structure of each molecule in ethene, the two carbons, is still trigonal planar.



sp Hybridization

sp Hybridization can explain the linear structure in molecules. In it, the 2s orbital and one of the 2p orbitals hybridize to form two sp orbitals, each consisting of 50% s and 50% p character. The front lobes face away from each other and form a straight line leaving a 180° angle between the two orbitals. This formation minimizes electron repulsion. Because only one p orbital was used, we are left with two unaltered 2p orbitals that the atom can use. These p orbitals are at right angles to one another and to the line formed by the two sp orbitals.

Energy changes occurring in hybridization

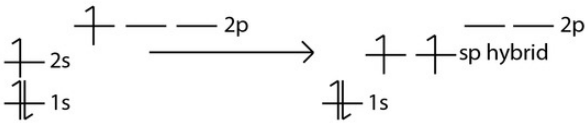


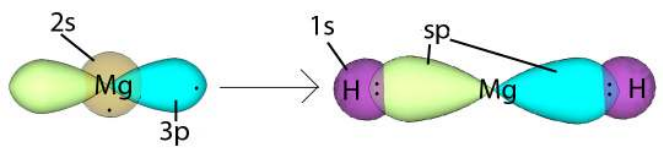
Figure 1: Notice how the energy of the electrons lowers when hybridized.

These p orbitals come into play in compounds such as ethyne where they form two addition? bonds, resulting in in a triple bond. This only happens when two atoms, such as two carbons, both have two p orbitals that each contain an electron. An sp hybrid orbital results when an s orbital is combined with p orbital (Figure 2). We will get two sp hybrid orbitals since we started with two orbitals (s and p). sp hybridization results in a pair of directional sp hybrid orbitals pointed in opposite directions. These hybridized orbitals result in higher electron density in the bonding region for a sigma bond toward the left of the atom and for another sigma bond toward the right. In addition, sp hybridization provides linear geometry with a bond angle of 180°.

Example: sp Hybridization in Magnesium Hydride

In magnesium hydride, the 3s orbital and one of the 3p orbitals from magnesium hybridize to form two sp orbitals. The two frontal lobes of the sp orbitals face away from each other forming a straight line leading to a linear structure. These two sp orbitals bond with the two 1s orbitals of the two hydrogen atoms through sp-s orbital overlap.

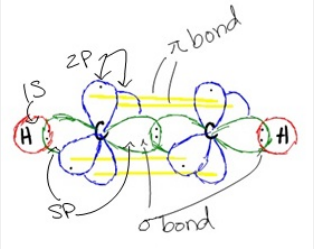
Hybridization

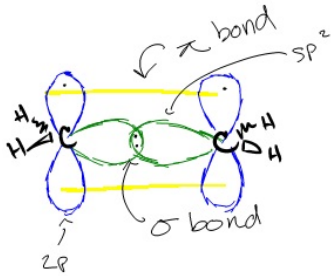


Example: sp Hybridization in Ethyne

The hybridization in ethyne is similar to the hybridization in magnesium hydride. For each carbon, the 2s orbital hybridizes with one of the 2p orbitals to form two sp hybridized orbitals. The frontal lobes of these orbitals face away from each other forming a straight line. The first bond consists of sp-sp orbital overlap between the two carbons. Another two bonds consist of s-sp orbital overlap between the sp hybridized orbitals of the carbons and the 1s orbitals of the hydrogens. This leaves us with two p orbitals on each carbon that have a single carbon in them. This allows for the formation of two ? bonds through p-p orbital overlap. The linear shape, or 180° angle, is formed because electron repulsion is minimized the greatest in this position.

Hybridization





References

1. John Olmsted, Gregory M. Williams Chemistry: The Molecular Science Jones & Bartlett Publishers 1996. 366-371
2. Francis A. Carey Advanced Organic Chemistry Springer 2001. 4-6
3. L. G. Wade, Jr. Whitman College *Organic Chemistry* Fifth Edition 2003

Problems

Using the Lewis Structures, try to figure out the hybridization (sp, sp^2, sp^3) of the indicated atom and indicate the atom's shape.

1. The carbon.



2. The oxygen.



3. The carbon on the right.



Answers

1. sp^2- Trigonal Planar

    The carbon has no lone pairs and is bonded to three hydrogens so we just need three hybrid orbitals, aka sp^2.

2. sp^3 - Tetrahedral

    Don't forget to take into account all the lone pairs. Every lone pair needs it own hybrid orbital. That makes three hybrid orbitals for lone pairs and the oxygen is bonded to one hydrogen which requires another sp^3 orbital. That makes 4 orbitals, aka sp^3.

3. sp - Linear

    The carbon is bonded to two other atoms, that means it needs two hybrid orbitals, aka sp.

An easy way to figure out what hybridization an atom has is to just count the number of atoms bonded to it and the number of lone pairs. Double and triple bonds still count as being only bonded to one atom. Use this method to go over the above problems again and make sure you understand it. It's a lot easier to figure out the hybridization this way.

Contributors

- Harpreet Chima (UCD), Farah Yasmeen

1.7: How Single Bonds Are Formed in Organic Compounds is shared under a not declared license and was authored, remixed, and/or curated by LibreTexts.

- **Hybrid Orbitals** is licensed CC BY-NC-SA 4.0.

1.8: How a Double Bond is Formed- The Bonds in Ethene

Structure and Bonding in Ethene-The Pi Bond

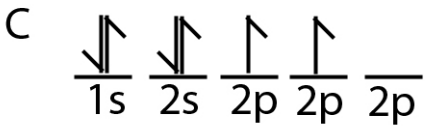
1.8: How a Double Bond is Formed- The Bonds in Ethene is shared under a not declared license and was authored, remixed, and/or curated by LibreTexts.

1.9: How a Triple Bond is Formed- The Bonds in Ethyne

Hybridization was introduced to explain molecular structure when the valence bond theory failed to correctly predict them. It is experimentally observed that bond angles in organic compounds are close to 109°, 120°, or 180°. According to Valence Shell Electron Pair Repulsion (VSEPR) theory, electron pairs repel each other and the bonds and lone pairs around a central atom are generally separated by the largest possible angles.

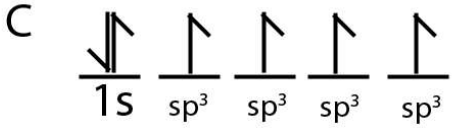
Introduction

Carbon is a perfect example showing the value of hybrid orbitals. Carbon's ground state configuration is:



According to Valence Bond Theory, carbon should form two covalent bonds, resulting in a CH_2, because it has two unpaired electrons in its electronic configuration.However, experiments have shown that $\boldsymbol{CH_2}$ is highly reactive and cannot exist outside of a reaction. Therefore, this does not explain how CH_4 can exist. To form **four** bonds the configuration of carbon must have **four** unpaired electrons.

One way CH_4 can be explained is, the 2s and the 3 2p orbitals combine to make four, equal energy sp^3 hybrid orbitals. That would give us the following configuration:



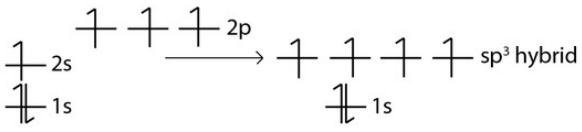
Now that carbon has four unpaired electrons it can have four equal energy bonds. The hybridization of orbitals is favored because hybridized orbitals are more directional which leads to greater overlap when forming bonds, therefore the bonds formed are stronger. This results in more stable compounds when hybridization occurs.

The next section will explain the various types of hybridization and how each type helps explain the structure of certain molecules.

sp^3 hybridization

sp^3 hybridization can explain the tetrahedral structure of molecules. In it, the 2s orbitals and all three of the 2p orbitals hybridize to form four sp^3 orbitals, each consisting of 75% p character and 25% s character. The frontal lobes align themselves in the manner shown below. In this structure, electron repulsion is minimized.

Energy changes occurring in hybridization

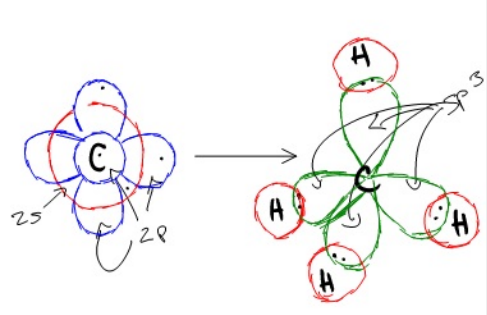


Hybridization of an s orbital with all three p orbitals (p_x , p_y, and p_z) results in four sp^3 hybrid orbitals. sp^3 hybrid orbitals are oriented at bond angle of 109.5° from each other. This 109.5° arrangement gives tetrahedral geometry (Figure 4).

Example: sp^3 Hybridization in Methane

Because carbon plays such a significant role in organic chemistry, we will be using it as an example here. Carbon's 2s and all three of its 2p orbitals hybridize to form four sp^3 orbitals. These orbitals then bond with four hydrogen atoms through sp^3-s orbital overlap, creating methane. The resulting shape is tetrahedral, since that minimizes electron repulsion.

Hybridization

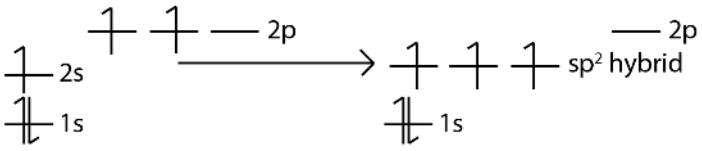


Lone Pairs: Remember to take into account lone pairs of electrons. These lone pairs cannot double bond so they are placed in their own hybrid orbital. This is why H_2O is tetrahedral. We can also build sp_3d and sp_3d_2 hybrid orbitals if we go beyond s and p subshells.

sp^2 hybridization

sp^2 hybridization can explain the trigonal planar structure of molecules. In it, the 2s orbitals and two of the 2p orbitals hybridize to form three sp orbitals, each consisting of 67% p and 33% s character. The frontal lobes align themselves in the trigonal planar structure, pointing to the corners of a triangle in order to minimize electron repulsion and to improve overlap. The remaining p orbital remains unchanged and is perpendicular to the plane of the three sp^2 orbitals.

Energy changes occurring in hybridization

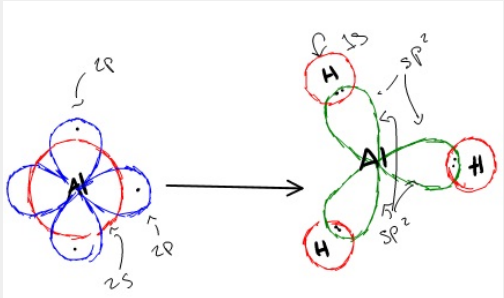


Hybridization of an s orbital with two p orbitals (p_x and p_y) results in three sp^2 hybrid orbitals that are oriented at 120° angle to each other (Figure 3). Sp^2 hybridization results in trigonal geometry.

figure3.gif

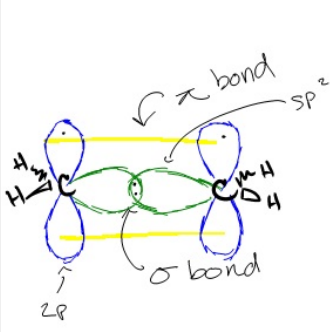
Example: sp^2 Hybridization in Aluminum Trihydride

In aluminum trihydride, one 2s orbital and two 2p orbitals hybridize to form three sp^2 orbitals that align themselves in the trigonal planar structure. The three Al sp^2 orbitals bond with with 1s orbitals from the three hydrogens through sp^2-s orbital overlap.



Example: sp^2 Hybridization in Ethene

Similar hybridization occurs in each carbon of ethene. For each carbon, one 2s orbital and two 2p orbitals hybridize to form three sp^2 orbitals. These hybridized orbitals align themselves in the trigonal planar structure. For each carbon, two of these sp orbitals bond with two 1s hydrogen orbitals through s-sp orbital overlap. The remaining sp^2 orbitals on each carbon are bonded with each other, forming a bond between each carbon through sp^2-sp^2 orbital overlap. This leaves us with the two p orbitals on each carbon that have a single carbon in them. These orbitals form a ? bonds through p-p orbital overlap, creating a double bond between the two carbons. Because a double bond was created, the overall structure of the ethene compound is linear. However, the structure of each molecule in ethene, the two carbons, is still trigonal planar.



sp Hybridization

sp Hybridization can explain the linear structure in molecules. In it, the 2s orbital and one of the 2p orbitals hybridize to form two sp orbitals, each consisting of 50% s and 50% p character. The front lobes face away from each other and form a straight line leaving a 180° angle between the two orbitals. This formation minimizes electron repulsion. Because only one p orbital was used, we are left with two unaltered 2p orbitals that the atom can use. These p orbitals are at right angles to one another and to the line formed by the two sp orbitals.

Energy changes occurring in hybridization

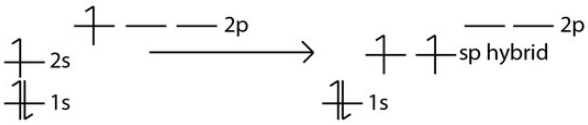


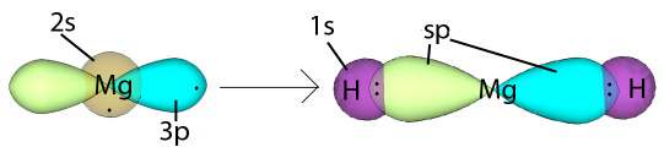
Figure 1: Notice how the energy of the electrons lowers when hybridized.

These p orbitals come into play in compounds such as ethyne where they form two addition? bonds, resulting in in a triple bond. This only happens when two atoms, such as two carbons, both have two p orbitals that each contain an electron. An sp hybrid orbital results when an s orbital is combined with p orbital (Figure 2). We will get two sp hybrid orbitals since we started with two orbitals (s and p). sp hybridization results in a pair of directional sp hybrid orbitals pointed in opposite directions. These hybridized orbitals result in higher electron density in the bonding region for a sigma bond toward the left of the atom and for another sigma bond toward the right. In addition, sp hybridization provides linear geometry with a bond angle of 180°.

Example: sp Hybridization in Magnesium Hydride

In magnesium hydride, the 3s orbital and one of the 3p orbitals from magnesium hybridize to form two sp orbitals. The two frontal lobes of the sp orbitals face away from each other forming a straight line leading to a linear structure. These two sp orbitals bond with the two 1s orbitals of the two hydrogen atoms through sp-s orbital overlap.

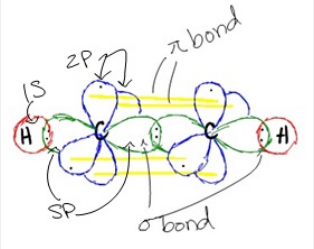
Hybridization

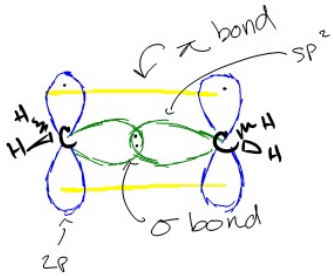


Example: sp Hybridization in Ethyne

The hybridization in ethyne is similar to the hybridization in magnesium hydride. For each carbon, the 2s orbital hybridizes with one of the 2p orbitals to form two sp hybridized orbitals. The frontal lobes of these orbitals face away from each other forming a straight line. The first bond consists of sp-sp orbital overlap between the two carbons. Another two bonds consist of s-sp orbital overlap between the sp hybridized orbitals of the carbons and the 1s orbitals of the hydrogens. This leaves us with two p orbitals on each carbon that have a single carbon in them. This allows for the formation of two ? bonds through p-p orbital overlap. The linear shape, or 180° angle, is formed because electron repulsion is minimized the greatest in this position.

Hybridization





References

1. John Olmsted, Gregory M. Williams Chemistry: The Molecular Science Jones & Bartlett Publishers 1996. 366-371
2. Francis A. Carey Advanced Organic Chemistry Springer 2001. 4-6
3. L. G. Wade, Jr. Whitman College *Organic Chemistry* Fifth Edition 2003

Problems

Using the Lewis Structures, try to figure out the hybridization (sp, sp^2, sp^3) of the indicated atom and indicate the atom's shape.

1. The carbon.



2. The oxygen.



3. The carbon on the right.



Answers

1. sp^2- Trigonal Planar

    The carbon has no lone pairs and is bonded to three hydrogens so we just need three hybrid orbitals, aka sp^2.

2. sp^3 - Tetrahedral

    Don't forget to take into account all the lone pairs. Every lone pair needs it own hybrid orbital. That makes three hybrid orbitals for lone pairs and the oxygen is bonded to one hydrogen which requires another sp^3 orbital. That makes 4 orbitals, aka sp^3.

3. sp - Linear

    The carbon is bonded to two other atoms, that means it needs two hybrid orbitals, aka sp.

An easy way to figure out what hybridization an atom has is to just count the number of atoms bonded to it and the number of lone pairs. Double and triple bonds still count as being only bonded to one atom. Use this method to go over the above problems again and make sure you understand it. It's a lot easier to figure out the hybridization this way.

Contributors

- Harpreet Chima (UCD), Farah Yasmeen

1.9: How a Triple Bond is Formed- The Bonds in Ethyne is shared under a not declared license and was authored, remixed, and/or curated by LibreTexts.

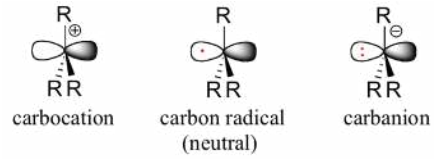
- **Hybrid Orbitals** is licensed CC BY-NC-SA 4.0.

1.10: Bonding in the Methyl Cation, the Methyl Radical, and the Methyl Anion

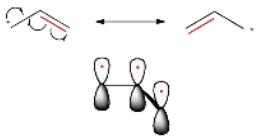
Solutions to exercises

17.1A: The geometry and relative stability of carbon radicals

As organic chemists, we are particularly interested in radical intermediates in which the unpaired electron resides on a carbon atom. Experimental evidence indicates that the three bonds in a carbon radical have trigonal planar geometry, and therefore the carbon is considered to be sp^2-hybridized with the unpaired electron occupying the perpendicular, unhybridized $2p_z$orbital. Contrast this picture with carbocation and carbanion intermediates, which are both also trigonal planar but whose $2p_z$ orbitals contain zero or two electrons, respectively.



The trend in the stability of carbon radicals parallels that of carbocations (section 8.4B): tertiary radicals, for example, are more stable than secondary radicals, followed by primary and methyl radicals. This should make intuitive sense, because radicals, like carbocations, can be considered to be electron deficient, and thus are stabilized by the electron-donating effects of nearby alkyl groups. Benzylic and allylic radicals are more stable than alkyl radicals due to resonance effects - an unpaired electron can be delocalized over a system of conjugated pi bonds. An allylic radical, for example, can be pictured as a system of three parallel $2p_z$ orbitals sharing three electrons.

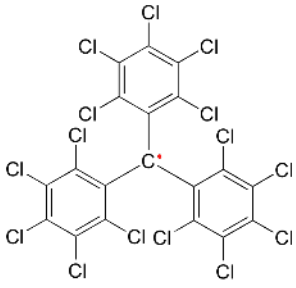


Template:ExampleStart

Exercise 17.1: Draw the structure of a benzylic radical compound, and then draw a resonance form showing how the radical is stabilized.

Template:ExampleEnd

With enough resonance stabilization, radicals can be made that are quite unreactive. One example of an inert organic radical structure is shown below.



In this molecule, the already extensive resonance stabilization is further enhanced by the ability of the chlorine atoms to shield the radical center from external reagents. The radical is, in some sense, inside a protective 'cage'.

Template:ExampleStart

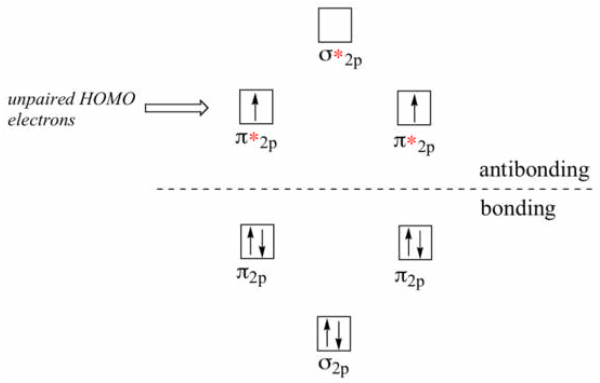
Exercise 17.2: Draw a resonance contributor of the structure above in which the unpaired electron is located on a chlorine atom.

Template:ExampleEnd

17.1B: The diradical character of triplet oxygen

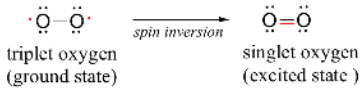
You may be surprised to learn that molecular oxygen (O_2) often reacts like a radical species - or more accurately, like a *di*radical, with *two separate unpaired valence electrons*. This puzzling phenomenon is best explained by molecular orbital theory (you may want to go back to chapter 2 at this point to review basic MO theory).

In molecular orbital energy diagram form, the configuration of O_2 looks like this:



When the molecular orbitals of O_2 are filled up with electrons according to Hund's rule (section 1.1C) , the HOMOs (Highest Occupied Molecular Orbitals) are the two antibonding π^*_{2p} orbitals, each holding a single, unpaired electron. This electron configuration, which describes oxygen in its lowest energy (ground) state, is referred to as the **triplet state** - the oxygen in the air around you is**triplet oxygen**. A higher energy state, in which the two highest energy electrons are paired in the same π^*_{2p} orbital, is called the **singlet state** of oxygen.

It is the last two unpaired electrons in triplet oxygen that react in radical-like fashion. For this reason, triplet O_2 is often depicted by a Lewis structure as a diradical, with a single covalent bond, four lone pairs, and two unpaired electrons. The excited singlet state is often depicted as a doubly-bonded molecule.



These Lewis-dot depictions, while only approximations and unsatisfactory in many respects, can nonetheless be helpful in illustrating how O_2 reacts. In any event, the molecular orbital picture of O_2 is not simply an academic exercise: the diradical model for triplet oxygen is key to understanding its reactivity in many enzymatic and non-enzymatic contexts. We will see one example of triplet oxygen reactivity in section 17.2D.

Organic Chemistry With a Biological Emphasis by Tim Soderberg (University of Minnesota, Morris)

1.10: Bonding in the Methyl Cation, the Methyl Radical, and the Methyl Anion is shared under a not declared license and was authored, remixed, and/or curated by LibreTexts.

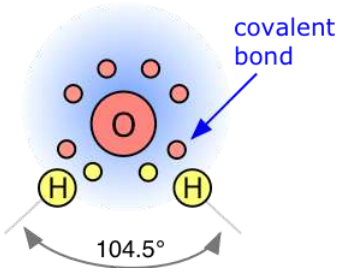
1.11: The Bonds in Water

Learning Objectives

- Identify three special properties of water that make it unusual for a molecule of its size, and explain how these result from hydrogen bonding.
- Explain what is meant by hydrogen bonding and the molecular structural features that bring it about.
- Describe the "structure", such as it is, of liquid water.
- Sketch out structural examples of hydrogen bonding in three small molecules other than H_2O.
- Describe the roles of hydrogen bonding in proteins and in DNA.

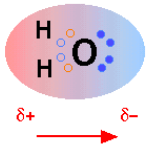
Most students of chemistry quickly learn to relate the structure of a molecule to its general properties. Thus we generally expect small molecules to form gases or liquids, and large ones to exist as solids under ordinary conditions. And then we come to H_2O, and are shocked to find that many of the predictions are way off, and that water (and by implication, life itself) should not even exist on our planet! In this section we will learn why this tiny combination of three nuclei and ten electrons possesses special properties that make it unique among the more than 15 million chemical species we presently know.

In water, each hydrogen nucleus is covalently bound to the central oxygen atom by a pair of electrons that are shared between them. In H_2O, only two of the six outer-shell electrons of oxygen are used for this purpose, leaving four electrons which are organized into two non-bonding pairs. The four electron pairs surrounding the oxygen tend to arrange themselves as far from each other as possible in order to minimize repulsions between these clouds of negative charge. This would ordinarily result in a tetrahedral geometry in which the angle between electron pairs (and therefore the H-O-H *bond angle*) is 109.5°. However, because the two non-bonding pairs remain closer to the oxygen atom, these exert a stronger repulsion against the two covalent bonding pairs, effectively pushing the two hydrogen atoms closer together. The result is a distorted tetrahedral arrangement in which the H—O—H angle is 104.5°.



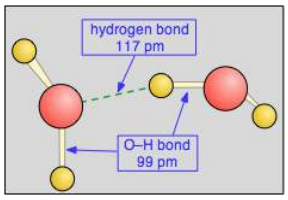
Water's large dipole moment leads to hydrogen bonding

The H_2O molecule is electrically neutral, but the positive and negative charges are not distributed uniformly. This is illustrated by the gradation in color in the schematic diagram here. The electronic (negative) charge is concentrated at the oxygen end of the molecule, owing partly to the nonbonding electrons (solid blue circles), and to oxygen's high nuclear charge which exerts stronger attractions on the electrons. This charge displacement constitutes an *electric dipole*, represented by the arrow at the bottom; you can think of this dipole as the electrical "image" of a water molecule.



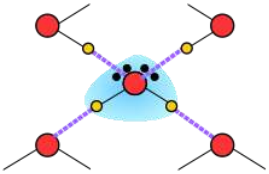
Opposite charges attract, so it is not surprising that the negative end of one water molecule will tend to orient itself so as to be close to the positive end of another molecule that happens to be nearby. The strength of this *dipole-dipole attraction* is less than that of a normal chemical bond, and so it is completely overwhelmed by ordinary thermal motions in the gas phase. However, when the H_2O molecules are crowded together in the liquid, these attractive forces exert a very noticeable effect, which we call (somewhat

misleadingly) *hydrogen bonding*. And at temperatures low enough to turn off the disruptive effects of thermal motions, water freezes into ice in which the hydrogen bonds form a rigid and stable network.



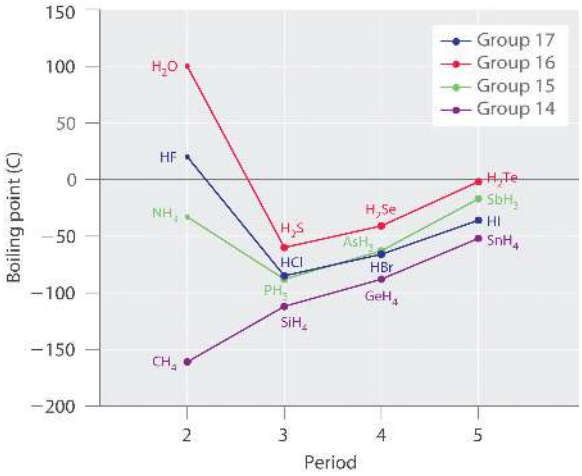
Notice that the hydrogen bond (shown by the dashed green line) is somewhat longer than the covalent O—H bond. It is also *much weaker*, about 23 kJ mol^{-1} compared to the O–H covalent bond strength of 492 kJ mol^{-1}.

Water has long been known to exhibit many physical properties that distinguish it from other small molecules of comparable mass. Although chemists refer to these as the "anomalous" properties of water, they are by no means mysterious; all are entirely predictable consequences of the way the size and nuclear charge of the oxygen atom conspire to distort the electronic charge clouds of the atoms of other elements when these are chemically bonded to the oxygen.



Boiling point

The most apparent peculiarity of water is its **very high boiling point** for such a light molecule. Liquid methane CH_4 (molecular weight 16) boils at –161°C. As you can see from this diagram, extrapolation of the boiling points of the various Group 16 hydrogen compounds to H_2O suggests that this substance should be a gas under normal conditions.

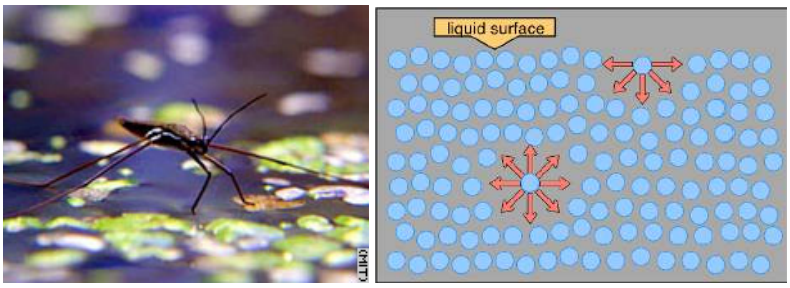


The Effects of Hydrogen Bonding on Boiling Points. These plots of the boiling points of the covalent hydrides of the elements of groups 14–17 show that the boiling points of the lightest members of each series for which hydrogen bonding is possible (HF, NH_3, and H_2O) are anomalously high for compounds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

Surface Tension

Compared to most other liquids, water also has a high **surface tension**. Have you ever watched an insect walk across the surface of a pond? The *water strider* takes advantage of the fact that the water surface acts like an elastic film that resists deformation when a small weight is placed on it. (If you are careful, you can also "float" a small paper clip or steel staple on the surface of water in a cup.) This is all due to the *surface tension* of the water. A molecule within the bulk of a liquid experiences attractions to neighboring molecules in all directions, but since these average out to zero, there is no net force on the molecule. For a molecule

that finds itself *at* the surface, the situation is quite different; it experiences forces only sideways and downward, and this is what creates the stretched-membrane effect.



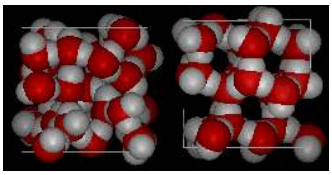
The distinction between molecules located at the surface and those deep inside is especially prominent in H_2O, owing to the strong hydrogen-bonding forces. The difference between the forces experienced by a molecule at the surface and one in the bulk liquid gives rise to the liquid's surface tension. This drawing highlights two H_2O molecules, one at the surface, and the other in the bulk of the liquid. The surface molecule is attracted to its neighbors below and to either side, but there are no attractions pointing in the 180° solid angle angle above the surface. As a consequence, a molecule at the surface will tend to be drawn into the bulk of the liquid. But since there must always be some surface, the overall effect is to minimize the surface area of a liquid.

The geometric shape that has the smallest ratio of surface area to volume is the *sphere*, so very small quantities of liquids tend to form spherical drops. As the drops get bigger, their weight deforms them into the typical tear shape.



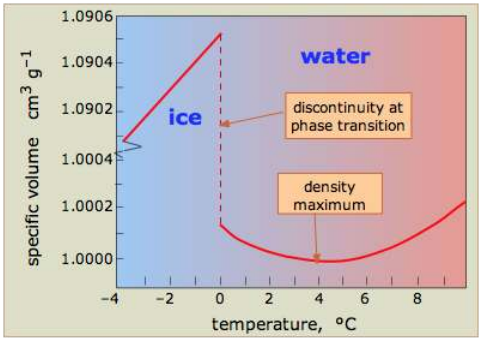
Ice floats on water

The most energetically favorable configuration of H_2O molecules is one in which each molecule is hydrogen-bonded to four neighboring molecules. Owing to the thermal motions described above, this ideal is never achieved in the liquid, but when water freezes to ice, the molecules settle into exactly this kind of an arrangement in the ice crystal. This arrangement requires that the molecules be somewhat farther apart then would otherwise be the case; as a consequence, ice, in which hydrogen bonding is at its maximum, has a more open structure, and thus a lower density than water.



Here are three-dimensional views of a typical local structure of water (left) and ice (right.) Notice the greater openness of the ice structure which is necessary to ensure the strongest degree of hydrogen bonding in a uniform, extended crystal lattice. The more crowded and jumbled arrangement in liquid water can be sustained only by the greater amount of thermal energy available above the freezing point.

When ice melts, the more vigorous thermal motion disrupts much of the hydrogen-bonded structure, allowing the molecules to pack more closely. Water is thus one of the very few substances whose solid form has a lower density than the liquid at the freezing point. Localized clusters of hydrogen bonds still remain, however; these are continually breaking and reforming as the thermal motions jiggle and shove the individual molecules. As the temperature of the water is raised above freezing, the extent and lifetimes of these clusters diminish, so the density of the water increases.



At higher temperatures, another effect, common to all substances, begins to dominate: as the temperature increases, so does the amplitude of thermal motions. This more vigorous jostling causes the average distance between the molecules to increase, reducing the density of the liquid; this is ordinary thermal expansion.

Because the two competing effects (hydrogen bonding at low temperatures and thermal expansion at higher temperatures) both lead to a decrease in density, it follows that there must be some temperature at which the density of water passes through a maximum. This temperature is 4° C; this is the temperature of the water you will find at the bottom of an ice-covered lake in which this most dense of all water has displaced the colder water and pushed it nearer to the surface.

Structure of Liquid Water

The nature of liquid water and how the H_2O molecules within it are organized and interact are questions that have attracted the interest of chemists for many years. There is probably no liquid that has received more intensive study, and there is now a huge literature on this subject. The following facts are well established:

- H_2O molecules attract each other through the special type of dipole-dipole interaction known as hydrogen bonding
- a hydrogen-bonded cluster in which four H_2Os are located at the corners of an imaginary tetrahedron is an especially favorable (low-potential energy) configuration, *but...*
- the molecules undergo rapid thermal motions on a time scale of picoseconds (10^{-12} second), so the lifetime of any specific clustered configuration will be fleetingly brief.

A variety of techniques including infrared absorption, neutron scattering, and nuclear magnetic resonance have been used to probe the microscopic structure of water. The information garnered from these experiments and from theoretical calculations has led to the development of around twenty "models" that attempt to explain the structure and behavior of water. More recently, computer simulations of various kinds have been employed to explore how well these models are able to predict the observed physical properties of water.

This work has led to a gradual refinement of our views about the structure of liquid water, but it has not produced any definitive answer. There are several reasons for this, but the principal one is that the very concept of "structure" (and of water "clusters") depends on both the time frame and volume under consideration. Thus, questions of the following kinds are still open:

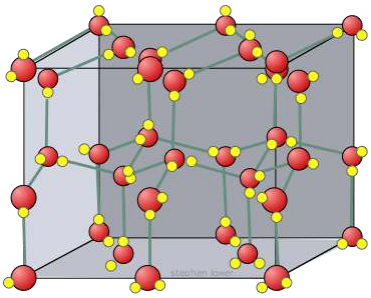
- How do you distinguish the members of a "cluster" from adjacent molecules that are not in that cluster?
- Since individual hydrogen bonds are continually breaking and re-forming on a picosecond time scale, do water clusters have any meaningful existence over longer periods of time? In other words, clusters are transient, whereas "structure" implies a molecular arrangement that is more enduring. Can we then legitimately use the term "clusters" in describing the structure of water?
- The possible locations of neighboring molecules around a given H_2O are limited by energetic and geometric considerations, thus giving rise to a certain amount of "structure" within any small volume element. It is not clear, however, to what extent these structures interact as the size of the volume element is enlarged. And as mentioned above, to what extent are these structures maintained for periods longer than a few picoseconds?

In the 1950's it was assumed that liquid water consists of a mixture of hydrogen-bonded clusters $(H_2O)_n$ in which n can have a variety of values, but little evidence for the existence of such aggregates was ever found. The present view, supported by computer-modeling and spectroscopy, is that on a very short time scale, water is more like a "gel" consisting of a single, huge hydrogen-

bonded cluster. On a 10^{-12}-10^{-9} sec time scale, rotations and other thermal motions cause individual hydrogen bonds to break and re-form in new configurations, inducing ever-changing local discontinuities whose extent and influence depends on the temperature and pressure.

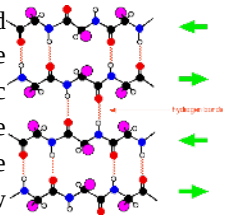
Ice

Ice, like all solids, has a well-defined structure; each water molecule is surrounded by four neighboring H_2Os. two of these are hydrogen-bonded to the oxygen atom on the central H_2O molecule, and each of the two hydrogen atoms is similarly bonded to another neighboring H_2O.



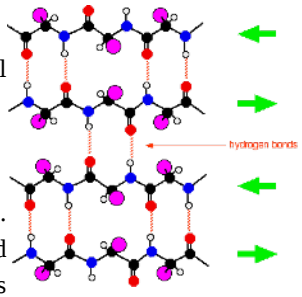
Ice forms crystals having a hexagonal lattice structure, which in their full development would tend to form hexagonal prisms very similar to those sometimes seen in quartz. This does occasionally happen, and anyone who has done much winter mountaineering has likely seen needle-shaped prisms of ice crystals floating in the air. Under most conditions, however, the snowflake crystals we see are flattened into the beautiful fractal-like hexagonal structures that are commonly observed.

Snowflakes



The H_2O molecules that make up the top and bottom plane faces of the prism are packed very closely and linked (through hydrogen bonding) to the molecules inside. In contrast to this, the molecules that make up the sides of the prism, and especially those at the hexagonal corners, are much more exposed, so that atmospheric H_2O molecules that come into contact with most places on the crystal surface attach very loosely and migrate along it until they are able to form hydrogen-bonded attachments to these corners, thus becoming part of the solid and extending the structure along these six directions. This process perpetuates itself as the new extensions themselves acquire a hexagonal structure.

Why is ice slippery?



At temperatures as low as 200 K, the surface of ice is highly disordered and water-like. As the temperature approaches the freezing point, this region of disorder extends farther down from the surface and acts as a lubricant.

The illustration is taken from from an article in the April 7, 2008 issue of C&EN honoring the physical chemist Gabor Somorjai who pioneered modern methods of studying surfaces.

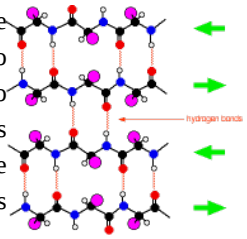
"Pure" water

To a chemist, the term "pure" has meaning only in the context of a particular application or process. The distilled or de-ionized water we use in the laboratory contains dissolved atmospheric gases and occasionally some silica, but their small amounts and relative inertness make these impurities insignificant for most purposes. When water of the highest obtainable purity is required for certain types of exacting measurements, it is commonly filtered, de-ionized, and triple-vacuum distilled. But even this "chemically pure" water is a mixture of isotopic species: there are two stable isotopes of both hydrogen (H^1 and H^2, the latter often denoted by D) and oxygen (O^{16} and O^{18}) which give rise to combinations such as H_2O^{18}, HDO^{16}, etc., all of which are readily identifiable in the infrared spectra of water vapor. And to top this off, the two hydrogen atoms in water contain protons whose magnetic moments can be parallel or antiparallel, giving rise to *ortho*- and *para*-water, respectively. The two forms are normally present in a *o/p* ratio of 3:1.

The amount of the **rare isotopes of oxygen and hydrogen in water** varies enough from place to place that it is now possible to determine the age and source of a particular water sample with some precision. These differences are reflected in the H and O

isotopic profiles of organisms. Thus the isotopic analysis of human hair can be a useful tool for crime investigations and anthropology research.

More about hydrogen bonding

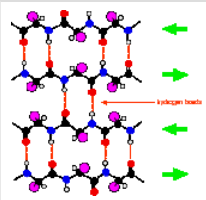
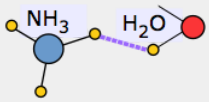
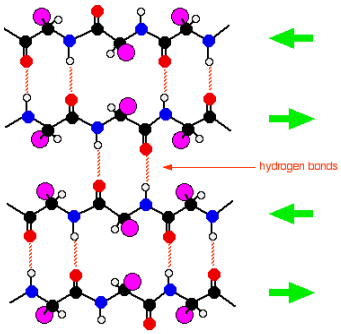
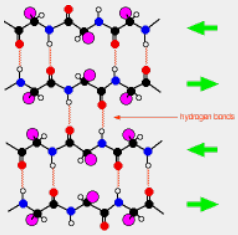
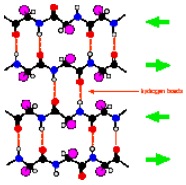
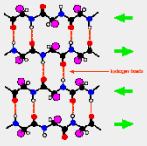
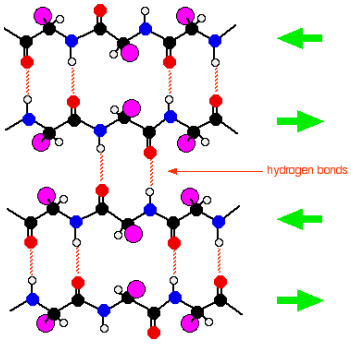
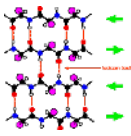


Hydrogen bonds form when the electron cloud of a hydrogen atom that is attached to one of the more electronegative atoms is distorted by that atom, leaving a partial positive charge on the hydrogen. Owing to the very small size of the hydrogen atom, the density of this partial charge is large enough to allow it to interact with the lone-pair electrons on a nearby electronegative atom. Although hydrogen bonding is commonly described as a form of dipole-dipole attraction, it is now clear that it involves a certain measure of electron-sharing (between the external non-bonding electrons and the hydrogen) as well, so these bonds possess some covalent character.

Hydrogen bonds are longer than ordinary covalent bonds, and they are also weaker. The experimental evidence for hydrogen bonding usually comes from X-ray diffraction studies on solids that reveal shorter-than-normal distances between hydrogen and other atoms.

Hydrogen bonding in small molecules

The following examples show something of the wide scope of hydrogen bonding in molecules.

	**Ammonia** (mp –78, bp –33°C) is hydrogen-bonded in the liquid and solid states.
	Hydrogen bonding is responsible for **ammonia**'s remarkably high solubility in water.
	Many **organic (carboxylic) acids** form hydrogen-bonded dimers in the solid state.
	Here the hydrogen bond acceptor is the π electron cloud of a benzene ring. This type of interaction is important in maintaining the shape of proteins.
	**Hydrogen fluoride** (mp –92, bp 33°C) is another common substance that is strongly hydrogen-bonded in its condensed phases.
	The **bifluoride ion** (for which no proper Lewis structure can be written) can be regarded as a complex ion held together by the strongest hydrogen bond known: about 155 kJ mol^{-1}.
	 "***As slow as molasses in the winter!***" Multiple hydroxyl groups provide lots of opportunities for hydrogen bonding and lead to the high viscosities of substances such as **glycerine** and **sugar syrups**.

Hydrogen bonding in biopolymers

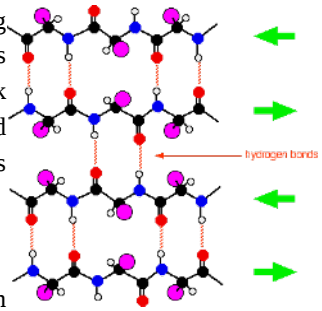
Hydrogen bonding plays an essential role in natural polymers of biological origin in two ways:

- Hydrogen bonding between adjacent polymer chains (intermolecular bonding);
- Hydrogen bonding between different parts of the same chain (intramolecular bonding;
- Hydrogen bonding of water molecules to –OH groups on the polymer chain ("bound water") that helps maintain the shape of the polymer.

The examples that follow are representative of several types of biopolymers.

Cellulose

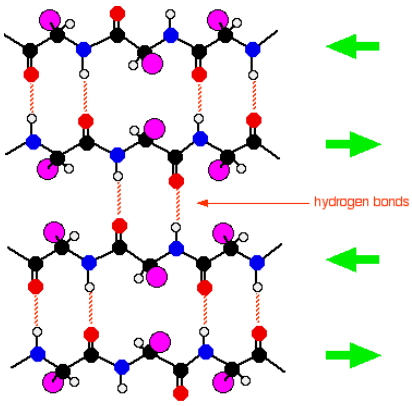
Cellulose is a linear polymer of glucose (see above), containing 300 to over 10,000 units, depending on the source. As the principal structural component of plants (along with lignin in trees), cellulose is the most abundant organic substance on the earth. The role of hydrogen bonding is to cross-link individual molecules to build up sheets as shown here. These sheets than stack up in a staggered array held together by van der Waals forces. Further hydrogen-bonding of adjacent stacks bundles them together into a stronger and more rigid structure.



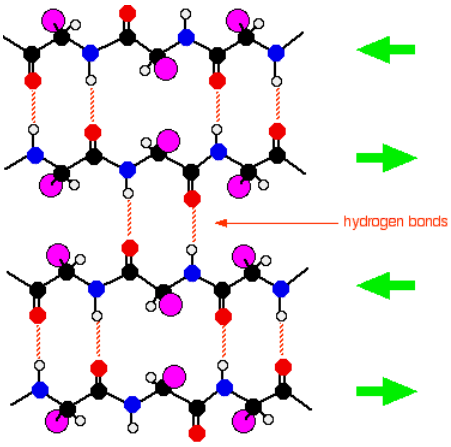
Proteins

These polymers made from amino acids R—CH(NH_2)COOH depend on intramolecular hydrogen bonding to maintain their shape (secondary and tertiary structure) which is essential for their important function as biological catalysts (enzymes). Hydrogen-bonded water molecules embedded in the protein are also important for their structural integrity.

The principal hydrogen bonding in proteins is between the -N—H groups of the "amino" parts with the -C=O groups of the "acid" parts. These interactions give rise to the two major types of the secondary structure which refers to the arrangement of the amino acid polymer chain:



alpha-helix
[images]



beta-sheet

Although carbon is not usually considered particularly electronegative, C—H----X hydrogen bonds are also now known to be significant in proteins.

DNA (Deoxyribonucleic acid)

Who you are is totally dependent on hydrogen bonds! DNA, as you probably know, is the most famous of the biopolymers owing to its central role in defining the structure and function of all living organisms. Each strand of DNA is built from a sequence of four different *nucleotide monomers* consisting of a *deoxyribose sugar*, *phosphate groups*, and a *nitrogenous base* conventionally identified by the letters A,T, C and G. DNA itself consists of two of these *polynucleotide chains* that are coiled around a common axis in a configuration something like the protein alpha helix depicted above. The sugar-and-phosphate backbones are on the outside so that the nucleotide bases are on the inside and facing each other. The two strands are held together by hydrogen bonds

that link a nitrogen atom of a nucleotide in one chain with a nitrogen or oxygen on the nucleotide that is across from it on the other chain.

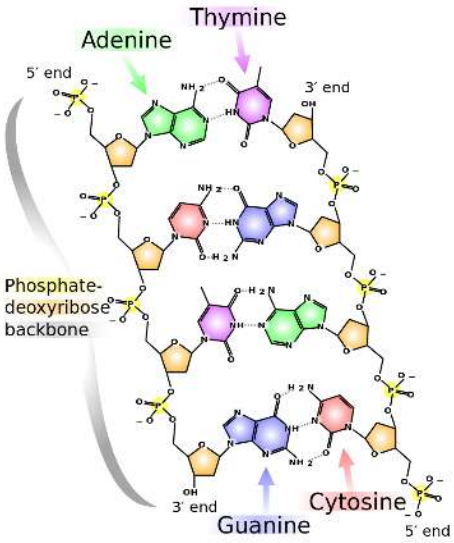


Figure: Chemical structure of DNA; hydrogen bonds shown as dotted lines. Image used with permisison from Wikipedia.

Efficient hydrogen bonding within this configuration can only occur between the pairs A-T and C-G, so these two complementary pairs constitute the "alphabet" that encodes the genetic information that gets transcribed whenever new protein molecules are built. Water molecules, hydrogen-bonded to the outer parts of the DNA helix, help stabilize it.

1.11: The Bonds in Water is shared under a not declared license and was authored, remixed, and/or curated by LibreTexts.

- **7.3: Hydrogen-Bonding and Water** by Stephen Lower is licensed CC BY 3.0. Original source: http://www.chem1.com/acad/webtext/virtualtextbook.html.

1.12: The Bonds in Ammonia and in the Ammonium Ion

Name: _____

Section: _____

Student ID#:_____

Work in groups on these problems. You should try to answer the questions without referring to your textbook. If you get stuck, try asking another group for help.

What is the first step that you must do in order to draw the electron dot formula for ammonia, NH_3?

The first step in drawing the electron dot formula for ammonia is to determine the number of bonding electrons for each of the atoms. The arabic numeral above the element's column in the periodic table gives you that number.

What are the numbers of bonding electrons for the nitrogen atom and the hydrogen atoms?

The nitrogen atom has 5 electrons and each of the three hydrogen atoms has 1 electron. The total number of electrons for ammonia will therefore be 8 electrons.

Draw a hydrogen atom next to a nitrogen atom and place a pair of electrons between these two atoms.

Now draw a second hydrogen atom next to the nitrogen atom and place a second pair of electrons between these atoms.

Now draw a third hydrogen atom next to the nitrogen atom and place a third pair of electrons between these atoms.

You have now used 6 of the 8 electrons. Place the remaining two electrons on the nitrogen atom. Remember that each hydrogen atom should not have more than 2 electrons and the nitrogen atom should have a total of 8 electrons.



The electron dot formula for ammonia is now complete. Note that the nitrogen atom now has three bonds. This is the normal number of bonds for a nitrogen atom when it does not have a charge.

Ammonia
NH_3

Click here to see an animated gif of this process...

1.12: The Bonds in Ammonia and in the Ammonium Ion is shared under a not declared license and was authored, remixed, and/or curated by LibreTexts.

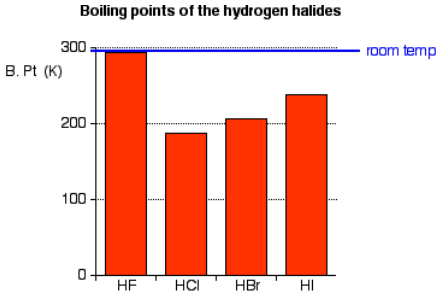
- **Ammonia (Worksheet)** by Mark Draganjac is licensed CC BY-NC-SA 4.0. Original source: http://myweb.astate.edu/mdraganj/worksheetlist.html.

1.13: The Bond in a Hydrogen Halide

This page discusses the acidity of the hydrogen halides: hydrogen fluoride, hydrogen chloride, hydrogen bromide and hydrogen iodide. It begins by describing their physical properties and synthesis and then explains what happens when they react with water to make acids such as hydrofluoric acid and hydrochloric acid.

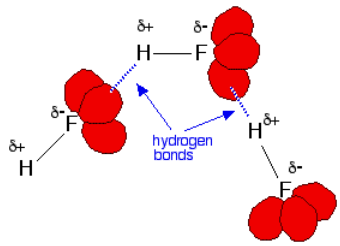
Physical properties

The hydrogen halides are colorless gases at room temperature, producing steamy fumes in moist air. The boiling points of these compounds are shown in the figure below:



Hydrogen fluoride has an abnormally high boiling point for a molecule of its size (293 K or 20°C), and can condense under cool conditions. This is due to the fact that hydrogen fluoride can form hydrogen bonds. Because fluorine is the most electronegative of all the elements, the fluorine-hydrogen bond is highly polarized. The hydrogen atom carries a high partial positive charge (δ+); the fluorine is fairly negatively charged (δ-).

In addition, each fluorine atom has 3 lone pairs of electrons. Fluorine's outer electrons are at the n=2 level, and the lone pairs represent small, highly charged regions of space. Hydrogen bonds form between the δ+ hydrogen on one HF molecule and a lone pair on the fluorine of another one.The figure below illustrates this association:



The other hydrogen halides do not form hydrogen bonds because the larger halogens are not as electronegative as fluorine; therefore, the bonds are less polar. In addition, their lone pairs are at higher energy levels, so the halogen does not carry such an intensely concentrated negative charge; therefore, other hydrogen atoms are not attracted as strongly.

Making hydrogen halides

There are several ways of synthesizing hydrogen halides; the method considered here is the reaction between an ionic halide, like sodium chloride, and an acid like concentrated phosphoric(V) acid, H_3PO_4, or concentrated sulfuric acid.

Making hydrogen chloride

When concentrated sulfuric acid is added to sodium chloride under cold conditions, the acid donates a proton to a chloride ion, forming hydrogen chloride. In the gas phase, it immediately escapes from the system.

$$Cl^- + H_2SO_4 \rightarrow HCl + HSO_4^-$$

The full equation for the reaction is:

$$NaCl + H_2SO_4 \rightarrow HCl + NaHSO_4$$

Sodium bisulfate is also formed in the reaction. Concentrated phosphoric(V) acid reacts similarly, according to the following equation:

$$Cl^- + H_3PO_4 \rightarrow HCl + H_2PO_4^-$$

The full ionic equation showing the formation of the salt, sodium biphosphate(V), is given below:

$$NaCl + H_3PO_4 \rightarrow HCl + NaH_2PO_4$$

Making other hydrogen halides

All hydrogen halides can be formed by the same method, using concentrated phosphoric(V) acid.

Concentrated sulfuric acid, however, behaves differently. Hydrogen fluoride can be made with sulfuric acid, but hydrogen bromide and hydrogen iodide cannot.

The problem is that concentrated sulfuric acid is an oxidizing agent, and as well as producing hydrogen bromide or hydrogen iodide, some of the halide ions are oxidized to bromine or iodine. Phosphoric acid does not have this ability because it is not an oxidant.

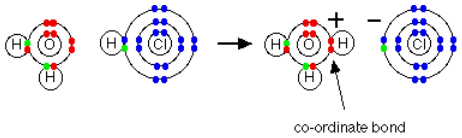
The acidity of the hydrogen halides

Hydrogen chloride as an acid

By the Bronsted-Lowry definition of an acid as a proton donor, hydrogen chloride is an acid because it transfers protons to other species. Consider its reaction with water.

Hydrogen chloride gas is soluble in water; its solvated form is hydrochloric acid. Hydrogen chloride fumes in moist air are caused by hydrogen chloride reacting with water vapor in the air to produce a cloud of concentrated hydrochloric acid.

A proton is donated from the hydrogen chloride to one of the lone pairs on a water molecule.



A coordinate (dative covalent) bond is formed between the oxygen and the transferred proton.

The equation for the reaction is the following:

$$H_2O + HCl \rightarrow H_3O^+ + Cl^-$$

The H_3O^+ ion is the hydroxonium ion (also known as the hydronium ion or the oxonium ion). This is the normal form of protons in water; sometimes it is shortened to the proton form, $H^+(aq)$, for brevity.

When hydrogen chloride dissolves in water (to produce hydrochloric acid), almost all the hydrogen chloride molecules react in this way. Hydrochloric acid is therefore a strong acid. An acid is strong if it is fully ionized in solution.

Hydrobromic acid and hydriodic acid as strong acids

Hydrogen bromide and hydrogen iodide dissolve in (and react with) water in exactly the same way as hydrogen chloride does. Hydrogen bromide forms hydrobromic acid; hydrogen iodide gives hydriodic acid. Both of these are also strong acids.

Hydrofluoric acid as an exception

By contrast, although hydrogen fluoride dissolves freely in water, hydrofluoric acid is only a weak acid; it is similar in strength to organic acids like methanoic acid. The complicated reason for this is discussed below.

The bond enthalpy of the H-F bond

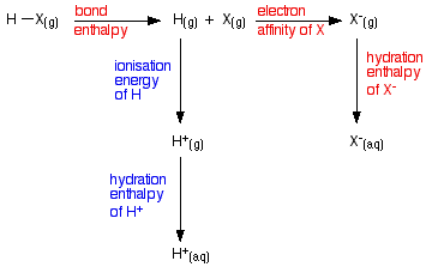
Because the fluorine atom is so small, the bond enthalpy (bond energy) of the hydrogen-fluorine bond is very high. The chart below gives values for all the hydrogen-halogen bond enthalpies:

	bond enthalpy (kJ mol^{-1})
H-F	+562
H-Cl	+431
H-Br	+366
H-I	+299

In order for ions to form when the hydrogen fluoride reacts with water, the H-F bond must be broken. It would seem reasonable to say that the relative reluctance of hydrogen fluoride to react with water is due to the large amount of energy needed to break that bond, but this explanation does not hold.

The energetics of the process from HX(g) to X^-(aq)

The energetics of this sequence are of interest:



All of these terms are involved in the overall enthalpy change as you convert $HX_{(g)}$ into its ions in water.

However, the terms involving the hydrogen are the same for every hydrogen halide. Only the values for the red terms in the diagram need be considered. The values are tabulated below:

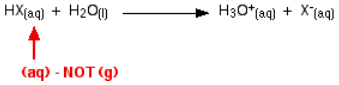
	bond enthalpy of HX (kJ mol^{-1})	electron affinity of X (kJ mol^{-1})	hydration enthalpy of X^- (kJ mol^{-1})	sum of these (kJ mol^{-1})
HF	+562	-328	-506	-272
HCl	+431	-349	-364	-282
HBr	+366	-324	-335	-293
HI	+299	-295	-293	-289

There is virtually no difference in the total HF and HCl values.

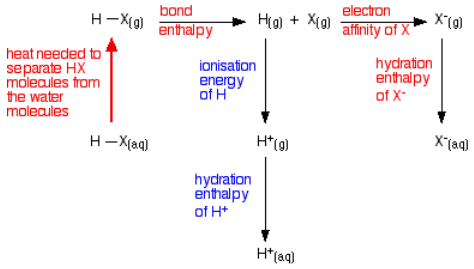
The large bond enthalpy of the H-F bond is offset by the large hydration enthalpy of the fluoride ion. There is a very strong attraction between the very small fluoride ion and the water molecules. This releases a lot of heat (the hydration enthalpy) when the fluoride ion becomes wrapped in water molecules.

Other attractions in the system

The energy terms considered previously have concerned HX molecules in the gas phase. To reach a more correct explanation, the molecules must first be considered as unreacted aqueous HX molecules. The equation for this is given below:



The equation is incorporated into an improved energy cycle as follows:



Unfortunately, values for the first step in the reaction are not readily available. However, in each case, the initial separation of the HX from water molecules is endothermic. Energy is required to break the intermolecular attractions between the HX molecules and water.

That energy is much greater for hydrogen fluoride because it forms hydrogen bonds with water. The other hydrogen halides experience only the weaker van der Waals dispersion forces or dipole-dipole attractions.

The overall enthalpy changes (including all the stages in the energy cycle) for the reactions are given in the table below:

$$HX(aq) + H_2O(l) \rightarrow H_3O^+(aq) + X^-(aq)$$

	enthalpy change (kJ mol^{-1})
HF	-13
HCl	-59
HBr	-63
H-I	-57

The enthalpy change for HF is much smaller in magnitude than that for the other three hydrogen halides, but it is still negative exothermic change. Therefore, more information is needed to explain why HF is a weak acid.

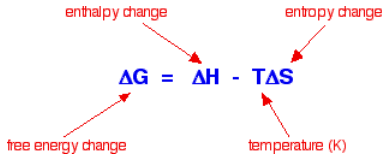
Entropy and free energy considerations

The free energy change, not the enthalpy change, determines the extent and direction of a reaction.

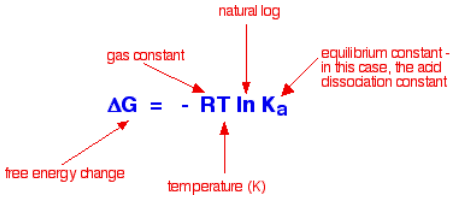
Free energy change is calculated from the enthalpy change, the temperature of the reaction and the entropy change during the reaction.

For simplicity, entropy can be thought of as a measure of the amount of disorder in a system. Entropy is given the symbol **S**. If a system becomes more disordered, then its entropy increases. If it becomes more ordered, its entropy decreases.

The key equation is given below:



In simple terms, for a reaction to happen, the free energy change must be negative. But more accurately, the free energy change can be used to calculate a value for the equilibrium constant for a reaction using the following expression:



The term K_a is the equilibrium constant for the reaction below:

$$HX(aq) + H_2O(l) \rightleftharpoons H_3O^+(aq) + X^-(aq)$$

The values for TΔS (needed to calculate ΔG) for the four reactions at a temperature of 298 K are tabulated below:

	$T_\Delta S$ (kJ mol^{-1})
HF	-29
HCl	-13
HBr	-4
H-I	+4

Notice that at the top of the group, the systems become more ordered when the HX reacts with the water. The entropy of the system (the amount of disorder) decreases, particularly for the hydrogen fluoride.

The reason for this is that the very strong attraction between H_3O^+ and $F^-_{(aq)}$ imposes a lot of order on the system, as does the attraction between the water molecules and the various ions present. These attractions are each greatest for the small fluoride ions.

The total effect on the free energy change, and therefore the value of the equilibrium constant, can now be considered. These values are calculated in the following table:

	$_\Delta H$ (kJ mol^{-1})	$T_\Delta S$ (kJ mol^{-1})	$_\Delta G$ (kJ mol^{-1})	K_a (mol dm^{-3})
HF	-13	-29	+16	1.6×10^{-3}
HCl	-59	-13	-46	1.2×10^{8}
HBr	-63	-4	-59	2.2×10^{10}
HI	-57	+4	-61	5.0×10^{10}

The values for these estimated equilibrium constants for HCl, HBr and HI are so high that the reaction can be considered "one-way". The ionization is virtually 100% complete. These are all strong acids, increasing in strength down the group.

By contrast, the estimated K_a for hydrofluoric acid is small. Hydrofluoric acid only ionizes to a limited extent in water. Therefore, it is a weak acid.

The estimated value for HF in the table can be compared to the experimental value:

- Experimental value: 5.6×10^{-4} mol dm^{-3}
- Estimated value: 1.6×10^{-3} mol dm^{-3}

These values differ by an order of magnitude, but because of the logarithmic relationship between the free energy and the equilibrium constant, a very small change in ΔG has a very large effect on K_a.

To have the values in close agreement, ΔG would have to increase from +16 to +18.5 kJ mol^{-1}. Given the uncertainty in the values used to calculate ΔG, the difference between the calculated value and the experimental value could easily fall within this range.

Summary: Why is hydrofluoric acid a weak acid?

The two main factors are:

- Entropy decreases dramatically when the hydrogen fluoride reacts with water. This is particularly noticeable with hydrogen fluoride because the attraction of the small fluoride ions produced imposes significant order on the surrounding water molecules and nearby hydronium ions. The effect decreases with larger halide ions.

- Very strong hydrogen bonding exists between the hydrogen fluoride molecules and water molecules. This costs a large amount of energy to break. This effect does not occur in the other hydrogen halides.

Contributors and Attributions

Jim Clark (Chemguide.co.uk)

1.13: The Bond in a Hydrogen Halide is shared under a not declared license and was authored, remixed, and/or curated by LibreTexts.

- **The Acidity of the Hydrogen Halides** by Jim Clark is licensed CC BY-NC 4.0.

1.14: Summary- Hybridization, Bond Lengths, Bond Strengths, and Bond Angles

Bond order is the number of chemical bonds between a pair of atoms and indicates the stability of a bond. For example, in diatomic nitrogen, N≡N, the bond order is 3; in acetylene, H−C≡C−H, the carbon-carbon bond order is also 3, and the C−H bond order is 1. Bond order and bond length indicate the type and strength of covalent bonds between atoms. Bond order and length are inversely proportional to each other: when bond order is increased, bond length is decreased.

Introduction

Chemistry deals with the way in which subatomic particles bond together to form atoms. Chemistry also focuses on the way in which atoms bond together to form molecules. In the atomic structure, electrons surround the atomic nucleus in regions called orbitals. Each orbital shell can hold a certain number of electrons. When the nearest orbital shell is full, new electrons start to gather in the next orbital shell out from the nucleus, and continue until that shell is also full. The collection of electrons continues in ever widening orbital shells as larger atoms have more electrons than smaller atoms. When two atoms bond to form a molecule, their electrons bond them together by mixing into openings in each others' orbital shells. As with the collection of electrons by the atom, the formation of bonds by the molecule starts at the nearest available orbital shell opening and expand outward.

Bond Order

Bond order is the number of bonding pairs of electrons between two atoms. In a covalent bond between two atoms, a single bond has a bond order of one, a double bond has a bond order of two, a triple bond has a bond order of three, and so on. To determine the bond order between two covalently bonded atoms, follow these steps:

1. Draw the Lewis structure.
2. Determine the type of bonds between the two atoms.
    - 0: No bond
    - 1: Single bond
    - 2: double bond
    - 3: triple bond

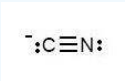
If the bond order is zero, the molecule cannot form. The higher bond orders indicate greater stability for the new molecule. In molecules that have resonance bonding, the bond order does not need to be an integer.

Example 1.14.1: CN^-

Determine the bond order for cyanide, CN^-.

Solution

1) Draw the Lewis structure.



2) Determine the type of bond between the two atoms.

Because there are 3 dashes, the bond is a triple bond. A triple bond corresponds to a bond order of 3.

Example 1.14.2: H_2

Determine the bond order for hydrogen gas, H_2.

Solution

1) Draw the Lewis structure.



2) Determine the type of bond between the two atoms.

There is only one pair of shared electrons (or dash), indicating is a single bond, with a bond order of 1.

Polyatomic molecules

If there are more than two atoms in the molecule, follow these steps to determine the bond order:

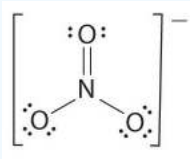
1. Draw the Lewis structure.
2. Count the total number of bonds.
3. Count the number of bond groups between individual atoms.
4. Divide the number of bonds between atoms by the total number of bond groups in the molecule.

Example 1.14.3: NO_3^-

Determine the bond order for nitrate, NO_3^-.

Solution

1) Draw the Lewis structure.



2) Count the total number of bonds.

4

The total number of bonds is 4.

3) Count the number of bond groups between individual atoms.

3

The number of bond groups between individual atoms is 3.

4) Divide the number of bonds between individual atoms by the total number of bonds.

$$\frac{4}{3} = 1.33 \tag{1.14.1}$$

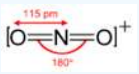
The bond order is 1.33

Example 1.14.4: NO_2^+

Determine the bond order for nitronium ion: NO_2^+.

Solution

1) Draw the Lewis Structure.



2) Count the total number of bonds.

4

The total number of bonds is 4.

3) Count the number of bond groups between individual atoms.

2

The number of bond groups between atoms is 2.

4) Divide the bond groups between individual atoms by the total number of bonds.

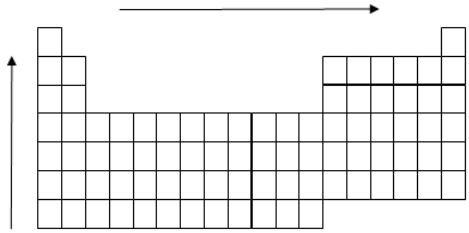
$$\frac{4}{2} = 2 \tag{1.14.2}$$

The bond order is 2.

A high bond order indicates more attraction between electrons. A higher bond order also means that the atoms are held together more tightly. With a lower bond order, there is less attraction between electrons and this causes the atoms to be held together more loosely. Bond order also indicates the stability of the bond. The higher the bond order, the more electrons holding the atoms together, and therefore the greater the stability.

Trends in the Periodic Table

Bond order increases across a period and decreases down a group.



Bond Length

Bond length is defined as the distance between the centers of two covalently bonded atoms. The length of the bond is determined by the number of bonded electrons (the bond order). The higher the bond order, the stronger the pull between the two atoms and the shorter the bond length. Generally, the length of the bond between two atoms is approximately the sum of the covalent radii of the two atoms. Bond length is reported in picometers. Therefore, bond length increases in the following order: triple bond < double bond < single bond.

To find the bond length, follow these steps:

1. Draw the Lewis structure.
2. Look up the chart below for the radii for the corresponding bond.
3. Find the sum of the two radii.

✔ 4

Determine the carbon-to-chlorine bond length in CCl_4.

Solution

Using Table A3, a C single bond has a length of 75 picometers and that a Cl single bond has a length of 99 picometers. When added together, the bond length of a C-Cl bond is approximately 174 picometers.

✔ 2

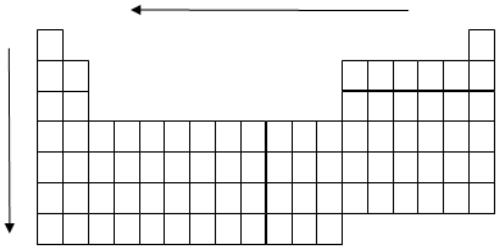
Determine the carbon-oxygen bond length in CO_2.

Solution

Using Table A3, we see that a C double bond has a length of 67 picometers and that an O double bond has a length of 57 picometers. When added together, the bond length of a C=O bond is approximately 124 picometers.

Trends in the Periodic Table

Because the bond length is proportional to the atomic radius, the bond length trends in the periodic table follow the same trends as atomic radii: bond length decreases across a period and increases down a group.



Problems

1. What is the bond order of O_2?
2. What is the bond order of NO_3^-?
3. What is the carbon-nitrogen bond length in HCN?
4. Is the carbon-to-oxygen bond length greater in CO_2 or CO?
5. What is the nitrogen-fluoride bond length in NF_3?

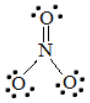
Solutions

1. First, write the Lewis structure for O_2.



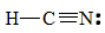
There is a double bond between the two oxygen atoms; therefore, the bond order of the molecule is 2.

2. The Lewis structure for NO_3^- is given below:



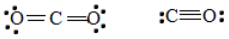
To find the bond order of this molecule, take the average of the bond orders. N=O has a bond order of two, and both N-O bonds have a bond order of one. Adding these together and dividing by the number of bonds (3) reveals that the bond order of nitrate is 1.33.

3. To find the carbon-nitrogen bond length in HCN, draw the Lewis structure of HCN.



The bond between carbon and nitrogen is a triple bond, and a triple bond between carbon and nitrogen has a bond length of approximately 60 + 54 =114 pm.

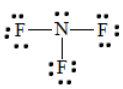
4. From the Lewis structures for CO_2 and CO, there is a double bond between the carbon and oxygen in CO_2 and a triple bond between the carbon and oxygen in CO.



Referring to the table above, a double bond between carbon and oxygen has a bond length of approximately 67 + 57 = 124 pm and a triple bond between carbon and oxygen has a bond length of approximately 60 + 53 =113 pm. Therefore, the bond length is greater in CO_2.

Another method makes use of the fact that the more electron bonds between the atoms, the tighter the electrons are pulling the atoms together. Therefore, the bond length is greater in CO_2.

5. To find the nitrogen-to-fluorine bond length in NF_3, draw the Lewis structure.



The bond between fluorine and nitrogen is a single bond. From the table above, a single bond between fluorine and nitrogen has a bond length of approximately 64 + 71 =135 pm.

References

1. Campbell, Neil A., Brad Williamson, and Robin J. Heyden. Biology: Exploring Life. Boston, Massachusetts: Pearson Prentice Hall, 2006.
2. Petrucci, Ralph H., Harwood, William S., Herring, F. G., and Madura Jeffrey D. General Chemistry: Principles & Modern Applications. 9th Ed. New Jersey: Pearson Education, Inc., 2007. Print.
3. Cordero, Beatriz, Verónica Gómez, Ana E. Platero-Prats, Marc Revés, Jorge Echeverría, Eduard Cremades, Flavia Barragán and Santiago Alvarez. Dalton's Transactions." Covalent radii revisited 2008:
4. Pekka Pyykkö and Michiko Atsumi, Chem. Eur. J. Molecular Double-Bond Covalent Radii for Elements Li–E112 2009

Contributors and Attributions

- Wikihow.com
- Anonymous

1.14: Summary- Hybridization, Bond Lengths, Bond Strengths, and Bond Angles is shared under a not declared license and was authored, remixed, and/or curated by LibreTexts.

- **Bond Order and Lengths** is licensed CC BY-NC-SA 4.0.

1.15: The Dipole Moments of Molecules

8.03 Bond Polarity and Dipole Moments

1.15: The Dipole Moments of Molecules is shared under a not declared license and was authored, remixed, and/or curated by LibreTexts.

SECTION OVERVIEW

1.16: An Introduction to Acids and Bases

An acid–base reaction is a chemical reaction that occurs between an acid and a base. Several theoretical frameworks provide alternative conceptions of the reaction mechanisms and their application in solving related problems; these are called acid–base theories, for example, Brønsted–Lowry acid–base theory. Their importance becomes apparent in analyzing acid–base reactions for gaseous or liquid species, or when acid or base character may be somewhat less apparent.

Topic hierarchy

Template:HideTOC

1.16: An Introduction to Acids and Bases is shared under a not declared license and was authored, remixed, and/or curated by LibreTexts.

1.17: pka and pH

Learning Objectives

- To define the pH scale as a measure of acidity of a solution
- Tell the origin and the logic of using the pH scale.
- Apply the same strategy for representing other types of quantities such as pK_a, pK_b, pK_w.

Auto-Ionization of Water

Because of its *amphoteric* nature (i.e., acts as both an acid or a base), water does not always remain as H_2O molecules. In fact, two water molecules react to form hydronium and hydroxide ions:

$$2\,H_2O\,(l) \rightleftharpoons H_3O^+\,(aq) + OH^-\,(aq) \tag{1.17.1}$$

This is also called the self-ionization of water. The concentration of H_3O^+ and OH^- are equal in pure water because of the 1:1 stoichiometric ratio of Equation 1.17.1. The molarity of H_3O^+ and OH^- in water are also both $1.0 \times 10^{-7}\,M$ at 25° C. Therefore, a constant of water (K_w) is created to show the equilibrium condition for the self-ionization of water. The product of the molarity of hydronium and hydroxide ion is always 1.0×10^{-14} (at room temperature).

$$K_w = [H_3O^+][OH^-] = 1.0 \times 10^{-14} \tag{1.17.2}$$

Equation 1.17.2 also applies to all aqueous solutions. However, K_w does change at different temperatures, which affects the pH range discussed below.

> *H^+ and H_3O^+ is often used interchangeably to represent the hydrated proton, commonly call the hydronium ion.*

Equation 1.17.1 can also be written as

$$H_2O \rightleftharpoons H^+ + OH^- \tag{1.17.3}$$

As expected for any equilibrium, the reaction can be shifted to the reactants or products:

- If an acid (H^+) is added to the water, the equilibrium shifts to the left and the OH^- ion concentration decreases
- If base (OH^-) is added to water, the equilibrium shifts to left and the H^+ concentration decreases.

pH and pOH

Because the constant of water, K_w is 1.0×10^{-14} (at 25° C), the pK_w is 14, the constant of water determines the range of the pH scale. To understand what the pK_w is, it is important to understand first what the "p" means in pOH and pH. The addition of the "p" reflects the negative of the logarithm, $-\log$. Therefore, the pH is the negative logarithm of the molarity of H, the pOH is the negative logarithm of the molarity of OH^-, and the pK_w is the negative logarithm of the constant of water:

$$pH = -\log[H^+] \tag{1.17.4}$$
$$pOH = -\log[OH^-] \tag{1.17.5}$$
$$pK_w = -\log[K_w] \tag{1.17.6}$$

At room temperature,

$$K_w = 1.0 \times 10^{-14} \tag{1.17.7}$$

So

$$pK_w = -\log[1.0 \times 10^{-14}] \tag{1.17.8}$$
$$= 14 \tag{1.17.9}$$

Using the properties of logarithms, Equation 1.17.8 can be rewritten as

$$10^{-pK_w} = 10^{-14}. \tag{1.17.10}$$

The equation also shows that each increasing unit on the scale decreases by the factor of ten on the concentration of $\mathbf{H^+}$. Combining Equations 1.17.4 - 1.17.6 and 1.17.8 results in this important relationship:

$$pK_w = pH + pOH = 14 \tag{1.17.11}$$

Equation 1.17.11 is correct only at room temperature since changing the temperature will change K_w.

> *The pH scale is logarithmic, meaning that an increase or decrease of an integer value changes the concentration by a tenfold. For example, a pH of 3 is ten times more acidic than a pH of 4. Likewise, a pH of 3 is one hundred times more acidic than a pH of 5. Similarly a pH of 11 is ten times more basic than a pH of 10.*

Properties of the pH Scale

From the simple definition of pH in Equation 1.17.4, the following properties can be identified:

- This scale is convenient to use, because it converts some odd expressions such as $\mathbf{1.23 \times 10^{-4}}$ into a single number of 3.91.
- This scale covers a very large range of $[\mathbf{H^+}]$, from 0.1 to 10^{-14}. When $[\mathbf{H^+}]$ is high, we usually do not use the pH value, but simply the $[\mathbf{H^+}]$. For example, when $[\mathbf{H^+}] = \mathbf{1.0}$, pH = 0. We seldom say the pH is 0, and that is why you consider pH = 0 such an odd expression. A pH = -0.30 is equivalent to a $[\mathbf{H^+}]$ of 2.0 M. Negative pH values are only for academic exercises. Using the concentrations directly conveys a better sense than the pH scales.
- The pH scale expands the division between zero and 1 in a linear scale or a compact scale into a large scale for comparison purposes. In mathematics, you learned that there are infinite values between 0 and 1, or between 0 and 0.1, or between 0 and 0.01 or between 0 and any small value. Using a log scale certainly converts infinite small quantities into infinite large quantities.
- The non-linearity of the pH scale in terms of $[\mathbf{H^+}]$ is easily illustrated by looking at the corresponding values for pH between 0.1 and 0.9 as follows:

pH	0	0.1	0.2	0.3	0.4	0.5	0.6	0.7	0.8	0.9
$[H^+]$	1	0.79	0.63	0.50	0.40	0.32	0.25	0.20	0.16	0.13

- Because the negative log of $[\mathbf{H^+}]$ is used in the pH scale, the pH scale *usually* has positive values. Furthermore, the larger the pH, the smaller the $[\mathbf{H^+}]$.

The Effective Range of the pH Scale

It is common that the pH scale is argued to range from 0-14 or perhaps 1-14, but neither is correct. The pH range does not have an upper nor lower bound, since as defined above, the pH is an indication of concentration of H^+. For example, at a pH of zero the hydronium ion concentration is one molar, while at pH 14 the hydroxide ion concentration is one molar. Typically the concentrations of H^+ in water in most solutions fall between a range of 1 M (pH=0) and 10^{-14} M (pH=14). Hence a range of 0 to 14 provides sensible (but not absolute) "bookends" for the scale. One can go somewhat below zero and somewhat above 14 in water, because the concentrations of hydronium ions or hydroxide ions can exceed one molar. Figure **1.17.1** depicts the pH scale with common solutions and where they are on the scale.

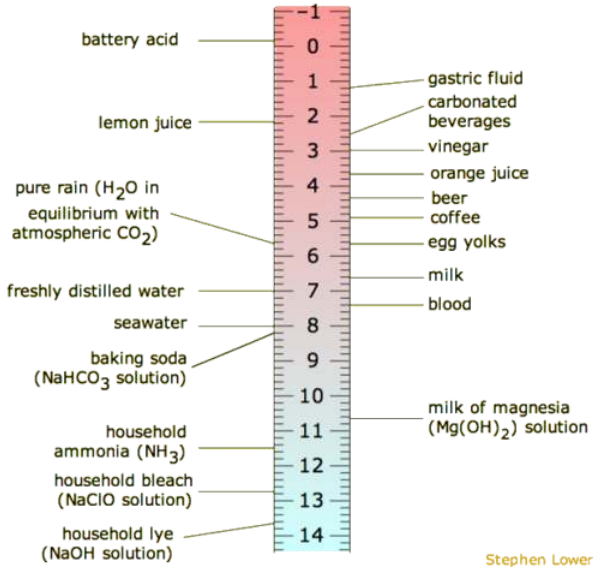


Figure **1.17.1**: Solutions and the placement of them on pH scale. (CC-BY-SA 3.0; Stephen Lower).

Quick Interpretation

- If pH >7, the solution is basic. The pOH should be looked in the perspective of OH^- instead of H^+. Whenever the value of pOH is less than 7, then it is considered basic. And therefore there are more OH^- than H^+ in the solution.
- At pH 7, the substance or solution is at neutral and means that the concentration of H^+ and OH^- ion is the same.
- If pH < 7, the solution is acidic. There are more H^+ than OH^- in an acidic solution.
- The pH scale **does not** have an upper nor lower bound.

Example 1.17.1

If the concentration of $NaOH$ in a solution is $2.5 \times 10^{-4}\ M$, what is the concentration of H_3O^+?

Solution

We can assume room temperature, so

$$1.0 \times 10^{-14} = [H_3O^+][OH^-]$$

to find the concentration of H_3O^+, solve for the $[H_3O^+]$.

$$\frac{1.0 \times 10^{-14}}{[OH^-]} = [H_3O^+] \tag{1.17.12}$$

$$\frac{1.0 \times 10^{-14}}{2.5 \times 10^{-4}} = [H_3O^+] = 4.0 \times 10^{-11}\ M \tag{1.17.13}$$

Example 1.17.2

a. Find the pH of a solution of 0.002 M of HCl.
b. Find the pH of a solution of 0.00005 M NaOH.

Solution

a. The equation for pH is -log [H+]

$$[H^+] = 2.0 \times 10^{-3}\ M$$

$$pH = -\log[2.0 \times 10^{-3}] = 2.70$$

b. The equation for pOH is -log [OH^-]

$$[OH^-] = 5.0 \times 10^{-5}\ M$$

$$pOH = -\log[5.0 \times 10^{-5}] = 4.30$$

$$pK_w = pH + pOH$$

and

$$pH = pK_w - pOH$$

then

$$pH = 14 - 4.30 = 9.70$$

Example 1.17.3: Soil

If moist soil has a pH of 7.84, what is the H^+ concentration of the soil solution?

Solution

$$pH = -\log[H^+]$$

$$7.84 = -\log[H^+]$$

$$[H^+] = 1.45 \times 10^{-8} M$$

Hint

Place -7.84 in your calculator and take the antilog (often inverse log or 10^x) = 1.45 x 10^{-8}M

Proper Definition of pH

The pH scale was originally introduced by the Danish biochemist S.P.L. Sørenson in 1909 using the symbol p_H. The letter *p* is derived from the German word *potenz* meaning power or exponent of, in this case, 10. In 1909, S.P.L. Sørenson published a paper in Biochem Z in which he discussed the effect of H^+ ions on the activity of enzymes. In the paper, he invented the term pH (purported to mean *pondus hydrogenii* in Latin) to describe this effect and defined it as the $-\log[H^+]$. In 1924, Sørenson realized that the pH of a solution is a function of the "activity" of the H^+ ion and not the concentration. Thus, he published a second paper on the subject. A better definition would be

$$pH = -\log\, a\{\mathrm{H}^+\} \tag{1.17.14}$$

where $a\{H^+\}$ denotes the activity (an effective concentration) of the H^+ ions. The activity of an ion is a function of many variables of which concentration is one.

- *Concentration* is abbreviated by using square brackets, e.g., $[H_3O^+]$ is the concentration of hydronium ion in solution.
- *Activity* is abbreviated by using "a" with curly brackets, e.g., $a\{H_3O^+\}$ is the activity of hydronium ions in solution

Because of the difficulty in accurately measuring the activity of the $\mathbf{H^+}$ ion for most solutions the International Union of Pure and Applied Chemistry (IUPAC) and the National Bureau of Standards (NBS) has defined pH as the reading on a pH meter that has been standardized against standard buffers. The following equation is used to calculate the pH of all solutions:

$$pH = \frac{F(E - E_{standard})}{RT\ \ln 10} + pH_{standard} \tag{1.17.15}$$

$$= \frac{5039.879(E - E_{standard})}{T} + pH_{standard} \tag{1.17.16}$$

with

- R is the ideal gas constant,
- F is the Faraday's constant, and
- T is absolute temperature (in K)

> The activity of the H^+ ion is determined as accurately as possible for the standard solutions used. The identity of these solutions vary from one authority to another, but all give the same values of pH to ± 0.005 pH unit. The historical definition of pH is correct for those solutions that are so dilute and so pure the H^+ ions are not influenced by anything but the solvent molecules (usually water).

When measuring pH, $[H^+]$ is in units of moles of H^+ per liter of solution. This is a reasonably accurate definition at low concentrations (the dilute limit) of H^+. At very high concentrations (10 M hydrochloric acid or sodium hydroxide, for example,) a significant fraction of the ions will be associated into neutral pairs such as $H^+Cl^–$, thus reducing the concentration of “available” ions to a smaller value which we will call the *effective concentration*. It is the *effective concentration* of H^+ and $OH^–$ that determines the pH and pOH. The pH scale as shown above is called sometimes "concentration pH scale" as opposed to the "thermodynamic pH scale". The main difference between both scales is that in thermodynamic pH scale one is interested not in H^+concentration, but in H^+activity. What a person measures in the solution is just activity, not the concentration. Thus it is thermodynamic pH scale that describes real solutions, not the concentration one.

For solutions in which ion concentrations don't exceed 0.1 M, the formulas pH = –log $[H^+]$ and pOH = –log$[OH^–]$ are generally reliable, but don't expect a 10.0 M solution of a strong acid to have a pH of exactly –1.00! However, this definition is only an approximation (albeit very good under most situations) of the proper definition of pH, which depends on the **activity** of the hydrogen ion:

$$pH = -\log a\{H^+\} \approx -\log[H^+] \tag{1.17.17}$$

The activity is a measure of the "effective concentration" of a substance, is often related to the true concentration via an activity coefficient, γ:

$$aH^+ = \gamma[H^+] \tag{1.17.18}$$

Calculating the activity coefficient requires detailed theories of how charged species interact in solution at high concentrations (e.g., the Debye-Hückel Theory). In most solutions the pH differs from the -log$[H^+]$ in the first decimal point. The following table gives experimentally determined pH values for a series of HCl solutions of increasing concentration at 25 °C.

Table **1.17.1**: HCl Solutions with corresponding pH values. Data taken from Christopher G. McCarty and Ed Vitz, Journal of Chemical Education, 83(5), 752 (2006) and G.N. Lewis, M. Randall, K. Pitzer, D.F. Brewer, Thermodynamics (McGraw-Hill: New York, 1961; pp. 233-34).

Molar Concentration of HCl	pH defined as Concentration	Experimentally Determined pH	Relative Deviation
0.00050	3.30	3.31	0.3%
0.0100	2	2.04	1.9%
0.100	1	1.10	9%
0.40	0.39	0.52	25%
7.6	-0.88	-1.85	52%

> *While the pH scale formally measures the activity of hydrogen ions in a substance or solution, it is typically approximated as the concentration of hydrogen ions; this approximation is applicable only under low concentrations.*

Living Systems

Molecules that make up or are produced by living organisms usually function within a narrow pH range (near neutral) and a narrow temperature range (body temperature). Many biological solutions, such as blood, have a pH near neutral. pH influences the structure and the function of many enzymes (protein catalysts) in living systems. Many of these enzymes have narrow ranges of pH activity. Cellular pH is so important that death may occur within hours if a person becomes acidotic (having increased acidity in the blood). As one can see pH is critical to life, biochemistry, and important chemical reactions. Common examples of how pH plays a very important role in our daily lives are given below:

- Water in swimming pool is maintained by checking its pH. Acidic or basic chemicals can be added if the water becomes too acidic or too basic.
- Whenever we get a heartburn, more acid build up in the stomach and causes pain. We needs to take antacid tablets (a base) to neutralize excess acid in the stomach.
- The pH of blood is slightly basic. A fluctuation in the pH of the blood can cause in serious harm to vital organs in the body.
- Certain diseases are diagnosed only by checking the pH of blood and urine.
- Certain crops thrive better at certain pH range.
- Enzymes activate at a certain pH in our body.

Table **1.17.2**: pH in Living Systems

Compartment	pH
Gastric Acid	1
Lysosomes	4.5
Granules of Chromaffin Cells	5.5
Human Skin	5.5
Urine	6
Neutral H_2O at 37 °C	6.81
Cytosol	7.2
Cerebrospinal Fluid	7.3
Blood	7.43-7.45
Mitochondrial Matrix	7.5
Pancreas Secretions	8.1

Problems

1. In a solution of $2.4 \times 10^{-3} M$ of HI, find the concentration of OH^-.
2. Determine the pH of a solution that is 0.0035 M HCl.
3. Determine the $[H_3O^+]$ of a solution with a pH = 5.65
4. If the pOH of NH_3, ammonia, in water is 4.74. What is the pH?
5. Pepsin, a digestive enzyme in our stomach, has a pH of 1.5. Find the concentration of OH^- in the stomach.

Solutions

1. We use the dissociation of water equation to find $[OH^-]$.
   $K_w = [H_3O^+][OH^-] = 1.0 \text{ X } 10^{-14}$
   Solve for $[OH^-]$
   $[OH^-] = (1.0 \text{ X } 10^{-14})/ [H_3O^+]$
   Plug in the molarity of HI and solve for OH^-.
   $[OH^-] = (1.0 \text{ X } 10^{-14})/ [2.4 \text{ X } 10^{-3}] = 4.17 \text{ X } 10^{-12}$ M.
2. $pH = -\log[H_3O^+]$
   Plug the molarity of the HCl in and solve for pH.
   $pH = -\log[0.0035] = 2.46$
3. $pH = -\log[H_3O^+]$
   Plug in the pH and solve for [H3O+]
   $5.65 = -\log[H_3O^+]$
   Move the negative sign to the pH. $-5.65 = \log[H_3O^+]$
   $10^{-5.65}=10^{\log[H_3O+]} = 2.24 \text{ X } 10^{-6}$ M

4. pH + pOH = 14
   Solve for pH.
   14 - pOH = pH
   14 - 4.74 = pH = 9.26
5. There are several ways to do this problem.
   Answer 1.
   pH + pOH = 14
   Solve for pOH.
   pOH = 14 - pH
   pOH = 14 - 1.5 = 12.5
   When the pOH is solved, solve for the concentration by using log.
   $pOH = -\log[OH^-]$
   $12.5 = -\log[OH^-]$
   $-12.5 = \log[OH^-]$
   $10^{-12.5} = 10^{\log[OH-]} = 3.16 \text{ X } 10^{-13}$ M.

   Answer 2.
   $pH = -\log[H^+]$
   Plug in the pH and solve for the molarity of H+ of pepsin.
   $1.5 = -\log[H^+]$
   $-1.5 = \log[H^+]$
   $10^{-1.5} = 10^{\log[H+]} = [H^+] = 0.032$
   Use the concentration of H^+ to solve for the concentration of OH^-.
   $[H^+][OH^-] = 1.0 \text{ X } 10^{-14}$
   Plug in the $[H^+]$ and solve for $[OH^-]$.
   $[OH^-] = (1.0 \text{ X } 10^{-14})/[H_3O^+]$
   $[OH^-] = (1.0 \text{ X } 10^{-14})/(0.032) = 3.125 \text{ X } 10^{-14}$ M

References

1. Petrucci, et al. "Self-Ionization of Water and the pH Scale." *General Chemistry: Principles & Modern Applications*. 7th ed. Upper Saddle River: Pearson Prentice Hall, 2007. 669-71.
2. Segel, Irwin H. "Acid and Base." *Biochemical Calculations*. 2nd ed. Wiley: BK Book, 1976. 12.
3. Christopher G. McCarty and Ed Vitz, Journal of Chemical Education, 83(5), 752 (2006)

Contributors and Attributions

- Emmellin Tung (UCD), Sharon Tsao (UCD), Divya Singh (UCD), Patrick Gormley (Lapeer Community School District)
- Chung (Peter) Chieh (Professor Emeritus, Chemistry @ University of Waterloo)

1.17: pka and pH is shared under a not declared license and was authored, remixed, and/or curated by LibreTexts.

- **The pH Scale** is licensed CC BY-NC-SA 4.0.

1.18: 1.18 Organic Acids and Bases

This page explains the acidity of simple organic acids and looks at the factors which affect their relative strengths.

Organic acids as weak acids

For the purposes of this topic, we are going to take the definition of an acid as "a substance which donates hydrogen ions (protons) to other things". We are going to get a measure of this by looking at how easily the acids release hydrogen ions to water molecules when they are in solution in water.

An acid in solution sets up this equilibrium:

$$AH + H_2O \rightleftharpoons A^- + H_3O^+$$

A hydroxonium ion is formed together with the anion (negative ion) from the acid.

This equilibrium is sometimes simplified by leaving out the water to emphasise the ionisation of the acid.

$$AH_{(aq)} \rightleftharpoons A^-_{(aq)} + H^+_{(aq)}$$

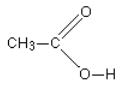
If you write it like this, you must include the state symbols - "(aq)". Writing $H^+_{(aq)}$ implies that the hydrogen ion is attached to a water molecule as H_3O^+. Hydrogen ions are always attached to something during chemical reactions.

The organic acids are weak in the sense that this ionisation is very incomplete. At any one time, most of the acid will be present in the solution as un-ionised molecules. For example, in the case of dilute ethanoic acid, the solution contains about 99% of ethanoic acid molecules - at any instant, only about 1% have actually ionised. The position of equilibrium therefore lies well to the left.

Comparing the strengths of weak acids

The strengths of weak acids are measured on the pK_a scale. The smaller the number on this scale, the stronger the acid is.

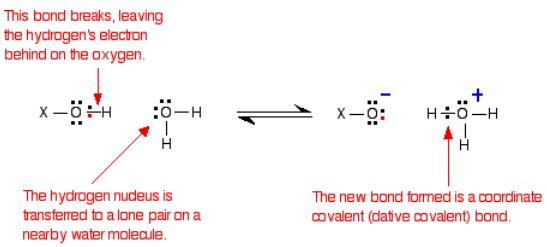
Three of the compounds we shall be looking at, together with their pK_a values are:

		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!

Why are these acids acidic?

In each case, the same bond gets broken - the bond between the hydrogen and oxygen in an -OH group. Writing the rest of the molecule as "X":



So . . . if the same bond is being broken in each case, why do these three compounds have such widely different acid strengths?

Differences in acid strengths between carboxylic acids, phenols and alcohols

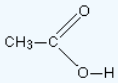
Two of the factors which influence the ionization of an acid are:

- the strength of the bond being broken,
- the stability of the ions being formed.

In these cases, you seem to be breaking the same oxygen-hydrogen bond each time, and so you might expect the strengths to be similar. The most important factor in determining the relative acid strengths of these molecules is the nature of the ions formed. You always get a hydroxonium ion - so that's constant - but the nature of the anion (the negative ion) varies markedly from case to case.

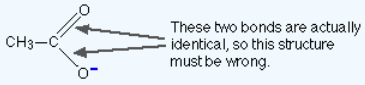
Example 1.18.1: Ethanoic Acid

Ethanoic acid has the structure:



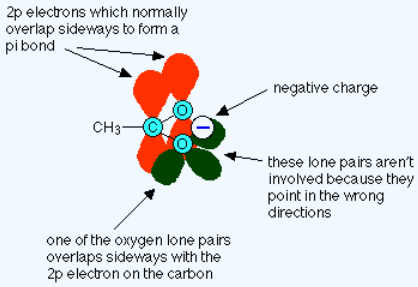
The acidic hydrogen is the one attached to the oxygen. When ethanoic acid ionises it forms the ethanoate ion, CH_3COO^-.

You might reasonably suppose that the structure of the ethanoate ion was as below, but measurements of bond lengths show that the two carbon-oxygen bonds are identical and somewhere in length between a single and a double bond.

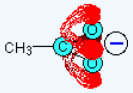


To understand why this is, you have to look in some detail at the bonding in the ethanoate ion. Like any other double bond, a carbon-oxygen double bond is made up of two different parts. One electron pair is found on the line between the two nuclei - this is known as a sigma bond. The other electron pair is found above and below the plane of the molecule in a pi bond. Pi bonds are made by sideways overlap between p orbitals on the carbon and the oxygen.

In an ethanoate ion, one of the lone pairs on the negative oxygen ends up almost parallel to these p orbitals, and overlaps with them

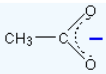


This leads to a delocalised pi system over the whole of the $-COO^-$ group, rather like that in benzene.



All the oxygen lone pairs have been left out of this diagram to avoid confusion. Because the oxygens are more electronegative than the carbon, the delocalised system is heavily distorted so that the electrons spend much more time in the region of the oxygen atoms.

So where is the negative charge in all this? It has been spread around over the whole of the $-COO^-$ group, but with the greatest chance of finding it in the region of the two oxygen atoms. Ethanoate ions can be drawn simply as:



The dotted line represents the delocalisation. The negative charge is written centrally on that end of the molecule to show that it isn't localised on one of the oxygen atoms. The more you can spread charge around, the more stable an ion becomes. In this case, if you delocalise the negative charge over several atoms, it is going to be much less attractive to hydrogen ions - and so you are less likely to re-form the ethanoic acid.

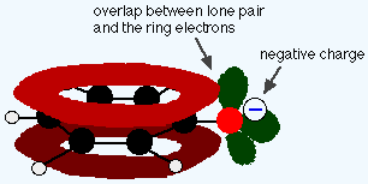
Example 1.18.2: Phenol

Phenols have an -OH group attached directly to a benzene ring. Phenol itself is the simplest of these with nothing else attached to the ring apart from the -OH group.

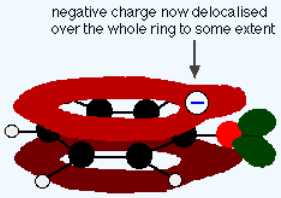


When the hydrogen-oxygen bond in phenol breaks, you get a phenoxide ion, $C_6H_5O^-$.

Delocalisation also occurs in this ion. This time, one of the lone pairs on the oxygen atom overlaps with the delocalised electrons on the benzene ring.

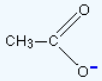


This overlap leads to a delocalisation which extends from the ring out over the oxygen atom. As a result, the negative charge is no longer entirely localised on the oxygen, but is spread out around the whole ion.

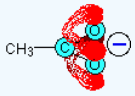


Why then is phenol a much weaker acid than ethanoic acid?

Think about the ethanoate ion again. If there wasn't any delocalisation, the charge would all be on one of the oxygen atoms, like this:



But the delocalisation spreads this charge over the whole of the COO group. Because oxygen is more electronegative than carbon, you can think of most of the charge being shared between the two oxygens (shown by the heavy red shading in this diagram).



If there wasn't any delocalisation, one of the oxygens would have a full charge which would be very attractive towards hydrogen ions. With delocalisation, that charge is spread over two oxygen atoms, and neither will be as attractive to a hydrogen ion as if one of the oxygens carried the whole charge.

That means that the ethanoate ion won't take up a hydrogen ion as easily as it would if there wasn't any delocalisation. Because some of it stays ionised, the formation of the hydrogen ions means that it is acidic.

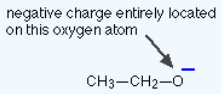
In the phenoxide ion, the single oxygen atom is still the most electronegative thing present, and the delocalised system will be heavily distorted towards it. That still leaves the oxygen atom with most of its negative charge.

What delocalisation there is makes the phenoxide ion more stable than it would otherwise be, and so phenol is acidic to an extent.

However, the delocalisation hasn't shared the charge around very effectively. There is still lots of negative charge around the oxygen to which hydrogen ions will be attracted - and so the phenol will readily re-form. Phenol is therefore only very weakly acidic.

Example 1.18.3: Ethanol

Ethanol, CH_3CH_2OH, is so weakly acidic that you would hardly count it as acidic at all. If the hydrogen-oxygen bond breaks to release a hydrogen ion, an ethoxide ion is formed:



This has nothing at all going for it. There is no way of delocalising the negative charge, which remains firmly on the oxygen atom. That intense negative charge will be highly attractive towards hydrogen ions, and so the ethanol will instantly re-form.

Since ethanol is very poor at losing hydrogen ions, it is hardly acidic at all.

Variations in acid strengths between different carboxylic acids

You might think that all carboxylic acids would have the same strength because each depends on the delocalization of the negative charge around the $-COO^-$ group to make the anion more stable, and so more reluctant to re-combine with a hydrogen ion.

In fact, the carboxylic acids have widely different acidities. One obvious difference is between methanoic acid, HCOOH, and the other simple carboxylic acids:

	pK_a
HCOOH	3.75
CH_3COOH	4.76
CH_3CH_2COOH	4.87
$CH_3CH_2CH_2COOH$	4.82

Remember that the higher the value for pK_a, the weaker the acid is.

Why is ethanoic acid weaker than methanoic acid? It again depends on the stability of the anions formed - on how much it is possible to delocalise the negative charge. The less the charge is delocalised, the less stable the ion, and the weaker the acid.

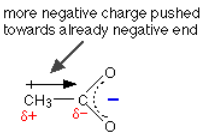
The methanoate ion (from methanoic acid) is:



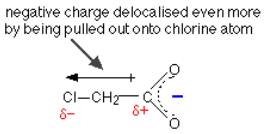
The only difference between this and the ethanoate ion is the presence of the CH_3 group in the ethanoate.

But that's important! Alkyl groups have a tendency to "push" electrons away from themselves. That means that there will be a small amount of extra negative charge built up on the $-COO^-$ group. Any build-up of charge will make the ion less stable, and more attractive to hydrogen ions.

Ethanoic acid is therefore weaker than methanoic acid, because it will re-form more easily from its ions.



The other alkyl groups have "electron-pushing" effects very similar to the methyl group, and so the strengths of propanoic acid and butanoic acid are very similar to ethanoic acid. The acids can be strengthened by pulling charge away from the -COO^- end. You can do this by attaching electronegative atoms like chlorine to the chain.



As the next table shows, the more chlorines you can attach the better:

	pK_a
CH_3COOH	4.76
$CH_2ClCOOH$	2.86
$CHCl_2COOH$	1.29
CCl_3COOH	0.65

Trichloroethanoic acid is quite a strong acid.

Attaching different halogens also makes a difference. Fluorine is the most electronegative and so you would expect it to be most successful at pulling charge away from the -COO^- end and so strengthening the acid.

	pK_a
CH_2FCOOH	2.66
$CH_2ClCOOH$	2.86
$CH_2BrCOOH$	2.90
CH_2ICOOH	3.17

The effect is there, but isn't as great as you might expect.

Finally, notice that the effect falls off quite quickly as the attached halogen gets further away from the -COO^- end. Here is what happens if you move a chlorine atom along the chain in butanoic acid.

	pK_a
$CH_3CH_2CH_2COOH$	4.82
$CH_3CH_2CHClCOOH$	2.84
$CH_3CHClCH_2COOH$	4.06
$CH_2ClCH_2CH_2COOH$	4.52

The chlorine is effective at withdrawing charge when it is next-door to the -COO^- group, and much less so as it gets even one carbon further away.

This page explains why simple organic bases are basic and looks at the factors which affect their relative strengths. For A'level purposes, all the bases we are concerned with are primary amines - compounds in which one of the hydrogens in an ammonia molecule, NH_3, is replaced either by an alkyl group or a benzene ring.

Ammonia as a weak base

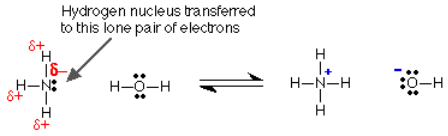
All of the compounds we are concerned with are derived from ammonia and so we'll start by looking at the reason for its basic properties. For the purposes of this topic, we are going to take the definition of a base as "a substance which combines with hydrogen ions (protons)". We are going to get a measure of this by looking at how easily the bases take hydrogen ions from water molecules when they are in solution in water.

Ammonia in solution sets up this equilibrium:

$$NH_3 + H_2O \rightleftharpoons NH_4^+ + OH^-$$

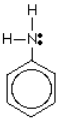
An ammonium ion is formed together with hydroxide ions. Because the ammonia is only a weak base, it doesn't hang on to the extra hydrogen ion very effectively and so the reaction is reversible. At any one time, about 99% of the ammonia is present as unreacted molecules. The position of equilibrium lies well to the left.

The ammonia reacts as a base because of the active lone pair on the nitrogen. Nitrogen is more electronegative than hydrogen and so attracts the bonding electrons in the ammonia molecule towards itself. That means that in addition to the lone pair, there is a build-up of negative charge around the nitrogen atom. That combination of extra negativity and active lone pair attracts the new hydrogen from the water.



Comparing the strengths of weak bases

The strengths of weak bases are measured on the pK_b scale. The smaller the number on this scale, the stronger the base is. Three of the compounds we shall be looking at, together with their pK_b values are:

		pK_b
ammonia		4.75
methylamine		3.36
phenylamine		9.38

Remember - the smaller the number the stronger the base. Comparing the other two to ammonia, you will see that methylamine is a stronger base, whereas phenylamine is very much weaker.

- Methylamine is typical of aliphatic primary amines - where the $-NH_2$ group is attached to a carbon chain. All aliphatic primary amines are stronger bases than ammonia.
- Phenylamine is typical of aromatic primary amines - where the $-NH_2$ group is attached directly to a benzene ring. These are very much weaker bases than ammonia.

Explaining the differences in base strengths

Two of the factors which influence the strength of a base are:

- the ease with which the lone pair picks up a hydrogen ion,

- the stability of the ions being formed.

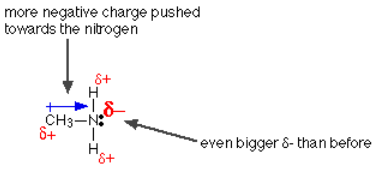
Why are aliphatic primary amines stronger bases than ammonia?

Methylamine

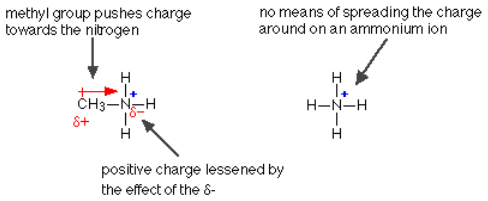
Methylamine has the structure:



The only difference between this and ammonia is the presence of the CH_3 group in the methylamine. But that's important! Alkyl groups have a tendency to "push" electrons away from themselves. That means that there will be a small amount of extra negative charge built up on the nitrogen atom. That extra negativity around the nitrogen makes the lone pair even more attractive towards hydrogen ions.



Making the nitrogen more negative helps the lone pair to pick up a hydrogen ion. What about the effect on the positive methylammonium ion formed? Is this more stable than a simple ammonium ion? Compare the methylammonium ion with an ammonium ion:



In the methylammonium ion, the positive charge is spread around the ion by the "electron-pushing" effect of the methyl group. The more you can spread charge around, the more stable an ion becomes. In the ammonium ion there isn't any way of spreading the charge.

To summarize:

- The nitrogen is more negative in methylamine than in ammonia, and so it picks up a hydrogen ion more readily.
- The ion formed from methylamine is more stable than the one formed from ammonia, and so is less likely to shed the hydrogen ion again.

Taken together, these mean that methylamine is a stronger base than ammonia.

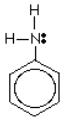
The other aliphatic primary amines

The other alkyl groups have "electron-pushing" effects very similar to the methyl group, and so the strengths of the other aliphatic primary amines are very similar to methylamine. For example:

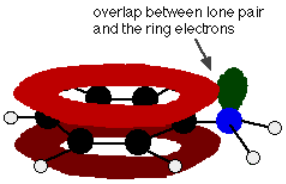
	pK_b
CH_3NH_2	3.36
$CH_3CH_2NH_2$	3.27
$CH_3CH_2CH_2NH_2$	3.16
$CH_3CH_2CH_2CH_2NH_2$	3.39

Why are aromatic primary amines much weaker bases than ammonia?

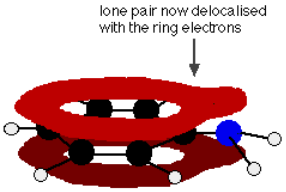
An aromatic primary amine is one in which the -NH_2 group is attached directly to a benzene ring. The only one you are likely to come across is phenylamine. Phenylamine has the structure:



The lone pair on the nitrogen touches the delocalized ring electrons . . .



. . . and becomes delocalized with them:



That means that the lone pair is no longer fully available to combine with hydrogen ions. The nitrogen is still the most electronegative atom in the molecule, and so the delocalized electrons will be attracted towards it, but the intensity of charge around the nitrogen is nothing like what it is in, say, an ammonia molecule.

The other problem is that if the lone pair is used to join to a hydrogen ion, it is no longer available to contribute to the delocalisation. That means that the delocalization would have to be disrupted if the phenylamine acts as a base. Delocalization makes molecules more stable, and so disrupting the delocalization costs energy and will not happen easily.

Taken together - the lack of intense charge around the nitrogen, and the need to break some delocalization - this means that phenylamine is a very weak base indeed.

1.18: 1.18 Organic Acids and Bases is shared under a not declared license and was authored, remixed, and/or curated by LibreTexts.

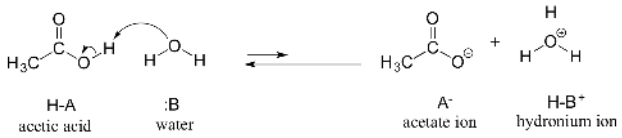
- **Organic Acids** by Jim Clark is licensed CC BY-NC 4.0.
- **Organic Bases** by Jim Clark is licensed CC BY-NC 4.0.

1.19: How to Predict the Outcome of an Acid-Base Reaction

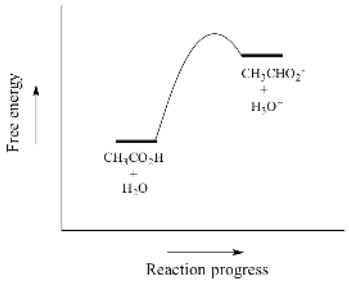
A: Defining the acidity constant

You are no doubt aware that some acids are stronger than others. The relative acidity of different compounds or functional groups – in other words, their relative capacity to donate a proton to a common base under identical conditions – is quantified by a number called the **acidity constant**, abbreviated $\mathbf{K_a}$. The common base chosen for comparison is water.

We will consider acetic acid as our first example. If we make a dilute solution of acetic acid in water, an acid-base reaction occurs between the acid (proton donor) and water (proton acceptor).



Acetic acid is a weak acid, so the equilibrium favors reactants over products - it is thermodynamically 'uphill', as indicated in the figure above by the relative length of the forward and reverse reaction arrows, and in the reaction coordinate diagram below in which products are higher energy than reactants.



As you know, the equilibrium constant K_{eq} is defined as:

$$K_{eq} = \frac{[\text{products}]}{[\text{reactants}]} = \frac{[CH_3COO^-][H_3O^+]}{[CH_3COOH][H_2O]}$$

Every equilibrium constant expressions is actually a ratio of the activities of all species involved in the reaction. To avoid the use of activities, and to simplify experimental measurements, the equilibrium constant of concentrations approximates the activities of solutes and gases in dilute solutions with their respective molarities. However, the activities of solids, pure liquids, and solvents are **not** approximated with their molarities. Instead these activities are defined to have a value equal to 1 (one).

Thus, if we acknowledge that the activity of water in a dilute solution is approximated with the value of unity (1), we can divide by 1 to get the common form of the expression for K_a, the acid constant for acetic acid:

$$K_a = K_{eq} = \frac{a_{H_3O^+} \cdot a_{CH_3COO^-}}{a_{CH_3COOH} \cdot a_{H_2O}} \approx \frac{[H_3O^+][CH_3COO^-]}{[CH_3COOH](1)} = \frac{[H_3O^+][CH_3COO^-]}{[CH_3COOH]} \tag{1.19.1}$$

In fact, for an dilute aqueous solution, the activity of water is approximated with the value of 1, so the generic dissociation constant for a given acid HA or HB^+ is expressed as:

$$HA + H_2O \rightleftharpoons :A^- + H_3O^+ \qquad HB^+ + H_2O \rightleftharpoons :B + H_3O^+$$

$$K_a = \frac{[:A^-][H_3O^+]}{[HA]} \quad or \quad K_a = \frac{[:B][H_3O^+]}{[HB^+]}$$

The value of K_a for acetic acid is 1.75 x 10^{-5} - much less than 1, indicating there is much more acetic acid in solution at equilibrium than acetate and hydronium ions.

Conversely, sulfuric acid, with a K_a of approximately 10^9, or hydrochloric acid, with a K_a of approximately 10^7, both undergo essentially complete dissociation in water: they are very strong acids.

A number like 1.75 x 10^{-5} is not very easy either to say, remember, or visualize, so chemists usually use a more convenient term to express relative acidity. The **pK_a** value of an acid is simply the log (base 10) of its K_a value.

$$pK_a = -\log K_a \quad Ka = 10^{-pKa}$$

Doing the math, we find that the pK_a of acetic acid is 4.8. The pK_a of sulfuric acid is -10, and of hydrochloric acid is -7. The use of pK_a values allows us to express the relative acidity of common compounds and functional groups on a numerical scale of about –10 (for a very strong acid) to 50 (for a compound that is not acidic at all). ***The lower the pK_a value, the stronger the acid.***

The ionizable (proton donating or accepting) functional groups relevant to biological organic chemistry generally have pK_a values ranging from about 5 to about 20. The most important of these are summarized below, with *very rough* pK_a values for the conjugate acid forms. More acidic groups with pK_a values near zero are also included for reference.

Approximate pK_a values to know

hydronium ion (H_3O^+) : **0**

protonated alcohol: **0**

protonated carbonyl: **0**

carboxylic acids: **5**

protonated imines: **7**

protonated amines: **10**

phenols: **10**

thiols: **10**

water: **14**

alcohols: **15-18**

alpha-carbon acids*: **20**

**alpha-carbon acids will be discussed later in this chapter*

You are strongly recommended to commit these rough values to memory now - then if you need a more precise value, you can always look it up in a pK_a table.

Caution! pKa is not the same as pH!

It is important to realize that pK_a is *not* the same thing as pH: the former is an inherent property of a compound or functional group, while the latter is a measure of hydronium ion concentration in a given aqueous solution:

$$pH = -\log [H_3O^+]$$

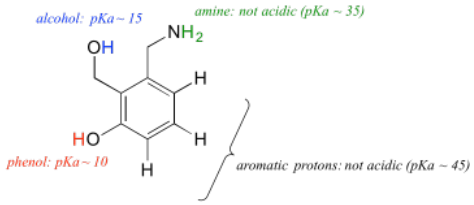
Knowing pK_a values not only allows us to compare acid strength, it also allows us to compare base strength. The key idea to remember is this: ***the stronger the conjugate acid, the weaker the conjugate base.*** We can determine that hydroxide ion is a stronger base than ammonia (NH_3), because ammonium ion (NH_4^+, $pK_a = 9.2$) is a stronger acid than water ($pK_a = 14.0$).

Exercise 7.2.1

Which is the stronger base, CH_3O^- or CH_3S^-? Acetate ion or ammonia? Hydroxide ion or acetate ion?

Solution

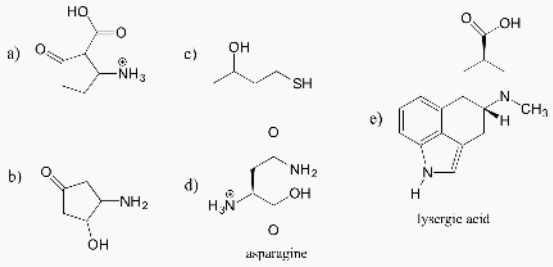
Let's put our understanding of the pK_a concept to use in the context of a more complex molecule. For example, what is the pK_a of the compound below?



We need to evaluate the potential acidity of *four* different types of protons on the molecule, and find the most acidic one. The aromatic protons are not all acidic - their pK_a is about 45. The amine group is also not acidic, its pK_a is about 35. (Remember, uncharged amines are basic: it is positively-charged *protonated* amines, with pKa values around 10, that are weakly acidic.) The alcohol proton has a pK_a of about 15, and the phenol proton has a pK_a of about 10: thus, the most acidic group on the molecule above is the phenol. (Be sure that you can recognize the difference between a phenol and an alcohol - remember, in a phenol the OH group is bound *directly* to the aromatic ring). If this molecule were to react with one molar equivalent of a strong base such as sodium hydroxide, it is the phenol proton which would be donated to form a phenolate anion.

Exercise 7.2.2

Identify the most acidic functional group on each of the molecules below, and give its approximate pK_a.



Solution

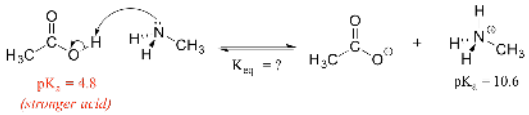
B: Using pK_a values to predict reaction equilibria

By definition, the pK_a value tells us the extent to which an acid will react with water as the base, but by extension we can also calculate the equilibrium constant for a reaction between any acid-base pair. Mathematically, it can be shown that:

$$K_{eq} = 10^{\Delta pKa}$$

. . . where ΔpK_a = (pK_a of product acid minus pK_a of reactant acid).

Consider a reaction between methylamine and acetic acid:

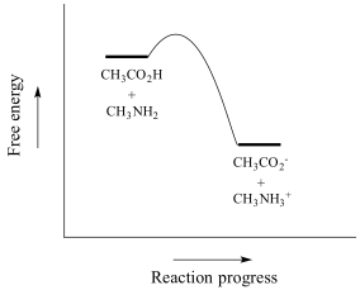


The first step is to identify the acid species on either side of the equation, and look up or estimate their pK_a values. On the left side, the acid is of course acetic acid while on the right side the acid is methyl ammonium ion (in other words, methyl ammonium ion is the acid in the reaction going from right to left). We can look up the precise pK_a values in table 7 (at the back of the book), but we already know (because we have this information memorized, right?!) that the pK_a of acetic acids is about 5, and methyl ammonium is about 10. More precise values are 4.8 and 10.6, respectively.

Without performing any calculations at all, you should be able to see that this equilibrium lies far to the right-hand side: acetic acid has a lower pK_a, meaning it is a stronger acid than methyl ammonium, and thus it wants to give up its proton more than methyl ammonium does. Doing the math, we see that

$$K_{eq} = 10^{\Delta pKa} = 10^{(10.6 - 4.8)} = 10^{5.8} = 6.3 \times 10^5$$

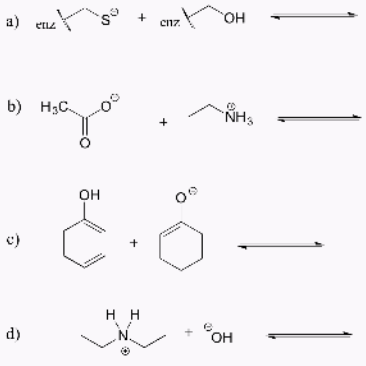
So K_{eq} is a very large number (much greater than 1) and the equilibrium for the reaction between acetic acid and methylamine lies far to the right-hand side of the equation, just as we had predicted. This also tells us that the reaction has a negative Gibbs free energy change, and is thermodynamically favorable.



If you had just wanted to quickly approximate the value of K_{eq} without benefit of precise pK_a information or a calculator, you could have approximated pK_a ~ 5 (for the carboxylic acid) and pK_a ~10 (for the ammonium ion) and calculated in your head that the equilibrium constant should be somewhere in the order of 10^5.

Exercise 7.2.3

Show the products of the following acid-base reactions, and roughly estimate the value of K_{eq}.



Solution

C: Organic molecules in buffered solution: the Henderson-Hasselbalch equation

The environment inside a living cell, where most biochemical reactions take place, is an aqueous buffer with pH ~ 7. Recall from your General Chemistry course that a buffer is a solution of a weak acid and its conjugate base. The key equation for working with buffers is the Henderson-Hasselbalch equation:

The Henderson-Hasselbalch equation:

$$pH = pK_a - \log\left(\frac{concentration\ of\ conjugate\ base}{concentration\ of\ weak\ acid}\right)$$

The equation tells us that if our buffer is an equimolar solution of a weak acid and its conjugate base, the pH of the buffer will equal the pK_a of the acid (because the log of 1 is equal to zero). If there is more of the acid form than the base, then of course the pH of the buffer is lower than the pK_a of the acid.

Exercise 7.2.4

What is the pH of an aqueous buffer solution that is 30 mM in acetic acid and 40 mM in sodium acetate? The pK_a of acetic acid is 4.8.

Solution

The Henderson-Hasselbalch equation is particularly useful when we want to think about the protonation state of different biomolecule functional groups in a pH 7 buffer. When we do this, we are always assuming that the concentration of the biomolecule is small compared to the concentration of the buffer components. (The actual composition of physiological buffer is complex, but it is primarily based on phosphoric and carbonic acids).

Imagine an aspartic acid residue located on the surface of a protein in a human cell. Being on the surface, the side chain is in full contact with the pH 7 buffer surrounding the protein. In what state is the side chain functional group: the protonated state (a carboxylic acid) or the deprotonated state (a carboxylate ion)? Using the Henderson-Hasselbalch equation, we fill in our values for the pH of the buffer and a rough pKa approximation of $pK_a = 5$ for the carboxylic acid functional group. Doing the math, we find that the ratio of carboxylate to carboxylic acid is about 100 to 1: the carboxylic acid is almost completely ionized (in the deprotonated state) inside the cell. This result extends to all other carboxylic acid groups you might find on natural biomolecules or drug molecules: in the physiological environment, carboxylic acids are almost completely deprotonated.

Now, let's use the equation again, this time for an amine functional group, such as the side chain of a lysine residue: inside a cell, are we likely to see a neutral amine ($R\text{-}NH_2$) or an ammonium cation ($R\text{-}NH_3^+$?) Using the equation with pH = 7 (for the biological buffer) and pKa = 10 (for the ammonium group), we find that the ratio of neutral amine to ammonium cation is about 1 to 100: the group is close to completely protonated inside the cell, so we will see $R\text{-}NH_3^+$, not $R\text{-}NH_2$.

We can do the same rough calculation for other common functional groups found in biomolecules. It will be very helpful going forward to commit the following to memory:

At physiological pH:

Carboxylic acids are deprotonated (in the carboxylate anion form)

Amines are protonated (in the ammonium cation form)

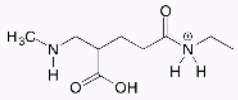
Thiols, phenols, alcohols, and amides are uncharged

Imines are a mixture of the protonated (cationic) and deprotonated (neutral) states

We will talk about the physiological protonation state of phosphate groups in chapter 9.

Exercise 7.2.5

The molecule below is ***not*** drawn in a reasonable protonation state for pH 7. Redraw it in with the functional groups in the correct protonation state.



Solution

While we are most interested in the state of molecules at pH 7, the Henderson-Hasselbalch equation can of course be used to determine the protonation state of functional groups in solutions buffered to other pH levels. The exercises below provide some practice in this type of calculation.

Exercise 7.2.6

What is the ratio of acetate ion to neutral acetic acid when a small amount of acetic acid (pK_a = 4.8) is dissolved in a buffer of pH 2.8? pH 3.8? pH 4.8? pH 5.8? pH 6.8?

Solution

Exercise 7.2.7

Would you expect phenol to be soluble in an aqueous solution buffered to pH 2? pH 7? pH 12? Explain your answer.

Solution

Exercise 7.2.8

Exercise 7.2.8: What is the approximate net charge on a tetrapeptide Cys-Asp-Lys-Glu in pH 7 buffer?

Solution

Next section⇒

Organic Chemistry With a Biological Emphasis by Tim Soderberg (University of Minnesota, Morris)

Modified by Tom Neils (Grand Rapids Community College)

1.19: How to Predict the Outcome of an Acid-Base Reaction is shared under a not declared license and was authored, remixed, and/or curated by LibreTexts.

1.20: How to Determine the Position of Equilibrium

1.20: How to Determine the Position of Equilibrium is shared under a not declared license and was authored, remixed, and/or curated by LibreTexts.

1.21: How the Structure of an Acid Affects its pka Value

1.21: How the Structure of an Acid Affects its pka Value is shared under a not declared license and was authored, remixed, and/or curated by LibreTexts.

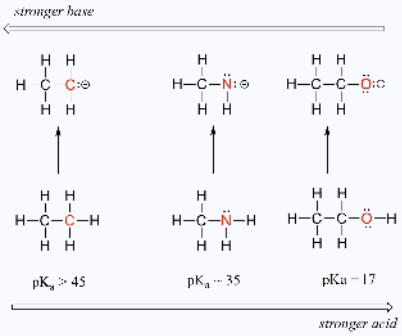
1.22: How Substituents Affect the Strength of an Acid

Now that we know how to quantify the strength of an acid or base, our next job is to gain an understanding of the fundamental reasons behind *why* one compound is more acidic or more basic than another. This is a big step: we are, for the first time, taking our knowledge of organic *structure* and applying it to a question of organic *reactivity*. Many of the ideas that we'll see for the first here will continue to apply throughout the book as we tackle many other organic reaction types.

A: Periodic trends

First, we will focus on individual atoms, and think about trends associated with the position of an element on the periodic table. We'll use as our first models the simple organic compounds ethane, methylamine, and ethanol, but the concepts apply equally to more complex biomolecules with the same functionalities, for example the side chains of the amino acids alanine (alkane), lysine (amine), and serine (alcohol).

Horizontal periodic trend in acidity and basicity



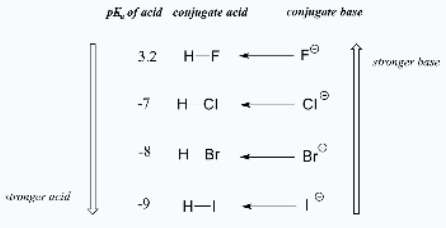
We can see a clear trend in acidity as we move from left to right along the second row of the periodic table from carbon to nitrogen to oxygen. The key to understanding this trend is to consider the hypothetical conjugate base in each case*: the more stable (weaker) the conjugate base, the stronger the acid*. Look at where the negative charge ends up in each conjugate base. In the conjugate base of ethane, the negative charge is borne by a carbon atom, while on the conjugate base of methylamine and ethanol the negative charge is located on a nitrogen and an oxygen, respectively. Remember that electronegativity also increases as we move from left to right along a row of the periodic table, meaning that oxygen is the most electronegative of the three atoms, and carbon the least.

The more electronegative an atom, the better able it is to bear a negative charge. Weaker bases have negative charges on more electronegative atoms; stronger bases have negative charges on less electronegative atoms.

Thus, the methoxide anion is the most stable (lowest energy, least basic) of the three conjugate bases, and the ethyl carbanion anion is the least stable (highest energy, most basic). Conversely, ethanol is the strongest acid, and ethane the weakest acid.

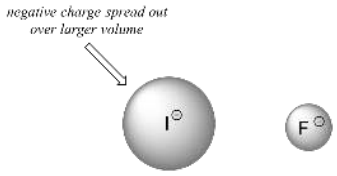
When moving vertically within a given column of the periodic table, we again observe a clear periodic trend in acidity. This is best illustrated with the haloacids and halides: basicity, like electronegativity, increases as we move up the column.

Vertical periodic trend in acidity and basicity



Conversely, acidity in the haloacids increases as we move *down* the column.

In order to make sense of this trend, we will once again consider the stability of the conjugate bases. Because fluorine is the most electronegative halogen element, we might expect fluoride to also be the least basic halogen ion. But in fact, it is the *least* stable, and the most basic! It turns out that when moving vertically in the periodic table, the *size* of the atom trumps its electronegativity with regard to basicity. The atomic radius of iodine is approximately twice that of fluorine, so in an iodide ion, the negative charge is spread out over a significantly larger volume:



This illustrates a fundamental concept in organic chemistry:

> ***Electrostatic charges, whether positive or negative, are more stable when they are 'spread out' over a larger area.***

We will see this idea expressed again and again throughout our study of organic reactivity, in many different contexts. For now, we are applying the concept only to the influence of atomic radius on base strength. Because fluoride is the least stable (most basic) of the halide conjugate bases, HF is the least acidic of the haloacids, only slightly stronger than a carboxylic acid. HI, with a pK_a of about -9, is almost as strong as sulfuric acid.

More importantly to the study of biological organic chemistry, this trend tells us that ***thiols are more acidic than alcohols***. The pK_a of the thiol group on the cysteine side chain, for example, is approximately 8.3, while the pK_a for the alcohol group on the serine side chain is on the order of 17.

Remember the concept of 'driving force' that we learned about in chapter 6? Recall that the driving force for a reaction is usually based on two factors: relative charge stability, and relative total bond energy. Let's see how this applies to a simple acid-base reaction between hydrochloric acid and fluoride ion:

$$HCl + F^- \rightarrow HF + Cl^-$$

We know that HCl (pK_a -7) is a stronger acid than HF (pK_a 3.2), so the equilibrium for the reaction lies on the product side: the reaction is exergonic, and a 'driving force' pushes reactant to product.

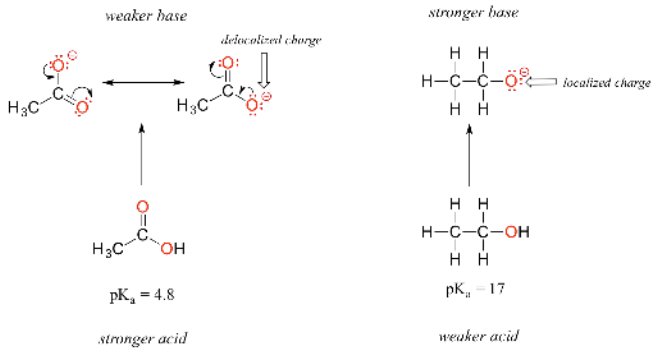
What explains this driving force? Consider first the charge factor: as we just learned, chloride ion (on the product side) is more stable than fluoride ion (on the reactant side). This partially accounts for the driving force going from reactant to product in this reaction: we are going from less stable ion to a more stable ion.

What about total bond energy, the other factor in driving force? If you consult a table of bond energies, you will see that the H-F bond on the product side is more energetic (stronger) than the H-Cl bond on the reactant side: 565 kJ/mol *vs* 427 kJ/mol, respectively). This also contributes to the driving force: we are moving from a weaker (less stable) bond to a stronger (more stable) bond.

B: Resonance effects

In the previous section we focused our attention on periodic trends - the differences in acidity and basicity between groups where the exchangeable proton was bound to different elements. Now, it is time to think about how the structure of different organic groups contributes to their relative acidity or basicity, even when we are talking about *the same element acting as the proton donor/acceptor*. The first model pair we will consider is ethanol and acetic acid, but the conclusions we reach will be equally valid for all alcohol and carboxylic acid groups.

Despite the fact that they are both oxygen acids, the pK_a values of ethanol and acetic acid are strikingly different. What makes a carboxylic acid so much more acidic than an alcohol? As before, we begin by considering the stability of the conjugate bases, remembering that a more stable (weaker) conjugate base corresponds to a stronger acid.

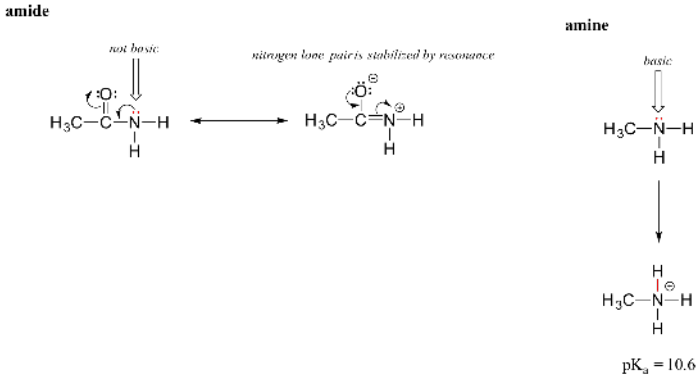


In both species, the negative charge on the conjugate base is located on oxygen, so periodic trends cannot be invoked. For acetic acid, however, there is a key difference: two resonance contributors can be drawn for the conjugate base, and the negative charge can be delocalized (shared) over two oxygen atoms. In the ethoxide ion, by contrast, the negative charge is localized, or 'locked' on the single oxygen – it has nowhere else to go. This makes the ethoxide ion much less stable.

Recall the important general statement that we made a little earlier: 'Electrostatic charges, whether positive or negative, are more stable when they are 'spread out' than when they are confined to one location.' Now, we are seeing this concept in another context, where 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 (and remember, pK_a is a log expression, so we are talking about a fator of 10^{12} between the K_a values for the two molecules!)

The resonance effect also nicely explains why a nitrogen atom is basic when it is in an amine, but *not* 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 minor but still important resonance contributor in which the nitrogen lone pair is part of a pi bond.



Whereas the 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 so comfortable - it is *not* part of a delocalized pi system, and is available to form a bond with any acidic proton that might be nearby.

If an amide group is protonated, it will be at the oxygen rather than the nitrogen.

Exercise 7.3.1

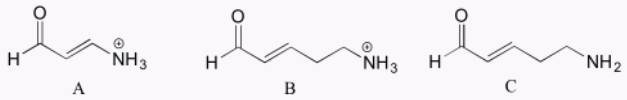
a) Draw the Lewis structure of nitric acid, HNO_3.

b) Nitric acid is a strong acid - it has a pK_a of -1.4. Make a structural argument to account for its strength. Your answer should involve the structure of nitrate, the conjugate base of nitric acid.

Solution

Exercise 7.3.2

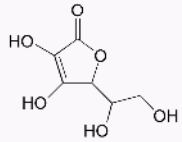
Rank the compounds below from most acidic to least acidic, and explain your reasoning.



Solution

Exercise 7.3.3

(challenging!) Often it requires some careful thought to predict the most acidic proton on a molecule. Ascorbic acid, also known as Vitamin C, has a pK_a of 4.1 - the fact that this is in the range of carboxylic acids suggest to us that the negative charge on the conjugate base can be delocalized by resonance to *two* oxygen atoms. Which if the four OH protons on the molecule is most acidic? Draw the structure of ascorbate, the conjugate base of ascorbic acid, then draw a second resonance contributor showing how the negative charge is delocalized to a second oxygen atom. *Hint* - try removing each OH group in turn, then use your resonance drawing skills to figure out whether or not delocalization of charge can occur.

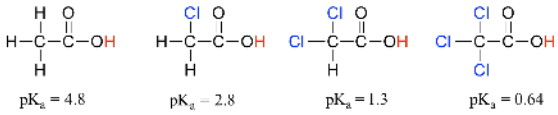


ascorbic acid
(Vitamin C)

Solution

C: Inductive effects

Compare the pK_a values of acetic acid and its mono-, di-, and tri-chlorinated derivatives:



The presence of the chlorine atoms clearly increases the acidity of the carboxylic acid group, but the argument here does not have to do with resonance delocalization, because no additional resonance contributors can be drawn for the chlorinated molecules. Rather, the explanation for this phenomenon involves something called the **inductive effect**. A chlorine atom is more electronegative than a hydrogen, and thus is able to 'induce', or 'pull' electron density towards itself, away from the carboxylate group. In effect, the chlorine atoms are helping to further spread out the electron density of the conjugate base, which as we know has a stabilizing effect. In this context, the chlorine substituent can be referred to as an **electron-withdrawing group**. Notice that the pKa-lowering effect of each chlorine atom, while significant, is not as dramatic as the delocalizing resonance effect illustrated by the difference in pK_a values between an alcohol and a carboxylic acid. In general, *resonance effects are more powerful than inductive effects*.

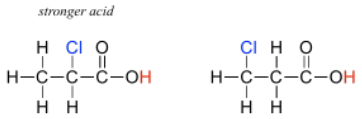
Because the inductive effect depends on electronegativity, fluorine substituents have a more pronounced pKa-lowered effect than chlorine substituents.



trichloroacetic acid
$pK_a = 0.64$

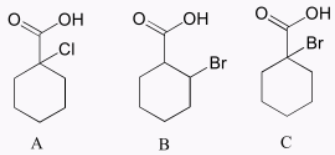
trifluoroacetic acid
$pK_a = -0.25$

In addition, the inductive takes place through covalent bonds, and its influence decreases markedly with distance – thus a chlorine two carbons away from a carboxylic acid group has a decreased effect compared to a chlorine just one carbon away.



Exercise 7.3.4

Rank the compounds below from most acidic to least acidic, and explain your reasoning.



Solution

Next section⇒

Organic Chemistry With a Biological Emphasis by Tim Soderberg (University of Minnesota, Morris)

1.22: How Substituents Affect the Strength of an Acid is shared under a not declared license and was authored, remixed, and/or curated by LibreTexts.

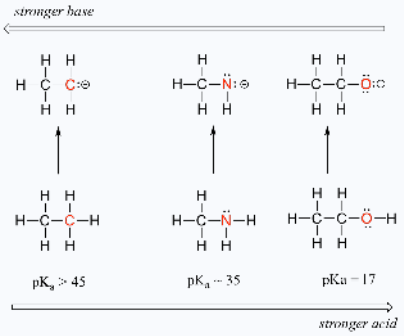
1.23: An Introduction to Delocalized Electrons

Now that we know how to quantify the strength of an acid or base, our next job is to gain an understanding of the fundamental reasons behind *why* one compound is more acidic or more basic than another. This is a big step: we are, for the first time, taking our knowledge of organic *structure* and applying it to a question of organic *reactivity*. Many of the ideas that we'll see for the first here will continue to apply throughout the book as we tackle many other organic reaction types.

A: Periodic trends

First, we will focus on individual atoms, and think about trends associated with the position of an element on the periodic table. We'll use as our first models the simple organic compounds ethane, methylamine, and ethanol, but the concepts apply equally to more complex biomolecules with the same functionalities, for example the side chains of the amino acids alanine (alkane), lysine (amine), and serine (alcohol).

Horizontal periodic trend in acidity and basicity



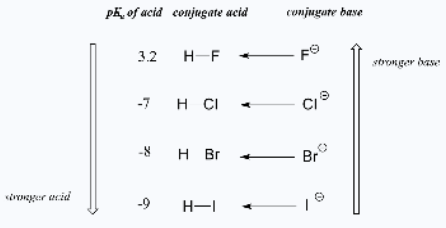
We can see a clear trend in acidity as we move from left to right along the second row of the periodic table from carbon to nitrogen to oxygen. The key to understanding this trend is to consider the hypothetical conjugate base in each case*: the more stable (weaker) the conjugate base, the stronger the acid*. Look at where the negative charge ends up in each conjugate base. In the conjugate base of ethane, the negative charge is borne by a carbon atom, while on the conjugate base of methylamine and ethanol the negative charge is located on a nitrogen and an oxygen, respectively. Remember that electronegativity also increases as we move from left to right along a row of the periodic table, meaning that oxygen is the most electronegative of the three atoms, and carbon the least.

The more electronegative an atom, the better able it is to bear a negative charge. Weaker bases have negative charges on more electronegative atoms; stronger bases have negative charges on less electronegative atoms.

Thus, the methoxide anion is the most stable (lowest energy, least basic) of the three conjugate bases, and the ethyl carbanion anion is the least stable (highest energy, most basic). Conversely, ethanol is the strongest acid, and ethane the weakest acid.

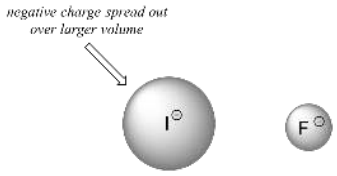
When moving vertically within a given column of the periodic table, we again observe a clear periodic trend in acidity. This is best illustrated with the haloacids and halides: basicity, like electronegativity, increases as we move up the column.

Vertical periodic trend in acidity and basicity



Conversely, acidity in the haloacids increases as we move *down* the column.

In order to make sense of this trend, we will once again consider the stability of the conjugate bases. Because fluorine is the most electronegative halogen element, we might expect fluoride to also be the least basic halogen ion. But in fact, it is the *least* stable, and the most basic! It turns out that when moving vertically in the periodic table, the *size* of the atom trumps its electronegativity with regard to basicity. The atomic radius of iodine is approximately twice that of fluorine, so in an iodide ion, the negative charge is spread out over a significantly larger volume:



This illustrates a fundamental concept in organic chemistry:

> ***Electrostatic charges, whether positive or negative, are more stable when they are 'spread out' over a larger area.***

We will see this idea expressed again and again throughout our study of organic reactivity, in many different contexts. For now, we are applying the concept only to the influence of atomic radius on base strength. Because fluoride is the least stable (most basic) of the halide conjugate bases, HF is the least acidic of the haloacids, only slightly stronger than a carboxylic acid. HI, with a pK_a of about -9, is almost as strong as sulfuric acid.

More importantly to the study of biological organic chemistry, this trend tells us that ***thiols are more acidic than alcohols***. The pK_a of the thiol group on the cysteine side chain, for example, is approximately 8.3, while the pK_a for the alcohol group on the serine side chain is on the order of 17.

Remember the concept of 'driving force' that we learned about in chapter 6? Recall that the driving force for a reaction is usually based on two factors: relative charge stability, and relative total bond energy. Let's see how this applies to a simple acid-base reaction between hydrochloric acid and fluoride ion:

$$HCl + F^- \rightarrow HF + Cl^-$$

We know that HCl (pK_a -7) is a stronger acid than HF (pK_a 3.2), so the equilibrium for the reaction lies on the product side: the reaction is exergonic, and a 'driving force' pushes reactant to product.

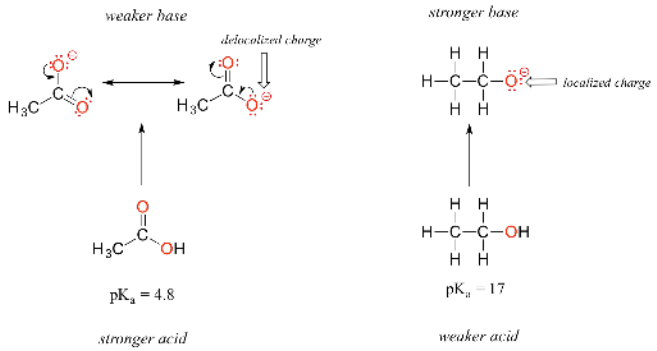
What explains this driving force? Consider first the charge factor: as we just learned, chloride ion (on the product side) is more stable than fluoride ion (on the reactant side). This partially accounts for the driving force going from reactant to product in this reaction: we are going from less stable ion to a more stable ion.

What about total bond energy, the other factor in driving force? If you consult a table of bond energies, you will see that the H-F bond on the product side is more energetic (stronger) than the H-Cl bond on the reactant side: 565 kJ/mol *vs* 427 kJ/mol, respectively). This also contributes to the driving force: we are moving from a weaker (less stable) bond to a stronger (more stable) bond.

B: Resonance effects

In the previous section we focused our attention on periodic trends - the differences in acidity and basicity between groups where the exchangeable proton was bound to different elements. Now, it is time to think about how the structure of different organic groups contributes to their relative acidity or basicity, even when we are talking about *the same element acting as the proton donor/acceptor*. The first model pair we will consider is ethanol and acetic acid, but the conclusions we reach will be equally valid for all alcohol and carboxylic acid groups.

Despite the fact that they are both oxygen acids, the pK_a values of ethanol and acetic acid are strikingly different. What makes a carboxylic acid so much more acidic than an alcohol? As before, we begin by considering the stability of the conjugate bases, remembering that a more stable (weaker) conjugate base corresponds to a stronger acid.

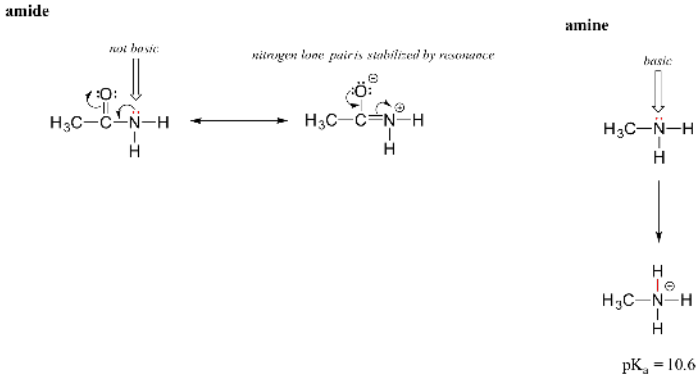


In both species, the negative charge on the conjugate base is located on oxygen, so periodic trends cannot be invoked. For acetic acid, however, there is a key difference: two resonance contributors can be drawn for the conjugate base, and the negative charge can be delocalized (shared) over two oxygen atoms. In the ethoxide ion, by contrast, the negative charge is localized, or 'locked' on the single oxygen – it has nowhere else to go. This makes the ethoxide ion much less stable.

Recall the important general statement that we made a little earlier: 'Electrostatic charges, whether positive or negative, are more stable when they are 'spread out' than when they are confined to one location.' Now, we are seeing this concept in another context, where 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 (and remember, pK_a is a log expression, so we are talking about a fator of 10^{12} between the K_a values for the two molecules!)

The resonance effect also nicely explains why a nitrogen atom is basic when it is in an amine, but *not* 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 minor but still important resonance contributor in which the nitrogen lone pair is part of a pi bond.



Whereas the 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 so comfortable - it is *not* part of a delocalized pi system, and is available to form a bond with any acidic proton that might be nearby.

If an amide group is protonated, it will be at the oxygen rather than the nitrogen.

Exercise 7.3.1

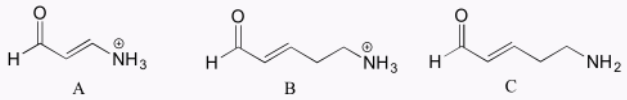
a) Draw the Lewis structure of nitric acid, HNO_3.

b) Nitric acid is a strong acid - it has a pK_a of -1.4. Make a structural argument to account for its strength. Your answer should involve the structure of nitrate, the conjugate base of nitric acid.

Solution

Exercise 7.3.2

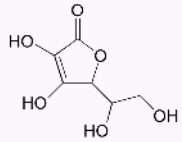
Rank the compounds below from most acidic to least acidic, and explain your reasoning.



Solution

Exercise 7.3.3

(challenging!) Often it requires some careful thought to predict the most acidic proton on a molecule. Ascorbic acid, also known as Vitamin C, has a pK_a of 4.1 - the fact that this is in the range of carboxylic acids suggest to us that the negative charge on the conjugate base can be delocalized by resonance to *two* oxygen atoms. Which if the four OH protons on the molecule is most acidic? Draw the structure of ascorbate, the conjugate base of ascorbic acid, then draw a second resonance contributor showing how the negative charge is delocalized to a second oxygen atom. *Hint* - try removing each OH group in turn, then use your resonance drawing skills to figure out whether or not delocalization of charge can occur.

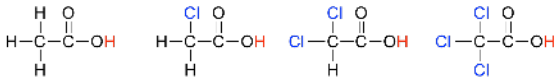


ascorbic acid
(Vitamin C)

Solution

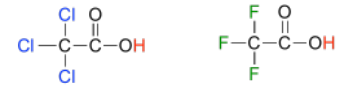
C: Inductive effects

Compare the pK_a values of acetic acid and its mono-, di-, and tri-chlorinated derivatives:



The presence of the chlorine atoms clearly increases the acidity of the carboxylic acid group, but the argument here does not have to do with resonance delocalization, because no additional resonance contributors can be drawn for the chlorinated molecules. Rather, the explanation for this phenomenon involves something called the **inductive effect**. A chlorine atom is more electronegative than a hydrogen, and thus is able to 'induce', or 'pull' electron density towards itself, away from the carboxylate group. In effect, the chlorine atoms are helping to further spread out the electron density of the conjugate base, which as we know has a stabilizing effect. In this context, the chlorine substituent can be referred to as an **electron-withdrawing group**. Notice that the pKa-lowering effect of each chlorine atom, while significant, is not as dramatic as the delocalizing resonance effect illustrated by the difference in pK_a values between an alcohol and a carboxylic acid. In general, *resonance effects are more powerful than inductive effects*.

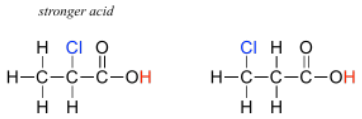
Because the inductive effect depends on electronegativity, fluorine substituents have a more pronounced pKa-lowered effect than chlorine substituents.



trichloroacetic acid
pK_a = 0.64

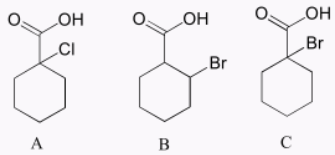
trifluoroacetic acid
pK_a = -0.25

In addition, the inductive takes place through covalent bonds, and its influence decreases markedly with distance – thus a chlorine two carbons away from a carboxylic acid group has a decreased effect compared to a chlorine just one carbon away.



Exercise 7.3.4

Rank the compounds below from most acidic to least acidic, and explain your reasoning.



Solution

Next section⇒

Organic Chemistry With a Biological Emphasis by Tim Soderberg (University of Minnesota, Morris)

1.23: An Introduction to Delocalized Electrons is shared under a not declared license and was authored, remixed, and/or curated by LibreTexts.

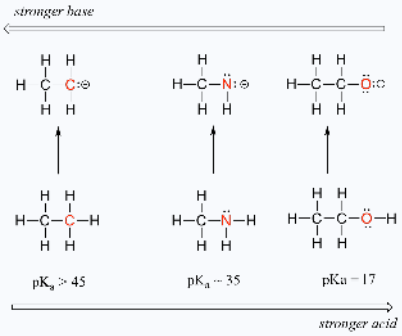
1.24: A Summary of the Factors that Determine Acid Strength

Now that we know how to quantify the strength of an acid or base, our next job is to gain an understanding of the fundamental reasons behind *why* one compound is more acidic or more basic than another. This is a big step: we are, for the first time, taking our knowledge of organic *structure* and applying it to a question of organic *reactivity*. Many of the ideas that we'll see for the first here will continue to apply throughout the book as we tackle many other organic reaction types.

A: Periodic trends

First, we will focus on individual atoms, and think about trends associated with the position of an element on the periodic table. We'll use as our first models the simple organic compounds ethane, methylamine, and ethanol, but the concepts apply equally to more complex biomolecules with the same functionalities, for example the side chains of the amino acids alanine (alkane), lysine (amine), and serine (alcohol).

Horizontal periodic trend in acidity and basicity



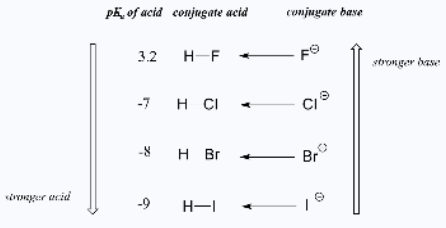
We can see a clear trend in acidity as we move from left to right along the second row of the periodic table from carbon to nitrogen to oxygen. The key to understanding this trend is to consider the hypothetical conjugate base in each case*: the more stable (weaker) the conjugate base, the stronger the acid*. Look at where the negative charge ends up in each conjugate base. In the conjugate base of ethane, the negative charge is borne by a carbon atom, while on the conjugate base of methylamine and ethanol the negative charge is located on a nitrogen and an oxygen, respectively. Remember that electronegativity also increases as we move from left to right along a row of the periodic table, meaning that oxygen is the most electronegative of the three atoms, and carbon the least.

The more electronegative an atom, the better able it is to bear a negative charge. Weaker bases have negative charges on more electronegative atoms; stronger bases have negative charges on less electronegative atoms.

Thus, the methoxide anion is the most stable (lowest energy, least basic) of the three conjugate bases, and the ethyl carbanion anion is the least stable (highest energy, most basic). Conversely, ethanol is the strongest acid, and ethane the weakest acid.

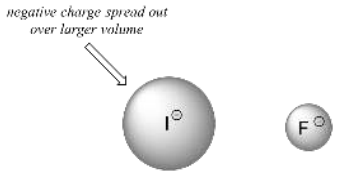
When moving vertically within a given column of the periodic table, we again observe a clear periodic trend in acidity. This is best illustrated with the haloacids and halides: basicity, like electronegativity, increases as we move up the column.

Vertical periodic trend in acidity and basicity



Conversely, acidity in the haloacids increases as we move *down* the column.

In order to make sense of this trend, we will once again consider the stability of the conjugate bases. Because fluorine is the most electronegative halogen element, we might expect fluoride to also be the least basic halogen ion. But in fact, it is the *least* stable, and the most basic! It turns out that when moving vertically in the periodic table, the *size* of the atom trumps its electronegativity with regard to basicity. The atomic radius of iodine is approximately twice that of fluorine, so in an iodide ion, the negative charge is spread out over a significantly larger volume:



This illustrates a fundamental concept in organic chemistry:

> ***Electrostatic charges, whether positive or negative, are more stable when they are 'spread out' over a larger area.***

We will see this idea expressed again and again throughout our study of organic reactivity, in many different contexts. For now, we are applying the concept only to the influence of atomic radius on base strength. Because fluoride is the least stable (most basic) of the halide conjugate bases, HF is the least acidic of the haloacids, only slightly stronger than a carboxylic acid. HI, with a pK_a of about -9, is almost as strong as sulfuric acid.

More importantly to the study of biological organic chemistry, this trend tells us that ***thiols are more acidic than alcohols***. The pK_a of the thiol group on the cysteine side chain, for example, is approximately 8.3, while the pK_a for the alcohol group on the serine side chain is on the order of 17.

Remember the concept of 'driving force' that we learned about in chapter 6? Recall that the driving force for a reaction is usually based on two factors: relative charge stability, and relative total bond energy. Let's see how this applies to a simple acid-base reaction between hydrochloric acid and fluoride ion:

$$HCl + F^- \rightarrow HF + Cl^-$$

We know that HCl (pK_a -7) is a stronger acid than HF (pK_a 3.2), so the equilibrium for the reaction lies on the product side: the reaction is exergonic, and a 'driving force' pushes reactant to product.

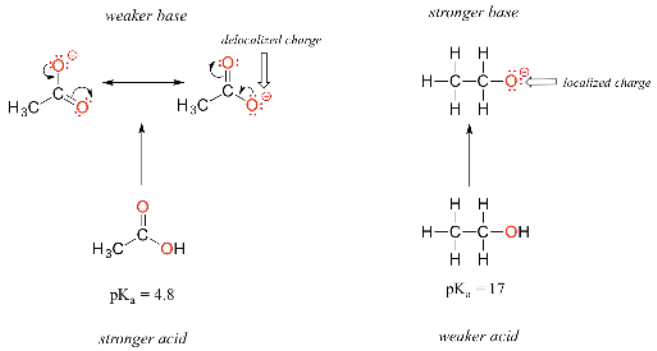
What explains this driving force? Consider first the charge factor: as we just learned, chloride ion (on the product side) is more stable than fluoride ion (on the reactant side). This partially accounts for the driving force going from reactant to product in this reaction: we are going from less stable ion to a more stable ion.

What about total bond energy, the other factor in driving force? If you consult a table of bond energies, you will see that the H-F bond on the product side is more energetic (stronger) than the H-Cl bond on the reactant side: 565 kJ/mol *vs* 427 kJ/mol, respectively). This also contributes to the driving force: we are moving from a weaker (less stable) bond to a stronger (more stable) bond.

B: Resonance effects

In the previous section we focused our attention on periodic trends - the differences in acidity and basicity between groups where the exchangeable proton was bound to different elements. Now, it is time to think about how the structure of different organic groups contributes to their relative acidity or basicity, even when we are talking about *the same element acting as the proton donor/acceptor*. The first model pair we will consider is ethanol and acetic acid, but the conclusions we reach will be equally valid for all alcohol and carboxylic acid groups.

Despite the fact that they are both oxygen acids, the pK_a values of ethanol and acetic acid are strikingly different. What makes a carboxylic acid so much more acidic than an alcohol? As before, we begin by considering the stability of the conjugate bases, remembering that a more stable (weaker) conjugate base corresponds to a stronger acid.

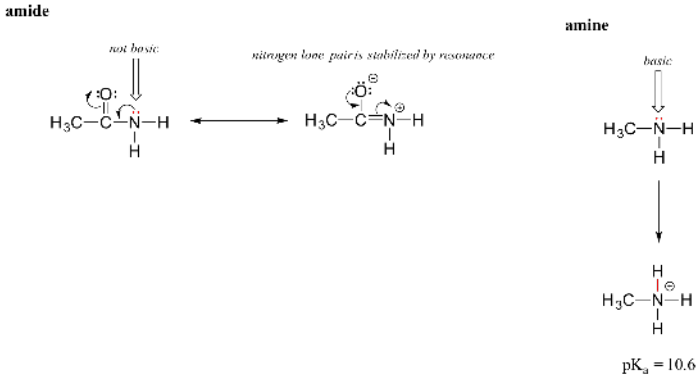


In both species, the negative charge on the conjugate base is located on oxygen, so periodic trends cannot be invoked. For acetic acid, however, there is a key difference: two resonance contributors can be drawn for the conjugate base, and the negative charge can be delocalized (shared) over two oxygen atoms. In the ethoxide ion, by contrast, the negative charge is localized, or 'locked' on the single oxygen – it has nowhere else to go. This makes the ethoxide ion much less stable.

Recall the important general statement that we made a little earlier: 'Electrostatic charges, whether positive or negative, are more stable when they are 'spread out' than when they are confined to one location.' Now, we are seeing this concept in another context, where 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 (and remember, pK_a is a log expression, so we are talking about a fator of 10^{12} between the K_a values for the two molecules!)

The resonance effect also nicely explains why a nitrogen atom is basic when it is in an amine, but *not* 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 minor but still important resonance contributor in which the nitrogen lone pair is part of a pi bond.



Whereas the 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 so comfortable - it is *not* part of a delocalized pi system, and is available to form a bond with any acidic proton that might be nearby.

If an amide group is protonated, it will be at the oxygen rather than the nitrogen.

Exercise 7.3.1

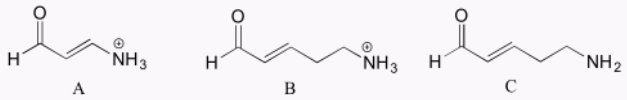
a) Draw the Lewis structure of nitric acid, HNO_3.

b) Nitric acid is a strong acid - it has a pK_a of -1.4. Make a structural argument to account for its strength. Your answer should involve the structure of nitrate, the conjugate base of nitric acid.

Solution

Exercise 7.3.2

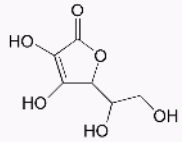
Rank the compounds below from most acidic to least acidic, and explain your reasoning.



Solution

Exercise 7.3.3

(challenging!) Often it requires some careful thought to predict the most acidic proton on a molecule. Ascorbic acid, also known as Vitamin C, has a pK_a of 4.1 - the fact that this is in the range of carboxylic acids suggest to us that the negative charge on the conjugate base can be delocalized by resonance to *two* oxygen atoms. Which if the four OH protons on the molecule is most acidic? Draw the structure of ascorbate, the conjugate base of ascorbic acid, then draw a second resonance contributor showing how the negative charge is delocalized to a second oxygen atom. *Hint* - try removing each OH group in turn, then use your resonance drawing skills to figure out whether or not delocalization of charge can occur.

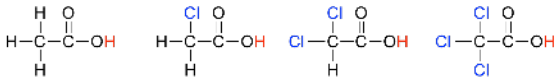


ascorbic acid
(Vitamin C)

Solution

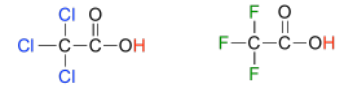
C: Inductive effects

Compare the pK_a values of acetic acid and its mono-, di-, and tri-chlorinated derivatives:



The presence of the chlorine atoms clearly increases the acidity of the carboxylic acid group, but the argument here does not have to do with resonance delocalization, because no additional resonance contributors can be drawn for the chlorinated molecules. Rather, the explanation for this phenomenon involves something called the **inductive effect**. A chlorine atom is more electronegative than a hydrogen, and thus is able to 'induce', or 'pull' electron density towards itself, away from the carboxylate group. In effect, the chlorine atoms are helping to further spread out the electron density of the conjugate base, which as we know has a stabilizing effect. In this context, the chlorine substituent can be referred to as an **electron-withdrawing group**. Notice that the pKa-lowering effect of each chlorine atom, while significant, is not as dramatic as the delocalizing resonance effect illustrated by the difference in pK_a values between an alcohol and a carboxylic acid. In general, *resonance effects are more powerful than inductive effects*.

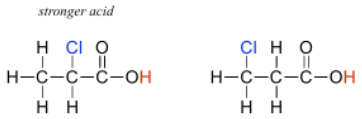
Because the inductive effect depends on electronegativity, fluorine substituents have a more pronounced pKa-lowered effect than chlorine substituents.



trichloroacetic acid
pK_a = 0.64

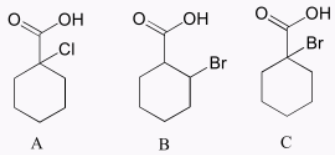
trifluoroacetic acid
pK_a = -0.25

In addition, the inductive takes place through covalent bonds, and its influence decreases markedly with distance – thus a chlorine two carbons away from a carboxylic acid group has a decreased effect compared to a chlorine just one carbon away.



Exercise 7.3.4

Rank the compounds below from most acidic to least acidic, and explain your reasoning.



Solution

Next section⇒

Organic Chemistry With a Biological Emphasis by Tim Soderberg (University of Minnesota, Morris)

1.24: A Summary of the Factors that Determine Acid Strength is shared under a not declared license and was authored, remixed, and/or curated by LibreTexts.

1.25: How pH Affects the Structure of an Organic Compound

The Henderson-Hasselbalch equation

1.25: How pH Affects the Structure of an Organic Compound is shared under a not declared license and was authored, remixed, and/or curated by LibreTexts.

SECTION OVERVIEW

1.26: Buffer Solutions

A buffer is a solution that can resist pH change upon the addition of an acidic or basic components. It is able to neutralize small amounts of added acid or base, thus maintaining the pH of the solution relatively stable. This is important for processes and/or reactions which require specific and stable pH ranges. Buffer solutions have a working pH range and capacity which dictate how much acid/base can be neutralized before pH changes, and the amount by which it will change.

1.27: Lewis Acids and Bases

Learning Objectives

Make sure you thoroughly understand the following essential ideas which have been presented above. It is especially important that you know the precise meanings of all the highlighted terms in the context of this topic.

- Write the equation for the proton transfer reaction involving a Brønsted-Lowry acid or base, and show how it can be interpreted as an electron-pair transfer reaction, clearly identifying the donor and acceptor.
- Give an example of a *Lewis acid-base reaction* that does not involve protons.
- Write equations illustrating the behavior of a given non-aqueous acid-base system.

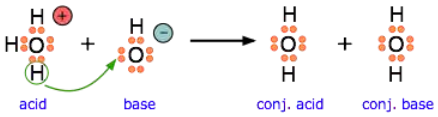
The Brønsted-Lowry proton donor-acceptor concept has been one of the most successful theories of Chemistry. But as with any such theory, it is fair to ask if this is not just a special case of a more general theory that could encompass an even broader range of chemical science. In 1916, G.N. Lewis of the University of California proposed that the *electron pair* is the dominant actor in acid-base chemistry. The Lewis theory did not become very well known until about 1923 (the same year that Brønsted and Lowry published their work), but since then it has been recognized as a very powerful tool for describing chemical reactions of widely different kinds and is widely used in organic and inorganic chemistry. According to Lewis,

- An *acid* is a substance that **accepts** a pair of electrons, and in doing so, forms a covalent bond with the entity that supplies the electrons.
- A *base* is a substance that **donates** an unshared pair of electrons to a recipient species with which the electrons can be shared.

> *In modern chemistry, electron donors are often referred to as nucleophiles, while acceptors are electrophiles.*

Proton-Transfer Reactions Involve Electron-Pair Transfer

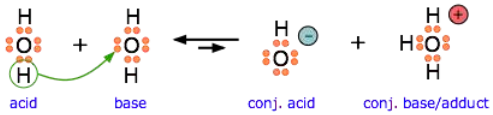
Just as any Arrhenius acid is also a Brønsted acid, any Brønsted acid is also a Lewis acid, so the various acid-base concepts are all "upward compatible". Although we do not really need to think about electron-pair transfers when we deal with ordinary aqueous-solution acid-base reactions, it is important to understand that it is the opportunity for electron-pair sharing that enables proton transfer to take place.



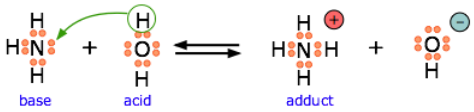
This equation for a simple acid-base neutralization shows how the Brønsted and Lewis definitions are really just different views of the same process. Take special note of the following points:

- The arrow shows the movement of a proton from the hydronium ion to the hydroxide ion.
- Note carefully that the electron-pairs themselves do not move; they remain attached to their central atoms. The electron pair on the base is "donated" to the acceptor (the proton) only in the sense that it ends up being *shared* with the acceptor, rather than being the exclusive property of the oxygen atom in the hydroxide ion.
- Although the hydronium ion is the nominal Lewis acid here, it does not itself accept an electron pair, but acts merely as the source of the proton that coordinates with the Lewis base.

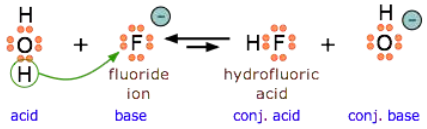
The point about the electron-pair remaining on the donor species is especially important to bear in mind. For one thing, it distinguishes a *Lewis acid-base reaction* from an *oxidation-reduction reaction*, in which a physical transfer of one or more electrons from donor to acceptor does occur. The product of a Lewis acid-base reaction is known formally as an "adduct" or "complex", although we do not ordinarily use these terms for simple proton-transfer reactions such as the one in the above example. Here, the proton combines with the hydroxide ion to form the "adduct" H_2O. The following examples illustrate these points for some other proton-transfer reactions that you should already be familiar with.



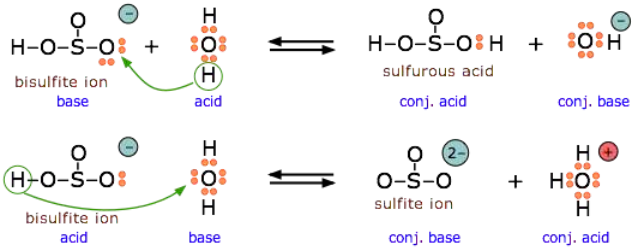
Another example, showing the autoprotolysis of water. Note that the conjugate base is also the adduct.



Ammonia is both a Brønsted and a Lewis base, owing to the unshared electron pair on the nitrogen. The reverse of this reaction represents the *hydrolysis* of the ammonium ion.



Because **HF** is a weak acid, fluoride salts behave as bases in aqueous solution. As a Lewis base, F^- accepts a proton from water, which is transformed into a hydroxide ion.



The bisulfite ion is *amphiprotic* and can act as an electron donor or acceptor.

Acid-base Reactions without Transferring Protons

The major utility of the Lewis definition is that it extends the concept of acids and bases beyond the realm of proton transfer reactions. The classic example is the reaction of boron trifluoride with ammonia to form an *adduct*:

$$\mathbf{BF_3 + NH_3 \rightarrow F_3B{-}NH_3} \tag{1.27.1}$$

One of the most commonly-encountered kinds of Lewis acid-base reactions occurs when electron-donating ligands form coordination complexes with transition-metal ions.

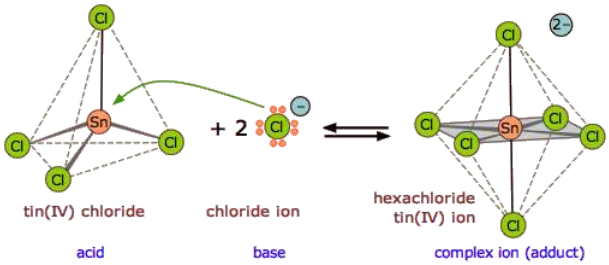


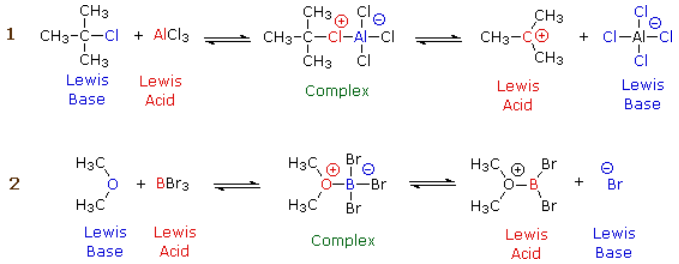
Figure **1.27.1**: The tin atom in $SnCl_4$ can expand its valence shell by utilizing a pair of d-orbitals, changing its hybridization from sp^3 to sp^3d^2.

? Exercise 1.27.1

Here are several more examples of Lewis acid-base reactions that **cannot** be accommodated within the Brønsted or Arrhenius models. Identify the Lewis acid and Lewis base in each reaction.

a. $Al(OH)_3 + OH^- \rightarrow Al(OH)_4^-$
b. $SnS_2 + S^{2-} \rightarrow SnS_3^{2-}$
c. $Cd(CN)_2 + 2\,CN^- \rightarrow Cd(CN)_4^{2+}$
d. $AgCl + 2\,NH_3 \rightarrow Ag(NH_3)_2^+ + Cl^-$
e. $Fe^{2+} + NO \rightarrow Fe(NO)^{2+}$
f. $Ni^{2+} + 6\,NH_3 \rightarrow Ni(NH_3)_5^{2+}$

Although organic chemistry is beyond the scope of these lessons, it is instructive to see how electron donors and acceptors play a role in chemical reactions. The following two diagrams show the mechanisms of two common types of reactions initiated by simple inorganic Lewis acids:



In each case, the species labeled "Complex" is an intermediate that decomposes into the products, which are conjugates of the original acid and base pairs. The electric charges indicated in the complexes are formal charges, but those in the products are "real".

In reaction 1, the incomplete octet of the aluminum atom in $AlCl_3$ serves as a better electron acceptor to the chlorine atom than does the isobutyl part of the base. In reaction 2, the pair of non-bonding electrons on the dimethyl ether coordinates with the electron-deficient boron atom, leading to a complex that breaks down by releasing a bromide ion.

Non-aqueous Protonic Acid-Base Systems

We ordinarily think of Brønsted-Lowry acid-base reactions as taking place in aqueous solutions, but this need not always be the case. A more general view encompasses a variety of acid-base *solvent systems*, of which the *water system* is only one (Table 1.27.1). Each of these has as its basis an amphiprotic solvent (one capable of undergoing autoprotolysis), in parallel with the familiar case of water.

The ammonia system is one of the most common non-aqueous system in Chemistry. Liquid ammonia boils at –33° C, and can conveniently be maintained as a liquid by cooling with dry ice (–77° C). It is a good solvent for substances that also dissolve in water, such as ionic salts and organic compounds since it is capable of forming hydrogen bonds. However, many other familiar substances can also serve as the basis of protonic solvent systems as Table 1.27.1 indicates:

Table 1.27.1: Popular Solvent systems

solvent	autoprotolysis reaction	pK_{ap}
water	$2\,H_2O \rightarrow H_3O^+ + OH^-$	14
ammonia	$2\,NH_3 \rightarrow NH_4^+ + NH_2^-$	33
acetic acid	$2\,CH_3COOH \rightarrow CH_3COOH_2^+ + CH_3COO^-$	13
ethanol	$2\,C_2H_5OH \rightarrow C_2H_5OH_2^+ + C_2H_5O^-$	19
hydrogen peroxide	$2\,HO\text{-}OH \rightarrow HO\text{-}OH_2^+ + HO\text{-}O^-$	13
hydrofluoric acid	$2\,HF \rightarrow H_2F^+ + F^-$	10
sulfuric acid	$2\,H_2SO_4 \rightarrow H_3SO_4^+ + HSO_4^-$	3.5

One use of nonaqueous acid-base systems is to examine the relative strengths of the strong acids and bases, whose strengths are "leveled" by the fact that they are all totally converted into H_3O^+ or OH^- ions in water. By studying them in appropriate non-aqueous solvents which are poorer acceptors or donors of protons, their relative strengths can be determined.

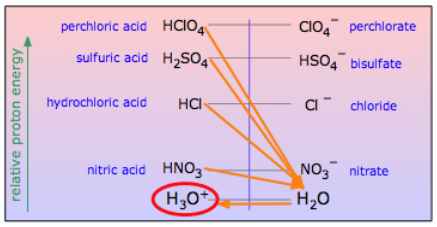


Figure **1.27.2**: Use of non-aqueous solvents allows the study of strong acids that are hindered by the "leveling" of the solvent.

1.27: Lewis Acids and Bases is shared under a not declared license and was authored, remixed, and/or curated by LibreTexts.

- **10.5: Lewis Acids and Bases** by Stephen Lower is licensed CC BY 3.0. Original source: http://www.chem1.com/acad/webtext/virtualtextbook.html.

CHAPTER OVERVIEW

2: Acids and Bases



Essential Organic Chemistry: 2nd Ed.
Bruice

Homework Problems
Homework Solutions

I II III IV V VI VII VIII IX X XI XII XIII XIV XV XVI XVII XVIII XIX XX XXI

Template:HideTOC

2.1: An Introduction to Acids and Bases
2.2: pka and pH
2.3: Organic Acids and Bases
2.4: How to Predict the Outcome of an Acid-Base Reaction
2.5: How to Determine the Position of Equilibrium
2.6: How the Structure of an Acid Affects its pka Value
2.7: How pH Affects the Structure of an Organic Compound
2.8: Buffer Solutions
2.9: Lewis Acids and Bases

2: Acids and Bases is shared under a not declared license and was authored, remixed, and/or curated by LibreTexts.

SECTION OVERVIEW

2.1: An Introduction to Acids and Bases

An acid–base reaction is a chemical reaction that occurs between an acid and a base. Several theoretical frameworks provide alternative conceptions of the reaction mechanisms and their application in solving related problems; these are called acid–base theories, for example, Brønsted–Lowry acid–base theory. Their importance becomes apparent in analyzing acid–base reactions for gaseous or liquid species, or when acid or base character may be somewhat less apparent.

Topic hierarchy

Template:HideTOC

2.1: An Introduction to Acids and Bases is shared under a not declared license and was authored, remixed, and/or curated by LibreTexts.

2.2: pka and pH

Learning Objectives

- To define the pH scale as a measure of acidity of a solution
- Tell the origin and the logic of using the pH scale.
- Apply the same strategy for representing other types of quantities such as pK_a, pK_b, pK_w.

Auto-Ionization of Water

Because of its *amphoteric* nature (i.e., acts as both an acid or a base), water does not always remain as H_2O molecules. In fact, two water molecules react to form hydronium and hydroxide ions:

$$2\,H_2O\,(l) \rightleftharpoons H_3O^+\,(aq) + OH^-\,(aq) \tag{2.2.1}$$

This is also called the self-ionization of water. The concentration of H_3O^+ and OH^- are equal in pure water because of the 1:1 stoichiometric ratio of Equation 2.2.1. The molarity of H_3O^+ and OH^- in water are also both $1.0 \times 10^{-7}\ M$ at 25° C. Therefore, a constant of water (K_w) is created to show the equilibrium condition for the self-ionization of water. The product of the molarity of hydronium and hydroxide ion is always 1.0×10^{-14} (at room temperature).

$$K_w = [H_3O^+][OH^-] = 1.0 \times 10^{-14} \tag{2.2.2}$$

Equation 2.2.2 also applies to all aqueous solutions. However, K_w does change at different temperatures, which affects the pH range discussed below.

> *H^+ and H_3O^+ is often used interchangeably to represent the hydrated proton, commonly call the hydronium ion.*

Equation 2.2.1 can also be written as

$$H_2O \rightleftharpoons H^+ + OH^- \tag{2.2.3}$$

As expected for any equilibrium, the reaction can be shifted to the reactants or products:

- If an acid (H^+) is added to the water, the equilibrium shifts to the left and the OH^- ion concentration decreases
- If base (OH^-) is added to water, the equilibrium shifts to left and the H^+ concentration decreases.

pH and pOH

Because the constant of water, K_w is 1.0×10^{-14} (at 25° C), the pK_w is 14, the constant of water determines the range of the pH scale. To understand what the pK_w is, it is important to understand first what the "p" means in pOH and pH. The addition of the "p" reflects the negative of the logarithm, $-\log$. Therefore, the pH is the negative logarithm of the molarity of H, the pOH is the negative logarithm of the molarity of OH^-, and the pK_w is the negative logarithm of the constant of water:

$$pH = -\log[H^+] \tag{2.2.4}$$
$$pOH = -\log[OH^-] \tag{2.2.5}$$
$$pK_w = -\log[K_w] \tag{2.2.6}$$

At room temperature,

$$K_w = 1.0 \times 10^{-14} \tag{2.2.7}$$

So

$$pK_w = -\log[1.0 \times 10^{-14}] \tag{2.2.8}$$
$$= 14 \tag{2.2.9}$$

Using the properties of logarithms, Equation 2.2.8 can be rewritten as

$$10^{-pK_w} = 10^{-14}. \tag{2.2.10}$$

The equation also shows that each increasing unit on the scale decreases by the factor of ten on the concentration of $\mathbf{H^+}$. Combining Equations 2.2.4 - 2.2.6 and 2.2.8 results in this important relationship:

$$pK_w = pH + pOH = 14 \tag{2.2.11}$$

Equation 2.2.11 is correct only at room temperature since changing the temperature will change K_w.

> *The pH scale is logarithmic, meaning that an increase or decrease of an integer value changes the concentration by a tenfold. For example, a pH of 3 is ten times more acidic than a pH of 4. Likewise, a pH of 3 is one hundred times more acidic than a pH of 5. Similarly a pH of 11 is ten times more basic than a pH of 10.*

Properties of the pH Scale

From the simple definition of pH in Equation 2.2.4, the following properties can be identified:

- This scale is convenient to use, because it converts some odd expressions such as $\mathbf{1.23 \times 10^{-4}}$ into a single number of 3.91.
- This scale covers a very large range of [$\mathbf{H^+}$], from 0.1 to 10^{-14}. When [$\mathbf{H^+}$] is high, we usually do not use the pH value, but simply the [$\mathbf{H^+}$]. For example, when $[\mathbf{H^+}] = \mathbf{1.0}$, pH = 0. We seldom say the pH is 0, and that is why you consider pH = 0 such an odd expression. A pH = -0.30 is equivalent to a [$\mathbf{H^+}$] of 2.0 M. Negative pH values are only for academic exercises. Using the concentrations directly conveys a better sense than the pH scales.
- The pH scale expands the division between zero and 1 in a linear scale or a compact scale into a large scale for comparison purposes. In mathematics, you learned that there are infinite values between 0 and 1, or between 0 and 0.1, or between 0 and 0.01 or between 0 and any small value. Using a log scale certainly converts infinite small quantities into infinite large quantities.
- The non-linearity of the pH scale in terms of [$\mathbf{H^+}$] is easily illustrated by looking at the corresponding values for pH between 0.1 and 0.9 as follows:

pH	0	0.1	0.2	0.3	0.4	0.5	0.6	0.7	0.8	0.9
[H^+]	1	0.79	0.63	0.50	0.40	0.32	0.25	0.20	0.16	0.13

- Because the negative log of [$\mathbf{H^+}$] is used in the pH scale, the pH scale *usually* has positive values. Furthermore, the larger the pH, the smaller the [$\mathbf{H^+}$].

The Effective Range of the pH Scale

It is common that the pH scale is argued to range from 0-14 or perhaps 1-14, but neither is correct. The pH range does not have an upper nor lower bound, since as defined above, the pH is an indication of concentration of H^+. For example, at a pH of zero the hydronium ion concentration is one molar, while at pH 14 the hydroxide ion concentration is one molar. Typically the concentrations of H^+ in water in most solutions fall between a range of 1 M (pH=0) and 10^{-14} M (pH=14). Hence a range of 0 to 14 provides sensible (but not absolute) "bookends" for the scale. One can go somewhat below zero and somewhat above 14 in water, because the concentrations of hydronium ions or hydroxide ions can exceed one molar. Figure **2.2.1** depicts the pH scale with common solutions and where they are on the scale.

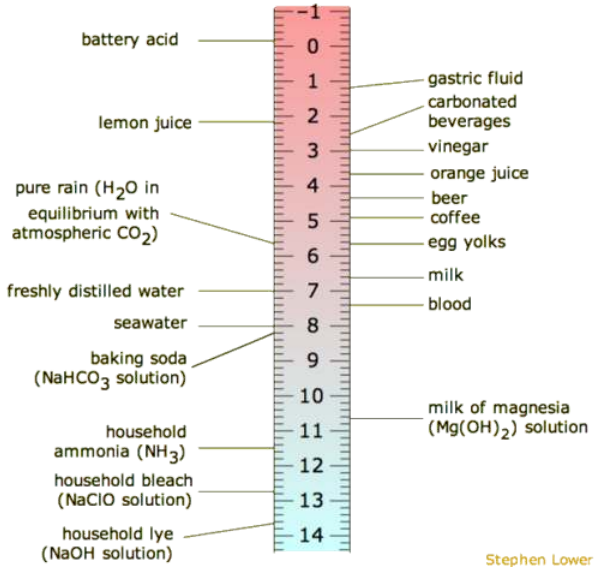


Figure **2.2.1**: Solutions and the placement of them on pH scale. (CC-BY-SA 3.0; Stephen Lower).

Quick Interpretation

- If pH >7, the solution is basic. The pOH should be looked in the perspective of OH^- instead of H^+. Whenever the value of pOH is less than 7, then it is considered basic. And therefore there are more OH^- than H^+ in the solution.
- At pH 7, the substance or solution is at neutral and means that the concentration of H^+ and OH^- ion is the same.
- If pH < 7, the solution is acidic. There are more H^+ than OH^- in an acidic solution.
- The pH scale **does not** have an upper nor lower bound.

Example 2.2.1

If the concentration of $NaOH$ in a solution is $2.5 \times 10^{-4}\ M$, what is the concentration of H_3O^+?

Solution

We can assume room temperature, so

$$1.0 \times 10^{-14} = [H_3O^+][OH^-]$$

to find the concentration of H_3O^+, solve for the $[H_3O^+]$.

$$\frac{1.0 \times 10^{-14}}{[OH^-]} = [H_3O^+] \tag{2.2.12}$$

$$\frac{1.0 \times 10^{-14}}{2.5 \times 10^{-4}} = [H_3O^+] = 4.0 \times 10^{-11}\ M \tag{2.2.13}$$

Example 2.2.2

a. Find the pH of a solution of 0.002 M of HCl.
b. Find the pH of a solution of 0.00005 M NaOH.

Solution

a. The equation for pH is -log [H+]

$$[H^+] = 2.0 \times 10^{-3}\ M$$

$$pH = -\log[2.0 \times 10^{-3}] = 2.70$$

b. The equation for pOH is -log [OH^-]

$$[OH^-] = 5.0 \times 10^{-5}\ M$$

$$pOH = -\log[5.0 \times 10^{-5}] = 4.30$$

$$pK_w = pH + pOH$$

and

$$pH = pK_w - pOH$$

then

$$pH = 14 - 4.30 = 9.70$$

Example 2.2.3: Soil

If moist soil has a pH of 7.84, what is the H^+ concentration of the soil solution?

Solution

$$pH = -\log[H^+]$$

$$7.84 = -\log[H^+]$$

$$[H^+] = 1.45 \times 10^{-8} M$$

Hint

Place -7.84 in your calculator and take the antilog (often inverse log or 10^x) = 1.45 x 10^{-8}M

Proper Definition of pH

The pH scale was originally introduced by the Danish biochemist S.P.L. Sørenson in 1909 using the symbol p_H. The letter *p* is derived from the German word *potenz* meaning power or exponent of, in this case, 10. In 1909, S.P.L. Sørenson published a paper in Biochem Z in which he discussed the effect of H^+ ions on the activity of enzymes. In the paper, he invented the term pH (purported to mean *pondus hydrogenii* in Latin) to describe this effect and defined it as the $-\log[H^+]$. In 1924, Sørenson realized that the pH of a solution is a function of the "activity" of the H^+ ion and not the concentration. Thus, he published a second paper on the subject. A better definition would be

$$pH = -\log\ a\{\mathrm{H}^+\} \tag{2.2.14}$$

where $a\{H^+\}$ denotes the activity (an effective concentration) of the H^+ ions. The activity of an ion is a function of many variables of which concentration is one.

- *Concentration* is abbreviated by using square brackets, e.g., $[H_3O^+]$ is the concentration of hydronium ion in solution.
- *Activity* is abbreviated by using "a" with curly brackets, e.g., $a\{H_3O^+\}$ is the activity of hydronium ions in solution

Because of the difficulty in accurately measuring the activity of the $\mathbf{H^+}$ ion for most solutions the International Union of Pure and Applied Chemistry (IUPAC) and the National Bureau of Standards (NBS) has defined pH as the reading on a pH meter that has been standardized against standard buffers. The following equation is used to calculate the pH of all solutions:

$$pH = \frac{F(E - E_{standard})}{RT\ \ln 10} + pH_{standard} \tag{2.2.15}$$

$$= \frac{5039.879(E - E_{standard})}{T} + pH_{standard} \tag{2.2.16}$$

with

- R is the ideal gas constant,
- F is the Faraday's constant, and
- T is absolute temperature (in K)

> The activity of the H^+ ion is determined as accurately as possible for the standard solutions used. The identity of these solutions vary from one authority to another, but all give the same values of pH to ± 0.005 pH unit. The historical definition of pH is correct for those solutions that are so dilute and so pure the H^+ ions are not influenced by anything but the solvent molecules (usually water).

When measuring pH, $[H^+]$ is in units of moles of H^+ per liter of solution. This is a reasonably accurate definition at low concentrations (the dilute limit) of H^+. At very high concentrations (10 M hydrochloric acid or sodium hydroxide, for example,) a significant fraction of the ions will be associated into neutral pairs such as $H^+Cl^–$, thus reducing the concentration of “available” ions to a smaller value which we will call the *effective concentration*. It is the *effective concentration* of H^+ and $OH^–$ that determines the pH and pOH. The pH scale as shown above is called sometimes "concentration pH scale" as opposed to the "thermodynamic pH scale". The main difference between both scales is that in thermodynamic pH scale one is interested not in H^+concentration, but in H^+activity. What a person measures in the solution is just activity, not the concentration. Thus it is thermodynamic pH scale that describes real solutions, not the concentration one.

For solutions in which ion concentrations don't exceed 0.1 M, the formulas pH = –log $[H^+]$ and pOH = –log$[OH^–]$ are generally reliable, but don't expect a 10.0 M solution of a strong acid to have a pH of exactly –1.00! However, this definition is only an approximation (albeit very good under most situations) of the proper definition of pH, which depends on the **activity** of the hydrogen ion:

$$pH = -\log a\{H^+\} \approx -\log[H^+] \tag{2.2.17}$$

The activity is a measure of the "effective concentration" of a substance, is often related to the true concentration via an activity coefficient, γ:

$$aH^+ = \gamma[H^+] \tag{2.2.18}$$

Calculating the activity coefficient requires detailed theories of how charged species interact in solution at high concentrations (e.g., the Debye-Hückel Theory). In most solutions the pH differs from the -log$[H^+]$ in the first decimal point. The following table gives experimentally determined pH values for a series of HCl solutions of increasing concentration at 25 °C.

Table **2.2.1**: HCl Solutions with corresponding pH values. Data taken from Christopher G. McCarty and Ed Vitz, Journal of Chemical Education, 83(5), 752 (2006) and G.N. Lewis, M. Randall, K. Pitzer, D.F. Brewer, Thermodynamics (McGraw-Hill: New York, 1961; pp. 233-34).

Molar Concentration of HCl	pH defined as Concentration	Experimentally Determined pH	Relative Deviation
0.00050	3.30	3.31	0.3%
0.0100	2	2.04	1.9%
0.100	1	1.10	9%
0.40	0.39	0.52	25%
7.6	-0.88	-1.85	52%

> *While the pH scale formally measures the activity of hydrogen ions in a substance or solution, it is typically approximated as the concentration of hydrogen ions; this approximation is applicable only under low concentrations.*

Living Systems

Molecules that make up or are produced by living organisms usually function within a narrow pH range (near neutral) and a narrow temperature range (body temperature). Many biological solutions, such as blood, have a pH near neutral. pH influences the structure and the function of many enzymes (protein catalysts) in living systems. Many of these enzymes have narrow ranges of pH activity. Cellular pH is so important that death may occur within hours if a person becomes acidotic (having increased acidity in the blood). As one can see pH is critical to life, biochemistry, and important chemical reactions. Common examples of how pH plays a very important role in our daily lives are given below:

- Water in swimming pool is maintained by checking its pH. Acidic or basic chemicals can be added if the water becomes too acidic or too basic.
- Whenever we get a heartburn, more acid build up in the stomach and causes pain. We needs to take antacid tablets (a base) to neutralize excess acid in the stomach.
- The pH of blood is slightly basic. A fluctuation in the pH of the blood can cause in serious harm to vital organs in the body.
- Certain diseases are diagnosed only by checking the pH of blood and urine.
- Certain crops thrive better at certain pH range.
- Enzymes activate at a certain pH in our body.

Table **2.2.2**: pH in Living Systems

Compartment	pH
Gastric Acid	1
Lysosomes	4.5
Granules of Chromaffin Cells	5.5
Human Skin	5.5
Urine	6
Neutral H_2O at 37 °C	6.81
Cytosol	7.2
Cerebrospinal Fluid	7.3
Blood	7.43-7.45
Mitochondrial Matrix	7.5
Pancreas Secretions	8.1

Problems

1. In a solution of $2.4 \times 10^{-3} M$ of HI, find the concentration of OH^-.
2. Determine the pH of a solution that is 0.0035 M HCl.
3. Determine the $[H_3O^+]$ of a solution with a pH = 5.65
4. If the pOH of NH_3, ammonia, in water is 4.74. What is the pH?
5. Pepsin, a digestive enzyme in our stomach, has a pH of 1.5. Find the concentration of OH^- in the stomach.

Solutions

1. We use the dissociation of water equation to find $[OH^-]$.
   $K_w = [H_3O^+][OH^-] = 1.0 \text{ X } 10^{-14}$
   Solve for $[OH^-]$
   $[OH^-] = (1.0 \text{ X } 10^{-14})/ [H_3O^+]$
   Plug in the molarity of HI and solve for OH^-.
   $[OH^-] = (1.0 \text{ X } 10^{-14})/ [2.4 \text{ X } 10^{-3}] = 4.17 \text{ X } 10^{-12}$ M.
2. $pH = -\log[H_3O^+]$
   Plug the molarity of the HCl in and solve for pH.
   $pH = -\log[0.0035] = 2.46$
3. $pH = -\log[H_3O^+]$
   Plug in the pH and solve for [H3O+]
   $5.65 = -\log[H_3O^+]$
   Move the negative sign to the pH. $-5.65 = \log[H_3O^+]$
   $10^{-5.65}=10^{\log[H_3O+]} = 2.24 \text{ X } 10^{-6}$ M

4. pH + pOH = 14
   Solve for pH.
   14 - pOH = pH
   14 - 4.74 = pH = 9.26
5. There are several ways to do this problem.
   Answer 1.
   pH + pOH = 14
   Solve for pOH.
   pOH = 14 - pH
   pOH = 14 - 1.5 = 12.5
   When the pOH is solved, solve for the concentration by using log.
   $pOH = -\log[OH^-]$
   $12.5 = -\log[OH^-]$
   $-12.5 = \log[OH^-]$
   $10^{-12.5} = 10^{\log[OH-]} = 3.16 \text{ X } 10^{-13}$ M.

   Answer 2.
   $pH = -\log[H^+]$
   Plug in the pH and solve for the molarity of H+ of pepsin.
   $1.5 = -\log[H^+]$
   $-1.5 = \log[H^+]$
   $10^{-1.5} = 10^{\log[H+]} = [H^+] = 0.032$
   Use the concentration of H^+ to solve for the concentration of OH^-.
   $[H^+][OH^-] = 1.0 \text{ X } 10^{-14}$
   Plug in the $[H^+]$ and solve for $[OH^-]$.
   $[OH^-] = (1.0 \text{ X } 10^{-14})/[H_3O^+]$
   $[OH^-] = (1.0 \text{ X } 10^{-14})/(0.032) = 3.125 \text{ X } 10^{-14}$ M

References

1. Petrucci, et al. "Self-Ionization of Water and the pH Scale." *General Chemistry: Principles & Modern Applications*. 7th ed. Upper Saddle River: Pearson Prentice Hall, 2007. 669-71.
2. Segel, Irwin H. "Acid and Base." *Biochemical Calculations*. 2nd ed. Wiley: BK Book, 1976. 12.
3. Christopher G. McCarty and Ed Vitz, Journal of Chemical Education, 83(5), 752 (2006)

Contributors and Attributions

- Emmellin Tung (UCD), Sharon Tsao (UCD), Divya Singh (UCD), Patrick Gormley (Lapeer Community School District)
- Chung (Peter) Chieh (Professor Emeritus, Chemistry @ University of Waterloo)

2.2: pka and pH is shared under a not declared license and was authored, remixed, and/or curated by LibreTexts.

- **The pH Scale** is licensed CC BY-NC-SA 4.0.

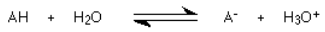
2.3: Organic Acids and Bases

This page explains the acidity of simple organic acids and looks at the factors which affect their relative strengths.

Organic acids as weak acids

For the purposes of this topic, we are going to take the definition of an acid as "a substance which donates hydrogen ions (protons) to other things". We are going to get a measure of this by looking at how easily the acids release hydrogen ions to water molecules when they are in solution in water.

An acid in solution sets up this equilibrium:



A hydroxonium ion is formed together with the anion (negative ion) from the acid.

This equilibrium is sometimes simplified by leaving out the water to emphasise the ionisation of the acid.



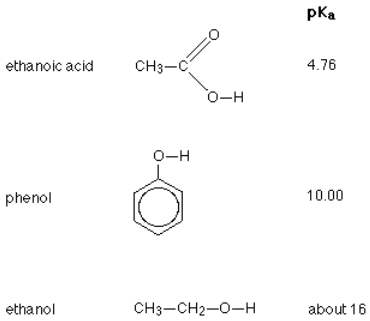
If you write it like this, you must include the state symbols - "(aq)". Writing $H^+_{(aq)}$ implies that the hydrogen ion is attached to a water molecule as H_3O^+. Hydrogen ions are always attached to something during chemical reactions.

The organic acids are weak in the sense that this ionisation is very incomplete. At any one time, most of the acid will be present in the solution as un-ionised molecules. For example, in the case of dilute ethanoic acid, the solution contains about 99% of ethanoic acid molecules - at any instant, only about 1% have actually ionised. The position of equilibrium therefore lies well to the left.

Comparing the strengths of weak acids

The strengths of weak acids are measured on the pK_a scale. The smaller the number on this scale, the stronger the acid is.

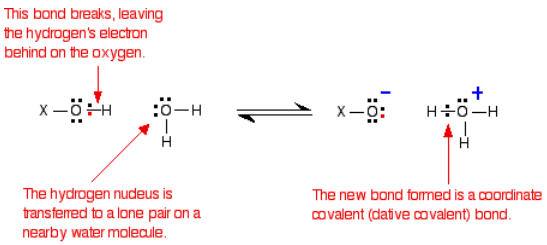
Three of the compounds we shall be looking at, together with their pK_a values are:



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!

Why are these acids acidic?

In each case, the same bond gets broken - the bond between the hydrogen and oxygen in an -OH group. Writing the rest of the molecule as "X":



So . . . if the same bond is being broken in each case, why do these three compounds have such widely different acid strengths?

Differences in acid strengths between carboxylic acids, phenols and alcohols

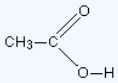
Two of the factors which influence the ionization of an acid are:

- the strength of the bond being broken,
- the stability of the ions being formed.

In these cases, you seem to be breaking the same oxygen-hydrogen bond each time, and so you might expect the strengths to be similar. The most important factor in determining the relative acid strengths of these molecules is the nature of the ions formed. You always get a hydroxonium ion - so that's constant - but the nature of the anion (the negative ion) varies markedly from case to case.

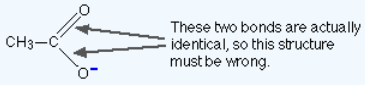
Example 2.3.1: Ethanoic Acid

Ethanoic acid has the structure:



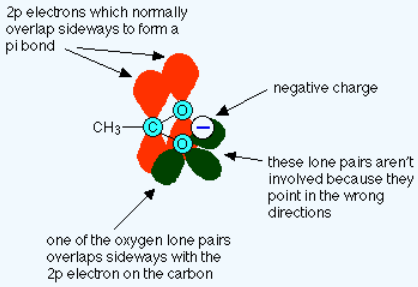
The acidic hydrogen is the one attached to the oxygen. When ethanoic acid ionises it forms the ethanoate ion, CH_3COO^-.

You might reasonably suppose that the structure of the ethanoate ion was as below, but measurements of bond lengths show that the two carbon-oxygen bonds are identical and somewhere in length between a single and a double bond.

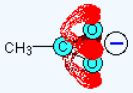


To understand why this is, you have to look in some detail at the bonding in the ethanoate ion. Like any other double bond, a carbon-oxygen double bond is made up of two different parts. One electron pair is found on the line between the two nuclei - this is known as a sigma bond. The other electron pair is found above and below the plane of the molecule in a pi bond. Pi bonds are made by sideways overlap between p orbitals on the carbon and the oxygen.

In an ethanoate ion, one of the lone pairs on the negative oxygen ends up almost parallel to these p orbitals, and overlaps with them

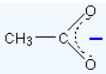


This leads to a delocalised pi system over the whole of the $-COO^-$ group, rather like that in benzene.



All the oxygen lone pairs have been left out of this diagram to avoid confusion. Because the oxygens are more electronegative than the carbon, the delocalised system is heavily distorted so that the electrons spend much more time in the region of the oxygen atoms.

So where is the negative charge in all this? It has been spread around over the whole of the $-COO^-$ group, but with the greatest chance of finding it in the region of the two oxygen atoms. Ethanoate ions can be drawn simply as:



The dotted line represents the delocalisation. The negative charge is written centrally on that end of the molecule to show that it isn't localised on one of the oxygen atoms. The more you can spread charge around, the more stable an ion becomes. In this case, if you delocalise the negative charge over several atoms, it is going to be much less attractive to hydrogen ions - and so you are less likely to re-form the ethanoic acid.

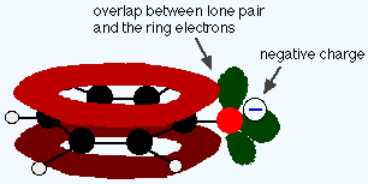
Example 2.3.2: Phenol

Phenols have an -OH group attached directly to a benzene ring. Phenol itself is the simplest of these with nothing else attached to the ring apart from the -OH group.

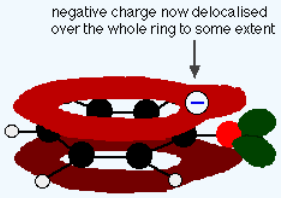


When the hydrogen-oxygen bond in phenol breaks, you get a phenoxide ion, $C_6H_5O^-$.

Delocalisation also occurs in this ion. This time, one of the lone pairs on the oxygen atom overlaps with the delocalised electrons on the benzene ring.

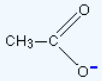


This overlap leads to a delocalisation which extends from the ring out over the oxygen atom. As a result, the negative charge is no longer entirely localised on the oxygen, but is spread out around the whole ion.

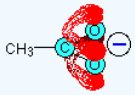


Why then is phenol a much weaker acid than ethanoic acid?

Think about the ethanoate ion again. If there wasn't any delocalisation, the charge would all be on one of the oxygen atoms, like this:



But the delocalisation spreads this charge over the whole of the COO group. Because oxygen is more electronegative than carbon, you can think of most of the charge being shared between the two oxygens (shown by the heavy red shading in this diagram).



If there wasn't any delocalisation, one of the oxygens would have a full charge which would be very attractive towards hydrogen ions. With delocalisation, that charge is spread over two oxygen atoms, and neither will be as attractive to a hydrogen ion as if one of the oxygens carried the whole charge.

That means that the ethanoate ion won't take up a hydrogen ion as easily as it would if there wasn't any delocalisation. Because some of it stays ionised, the formation of the hydrogen ions means that it is acidic.

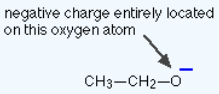
In the phenoxide ion, the single oxygen atom is still the most electronegative thing present, and the delocalised system will be heavily distorted towards it. That still leaves the oxygen atom with most of its negative charge.

What delocalisation there is makes the phenoxide ion more stable than it would otherwise be, and so phenol is acidic to an extent.

However, the delocalisation hasn't shared the charge around very effectively. There is still lots of negative charge around the oxygen to which hydrogen ions will be attracted - and so the phenol will readily re-form. Phenol is therefore only very weakly acidic.

Example 2.3.3: Ethanol

Ethanol, CH_3CH_2OH, is so weakly acidic that you would hardly count it as acidic at all. If the hydrogen-oxygen bond breaks to release a hydrogen ion, an ethoxide ion is formed:



This has nothing at all going for it. There is no way of delocalising the negative charge, which remains firmly on the oxygen atom. That intense negative charge will be highly attractive towards hydrogen ions, and so the ethanol will instantly re-form.

Since ethanol is very poor at losing hydrogen ions, it is hardly acidic at all.

Variations in acid strengths between different carboxylic acids

You might think that all carboxylic acids would have the same strength because each depends on the delocalization of the negative charge around the $-COO^-$ group to make the anion more stable, and so more reluctant to re-combine with a hydrogen ion.

In fact, the carboxylic acids have widely different acidities. One obvious difference is between methanoic acid, HCOOH, and the other simple carboxylic acids:

	pK_a
HCOOH	3.75
CH_3COOH	4.76
CH_3CH_2COOH	4.87
$CH_3CH_2CH_2COOH$	4.82

Remember that the higher the value for pK_a, the weaker the acid is.

Why is ethanoic acid weaker than methanoic acid? It again depends on the stability of the anions formed - on how much it is possible to delocalise the negative charge. The less the charge is delocalised, the less stable the ion, and the weaker the acid.

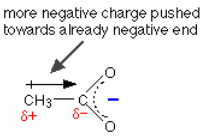
The methanoate ion (from methanoic acid) is:



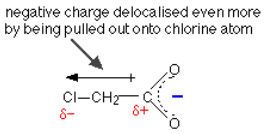
The only difference between this and the ethanoate ion is the presence of the CH_3 group in the ethanoate.

But that's important! Alkyl groups have a tendency to "push" electrons away from themselves. That means that there will be a small amount of extra negative charge built up on the $-COO^-$ group. Any build-up of charge will make the ion less stable, and more attractive to hydrogen ions.

Ethanoic acid is therefore weaker than methanoic acid, because it will re-form more easily from its ions.



The other alkyl groups have "electron-pushing" effects very similar to the methyl group, and so the strengths of propanoic acid and butanoic acid are very similar to ethanoic acid. The acids can be strengthened by pulling charge away from the -COO^- end. You can do this by attaching electronegative atoms like chlorine to the chain.



As the next table shows, the more chlorines you can attach the better:

	pK_a
CH_3COOH	4.76
$CH_2ClCOOH$	2.86
$CHCl_2COOH$	1.29
CCl_3COOH	0.65

Trichloroethanoic acid is quite a strong acid.

Attaching different halogens also makes a difference. Fluorine is the most electronegative and so you would expect it to be most successful at pulling charge away from the -COO^- end and so strengthening the acid.

	pK_a
CH_2FCOOH	2.66
$CH_2ClCOOH$	2.86
$CH_2BrCOOH$	2.90
CH_2ICOOH	3.17

The effect is there, but isn't as great as you might expect.

Finally, notice that the effect falls off quite quickly as the attached halogen gets further away from the -COO^- end. Here is what happens if you move a chlorine atom along the chain in butanoic acid.

	pK_a
$CH_3CH_2CH_2COOH$	4.82
$CH_3CH_2CHClCOOH$	2.84
$CH_3CHClCH_2COOH$	4.06
$CH_2ClCH_2CH_2COOH$	4.52

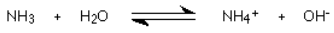
The chlorine is effective at withdrawing charge when it is next-door to the -COO^- group, and much less so as it gets even one carbon further away.

This page explains why simple organic bases are basic and looks at the factors which affect their relative strengths. For A'level purposes, all the bases we are concerned with are primary amines - compounds in which one of the hydrogens in an ammonia molecule, NH_3, is replaced either by an alkyl group or a benzene ring.

Ammonia as a weak base

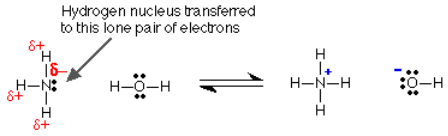
All of the compounds we are concerned with are derived from ammonia and so we'll start by looking at the reason for its basic properties. For the purposes of this topic, we are going to take the definition of a base as "a substance which combines with hydrogen ions (protons)". We are going to get a measure of this by looking at how easily the bases take hydrogen ions from water molecules when they are in solution in water.

Ammonia in solution sets up this equilibrium:



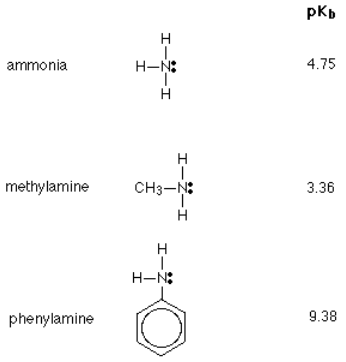
An ammonium ion is formed together with hydroxide ions. Because the ammonia is only a weak base, it doesn't hang on to the extra hydrogen ion very effectively and so the reaction is reversible. At any one time, about 99% of the ammonia is present as unreacted molecules. The position of equilibrium lies well to the left.

The ammonia reacts as a base because of the active lone pair on the nitrogen. Nitrogen is more electronegative than hydrogen and so attracts the bonding electrons in the ammonia molecule towards itself. That means that in addition to the lone pair, there is a build-up of negative charge around the nitrogen atom. That combination of extra negativity and active lone pair attracts the new hydrogen from the water.



Comparing the strengths of weak bases

The strengths of weak bases are measured on the pK_b scale. The smaller the number on this scale, the stronger the base is. Three of the compounds we shall be looking at, together with their pK_b values are:



Remember - the smaller the number the stronger the base. Comparing the other two to ammonia, you will see that methylamine is a stronger base, whereas phenylamine is very much weaker.

- Methylamine is typical of aliphatic primary amines - where the $-NH_2$ group is attached to a carbon chain. All aliphatic primary amines are stronger bases than ammonia.
- Phenylamine is typical of aromatic primary amines - where the $-NH_2$ group is attached directly to a benzene ring. These are very much weaker bases than ammonia.

Explaining the differences in base strengths

Two of the factors which influence the strength of a base are:

- the ease with which the lone pair picks up a hydrogen ion,

- the stability of the ions being formed.

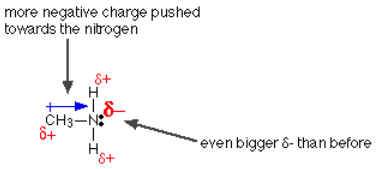
Why are aliphatic primary amines stronger bases than ammonia?

Methylamine

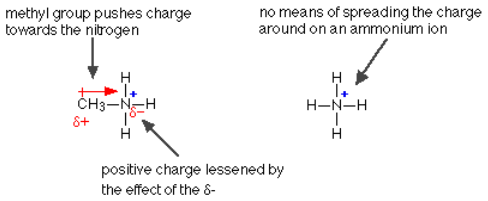
Methylamine has the structure:



The only difference between this and ammonia is the presence of the CH_3 group in the methylamine. But that's important! Alkyl groups have a tendency to "push" electrons away from themselves. That means that there will be a small amount of extra negative charge built up on the nitrogen atom. That extra negativity around the nitrogen makes the lone pair even more attractive towards hydrogen ions.



Making the nitrogen more negative helps the lone pair to pick up a hydrogen ion. What about the effect on the positive methylammonium ion formed? Is this more stable than a simple ammonium ion? Compare the methylammonium ion with an ammonium ion:



In the methylammonium ion, the positive charge is spread around the ion by the "electron-pushing" effect of the methyl group. The more you can spread charge around, the more stable an ion becomes. In the ammonium ion there isn't any way of spreading the charge.

To summarize:

- The nitrogen is more negative in methylamine than in ammonia, and so it picks up a hydrogen ion more readily.
- The ion formed from methylamine is more stable than the one formed from ammonia, and so is less likely to shed the hydrogen ion again.

Taken together, these mean that methylamine is a stronger base than ammonia.

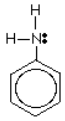
The other aliphatic primary amines

The other alkyl groups have "electron-pushing" effects very similar to the methyl group, and so the strengths of the other aliphatic primary amines are very similar to methylamine. For example:

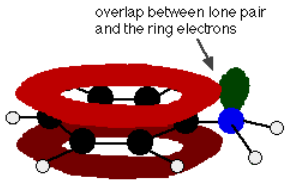
	pK_b
CH_3NH_2	3.36
$CH_3CH_2NH_2$	3.27
$CH_3CH_2CH_2NH_2$	3.16
$CH_3CH_2CH_2CH_2NH_2$	3.39

Why are aromatic primary amines much weaker bases than ammonia?

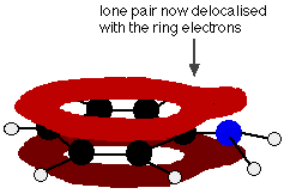
An aromatic primary amine is one in which the -NH_2 group is attached directly to a benzene ring. The only one you are likely to come across is phenylamine. Phenylamine has the structure:



The lone pair on the nitrogen touches the delocalized ring electrons . . .



. . . and becomes delocalized with them:



That means that the lone pair is no longer fully available to combine with hydrogen ions. The nitrogen is still the most electronegative atom in the molecule, and so the delocalized electrons will be attracted towards it, but the intensity of charge around the nitrogen is nothing like what it is in, say, an ammonia molecule.

The other problem is that if the lone pair is used to join to a hydrogen ion, it is no longer available to contribute to the delocalisation. That means that the delocalization would have to be disrupted if the phenylamine acts as a base. Delocalization makes molecules more stable, and so disrupting the delocalization costs energy and will not happen easily.

Taken together - the lack of intense charge around the nitrogen, and the need to break some delocalization - this means that phenylamine is a very weak base indeed.

2.3: Organic Acids and Bases is shared under a not declared license and was authored, remixed, and/or curated by LibreTexts.

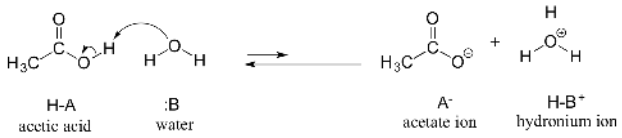
- **Organic Acids** by Jim Clark is licensed CC BY-NC 4.0.
- **Organic Bases** by Jim Clark is licensed CC BY-NC 4.0.

2.4: How to Predict the Outcome of an Acid-Base Reaction

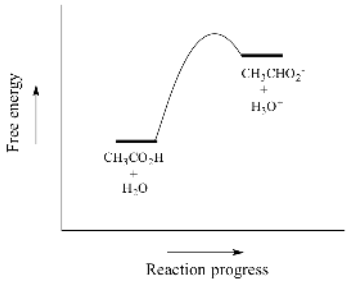
A: Defining the acidity constant

You are no doubt aware that some acids are stronger than others. The relative acidity of different compounds or functional groups – in other words, their relative capacity to donate a proton to a common base under identical conditions – is quantified by a number called the **acidity constant**, abbreviated $\mathbf{K_a}$. The common base chosen for comparison is water.

We will consider acetic acid as our first example. If we make a dilute solution of acetic acid in water, an acid-base reaction occurs between the acid (proton donor) and water (proton acceptor).



Acetic acid is a weak acid, so the equilibrium favors reactants over products - it is thermodynamically 'uphill', as indicated in the figure above by the relative length of the forward and reverse reaction arrows, and in the reaction coordinate diagram below in which products are higher energy than reactants.



As you know, the equilibrium constant K_{eq} is defined as:

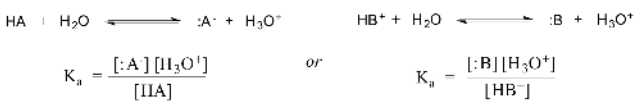
$$K_{eq} = \frac{[\text{products}]}{[\text{reactants}]} = \frac{[CH_3COO^-][H_3O^+]}{[CH_3COOH][H_2O]}$$

Every equilibrium constant expressions is actually a ratio of the activities of all species involved in the reaction. To avoid the use of activities, and to simplify experimental measurements, the equilibrium constant of concentrations approximates the activities of solutes and gases in dilute solutions with their respective molarities. However, the activities of solids, pure liquids, and solvents are **not** approximated with their molarities. Instead these activities are defined to have a value equal to 1 (one).

Thus, if we acknowledge that the activity of water in a dilute solution is approximated with the value of unity (1), we can divide by 1 to get the common form of the expression for K_a, the acid constant for acetic acid:

$$K_a = K_{eq} = \frac{a_{H_3O^+} \cdot a_{CH_3COO^-}}{a_{CH_3COOH} \cdot a_{H_2O}} \approx \frac{[H_3O^+][CH_3COO^-]}{[CH_3COOH](1)} = \frac{[H_3O^+][CH_3COO^-]}{[CH_3COOH]} \tag{2.4.1}$$

In fact, for an dilute aqueous solution, the activity of water is approximated with the value of 1, so the generic dissociation constant for a given acid HA or HB^+ is expressed as:



The value of K_a for acetic acid is 1.75 x 10^{-5} - much less than 1, indicating there is much more acetic acid in solution at equilibrium than acetate and hydronium ions.

Conversely, sulfuric acid, with a K_a of approximately 10^9, or hydrochloric acid, with a K_a of approximately 10^7, both undergo essentially complete dissociation in water: they are very strong acids.

A number like 1.75 x 10^{-5} is not very easy either to say, remember, or visualize, so chemists usually use a more convenient term to express relative acidity. The **pK_a** value of an acid is simply the log (base 10) of its K_a value.

$$pK_a = -\log K_a \quad Ka = 10^{-pKa}$$

Doing the math, we find that the pK_a of acetic acid is 4.8. The pK_a of sulfuric acid is -10, and of hydrochloric acid is -7. The use of pK_a values allows us to express the relative acidity of common compounds and functional groups on a numerical scale of about –10 (for a very strong acid) to 50 (for a compound that is not acidic at all). ***The lower the pK_a value, the stronger the acid.***

The ionizable (proton donating or accepting) functional groups relevant to biological organic chemistry generally have pK_a values ranging from about 5 to about 20. The most important of these are summarized below, with *very rough* pK_a values for the conjugate acid forms. More acidic groups with pK_a values near zero are also included for reference.

Approximate pK_a values to know

hydronium ion (H_3O^+) : **0**

protonated alcohol: **0**

protonated carbonyl: **0**

carboxylic acids: **5**

protonated imines: **7**

protonated amines: **10**

phenols: **10**

thiols: **10**

water: **14**

alcohols: **15-18**

alpha-carbon acids*: **20**

**alpha-carbon acids will be discussed later in this chapter*

You are strongly recommended to commit these rough values to memory now - then if you need a more precise value, you can always look it up in a pK_a table.

Caution! pKa is not the same as pH!

It is important to realize that pK_a is *not* the same thing as pH: the former is an inherent property of a compound or functional group, while the latter is a measure of hydronium ion concentration in a given aqueous solution:

$$pH = -\log [H_3O^+]$$

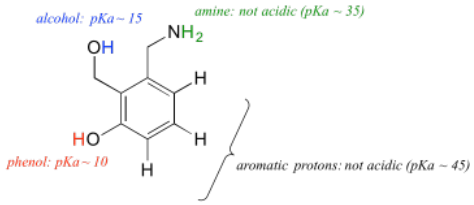
Knowing pK_a values not only allows us to compare acid strength, it also allows us to compare base strength. The key idea to remember is this: ***the stronger the conjugate acid, the weaker the conjugate base.*** We can determine that hydroxide ion is a stronger base than ammonia (NH_3), because ammonium ion (NH_4^+, $pK_a = 9.2$) is a stronger acid than water ($pK_a = 14.0$).

Exercise 7.2.1

Which is the stronger base, CH_3O^- or CH_3S^-? Acetate ion or ammonia? Hydroxide ion or acetate ion?

Solution

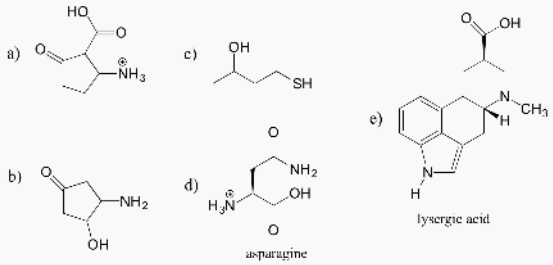
Let's put our understanding of the pK_a concept to use in the context of a more complex molecule. For example, what is the pK_a of the compound below?



We need to evaluate the potential acidity of *four* different types of protons on the molecule, and find the most acidic one. The aromatic protons are not all acidic - their pK_a is about 45. The amine group is also not acidic, its pK_a is about 35. (Remember, uncharged amines are basic: it is positively-charged *protonated* amines, with pKa values around 10, that are weakly acidic.) The alcohol proton has a pK_a of about 15, and the phenol proton has a pK_a of about 10: thus, the most acidic group on the molecule above is the phenol. (Be sure that you can recognize the difference between a phenol and an alcohol - remember, in a phenol the OH group is bound *directly* to the aromatic ring). If this molecule were to react with one molar equivalent of a strong base such as sodium hydroxide, it is the phenol proton which would be donated to form a phenolate anion.

Exercise 7.2.2

Identify the most acidic functional group on each of the molecules below, and give its approximate pK_a.



Solution

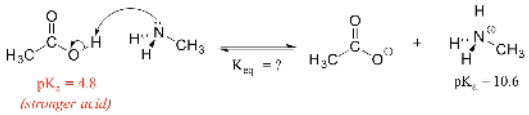
B: Using pK_a values to predict reaction equilibria

By definition, the pK_a value tells us the extent to which an acid will react with water as the base, but by extension we can also calculate the equilibrium constant for a reaction between any acid-base pair. Mathematically, it can be shown that:

$$K_{eq} = 10^{\Delta pKa}$$

. . . where ΔpK_a = (pK_a of product acid minus pK_a of reactant acid).

Consider a reaction between methylamine and acetic acid:

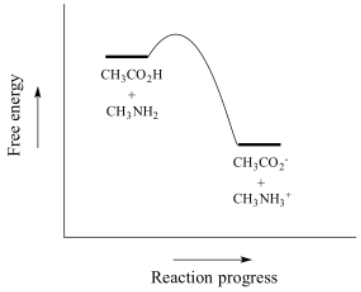


The first step is to identify the acid species on either side of the equation, and look up or estimate their pK_a values. On the left side, the acid is of course acetic acid while on the right side the acid is methyl ammonium ion (in other words, methyl ammonium ion is the acid in the reaction going from right to left). We can look up the precise pK_a values in table 7 (at the back of the book), but we already know (because we have this information memorized, right?!) that the pK_a of acetic acids is about 5, and methyl ammonium is about 10. More precise values are 4.8 and 10.6, respectively.

Without performing any calculations at all, you should be able to see that this equilibrium lies far to the right-hand side: acetic acid has a lower pK_a, meaning it is a stronger acid than methyl ammonium, and thus it wants to give up its proton more than methyl ammonium does. Doing the math, we see that

$$K_{eq} = 10^{\Delta pKa} = 10^{(10.6 - 4.8)} = 10^{5.8} = 6.3 \times 10^5$$

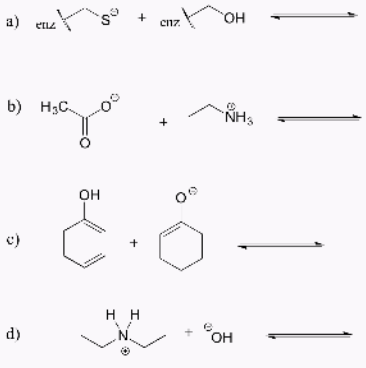
So K_{eq} is a very large number (much greater than 1) and the equilibrium for the reaction between acetic acid and methylamine lies far to the right-hand side of the equation, just as we had predicted. This also tells us that the reaction has a negative Gibbs free energy change, and is thermodynamically favorable.



If you had just wanted to quickly approximate the value of K_{eq} without benefit of precise pK_a information or a calculator, you could have approximated pK_a ~ 5 (for the carboxylic acid) and pK_a ~10 (for the ammonium ion) and calculated in your head that the equilibrium constant should be somewhere in the order of 10^5.

Exercise 7.2.3

Show the products of the following acid-base reactions, and roughly estimate the value of K_{eq}.



Solution

C: Organic molecules in buffered solution: the Henderson-Hasselbalch equation

The environment inside a living cell, where most biochemical reactions take place, is an aqueous buffer with pH ~ 7. Recall from your General Chemistry course that a buffer is a solution of a weak acid and its conjugate base. The key equation for working with buffers is the Henderson-Hasselbalch equation:

The Henderson-Hasselbalch equation:

$$pH = pK_a - \log\left(\frac{concentration\ of\ conjugate\ base}{concentration\ of\ weak\ acid}\right)$$

The equation tells us that if our buffer is an equimolar solution of a weak acid and its conjugate base, the pH of the buffer will equal the pK_a of the acid (because the log of 1 is equal to zero). If there is more of the acid form than the base, then of course the pH of the buffer is lower than the pK_a of the acid.

Exercise 7.2.4

What is the pH of an aqueous buffer solution that is 30 mM in acetic acid and 40 mM in sodium acetate? The pK_a of acetic acid is 4.8.

Solution

The Henderson-Hasselbalch equation is particularly useful when we want to think about the protonation state of different biomolecule functional groups in a pH 7 buffer. When we do this, we are always assuming that the concentration of the biomolecule is small compared to the concentration of the buffer components. (The actual composition of physiological buffer is complex, but it is primarily based on phosphoric and carbonic acids).

Imagine an aspartic acid residue located on the surface of a protein in a human cell. Being on the surface, the side chain is in full contact with the pH 7 buffer surrounding the protein. In what state is the side chain functional group: the protonated state (a carboxylic acid) or the deprotonated state (a carboxylate ion)? Using the Henderson-Hasselbalch equation, we fill in our values for the pH of the buffer and a rough pKa approximation of $pK_a = 5$ for the carboxylic acid functional group. Doing the math, we find that the ratio of carboxylate to carboxylic acid is about 100 to 1: the carboxylic acid is almost completely ionized (in the deprotonated state) inside the cell. This result extends to all other carboxylic acid groups you might find on natural biomolecules or drug molecules: in the physiological environment, carboxylic acids are almost completely deprotonated.

Now, let's use the equation again, this time for an amine functional group, such as the side chain of a lysine residue: inside a cell, are we likely to see a neutral amine ($R\text{-}NH_2$) or an ammonium cation ($R\text{-}NH_3^+$?) Using the equation with pH = 7 (for the biological buffer) and pKa = 10 (for the ammonium group), we find that the ratio of neutral amine to ammonium cation is about 1 to 100: the group is close to completely protonated inside the cell, so we will see $R\text{-}NH_3^+$, not $R\text{-}NH_2$.

We can do the same rough calculation for other common functional groups found in biomolecules. It will be very helpful going forward to commit the following to memory:

At physiological pH:

Carboxylic acids are deprotonated (in the carboxylate anion form)

Amines are protonated (in the ammonium cation form)

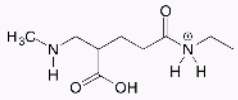
Thiols, phenols, alcohols, and amides are uncharged

Imines are a mixture of the protonated (cationic) and deprotonated (neutral) states

We will talk about the physiological protonation state of phosphate groups in chapter 9.

Exercise 7.2.5

The molecule below is ***not*** drawn in a reasonable protonation state for pH 7. Redraw it in with the functional groups in the correct protonation state.



Solution

While we are most interested in the state of molecules at pH 7, the Henderson-Hasselbalch equation can of course be used to determine the protonation state of functional groups in solutions buffered to other pH levels. The exercises below provide some practice in this type of calculation.

Exercise 7.2.6

What is the ratio of acetate ion to neutral acetic acid when a small amount of acetic acid (pK_a = 4.8) is dissolved in a buffer of pH 2.8? pH 3.8? pH 4.8? pH 5.8? pH 6.8?

Solution

Exercise 7.2.7

Would you expect phenol to be soluble in an aqueous solution buffered to pH 2? pH 7? pH 12? Explain your answer.

Solution

Exercise 7.2.8

Exercise 7.2.8: What is the approximate net charge on a tetrapeptide Cys-Asp-Lys-Glu in pH 7 buffer?

Solution

Next section⇒

Organic Chemistry With a Biological Emphasis by Tim Soderberg (University of Minnesota, Morris)

Modified by Tom Neils (Grand Rapids Community College)

2.4: How to Predict the Outcome of an Acid-Base Reaction is shared under a not declared license and was authored, remixed, and/or curated by LibreTexts.

2.5: How to Determine the Position of Equilibrium

2.5: How to Determine the Position of Equilibrium is shared under a not declared license and was authored, remixed, and/or curated by LibreTexts.

2.6: How the Structure of an Acid Affects its pka Value

2.6: How the Structure of an Acid Affects its pka Value is shared under a not declared license and was authored, remixed, and/or curated by LibreTexts.

2.7: How pH Affects the Structure of an Organic Compound

The Henderson-Hasselbalch equation

2.7: How pH Affects the Structure of an Organic Compound is shared under a not declared license and was authored, remixed, and/or curated by LibreTexts.

SECTION OVERVIEW

2.8: Buffer Solutions

A buffer is a solution that can resist pH change upon the addition of an acidic or basic components. It is able to neutralize small amounts of added acid or base, thus maintaining the pH of the solution relatively stable. This is important for processes and/or reactions which require specific and stable pH ranges. Buffer solutions have a working pH range and capacity which dictate how much acid/base can be neutralized before pH changes, and the amount by which it will change.

2.9: Lewis Acids and Bases

Learning Objectives

Make sure you thoroughly understand the following essential ideas which have been presented above. It is especially important that you know the precise meanings of all the highlighted terms in the context of this topic.

- Write the equation for the proton transfer reaction involving a Brønsted-Lowry acid or base, and show how it can be interpreted as an electron-pair transfer reaction, clearly identifying the donor and acceptor.
- Give an example of a *Lewis acid-base reaction* that does not involve protons.
- Write equations illustrating the behavior of a given non-aqueous acid-base system.

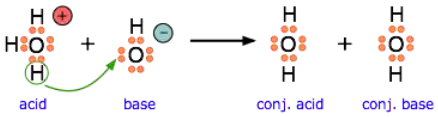
The Brønsted-Lowry proton donor-acceptor concept has been one of the most successful theories of Chemistry. But as with any such theory, it is fair to ask if this is not just a special case of a more general theory that could encompass an even broader range of chemical science. In 1916, G.N. Lewis of the University of California proposed that the *electron pair* is the dominant actor in acid-base chemistry. The Lewis theory did not become very well known until about 1923 (the same year that Brønsted and Lowry published their work), but since then it has been recognized as a very powerful tool for describing chemical reactions of widely different kinds and is widely used in organic and inorganic chemistry. According to Lewis,

- An *acid* is a substance that **accepts** a pair of electrons, and in doing so, forms a covalent bond with the entity that supplies the electrons.
- A *base* is a substance that **donates** an unshared pair of electrons to a recipient species with which the electrons can be shared.

> *In modern chemistry, electron donors are often referred to as nucleophiles, while acceptors are electrophiles.*

Proton-Transfer Reactions Involve Electron-Pair Transfer

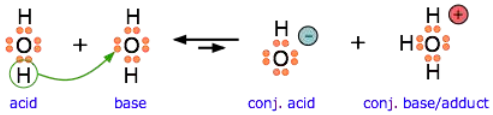
Just as any Arrhenius acid is also a Brønsted acid, any Brønsted acid is also a Lewis acid, so the various acid-base concepts are all "upward compatible". Although we do not really need to think about electron-pair transfers when we deal with ordinary aqueous-solution acid-base reactions, it is important to understand that it is the opportunity for electron-pair sharing that enables proton transfer to take place.



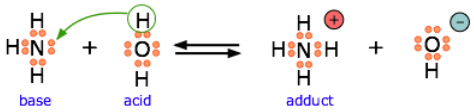
This equation for a simple acid-base neutralization shows how the Brønsted and Lewis definitions are really just different views of the same process. Take special note of the following points:

- The arrow shows the movement of a proton from the hydronium ion to the hydroxide ion.
- Note carefully that the electron-pairs themselves do not move; they remain attached to their central atoms. The electron pair on the base is "donated" to the acceptor (the proton) only in the sense that it ends up being *shared* with the acceptor, rather than being the exclusive property of the oxygen atom in the hydroxide ion.
- Although the hydronium ion is the nominal Lewis acid here, it does not itself accept an electron pair, but acts merely as the source of the proton that coordinates with the Lewis base.

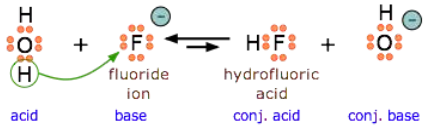
The point about the electron-pair remaining on the donor species is especially important to bear in mind. For one thing, it distinguishes a *Lewis acid-base reaction* from an *oxidation-reduction reaction*, in which a physical transfer of one or more electrons from donor to acceptor does occur. The product of a Lewis acid-base reaction is known formally as an "adduct" or "complex", although we do not ordinarily use these terms for simple proton-transfer reactions such as the one in the above example. Here, the proton combines with the hydroxide ion to form the "adduct" H_2O. The following examples illustrate these points for some other proton-transfer reactions that you should already be familiar with.



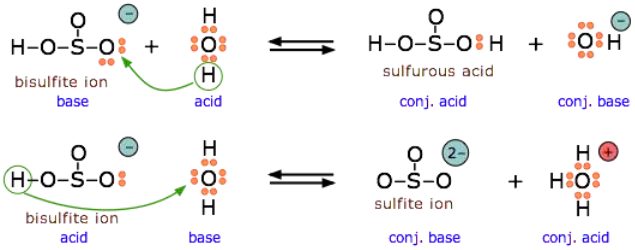
Another example, showing the autoprotolysis of water. Note that the conjugate base is also the adduct.



Ammonia is both a Brønsted and a Lewis base, owing to the unshared electron pair on the nitrogen. The reverse of this reaction represents the *hydrolysis* of the ammonium ion.



Because **HF** is a weak acid, fluoride salts behave as bases in aqueous solution. As a Lewis base, F^- accepts a proton from water, which is transformed into a hydroxide ion.



The bisulfite ion is *amphiprotic* and can act as an electron donor or acceptor.

Acid-base Reactions without Transferring Protons

The major utility of the Lewis definition is that it extends the concept of acids and bases beyond the realm of proton transfer reactions. The classic example is the reaction of boron trifluoride with ammonia to form an *adduct*:

$$\mathbf{BF_3 + NH_3 \rightarrow F_3B{-}NH_3} \tag{2.9.1}$$

One of the most commonly-encountered kinds of Lewis acid-base reactions occurs when electron-donating ligands form coordination complexes with transition-metal ions.

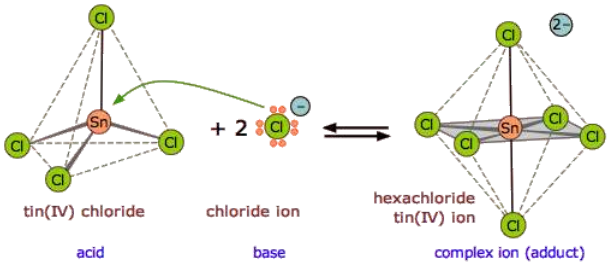


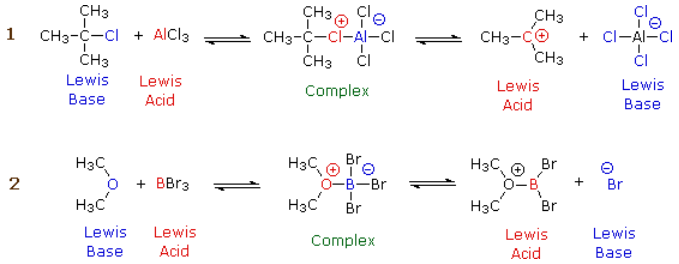
Figure **2.9.1**: The tin atom in $SnCl_4$ can expand its valence shell by utilizing a pair of d-orbitals, changing its hybridization from sp^3 to sp^3d^2.

? Exercise 2.9.1

Here are several more examples of Lewis acid-base reactions that **cannot** be accommodated within the Brønsted or Arrhenius models. Identify the Lewis acid and Lewis base in each reaction.

a. $Al(OH)_3 + OH^- \rightarrow Al(OH)_4^-$
b. $SnS_2 + S^{2-} \rightarrow SnS_3^{2-}$
c. $Cd(CN)_2 + 2\,CN^- \rightarrow Cd(CN)_4^{2+}$
d. $AgCl + 2\,NH_3 \rightarrow Ag(NH_3)_2^+ + Cl^-$
e. $Fe^{2+} + NO \rightarrow Fe(NO)^{2+}$
f. $Ni^{2+} + 6\,NH_3 \rightarrow Ni(NH_3)_5^{2+}$

Although organic chemistry is beyond the scope of these lessons, it is instructive to see how electron donors and acceptors play a role in chemical reactions. The following two diagrams show the mechanisms of two common types of reactions initiated by simple inorganic Lewis acids:



In each case, the species labeled "Complex" is an intermediate that decomposes into the products, which are conjugates of the original acid and base pairs. The electric charges indicated in the complexes are formal charges, but those in the products are "real".

In reaction 1, the incomplete octet of the aluminum atom in $AlCl_3$ serves as a better electron acceptor to the chlorine atom than does the isobutyl part of the base. In reaction 2, the pair of non-bonding electrons on the dimethyl ether coordinates with the electron-deficient boron atom, leading to a complex that breaks down by releasing a bromide ion.

Non-aqueous Protonic Acid-Base Systems

We ordinarily think of Brønsted-Lowry acid-base reactions as taking place in aqueous solutions, but this need not always be the case. A more general view encompasses a variety of acid-base *solvent systems*, of which the *water system* is only one (Table **2.9.1**). Each of these has as its basis an amphiprotic solvent (one capable of undergoing autoprotolysis), in parallel with the familiar case of water.

The ammonia system is one of the most common non-aqueous system in Chemistry. Liquid ammonia boils at –33° C, and can conveniently be maintained as a liquid by cooling with dry ice (–77° C). It is a good solvent for substances that also dissolve in water, such as ionic salts and organic compounds since it is capable of forming hydrogen bonds. However, many other familiar substances can also serve as the basis of protonic solvent systems as Table **2.9.1** indicates:

Table **2.9.1**: Popular Solvent systems

solvent	autoprotolysis reaction	pK_{ap}
water	$2\,H_2O \rightarrow H_3O^+ + OH^-$	14
ammonia	$2\,NH_3 \rightarrow NH_4^+ + NH_2^-$	33
acetic acid	$2\,CH_3COOH \rightarrow CH_3COOH_2^+ + CH_3COO^-$	13
ethanol	$2\,C_2H_5OH \rightarrow C_2H_5OH_2^+ + C_2H_5O^-$	19
hydrogen peroxide	$2\,HO\text{-}OH \rightarrow HO\text{-}OH_2^+ + HO\text{-}O^-$	13
hydrofluoric acid	$2\,HF \rightarrow H_2F^+ + F^-$	10
sulfuric acid	$2\,H_2SO_4 \rightarrow H_3SO_4^+ + HSO_4^-$	3.5

One use of nonaqueous acid-base systems is to examine the relative strengths of the strong acids and bases, whose strengths are "leveled" by the fact that they are all totally converted into H_3O^+ or OH^- ions in water. By studying them in appropriate non-aqueous solvents which are poorer acceptors or donors of protons, their relative strengths can be determined.

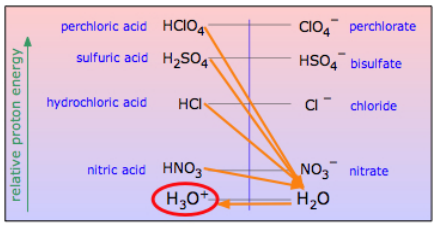


Figure **2.9.2**: Use of non-aqueous solvents allows the study of strong acids that are hindered by the "leveling" of the solvent.

2.9: Lewis Acids and Bases is shared under a not declared license and was authored, remixed, and/or curated by LibreTexts.

- **10.5: Lewis Acids and Bases** by Stephen Lower is licensed CC BY 3.0. Original source: http://www.chem1.com/acad/webtext/virtualtextbook.html.

CHAPTER OVERVIEW

3: An Introduction to Organic Compounds- Nomenclature, Physical Properties, and Representation of Structure



Essential Organic Chemistry: 2nd Ed.
Bruice

Homework Problems
Homework Solutions

I II III IV V VI VII VIII IX X XI XII XIII XIV XV XVI XVII XVIII XIX XX XXI

Template:HideTOC

3.1: How Alkyl Substituents Are Named
3.2: The Nomenclature of Alkanes
3.3: The Nomenclature of Cycloalkanes • Skeletal Structures
3.4: The Nomenclature of Alkyl Halides
3.5: The Structures of Alkyl Halides, Alcohols, Ethers, and Amines
3.6: The Physical Properties of Alkanes, Alkyl Halides, Alcohols, Ethers, and Amines
3.7: Rotation Occurs About Carbon-Carbon Single Bonds
3.8: Some Cycloalkanes Have Angle Strain
3.9: Conformers of Cyclohexane
3.10: Conformers of Monosubstituted Cyclohexanes
3.11: Conformers of Disubstituted Cyclohexanes
3.12: Fused Cyclohexane Rings

3: An Introduction to Organic Compounds- Nomenclature, Physical Properties, and Representation of Structure is shared under a not declared license and was authored, remixed, and/or curated by LibreTexts.

3.1: How Alkyl Substituents Are Named

The names of all alkanes end with *-ane*. Whether or not the carbons are linked together end-to-end in a ring (called *cyclic alkanes* or *cycloalkanes*) or whether they contain side chains and branches, the name of every carbon-hydrogen chain that lacks any double bonds or functional groups will end with the suffix *-ane*.

Alkanes with unbranched carbon chains are simply named by the number of carbons in the chain. The first four members of the series (in terms of number of carbon atoms) are named as follows:

1. CH_4 = **methane** = one hydrogen-saturated carbon
2. C_2H_6 = **ethane** = two hydrogen-saturated carbons
3. C_3H_8 = **propane** = three hydrogen-saturated carbons
4. C_4H_{10} = **butane** = four hydrogen-saturated carbons

Alkanes with five or more carbon atoms are named by adding the suffix *-ane* to the appropriate numerical multiplier, except the terminal *-a* is removed from the basic numerical term. Hence, C_5H_{12} is called *pentane*, C_6H_{14} is called *hexane*, C_7H_{16} is called *heptane* and so forth.

Straight-chain alkanes are sometimes indicated by the prefix *n-* (for normal) to distinguish them from branched-chain alkanes having the same number of carbon atoms. Although this is not strictly necessary, the usage is still common in cases where there is an important difference in properties between the straight-chain and branched-chain isomers: e.g. *n-hexane* is a neurotoxin while its branched-chain isomers are not.

IUPAC nomenclature

The IUPAC nomenclature is a system on which most organic chemists have agreed to provide guidelines to allow them to learn from each others' works. Nomenclature, in other words, provides a foundation of language for organic chemistry.

Number of Hydrogen to Carbons

This equation describes the relationship between the number of hydrogen and carbon atoms in alkanes:

$$\mathbf{H = 2C + 2}$$

where "C" and "H" are used to represent the number of carbon and hydrogen atoms present in one molecule. If C = 2, then H = 6.

Many textbooks put this in the following format:

$$\mathbf{C_nH_{2n+2}}$$

where "C_n" and "H_{2n+2}" represent the number of carbon and hydrogen atoms present in one molecule. If $C_n = 3$, then $H_{2n+2} = 2(3) + 2 = 8$. (For this formula look to the "n" for the number, the "C" and the "H" letters themselves do not change.)

Progressively longer hydrocarbon chains can be made and are named systematically, depending on the number of carbons in the longest chain.

The following table contains the systematic names for the first twenty straight chain alkanes. It will be important to familiarize yourself with these names because they will be the basis for naming many other organic molecules throughout your course of study.

Drawing Hydrocarbons

Recall that when carbon makes four bonds, it adopts the tetrahedral geometry. In the tetrahedral geometry, only two bonds can occupy a plane simultaneously. The other two bonds point in back or in front of this plane. In order to represent the tetrahedral geometry in two dimensions, solid wedges are used to represent bonds pointing out of the plane of the drawing toward the viewer, and dashed wedges are used to represent bonds pointing out of the plane of the drawing away from the viewer. Consider the following representation of the molecule methane:



***Figure 1**: Two dimensional representation of methane*

In the above drawing, the two hydrogens connected by solid lines, as well as the carbon in the center of the molecule, exist in a plane (specifically, the plane of the computer monitor / piece of paper, etc.). The hydrogen connected by a solid wedge points out of this plane toward the viewer, and the hydrogen connected by the dashed wedge points behind this plane and away from the viewer.

In drawing hydrocarbons, it can be time-consuming to write out each atom and bond individually. In organic chemistry, hydrocarbons can be represented in a shorthand notation called a **skeletal structure**. In a skeletal structure, only the bonds between carbon atoms are represented. Individual carbon and hydrogen atoms are not drawn, and bonds to hydrogen are not drawn. In the case that the molecule contains just single bonds (sp^3 bonds), these bonds are drawn in a "zig-zag" fashion. This is because in the tetrahedral geometry all bonds point as far away from each other as possible, and the structure is not linear. Consider the following representations of the molecule propane:

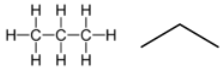
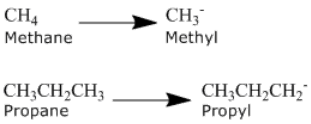


Figure 2: Full structure of propane and skeletal structure of propane

Only the bonds between carbons have been drawn, and these have been drawn in a "zig-zag" manner. Note that there is no representation of hydrogens in a skeletal structure. Since, in the absence of double or triple bonds, carbon makes four bonds total, the presence of hydrogens is implicit. Whenever an insufficient number of bonds to a carbon atom are specified in the structure, it is assumed that the rest of the bonds are made to hydrogens. For example, if the carbon atom makes only one explicit bond, there are three hydrogens implicitly attached to it. If it makes two explicit bonds, there are two hydrogens implicitly attached, etc. Note also that two lines are sufficient to represent three carbon atoms. It is the bonds only that are being drawn out, and it is understood that there are carbon atoms (with three hydrogens attached!) at the terminal ends of the structure.

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 above.

Name	Molecular Formula	Condensed Structural Formula
Methane	CH_4	CH_4
Ethane	C_2H_6	CH_3CH_3
Propane	C_3H_8	$CH_3CH_2CH_3$
Butane	C_4H_{10}	$CH_3(CH_2)_2CH_3$
Pentane	C_5H_{12}	$CH_3(CH_2)_3CH_3$
Hexane	C_6H_{14}	$CH_3(CH_2)_4CH_3$
Heptane	C_7H_{16}	$CH_3(CH_2)_5CH_3$
Octane	C_8H_{18}	$CH_3(CH_2)_6CH_3$
Nonane	C_9H_{20}	$CH_3(CH_2)_7CH_3$
Decane	$C_{10}H_{22}$	$CH_3(CH_2)_8CH_3$
Undecane	$C_{11}H_{24}$	$CH_3(CH_2)_9CH_3$
Dodecane	$C_{12}H_{26}$	$CH_3(CH_2)_{10}CH_3$
Tridecane	$C_{13}H_{28}$	$CH_3(CH_2)_{11}CH_3$
Tetradecane	$C_{14}H_{30}$	$CH_3(CH_2)_{12}CH_3$
Pentadecane	$C_{15}H_{32}$	$CH_3(CH_2)_{13}CH_3$
Hexadecane	$C_{16}H_{34}$	$CH_3(CH_2)_{14}CH_3$
Heptadecane	$C_{17}H_{36}$	$CH_3(CH_2)_{15}CH_3$
Octadecane	$C_{18}H_{38}$	$CH_3(CH_2)_{16}CH_3$
Nonadecane	$C_{19}H_{40}$	$CH_3(CH_2)_{17}CH_3$
Eicosane	$C_{20}H_{42}$	$CH_3(CH_2)_{18}CH_3$

Using Common Names with Branched Alkanes

Certain branched alkanes have common names that are still widely used today. These common names make use of prefixes, such as ***iso***-, ***sec***-, ***tert***-, and ***neo***-. The prefix ***iso***-, which stands for isomer, is commonly given to 2-methyl alkanes. In other words, if there is methyl group located on the second carbon of a carbon chain, we can use the prefix ***iso***-. The prefix will be placed in front of the alkane name that indicates the *total* number of carbons. Examples:

- isopentane which is the same as 2-methylbutane
- isobutane which is the same as 2-methylpropane

To assign the prefixes ***sec***-, which stands for secondary, and ***tert***-, for tertiary, it is important that we first learn how to classify carbon molecules. If a carbon is attached to only one other carbon, it is called a **primary** carbon. If a carbon is attached to two other carbons, it is called a **seconday** carbon. A **tertiary** carbon is attached to three other carbons and last, a **quaternary** carbon is attached to four other carbons. Examples:

- 4-*sec*-butylheptane (30g)
- 4-*tert*-butyl-5-isopropylhexane (30d); if using this example, may want to move sec/tert after iso disc

The prefix ***neo***- refers to a substituent whose second-to-last carbon of the chain is trisubstituted (has three methyl groups attached to it). A neo-pentyl has five carbons total. Examples:

- neopentane

- neoheptane

Alkoxy Groups

Alkoxides consist of an organic group bonded to a negatively charged oxygen atom. In the general form, alkoxides are written as RO^-, where R represents the organic substituent. Similar to the alkyl groups above, the concept of naming alkoxides can be applied to any of the straight chain alkanes provided in the table above.

RO^-
Alkoxy

CH_3O^-
Methoxy

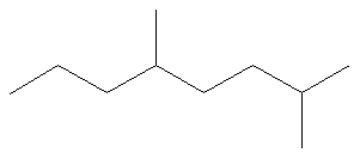
$CH_3CH_2O^-$
Ethoxy

Three Principles of Naming

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 substitute 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 substitutes and/or functional groups are written in alphabetical order.

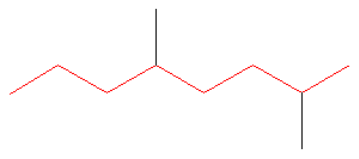
Example 1

What is the name of the following molecule?

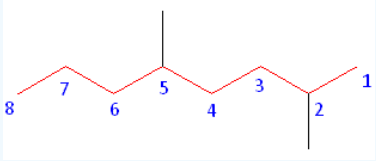


Solution

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 red and consists of eight carbons.



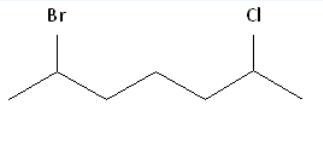
Rule #2: Carbons bonded to a functional group must have the lowest possible carbon number. If there are no functional groups, then any substitute present must have the lowest possible number. Because this example does not contain any functional groups, we only need to be concerned with the two substitutes 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.

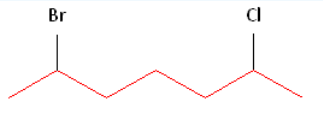
Example 2

What is the name of the following molecule?

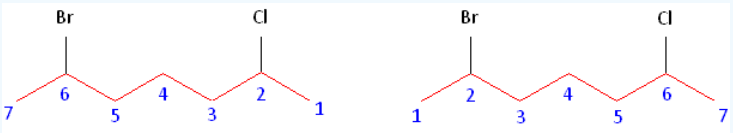


Solution

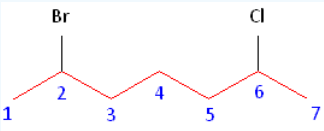
Rule #1: Choose the longest, most substituted carbon chain containing a functional group. This example contains two functional groups, bromine and chlorine. The longest carbon chain has been highlighted in red and consists of seven carbons.



Rule #2: Carbons bonded to a functional group must have the lowest possible carbon number. If there are no functional groups, then any substitute present must have the lowest possible number. In this example, numbering the chain from 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.

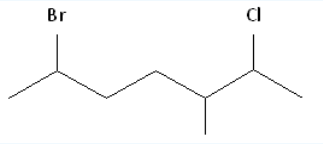


Rule #3: After applying the first two rules, take the alphabetical order into consideration. Alphabetically, bromine comes before chlorine. Therefore, bromine is assigned the second carbon position, and chlorine is assigned the sixth carbon position.



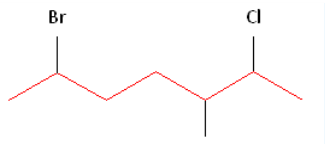
Example 3

What is the name of the follow molecule?

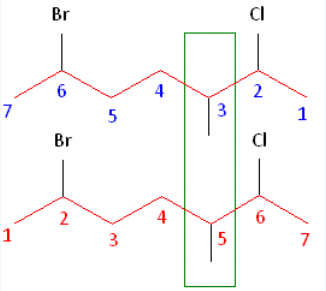


Solution

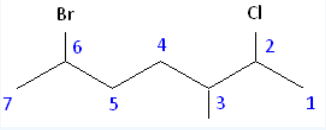
Rule #1: Choose the longest, most substituted carbon chain containing a functional group. This example contains two functional groups, bromine and chlorine, and one substitute, the methyl group. The longest carbon chain has been highlighted in red and consists of seven carbons.



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.

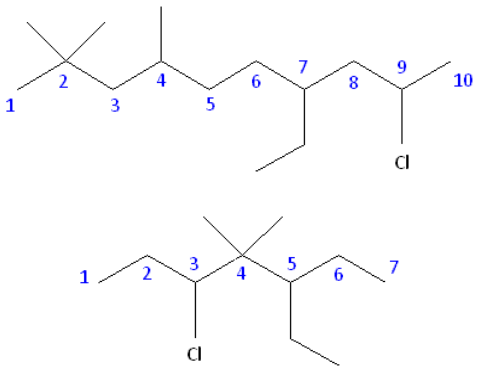
Rule #3: After applying the first two rules, take the alphabetical order into consideration. Alphabetically, bromine comes before chlorine. Therefore, bromine is assigned the second carbon position, and chlorine is assigned the sixth carbon position.

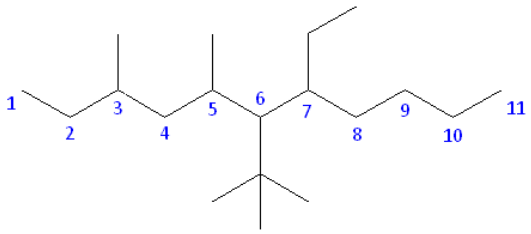
Parent chain: heptane 2-Chloro 3-Methyl 6-Bromo

6-bromo-2-chloro-3-methylheptane

Problems

What is the name of the follow molecules?





Contributors

- Jonathan Mooney (McGill University)
- Template:ContribWikiOrgo

3.1: How Alkyl Substituents Are Named is shared under a not declared license and was authored, remixed, and/or curated by LibreTexts.

- **Nomenclature of Alkanes** is licensed CC BY-NC-SA 4.0.

3.2: The Nomenclature of Alkanes

Nomenclature of Alkanes

3.2: The Nomenclature of Alkanes is shared under a not declared license and was authored, remixed, and/or curated by LibreTexts.

3.3: The Nomenclature of Cycloalkanes • Skeletal Structures

Nomenclature of Cycloalkanes

3.3: The Nomenclature of Cycloalkanes • Skeletal Structures is shared under a not declared license and was authored, remixed, and/or curated by LibreTexts.

3.4: The Nomenclature of Alkyl Halides

Nomenclature of Alkanes

3.4: The Nomenclature of Alkyl Halides is shared under a not declared license and was authored, remixed, and/or curated by LibreTexts.

SECTION OVERVIEW

3.5: The Structures of Alkyl Halides, Alcohols, Ethers, and Amines

Alkyl halides (also known as haloalkanes) are compounds in which one or more hydrogen atoms in an alkane have been replaced by halogen atoms (fluorine, chlorine, bromine or iodine). The halogen atoms significantly alters the physical properties of the molecules including electronegativity, bond length, bond strength, and molecular size.

Topic hierarchy

3.5: The Structures of Alkyl Halides, Alcohols, Ethers, and Amines is shared under a not declared license and was authored, remixed, and/or curated by LibreTexts.

SECTION OVERVIEW

3.6: The Physical Properties of Alkanes, Alkyl Halides, Alcohols, Ethers, and Amines

Physical Properties of Alkanes

Alkyl halides (also known as haloalkanes) are compounds in which one or more hydrogen atoms in an alkane have been replaced by halogen atoms (fluorine, chlorine, bromine or iodine). The halogen atoms significantly alters the physical properties of the molecules including electronegativity, bond length, bond strength, and molecular size.

Topic hierarchy

Boiling Point and Water Solubility

It is instructive to compare the boiling points and water solubility of amines with those of corresponding alcohols and ethers. The dominant factor here is hydrogen bonding, and the first table below documents the powerful intermolecular attraction that results from -O-H---O- hydrogen bonding in alcohols (light blue columns). Corresponding -N-H---N- hydrogen bonding is weaker, as the lower boiling points of similarly sized amines (light green columns) demonstrate. Alkanes provide reference compounds in which hydrogen bonding is not possible, and the increase in boiling point for equivalent 1º-amines is roughly half the increase observed for equivalent alcohols.

Compound	CH_3CH_3	CH_3OH	CH_3NH_2	$CH_3CH_2CH_3$	CH_3CH_2OH	$CH_3CH_2NH_2$
Mol.Wt.	30	32	31	44	46	45
Boiling Point ºC	-88.6º	65º	-6.0º	-42º	78.5º	16.6º

The second table illustrates differences associated with isomeric 1º, 2º & 3º-amines, as well as the influence of chain branching. Since 1º-amines have two hydrogens available for hydrogen bonding, we expect them to have higher boiling points than isomeric 2º-amines, which in turn should boil higher than isomeric 3º-amines (no hydrogen bonding). Indeed, 3º-amines have boiling points similar to equivalent sized ethers; and in all but the smallest compounds, corresponding ethers, 3º-amines and alkanes have similar boiling points. In the examples shown here, it is further demonstrated that chain branching reduces boiling points by 10 to 15 ºC.

Compound	$CH_3(CH_2)_2CH_3$	$CH_3(CH_2)_2OH$	$CH_3(CH_2)_2NH_2$	$CH_3CH_2NHCH_3$	$(CH_3)_3CH$	$(CH_3)_2CHOH$	$(CH_3)_2CHNH_2$	$(CH_3)_3N$
Mol.Wt.	58	60	59	59	58	60	59	59
Boiling Point ºC	-0.5º	97º	48º	37º	-12º	82º	34º	3º

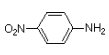
The water solubility of 1º and 2º-amines is similar to that of comparable alcohols. As expected, the water solubility of 3º-amines and ethers is also similar. These comparisons, however, are valid only for pure compounds in neutral water. The basicity of amines (next section) allows them to be dissolved in dilute mineral acid solutions, and this property facilitates their separation from neutral compounds such as alcohols and hydrocarbons by partitioning between the phases of non-miscible solvents.

Basicity of Amines

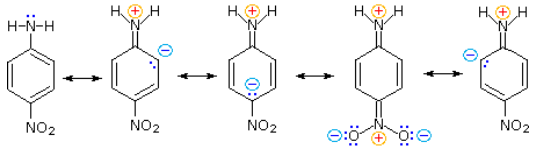
A review of basic acid-base concepts should be helpful to the following discussion. Like ammonia, most amines are Brønsted and Lewis bases, but their base strength can be changed enormously by substituents. It is common to compare basicity's quantitatively by using the

pK_a's of their conjugate acids rather than their pK_b's. Since $pK_a + pK_b = 14$, **the higher the pK_a the stronger the base**, in contrast to the usual inverse relationship of pK_a with acidity. Most simple alkyl amines have pK_a's in the range 9.5 to 11.0, and their water solutions are basic (have a pH of 11 to 12, depending on concentration). The first four compounds in the following table, including ammonia, fall into that category.

The last five compounds (colored cells) are significantly weaker bases as a consequence of three factors. The first of these is the hybridization of the nitrogen. In pyridine the nitrogen is sp^2 hybridized, and in nitriles (last entry) an sp hybrid nitrogen is part of the triple bond. In each of these compounds (shaded red) the non-bonding electron pair is localized on the nitrogen atom, but increasing s-character brings it closer to the nitrogen nucleus, reducing its tendency to bond to a proton.

Compound				NH_3						$CH_3C{\equiv}N$
pK_a	11.0	10.7	10.7	9.3	5.2	4.6	1.0	0.0	-1.0	-10.0

Secondly, aniline and p-nitroaniline (first two green shaded structures) are weaker bases due to delocalization of the nitrogen non-bonding electron pair into the aromatic ring (and the nitro substituent). This is the same delocalization that results in activation of a benzene ring toward electrophilic substitution. The following resonance equations, which are similar to those used to explain the enhanced acidity of ortho and para-nitrophenols illustrate electron pair delocalization in p-nitroaniline. Indeed, aniline is a weaker base than cyclohexyl amine by roughly a million fold, the same factor by which phenol is a stronger acid than cyclohexanol. This electron pair delocalization is accompanied by a degree of rehybridization of the amino nitrogen atom, but the electron pair delocalization is probably the major factor in the reduced basicity of these compounds. A similar electron pair delocalization is responsible for the very low basicity (and nucleophilic reactivity) of amide nitrogen atoms (last green shaded structure). This feature was instrumental in moderating the influence of amine substituents on aromatic ring substitution, and will be discussed further in the section devoted to carboxylic acid derivatives.

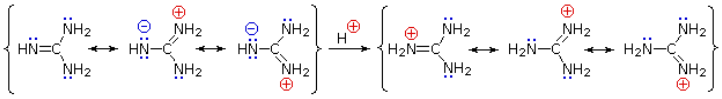


Reduced Basicity of *para*-Nitroaniline due to Electron Pair Delocalization

Conjugated amine groups influence the basicity of an existing amine. Although 4-dimethylaminopyridine (DMAP) might appear to be a base similar in strength to pyridine or N,N-dimethylaniline, it is actually more than ten thousand times stronger, thanks to charge delocalization in its conjugate acid. The structure in the gray box shows the locations over which positive charge (colored red) is delocalized in the conjugate acid. This compound is often used as a catalyst for acyl transfer reactions.

Finally, the very low basicity of pyrrole (shaded blue) reflects the exceptional delocalization of the nitrogen electron pair associated with its incorporation in an aromatic ring. Indole (pK_a = -2) and imidazole (pK_a = 7.0), see above, also have similar heterocyclic aromatic rings. Imidazole is over a million times more basic than pyrrole because the sp^2 nitrogen that is part of one double bond is structurally similar to pyridine, and has a comparable basicity.

Although resonance delocalization generally reduces the basicity of amines, a dramatic example of the reverse effect is found in the compound guanidine (pK_a = 13.6). Here, as shown below, resonance stabilization of the base is small, due to charge separation, while the conjugate acid is stabilized strongly by charge delocalization. Consequently, aqueous solutions of guanidine are nearly as basic as are solutions of sodium hydroxide.



guanidine base
small stabilization

guanidinium conjugate acid
large stabilization

The relationship of amine basicity to the acidity of the corresponding conjugate acids may be summarized in a fashion analogous to that noted earlier for acids:

Strong bases have weak conjugate acids, and weak bases have strong conjugate acids.

Acidity of Amines

We normally think of amines as bases, but it must be remembered that 1º and 2º-amines are also very weak acids (ammonia has a pK_a = 34). In this respect it should be noted that **pK_a is being used as a measure of the acidity of the amine itself rather than its conjugate acid, as in the previous section**. For ammonia this is expressed by the following hypothetical equation:

$NH_3 + H_2O \longrightarrow NH_2^{(-)} + H_2O\text{-}H^{(+)}$

The same factors that decreased the basicity of amines increase their acidity. This is illustrated by the following examples, which are shown in order of increasing acidity. It should be noted that the first four examples have the same order and degree of increased acidity as they exhibited decreased basicity in the previous table. The first compound is a typical 2º-amine, and the three next to it are characterized by varying degrees of nitrogen electron pair delocalization. The last two compounds (shaded blue) show the influence of adjacent sulfonyl and carbonyl groups on N-H acidity. From previous discussion it should be clear that the basicity of these nitrogens is correspondingly reduced.

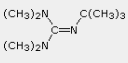
Compound					$C_6H_5SO_2NH_2$	
pK_a	33	27	19	15	10	9.6

The acids shown here may be converted to their conjugate bases by reaction with bases derived from weaker acids (stronger bases). Three examples of such reactions are shown below, with the acidic hydrogen colored red in each case. For complete conversion to the conjugate base, as shown, a reagent base roughly a million times stronger is required.

$C_6H_5SO_2NH_2 + KOH \longrightarrow C_6H_5SO_2NH^{(-)}\ K^{(+)} + H_2O$	a sulfonamide base
$(CH_3)_3COH + NaH \longrightarrow (CH_3)_3CO^{(-)}\ Na^{(+)} + H_2$	an alkoxide base
$(C_2H_5)_2NH + C_4H_9Li \longrightarrow (C_2H_5)_2N^{(-)}\ Li^{(+)} + C_4H_{10}$	an amide base

Important Reagent Bases

The significance of all these acid-base relationships to practical organic chemistry lies in the need for organic bases of varying strength, as reagents tailored to the requirements of specific reactions. The common base sodium hydroxide is not soluble in many organic solvents, and is therefore not widely used as a reagent in organic reactions. Most base reagents are alkoxide salts, amines or amide salts. Since alcohols are much stronger acids than amines, their conjugate bases are weaker than amide bases, and fill the gap in base strength between amines and amide salts. In the following table, pK_a again refers to the conjugate acid of the base drawn above it.

Base Name	Pyridine	Triethyl Amine	Hünig's Base	Barton's Base	Potassium t-Butoxide	Sodium HMDS	LDA
Formula		$(C_2H_5)_3N$			$(CH_3)_3CO^{(-)}\ K^{(+)}$	$[(CH_3)_3Si]_2N^{(-)}\ Na^{(+)}$	$[(CH_3)_2CH]_2N^{(-)}$
pK_a	5.3	10.7	11.4	14	19	26	35.7

Pyridine is commonly used as an acid scavenger in reactions that produce mineral acid co-products. Its basicity and nucleophilicity may be modified by steric hindrance, as in the case of 2,6-dimethylpyridine (pK_a=6.7), or resonance stabilization, as in the case of 4-dimethylaminopyridine (pK_a=9.7). Hünig's base is relatively non-nucleophilic (due to steric hindrance), and like DBU is often used as the base in E2 elimination reactions conducted in non-polar solvents. Barton's base is a strong, poorly-nucleophilic, neutral base that serves in cases where electrophilic substitution of DBU or other amine bases is a problem. The alkoxides are stronger bases that are often used in the corresponding alcohol as solvent, or for greater reactivity in DMSO. Finally, the two amide bases see widespread use in generating enolate bases from carbonyl compounds and other weak carbon acids.

Nonionic Superbases

An interesting group of neutral, highly basic compounds of nitrogen and phosphorus have been prepared, and are referred to as superbases. To see examples of these compounds Click Here.

Contributors

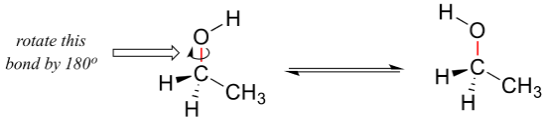
- William Reusch, Professor Emeritus (Michigan State U.), Virtual Textbook of Organic Chemistry

3.6: The Physical Properties of Alkanes, Alkyl Halides, Alcohols, Ethers, and Amines is shared under a not declared license and was authored, remixed, and/or curated by LibreTexts.

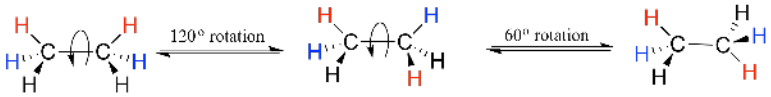
3.7: Rotation Occurs About Carbon-Carbon Single Bonds

Before we begin our exploration of stereochemistry and chirality, we first need to consider the subject of **conformational isomerism**, which has to do with rotation about single bonds.

We learned in section 2.1 that single bonds in organic molecules are free to rotate, due to the 'end-to-end' (sigma) nature of their orbital overlap. Consider the carbon-oxygen bond in ethanol, for example: with a 180° rotation about this bond, the shape of the molecule would look quite different:

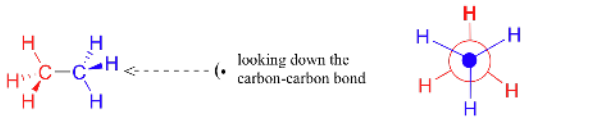


Or ethane: rotation about the carbon-carbon sigma bond results in many different possible three-dimensional arrangements of the atoms.



These different arrangements, resulting from sigma bond rotation, are referred to in organic chemistry as **conformations**. Any one specific conformation is called a **conformational isomer**, or **conformer**.

In order to better visualize different conformations of a molecule, it is convenient to use a drawing convention called the **Newman projection**. In a Newman projection, we look lengthwise down a specific bond of interest – in this case, the carbon-carbon bond in ethane. We depict the 'front' atom as a dot, and the 'back' atom as a larger circle.



'staggered' conformation
(Newman projection)

The six carbon-hydrogen bonds are shown as solid lines protruding from the two carbons. Note that we do *not* draw bonds as solid or dashed wedges in a Newman projection.

Looking down the C-C bond in this way, the angle formed between a C-H bond on the front carbon and a C-H bond on the back carbon is referred to as a **dihedral angle**. (The dihedral angle between the hour hand and the minute hand on a clock is 0° at noon, 90° at 3:00, and so forth).

The lowest energy conformation of ethane, shown in the figure above, is called the '**staggered'** conformation: all of the dihedral angles are 60°, and the distance between the front and back C-H bonds is maximized.

If we now rotate the front CH_3 group 60° clockwise, the molecule is in the highest energy '**eclipsed**' conformation, where the dihedral angles are all 0° (we stagger the bonds slightly in our Newman projection drawing so that we can see them all).



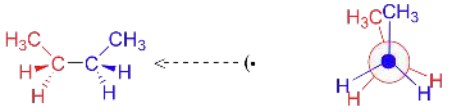
'eclipsed' conformation

The energy of the eclipsed conformation, where the electrons in the front and back C-H bonds are closer together, is approximately 12 kJ/mol higher than that of the staggered conformation.

Another 60° rotation returns the molecule to a second staggered conformation. This process can be continued all around the 360° circle, with three possible eclipsed conformations and three staggered conformations, in addition to an infinite number of

conformations in between these two extremes.

Now let's consider butane, with its four-carbon chain. There are now three rotating carbon-carbon bonds to consider, but we will focus on the middle bond between C_2 and C_3. Below are two representations of butane in a conformation which puts the two CH_3 groups (C_1 and C_4) in the eclipsed position, with the two C-C bonds at a 0° dihedral angle.



eclipsed (A)

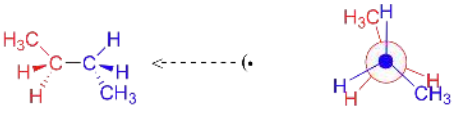
If we rotate the front, (blue) carbon by 60° clockwise, the butane molecule is now in a staggered conformation.



gauche

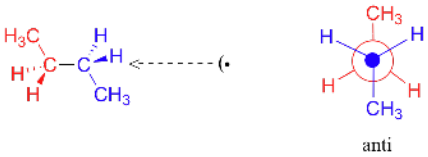
This is more specifically referred to as the **gauche** conformation of butane. Notice that although they are staggered, the two methyl groups are not as far apart as they could possibly be.

A further rotation of 60° gives us a second eclipsed conformation (B) in which both methyl groups are lined up with hydrogen atoms.



eclipsed (B)

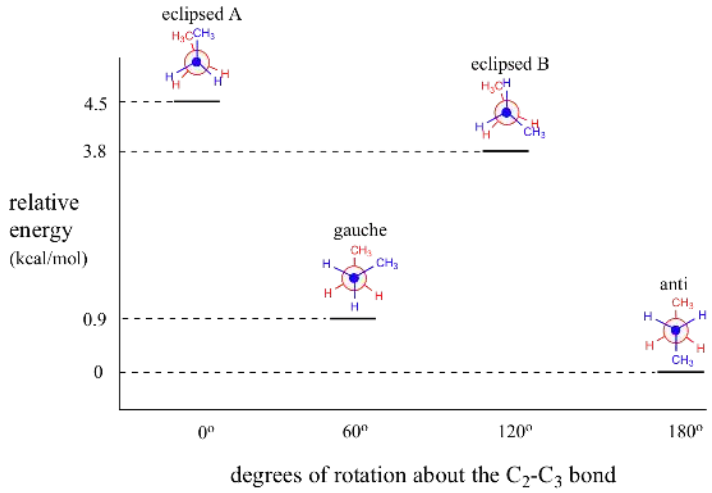
One more 60 rotation produces another staggered conformation called the **anti** conformation, where the two methyl groups are positioned opposite each other (a dihedral angle of 180°).



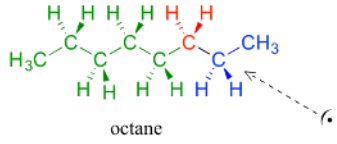
anti

As with ethane, the staggered conformations of butane are energy 'valleys', and the eclipsed conformations are energy 'peaks'. However, in the case of butane there are two different valleys, and two different peaks. The gauche conformation is a higher energy valley than the anti conformation due to **steric strain**, which is the repulsive interaction caused by the two bulky methyl groups being forced too close together. Clearly, steric strain is lower in the anti conformation. In the same way, steric strain causes the eclipsed A conformation - where the two methyl groups are as close together as they can possibly be - to be higher in energy than the two eclipsed B conformations.

The diagram below summarizes the relative energies for the various eclipsed, staggered, and gauche conformations.



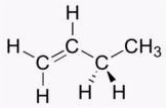
Because the anti conformation is lowest in energy (and also simply for ease of drawing), it is conventional to draw open-chain alkanes in a 'zigzag' form, which implies anti conformation at all carbon-carbon bonds. The figure below shows, as an example, a Newman projection looking down the C_2-C_3 bond of octane.





Exercise 3.1: Draw Newman projections of the lowest and highest energy conformations of propane.

Exercise 3.2: Draw a Newman projection, looking down the C_2-C_3 bond, of 1-butene in the conformation shown below (C_2 should be your *front* carbon).



Solutions to exercises

Online lectures from Kahn Academy

Newman projections part I

Newman projections part II

Organic Chemistry With a Biological Emphasis by Tim Soderberg (University of Minnesota, Morris)

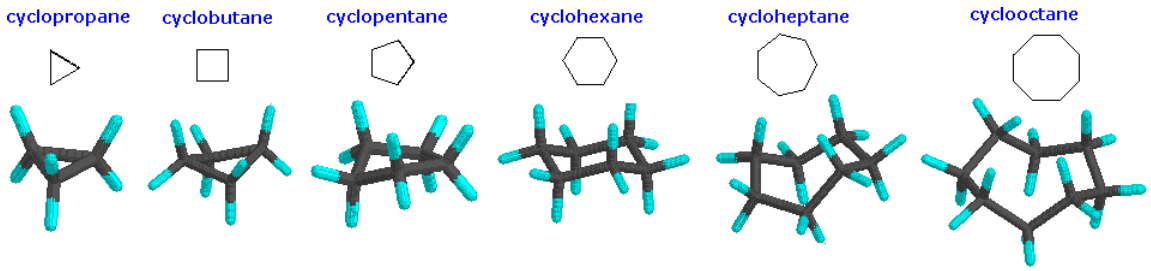
3.7: Rotation Occurs About Carbon-Carbon Single Bonds is shared under a not declared license and was authored, remixed, and/or curated by LibreTexts.

3.8: Some Cycloalkanes Have Angle Strain

Cycloalkanes are very important in components of food, pharmaceutical drugs, and much more. However, to use cycloalkanes in such applications, we must know the effects, functions, properties, and structures of cycloalkanes. Cycloalkanes are alkanes that are in the form of a ring; hence, the prefix cyclo-. Stable cycloalkanes cannot be formed with carbon chains of just any length. Recall that in alkanes, carbon adopts the sp^3 tetrahedral geometry in which the angles between bonds are 109.5°. For some cycloalkanes to form, the angle between bonds must deviate from this ideal angle, an effect known as **angle strain**. Additionally, some hydrogen atoms may come into closer proximity with each other than is desirable (become eclipsed), an effect called **torsional strain**. These destabilizing effects, angle strain and torsional strain are known together as **ring strain**. The smaller cycloalkanes, cyclopropane and cyclobutane, have particularly high ring strains because their bond angles deviate substantially from 109.5° and their hydrogens eclipse each other. Cyclopentane is a more stable molecule with a small amount of ring strain, while **cyclohexane** is able to adopt the perfect geometry of a cycloalkane in which all angles are the ideal 109.5° and no hydrogens are eclipsed; it has no ring strain at all. Cycloalkanes larger than cyclohexane have ring strain and are not commonly encountered in organic chemistry.

Ring Strain and the Structures of Cycloalkanes

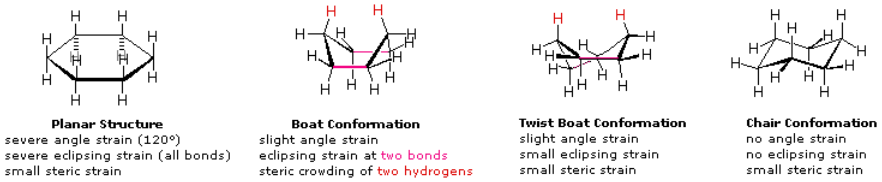
There are many forms of cycloalkanes, such as cyclopropane, cyclobutane, cyclopentane, cyclohexane, among others. The process of naming cycloalkanes is the same as naming alkanes but the addition of the prefix cyclo- is required. Cyclobutane is in a form of a square, which is highly unfavorable and unstable (this will be explained soon). There are different drawings for cyclobutane, but they are equivalent to each other. Cyclobutane can reduce the ring string by puckering the square cyclobutane. Cyclopentane takes the shape of a pentagon and cyclohexane is in the shape of a hexagon.



Chair Conformation of Cyclohexane - Equitorial and Axial

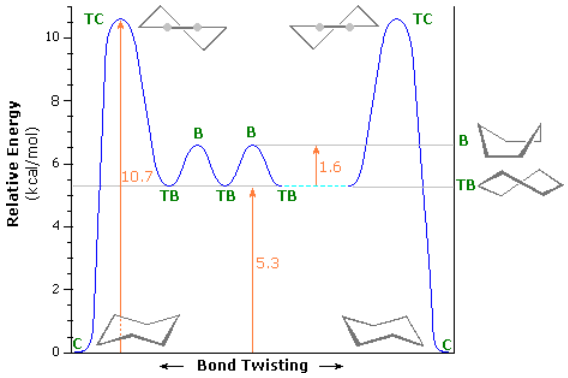
There are two ways to draw cyclohexane because it can be in a hexagon shape or in a different conformational form called the **chair** conformation and the **boat** conformation.

- The chair conformation drawing is more favored than the boat because of the energy, the steric hindrance, and a new strain called the **transannular strain**.
- The boat conformation is not the favored conformation because it is less stable and has a steric repulsion between the two H's, shown with the pink curve. This is known as the transannular strain, which means that the strain results from steric crowding of two groups across a ring. The boat is less stable than the chair by 6.9 kcal/mol. The boat conformation, however, is flexible, and when we twist one of the C-C bonds, it reduces the transannular strain.
- When we twist the C-C bond in a boat, it becomes a twisted boat.



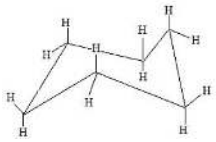
Some Conformations of Cyclohexane Rings. (William Reusch, MSU)

Although there are multiple ways to draw cyclohexane, the most stable and major conformer is the chair because is has a lower activation barrier from the energy diagram.

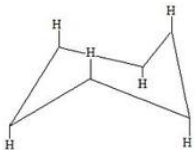


Conformational Energy Profile of Cyclohexane. (William Reusch, MSU).

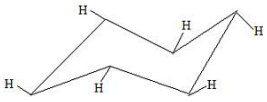
The transition state structure is called a **half chair**. This energy diagram shows that the chair conformation is lower in energy; therefore, it is more stable. The chair conformation is more stable because it does not have any steric hindrance or steric repulsion between the hydrogen bonds. By drawing cyclohexane in a chair conformation, we can see how the H's are positioned. There are two positions for the H's in the chair conformation, which are in an axial or an equitorial formation.



This is how a chair conformation looks, but you're probably wondering which H's are in the equitorial and axial form. Here are more pictures to help.



These are hydrogens in the axial form.



These hydrogens are in an equitorial form. Of these two positions of the H's, the equitorial form will be the most stable because the hydrogen atoms, or perhaps the other substituents, will not be touching each other. This is the best time to build a chair conformation in an equitorial and an axial form to demonstrate the stability of the equitorial form.

Ring Strain

Cycloalkanes tend to give off a very high and non-favorable energy, and the spatial orientation of the atoms is called the ring strain. When atoms are close together, their proximity is highly unfavorable and causes steric hindrance. The reason we do not want ring strain and steric hindrance is because heat will be released due to an increase in energy; therefore, a lot of that energy is stored in the bonds and molecules, causing the ring to be unstable and reactive. Another reason we try to avoid ring strain is because it will affect the structures and the conformational function of the smaller cycloalkanes. One way to determine the presence of ring strain is by its heat of combustion. By comparing the heat of combustion with the value measured for the straight chain molecule, we can determine the stability of the ring. There are two types of strain, which are eclipsing/torsional strain and bond angle strain. Bond angle strain causes a ring to have a poor overlap between the atoms, resulting in weak and reactive C-C bonds. An eclipsed spatial arrangement of the atoms on the cycloalkanes results in high energy.

With so many cycloalkanes, which ones have the highest ring strain and are very unlikely to stay in its current form? The figures below show cyclopropane, cyclobutane, and cyclopentane, respectively. Cyclopropane is one of the cycloalkanes that has an

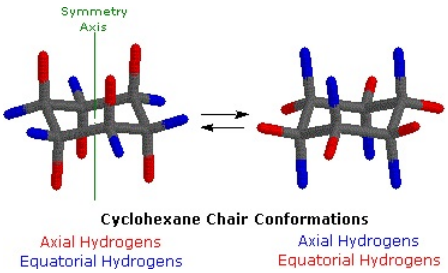
incredibly high and unfavorable energy, followed by cyclobutane as the next strained cycloalkane. Any ring that is small (with three to four carbons) has a significant amount of ring strain; cyclopropane and cyclobutane are in the category of small rings. A ring with five to seven carbons is considered to have minimal to zero strain, and typical examples are cyclopentane, cyclohexane, and cycloheptane. However, a ring with eight to twelve carbons is considered to have a moderate strain, and if a ring has beyond twelve carbons, it has minimal strain.

There are different types of ring strain:

- **Transannular strain** isdefined as the crowding of the two groups in a ring.
- **Eclipsing strain,** also known as torsional strain, is intramolecular strain due to the bonding interaction between two eclipsed atoms or groups.
- **Bond angle strain** is present when there is a poor overlap between the atoms. There must be an ideal bond angle to achieve the maximum bond strength and that will allow the overlapping of the atomic/hybrid orbitals.

Cyclohexane

Most of the time, cyclohexane adopts the fully staggered, ideal angle **chair conformation**. In the chair conformation, if any carbon-carbon bond were examined, it would be found to exist with its substituents in the staggered conformation and all bonds would be found to possess an angle of 109.5°.



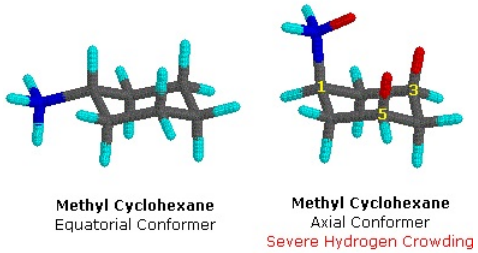
Cyclohexane in the chair conformation. (William Reusch, MSU).

In the chair conformation, hydrogen atoms are labeled according to their location. Those hydrogens which exist above or below the plane of the molecule (shown with red bonds above) are called **axial**. Those hydrogens which exist in the plane of the molecule (shown with blue bonds above) are called **equatorial**.

Although the chair conformation is the most stable conformation that cyclohexane can adopt, there is enough thermal energy for it to also pass through less favorable conformations before returning to a different chair conformation. When it does so, the axial and equatorial substituents change places. The passage of cyclohexane from one chair conformation to another, during which the axial substituents switch places with the equatorial substituents, is called a **ring flip**.

Methylcyclohexane

Methylcyclohexane is cyclohexane in which one hydrogen atom is replaced with a methyl group substituent. Methylcyclohexane can adopt two basic chair conformations: one in which the methyl group is axial, and one in which it is equatorial. Methylcyclohexane strongly prefers the equatorial conformation. In the axial conformation, the methyl group comes in close proximity to the axial hydrogens, an energetically unfavorable effect known as a **1,3-diaxial interaction** (Figure 3). Thus, the equatorial conformation is preferred for the methyl group. In most cases, if the cyclohexane ring contains a substituent, the substituent will prefer the equatorial conformation.



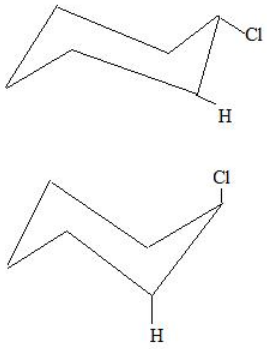
Methylcyclohexane in the chair conformation. (William Reusch, MSU).

References

1. Bachrach, Steven M. Computational Organic Chemistry. Wiley- Interscience. (2007).
2. McMurray, John E. Organic Chemistry Sixth Edition. Brooks Cole. (2003).
3. Vollhardt and Schore. Organic Chemistry Structure and Function Fifth Edition. New York. (2007).

Problems

1. Trans- 1,2-dimethylcyclopropane is more stable than cis-1,2-dimethylcyclopropane. Why? Drawing a picture of the two will help your explanation.
2. Out of all the cycloalkanes, which one has the most ring strain and which one is strain free? Explain.
3. Which of these chair conformations are the most stable and why?



3.

4. What does it mean when people say "increase in heat leads to increase in energy" and how does that statement relate to ring strains?
5. Why is that the bigger rings have lesser strains compared to smaller rings?

Answers

1. The cis isomer suffers from steric hindrance and has a larger heat of combustion.
2. Cyclopropane- ring strain. Cyclohexane chair conformation- ring strain free.
3. Top one is more stable because it is in an equitorial conformation. When assembling it with the OChem Molecular Structure Tool Kit, equitorial formation is more spread out.
4. When there is an increase in heat there will be an increase of energy released therefore there will be a lot of energy stored in the bond and molecule making it unstable.
5. Smaller rings are more compacts, which leads to steric hindrance and the angles for these smaller rings are harder to get ends to meet. Bigger rings tend to have more space and that the atoms attached to the ring won't be touching each other as much as atoms attached to the smaller ring.

Contributors

- Jonathan Mooney (McGill University)

3.8: Some Cycloalkanes Have Angle Strain is shared under a not declared license and was authored, remixed, and/or curated by LibreTexts.

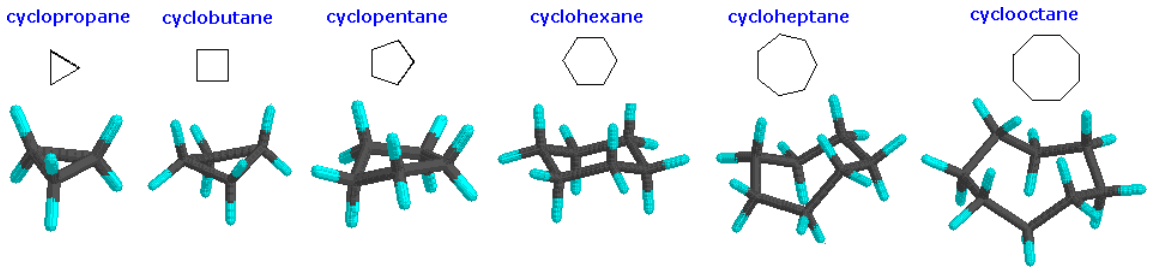
- **Ring Strain and the Structure of Cycloalkanes** is licensed CC BY-NC-SA 4.0.

3.9: Conformers of Cyclohexane

Cycloalkanes are very important in components of food, pharmaceutical drugs, and much more. However, to use cycloalkanes in such applications, we must know the effects, functions, properties, and structures of cycloalkanes. Cycloalkanes are alkanes that are in the form of a ring; hence, the prefix cyclo-. Stable cycloalkanes cannot be formed with carbon chains of just any length. Recall that in alkanes, carbon adopts the sp^3 tetrahedral geometry in which the angles between bonds are 109.5°. For some cycloalkanes to form, the angle between bonds must deviate from this ideal angle, an effect known as **angle strain**. Additionally, some hydrogen atoms may come into closer proximity with each other than is desirable (become eclipsed), an effect called **torsional strain**. These destabilizing effects, angle strain and torsional strain are known together as **ring strain**. The smaller cycloalkanes, cyclopropane and cyclobutane, have particularly high ring strains because their bond angles deviate substantially from 109.5° and their hydrogens eclipse each other. Cyclopentane is a more stable molecule with a small amount of ring strain, while **cyclohexane** is able to adopt the perfect geometry of a cycloalkane in which all angles are the ideal 109.5° and no hydrogens are eclipsed; it has no ring strain at all. Cycloalkanes larger than cyclohexane have ring strain and are not commonly encountered in organic chemistry.

Ring Strain and the Structures of Cycloalkanes

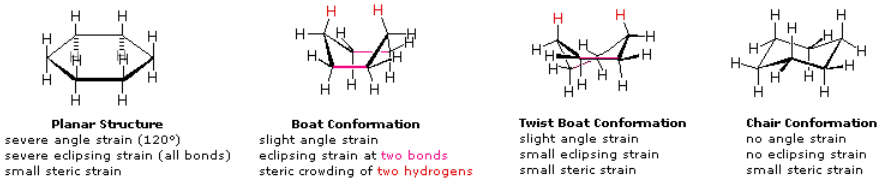
There are many forms of cycloalkanes, such as cyclopropane, cyclobutane, cyclopentane, cyclohexane, among others. The process of naming cycloalkanes is the same as naming alkanes but the addition of the prefix cyclo- is required. Cyclobutane is in a form of a square, which is highly unfavorable and unstable (this will be explained soon). There are different drawings for cyclobutane, but they are equivalent to each other. Cyclobutane can reduce the ring string by puckering the square cyclobutane. Cyclopentane takes the shape of a pentagon and cyclohexane is in the shape of a hexagon.



Chair Conformation of Cyclohexane - Equitorial and Axial

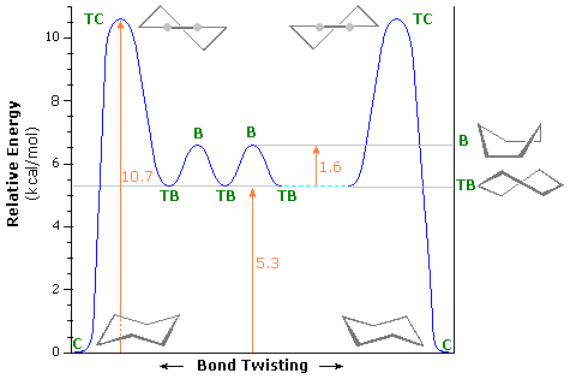
There are two ways to draw cyclohexane because it can be in a hexagon shape or in a different conformational form called the **chair** conformation and the **boat** conformation.

- The chair conformation drawing is more favored than the boat because of the energy, the steric hindrance, and a new strain called the **transannular strain**.
- The boat conformation is not the favored conformation because it is less stable and has a steric repulsion between the two H's, shown with the pink curve. This is known as the transannular strain, which means that the strain results from steric crowding of two groups across a ring. The boat is less stable than the chair by 6.9 kcal/mol. The boat conformation, however, is flexible, and when we twist one of the C-C bonds, it reduces the transannular strain.
- When we twist the C-C bond in a boat, it becomes a twisted boat.



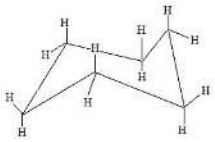
Some Conformations of Cyclohexane Rings. (William Reusch, MSU)

Although there are multiple ways to draw cyclohexane, the most stable and major conformer is the chair because is has a lower activation barrier from the energy diagram.

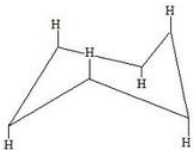


Conformational Energy Profile of Cyclohexane. (William Reusch, MSU).

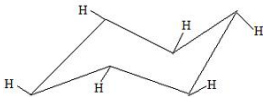
The transition state structure is called a **half chair**. This energy diagram shows that the chair conformation is lower in energy; therefore, it is more stable. The chair conformation is more stable because it does not have any steric hindrance or steric repulsion between the hydrogen bonds. By drawing cyclohexane in a chair conformation, we can see how the H's are positioned. There are two positions for the H's in the chair conformation, which are in an axial or an equitorial formation.



This is how a chair conformation looks, but you're probably wondering which H's are in the equitorial and axial form. Here are more pictures to help.



These are hydrogens in the axial form.



These hydrogens are in an equitorial form. Of these two positions of the H's, the equitorial form will be the most stable because the hydrogen atoms, or perhaps the other substituents, will not be touching each other. This is the best time to build a chair conformation in an equitorial and an axial form to demonstrate the stability of the equitorial form.

Ring Strain

Cycloalkanes tend to give off a very high and non-favorable energy, and the spatial orientation of the atoms is called the ring strain. When atoms are close together, their proximity is highly unfavorable and causes steric hindrance. The reason we do not want ring strain and steric hindrance is because heat will be released due to an increase in energy; therefore, a lot of that energy is stored in the bonds and molecules, causing the ring to be unstable and reactive. Another reason we try to avoid ring strain is because it will affect the structures and the conformational function of the smaller cycloalkanes. One way to determine the presence of ring strain is by its heat of combustion. By comparing the heat of combustion with the value measured for the straight chain molecule, we can determine the stability of the ring. There are two types of strain, which are eclipsing/torsional strain and bond angle strain. Bond angle strain causes a ring to have a poor overlap between the atoms, resulting in weak and reactive C-C bonds. An eclipsed spatial arrangement of the atoms on the cycloalkanes results in high energy.

With so many cycloalkanes, which ones have the highest ring strain and are very unlikely to stay in its current form? The figures below show cyclopropane, cyclobutane, and cyclopentane, respectively. Cyclopropane is one of the cycloalkanes that has an

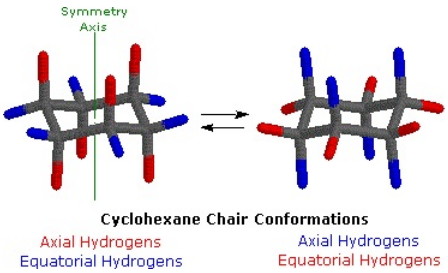
incredibly high and unfavorable energy, followed by cyclobutane as the next strained cycloalkane. Any ring that is small (with three to four carbons) has a significant amount of ring strain; cyclopropane and cyclobutane are in the category of small rings. A ring with five to seven carbons is considered to have minimal to zero strain, and typical examples are cyclopentane, cyclohexane, and cycloheptane. However, a ring with eight to twelve carbons is considered to have a moderate strain, and if a ring has beyond twelve carbons, it has minimal strain.

There are different types of ring strain:

- **Transannular strain** isdefined as the crowding of the two groups in a ring.
- **Eclipsing strain,** also known as torsional strain, is intramolecular strain due to the bonding interaction between two eclipsed atoms or groups.
- **Bond angle strain** is present when there is a poor overlap between the atoms. There must be an ideal bond angle to achieve the maximum bond strength and that will allow the overlapping of the atomic/hybrid orbitals.

Cyclohexane

Most of the time, cyclohexane adopts the fully staggered, ideal angle **chair conformation**. In the chair conformation, if any carbon-carbon bond were examined, it would be found to exist with its substituents in the staggered conformation and all bonds would be found to possess an angle of 109.5°.



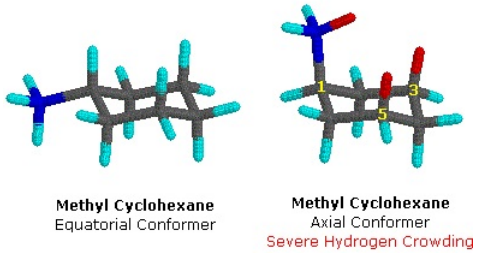
Cyclohexane in the chair conformation. (William Reusch, MSU).

In the chair conformation, hydrogen atoms are labeled according to their location. Those hydrogens which exist above or below the plane of the molecule (shown with red bonds above) are called **axial**. Those hydrogens which exist in the plane of the molecule (shown with blue bonds above) are called **equatorial**.

Although the chair conformation is the most stable conformation that cyclohexane can adopt, there is enough thermal energy for it to also pass through less favorable conformations before returning to a different chair conformation. When it does so, the axial and equatorial substituents change places. The passage of cyclohexane from one chair conformation to another, during which the axial substituents switch places with the equatorial substituents, is called a **ring flip**.

Methylcyclohexane

Methylcyclohexane is cyclohexane in which one hydrogen atom is replaced with a methyl group substituent. Methylcyclohexane can adopt two basic chair conformations: one in which the methyl group is axial, and one in which it is equatorial. Methylcyclohexane strongly prefers the equatorial conformation. In the axial conformation, the methyl group comes in close proximity to the axial hydrogens, an energetically unfavorable effect known as a **1,3-diaxial interaction** (Figure 3). Thus, the equatorial conformation is preferred for the methyl group. In most cases, if the cyclohexane ring contains a substituent, the substituent will prefer the equatorial conformation.



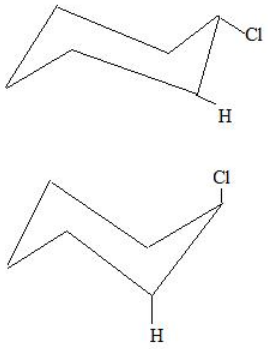
Methylcyclohexane in the chair conformation. (William Reusch, MSU).

References

1. Bachrach, Steven M. Computational Organic Chemistry. Wiley- Interscience. (2007).
2. McMurray, John E. Organic Chemistry Sixth Edition. Brooks Cole. (2003).
3. Vollhardt and Schore. Organic Chemistry Structure and Function Fifth Edition. New York. (2007).

Problems

1. Trans- 1,2-dimethylcyclopropane is more stable than cis-1,2-dimethylcyclopropane. Why? Drawing a picture of the two will help your explanation.
2. Out of all the cycloalkanes, which one has the most ring strain and which one is strain free? Explain.
3. Which of these chair conformations are the most stable and why?



3.

4. What does it mean when people say "increase in heat leads to increase in energy" and how does that statement relate to ring strains?
5. Why is that the bigger rings have lesser strains compared to smaller rings?

Answers

1. The cis isomer suffers from steric hindrance and has a larger heat of combustion.
2. Cyclopropane- ring strain. Cyclohexane chair conformation- ring strain free.
3. Top one is more stable because it is in an equitorial conformation. When assembling it with the OChem Molecular Structure Tool Kit, equitorial formation is more spread out.
4. When there is an increase in heat there will be an increase of energy released therefore there will be a lot of energy stored in the bond and molecule making it unstable.
5. Smaller rings are more compacts, which leads to steric hindrance and the angles for these smaller rings are harder to get ends to meet. Bigger rings tend to have more space and that the atoms attached to the ring won't be touching each other as much as atoms attached to the smaller ring.

Contributors

- Jonathan Mooney (McGill University)

3.9: Conformers of Cyclohexane is shared under a not declared license and was authored, remixed, and/or curated by LibreTexts.

- **Ring Strain and the Structure of Cycloalkanes** is licensed CC BY-NC-SA 4.0.

3.10: Conformers of Monosubstituted Cyclohexanes

Rings: cis/trans and axial/equatorial relationships

3.10: Conformers of Monosubstituted Cyclohexanes is shared under a not declared license and was authored, remixed, and/or curated by LibreTexts.

3.11: Conformers of Disubstituted Cyclohexanes

Rings: cis/trans and axial/equatorial relationships

3.11: Conformers of Disubstituted Cyclohexanes is shared under a not declared license and was authored, remixed, and/or curated by LibreTexts.

3.12: Fused Cyclohexane Rings

Generally, there are two types of inorganic compounds that can be formed: ionic compounds and molecular compounds. Nomenclature is the process of naming chemical compounds with different names so that they can be easily identified as separate chemicals. Inorganic compounds are compounds that do not deal with the formation of carbohydrates, or simply all other compounds that do not fit into the description of an organic compound. For example, organic compounds include molecules with carbon rings and/or chains with hydrogen atoms (see picture below). Inorganic compounds, the topic of this section, are every other molecule that does not include these distinctive carbon and hydrogen structures.

Compounds between Metals and Nonmetals (Cation and Anion)

Compounds made of a metal and nonmetal are commonly known as Ionic Compounds, where the compound name has an ending of ***–ide***. Cations have positive charges while anions have negative charges. The net charge of any ionic compound must be zero which also means it must be electrically neutral. For example, one Na^+ is paired with one Cl^-; one Ca^{2+} is paired with two Br^-. There are two rules that must be followed through:

- The **cation** (metal) is always named first with its name unchanged
- The **anion** (nonmetal) is written after the cation, modified to end in ***–ide***

Table 1: Cations and Anions:

+1 Charge	+2 Charge	-1 Charge	-2 Charge	-3 Charge	-4 Charge
Group 1A elements	**Group 2A elements**	**Group 7A elements**	**Group 6A elements**	**Group 5A elements**	**Group 4A elements**
Hydrogen: H^+	Beryllium: Be^{2+}	Hydride: H^-	Oxide: O^{2-}	Nitride: N^{3-}	Carbide: C^{4-}
Lithium: Li^+	Magnesium: Mg^{2+}	Fluoride: F^-	Sulfide: S^{2-}	Phosphide: P^{3-}	
Soduim: Na^+	Calcium: Ca^{2+}	Chloride: Cl^-			
Potassium: K^+	Strontium: Sr^{2+}	Bromide: Br^-			
Rubidium: Rb^+	Barium: Ba^{2+}	Iodide: I^-			
Cesium: Cs^+					

Example 1

$Na^+ + Cl^- = NaCl$; $Ca^{2+} + 2Br^- = CaBr_2$

Sodium + Chlorine = Sodium Chlor**ide;** Calcium + Bromine = Calcium Brom**ide**

The transition metals may form more than one ion, thus it is needed to be specified which particular ion we are talking about. This is indicated by assigning a Roman numeral after the metal. The Roman numeral denotes the charge and the oxidation state of the transition metal ion. For example, iron can form two common ions, Fe^{2+} and Fe^{3+}. To distinguish the difference, Fe^{2+} would be named iron (II) and Fe^{3+} would be named iron (III).

Table of Transition Metal and Metal Cations:

+1 Charge	+2 Charge	+3 Charge	+4 Charge
Copper(I): Cu^{+}	Copper(II): Cu^{2+}	Aluminum: Al^{3+}	Lead(IV): Pb^{4+}
Silver: Ag^{+}	Iron(II): Fe^{2+}	Iron(III): Fe^{3+}	Tin(IV): Sn^{4+}
	Cobalt(II): Co^{2+}	Cobalt(III): Co^{3+}	
	Tin(II): Sn^{2+}		
	Lead(II): Pb^{2+}		
	Nickel: Ni^{2+}		
	Zinc: Zn^{2+}		

Example 2

Ions:	Fe^{2+} + $2Cl^{-}$	Fe^{3+} + $3Cl^{-}$
Compound:	$FeCl_2$	$FeCl_3$
Nomenclature	Iron (II) Chloride	Iron (III) Chloride

However, some of the transition metals' charges have specific Latin names. Just like the other nomenclature rules, the ion of the transition metal that has the lower charge has the Latin name ending with **-ous** and the one with the the higher charge has a Latin name ending with **-ic**. The most common ones are shown in the table below:

Transition Metal Ion with Roman Numeral	Latin name
Copper (I): Cu^{+}	Cuprous
Copper (II): Cu^{2+}	Cupric
Iron (II): Fe^{2+}	Ferrous
Iron (III): Fe^{3+}	Ferric
Lead (II): Pb^{2+}	Plumbous
Lead (IV): Pb^{4+}	Plumbic
Mercury (I): Hg_2^{2+}	Mercurous
Mercury (II): Hg^{2+}	Mercuric
Tin (II): Sn^{2+}	Stannous
Tin (IV): Sn^{4+}	Stannic

Several exceptions apply to the Roman numeral assignment: Aluminum, Zinc, and Silver. Although they belong to the transition metal category, these metals do not have Roman numerals written after their names because these metals only exist in one ion. Instead of using Roman numerals, the different ions can also be presented in plain words. The metal is changed to end in ***–ous*** or ***–ic***.

- ***-ous*** ending is used for the **lower** oxidation state
- ***-ic*** ending is used for the **higher** oxidation state

Example 3

Compound	Cu_2O	CuO	$FeCl_2$	$FeCl_3$
Charge	Charge of copper is +1	Charge of copper is +2	Charge of iron is +2	Charge of iron is +3
Nomenclature	Cuprous Oxide	Cupric Oxide	Ferrous Chloride	Ferric Chloride

However, this **-ous/-ic** system is inadequate in some cases, so the Roman numeral system is preferred. This system is used commonly in naming acids, where H_2SO_4 is commonly known as Sulfuric Acid, and H_2SO_3 is known as Sulfurous Acid.

Compounds between Nonmetals and Nonmetals

Compounds that consist of a nonmetal bonded to a nonmetal are commonly known as **Molecular Compounds**, where the element with the positive oxidation state is written first. In many cases, nonmetals form more than one binary compound, so **prefixes** are used to distinguish them.

# of Atoms	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**
Prefixes	Mono-	Di-	Tri-	Tetra-	Penta-	Hexa-	Hepta-	Octa-	Nona-	Deca-

Example 4

CO = carbon ***mon***oxide BCl_3 = boron***tri***chloride

CO_2 = carbon ***di***oxide N_2O_5 =***di***nitrogen ***pent***oxide

The prefix ***mono***- is not used for the first element. If there is not a prefix before the first element, it is assumed that there is only one atom of that element.

Binary Acids

Although HF can be named hydrogen fluoride, it is given a different name for emphasis that it is an acid. An acid is a substance that dissociates into hydrogen ions (H^+) and anions in water. A quick way to identify acids is to see if there is an H (denoting hydrogen) in front of the molecular formula of the compound. To name acids, the prefix ***hydro***- is placed in front of the nonmetal modified to end with ***–ic***. The state of acids is aqueous (aq) because acids are found in water.

Some common binary acids include:

HF (g) = hydrogen fluor**ide** -> HF (aq) = ***hydro***fluor***ic*** acid

HBr (g) = hydrogen brom**ide** -> HBr (aq) = ***hydro***brom***ic*** acid

HCl (g) = hydrogen chlor**ide** -> HCl (aq) = ***hydro***chlor***ic*** acid

H_2S (g) = hydrogen sulf**ide** -> H_2S (aq) = ***hydro***sulfur***ic***acid

It is important to include (aq) after the acids because the same compounds can be written in gas phase with hydrogen named first followed by the anion ending with ***–ide***.

Example 5

hypo____ite ____ite ____ate per____ate

ClO^- ClO_2^- ClO_3^- ClO_4^-

hypo*chlor*ite *chlor*ite *chlor*ate per*chlor*ate

---------->

As indicated by the arrow, moving to the right, the following trends occur:

Increasing number of oxygen atoms

Increasing oxidation state of the nonmetal

(Usage of this example can be seen from the set of compounds containing Cl and O)

This occurs because the number of oxygen atoms are increasing from hypochlorite to perchlorate, yet the overall charge of the polyatomic ion is still -1. To correctly specify how many oxygen atoms are in the ion, prefixes and suffixes are again used.

Polyatomic Ions

In **polyatomic ions**, polyatomic (meaning two or more atoms) are joined together by **covalent bonds**. Although there may be a element with positive charge like H^+, it is not joined with another element with an ionic bond. This occurs because if the atoms formed an ionic bond, then it would have already become a compound, thus not needing to gain or loose any electrons. Polyatomic anions are more common than polyatomic cations as shown in the chart below. Polyatomic anions have negative charges while polyatomic cations have positive charges. To indicate different polyatomic ions made up of the same elements, the name of the ion is modified according to the example below:

Table: Common Polyatomic ions

Name: Cation/Anion	Formula
Ammonium ion	NH_4^+
Hydronium ion	H_3O^+
Acetate ion	$C_2H_3O_2^-$
Arsenate ion	AsO_4^{3-}
Carbonate ion	CO_3^{2-}
Hypochlorite ion	ClO^-
Chlorite ion	ClO_2^-
Chlorate ion	ClO_3^-
Perchlorate ion	ClO_4^-
Chromate ion	CrO_4^{2-}
Dichromate ion	$Cr_2O_7^{2-}$
Cyanide ion	CN^-
Hydroxide ion	OH^-
Nitrite ion	NO_2^-
Nitrate ion	NO_3^-
Oxalate ion	$C_2O_4^{2-}$
Permanganate ion	MnO_4^-
Phosphate ion	PO_4^{3-}
Sulfite ion	SO_3^{2-}
Sulfate ion	SO_4^{2-}
Thiocyanate ion	SCN^-
Thiosulfate ion	$S_2O_3^{2-}$

To combine the topic of acids and polyatomic ions, there is nomenclature of aqueous acids. Such acids include sulfuric acid (H_2SO_4) or carbonic acid (H_2CO_3). To name them, follow these quick, simple rules:

1. If the ion ends in **-ate** and is added with an acid, the acid name will have an **-ic** ending. Examples: nitrate ion (NO_3^-) + H^+ (denoting formation of acid) = nitr**ic** acid (HNO_3)
2. If the ion ends in **-ite** and is added with an acid, then the acid name will have an **-ous** ending. Example: nitite ion (NO_2^-) + H^+ (denoting formation of acid) = nitr**ous** acid (HNO_2)

References

1. Pettrucci, Ralph H. General Chemistry: Principles and Modern Applications. 9th. Upper Saddle River: Pearson Prentice Hall, 2007
2. Nomenclature of Inorganic Chemistry, Recommendations 1990, Oxford:Blackwell Scientific Publications. (1990)
3. International Union of Pure and Applied Chemistry (2005). Nomenclature of Inorganic Chemistry (IUPAC Recommendations 2005). Cambridge (UK): RSC–IUPAC. ISBN 0-85404-438-8. Electronic version..
4. Biochemical Nomenclature and Related Documents, London:Portland Press, 1992.

Problems

1. What is the correct formula for Calcium Carbonate?

    a. $Ca^+ + CO_2^-$

    b. $CaCO_2^-$

    c. $CaCO_3$

    d. $2CaCO_3$

2. What is the correct name for FeO?

    a. Iron oxide

    b. Iron dioxide

    c. Iron(III) oxide

    d. Iron(II) oxide

3. What is the correct name for $Al(NO_3)_3$?

    a. Aluminum nitrate

    b. Aluminum(III) nitrate

    c. Aluminum nitrite

    d. Aluminum nitrogen trioxide

4. What is the correct formula of phosphorus trichloride?

    a. P_2Cl_2

    b. PCl_3

    c. PCl_4

    d. P_4Cl_2

5. What is the correct formula of lithium perchlorate?

    a. Li_2ClO_4

    b. $LiClO_2$

    c. LiClO

    d. None of these

6. Write the correct name for these compounds.

a. BeC_2O_4:

b. NH_4MnO_4:

c. CoS_2O_3:

7. What is $W(HSO_4)_5$?

8. How do you write diphosphorus trioxide?

9. What is H_3P?

10. By adding oxygens to the molecule in number 9, we now have H_3PO_4? What is the name of this molecule?

Answer

1.C; Calcium + Carbonate --> $Ca^{2+} + CO_3^{2-}$ --> $CaCO_3$

2.D; FeO --> Fe + O^{2-} --> Iron must have a charge of +2 to make a neutral compound --> $Fe^{2+} + O^{2-}$ --> Iron(II) Oxide

3.A; $Al(NO_3)_3$ --> $Al^{3+} + (NO_3^-)_3$ --> Aluminum nitrate

4.B; Phosphorus trichloride --> P + 3Cl --> PCl_3

5.D, $LiClO_4$; Lithium perchlorate --> $Li^+ + ClO_4^-$ --> $LiClO_4$

6. a. Beryllium Oxalate; BeC_2O_4 --> $Be^{2+} + C_2O_4^{2-}$ --> Beryllium Oxalate

b. Ammonium Permanganate; NH_4MnO_4 --> $NH_4^+ + MnO_4^-$ --> Ammonium Permanganate

c. Cobalt (II) Thiosulfate; CoS_2O_3 --> Co + $S_2O_3^{2-}$ --> Cobalt must have +2 charge to make a neutral compund --> $Co^{2+} + S_2O_3^{2-}$ --> Cobalt(II) Thiosulfate

7. Tungsten (V) hydrogen sulfate

8. P_2O_3

9. Hydrophosphoric Acid

10. Phosphoric Acid

Contributors and Attributions

- Pui Yan Ho (UCD), Alex Moskaluk (UCD), Emily Nguyen (UCD)

3.12: Fused Cyclohexane Rings is shared under a not declared license and was authored, remixed, and/or curated by LibreTexts.

- **Nomenclature of Inorganic Compounds** is licensed CC BY-NC-SA 4.0.

CHAPTER OVERVIEW

4: Alkenes- Structure, Nomenclature, and an Introduction to Reactivity



Essential Organic Chemistry: 2nd Ed.
Bruice

Homework Problems
Homework Solutions

I II III IV V VI VII VIII IX X XI XII XIII XIV XV XVI XVII XVIII XIX XX XXI

Template:HideTOC

- 4.1: Molecular Formulas and the Degree of Unsaturation
- 4.2: The Nomenclature of Alkenes
- 4.3: The Structures of Alkenes
- 4.4: Alkenes Can Have Cis and Trans Isomers
- 4.5: Naming Alkenes Using the E Z System
- 4.6: How Alkenes React (Curved Arrows Show the Flow of Electrons)
- 4.7: A Reaction Coordinate Diagram Describes the Energy Changes That Take Place During a Reaction

---

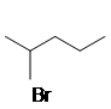
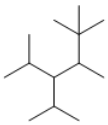
4: Alkenes- Structure, Nomenclature, and an Introduction to Reactivity is shared under a not declared license and was authored, remixed, and/or curated by LibreTexts.

4.1: Molecular Formulas and the Degree of Unsaturation

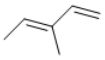
There are many ways one can go about determining the structure of an unknown organic molecule. Although, nuclear magnetic resonance (NMR) and infrared radiation (IR) are the primary ways of determining molecular structures, calculating the degrees of unsaturation is useful information since knowing the degrees of unsaturation make it easier for one to figure out the molecular structure; it helps one double-check the number of π bonds and/or cyclic rings.

Saturated vs. Unsaturated Molecules

In the lab, saturation may be thought of as the point when a solution cannot dissolve anymore of a substance added to it. In terms of degrees of unsaturation, a molecule only containing single bonds with no rings is considered saturated.

$CH_3CH_2CH_3$			1-methyoxypentane

Unlike saturated molecules, unsaturated molecules contain double bond(s), triple bond(s) and/or ring(s).

$CH_3CH{=}CHCH_3$				3-chloro-5-octyne

Calculating Degrees of Unsaturation (DoU)

Degree of Unsaturation (DoU) is also known as **Double Bond Equivalent**. If the molecular formula is given, plug in the numbers into this formula:

$$DoU = \frac{2C + 2 + N - X - H}{2} \tag{4.1.1}$$

- C is the number of carbons
- N is the number of nitrogens
- X is the number of halogens (F, Cl, Br, I)
- H is the number of hydrogens

As stated before, a saturated molecule contains only single bonds and no rings. Another way of interpreting this is that a saturated molecule has the maximum number of hydrogen atoms possible to be an acyclic alkane. Thus, the number of hydrogens can be represented by 2C+2, which is the general molecular representation of an alkane. As an example, for the molecular formula C_3H_4 the number of actual hydrogens needed for the compound to be saturated is 8 *[2C+2=(2x3)+2=8]*. The compound needs 4 more hydrogens in order to be fully saturated *(expected number of hydrogens-observed number of hydrogens=8-4=4)*. Degrees of unsaturation is equal to 2, or half the number of hydrogens the molecule needs to be classified as saturated. Hence, the DoB formula divides by 2. The formula subtracts the number of X's because a halogen (X) replaces a hydrogen in a compound. For instance, in chloroethane, C_2H_5Cl, there is one less hydrogen compared to ethane, C_2H_6.

For a compound to be saturated, there is one more hydrogen in a molecule when nitrogen is present. Therefore, we add the number of nitrogens (N). This can be seen with C_3H_9N compared to C_3H_8. Oxygen and sulfur are not included in the formula because saturation is unaffected by these elements. As seen in alcohols, the same number of hydrogens in ethanol, C_2H_5OH, matches the number of hydrogens in ethane, C_2H_6.

The following chart illustrates the possible combinations of the number of double bond(s), triple bond(s), and/or ring(s) for a given degree of unsaturation. Each row corresponds to a different combination.

- One degree of unsaturation is equivalent to 1 ring or 1 double bond (1 π bond).
- Two degrees of unsaturation is equivalent to 2 double bonds, 1 ring and 1 double bond, 2 rings, or 1 triple bond (2 π bonds).

DoU	**Possible combinations of rings/ bonds**		
	# of rings	# of double bonds	# of triple bonds
1	1	0	0
	0	1	0
2	2	0	0
	0	2	0
	0	0	1
	1	1	0
3	3	0	0
	2	1	0
	1	2	0
	0	1	1
	0	3	0
	1	0	1

Remember, the degrees of unsaturation only gives the sum of double bonds, triple bonds and/or rings. For instance, a degree of unsaturation of 3 can contain 3 rings, 2 rings+1 double bond, 1 ring+2 double bonds, 1 ring+1 triple bond, 1 double bond+1 triple bond, *or* 3 double bonds.

Example: Benzene

What is the Degree of Unsaturation for Benzene?

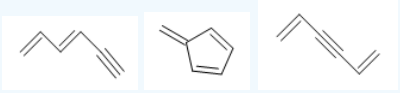
Solution

The molecular formula for benzene is C_6H_6. Thus,

DoU= 4, where C=6, N=0,X=0, and H=6. 1 DoB can equal 1 ring or 1 double bond. This corresponds to benzene containing 1 ring and 3 double bonds.



However, when given the molecular formula C_6H_6, benzene is only one of many possible structures (isomers). The following structures all have DoB of 4 and have the same molecular formula as benzene.

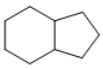
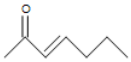
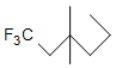


References

1. Vollhardt, K. P.C. & Shore, N. (2007). *Organic Chemistry* (5thEd.). New York: W. H. Freeman. (473-474)
2. Shore, N. (2007). *Study Guide and Solutions Manual for Organic Chemistry* (5th Ed.). New York: W.H. Freeman. (201)

Problems

1. Are the following molecules saturated or unsaturated:

1.  (b.)  (c.)  (d.) $C_{10}H_6N_4$

2. Using the molecules from 1., give the degrees of unsaturation for each.
3. Calculate the degrees of unsaturation for the following molecular formulas:
    1. (a.) C_9H_{20} (b.) C_7H_8 (c.) C_5H_7Cl (d.) $C_9H_9NO_4$
4. Using the molecular formulas from 3, are the molecules unsaturated or saturated.
5. Using the molecular formulas from 3, if the molecules are unsaturated, how many rings/double bonds/triple bonds are predicted?

Answers

1.

(a.) **unsaturated** (E*ven though rings only contain single bonds, rings are considered unsaturated.)*

(b.) **unsaturated**

(c.) **saturated**

(d.) **unsaturated**

2. *If the molecular structure is given, the easiest way to solve is to count the number of double bonds, triple bonds and/or rings. However, you can also determine the molecular formula and solve for the degrees of unsaturation by using the formula.*

(a.) **2**

(b.) **2** *(one double bond and the double bond from the carbonyl)*

(c.) **0**

(d.) **10**

3. *Use the formula to solve*

(a.) **0**

(b.) **4**

(c.) **2**

(d.) **6**

4.

(a.) **saturated**

(b.) **unsaturated**

(c.) **unsaturated**

(d.) **unsaturated**

5.

(a.) **0** (Remember-a saturated molecule only contains single bonds)

(b.) *The molecule can contain any of these combinations* **(i) 4 double bonds (ii) 4 rings (iii) 2 double bonds+2 rings (iv) 1 double bond+3 rings (v) 3 double bonds+1 ring (vi) 1 triple bond+2 rings (vii) 2 triple bonds (viii) 1 triple bond+1 double bond+1 ring (ix) 1 triple bond+2 double bonds**

(c.) **(i) 1 triple bond (ii) 1 ring+1 double bond (iii) 2 rings (iv) 2 double bonds**

(d.) **(i) 3 triple bonds (ii) 2 triple bonds+2 double bonds (iii) 2 triple bonds+1 double bond+1 ring (iv)...** *(As you can see, the degrees of unsaturation only gives the sum of double bonds, triple bonds and/or ring. Thus, the formula may give numerous possible structures for a given molecular formula.)*

Contributors

- Kim Quach (UCD)

4.1: Molecular Formulas and the Degree of Unsaturation is shared under a not declared license and was authored, remixed, and/or curated by LibreTexts.

- **Degree of Unsaturation** is licensed CC BY-NC-SA 4.0.

4.2: The Nomenclature of Alkenes

Naming the Alkenes

4.2: The Nomenclature of Alkenes is shared under a not declared license and was authored, remixed, and/or curated by LibreTexts.

4.3: The Structures of Alkenes

Background of Alkenes

4.3: The Structures of Alkenes is shared under a not declared license and was authored, remixed, and/or curated by LibreTexts.

4.4: Alkenes Can Have Cis and Trans Isomers

Background of Alkenes

4.4: Alkenes Can Have Cis and Trans Isomers is shared under a not declared license and was authored, remixed, and/or curated by LibreTexts.

4.5: Naming Alkenes Using the E Z System

Naming the Alkenes

4.5: Naming Alkenes Using the E Z System is shared under a not declared license and was authored, remixed, and/or curated by LibreTexts.

4.6: How Alkenes React (Curved Arrows Show the Flow of Electrons)

Addition Reactions of Alkenes

4.6: How Alkenes React (Curved Arrows Show the Flow of Electrons) is shared under a not declared license and was authored, remixed, and/or curated by LibreTexts.

4.7: A Reaction Coordinate Diagram Describes the Energy Changes That Take Place During a Reaction

Review of thermodynamics and kinetics

4.7: A Reaction Coordinate Diagram Describes the Energy Changes That Take Place During a Reaction is shared under a not declared license and was authored, remixed, and/or curated by LibreTexts.

CHAPTER OVERVIEW

5: The Reactions of Alkenes and Alkynes- An Introduction to Multistep Synthesis



Essential Organic Chemistry: 2nd Ed.
Bruice

Homework Problems
Homework Solutions

I II III IV V VI VII VIII IX X XI XII XIII XIV XV XVI XVII XVIII XIX XX XXI

Template:HideTOC

5.1: The Addition of a Hydrogen Halide to an Alkene
5.2: Carbocation Stability Depends on the Number of Alkyl Groups Attached to the Positively Charged Carbon
5.3: Electrophilic Addition Reactions Are Regioselective
5.4: The Addition of Water to an Alkene
5.5: The Addition of an Alcohol to an Alkene
5.6: The Nomenclature of Alkynes
5.7: The Structure of Alkynes
5.8: The Physical Properties of Unsaturated Hydrocarbons
5.9: The Addition of Hydrogen Halides and Addition of Halogens to an Alkyne
5.10: The Addition of Hydrogen to Alkenes and Alkynes
5.11: A Hydrogen Bonded to an sp Carbon is “Acidic”
5.12: Synthesis Using Acetylide Ions
5.13: An Introduction to Multistep Synthesis

5: The Reactions of Alkenes and Alkynes- An Introduction to Multistep Synthesis is shared under a not declared license and was authored, remixed, and/or curated by LibreTexts.

5.1: The Addition of a Hydrogen Halide to an Alkene

Electrophilic Addition of Hydrogen Halides

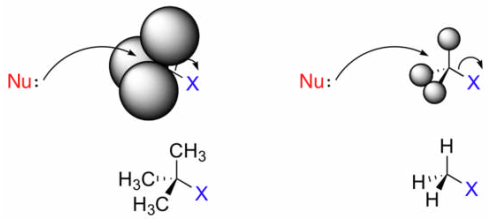
5.1: The Addition of a Hydrogen Halide to an Alkene is shared under a not declared license and was authored, remixed, and/or curated by LibreTexts.

5.2: Carbocation Stability Depends on the Number of Alkyl Groups Attached to the Positively Charged Carbon

In the vast majority of the nucleophilic substitution reactions you will see in this and other organic chemistry texts, the electrophilic atom is a carbon which is bonded to an electronegative atom, usually oxygen, nitrogen, sulfur, or a halogen. The concept of electrophilicity is relatively simple: an electron-poor atom is an attractive target for something that is electron-rich, *i.e.* a nucleophile. However, we must also consider the effect of steric hindrance on electrophilicity. In addition, we must discuss how the nature of the electrophilic carbon, and more specifically the stability of a potential carbocationic intermediate, influences the S_N1 vs. S_N2 character of a nucleophilic substitution reaction.

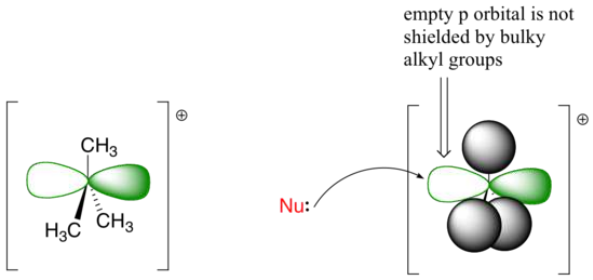
8.4A: Steric effects on electrophilicity

Consider two hypothetical S_N2 reactions: one in which the electrophile is a methyl carbon and another in which it is tertiary carbon.



Because the three substituents on the methyl carbon electrophile are tiny hydrogens, the nucleophile has a relatively clear path for backside attack. However, backside attack on the tertiary carbon is blocked by the bulkier methyl groups. Once again, steric hindrance - this time caused by bulky groups attached to the electrophile rather than to the nucleophile - hinders the progress of an associative nucleophilic (S_N2) displacement.

The factors discussed in the above paragraph, however, do not prevent a sterically-hindered carbon from being a good electrophile - they only make it less likely to be attacked in a *concerted S_N2 reaction*. Nucleophilic substitution reactions in which the electrophilic carbon is sterically hindered are more likely to occur by a two-step, dissociative (S_N1) mechanism. This makes perfect sense from a geometric point of view: the limitations imposed by sterics are significant mainly in an S_N2 displacement, when the electrophile being attacked is a sp^3-hybridized tetrahedral carbon with its relatively 'tight' angles of 109.4^o. Remember that in an S_N1 mechanism, the nucleophile attacks an sp^2-hybridized carbocation intermediate, which has trigonal planar geometry with 'open' 120 angles.



With this open geometry, the empty p orbital of the electrophilic carbocation is no longer significantly shielded from the approaching nucleophile by the bulky alkyl groups. A carbocation is a very potent electrophile, and the nucleophilic step occurs very rapidly compared to the first (ionization) step.

8.4B: Stability of carbocation intermediates

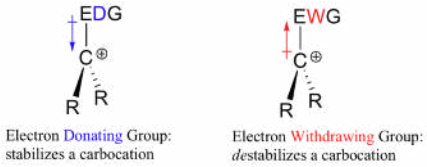
We know that the rate-limiting step of an S_N1 reaction is the first step - formation of the this carbocation intermediate. The rate of this step – and therefore, the rate of the overall substitution reaction – depends on the activation energy for the process in which the bond between the carbon and the leaving group breaks and a carbocation forms. According to Hammond's postulate (section 6.2B), the more stable the carbocation intermediate is, the faster this first bond-breaking step will occur. In other words, the likelihood of a

nucleophilic substitution reaction proceeding by a dissociative (S_N1) mechanism depends to a large degree on the stability of the carbocation intermediate that forms.

The critical question now becomes, *what stabilizes a carbocation*?

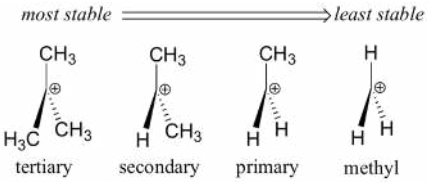
Think back to Chapter 7, when we were learning how to evaluate the strength of an acid. The critical question was “how stable is the conjugate base that results when this acid donates its proton"? In many cases, this conjugate base was an anion – a center of excess electron density. Anything that can draw some of this electron density away– in other words, any electron withdrawing group – will stabilize the anion.

So if it takes an electron *withdrawing* group to stabilize a negative charge, what will stabilize a positive charge? An electron *donating* group!



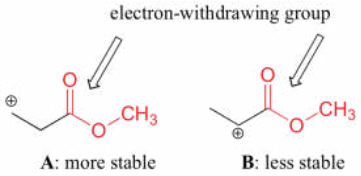
A positively charged species such as a carbocation is very electron-poor, and thus anything which donates electron density to the center of electron poverty will help to stabilize it. Conversely, a carbocation will be *destabilized* by an electron withdrawing group.

Alkyl groups – methyl, ethyl, and the like – are weak electron donating groups, and thus stabilize nearby carbocations. What this means is that, in general, *more substituted carbocations are more stable*: a tert-butyl carbocation, for example, is more stable than an isopropyl carbocation. Primary carbocations are highly unstable and not often observed as reaction intermediates; methyl carbocations are even less stable.



Alkyl groups are electron donating and carbocation-stabilizing because the electrons around the neighboring carbons are drawn towards the nearby positive charge, thus slightly reducing the electron poverty of the positively-charged carbon.

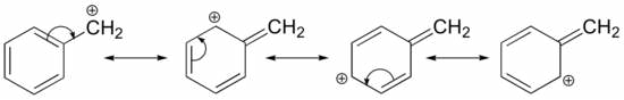
It is not accurate to say, however, that carbocations with higher substitution are *always* more stable than those with less substitution. Just as electron-donating groups can stabilize a carbocation, electron-withdrawing groups act to destabilize carbocations. Carbonyl groups are electron-withdrawing by inductive effects, due to the polarity of the C=O double bond. It is possible to demonstrate in the laboratory (see section 16.1D) that carbocation A below is more stable than carbocation B, even though A is a primary carbocation and B is secondary.



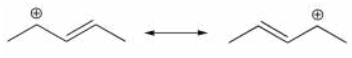
The difference in stability can be explained by considering the electron-withdrawing inductive effect of the ester carbonyl. Recall that inductive effects - whether electron-withdrawing or donating - are relayed through covalent bonds and that the strength of the effect decreases rapidly as the number of intermediary bonds increases. In other words, the effect decreases with distance. In species B the positive charge is closer to the carbonyl group, thus the destabilizing electron-withdrawing effect is stronger than it is in species A.

In the next chapter we will see how the carbocation-destabilizing effect of electron-withdrawing fluorine substituents can be used in experiments designed to address the question of whether a biochemical nucleophilic substitution reaction is S_N1 or S_N2.

Stabilization of a carbocation can also occur through resonance effects, and as we have already discussed in the acid-base chapter, resonance effects as a rule are more powerful than inductive effects. Consider the simple case of a **benzylic** carbocation:

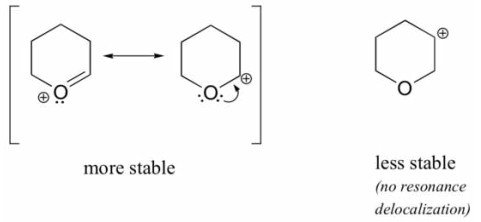


This carbocation is comparatively stable. In this case, electron donation is a resonance effect. Three additional resonance structures can be drawn for this carbocation in which the positive charge is located on one of three aromatic carbons. The positive charge is not isolated on the benzylic carbon, rather it is delocalized around the aromatic structure: this delocalization of charge results in significant stabilization. As a result, benzylic and **allylic** carbocations (where the positively charged carbon is conjugated to one or more non-aromatic double bonds) are significantly more stable than even tertiary alkyl carbocations.



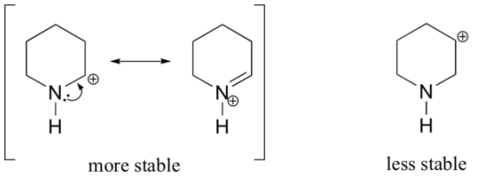
an allylic carbocation

Because heteroatoms such as oxygen and nitrogen are more electronegative than carbon, you might expect that they would by definition be electron withdrawing groups that destabilize carbocations. In fact, the opposite is often true: if the oxygen or nitrogen atom is in the correct position, the overall effect is carbocation stabilization. This is due to the fact that although these heteroatoms are electron *withdrawing* groups by induction, they are electron *donating* groups by resonance, and it is this resonance effect which is more powerful. (We previously encountered this same idea when considering the relative acidity and basicity of phenols and aromatic amines in section 7.4). Consider the two pairs of carbocation species below:



more stable

less stable
(no resonance delocalization)

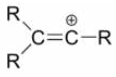


more stable

less stable
(no resonance delocalization)

In the more stable carbocations, the heteroatom acts as an electron donating group by resonance: in effect, the lone pair on the heteroatom is available to delocalize the positive charge. In the less stable carbocations the positively-charged carbon is more than one bond away from the heteroatom, and thus no resonance effects are possible. In fact, in these carbocation species the heteroatoms actually *destabilize* the positive charge, because they are electron withdrawing by induction.

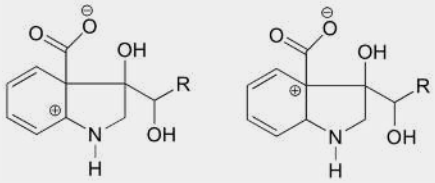
Finally, **vinylic** carbocations, in which the positive charge resides on a double-bonded carbon, are very unstable and thus unlikely to form as intermediates in any reaction.



a vinylic carbocation
(very unstable)

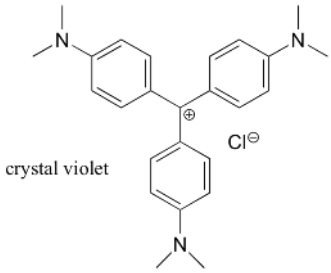
Example 8.10

Exercise 8.10: In which of the structures below is the carbocation expected to be more stable? Explain.



Solution

For the most part, carbocations are very high-energy, transient intermediate species in organic reactions. However, there are some unusual examples of very stable carbocations that take the form of organic salts. Crystal violet is the common name for the chloride salt of the carbocation whose structure is shown below. Notice the structural possibilities for extensive resonance delocalization of the positive charge, and the presence of three electron-donating amine groups.



Example 8.11

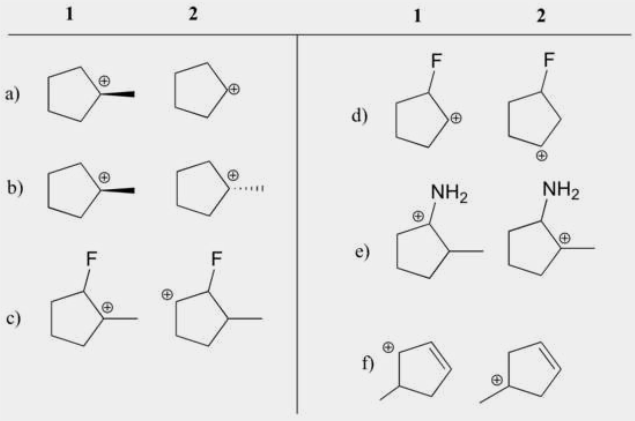
Draw a resonance structure of the crystal violet cation in which the positive charge is delocalized to one of the nitrogen atoms.

Solution

When considering the possibility that a nucleophilic substitution reaction proceeds *via* an S_N1 pathway, it is critical to evaluate the stability of the hypothetical carbocation intermediate. If this intermediate is not sufficiently stable, an S_N1 mechanism must be considered unlikely, and the reaction probably proceeds by an S_N2 mechanism. In the next chapter we will see several examples of biologically important S_N1 reactions in which the positively charged intermediate is stabilized by inductive and resonance effects inherent in its own molecular structure.

Example 8.12

State which carbocation in each pair below is more stable, or if they are expected to be approximately equal. Explain your reasoning.



Solution

5.2: Carbocation Stability Depends on the Number of Alkyl Groups Attached to the Positively Charged Carbon is shared under a not declared license and was authored, remixed, and/or curated by LibreTexts.

5.3: Electrophilic Addition Reactions Are Regioselective

Regioselectivity and the Markovnikov Rule

5.3: Electrophilic Addition Reactions Are Regioselective is shared under a not declared license and was authored, remixed, and/or curated by LibreTexts.

5.4: The Addition of Water to an Alkene

Addition of electrophilic reagents to alkenes

5.4: The Addition of Water to an Alkene is shared under a not declared license and was authored, remixed, and/or curated by LibreTexts.

5.5: The Addition of an Alcohol to an Alkene

Addition of electrophilic reagents to alkenes

5.5: The Addition of an Alcohol to an Alkene is shared under a not declared license and was authored, remixed, and/or curated by LibreTexts.

5.6: The Nomenclature of Alkynes

Naming the Alkynes

5.6: The Nomenclature of Alkynes is shared under a not declared license and was authored, remixed, and/or curated by LibreTexts.

5.7: The Structure of Alkynes

Properties and Bonding in the Alkynes

5.7: The Structure of Alkynes is shared under a not declared license and was authored, remixed, and/or curated by LibreTexts.

5.8: The Physical Properties of Unsaturated Hydrocarbons

Properties and Bonding in the Alkynes

5.8: The Physical Properties of Unsaturated Hydrocarbons is shared under a not declared license and was authored, remixed, and/or curated by LibreTexts.

5.9: The Addition of Hydrogen Halides and Addition of Halogens to an Alkyne

Anti-Markovnikov Additions to Triple Bonds

5.9: The Addition of Hydrogen Halides and Addition of Halogens to an Alkyne is shared under a not declared license and was authored, remixed, and/or curated by LibreTexts.

5.10: The Addition of Hydrogen to Alkenes and Alkynes

Catalytic Hydrogenation of Alkenes

Hydration of Alkynes

5.10: The Addition of Hydrogen to Alkenes and Alkynes is shared under a not declared license and was authored, remixed, and/or curated by LibreTexts.

5.11: A Hydrogen Bonded to an sp Carbon is “Acidic”

Acidity of Terminal Alkynes

5.11: A Hydrogen Bonded to an sp Carbon is “Acidic” is shared under a not declared license and was authored, remixed, and/or curated by LibreTexts.

5.12: Synthesis Using Acetylide Ions

Nucleophilic Reactivity of Deprotonated Alkynes

5.12: Synthesis Using Acetylide Ions is shared under a not declared license and was authored, remixed, and/or curated by LibreTexts.

5.13: An Introduction to Multistep Synthesis

under construction

5.13: An Introduction to Multistep Synthesis is shared under a not declared license and was authored, remixed, and/or curated by LibreTexts.

CHAPTER OVERVIEW

6: Isomers and Stereochemistry



Essential Organic Chemistry: 2nd Ed.
Bruice

Homework Problems
Homework Solutions

I II III IV V VI VII VIII IX X XI XII XIII XIV XV XVI XVII XVIII XIX XX XXI

Template:HideTOC

6.1: Cis-Trans Isomers Result from Restricted Rotation
6.2: A Chiral Object Has a Nonsuperimposable Mirror Image
6.3: An Asymmetric Center Is a Cause of Chirality in a Molecule
6.4: Isomers with One Asymmetric Center
6.5: Asymmetric Centers and Stereocenters
6.6: How to Draw Enantiomers
6.7: Naming Enantiomers by the R,S System
6.8: Chiral Compounds Are Optically Active
6.9: How Specific Rotation is Measured
6.10: Enantiomeric Excess
6.11: Isomers with More than One Asymmetric Center
6.12: Meso Compounds Have Asymmetric Centers but Are Optically Inactive
6.13: How to Name Isomers with More than One Asymmetric Center
6.14: Reactions of Compounds that Contain an Asymmetric Center
6.15: Using Reactions that Do Not Break Bonds to an Asymmetric Center to Determine Relative Configurations
6.16: How Enantiomers Can Be Separated
6.17: Nitrogen and Phosphorus Atoms Can Be Asymmetric Centers
6.18: Stereochemistry of Reactions- Regioselective, Stereoselective, and Stereospecific Reactions
6.19: The Stereochemistry of Electrophilic addition Reactions of Alkenes
6.20: The Stereochemistry of Enzyme-Catalyzed Reactions
6.21: Enantiomers Can Be Distinguished by Biological Molecules

---

6: Isomers and Stereochemistry is shared under a not declared license and was authored, remixed, and/or curated by LibreTexts.

6.1: Cis-Trans Isomers Result from Restricted Rotation

Several organic compounds may have identical compositions but will have widely different physical and chemical properties because the arrangement of the atoms is different. Isomers and identical compounds both have the same number of each kind of element in a formula. A simple count will establish this fact.

Introduction

As a consequence of the double bond, some alkene compounds exhibit a unique type of isomerism. Rotation around a single bond occurs readily, while rotation around a double bond is restricted. The pi bond prevents rotation because of the electron overlap both above and below the plane of the atoms.

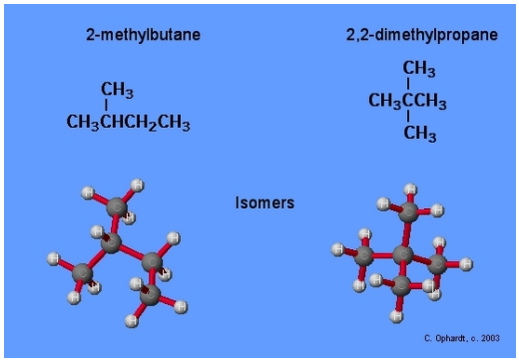
A single bond is analogous to two boards nailed together with one nail. A double bond is analogous to two boards nailed together with two nails. In the first case you can twist the boards, while in the second case you cannot twist them.

Geometric Isomers are compounds with different spatial arrangements of groups attached to the carbons of a double bond. In alkenes, the carbon-carbon double bond is rigidly fixed. Even though the attachment of atoms is the same, the geometry (the way the atoms "see" each other) is different.

When looking for geometric isomers, a guiding principle is that there **MUST BE TWO DIFFERENT "GROUPS" ON EACH CARBON OF THE DOUBLE BOND**. A "group" can be hydrogen, alkyls, halogens, etc.

Identical compounds may appear to have different arrangements as written, but closer examination by rotation or turning will result in the molecules being superimposed. If they are super impossible or if they have identical names, then the two compounds are in fact identical.

Isomers of compounds have a different arrangement of the atoms. Isomer compounds will differ from identical compounds by the arrangement of the atoms. See **example below.**

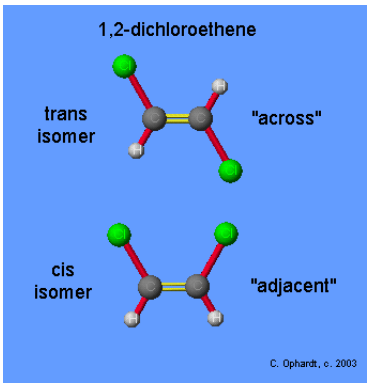


Both compounds have the same number of atoms, C_5H_{12}. They are isomers because in the left molecule the root is 4 carbons with one branch. In the right molecule, the root is 3 carbons with 2 branches. They are **isomers** because they have the same number of atoms but different arrangements of those atoms.

Completely different compounds: If the number of each element is different, the two compounds are merely completely different. A simple count of the atoms will reveal them as different.

1,2-dichlorethene

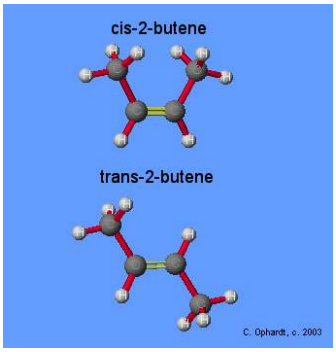
In the example on the left, the chlorine atoms can be opposite or across from each other in which case it is called the **"trans" isomer**. If the the chlorine atoms are next to or adjacent each other, the isomer is called " **cis**".



If one carbon of the double bond has two identical groups such as 2 H's or 2 Cl's or 2 CH_3 etc. there cannot be any geometric isomers.

2-butene

Consider the longest chain containing the double bond: If two groups (attached to the carbons of the double bond) are on the same side of the double bond, the isomer is a **cis** alkene. If the two groups lie on opposite sides of the double bond, the isomer is a **trans** alkene. One or more of the "groups" may or may not be part of the longest chain. In the case on the left, the "group" is a methyl - but is actually part of the longest chain.



A common mistake is to name this compound as 1,2-dimethylethene. Look at all carbons for the longest continuous chain - the root is 4 carbons - butene.

Problems

For the structures below:
a. Draw both cis/trans isomers, if any, of the structure based upon the name.

b. Look at the graphic and state whether the compound is cis, trans, or not cis/trans isomers.

- 2-methyl-2-butene
- 3-methyl-2-pentene
- 1-pentene

Contributors

- Charles Ophardt, Professor Emeritus, Elmhurst College; Virtual Chembook

---

6.1: Cis-Trans Isomers Result from Restricted Rotation is shared under a not declared license and was authored, remixed, and/or curated by LibreTexts.

- **Cis & Trans Isomers of Alkanes** is licensed CC BY-NC-SA 4.0.

6.2: A Chiral Object Has a Nonsuperimposable Mirror Image

Chirality

6.2: A Chiral Object Has a Nonsuperimposable Mirror Image is shared under a not declared license and was authored, remixed, and/or curated by LibreTexts.

6.3: An Asymmetric Center Is a Cause of Chirality in a Molecule

Enantiomers

6.3: An Asymmetric Center Is a Cause of Chirality in a Molecule is shared under a not declared license and was authored, remixed, and/or curated by LibreTexts.

6.4: Isomers with One Asymmetric Center

Enantiomers

6.4: Isomers with One Asymmetric Center is shared under a not declared license and was authored, remixed, and/or curated by LibreTexts.

6.5: Asymmetric Centers and Stereocenters

To better understand the molecular origins of the ideal gas law,

$$PV = nRT \tag{6.5.1}$$

the basics of the **Kinetic Molecular Theory of Gases** (**KMT**) should be understood. This model is used to describe the behavior of gases. More specifically, it is used to explain macroscopic properties of a gas, such as pressure and temperature, in terms of its microscopic components, such as atoms. Like the ideal gas law, this theory was developed in reference to ideal gases, although it can be applied reasonably well to real gases.

In order to apply the kinetic model of gases, five assumptions are made:

1. Gases are made up of particles with no defined volume but with a defined mass. In other words their volume is miniscule compared to the distance between themselves and other molecules.
2. Gas particles undergo no intermolecular attractions or repulsions. This assumption implies that the particles possess no potential energy and thus their total energy is simply equal to their kinetic energies.
3. Gas particles are in continuous, random motion.
4. Collisions between gas particles are completely elastic. In other words, there is no net loss or gain of kinetic energy when particles collide.
5. The average kinetic energy is the same for all gases at a given temperature, regardless of the identity of the gas. Furthermore, this kinetic energy is proportional to the absolute temperature of the gas.

Temperature and KMT

The last assumption can be written in equation form as:

$$KE = \frac{1}{2}mv^2 = \frac{3}{2}k_BT \tag{6.5.2}$$

where

- k_B is Boltzmann's constant ($k_B = 1.381\times10^{-23}$ m^2 kg s^{-2} K^{-1}) and
- T is the absolution temperature (in Kelvin)

This equation says that the speed of gas particles is related to their absolute temperature. In other words, as their temperature increases, their speed increases, and finally their total energy increases as well. However, it is impossible to define the speed of any *one* gas particle. As such, the speeds of gases are defined in terms of their root-mean-square speed.

Pressure and KMT

The macroscopic phenomena of pressure can be explained in terms of the kinetic molecular theory of gases. Assume the case in which a gas molecule (represented by a sphere) is in a box, length *L* (Figure 1). Through using the assumptions laid out above, and considering the sphere is only moving in the x-direction, we can examine the instance of the sphere colliding elastically with one of the walls of the box.

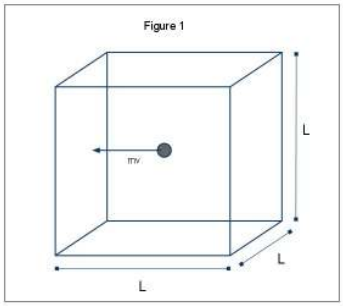


Figure 1

The momentum of this collision is given by $p=mv$, in this case $p=mv_x$, since we are only considering the x dimension. The total momentum change for this collision is then given by

$$mv_x - m(-v_x) = 2mv_x \tag{6.5.3}$$

Given that the amount of time it takes between collisions of the molecule with the wall is L/v_x we can give the frequency of collisions of the molecule against a given wall of the box per unit time as $v_x/2L$. One can now solve for the change in momentum per unit of time:

$$(2mv_x)(v_x/2L) = mv_x^2/L \tag{6.5.4}$$

Solving for momentum per unit of time gives the force exerted by an object ($F=ma=p/time$). With the expression that $F=mv_x^2/L$ one can now solve for the pressure exerted by the molecular collision, where area is given as the area of one wall of the box, $A=L^2$:

$$P = \frac{F}{A} \tag{6.5.5}$$

$$P = \frac{mv_x^2}{[L(L^2)}} \tag{6.5.6}$$

The expression can now be written in terms of the pressure associated with collisions from N number of molecules:

$$P = \frac{Nmv_x^2}{V} \tag{6.5.7}$$

This expression can now be adjusted to account for movement in the x, y and z directions by using mean-square velocity for three dimensions and a large value of N. The expression now is written as:

$$P = \frac{Nm\bar{v}^2}{3V} \tag{6.5.8}$$

This expression now gives pressure, a macroscopic quality, in terms of atomic motion. The significance of the above relationship is that pressure is proportional to the mean-square velocity of molecules in a given container. Therefore, as molecular velocity increases so does the pressure exerted on the container.

References

1. Oxtoby, Gillis and Campion. *Principles of Modern Chemistry*. 6th Edition. California: Thomson Brooks/Cole. 2008.
2. Chang, Raymond. *Physical Chemistry for the Biosciences*. California: University Science Books. 2005.

Contributors and Attributions

- Sevini Shahbaz, Andrew Cooley

6.5: Asymmetric Centers and Stereocenters is shared under a not declared license and was authored, remixed, and/or curated by LibreTexts.

- **Kinetic Molecular Theory of Gases** is licensed CC BY-NC-SA 4.0.

6.6: How to Draw Enantiomers

When examining the ideal gas laws in conjunction with the kinetic theory of gases, we gain insights into the behavior of ideal gas. We can then predict how gas particles behaviors such as gas molecular speed, effusion rates, distances traveled by gas molecules. Graham's Law, which was formulated by the Scottish physical chemist Thomas Graham, is an important law that connects gas properties to the kinetic theory of gases.

Introduction

The Kinetic Molecular Theory states that the average energy of molecules is proportional to absolute temperature as illustrated by the following equation:

$$e_K = \frac{3}{2}\frac{R}{N_A}T \tag{6.6.1}$$

where

- $\mathbf{e_k}$ is the average translation kinetic energy,
- **R** is the gas constant,
- $\mathbf{N_A}$ is Avogadro's number, and
- **T** is temperature in Kelvins.

Since R and N_A are constants, this means that the Kelvin temperature (T) of a gas is directly proportional to the average kinetic energy of its molecules. This means that at a given temperature, different gases (for example He or O_2) will the same average kinetic energy.

Graham's Law

Gas molecules move constantly and randomly throughout the volume of the container they occupy. When examining the gas molecules individually, we see that not all of the molecules of a particular gas at a given temperature move at exactly the same speed. This means that each molecule of a gas have slightly different kinetic energy. To calculate the average kinetic energy (e_K) of a sample of a gas, we use an average speed of the gas, called the root mean square speed (u_{rms}).

$$e_K = \frac{1}{2}mu_{rms}^2 \tag{6.6.2}$$

with

- $\mathbf{e_K}$ is the kinetic energy measures in Joules
- **m** is mass of a molecule of gas (kg)
- $\mathbf{u_{rms}}$ is the root mean square speed (m/s)

The root mean square speed, u_{rms}, can be determined from the temperature and molar mass of a gas.

$$u_{rms} = \sqrt{\frac{3RT}{M}} \tag{6.6.3}$$

with

- **R** the ideal gas constant (8.314 kg*m^2/s^2*mol*K)
- **T** temperature (Kelvin)
- **M** molar mass (kg/mol)

When examining the root mean square speed equation, we can see that the changes in temperature (T) and molar mass (M) affect the speed of the gas molecules. The speed of the molecules in a gas is proportional to the temperature and is inversely proportional to molar mass of the gas. In other words, as the temperature of a sample of gas is increased, the molecules speed up and the root mean square molecular speed increases as a result.

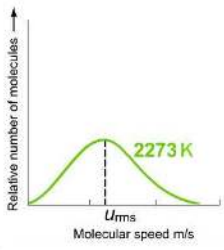


Figure **6.6.1**: As the temperature of a gas sample increases from left to right, the molecular speed distribution increases indicate by the shift of the peaks form left to right from each graph.

Graham's Law states that the rate of effusion of two different gases at the same conditions are inversely proportional to the square roots of their molar masses as given by the following equation:

$$\frac{Rate\ of\ effusion\ of\ A}{Rate\ of\ effusion\ of\ B} = \frac{(u_rms)_A}{(u_rms)_B} = \frac{\sqrt{3RT/M_A}}{\sqrt{3RT/M_B}} = \frac{\sqrt{M_B}}{\sqrt{M_A}} \tag{6.6.4}$$

In according with the Kinetic Molecular Theory, each gas molecule moves independently. However, the net rate at which gas molecules move depend on their average speed. By examining the equation above, we can conclude that the heavier the molar mass of the gas molecules slower the gas molecules move. And conversely, lighter the molar mass of the gas molecules the faster the gas molecules move.

Limitations of Graham's Law

Graham's Law can only be applied to gases at low pressures so that gas molecules escape through the tiny pinhole slowly. In addition, the pinhole must be tiny so that no collisions occur as the gas molecules pass through. Since Graham's Law is an extension of the Ideal Gas Law, gases that follows Graham's Law also follows the Ideal Gas Law.

Molecular Effusion

The random and rapid motion of tiny gas molecules results in effusion. **Effusion** is the escape of gas molecules through a tiny hole or pinhole.

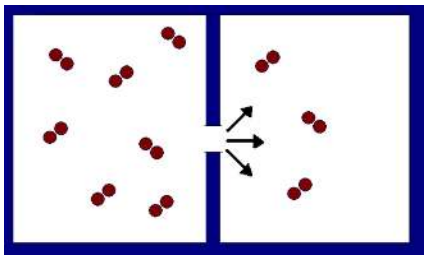


Figure **6.6.1**: Illustration of gas molecules escaping through a small opening. This is a phenomenon called effusion.

The behavior of helium gas in balloons is an example of effusion. The balloons are made of latex which is porous material that the small helium atom can effuse through. The helium inside a newly inflated balloon will eventually effuse out. This is the reason why balloons will deflate after a period of time. Molecular speeds are also used to explain why small molecules (such as He) diffuse more rapidly than larger molecules (O_2). That is the reason why a balloon filled with helium gas will deflate faster than a balloon filled with oxygen gas.

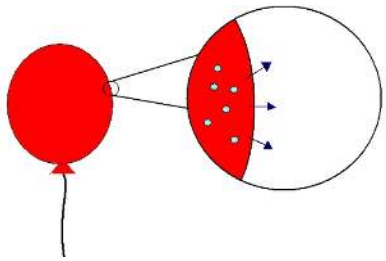


Figure **6.6.1**: Example of effusion. The escaping of helium molecules from an inflated balloon causes the deflation of the balloon after a period of time.

The effusion rate, r, is inversely proportional to the square root of its molar mass, M.

$$r \propto \sqrt{\frac{1}{M}} \tag{6.6.5}$$

When there are two different gases the equation for effusion becomes

$$\frac{Rate\ of\ effusion\ of\ A}{Rate\ of\ effusion\ of\ B} = \frac{\sqrt{3RT/M_A}}{\sqrt{3RT/M_B}} \tag{6.6.6}$$

M_A is the molar mass of gas A, M_B is the molar mass of gas B, T Temperature in Kelvin, R is the ideal gas constant.

From the equation above,

Rates of effusion of two gases

The relative rates of effusion of two gases at the same temperature is given as:

$$\frac{Rate\ of\ effusion\ of\ gas\ 1}{Rate\ of\ effusion\ of\ gas\ 2} = \frac{\sqrt{M_2}}{\sqrt{M_1}} \tag{6.6.7}$$

Units used to express rate of effusion includes: moles/seconds, moles/minutes, grams/seconds, grams/minutes.

Relative distances of two gases

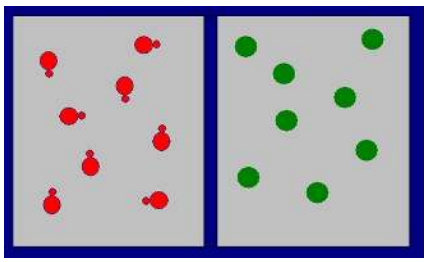
The relative distances traveled by the two gases is given as:

$$\frac{Distance\ traveled\ by\ gas\ 1}{Distance\ traveled\ by\ gas\ 2} = \frac{\sqrt{M_2}}{\sqrt{M_1}} \tag{6.6.8}$$

By examine the Graham's law as stated above, we can conclude that a lighter gas will effuse or travel more rapidly than a heavier gas. Mathematically speaking, a gas with smaller molar mass will effuse faster than a gas with larger molar mass under the same condition.

Molecular Diffusion

Similar to effusion, the process of **diffusion** is the spread of gas molecules through space or through a second substance such as the atmosphere.



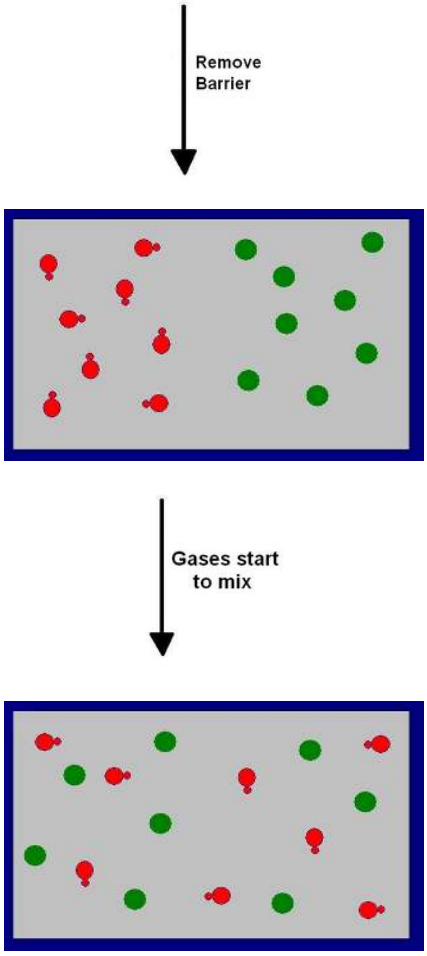
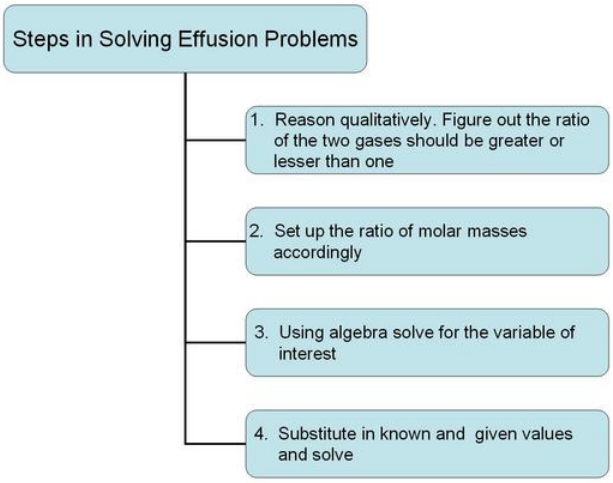


Figure **6.6.4**. The passage of one gas through another substance. In this example, the other substance is another gas.

Diffusion has many useful applications. Here is an example of diffusion that is use in everyday households. Natural gas is odorless and used commercially daily. An undetected leakage can be very dangerous as it is highly flammable and can cause an explosion when it comes in contact with an ignition source. In addition, the long term breathing of natural gas can lead to asphyxiation. Fortunately, chemists have discovered a way to easily detect natural gas occur leak by adding a small quantity of a gaseous organic sulfur compound named methyl mercaptan, CH_3SH, to the natural gas. When a leak happens, the diffusion of the odorous methyl mercaptan in the natural gas will serve as a sign of warning.

General guideline in solving effusion problems

The following flowchart outlines the steps in solving quantitative problems involving Graham's Law. It can be used as a general guideline.



Example 6.6.1

Calculate the root mean square speed, u_{rms}, in m/s of helium at 30^oC.

Solution

Start by converting the molar mass for helium from g/mol to kg/mol.

$$M = (4.00\ g/mol) \times \frac{1\ kg}{1000\ g}$$

$$M = 4.00 \times 10^{-3}\ kg/mol$$

Now, using the equation for u_{rms} substitute in the proper values for each variable and perform the calculation.

$$u_{rms} = \sqrt{\frac{3RT}{M}} \tag{6.6.9}$$

$$u_{rms} = \sqrt{\frac{3 \times (8.314\ kg\ m^2/s^2 * mol * K)(303K)}{4.00 \times 10^{-3} kg/mol}} \tag{6.6.10}$$

$$u_{rms} = 1.37 \times 10^3\ m/s \tag{6.6.11}$$

Example 6.6.2

What is the ratio of u_{rms} values for helium vs. xenon at 30^oC. Which is higher and why?

Solution

There are two approaches to solve this problem: the hard way and the easy way

Hard way:

The u_{rms} speed of helium is calculated from the above example.

First convert the molar mass of xenon from g/mol to kg/mol as we did for helium in example 1

$$M_{Xe} = (131.3\ g/mol) \times \frac{1\ kg}{1000\ g}$$

$$M = 0.1313\ kg/mol$$

Now, using the equation for the u_{rms}, insert the given and known values and solve for the variable of interest.

$$u_{rms} = \sqrt{\frac{3(8.314\ kg\ m^2/s^2 * mol * K)(303\ K)}{0.1313\ kg/mol}} \tag{6.6.12}$$

$$u_{rms} = 2.40 \times 10^2\ m/s \tag{6.6.13}$$

Compare the two values for xenon and helium and decide which is greater.

- $u_{Xe} = 2.4 \times 10^2\ m/s$
- $u_{He} = 1.37 \times 10^3\ m/s$

So the ratio of RMS speeds is

$$\frac{u_{Xe}}{u_{He}} \approx 0.18 \tag{6.6.14}$$

Helium has the higher u_{rms} speed. This is in according with Graham's Law, because helium atoms are much lighter than xenon atoms.

Easy Way:

Since the temperature is the same for both gases, only the square root of the ratio of molar mass is needed to be calculated.

$$\sqrt{\frac{M_{He}}{M_{Xe}}} = \sqrt{\frac{4.00\ g/mol}{131.3\ g/mol}} \approx 0.18 \tag{6.6.15}$$

In either approach, helium has a faster RMS speed than xenon and this is due exclusively to its smaller mass.

Example 6.6.3

If oxygen effuses from a container in 5.00 minutes, what is the molecular weight of a gas with the same given quantity of molecules effusing from the same container in 4.00 min?

Solution

Let oxygen be gas A and its rate is 1/5.00 minutes because it takes that much time for a certain quantity of oxygen to effuse and its molecular weight is 32 grams/mole (O_2 (g)). Let the unknown gas be B and its rate is 1/4.00 minutes and M_b be the molecular weight of the unknown gas.

First, choose the appropriate equation,

$$\frac{Rate\ effusion\ of\ gas\ A}{Rate\ effusion\ of\ gas\ B} = \frac{\sqrt{M_B}}{\sqrt{M_A}}$$

Second, using algebra, solve for the variable of interest on one side of the equation and plug in known and given values from the problem.

$$\sqrt{M_B} = \frac{(Rate\ effusion\ of\ gas\ A)(\sqrt{M_A})}{Rate\ effusion\ of\ gas\ B}$$

$$\sqrt{M_B} = \frac{(1/5.00\ minutes)(\sqrt{32\ grams/mole})}{1/4.00\ minutes}$$

$$\sqrt{M_B} = 4.525$$

$$M_B = (4.525)^2 = 20.5\ grams/mole$$

Example 6.6.4

Oxygen, O_2 (g), effuses from a container at the rate of 3.64 mL/sec, what is the molecular weight of a gas effusing from the same container under identical conditions at 4.48 mL/sec?

Solution

Let label oxygen as gas A. Therefore, rate of effusion of gas A is equaled to 3.64 mL/sec and the molecular weight is 32 grams/mole. The unknown gas is B and its rate of effusion is 4.48 mL/sec. We are solving for the molecular weight of gas B which is labeled as M_B.

First, choose the appropriate equation,

$$\frac{Rate\ effusion\ of\ gas\ A}{Rate\ effusion\ of\ gas\ B} = \frac{\sqrt{M_B}}{\sqrt{M_A}}$$

$$\sqrt{M_B} = \frac{(Rate\ effusion\ of\ gas\ A)(\sqrt{M_A})}{Rate\ effusion\ of\ gas\ B}$$

Second, using algebra, solve for the variable of interest on one side of the equation and plug in known and given values from the problem.

$$\sqrt{M_B} = \frac{(Rate\ effusion\ of\ gas\ A)(\sqrt{M_A})}{Rate\ effusion\ of\ gas\ B}$$

$$\sqrt{M_B} = \frac{(3.64\ mL/sec)(\sqrt{32\ grams/mole})}{4.48\ mL/sec}$$

$$\sqrt{M_B} = 4.50$$

$$M_B = (4.50)^2 = 20.2\ grams/mole$$

Example 6.6.5

Which answer(s) are true when comparing 1.0 mol O_2 (g) at STP (Standard Temperature and Pressure) and 0.50 mole of S_2 (g) at STP?

The two gases have equal through the same orifice, a tiny opening:

a. average molecular kinetic energies
b. root-mean-square speeds
c. masses
d. volumes
e. densities
f. effusion rates

Solution

The average kinetic energy of gas molecules depends on only the Temperature as exemplifies in this equation:

$$e_K = \frac{3}{2}\frac{R}{N_A}T$$

In addition, the mass of 0.50 mole of S_2 is the same as that of 1.0 mole of O_2. The rest of the choices are false.

Therefore, the correct answers are (a) and (c).

References

1. Petrucci, RH et al. (2007). *General Chemistry: Principles and Modern Applications*. New Jersey: Pearson Prentice Hall. p. 201-209.
2. Oxtoby, DW et al. (2008). *Principles of Modern Chemistry*. Belmont, California: Thomson Brooks/Cole. p.379-386
3. Gilbert, TR et al. (June 2003). *Chemistry: The Science in Context*. New York: W.W. Norton & Company. Chapter 8

Contributors and Attributions

- Tram Anh Dao

6.6: How to Draw Enantiomers is shared under a not declared license and was authored, remixed, and/or curated by LibreTexts.

- **Connecting Gas Properties to Kinetic Theory of Gases** is licensed CC BY-NC-SA 4.0.

6.7: Naming Enantiomers by the R,S System

To name the enantiomers of a compound unambiguously, their names must include the "handedness" of the molecule. The method for this is formally known as R/S nomenclature.

Introduction

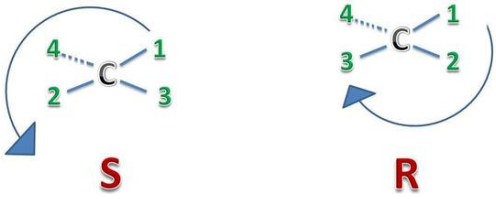
The method of unambiguously assigning the handedness of molecules was originated by three chemists: R.S. Cahn, C. Ingold, and V. Prelog and is also often called the **Cahn-Ingold-Prelog rules**. In addition to the Cahn-Ingold system, there are two ways of experimentally determining the absolute configuration of an enantiomer:

1. X-ray diffraction analysis. Note that there is no correlation between the sign of rotation and the structure of a particular enantiomer.
2. Chemical correlation with a molecule whose structure has already been determined via X-ray diffraction.

However, for non-laboratory purposes, it is beneficial to focus on the R/S system. The sign of optical rotation, although different for the two enantiomers of a chiral molecule, at the same temperature, **cannot** be used to establish the absolute configuration of an enantiomer; this is because the sign of optical rotation for a particular enantiomer may change when the temperature changes.

Stereocenters are labeled R or S

The "right hand" and "left hand" nomenclature is used to name the enantiomers of a chiral compound. The stereocenters are labeled as R or S.



Consider the first picture: a curved arrow is drawn from the highest priority (*1*) substituent to the lowest priority *(4)* substituent. If the arrow points in a counterclockwise direction (**left** when leaving the 12 o' clock position), the configuration at stereocenter is considered ***S*** ("Sinister" → Latin= "left"). If, however, the arrow points clockwise,(**Right** when leaving the 12 o' clock position) then the stereocenter is labeled ***R*** ("Rectus" → Latin= "right"). The ***R*** *or* ***S*** is then added as a prefix, in parenthesis, to the name of the enantiomer of interest. For example: (*R*)-2-Bromobutane and (*S*)-2,3- Dihydroxypropanal.

Sequence rules to assign priorities to substituents

Before applying the R and S nomenclature to a stereocenter, the substituents must be prioritized according to the following rules:

Rule 1

First, examine at the atoms directly attached to the stereocenter of the compound. A substituent with a higher atomic number takes precedence over a substituent with a lower atomic number. Hydrogen is the lowest possible priority substituent, because it has the lowest atomic number.

1. When dealing with isotopes, the atom with the higher atomic mass receives higher priority.
2. When visualizing the molecule, the lowest priority substituent should always point away from the viewer (a dashed line indicates this). To understand how this works or looks, imagine that a clock and a pole. Attach the pole to the back of the clock, so that when when looking at the face of the clock the pole points away from the viewer in the same way the lowest priority substituent should point away.
3. Then, draw an arrow from the highest priority atom to the 2nd highest priority atom to the 3rd highest priority atom. Because the 4th highest priority atom is placed in the back, the arrow should appear like it is going across the face of a clock. If it is going clockwise, then it is an R-enantiomer; If it is going counterclockwise, it is an S-enantiomer.

When looking at a problem with wedges and dashes, if the lowest priority atom is not on the dashed line pointing away, the molecule must be rotated.

Remember that

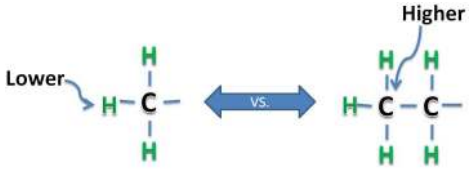
- Wedges indicate coming towards the viewer.
- Dashes indicate pointing away from the viewer.

Rule 2

If there are two substituents with equal rank, proceed along the two substituent chains until there is a point of difference. First, determine which of the chains has the first connection to an atom with the highest priority (the highest atomic number). That chain has the higher priority.

If the chains are similar, proceed down the chain, until a point of difference.

For example: an ethyl substituent takes priority over a methyl substituent. At the connectivity of the stereocenter, both have a carbon atom, which are equal in rank. Going down the chains, a methyl has only has hydrogen atoms attached to it, whereas the ethyl has another carbon atom. The carbon atom on the ethyl is the first point of difference and has a higher atomic number than hydrogen; therefore the ethyl takes priority over the methyl.



The "H-" (left) ranks lower than the "C-" (right) based on the first point of difference and their relative molecular weights

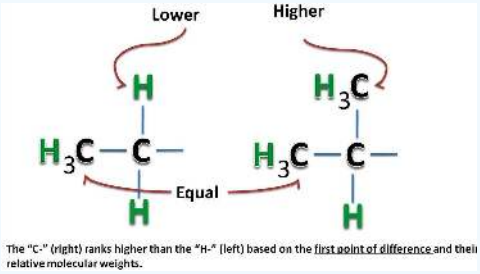
Rule 3

If a chain is connected to the same kind of atom twice or three times, check to see if the atom it is connected to has a greater atomic number than any of the atoms that the competing chain is connected to.

- If none of the atoms connected to the competing chain(s) at the same point has a greater atomic number: the chain bonded to the same atom multiple times has the greater priority
- If however, one of the atoms connected to the competing chain has a higher atomic number: that chain has the higher priority.

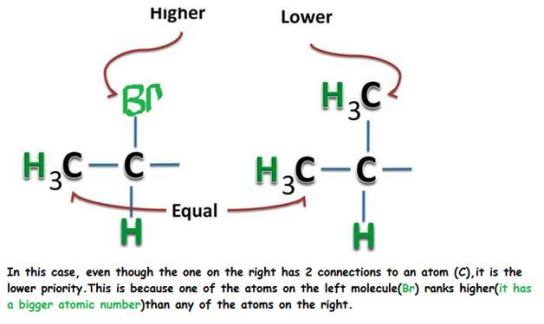
Example 2

A 1-methylethyl substituent takes precedence over an ethyl substituent. Connected to the first carbon atom, ethyl only has one other carbon, whereas the 1-methylethyl has two carbon atoms attached to the first; this is the first point of difference. Therefore, 1-methylethyl ranks higher in priority than ethyl, as shown below:

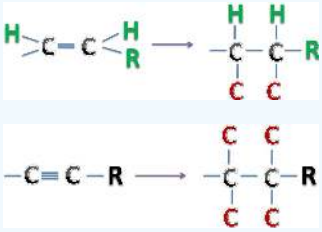


The "C-" (right) ranks higher than the "H-" (left) based on the first point of difference and their relative molecular weights.

However:

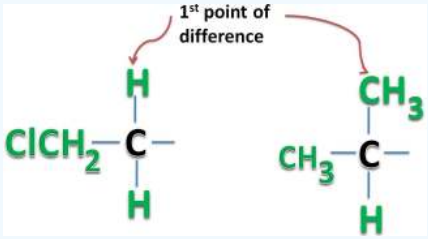


Remember that being double or triple bonded to an atom means that the atom is connected to the same atom twice. In such a case, follow the same method as above.

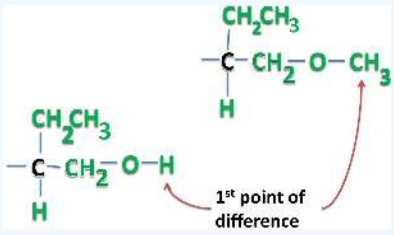


Caution!!

Keep in mind that priority is determined by the **first** point of difference along the two similar substituent chains. After the first point of difference, the rest of the chain is irrelevant.



When looking for the first point of difference on similar substituent chains, one may encounter branching. If there is branching, choose the branch that is higher in priority. If the two substituents have similar branches, rank the elements within the branches until a point of difference.



After all your substituents have been prioritized in the correct manner, you can now name/label the molecule **R** or **S.**

1. Put the lowest priority substituent in the back (dashed line).
2. Proceed from 1 to 2 to 3. (it is helpful to draw or imagine an arcing arrow that goes from 1--> 2-->3)
3. Determine if the direction from 1 to 2 to 3 clockwise or counterclockwise.

i) If it is **clockwise** it is **R.**
ii) if it is **counterclockwise** it is **S**.

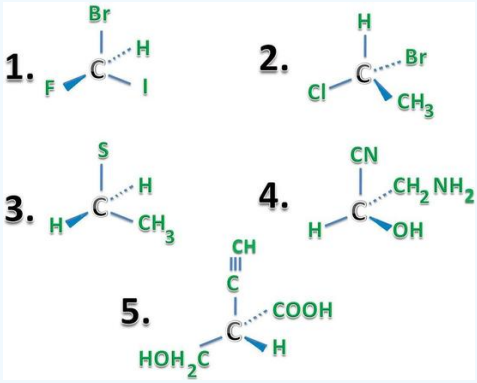
USE YOUR MODELING KIT: Models assist in visualizing the structure. When using a model, make sure the lowest priority is pointing away from you. Then determine the direction from the highest priority substituent to the lowest: clockwise (R) or counterclockwise (S).

IF YOU DO NOT HAVE A MODELING KIT: remember that the dashes mean the bond is going into the screen and the wedges means that bond is coming out of the screen. If the lowest priority bond is not pointing to the back, mentally rotate it so that it is. However, it is very useful when learning organic chemistry to use models.

If you have a modeling kit use it to help you solve the following practice problems.

? Exercise 6.7.1

Are the following R or S?



Answer

1. **S:** I > Br > F > H. The lowest priority substituent, H, is already going towards the back. It turns left going from I to Br to F, so it's a S.
2. **R:** Br > Cl > CH_3 > H. You have to switch the H and Br in order to place the H, the lowest priority, in the back. Then, going from Br to Cl, CH_3 is turning to the right, giving you a R.
3. **Neither R or S**: This molecule is achiral. Only chiral molecules can be named R or S.
4. **R:** OH > CN > CH_2NH_2 > H. The H, the lowest priority, has to be switched to the back. Then, going from OH to CN to CH_2NH_2, you are turning right, giving you a R. **(5)**
5. **S:** $-COOH$ > $-CH_2OH$ > $C{\equiv}CH$ > H. Then, going from $-COOH$ to $-CH_2OH$ to $-C{\equiv}CH$ you are turning left, giving you a S configuration.

References

1. Schore and Vollhardt. *Organic Chemistry Structure and Function.* New York:W.H. Freeman and Company, 2007.
2. McMurry, John and Simanek, Eric. *Fundamentals of Organic Chemistry*. 6th Ed. Brooks Cole, 2006.

6.7: Naming Enantiomers by the R,S System is shared under a not declared license and was authored, remixed, and/or curated by LibreTexts.

- **Absolute Configuration - R-S Sequence Rules** by Ekta Patel, Ifemayowa Aworanti is licensed CC BY-NC-SA 4.0.

6.8: Chiral Compounds Are Optically Active

Optical activity

6.8: Chiral Compounds Are Optically Active is shared under a not declared license and was authored, remixed, and/or curated by LibreTexts.

6.9: How Specific Rotation is Measured

Optical activity

6.9: How Specific Rotation is Measured is shared under a not declared license and was authored, remixed, and/or curated by LibreTexts.

6.10: Enantiomeric Excess

What do you notice about these three pictures? Count the number of left gloves and right gloves.



6 left and 6 right gloves, correct?

What about this one:

I count 8 right gloves, 4 left gloves. So there's a slight excess of right gloves here.

Finally, this figure:

ONLY right hand gloves here. 12 right gloves, zero left gloves.

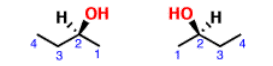
Application to organic chemistry?

Gloves are chiral objects. That is, they lack an internal plane of symmetry. Left gloves and right gloves are mirror images of each other, but they can't be superimposed. In chemistry, there's a word we have to describe a pair of non-superimposable mirror images – they're called enantiomers.

Tying it back to the drawings, we can have three types of situations.

1. **Racemic Mixture**: In the first drawing, we have an equal number of left and right gloves (i.e. enantiomers). This is called a racemic mixture of enantiomers.
2. **Enantiomeric excess**: In the second drawing, we have an excess of right gloves compared to left gloves. In a situtation like this we can say we have an "enantiomeric excess" of gloves, or alternatively, the mixture is "enantioenriched" in the right-hand glove. [We can also calculate the "excess" here: the mixture is 66% right and 33% left - so we have a 33% "excess" of the right-hand enantiomer].
3. **Enantiomeric pure:** In the third drawing, we have only right-hand gloves. This is said to be an "enantiomerically pure" mixture of gloves, since we have only one enantiomer present.

To tie it back to chemistry, let's say we have a solution of a chiral molecule, like 2-butanol, which can exist as either the (R)-enantiomer or the (S)-enantiomer.



(S)-2-butanol *(R)*-2-butanol

- A solution containing equal amounts of (R)-2-butanol and (S)-2-butanol is a racemic mixture.
- A solution containing an excess of either the (R)-enantiomer or the (S)-enantiomer would be enantioenriched.
- A solution containing only the (R)-enantiomer or the (S)-enantiomer will be enantiomerically pure**.**

Contributors

James Ashenhurst (MasterOrganicChemistry.com)

- A big thanks to Agnieszka at IlluScientia for the glove drawings.

4.5.1 Enantiomeric Excess and Optical Purity

Enantiomeric Excess

For non-racemic mixtures of enantiomers, one enantiomer is more abundant than the other. The composition of these mixtures is described by the **enantiomeric excess**, which is the difference between the relative abundance of the two enantiomers. Therefore, if a mixture contains 75% of the R enantiomer and 25% S, the enantiomeric excess if 50%. Similarly, a mixture that is 95% of one enantiomer, the enantiomeric excess is 90%, etc.

Enantiomeric excess is useful because it reflects the optical activity of the mixture. The standard optical rotation by the mixture ($[\alpha]_{mix}$) is equal to the product of the standard optical rotation of the major isomer ($[\alpha]_{major}$) and the enantiomeric excess (EE):

$$[\alpha]_{mix} = EE \times [\alpha]_{major} \tag{6.10.1}$$

In the same way, the enantiomeric excess in a mixture can be measured if the optical rotation of the pure enantiomer is known.

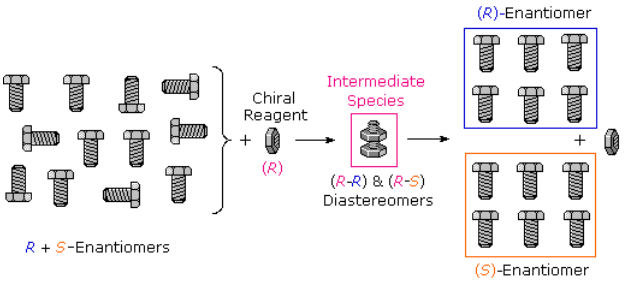
Diastereomeric Excess

A similar approach can be used to describe mixtures of diastereomers, resulting in the **diastereomeric excess**.

4.5.2 Resolution of Enantiomers

As noted earlier, chiral compounds synthesized from achiral starting materials and reagents are generally racemic (i.e. a 50:50 mixture of enantiomers). Separation of racemates into their component enantiomers is a process called **resolution**. Since enantiomers have identical physical properties, such as solubility and melting point, resolution is extremely difficult. Diastereomers, on the other hand, have different physical properties, and this fact is used to achieve resolution of racemates. Reaction of a racemate with an enantiomerically pure chiral reagent gives a mixture of diastereomers, which can be separated. Reversing the first reaction then leads to the separated enantiomers plus the recovered reagent.

Many kinds of chemical and physical reactions, including salt formation, may be used to achieve the diastereomeric intermediates needed for separation. The following diagram illustrates this general principle by showing how a nut having a right-handed thread (R) could serve as a "reagent" to discriminate and separate a mixture of right- and left-handed bolts of identical size and weight. Only the two right-handed partners can interact to give a fully-threaded intermediate, so separation is fairly simple. The resolving moiety, i.e. the nut, is then removed, leaving the bolts separated into their right and left-handed forms. Chemical reactions of enantiomers are normally not so dramatically different, but a practical distinction is nevertheless possible.



To learn more about chemical procedures for achieving resolution Click Here.

Contributors

- William Reusch, Professor Emeritus (Michigan State U.), Virtual Textbook of Organic Chemistry

Further Reading on Racemic Mixtures

Cliffs Notes

Racemic Mixtures: Resolving Enantiomers

Web Pages

Racemic Mixtures

Racemic Mixtures and Enantiomeric Excess

Further Reading on Enantiomeric Excess and Optical Purity

Carey 4th Edition On-Line Activity

Determining Optical Purity

6.10: Enantiomeric Excess is shared under a not declared license and was authored, remixed, and/or curated by LibreTexts.

- **Racemic Mixtures** is licensed CC BY-NC-SA 4.0.
- **Mixtures of Stereoisomers** is licensed CC BY-NC-SA 4.0.
- **Resolution of Racemates** by William Reusch is licensed CC BY-NC-SA 4.0.

6.11: Isomers with More than One Asymmetric Center

Compounds with two or more chiral centers

6.11: Isomers with More than One Asymmetric Center is shared under a not declared license and was authored, remixed, and/or curated by LibreTexts.

6.12: Meso Compounds Have Asymmetric Centers but Are Optically Inactive

Meso compounds

6.12: Meso Compounds Have Asymmetric Centers but Are Optically Inactive is shared under a not declared license and was authored, remixed, and/or curated by LibreTexts.

6.13: How to Name Isomers with More than One Asymmetric Center

Diastereomers are stereoisomers that are not related as object and mirror image and are not enantiomers. Unlike enatiomers which **are mirror images** of each other and **non-sumperimposable**, diastereomers are **not mirror images** of each other and **non-superimposable**. Diastereomers can have different physical properties and reactivity. They have different melting points and boiling points and different densities. They have **two or more** stereocenters.

Introduction

It is easy to mistake between diasteromers and enantiomers. For example, we have four steroisomers of 3-bromo-2-butanol. The four possible combination are SS, RR, SR and RS (Figure 1). One of the molecule is the enantiomer of its mirror image molecule and diasteromer of each of the other two molecule (SS is enantiomer of RR and diasteromer of RS and SR). SS's mirror image is RR and they are not superimposable, so they are enantiomers. RS and SR are not mirror image of SS and are not superimposable to each other, so they are diasteromers.

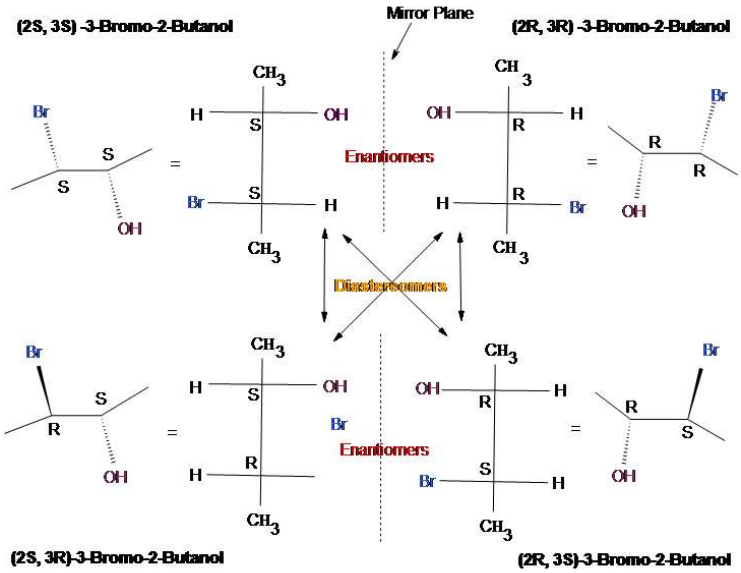


Figure 1

Diastereomers vs. Enantiomers vs. Meso Compounds

Tartaric acid, $C_4H_6O_6$, is an organic compound that can be found in grape, bananas, and in wine. The structures of tartaric acid itself is really interesting. Naturally, it is in the form of (R,R) stereocenters. Artificially, it can be in the meso form (R,S), which is achiral. R,R tartaric acid is enantiomer to is mirror image which is S,S tartaric acid and diasteromers to meso-tartaric acid (figure 2).

(R,R) and (S,S) tartaric acid have similar physical properties and reactivity. However, meso-tartaric acid have different physical properties and reactivity. For example, melting point of (R,R) & (S,S) tartaric is about 170 degree Celsius, and melting point of meso-tartaric acid is about 145 degree Celsius.

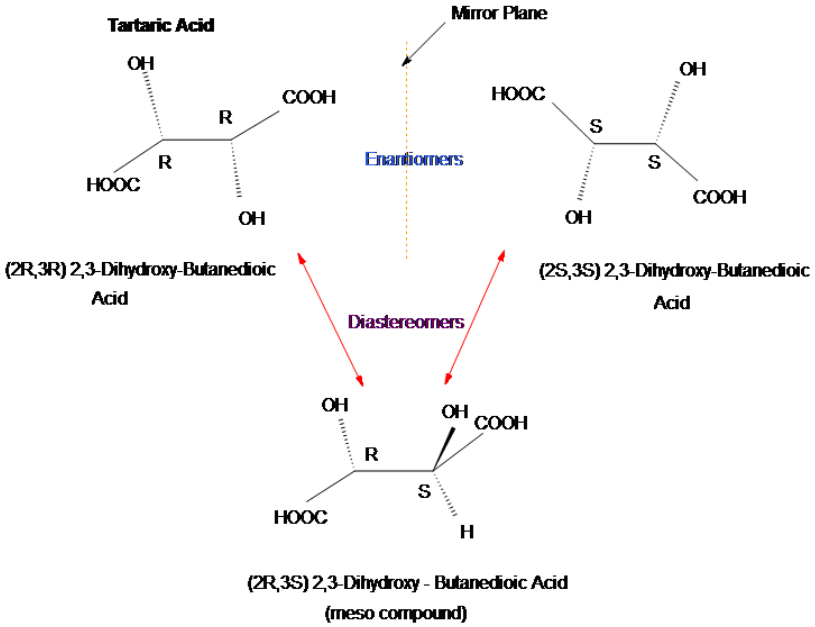
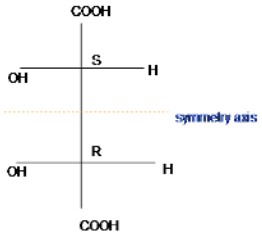


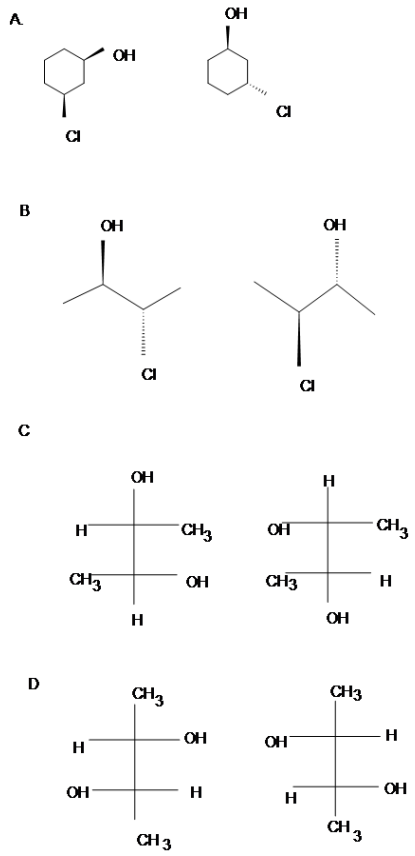
Figure 2

To identify meso, meso compound is superimposed on its mirror image, and has an internal plane that is symmetry (figure 3). Meso-tartaric acid is achiral and optically unactive.



Problems

Identify which of the following pair is enantiomers, diastereomers or meso compounds.



Answer

a. Diasteromers
b. Identical
c. Meso
d. Enantiomers

Outside Links

- http://www.sparknotes.com/chemistry/...section2.rhtml
- http://en.Wikipedia.org/wiki/Diastereomer
- http://en.Wikipedia.org/wiki/Tartaric_acid

6.13: How to Name Isomers with More than One Asymmetric Center is shared under a not declared license and was authored, remixed, and/or curated by LibreTexts.

- **Diastereomers** is licensed CC BY-NC-SA 4.0.

6.14: Reactions of Compounds that Contain an Asymmetric Center

The earth's stratospheric ozone layer plays a critical role in absorbing ultraviolet radiation emitted by the sun. In the last thirty years, it has been discovered that stratospheric ozone is depleting as a result of anthropogenic pollutants. There are a number of chemical reactions that can deplete stratospheric ozone; however, some of the most significant of these involves the catalytic destruction of ozone by halogen radicals such as chlorine and bromine.

Introduction

The atmosphere of the Earth is divided into five layers. In order of closest and thickest to farthest and thinnest the layers are listed as follows: troposphere, stratosphere, mesosphere, thermosphere and exosphere. The majority of the ozone in the atmosphere resides in the stratosphere, which extends from six miles above the Earth’s surface to 31 miles. Humans rely heavily on the absorption of ultraviolet B rays by the ozone layer because UV-B radiation causes skin cancer and can lead to genetic damage. The ozone layer has historically protected the Earth from the harmful UV rays, although in recent decades this protection has diminished due to stratospheric ozone depletion.

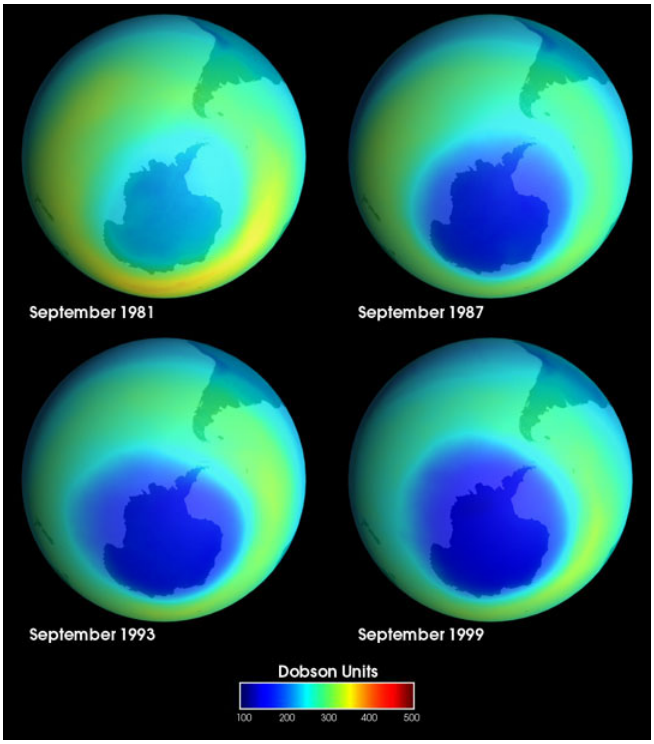


Figure courtesy of NASA.

Ozone depletion is largely a result of man-made substances. Humans have introduced gases and chemicals into the atmosphere that have rapidly depleted the ozone layer in the last century. This depletion makes humans more vulnerable to the UV-B rays which are known to cause skin cancer as well as other genetic deformities. The possibility of ozone depletion was first introduced by scientists in the late 1960's as dreams of super sonic transport began to become a reality. Scientists had long been aware that nitric oxide (NO) can catalytically react with ozone (O_3) to produce O_2 molecules; however, NO molecules produced at ground level have a half life far too short to make it into the stratosphere. It was not until the advent of commercial super sonic jets (which fly in the stratosphere and at an altitude much higher then conventional jets) that the potential for NO to react with stratospheric ozone became a possibility. The threat of ozone depletion from commercial super sonic transport was so great that it is often cited as the main reason why the US federal government pulled support for its development in 1971. Fear of ozone depletion was abated until 1974 when Sherwood Rowland and Mario Molina discovered that chlorofluorocarbons could be photolyzed by high energy photons in the stratosphere. They discovered that this process could releasing chlorine radicals that would catalytically react with O_3 and destroy the molecule. This process is called the Rowland-Molina theory of O_3 depletion.

The Chapman Cycle

The stratosphere is in a constant cycle with oxygen molecules and their interaction with ultraviolet rays. This process is considered a cycle because of its constant conversion between different molecules of oxygen. The ozone layer is created when ultraviolet rays react with oxygen molecules (O_2) to create ozone (O_3) and atomic oxygen (O). This process is called the *Chapman cycle*.

Step 1: An oxygen molecules is photolyzed by solar radiation, creating two oxygen radicals:

$$h\nu + O_2 \rightarrow 2O^{\cdot}$$

Step 2: Oxygen radicals then react with molecular oxygen to produce ozone:

$$O_2 + O^{\cdot} \rightarrow O_3$$

Step 3: Ozone then reacts with an additional oxygen radical to form molecular oxygen:

$$O_3 + O^{\cdot} \rightarrow 2O_2$$

Step 4: Ozone can also be recycled into molecular oxygen by reacting with a photon:

$$O_3 + h\nu \rightarrow O_2 + O^{\cdot}$$

It is important to keep in mind that ozone is constantly being created and destroyed by the Chapman cycle and that these reactions are natural processes, which have been taking place for millions of years. Because of this, the thickness the ozone layer at any particular time can vary greatly. It is also important to know that O_2 is constantly being introduced into the atmosphere through photosynthesis, so the ozone layer has the capability of regenerating itself.

Chemistry of Ozone Depletion

CFC molecules are made up of chlorine, fluorine and carbon atoms and are extremely stable. This extreme stability allows CFC's to slowly make their way into the stratosphere (most molecules decompose before they can cross into the stratosphere from the troposphere). This prolonged life in the atmosphere allows them to reach great altitudes where photons are more energetic. When the CFC's come into contact with these high energy photons, their individual components are freed from the whole. The following reaction displays how Cl atoms have an ozone destroying cycle:

$$Cl + O_3 \rightarrow ClO + O_2 \qquad \textbf{(step 1)}$$

$$ClO + O^{\cdot} \rightarrow Cl + O_2 \qquad \textbf{(step 2)}$$

$$O_3 + O^{\cdot} \rightarrow 2O_2 \qquad \textbf{(Overall reaction)}$$

Chlorine is able to destroy so much of the ozone because it acts as a catalyst. Chlorine initiates the breakdown of ozone and combines with a freed oxygen to create two oxygen molecules. After each reaction, chlorine begins the destructive cycle again with another ozone molecule. One chlorine atom can thereby destroy thousands of ozone molecules. Because ozone molecules are being broken down they are unable to absorb any ultraviolet light so we experience more intense UV radiation at the earths surface.

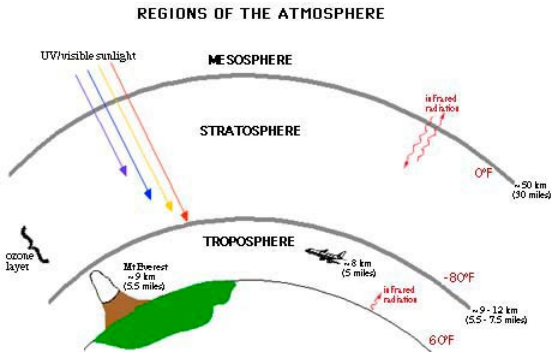


Figure courtesy of NOAA.

From 1985 to 1988, researchers studying atmospheric properties over the south pole continually noticed significantly reduced concentrations of ozone directly over the continent of Antarctica. For three years it was assumed that the ozone data was incorrect

and was due to some type of instrument malfunction. In 1988, researchers finally realized their error and concluded that an enormous hole in the ozone layer had indeed developed over Antarctica. Examination of NASA satellite data later showed that the hole had begun to develop in the mid 1970's.

The ozone hole over Antarctica is formed by a slew of unique atmospheric conditions over the continent that combine to create an ideal environment for ozone destruction.

- Because Antarctica is surrounded by water, winds over the continent blow in a unique clockwise direction creating a so called "polar vortex" that effectively contains a single static air mass over the continent. As a result, air over Antarctica does not mix with air in the rest of the earth's atmosphere.
- Antarctica has the coldest winter temperatures on earth, often reaching -110 F. These chilling temperatures result in the formation of polar stratospheric clouds (PSC's) which are a conglomeration of frozen H_2O and HNO_3. Due to their extremely cold temperatures, PSC's form an electrostatic attraction with CFC molecules as well as other halogenated compounds

As spring comes to Antarctica, the PSC's melt in the stratosphere and release all of the halogenated compounds that were previously absorbed to the cloud. In the antarctic summer, high energy photons are able to photolyze the halogenated compounds, freeing halogen radicals that then catalytically destroy O_3. Because Antarctica is constantly surrounded by a polar vortex, radical halogens are not able to be diluted over the entire globe. The ozone hole develops as result of this process.

Resent research suggests that the strength of the polar vortex from any given year is directly correlated to the size of the ozone hole. In years with a strong polar vortex, the ozone hole is seen to expand in diameter, whereas in years with a weaker polar vortex, the ozone hole is noted to shrink

Ozone Depleting Substances

The following substances are listed as ozone depleting substances under Title VI of the United State Clean Air Act:

Table **6.14.1**: Ozone Depleting Substances And Their Ozone-Depletion Potential. Taken directly from the Clean Air Act, as of June 2010.

Substance	Ozone- depletion potential
chlorofluorocarbon-11 (CFC–11)	1.0
chlorofluorocarbon-12 (CFC–12)	1.0
chlorofluorocarbon-13 (CFC–13)	1.0
chlorofluorocarbon-111 (CFC–111)	1.0
chlorofluorocarbon-112 (CFC–112)	1.0
chlorofluorocarbon-113 (CFC–113)	0.8
chlorofluorocarbon-114 (CFC–114)	1.0
chlorofluorocarbon-115 (CFC–115)	0.6
chlorofluorocarbon-211 (CFC–211)	1.0
chlorofluorocarbon-212 (CFC–212)	1.0
chlorofluorocarbon-213 (CFC–213)	1.0
chlorofluorocarbon-214 (CFC–214)	1.0
chlorofluorocarbon-215 (CFC–215)	1.0
chlorofluorocarbon-216 (CFC–216)	1.0
chlorofluorocarbon-217 (CFC–217)	1.0
halon-1211	3.0
halon-1301	10.0
halon-2402	6.0
carbon tetrachloride	1.1
methyl chloroform	0.1
hydrochlorofluorocarbon-22 (HCFC–22)	0.05
hydrochlorofluorocarbon-123 (HCFC–123)	0.02
hydrochlorofluorocarbon-124 (HCFC–124)	0.02
hydrochlorofluorocarbon-141(b) (HCFC–141(b))	0.1
hydrochlorofluorocarbon-142(b) (HCFC–142(b))	0.06

References

1. Dessler, Andrew. The Chemistry and Physics of Stratospheric Ozone. San Diego, Ca: Academic Press, 2000
2. Hoffman, Matthew J. Ozone Depletion and Climate Change. Albany, NY: State University of New York Press, 2005
3. Parson, Edward A. Protecting the Ozone Layer: Science and Strategy. New York: Oxford University Press, 2003.
4. Petrucci, Ralph H., William S. Harwood, and Geoff E. Herring. General Chemistry : Principles and Modern Applications. 9th ed. Upper Saddle River: Prentice Hall, 2006.
5. Varotsos, Costas, Kirill Ya. Kondratyev. Atmospheric Ozone Variability: Implications for Climate Change, Human Health and Ecosystems. Chichester, UK: Praxis Publishing Ltd, 2000
6. Godish, Thad. Air Quality. 4th ed. Florida: CRC Press LLC, 2004.
7. United States Clean Air Act: as of June 3rd, 2010.

General Questions

- What are the causes of the depletion of our ozone layer?
  - the release of free radicals, the use of CFC's, the excessive burning of fossil fuels
- What is the chemical reaction that displays how ozone is created?
  - UV + O_2 -> 2O + heat, O_2 + O -> O_3, O_3 + O -> $2O_2$
- Which reactions demonstrate the destruction of the ozone layer?
  - Cl + O_3 ------> ClO + O_2 and ClO + O ------> Cl + O
- How do CFC's destroy the ozone layer?
  - the atomic chlorine freed from CFC reacts in a catalytic manner with ozone and atomic oxygen to make more oxygen molecules
- Why should regulations be enforced now in regards to pollution and harmful chemicals?
  - without regulation, the production and use of chemicals will run out of hand and do irreversible damage to the stratosphere
- What type of atom in the CFC molecule is most destructive to the ozone?
  - chlorine
- In which layer of the atmosphere does the ozone layer?
  - the stratosphere, the second closest to the Earth's surface
- What cycle is responsible for ozone in the stratosphere?
  - the Chapman cycle
- What factor is responsible for breaking up stable molecules?
  - ultraviolet rays from the sun

6.14: Reactions of Compounds that Contain an Asymmetric Center is shared under a not declared license and was authored, remixed, and/or curated by LibreTexts.

- **7.3: Depletion of the Ozone Layer** by Anne Keith, Caroline Tran, Dan Chong, Jordan Shively is licensed CC BY-NC-SA 4.0.

6.15: Using Reactions that Do Not Break Bonds to an Asymmetric Center to Determine Relative Configurations

The earth's stratospheric ozone layer plays a critical role in absorbing ultraviolet radiation emitted by the sun. In the last thirty years, it has been discovered that stratospheric ozone is depleting as a result of anthropogenic pollutants. There are a number of chemical reactions that can deplete stratospheric ozone; however, some of the most significant of these involves the catalytic destruction of ozone by halogen radicals such as chlorine and bromine.

Introduction

The atmosphere of the Earth is divided into five layers. In order of closest and thickest to farthest and thinnest the layers are listed as follows: troposphere, stratosphere, mesosphere, thermosphere and exosphere. The majority of the ozone in the atmosphere resides in the stratosphere, which extends from six miles above the Earth's surface to 31 miles. Humans rely heavily on the absorption of ultraviolet B rays by the ozone layer because UV-B radiation causes skin cancer and can lead to genetic damage. The ozone layer has historically protected the Earth from the harmful UV rays, although in recent decades this protection has diminished due to stratospheric ozone depletion.

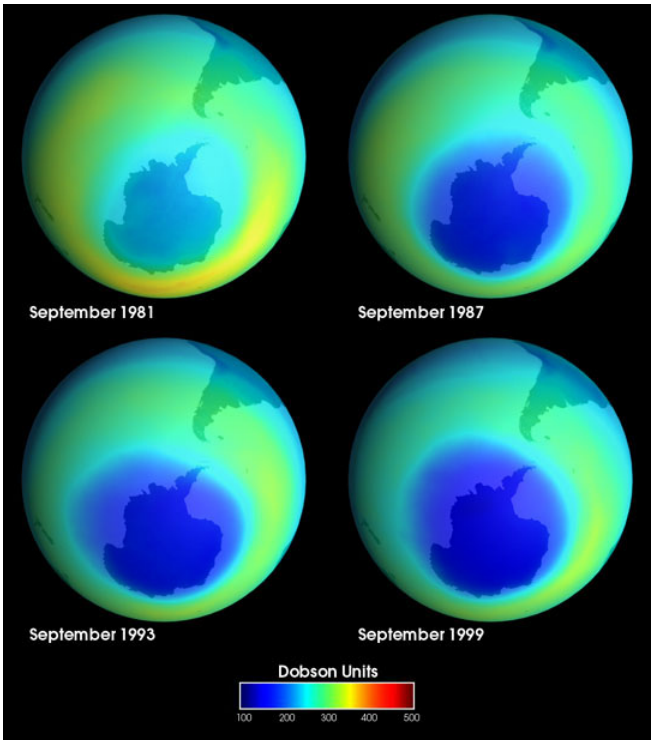


Figure courtesy of NASA.

Ozone depletion is largely a result of man-made substances. Humans have introduced gases and chemicals into the atmosphere that have rapidly depleted the ozone layer in the last century. This depletion makes humans more vulnerable to the UV-B rays which are known to cause skin cancer as well as other genetic deformities. The possibility of ozone depletion was first introduced by scientists in the late 1960's as dreams of super sonic transport began to become a reality. Scientists had long been aware that nitric oxide (NO) can catalytically react with ozone (O_3) to produce O_2 molecules; however, NO molecules produced at ground level have a half life far too short to make it into the stratosphere. It was not until the advent of commercial super sonic jets (which fly in the stratosphere and at an altitude much higher then conventional jets) that the potential for NO to react with stratospheric ozone became a possibility. The threat of ozone depletion from commercial super sonic transport was so great that it is often cited as the main reason why the US federal government pulled support for its development in 1971. Fear of ozone depletion was abated until 1974 when Sherwood Rowland and Mario Molina discovered that chlorofluorocarbons could be photolyzed by high energy photons in the stratosphere. They discovered that this process could releasing chlorine radicals that would catalytically react with O_3 and destroy the molecule. This process is called the Rowland-Molina theory of O_3 depletion.

The Chapman Cycle

The stratosphere is in a constant cycle with oxygen molecules and their interaction with ultraviolet rays. This process is considered a cycle because of its constant conversion between different molecules of oxygen. The ozone layer is created when ultraviolet rays react with oxygen molecules (O_2) to create ozone (O_3) and atomic oxygen (O). This process is called the *Chapman cycle*.

Step 1: An oxygen molecules is photolyzed by solar radiation, creating two oxygen radicals:

$$h\nu + O_2 \rightarrow 2O^{\cdot}$$

Step 2: Oxygen radicals then react with molecular oxygen to produce ozone:

$$O_2 + O^{\cdot} \rightarrow O_3$$

Step 3: Ozone then reacts with an additional oxygen radical to form molecular oxygen:

$$O_3 + O^{\cdot} \rightarrow 2O_2$$

Step 4: Ozone can also be recycled into molecular oxygen by reacting with a photon:

$$O_3 + h\nu \rightarrow O_2 + O^{\cdot}$$

It is important to keep in mind that ozone is constantly being created and destroyed by the Chapman cycle and that these reactions are natural processes, which have been taking place for millions of years. Because of this, the thickness the ozone layer at any particular time can vary greatly. It is also important to know that O_2 is constantly being introduced into the atmosphere through photosynthesis, so the ozone layer has the capability of regenerating itself.

Chemistry of Ozone Depletion

CFC molecules are made up of chlorine, fluorine and carbon atoms and are extremely stable. This extreme stability allows CFC's to slowly make their way into the stratosphere (most molecules decompose before they can cross into the stratosphere from the troposphere). This prolonged life in the atmosphere allows them to reach great altitudes where photons are more energetic. When the CFC's come into contact with these high energy photons, their individual components are freed from the whole. The following reaction displays how Cl atoms have an ozone destroying cycle:

$$Cl + O_3 \rightarrow ClO + O_2 \qquad \textbf{(step 1)}$$

$$ClO + O^{\cdot} \rightarrow Cl + O_2 \qquad \textbf{(step 2)}$$

$$O_3 + O^{\cdot} \rightarrow 2O_2 \qquad \textbf{(Overall reaction)}$$

Chlorine is able to destroy so much of the ozone because it acts as a catalyst. Chlorine initiates the breakdown of ozone and combines with a freed oxygen to create two oxygen molecules. After each reaction, chlorine begins the destructive cycle again with another ozone molecule. One chlorine atom can thereby destroy thousands of ozone molecules. Because ozone molecules are being broken down they are unable to absorb any ultraviolet light so we experience more intense UV radiation at the earths surface.

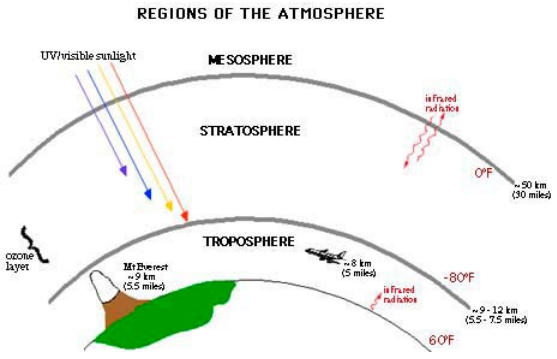


Figure courtesy of NOAA.

From 1985 to 1988, researchers studying atmospheric properties over the south pole continually noticed significantly reduced concentrations of ozone directly over the continent of Antarctica. For three years it was assumed that the ozone data was incorrect

and was due to some type of instrument malfunction. In 1988, researchers finally realized their error and concluded that an enormous hole in the ozone layer had indeed developed over Antarctica. Examination of NASA satellite data later showed that the hole had begun to develop in the mid 1970's.

The ozone hole over Antarctica is formed by a slew of unique atmospheric conditions over the continent that combine to create an ideal environment for ozone destruction.

- Because Antarctica is surrounded by water, winds over the continent blow in a unique clockwise direction creating a so called "polar vortex" that effectively contains a single static air mass over the continent. As a result, air over Antarctica does not mix with air in the rest of the earth's atmosphere.
- Antarctica has the coldest winter temperatures on earth, often reaching -110 F. These chilling temperatures result in the formation of polar stratospheric clouds (PSC's) which are a conglomeration of frozen H_2O and HNO_3. Due to their extremely cold temperatures, PSC's form an electrostatic attraction with CFC molecules as well as other halogenated compounds

As spring comes to Antarctica, the PSC's melt in the stratosphere and release all of the halogenated compounds that were previously absorbed to the cloud. In the antarctic summer, high energy photons are able to photolyze the halogenated compounds, freeing halogen radicals that then catalytically destroy O_3. Because Antarctica is constantly surrounded by a polar vortex, radical halogens are not able to be diluted over the entire globe. The ozone hole develops as result of this process.

Resent research suggests that the strength of the polar vortex from any given year is directly correlated to the size of the ozone hole. In years with a strong polar vortex, the ozone hole is seen to expand in diameter, whereas in years with a weaker polar vortex, the ozone hole is noted to shrink

Ozone Depleting Substances

The following substances are listed as ozone depleting substances under Title VI of the United State Clean Air Act:

Table **6.15.1**: Ozone Depleting Substances And Their Ozone-Depletion Potential. Taken directly from the Clean Air Act, as of June 2010.

Substance	Ozone- depletion potential
chlorofluorocarbon-11 (CFC–11)	1.0
chlorofluorocarbon-12 (CFC–12)	1.0
chlorofluorocarbon-13 (CFC–13)	1.0
chlorofluorocarbon-111 (CFC–111)	1.0
chlorofluorocarbon-112 (CFC–112)	1.0
chlorofluorocarbon-113 (CFC–113)	0.8
chlorofluorocarbon-114 (CFC–114)	1.0
chlorofluorocarbon-115 (CFC–115)	0.6
chlorofluorocarbon-211 (CFC–211)	1.0
chlorofluorocarbon-212 (CFC–212)	1.0
chlorofluorocarbon-213 (CFC–213)	1.0
chlorofluorocarbon-214 (CFC–214)	1.0
chlorofluorocarbon-215 (CFC–215)	1.0
chlorofluorocarbon-216 (CFC–216)	1.0
chlorofluorocarbon-217 (CFC–217)	1.0
halon-1211	3.0
halon-1301	10.0
halon-2402	6.0
carbon tetrachloride	1.1
methyl chloroform	0.1
hydrochlorofluorocarbon-22 (HCFC–22)	0.05
hydrochlorofluorocarbon-123 (HCFC–123)	0.02
hydrochlorofluorocarbon-124 (HCFC–124)	0.02
hydrochlorofluorocarbon-141(b) (HCFC–141(b))	0.1
hydrochlorofluorocarbon-142(b) (HCFC–142(b))	0.06

References

1. Dessler, Andrew. The Chemistry and Physics of Stratospheric Ozone. San Diego, Ca: Academic Press, 2000
2. Hoffman, Matthew J. Ozone Depletion and Climate Change. Albany, NY: State University of New York Press, 2005
3. Parson, Edward A. Protecting the Ozone Layer: Science and Strategy. New York: Oxford University Press, 2003.
4. Petrucci, Ralph H., William S. Harwood, and Geoff E. Herring. General Chemistry : Principles and Modern Applications. 9th ed. Upper Saddle River: Prentice Hall, 2006.
5. Varotsos, Costas, Kirill Ya. Kondratyev. Atmospheric Ozone Variability: Implications for Climate Change, Human Health and Ecosystems. Chichester, UK: Praxis Publishing Ltd, 2000
6. Godish, Thad. Air Quality. 4th ed. Florida: CRC Press LLC, 2004.
7. United States Clean Air Act: as of June 3rd, 2010.

General Questions

- What are the causes of the depletion of our ozone layer?
  - the release of free radicals, the use of CFC's, the excessive burning of fossil fuels
- What is the chemical reaction that displays how ozone is created?
  - UV + O_2 -> 2O + heat, O_2 + O -> O_3, O_3 + O -> $2O_2$
- Which reactions demonstrate the destruction of the ozone layer?
  - Cl + O_3 ------> ClO + O_2 and ClO + O ------> Cl + O
- How do CFC's destroy the ozone layer?
  - the atomic chlorine freed from CFC reacts in a catalytic manner with ozone and atomic oxygen to make more oxygen molecules
- Why should regulations be enforced now in regards to pollution and harmful chemicals?
  - without regulation, the production and use of chemicals will run out of hand and do irreversible damage to the stratosphere
- What type of atom in the CFC molecule is most destructive to the ozone?
  - chlorine
- In which layer of the atmosphere does the ozone layer?
  - the stratosphere, the second closest to the Earth's surface
- What cycle is responsible for ozone in the stratosphere?
  - the Chapman cycle
- What factor is responsible for breaking up stable molecules?
  - ultraviolet rays from the sun

6.15: Using Reactions that Do Not Break Bonds to an Asymmetric Center to Determine Relative Configurations is shared under a not declared license and was authored, remixed, and/or curated by LibreTexts.

- **7.3: Depletion of the Ozone Layer** by Anne Keith, Caroline Tran, Dan Chong, Jordan Shively is licensed CC BY-NC-SA 4.0.

6.16: How Enantiomers Can Be Separated

Resolution of enantiomers

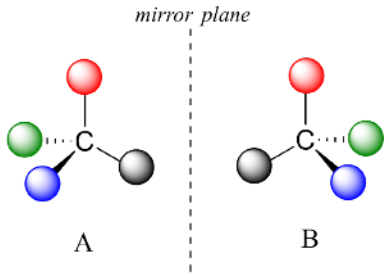
6.16: How Enantiomers Can Be Separated is shared under a not declared license and was authored, remixed, and/or curated by LibreTexts.

6.17: Nitrogen and Phosphorus Atoms Can Be Asymmetric Centers

We turn now to concept of chirality that formed the basis of the story about Louis Pasteur in the beginning of this chapter. Recall that the term **chiral**, from the Greek work for 'hand', refers to anything which cannot be superimposed on its own mirror image. Your hands, of course, are chiral - you cannot superimpose your left hand on your right, and you cannot fit your left hand into a right-handed glove (which is also a chiral object). Another way of saying this is that your hands do not have a **mirror plane of symmetry**: you cannot find any plane which bisects your hand in such a way that one side of the plane is a mirror image of the other side. *Chiral objects do not have a plane of symmetry*.

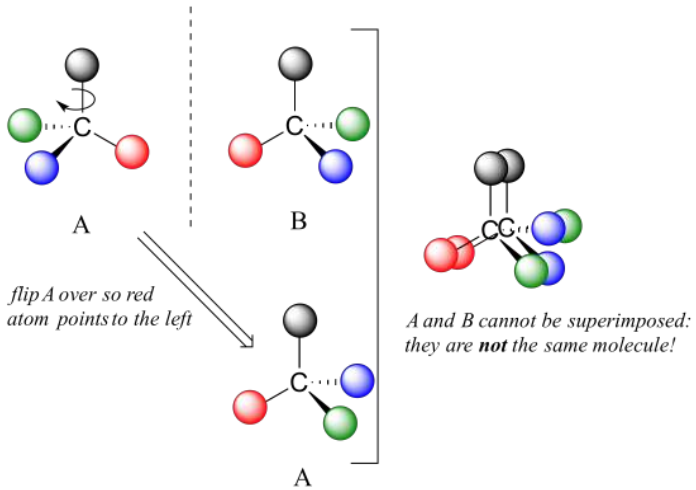
Your face, on the other hand is **achiral** - lacking chirality - because, some small deviations notwithstanding, you could superimpose your face onto its mirror image. If someone were to show you a mirror image photograph of your face, you could line the image up, point-for-point, with your actual face. Your face has a plane of symmetry, because the left side is the mirror image of the right side.

What Pasteur, Biot, and their contemporaries did not yet fully understand when Pasteur made his discovery of molecular chirality was the *source* of chirality at the molecular level. It stood to reason that a chiral molecule is one that does not contain a plane of symmetry, and thus cannot be superimposed on its mirror image. We now know that chiral molecules contain one or more **chiral centers**, which are almost always tetrahedral (sp^3-hybridized) carbons with four different substituents. Consider the cartoon molecule A below: a tetrahedral carbon, with four different substituents denoted by balls of four different colors (for the time being, don't worry about exactly what these substituents could be - we will see real examples very soon).



The mirror image of A, which we will call B, is drawn on the right side of the figure, and an imaginary mirror is in the middle. Notice that every point on A lines up through the mirror with the same point on B: in other words, if A looked in the mirror, it would see B looking back.

Now, if we flip compound A over and try to superimpose it point for point on compound B, we find that we cannot do it: if we superimpose any two colored balls, then the other two are misaligned.

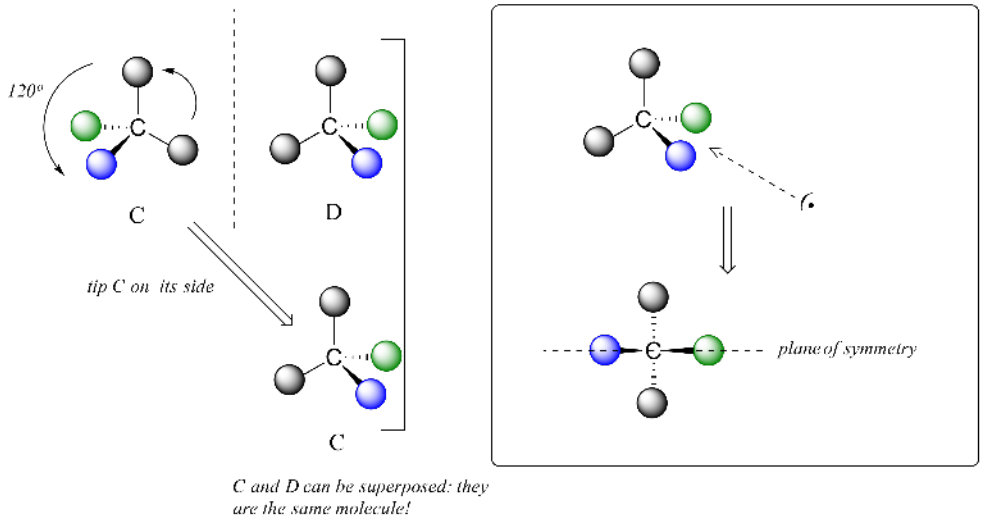


A is not superimposable on its mirror image (B), thus by definition A is a chiral molecule. It follows that B also is not superimposable on *its* mirror image (A), and thus it is also a chiral molecule. Also notice in the figure below (and convince yourself with models) that neither A nor B has an internal plane of symmetry.

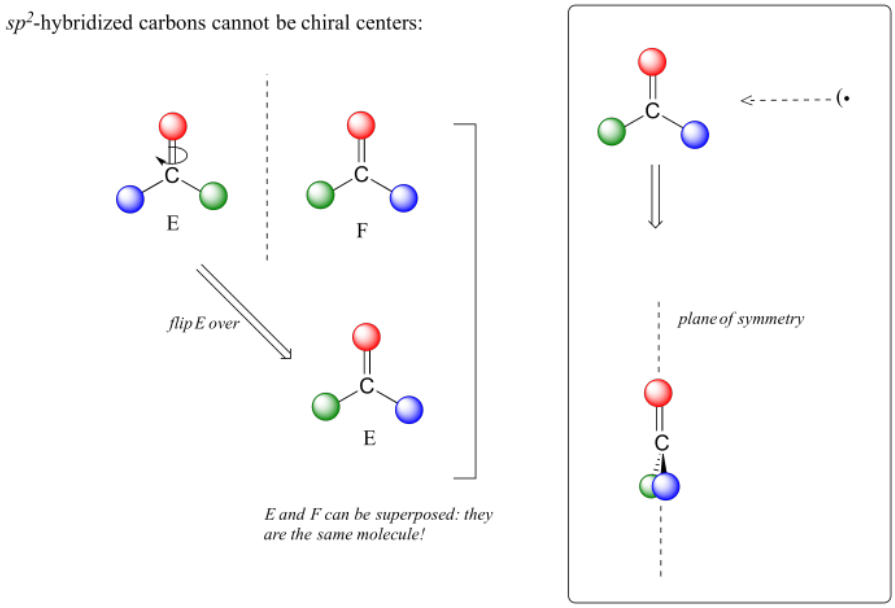
A and B are **stereoisomers**: molecules with the same molecular formula and the same bonding arrangement, but *a different arrangement of atoms in space*. There are two types of stereoisomers: enantiomers and diastereomers. **Enantiomers** are pairs of stereoisomers which are mirror images of each other: thus, A and B are enantiomers. It should be self-evident that a chiral molecule will always have one (and *only* one) enantiomer: enantiomers come in pairs. Enantiomers have identical physical properties (melting point, boiling point, density, and so on). However, enantiomers do differ in how they interact with polarized light (we will learn more about this soon) and they may also interact in very different ways with other chiral molecules - proteins, for example. We will begin to explore this last idea in later in this chapter, and see many examples throughout the remainder of our study of biological organic chemistry.

Diastereomers are stereoisomers which are *not* mirror images of each other. For now, we will concentrate on understanding enantiomers, and come back to diastereomers later.

We defined a chiral center as a tetrahedral carbon with four different substituents. If, instead, a tetrahedral carbon has two identical substituents (two black atoms in the cartoon figure below), then of course it still has a mirror image (*everything* has a mirror image, unless we are talking about a vampire!) However, it is superimposable on its mirror image, and has a plane of symmetry.



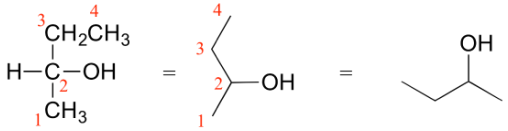
This molecule is **achiral** (lacking chirality). Using the same reasoning, we can see that a trigonal planar (sp^2-hybridized) carbon is also not a chiral center.



Notice that structure E can be superimposed on F, its mirror image - all you have to do is pick E up, flip it over, and it is the same as F. This molecule has a plane of symmetry, and is achiral.

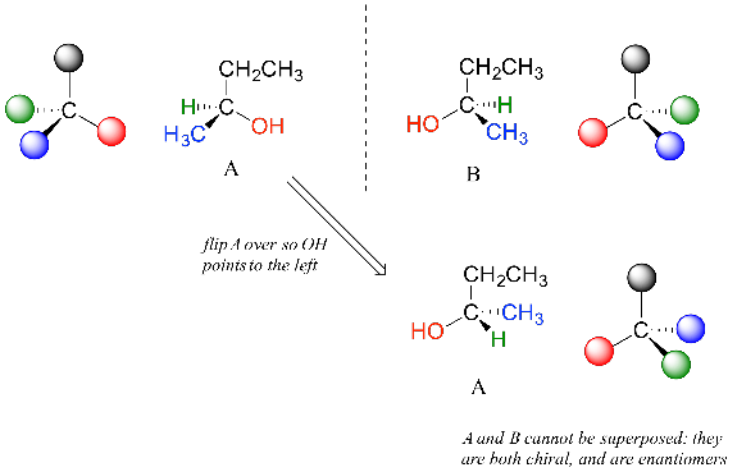
Let's apply our general discussion to real molecules. For now, we will limit our discussion to molecules with a single chiral center. It turns out that tartaric acid, the subject of our chapter introduction, has *two* chiral centers, so we will come back to it later.

Consider 2-butanol, drawn in two dimensions below.



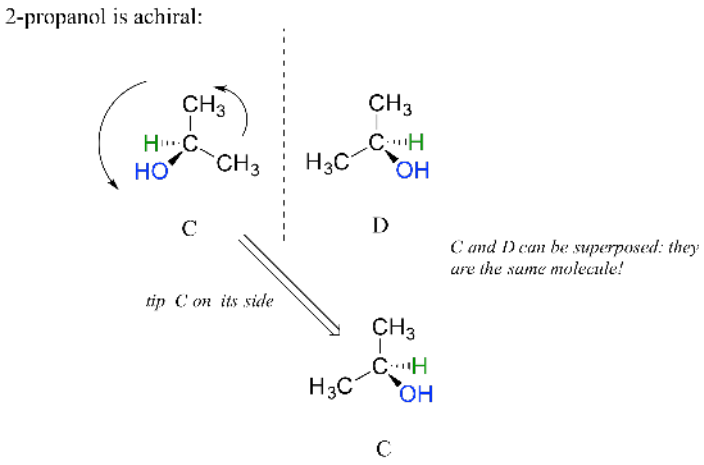
2-butanol
(drawn in 2D)

Carbon #2 is a chiral center: it is sp^3-hybridized and tetrahedral (even though it is not drawn that way above), and the four things attached to is are different: a hydrogen, a methyl ($-CH_3$) group, an ethyl ($-CH_2CH_3$) group, and a hydroxyl (OH) group. Let's draw the bonding at C_2 in three dimensions, and call this structure A. We will also draw the mirror image of A, and call this structure B.



When we try to superimpose A onto B, we find that we cannot do it. A and B are both chiral molecules, and they are enantiomers of each other.

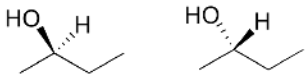
2-propanol, unlike 2-butanol, is *not* a chiral molecule. Carbon #2 is bonded to two identical substituents (methyl groups), and so it is not a chiral center.



Notice that 2-propanol is superimposable on its own mirror image.

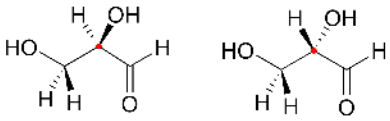
When we look at very simple molecules like 2-butanol, it is not difficult to draw out the mirror image and recognize that it is not superimposable. However, with larger, more complex molecules, this can be a daunting challenge in terms of drawing and three-dimensional visualization. The easy way to determine if a molecule is chiral is simply to look for the presence of one or more chiral centers: molecules with chiral centers will (almost always) be chiral. We insert the 'almost always' caveat here because it is possible to come up with the exception to this rule - we will have more to say on this later, but don't worry about it for now.

Here's another trick to make your stereochemical life easier: if you want to draw the enantiomer of a chiral molecule, it is not necessary to go to the trouble of drawing the point-for-point mirror image, as we have done up to now for purposes of illustration. Instead, keep the carbon skeleton the same, and simply reverse the solid and dashed wedge bonds on the chiral carbon: that accomplishes the same thing. You should use models to convince yourself that this is true, and also to convince yourself that swapping *any two substituents* about the chiral carbon will result in the formation of the enantiomer.

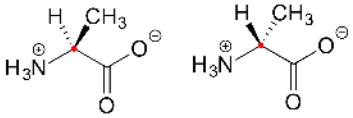


two enantiomers of 2-butanol

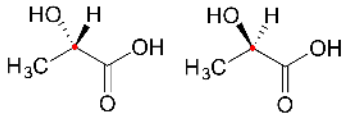
Here are four more examples of chiral biomolecules, each one shown as a pair of enantiomers, with chiral centers marked by red dots.



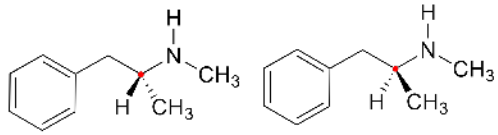
glyceraldehyde



alanine

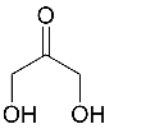


lactic acid

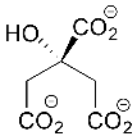


methamphetamine

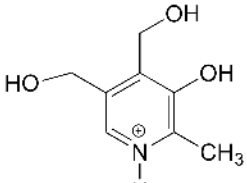
Here are some examples of ***achiral*** biomolecules - convince yourself that none of them contain a chiral center:



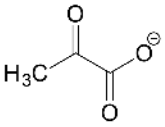
dihydroxyacetone



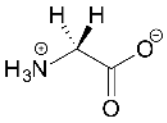
citrate



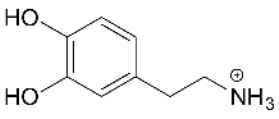
pyridoxine
(vitamin B_6)



pyruvate



glycine
(amino acid)



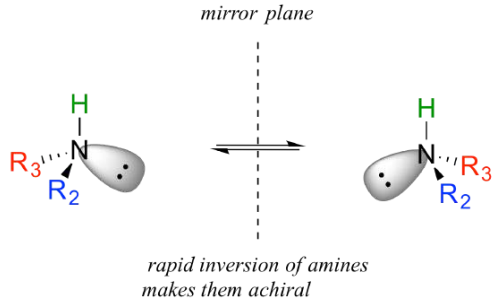
dopamine
(neurotransmitter)

When looking for chiral centers, it is important to recognize that the question of whether or not the dashed/solid wedge drawing convention is used is irrelevant. Chiral molecules are sometimes drawn without using wedges (although obviously this means that stereochemical information is being omitted). Conversely, wedges may be used on carbons that are *not* chiral centers – look, for example, at the drawings of glycine and citrate in the figure above.

Can a chiral center be something other than a tetrahedral carbon with four different substituents? The answer to this question is 'yes' - however, these alternative chiral centers are very rare in the context of biological organic chemistry, and outside the scope of our discussion here.

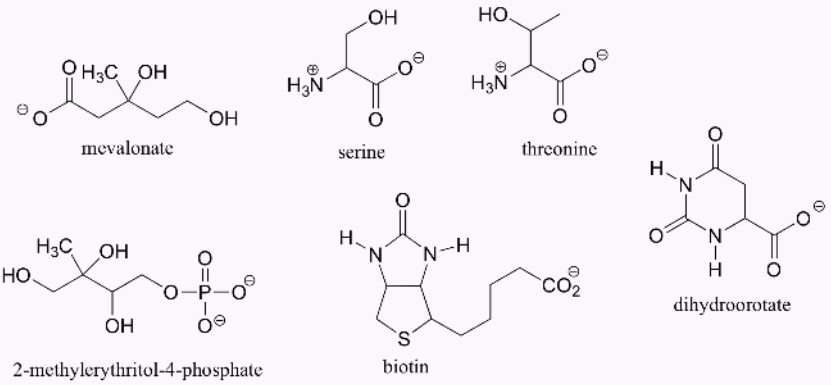
You may also have wondered about amines: shouldn't we consider a secondary or tertiary amine to be a chiral center, as they are tetrahedral and attached to four different substituents, if the lone-pair electrons are counted as a 'substituent'? Put another way, isn't an amine non-superimposable on its mirror image?

The answer: yes it is, in the static picture, but in reality, the nitrogen of an amine is rapidly and reversibly inverting, or turning inside out, at room temperature.



If you have trouble picturing this, take an old tennis ball and cut it in half. Then, take one of the concave halves and flip it inside out, then back again: this is what the amine is doing. The end result is that the two 'enantiomers' if the amine are actually two rapidly interconverting forms of the same molecule, and thus the amine itself is not a chiral center. This inversion process does *not* take place on a tetrahedral carbon, which of course has no lone-pair electrons.

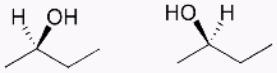
Exercise 3.8: Locate all of the chiral centers (there may be more than one in a molecule). Remember, hydrogen atoms bonded to carbon usually are not drawn in the line structure convention - but they are still there!



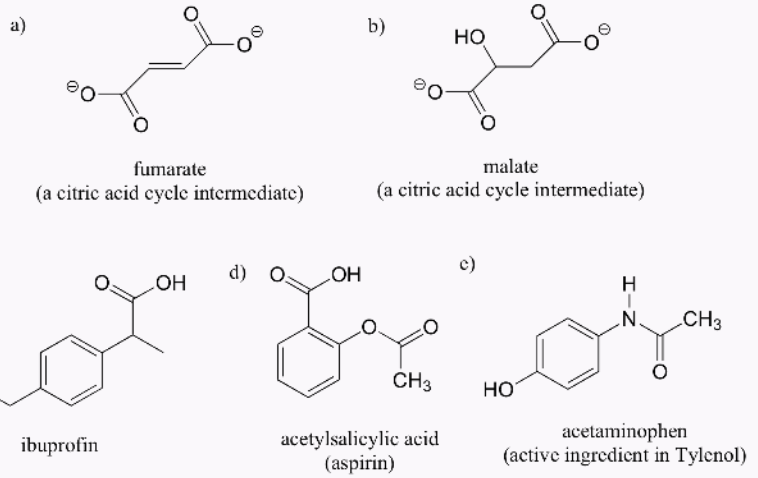
Exercise 3.9:

a) Draw two enantiomers of i) mevalonate and ii) serine.

b) Are the two 2-butanol structures below enantiomers?



Exercise 3.10: Label the molecules below as chiral or achiral, and locate all chiral centers.



Solutions to exercises

Kahn Academy video tutorials

Chirality

Enantiomers

Organic Chemistry With a Biological Emphasis by Tim Soderberg (University of Minnesota, Morris)

6.17: Nitrogen and Phosphorus Atoms Can Be Asymmetric Centers is shared under a not declared license and was authored, remixed, and/or curated by LibreTexts.

6.18: Stereochemistry of Reactions- Regioselective, Stereoselective, and Stereospecific Reactions

Stereochemistry of Addition to Alkenes

6.18: Stereochemistry of Reactions- Regioselective, Stereoselective, and Stereospecific Reactions is shared under a not declared license and was authored, remixed, and/or curated by LibreTexts.

6.19: The Stereochemistry of Electrophilic addition Reactions of Alkenes

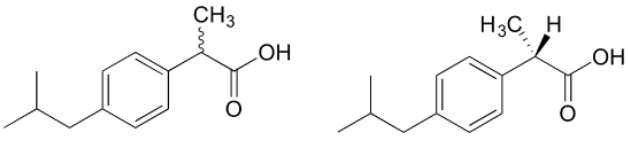
Stereochemistry of Addition to Alkenes{es} }}

6.19: The Stereochemistry of Electrophilic addition Reactions of Alkenes is shared under a not declared license and was authored, remixed, and/or curated by LibreTexts.

6.20: The Stereochemistry of Enzyme-Catalyzed Reactions

While challenging to understand and visualize, the stereochemistry concepts we have explored in this chapter are integral to the study of living things. The vast majority of biological molecules contain chiral centers and/or stereogenic alkene groups. Most importantly, proteins are chiral, which of course includes all of the the enzymes which catalyze the chemical reactions of a cell, the receptors which transmit information within or between cells, and the antibodies which bind specifically to potentially harmful invaders. You know from your biology classes that proteins, because they fold up into a specific three dimensional shape, are able to very specifically recognize and bind to other organic molecules. The ligand or substrate bound by a particular protein could be a small organic molecule such as pyruvate all the way up to a large biopolymer such as a specific region of DNA, RNA, or another protein. Because they are chiral molecules, *proteins are very sensitive to the stereochemistry of their ligands*: a protein may bind specifically to (*R*)-glyceraldehyde, for example, but not bind to (*S*)-glyceraldehyde, just as your right hand will not fit into a left-handed baseball glove (see end of chapter for a link to an animation illustrating this concept).

The over-the-counter painkiller ibuprofen is currently sold as a racemic mixture, but only the *S* enantiomer is effective, due to the specific way it is able to bind to and inhibit the action of prostaglandin H_2 synthase, an enzyme in the body's inflammation response process.



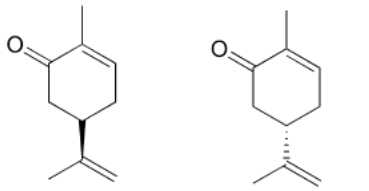
racemic ibuprofen

(*S*)-ibuprofen
(active enantiomer)

The *R* enantiomer of ibuprofen does not bind to prostaglandin H_2 synthase in the same way as the *S* enantiomer, and as a consequence does not exert the same inhibitory effect on the enzyme's action (see *Nature Chemical Biology* **2011**, *7*, 803 for more details). Fortunately, (*R*)-ibuprofen apparently does not cause any harmful side effects, and is in fact isomerized gradually by an enzyme in the body to (*S*)-ibuprofen.

Earlier in this chapter we discussed the tragic case of thalidomide, and mentioned that it appears that it is specifically the *S* enantiomer which caused birth defects. Many different proposals have been made over the past decades to try to explain the teratogenic (birth defect-causing) effect of the drug, but a clear understanding still evades the scientific community. In 2010, however, a team in Japan reported evidence that thalidomide binds specifically to a protein called 'thereblon'. Furthermore, when production of thereblon is blocked in female zebra fish, developmental defects occur in her offspring which are very similar to the defects caused by the administration of thalidomide, pointing to the likelihood that thalidomide binding somehow inactivates the protein, thus initiating the teratogenic effect. (http://news.sciencemag.org/2010/03/t...-partner-crime)

You can, with a quick trip to the grocery store, directly experience the biological importance of stereoisomerism. Carvone is a chiral, plant-derived molecule that contributes to the smell of spearmint in the *R* form and caraway (a spice) in the *S* form.



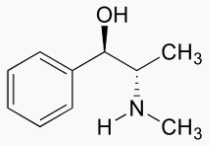
(*R*)-carvone
(spearmint odor)

(*S*)-carvone
(caraway odor)

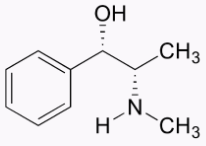
Although details are not known, the two enantiomers presumably interact differently with one or more smell receptor proteins in your nose, generating the transmission of different chemical signals to the olfactory center of your brain.

Exercise 3.28: Ephedrine, found in the Chinese traditional medicine *ma huang*, is a stimulant and appetite suppressant. Both pseudoephedrine and levomethamphetamine are active ingredients in over-the-counter nasal decongestants. Methamphetamine

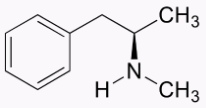
is a highly addictive and illegal stimulant, and is usually prepared in illicit 'meth labs' using pseudoephedrine as a starting point.



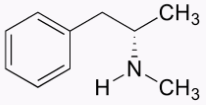
ephedrine



pseudoephedrine



methamphetamine

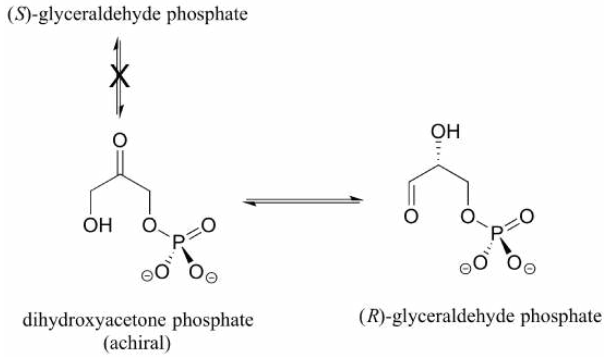


levomethamphetamine

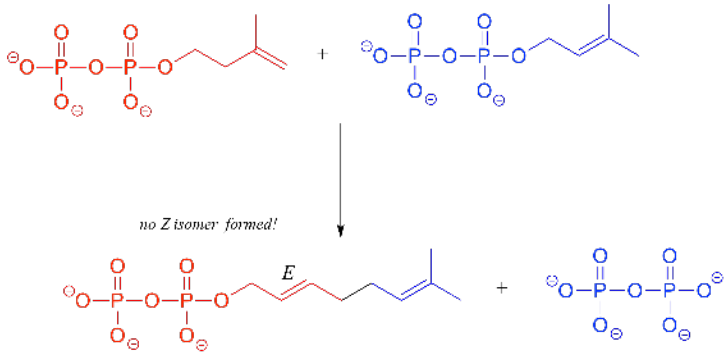
What is the relationship between ephedrine and pseudoephedrine? Between methamphetamine and levomethamphetamine? Between pseudoephedrine and methamphetamine? Your choices are: not isomers, constitutional isomers, diastereomers, enantiomers, or same molecule.

Solutions to exercises

Enzymes are very specific with regard to the stereochemistry of the reactions they catalyze. *When the product of a biochemical reaction contains a chiral center or a stereogenic alkene, with very few exceptions only one stereoisomer of the product is formed.* In the glycolysis pathway, for example, the enzyme triose-phosphate isomerase catalyzes the reversible interconversion between dihydroxyacetone (which is achiral) and (*R*)-glyceraldehyde phosphate. The (*S*)-glyceraldehyde enantiomer is not formed by this enzyme in the left-to-right reaction, and is not used as a starting compound in the right-to-left reaction - it does not 'fit' in the active site of the enzyme.



In the isoprenoid biosynthesis pathway, two five-carbon building-block molecules combine to form a ten-carbon chain containing an *E*-alkene group. The enzyme does *not* catalyze formation of the *Z* diastereomer.



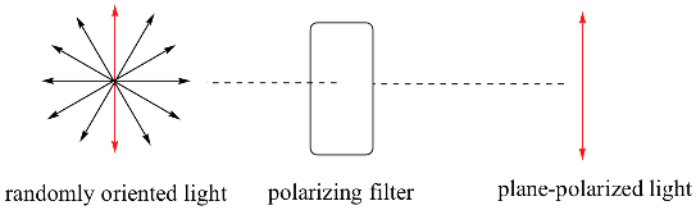
In chapters 9-17 of this book, and continuing on into your study of biological and organic chemistry, you will be learning about how enzymes are able to achieve these feats of stereochemical specificity. If you take a more advanced class in organic synthesis, you will also learn how laboratory chemists are figuring out ingenious ways to exert control over the stereochemical outcomes of nonenzymatic reactions, an area of chemistry that is particularly important in the pharmaceutical industry.

Organic Chemistry With a Biological Emphasis by Tim Soderberg (University of Minnesota, Morris)

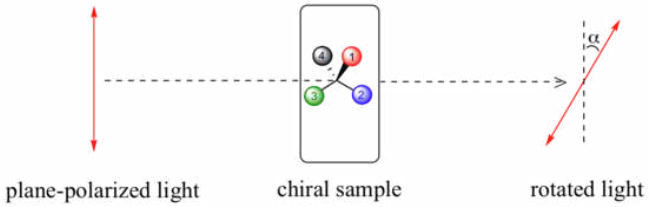
6.20: The Stereochemistry of Enzyme-Catalyzed Reactions is shared under a not declared license and was authored, remixed, and/or curated by LibreTexts.

6.21: Enantiomers Can Be Distinguished by Biological Molecules

Chiral molecules, as we learned in the introduction to this chapter, have an interesting optical property. You may know from studying physics that light waves are oscillating electric and magnetic fields. In ordinary light, the oscillation is randomly oriented in an infinite number of planes. When ordinary light is passed through a polarizer, all planes of oscillation are filtered out except one, resulting in **plane-polarized light**.



A beam of plane-polarized light, when passed through a sample of a chiral compound, interacts with the compound in such a way that the angle of oscillation will rotate. This property is called **optical activity**.



If a compound rotates plane polarized light in the clockwise (+) direction, it is said to be **dextrorotatory**, while if it rotates light in the counterclockwise (-) direction it is **levorotatory**. (We mentioned L- and D-amino acids in the previous section: the L-amino acids are levorotatory). The magnitude of the observed optical activity is dependent on temperature, the wavelength of light used, solvent, concentration of the chiral sample, and the path length of the sample tube (path length is the length that the plane-polarized light travels through the chiral sample). Typically, optical activity measurements are made in a 1 decimeter (10 cm) path-length sample tube at 25 °C, using as a light source the so-called “D-line” from a sodium lamp, which has a wavelength of 589 nm. The **specific rotation** of a pure chiral compound at 25° is expressed by the expression:

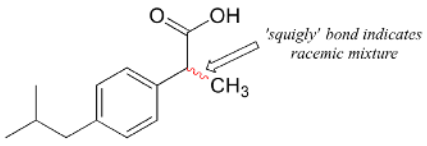
specific rotation:

$$[\alpha]_D^{25} = \frac{\alpha_{obs}}{lc}$$

. . . where alpha$_{(obs)}$ is the observed rotation, *l* is path length in decimeters, and *c* is the concentration of the sample in grams per 100 mL. In other words, the specific rotation of a chiral compound is the optical rotation that is observed when 1 g of the compound is dissolved in enough of a given solvent to make 100 mL solution, and the rotation is measured in a 1 dm cuvette at 25 ^{o}C using light from a sodium lamp.

Every chiral molecule has a characteristic specific rotation, which is recorded in the chemical literature as a physical property just like melting point or density. Different enantiomers of a compound will always rotate plane-polarized light with an equal but opposite magnitude. (*S*)-ibuprofen, for example, has a specific rotation of +54.5^{o} (dextrorotatory) in methanol, while (*R*)-ibuprofen has a specific rotation of -54.5^{o}. *There is no relationship between chiral compound's R/S designation and the direction of its specific rotation.* For example, the *S* enantiomer of ibuprofen is dextrorotatory, but the *S* enantiomer of glyceraldehyde is levorotatory.

A 50:50 mixture of two enantiomers (a racemic mixture) will have no observable optical activity, because the two optical activities cancel each other out. In a structural drawing, a 'squigly' bond from a chiral center indicates a mixture of both *R* and *S* configurations.



(+/-) ibuprofen
(racemic)

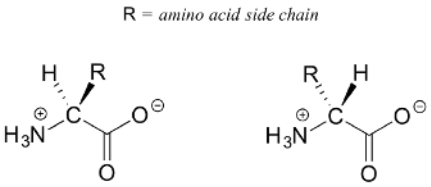
Chiral molecules are often labeled according to whether they are dextrorotatory or levorotatory as well as by their *R/S* designation. For example, the pure enantiomers of ibuprofen are labeled (*S*)-(+)-ibuprofen and (*R*)-(-)-ibuprofen, while (±)-ibuprofen refers to the racemic mixture, which is the form in which the drug is sold to consumers.

Exercise 3.14: The specific rotation of (*R*)-limonene is +11.5° in ethanol. What is the expected observed rotation of a sample of 6.00 g (*S*)-limonene dissolved in ethanol to a total volume of 80.0 mL in a 1.00 dm (10.0 cm) pathlength cuvette?

Exercise 3.15: The specific rotation of (*S*)-carvone is +61°, measured 'neat' (pure liquid sample, no solvent). The optical rotation of a mixture of *R* and *S* carvone is measured at -23°. Which enantiomer is in excess in the mixture?

Solutions to exercises

All of the twenty natural amino acids except glycine have a chiral center at their alpha-carbon (recall that basic amino acid structure and terminology was introduced in section 1.3). Virtually all of the amino acids found in nature, both in the form of free amino acids or incorporated into peptides and proteins, have what is referred to in the biochemical literature as the 'L' configuration:



L-amino acids
(common in nature)

D-amino acids
(rare in nature)

The 'L' indicates that these amino acid stereoisomers are levorotatory. All but one of the 19 L-amino acids have *S* stereochemistry at the a-carbon, using the rules of the *R/S* naming system.

D-amino acids (the D stands for dextrorotatory) are very rare in nature, but we will learn about an interesting example of a peptide containing one D-amino acid residue later in chapter 12.

Exercise 3.16: Which of the 20 common L-amino acids found in nature has the *R* configuration? Refer to the amino acid table for structures.

Solutions to exercises

Khan Academy video tutorial on optical acitivity

Organic Chemistry With a Biological Emphasis by Tim Soderberg (University of Minnesota, Morris)

6.21: Enantiomers Can Be Distinguished by Biological Molecules is shared under a not declared license and was authored, remixed, and/or curated by LibreTexts.

CHAPTER OVERVIEW

7: Delocalized Electrons and Their Effect on Stability, Reactivity, and pKa (Ultraviolet and Visible Spectroscopy)



Essential Organic Chemistry: 2nd Ed.

Bruice

Homework Problems
Homework Solutions

I II III IV V VI VII VIII IX X XI XII XIII XIV XV XVI XVII XVIII XIX XX XXI

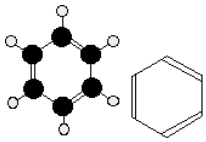
Template:HideTOC

- 7.1: Delocalized Electrons Explain Benzene's Structure
- 7.2: The Bonding in Benzene
- 7.3: Resonance Contributors and the Resonance Hybrid
- 7.4: How to Draw Resonance Contributors
- 7.5: The Predicted Stabilities of Resonance Contributors
- 7.6: Delocalized Energy Is the Additional Stability Delocalized Electrons Give to a Compound
- 7.7: Examples That Show How Delocalized Electrons Affect Stability
- 7.8: A Molecular Orbital Description of Stability
- 7.9: How Delocalized Electrons Affect pKa Values
- 7.10: Delocalized Electrons Can Affect the Product of a Reaction
- 7.11: Thermodynamic Versus Kinetic Control of Reactions
- 7.12: The Diels-Adler Reaction Is a 1,4-Addition Reaction

7: Delocalized Electrons and Their Effect on Stability, Reactivity, and pKa (Ultraviolet and Visible Spectroscopy) is shared under a not declared license and was authored, remixed, and/or curated by LibreTexts.

7.1: Delocalized Electrons Explain Benzene's Structure

Kekulé was the first to suggest a sensible structure for benzene. The carbons are arranged in a hexagon, and he suggested alternating double and single bonds between them. Each carbon atom has a hydrogen attached to it.



This diagram is often simplified by leaving out all the carbon and hydrogen atoms! In diagrams of this sort, there is a carbon atom at each corner. You have to count the bonds leaving each carbon to work out how many hydrogens there are attached to it. In this case, each carbon has three bonds leaving it. Because carbon atoms form four bonds, that means you are a bond missing - and that must be attached to a hydrogen atom.

Problems with the Kekulé structure

Although the Kekulé structure was a good attempt in its time, there are serious problems with it regarding chemistry, structure and stability.

The Kekulé structure has problems with the chemistry. Because of the three double bonds, you might expect benzene to have reactions like ethene - only more so! Ethene undergoes addition reactions in which one of the two bonds joining the carbon atoms breaks, and the electrons are used to bond with additional atoms. Benzene rarely does this. Instead, it usually undergoes substitution reactions in which one of the hydrogen atoms is replaced by something new.

The Kekulé structure has problems with the shape. Benzene is a planar molecule (all the atoms lie in one plane), and that would also be true of the Kekulé structure. The problem is that C-C single and double bonds are different lengths.

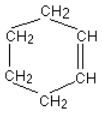
- C-C (0.154 nm)
- C=C (0.134 nm)

That would mean that the hexagon would be irregular if it had the Kekulé structure, with alternating shorter and longer sides. In real benzene all the bonds are exactly the same - intermediate in length between C-C and C=C at 0.139 nm. Real benzene is a perfectly regular hexagon.

The Kekulé structure has problems with the stability of benzene. Real benzene is a lot more stable than the Kekulé structure would give it credit for. Every time you do a thermochemistry calculation based on the Kekulé structure, you get an answer which is wrong by about 150 kJ mol^{-1}. This is most easily shown using enthalpy changes of hydrogenation. Hydrogenation is the addition of hydrogen to something. If, for example, you hydrogenate ethene you get ethane:

$$\mathbf{CH_2{=}CH_2 + H_2 \rightarrow CH_3CH_3} \quad (1)$$

In order to do a fair comparison with benzene (a ring structure) we're going to compare it with cyclohexene. Cyclohexene, C_6H_{10}, is a ring of six carbon atoms containing just one C=C.



When hydrogen is added to this, cyclohexane, C_6H_{12}, is formed. The "CH" groups become CH_2 and the double bond is replaced by a single one. The structures of cyclohexene and cyclohexane are usually simplified in the same way that the Kekulé structure for benzene is simplified - by leaving out all the carbons and hydrogens.


cyclohexene

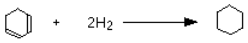

cyclohexane

In the cyclohexane case, for example, there is a carbon atom at each corner, and enough hydrogens to make the total bonds on each carbon atom up to four. In this case, then, each corner represents CH_2. The hydrogenation equation could be written:

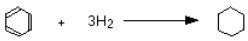


The enthalpy change during this reaction is -120 kJ mol^{-1}. In other words, when 1 mole of cyclohexene reacts, 120 kJ of heat energy is evolved. Where does this heat energy come from? When the reaction happens, bonds are broken (C=C and H-H) and this costs energy. Other bonds have to be made, and this releases energy. Because the bonds made are stronger than those broken, more energy is released than was used to break the original bonds and so there is a net evolution of heat energy.

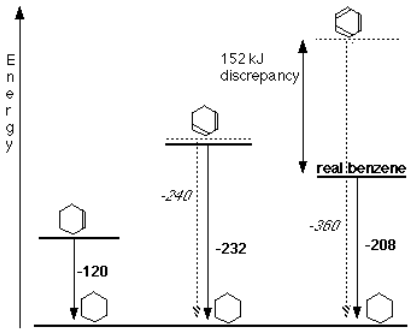
If the ring had two double bonds in it initially (cyclohexa-1,3-diene), exactly twice as many bonds would have to be broken and exactly twice as many made. In other words, you would expect the enthalpy change of hydrogenation of cyclohexa-1,3-diene to be exactly twice that of cyclohexene - that is, -240 kJ mol^{-1}.



In fact, the enthalpy change is -232 kJ mol^{-1} - which isn't far off what we are predicting. Applying the same argument to the Kekulé structure for benzene (what might be called cyclohexa-1,3,5-triene), you would expect an enthalpy change of -360 kJ mol^{-1}, because there are exactly three times as many bonds being broken and made as in the cyclohexene case.



In fact what you get is -208 kJ mol^{-1} - not even within distance of the predicted value! This is very much easier to see on an enthalpy diagram. Notice that in each case heat energy is released, and in each case the product is the same (cyclohexane). That means that all the reactions "fall down" to the same end point.



Heavy lines, solid arrows and bold numbers represent real changes. Predicted changes are shown by dotted lines and italics. The most important point to notice is that real benzene is much lower down the diagram than the Kekulé form predicts. The lower down a substance is, the more energetically stable it is. This means that real benzene is about 150 kJ mol^{-1} more stable than the Kekulé structure gives it credit for. This increase in stability of benzene is known as the **delocalization energy** or **resonance energy** of benzene.

Contributors

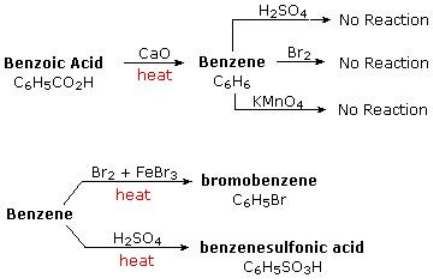
Jim Clark (Chemguide.co.uk)

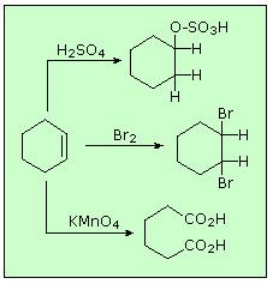
7.1: Delocalized Electrons Explain Benzene's Structure is shared under a not declared license and was authored, remixed, and/or curated by LibreTexts.

- **Bonding in Benzene: the Kekulé Structure** by Jim Clark is licensed CC BY-NC 4.0.

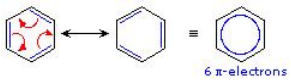
7.2: The Bonding in Benzene

Because of the low hydrogen to carbon ratio in aromatic compounds (note that the H:C ratio in an alkane is >2), chemists expected their structural formulas would contain a large number of double or triple bonds. Since double bonds are easily cleaved by oxidative reagents such as potassium permanganate or ozone, and rapidly add bromine and chlorine, these reactions were applied to these aromatic compounds. Surprisingly, products that appeared to retain many of the double bonds were obtained, and these compounds exhibited a high degree of chemical stability compared with known alkenes and cycloalkenes (aliphatic compounds). On treatment with hot permanganate solution, cinnamaldehyde gave a stable, crystalline $C_7H_6O_2$ compound, now called benzoic acid. The H:C ratio in benzoic acid is <1, again suggesting the presence of several double bonds. Benzoic acid was eventually converted to the stable hydrocarbon benzene, C_6H_6, which also proved unreactive to common double bond transformations, as shown below. For comparison, reactions of cyclohexene, a typical alkene, with these reagents are also shown (green box). As experimental evidence for a wide assortment of compounds was acquired, those incorporating this exceptionally stable six-carbon core came to be called "aromatic".



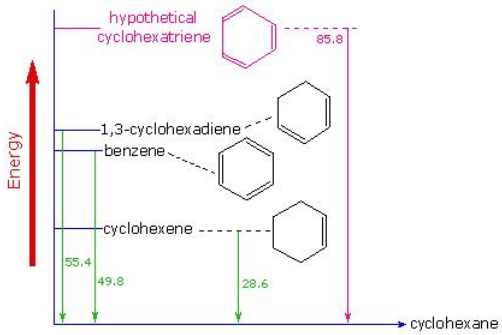


If benzene is forced to react by increasing the temperature and/or by addition of a catalyst, It undergoes **substitution reactions** rather than the addition reactions that are typical of alkenes. This further confirms the previous indication that the six-carbon benzene core is unusually stable to chemical modification. The conceptual contradiction presented by a high degree of unsaturation (low H:C ratio) and high chemical stability for benzene and related compounds remained an unsolved puzzle for many years. Eventually, the presently accepted structure of a regular-hexagonal, planar ring of carbons was adopted, and the exceptional thermodynamic and chemical stability of this system was attributed to resonance stabilization of a conjugated cyclic triene.

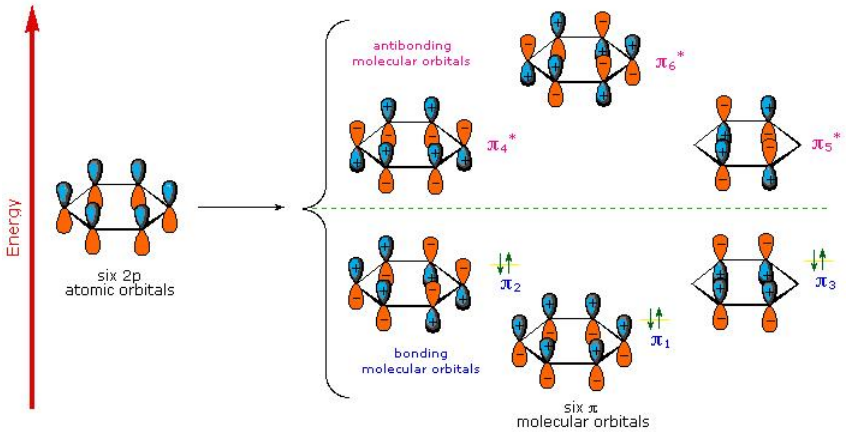
Benzene:	

Here, two structurally and energetically equivalent electronic structures for a stable compound are written, but no single structure provides an accurate or even an adequate representation of the true molecule. The six-membered ring in benzene is a perfect hexagon (all carbon-carbon bonds have an identical length of 1.40 Å). The cyclohexatriene contributors would be expected to show alternating bond lengths, the double bonds being shorter (1.34 Å) than the single bonds (1.54 Å). An alternative representation for benzene (circle within a hexagon) emphasizes the pi-electron delocalization in this molecule, and has the advantage of being a single diagram. In cases such as these, the electron delocalization described by resonance enhances the stability of the molecules, and compounds composed of such molecules often show exceptional stability and related properties.

Evidence for the enhanced thermodynamic stability of benzene was obtained from measurements of the heat released when double bonds in a six-carbon ring are hydrogenated (hydrogen is added catalytically) to give cyclohexane as a common product. In the following diagram cyclohexane represents a low-energy reference point. Addition of hydrogen to cyclohexene produces cyclohexane and releases heat amounting to 28.6 kcal per mole. If we take this value to represent the energy cost of introducing one double bond into a six-carbon ring, we would expect a cyclohexadiene to release 57.2 kcal per mole on complete hydrogenation, and 1,3,5-cyclohexatriene to release 85.8 kcal per mole. These **heats of hydrogenation** would reflect the relative thermodynamic stability of the compounds. In practice, 1,3-cyclohexadiene is slightly more stable than expected, by about 2 kcal, presumably due to conjugation of the double bonds. **Benzene, however, is an extraordinary 36 kcal/mole more stable than expected**. This sort of stability enhancement is now accepted as a characteristic of all aromatic compounds.



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



The Molecular Orbitals of Benzene

Contributors

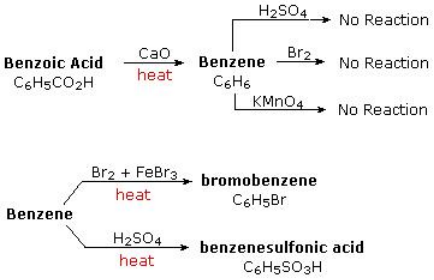
William Reusch, Professor Emeritus (Michigan State U.), Virtual Textbook of Organic Chemistry

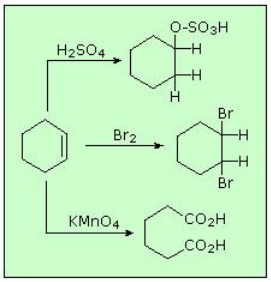
7.2: The Bonding in Benzene is shared under a not declared license and was authored, remixed, and/or curated by LibreTexts.

- **Properties of Benzene** is licensed CC BY-NC-SA 4.0.

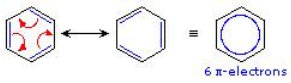
7.3: Resonance Contributors and the Resonance Hybrid

Because of the low hydrogen to carbon ratio in aromatic compounds (note that the H:C ratio in an alkane is >2), chemists expected their structural formulas would contain a large number of double or triple bonds. Since double bonds are easily cleaved by oxidative reagents such as potassium permanganate or ozone, and rapidly add bromine and chlorine, these reactions were applied to these aromatic compounds. Surprisingly, products that appeared to retain many of the double bonds were obtained, and these compounds exhibited a high degree of chemical stability compared with known alkenes and cycloalkenes (aliphatic compounds). On treatment with hot permanganate solution, cinnamaldehyde gave a stable, crystalline $C_7H_6O_2$ compound, now called benzoic acid. The H:C ratio in benzoic acid is <1, again suggesting the presence of several double bonds. Benzoic acid was eventually converted to the stable hydrocarbon benzene, C_6H_6, which also proved unreactive to common double bond transformations, as shown below. For comparison, reactions of cyclohexene, a typical alkene, with these reagents are also shown (green box). As experimental evidence for a wide assortment of compounds was acquired, those incorporating this exceptionally stable six-carbon core came to be called "aromatic".



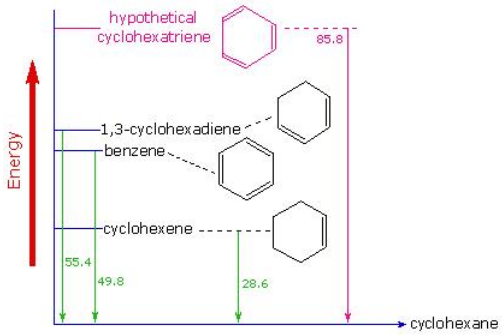


If benzene is forced to react by increasing the temperature and/or by addition of a catalyst, It undergoes **substitution reactions** rather than the addition reactions that are typical of alkenes. This further confirms the previous indication that the six-carbon benzene core is unusually stable to chemical modification. The conceptual contradiction presented by a high degree of unsaturation (low H:C ratio) and high chemical stability for benzene and related compounds remained an unsolved puzzle for many years. Eventually, the presently accepted structure of a regular-hexagonal, planar ring of carbons was adopted, and the exceptional thermodynamic and chemical stability of this system was attributed to resonance stabilization of a conjugated cyclic triene.

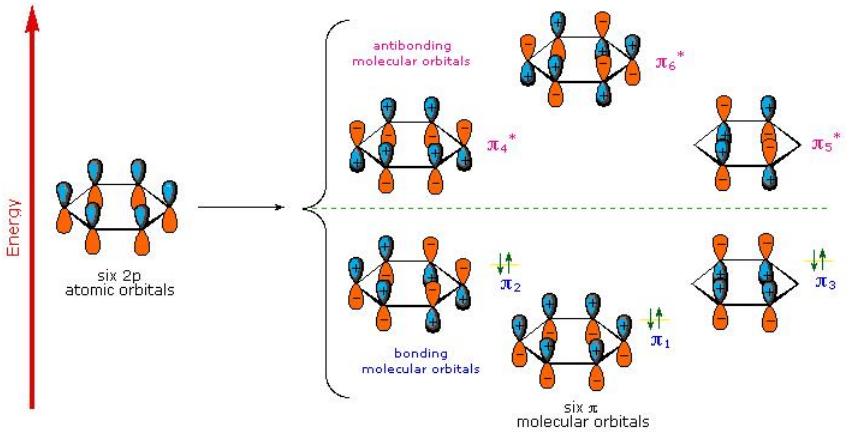
Benzene:	

Here, two structurally and energetically equivalent electronic structures for a stable compound are written, but no single structure provides an accurate or even an adequate representation of the true molecule. The six-membered ring in benzene is a perfect hexagon (all carbon-carbon bonds have an identical length of 1.40 Å). The cyclohexatriene contributors would be expected to show alternating bond lengths, the double bonds being shorter (1.34 Å) than the single bonds (1.54 Å). An alternative representation for benzene (circle within a hexagon) emphasizes the pi-electron delocalization in this molecule, and has the advantage of being a single diagram. In cases such as these, the electron delocalization described by resonance enhances the stability of the molecules, and compounds composed of such molecules often show exceptional stability and related properties.

Evidence for the enhanced thermodynamic stability of benzene was obtained from measurements of the heat released when double bonds in a six-carbon ring are hydrogenated (hydrogen is added catalytically) to give cyclohexane as a common product. In the following diagram cyclohexane represents a low-energy reference point. Addition of hydrogen to cyclohexene produces cyclohexane and releases heat amounting to 28.6 kcal per mole. If we take this value to represent the energy cost of introducing one double bond into a six-carbon ring, we would expect a cyclohexadiene to release 57.2 kcal per mole on complete hydrogenation, and 1,3,5-cyclohexatriene to release 85.8 kcal per mole. These **heats of hydrogenation** would reflect the relative thermodynamic stability of the compounds. In practice, 1,3-cyclohexadiene is slightly more stable than expected, by about 2 kcal, presumably due to conjugation of the double bonds. **Benzene, however, is an extraordinary 36 kcal/mole more stable than expected**. This sort of stability enhancement is now accepted as a characteristic of all aromatic compounds.



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



The Molecular Orbitals of Benzene

Contributors

William Reusch, Professor Emeritus (Michigan State U.), Virtual Textbook of Organic Chemistry

7.3: Resonance Contributors and the Resonance Hybrid is shared under a not declared license and was authored, remixed, and/or curated by LibreTexts.

- **Properties of Benzene** is licensed CC BY-NC-SA 4.0.

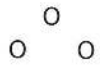
7.4: How to Draw Resonance Contributors

Resonance is a mental exercise within the Valence Bond Theory of bonding that describes the delocalization of electrons within molecules. It involves constructing multiple Lewis structures that, when combined, represent the full electronic structure of the molecule. **Resonance structures** are used when a single Lewis structure cannot fully describe the bonding; the combination of possible resonance structures is defined as a **resonance hybrid**, which represents the overall delocalization of electrons within the molecule. In general, molecules with multiple resonance structures will be more stable than one with fewer and some resonance structures contribute more to the stability of the molecule than others - formal charges aid in determining this.

Introduction

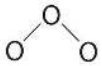
Resonance is a way of describing delocalized electrons within certain molecules or polyatomic ions where the bonding cannot be expressed by a single Lewis formula. A molecule or ion with such delocalized electrons is represented by several resonance structures. The nuclear skeleton of the Lewis Structure of these resonance structures remains the same, only the electron locations differ. Such is the case for ozone ($\mathbf{O_3}$), an allotrope of oxygen with a V-shaped structure and an O–O–O angle of 117.5°. Let's motivate the discussion by building the Lewis structure for ozone.

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



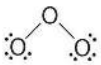
2. Each O atom has 6 valence electrons, for a total of 18 valence electrons.

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



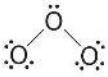
with 14 electrons left over.

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

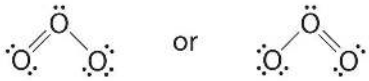


and have 2 electrons left over.

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

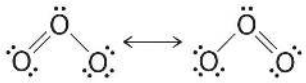


6. The central oxygen has only 6 electrons. We must convert one lone pair on a terminal oxygen atom to a bonding pair of electrons —but which one? Depending on which one we choose, we obtain either



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

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



The double-headed arrow indicates that the actual electronic structure is an *average* of those shown, not that the molecule oscillates between the two structures.

> *When it is possible to write more than one equivalent resonance structure for a molecule or ion, the actual structure is the average of the resonance structures.*

The electrons appear to "shift" between different resonance structures and while not strictly correct as each resonance structure is just a limitation of using the Lewis structure perspective to describe these molecules. A more accurate description of the electron structure of the molecule requires considering multiple resonance structures simultaneously.

Delocalization and Resonance Structures Rules

1. Resonance structures should have the same number of electrons, do not add or subtract any electrons. (check the number of electrons by simply counting them).
2. Each resonance structures follows the rules of writing Lewis Structures.
3. The hybridization of the structure must stay the same.
4. The skeleton of the structure can not be changed (only the electrons move).
5. Resonance structures must also have the same number of lone pairs.

"Pick the Correct Arrow for the Job"

Most arrows in chemistry cannot be used interchangeably and care must be given to selecting the correct arrow for the job.

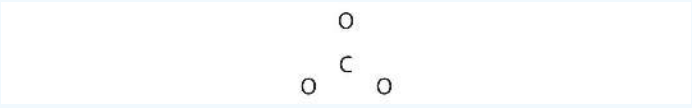
- ↔: A double headed arrow on both ends of the arrow between Lewis structures is used to show resonance
- ⇌: Double harpoons are used to designate equilibria
- ⇀: A single harpoon on one end indicates the movement of **one** electron
- →: A double headed arrow on one end is used to indicate the movement of **two** electrons

Example 7.4.2: Carbonate Ion

Identify the resonance structures for the carbonate ion: CO_3^{2-}.

Solution

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

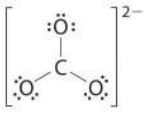


2. Carbon has 4 valence electrons, each oxygen has 6 valence electrons, and there are 2 more for the −2 charge. This gives 4 + (3 × 6) + 2 = 24 valence electrons.

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

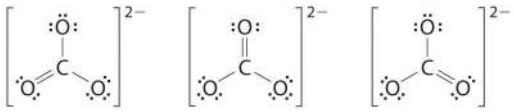


4. We divide the remaining 18 electrons equally among the three oxygen atoms by placing three lone pairs on each and indicating the −2 charge:

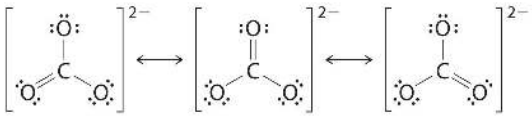


5. No electrons are left for the central atom.

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:



The actual structure is an average of these three resonance structures.

Like ozone, the electronic structure of the carbonate ion cannot be described by a single Lewis electron structure. Unlike O_3, though, the actual structure of CO_3^{2-} is an average of *three* resonance structures.

Using Formal Charges to Identify viable Resonance Structures

While each resonance structure contributes to the total electronic structure of the molecule, they may not contribute equally. Assigning Formal charges to atoms in the molecules is one mechanism to identify the viability of a resonance structure and determine its relative magnitude among other structures. The formal charge on an atom in a covalent species is the net charge the atom would bear if the electrons in all the bonds to the atom were equally shared. Alternatively the formal charge on an atom in a covalent species is the net charge the atom would bear if all bonds to the atom were nonpolar covalent bonds. To determine the formal charge on a given atom in a covalent species, use the following formula:

$$\begin{aligned}\textbf{Formal Charge} &= (\textbf{number of valence electrons in free orbital}) \\ &- (\textbf{number of lone-pair electrons}) - \frac{1}{2}(\textbf{ number bond pair electrons})\end{aligned} \tag{7.4.1}$$

Rules for estimating stability of resonance structures

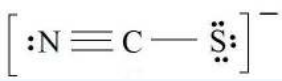
1. The **greater the number of covalent bonds**, the greater the stability since more atoms will have complete octets
2. The structure with the **least number of formal charges** is more stable
3. The structure with the **least separation of formal charge** is more stable
4. A structure with a **negative charge on the more electronegative atom** will be more stable
5. **Positive charges on the least electronegative atom** (most electropositive) is more stable
6. Resonance forms that are equivalent have no difference in stability and contribute equally (eg. benzene)

Example 7.4.3: Thiocyanate Ion

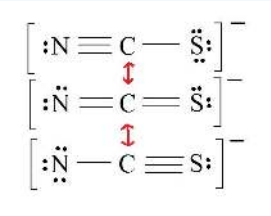
Consider the thiocyanate (CNS^-) ion.

Solution

1. Find the Lewis Structure of the molecule. (Remember the Lewis Structure rules.)



2. Resonance: All elements want an octet, and we can do that in multiple ways by moving the terminal atom's electrons around (bonds too).

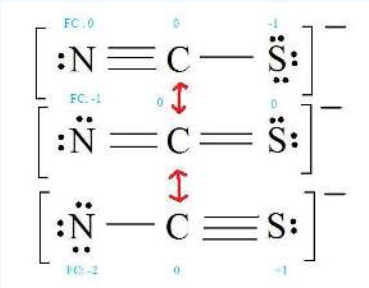


3. Assign Formal Charges via Equation 7.4.1.

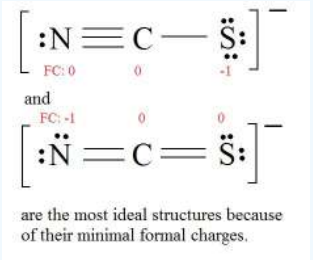
$$\text{Formal Charge} = (\text{number of valence electrons in free orbital}) - (\text{number of lone-pair electrons}) - \left(\tfrac{1}{2}\ \text{number bond pair electrons}\right)$$

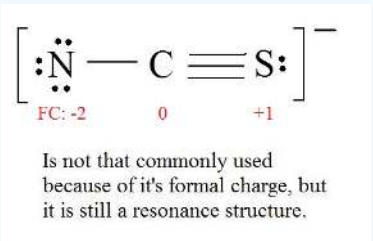
Remember to determine the number of valence electron each atom has before assigning Formal Charges

C = 4 valence e^-, N = 5 valence e^-, S = 6 valence e^-, also add an extra electron for the (-1) charge. The total of valence electrons is 16.



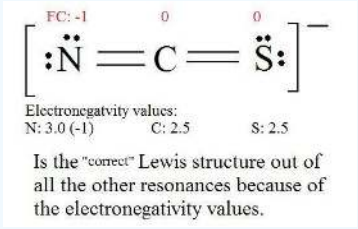
4. Find the most ideal resonance structure. (Note: It is the one with the least formal charges that adds up to zero or to the molecule's overall charge.)





5. Now we have to look at electronegativity for the "Correct" Lewis structure.

The most electronegative atom usually has the negative formal charge, while the least electronegative atom usually has the positive formal charges.



It is useful to combine the resonance structures into a single structure called the **Resonance Hybrid** that describes the bonding of the molecule. The general approach is described below:

1. Draw the Lewis Structure & Resonance for the molecule (using solid lines for bonds).
2. Where there **can** be a double or triple bond, draw a dotted line (-----) for the bond.
3. Draw only the lone pairs found in all resonance structures, do not include the lone pairs that are not on all of the resonance structures.

Example 7.4.4: Benzene

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

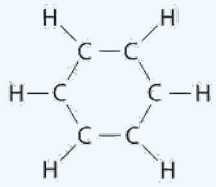
Asked for: resonance structures

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.

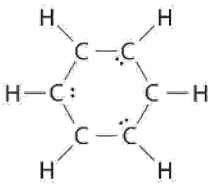
Solution:

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:



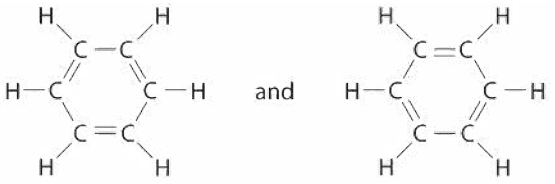
Each carbon atom in this structure has only 6 electrons and has a formal charge of +1, but we have used only 24 of the 30 valence electrons.

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

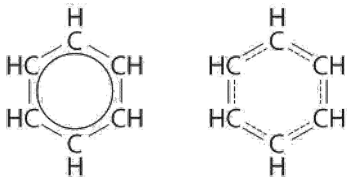


Three carbon atoms now have an octet configuration and a formal charge of −1, while three carbon atoms have only 6 electrons and a formal charge of +1. We can convert each lone pair to a bonding electron pair, which gives each atom an octet of electrons and a formal charge of 0, by making three C=C double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

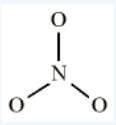
Example 7.4.5: Nitrate Ion

Draw the possible resonance structures for the Nitrate ion NO_3^-.

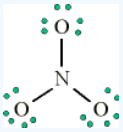
Solution

1. Count up the valence electrons: (1*5) + (3*6) + 1(ion) = **24** electrons

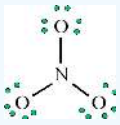
2. Draw the bond connectivities:



3. Add octet electrons to the atoms bonded to the center atom:

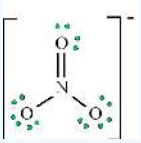


4. Place any leftover electrons (24-24 = **0**) on the center atom:



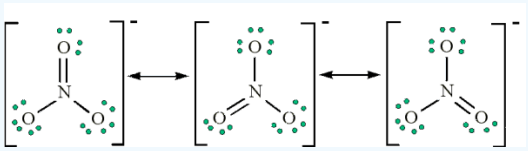
5. Does the central atom have an octet?

- **NO**, it has 6 electrons
- Add a multiple bond (first try a double bond) to see if the central atom can achieve an octet:



6. Does the central atom have an octet?

- YES
- Are there possible resonance structures? YES



Note: We would expect that the bond lengths in the NO_3^- ion to be somewhat shorter than a single bond.

References

1. Petrucci, Ralph H., et al. *General Chemistry: Principles and Modern Applications*. New Jersey: Pearson Prentice Hall, 2007.
2. Ahmad, Wan-Yaacob and Zakaria, Mat B. "Drawing Lewis Structures from Lewis Symbols: A Direct Electron Pairing Approach." Journal of Chemical Education: Journal 77.3.

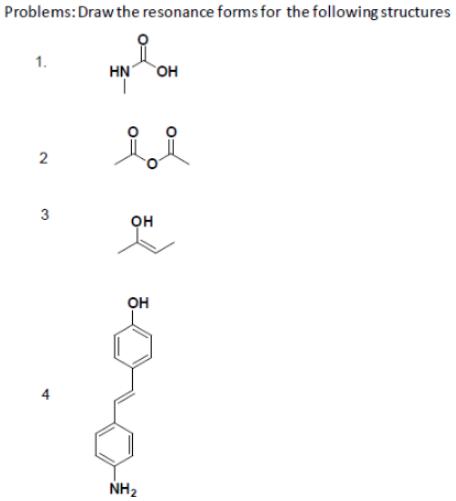
Problems

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

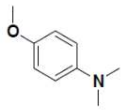


2. Draw the Lewis Dot Structure for SO_4^{2-} and all possible resonance structures. Which of the following resonance structure is not favored among the Lewis Structures? Explain why. Assign Formal Charges.
3. Draw the Lewis Dot Structure for CH_3COO^- and all possible resonance structures. Assign Formal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

Problems #2



5



Based on resonance conformation which structure is more stable?

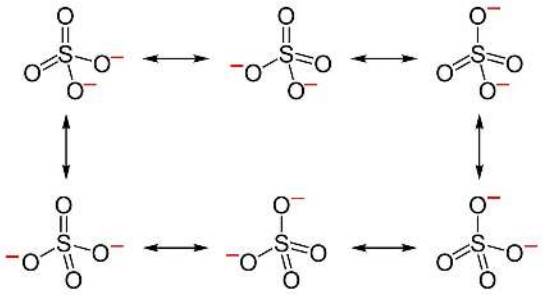
6



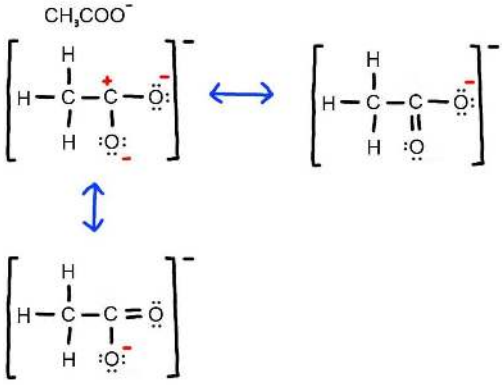
Answers

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

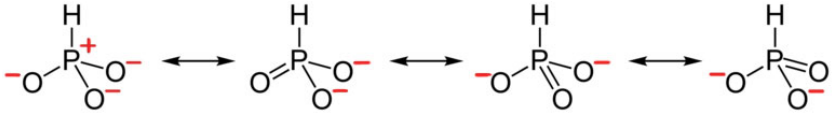
2. Below are the all Lewis dot structure with formal charges (in red) for Sulfate ($\mathbf{SO_4^{2-}}$). There isn't a most favorable resonance of the Sulfate ion because they are all identical in charge and there is no change in Electronegativity between the Oxygen atoms.



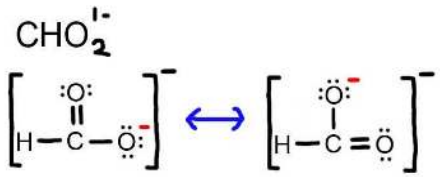
3. Below is the resonance for $\mathbf{CH_3COO^-}$, formal charges are displayed in red. The Lewis Structure with the most formal charges is not desirable, because we want the Lewis Structure with the least formal charge.



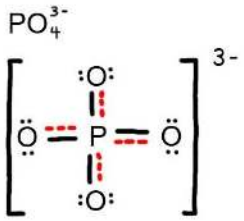
4. The resonance for $\mathbf{HPO_3^{2-}}$, and the formal charges (in red).



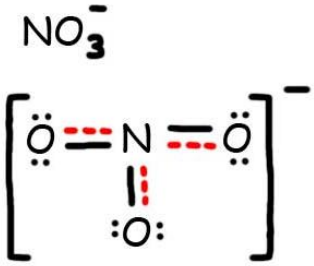
5. The resonance for $\mathbf{CHO_2^{1-}}$, and the formal charges (in red).



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

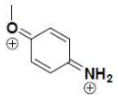


7. The resonance hybrid for $\mathbf{NO_3^-}$, hybrid bonds are in red.



Problems #2

5



6



This is more stable

Contributors and Attributions

- Sharon Wei (UCD), Liza Chu (UCD)

7.4: How to Draw Resonance Contributors is shared under a not declared license and was authored, remixed, and/or curated by LibreTexts.

- **Resonance** is licensed CC BY-NC-SA 4.0.

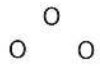
7.5: The Predicted Stabilities of Resonance Contributors

Resonance is a mental exercise within the Valence Bond Theory of bonding that describes the delocalization of electrons within molecules. It involves constructing multiple Lewis structures that, when combined, represent the full electronic structure of the molecule. **Resonance structures** are used when a single Lewis structure cannot fully describe the bonding; the combination of possible resonance structures is defined as a **resonance hybrid**, which represents the overall delocalization of electrons within the molecule. In general, molecules with multiple resonance structures will be more stable than one with fewer and some resonance structures contribute more to the stability of the molecule than others - formal charges aid in determining this.

Introduction

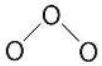
Resonance is a way of describing delocalized electrons within certain molecules or polyatomic ions where the bonding cannot be expressed by a single Lewis formula. A molecule or ion with such delocalized electrons is represented by several resonance structures. The nuclear skeleton of the Lewis Structure of these resonance structures remains the same, only the electron locations differ. Such is the case for ozone ($\mathbf{O_3}$), an allotrope of oxygen with a V-shaped structure and an O–O–O angle of 117.5°. Let's motivate the discussion by building the Lewis structure for ozone.

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



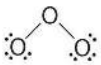
2. Each O atom has 6 valence electrons, for a total of 18 valence electrons.

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



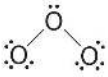
with 14 electrons left over.

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

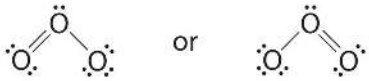


and have 2 electrons left over.

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

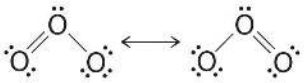


6. The central oxygen has only 6 electrons. We must convert one lone pair on a terminal oxygen atom to a bonding pair of electrons —but which one? Depending on which one we choose, we obtain either



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

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



The double-headed arrow indicates that the actual electronic structure is an *average* of those shown, not that the molecule oscillates between the two structures.

> *When it is possible to write more than one equivalent resonance structure for a molecule or ion, the actual structure is the average of the resonance structures.*

The electrons appear to "shift" between different resonance structures and while not strictly correct as each resonance structure is just a limitation of using the Lewis structure perspective to describe these molecules. A more accurate description of the electron structure of the molecule requires considering multiple resonance structures simultaneously.

Delocalization and Resonance Structures Rules

1. Resonance structures should have the same number of electrons, do not add or subtract any electrons. (check the number of electrons by simply counting them).
2. Each resonance structures follows the rules of writing Lewis Structures.
3. The hybridization of the structure must stay the same.
4. The skeleton of the structure can not be changed (only the electrons move).
5. Resonance structures must also have the same number of lone pairs.

"Pick the Correct Arrow for the Job"

Most arrows in chemistry cannot be used interchangeably and care must be given to selecting the correct arrow for the job.

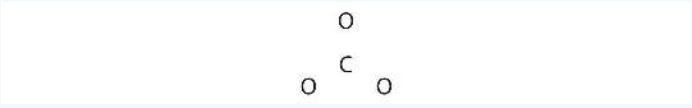
- ↔: A double headed arrow on both ends of the arrow between Lewis structures is used to show resonance
- ⇌: Double harpoons are used to designate equilibria
- ⇀: A single harpoon on one end indicates the movement of **one** electron
- →: A double headed arrow on one end is used to indicate the movement of **two** electrons

Example 7.5.2: Carbonate Ion

Identify the resonance structures for the carbonate ion: CO_3^{2-}.

Solution

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

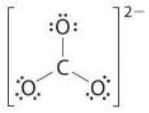


2. Carbon has 4 valence electrons, each oxygen has 6 valence electrons, and there are 2 more for the −2 charge. This gives 4 + (3 × 6) + 2 = 24 valence electrons.

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

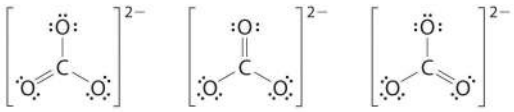


4. We divide the remaining 18 electrons equally among the three oxygen atoms by placing three lone pairs on each and indicating the −2 charge:

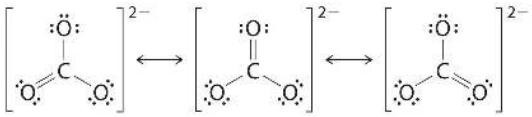


5. No electrons are left for the central atom.

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:



The actual structure is an average of these three resonance structures.

Like ozone, the electronic structure of the carbonate ion cannot be described by a single Lewis electron structure. Unlike O_3, though, the actual structure of CO_3^{2-} is an average of *three* resonance structures.

Using Formal Charges to Identify viable Resonance Structures

While each resonance structure contributes to the total electronic structure of the molecule, they may not contribute equally. Assigning Formal charges to atoms in the molecules is one mechanism to identify the viability of a resonance structure and determine its relative magnitude among other structures. The formal charge on an atom in a covalent species is the net charge the atom would bear if the electrons in all the bonds to the atom were equally shared. Alternatively the formal charge on an atom in a covalent species is the net charge the atom would bear if all bonds to the atom were nonpolar covalent bonds. To determine the formal charge on a given atom in a covalent species, use the following formula:

$$\begin{aligned}\textbf{Formal Charge} &= (\textbf{number of valence electrons in free orbital}) \\ &- (\textbf{number of lone-pair electrons}) - \frac{1}{2}(\textbf{ number bond pair electrons})\end{aligned} \tag{7.5.1}$$

Rules for estimating stability of resonance structures

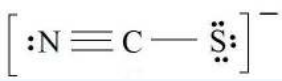
1. The **greater the number of covalent bonds**, the greater the stability since more atoms will have complete octets
2. The structure with the **least number of formal charges** is more stable
3. The structure with the **least separation of formal charge** is more stable
4. A structure with a **negative charge on the more electronegative atom** will be more stable
5. **Positive charges on the least electronegative atom** (most electropositive) is more stable
6. Resonance forms that are equivalent have no difference in stability and contribute equally (eg. benzene)

Example 7.5.3: Thiocyanate Ion

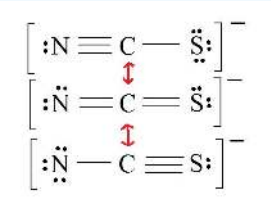
Consider the thiocyanate (CNS^-) ion.

Solution

1. Find the Lewis Structure of the molecule. (Remember the Lewis Structure rules.)



2. Resonance: All elements want an octet, and we can do that in multiple ways by moving the terminal atom's electrons around (bonds too).

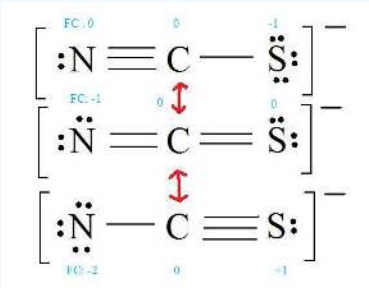


3. Assign Formal Charges via Equation 7.5.1.

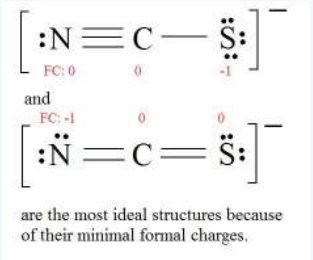
$$\text{Formal Charge} = (\text{number of valence electrons in free orbital}) - (\text{number of lone-pair electrons}) - \left(\tfrac{1}{2}\ \text{number bond pair electrons}\right)$$

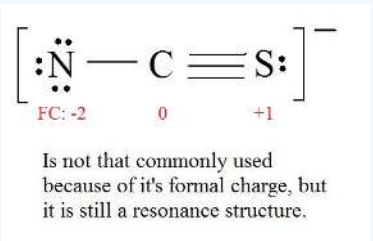
Remember to determine the number of valence electron each atom has before assigning Formal Charges

C = 4 valence e^-, N = 5 valence e^-, S = 6 valence e^-, also add an extra electron for the (-1) charge. The total of valence electrons is 16.



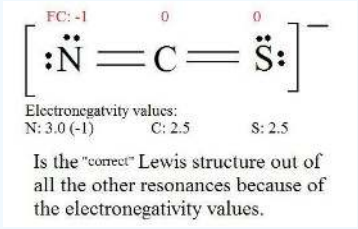
4. Find the most ideal resonance structure. (Note: It is the one with the least formal charges that adds up to zero or to the molecule's overall charge.)





5. Now we have to look at electronegativity for the "Correct" Lewis structure.

The most electronegative atom usually has the negative formal charge, while the least electronegative atom usually has the positive formal charges.



It is useful to combine the resonance structures into a single structure called the **Resonance Hybrid** that describes the bonding of the molecule. The general approach is described below:

1. Draw the Lewis Structure & Resonance for the molecule (using solid lines for bonds).
2. Where there **can** be a double or triple bond, draw a dotted line (-----) for the bond.
3. Draw only the lone pairs found in all resonance structures, do not include the lone pairs that are not on all of the resonance structures.

Example 7.5.4: Benzene

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

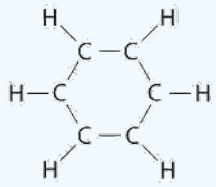
Asked for: resonance structures

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.

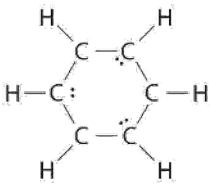
Solution:

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:



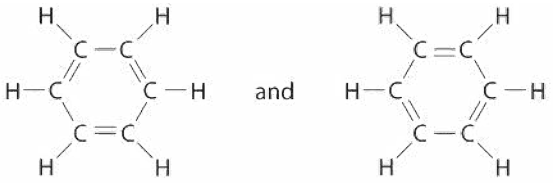
Each carbon atom in this structure has only 6 electrons and has a formal charge of +1, but we have used only 24 of the 30 valence electrons.

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

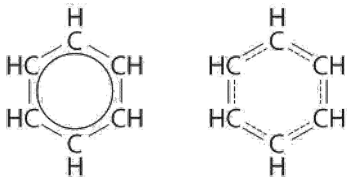


Three carbon atoms now have an octet configuration and a formal charge of −1, while three carbon atoms have only 6 electrons and a formal charge of +1. We can convert each lone pair to a bonding electron pair, which gives each atom an octet of electrons and a formal charge of 0, by making three C=C double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

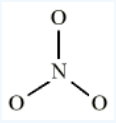
Example 7.5.5: Nitrate Ion

Draw the possible resonance structures for the Nitrate ion NO_3^-.

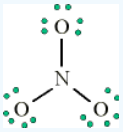
Solution

1. Count up the valence electrons: (1*5) + (3*6) + 1(ion) = **24** electrons

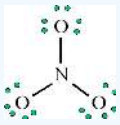
2. Draw the bond connectivities:



3. Add octet electrons to the atoms bonded to the center atom:

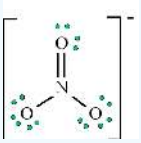


4. Place any leftover electrons (24-24 = **0**) on the center atom:



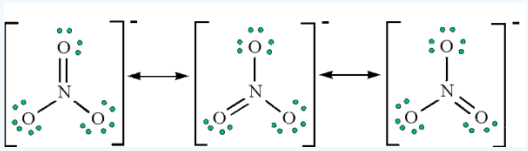
5. Does the central atom have an octet?

- **NO**, it has 6 electrons
- Add a multiple bond (first try a double bond) to see if the central atom can achieve an octet:



6. Does the central atom have an octet?

- YES
- Are there possible resonance structures? YES



Note: We would expect that the bond lengths in the NO_3^- ion to be somewhat shorter than a single bond.

References

1. Petrucci, Ralph H., et al. *General Chemistry: Principles and Modern Applications*. New Jersey: Pearson Prentice Hall, 2007.
2. Ahmad, Wan-Yaacob and Zakaria, Mat B. "Drawing Lewis Structures from Lewis Symbols: A Direct Electron Pairing Approach." Journal of Chemical Education: Journal 77.3.

Problems

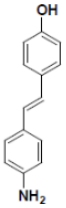
1. True or False, The picture below is a resonance structure?



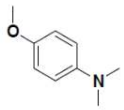
2. Draw the Lewis Dot Structure for SO_4^{2-} and all possible resonance structures. Which of the following resonance structure is not favored among the Lewis Structures? Explain why. Assign Formal Charges.
3. Draw the Lewis Dot Structure for CH_3COO^- and all possible resonance structures. Assign Formal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

Problems #2

Problems: Draw the resonance forms for the following structures

1. 
2. 
3. 
4. 

5



Based on resonance conformation which structure is more stable?

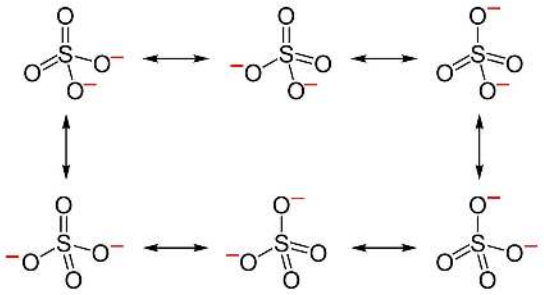
6



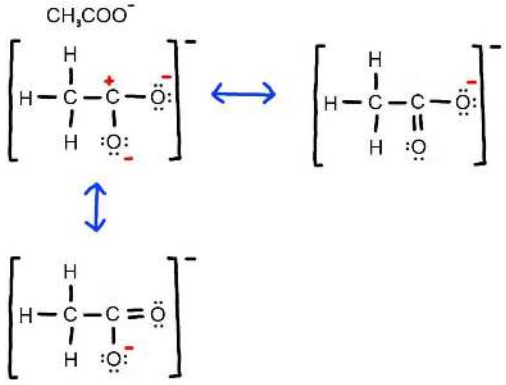
Answers

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

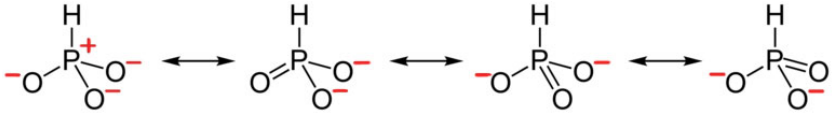
2. Below are the all Lewis dot structure with formal charges (in red) for Sulfate ($\mathbf{SO_4^{2-}}$). There isn't a most favorable resonance of the Sulfate ion because they are all identical in charge and there is no change in Electronegativity between the Oxygen atoms.



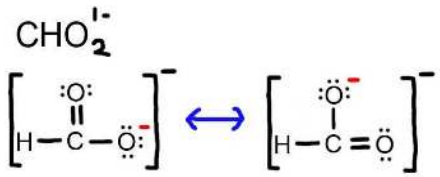
3. Below is the resonance for $\mathbf{CH_3COO^-}$, formal charges are displayed in red. The Lewis Structure with the most formal charges is not desirable, because we want the Lewis Structure with the least formal charge.



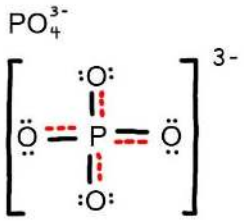
4. The resonance for $\mathbf{HPO_3^{2-}}$, and the formal charges (in red).



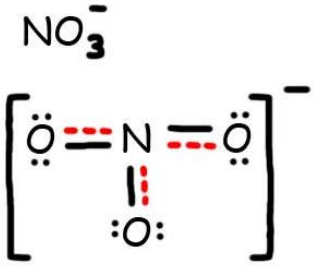
5. The resonance for $\mathbf{CHO_2^{1-}}$, and the formal charges (in red).



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

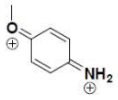


7. The resonance hybrid for $\mathbf{NO_3^-}$, hybrid bonds are in red.



Problems #2

5



6



This is more stable

Contributors and Attributions

- Sharon Wei (UCD), Liza Chu (UCD)

7.5: The Predicted Stabilities of Resonance Contributors is shared under a not declared license and was authored, remixed, and/or curated by LibreTexts.

- **Resonance** is licensed CC BY-NC-SA 4.0.

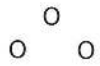
7.6: Delocalized Energy Is the Additional Stability Delocalized Electrons Give to a Compound

Resonance is a mental exercise within the Valence Bond Theory of bonding that describes the delocalization of electrons within molecules. It involves constructing multiple Lewis structures that, when combined, represent the full electronic structure of the molecule. **Resonance structures** are used when a single Lewis structure cannot fully describe the bonding; the combination of possible resonance structures is defined as a **resonance hybrid**, which represents the overall delocalization of electrons within the molecule. In general, molecules with multiple resonance structures will be more stable than one with fewer and some resonance structures contribute more to the stability of the molecule than others - formal charges aid in determining this.

Introduction

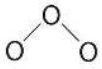
Resonance is a way of describing delocalized electrons within certain molecules or polyatomic ions where the bonding cannot be expressed by a single Lewis formula. A molecule or ion with such delocalized electrons is represented by several resonance structures. The nuclear skeleton of the Lewis Structure of these resonance structures remains the same, only the electron locations differ. Such is the case for ozone ($\mathbf{O_3}$), an allotrope of oxygen with a V-shaped structure and an O–O–O angle of 117.5°. Let's motivate the discussion by building the Lewis structure for ozone.

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



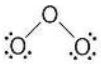
2. Each O atom has 6 valence electrons, for a total of 18 valence electrons.

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



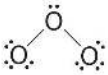
with 14 electrons left over.

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

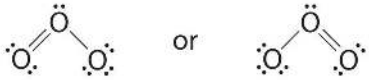


and have 2 electrons left over.

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

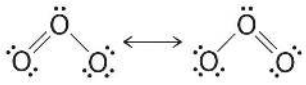


6. The central oxygen has only 6 electrons. We must convert one lone pair on a terminal oxygen atom to a bonding pair of electrons —but which one? Depending on which one we choose, we obtain either



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

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



The double-headed arrow indicates that the actual electronic structure is an *average* of those shown, not that the molecule oscillates between the two structures.

> *When it is possible to write more than one equivalent resonance structure for a molecule or ion, the actual structure is the average of the resonance structures.*

The electrons appear to "shift" between different resonance structures and while not strictly correct as each resonance structure is just a limitation of using the Lewis structure perspective to describe these molecules. A more accurate description of the electron structure of the molecule requires considering multiple resonance structures simultaneously.

Delocalization and Resonance Structures Rules

1. Resonance structures should have the same number of electrons, do not add or subtract any electrons. (check the number of electrons by simply counting them).
2. Each resonance structures follows the rules of writing Lewis Structures.
3. The hybridization of the structure must stay the same.
4. The skeleton of the structure can not be changed (only the electrons move).
5. Resonance structures must also have the same number of lone pairs.

"Pick the Correct Arrow for the Job"

Most arrows in chemistry cannot be used interchangeably and care must be given to selecting the correct arrow for the job.

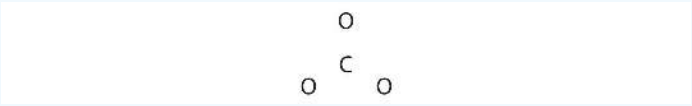
- ↔: A double headed arrow on both ends of the arrow between Lewis structures is used to show resonance
- ⇌: Double harpoons are used to designate equilibria
- ⇀: A single harpoon on one end indicates the movement of **one** electron
- →: A double headed arrow on one end is used to indicate the movement of **two** electrons

Example 7.6.2: Carbonate Ion

Identify the resonance structures for the carbonate ion: CO_3^{2-}.

Solution

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

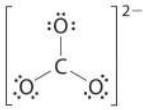


2. Carbon has 4 valence electrons, each oxygen has 6 valence electrons, and there are 2 more for the −2 charge. This gives 4 + (3 × 6) + 2 = 24 valence electrons.

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

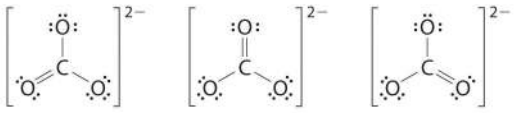


4. We divide the remaining 18 electrons equally among the three oxygen atoms by placing three lone pairs on each and indicating the −2 charge:

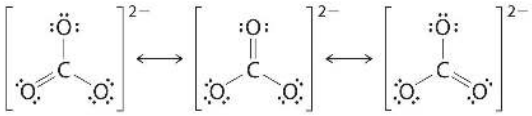


5. No electrons are left for the central atom.

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:



The actual structure is an average of these three resonance structures.

Like ozone, the electronic structure of the carbonate ion cannot be described by a single Lewis electron structure. Unlike O_3, though, the actual structure of CO_3^{2-} is an average of *three* resonance structures.

Using Formal Charges to Identify viable Resonance Structures

While each resonance structure contributes to the total electronic structure of the molecule, they may not contribute equally. Assigning Formal charges to atoms in the molecules is one mechanism to identify the viability of a resonance structure and determine its relative magnitude among other structures. The formal charge on an atom in a covalent species is the net charge the atom would bear if the electrons in all the bonds to the atom were equally shared. Alternatively the formal charge on an atom in a covalent species is the net charge the atom would bear if all bonds to the atom were nonpolar covalent bonds. To determine the formal charge on a given atom in a covalent species, use the following formula:

$$\begin{aligned}\text{Formal Charge} &= (\text{number of valence electrons in free orbital}) \\ &- (\text{number of lone-pair electrons}) - \frac{1}{2}(\text{ number bond pair electrons})\end{aligned} \tag{7.6.1}$$

Rules for estimating stability of resonance structures

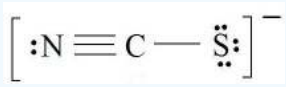
1. The **greater the number of covalent bonds**, the greater the stability since more atoms will have complete octets
2. The structure with the **least number of formal charges** is more stable
3. The structure with the **least separation of formal charge** is more stable
4. A structure with a **negative charge on the more electronegative atom** will be more stable
5. **Positive charges on the least electronegative atom** (most electropositive) is more stable
6. Resonance forms that are equivalent have no difference in stability and contribute equally (eg. benzene)

Example 7.6.3: Thiocyanate Ion

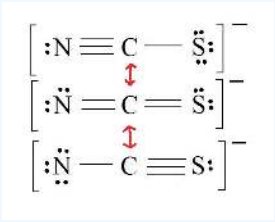
Consider the thiocyanate (CNS^-) ion.

Solution

1. Find the Lewis Structure of the molecule. (Remember the Lewis Structure rules.)



2. Resonance: All elements want an octet, and we can do that in multiple ways by moving the terminal atom's electrons around (bonds too).

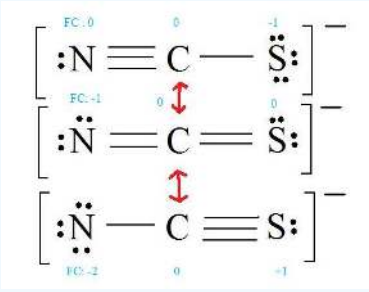


3. Assign Formal Charges via Equation 7.6.1.

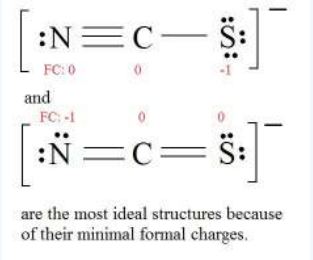
$$\text{Formal Charge} = (\text{number of valence electrons in free orbital}) - (\text{number of lone-pair electrons}) - \left(\tfrac{1}{2}\ \text{number bond pair electrons}\right)$$

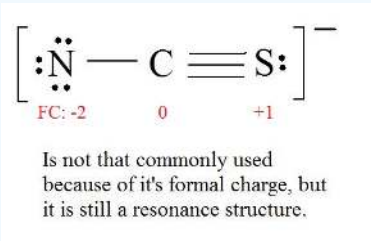
Remember to determine the number of valence electron each atom has before assigning Formal Charges

C = 4 valence e^-, N = 5 valence e^-, S = 6 valence e^-, also add an extra electron for the (-1) charge. The total of valence electrons is 16.



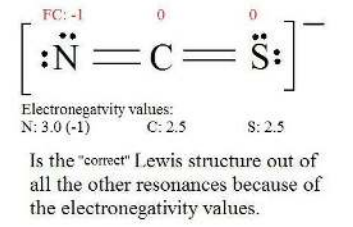
4. Find the most ideal resonance structure. (Note: It is the one with the least formal charges that adds up to zero or to the molecule's overall charge.)





5. Now we have to look at electronegativity for the "Correct" Lewis structure.

The most electronegative atom usually has the negative formal charge, while the least electronegative atom usually has the positive formal charges.



It is useful to combine the resonance structures into a single structure called the **Resonance Hybrid** that describes the bonding of the molecule. The general approach is described below:

1. Draw the Lewis Structure & Resonance for the molecule (using solid lines for bonds).
2. Where there **can** be a double or triple bond, draw a dotted line (-----) for the bond.
3. Draw only the lone pairs found in all resonance structures, do not include the lone pairs that are not on all of the resonance structures.

Example 7.6.4: Benzene

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

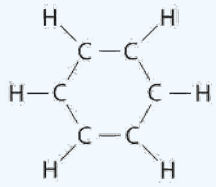
Asked for: resonance structures

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.

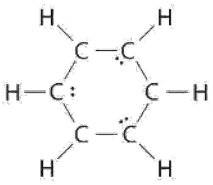
Solution:

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:



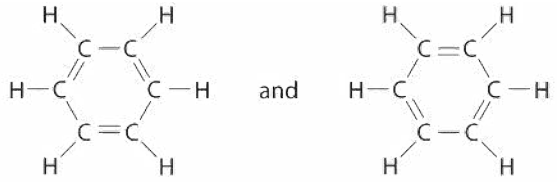
Each carbon atom in this structure has only 6 electrons and has a formal charge of +1, but we have used only 24 of the 30 valence electrons.

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

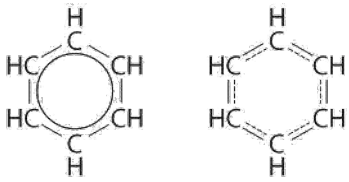


Three carbon atoms now have an octet configuration and a formal charge of −1, while three carbon atoms have only 6 electrons and a formal charge of +1. We can convert each lone pair to a bonding electron pair, which gives each atom an octet of electrons and a formal charge of 0, by making three C=C double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

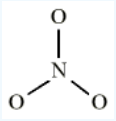
Example 7.6.5: Nitrate Ion

Draw the possible resonance structures for the Nitrate ion $\mathbf{NO_3^-}$.

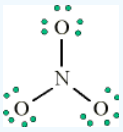
Solution

1. Count up the valence electrons: (1*5) + (3*6) + 1(ion) = **24** electrons

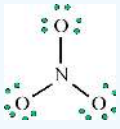
2. Draw the bond connectivities:



3. Add octet electrons to the atoms bonded to the center atom:

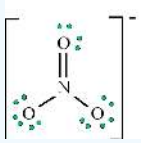


4. Place any leftover electrons (24-24 = **0**) on the center atom:



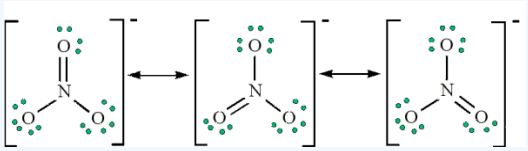
5. Does the central atom have an octet?

- **NO**, it has 6 electrons
- Add a multiple bond (first try a double bond) to see if the central atom can achieve an octet:



6. Does the central atom have an octet?

- YES
- Are there possible resonance structures? YES



Note: We would expect that the bond lengths in the NO_3^- ion to be somewhat shorter than a single bond.

References

1. Petrucci, Ralph H., et al. *General Chemistry: Principles and Modern Applications*. New Jersey: Pearson Prentice Hall, 2007.
2. Ahmad, Wan-Yaacob and Zakaria, Mat B. "Drawing Lewis Structures from Lewis Symbols: A Direct Electron Pairing Approach." Journal of Chemical Education: Journal 77.3.

Problems

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



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

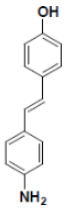
Problems #2

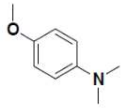
Problems: Draw the resonance forms for the following structures

1. 

2 

3 

4 

5 

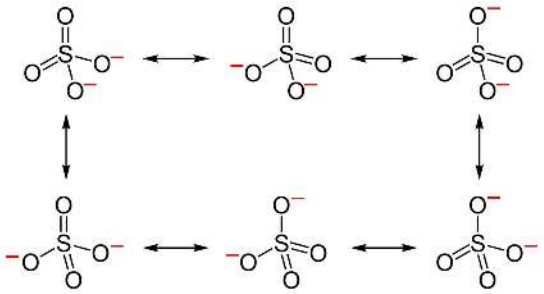
Based on resonance conformation which structure is more stable?

6 

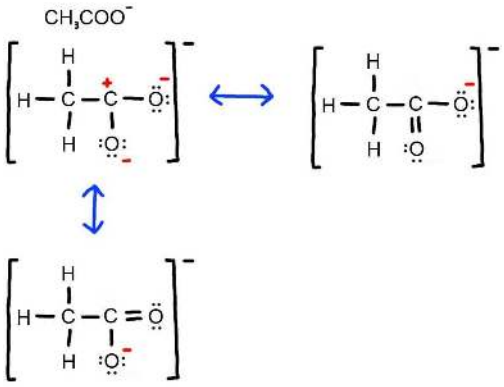
Answers

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

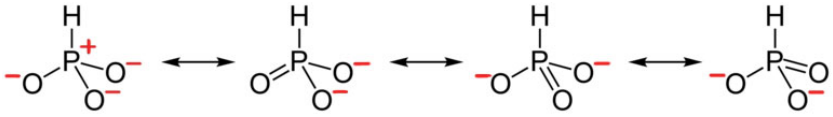
2. Below are the all Lewis dot structure with formal charges (in red) for Sulfate ($\mathbf{SO_4^{2-}}$). There isn't a most favorable resonance of the Sulfate ion because they are all identical in charge and there is no change in Electronegativity between the Oxygen atoms.



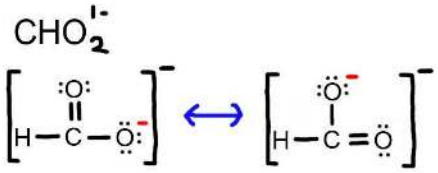
3. Below is the resonance for $\mathbf{CH_3COO^-}$, formal charges are displayed in red. The Lewis Structure with the most formal charges is not desirable, because we want the Lewis Structure with the least formal charge.



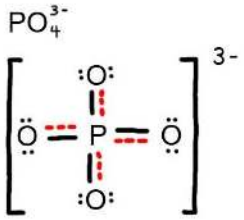
4. The resonance for **HPO_3^{2-}**, and the formal charges (in red).



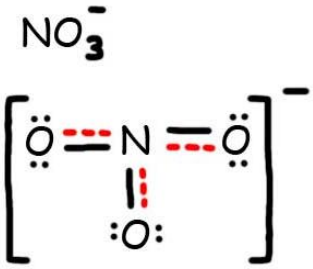
5. The resonance for **CHO_2^{1-}**, and the formal charges (in red).



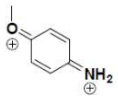
6. The resonance hybrid for **PO_4^{3-}**, hybrid bonds are in red.



7. The resonance hybrid for **NO_3^-**, hybrid bonds are in red.



Problems #2

5 

6 

This is more stable

Contributors and Attributions

- Sharon Wei (UCD), Liza Chu (UCD)

7.6: Delocalized Energy Is the Additional Stability Delocalized Electrons Give to a Compound is shared under a not declared license and was authored, remixed, and/or curated by LibreTexts.

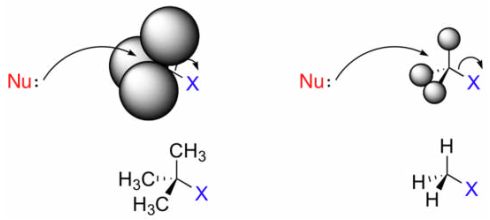
- **Resonance** is licensed CC BY-NC-SA 4.0.

7.7: Examples That Show How Delocalized Electrons Affect Stability

In the vast majority of the nucleophilic substitution reactions you will see in this and other organic chemistry texts, the electrophilic atom is a carbon which is bonded to an electronegative atom, usually oxygen, nitrogen, sulfur, or a halogen. The concept of electrophilicity is relatively simple: an electron-poor atom is an attractive target for something that is electron-rich, *i.e.* a nucleophile. However, we must also consider the effect of steric hindrance on electrophilicity. In addition, we must discuss how the nature of the electrophilic carbon, and more specifically the stability of a potential carbocationic intermediate, influences the S_N1 vs. S_N2 character of a nucleophilic substitution reaction.

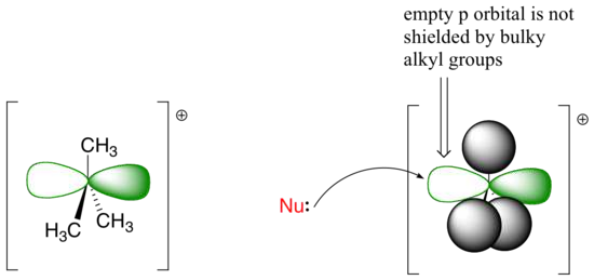
8.4A: Steric effects on electrophilicity

Consider two hypothetical S_N2 reactions: one in which the electrophile is a methyl carbon and another in which it is tertiary carbon.



Because the three substituents on the methyl carbon electrophile are tiny hydrogens, the nucleophile has a relatively clear path for backside attack. However, backside attack on the tertiary carbon is blocked by the bulkier methyl groups. Once again, steric hindrance - this time caused by bulky groups attached to the electrophile rather than to the nucleophile - hinders the progress of an associative nucleophilic (S_N2) displacement.

The factors discussed in the above paragraph, however, do not prevent a sterically-hindered carbon from being a good electrophile - they only make it less likely to be attacked in a *concerted S_N2 reaction*. Nucleophilic substitution reactions in which the electrophilic carbon is sterically hindered are more likely to occur by a two-step, dissociative (S_N1) mechanism. This makes perfect sense from a geometric point of view: the limitations imposed by sterics are significant mainly in an S_N2 displacement, when the electrophile being attacked is a sp^3-hybridized tetrahedral carbon with its relatively 'tight' angles of 109.4º. Remember that in an S_N1 mechanism, the nucleophile attacks an sp^2-hybridized carbocation intermediate, which has trigonal planar geometry with 'open' 120 angles.



With this open geometry, the empty p orbital of the electrophilic carbocation is no longer significantly shielded from the approaching nucleophile by the bulky alkyl groups. A carbocation is a very potent electrophile, and the nucleophilic step occurs very rapidly compared to the first (ionization) step.

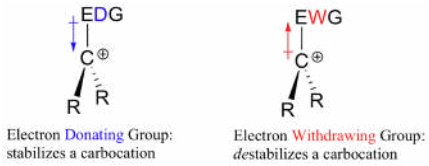
8.4B: Stability of carbocation intermediates

We know that the rate-limiting step of an S_N1 reaction is the first step - formation of the this carbocation intermediate. The rate of this step – and therefore, the rate of the overall substitution reaction – depends on the activation energy for the process in which the bond between the carbon and the leaving group breaks and a carbocation forms. According to Hammond's postulate (section 6.2B), the more stable the carbocation intermediate is, the faster this first bond-breaking step will occur. In other words, the likelihood of a nucleophilic substitution reaction proceeding by a dissociative (S_N1) mechanism depends to a large degree on the stability of the carbocation intermediate that forms.

The critical question now becomes, *what stabilizes a carbocation*?

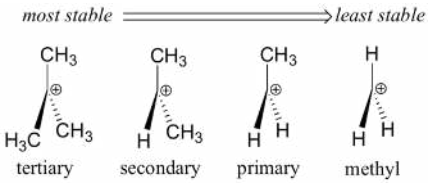
Think back to Chapter 7, when we were learning how to evaluate the strength of an acid. The critical question was "how stable is the conjugate base that results when this acid donates its proton"? In many cases, this conjugate base was an anion – a center of excess electron density. Anything that can draw some of this electron density away– in other words, any electron withdrawing group – will stabilize the anion.

So if it takes an electron *withdrawing* group to stabilize a negative charge, what will stabilize a positive charge? An electron *donating* group!



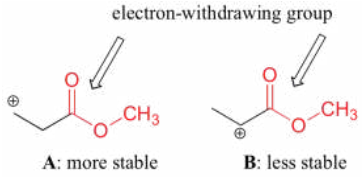
A positively charged species such as a carbocation is very electron-poor, and thus anything which donates electron density to the center of electron poverty will help to stabilize it. Conversely, a carbocation will be *destabilized* by an electron withdrawing group.

Alkyl groups – methyl, ethyl, and the like – are weak electron donating groups, and thus stabilize nearby carbocations. What this means is that, in general, *more substituted carbocations are more stable*: a tert-butyl carbocation, for example, is more stable than an isopropyl carbocation. Primary carbocations are highly unstable and not often observed as reaction intermediates; methyl carbocations are even less stable.



Alkyl groups are electron donating and carbocation-stabilizing because the electrons around the neighboring carbons are drawn towards the nearby positive charge, thus slightly reducing the electron poverty of the positively-charged carbon.

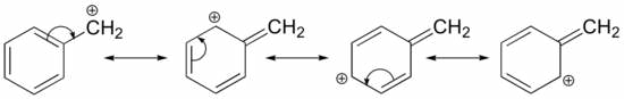
It is not accurate to say, however, that carbocations with higher substitution are *always* more stable than those with less substitution. Just as electron-donating groups can stabilize a carbocation, electron-withdrawing groups act to destabilize carbocations. Carbonyl groups are electron-withdrawing by inductive effects, due to the polarity of the C=O double bond. It is possible to demonstrate in the laboratory (see section 16.1D) that carbocation A below is more stable than carbocation B, even though A is a primary carbocation and B is secondary.



The difference in stability can be explained by considering the electron-withdrawing inductive effect of the ester carbonyl. Recall that inductive effects - whether electron-withdrawing or donating - are relayed through covalent bonds and that the strength of the effect decreases rapidly as the number of intermediary bonds increases. In other words, the effect decreases with distance. In species B the positive charge is closer to the carbonyl group, thus the destabilizing electron-withdrawing effect is stronger than it is in species A.

In the next chapter we will see how the carbocation-destabilizing effect of electron-withdrawing fluorine substituents can be used in experiments designed to address the question of whether a biochemical nucleophilic substitution reaction is S_N1 or S_N2.

Stabilization of a carbocation can also occur through resonance effects, and as we have already discussed in the acid-base chapter, resonance effects as a rule are more powerful than inductive effects. Consider the simple case of a **benzylic** carbocation:

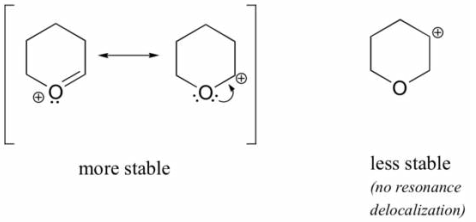


This carbocation is comparatively stable. In this case, electron donation is a resonance effect. Three additional resonance structures can be drawn for this carbocation in which the positive charge is located on one of three aromatic carbons. The positive charge is not isolated on the benzylic carbon, rather it is delocalized around the aromatic structure: this delocalization of charge results in significant stabilization. As a result, benzylic and **allylic** carbocations (where the positively charged carbon is conjugated to one or more non-aromatic double bonds) are significantly more stable than even tertiary alkyl carbocations.



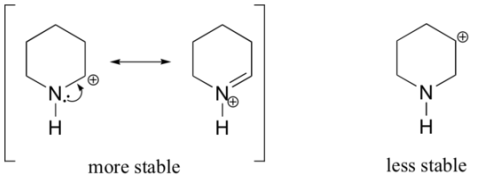
an allylic carbocation

Because heteroatoms such as oxygen and nitrogen are more electronegative than carbon, you might expect that they would by definition be electron withdrawing groups that destabilize carbocations. In fact, the opposite is often true: if the oxygen or nitrogen atom is in the correct position, the overall effect is carbocation stabilization. This is due to the fact that although these heteroatoms are electron *withdrawing* groups by induction, they are electron *donating* groups by resonance, and it is this resonance effect which is more powerful. (We previously encountered this same idea when considering the relative acidity and basicity of phenols and aromatic amines in section 7.4). Consider the two pairs of carbocation species below:



more stable

less stable
(no resonance delocalization)

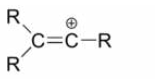


more stable

less stable
(no resonance delocalization)

In the more stable carbocations, the heteroatom acts as an electron donating group by resonance: in effect, the lone pair on the heteroatom is available to delocalize the positive charge. In the less stable carbocations the positively-charged carbon is more than one bond away from the heteroatom, and thus no resonance effects are possible. In fact, in these carbocation species the heteroatoms actually *destabilize* the positive charge, because they are electron withdrawing by induction.

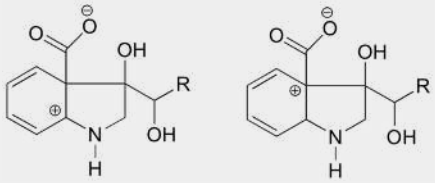
Finally, **vinylic** carbocations, in which the positive charge resides on a double-bonded carbon, are very unstable and thus unlikely to form as intermediates in any reaction.



a vinylic carbocation
(very unstable)

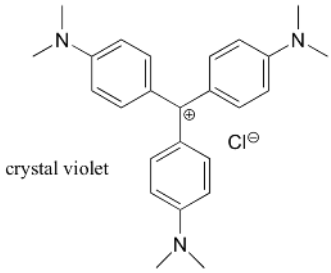
Example 8.10

Exercise 8.10: In which of the structures below is the carbocation expected to be more stable? Explain.



Solution

For the most part, carbocations are very high-energy, transient intermediate species in organic reactions. However, there are some unusual examples of very stable carbocations that take the form of organic salts. Crystal violet is the common name for the chloride salt of the carbocation whose structure is shown below. Notice the structural possibilities for extensive resonance delocalization of the positive charge, and the presence of three electron-donating amine groups.



Example 8.11

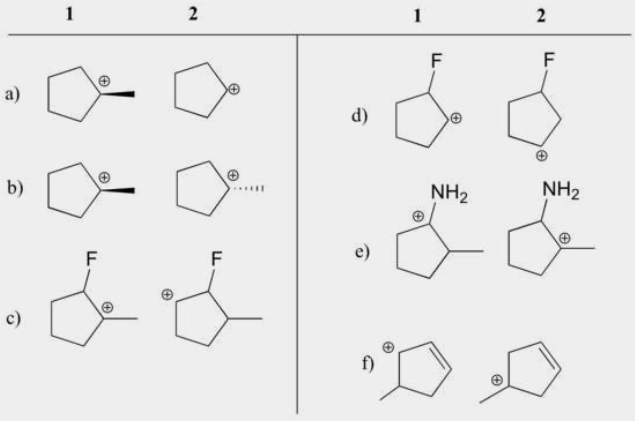
Draw a resonance structure of the crystal violet cation in which the positive charge is delocalized to one of the nitrogen atoms.

Solution

When considering the possibility that a nucleophilic substitution reaction proceeds *via* an S_N1 pathway, it is critical to evaluate the stability of the hypothetical carbocation intermediate. If this intermediate is not sufficiently stable, an S_N1 mechanism must be considered unlikely, and the reaction probably proceeds by an S_N2 mechanism. In the next chapter we will see several examples of biologically important S_N1 reactions in which the positively charged intermediate is stabilized by inductive and resonance effects inherent in its own molecular structure.

Example 8.12

State which carbocation in each pair below is more stable, or if they are expected to be approximately equal. Explain your reasoning.



Solution

Organic Chemistry With a Biological Emphasis by Tim Soderberg (University of Minnesota, Morris)

Further Reading

MasterOrganicChemistry

Introduction to Rearrangement Reactions

Rearrangement Reactions – Hydride Shifts

Rearrangement Reactions – Alkyl Shifts

3 Factors That Stabilize Carbocations

Carey 4th Edition On-Line Activity

Properties and Structures of Carbocations

Khan Academy

Properties and Structures of Carbocations

Web Pages

Relative stabilities of carbocations

Practice Problems

Carbocation rearrangement practice

7.7: Examples That Show How Delocalized Electrons Affect Stability is shared under a not declared license and was authored, remixed, and/or curated by LibreTexts.

7.8: A Molecular Orbital Description of Stability

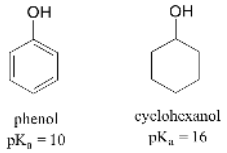
Molecular orbitals

7.8: A Molecular Orbital Description of Stability is shared under a not declared license and was authored, remixed, and/or curated by LibreTexts.

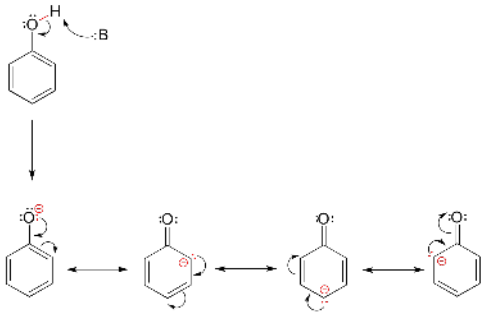
7.9: How Delocalized Electrons Affect pKa Values

Resonance effects on acidity

Resonance effects involving aromatic structures can have a dramatic influence on acidity and basicity. Notice, for example, the difference in acidity between phenol and cyclohexanol.



Looking at the conjugate base of phenol, we see that the negative charge can be delocalized by resonance to three different carbons on the aromatic ring.

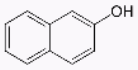


Although these are all minor resonance contributors (negative charge is placed on a carbon rather than the more electronegative oxygen), they nonetheless have a significant effect on the acidity of the phenolic proton. Essentially, the benzene ring is acting as an electron-withdrawing group by resonance.

As we begin to study in detail the mechanisms of biological organic reactions, we'll see that the phenol side chain of the amino acid tyrosine (see table 5 at the back of the book), with its relatively acidic $pK_a$of 9-10, often acts as a catalytic proton donor/acceptor in enzyme active sites.

Exercise 7.4.1

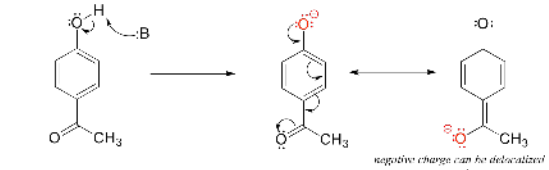
Draw the conjugate base of 2-napthol (the major resonance contributor), and on your drawing indicate with arrows all of the atoms to which the negative charge can be delocalized by resonance.



2-napthol

Solution

The base-stabilizing effect of an aromatic ring can be accentuated by the presence of an additional electron-withdrawing substituent, such as a carbonyl. For the conjugate base of the phenol derivative below, an additional resonance contributor can be drawn in which the negative formal charge is placed on the carbonyl oxygen.



para-hydroxyacetophenone
(pKa = 4.2)

Now the negative charge on the conjugate base can be spread out over *two* oxygens (in addition to three aromatic carbons). The phenol acid therefore has a pK_a similar to that of a carboxylic acid, where the negative charge on the conjugate base is also

delocalized to two oxygen atoms. The ketone group is acting as an electron withdrawing group - it is 'pulling' electron density towards itself, through both inductive and resonance effects.

Exercise 7.4.2

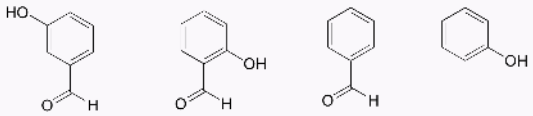
The position of the electron-withdrawing substituent relative to the phenol hydroxyl is very important in terms of its effect on acidity. Which of the two substituted phenols below is more acidic? Use resonance drawings to explain your answer.



Solution

Exercise 7.4.3

Rank the four compounds below from most acidic to least.



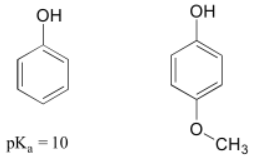
Solution

Exercise 7.4.4

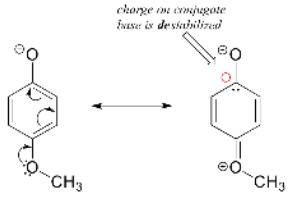
Nitro groups are very powerful electron-withdrawing groups. The phenol derivative picric acid (2,4,6 -trinitrophenol) has a pK_a of 0.25, lower than that of trifluoroacetic acid. Use a resonance argument to explain why picric acid has such a low pK_a.

Solution

Consider the acidity of 4-methoxyphenol, compared to phenol:



Notice that the methoxy group increases the pK_a of the phenol group - it makes it *less* acidic. Why is this? At first inspection, you might assume that the methoxy substituent, with its electronegative oxygen, would be an electron-withdrawing group by induction. That is correct, but only to a point. The oxygen atom does indeed exert an electron-withdrawing inductive effect, but the lone pairs on the oxygen cause the exact opposite effect – *the methoxy group is an* ***electron-donating group by resonance***. A resonance contributor can be drawn in which a formal negative charge is placed on the carbon adjacent to the negatively-charged phenolate oxygen.



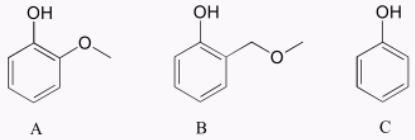
Because of like-charge repulsion, this *destabilizes* the negative charge on the phenolate oxygen, making it more basic. It may help to visualize the methoxy group ‘pushing’ electrons towards the lone pair electrons of the phenolate oxygen, causing them to be less 'comfortable' and more reactive. The example above is a somewhat confusing but quite common situation in organic chemistry - a functional group, in this case a methoxy group, is exerting both an inductive effect and a resonance effect, *but in opposite directions* (the inductive effect is electron-withdrawing, the resonance effect is electron-donating). As a general rule a resonance

effect is more powerful than an inductive effect - so overall, the methoxy group is acting as an electron donating group. A good rule of thumb to remember:

When resonance and induction compete, resonance usually wins!

Exercise 7.4.5

Rank the three compounds below from lowest pKa to highest, and explain your reasoning. *Hint* - think about both resonance and inductive effects!



A B C

Solution

Next section⇒

Organic Chemistry With a Biological Emphasis by Tim Soderberg (University of Minnesota, Morris)

7.9: How Delocalized Electrons Affect pKa Values is shared under a not declared license and was authored, remixed, and/or curated by LibreTexts.

SECTION OVERVIEW

7.10: Delocalized Electrons Can Affect the Product of a Reaction

Topic hierarchy

7.10: Delocalized Electrons Can Affect the Product of a Reaction is shared under a not declared license and was authored, remixed, and/or curated by LibreTexts.

SECTION OVERVIEW

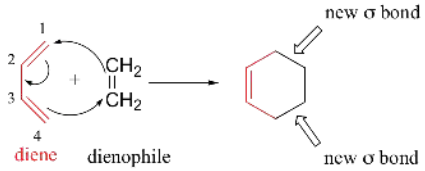
7.11: Thermodynamic Versus Kinetic Control of Reactions

Topic hierarchy

7.11: Thermodynamic Versus Kinetic Control of Reactions is shared under a not declared license and was authored, remixed, and/or curated by LibreTexts.

7.12: The Diels-Adler Reaction Is a 1,4-Addition Reaction

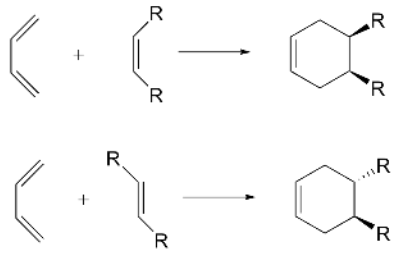
We end this chapter with a discussion of a type of reaction that is different from anything we have seen before. In the Diels-Alder cycloaddition reaction, a conjugated diene reacts with an alkene to form a ring structure.



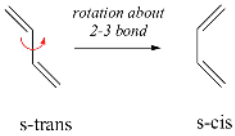
In a Diels-Alder reaction, the alkene reacting partner is referred to as the **dienophile**. Essentially, this process involves overlap of the 2p orbitals on carbons 1 and 4 of the diene with 2p orbitals on the two sp^2-hybridized carbons of the dienophile. Both of these new overlaps end up forming new sigma bonds, and a new pi bond is formed between carbon 2 and 3 of the diene.

One of the most important things to understand about this process is that it is *concerted* – all of the electron rearrangement takes place at once, with no carbocation intermediates.

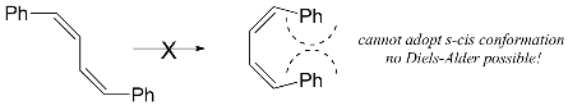
The Diels-Alder reaction is enormously useful for synthetic organic chemists, not only because ring-forming reactions are useful in general but also because in many cases two new stereocenters are formed, and the reaction is inherently stereospecific. A *cis* dienophile will generate a ring with *cis* substitution, while a *trans* dienophile will generate a ring with *trans* substitution:



In order for a Diels-Alder reaction to occur, the diene molecule must adopt what is called the **s-cis conformation**:



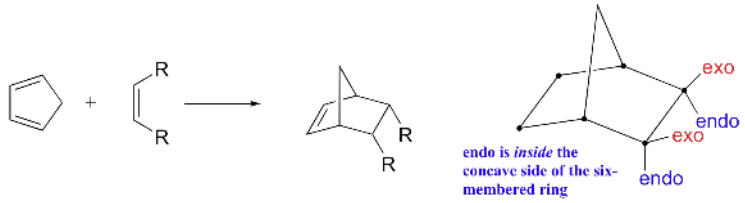
The s-cis conformation is higher in energy than the s-trans conformation, due to steric hindrance. For some dienes, extreme steric hindrance causes the s-cis conformation to be highly strained, and for this reason such dienes do not readily undergo Diels-Alder reactions.



Cyclic dienes, on the other hand, are 'locked' in the s-cis conformation, and are especially reactive. The result of a Diels-Alder reaction involving a cyclic diene is a **bicyclic** structure:

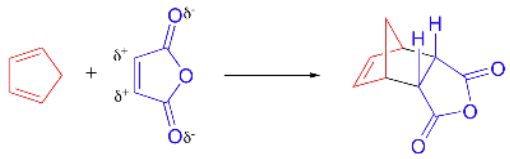


Here, we see another element of stereopecificity: Diels-Alder reactions with cyclic dienes favor the formation of bicyclic structures in which substituents are in the **endo position**.



The endo position on a bicyclic structure refers to the position that is *inside* the concave shape of the larger (six-membered) ring. As you might predict, the **exo position** refers to the *outside* position.

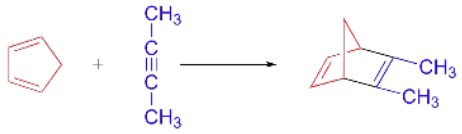
The rate at which a Diels-Alder reaction takes place depends on electronic as well as steric factors. A particularly rapid Diels-Alder reaction takes place between cyclopentadiene and maleic anhydride.



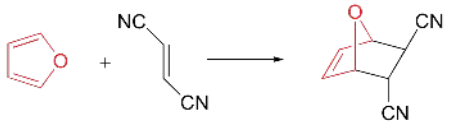
We already know that cyclopentadiene is a good diene because of its inherent s-cis conformation. Maleic anhydride is also a very good dienophile, because the electron-withdrawing effect of the carbonyl groups causes the two alkene carbons to be electron-poor, and thus a good target for attack by the pi electrons in the diene.

In general, Diels-Alder reactions proceed fastest with electron-donating groups on the diene (eg. alkyl groups) and electron-withdrawing groups on the dienophile.

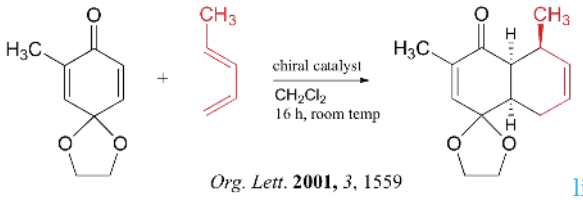
Alkynes can also serve as dienophiles in Diels-Alder reactions:



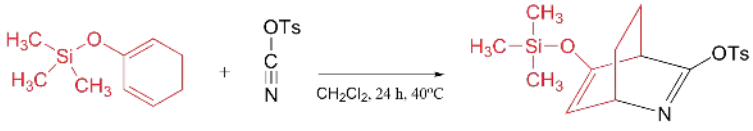
Below are just three examples of Diels-Alder reactions that have been reported in recent years:



J. Med. Chem. **2008,** *51*, 424 link



Org. Lett. **2001,** *3*, 1559 link



J. Org. Chem. **2003,** *68*, 8256 link

The Diels-Alder reaction is just one example of a **pericyclic** reaction: this is a general term that refers to concerted rearrangements that proceed though cyclic transition states. Two well-studied intramolecular pericyclic reactions are known as the Cope rearrangement . . .

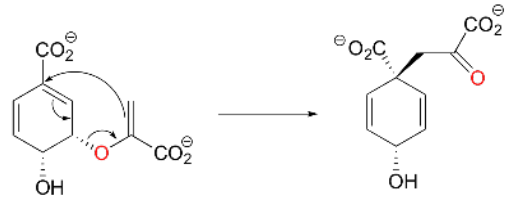


. . .and the Claisen rearrangement (when an oxygen is involved):



Notice that the both of these reactions require compounds in which two double bonds are separated by three single bonds.

Pericyclic reactions are rare in biological chemistry, but here is one example: the Claisen rearrangement catalyzed by chorismate mutase in the aromatic amino acid biosynthetic pathway.



chorismate prephenate

The study of pericyclic reactions is an area of physical organic chemistry that blossomed in the mid-1960s, due mainly to the work of R.B. Woodward, Roald Hoffman, and Kenichi Fukui. The **Woodward-Hoffman rules** for pericyclic reactions (and a simplified version introduced by Fukui) use molecular orbital theory to explain why some pericyclic processes take place and others do not. A full discussion is beyond the scope of this text, but if you go on to study organic chemistry at the advanced undergraduate or graduate level you are sure to be introduced to this fascinating area of inquiry.

Organic Chemistry With a Biological Emphasis by Tim Soderberg (University of Minnesota, Morris)

7.12: The Diels-Adler Reaction Is a 1,4-Addition Reaction is shared under a not declared license and was authored, remixed, and/or curated by LibreTexts.

CHAPTER OVERVIEW

8: Aromaticity- Reactions of Benzene and Substituted Benzenes



Essential Organic Chemistry: 2nd Ed.
Bruice

Homework Problems
Homework Solutions

I II III IV V VI VII VIII IX X XI XII XIII XIV XV XVI XVII XVIII XIX XX XXI

Template:HideTOC

8.1: The Two Criteria for Aromaticity
8.2: Applying the Criteria for Aromaticity
8.3: Aromatic Heterocyclic Compounds
8.4: The Nomenclature of Monosubstituted Benzenes
8.5: How Benzene Reacts
8.6: The General Mechanism for Electrophilic Aromatic Substitution Reactions
8.7: Halogenation of Benzene
8.8: Nitration of Benzene
8.9: Sulfonation of Benzene
8.10: The Friedel-Crafts Acylation of Benzene
8.11: The Friedel-Crafts Alkylation of Benzene
8.12: The Nomenclature of Disubstituted and Polysubstituted Benzenes
8.13: The Effect of Substituents on Reactivity
8.14: The Effect of Substituents on Orientation
8.15: The Effect of Substituents on pKa

8: Aromaticity- Reactions of Benzene and Substituted Benzenes is shared under a not declared license and was authored, remixed, and/or curated by LibreTexts.

8.1: The Two Criteria for Aromaticity

This page was auto-generated because a user created a sub-page to this page.

8.1: The Two Criteria for Aromaticity is shared under a not declared license and was authored, remixed, and/or curated by LibreTexts.

- **Aromaticity** is licensed CC BY-NC-SA 4.0.

8.2: Applying the Criteria for Aromaticity

Other Aromatic Systems

8.2: Applying the Criteria for Aromaticity is shared under a not declared license and was authored, remixed, and/or curated by LibreTexts.

8.3: Aromatic Heterocyclic Compounds

Other Aromatic Systems

8.3: Aromatic Heterocyclic Compounds is shared under a not declared license and was authored, remixed, and/or curated by LibreTexts.

8.4: The Nomenclature of Monosubstituted Benzenes

Benzene, C_6H_6, is an organic aromatic compound with many interesting properties. Unlike aliphatic (straight chain carbons) or other cyclic organic compounds, the structure of benzene (3 conjugated π bonds) allows benzene and its derived products to be useful in fields such as health, laboratory, and other applications such as rubber synthesis.

Introduction

Benzene derived products are well known to be pleasantly fragrant. For this reason, organic compounds containing benzene rings were classified as being "aromatic" (sweet smelling) amongst scientists in the early 19th century when a relation was established between benzene derived compounds and sweet/spicy fragrances. There is a misconception amongst the scientific community, however, that all aromatics are sweet smelling and that all sweet smelling compounds would have a benzene ring in its structure. This is false, since non-aromatic compounds, such as camphor, extracted from the camphor laurel tree, release a strong, minty aroma, yet it lacks the benzene ring in its structure (Figure 1). On the other hand, benzene itself gives off a rather strong and unpleasant smell that would otherwise invalidate the definition of an aromatic (sweet-smelling) compound. Despite this inconsistency, however, the term aromatic continues to be used today in order to designate molecules with benzene-like rings in their structures. For a modern, chemical definition of aromaticity, refer to sections Aromaticity and Hückel's Rule.

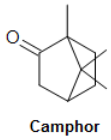


Figure 1. *Top-view of camphor, along with its* ***monoterpene*** *unit. Notice how camphor lacks the benzene ring to be "aromatic".*

Many aromatic compounds are however, sweet/pleasant smelling. Eugenol, for example, is extracted from essential oils of cloves and it releases a spicy, clove-like aroma used in perfumes. In addition, it is also used in dentistry as an analgesic.

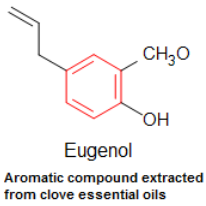


Figure 2. *Eugenol, an aromatic compound extracted from clove essential oils. Used in perfumes and as an analgesic. The benzene ring is labeled in red in the eugenol molecule.*

Is it cyclohexane or is it benzene?

Due to the similarity between benzene and cyclohexane, the two is often confused with each other in beginning organic chemistry students.

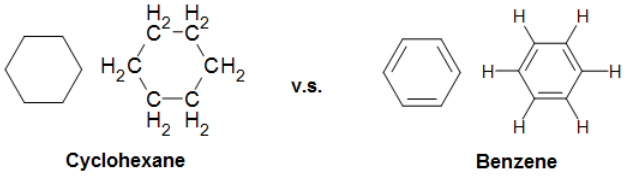


Figure 3. *Structure comparison between cyclohexane and benzene*

If you were to count the number of carbons and hydrogens in **cyclohexane**, you will notice that its molecular formula is $\mathbf{C_6H_{12}}$. Since the carbons in the **cyclohexane** ring is **fully saturated** with hydrogens (carbon is bound to 2 hydrogens and 2 adjacent carbons), no double bonds are formed in the cyclic ring. In contrast, **benzene** is only saturated with one hydrogen per carbon,

leading to its molecular formula of C_6H_6. In order to stabilize this structure, 3 conjugated π (double) bonds are formed in the benzene ring in order for carbon to have four adjacent bonds.

> *In other words, cyclohexane is not the same as benzene! These two compounds have different molecular formulas and their chemical and physical properties are not the same. The **hydrogenation** technique can be used by chemists to convert from benzene to cyclohexane by saturating the benzene ring with missing hydrogens.*

A special catalyst is required to hydrogenate benzene rings due to its unusual stability and configuration. Normal catalytic hydrogenation techniques will not hydrogenate benzene and yield any meaningful products.

What about Resonance?

Benzene can be drawn a number of different ways. This is because benzene's conjugated pi electrons freely resonate within the cyclic ring, thus resulting in its two resonance forms.

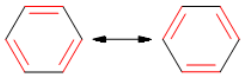


Figure 4. *The Figure to the left shows the two resonance forms of benzene. The **delocalized electrons** are moved from one carbon to the next, thus providing **stabilization** energy. Ring structures stabilized by the movement of delocalized electrons are sometimes referred to as **arenes**.*



As the electrons in the benzene ring can resonate within the ring at a fairly high rate, a simplified notation is often used to designate the two different resonance forms. This notation is shown above, with the initial three pi bonds (#1, #2) replaced with an inner ring circle (#3). Alternatively, the circle within the benzene ring can also be dashed to show the same resonance forms (#4).

The Formation of the Phenyl Group and its Derivatives

The phenyl group can be formed by taking benzene, and removing a hydrogen from it. The resulting molecular formula for the fragment is C_6H_5. NOTE: Although the molecular formula of the phenyl group is C_6H_5, the phenyl group would always have something attached to where the hydrogen was removed. Thus, the formula is often written as Ph-R, where Ph refers to the Phenyl group, and R refers to the R group attached to where the hydrogen was removed.

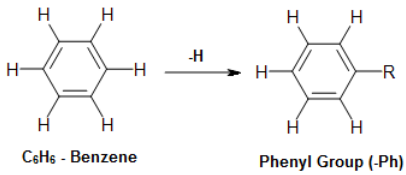


Figure 5. *Figure demonstrating the removal of hydrogen to form the phenyl group.*

Different R groups on the phenyl group allows different benzene derivatives to be formed. Phenol, Ph-OH, or C_6H_5OH, for example, is formed when an alcohol (-OH) group displaces a hydrogen atom on the benzene ring. Benzene, for this very same reason, can be formed from the phenyl group by reattaching the hydrogen back its place of removal. Thus benzene, similar to phenol, can be abbreviated Ph-H, or C_6H_6.

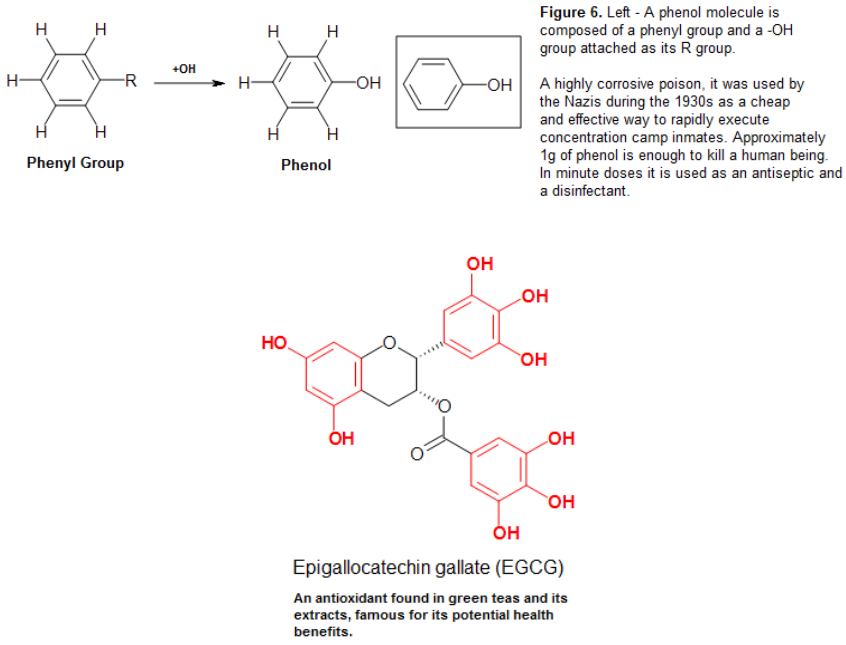


Figure 7: *Epigallocatechin gallate (EGCG), an antioxidant found in green teas and its extracts, is famous for its potential health benefits. The molecule is a type of catechin, which is composed of multiple phenol (labeled in red) units (polyphenols - see polycyclic aromatics). Since catechins are usually found in plant extracts, they are often referred as plant polyphenolic antioxidants.*

As you can see above, these are only some of the many possibilities of the benzene derived products that have special uses in human health and other industrial fields.

Nomenclature of Benzene Derived Compounds

Unlike aliphatic organics, nomenclature of benzene-derived compounds can be confusing because a single aromatic compound can have multiple possible names (such as common and systematic names) be associated with its structure. In these sections, we will analyze some of the ways these compounds can be named.

Simple Benzene Naming

Some common substituents, like NO_2, Br, and Cl, can be named this way when it is attached to a phenyl group. Long chain carbons attached can also be named this way. The general format for this kind of naming is:

(positions of substituents (if >1)- + # (di, tri, ...) + substituent)$_n$ + benzene.

For example, chlorine (Cl) attached to a phenyl group would be named **chlorobenzene (chloro + benzene)**. Since there is only one substituent on the benzene ring, we do not have to indicate its position on the benzene ring (as it can freely rotate around and you would end up getting the same compound.)

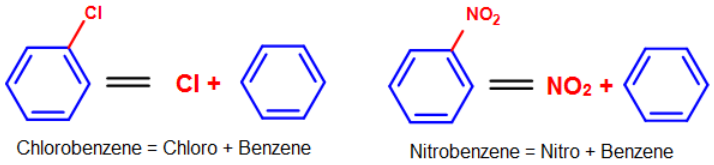


Figure 8. Example of simple benzene naming with chlorine and NO_2 as substituents.

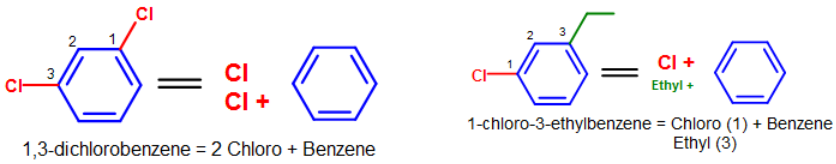


Figure 9. *More complicated simple benzene naming examples - Note that standard nomenclature priority rules are applied here, causing the numbering of carbons to switch. See Nomenclature of Organic Compounds for a review on naming and priority rules.*

Ortho-, Meta-, Para- (OMP) Nomenclature for Disubstituted Benzenes

Instead of using numbers to indicate substituents on a benzene ring, ***ortho- (o-), meta- (m-), or para (p-)*** can be used in place of positional markers when there are **two** substituents on the benzene ring (disubstituted benzenes). They are defined as the following:

- ***ortho- (o-):*** 1,2- (next to each other in a benzene ring)
- ***meta- (m):*** 1,3- (separated by one carbon in a benzene ring)
- ***para- (p):*** 1,4- (across from each other in a benzene ring)

Using the same example above in Figure 9a (1,3-dichlorobenzene), we can use the ortho-, meta-, para- nomenclature to transform the chemical name into m-dichlorobenzene, as shown in the Figure below.

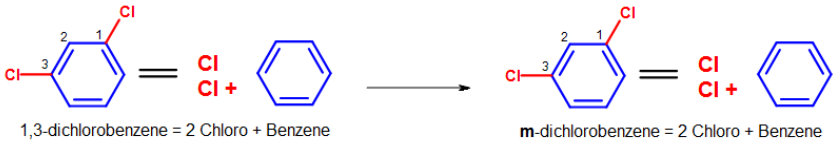


Figure 10. *Transformation of 1,3-dichlorobenzene into m-dichlorobenzene.*

Here are some other examples of ortho-, meta-, para- nomenclature used in context:

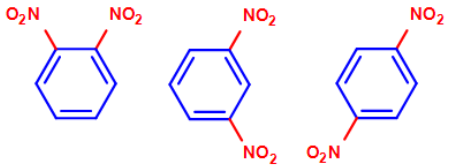


Figure 11. Example of o-, m-, p- nomenclature.
Listed in order:
1) o-dinitrobenzene
2) m-dinitrobenzene
3) p-dinitrobenzene

However, the substituents used in ortho-, meta-, para- nomenclature do not have to be the same. For example, we can use chlorine and a nitro group as substituents in the benzene ring.

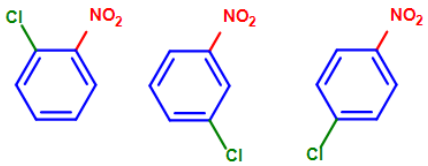
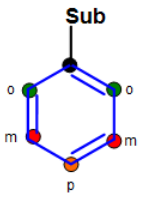


Figure 12. Example of o-, m-, p- nomenclature.
Listed in order:
1) o-nitrochlorobenzene
2) m-nitrochlorobenzene
3) p-nitrochlorobenzene
Note that the two substituents do not have to be the same.

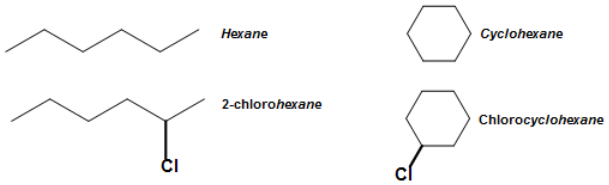
In conclusion, these can be pieced together into a summary diagram, as shown below:

Figure 13. A benzene ring with a primary substituent and the possible locations for the secondary substituent.
As shown:
1,2- (green) = ortho, o-
1,3- (red) = meta, m-
1,4- (orange) = para, p-
For clarity, the benzene ring has been rotated 30° relatively to the other benzenes in this article.



Base Name Nomenclature

In addition to simple benzene naming and OMP nomenclature, benzene derived compounds are also sometimes used as **bases**. The concept of a base is similar to the nomenclature of aliphatic and cyclic compounds, where the parent for the organic compound is used as a base (a name for its chemical name. For example, the following compounds have the base names ***hexane*** and ***cyclohexane***, respectively. See Nomenclature of Organic Compounds for a review on naming organic compounds.



Benzene, similar to these compounds shown above, also has base names from its derived compounds. **Phenol (C_6H_5OH)**, as introduced previously in this article, for example, serves as a base when other substituents are attached to it. This is best illustrated in the diagram below.

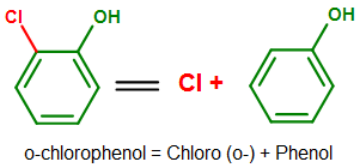


Figure 14. *An example showing phenol as a base in its chemical name. Note how benzene no longer serves as a base when an OH group is added to the benzene ring.*

Alternatively, we can use the numbering system to indicate this compound. When the numbering system is used, the carbon where the substituent is attached on the base will be given the first priority and named as carbon #1 (C_1). The normal priority rules then apply in the nomenclature process (give the rest of the substituents the lowest numbering as you could).

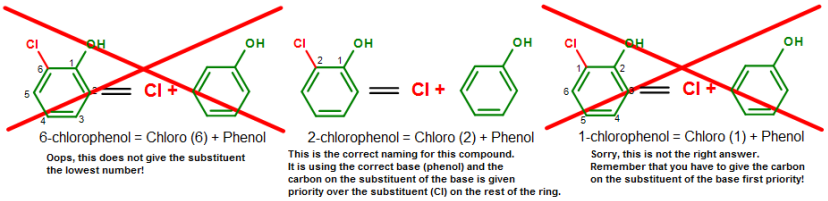


Figure 15. *The naming process for 2-chlorophenol (o-chlorophenol). Note that 2-chlorophenol = o-chlorophenol.*

Below is a list of commonly seen benzene-derived compounds. Some of these mono-substituted compounds (labeled in red and green), such as phenol or toluene, can be used in place of benzene for the chemical's base name.

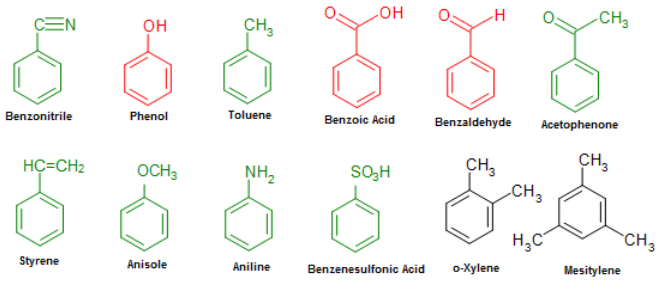


Figure 16. Common benzene derived compounds with various substituents.

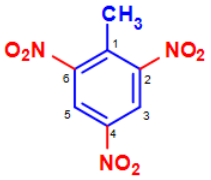


Figure 17. 2,4,6-Trinitrotoluene, or **TNT**, a common explosive used for both industrial and military purposes, is consisted of a **toluene** base (labeled in blue), along with three **nitro** groups attached as substituents (labeled in red).
The explosive is characteristic for its resistance to external shock and friction, making it useful in many applications where other highly sensitive explosives would simultaneously detonate.

Common vs. Systematic (IUPAC) Nomenclature

According to the indexing preferences of the *Chemical Abstracts*, **phenol, benzaldehyde, and benzoic acid (labeled in red in Figure 16)** are some of the common names that are retained in the IUPAC (systematic) nomenclature. Other names such as toluene, styrene, naphthalene, or phenanthrene can also be seen in the IUPAC system in the same way. While the use of other common names are usually acceptable in IUPAC, their use are discouraged in the nomenclature of compounds.

Nomenclature for compounds which has such discouraged names will be named by the simple benzene naming system. An example of this would include **toluene derivatives like TNT.** (Note that toluene by itself is retained by the IUPAC nomenclature, but its derivatives, which contains additional substituents on the benzene ring, might be excluded from the convention). For this reason, the **common chemical name** 2,4,6-trinitrotoluene, or TNT, as shown in Figure 17, would not be advisable under the IUPAC (**systematic**) nomenclature.

In order to correctly name TNT under the IUPAC system, the simple benzene naming system should be used:

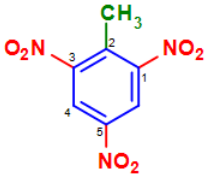


Figure 18. TNT, as named under the IUPAC nomenclature.
Note that since the IUPAC nomenclature does not recognize toluene as the primary base of this compound, substituent priorities are reverted to normal defaults.
As a result, TNT in IUPAC is named (systematic name):
2-methyl-1,3,5-trinitrobenzene

Figure 18. *Systematic (IUPAC) name of 2,4,6-trinitrotoluene (common name), or TNT. Note that the methyl group is individually named due to the exclusion of toluene from the IUPAC nomenclature.*

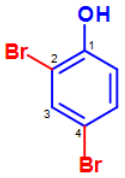


Figure 19. 2,4-dibromophenol, as shown in this diagram, is valid in both the common nomenclature as well as the IUPAC nomenclature.
As mentioned previously, **phenol, benzoic acid, and benzaldehyde** substituents are allowed to be used in the IUPAC naming conventions and the base naming priority rules are applied in the nomenclature process.

Figure 19. *The common name 2,4-dibromophenol, is shared by the IUPAC systematic nomenclature. Only substituents* ***phenol, benzoic acid, and benzaldehyde*** *share this commonality.*

Since the IUPAC nomenclature primarily rely on the simple benzene naming system for the nomenclature of different benzene derived compounds, the OMP (ortho-, meta-, para-) system is not accepted in the IUPAC nomenclature. For this reason, the OMP system will yield common names that can be converted to systematic names by using the same method as above. For example, o-Xylene from the OMP system can be named 1,2-dimethylbenzene by using simple benzene naming (IUPAC standard).

The Phenyl and Benzyl Groups

The Phenyl Group

As mentioned previously, the phenyl group (Ph-R, C_6H_5-R) can be formed by removing a hydrogen from benzene and attaching a substituent to where the hydrogen was removed. To this phenomenon, we can name compounds formed this way by applying this rule: **(phenyl + substituent)**. For example, a chlorine attached in this manner would be named **phenyl chloride**, and a bromine attached in this manner would be named **phenyl bromide**. (See below diagram)

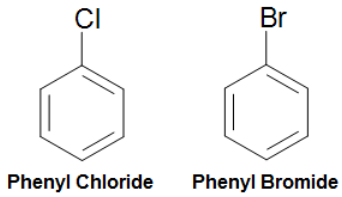


Figure 20. *Naming of Phenyl Chloride and Phenyl Bromide*

While compounds like these are usually named by simple benzene type naming (chlorobenzene and bromobenzene), the phenyl group naming is usually applied to benzene rings where a substituent with six or more carbons is attached, such as in the diagram below.

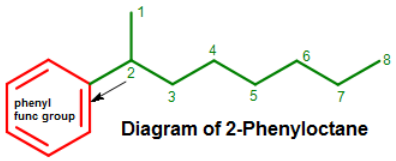


Figure 21. *Diagram of 2-phenyloctane.*

Although the diagram above might be a little daunting to understand at first, it is not as difficult as it seems after careful analysis of the structure is made. By looking for the longest chain in the compound, it should be clear that the longest chain is eight (8) carbons long (octane, as shown in green) and that a benzene ring is attached to the second position of this longest chain (labeled in red). As this rule suggests that the benzene ring will act as a function group (a substituent) whenever a substituent of more than six (6) carbons is attached to it, the name "benzene" is changed to **phenyl** and is used the same way as any other substituents, such as **methyl, ethyl, or bromo.** Putting it all together, the name can be derived as: **2-phenyloctane** (phenyl is attached at the second position of the longest carbon chain, octane).

The Benzyl Group

The benzyl group (abbv. Bn), similar to the phenyl group, is formed by manipulating the benzene ring. In the case of the benzyl group, it is formed by taking the phenyl group and adding a CH_2 group to where the hydrogen was removed. Its molecular fragment can be written as $C_6H_5CH_2$-R, $PhCH_2$-R, or Bn-R. Nomenclature of benzyl group based compounds are very similar to the phenyl group compounds. For example, a chlorine attached to a benzyl group would simply be called benzyl chloride, whereas an OH group attached to a benzyl group would simply be called benzyl alcohol.

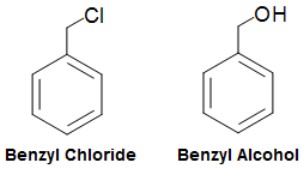


Figure 22. *Benzyl Group Nomenclature*

Additionally, other substituents can attach on the benzene ring in the presence of the benzyl group. An example of this can be seen in the Figure below:

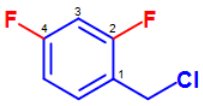
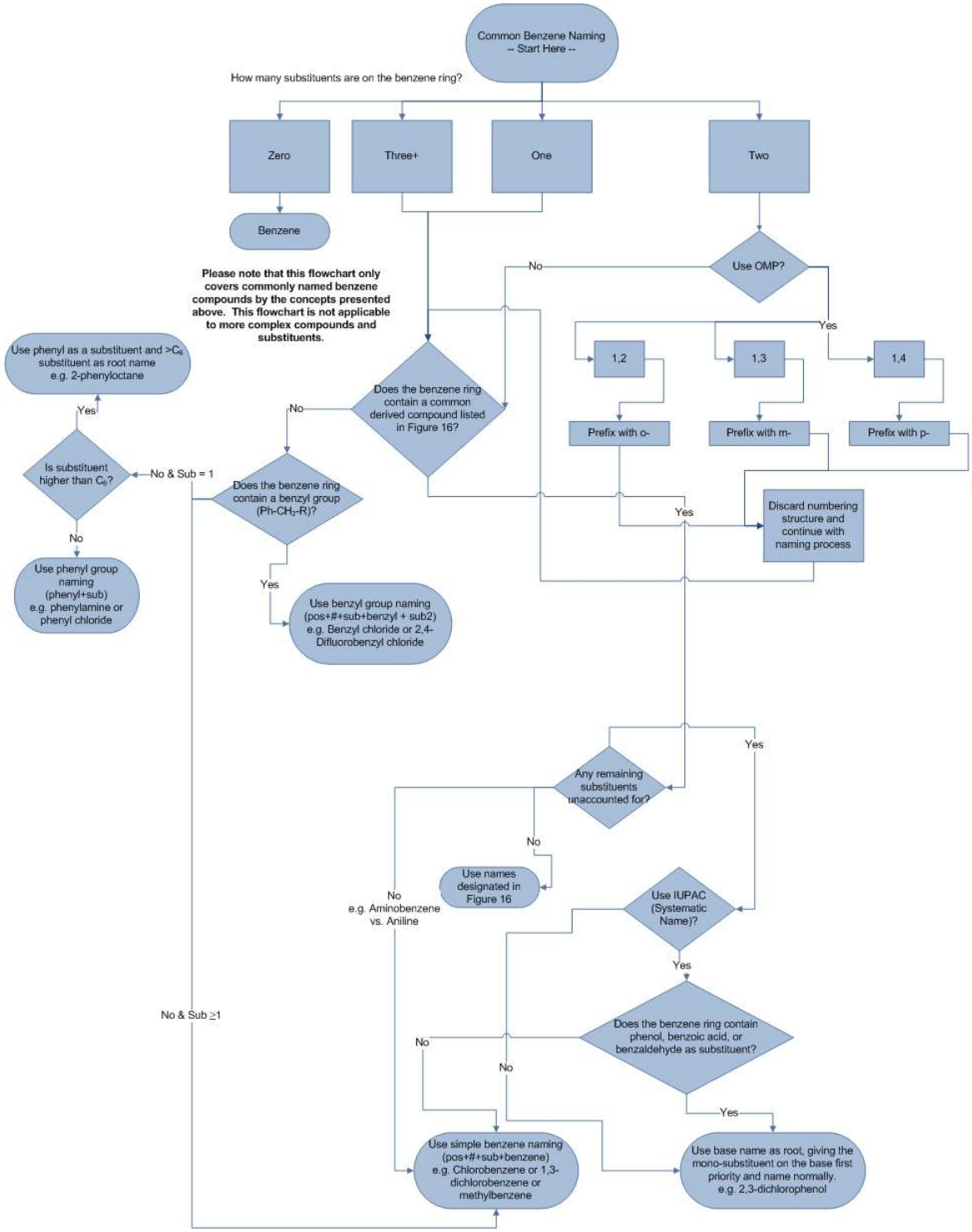


Figure 23. *Nomenclature of 2,4-difluorobenzyl chloride. Similar to the base name nomenclatures system, the carbon in which th base substitutent is attached on the benzene ring is given the first priority and the rest of the substituents are given the lowest number order possible.*

Similar to the base name nomenclature system, the carbon in which the base substituent is attached on the benzene ring is given the first priority and the rest of the substituents are given the lowest number order possible. Under this consideration, the above compound can be named: **2,4-difluorobenzyl chloride.**

Commonly Named Benzene Compounds Nomenclature Summary Flowchart

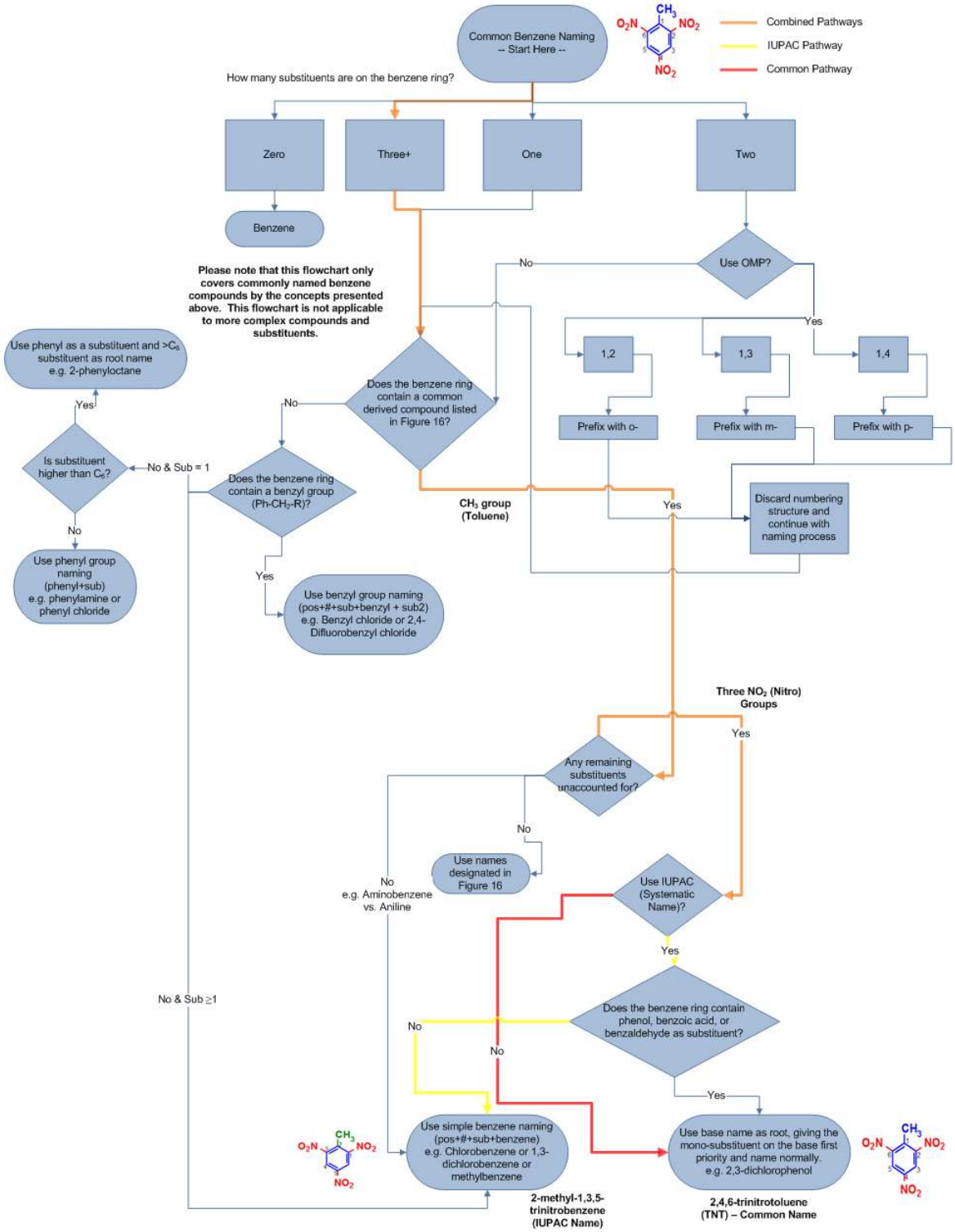


Summary Flowchart (Figure 24). *Summary of nomenclature rules used in commonly benzene derived compounds.*

As benzene derived compounds can be extremely complex, only compounds covered in this article and other commonly named compounds can be named using this flowchart.

Determination of Common and Systematic Names using Flowchart

To demonstrate how this flowchart can be used to name TNT in its common and systematic (IUPAC) name, a replica of the flowchart with the appropriate flow paths are shown below:

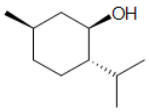


References

1. Nicolaou, K. C., & Montagnon, T. (2008). *Molecules That Changed the World.* KGaA, Weinheim: Wiley-VCH. p. 54
2. Pitman, V. (2004). *Aromatherapy.* Great Britain, UK: Nelson Thornes. p.135-136

3. Burton, G. (2000). *Chemical Ideas.* Bicester, Oxon: Heinemann. p.290-292
4. Vollhardt, K. P.C. & Shore, N. (2007). *Organic Chemistry* (5th Ed.). New York: W. H. Freeman. p. 667-669
5. Schnaubelt, K. (1999). *Medical Aromatherapy.* Berkeley, CA: Frog Books. p. 211-213
6. Patrick, G. L. (2004). *Organic Chemistry.* New York, NY: Taylor & Francis. p. 135-136
7. Talbott, S. M. (2002). *A Guide to Understanding Dietary Supplements.* Binghamton, NY: Haworth Press. p. 616-619
8. Lifton, R. J. (2000). *The Nazi doctors.* New York, NY: Basic Books. p. 255-261
9. Myers, R. L., & Myers, R. L. (2007). *The 100 most important chemical compounds.* Westport, CT: Greenwood Publishing Group. p. 281-282

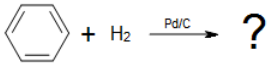
Practice Problems



Q1) (True/False) The compound above contains a benzene ring and thus is aromatic.

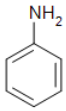
Q2) Benzene unusual stability is caused by how many conjugated pi bonds in its cyclic ring? ____

Q3) Menthol, a topical analgesic used in many ointments for the relief of pain, releases a peppermint aroma upon exposure to the air. Based on this conclusion, can you imply that a benzene ring is present in its chemical structure? Why or why not?

Q4) 

Q5) At normal conditions, benzene has ___ resonance structures.

Q6) Which of the following name(s) is/are correct for the following compound?

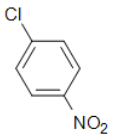


a) nitrohydride benzene
b) phenylamine
c) phenylamide
d) aniline
e) nitrogenhydrogen benzene
f) All of the above is correct

Q7) Convert 1,4-dimethylbenzene into its common name.

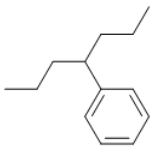
Q8) TNT's common name is: _____

Q9) Name the following compound using OMP nomenclature:

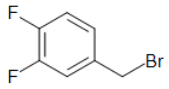


Q10) Draw the structure of 2,4-dinitrotoluene.

Q11) Name the following compound:



Q12) Which of the following is the correct name for the following compound?



a) 3,4-difluorobenzyl bromide
b) 1,2-difluorobenzyl bromide
c) 4,5-difluorobenzyl bromide
d) 1,2-difluoroethyl bromide
e) 5,6-difluoroethyl bromide
f) 4,5-difluoroethyl bromide

Q13) (True/False) Benzyl chloride can be abbreviated Bz-Cl.

Q14) Benzoic Acid has what R group attached to its phenyl functional group?

Q15) (True/False) A single aromatic compound can have multiple names indicating its structure.

Q16) List the corresponding positions for the OMP system (o-, m-, p-).

Q17) A scientist has conducted an experiment on an unknown compound. He was able to determine that the unknown compound contains a cyclic ring in its structure as well as an alcohol (-OH) group attached to the ring. What is the unknown compound?
a) Cyclohexanol
b) Cyclicheptanol
c) Phenol
d) Methanol
e) Bleach
f) Cannot determine from the above information

Q18) Which of the following statements is **false** for the compound, phenol?
a) Phenol is a benzene derived compound.
b) Phenol can be made by attaching an -OH group to a phenyl group.
c) Phenol is highly toxic to the body even in small doses.
d) Phenol can be used as a catalyst in the hydrogenation of benzene into cyclohexane.
e) Phenol is used as an antiseptic in minute doses.
f) Phenol is amongst one of the three common names retained in the IUPAC nomenclature.

Answer Key to Practice Questions

Q1) False, this compound does not contain a benzene ring in its structure.

Q2) 3

Q3) No, a substance that is fragrant does not imply a benzene ring is in its structure. See camphor example (Figure 1)

Q4) No reaction, benzene requires a special catalyst to be hydrogenated due to its unusual stability given by its three conjugated pi bonds.

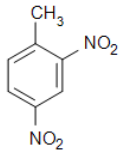
Q5) 2

Q6) b, d

Q7) p-Xylene

Q8) 2,4,6-trinitrotoluene

Q9) p-chloronitrobenzene

Q10) 

Q11) 4-phenylheptane

Q12) a

Q13) False, the correct abbreviation for the benzyl group is Bn, not Bz. The correct abbreviation for Benzyl chloride is Bn-Cl.

Q14) COOH

Q15) True. TNT, for example, has the common name 2,4,6-trinitrotoluene and its systematic name is 2-methyl-1,3,5-trinitrobenzene.

Q16) Ortho - 1,2 ; Meta - 1,3 ; Para - 1,4

Q17) The correct answer is f). We cannot determine what structure this is since the question does not tell us what kind of cyclic ring the -OH group is attached on. Just as cyclohexane can be cyclic, benzene and cycloheptane can also be cyclic.

Q18) d

Contributors

- David Lam

8.4: The Nomenclature of Monosubstituted Benzenes is shared under a not declared license and was authored, remixed, and/or curated by LibreTexts.

- **Nomenclature of Arenes** is licensed CC BY-NC-SA 4.0.

8.5: How Benzene Reacts

Substitution Reactions of Benzene and Other Aromatic Compounds

8.5: How Benzene Reacts is shared under a not declared license and was authored, remixed, and/or curated by LibreTexts.

8.6: The General Mechanism for Electrophilic Aromatic Substitution Reactions

Electrophilic Aromatic Substitution

8.6: The General Mechanism for Electrophilic Aromatic Substitution Reactions is shared under a not declared license and was authored, remixed, and/or curated by LibreTexts.

8.7: Halogenation of Benzene

Halogenation of Benzene-The Need for a Catalyst

8.7: Halogenation of Benzene is shared under a not declared license and was authored, remixed, and/or curated by LibreTexts.

8.8: Nitration of Benzene

Nitration and Sulfonation of Benzene

8.8: Nitration of Benzene is shared under a not declared license and was authored, remixed, and/or curated by LibreTexts.

8.9: Sulfonation of Benzene

Nitration and Sulfonation of Benzene

8.9: Sulfonation of Benzene is shared under a not declared license and was authored, remixed, and/or curated by LibreTexts.

8.10: The Friedel-Crafts Acylation of Benzene

Friedel-Crafts Acylation

8.10: The Friedel-Crafts Acylation of Benzene is shared under a not declared license and was authored, remixed, and/or curated by LibreTexts.

8.11: The Friedel-Crafts Alkylation of Benzene

This page gives you the facts and a simple, uncluttered mechanism for the electrophilic substitution reaction between benzene and chloromethane in the presence of an aluminium chloride catalyst. Any other chloroalkane would work similarly.

The electrophilic substitution reaction between benzene and chloromethane

Alkylation means substituting an alkyl group into something - in this case into a benzene ring. A hydrogen on the ring is replaced by a group like methyl or ethyl and so on.

Benzene is treated with a chloroalkane (for example, chloromethane or chloroethane) in the presence of aluminum chloride as a catalyst. On this page, we will look at substituting a methyl group, but any other alkyl group could be used in the same way. Substituting a methyl group gives methylbenzene - once known as toluene.

$$C_6H_6 + CH_3Cl \rightarrow C_6H_5CH_3 + HCl \tag{8.11.1}$$

or better:



The aluminium chloride isn't written into these equations because it is acting as a catalyst. If you wanted to include it, you could write $AlCl_3$ over the top of the arrow.

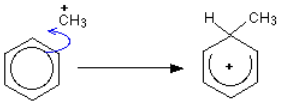
The formation of the electrophile

The electrophile is CH_3^+. It is formed by reaction between the chloromethane and the aluminum chloride catalyst.

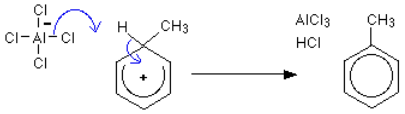
$$CH_3Cl + AlCl_3 \rightarrow^+ CH_3 + AlCl_4^- \tag{8.11.2}$$

The electrophilic substitution mechanism

Stage one



Stage two



The hydrogen is removed by the $AlCl_4^-$ ion wh ich was formed at the same time as the CH_3^+ ele ctrophile . The aluminum chloride catalyst is re-generated in this second stage.

Contributors

Jim Clark (Chemguide.co.uk)

8.11: The Friedel-Crafts Alkylation of Benzene is shared under a not declared license and was authored, remixed, and/or curated by LibreTexts.

- **The Friedel-Crafts Alkylation of Benzene** by Jim Clark is licensed CC BY-NC 4.0.

8.12: The Nomenclature of Disubstituted and Polysubstituted Benzenes

Benzene, C_6H_6, is an organic aromatic compound with many interesting properties. Unlike aliphatic (straight chain carbons) or other cyclic organic compounds, the structure of benzene (3 conjugated π bonds) allows benzene and its derived products to be useful in fields such as health, laboratory, and other applications such as rubber synthesis.

Introduction

Benzene derived products are well known to be pleasantly fragrant. For this reason, organic compounds containing benzene rings were classified as being "aromatic" (sweet smelling) amongst scientists in the early 19th century when a relation was established between benzene derived compounds and sweet/spicy fragrances. There is a misconception amongst the scientific community, however, that all aromatics are sweet smelling and that all sweet smelling compounds would have a benzene ring in its structure. This is false, since non-aromatic compounds, such as camphor, extracted from the camphor laurel tree, release a strong, minty aroma, yet it lacks the benzene ring in its structure (Figure 1). On the other hand, benzene itself gives off a rather strong and unpleasant smell that would otherwise invalidate the definition of an aromatic (sweet-smelling) compound. Despite this inconsistency, however, the term aromatic continues to be used today in order to designate molecules with benzene-like rings in their structures. For a modern, chemical definition of aromaticity, refer to sections Aromaticity and Hückel's Rule.

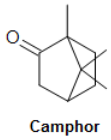


Figure 1. *Top-view of camphor, along with its* ***monoterpene*** *unit. Notice how camphor lacks the benzene ring to be "aromatic".*

Many aromatic compounds are however, sweet/pleasant smelling. Eugenol, for example, is extracted from essential oils of cloves and it releases a spicy, clove-like aroma used in perfumes. In addition, it is also used in dentistry as an analgesic.

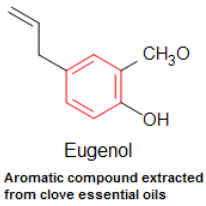


Figure 2. *Eugenol, an aromatic compound extracted from clove essential oils. Used in perfumes and as an analgesic. The benzene ring is labeled in red in the eugenol molecule.*

Is it cyclohexane or is it benzene?

Due to the similarity between benzene and cyclohexane, the two is often confused with each other in beginning organic chemistry students.

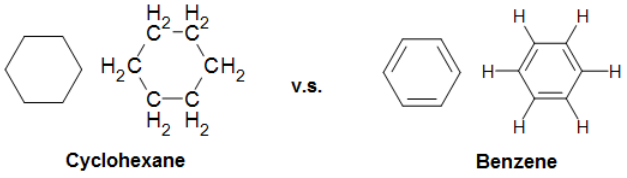


Figure 3. *Structure comparison between cyclohexane and benzene*

If you were to count the number of carbons and hydrogens in **cyclohexane**, you will notice that its molecular formula is $\mathbf{C_6H_{12}}$. Since the carbons in the **cyclohexane** ring is **fully saturated** with hydrogens (carbon is bound to 2 hydrogens and 2 adjacent carbons), no double bonds are formed in the cyclic ring. In contrast, **benzene** is only saturated with one hydrogen per carbon,

leading to its molecular formula of C_6H_6. In order to stabilize this structure, 3 conjugated π (double) bonds are formed in the benzene ring in order for carbon to have four adjacent bonds.

> *In other words, cyclohexane is not the same as benzene! These two compounds have different molecular formulas and their chemical and physical properties are not the same. The **hydrogenation** technique can be used by chemists to convert from benzene to cyclohexane by saturating the benzene ring with missing hydrogens.*

A special catalyst is required to hydrogenate benzene rings due to its unusual stability and configuration. Normal catalytic hydrogenation techniques will not hydrogenate benzene and yield any meaningful products.

What about Resonance?

Benzene can be drawn a number of different ways. This is because benzene's conjugated pi electrons freely resonate within the cyclic ring, thus resulting in its two resonance forms.

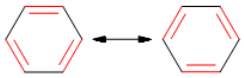


Figure 4. *The Figure to the left shows the two resonance forms of benzene. The **delocalized electrons** are moved from one carbon to the next, thus providing **stabilization** energy. Ring structures stabilized by the movement of delocalized electrons are sometimes referred to as **arenes**.*



As the electrons in the benzene ring can resonate within the ring at a fairly high rate, a simplified notation is often used to designate the two different resonance forms. This notation is shown above, with the initial three pi bonds (#1, #2) replaced with an inner ring circle (#3). Alternatively, the circle within the benzene ring can also be dashed to show the same resonance forms (#4).

The Formation of the Phenyl Group and its Derivatives

The phenyl group can be formed by taking benzene, and removing a hydrogen from it. The resulting molecular formula for the fragment is C_6H_5. NOTE: Although the molecular formula of the phenyl group is C_6H_5, the phenyl group would always have something attached to where the hydrogen was removed. Thus, the formula is often written as Ph-R, where Ph refers to the Phenyl group, and R refers to the R group attached to where the hydrogen was removed.

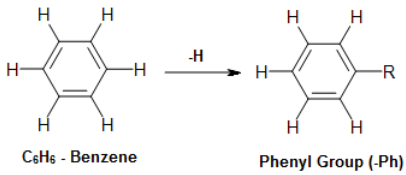


Figure 5. *Figure demonstrating the removal of hydrogen to form the phenyl group.*

Different R groups on the phenyl group allows different benzene derivatives to be formed. Phenol, Ph-OH, or C_6H_5OH, for example, is formed when an alcohol (-OH) group displaces a hydrogen atom on the benzene ring. Benzene, for this very same reason, can be formed from the phenyl group by reattaching the hydrogen back its place of removal. Thus benzene, similar to phenol, can be abbreviated Ph-H, or C_6H_6.

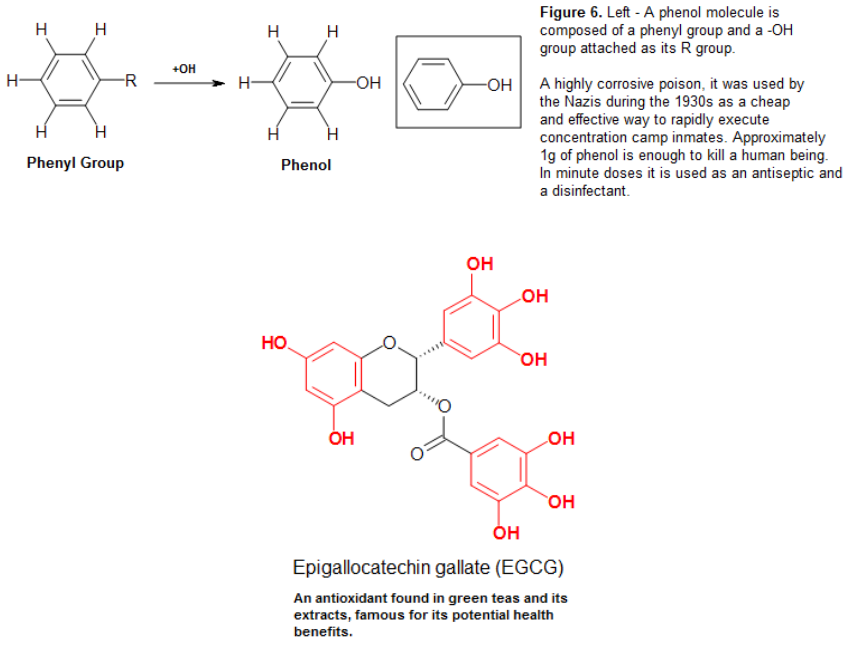


Figure 7: *Epigallocatechin gallate (EGCG), an antioxidant found in green teas and its extracts, is famous for its potential health benefits. The molecule is a type of catechin, which is composed of multiple phenol (labeled in red) units (polyphenols - see polycyclic aromatics). Since catechins are usually found in plant extracts, they are often referred as plant polyphenolic antioxidants.*

As you can see above, these are only some of the many possibilities of the benzene derived products that have special uses in human health and other industrial fields.

Nomenclature of Benzene Derived Compounds

Unlike aliphatic organics, nomenclature of benzene-derived compounds can be confusing because a single aromatic compound can have multiple possible names (such as common and systematic names) be associated with its structure. In these sections, we will analyze some of the ways these compounds can be named.

Simple Benzene Naming

Some common substituents, like NO_2, Br, and Cl, can be named this way when it is attached to a phenyl group. Long chain carbons attached can also be named this way. The general format for this kind of naming is:

(positions of substituents (if >1)- + # (di, tri, ...) + substituent)$_n$ + benzene.

For example, chlorine (Cl) attached to a phenyl group would be named **chlorobenzene (chloro + benzene)**. Since there is only one substituent on the benzene ring, we do not have to indicate its position on the benzene ring (as it can freely rotate around and you would end up getting the same compound.)

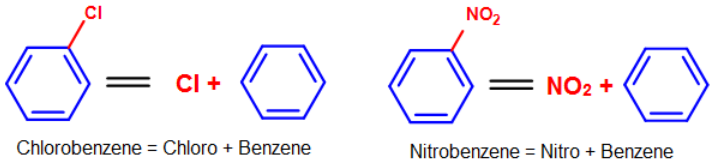


Figure 8. Example of simple benzene naming with chlorine and NO_2 as substituents.

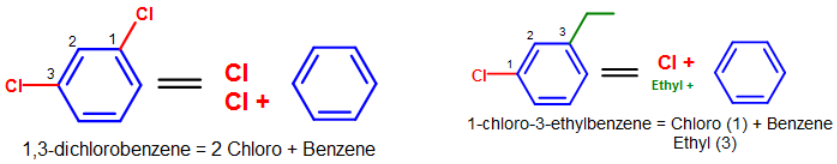


Figure 9. *More complicated simple benzene naming examples - Note that standard nomenclature priority rules are applied here, causing the numbering of carbons to switch. See Nomenclature of Organic Compounds for a review on naming and priority rules.*

Ortho-, Meta-, Para- (OMP) Nomenclature for Disubstituted Benzenes

Instead of using numbers to indicate substituents on a benzene ring, ***ortho- (o-), meta- (m-), or para (p-)*** can be used in place of positional markers when there are **two** substituents on the benzene ring (disubstituted benzenes). They are defined as the following:

- ***ortho- (o-):*** 1,2- (next to each other in a benzene ring)
- ***meta- (m):*** 1,3- (separated by one carbon in a benzene ring)
- ***para- (p):*** 1,4- (across from each other in a benzene ring)

Using the same example above in Figure 9a (1,3-dichlorobenzene), we can use the ortho-, meta-, para- nomenclature to transform the chemical name into m-dichlorobenzene, as shown in the Figure below.

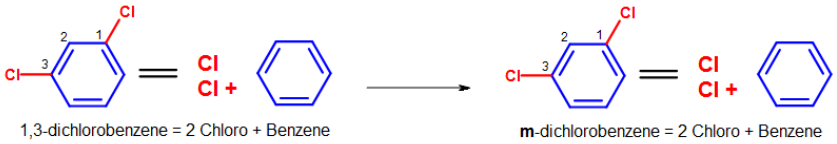


Figure 10. *Transformation of 1,3-dichlorobenzene into m-dichlorobenzene.*

Here are some other examples of ortho-, meta-, para- nomenclature used in context:

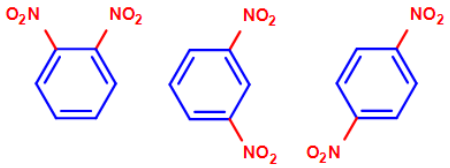


Figure 11. Example of o-, m-, p- nomenclature.
Listed in order:
1) o-dinitrobenzene
2) m-dinitrobenzene
3) p-dinitrobenzene

However, the substituents used in ortho-, meta-, para- nomenclature do not have to be the same. For example, we can use chlorine and a nitro group as substituents in the benzene ring.

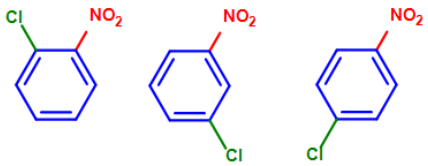
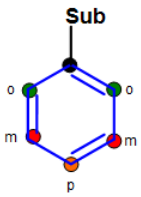


Figure 12. Example of o-, m-, p- nomenclature.
Listed in order:
1) o-nitrochlorobenzene
2) m-nitrochlorobenzene
3) p-nitrochlorobenzene
Note that the two substituents do not have to be the same.

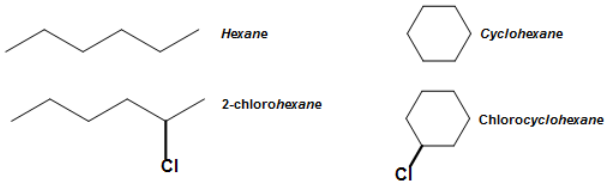
In conclusion, these can be pieced together into a summary diagram, as shown below:

Figure 13. A benzene ring with a primary substituent and the possible locations for the secondary substituent.
As shown:
1,2- (green) = ortho, o-
1,3- (red) = meta, m-
1,4- (orange) = para, p-
For clarity, the benzene ring has been rotated 30° relatively to the other benzenes in this article.



Base Name Nomenclature

In addition to simple benzene naming and OMP nomenclature, benzene derived compounds are also sometimes used as **bases**. The concept of a base is similar to the nomenclature of aliphatic and cyclic compounds, where the parent for the organic compound is used as a base (a name for its chemical name. For example, the following compounds have the base names ***hexane*** and ***cyclohexane***, respectively. See Nomenclature of Organic Compounds for a review on naming organic compounds.



Benzene, similar to these compounds shown above, also has base names from its derived compounds. **Phenol (C_6H_5OH)**, as introduced previously in this article, for example, serves as a base when other substituents are attached to it. This is best illustrated in the diagram below.

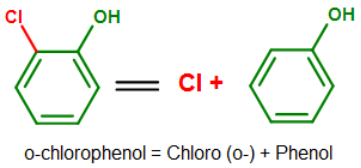


Figure 14. *An example showing phenol as a base in its chemical name. Note how benzene no longer serves as a base when an OH group is added to the benzene ring.*

Alternatively, we can use the numbering system to indicate this compound. When the numbering system is used, the carbon where the substituent is attached on the base will be given the first priority and named as carbon #1 (C_1). The normal priority rules then apply in the nomenclature process (give the rest of the substituents the lowest numbering as you could).

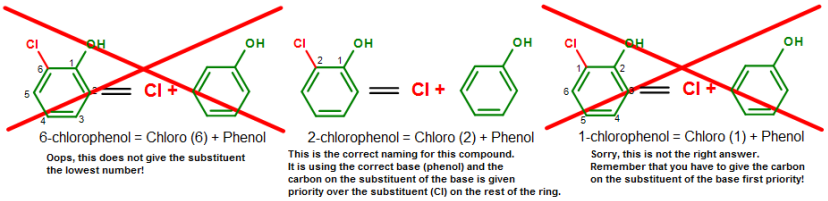


Figure 15. *The naming process for 2-chlorophenol (o-chlorophenol). Note that 2-chlorophenol = o-chlorophenol.*

Below is a list of commonly seen benzene-derived compounds. Some of these mono-substituted compounds (labeled in red and green), such as phenol or toluene, can be used in place of benzene for the chemical's base name.

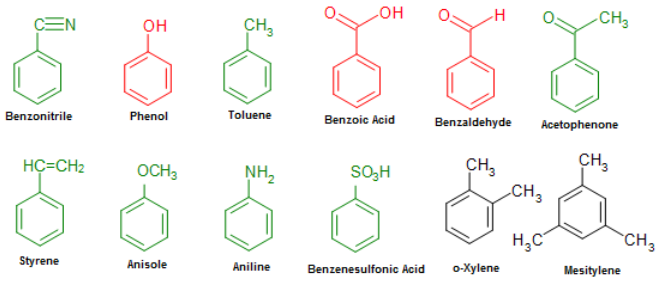


Figure 16. Common benzene derived compounds with various substituents.

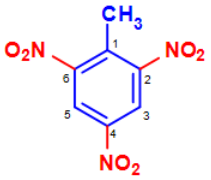


Figure 17. 2,4,6-Trinitrotoluene, or **TNT**, a common explosive used for both industrial and military purposes, is consisted of a **toluene** base (labeled in blue), along with three **nitro** groups attached as substituents (labeled in red). The explosive is characteristic for its resistance to external shock and friction, making it useful in many applications where other highly sensitive explosives would simultaneously detonate.

Common vs. Systematic (IUPAC) Nomenclature

According to the indexing preferences of the *Chemical Abstracts*, **phenol, benzaldehyde, and benzoic acid (labeled in red in Figure 16)** are some of the common names that are retained in the IUPAC (systematic) nomenclature. Other names such as toluene, styrene, naphthalene, or phenanthrene can also be seen in the IUPAC system in the same way. While the use of other common names are usually acceptable in IUPAC, their use are discouraged in the nomenclature of compounds.

Nomenclature for compounds which has such discouraged names will be named by the simple benzene naming system. An example of this would include **toluene derivatives like TNT.** (Note that toluene by itself is retained by the IUPAC nomenclature, but its derivatives, which contains additional substituents on the benzene ring, might be excluded from the convention). For this reason, the **common chemical name** 2,4,6-trinitrotoluene, or TNT, as shown in Figure 17, would not be advisable under the IUPAC (**systematic**) nomenclature.

In order to correctly name TNT under the IUPAC system, the simple benzene naming system should be used:

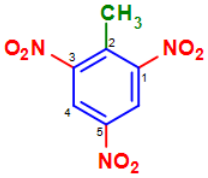


Figure 18. TNT, as named under the IUPAC nomenclature. Note that since the IUPAC nomenclature does not recognize toluene as the primary base of this compound, substituent priorities are reverted to normal defaults. As a result, TNT in IUPAC is named (systematic name): **2-methyl-1,3,5-trinitrobenzene**

Figure 18. *Systematic (IUPAC) name of 2,4,6-trinitrotoluene (common name), or TNT. Note that the methyl group is individually named due to the exclusion of toluene from the IUPAC nomenclature.*

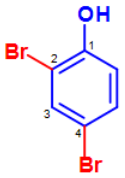


Figure 19. 2,4-dibromophenol, as shown in this diagram, is valid in both the common nomenclature as well as the IUPAC nomenclature. As mentioned previously, **phenol, benzoic acid, and benzaldehyde** substituents are allowed to be used in the IUPAC naming conventions and the base naming priority rules are applied in the nomenclature process.

Figure 19. *The common name 2,4-dibromophenol, is shared by the IUPAC systematic nomenclature. Only substituents* ***phenol, benzoic acid, and benzaldehyde*** *share this commonality.*

Since the IUPAC nomenclature primarily rely on the simple benzene naming system for the nomenclature of different benzene derived compounds, the OMP (ortho-, meta-, para-) system is not accepted in the IUPAC nomenclature. For this reason, the OMP system will yield common names that can be converted to systematic names by using the same method as above. For example, o-Xylene from the OMP system can be named 1,2-dimethylbenzene by using simple benzene naming (IUPAC standard).

The Phenyl and Benzyl Groups

The Phenyl Group

As mentioned previously, the phenyl group (Ph-R, C_6H_5-R) can be formed by removing a hydrogen from benzene and attaching a substituent to where the hydrogen was removed. To this phenomenon, we can name compounds formed this way by applying this rule: **(phenyl + substituent)**. For example, a chlorine attached in this manner would be named **phenyl chloride**, and a bromine attached in this manner would be named **phenyl bromide**. (See below diagram)

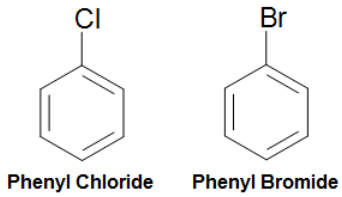


Figure 20. *Naming of Phenyl Chloride and Phenyl Bromide*

While compounds like these are usually named by simple benzene type naming (chlorobenzene and bromobenzene), the phenyl group naming is usually applied to benzene rings where a substituent with six or more carbons is attached, such as in the diagram below.

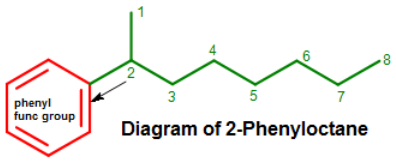


Figure 21. *Diagram of 2-phenyloctane.*

Although the diagram above might be a little daunting to understand at first, it is not as difficult as it seems after careful analysis of the structure is made. By looking for the longest chain in the compound, it should be clear that the longest chain is eight (8) carbons long (octane, as shown in green) and that a benzene ring is attached to the second position of this longest chain (labeled in red). As this rule suggests that the benzene ring will act as a function group (a substituent) whenever a substituent of more than six (6) carbons is attached to it, the name "benzene" is changed to **phenyl** and is used the same way as any other substituents, such as **methyl, ethyl, or bromo.** Putting it all together, the name can be derived as: **2-phenyloctane** (phenyl is attached at the second position of the longest carbon chain, octane).

The Benzyl Group

The benzyl group (abbv. Bn), similar to the phenyl group, is formed by manipulating the benzene ring. In the case of the benzyl group, it is formed by taking the phenyl group and adding a CH_2 group to where the hydrogen was removed. Its molecular fragment can be written as $C_6H_5CH_2$-R, $PhCH_2$-R, or Bn-R. Nomenclature of benzyl group based compounds are very similar to the phenyl group compounds. For example, a chlorine attached to a benzyl group would simply be called benzyl chloride, whereas an OH group attached to a benzyl group would simply be called benzyl alcohol.

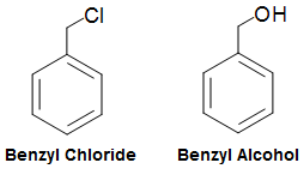


Figure 22. *Benzyl Group Nomenclature*

Additionally, other substituents can attach on the benzene ring in the presence of the benzyl group. An example of this can be seen in the Figure below:

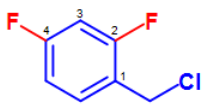
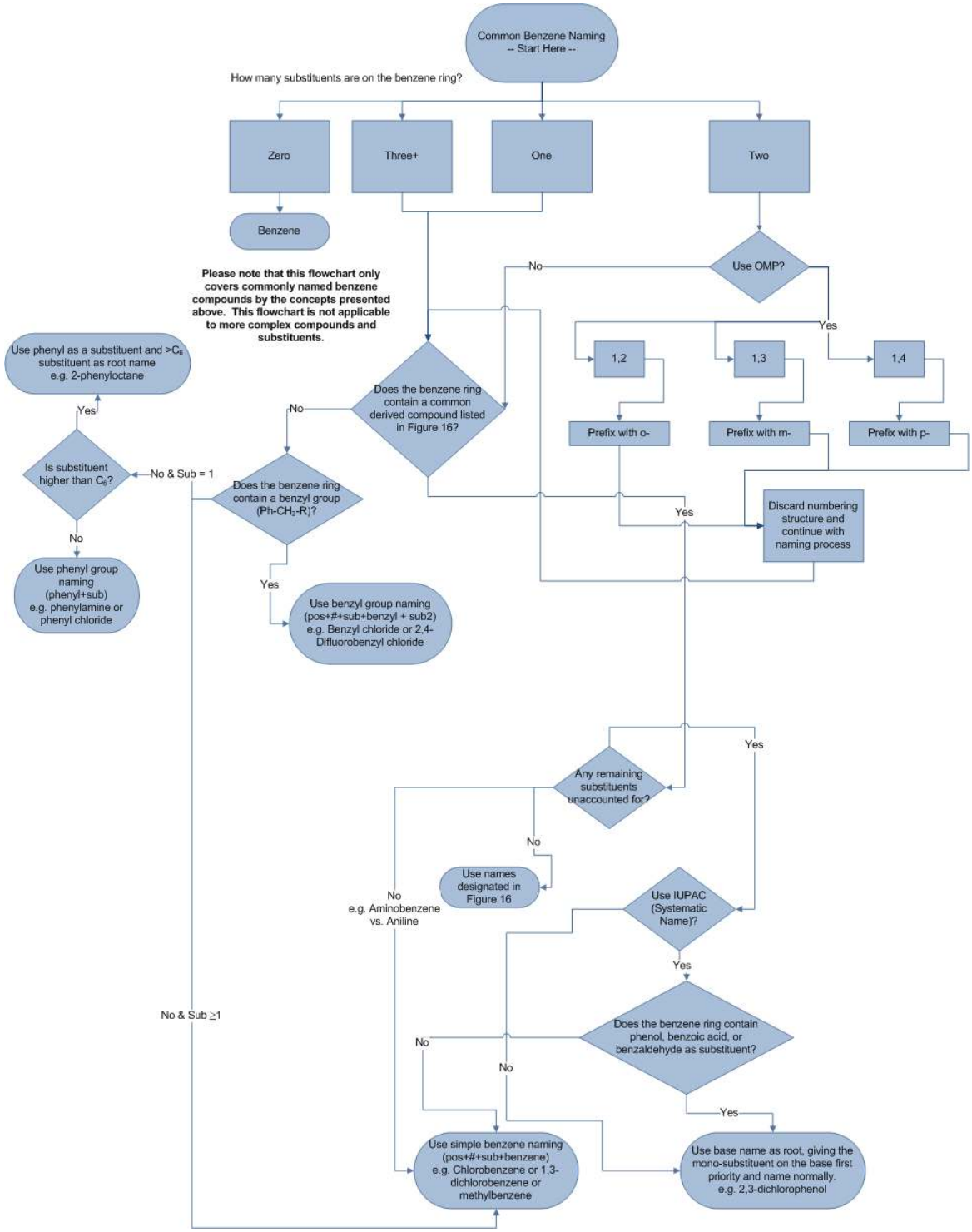


Figure 23. *Nomenclature of 2,4-difluorobenzyl chloride. Similar to the base name nomenclatures system, the carbon in which th base substitutent is attached on the benzene ring is given the first priority and the rest of the substituents are given the lowest number order possible.*

Similar to the base name nomenclature system, the carbon in which the base substituent is attached on the benzene ring is given the first priority and the rest of the substituents are given the lowest number order possible. Under this consideration, the above compound can be named: **2,4-difluorobenzyl chloride.**

Commonly Named Benzene Compounds Nomenclature Summary Flowchart

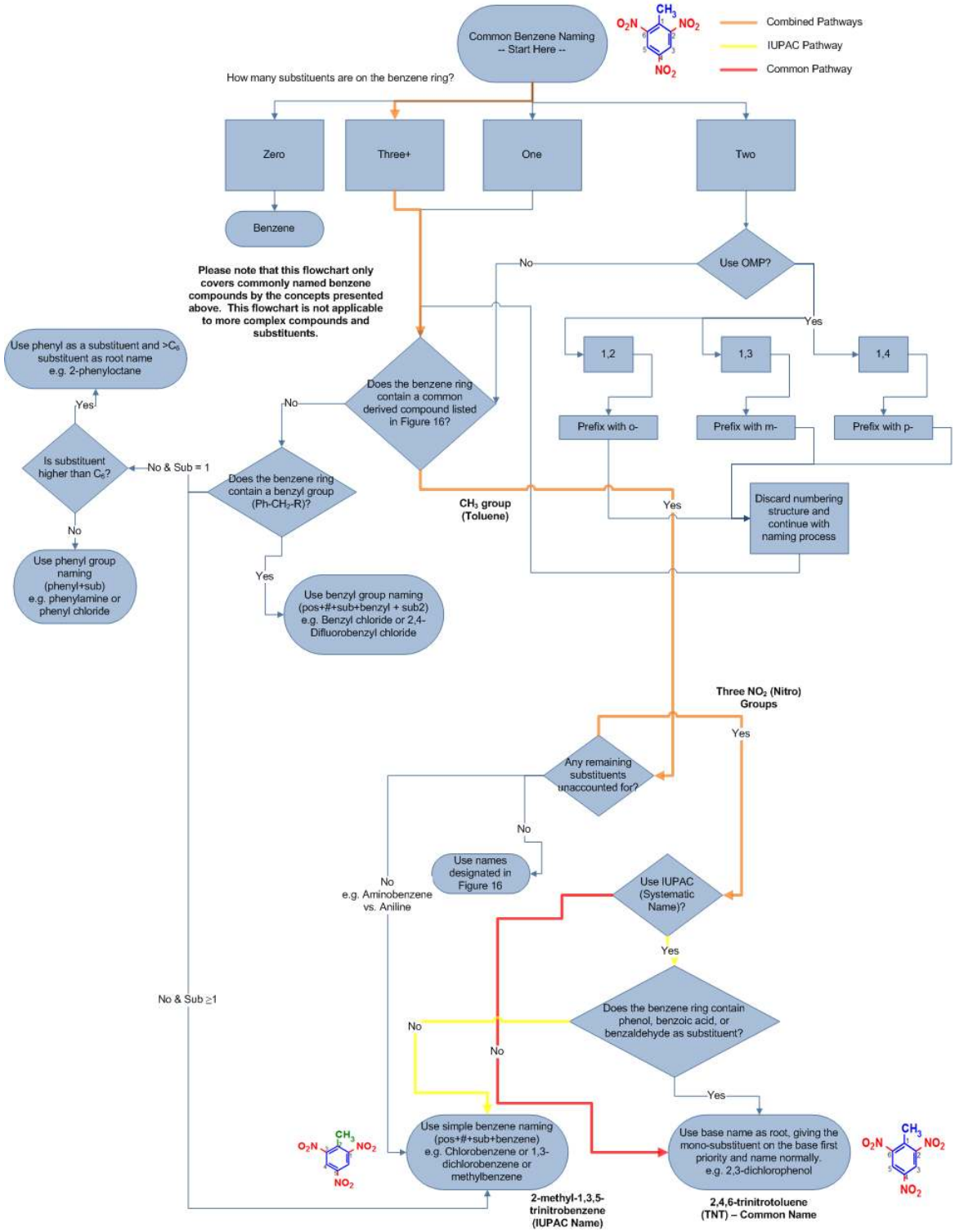


Summary Flowchart (Figure 24). *Summary of nomenclature rules used in commonly benzene derived compounds.*

As benzene derived compounds can be extremely complex, only compounds covered in this article and other commonly named compounds can be named using this flowchart.

Determination of Common and Systematic Names using Flowchart

To demonstrate how this flowchart can be used to name TNT in its common and systematic (IUPAC) name, a replica of the flowchart with the appropriate flow paths are shown below:

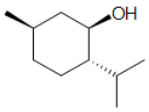


References

1. Nicolaou, K. C., & Montagnon, T. (2008). *Molecules That Changed the World.* KGaA, Weinheim: Wiley-VCH. p. 54
2. Pitman, V. (2004). *Aromatherapy.* Great Britain, UK: Nelson Thornes. p.135-136

3. Burton, G. (2000). *Chemical Ideas.* Bicester, Oxon: Heinemann. p.290-292
4. Vollhardt, K. P.C. & Shore, N. (2007). *Organic Chemistry* (5th Ed.). New York: W. H. Freeman. p. 667-669
5. Schnaubelt, K. (1999). *Medical Aromatherapy.* Berkeley, CA: Frog Books. p. 211-213
6. Patrick, G. L. (2004). *Organic Chemistry.* New York, NY: Taylor & Francis. p. 135-136
7. Talbott, S. M. (2002). *A Guide to Understanding Dietary Supplements.* Binghamton, NY: Haworth Press. p. 616-619
8. Lifton, R. J. (2000). *The Nazi doctors.* New York, NY: Basic Books. p. 255-261
9. Myers, R. L., & Myers, R. L. (2007). *The 100 most important chemical compounds.* Westport, CT: Greenwood Publishing Group. p. 281-282

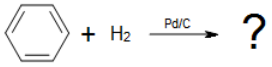
Practice Problems



Q1) (True/False) The compound above contains a benzene ring and thus is aromatic.

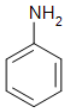
Q2) Benzene unusual stability is caused by how many conjugated pi bonds in its cyclic ring? ____

Q3) Menthol, a topical analgesic used in many ointments for the relief of pain, releases a peppermint aroma upon exposure to the air. Based on this conclusion, can you imply that a benzene ring is present in its chemical structure? Why or why not?

Q4) 

Q5) At normal conditions, benzene has ___ resonance structures.

Q6) Which of the following name(s) is/are correct for the following compound?

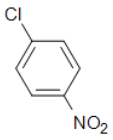


a) nitrohydride benzene
b) phenylamine
c) phenylamide
d) aniline
e) nitrogenhydrogen benzene
f) All of the above is correct

Q7) Convert 1,4-dimethylbenzene into its common name.

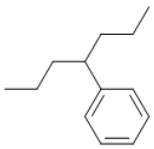
Q8) TNT's common name is: _____

Q9) Name the following compound using OMP nomenclature:

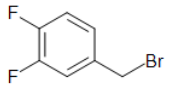


Q10) Draw the structure of 2,4-dinitrotoluene.

Q11) Name the following compound:



Q12) Which of the following is the correct name for the following compound?



a) 3,4-difluorobenzyl bromide
b) 1,2-difluorobenzyl bromide
c) 4,5-difluorobenzyl bromide
d) 1,2-difluoroethyl bromide
e) 5,6-difluoroethyl bromide
f) 4,5-difluoroethyl bromide

Q13) (True/False) Benzyl chloride can be abbreviated Bz-Cl.

Q14) Benzoic Acid has what R group attached to its phenyl functional group?

Q15) (True/False) A single aromatic compound can have multiple names indicating its structure.

Q16) List the corresponding positions for the OMP system (o-, m-, p-).

Q17) A scientist has conducted an experiment on an unknown compound. He was able to determine that the unknown compound contains a cyclic ring in its structure as well as an alcohol (-OH) group attached to the ring. What is the unknown compound?
a) Cyclohexanol
b) Cyclicheptanol
c) Phenol
d) Methanol
e) Bleach
f) Cannot determine from the above information

Q18) Which of the following statements is **false** for the compound, phenol?
a) Phenol is a benzene derived compound.
b) Phenol can be made by attaching an -OH group to a phenyl group.
c) Phenol is highly toxic to the body even in small doses.
d) Phenol can be used as a catalyst in the hydrogenation of benzene into cyclohexane.
e) Phenol is used as an antiseptic in minute doses.
f) Phenol is amongst one of the three common names retained in the IUPAC nomenclature.

Answer Key to Practice Questions

Q1) False, this compound does not contain a benzene ring in its structure.

Q2) 3

Q3) No, a substance that is fragrant does not imply a benzene ring is in its structure. See camphor example (Figure 1)

Q4) No reaction, benzene requires a special catalyst to be hydrogenated due to its unusual stability given by its three conjugated pi bonds.

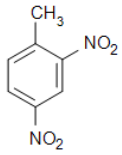
Q5) 2

Q6) b, d

Q7) p-Xylene

Q8) 2,4,6-trinitrotoluene

Q9) p-chloronitrobenzene

Q10) 

Q11) 4-phenylheptane

Q12) a

Q13) False, the correct abbreviation for the benzyl group is Bn, not Bz. The correct abbreviation for Benzyl chloride is Bn-Cl.

Q14) COOH

Q15) True. TNT, for example, has the common name 2,4,6-trinitrotoluene and its systematic name is 2-methyl-1,3,5-trinitrobenzene.

Q16) Ortho - 1,2 ; Meta - 1,3 ; Para - 1,4

Q17) The correct answer is f). We cannot determine what structure this is since the question does not tell us what kind of cyclic ring the -OH group is attached on. Just as cyclohexane can be cyclic, benzene and cycloheptane can also be cyclic.

Q18) d

Contributors

- David Lam

8.12: The Nomenclature of Disubstituted and Polysubstituted Benzenes is shared under a not declared license and was authored, remixed, and/or curated by LibreTexts.

- **Nomenclature of Arenes** is licensed CC BY-NC-SA 4.0.

8.13: The Effect of Substituents on Reactivity

Electrophilic Substitution of Disubstituted Benzene Rings

8.13: The Effect of Substituents on Reactivity is shared under a not declared license and was authored, remixed, and/or curated by LibreTexts.

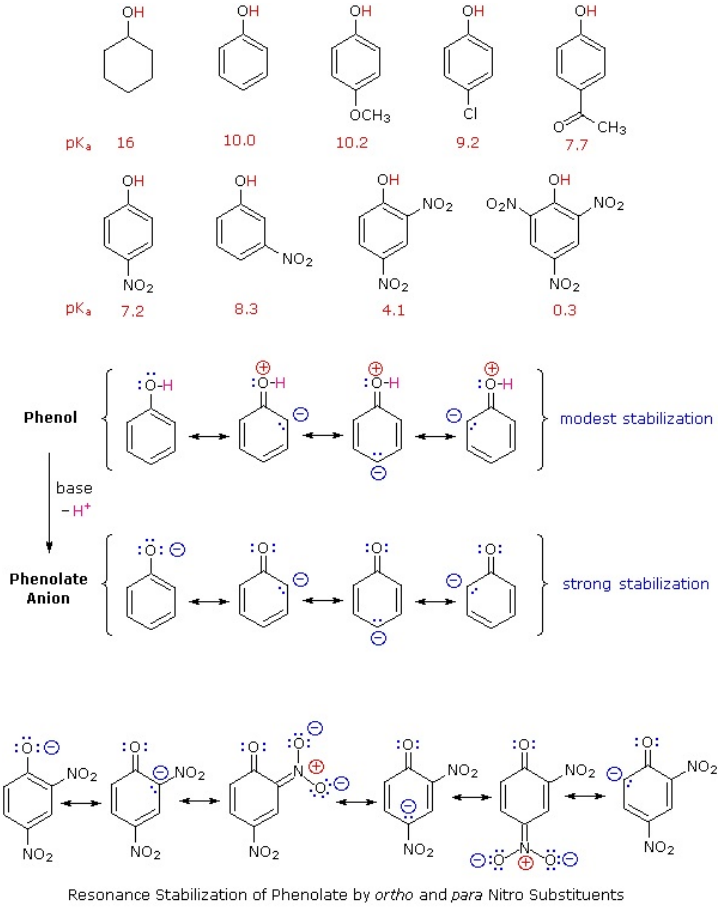
8.14: The Effect of Substituents on Orientation

Electrophilic Substitution of Disubstituted Benzene Rings

8.14: The Effect of Substituents on Orientation is shared under a not declared license and was authored, remixed, and/or curated by LibreTexts.

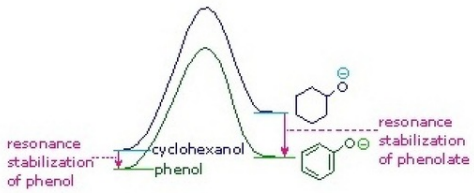
8.15: The Effect of Substituents on pKa

Substitution of the hydroxyl hydrogen atom is even more facile with phenols, which are roughly a million times more acidic than equivalent alcohols. This phenolic acidity is further enhanced by electron-withdrawing substituents ortho and para to the hydroxyl group, as displayed in the following diagram. The alcohol cyclohexanol is shown for reference at the top left. It is noteworthy that the influence of a nitro substituent is over ten times stronger in the para-location than it is meta, despite the fact that the latter position is closer to the hydroxyl group. Furthermore additional nitro groups have an additive influence if they are positioned in ortho or para locations. The trinitro compound shown at the lower right is a very strong acid called picric acid.



Resonance Stabilization of Phenolate by *ortho* and *para* Nitro Substituents

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. Formulas illustrating this electron delocalization will be displayed when the "Resonance Structures" button beneath the previous diagram is clicked. 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

William Reusch, Professor Emeritus (Michigan State U.), Virtual Textbook of Organic Chemistry

---

8.15: The Effect of Substituents on pKa is shared under a not declared license and was authored, remixed, and/or curated by LibreTexts.

- **Acidity of Substituted Phenols** by William Reusch is licensed CC BY-NC-SA 4.0.

CHAPTER OVERVIEW

9: Substitution and Elimination Reactions of Alkyl Halides



Essential Organic Chemistry: 2nd Ed.
Bruice

Homework Problems
Homework Solutions

I II III IV V VI VII VIII IX X XI XII XIII XIV XV XVI XVII XVIII XIX XX XXI

Template:HideTOC

9.1: How Alkyl Halides React
9.2: The Mechanism For an \(S_N2\) Reaction
9.3: Factors That Affect \(S_N2\) Reactions
9.4: The Mechanism for an \(S_N1\) Reaction
9.5: Factors That Affect \(S_N1\) Reactions
9.6: Comparing the \(S_N2\) and \(S_N1\) Reactions of Alkyl Halides
9.7: Elimination Reaction of Alkyl Halides
9.8: Products of Elimination Reactions
9.9: Comparing the E2 and E1 Reactions of Alkyl Halides
9.10: Does an Alkyl Halide Undergo SN2, E2 Reactions or SN1 Reactions?
9.11: Does an Alkyl Halide Undergo SN2/E2 Reactions or SN1/E1 Reactions?
9.12: Solvent Effects
9.13: Using Substitution Reactions to Synthesize Organic Compounds
9.14: Biological Methylating Reagents

9: Substitution and Elimination Reactions of Alkyl Halides is shared under a not declared license and was authored, remixed, and/or curated by LibreTexts.

SECTION OVERVIEW

9.1: How Alkyl Halides React

The high reactivity of alkyl halides can be explained in terms of the nature of C — X bond which is highly polarized covalent bond due to large difference in the electronegativities of carbon and halogen atoms.

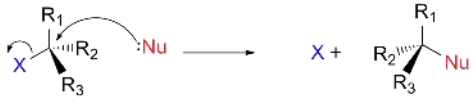
Topic hierarchy

9.1: How Alkyl Halides React is shared under a not declared license and was authored, remixed, and/or curated by LibreTexts.

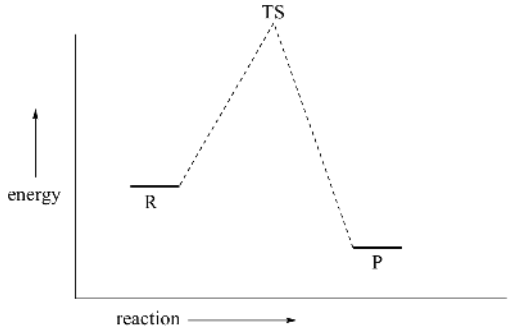
9.2: The Mechanism For an S_N2 Reaction

The S_N2 mechanism

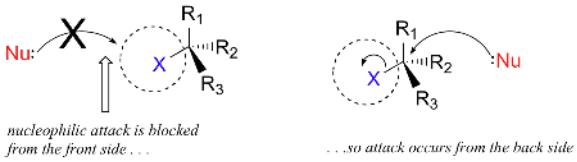
There are two mechanistic models for how an alkyl halide can undergo nucleophilic substitution. In the first picture, the reaction takes place in a single step, and bond-forming and bond-breaking occur simultaneously. (In all figures in this section, 'X' indicates a halogen substituent).



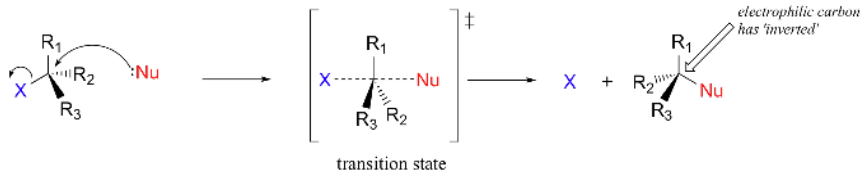
This is called an '**S_N2**' mechanism. In the term S_N2, S stands for 'substitution', the subscript N stands for 'nucleophilic', and the number 2 refers to the fact that this is a **bimolecular reaction**: the overall rate depends on a step in which two separate molecules (the nucleophile and the electrophile) collide. A potential energy diagram for this reaction shows the transition state (TS) as the highest point on the pathway from reactants to products.



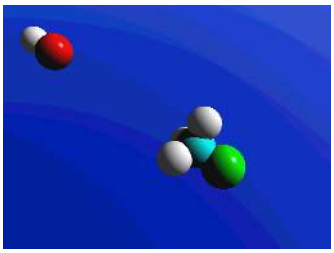
If you look carefully at the progress of the S_N2 reaction, you will realize something very important about the outcome. The nucleophile, being an electron-rich species, must attack the electrophilic carbon from the *back side* relative to the location of the leaving group. Approach from the front side simply doesn't work: the leaving group - which is also an electron-rich group - blocks the way.



The result of this backside attack is that the stereochemical configuration at the central carbon *inverts* as the reaction proceeds. In a sense, the molecule is turned inside out. At the transition state, the electrophilic carbon and the three 'R' substituents all lie on the same plane.

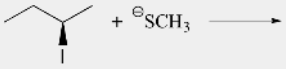


What this means is that S_N2 reactions whether enzyme catalyzed or not, are inherently stereoselective: when the substitution takes place at a stereocenter, we can confidently predict the stereochemical configuration of the product. Below is an animation illustrating the principles we have just learned, showing the S_N2 reaction between hydroxide ion and methyl iodide. Notice how backside attack by the hydroxide nucleophile results in inversion at the tetrahedral carbon electrophile.



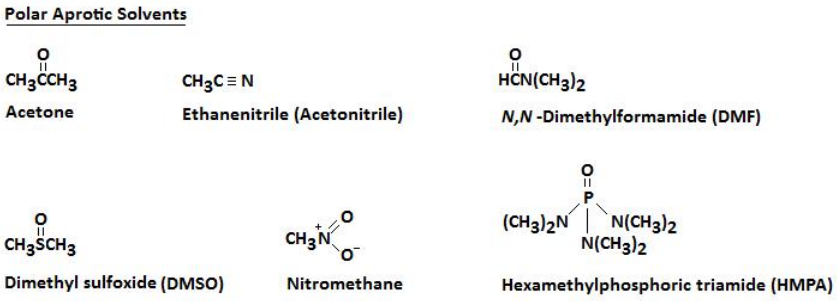
Exercise

Predict the structure of the product in this S_N2 reaction. Be sure to specify stereochemistry.

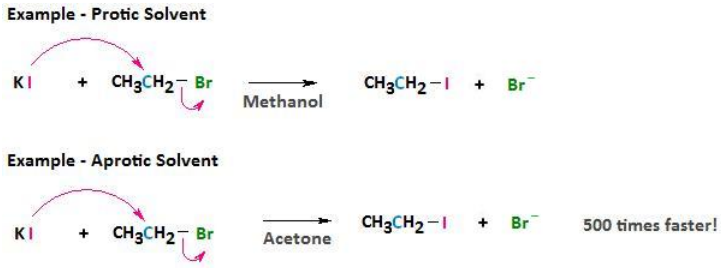


Influence of the solvent in an S_N2 reaction

The rate of an SN2 reaction is significantly influenced by the solvent in which the reaction takes place. The use of **protic solvents** (those, such as water or alcohols, with hydrogen-bond donating capability) decreases the power of the nucleophile, because of strong hydrogen-bond interactions between solvent protons and the reactive lone pairs on the nucleophile. A less powerful nucleophile in turn means a slower SN2 reaction. SN2 reactions are faster in **polar, aprotic solvents:** those that lack hydrogen-bond donating capability. Below are several polar aprotic solvents that are commonly used in the laboratory:

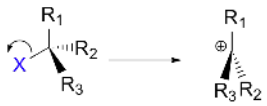


These aprotic solvents are polar but, because they do not form hydrogen bonds with the anionic nucleophile, there is a relatively weak interaction between the aprotic solvent and the nucleophile. By using an aprotic solvent we can raise the reactivity of the nucleophile. This can sometimes have dramatic effects on the rate at which a nucleophilic substitution reaction can occur. For example, if we consider the reaction between bromoethane and potassium iodide, the reaction occurs 500 times faster in acetone than in methanol.

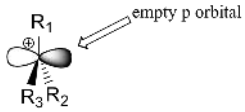


The S_N1 mechanism

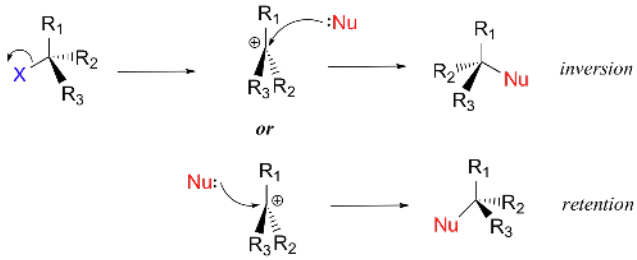
A second model for a nucleophilic substitution reaction is called the '**dissociative**', or '**S_N1**' mechanism: in this picture, the C-X bond breaks *first*, before the nucleophile approaches:



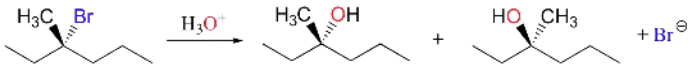
This results in the formation of a carbocation: because the central carbon has only three bonds, it bears a formal charge of +1. Recall that a carbocation should be pictured as sp^2 hybridized, with trigonal planar geometry. Perpendicular to the plane formed by the three sp^2 hybrid orbitals is an empty, unhybridized *p* orbital.



In the second step of this two-step reaction, the nucleophile attacks the empty, 'electron hungry' *p* orbital of the carbocation to form a new bond and return the carbon to tetrahedral geometry.

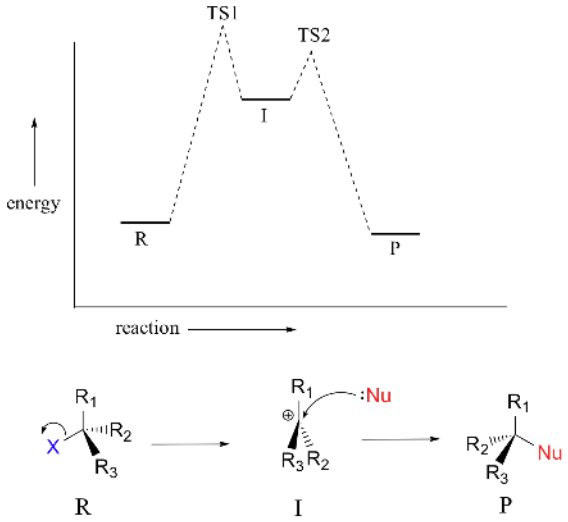


We saw that S_N2 reactions result specifically in inversion of stereochemistry at the electrophilic carbon center. What about the stereochemical outcome of S_N1 reactions? In the model S_N1 reaction shown above, the leaving group dissociates completely from the vicinity of the reaction before the nucleophile begins its attack. Because the leaving group is no longer in the picture, the nucleophile is free to attack from either side of the planar, sp^2-hybridized carbocation electrophile. This means that about half the time the product has the same stereochemical configuration as the starting material (retention of configuration), and about half the time the stereochemistry has been inverted. In other words, *racemization* has occurred at the carbon center. As an example, the tertiary alkyl bromide below would be expected to form a racemic mix of *R* and *S* alcohols after an S_N1 reaction with water as the incoming nucleophile.



Exercise
Draw the structure of the intermediate in the two-step nucleophilic substitution reaction above.

The S_N1 reaction we see an example of a reaction intermediate, a very important concept in the study of organic reaction mechanisms that was introduced earlier in the module on organic reactivity Recall that many important organic reactions do not occur in a single step; rather, they are the sum of two or more discreet bond-forming / bond-breaking steps, and involve transient intermediate species that go on to react very quickly. In the S_N1 reaction, the carbocation species is a reaction intermediate. A potential energy diagram for an S_N1 reaction shows that the carbocation intermediate can be visualized as a kind of valley in the path of the reaction, higher in energy than both the reactant and product but lower in energy than the two transition states.



Exercise

Draw structures representing TS1 and TS2 in the reaction above. Use the solid/dash wedge convention to show three dimensions.

Recall that the first step of the reaction above, in which two charged species are formed from a neutral molecule, is much the slower of the two steps, and is therefore rate-determining. This is illustrated by the energy diagram, where the activation energy for the first step is higher than that for the second step. Also recall that an S_N1 reaction has *first order* kinetics, because the rate determining step involves one molecule splitting apart, not two molecules colliding.

Exercise

Consider two nucleophilic substitutions that occur uncatalyzed in solution. Assume that reaction A is S_N2, and reaction B is S_N1. Predict, in each case, what would happen to the rate of the reaction if the concentration of the nucleophile were doubled, while all other conditions remained constant.

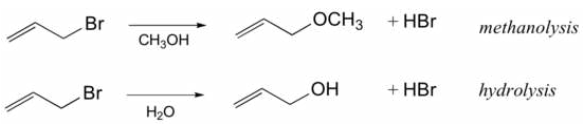
A: $CH_3I + CH_3S^{\ominus} \xrightarrow{S_N2}$

B: $(CH_3)_3CBr + CH_3SH \xrightarrow{S_N1}$

Influence of the solvent in an SN1 reaction

Since the hydrogen atom in a polar protic solvent is highly positively charged, it can interact with the anionic nucleophile which would negatively affect an SN2, but it does not affect an SN1 reaction because the nucleophile is not a part of the rate-determining step. Polar protic solvents actually speed up the rate of the unimolecular substitution reaction because the large dipole moment of the solvent helps to stabilize the transition state. The highly positive and highly negative parts interact with the substrate to lower the energy of the transition state. Since the carbocation is unstable, anything that can stabilize this even a little will speed up the reaction.

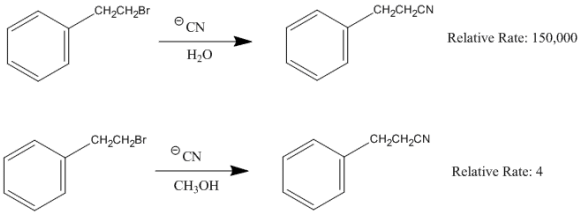
Sometimes in an SN1 reaction the solvent acts as the nucleophile. This is called a solvolysis reaction.The S_N1 reaction of allyl bromide in methanol is an example of what we would call **methanolysis**, while if water is the solvent the reaction would be called **hydrolysis**:



The polarity and the ability of the solvent to stabilize the intermediate carbocation is very important as shown by the relative rate data for the solvolysis (see table below). The dielectric constant of a solvent roughly provides a measure of the solvent's polarity. A dielectric constant below 15 is usually considered non-polar. Basically, the dielectric constant can be thought of as the solvent's ability to reduce the internal charge of the solvent. So for our purposes, the higher the dielectric constant the more polar the substance and in the case of S_N1 reactions, the faster the rate.

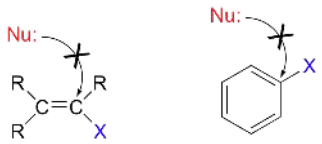
Solvent	Dielectric Constant	Relative Rate
• CH_3CO_2H • CH_3OH • H_2O	• 6 • 33 • 78	• 1 • 4 • 150,000

Below is the same reaction conducted in two different solvents and the relative rate that corresponds with it.



Exercise
Draw a complete curved-arrow mechanism for the methanolysis reaction of allyl bromide shown above.

One more important point must be made before continuing: nucleophilic substitutions as a rule occur at sp^3-hybridized carbons, and *not* where the leaving group is attached to an sp^2-hybridized carbon::



Bonds on sp^2-hybridized carbons are inherently shorter and stronger than bonds on sp^3-hybridized carbons, meaning that it is harder to break the C-X bond in these substrates. S_N2 reactions of this type are unlikely also because the (hypothetical) electrophilic carbon is protected from nucleophilic attack by electron density in the p bond. S_N1 reactions are highly unlikely, because the resulting carbocation intermediate, which would be sp-hybridized, would be very unstable (we'll discuss the relative stability of carbocation intermediates in a later section of this module).

Before we look at some real-life nucleophilic substitution reactions in the next chapter, we will spend some time in the remainder of this module focusing more closely on the three principal partners in the nucleophilic substitution reaction: the nucleophile, the electrophile, and the leaving group.

Practice Problems

9.2: The Mechanism For an S_N2 Reaction is shared under a not declared license and was authored, remixed, and/or curated by LibreTexts.

- **Substitution reactions of alkyl halides: two mechanisms** is licensed CC BY-NC-SA 4.0.

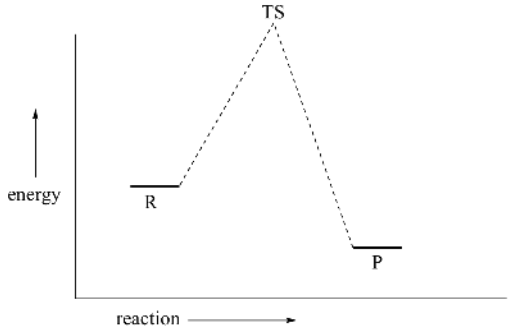
9.3: Factors That Affect S_N2 Reactions

The S_N2 mechanism

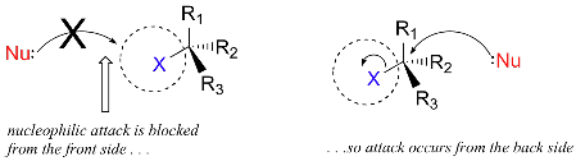
There are two mechanistic models for how an alkyl halide can undergo nucleophilic substitution. In the first picture, the reaction takes place in a single step, and bond-forming and bond-breaking occur simultaneously. (In all figures in this section, 'X' indicates a halogen substituent).



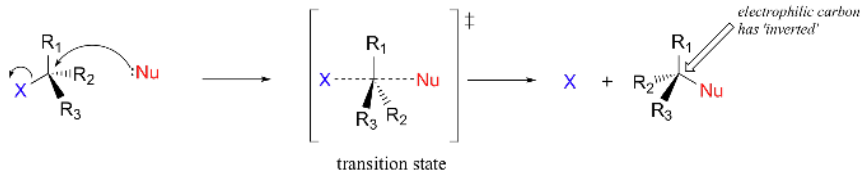
This is called an '**S_N2**' mechanism. In the term S_N2, S stands for 'substitution', the subscript N stands for 'nucleophilic', and the number 2 refers to the fact that this is a **bimolecular reaction**: the overall rate depends on a step in which two separate molecules (the nucleophile and the electrophile) collide. A potential energy diagram for this reaction shows the transition state (TS) as the highest point on the pathway from reactants to products.



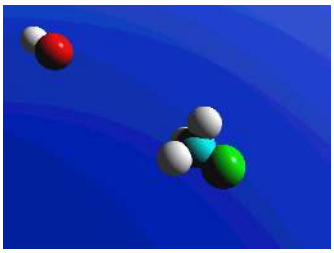
If you look carefully at the progress of the S_N2 reaction, you will realize something very important about the outcome. The nucleophile, being an electron-rich species, must attack the electrophilic carbon from the *back side* relative to the location of the leaving group. Approach from the front side simply doesn't work: the leaving group - which is also an electron-rich group - blocks the way.



The result of this backside attack is that the stereochemical configuration at the central carbon *inverts* as the reaction proceeds. In a sense, the molecule is turned inside out. At the transition state, the electrophilic carbon and the three 'R' substituents all lie on the same plane.

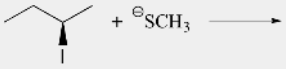


What this means is that S_N2 reactions whether enzyme catalyzed or not, are inherently stereoselective: when the substitution takes place at a stereocenter, we can confidently predict the stereochemical configuration of the product. Below is an animation illustrating the principles we have just learned, showing the S_N2 reaction between hydroxide ion and methyl iodide. Notice how backside attack by the hydroxide nucleophile results in inversion at the tetrahedral carbon electrophile.



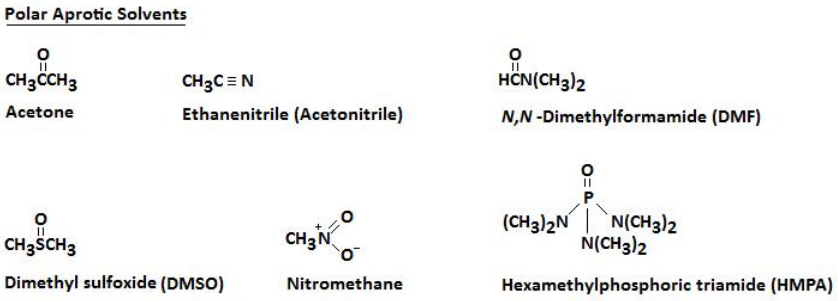
Exercise

Predict the structure of the product in this S_N2 reaction. Be sure to specify stereochemistry.

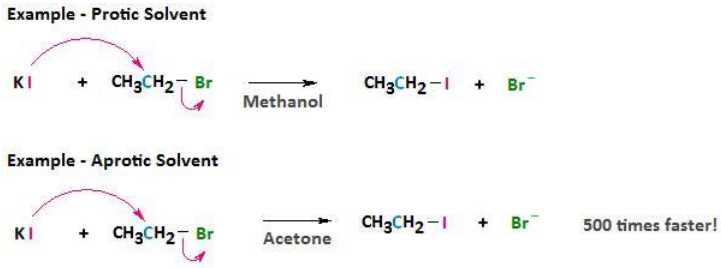


Influence of the solvent in an S_N2 reaction

The rate of an SN2 reaction is significantly influenced by the solvent in which the reaction takes place. The use of **protic solvents** (those, such as water or alcohols, with hydrogen-bond donating capability) decreases the power of the nucleophile, because of strong hydrogen-bond interactions between solvent protons and the reactive lone pairs on the nucleophile. A less powerful nucleophile in turn means a slower SN2 reaction. SN2 reactions are faster in **polar, aprotic solvents:** those that lack hydrogen-bond donating capability. Below are several polar aprotic solvents that are commonly used in the laboratory:

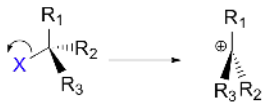


These aprotic solvents are polar but, because they do not form hydrogen bonds with the anionic nucleophile, there is a relatively weak interaction between the aprotic solvent and the nucleophile. By using an aprotic solvent we can raise the reactivity of the nucleophile. This can sometimes have dramatic effects on the rate at which a nucleophilic substitution reaction can occur. For example, if we consider the reaction between bromoethane and potassium iodide, the reaction occurs 500 times faster in acetone than in methanol.

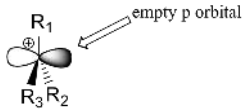


The S_N1 mechanism

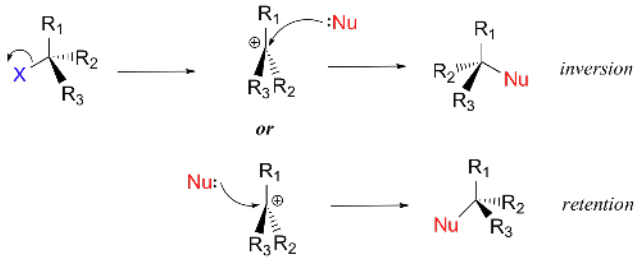
A second model for a nucleophilic substitution reaction is called the '**dissociative**', or '**S_N1**' mechanism: in this picture, the C-X bond breaks *first*, before the nucleophile approaches:



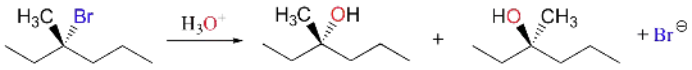
This results in the formation of a carbocation: because the central carbon has only three bonds, it bears a formal charge of +1. Recall that a carbocation should be pictured as sp^2 hybridized, with trigonal planar geometry. Perpendicular to the plane formed by the three sp^2 hybrid orbitals is an empty, unhybridized *p* orbital.



In the second step of this two-step reaction, the nucleophile attacks the empty, 'electron hungry' *p* orbital of the carbocation to form a new bond and return the carbon to tetrahedral geometry.

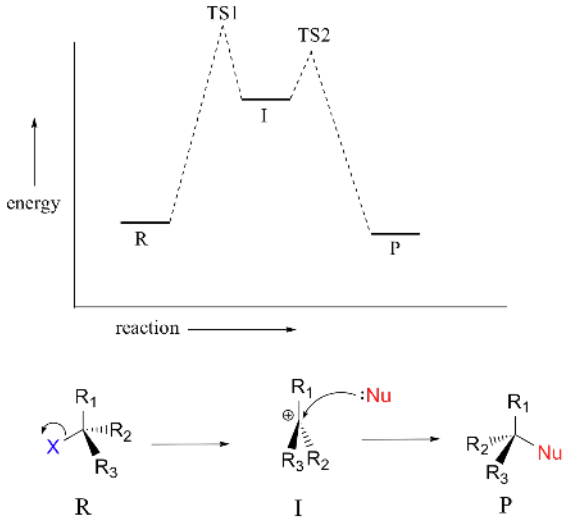


We saw that S_N2 reactions result specifically in inversion of stereochemistry at the electrophilic carbon center. What about the stereochemical outcome of S_N1 reactions? In the model S_N1 reaction shown above, the leaving group dissociates completely from the vicinity of the reaction before the nucleophile begins its attack. Because the leaving group is no longer in the picture, the nucleophile is free to attack from either side of the planar, sp^2-hybridized carbocation electrophile. This means that about half the time the product has the same stereochemical configuration as the starting material (retention of configuration), and about half the time the stereochemistry has been inverted. In other words, *racemization* has occurred at the carbon center. As an example, the tertiary alkyl bromide below would be expected to form a racemic mix of *R* and *S* alcohols after an S_N1 reaction with water as the incoming nucleophile.



Exercise
Draw the structure of the intermediate in the two-step nucleophilic substitution reaction above.

The S_N1 reaction we see an example of a reaction intermediate, a very important concept in the study of organic reaction mechanisms that was introduced earlier in the module on organic reactivity Recall that many important organic reactions do not occur in a single step; rather, they are the sum of two or more discreet bond-forming / bond-breaking steps, and involve transient intermediate species that go on to react very quickly. In the S_N1 reaction, the carbocation species is a reaction intermediate. A potential energy diagram for an S_N1 reaction shows that the carbocation intermediate can be visualized as a kind of valley in the path of the reaction, higher in energy than both the reactant and product but lower in energy than the two transition states.



Exercise

Draw structures representing TS1 and TS2 in the reaction above. Use the solid/dash wedge convention to show three dimensions.

Recall that the first step of the reaction above, in which two charged species are formed from a neutral molecule, is much the slower of the two steps, and is therefore rate-determining. This is illustrated by the energy diagram, where the activation energy for the first step is higher than that for the second step. Also recall that an S_N1 reaction has *first order* kinetics, because the rate determining step involves one molecule splitting apart, not two molecules colliding.

Exercise

Consider two nucleophilic substitutions that occur uncatalyzed in solution. Assume that reaction A is S_N2, and reaction B is S_N1. Predict, in each case, what would happen to the rate of the reaction if the concentration of the nucleophile were doubled, while all other conditions remained constant.

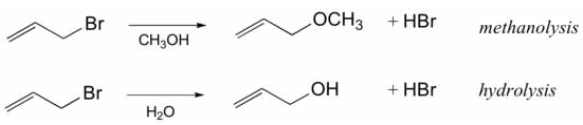
A: $CH_3I + CH_3S^{\ominus} \xrightarrow{S_N2}$

B: $(CH_3)_3CBr + CH_3SH \xrightarrow{S_N1}$

Influence of the solvent in an SN1 reaction

Since the hydrogen atom in a polar protic solvent is highly positively charged, it can interact with the anionic nucleophile which would negatively affect an SN2, but it does not affect an SN1 reaction because the nucleophile is not a part of the rate-determining step. Polar protic solvents actually speed up the rate of the unimolecular substitution reaction because the large dipole moment of the solvent helps to stabilize the transition state. The highly positive and highly negative parts interact with the substrate to lower the energy of the transition state. Since the carbocation is unstable, anything that can stabilize this even a little will speed up the reaction.

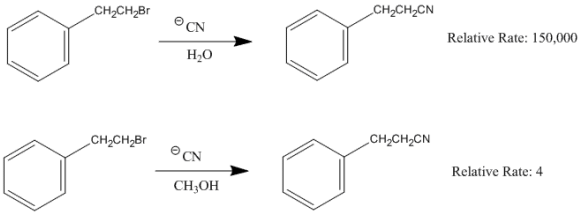
Sometimes in an SN1 reaction the solvent acts as the nucleophile. This is called a solvolysis reaction.The S_N1 reaction of allyl bromide in methanol is an example of what we would call **methanolysis**, while if water is the solvent the reaction would be called **hydrolysis**:



The polarity and the ability of the solvent to stabilize the intermediate carbocation is very important as shown by the relative rate data for the solvolysis (see table below). The dielectric constant of a solvent roughly provides a measure of the solvent's polarity. A dielectric constant below 15 is usually considered non-polar. Basically, the dielectric constant can be thought of as the solvent's ability to reduce the internal charge of the solvent. So for our purposes, the higher the dielectric constant the more polar the substance and in the case of S_N1 reactions, the faster the rate.

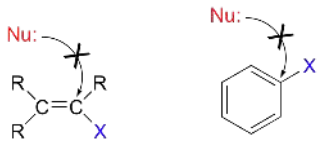
Solvent	Dielectric Constant	Relative Rate
• CH_3CO_2H • CH_3OH • H_2O	• 6 • 33 • 78	• 1 • 4 • 150,000

Below is the same reaction conducted in two different solvents and the relative rate that corresponds with it.



Exercise
Draw a complete curved-arrow mechanism for the methanolysis reaction of allyl bromide shown above.

One more important point must be made before continuing: nucleophilic substitutions as a rule occur at sp^3-hybridized carbons, and *not* where the leaving group is attached to an sp^2-hybridized carbon::



Bonds on sp^2-hybridized carbons are inherently shorter and stronger than bonds on sp^3-hybridized carbons, meaning that it is harder to break the C-X bond in these substrates. S_N2 reactions of this type are unlikely also because the (hypothetical) electrophilic carbon is protected from nucleophilic attack by electron density in the p bond. S_N1 reactions are highly unlikely, because the resulting carbocation intermediate, which would be sp-hybridized, would be very unstable (we'll discuss the relative stability of carbocation intermediates in a later section of this module).

Before we look at some real-life nucleophilic substitution reactions in the next chapter, we will spend some time in the remainder of this module focusing more closely on the three principal partners in the nucleophilic substitution reaction: the nucleophile, the electrophile, and the leaving group.

Practice Problems

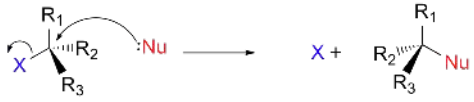
9.3: Factors That Affect S_N2 Reactions is shared under a not declared license and was authored, remixed, and/or curated by LibreTexts.

- **Substitution reactions of alkyl halides: two mechanisms** is licensed CC BY-NC-SA 4.0.

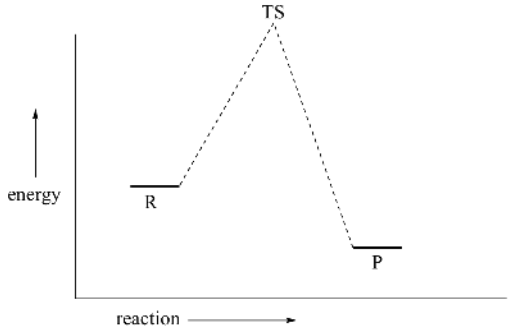
9.4: The Mechanism for an S_N1 Reaction

The S_N2 mechanism

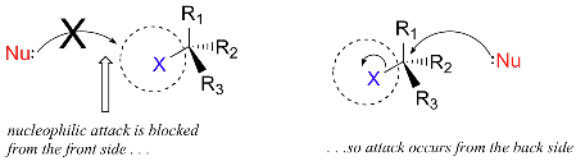
There are two mechanistic models for how an alkyl halide can undergo nucleophilic substitution. In the first picture, the reaction takes place in a single step, and bond-forming and bond-breaking occur simultaneously. (In all figures in this section, 'X' indicates a halogen substituent).



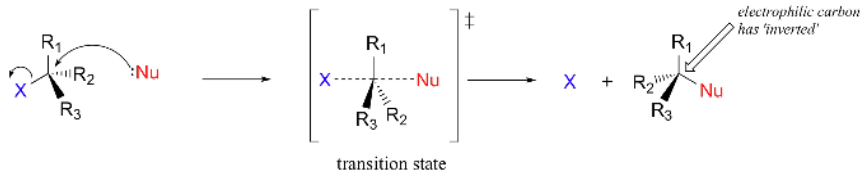
This is called an '**S_N2**' mechanism. In the term S_N2, S stands for 'substitution', the subscript N stands for 'nucleophilic', and the number 2 refers to the fact that this is a **bimolecular reaction**: the overall rate depends on a step in which two separate molecules (the nucleophile and the electrophile) collide. A potential energy diagram for this reaction shows the transition state (TS) as the highest point on the pathway from reactants to products.



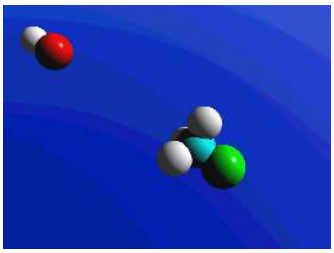
If you look carefully at the progress of the S_N2 reaction, you will realize something very important about the outcome. The nucleophile, being an electron-rich species, must attack the electrophilic carbon from the *back side* relative to the location of the leaving group. Approach from the front side simply doesn't work: the leaving group - which is also an electron-rich group - blocks the way.



The result of this backside attack is that the stereochemical configuration at the central carbon *inverts* as the reaction proceeds. In a sense, the molecule is turned inside out. At the transition state, the electrophilic carbon and the three 'R' substituents all lie on the same plane.

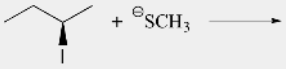


What this means is that S_N2 reactions whether enzyme catalyzed or not, are inherently stereoselective: when the substitution takes place at a stereocenter, we can confidently predict the stereochemical configuration of the product. Below is an animation illustrating the principles we have just learned, showing the S_N2 reaction between hydroxide ion and methyl iodide. Notice how backside attack by the hydroxide nucleophile results in inversion at the tetrahedral carbon electrophile.



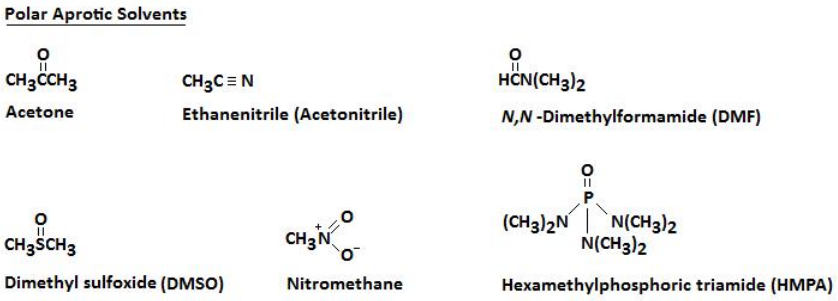
Exercise

Predict the structure of the product in this S_N2 reaction. Be sure to specify stereochemistry.

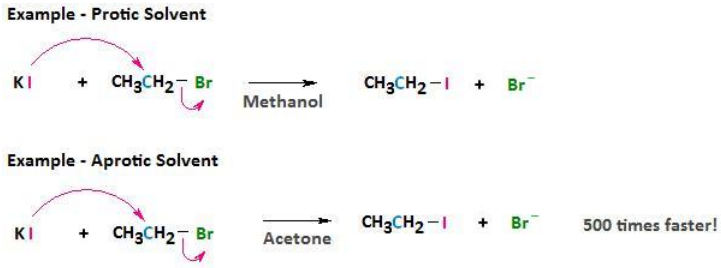


Influence of the solvent in an S_N2 reaction

The rate of an SN2 reaction is significantly influenced by the solvent in which the reaction takes place. The use of **protic solvents** (those, such as water or alcohols, with hydrogen-bond donating capability) decreases the power of the nucleophile, because of strong hydrogen-bond interactions between solvent protons and the reactive lone pairs on the nucleophile. A less powerful nucleophile in turn means a slower SN2 reaction. SN2 reactions are faster in **polar, aprotic solvents:** those that lack hydrogen-bond donating capability. Below are several polar aprotic solvents that are commonly used in the laboratory:

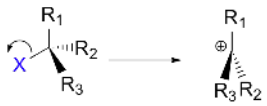


These aprotic solvents are polar but, because they do not form hydrogen bonds with the anionic nucleophile, there is a relatively weak interaction between the aprotic solvent and the nucleophile. By using an aprotic solvent we can raise the reactivity of the nucleophile. This can sometimes have dramatic effects on the rate at which a nucleophilic substitution reaction can occur. For example, if we consider the reaction between bromoethane and potassium iodide, the reaction occurs 500 times faster in acetone than in methanol.

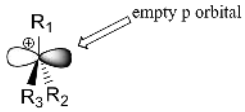


The S_N1 mechanism

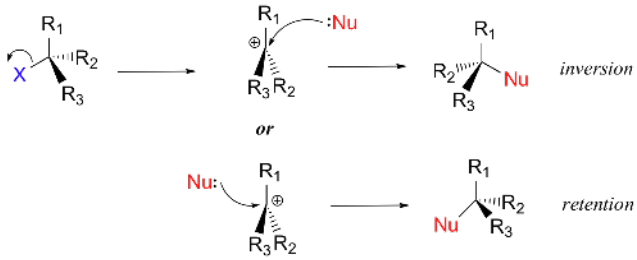
A second model for a nucleophilic substitution reaction is called the '**dissociative**', or '**S_N1**' mechanism: in this picture, the C-X bond breaks *first*, before the nucleophile approaches:



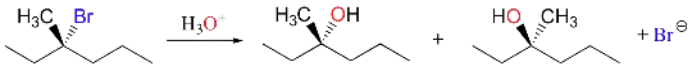
This results in the formation of a carbocation: because the central carbon has only three bonds, it bears a formal charge of +1. Recall that a carbocation should be pictured as sp^2 hybridized, with trigonal planar geometry. Perpendicular to the plane formed by the three sp^2 hybrid orbitals is an empty, unhybridized *p* orbital.



In the second step of this two-step reaction, the nucleophile attacks the empty, 'electron hungry' *p* orbital of the carbocation to form a new bond and return the carbon to tetrahedral geometry.

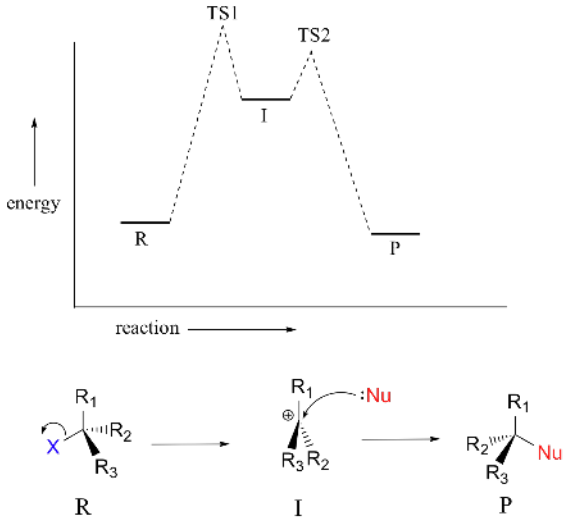


We saw that S_N2 reactions result specifically in inversion of stereochemistry at the electrophilic carbon center. What about the stereochemical outcome of S_N1 reactions? In the model S_N1 reaction shown above, the leaving group dissociates completely from the vicinity of the reaction before the nucleophile begins its attack. Because the leaving group is no longer in the picture, the nucleophile is free to attack from either side of the planar, sp^2-hybridized carbocation electrophile. This means that about half the time the product has the same stereochemical configuration as the starting material (retention of configuration), and about half the time the stereochemistry has been inverted. In other words, *racemization* has occurred at the carbon center. As an example, the tertiary alkyl bromide below would be expected to form a racemic mix of *R* and *S* alcohols after an S_N1 reaction with water as the incoming nucleophile.



Exercise
Draw the structure of the intermediate in the two-step nucleophilic substitution reaction above.

The S_N1 reaction we see an example of a reaction intermediate, a very important concept in the study of organic reaction mechanisms that was introduced earlier in the module on organic reactivity Recall that many important organic reactions do not occur in a single step; rather, they are the sum of two or more discreet bond-forming / bond-breaking steps, and involve transient intermediate species that go on to react very quickly. In the S_N1 reaction, the carbocation species is a reaction intermediate. A potential energy diagram for an S_N1 reaction shows that the carbocation intermediate can be visualized as a kind of valley in the path of the reaction, higher in energy than both the reactant and product but lower in energy than the two transition states.



Exercise

Draw structures representing TS1 and TS2 in the reaction above. Use the solid/dash wedge convention to show three dimensions.

Recall that the first step of the reaction above, in which two charged species are formed from a neutral molecule, is much the slower of the two steps, and is therefore rate-determining. This is illustrated by the energy diagram, where the activation energy for the first step is higher than that for the second step. Also recall that an S_N1 reaction has *first order* kinetics, because the rate determining step involves one molecule splitting apart, not two molecules colliding.

Exercise

Consider two nucleophilic substitutions that occur uncatalyzed in solution. Assume that reaction A is S_N2, and reaction B is S_N1. Predict, in each case, what would happen to the rate of the reaction if the concentration of the nucleophile were doubled, while all other conditions remained constant.

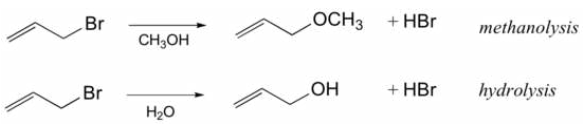
A: $CH_3I + CH_3S^{\ominus} \xrightarrow{S_N2}$

B: $(CH_3)_3CBr + CH_3SH \xrightarrow{S_N1}$

Influence of the solvent in an SN1 reaction

Since the hydrogen atom in a polar protic solvent is highly positively charged, it can interact with the anionic nucleophile which would negatively affect an SN2, but it does not affect an SN1 reaction because the nucleophile is not a part of the rate-determining step. Polar protic solvents actually speed up the rate of the unimolecular substitution reaction because the large dipole moment of the solvent helps to stabilize the transition state. The highly positive and highly negative parts interact with the substrate to lower the energy of the transition state. Since the carbocation is unstable, anything that can stabilize this even a little will speed up the reaction.

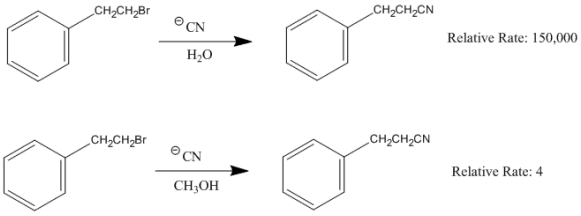
Sometimes in an SN1 reaction the solvent acts as the nucleophile. This is called a solvolysis reaction.The S_N1 reaction of allyl bromide in methanol is an example of what we would call **methanolysis**, while if water is the solvent the reaction would be called **hydrolysis**:



The polarity and the ability of the solvent to stabilize the intermediate carbocation is very important as shown by the relative rate data for the solvolysis (see table below). The dielectric constant of a solvent roughly provides a measure of the solvent's polarity. A dielectric constant below 15 is usually considered non-polar. Basically, the dielectric constant can be thought of as the solvent's ability to reduce the internal charge of the solvent. So for our purposes, the higher the dielectric constant the more polar the substance and in the case of S_N1 reactions, the faster the rate.

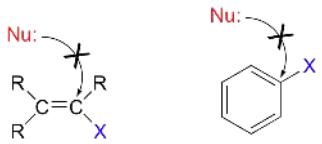
Solvent	Dielectric Constant	Relative Rate
• CH_3CO_2H • CH_3OH • H_2O	• 6 • 33 • 78	• 1 • 4 • 150,000

Below is the same reaction conducted in two different solvents and the relative rate that corresponds with it.



Exercise
Draw a complete curved-arrow mechanism for the methanolysis reaction of allyl bromide shown above.

One more important point must be made before continuing: nucleophilic substitutions as a rule occur at sp^3-hybridized carbons, and *not* where the leaving group is attached to an sp^2-hybridized carbon::



Bonds on sp^2-hybridized carbons are inherently shorter and stronger than bonds on sp^3-hybridized carbons, meaning that it is harder to break the C-X bond in these substrates. S_N2 reactions of this type are unlikely also because the (hypothetical) electrophilic carbon is protected from nucleophilic attack by electron density in the p bond. S_N1 reactions are highly unlikely, because the resulting carbocation intermediate, which would be sp-hybridized, would be very unstable (we'll discuss the relative stability of carbocation intermediates in a later section of this module).

Before we look at some real-life nucleophilic substitution reactions in the next chapter, we will spend some time in the remainder of this module focusing more closely on the three principal partners in the nucleophilic substitution reaction: the nucleophile, the electrophile, and the leaving group.

Practice Problems

9.4: The Mechanism for an S_N1 Reaction is shared under a not declared license and was authored, remixed, and/or curated by LibreTexts.

- **Substitution reactions of alkyl halides: two mechanisms** is licensed CC BY-NC-SA 4.0.

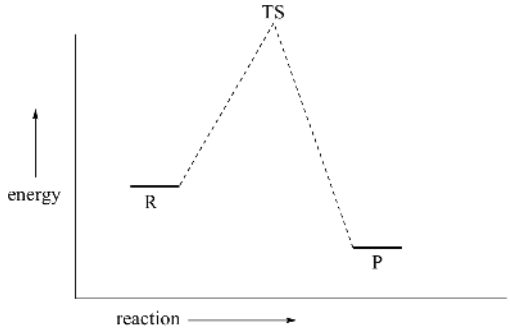
9.5: Factors That Affect S_N1 Reactions

The S_N2 mechanism

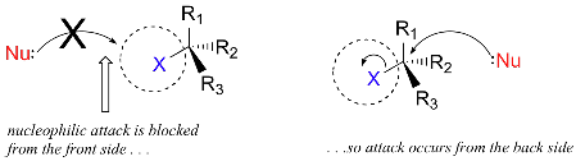
There are two mechanistic models for how an alkyl halide can undergo nucleophilic substitution. In the first picture, the reaction takes place in a single step, and bond-forming and bond-breaking occur simultaneously. (In all figures in this section, 'X' indicates a halogen substituent).



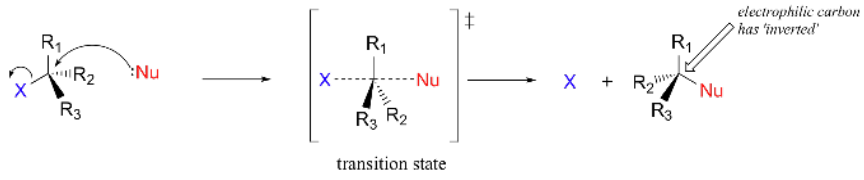
This is called an '**S_N2**' mechanism. In the term S_N2, S stands for 'substitution', the subscript N stands for 'nucleophilic', and the number 2 refers to the fact that this is a **bimolecular reaction**: the overall rate depends on a step in which two separate molecules (the nucleophile and the electrophile) collide. A potential energy diagram for this reaction shows the transition state (TS) as the highest point on the pathway from reactants to products.



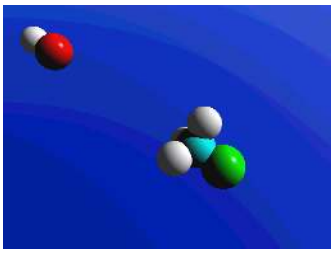
If you look carefully at the progress of the S_N2 reaction, you will realize something very important about the outcome. The nucleophile, being an electron-rich species, must attack the electrophilic carbon from the *back side* relative to the location of the leaving group. Approach from the front side simply doesn't work: the leaving group - which is also an electron-rich group - blocks the way.



The result of this backside attack is that the stereochemical configuration at the central carbon *inverts* as the reaction proceeds. In a sense, the molecule is turned inside out. At the transition state, the electrophilic carbon and the three 'R' substituents all lie on the same plane.

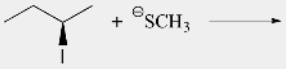


What this means is that S_N2 reactions whether enzyme catalyzed or not, are inherently stereoselective: when the substitution takes place at a stereocenter, we can confidently predict the stereochemical configuration of the product. Below is an animation illustrating the principles we have just learned, showing the S_N2 reaction between hydroxide ion and methyl iodide. Notice how backside attack by the hydroxide nucleophile results in inversion at the tetrahedral carbon electrophile.



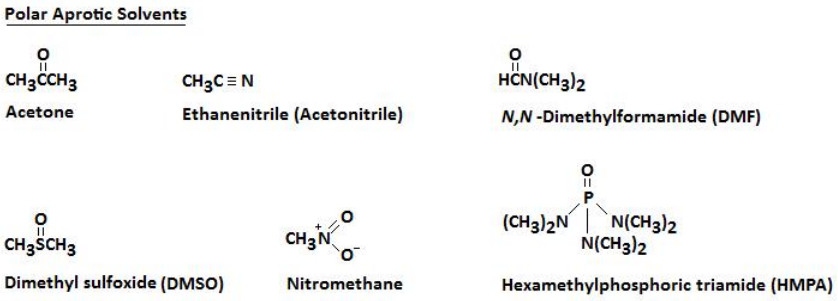
Exercise

Predict the structure of the product in this S_N2 reaction. Be sure to specify stereochemistry.

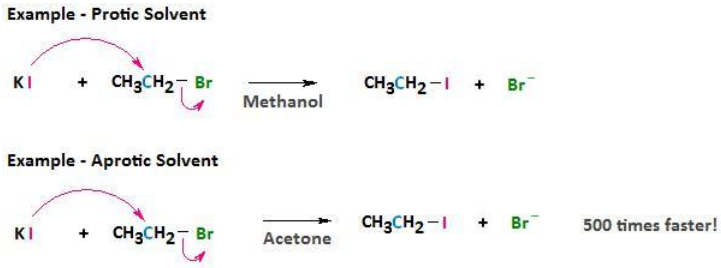


Influence of the solvent in an S_N2 reaction

The rate of an SN2 reaction is significantly influenced by the solvent in which the reaction takes place. The use of **protic solvents** (those, such as water or alcohols, with hydrogen-bond donating capability) decreases the power of the nucleophile, because of strong hydrogen-bond interactions between solvent protons and the reactive lone pairs on the nucleophile. A less powerful nucleophile in turn means a slower SN2 reaction. SN2 reactions are faster in **polar, aprotic solvents:** those that lack hydrogen-bond donating capability. Below are several polar aprotic solvents that are commonly used in the laboratory:

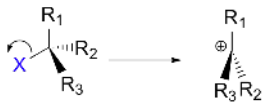


These aprotic solvents are polar but, because they do not form hydrogen bonds with the anionic nucleophile, there is a relatively weak interaction between the aprotic solvent and the nucleophile. By using an aprotic solvent we can raise the reactivity of the nucleophile. This can sometimes have dramatic effects on the rate at which a nucleophilic substitution reaction can occur. For example, if we consider the reaction between bromoethane and potassium iodide, the reaction occurs 500 times faster in acetone than in methanol.

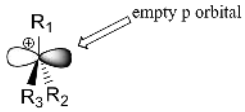


The S_N1 mechanism

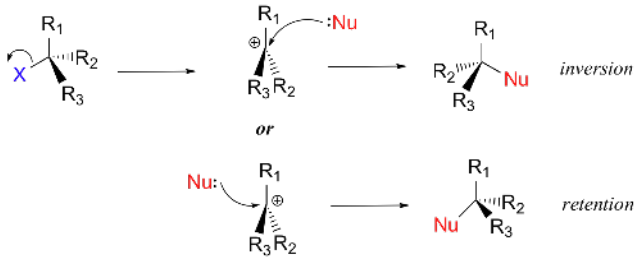
A second model for a nucleophilic substitution reaction is called the '**dissociative**', or '**S_N1**' mechanism: in this picture, the C-X bond breaks *first*, before the nucleophile approaches:



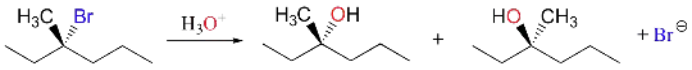
This results in the formation of a carbocation: because the central carbon has only three bonds, it bears a formal charge of +1. Recall that a carbocation should be pictured as sp^2 hybridized, with trigonal planar geometry. Perpendicular to the plane formed by the three sp^2 hybrid orbitals is an empty, unhybridized *p* orbital.



In the second step of this two-step reaction, the nucleophile attacks the empty, 'electron hungry' *p* orbital of the carbocation to form a new bond and return the carbon to tetrahedral geometry.

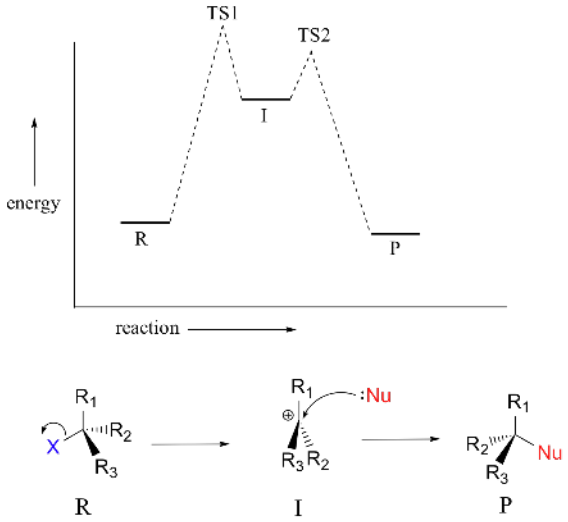


We saw that S_N2 reactions result specifically in inversion of stereochemistry at the electrophilic carbon center. What about the stereochemical outcome of S_N1 reactions? In the model S_N1 reaction shown above, the leaving group dissociates completely from the vicinity of the reaction before the nucleophile begins its attack. Because the leaving group is no longer in the picture, the nucleophile is free to attack from either side of the planar, sp^2-hybridized carbocation electrophile. This means that about half the time the product has the same stereochemical configuration as the starting material (retention of configuration), and about half the time the stereochemistry has been inverted. In other words, *racemization* has occurred at the carbon center. As an example, the tertiary alkyl bromide below would be expected to form a racemic mix of *R* and *S* alcohols after an S_N1 reaction with water as the incoming nucleophile.



Exercise
Draw the structure of the intermediate in the two-step nucleophilic substitution reaction above.

The S_N1 reaction we see an example of a reaction intermediate, a very important concept in the study of organic reaction mechanisms that was introduced earlier in the module on organic reactivity Recall that many important organic reactions do not occur in a single step; rather, they are the sum of two or more discreet bond-forming / bond-breaking steps, and involve transient intermediate species that go on to react very quickly. In the S_N1 reaction, the carbocation species is a reaction intermediate. A potential energy diagram for an S_N1 reaction shows that the carbocation intermediate can be visualized as a kind of valley in the path of the reaction, higher in energy than both the reactant and product but lower in energy than the two transition states.



Exercise

Draw structures representing TS1 and TS2 in the reaction above. Use the solid/dash wedge convention to show three dimensions.

Recall that the first step of the reaction above, in which two charged species are formed from a neutral molecule, is much the slower of the two steps, and is therefore rate-determining. This is illustrated by the energy diagram, where the activation energy for the first step is higher than that for the second step. Also recall that an S_N1 reaction has *first order* kinetics, because the rate determining step involves one molecule splitting apart, not two molecules colliding.

Exercise

Consider two nucleophilic substitutions that occur uncatalyzed in solution. Assume that reaction A is S_N2, and reaction B is S_N1. Predict, in each case, what would happen to the rate of the reaction if the concentration of the nucleophile were doubled, while all other conditions remained constant.

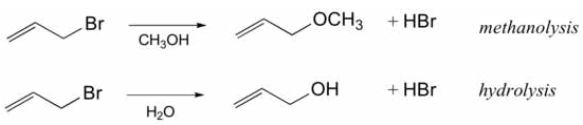
A: $CH_3I + CH_3S^{\ominus} \xrightarrow{S_N2}$

B: $(CH_3)_3CBr + CH_3SH \xrightarrow{S_N1}$

Influence of the solvent in an SN1 reaction

Since the hydrogen atom in a polar protic solvent is highly positively charged, it can interact with the anionic nucleophile which would negatively affect an SN2, but it does not affect an SN1 reaction because the nucleophile is not a part of the rate-determining step. Polar protic solvents actually speed up the rate of the unimolecular substitution reaction because the large dipole moment of the solvent helps to stabilize the transition state. The highly positive and highly negative parts interact with the substrate to lower the energy of the transition state. Since the carbocation is unstable, anything that can stabilize this even a little will speed up the reaction.

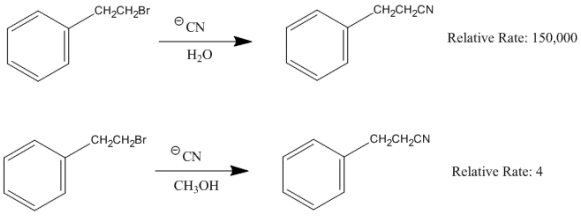
Sometimes in an SN1 reaction the solvent acts as the nucleophile. This is called a solvolysis reaction.The S_N1 reaction of allyl bromide in methanol is an example of what we would call **methanolysis**, while if water is the solvent the reaction would be called **hydrolysis**:



The polarity and the ability of the solvent to stabilize the intermediate carbocation is very important as shown by the relative rate data for the solvolysis (see table below). The dielectric constant of a solvent roughly provides a measure of the solvent's polarity. A dielectric constant below 15 is usually considered non-polar. Basically, the dielectric constant can be thought of as the solvent's ability to reduce the internal charge of the solvent. So for our purposes, the higher the dielectric constant the more polar the substance and in the case of S_N1 reactions, the faster the rate.

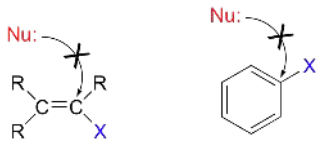
Solvent	Dielectric Constant	Relative Rate
• CH_3CO_2H • CH_3OH • H_2O	• 6 • 33 • 78	• 1 • 4 • 150,000

Below is the same reaction conducted in two different solvents and the relative rate that corresponds with it.



Exercise
Draw a complete curved-arrow mechanism for the methanolysis reaction of allyl bromide shown above.

One more important point must be made before continuing: nucleophilic substitutions as a rule occur at sp^3-hybridized carbons, and *not* where the leaving group is attached to an sp^2-hybridized carbon::



Bonds on sp^2-hybridized carbons are inherently shorter and stronger than bonds on sp^3-hybridized carbons, meaning that it is harder to break the C-X bond in these substrates. S_N2 reactions of this type are unlikely also because the (hypothetical) electrophilic carbon is protected from nucleophilic attack by electron density in the p bond. S_N1 reactions are highly unlikely, because the resulting carbocation intermediate, which would be sp-hybridized, would be very unstable (we'll discuss the relative stability of carbocation intermediates in a later section of this module).

Before we look at some real-life nucleophilic substitution reactions in the next chapter, we will spend some time in the remainder of this module focusing more closely on the three principal partners in the nucleophilic substitution reaction: the nucleophile, the electrophile, and the leaving group.

Practice Problems

9.5: Factors That Affect S_N1 Reactions is shared under a not declared license and was authored, remixed, and/or curated by LibreTexts.

- **Substitution reactions of alkyl halides: two mechanisms** is licensed CC BY-NC-SA 4.0.

9.6: Comparing the $S\ N\ 2$ and $S\ N\ 1$ Reactions of Alkyl Halides

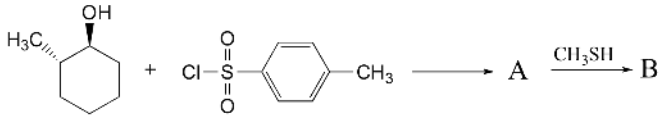
8.5A: What makes a good leaving group?

In our general discussion of nucleophilic substitution reactions, we have until now been designating the leaving group simply as “X". As you may imagine, however, the nature of the leaving group is an important consideration: if the C-X bond does not break, the new bond between the nucleophile and electrophilic carbon cannot form, regardless of whether the substitution is S_N1 or S_N2.

When the C-X bond breaks in a nucleophilic substitution, the pair of electrons in the bond goes with the leaving group. In this way, the leaving group is analogous to the conjugate base in a Brønsted-Lowry acid-base reaction. When we were evaluating the strength of acids in chapter 7, what we were really doing was evaluating the stability of the conjugate base that resulted from the proton transfer. All of the concepts that we used to evaluate the stability of conjugate bases we can use again to evaluate leaving groups – essentially they are one and the same. In other words, the trends in basicity are parallel to the trends in leaving group potential - the weaker the base, the better the leaving group. Just as with conjugate bases, the most important question regarding leaving groups is this: when a leaving group leaves and takes a pair of electrons with it, how well is the extra electron density stabilized?

In laboratory synthesis reactions, halides often act as leaving groups. Iodide, which is the *least* basic of the four main halides, is also the *best* leaving group – it is the most stable as a negative ion. Fluoride is the least effective leaving group among the halides, because fluoride anion is the most basic.

Exercise 8.14: Predict the structures of A and B in the following reaction:



Solution

Template:ExampleEnd

8.5D: **Predicting S_N1 vs. S_N2 mechanisms; competition between nucleophilic substitution and elimination reactions**

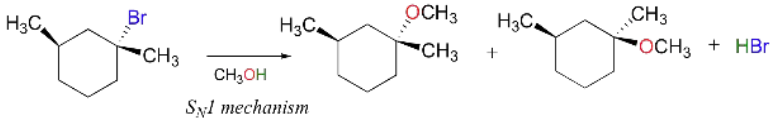
When considering whether a nucleophilic substitution is likely to occur via an S_N1 or S_N2 mechanism, we really need to consider three factors:

1) **The electrophile:** when the leaving group is attached to a methyl group or a primary carbon, an S_N2 mechanism is favored (here the electrophile is unhindered by surrounded groups, and any carbocation intermediate would be high-energy and thus unlikely). When the leaving group is attached to a tertiary, allylic, or benzylic carbon, a carbocation intermediate will be relatively stable and thus an S_N1 mechanism is favored.

2) **The nucleophile**: powerful nucleophiles, especially those with negative charges, favor the S_N2 mechanism. Weaker nucleophiles such as water or alcohols favor the S_N1 mechanism.

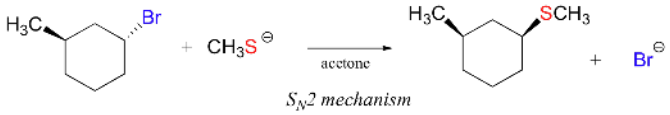
3) **The solvent**: Polar aprotic solvents favor the S_N2 mechanism by enhancing the reactivity of the nucleophile. Polar protic solvents favor the S_N1 mechanism by stabilizing the carbocation intermediate. S_N1 reactions are frequently solvolysis reactions.

For example, the reaction below has a tertiary alkyl bromide as the electrophile, a weak nucleophile, and a polar protic solvent (we’ll assume that methanol is the solvent). Thus we’d confidently predict an S_N1 reaction mechanism. Because substitution occurs at a chiral carbon, we can also predict that the reaction will proceed with racemization.



S_N1 mechanism

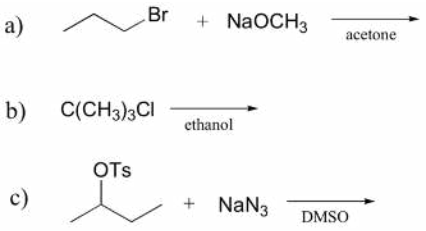
In the reaction below, on the other hand, the electrophile is a secondary alkyl bromide – with these, both S_N1 and S_N2 mechanisms are possible, depending on the nucleophile and the solvent. In this example, the nucleophile (a thiolate anion) is strong, and a polar protic solvent is used – so the S_N2 mechanism is heavily favored. The reaction is expected to proceed with inversion of configuration.



S_N2 mechanism

Template:ExampleStart

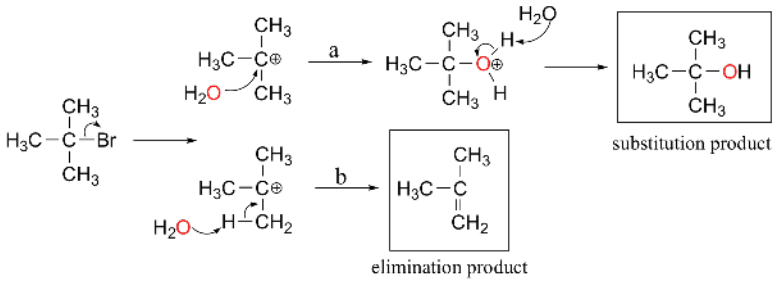
Exercise 8.15: Determine whether each substitution reaction shown below is likely to proceed by an S_N1 or S_N2 mechanism.



Solution

Template:ExampleEnd

In all of our discussion so far about nucleophilic substitutions, we have ignored another important possibility. In many cases, including the two examples above, substitution reactions compete with a type of reaction known as **elimination**. Consider, for example, the two courses that a reaction could take when *tert*-butyl bromide reacts with water:



We begin with formation of the carbocation intermediate. In pathway 'a', water acts as a nucleophile – this is, of course, the familiar S_N1 reaction. However, a water molecule encountering the carbocation intermediate could alternatively act as a *base* rather than as a nucleophile, plucking a proton from one of the methyl carbons and causing the formation of a new carbon-carbon p bond. This alternative pathway is called an elimination reaction, and in fact with the conditions above, both the substitution and the elimination pathways will occur in competition with each other.

We will have lots more to say about elimination reactions in chapter 14, focusing on biochemical eliminations but also thinking about the competition between substitution and elimination that occurs with many nonenzymatic reactions.

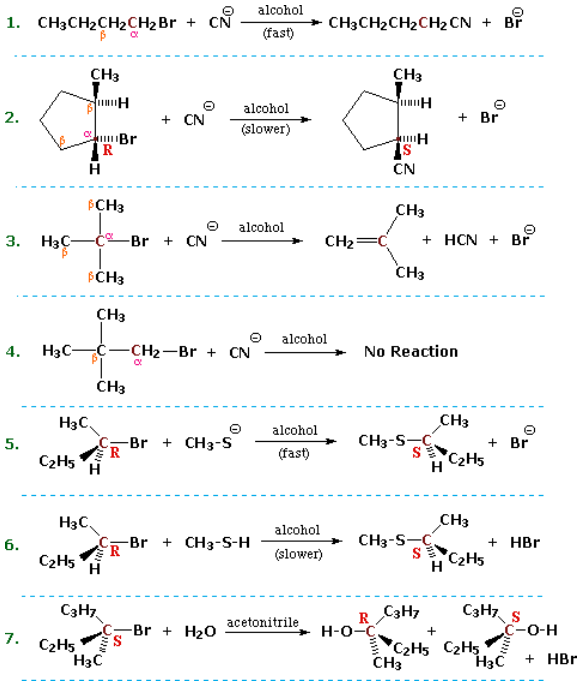
Organic Chemistry With a Biological Emphasis by Tim Soderberg (University of Minnesota, Morris)

9.6: Comparing the S_N2 and S_N1 Reactions of Alkyl Halides is shared under a not declared license and was authored, remixed, and/or curated by LibreTexts.

9.7: Elimination Reaction of Alkyl Halides

Certain types of reactions that are likely to occur with alkyl halides. In describing these, it is useful to designate the halogen-bearing carbon as **alpha** and the carbon atom(s) adjacent to it as **beta**, as noted in the first four equations shown below. Replacement or substitution of the halogen on the α-carbon (colored maroon) by a nucleophilic reagent is a commonly observed reaction, as shown in equations **1, 2, 5, 6 & 7** below.

Also, since the electrophilic character introduced by the halogen extends to the β-carbons, and since nucleophiles are also bases, the possibility of base induced H-X elimination must also be considered, as illustrated by equation **3**. Finally, there are some combinations of alkyl halides and nucleophiles that fail to show any reaction over a 24 hour period, such as the example in equation **4**. For consistency, alkyl bromides have been used in these examples. Similar reactions occur when alkyl chlorides or iodides are used, but the speed of the reactions and the exact distribution of products will change.

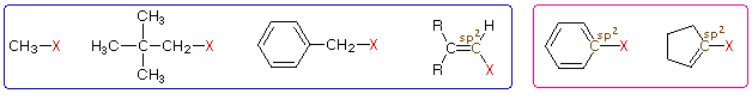


In order to understand why some combinations of alkyl halides and nucleophiles give a substitution reaction, whereas other combinations give elimination, and still others give no observable reaction, we must investigate systematically the way in which changes in reaction variables perturb the course of the reaction. The following general equation summarizes the factors that will be important in such an investigation.



One conclusion, relating the structure of the R-group to possible products, should be immediately obvious. **If R- has no beta-hydrogens an elimination reaction is not possible**, unless a structural rearrangement occurs first. The first four halides shown on the left below do not give elimination reactions on treatment with base, because they have no β-hydrogens. The two halides on the right do not normally undergo such reactions because the potential elimination products have highly strained double or triple bonds.

It is also worth noting that sp^2 hybridized C–X compounds, such as the three on the right, do not normally undergo nucleophilic substitution reactions, unless other functional groups perturb the double bond(s).



Using the general reaction shown above as our reference, we can identify the following variables and observables.

Variables	**R** change α-carbon from 1º to 2º to 3º if the α-carbon is a chiral center, set as (*R*) or (*S*) **X** change from Cl to Br to I (F is relatively unreactive) **Nu:** change from anion to neutral; change basicity; change polarizability **Solvent** polar vs. non-polar; protic vs. non-protic
Observables	**Products** substitution, elimination, no reaction. **Stereospecificity** if the α-carbon is a chiral center what happens to its configuration? **Reaction Rate** measure as a function of reactant concentration.

When several reaction variables may be changed, it is important to isolate the effects of each during the course of study. In other words: **only one variable should be changed at a time**, the others being held as constant as possible. For example, we can examine the effect of changing the halogen substituent from Cl to Br to I, using ethyl as a common R–group, cyanide anion as a common nucleophile, and ethanol as a common solvent. We would find a common substitution product, C_2H_5–CN, in all cases, but the speed or rate of the reaction would increase in the order: Cl < Br < I. This reactivity order reflects both the strength of the C–X bond, and the stability of $X^{(-)}$ as a leaving group, and leads to the general conclusion that alkyl iodides are the most reactive members of this functional class.

Contributors

- William Reusch, Professor Emeritus (Michigan State U.), Virtual Textbook of Organic Chemistry

9.7: Elimination Reaction of Alkyl Halides is shared under a not declared license and was authored, remixed, and/or curated by LibreTexts.

- **Substitution and Elimination Reactions of Alkyl Halides** by William Reusch is licensed CC BY-NC-SA 4.0.

9.8: Products of Elimination Reactions

9.8: Products of Elimination Reactions is shared under a not declared license and was authored, remixed, and/or curated by LibreTexts.

9.9: Comparing the E2 and E1 Reactions of Alkyl Halides

Having discussed the many factors that influence nucleophilic substitution and elimination reactions of alkyl halides, we must now consider the practical problem of predicting the most likely outcome when a given alkyl halide is reacted with a given nucleophile. As we noted earlier, several variables must be considered, **the most important being the structure of the alkyl group and the nature of the nucleophilic reactant**.In general, in order for an SN1 or E1 reaction to occur, the relevant carbocation intermediate must be relatively stable. Strong nucleophile favor substitution, and strong bases, especially strong hindered bases (such as tert-butoxide) favor elimination.

The nature of the halogen substituent on the alkyl halide is usually not very significant if it is Cl, Br or I. In cases where both S_N2 and E2 reactions compete, chlorides generally give more elimination than do iodides, since the greater electronegativity of chlorine increases the acidity of beta-hydrogens. Indeed, although alkyl fluorides are relatively unreactive, when reactions with basic nucleophiles are forced, elimination occurs (note the high electronegativity of fluorine).

The following table summarizes the expected outcome of alkyl halide reactions with nucleophiles. It is assumed that the alkyl halides have one or more beta-hydrogens, making elimination possible; and that low dielectric solvents (e.g. acetone, ethanol, tetrahydrofuran & ethyl acetate) are used. When a high dielectric solvent would significantly influence the reaction this is noted in red. **Note that halogens bonded to sp^2 or sp hybridized carbon atoms do not normally undergo substitution or elimination reactions with nucleophilic reagents**.

Nucleophile		
Anionic Nucleophiles (Weak Bases: I^-, Br^-, SCN^-, N_3^-, $CH_3CO_2^-$, RS^-, CN^- etc.) pK_a's from -9 to 10 (left to right)	**Anionic Nucleophiles** (Strong Bases: HO^-, RO^-) pK_a's > 15	**Neutral Nucleophiles** (H_2O, ROH, RSH, R_3N) pK_a's ranging from -2 to 11

Alkyl Group			
Primary RCH_2-	Rapid S_N2 substitution. The rate may be reduced by substitution of β-carbons, as in the case of neopentyl.	Rapid S_N2 substitution. E2 elimination may also occur. *e.g.* $ClCH_2CH_2Cl + KOH \longrightarrow CH_2=CHCl$	S_N2 substitution. (N ≈ S >>O)
Secondary R_2CH-	S_N2 substitution and / or E2 elimination (depending on the basicity of the nucleophile). Bases weaker than acetate (pK_a = 4.8) give less elimination. The rate of substitution may be reduced by branching at the β-carbons, and this will increase elimination.	E2 elimination will dominate.	S_N2 substitution. (N ≈ S >>O) In high dielectric ionizing solvents, such as water, dimethyl sulfoxide & acetonitrile, S_N1 and E1 products may be formed slowly.
Tertiary R_3C-	E2 elimination will dominate with most nucleophiles (even if they are weak bases). No S_N2 substitution due to steric hindrance. In high dielectric ionizing solvents, such as water, dimethyl sulfoxide & acetonitrile, S_N1 and E1 products may be expected.	E2 elimination will dominate. No S_N2 substitution will occur. In high dielectric ionizing solvents S_N1 and E1 products may be formed.	E2 elimination with nitrogen nucleophiles (they are bases). No S_N2 substitution. In high dielectric ionizing solvents S_N1 and E1 products may be formed.
Allyl, Benzyl $H_2C=CH-CH_2-$	Rapid S_N2 substitution for 1º and 2º-halides. For 3º-halides a very slow S_N2 substitution or, if the nucleophile is moderately basic, E2 elimination. In high dielectric ionizing solvents, such as water, dimethyl sulfoxide & acetonitrile, S_N1 and E1 products may be observed.	Rapid S_N2 substitution for 1º halides. E2 elimination will compete with substitution in 2º-halides, and dominate in the case of 3º-halides. In high dielectric ionizing solvents S_N1 and E1 products may be formed.	Nitrogen and sulfur nucleophiles will give S_N2 substitution in the case of 1º and 2º-halides. 3º-halides will probably give E2 elimination with nitrogen nucleophiles (they are bases). In high dielectric ionizing solvents S_N1 and E1 products may be formed. Water hydrolysis will be favorable for 2º & 3º-halides.

$CH_2=CHCH_2-$		
Benzyl $C_6H_5CH_2-$	Rapid S_N2 substitution for 1º and 2º-halides. For 3º-halides a very slow S_N2 substitution or, if the nucleophile is moderately basic, E2 elimination. In high dielectric ionizing solvents, such as water, dimethyl sulfoxide & acetonitrile, S_N1 and E1 products may be observed.	Rapid S_N2 substitution for 1º halides (note there are no β hydrogens). E2 elimination will compete with substitution in 2º-halides, and dominate in the case of 3º-halides. In high dielectric ionizing solvents S_N1 and E1 products may be formed.	Nitrogen and sulfur nucleophiles will give S_N2 substitution in the case of 1º and 2º-halides. 3º-halides will probably give E2 elimination with nitrogen nucleophiles (they are bases). In high dielectric ionizing solvents S_N1 and E1 products may be formed. Water hydrolysis will be favorable for 2º & 3º-halides.

Contributors

William Reusch, Professor Emeritus (Michigan State U.), Virtual Textbook of Organic Chemistry

9.9: Comparing the E2 and E1 Reactions of Alkyl Halides is shared under a not declared license and was authored, remixed, and/or curated by LibreTexts.

- **Competition between substitution and elimination** is licensed CC BY-NC-SA 4.0.

9.10: Does an Alkyl Halide Undergo SN2, E2 Reactions or SN1 Reactions?

This page was auto-generated because a user created a sub-page to this page.

9.10: Does an Alkyl Halide Undergo SN2, E2 Reactions or SN1 Reactions? is shared under a not declared license and was authored, remixed, and/or curated by LibreTexts.

9.11: Does an Alkyl Halide Undergo SN2/E2 Reactions or SN1/E1 Reactions?

9.11: Does an Alkyl Halide Undergo SN2/E2 Reactions or SN1/E1 Reactions? is shared under a not declared license and was authored, remixed, and/or curated by LibreTexts.

9.12: Solvent Effects

Nucleophilicity

Recall the definitions of electrophile and nucleophile:

> **Electrophile**: An electron deficient atom, ion or molecule that has an affinity for an electron pair, and will bond to a base or nucleophile.
> **Nucleophile**: An atom, ion or molecule that has an electron pair that may be donated in forming a covalent bond to an electrophile (or Lewis acid).

If we use a common alkyl halide, such as methyl bromide, and a common solvent, ethanol, we can examine the rate at which various nucleophiles substitute the methyl carbon. **Nucleophilicity** is thereby related to the relative rate of substitution reactions at the halogen-bearing carbon atom of the reference alkyl halide. The most reactive nucleophiles are said to be more nucleophilic than less reactive members of the group. The nucleophilicities of some common $Nu:^{(-)}$ reactants vary as shown in the following

Nucleophilicity: $CH_3CO_2^{(-)} < Cl^{(-)} < Br^{(-)} < N_3^{(-)} < CH_3O^{(-)} < CN^{(-)} \approx SCN^{(-)} < I^{(-)} < CH_3S^{(-)}$

The reactivity range encompassed by these reagents is over 5,000 fold, thiolate being the most reactive. Note that by using methyl bromide as the reference substrate, the complication of competing elimination reactions is avoided. The nucleophiles used in this study were all anions, but this is not a necessary requirement for these substitution reactions. Indeed reactions **6 & 7**, presented at the beginning of this section, are examples of neutral nucleophiles participating in substitution reactions. The cumulative results of studies of this kind has led to useful empirical rules pertaining to nucleophilicity:

1. **(i)** For a given element, negatively charged species are more nucleophilic (and basic) than are equivalent neutral species.
2. **(ii)** For a given period of the periodic table, nucleophilicity (and basicity) decreases on moving from left to right.
3. **(iii)** For a given group of the periodic table, nucleophilicity increases from top to bottom (*i.e.* with increasing size), although there is a solvent dependence due to hydrogen bonding. Basicity varies in the opposite manner.

Solvent Effects

Solvation of nucleophilic anions markedly influences their reactivity. The nucleophilicities cited above were obtained from reactions in methanol solution. Polar, protic solvents such as water and alcohols solvate anions by hydrogen bonding interactions, as shown in the diagram below.

These solvated species are more stable and less reactive than the unsolvated "naked" anions. Polar, aprotic solvents such as DMSO (dimethyl sulfoxide), DMF (dimethylformamide) and acetonitrile do not solvate anions nearly as well as methanol, but provide good solvation of the accompanying cations. Consequently, most of the nucleophiles discussed here react more rapidly in solutions prepared from these solvents. These solvent effects are more pronounced for small basic anions than for large weakly basic anions. Thus, for reaction in DMSO solution we observe the following reactivity order:

Nucleophilicity: $I^{(-)} < SCN^{(-)} < Br^{(-)} < Cl^{(-)} \approx N_3^{(-)} < CH_3CO_2^{(-)} < CN^{(-)} \approx CH_3S^{(-)} < CH_3O^{(-)}$

Note that this order is roughly the order of increasing basicity.

Contributors

- William Reusch, Professor Emeritus (Michigan State U.), Virtual Textbook of Organic Chemistry

9.12: Solvent Effects is shared under a not declared license and was authored, remixed, and/or curated by LibreTexts.

- **Nucleophilicity and Solvent Effects** by William Reusch is licensed CC BY-NC-SA 4.0.

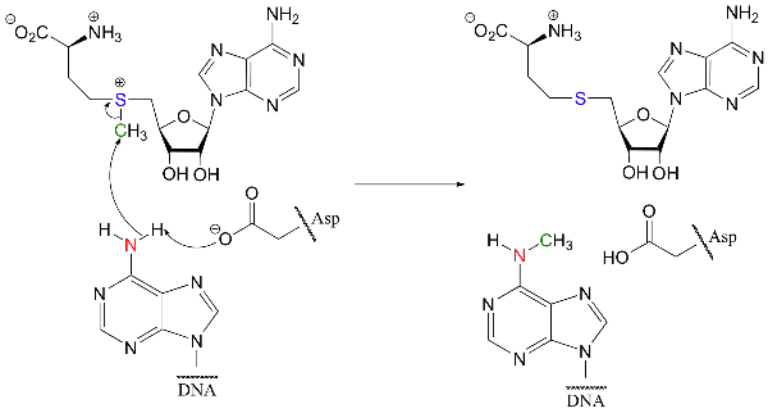
9.13: Using Substitution Reactions to Synthesize Organic Compounds

9.13: Using Substitution Reactions to Synthesize Organic Compounds is shared under a not declared license and was authored, remixed, and/or curated by LibreTexts.

9.14: Biological Methylating Reagents

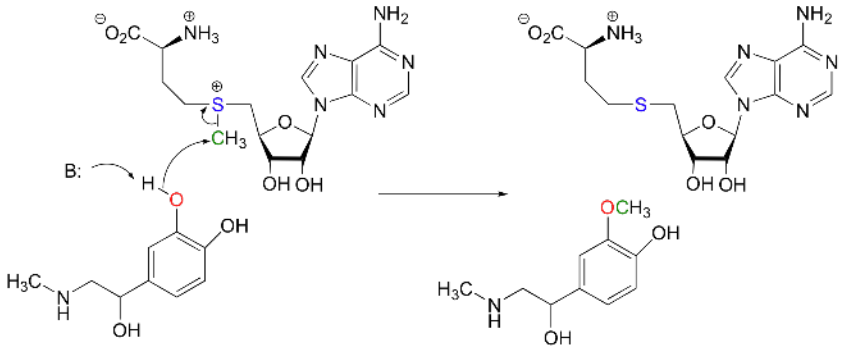
9.1A: SAM methyltransferases

Some of the most important examples of S_N2 reactions in biochemistry are those catalyzed by S-adenosyl methionine (SAM) – dependent methyltransferase enzymes. We have already seen, in chapter 6 and again in chapter 8, how a methyl group is transferred in an S_N2 reaction from SAM to the amine group on the nucleotide base adenosine:



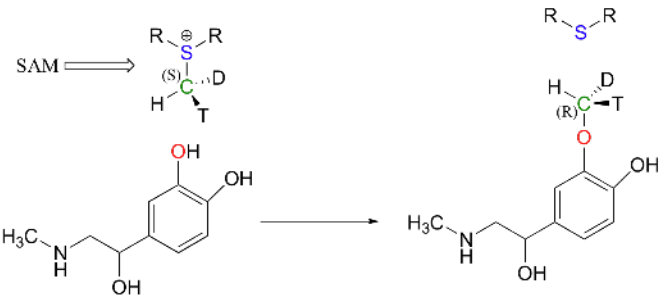
(*Nucleic Acids Res.* **2000**, *28*, 3950).

Another SAM-dependent methylation reaction is catalyzed by an enzyme called catechol-O-methyltransferase. The substrate here is epinephrine, also known as adrenaline.



Notice that in this example, the attacking nucleophile is an alcohol rather than an amine (that's why the enzyme is called an O-methyltransferase). In both cases, though, a basic amino acid side chain is positioned in the active site in just the right place to deprotonate the nucleophilic group as it attacks, increasing its nucleophilicity. The electrophile in both reactions is a methyl carbon, so there is little steric hindrance to slow down the nucleophilic attack. The methyl carbon is electrophilic because it is bonded to a positively-charged sulfur, which is a powerful electron withdrawing group. The positive charge on the sulfur also makes it an excellent leaving group, as the resulting product will be a neutral and very stable sulfide. All in all, in both reactions we have a reasonably good nucleophile, an electron-poor, unhindered electrophile, and an excellent leaving group.

Because the electrophilic carbon in these reactions is a methyl carbon, a stepwise S_N1-like mechanism is extremely unlikely: a methyl carbocation is very high in energy and thus is not a reasonable intermediate to propose. We can confidently predict that this reaction is S_N2. Does this S_N2 reaction occur, as expected, with inversion of stereochemistry? Of course, the electrophilic methyl carbon in these reactions is achiral, so inversion is not apparent. To demonstrate inversion, the following experiment has been carried out with catechol-O-methyltransferase:



Here, the methyl group of SAM was made to be chiral by incorporating hydrogen isotopes tritium (^{3}H, T) and deuterium (^{2}H, D). The researchers determined that the reaction occurred with inversion of configuration, as expected for an S_N2 displacement (*J. Biol. Chem.* **1980,** *255,* 9124).

Template:ExampleStart

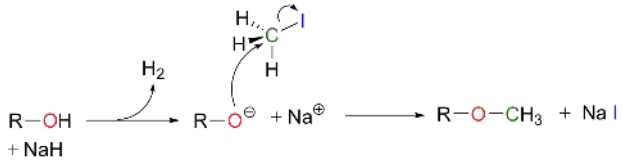
Exercise 9.1: SAM is formed by a nucleophilic substitution reaction between methionine and adenosine triphosphate (ATP). Propose a mechanism for this reaction.

Solution

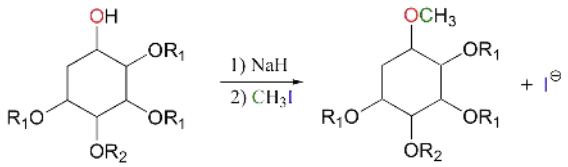
ParseError: EOF expected (click for details)

9.1B: Synthetic parallel – the Williamson ether synthesis

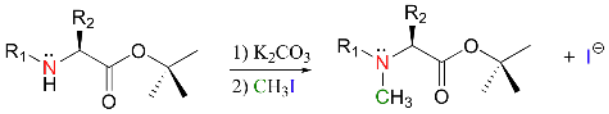
Synthetic organic chemists often use reactions in the laboratory that are conceptually very similar to the SAM-dependent methylation reactions described above. In what is referred to as "O-methylation", an alcohol is first deprotonated by a strong base, typically sodium hydride (this is essentially an irreversible deprotonation, as the hydrogen gas produced can easily be removed from the reaction vessel).



The alkoxide ion, a powerful nucleophile, is then allowed to attack the electrophilic carbon in iodomethane, displacing iodide in an S_N2 reaction. Recall (section 7.3A) that iodide ion is the least basic - and thus the best leaving group - among the halogens commonly used in the synthetic lab. CH_3I is one of the most commonly used lab reagents for methyl transfer reactions, and is the lab equivalent of SAM. In the synthesis of a modified analog of the signaling molecule *myo*-inisitol triphosphate, an alcohol group was methylated using sodium hydride and iodomethane (*Carbohydrate Research* **2004,** *339,* 51):



Methylation of amines (N-methylation) by iodomethane is also possible. A recent study concerning the optimization of peptide synthesis methods involved the following reaction (*J. Org. Chem.* **2000** *65,* 2309):



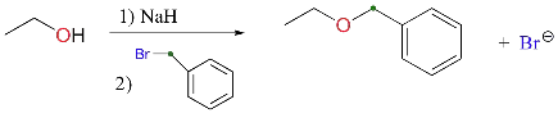
Template:ExampleStart

Exercise 9.2: Notice that in the N-methylation reaction a weak base (potassium carbonate) is used, rather than the very strong base (sodium hydride) that was used in the o-methylation reaction. Why is this weak base sufficient for N-methylation but not for o-methylation? In your answer, draw a step-by step mechanism for both reactions, and think carefully about pK_a values and where in each mechanism the deprotonation step occurs.

Solution

Template:ExampleEnd

The methylation of an alcohol by iodomethane is just one example of what is generally referred to as the **Williamson ether synthesis**, in which alcohols are first deprotonated by a strong base and then allowed to attack an alkyl halide electrophile. Below we see the condensation between ethanol and benzyl bromide:



It is important to note that this reaction does not work well at all if secondary or tertiary alkyl halides are used: remember that the alkoxide ion is a strong base as well as a nucleophile, and elimination will compete with nucleophilic substitution (Section 8.5D).

Organic Chemistry With a Biological Emphasis by Tim Soderberg (University of Minnesota, Morris)

9.14: Biological Methylating Reagents is shared under a not declared license and was authored, remixed, and/or curated by LibreTexts.

CHAPTER OVERVIEW

10: Reactions of Alcohols, Amines, Ethers, and Epoxides



Essential Organic Chemistry: 2nd Ed.
Bruice

Homework Problems
Homework Solutions

I II III IV V VI VII VIII IX X XI XII XIII XIV XV XVI XVII XVIII XIX XX XXI

Template:HideTOC

- 10.1: Nomenclature of Alcohols
- 10.2: Substitution Reactions of Alcohols
- 10.3: Elimination Reactions of Alcohols- Dehydration
- 10.4: Oxidation of Alcohols
- 10.5: Amines Do Not Undergo Substitution or Elimination Reactions
- 10.6: Nomenclature of Ethers
- 10.7: Nucleophilic Substitution Reactions of Ethers
- 10.8: Nucleophilic Substitution Reactions of Epoxides
- 10.9: Using Carbocation Stability to Determine the Carcinogenicity of an Arene Oxide

---

10: Reactions of Alcohols, Amines, Ethers, and Epoxides is shared under a not declared license and was authored, remixed, and/or curated by LibreTexts.

10.1: 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	$C_8H_{17}OH$

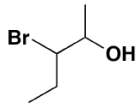
Rules for naming the alcohols

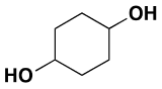
1. Find the longest chain containing the hydroxy group (OH). If there is a chain with more carbons than the one containing the OH group it will be named as a subsitutent.
2. Place the OH on the lowest possible number for the chain. With the exception of carbonyl groups such as ketones and aldehydes, 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.**

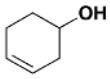
Examples

Ethan**e**: CH_3CH_3 ----->Ethan**ol**:  (the alcohol found in beer, wine and other consumed sprits)

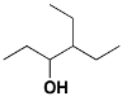
Secondary alcohol:  2-propanol

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

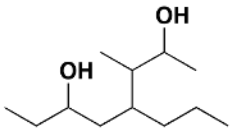
References

- 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)

10.1: Nomenclature of Alcohols is shared under a not declared license and was authored, remixed, and/or curated by LibreTexts.

- **Nomenclature of Alcohols** is licensed CC BY-NC-SA 4.0.

10.2: Substitution Reactions of Alcohols

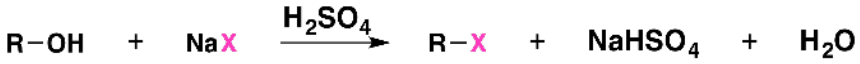
When alcohols react with a hydrogen halide, a substitution occurs, producing an alkyl halide and water:



Scope of Reaction

- The order of reactivity of alcohols is 3° > 2° > 1° methyl.
- The order of reactivity of the hydrogen halides is HI > HBr > HCl (HF is generally unreactive).

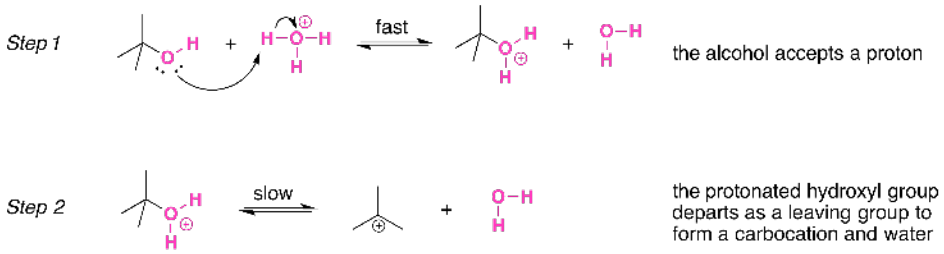
The reaction is acid catalyzed. Alcohols react with the strongly acidic hydrogen halides HCl, HBr, and HI, but they do not react with nonacidic NaCl, NaBr, or NaI. Primary and secondary alcohols can be converted to alkyl chlorides and bromides by allowing them to react with a mixture of a sodium halide and sulfuric acid:



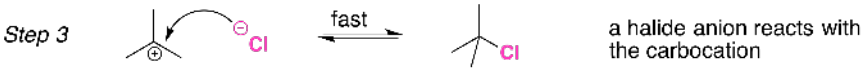
Mechanisms of the Reactions of Alcohols with HX

Secondary, tertiary, allylic, and benzylic alcohols appear to react by a mechanism that involves the formation of a carbocation in an S_N1 reaction with the protonated alcohol acting as the substrate.

The S_N1 mechanism is illustrated by the reaction tert-butyl alcohol and aqueous hydrochloric acid (H_3O^+, Cl^-). The first two steps in this S_n1 substitution mechanism are protonation of the alcohol to form an oxonium ion. Although the oxonium ion is formed by protonation of the alcohol, it can also be viewed as a Lewis acid-base complex between the cation (R^+) and H_2O. Protonation of the alcohol converts a poor leaving group (OH-) to a good leaving group (\)H_2O_), which makes the dissociation step of the S_N1 mechanism more favorable.



In step 3, the carbocation reacts with a nucleophile (a halide ion) to complete the substitution.

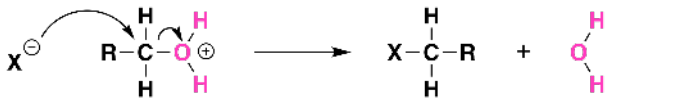


When we convert an alcohol to an alkyl halide, we perform the reaction in the presence of acid and in the presence of halide ions and not at elevated temperatures. Halide ions are good nucleophiles (they are much stronger nucleophiles than water), and because halide ions are present in a high concentration, most of the carbocations react with an electron pair of a halide ion to form a more stable species, the alkyl halide product. The overall result is an S_n1 reaction.

Primary Alcohols

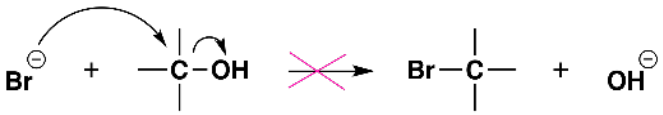
Not all acid-catalyzed conversions of alcohols to alkyl halides proceed through the formation of carbocations. Primary alcohols and methanol react to form alkyl halides under acidic conditions by an S_N2 mechanism.

In these reactions, the function of the acid is to produce a *protonated alcohol*. The halide ion then displaces a molecule of water (a good leaving group) from carbon; this produces an alkyl halide:



(protonated 1° alcohol or methanol) (A good leaving group)

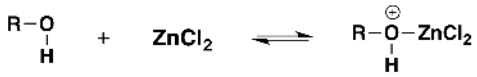
Again, acid is required. Although halide ions (particularly iodide and bromide ions) are strong nucleophiles, they are not strong enough to carry out substitution reactions with alcohols themselves. Direct displacement of the hydroxyl group does not occur because the leaving group would have to be a strongly basic hydroxide ion:

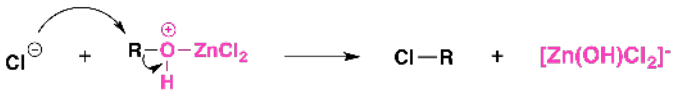


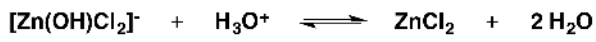
We can see now why the reactions of alcohols with hydrogen halides are acid-promoted.

The role of acid catalysis

Acid protonates the alcohol hydroxyl group, making it a good leaving group. However, other strong Lewis acids can be used instead of hydrohalic acids. Because the chloride ion is a weaker nucleophile than bromide or iodide ions, hydrogen chloride does not react with primary or secondary alcohols unless zinc chloride or a similar Lewis acid is added to the reaction mixture as well. Zinc chloride, a good Lewis acid, forms a complex with the alcohol through association with an unshared pair of electrons on the oxygen atom. This enhances the hydroxyl's leaving group potential sufficiently so that chloride can displace it.







Rearrangement

As we might expect, many reactions of alcohols with hydrogen halides, particularly those in which carbocations are formed, are accompanied by rearrangements. The general rule is that if rearrangement CAN OCCUR (to form more stable or equally stable cations), it will! In these reactions, mixtures of products can be formed.

Contributors

- Prof. Paul G. Wenthold (Purdue University)

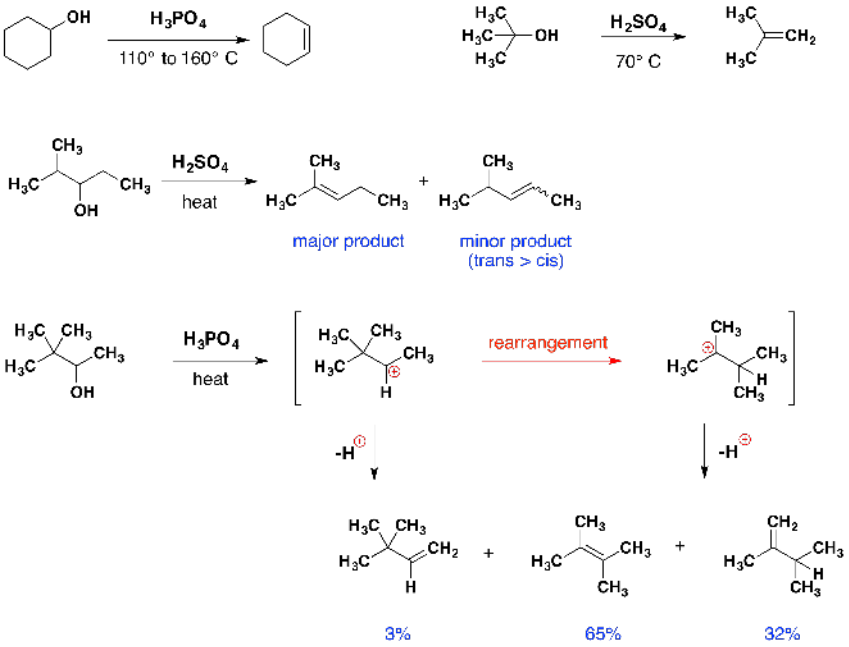
10.2: Substitution Reactions of Alcohols is shared under a not declared license and was authored, remixed, and/or curated by LibreTexts.

- **Reactions of alcohols with hydrohalic acids (HX)** is licensed CC BY-NC-SA 4.0.

10.3: Elimination Reactions of Alcohols- Dehydration

The discussion of alkyl halide reactions noted that 2º and 3º-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.

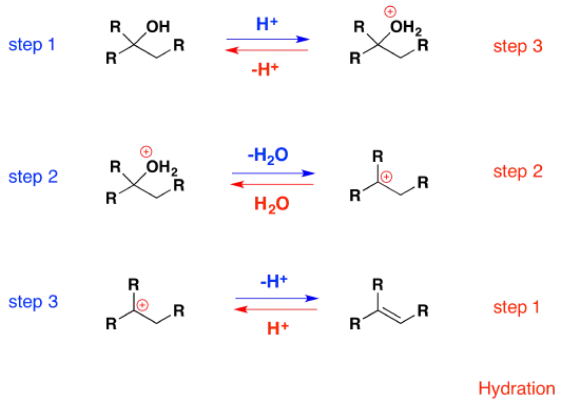
The elimination of water from an alcohol is called **dehydration**. Recalling that water is a much better leaving group than hydroxide ion, it is sensible to use acid-catalysis rather than base-catalysis in such reactions. Four examples of this useful technique are shown below. Note that hydrohalic acids (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 3º-alcohol suggests the predominant E1 character for the reaction. This agrees with the tendency of branched 1º and 2º-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.

Dehydration



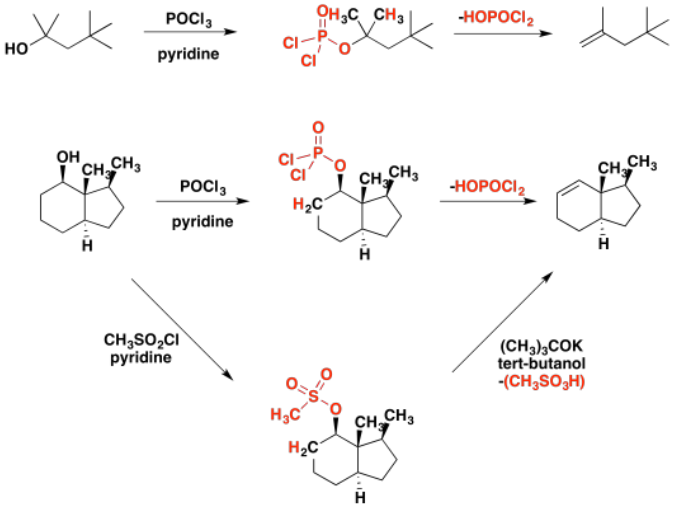
Energy Profile

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 3º-sulfonate derivatives are sometimes unstable, this procedure is best used with 1º and 2º-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 3º-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 2º-alcohols, but for unhindered and 1º-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 3º-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 2º-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

---

10.3: Elimination Reactions of Alcohols- Dehydration is shared under a not declared license and was authored, remixed, and/or curated by LibreTexts.

- **Elimination Reactions of Alcohols** by William Reusch is licensed CC BY-NC-SA 4.0.

10.4: Oxidation of Alcohols

This page looks at the oxidation of alcohols using acidified sodium or potassium dichromate(VI) solution. This reaction is used to make aldehydes, ketones and carboxylic acids, and as a way of distinguishing between primary, secondary and tertiary alcohols.

Oxidizing the different types of alcohols

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, then the orange solution containing the dichromate(VI) ions is reduced to a green solution containing chromium(III) ions. The electron-half-equation for this reaction is as follows:

$$Cr_2O_7^{2-} + 14H^+ + 6e^- \rightarrow 2Cr^{3+} + 7H_2O \tag{10.4.1}$$

Primary alcohols

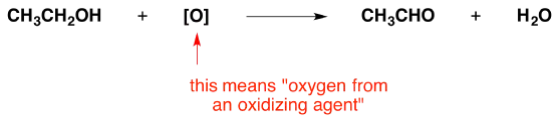
Primary alcohols can be oxidized to either aldehydes or carboxylic acids, depending on the reaction conditions. In the case of the formation of carboxylic acids, the alcohol is first oxidized to an aldehyde, which is then oxidized further to the acid.

An aldehyde is obtained if an excess amount of the alcohol is used, and the aldehyde is distilled off as soon as it forms. An excess of the alcohol means that there is not enough oxidizing agent present to carry out the second stage, and removing the aldehyde as soon as it is formed means that it is not present to be oxidized anyway!

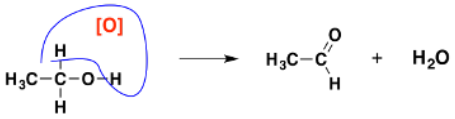
If you used ethanol as a typical primary alcohol, you would produce the aldehyde ethanal, CH_3CHO. The full equation for this reaction is fairly complicated, and you need to understand the electron-half-equations in order to work it out.

$$3CH_3CH_2OH + Cr_2O_7^{2-} + 8H^+ \rightarrow 3CH_3CHO + 2Cr^{3+} + 7H_2O \tag{10.4.2}$$

In organic chemistry, simplified versions are often used that concentrate on what is happening to the organic substances. To do that, oxygen from an oxidizing agent is represented as $[O]$. That would produce the much simpler equation:



It also helps in remembering what happens. You can draw simple structures to show the relationship between the primary alcohol and the aldehyde formed.



Full oxidation to carboxylic acids

An excess of the oxidizing agent must be used, and the aldehyde formed as the half-way product should remain in the mixture. The alcohol is heated under reflux with an excess of the oxidizing agent. When the reaction is complete, the carboxylic acid is distilled off. The full equation for the oxidation of ethanol to ethanoic acid is as follows:

$$3CH_3CH_2OH + 2Cr_2O_7^{2-} + 16H+ \rightarrow 3CH_3COOH + 4Cr^{3+} + 11H_2O \tag{10.4.3}$$

The more typical simplified version looks like this:

$$CH_3CH_2OH + 2[O] \rightarrow CH_3COOH + H_2O \tag{10.4.4}$$

Alternatively, you could write separate equations for the two stages of the reaction - the formation of ethanal and then its subsequent oxidation.

$$CH_3CH_2OH + [O] \rightarrow CH_3CHO + H_2O \tag{10.4.5}$$

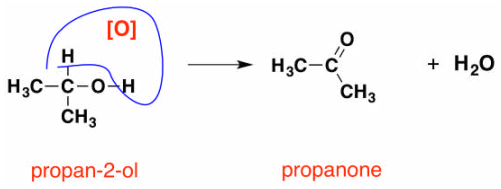
$$CH_3CHO + [O] \rightarrow CH_3COOH \tag{10.4.6}$$

This is what is happening in the second stage:



Secondary alcohols

Secondary alcohols are oxidized to ketones - and that's it. For example, if you heat the secondary alcohol propan-2-ol with sodium or potassium dichromate(VI) solution acidified with dilute sulfuric acid, propanone is formed. Changing the reaction conditions makes no difference to the product. Folloiwng is the simple version of the equation, showing the relationship between the structures:

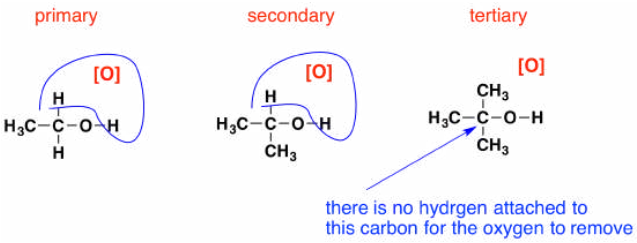


If you look back at the second stage of the primary alcohol reaction, you will see that an oxygen inserted between the carbon and the hydrogen in the aldehyde group to produce the carboxylic acid. In this case, there is no such hydrogen - and the reaction has nowhere further to go.

Tertiary alcohols

Tertiary alcohols are not oxidized by acidified sodium or potassium dichromate(VI) solution - there is no reaction whatsoever. If you look at what is happening with primary and secondary alcohols, you will see that the oxidizing agent is removing the hydrogen from the -OH group, and a hydrogen from the carbon atom is attached to the -OH. Tertiary alcohols don't have a hydrogen atom attached to that carbon.

You need to be able to remove those two particular hydrogen atoms in order to set up the carbon-oxygen double bond.

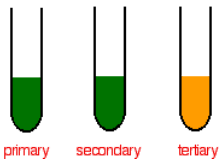


Using these reactions as a test for the different types of alcohols

First, the presence of an alcohol must be confirmed by testing for the -OH group. The liquid would need to be verified as neutral, free of water and that it reacted with solid phosphorus(V) chloride to produce a burst of acidic steamy hydrogen chloride fumes. A few drops of the alcohol would be added to a test tube containing potassium dichromate(VI) solution acidified with dilute sulfuric acid. The tube would be warmed in a hot water bath.

Determining the tertiary alcohol

In the case of a primary or secondary alcohol, the orange solution turns green. With a tertiary alcohol, there is no color change. After heating, the following colors are observed:

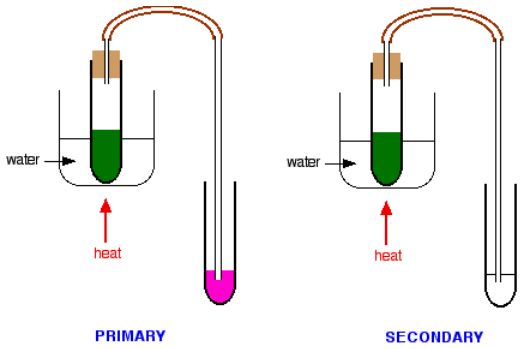


Distinguishing between the primary and secondary alcohols

A sufficient amount of the aldehyde (from oxidation of a primary alcohol) or ketone (from a secondary alcohol) must be produced to be able to test them. There are various reactions that aldehydes undergo that ketones do not. These include the reactions with Tollens' reagent, Fehling's solution and Benedict's solution, and these reactions are covered on a separate page.

These tests can be difficult to carry out, and the results are not always as clear-cut as the books say. A much simpler but fairly reliable test is to use *Schiff's reagent*. Schiff's reagent is a fuchsin dye decolorized by passing sulfur dioxide through it. In the presence of even small amounts of an aldehyde, it turns bright magenta.

It must, however, be used absolutely cold, because ketones react with it very slowly to give the same color. If you heat it, obviously the change is faster - and potentially confusing. While you are warming the reaction mixture in the hot water bath, you can pass any vapors produced through some Schiff's reagent.



- If the Schiff's reagent quickly becomes magenta, then you are producing an aldehyde from a primary alcohol.
- If there is no color change in the Schiff's reagent, or only a trace of pink color within a minute or so, then you are not producing an aldehyde; therefore, no primary alcohol is present.

Because of the color change to the acidified potassium dichromate(VI) solution, you must, therefore, have a secondary alcohol. You should check the result as soon as the potassium dichromate(VI) solution turns green - if you leave it too long, the Schiff's reagent might start to change color in the secondary alcohol case as well.

Contributors

- Jim Clark (Chemguide.co.uk)

10.4: Oxidation of Alcohols is shared under a not declared license and was authored, remixed, and/or curated by LibreTexts.

- **The Oxidation of Alcohols** by Jim Clark is licensed CC BY-NC 4.0.

10.5: Amines Do Not Undergo Substitution or Elimination Reactions

The rate of a chemical reaction is the *change* in concentration over the *change* in time.

Introduction

The rate of a chemical reaction is the *change* in concentration over the *change* in time and is a metric of the "speed" at which a chemical reactions occurs and can be defined in terms of two observables:

1. The Rate of Disappearance of Reactants

$$-\frac{\Delta[Reactants]}{\Delta t}$$

   Note this is negative because it measures the rate of disappearance of the reactants.
2. The Rate of Formation of Products

$$\frac{\Delta[Products]}{\Delta t}$$

   This is the rate at which the products are formed.

They both are linked via the balanced chemical reactions and can both be used to measure the reaction rate.

Outside links

- http://en.Wikipedia.org/wiki/Reaction_rate
- www.chm.davidson.edu/vce/kinetics/ReactionRates.html(this website lets you play around with reaction rates and will help your understanding)
- goldbook.iupac.org/R05156.html
- www.youtube.com/watch?v=FfoQsZa8F1c YouTube video of a very fast exothermic reaction.

References

1. Petrucci et al. General Chemistry: Principles & Modern Applications, 9th Edition. New Jersey: Prentice-Hall Inc., 2007.
2. Connors, Kenneth. Chemical Kinetics: The Study of Reaction Rates in Solution. New York City: VCH Publishers, Inc., 1990.

Problems

1. Consider the reaction $2A + B \longrightarrow C$. The concentration of [A] is 0.54321M and the rate of reaction is $3.45 \times 10^{-6} M/s$. What Concentration will [A] be 3 minutes later?
2. Consider the reaction $A + B \longrightarrow C$. The rate of reaction is 1.23*10-4. [A] will go from a 0.4321 M to a 0.4444 M concentration in what length of time?
3. Write the rate of the chemical reaction with respect to the variables for the given equation.

$$2A + 3B \rightarrow C + 2D$$

4. True or False: The Average Rate and Instantaneous Rate are equal to each other.
5. How is the rate of formation of a product related to the rates of the disappearance of reactants.

Contributors

- Albert Law, Victoria Blanchard, Donald Le

10.5: Amines Do Not Undergo Substitution or Elimination Reactions is shared under a not declared license and was authored, remixed, and/or curated by LibreTexts.

- **2.5.2: The Rate of a Chemical Reaction** is licensed CC BY-NC-SA 4.0.

10.6: Nomenclature of Ethers

Ethers are compounds having two alkyl or aryl groups bonded to an oxygen atom, as in the formula $R^1–O–R^2$. The ether functional group does not have a characteristic IUPAC nomenclature suffix, so it is necessary to designate it as a substituent. To do so the common alkoxy substituents are given names derived from their alkyl component (below):

Alkyl Group	Name		Alkoxy Group	Name
$CH_3–$	Methyl		$CH_3O–$	Methoxy
$CH_3CH_2–$	Ethyl		$CH_3CH_2O–$	Ethoxy
$(CH_3)_2CH–$	Isopropyl		$(CH_3)_2CHO–$	Isopropoxy
$(CH_3)_3C–$	tert-Butyl		$(CH_3)_3CO–$	tert-Butoxy
$C_6H_5–$	Phenyl		$C_6H_5O–$	Phenoxy

Ethers can be named by naming each of the two carbon groups as a separate word followed by a space and the word ether. The -OR group can also be named as a substituent using the group name, alkox

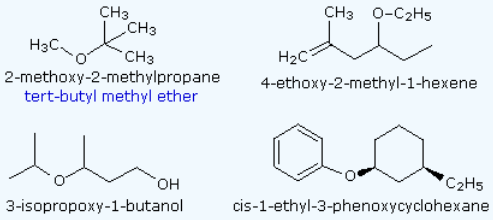
Example 10.6.1

CH_3-CH_2-O-CH_3 is called ethyl methyl ether or methoxyethane.

The smaller, shorter alkyl group becomes the alkoxy substituent. The larger, longer alkyl group side becomes the alkane base name. Each alkyl group on each side of the oxygen is numbered separately. The numbering priority is given to the carbon closest to the oxgen. The alkoxy side (shorter side) has an "-oxy" ending with its corresponding alkyl group. For example, $CH_3CH_2CH_2CH_2CH_2$-O-$CH_2CH_2CH_3$ is 1-propoxypentane. If there is cis or trans stereochemistry, the same rule still applies.

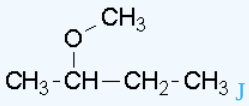
Examples 10.6.2

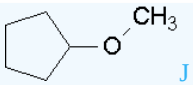
- $\boldsymbol{CH_3CH_2OCH_2CH_3}$, diethyl ether (sometimes referred to as just ether)
- $\boldsymbol{CH_3OCH_2CH_2OCH_3}$, ethylene glycol dimethyl ether (glyme).



Exercises 10.6.2

Try to name the following compounds using these conventions:





J

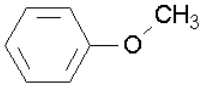
Try to draw structures for the following compounds:

- 2-pentyl 1-propyl ether J
- 1-(2-propoxy)cyclopentene J

Common names

Simple ethers are given common names in which the alkyl groups bonded to the oxygen are named in alphabetical order followed by the word "ether". The top left example shows the common name in blue under the IUPAC name. Many simple ethers are symmetrical, in that the two alkyl substituents are the same. These are named as "dialkyl ethers".

- **anisole** (try naming anisole by the other two conventions. J)



- **oxirane**



1,2-epoxyethane, ethylene oxide, dimethylene oxide, oxacyclopropane,

- **furan (this compound is aromatic)**



tetrahydrofuran



oxacyclopentane, 1,4-epoxybutane, tetramethylene oxide,

- **dioxane**



1,4-dioxacyclohexane

? Exercise 10.6.2

Try to draw structures for the following compounds-

- 3-bromoanisole J
- 2-methyloxirane J
- 3-ethylfuran J

Heterocycles

In cyclic ethers (heterocycles), one or more carbons are replaced with oxygen. Often, it's called heteroatoms, when carbon is replaced by an oxygen or any atom other than carbon or hydrogen. In this case, the stem is called the oxacycloalkane, where the

prefix "oxa-" is an indicator of the replacement of the carbon by an oxygen in the ring. These compounds are numbered starting at the oxygen and continues around the ring. For example,



1,4-dioxacyclohexane



1-oxacyclopentane

If a substituent is an alcohol, the alcohol has higher priority. However, if a substituent is a halide, ether has higher priority. If there is both an alcohol group and a halide, alcohol has higher priority. The numbering begins with the end that is closest to the higher priority substituent. There are ethers that are contain multiple ether groups that are called cyclic polyethers or crown ethers. These are also named using the IUPAC system.

Sulfides

Sulfur analogs of ethers (R–S–R') are called **sulfides**, e.g., $(CH_3)_3C–S–CH_3$ is tert-butyl methyl sulfide. Sulfides are chemically more reactive than ethers, reflecting the greater nucleophilicity of sulfur relative to oxygen.

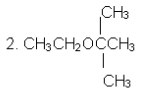
References

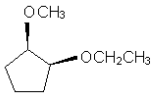
1. Schore, Neil E. and Vollhardt, K. Peter C. Organic Chemistry: Structure and Function. New York: Bleyer, Brennan, 2007.
2. Winter, Arthur. Organic Chemistry for Dummies. Hoboken, New Jersey: Wiley, 2005.
3. Pellegrini, Frank. Cliffs QuickReview Organic Chemistry II. Foster City, CA: Wiley, 2000

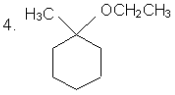
Problems

Name the following ethers:

1. $CH_3CH_2OCH_2CH_3$

2. 

3. 

4. 

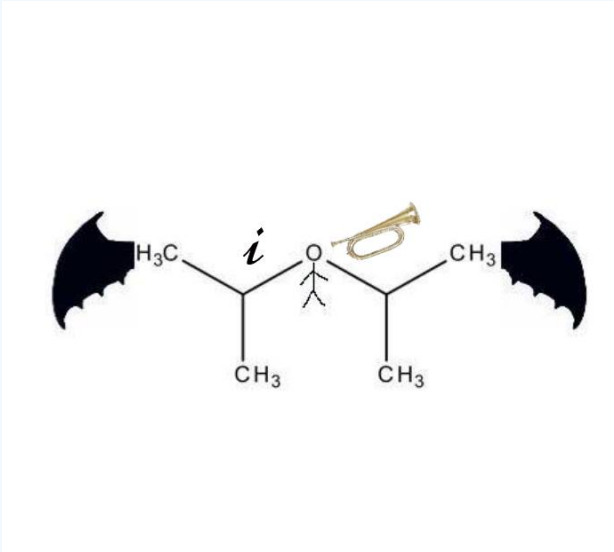
5. 

6. 

(Answers to problems above: 1. diethyl ether; 2. 2-ethoxy-2-methyl-1-propane; 3. cis-1-ethoxy-2-methoxycyclopentane; 4. 1-ethoxy-1-methylcyclohexane; 5. oxacyclopropane; 6. 2,2-Dimethyloxacyclopropane)

Exercise 10.6.3

What would you call



(CC-BY; Dan Johnson via Twitter)

Answer

A one-eyed one-horned flying propyl people ether

Contributors

- William Reusch, Professor Emeritus (Michigan State U.), Virtual Textbook of Organic Chemistry
- Richard Banks (Boise State University)

10.6: Nomenclature of Ethers is shared under a not declared license and was authored, remixed, and/or curated by LibreTexts.

- **Nomenclature of Ethers** by William Reusch is licensed CC BY-NC-SA 4.0.

10.7: Nucleophilic Substitution Reactions of Ethers

The rate of a chemical reaction is the *change* in concentration over the *change* in time.

Introduction

The rate of a chemical reaction is the *change* in concentration over the *change* in time and is a metric of the "speed" at which a chemical reactions occurs and can be defined in terms of two observables:

1. The Rate of Disappearance of Reactants

$$-\frac{\Delta[Reactants]}{\Delta t}$$

   Note this is negative because it measures the rate of disappearance of the reactants.
2. The Rate of Formation of Products

$$\frac{\Delta[Products]}{\Delta t}$$

   This is the rate at which the products are formed.

They both are linked via the balanced chemical reactions and can both be used to measure the reaction rate.

Outside links

- http://en.Wikipedia.org/wiki/Reaction_rate
- www.chm.davidson.edu/vce/kinetics/ReactionRates.html(this website lets you play around with reaction rates and will help your understanding)
- goldbook.iupac.org/R05156.html
- www.youtube.com/watch?v=FfoQsZa8F1c YouTube video of a very fast exothermic reaction.

References

1. Petrucci et al. General Chemistry: Principles & Modern Applications, 9th Edition. New Jersey: Prentice-Hall Inc., 2007.
2. Connors, Kenneth. Chemical Kinetics: The Study of Reaction Rates in Solution. New York City: VCH Publishers, Inc., 1990.

Problems

1. Consider the reaction $2A + B \longrightarrow C$. The concentration of [A] is 0.54321M and the rate of reaction is $3.45 \times 10^{-6} M/s$. What Concentration will [A] be 3 minutes later?
2. Consider the reaction $A + B \longrightarrow C$. The rate of reaction is 1.23*10-4. [A] will go from a 0.4321 M to a 0.4444 M concentration in what length of time?
3. Write the rate of the chemical reaction with respect to the variables for the given equation.

$$2A + 3B \rightarrow C + 2D$$

4. True or False: The Average Rate and Instantaneous Rate are equal to each other.
5. How is the rate of formation of a product related to the rates of the disappearance of reactants.

Contributors

- Albert Law, Victoria Blanchard, Donald Le

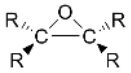
10.7: Nucleophilic Substitution Reactions of Ethers is shared under a not declared license and was authored, remixed, and/or curated by LibreTexts.

- **2.5.2: The Rate of a Chemical Reaction** is licensed CC BY-NC-SA 4.0.

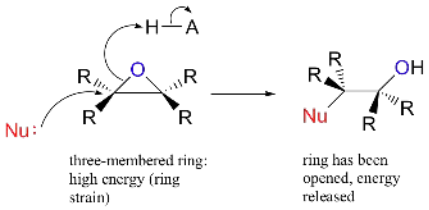
10.8: Nucleophilic Substitution Reactions of Epoxides

8.6A: Epoxide structure

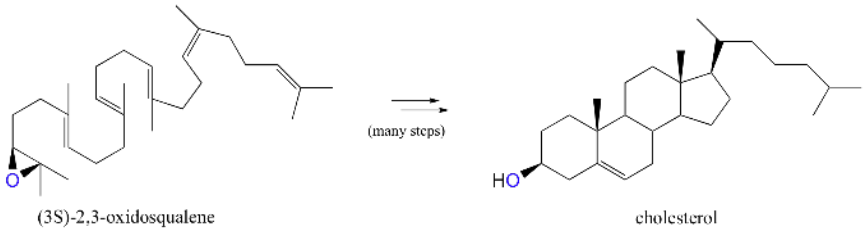
Epoxides (also known as **oxiranes**) are three-membered ring structures in which one of the vertices is an oxygen and the other two are carbons.



The carbons in an epoxide group are very reactive electrophiles, due in large part to the fact that substantial ring strain is relieved when the ring opens upon nucleophilic attack.



Epoxides are very important intermediates in laboratory organic synthesis, and are also found as intermediate products in some biosynthetic pathways. The compound (3S)-2,3-oxidosqualene, for example, is an important intermediate in the biosynthesis of cholesterol (we'll see the epoxide ring-opening step in chapter 15):

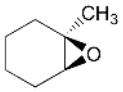


Both in the laboratory and in the cell, epoxides are usually formed by the oxidation of an alkene. These reactions will be discussed in detail in chapter 16.

Exercise 8.17: Predict the major product(s) of the ring opening reaction that occurs when the epoxide shown below is treated with:

a) ethanol and a small amount of sodium hydroxide

b) ethanol and a small amount of sulfuric acid



*Hint: be sure to consider both regiochemistry **and** stereochemistry!*

Solution

Template:ExampleEnd

Organic Chemistry With a Biological Emphasis by Tim Soderberg (University of Minnesota, Morris)

10.8: Nucleophilic Substitution Reactions of Epoxides is shared under a not declared license and was authored, remixed, and/or curated by LibreTexts.

10.9: Using Carbocation Stability to Determine the Carcinogenicity of an Arene Oxide

10.9: Using Carbocation Stability to Determine the Carcinogenicity of an Arene Oxide is shared under a not declared license and was authored, remixed, and/or curated by LibreTexts.

CHAPTER OVERVIEW

11: Carbonyl Compounds I- Reactions of Carboxylic Acids and Carboxylic Derivatives



Essential Organic Chemistry: 2nd Ed.
Bruice

Homework Problems
Homework Solutions

I II III IV V VI VII VIII IX X XI XII XIII XIV XV XVI XVII XVIII XIX XX XXI

Template:HideTOC

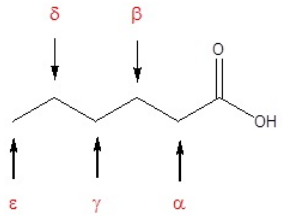
- 11.1: The Nomenclature of Carboxylic Acids and Carboxylic Acid Derivatives
- 11.2: The Structures of Carboxylic Acids and Carboxylic Acid Derivatives
- 11.3: The Physical Properties of Carbonyl Compounds
- 11.4: Carboxylic Acids and Carboxylic Acid Derivatives found in Nature
- 11.5: How Carboxylic Acids and Carboxylic Acids Compounds React
- 11.6: Relative Reactivities of Carboxylic Acids and Carboxylic Acid Derivatives
- 11.7: Reactions of Acyl Halides
- 11.8: Reactions of Esters
- 11.9: Acid-Catalyzed Ester Hydrolysis
- 11.10: Soaps, Detergents, and Micelles
- 11.11: Reactions of Carboxylic Acids
- 11.12: Reactions of Amides
- 11.13: Acid-Catalyzed Amide Hydrolysis
- 11.14: The Synthesis of Carboxylic Acid Derivatives
- 11.15: Nitriles

11: Carbonyl Compounds I- Reactions of Carboxylic Acids and Carboxylic Derivatives is shared under a not declared license and was authored, remixed, and/or curated by LibreTexts.

11.1: The Nomenclature of Carboxylic Acids and Carboxylic Acid Derivatives

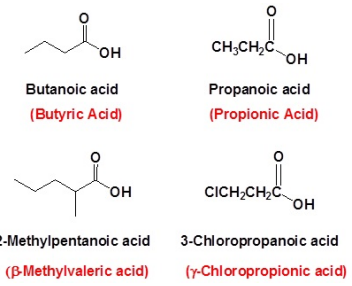
The IUPAC system of nomenclature assigns a characteristic suffix to these classes. The **–e** ending is removed from the name of the parent chain and is replaced **-anoic acid**. Since a carboxylic acid group must always lie at the end of a carbon chain, it is always is given the #1 location position 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.



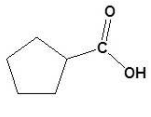
Formula	Common Name	Source	IUPAC Name	Melting Point	Boiling Point
HCO_2H	formic acid	ants (L. formica)	methanoic acid	8.4 ºC	101 ºC
CH_3CO_2H	acetic acid	vinegar (L. acetum)	ethanoic acid	16.6 ºC	118 ºC
$CH_3CH_2CO_2H$	propionic acid	milk (Gk. protus prion)	propanoic acid	-20.8 ºC	141 ºC
$CH_3(CH_2)_2CO_2H$	butyric acid	butter (L. butyrum)	butanoic acid	-5.5 ºC	164 ºC
$CH_3(CH_2)_3CO_2H$	valeric acid	valerian root	pentanoic acid	-34.5 ºC	186 ºC
$CH_3(CH_2)_4CO_2H$	caproic acid	goats (L. caper)	hexanoic acid	-4.0 ºC	205 ºC
$CH_3(CH_2)_5CO_2H$	enanthic acid	vines (Gk. oenanthe)	heptanoic acid	-7.5 ºC	223 ºC
$CH_3(CH_2)_6CO_2H$	caprylic acid	goats (L. caper)	octanoic acid	16.3 ºC	239 ºC
$CH_3(CH_2)_7CO_2H$	pelargonic acid	pelargonium (an herb)	nonanoic acid	12.0 ºC	253 ºC
$CH_3(CH_2)_8CO_2H$	capric acid	goats (L. caper)	decanoic acid	31.0 ºC	219 ºC

Example (Common Names Are in Red)

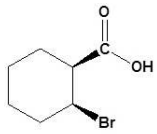


Naming carboxyl groups added to a ring

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.



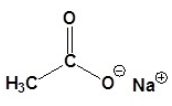
Cyclopentanecarboxylic acid



Cis-2-Bromocyclohexanecarboxylic acid

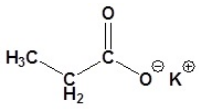
Naming carboxylates

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)

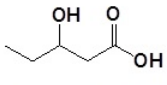


Potassium Propanoate

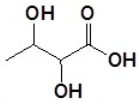
(Potassium propionate)

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.

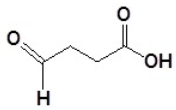


3-Hydroxypentanoic acid

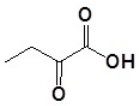


2,3-Dihydroxybutanoic acid

In the case of molecules containing a carboxylic acid and aldehydes and/or ketones functional groups the carbonyl is named as a "Oxo" substituent.

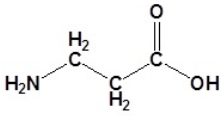


4-Oxobutanoic acid

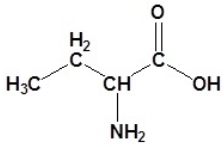


2-Oxobutanoic acid

In the case of molecules containing a carboxylic acid an amine functional group the amine is named as an "amino" substituent.



3-Aminopropanoic acid

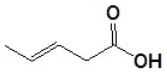


2-Aminobutanoic acid

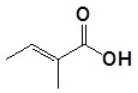
When carboxylic acids are included with an alkene the following order is followed:

(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.



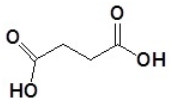
Trans-3-pentenoic acid



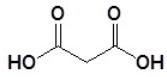
(E)-2-Methyl-2-butenoic acid

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

---

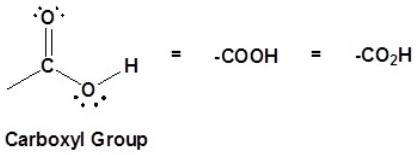
11.1: The Nomenclature of Carboxylic Acids and Carboxylic Acid Derivatives is shared under a not declared license and was authored, remixed, and/or curated by LibreTexts.

- **Nomenclature of Carboxylic Acids** by William Reusch is licensed CC BY-NC-SA 4.0.

11.2: The Structures of Carboxylic Acids and Carboxylic Acid Derivatives

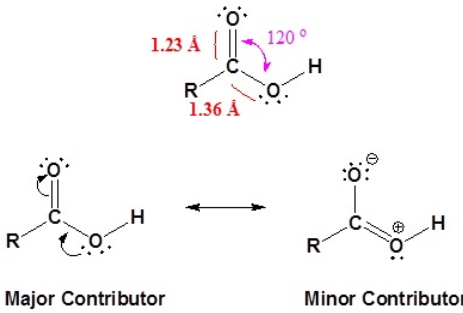
Structure of the carboxyl acid group

Carboxylic acids are organic compounds which incorporate a carboxyl functional group, CO_2H. The name carboxyl comes from the fact that a carbonyl and a hydroxyl group are attached to the same carbon.



Carboxyl Group

The carbon and oxygen in the carbonyl are both sp2 hybridized which give a carbonyl group a basic trigonal shape. The hydroxyl oxygen is also sp2 hybridized which allows one of its lone pair electrons to conjugate with the pi system of the carbonyl group. This make the carboxyl group planar an can represented with the following resonance structure.



Major Contributor Minor Contributor

Carboxylic acids are named such because they can donate a hydrogen to produce a carboxylate ion. The factors which affect the acidity of carboxylic acids will be discussed later.



Carboxylic acid Carboxylate ion

Physical Properties of Some Carboxylic Acids

Formula	Common Name	Source	IUPAC Name	Melting Point	Boiling Point
HCO_2H	formic acid	ants (L. formica)	methanoic acid	8.4 ºC	101 ºC
CH_3CO_2H	acetic acid	vinegar (L. acetum)	ethanoic acid	16.6 ºC	118 ºC
$CH_3CH_2CO_2H$	propionic acid	milk (Gk. protus prion)	propanoic acid	-20.8 ºC	141 ºC
$CH_3(CH_2)_2CO_2H$	butyric acid	butter (L. butyrum)	butanoic acid	-5.5 ºC	164 ºC
$CH_3(CH_2)_3CO_2H$	valeric acid	valerian root	pentanoic acid	-34.5 ºC	186 ºC
$CH_3(CH_2)_4CO_2H$	caproic acid	goats (L. caper)	hexanoic acid	-4.0 ºC	205 ºC
$CH_3(CH_2)_5CO_2H$	enanthic acid	vines (Gk. oenanthe)	heptanoic acid	-7.5 ºC	223 ºC
$CH_3(CH_2)_6CO_2H$	caprylic acid	goats (L. caper)	octanoic acid	16.3 ºC	239 ºC
$CH_3(CH_2)_7CO_2H$	pelargonic acid	pelargonium (an herb)	nonanoic acid	12.0 ºC	253 ºC
$CH_3(CH_2)_8CO_2H$	capric acid	goats (L. caper)	decanoic acid	31.0 ºC	219 ºC

Saturated			Unsaturated		
Formula	Common Name	Melting Point	Formula	Common Name	Melting Point
$CH_3(CH_2)_{10}CO_2H$	lauric acid	45 ºC	$CH_3(CH_2)_5CH{=}CH(CH_2)_7CO_2H$	palmitoleic acid	0 ºC
$CH_3(CH_2)_{12}CO_2H$	myristic acid	55 ºC	$CH_3(CH_2)_7CH{=}CH(CH_2)_7CO_2H$	oleic acid	13 ºC
$CH_3(CH_2)_{14}CO_2H$	palmitic acid	63 ºC	$CH_3(CH_2)_4CH{=}CHCH_2CH{=}CH(CH_2)_7CO_2H$	linoleic acid	-5 ºC
$CH_3(CH_2)_{16}CO_2H$	stearic acid	69 ºC	$CH_3CH_2CH{=}CHCH_2CH{=}CHCH_2CH{=}CH(CH_2)_7CO_2H$	linolenic acid	-11 ºC
$CH_3(CH_2)_{18}CO_2H$	arachidic acid	76 ºC	$CH_3(CH_2)_4(CH{=}CHCH_2)_4(CH_2)_2CO_2H$	arachidonic acid	-49 ºC

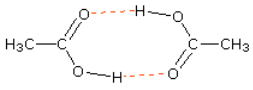
The table at the beginning of this page gave the melting and boiling points for a homologous group of carboxylic acids having from one to ten carbon atoms. The boiling points increased with size in a regular manner, but the melting points did not. Unbranched acids made up of an even number of carbon atoms have melting points higher than the odd numbered homologs having one more or one less carbon. This reflects differences in intermolecular attractive forces in the crystalline state. In the table of fatty acids we see that the presence of a cis-double bond significantly lowers the melting point of a compound. Thus, palmitoleic acid melts over 60º lower than palmitic acid, and similar decreases occur for the C_{18} and C_{20} compounds. Again, changes in crystal packing and intermolecular forces are responsible.

The factors that influence the relative boiling points and water solubilities of various types of compounds were discussed earlier. In general, dipolar attractive forces between molecules act to increase the boiling point of a given compound, with hydrogen bonds being an extreme example. Hydrogen bonding is also a major factor in the water solubility of covalent compounds To refresh your understanding of these principles Click Here. The following table lists a few examples of these properties for some similar sized polar compounds (the non-polar hydrocarbon hexane is provided for comparison).

Physical Properties of Some Organic Compounds

Formula	IUPAC Name	Molecular Weight	Boiling Point	Water Solubility
$CH_3(CH_2)_2CO_2H$	butanoic acid	88	164 ºC	very soluble
$CH_3(CH_2)_4OH$	1-pentanol	88	138 ºC	slightly soluble
$CH_3(CH_2)_3CHO$	pentanal	86	103 ºC	slightly soluble
$CH_3CO_2C_2H_5$	ethyl ethanoate	88	77 ºC	moderately soluble
$CH_3CH_2CO_2CH_3$	methyl propanoate	88	80 ºC	slightly soluble
$CH_3(CH_2)_2CONH_2$	butanamide	87	216 ºC	soluble
$CH_3CON(CH_3)_2$	N,N-dimethylethanamide	87	165 ºC	very soluble
$CH_3(CH_2)_4NH_2$	1-aminobutane	87	103 ºC	very soluble
$CH_3(CH_2)_3CN$	pentanenitrile	83	140 ºC	slightly soluble
$CH_3(CH_2)_4CH_3$	hexane	86	69 ºC	insoluble

The first five entries all have oxygen functional groups, and the relatively high boiling points of the first two is clearly due to hydrogen bonding. Carboxylic acids have exceptionally high boiling points, due in large part to dimeric associations involving two hydrogen bonds. A structural formula for the dimer of acetic acid is shown here. When the mouse pointer passes over the drawing, an electron cloud diagram will appear. The high boiling points of the amides and nitriles are due in large part to strong dipole attractions, supplemented in some cases by hydrogen bonding.



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.

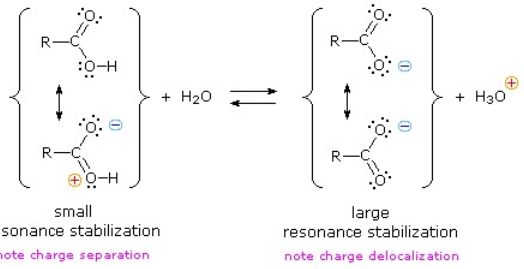
Compound	pK_a		Compound	pK_a
HCO_2H	3.75		$CH_3CH_2CH_2CO_2H$	4.82
CH_3CO_2H	4.74		$ClCH_2CH_2CH_2CO_2H$	4.53
FCH_2CO_2H	2.65		$CH_3CHClCH_2CO_2H$	4.05
$ClCH_2CO_2H$	2.85		$CH_3CH_2CHClCO_2H$	2.89
$BrCH_2CO_2H$	2.90		$C_6H_5CO_2H$	4.20
ICH_2CO_2H	3.10		$p\text{-}O_2NC_6H_4CO_2H$	3.45
Cl_3CCO_2H	0.77		$p\text{-}CH_3OC_6H_4CO_2H$	4.45

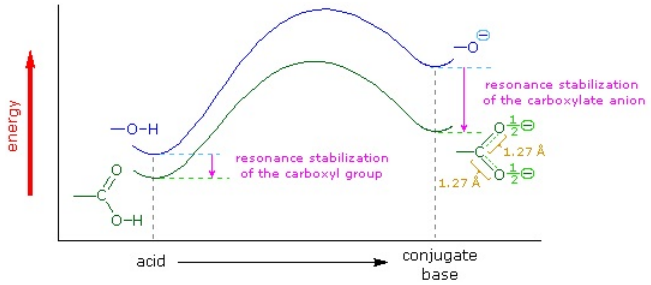
Why should the presence of a carbonyl group adjacent to a hydroxyl group have such a profound effect on the acidity of the hydroxyl proton? To answer this question we must return to the nature of acid-base equilibria and the definition of pK_a , illustrated by the general equations given below. These relationships were described in an previous section of this text.

$$H\text{–}A + H_2O \rightleftharpoons H_3O^{\oplus} + A:^{\ominus} \qquad K_{eq} = \frac{[H_3O^{\oplus}]\,[A:^{\ominus}]}{[HA]\,[H_2O]}$$

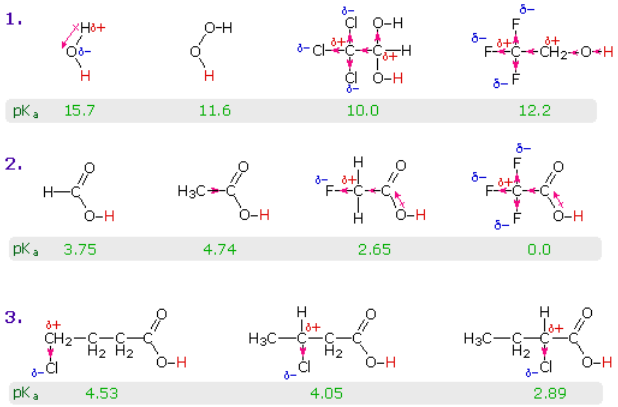
$$K_a = \frac{[H_3O^{\oplus}]\,[A:^{\ominus}]}{[HA]} \qquad pK_a = -\log K_a = \log\left(\frac{1}{K_a}\right)$$

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 displayed by clicking the "Toggle Display" button.





The resonance effect described here is undoubtedly the major contributor to the exceptional acidity of carboxylic acids. However, inductive effects also play a role. For example, alcohols have pK_a's of 16 or greater but their acidity is increased by electron withdrawing substituents on the alkyl group. The following diagram illustrates this factor for several simple inorganic and organic compounds (row #1), and shows how inductive electron withdrawal may also increase the acidity of carboxylic acids (rows #2 & 3). The acidic hydrogen is colored red in all examples.



Water is less acidic than hydrogen peroxide because hydrogen is less electronegative than oxygen, and the covalent bond joining these atoms is polarized in the manner shown. Alcohols are slightly less acidic than water, due to the poor electronegativity of carbon, but chloral hydrate, $Cl_3CCH(OH)_2$, and 2,2,2,-trifluoroethanol are significantly more acidic than water, due to inductive electron withdrawal by the electronegative halogens (and the second oxygen in chloral hydrate). In the case of carboxylic acids, if the electrophilic character of the carbonyl carbon is decreased the acidity of the carboxylic acid will also decrease. Similarly, an increase in its electrophilicity will increase the acidity of the acid. Acetic acid is ten times weaker an acid than formic acid (first two entries in the second row), confirming the electron donating character of an alkyl group relative to hydrogen, as noted earlier in a discussion of carbocation stability. Electronegative substituents increase acidity by inductive electron withdrawal. As expected, the higher the electronegativity of the substituent the greater the increase in acidity (F > Cl > Br > I), and the closer the substituent is to the carboxyl group the greater is its effect (isomers in the 3rd row). Substituents also influence the acidity of benzoic acid derivatives, but resonance effects compete with inductive effects. The methoxy group is electron donating and the nitro group is electron withdrawing (last three entries in the table of pK_a values).

For additional information about substituent effects on the acidity of carboxylic acids Click Here

Vinylagous Acids

Compounds in which an enolic hydroxyl group is conjugated with a carbonyl group also show enhanced acidity. To see examples of such compounds Click Here

Contributors

Prof. Steven Farmer (Sonoma State University)

William Reusch, Professor Emeritus (Michigan State U.), Virtual Textbook of Organic Chemistry

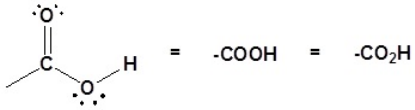
11.2: The Structures of Carboxylic Acids and Carboxylic Acid Derivatives is shared under a not declared license and was authored, remixed, and/or curated by LibreTexts.

- **Physical Properties of Carboxylic Acids** is licensed CC BY-NC-SA 4.0.

11.3: The Physical Properties of Carbonyl Compounds

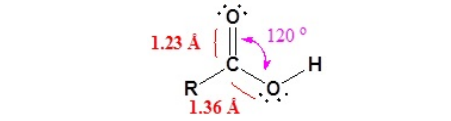
Structure of the carboxyl acid group

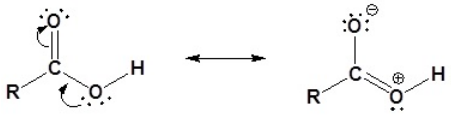
Carboxylic acids are organic compounds which incorporate a carboxyl functional group, CO_2H. The name carboxyl comes from the fact that a carbonyl and a hydroxyl group are attached to the same carbon.



Carboxyl Group

The carbon and oxygen in the carbonyl are both sp2 hybridized which give a carbonyl group a basic trigonal shape. The hydroxyl oxygen is also sp2 hybridized which allows one of its lone pair electrons to conjugate with the pi system of the carbonyl group. This make the carboxyl group planar an can represented with the following resonance structure.





Major Contributor Minor Contributor

Carboxylic acids are named such because they can donate a hydrogen to produce a carboxylate ion. The factors which affect the acidity of carboxylic acids will be discussed later.



Carboxylic acid Carboxylate ion

Physical Properties of Some Carboxylic Acids

Formula	Common Name	Source	IUPAC Name	Melting Point	Boiling Point
HCO_2H	formic acid	ants (L. formica)	methanoic acid	8.4 ºC	101 ºC
CH_3CO_2H	acetic acid	vinegar (L. acetum)	ethanoic acid	16.6 ºC	118 ºC
$CH_3CH_2CO_2H$	propionic acid	milk (Gk. protus prion)	propanoic acid	-20.8 ºC	141 ºC
$CH_3(CH_2)_2CO_2H$	butyric acid	butter (L. butyrum)	butanoic acid	-5.5 ºC	164 ºC
$CH_3(CH_2)_3CO_2H$	valeric acid	valerian root	pentanoic acid	-34.5 ºC	186 ºC
$CH_3(CH_2)_4CO_2H$	caproic acid	goats (L. caper)	hexanoic acid	-4.0 ºC	205 ºC
$CH_3(CH_2)_5CO_2H$	enanthic acid	vines (Gk. oenanthe)	heptanoic acid	-7.5 ºC	223 ºC
$CH_3(CH_2)_6CO_2H$	caprylic acid	goats (L. caper)	octanoic acid	16.3 ºC	239 ºC
$CH_3(CH_2)_7CO_2H$	pelargonic acid	pelargonium (an herb)	nonanoic acid	12.0 ºC	253 ºC
$CH_3(CH_2)_8CO_2H$	capric acid	goats (L. caper)	decanoic acid	31.0 ºC	219 ºC

Saturated			Unsaturated		
Formula	Common Name	Melting Point	Formula	Common Name	Melting Point
$CH_3(CH_2)_{10}CO_2H$	lauric acid	45 ºC	$CH_3(CH_2)_5CH{=}CH(CH_2)_7CO_2H$	palmitoleic acid	0 ºC
$CH_3(CH_2)_{12}CO_2H$	myristic acid	55 ºC	$CH_3(CH_2)_7CH{=}CH(CH_2)_7CO_2H$	oleic acid	13 ºC
$CH_3(CH_2)_{14}CO_2H$	palmitic acid	63 ºC	$CH_3(CH_2)_4CH{=}CHCH_2CH{=}CH(CH_2)_7CO_2H$	linoleic acid	-5 ºC
$CH_3(CH_2)_{16}CO_2H$	stearic acid	69 ºC	$CH_3CH_2CH{=}CHCH_2CH{=}CHCH_2CH{=}CH(CH_2)_7CO_2H$	linolenic acid	-11 ºC
$CH_3(CH_2)_{18}CO_2H$	arachidic acid	76 ºC	$CH_3(CH_2)_4(CH{=}CHCH_2)_4(CH_2)_2CO_2H$	arachidonic acid	-49 ºC

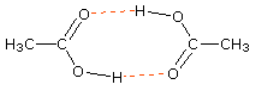
The table at the beginning of this page gave the melting and boiling points for a homologous group of carboxylic acids having from one to ten carbon atoms. The boiling points increased with size in a regular manner, but the melting points did not. Unbranched acids made up of an even number of carbon atoms have melting points higher than the odd numbered homologs having one more or one less carbon. This reflects differences in intermolecular attractive forces in the crystalline state. In the table of fatty acids we see that the presence of a cis-double bond significantly lowers the melting point of a compound. Thus, palmitoleic acid melts over 60º lower than palmitic acid, and similar decreases occur for the C_{18} and C_{20} compounds. Again, changes in crystal packing and intermolecular forces are responsible.

The factors that influence the relative boiling points and water solubilities of various types of compounds were discussed earlier. In general, dipolar attractive forces between molecules act to increase the boiling point of a given compound, with hydrogen bonds being an extreme example. Hydrogen bonding is also a major factor in the water solubility of covalent compounds To refresh your understanding of these principles Click Here. The following table lists a few examples of these properties for some similar sized polar compounds (the non-polar hydrocarbon hexane is provided for comparison).

Physical Properties of Some Organic Compounds

Formula	IUPAC Name	Molecular Weight	Boiling Point	Water Solubility
$CH_3(CH_2)_2CO_2H$	butanoic acid	88	164 ºC	very soluble
$CH_3(CH_2)_4OH$	1-pentanol	88	138 ºC	slightly soluble
$CH_3(CH_2)_3CHO$	pentanal	86	103 ºC	slightly soluble
$CH_3CO_2C_2H_5$	ethyl ethanoate	88	77 ºC	moderately soluble
$CH_3CH_2CO_2CH_3$	methyl propanoate	88	80 ºC	slightly soluble
$CH_3(CH_2)_2CONH_2$	butanamide	87	216 ºC	soluble
$CH_3CON(CH_3)_2$	N,N-dimethylethanamide	87	165 ºC	very soluble
$CH_3(CH_2)_4NH_2$	1-aminobutane	87	103 ºC	very soluble
$CH_3(CH_2)_3CN$	pentanenitrile	83	140 ºC	slightly soluble
$CH_3(CH_2)_4CH_3$	hexane	86	69 ºC	insoluble

The first five entries all have oxygen functional groups, and the relatively high boiling points of the first two is clearly due to hydrogen bonding. Carboxylic acids have exceptionally high boiling points, due in large part to dimeric associations involving two hydrogen bonds. A structural formula for the dimer of acetic acid is shown here. When the mouse pointer passes over the drawing, an electron cloud diagram will appear. The high boiling points of the amides and nitriles are due in large part to strong dipole attractions, supplemented in some cases by hydrogen bonding.



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.

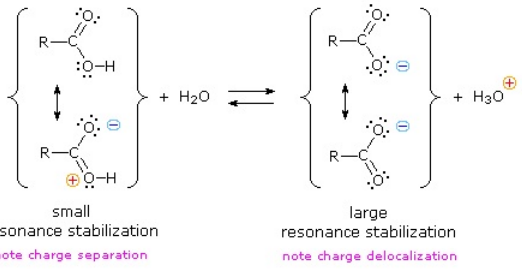
Compound	pK_a		Compound	pK_a
HCO_2H	3.75		$CH_3CH_2CH_2CO_2H$	4.82
CH_3CO_2H	4.74		$ClCH_2CH_2CH_2CO_2H$	4.53
FCH_2CO_2H	2.65		$CH_3CHClCH_2CO_2H$	4.05
$ClCH_2CO_2H$	2.85		$CH_3CH_2CHClCO_2H$	2.89
$BrCH_2CO_2H$	2.90		$C_6H_5CO_2H$	4.20
ICH_2CO_2H	3.10		$p\text{-}O_2NC_6H_4CO_2H$	3.45
Cl_3CCO_2H	0.77		$p\text{-}CH_3OC_6H_4CO_2H$	4.45

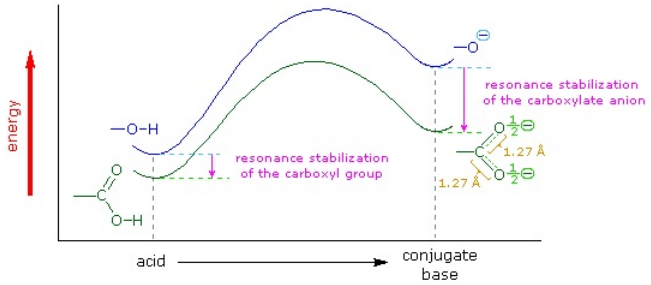
Why should the presence of a carbonyl group adjacent to a hydroxyl group have such a profound effect on the acidity of the hydroxyl proton? To answer this question we must return to the nature of acid-base equilibria and the definition of pK_a , illustrated by the general equations given below. These relationships were described in an previous section of this text.

$$H\text{–}A + H_2O \rightleftharpoons H_3O^{\oplus} + A:^{\ominus} \qquad K_{eq} = \frac{[H_3O^{\oplus}]\,[A:^{\ominus}]}{[HA]\,[H_2O]}$$

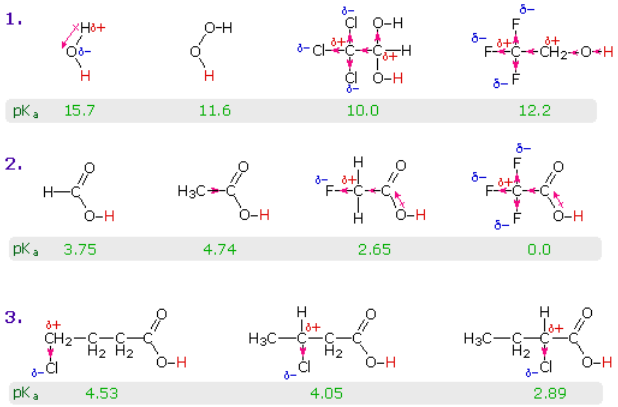
$$K_a = \frac{[H_3O^{\oplus}]\,[A:^{\ominus}]}{[HA]} \qquad pK_a = -\log K_a = \log\left(\frac{1}{K_a}\right)$$

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 displayed by clicking the "Toggle Display" button.





The resonance effect described here is undoubtedly the major contributor to the exceptional acidity of carboxylic acids. However, inductive effects also play a role. For example, alcohols have pK_a's of 16 or greater but their acidity is increased by electron withdrawing substituents on the alkyl group. The following diagram illustrates this factor for several simple inorganic and organic compounds (row #1), and shows how inductive electron withdrawal may also increase the acidity of carboxylic acids (rows #2 & 3). The acidic hydrogen is colored red in all examples.



Water is less acidic than hydrogen peroxide because hydrogen is less electronegative than oxygen, and the covalent bond joining these atoms is polarized in the manner shown. Alcohols are slightly less acidic than water, due to the poor electronegativity of carbon, but chloral hydrate, $Cl_3CCH(OH)_2$, and 2,2,2,-trifluoroethanol are significantly more acidic than water, due to inductive electron withdrawal by the electronegative halogens (and the second oxygen in chloral hydrate). In the case of carboxylic acids, if the electrophilic character of the carbonyl carbon is decreased the acidity of the carboxylic acid will also decrease. Similarly, an increase in its electrophilicity will increase the acidity of the acid. Acetic acid is ten times weaker an acid than formic acid (first two entries in the second row), confirming the electron donating character of an alkyl group relative to hydrogen, as noted earlier in a discussion of carbocation stability. Electronegative substituents increase acidity by inductive electron withdrawal. As expected, the higher the electronegativity of the substituent the greater the increase in acidity (F > Cl > Br > I), and the closer the substituent is to the carboxyl group the greater is its effect (isomers in the 3rd row). Substituents also influence the acidity of benzoic acid derivatives, but resonance effects compete with inductive effects. The methoxy group is electron donating and the nitro group is electron withdrawing (last three entries in the table of pK_a values).

For additional information about substituent effects on the acidity of carboxylic acids Click Here

Vinylagous Acids

Compounds in which an enolic hydroxyl group is conjugated with a carbonyl group also show enhanced acidity. To see examples of such compounds Click Here

Contributors

Prof. Steven Farmer (Sonoma State University)

William Reusch, Professor Emeritus (Michigan State U.), Virtual Textbook of Organic Chemistry

11.3: The Physical Properties of Carbonyl Compounds is shared under a not declared license and was authored, remixed, and/or curated by LibreTexts.

- **Physical Properties of Carboxylic Acids** is licensed CC BY-NC-SA 4.0.

11.4: Carboxylic Acids and Carboxylic Acid Derivatives found in Nature

Carboxylic acids are widespread in nature, often combined with other functional groups. Simple alkyl carboxylic acids, composed of four to ten carbon atoms, are liquids or low melting solids having very unpleasant odors. The **fatty acids** are important components of the biomolecules known as lipids, especially fats and oils. As shown in the following table, these long-chain carboxylic acids are usually referred to by their common names, which in most cases reflect their sources. A mnemonic phrase for the C_{10} to C_{20} natural fatty acids capric, lauric, myristic, palmitic, stearic and arachidic is: "**C**urly, **L**arry & **M**oe **P**erform **S**illy **A**ntics" (note that the names of the three stooges are in alphabetical order).

Table: **11.4.1**: *Saturated Fatty Acids*

Formula	Common Name	Melting Point
$CH_3(CH_2)_{10}CO_2H$	lauric acid	45 ºC
$CH_3(CH_2)_{12}CO_2H$	myristic acid	55 ºC
$CH_3(CH_2)_{14}CO_2H$	palmitic acid	63 ºC
$CH_3(CH_2)_{16}CO_2H$	stearic acid	69 ºC
$CH_3(CH_2)_{18}CO_2H$	arachidic acid	76 ºC

Interestingly, the molecules of most natural fatty acids have an *even number of carbon atoms*. Analogous compounds composed of odd numbers of carbon atoms are perfectly stable and have been made synthetically. Since nature makes these long-chain acids by linking together acetate units, it is not surprising that the carbon atoms composing the natural products are multiples of two. The double bonds in the unsaturated compounds listed on the right are all cis (or Z).

Table **11.4.2**: *Unsaturated Fatty Acids*

Formula	Common Name	Melting Point
$CH_3(CH_2)_5CH{=}CH(CH_2)_7CO_2H$	palmitoleic acid	0 ºC
$CH_3(CH_2)_7CH{=}CH(CH_2)_7CO_2H$	oleic acid	13 ºC
$CH_3(CH_2)_4CH{=}CHCH_2CH{=}CH(CH_2)_7CO_2H$	linoleic acid	-5 ºC
$CH_3CH_2CH{=}CHCH_2CH{=}CHCH_2CH{=}CH(CH_2)_7CO_2H$	linolenic acid	-11 ºC
$CH_3(CH_2)_4(CH{=}CHCH_2)_4(CH_2)_2CO_2H$	arachidonic acid	-49 ºC

The following formulas are examples of other naturally occurring carboxylic acids. The molecular structures range from simple to complex, often incorporate a variety of other functional groups, and many are chiral.

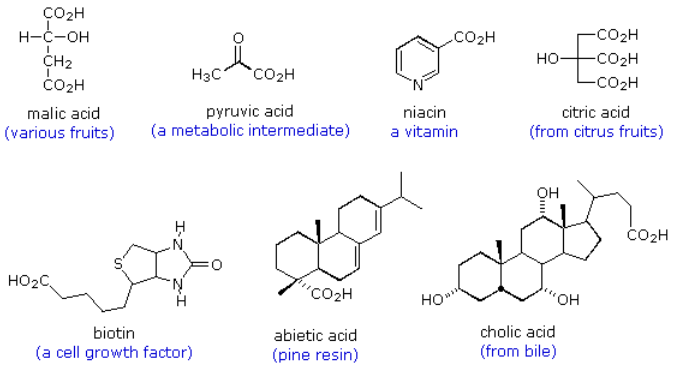


Figure 1: Naturally occurring carboxylic acids.

Contributors

- William Reusch, Professor Emeritus (Michigan State U.), Virtual Textbook of Organic Chemistry

---

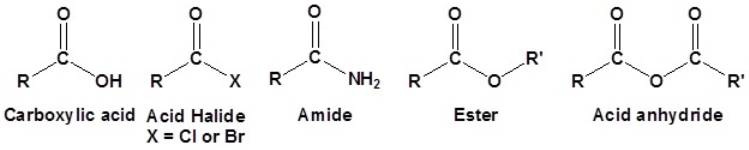
11.4: Carboxylic Acids and Carboxylic Acid Derivatives found in Nature is shared under a not declared license and was authored, remixed, and/or curated by LibreTexts.

- **Fatty Acids** by William Reusch is licensed CC BY-NC-SA 4.0.

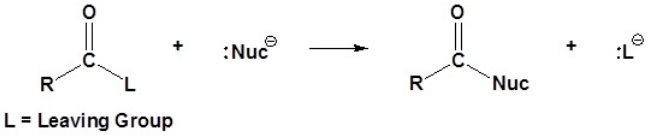
11.5: How Carboxylic Acids and Carboxylic Acids Compounds React

Introduction

Carboxylic acid derivatives are a group of functional groups whose chemistry is closely related. The main difference is the presence of an electronegative substituent that can act as a leaving group during nucleophile substitution reactions. Although there are many types of carboxylic acid derivatives known we will be focusing on just four: Acid halides, Acid anhydrides, Esters, and Amides.

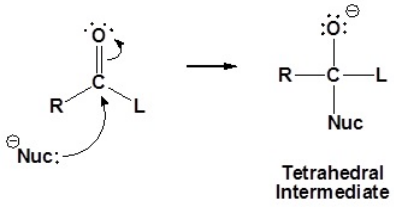


General reaction

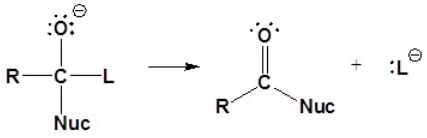


General mechanism

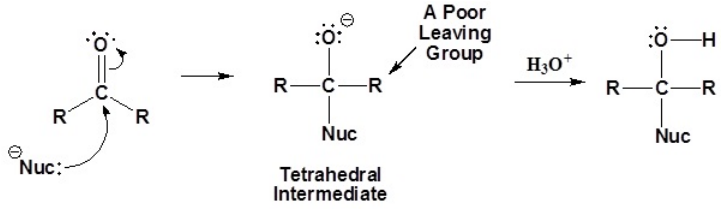
1) Nucleophilic attack on the carbonyl



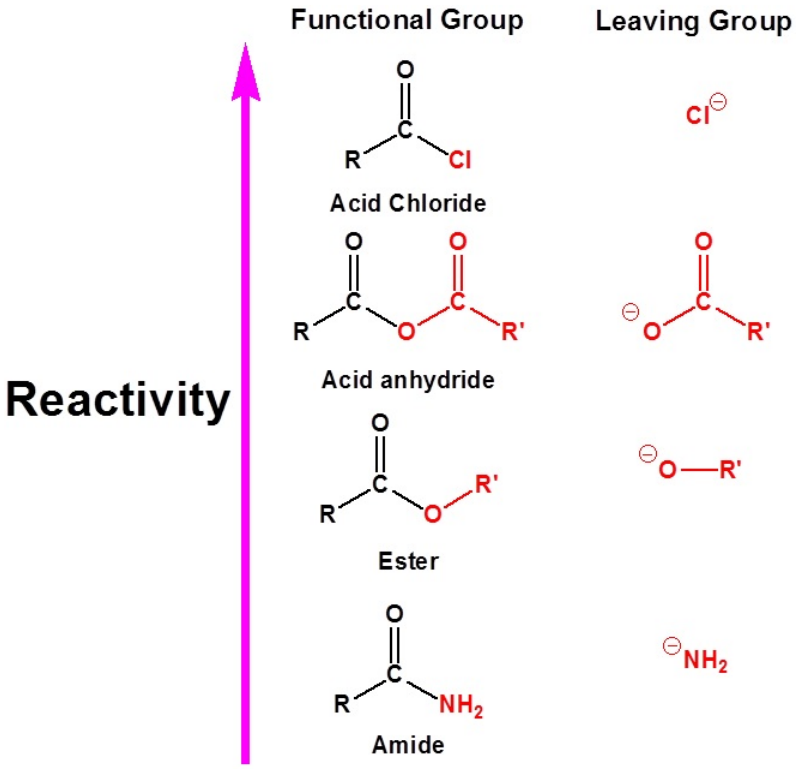
2) Leaving group is removed



Although aldehydes and ketones also contain a carbonyl their chemistry is distinctly different because they do not contain a suitable leaving group. Once the tetrahedral intermediate is formed aldehydes and ketones cannot reform the carbonyl. Because of this aldehydes and ketones typically undergo nucleophilic additions and not substitutions.



The relative reactivity of carboxylic acid derivatives toward nucleophile substitutions is related to the electronegative leaving group's ability to activate the carbonyl. The more electronegative leaving groups withdrawn electron density from the carbonyl, thereby, increasing its electrophilicity.



Contributors

Prof. Steven Farmer (Sonoma State University)

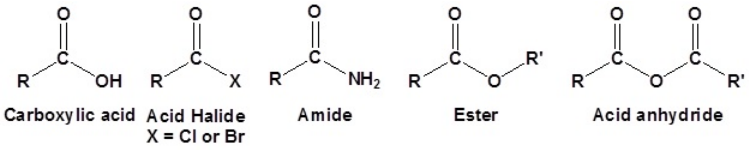
11.5: How Carboxylic Acids and Carboxylic Acids Compounds React is shared under a not declared license and was authored, remixed, and/or curated by LibreTexts.

- **General mechanism of ester reactions** is licensed CC BY-NC-SA 4.0.

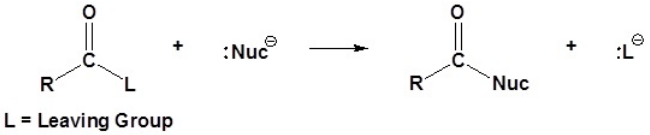
11.6: Relative Reactivities of Carboxylic Acids and Carboxylic Acid Derivatives

Introduction

Carboxylic acid derivatives are a group of functional groups whose chemistry is closely related. The main difference is the presence of an electronegative substituent that can act as a leaving group during nucleophile substitution reactions. Although there are many types of carboxylic acid derivatives known we will be focusing on just four: Acid halides, Acid anhydrides, Esters, and Amides.

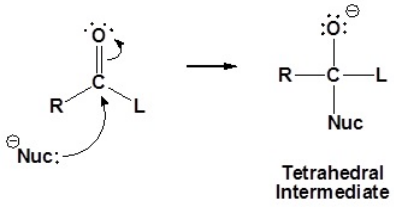


General reaction

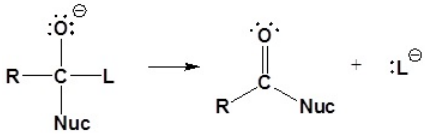


General mechanism

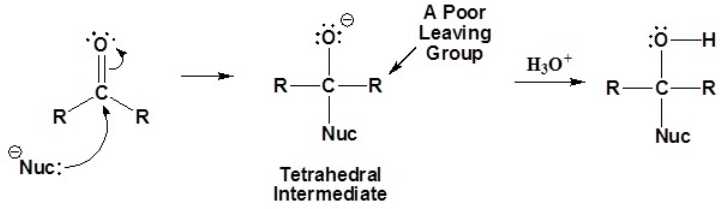
1) Nucleophilic attack on the carbonyl



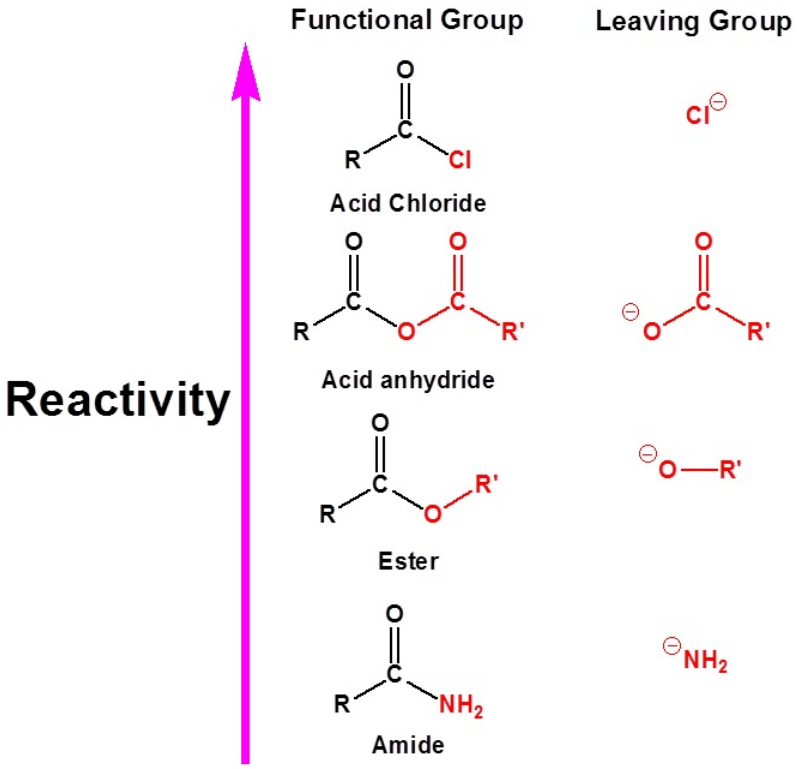
2) Leaving group is removed



Although aldehydes and ketones also contain a carbonyl their chemistry is distinctly different because they do not contain a suitable leaving group. Once the tetrahedral intermediate is formed aldehydes and ketones cannot reform the carbonyl. Because of this aldehydes and ketones typically undergo nucleophilic additions and not substitutions.



The relative reactivity of carboxylic acid derivatives toward nucleophile substitutions is related to the electronegative leaving group's ability to activate the carbonyl. The more electronegative leaving groups withdrawn electron density from the carbonyl, thereby, increasing its electrophilicity.



Contributors

Prof. Steven Farmer (Sonoma State University)

11.6: Relative Reactivities of Carboxylic Acids and Carboxylic Acid Derivatives is shared under a not declared license and was authored, remixed, and/or curated by LibreTexts.

- **General mechanism of ester reactions** is licensed CC BY-NC-SA 4.0.

SECTION OVERVIEW

11.7: Reactions of Acyl Halides

Topic hierarchy

11.7: Reactions of Acyl Halides is shared under a not declared license and was authored, remixed, and/or curated by LibreTexts.

SECTION OVERVIEW

11.8: Reactions of Esters

Topic hierarchy

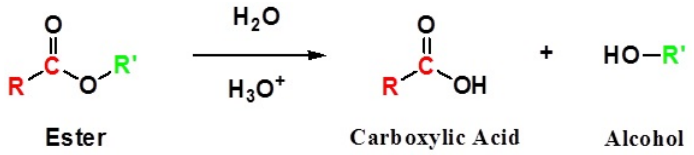
11.8: Reactions of Esters is shared under a not declared license and was authored, remixed, and/or curated by LibreTexts.

11.9: Acid-Catalyzed Ester Hydrolysis

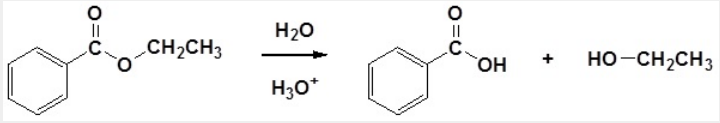
Introduction

Esters can be cleaved back into a carboxylic acid and an alcohol by reaction with water and a catalytic amount of acid.

General Reaction

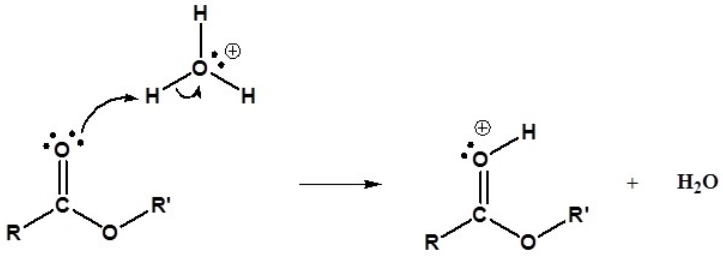


Example 1:

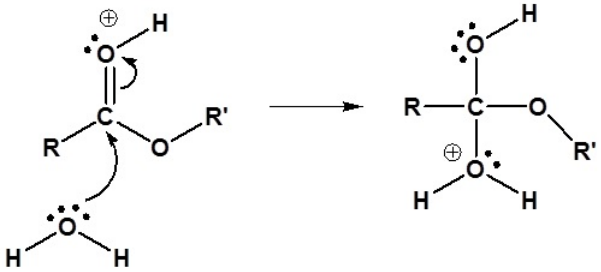


Mechanism

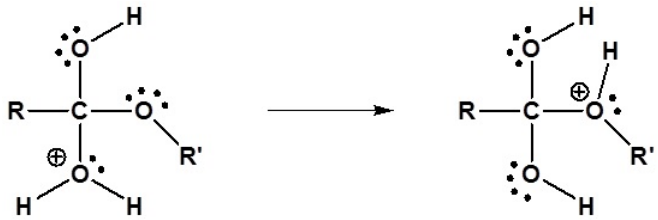
1) Protonation of the Carbonyl



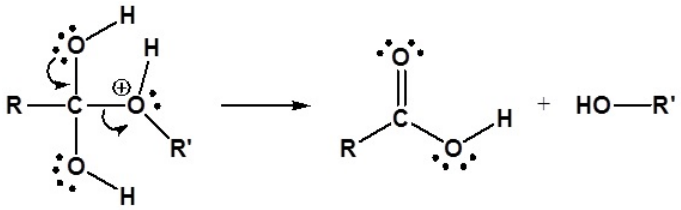
2) Nucleophilic attack by water



3) Proton transfer



4) Leaving group removal



Contributors

Prof. Steven Farmer (Sonoma State University)

11.9: Acid-Catalyzed Ester Hydrolysis is shared under a not declared license and was authored, remixed, and/or curated by LibreTexts.

- **Acid Catalyzed Hydrolysis of Esters (II)** is licensed CC BY-NC-SA 4.0.

11.10: Soaps, Detergents, and Micelles

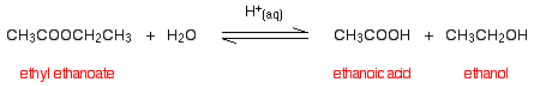
This page describes ways of hydrolyzing esters - splitting them into carboxylic acids (or their salts) and alcohols by the action of water, dilute acid or dilute alkali. It starts by looking at the hydrolysis of simple esters like ethyl ethanoate, and goes on to look at hydrolyzing bigger, more complicated ones to make soap.

Technically, hydrolysis is a reaction with water. That is exactly what happens when esters are hydrolyzed by water or by dilute acids such as dilute hydrochloric acid. The alkaline hydrolysis of esters actually involves reaction with hydroxide ions, but the overall result is so similar that it is lumped together with the other two.

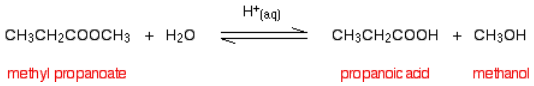
Hydrolysis using water or dilute acid

The reaction with pure water is so slow that it is never used. The reaction is catalyzed by dilute acid, and so the ester is heated under reflux with a dilute acid like dilute hydrochloric acid or dilute sulfuric acid. Here are two simple examples of hydrolysis using an acid catalyst.

First, hydrolyzing ethyl ethanoate:



. . . and then hydrolyzing methyl propanoate:

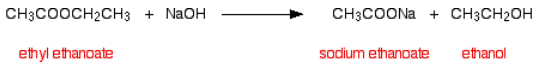


Notice that the reactions are reversible. To make the hydrolysis as complete as possible, you would have to use an excess of water. The water comes from the dilute acid, and so you would mix the ester with an excess of dilute acid.

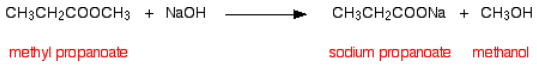
Hydrolysis using dilute alkali

This is the usual way of hydrolyzing esters. The ester is heated under reflux with a dilute alkali like sodium hydroxide solution. There are two advantages of doing this rather than using a dilute acid. The reactions are one-way rather than reversible, and the products are easier to separate. Taking the same esters as above, but using sodium hydroxide solution rather than a dilute acid:

First, hydrolyzing ethyl ethanoate using sodium hydroxide solution:



and then hydrolyzing methyl propanoate in the same way:



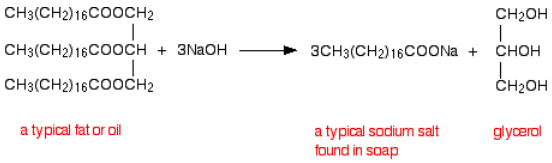
Notice that you get the sodium salt formed rather than the carboxylic acid itself. This mixture is relatively easy to separate. Provided you use an excess of sodium hydroxide solution, there will not be any ester left - so you don't have to worry about that. The alcohol formed can be distilled off. That's easy!

If you want the acid rather than its salt, all you have to do is to add an excess of a strong acid like dilute hydrochloric acid or dilute sulfuric acid to the solution left after the first distillation. If you do this, the mixture is flooded with hydrogen ions. These are picked up by the ethanoate ions (or propanoate ions or whatever) present in the salts to make ethanoic acid (or propanoic acid, etc). Because these are weak acids, once they combine with the hydrogen ions, they tend to stay combined. The carboxylic acid can now be distilled off.

Hydrolyzing complicated esters to make soap

This next bit deals with the alkaline hydrolysis (using sodium hydroxide solution) of the big esters found in animal and vegetable fats and oils. If the large esters present in animal or vegetable fats and oils are heated with concentrated sodium hydroxide solution

exactly the same reaction happens as with the simple esters. A salt of a carboxylic acid is formed - in this case, the sodium salt of a big acid such as octadecanoic acid (stearic acid). These salts are the important ingredients of soap - the ones that do the cleaning. An alcohol is also produced - in this case, the more complicated alcohol, propane-1,2,3-triol (glycerol).



Because of its relationship with soap making, the alkaline hydrolysis of esters is sometimes known as saponification.

Contributors

- Jim Clark (Chemguide.co.uk)

11.10: Soaps, Detergents, and Micelles is shared under a not declared license and was authored, remixed, and/or curated by LibreTexts.

- **The Hydrolysis of Esters** by Jim Clark is licensed CC BY-NC 4.0.

SECTION OVERVIEW

11.11: Reactions of Carboxylic Acids

Topic hierarchy

11.11: Reactions of Carboxylic Acids is shared under a not declared license and was authored, remixed, and/or curated by LibreTexts.

SECTION OVERVIEW

11.12: Reactions of Amides

Amides are reasonably reactive, usually via an attack on the carbonyl breaking the carbonyl double bond and forming a tetrahedral intermediate. Thiols, hydroxyls and amines are all known to serve as nucleophiles. Owing to their resonance stabilization, amides are less reactive under physiological conditions than esters.

Topic hierarchy

11.12: Reactions of Amides is shared under a not declared license and was authored, remixed, and/or curated by LibreTexts.

11.13: Acid-Catalyzed Amide Hydrolysis

Technically, hydrolysis is a reaction with water. That is exactly what happens when amides are hydrolyzed in the presence of dilute acids such as dilute hydrochloric acid. The acid acts as a catalyst for the reaction between the amide and water. The alkaline hydrolysis of amides actually involves reaction with hydroxide ions, but the result is similar enough that it is still classed as hydrolysis.

Hydrolysis under acidic conditions

Taking ethanamide as a typical amide. If ethanamide is heated with a dilute acid (such as dilute hydrochloric acid), ethanoic acid is formed together with ammonium ions. So, if you were using hydrochloric acid, the final solution would contain ammonium chloride and ethanoic acid.

$$CH_3CONH_2 + H_2O + HCl \; rightarrow CH_3COOH + NH_4^+Cl^- \tag{11.13.1}$$

Hydrolysis under alkaline conditions

Also, if ethanamide is heated with sodium hydroxide solution, ammonia gas is given off and you are left with a solution containing sodium ethanoate.

$$CH_3CONH_2 + NaOH \rightarrow CH_3COONa + NH_3 \tag{11.13.2}$$

Using alkaline hydrolysis to test for an amide

If you add sodium hydroxide solution to an unknown organic compound, and it gives off ammonia on heating (but not immediately in the cold), then it is an amide. You can recognize the ammonia by smell and because it turns red litmus paper blue.

The possible confusion using this test is with ammonium salts. Ammonium salts also produce ammonia with sodium hydroxide solution, but in this case there is always enough ammonia produced in the cold for the smell to be immediately obvious.

Contributors

- Jim Clark (Chemguide.co.uk)

11.13: Acid-Catalyzed Amide Hydrolysis is shared under a not declared license and was authored, remixed, and/or curated by LibreTexts.

- **The Hydrolysis of Amides** by Jim Clark is licensed CC BY-NC 4.0.

11.14: The Synthesis of Carboxylic Acid Derivatives

Applications of Condensation Reactions to Synthesis

The construction of complex molecules by a series of suitable reactions carried out from simple starting compounds is called **synthesis**. Synthesis is not only of immense practical importance (aspirin and nylon are two examples of commercially valuable synthetic compounds), but it also allows us to prepare novel molecules with which to test our understanding of structure and reactivity. Three challenges must be met in devising a synthesis for a specific compound:

1. The carbon atom framework or skeleton that is found in the desired compound (the target) must be assembled.
2. The functional groups that characterize the target compound must be introduced or transformed from other groups at appropriate locations.
3. If centers of stereoisomerism are present, they must be fixed in a proper manner.

Recognition of these tasks does not imply that they are independent of each other, or should be approached and solved separately. A successful plan or strategy for a synthesis must correlate each step with all these goals, so that an efficient and practical solution to making the target molecule is achieved. Nevertheless, it is useful to classify the various reactions we have studied with respect to their ability to **(i)** enlarge or expand a given structure, **(ii)** transform or relocate existing functional groups, and **(iii)** do both of these in a stereoselective fashion. The organization of this text by functional group behavior partially satisfies the second point, and the following discussion focuses on the first.

1. Carbon-Carbon Bond Formation

A useful assortment of carbon-carbon bond forming reactions have been described in this and earlier chapters. These include:

(1) Friedel-Crafts alkylation and acylation.

(2) Diels-Alder cycloaddition.

(3) addition of organometallic reagents to aldehydes, ketones & carboxylic acid derivatives.

(4) alkylation of acetylide anions.

(5) alkylation of enolate anions.

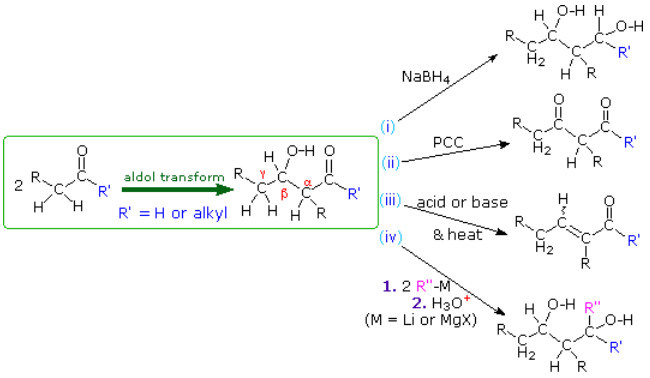
(6) Claisen and aldol condensations.

With the exception of Friedel-Crafts alkylation these reactions all give products having one or more functional groups at or adjacent to the bonding sites. As a result, subsequent functional group introduction or modification may be carried out in a relatively straightforward manner. This will be illustrated for aldol and Claisen condensations in the following section.

2. Modification of Condensation Products

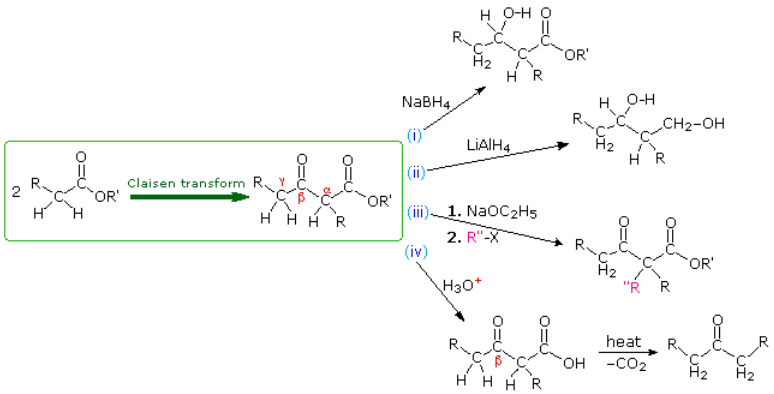
A. Reactions of Aldol Products

The aldol reaction produces beta-hydroxyaldehydes or ketones, and a number of subsequent reactions may be carried out with these products. As shown in the following diagram, they may be (i) reduced to 1,3-diols, (ii) a 2º-hydroxyl group may be oxidized to a carbonyl group, (iii) acid or base catalyzed beta-dehydration may produce an unsaturated aldehyde or ketone, and (iv) organometallic reagents may be added to the carbonyl group (assuming the hydroxyl group is protected as an ether or a second equivalent of reagent is used).



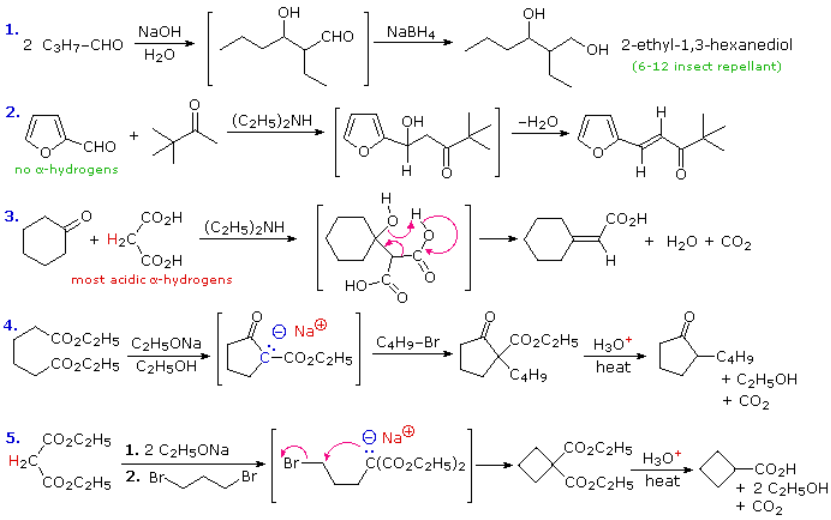
B. Reactions of Claisen Products

The Claisen condensation produces beta-ketoesters. These products may then be modified or enhanced by further reactions. Among these, the following diagram illustrates (i) partial reduction of the ketone with $NaBH_4$, (ii) complete reduction to a 1,3-diol by $LiAlH_4$, (iii) enolate anion alkylation, and (iv) ester hydrolysis followed by thermal decarboxylation of the resulting beta-ketoacid.



C. Synthesis Examples

To illustrate how the reaction sequences described above may be used to prepare a variety of different compounds, five examples are provided here. The first is a typical aldol reaction followed by reduction to a 1,3-diol (2-ethyl-1,3-hexanediol). In the second example, the absence of alpha-hydrogens on the aldehyde favors the mixed condensation, and conjugation of the double bond facilitates dehydration. The doubly-activated methylene group of malonic and acetoacetic acids or esters makes them good donors in any condensation, as is demonstrated by the third aldol-like reaction. A concerted dehydrative-decarboxylation (shown by the magenta arrows) leads to the unsaturated carboxylic acid product. Amine bases are often used as catalysts for aldol reactions, as in equations #2 & 3. The fourth reaction demonstrates that the conjugate base of the beta-ketoester products from Claisen or Dieckmann condensation may be alkylated directly. Thermal decarboxylation of the resulting beta-ketoacid gives a mono-alkylated cyclic ketone. Finally, both acidic methylene hydrogens in malonic ester or ethyl acetoacetate may be substituted, and the irreversible nature of such alkylations permits strained rings to be formed. In this case thermal decarboxylation of a substituted malonic acid generates a carboxylic acid. In all these examples the remaining functional groups could be used for additional synthetic operations.

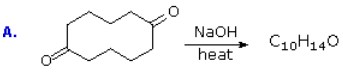


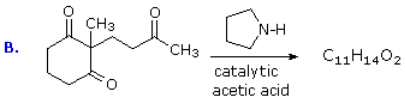
Vinylagous Reactions

A large family of vinylagous reactions, related to the condensations, acylations and alkylations described here, increase the bond forming options available to the synthetic chemist. To learn more about these versatile reactions Click Here

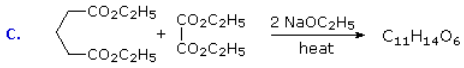
Some Exercises

If you understand the previous discussion of reactions useful in synthesis you should try the following problems. Some of them are complex so don't be concerned if you don't solve them all immediately. Analyze each problem carefully, and try to learn from it. The solutions will be displayed by clicking the answer button under the diagram.



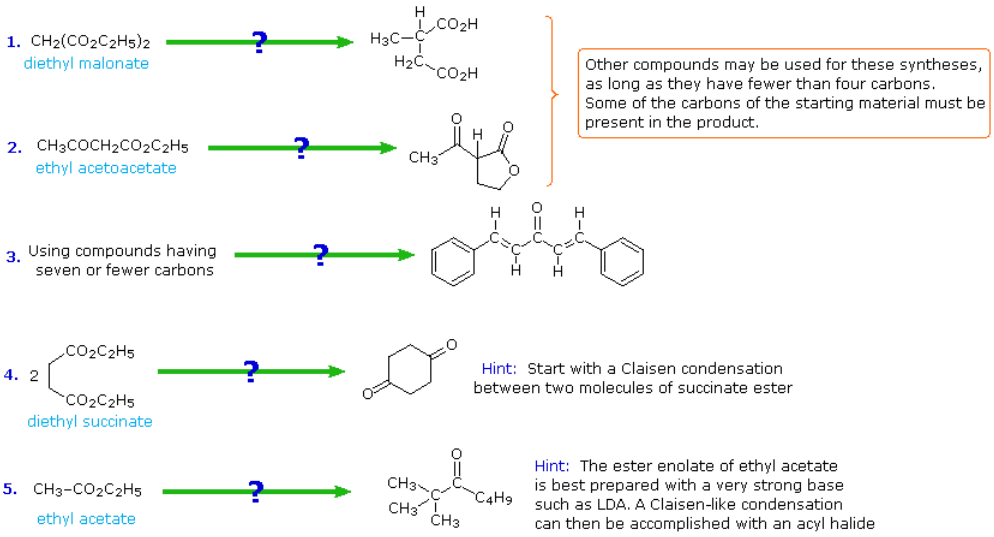


The molecular formulas for the products from each of the condensation reactions to the left are given. Deduce the structural formula for each, and write a mechanism for the reaction.



Show Products

The following problems ask you to devise a synthesis for a given target molecule. The first two problems make use of the common starting materials, diethyl malonate and ethyl acetoacetate. The third problem leaves the choice of materials open. The nature of the target molecule suggests that an aldol condensation might be useful. The fourth problem must be solved by using diethyl succinate as the only reagent. Finally, other reactants composed of no more than five carbon atoms may be used in the last problem.



Contributors

William Reusch, Professor Emeritus (Michigan State U.), Virtual Textbook of Organic Chemistry

---

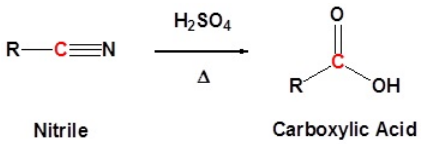
11.14: The Synthesis of Carboxylic Acid Derivatives is shared under a not declared license and was authored, remixed, and/or curated by LibreTexts.

- **Carboxylic Derivatives - Synthesis Applications** by William Reusch is licensed CC BY-NC-SA 4.0.

11.15: Nitriles

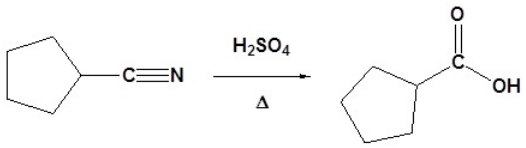
Nitriles can be converted to carboxylic acid with heating in sulfuric acid. During the reaction an amide intermediate is formed.

General Reaction



Nitrile Carboxylic Acid

Example



Contributors

Prof. Steven Farmer (Sonoma State University)

11.15: Nitriles is shared under a not declared license and was authored, remixed, and/or curated by LibreTexts.

- **Conversion of nitriles to carboxylic acids** is licensed CC BY-NC-SA 4.0.

CHAPTER OVERVIEW

12: Carbonyl Compounds II- Reactions of Aldehydes and Ketones • More Reactions of Carboxylic Acid Derivatives



Essential Organic Chemistry: 2nd Ed.

Bruice

Homework Problems
Homework Solutions

I II III IV V VI VII VIII IX X XI XII XIII XIV XV XVI XVII XVIII XIX XX XXI

Template:HideTOC

- 12.1: The Nomenclature of Aldehydes and Ketones
- 12.2: The Relative Reactivities of Carbonyl Compounds
- 12.3: How Aldehydes and Ketones React
- 12.4: Gringard Reagents
- 12.5: Reactions of Carbonyl Compounds with Hydride Ion
- 12.6: Reactions of Aldehydes and Ketones with Amines
- 12.7: Reactions of Aldehydes and Ketones with Water
- 12.8: Reactions of Aldehydes and Ketones with Alcohols
- 12.9: Nucleophilic Addition to α, β- Unsaturated Carboxylic Acid Derivatives
- 12.10: Nucleophilic Addition to α, β- Unsaturated Carbonyl Compounds
- 12.11: Protecting Groups
- 12.12: Addition of Sulfur Nucleophiles
- 12.13: The Wittig Reaction Forms an Alkene
- 12.14: Stereochemistry of Nucleophilic Addition Reactions- Re and Si Faces
- 12.15: Designing a Synthesis VI- Disconnections, Synthons, and Synthetic Equivalents
- 12.16: Enzyme-Catalyzed Additions to α, β- Unsaturated Carbonyl Compounds

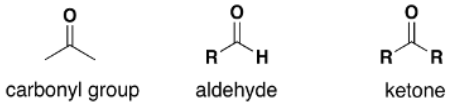
---

12: Carbonyl Compounds II- Reactions of Aldehydes and Ketones • More Reactions of Carboxylic Acid Derivatives is shared under a not declared license and was authored, remixed, and/or curated by LibreTexts.

12.1: The 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 *dehyd*ration 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.

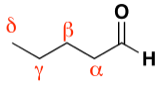
Aldehydes and ketones are organic compounds which incorporate a **carbonyl functional group**, C=O. The carbon atom of this group has two remaining bonds that may be occupied by hydrogen, alkyl or aryl substituents. If at least one of these substituents is hydrogen, the compound is an **aldehyde**. If 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.



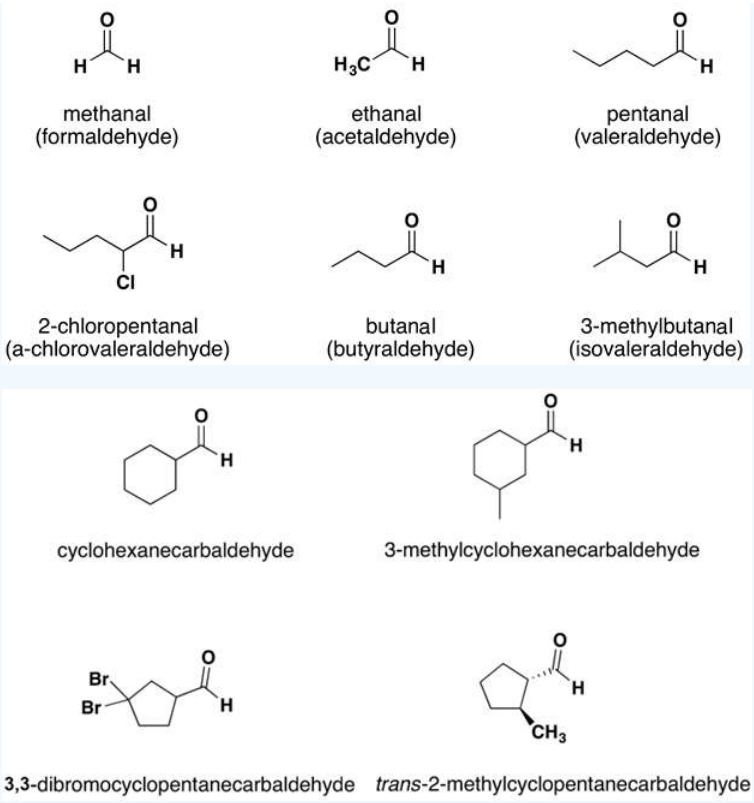
If the aldehyde moiety  (-CHO) is attached to a ring the suffix ***–carbaldehyde*** is added to the name of the ring. The carbon attached to this moiety will get the #1 location number in naming the ring.

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.

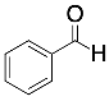
Example 1

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

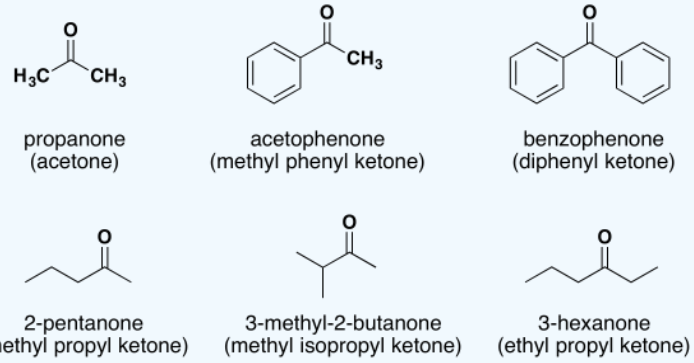
The IUPAC system of nomenclature assigns a characteristic suffix of **-one** to ketones. A ketone carbonyl function may be located anywhere within a chain or ring, and its position is usually given by a location number. Chain numbering normally starts from the end nearest the carbonyl group. Very simple 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*.

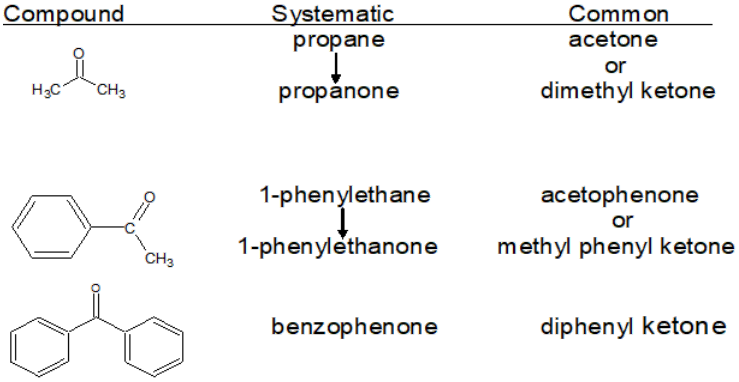
Example 2

The IUPAC system names are given on top while the common name is given on the bottom in parentheses.



Ketone Common Names to Memorize

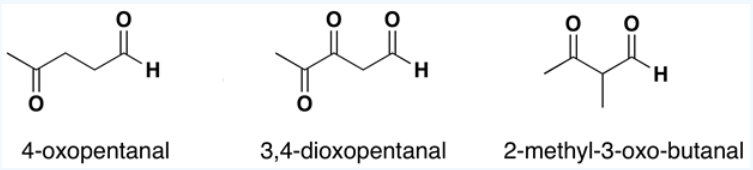
There are some common names that are still used and need to be memorized. Recognizing the patterns can be helpful.



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.

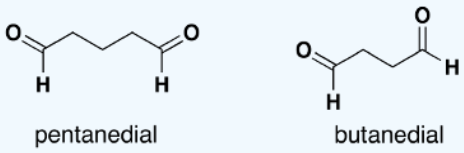
Example 3



Naming Dialdehydes and Diketones

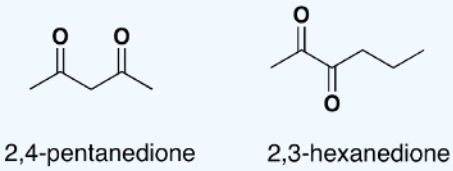
For dialdehydes the location numbers for both carbonyls are omitted because the aldehyde functional groups are expected to occupy the ends of the parent chain. The ending **–dial** is added to the end of the parent chain name.

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

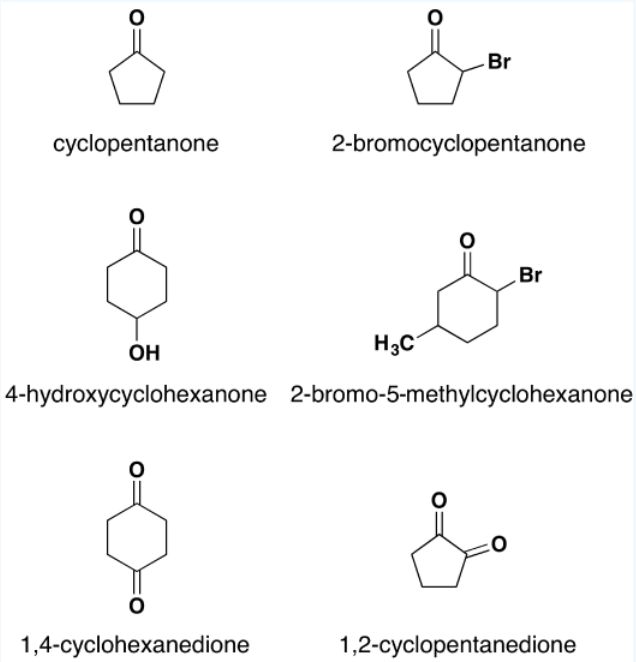


Naming Cyclic Ketones and Diketones

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.

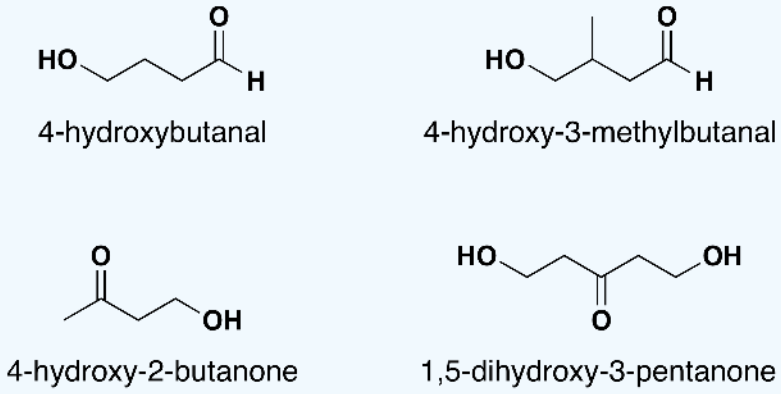
Example 6



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



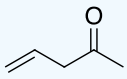
Naming Carbonyls and Alkenes in the Same Molecule

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:

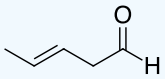
*(Location number of the alkene)-(Prefix name for the longest carbon chain minus the -**ane** ending)-(an -**en** ending to indicate the presence of an alkene)-(the location number of the carbonyl if a ketone is present)-(either an –**one** or and -**anal** ending).*

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.

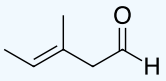
Example 8



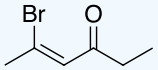
4-penten-2-one



trans-3-pentenal
or (*E*)-3-pentenal



(*E*)-3-methyl-3-pentenal

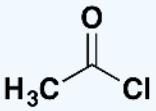


(*Z*)-5-bromo-4-hexen-3-one

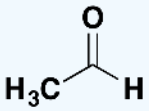
Aldehydes and Ketones as Fragments

- *Alkanoyl* is the common name of the fragment, though the older naming, *acyl*, is still widely used.
- *Formyl* is the common name of the fragment.
- *Acety* is the common name of the CH_3-C=O- fragment.

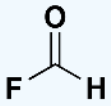
Example 9



acetyl chloride



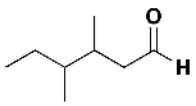
acetylaldehyde

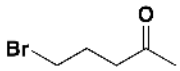


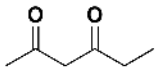
formyl fluoride

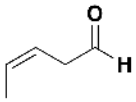
Additional Examples of Carbonyl Nomenclature

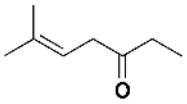
1) Please give the IUPAC name for each compound:

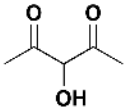
A) 

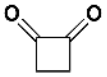
B) 

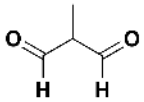
C) 

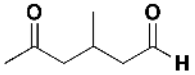
D) 

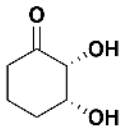
E) 

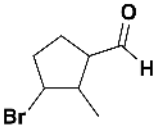
F) 

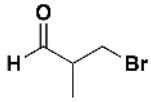
G) 

H) 

I) 

J) 

K) 

L) 

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

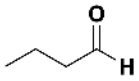
G) 3-oxobutanal

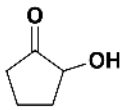
H) *cis*-3-bromocyclohexanecarboaldehyde

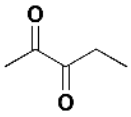
I) butanedial

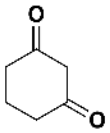
J) *trans*-2-methyl-3-hexenal

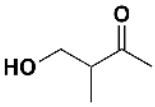
Answers to question 2:

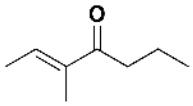
A) 

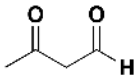
B) 

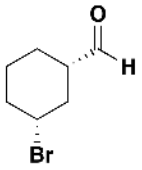
C) 

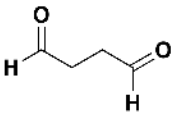
D) 

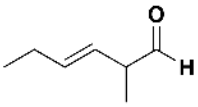
E) 

F) 

G) 

H) 

I) 

J) 

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

- Prof. Steven Farmer (Sonoma State University)
- William Reusch, Professor Emeritus (Michigan State U.), Virtual Textbook of Organic Chemistry

12.1: The Nomenclature of Aldehydes and Ketones is shared under a not declared license and was authored, remixed, and/or curated by LibreTexts.

- **Nomenclature of Aldehydes & Ketones** is licensed CC BY-NC-SA 4.0.

SECTION OVERVIEW

12.2: The Relative Reactivities of Carbonyl Compounds

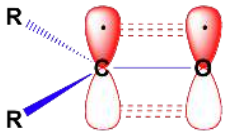
The concept of an ideal solution is fundamental to chemical thermodynamics and its applications, such as the use of colligative properties. An **ideal solution** or ideal mixture is a solution in which the enthalpy of solution ($\Delta H_{solution} = 0$) is zero; with the closer to zero the enthalpy of solution, the more "ideal" the behavior of the solution becomes. Since the enthalpy of mixing (solution) is zero, the change in Gibbs energy on mixing is determined solely by the entropy of mixing ($\Delta S_{solution}$).

Template:HideTOC

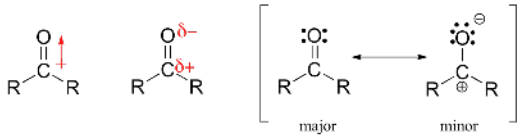
12.2: The Relative Reactivities of Carbonyl Compounds is shared under a not declared license and was authored, remixed, and/or curated by LibreTexts.

12.3: How Aldehydes and Ketones React

Before we consider in detail the reactivity of aldehydes and ketones, we need to look back and remind ourselves of what the bonding picture looks like in a carbonyl. Carbonyl carbons are sp^2 hybridized, with the three sp^2 orbitals forming soverlaps with orbitals on the oxygen and on the two carbon or hydrogen atoms. These three bonds adopt trigonal planar geometry. The remaining unhybridized 2p orbital on the central carbonyl carbon is perpendicular to this plane, and forms a 'side-by-side' pbond with a 2p orbital on the oxygen.

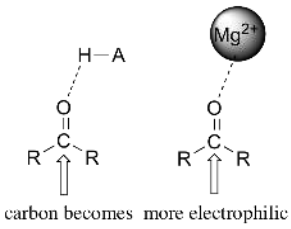


The carbon-oxygen double bond is polar: oxygen is more electronegative than carbon, so electron density is higher on the oxygen side of the bond and lower on the carbon side. Recall that bond polarity can be depicted with a dipole arrow, or by showing the oxygen as holding a partial negative charge and the carbonyl carbon a partial positive charge.



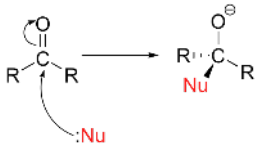
A third way to illustrate the carbon-oxygen dipole is to consider the two main resonance contributors of a carbonyl group: the major form, which is what you typically see drawn in Lewis structures, and a minor but very important contributor in which both electrons in the pbond are localized on the oxygen, giving it a full negative charge. The latter depiction shows the carbon with an empty 2p orbital and a full positive charge.

The result of carbonyl bond polarization, however it is depicted, is straightforward to predict. The carbon, because it is electron-poor, is an electrophile: it is a great target for attack by an electron-rich nucleophilic group. Because the oxygen end of the carbonyl double bond bears a partial negative charge, anything that can help to stabilize this charge by accepting some of the electron density will increase the bond's polarity and make the carbon more electrophilic. Very often a general acid group serves this purpose, donating a proton to the carbonyl oxygen.

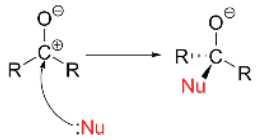


The same effect can also be achieved if a Lewis acid, such as a magnesium ion, is located near the carbonyl oxygen.

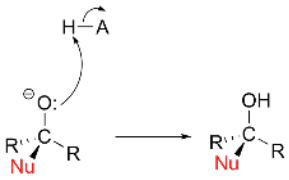
Unlike the situation in a nucleophilic substitution reaction, when a nucleophile attacks an aldehyde or ketone carbon there is no leaving group – the incoming nucleophile simply 'pushes' the electrons in the pi bond up to the oxygen.



Alternatively, if you start with the minor resonance contributor, you can picture this as an attack by a nucleophile on a carbocation.



After the carbonyl is attacked by the nucleophile, the negatively charged oxygen has the capacity to act as a nucleophile. However, most commonly the oxygen acts instead as a base, abstracting a proton from a nearby acid group in the solvent or enzyme active site.



This very common type of reaction is called a **nucleophilic addition**. In many biologically relevant examples of nucleophilic addition to carbonyls, the nucleophile is an alcohol oxygen or an amine nitrogen, or occasionally a thiol sulfur. In one very important reaction type known as an aldol reaction (which we will learn about in section 13.3) the nucleophile attacking the carbonyl is a resonance-stabilized carbanion. In this chapter, we will concentrate on reactions where the nucleophile is an oxygen or nitrogen.

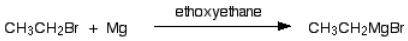
. . . on to the next section . . .

Organic Chemistry With a Biological Emphasis by Tim Soderberg (University of Minnesota, Morris)

12.3: How Aldehydes and Ketones React is shared under a not declared license and was authored, remixed, and/or curated by LibreTexts.

12.4: Gringard Reagents

A Grignard reagent has a formula RMgX where X is a halogen, and R is an alkyl or aryl (based on a benzene ring) group. For the purposes of this page, we shall take R to be an alkyl group (e.g., CH_3CH_2MgBr). Grignard reagents are made by adding the halogenoalkane to small bits of magnesium in a flask containing ethoxyethane (commonly called diethyl ether or just "ether"). The flask is fitted with a reflux condenser, and the mixture is warmed over a water bath for 20 - 30 minutes.

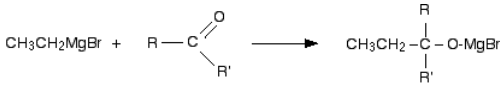


Everything must be perfectly dry because Grignard reagents react with water. Any reactions using the Grignard reagent are carried out with the mixture produced from this reaction; you cannot separate it out in any way. Any excess Grignard reagent must be quenched before disposal.

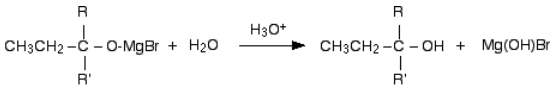
Reactions of Grignard reagents with aldehydes and ketones

These are reactions of the carbon-oxygen double bond, and so aldehydes and ketones react in exactly the same way - all that changes are the groups that happen to be attached to the carbon-oxygen double bond. It is much easier to understand what is going on by looking closely at the general case (using "R" groups rather than specific groups) - and then slotting in the various real groups as and when you need to. The "R" groups can be either hydrogen or alkyl in any combination.

In the first stage, the Grignard reagent adds across the carbon-oxygen double bond:



Dilute acid is then added to this to hydrolyse it.



An alcohol is formed. One of the key uses of Grignard reagents is the ability to make complicated alcohols easily. What sort of alcohol you get depends on the carbonyl compound you started with - in other words, what R and R' are.

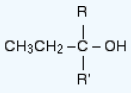
Example 12.4.1: Reaction with Methanal

Methanal is the simplest possible aldehyde with hydrogen as both R groups.



methanal

Assuming that you are starting with CH_3CH_2MgBr and using the general equation above, the alcohol you get always has the form:



Since both R groups are hydrogen atoms, the final product will be:

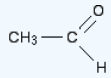


a primary alcohol

A primary alcohol is formed. A primary alcohol has only one alkyl group attached to the carbon atom with the -OH group on it. You could obviously get a different primary alcohol if you started from a different Grignard reagent.

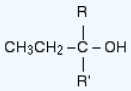
Example 12.4.2: Reaction with Aldehyde

The next biggest aldehyde is ethanal with one of the R groups is hydrogen and the other CH_3.



ethanal

Again, think about how that relates to the general case. The alcohol formed is:



So this time the final product has one CH_3 group and one hydrogen attached:



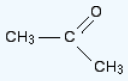
a secondary alcohol

A secondary alcohol has two alkyl groups (the same or different) attached to the carbon with the -OH group on it. You could change the nature of the final secondary alcohol by either:

- changing the nature of the Grignard reagent - which would change the CH_3CH_2 group into some other alkyl group;
- changing the nature of the aldehyde - which would change the CH_3 group into some other alkyl group.

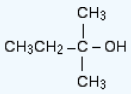
Example 12.4.3: Reactions with Propanone

Ketones have two alkyl groups attached to the carbon-oxygen double bond. The simplest one is propanone.



propanone

This time when you replace the R groups in the general formula for the alcohol produced you get a tertiary alcohol.



a tertiary alcohol

A tertiary alcohol has three alkyl groups attached to the carbon with the -OH attached. The alkyl groups can be any combination of same or different. You could ring the changes on the product by:

- changing the nature of the Grignard reagent - which would change the CH_3CH_2 group into some other alkyl group;
- changing the nature of the ketone - which would change the CH_3 groups into whatever other alkyl groups you choose to have in the original ketone.

Contributors

- Jim Clark (Chemguide.co.uk)

12.4: Gringard Reagents is shared under a not declared license and was authored, remixed, and/or curated by LibreTexts.

- **Reactions with Grignard Reagents** by Jim Clark is licensed CC BY-NC 4.0.

12.5: Reactions of Carbonyl Compounds with Hydride Ion

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:

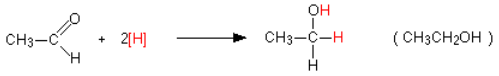


lithium tetrahydridoaluminate sodium tetrahydridoborate

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

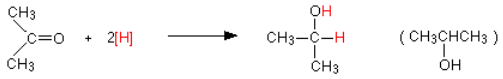
You get exactly the same organic product whether you use lithium tetrahydridoaluminate or sodium tetrahydridoborate. For example, with ethanal you get ethanol:



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:

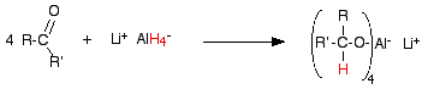


Reduction of a ketone leads to a secondary alcohol.

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.

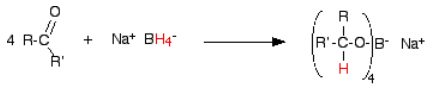


The alcohol formed can be recovered from the mixture by fractional distillation.

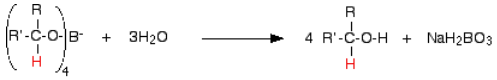
Using sodium tetrahydridoborate (sodium borohydride)

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

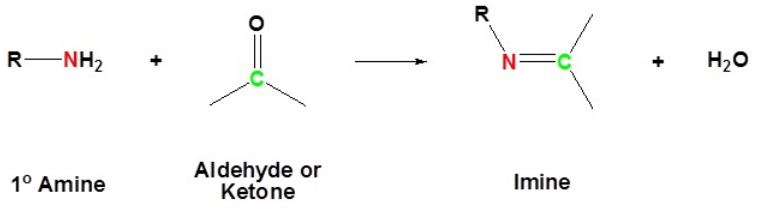
- Jim Clark (Chemguide.co.uk)

12.5: Reactions of Carbonyl Compounds with Hydride Ion is shared under a not declared license and was authored, remixed, and/or curated by LibreTexts.

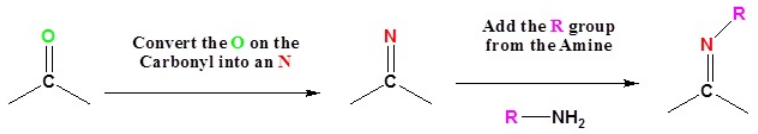
- **Reduction of Aldehydes and Ketones** by Jim Clark is licensed CC BY-NC 4.0.

12.6: Reactions of Aldehydes and Ketones with Amines

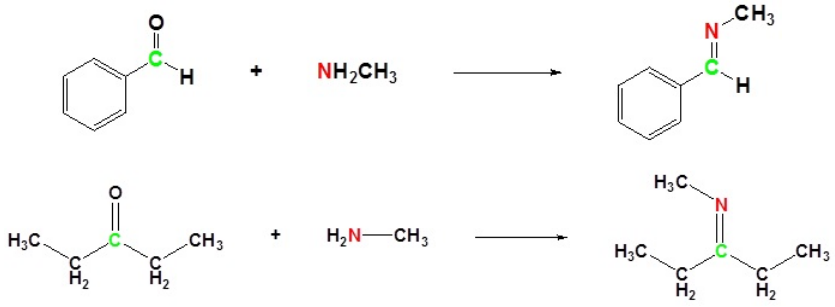
The reaction of aldehydes and ketones with ammonia or 1º-amines forms imine derivatives, also known as Schiff bases (compounds having a C=N function). Water is eliminated in the reaction, which is acid-catalyzed and reversible in the same sense as acetal formation. The pH for reactions which form imine compounds must be carefully controlled. The rate at which these imine compounds are formed is generally greatest near a pH of 5, and drops at higher and lower pH's. At high pH there will not be enough acid to protonate the OH in the intermediate to allow for removal as H_2O. At low pH most of the amine reactant will be tied up as its ammonium conjugate acid and will become non-nucleophilic.



Converting reactants to products simply

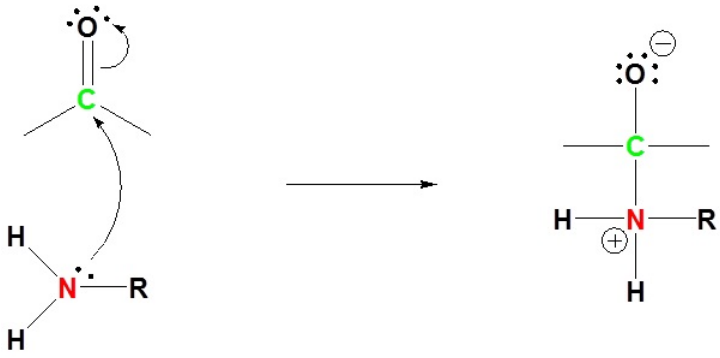


Examples of imine forming reactions

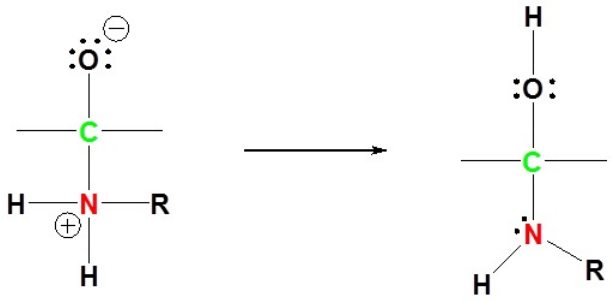


Mechanism of imine formation

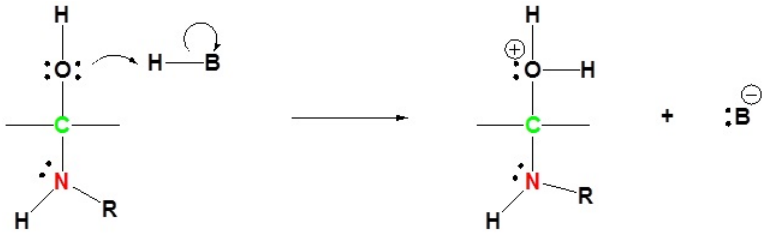
1) Nucleophilic attack



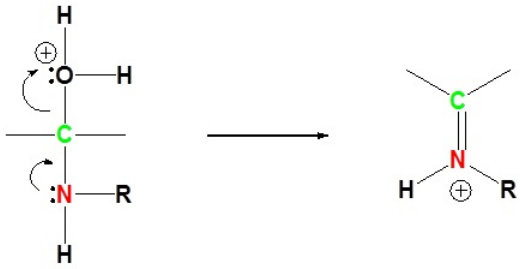
2) Proton transfer



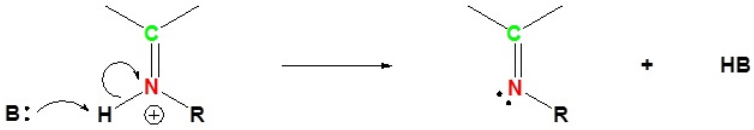
3) Protonation of OH



4) Removal of water

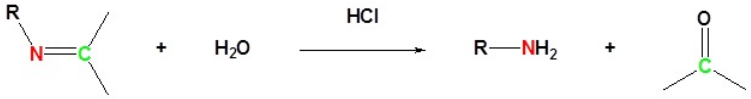


5) Deprotonation



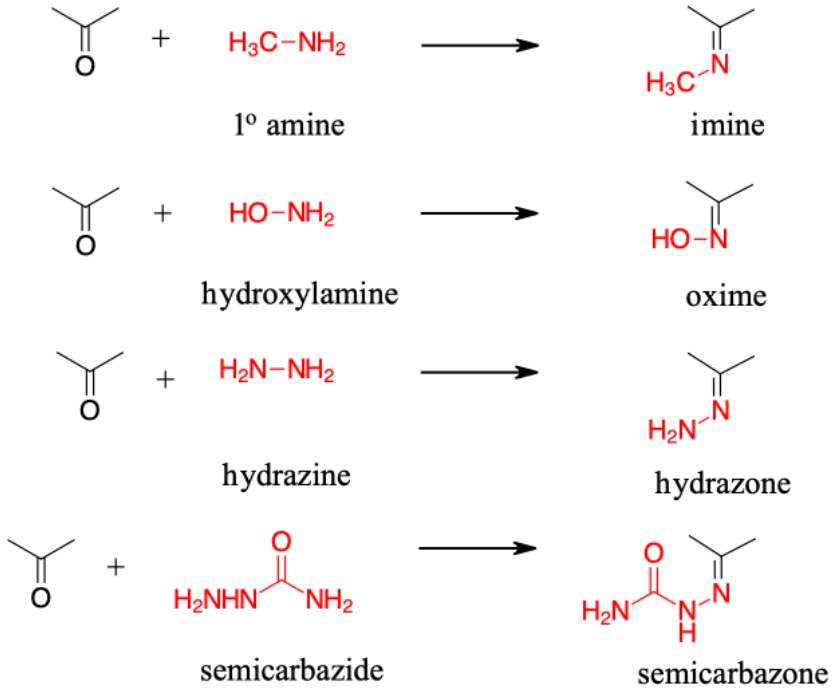
Reversibility of imine forming reactions

Imines can be hydrolyzed back to the corresponding primary amine under acidic conditons.



Reactions involving other reagents of the type Y-NH_2

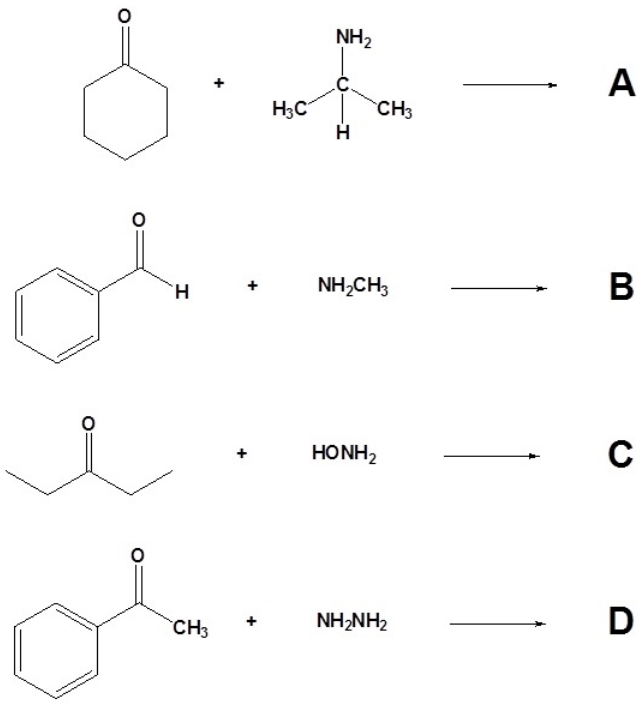
Imines are sometimes difficult to isolate and purify due to their sensitivity to hydrolysis. Consequently, other reagents of the type Y–NH_2 have been studied, and found to give stable products (R_2C=N–Y) useful in characterizing the aldehydes and ketones from which they are prepared. Some of these reagents are listed in the following table, together with the structures and names of their carbonyl reaction products. Hydrazones are used as part of the Wolff-Kishner reduction and will be discussed in more detail in another module.



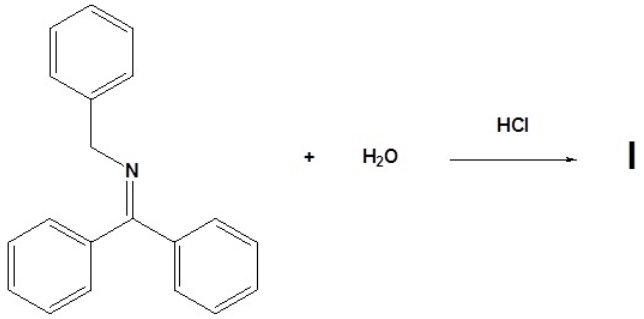
With the exception of unsubstituted hydrazones, these derivatives are easily prepared and are often crystalline solids - even when the parent aldehyde or ketone is a liquid. Since melting points can be determined more quickly and precisely than boiling points, derivatives such as these are useful for comparison and identification of carbonyl compounds. It should be noted that although semicarbazide has two amino groups ($–NH_2$) only one of them is a reactive amine. The other is amide-like and is deactivated by the adjacent carbonyl group.

Problems

1)Please draw the products of the following reactions.



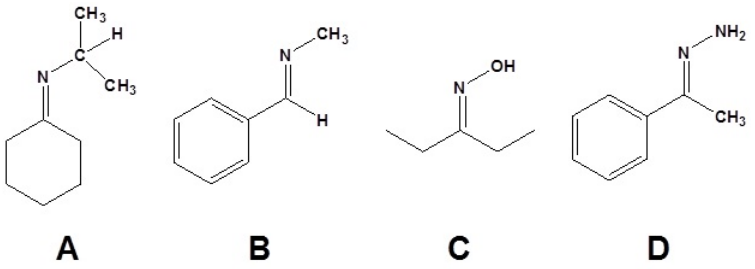
2) Please draw the structure of the reactant needed to produce the indicated product.



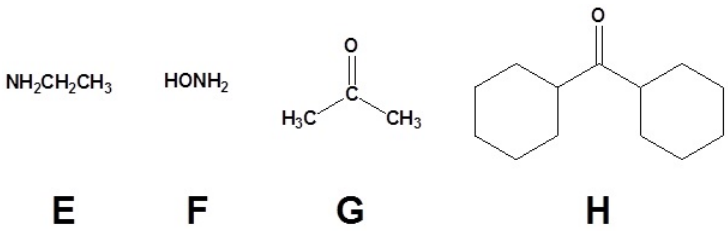
3) Please draw the products of the following reactions.

Answers

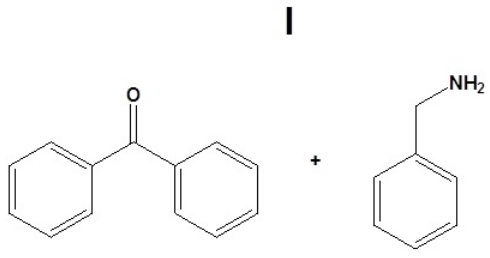
1)



2)



3)



Contributors

Prof. Steven Farmer (Sonoma State University)

William Reusch, Professor Emeritus (Michigan State U.), Virtual Textbook of Organic Chemistry

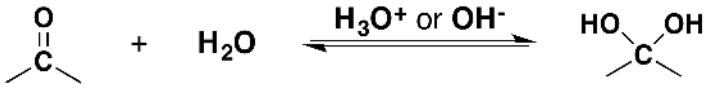
---

12.6: Reactions of Aldehydes and Ketones with Amines is shared under a not declared license and was authored, remixed, and/or curated by LibreTexts.

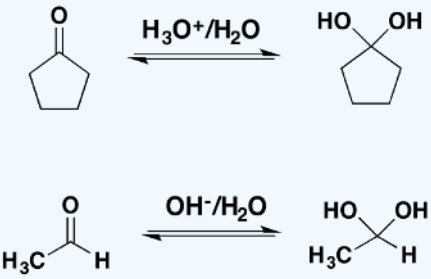
- **Reaction with Primary Amines to form Imines** is licensed CC BY-NC-SA 4.0.

12.7: Reactions of Aldehydes and Ketones with Water

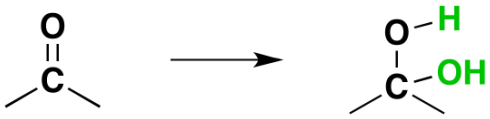
It has been demonstrated that water, in the presence of an acid or a base, adds rapidly to the carbonyl function of aldehydes and ketones establishing a reversible equilibrium with a **hydrate** (geminal-diol or *gem*-diol). The word germinal or gem comes from the Latin word for twin, *geminus*.



Example 1

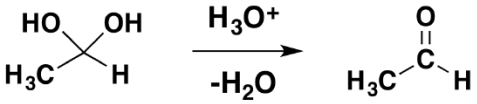


Going from Reactants to Products Simplified



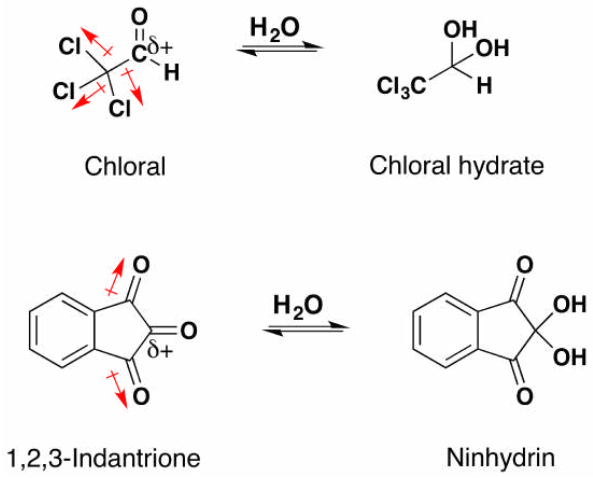
Reversibility of the Reaction

Isolation of *gem*-diols is difficult because the reaction is reversibly. Removal of the water during a reaction can cause the conversion of a gem-diol back to the corresponding carbonyl.



Factors Affecting the *Gem*-diol Equilibrium

In most cases the resulting *gem*-diol is unstable relative to the reactants and cannot be isolated. Exceptions to this rule exist, one being formaldehyde where the weaker pi-component of the carbonyl double bond, relative to other aldehydes or ketones, and the small size of the hydrogen substituents favor addition. Thus, a solution of formaldehyde in water (formalin) is almost exclusively the hydrate, or polymers of the hydrate. The addition of electron donating alkyl groups stabilized the partial positive charge on the carbonyl carbon and decreases the amount of *gem*-diol product at equilibrium. Because of this ketones tend to form less than 1% of the hydrate at equilibrium. Likewise, the addition of strong electron-withdrawing groups destabilizes the carbonyl and tends to form stable *gem*-diols. Two examples of this are chloral, and 1,2,3-indantrione. It should be noted that chloral hydrate is a sedative and has been added to alcoholic beverages to make a “Knock-out” drink also called a Mickey Finn. Also, ninhydrin is commonly used by forensic investigators to resolve finger prints.

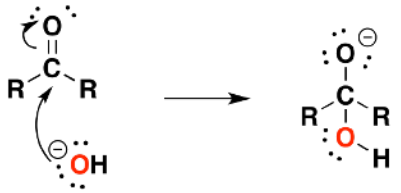


Mechanism of *Gem*-diol Formation

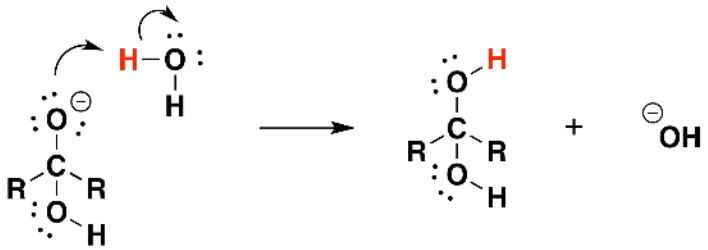
The mechanism is catalyzed by the addition of an acid or base. Note! This may speed up the reaction but is has not effect on the equilibriums discussed above. Basic conditions speed up the reaction because hydroxide is a better nucleophilic than water. Acidic conditions speed up the reaction because the protonated carbonyl is more electrophilic.

Under Basic conditions

1) Nucleophilic attack by hydroxide

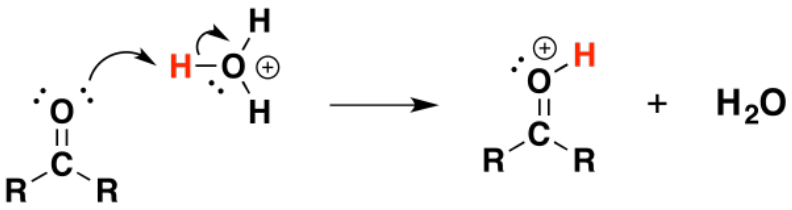


2) Protonation of the alkoxide

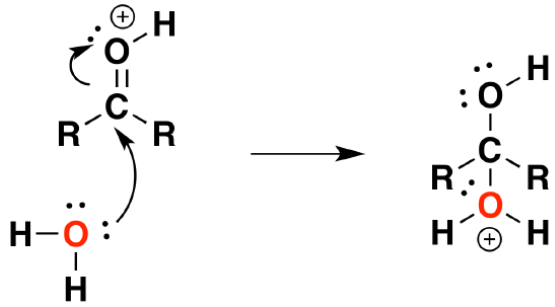


Under Acidic conditions

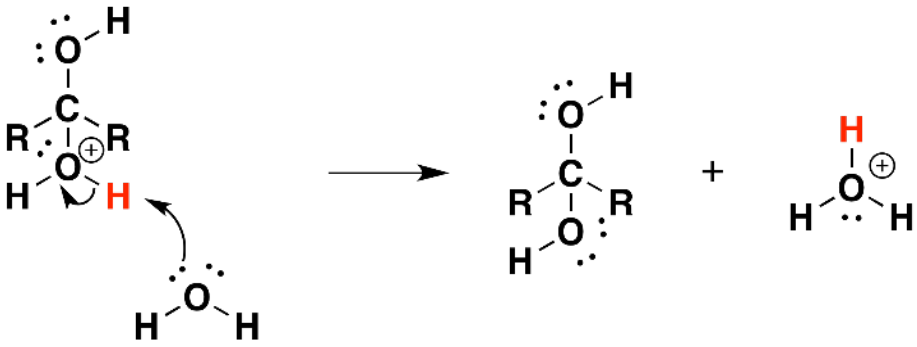
1) Protonation of the carbonyl



2) Nucleophilic attack by water

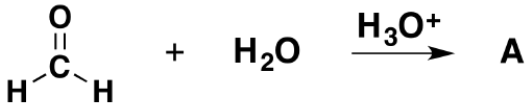


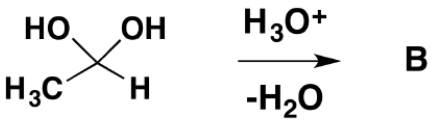
3) Deprotonation

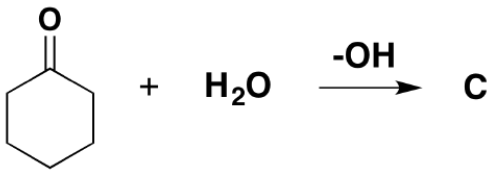


Problems

1) Draw the expected products of the following reactions.



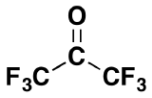




2) Of the following pairs of molecules which would you expect to form a larger percentage of *gem*-diol at equilibrium? Please explain your answer.

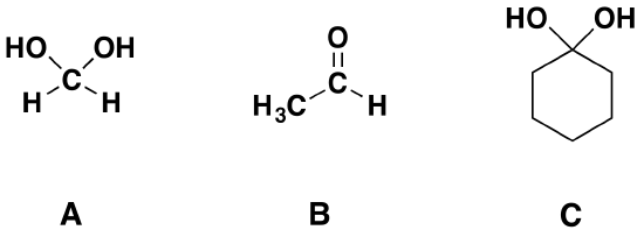


3) Would you expect the following molecule to form appreciable amount of *gem*-diol in water? Please explain your answer.



Answers

1)



A B C

2) The compound on the left would. Fluorine is more electronegative than bromine and would remove more electron density from the carbonyl carbon. This would destabilize the carbonyl allowing for more *gem*-diol to form.

3) Although ketones tend to not form *gem*-diols this compound exists almost entirely in the *gem*-diol form when placed in water. Ketones tend to not form *gem*-diols because of the stabilizing effect of the electron donating alkyl group. However, in this case the electron donating effects of alkyl group is dominated by the presence of six highly electronegative fluorines.

Contributors

- Prof. Steven Farmer (Sonoma State University)
- William Reusch, Professor Emeritus (Michigan State U.), Virtual Textbook of Organic Chemistry

12.7: Reactions of Aldehydes and Ketones with Water is shared under a not declared license and was authored, remixed, and/or curated by LibreTexts.

- **Addition of Water to form Hydrates (Gem-Diols)** is licensed CC BY-NC-SA 4.0.

12.8: Reactions of Aldehydes and Ketones with Alcohols

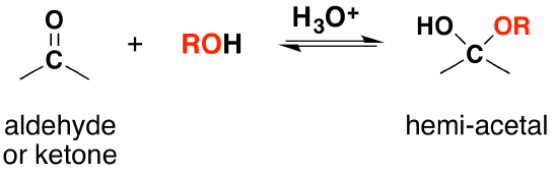
In this organic chemistry topic, we shall see how alcohols (R-OH) add to carbonyl groups. Carbonyl groups are characterized by a carbon-oxygen double bond. The two main functional groups that consist of this carbon-oxygen double bond are Aldehydes and Ketones.

Introduction

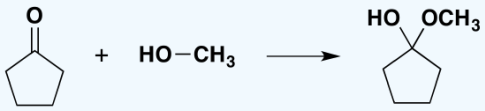
It has been demonstrated that water adds rapidly to the carbonyl function of aldehydes and ketones to form geminal-diol. In a similar reaction alcohols add reversibly to aldehydes and ketones to form hemiacetals (h*emi*, Greek, half). This reaction can continue by adding another alcohol to form an acetal. 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.

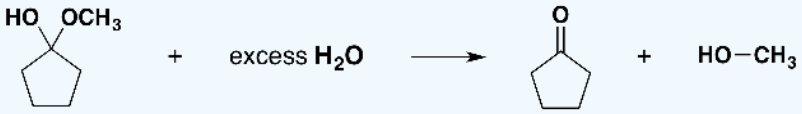
Formation of Hemiacetals



Example 1: Formation of Hemiacetals

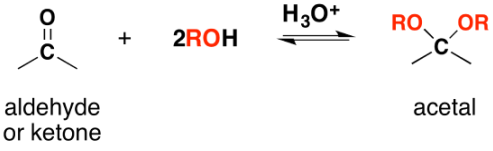


Example 2: Hemiacetal Reversibility

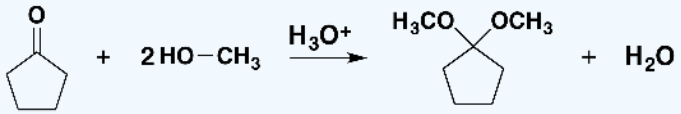


Formation of Acetals

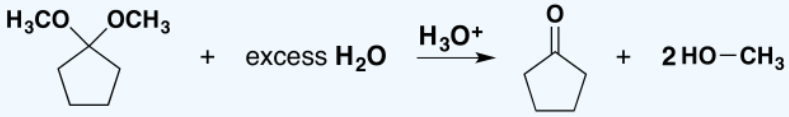
Acetals are geminal-diether derivatives of aldehydes or ketones, formed by reaction with two equivalents (or an excess amount) of an alcohol and elimination of water. Ketone derivatives of this kind were once called ketals, but modern usage has dropped that term. It is important to note that a hemiacetal is formed as an intermediate during the formation of an acetal.



Example 3: Formation of Acetals



Example 4: Acetal Reversibility



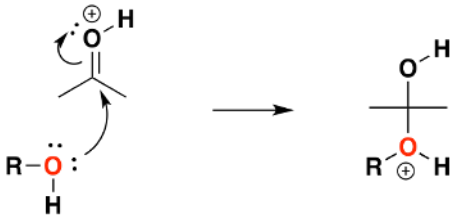
Mechanism for Hemiacetal and Acetal Formation

The mechanism shown here applies to both acetal and hemiacetal formation

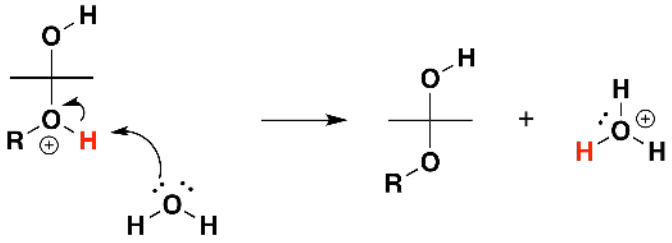
1) Protonation of the carbonyl



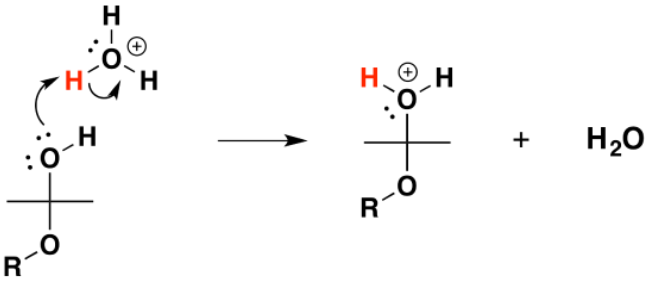
2) Nucleophilic attack by the alcohol



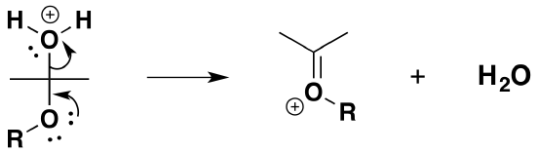
3) Deprotonation to form a hemiacetal



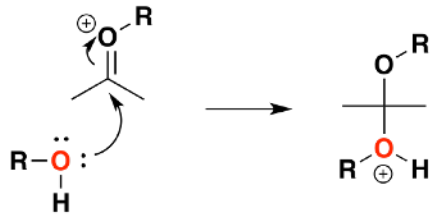
4) Protonation of the alcohol



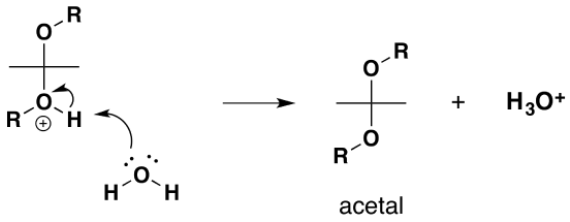
5) Removal of water



6) Nucleophilic attack by the alcohol

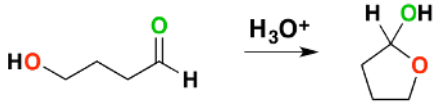


7) Deprotonation by water

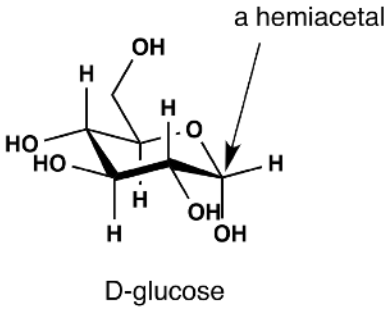


Formation of Cyclic Hemiacetal and Acetals

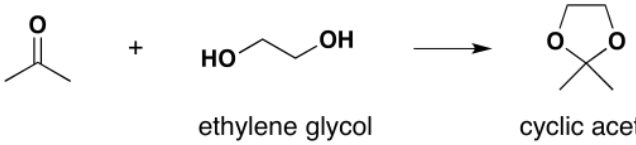
Molecules which have an alcohol and a carbonyl can undergo an intramolecular reaction to form a cyclic hemiacetal.



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.



Carbonyls reacting with diol produce a cyclic acetal. A common diol used to form cyclic acetals is ethylene glycol.

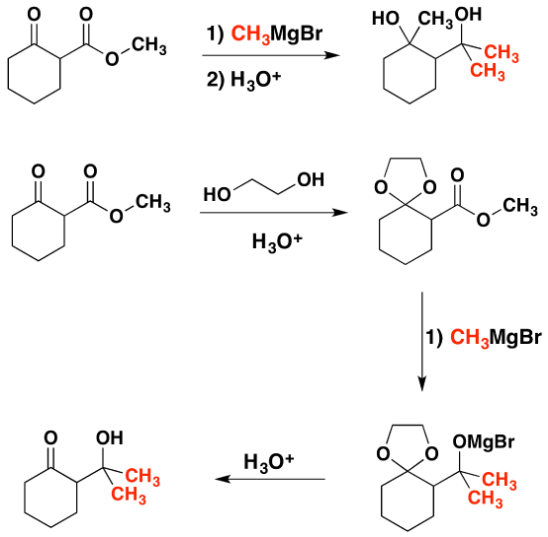


Acetals as Protecting Groups

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

- Prof. Steven Farmer (Sonoma State University)
- William Reusch, Professor Emeritus (Michigan State U.), Virtual Textbook of Organic Chemistry
- Ekram Alexander and Ahmed Rahim (UCD)

12.8: Reactions of Aldehydes and Ketones with Alcohols is shared under a not declared license and was authored, remixed, and/or curated by LibreTexts.

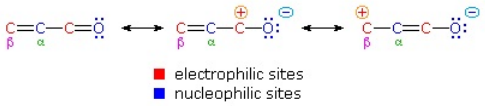
- **Addition of Alcohols to form Hemiacetals and Acetals** is licensed CC BY-NC-SA 4.0.

12.9: Nucleophilic Addition to α, β- Unsaturated Carboxylic Acid Derivatives

12.9: Nucleophilic Addition to α, β- Unsaturated Carboxylic Acid Derivatives is shared under a not declared license and was authored, remixed, and/or curated by LibreTexts.

12.10: Nucleophilic Addition to α, β- Unsaturated Carbonyl Compounds

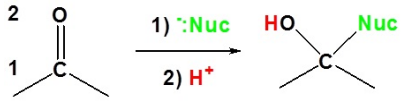
One of the largest and most diverse classes of reactions is composed of nucleophilic additions to a carbonyl group. Conjugation of a double bond to a carbonyl group transmits the electrophilic character of the carbonyl carbon to the beta-carbon of the double bond. These conjugated carbonyl are called enones or α, β unsaturated carbonyls. A resonance description of this transmission is shown below.



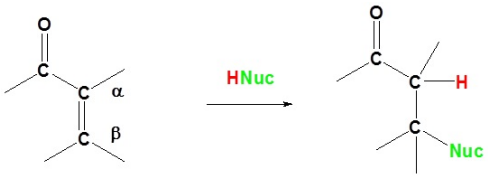
From this formula it should be clear that nucleophiles may attack either at the carbonyl carbon, as for any aldehyde, ketone or carboxylic acid derivative, or at the beta-carbon. These two modes of reaction are referred to as 1,2-addition and 1,4-addition respectively. A 1,4-addition is also called a conjugate addition.

Basic reaction of 1,2 addition

Here the nucleophile adds to the carbon which is in the one position. The hydrogen adds to the oxygen which is in the two position.



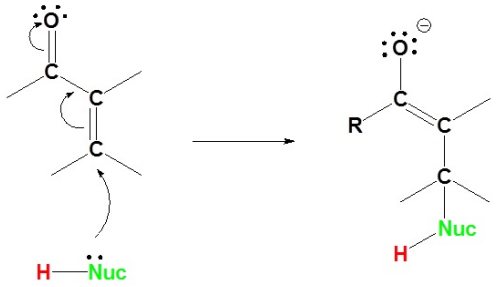
Basic reaction of 1,4 addition



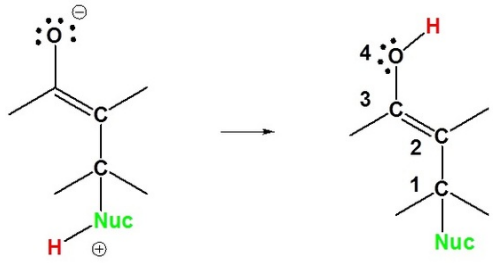
In 1,4 addition the Nucleophile is added to the carbon β to the carbonyl while the hydrogen is added to the carbon α to the carbonyl.

Mechanism for 1,4 addition

1) Nucleophilic attack on the carbon β to the carbonyl

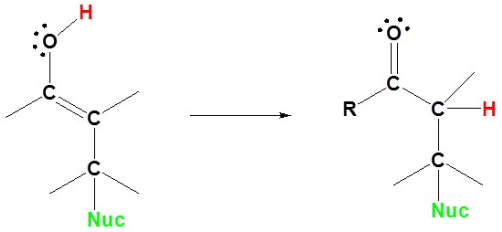


2) Proton Transfer

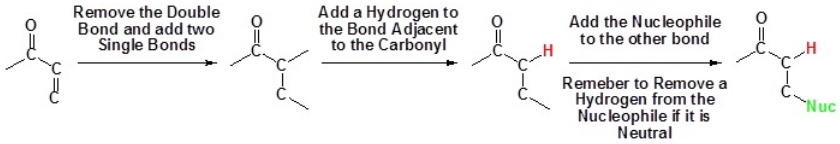


Here we can see why this addition is called 1,4. The nucleophile bonds to the carbon in the one position and the hydrogen adds to the oxygen in the four position.

3) Tautomerization



Going from reactant to products simplified



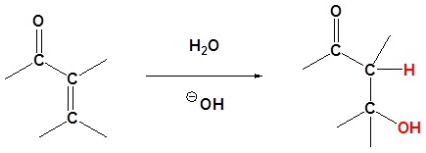
1,2 vs. 1,4 addition

Whether 1,2 or 1,4-addition occurs depends on multiple variables but mostly it is determined by the nature of the nucleophile. During the addition of a nucleophile there is a competition between 1,2 and 1,4 addition products. If the nucleophile is a strong base, such as Grignard reagents, both the 1,2 and 1,4 reactions are irreversible and therefor are under kinetic control. Since 1,2-additions to the carbonyl group are fast, we would expect to find a predominance of 1,2-products from these reactions.

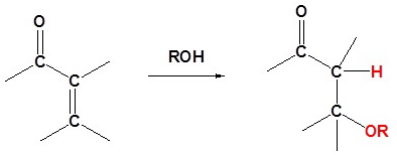
If the nucleophile is a weak base, such as alcohols or amines, then the 1,2 addition is usually reversible. This means the competition between 1,2 and 1,4 addition is under thermodynamic control. In this case 1,4-addition dominates because the stable carbonyl group is retained.

Nucleophiles which add 1,4 to α, β unsaturated carbonyls

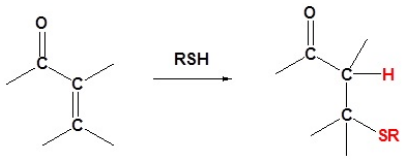
Water



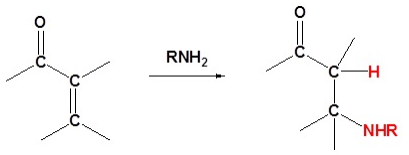
Alcohols



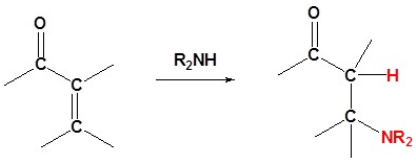
Thiols



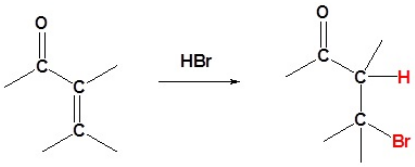
1° Amines



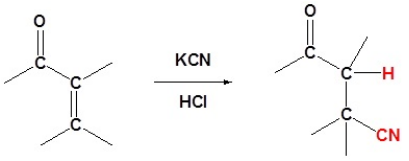
2° Amines



HBr



Cyanides



Gilman Reagents

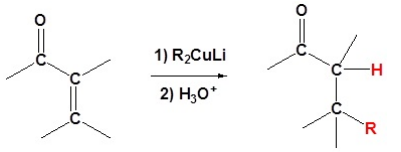
Another important reaction exhibited by organometallic reagents is metal exchange. Organolithium reagents react with cuprous iodide to give a lithium dimethylcopper reagent, which is referred to as a Gilman reagent. Gilman reagents are a source of carbanion like nucleophiles similar to Grignard and Organo lithium reagents. However, the reactivity of organocuprate reagents is slightly different and this difference will be exploited in different situations. In the case of α, β unsaturated carbonyls organocuprate reagents allow for an 1,4 addition of an alkyl group. As we will see later Grignard and Organolithium reagents add alkyl groups 1,2 to α, β unsaturated carbonyls

Organocuprate reagents are made from the reaction of organolithium reagents and CuI

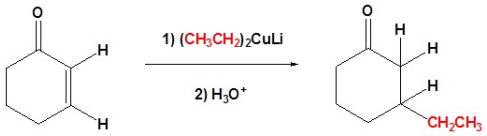
$$2RLi + CuI \rightarrow R_2CuLi + LiI \tag{12.10.1}$$

This acts as a source of R:$^-$

$$2CH_3Li + CuI \rightarrow (CH_3)_2CuLi + LiI \tag{12.10.2}$$

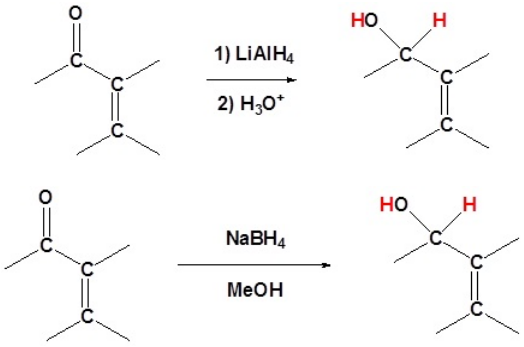


Example

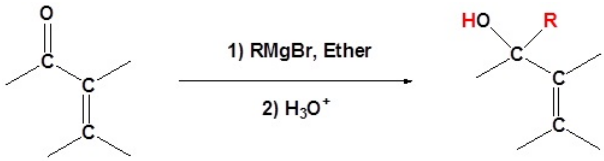


Nucleophiles which add 1,2 to α, β unsaturated carbonyls

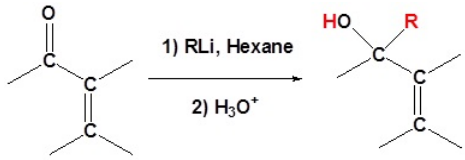
Metal Hydrides



Grignard Reagents



Organolithium Reagents



Contributors

Prof. Steven Farmer (Sonoma State University)

William Reusch, Professor Emeritus (Michigan State U.), Virtual Textbook of Organic Chemistry

---

12.10: Nucleophilic Addition to α, β- Unsaturated Carbonyl Compounds is shared under a not declared license and was authored, remixed, and/or curated by LibreTexts.

- **Conjugate Addition Reactions** is licensed CC BY-NC-SA 4.0.

12.11: Protecting Groups

12.11: Protecting Groups is shared under a not declared license and was authored, remixed, and/or curated by LibreTexts.

12.12: Addition of Sulfur Nucleophiles

12.12: Addition of Sulfur Nucleophiles is shared under a not declared license and was authored, remixed, and/or curated by LibreTexts.

12.13: The Wittig Reaction Forms an Alkene

Organophosphorus ylides react with aldehydes or ketones to give substituted alkenes in a transformation called the Wittig reaction. This reaction is named for George Wittig who was awarded the Nobel prize for this work in 1979. A principal advantage of alkene synthesis by the Wittig reaction is that the location of the double bond is absolutely fixed, in contrast to the mixtures often produced by alcohol dehydration.

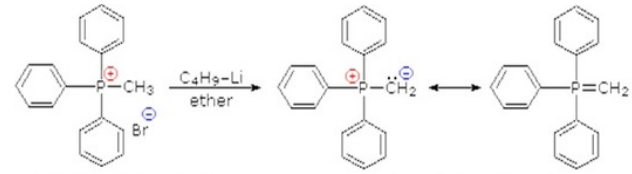
Preparation of Phosphorus Ylides

It has been noted that dipolar phosphorus compounds are stabilized by p-d bonding. This bonding stabilization extends to carbanions adjacent to phosphonium centers, and the zwitterionic conjugate bases derived from such cations are known as ylides. An **ylide** is defined as a compound with opposite charges on adjacent atoms both of which have complete octets. For the Wittig reaction discussed below an organophosphorus ylide, also called Wittig reagents, will be used. The ability of phosphorus to hold more than eight valence electrons allows for a resonance structure to be drawn forming a double bonded structure.



An Ylide

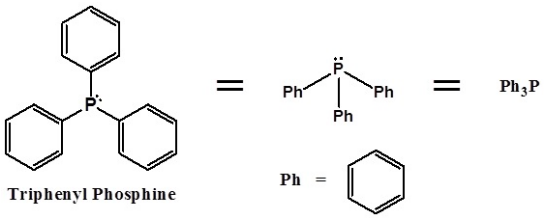
The stabilization of the carbanion provided by the phosphorus causes an increase in acidity (pKa ~35). Very strong bases, such as butyl lithium, are required for complete formation of ylides.



The ylides shown here are all strong bases. Like other strongly basic organic reagents, they are protonated by water and alcohols, and are sensitive to oxygen. Water decomposes phosphorous ylides to hydrocarbons and phosphine oxides, as shown.

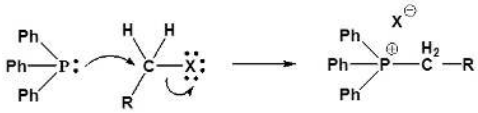
$$R_3P{=}CR'_2 \;+\; H_2O \longrightarrow R_3P{=}O \;+\; R'_2CH_2$$

Although many ylides are commercially available it is often necessary to create them synthetically. Ylides can be synthesized from an alkyl halide and a trialkyl phosphine. Typically triphenyl phosphine is used to synthesize ylides. Because a S_N2 reaction is used in the ylide synthesis methyl and primary halides perform the best. Secondary halides can also be used but the yields are generally lower. This should be considered when planning out a synthesis which involves a synthesized Wittig reagent.

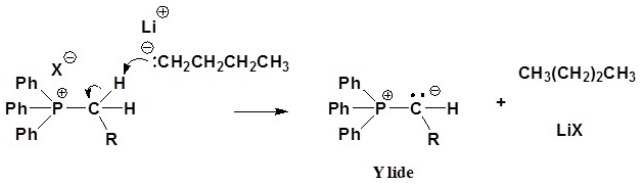


Mechanism of ylide formation

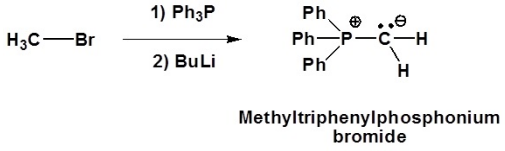
1) S_N2 reaction



2) Deprotonation

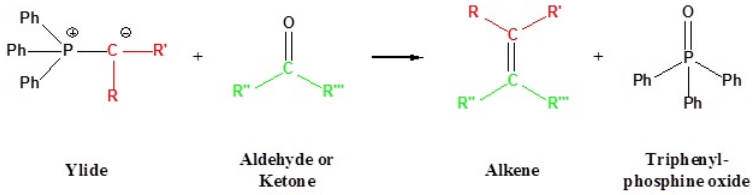


Examples of ylide formation

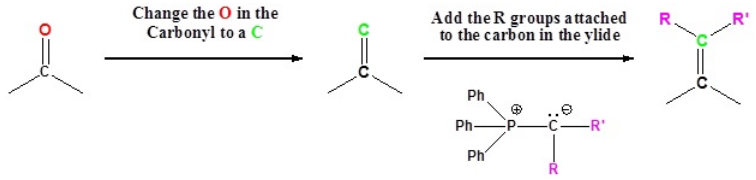


The Wittig Reaction

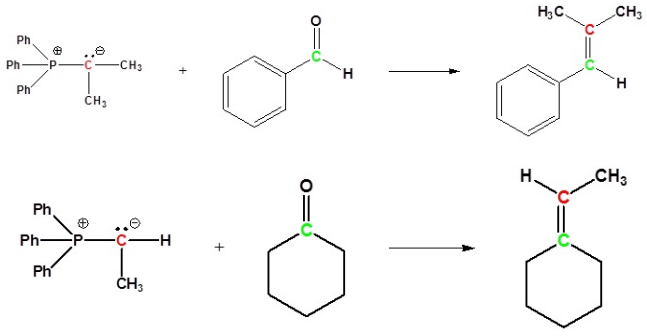
The most important use of ylides in synthesis comes from their reactions with aldehydes and ketones, which are initiated in every case by a covalent bonding of the nucleophilic alpha-carbon to the electrophilic carbonyl carbon. Ylides react to give substituted alkenes in a transformation called the Wittig reaction. This reaction is named for George Wittig who was awarded the Nobel prize for this work in 1979. A principal advantage of alkene synthesis by the Wittig reaction is that the location of the double bond is absolutely fixed, in contrast to the mixtures often produced by alcohol dehydration.



Going from reactants to products simplified



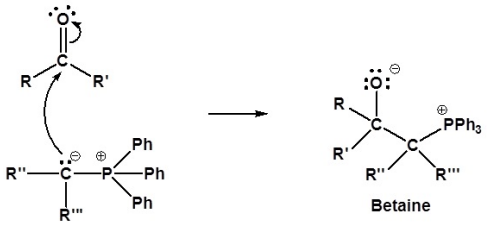
Examples of the Wittig reaction



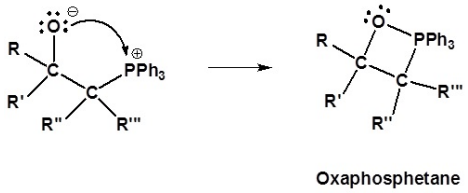
Mechanism of the Wittig reaction

Following the initial carbon-carbon bond formation, two intermediates have been identified for the Wittig reaction, a dipolar charge-separated species called a betaine and a four-membered heterocyclic structure referred to as an oxaphosphatane. Cleavage of the oxaphosphatane to alkene and phosphine oxide products is exothermic and irreversible.

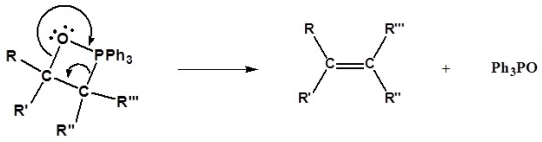
1) Nucleophillic attack on the carbonyl



2) Formation of a 4 membered ring

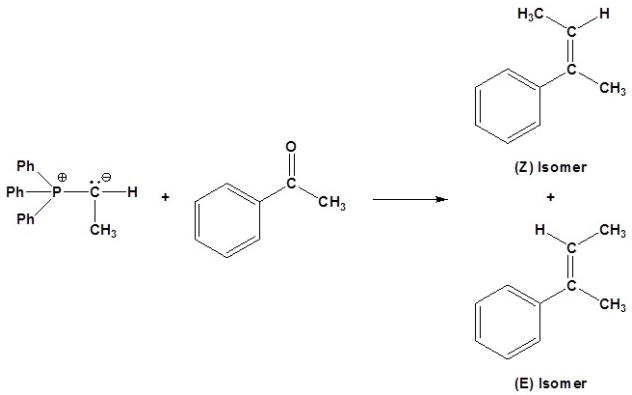


3) Formation of the alkene



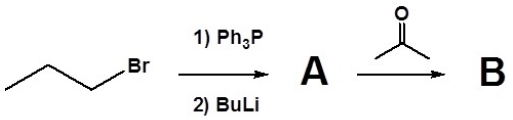
Limitation of the Wittig reaction

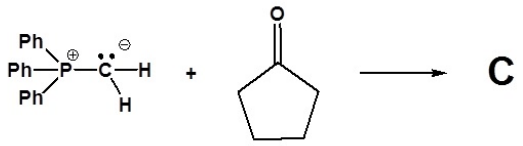
If possible both E and Z isomer of the double bond will be formed. This should be considered when planning a synthesis involving a Wittig Reaction.

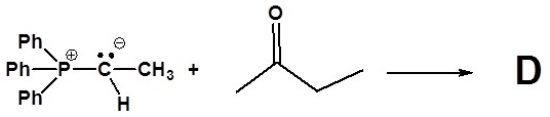


Problems

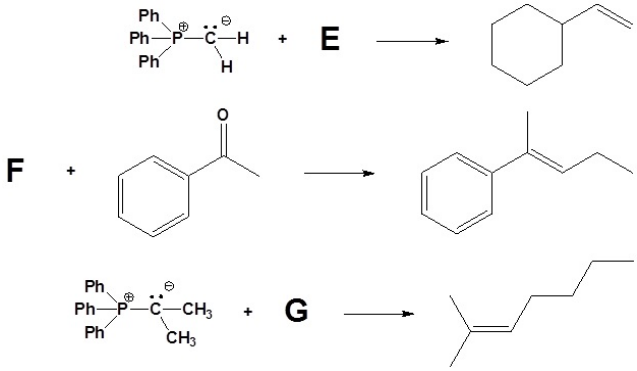
1) Please write the product of the following reactions.







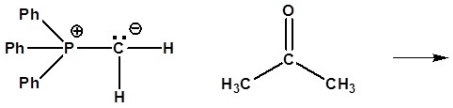
2) Please indicate the starting material required to produce the product.



3) Please draw the structure of the oxaphosphetane which is made during the mechanism of the reaction given that produces product **C**.

4) Please draw the structure of the betaine which is made during the mechanism of the reaction given that produces product **D**.

5) Please give a detailed mechanism and the final product of this reaction

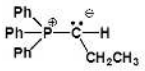


6) It has been shown that reacting and epoxide with triphenylphosphine forms an alkene. Please propose a mechanism for this reaction. Review the section on epoxide reactions if you need help.

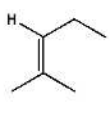


Answers

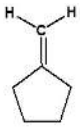
1)



A



B

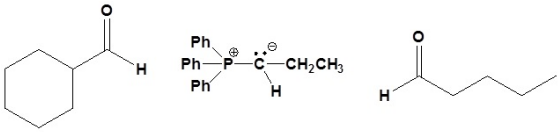


C



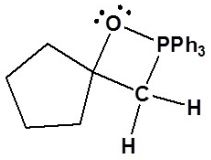
D

2)

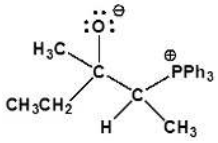


E F G

3)

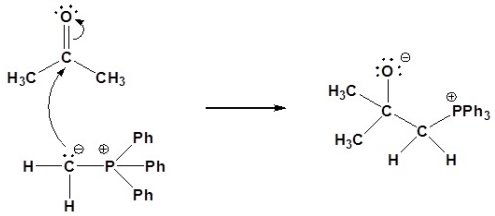


4)

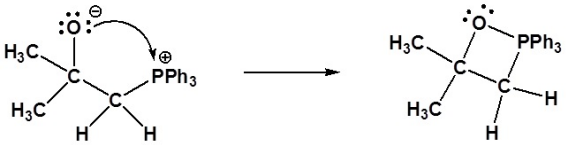


5)

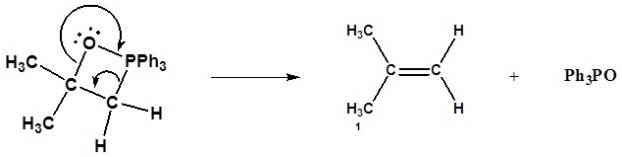
Nucleophillic attack on the carbonyl



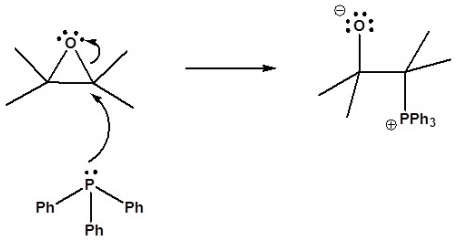
Formation of a 4 membered ring



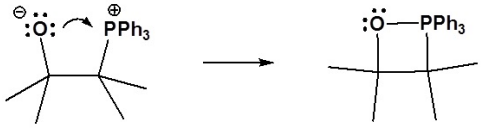
Formation of the alkene



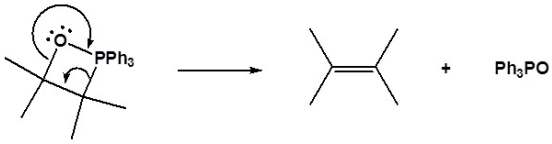
6) Nucleophillic attack on the epoxide



Formation of a 4 membered ring



Formation of the alkene



Contributors

Prof. Steven Farmer (Sonoma State University)

William Reusch, Professor Emeritus (Michigan State U.), Virtual Textbook of Organic Chemistry

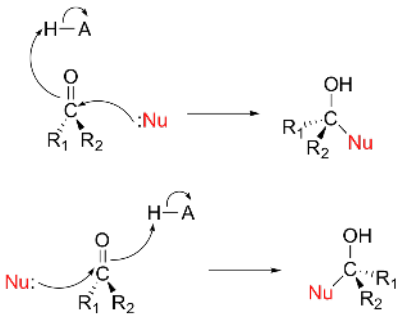
---

12.13: The Wittig Reaction Forms an Alkene is shared under a not declared license and was authored, remixed, and/or curated by LibreTexts.

- **The Wittig Reaction** is licensed CC BY-NC-SA 4.0.

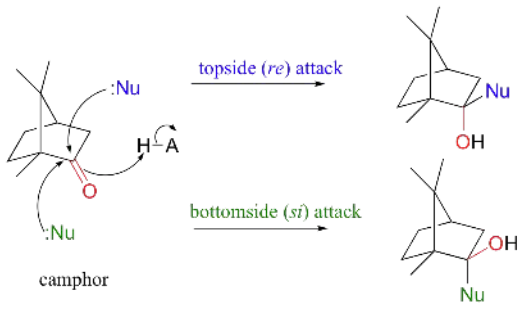
12.14: Stereochemistry of Nucleophilic Addition Reactions- Re and Si Faces

Notice that in the course of the nucleophilic addition pictured above, the hybridization of the carbonyl carbon changes from sp^2 to sp^3, meaning that the bond geometry changes from trigonal planar to tetrahedral. It is also important to note that if the starting carbonyl is asymmetric (in other words, if the two R groups are not equivalent), then a new stereocenter has been created. The configuration of the new stereocenter depends upon which side of the carbonyl plane the nucleophile attacks from.



If the reaction is catalyzed by an enzyme, the stereochemistry of addition is tightly controlled, and leads to one specific stereoisomer - this is because the nucleophilic and electrophilic substrates are bound in a specific positions within the active site, so that attack must occur specifically from one side. If, however, the reaction occurs uncatalyzed in solution, then either side of the carbonyl is equally likely to be attacked, and the result will be a 50:50 racemic mixture.

This is the rule for most nonenzymatic reactions, but as with most rules, there are exceptions. If, for example, the geometry of the carbonyl-containing molecule is constrained in such a way that approach by the nucleophile is less hindered from one side, a 50:50 racemic mixture will not necessarily result. Consider camphor, the distinctive-smelling compound found in many cosmetics and skin creams.



Upon inspection it is clear that topside attack and bottom side attack by a nucleophile are nonequivalent in terms of steric hindrance. A relatively simple experiment shows that, when the incoming nucleophile is a hydride ion from the common synthetic reducing agent sodium borohydride (a reaction type we will study in a later chapter), the product of bottom side attack predominates by a ratio of about 6 to 1 (see section 16.4D for more details on this experiment). We can infer from this result that approach from the bottom (*si*) face of the carbonyl in camphor is less hindered.

. . . on to the next section . . .

Organic Chemistry With a Biological Emphasis by Tim Soderberg (University of Minnesota, Morris)

12.14: Stereochemistry of Nucleophilic Addition Reactions- Re and Si Faces is shared under a not declared license and was authored, remixed, and/or curated by LibreTexts.

12.15: Designing a Synthesis VI- Disconnections, Synthons, and Synthetic Equivalents

12.15: Designing a Synthesis VI- Disconnections, Synthons, and Synthetic Equivalents is shared under a not declared license and was authored, remixed, and/or curated by LibreTexts.

12.16: Enzyme-Catalyzed Additions to α, β- Unsaturated Carbonyl Compounds

12.16: Enzyme-Catalyzed Additions to α, β- Unsaturated Carbonyl Compounds is shared under a not declared license and was authored, remixed, and/or curated by LibreTexts.

CHAPTER OVERVIEW

13: Carbonyl Compounds III- Reactions at the α- Carbon



Essential Organic Chemistry: 2nd Ed.
Bruice

Homework Problems
Homework Solutions

I II III IV V VI VII VIII IX X XI XII XIII XIV XV XVI XVII XVIII XIX XX XXI

Template:HideTOC

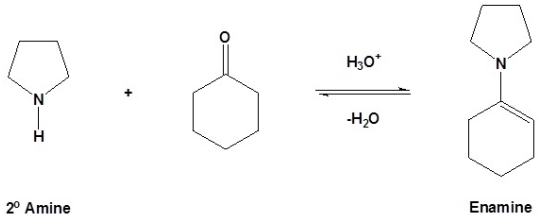
13.1: Alkylation and Acylation of the α-Carbon Using an Enamine Intermediate
13.2: Alkylation of the β-Carbon- The Michael Reaction
13.3: An Aldol Addition Forms β-Hydroxaldehydes or β-Hydroxyketones
13.4: Dehydration of Aldol Addition Products Form α, β-Unsaturated Aldehydes and Ketones
13.5: The Crossed Aldol Addition
13.6: A Claisen Condensation Forms a β-Keto Ester
13.7: Other Crossen Condensations
13.8: Intramolecular Condensation and Addition Reactions
13.9: The Robinson Annulation
13.10: Carboxylic Acids with a Carbonyl Group at the 3-Position can be Decarboxylated
13.11: The Acidity of an α- Hydrogen
13.12: The Malonic Ester Synthesis- A Way to Synthesize a Carboxylic Acid
13.13: The Acetoacetic Ester Synthesis- A Way to Synthesize a Methyl Ketone
13.14: Designing a Synthesis VII- Making New Carbon-Carbon Bonds
13.15: Reactions at the α-Carbon in Biological Systems
13.16: Keto-Enol Tautomers
13.17: Keto-Enol Interconversion
13.18: How Enolate Ions and Enols React
13.19: Halogenation of the α- Carbon and Aldehydes and Ketones
13.20: Halogenation of the α- Carbon of Carboxylic Acids- The Hell-Volhard-Zelinski Reaction
13.21: α- Halogenated Carbonyl Compounds Are Useful in Synthesis
13.22: Using LDA to Form an Enolate Ion
13.23: Alkylating the α-Carbon of Carbonyl Compounds

13: Carbonyl Compounds III- Reactions at the α- Carbon is shared under a not declared license and was authored, remixed, and/or curated by LibreTexts.

13.1: Alkylation and Acylation of the α-Carbon Using an Enamine Intermediate

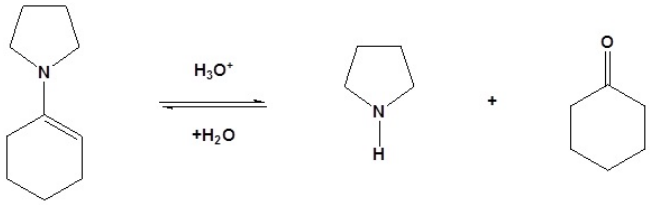
As previously seen, aldehydes and ketones react with 2° amines to reversibly form enamines.

Example



2° Amine Enamine

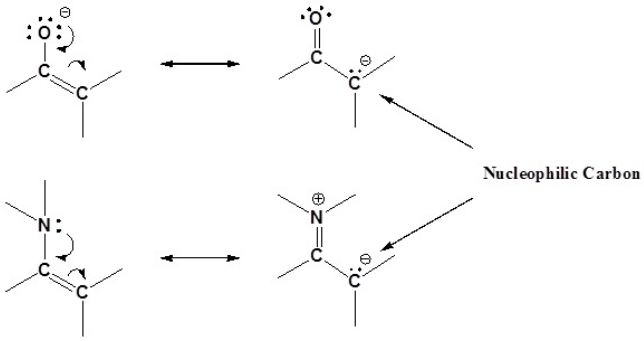
Reversible



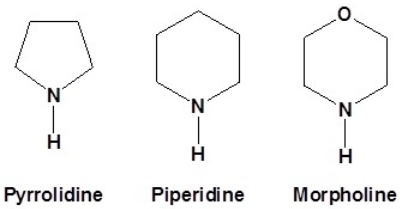
Enamines act as nucleophiles in a fashion similar to enolates. Because of this enamines can be used as synthetic equivalents as enolates in many reactions. This process requires a three steps:

1. Formation of the enamine,
2. Reaction with an eletrophile to form an iminium salt,
3. Hydrolysis of the iminium salt to reform the aldehyde or ketone.

Some of the advantages of using an enamine over and enolate are enamines are neutral, easier to prepare, and usually prevent the overreaction problems plagued by enolates. These reactions are generally known as the Stork enamine reaction after Gilbert Stork of Columbia University who originated the work.



Typically we use the following 2° amines for enamine reactions

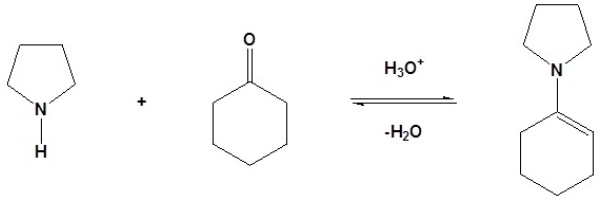


Pyrrolidine Piperidine Morpholine

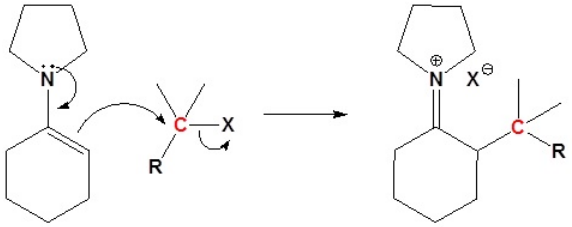
Alkylation of an Enamine

Enamined undergo an S_N2 reaction with reactive alkyl halides to give the iminium salt. The iminium salt can be hydrolyzed back into the carbonyl.

Step 1: Formation of an enamine

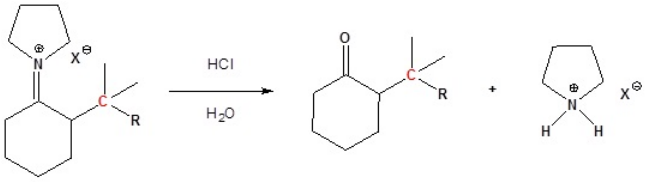


Step 2: S_N2 Alkylation

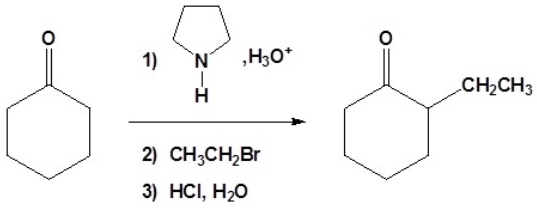


Iminium Salt

Step 3: Reform the carbonyl by hydrolysis



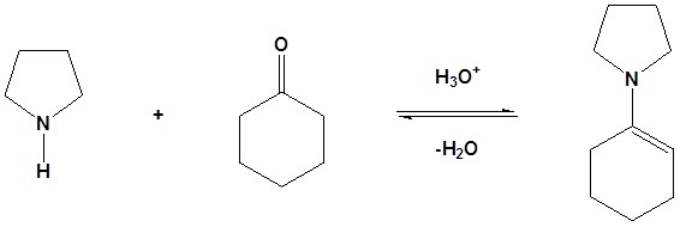
All three steps together:



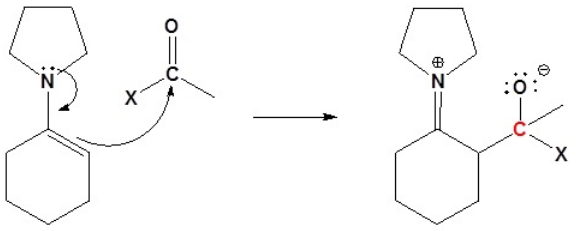
Acylation of Enamines

Enamine can react with acid halides to form β-dicarbonyls

1) Formation of the enamine

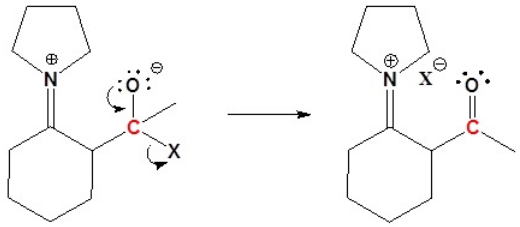


2) Nucleophilic attack

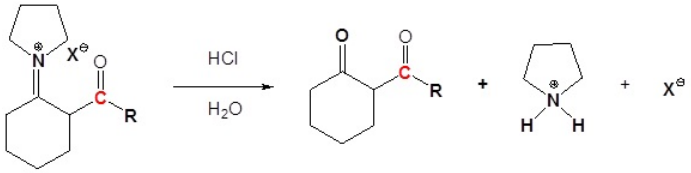


Iminium Salt

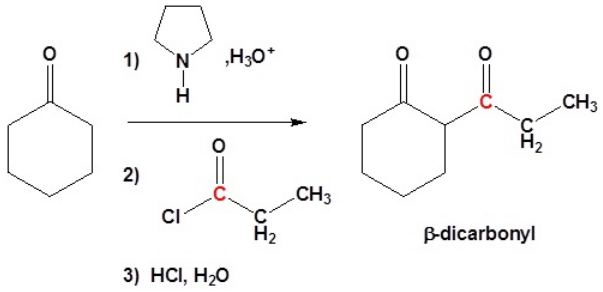
3) Leaving group removal



4) Reform the carbonyl by hydrolysis



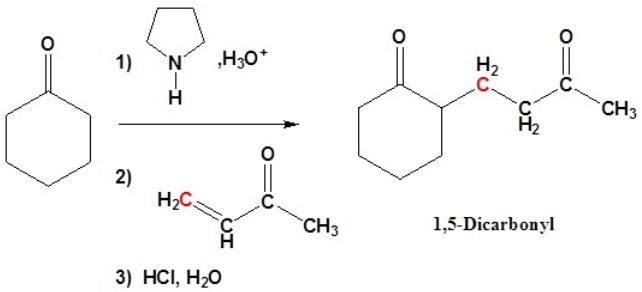
All three steps together:



β-dicarbonyl

Michael Addition using Enamines

Enamines, like other weak bases, add 1,4 to enones. The end product is a 1,5 dicarbonyl compound.



1,5-Dicarbonyl

Contributors

- Prof. Steven Farmer (Sonoma State University)

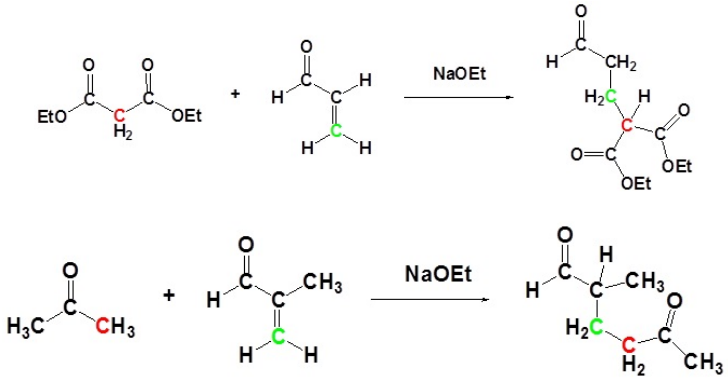
13.1: Alkylation and Acylation of the α-Carbon Using an Enamine Intermediate is shared under a not declared license and was authored, remixed, and/or curated by LibreTexts.

- **Enamine Reactions** is licensed CC BY-NC-SA 4.0.

13.2: Alkylation of the β-Carbon- The Michael Reaction

Enolates undergo 1,4 addition to α, β-unsaturated carbonyl compounds is a process called a Michael addition. The reaction is named after American chemist Arthur Michael (1853-1942).

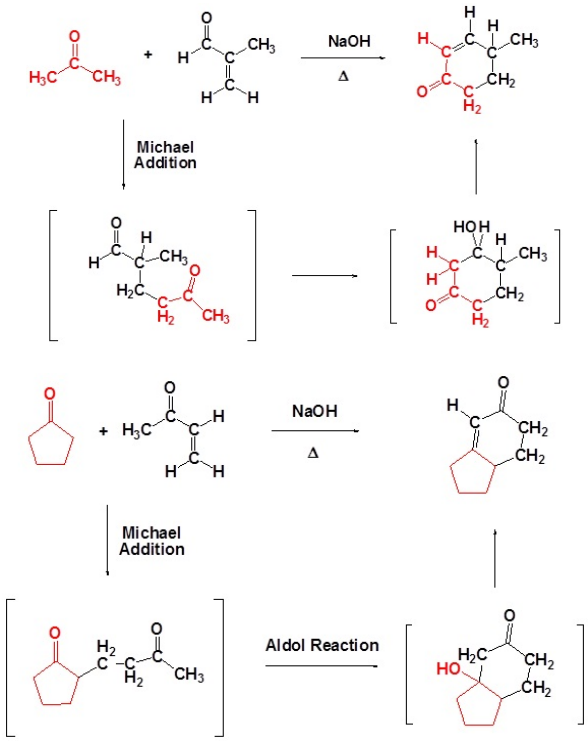
Examples of Michael Additions



Robinson Annulation

Many times the product of a Michael addition produces a dicarbonyl which can then undergo an intramolecular aldol reaction. These two processes together in one reaction creates two new carbon-carbon bonds and also creates a ring. Ring-forming reactions are called annulations after the Latin work for ring annulus. The reaction is named after English chemist Sir Robert Robinson (1886-1975) who developed it. He received the Nobel prize in chemistry in 1947. Remember that during annulations five and six membered rings are preferred.

Examples of Robinson Annulations



Contributors

- Prof. Steven Farmer (Sonoma State University)

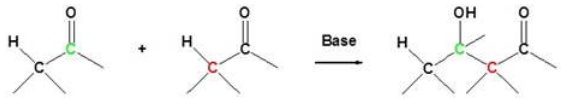
13.2: Alkylation of the β-Carbon- The Michael Reaction is shared under a not declared license and was authored, remixed, and/or curated by LibreTexts.

- **Michael Additions & Robinson Annulation** is licensed CC BY-NC-SA 4.0.

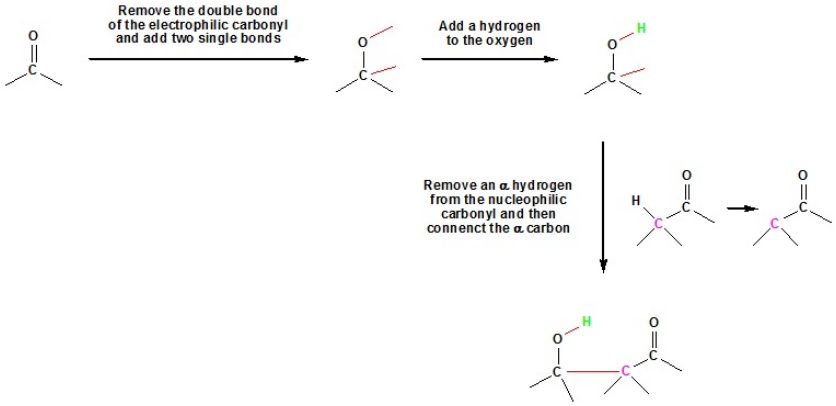
13.3: An Aldol Addition Forms β-Hydroxaldehydes or β-Hydroxyketones

A useful carbon-carbon bond-forming reaction known as the **Aldol Reaction** is yet another example of electrophilic substitution at the alpha carbon in enolate anions. The fundamental transformation in this reaction is a dimerization of an aldehyde (or ketone) to a beta-hydroxy aldehyde (or ketone) by alpha C–H addition of one reactant molecule to the carbonyl group of a second reactant molecule. Due to the carbanion like nature of enolates they can add to carbonyls in a similar manner as Grignard reagents. For this reaction to occur at least one of the reactants must have α hydrogens.

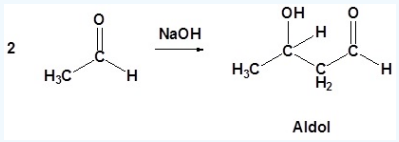
General Aldol reaction

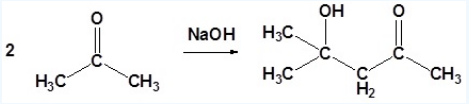


Going from reactants to products simply



Example 1: Aldol Reactions

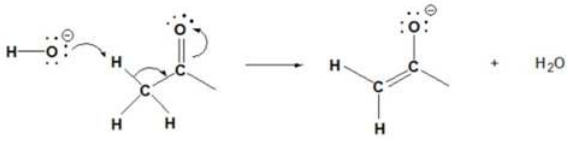




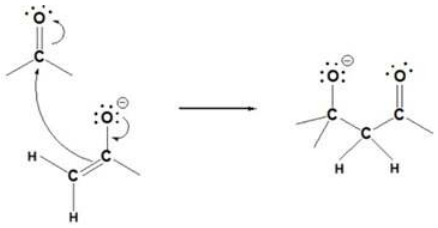
Aldol Reaction Mechanism

A three step mechanism:

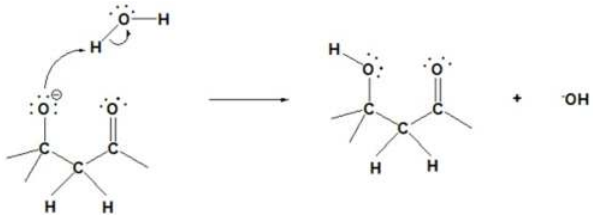
Step 1: Enolate formation



Step 2: Nucleophilic attack by the enolate



Step 3: Protonation



Aldol Condensation: the dehydration of Aldol products to synthesize α, β unsaturated carbonyl (enones)

The products of aldol reactions often undergo a subsequent elimination of water, made up of an alpha-hydrogen and the beta-hydroxyl group. The product of this ***β*-elimination** reaction is an α,β-unsaturated aldehyde or ketone. Base-catalyzed elimination occurs with heating. The additional stability provided by the conjugated carbonyl system of the product makes some aldol reactions thermodynamically and mixtures of stereoisomers (E & Z) are obtained from some reactions. Reactions in which a larger molecule is formed from smaller components, with the elimination of a very small by-product such as water, are termed **Condensations**. Hence, the following examples are properly referred to as **aldol condensations**. Overall the general reaction involves a dehydration of an aldol product to form an alkene:

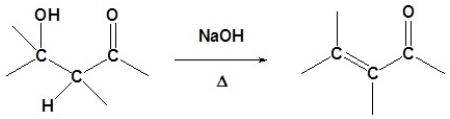


***Figure**: General reaction for an aldol condensation*

Going from reactants to products simply

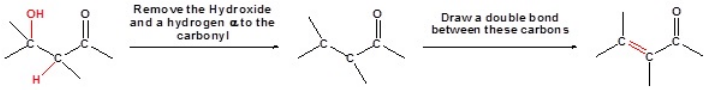
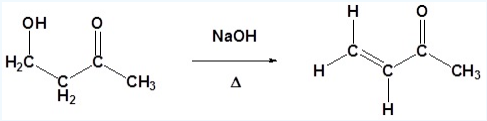


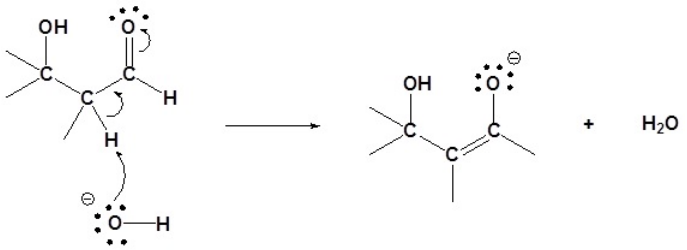
***Figure**: The aldol condensatio* example

Example 2: Aldol Condensation

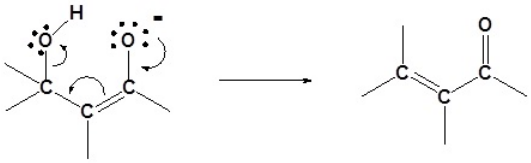


Aldol Condensation Mechanism

1) Form enolate

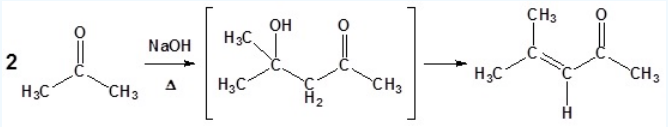


2) Form enone



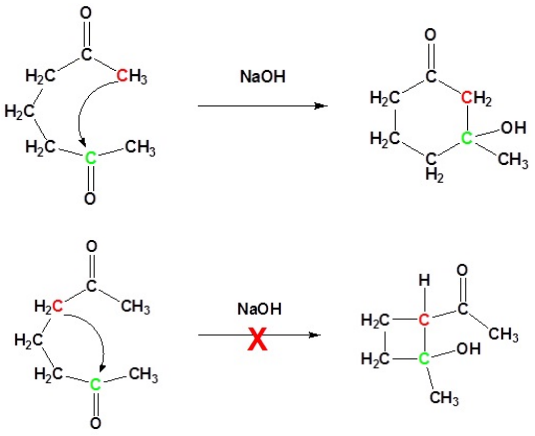
When performing both reactions together always consider the aldol product first then convert to the enone. Note! The double bond always forms in conjugation with the carbonyl.

Example 3

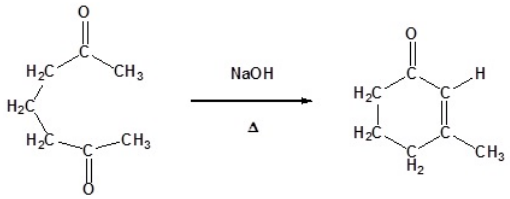


Intramolecular aldol reaction

Molecules which contain two carbonyl functionalities have the possibility of forming a ring through an intramolecular aldol reaction. In most cases two sets of α hydrogens need to be considered. As with most ring forming reaction five and six membered rings are preferred.



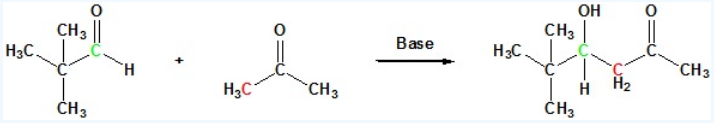
As with other aldol reaction the addition of heat causes an aldol condensation to occur.



Mixed Aldol Reaction and Condensations

In examples of aldol reactions and condensations using a common reactant as both the enolic donor and the electrophilic acceptor, the product is a dimer of the reactant carbonyl compound. Aldol condensations between different carbonyl reactants are called **crossed** or **mixed** reactions, and under certain conditions, such crossed aldol condensations can be effective.

Example 4: Mixed Aldol Reactions



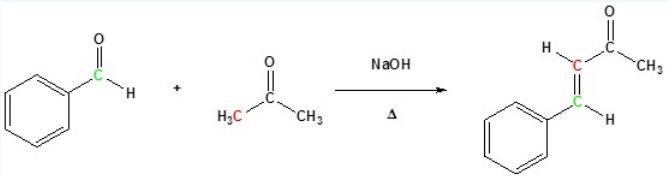
The success of these mixed aldol reactions is due to two factors. First, aldehydes are more reactive acceptor electrophiles than ketones, and formaldehyde is more reactive than other aldehydes. Second, aldehydes lacking alpha-hydrogens can only function as acceptor reactants, and this reduces the number of possible products by half. Mixed aldols in which both reactants can serve as donors and acceptors generally give complex mixtures of both dimeric (homo) aldols and crossed aldols. Because of this most mixed aldol reactions are usually not performed unless one reactant has no alpha hydrogens.

The following abbreviated formulas illustrate the possible products in such a case, red letters representing the acceptor component and blue the donor. If all the reactions occurred at the same rate, equal quantities of the four products would be obtained. Separation and purification of the components of such a mixture would be difficult.

$$\mathrm{AACH_2CHO + BCH_2CHO + NaOH \rightarrow A{-}A + B{-}B + A{-}B + B{-}A}$$

The aldol condensation of ketones with aryl aldehydes to form α,β-unsaturated derivatives is called the **Claisen-Schmidt** reaction.

Example 4: Claisen-Schmidt Reaction



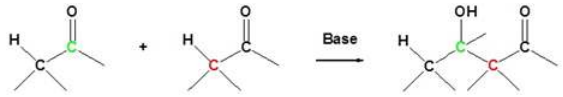
13.3: An Aldol Addition Forms β-Hydroxaldehydes or β-Hydroxyketones is shared under a not declared license and was authored, remixed, and/or curated by LibreTexts.

- **Aldol Reaction** by Steven Farmer is licensed CC BY 4.0.

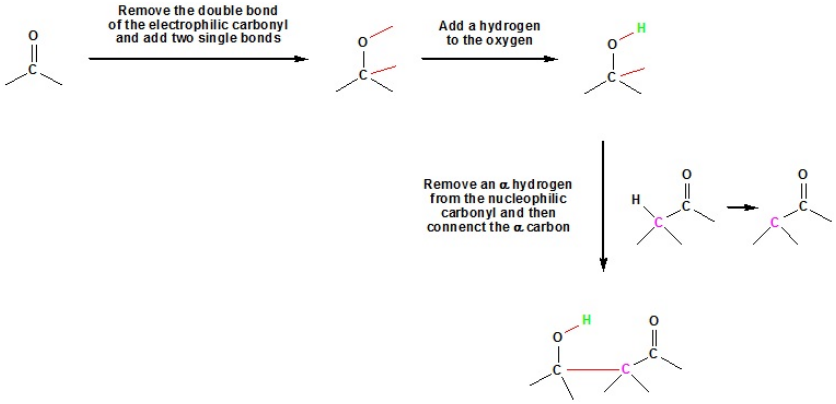
13.4: Dehydration of Aldol Addition Products Form α, β-Unsaturated Aldehydes and Ketones

A useful carbon-carbon bond-forming reaction known as the **Aldol Reaction** is yet another example of electrophilic substitution at the alpha carbon in enolate anions. The fundamental transformation in this reaction is a dimerization of an aldehyde (or ketone) to a beta-hydroxy aldehyde (or ketone) by alpha C–H addition of one reactant molecule to the carbonyl group of a second reactant molecule. Due to the carbanion like nature of enolates they can add to carbonyls in a similar manner as Grignard reagents. For this reaction to occur at least one of the reactants must have α hydrogens.

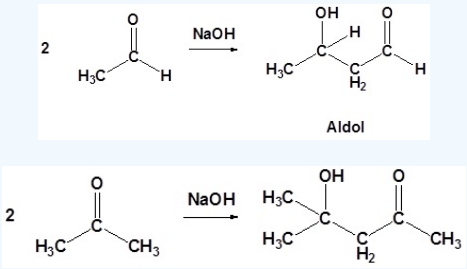
General Aldol reaction



Going from reactants to products simply



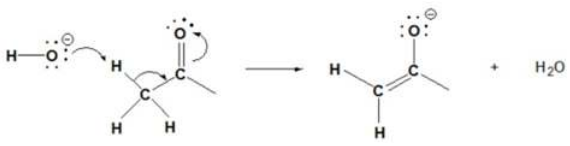
Example 1: Aldol Reactions



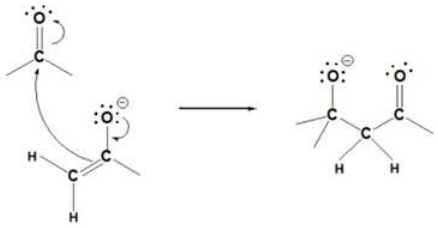
Aldol Reaction Mechanism

A three step mechanism:

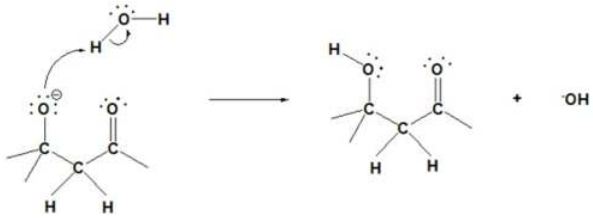
Step 1: Enolate formation



Step 2: Nucleophilic attack by the enolate



Step 3: Protonation



Aldol Condensation: the dehydration of Aldol products to synthesize α, β unsaturated carbonyl (enones)

The products of aldol reactions often undergo a subsequent elimination of water, made up of an alpha-hydrogen and the beta-hydroxyl group. The product of this ***β*-elimination** reaction is an α,β-unsaturated aldehyde or ketone. Base-catalyzed elimination occurs with heating. The additional stability provided by the conjugated carbonyl system of the product makes some aldol reactions thermodynamically and mixtures of stereoisomers (E & Z) are obtained from some reactions. Reactions in which a larger molecule is formed from smaller components, with the elimination of a very small by-product such as water, are termed **Condensations**. Hence, the following examples are properly referred to as **aldol condensations**. Overall the general reaction involves a dehydration of an aldol product to form an alkene:

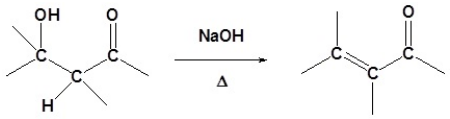


***Figure**: General reaction for an aldol condensation*

Going from reactants to products simply

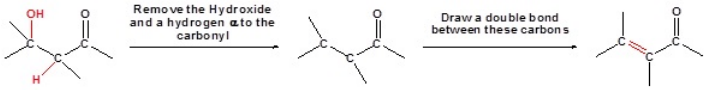
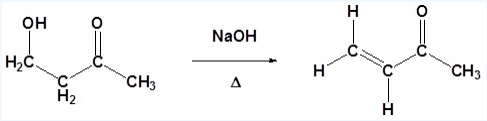


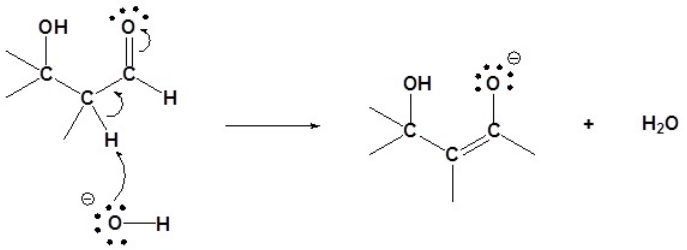
***Figure**: The aldol condensatio* example

Example 2: Aldol Condensation

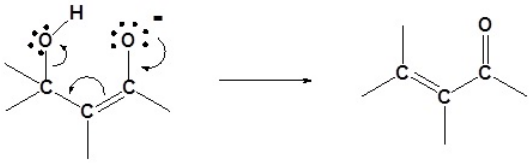


Aldol Condensation Mechanism

1) Form enolate

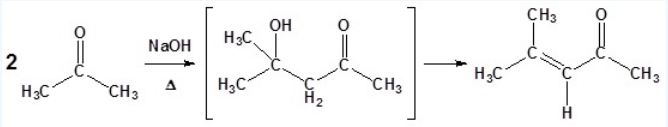


2) Form enone



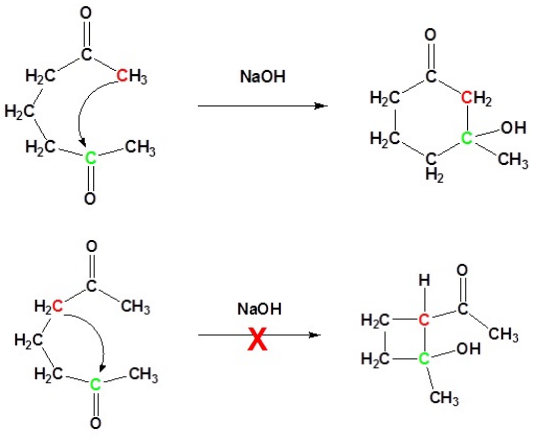
When performing both reactions together always consider the aldol product first then convert to the enone. Note! The double bond always forms in conjugation with the carbonyl.

Example 3

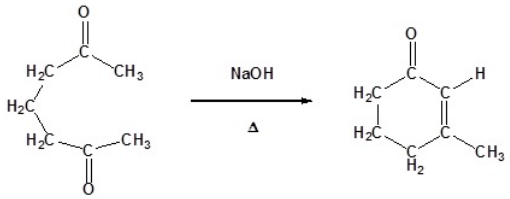


Intramolecular aldol reaction

Molecules which contain two carbonyl functionalities have the possibility of forming a ring through an intramolecular aldol reaction. In most cases two sets of α hydrogens need to be considered. As with most ring forming reaction five and six membered rings are preferred.



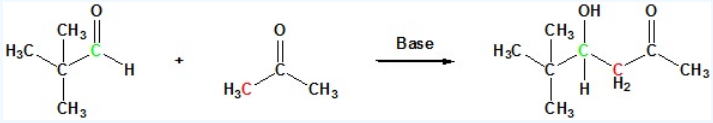
As with other aldol reaction the addition of heat causes an aldol condensation to occur.



Mixed Aldol Reaction and Condensations

In examples of aldol reactions and condensations using a common reactant as both the enolic donor and the electrophilic acceptor, the product is a dimer of the reactant carbonyl compound. Aldol condensations between different carbonyl reactants are called **crossed** or **mixed** reactions, and under certain conditions, such crossed aldol condensations can be effective.

Example 4: Mixed Aldol Reactions



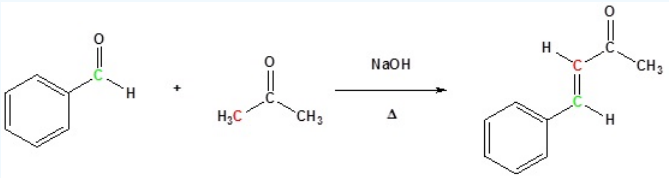
The success of these mixed aldol reactions is due to two factors. First, aldehydes are more reactive acceptor electrophiles than ketones, and formaldehyde is more reactive than other aldehydes. Second, aldehydes lacking alpha-hydrogens can only function as acceptor reactants, and this reduces the number of possible products by half. Mixed aldols in which both reactants can serve as donors and acceptors generally give complex mixtures of both dimeric (homo) aldols and crossed aldols. Because of this most mixed aldol reactions are usually not performed unless one reactant has no alpha hydrogens.

The following abbreviated formulas illustrate the possible products in such a case, red letters representing the acceptor component and blue the donor. If all the reactions occurred at the same rate, equal quantities of the four products would be obtained. Separation and purification of the components of such a mixture would be difficult.

$$\mathrm{AACH_2CHO + BCH_2CHO + NaOH \rightarrow A{-}A + B{-}B + A{-}B + B{-}A}$$

The aldol condensation of ketones with aryl aldehydes to form α,β-unsaturated derivatives is called the **Claisen-Schmidt** reaction.

Example 4: Claisen-Schmidt Reaction



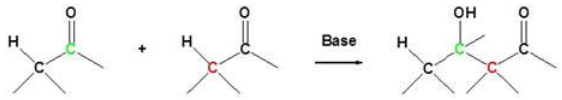
13.4: Dehydration of Aldol Addition Products Form α, β-Unsaturated Aldehydes and Ketones is shared under a not declared license and was authored, remixed, and/or curated by LibreTexts.

- **Aldol Reaction** by Steven Farmer is licensed CC BY 4.0.

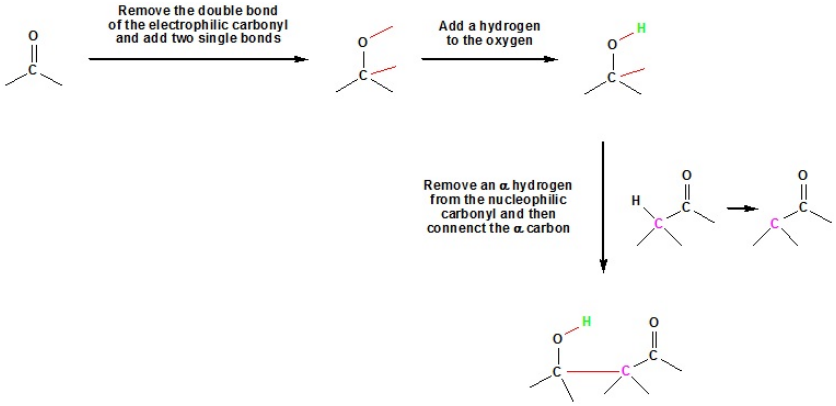
13.5: The Crossed Aldol Addition

A useful carbon-carbon bond-forming reaction known as the **Aldol Reaction** is yet another example of electrophilic substitution at the alpha carbon in enolate anions. The fundamental transformation in this reaction is a dimerization of an aldehyde (or ketone) to a beta-hydroxy aldehyde (or ketone) by alpha C–H addition of one reactant molecule to the carbonyl group of a second reactant molecule. Due to the carbanion like nature of enolates they can add to carbonyls in a similar manner as Grignard reagents. For this reaction to occur at least one of the reactants must have α hydrogens.

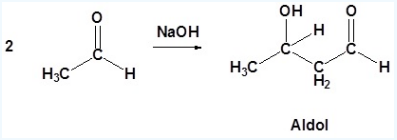
General Aldol reaction

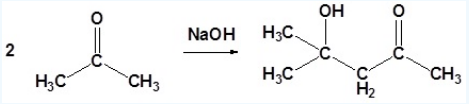


Going from reactants to products simply



Example 1: Aldol Reactions

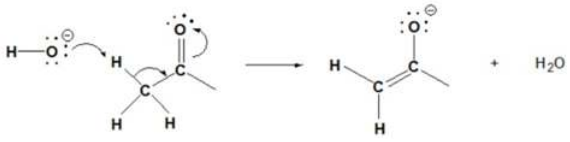




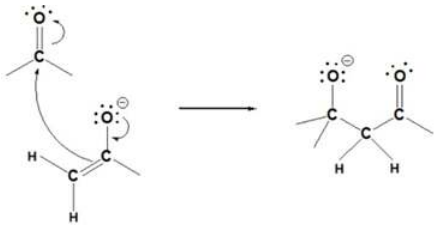
Aldol Reaction Mechanism

A three step mechanism:

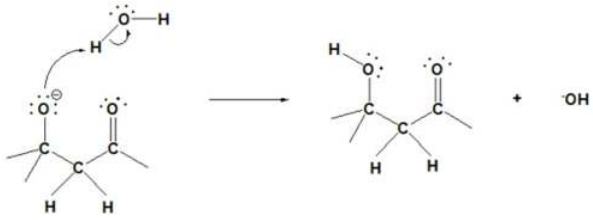
Step 1: Enolate formation



Step 2: Nucleophilic attack by the enolate



Step 3: Protonation



Aldol Condensation: the dehydration of Aldol products to synthesize α, β unsaturated carbonyl (enones)

The products of aldol reactions often undergo a subsequent elimination of water, made up of an alpha-hydrogen and the beta-hydroxyl group. The product of this ***β*-elimination** reaction is an α,β-unsaturated aldehyde or ketone. Base-catalyzed elimination occurs with heating. The additional stability provided by the conjugated carbonyl system of the product makes some aldol reactions thermodynamically and mixtures of stereoisomers (E & Z) are obtained from some reactions. Reactions in which a larger molecule is formed from smaller components, with the elimination of a very small by-product such as water, are termed **Condensations**. Hence, the following examples are properly referred to as **aldol condensations**. Overall the general reaction involves a dehydration of an aldol product to form an alkene:

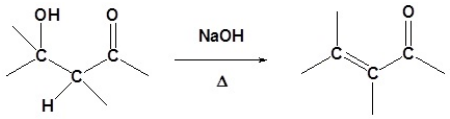


***Figure**: General reaction for an aldol condensation*

Going from reactants to products simply

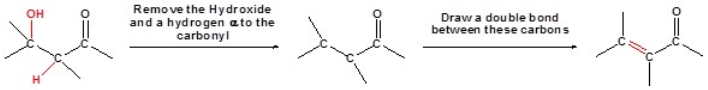
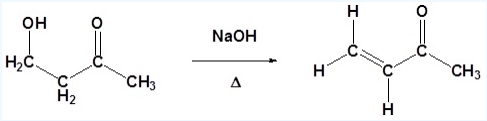


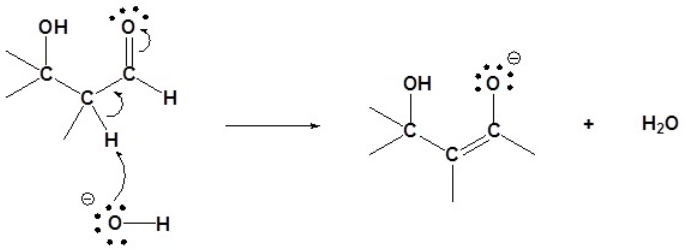
***Figure**: The aldol condensatio* example

Example 2: Aldol Condensation

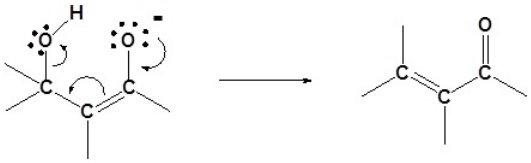


Aldol Condensation Mechanism

1) Form enolate

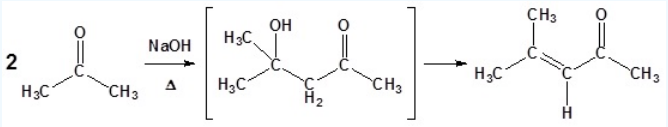


2) Form enone



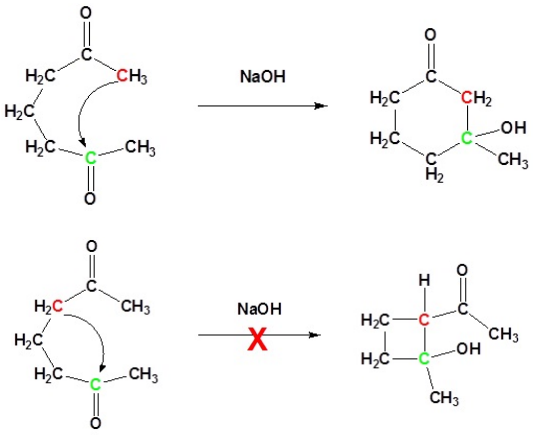
When performing both reactions together always consider the aldol product first then convert to the enone. Note! The double bond always forms in conjugation with the carbonyl.

Example 3

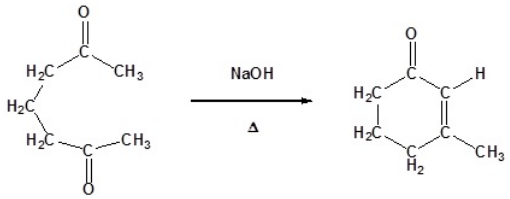


Intramolecular aldol reaction

Molecules which contain two carbonyl functionalities have the possibility of forming a ring through an intramolecular aldol reaction. In most cases two sets of α hydrogens need to be considered. As with most ring forming reaction five and six membered rings are preferred.



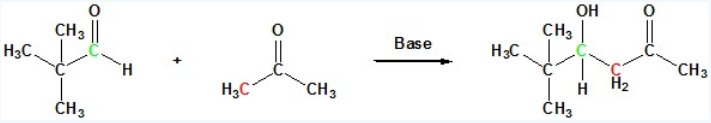
As with other aldol reaction the addition of heat causes an aldol condensation to occur.



Mixed Aldol Reaction and Condensations

In examples of aldol reactions and condensations using a common reactant as both the enolic donor and the electrophilic acceptor, the product is a dimer of the reactant carbonyl compound. Aldol condensations between different carbonyl reactants are called **crossed** or **mixed** reactions, and under certain conditions, such crossed aldol condensations can be effective.

Example 4: Mixed Aldol Reactions



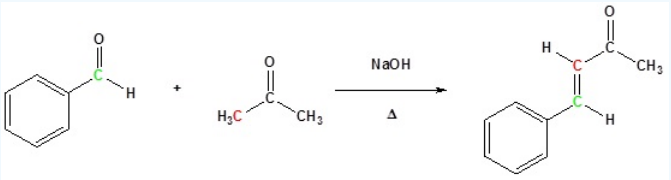
The success of these mixed aldol reactions is due to two factors. First, aldehydes are more reactive acceptor electrophiles than ketones, and formaldehyde is more reactive than other aldehydes. Second, aldehydes lacking alpha-hydrogens can only function as acceptor reactants, and this reduces the number of possible products by half. Mixed aldols in which both reactants can serve as donors and acceptors generally give complex mixtures of both dimeric (homo) aldols and crossed aldols. Because of this most mixed aldol reactions are usually not performed unless one reactant has no alpha hydrogens.

The following abbreviated formulas illustrate the possible products in such a case, red letters representing the acceptor component and blue the donor. If all the reactions occurred at the same rate, equal quantities of the four products would be obtained. Separation and purification of the components of such a mixture would be difficult.

$$\mathbf{A}\mathbf{A}CH_2CHO + \mathbf{B}CH_2CHO + NaOH \rightarrow A\text{–}A + B\text{–}B + A\text{–}B + B\text{–}A$$

The aldol condensation of ketones with aryl aldehydes to form α,β-unsaturated derivatives is called the **Claisen-Schmidt** reaction.

Example 4: Claisen-Schmidt Reaction



13.5: The Crossed Aldol Addition is shared under a not declared license and was authored, remixed, and/or curated by LibreTexts.

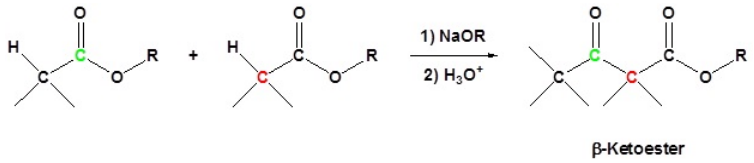
- **Aldol Reaction** by Steven Farmer is licensed CC BY 4.0.

13.6: A Claisen Condensation Forms a β-Keto Ester

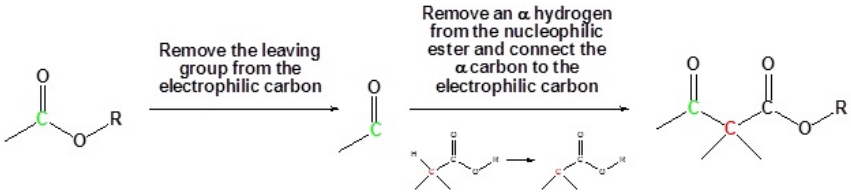
Because esters can contain α hydrogens they can undergo a condensation reaction similar to the aldol reaction called a **Claisen Condensation**. In a fashion similar to the aldol, one ester acts as a nucleophile while a second ester acts as the electrophile. During the reaction a new carbon-carbon bond is formed; the product is a β-keto ester. A major difference with the aldol reaction is the fact that hydroxide cannot be used as a base because it could possibly react with the ester. Instead, an alkoxide version of the alcohol used to synthesize the ester is used to prevent transesterification side products.

Claisen Condensation

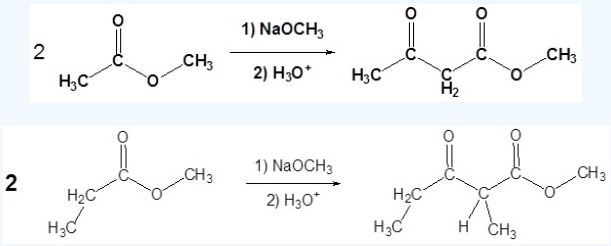
Basic reaction



Going from reactants to products simply



Example 1: Claisen Condensation

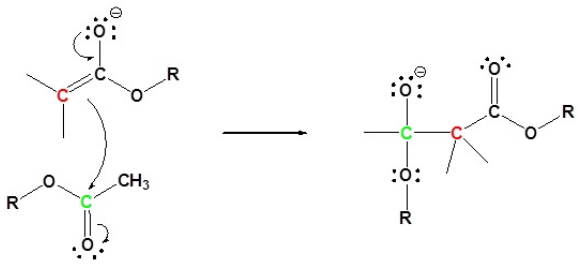


Claisen Condensation Mechanism

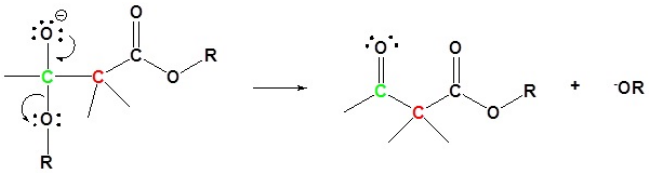
1) Enolate formation



2) Nucleophilic attack



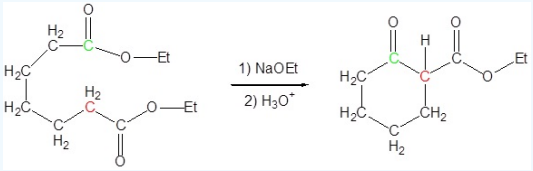
3) Removal of leaving group



Dieckmann Condensation

A diester can undergo an intramolecular reaction called a Dieckmann condensation.

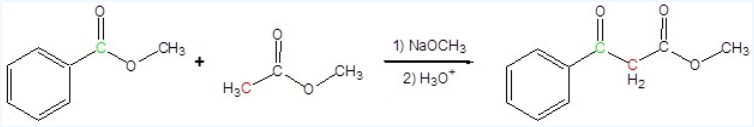
Example 2: Dieckman Condensation



Crossed Claisen Condensation

Claisen condensations between different ester reactants are called **Crossed Claisen** reactions. Crossed Claisen reactions in which both reactants can serve as donors and acceptors generally give complex mixtures. Because of this most Crossed Claisen reactions are usually not performed unless one reactant has no alpha hydrogens.

Example 3: Crossed Claisen Condensation



Contributors

- Prof. Steven Farmer (Sonoma State University)

13.6: A Claisen Condensation Forms a β-Keto Ester is shared under a not declared license and was authored, remixed, and/or curated by LibreTexts.

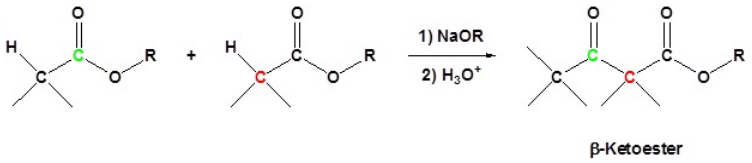
- **Claisen Reactions** is licensed CC BY-NC-SA 4.0.

13.7: Other Crossen Condensations

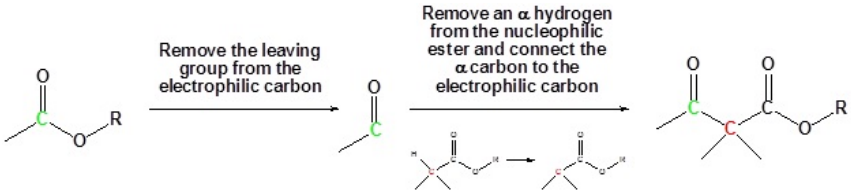
Because esters can contain α hydrogens they can undergo a condensation reaction similar to the aldol reaction called a **Claisen Condensation**. In a fashion similar to the aldol, one ester acts as a nucleophile while a second ester acts as the electrophile. During the reaction a new carbon-carbon bond is formed; the product is a β-keto ester. A major difference with the aldol reaction is the fact that hydroxide cannot be used as a base because it could possibly react with the ester. Instead, an alkoxide version of the alcohol used to synthesize the ester is used to prevent transesterification side products.

Claisen Condensation

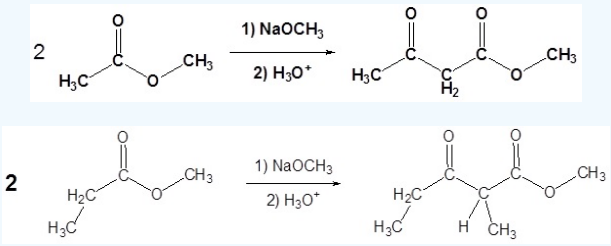
Basic reaction



Going from reactants to products simply



Example 1: Claisen Condensation

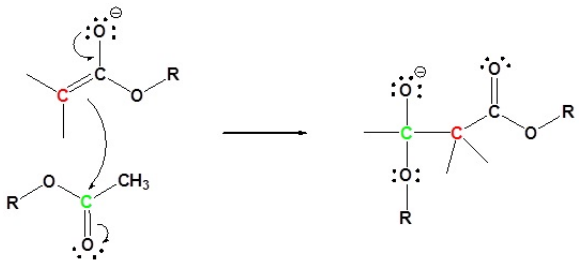


Claisen Condensation Mechanism

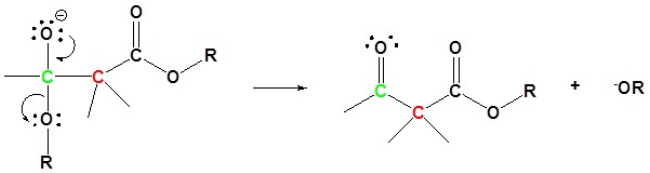
1) Enolate formation



2) Nucleophilic attack



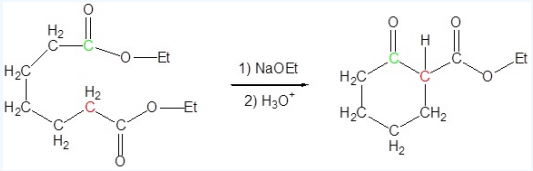
3) Removal of leaving group



Dieckmann Condensation

A diester can undergo an intramolecular reaction called a Dieckmann condensation.

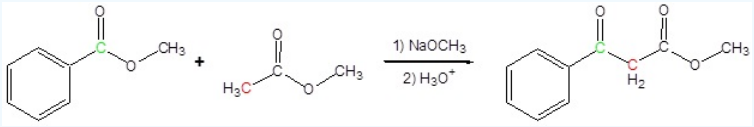
Example 2: Dieckman Condensation



Crossed Claisen Condensation

Claisen condensations between different ester reactants are called **Crossed Claisen** reactions. Crossed Claisen reactions in which both reactants can serve as donors and acceptors generally give complex mixtures. Because of this most Crossed Claisen reactions are usually not performed unless one reactant has no alpha hydrogens.

Example 3: Crossed Claisen Condensation



Contributors

- Prof. Steven Farmer (Sonoma State University)

13.7: Other Crossen Condensations is shared under a not declared license and was authored, remixed, and/or curated by LibreTexts.

- **Claisen Reactions** is licensed CC BY-NC-SA 4.0.

13.8: Intramolecular Condensation and Addition Reactions

13.8: Intramolecular Condensation and Addition Reactions is shared under a not declared license and was authored, remixed, and/or curated by LibreTexts.

13.9: The Robinson Annulation

Objectives

After completing this section, you should be able to

1. write an equation to illustrate the Robinson annulation reaction.
2. identify the cyclic product formed when a 1,5-diketone is treated with base.
3. identify the carbonyl compounds and any other reagents needed to synthesize a given cyclic compound by a series of reactions, one of which is a Robinson annulation.

Key Terms

- Robinson annulation reaction

Study Notes

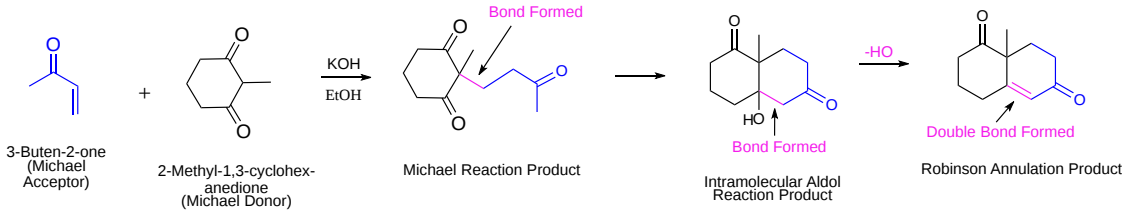
The building of an alicyclic compound from acyclic starting materials can present an interesting challenge to the synthetic organic chemist. One route by which such a synthesis can be achieved is through the use of the Robinson annulation reaction. This reaction, which may at first look very complex, can be readily understood once you realize that it simply involves a Michael reaction followed by an intramolecular aldol condensation. Both of these steps involve attack by enolate anions.

As in some of the other syntheses that you have studied, when you are simply given the structure of a compound and asked how it could have been prepared, it can be difficult to recognize which reactions might have been used. In this instance, keep in mind that you have studied relatively few reactions which have resulted in the formation of an alicyclic compound. Thus, when asked how such a compound might be prepared, you should keep the possibility of using a Robinson annulation reaction in mind.

The Robinson Annulation

Many times the product of a Michael addition produces a dicarbonyl which can then undergo an intramolecular aldol reaction. These two processes together in one reaction creates two new carbon-carbon bonds and also creates a ring. Ring-forming reactions are called annulations after the Latin work for ring annulus. The reaction is named after English chemist Sir Robert Robinson (1886-1975) who developed it. He received the Nobel prize in chemistry in 1947. Remember that during annulations five and six membered rings are preferred.

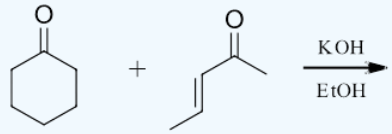
The nucleophilic enolate donor is typically an enolate ion or enamine of a cyclic ketone, β-keto ester or β-diketone. The electrophilic acceptor is usually an α, β-unsaturated ketone. In the example below, 2-methyl-1,3-cyclohexanedione is deprotonated to form an enolate which affects a Michael reaction addition on 3-buten-2-one forming a C-C bond. The product contains a 1,5-diketone fragment which can undergo an intramolecular aldol condensation. This occurs through creation of a new enolate at the methyl ketone which undergoes an intramolecular aldol reaction. A new C-C bond is formed to one of the ring carbonyls, creating a new six-membered ring. In the last step, the resulting alcohol is eliminated to form a α, β-unsaturated ketone as the final Robinson annulation product. Because the Robinson Annulation involves an aldol reaction, a full equivalent of base is required.



Example

? Example

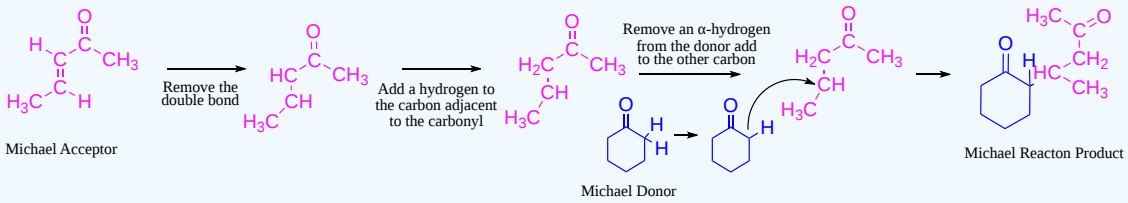
Draw the product of the following Robinson Annulation.



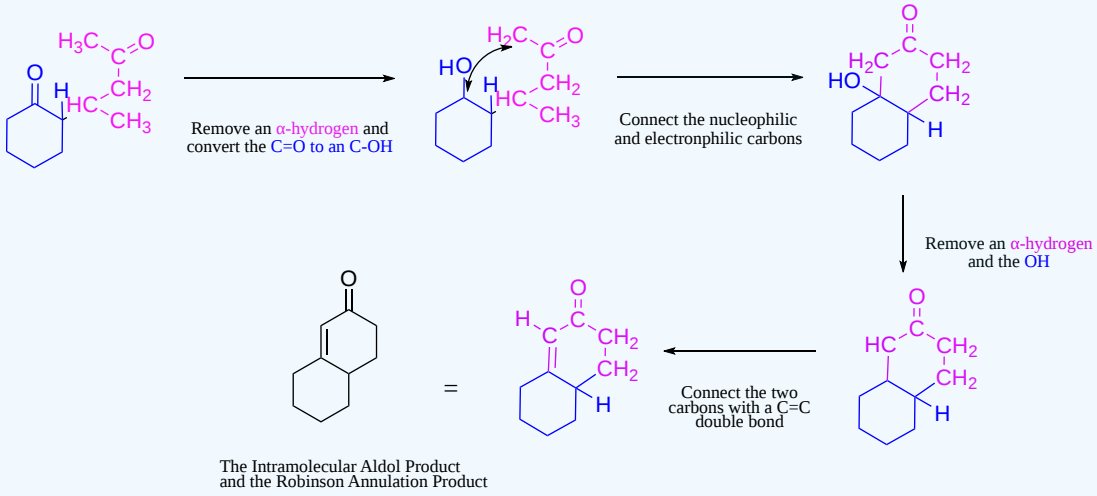
Analysis

When considering the product of a Robinson annulation it is usually best to consider each reaction individually. Use the steps discussed in Section 23.10 to convert the starting materials into the product of a Michael reaction, then into the product of an intramolecular aldol condensation. If the starting materials are drawn in a skeletal structure it may be helpful to convert to a condensed formula to better keep track of carbons and hydrogens.

Formation of the Michael reaction product

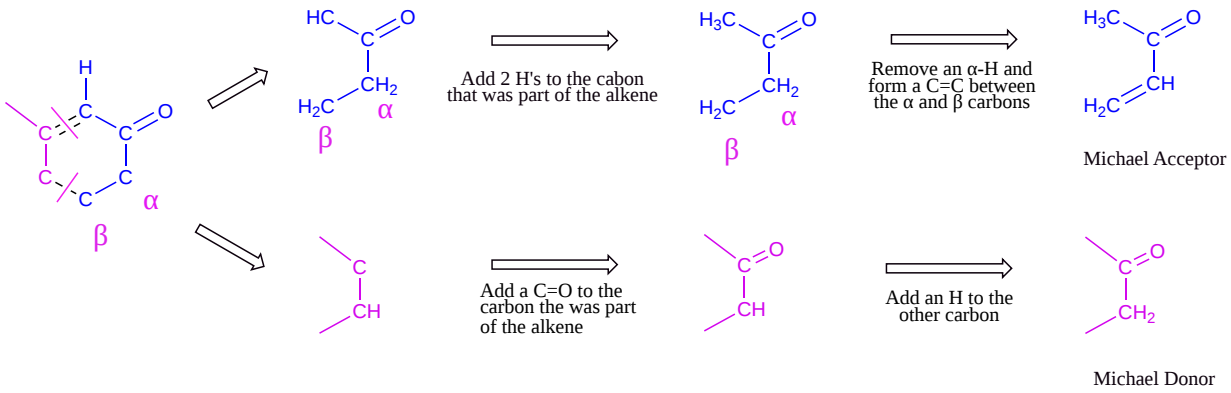


Formation of the intramolecular Aldol condensation product



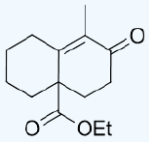
Planning a Synthesis Using a Robinson Annulation

The presence of a cyclic, six-membered α, β-unsaturated ketone in a target molecule suggest that a Robinson Annulation may be utilized in its synthesis. The key bond cleavages are the C=C bond of the α, β-unsaturated ketone and the C-C bond between carbons in the a and g on the opposite alkyl chain of the ketone.

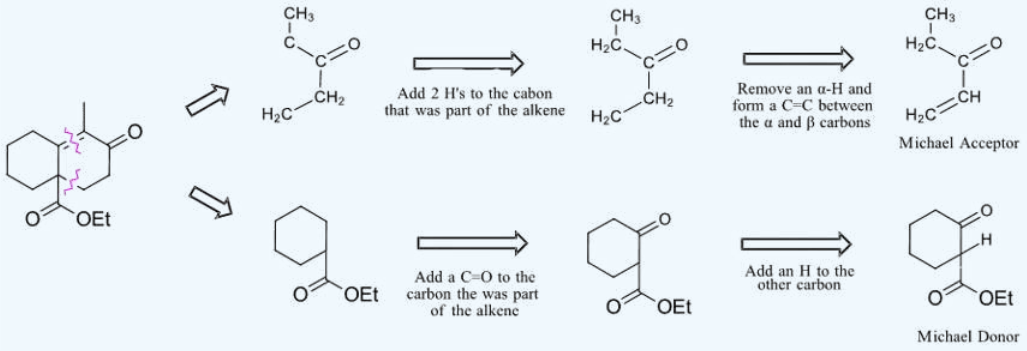


? Example

What would be the starting materials used if the following molecule was made using a Robinson annulation?

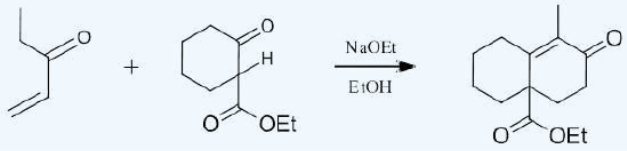


Analysis



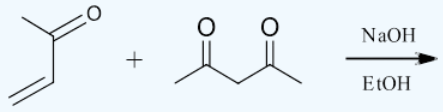
Solution

It is necessary to use sodium ethoxide as the reaction base due to the presence of an ester.

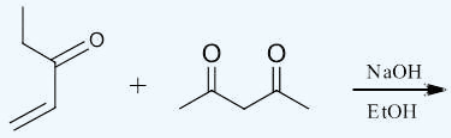


? Exercise 13.9.1

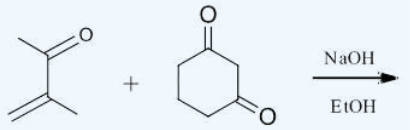
Provide products of the following Robinson annulations.

a. 

b.

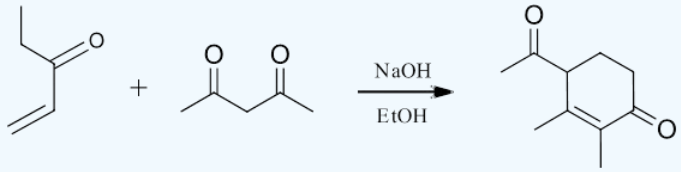


c.

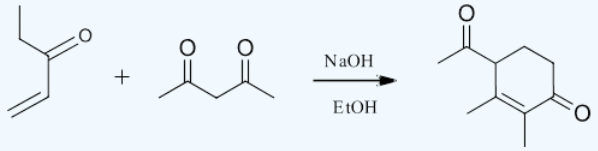


Answer

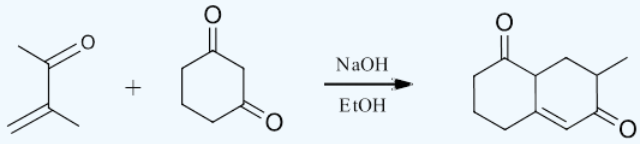
a.



b.

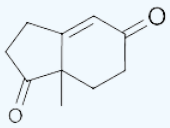


c.

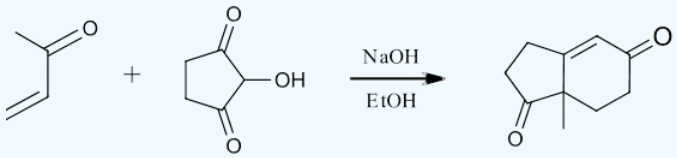


? Exercise 13.9.2

What would be the starting materials required to make the following molecule using a Robinson annulation?



Answer

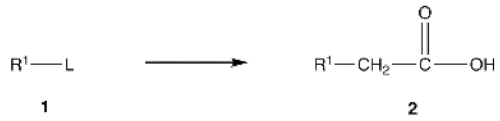


13.9: The Robinson Annulation is shared under a not declared license and was authored, remixed, and/or curated by LibreTexts.

- **23.12: The Robinson Annulation Reaction** by Dietmar Kennepohl, Layne Morsch, Steven Farmer is licensed CC BY-SA 4.0.

13.10: Carboxylic Acids with a Carbonyl Group at the 3-Position can be Decarboxylated

Malonic ester is a reagent specifically used in a reaction which converts alkyl halides to carboxylic acids called the Malonic Ester Synthesis. Malonic ester synthesis is a synthetic procedure used to convert a compound that has the general structural formula 1 into a carboxylic acid that has the general structural formula 2.



1 2

- reaction 1:

  reaction 2:



  reaction 3:



  reaction 4:



  A more direct method to convert **3** into **4** is the reaction of **3** with the enolate ion **(5)** of ethyl acetate followed by hydrolysis of the resultant ester.



  However, the generation of **5** from ethyl acetate quantitatively in high yield is not an easy task because the reaction requires a very strong base, such as LDA, and must be carried out at very low temperature under strictly anhydrous conditions.



Malonic ester synthesis provides a more convenient alternative to convert **3** to **4**.

Malonic ester synthesis can be adapted to synthesize compounds that have the general structural formula **6**.



R^3, R^4 = identical or different alkyl groups

eg:



reaction 1:



reaction 2:



reaction 1 (repeat):



reaction 2 (repeat):



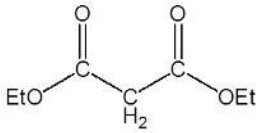
reaction 3:



reaction 4:



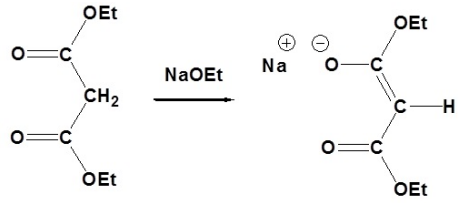
Malonic Ester Synthesis



Et = -CH_2CH_3

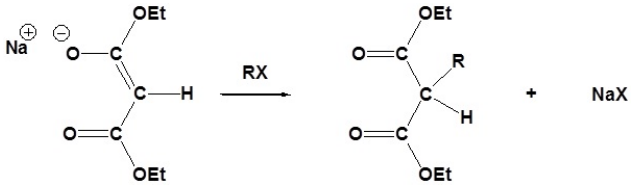
Malonic Ester

Due to the fact that Malonic ester's α hydrogens are adjacent to two carbonyls, they can be deprotonated by sodium ethoxide (NaOEt) to form Sodio Malonic Ester.

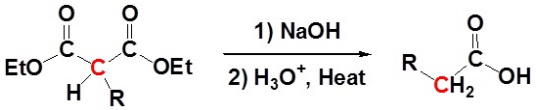


Malonic Ester **Sodio Malonic Ester**

Because Sodio Malonic Ester is an enolate, it can then be alkylated with alkyl halides.

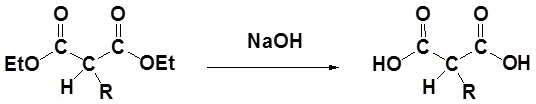


After alkylation the product can be converted to a dicarboxylic acid through saponification and subsequently one of the carboxylic acids can be removed through a decarboxylation step.

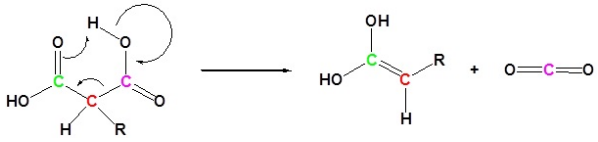


Mechanism

1) Saponification



2) Decarboxylation



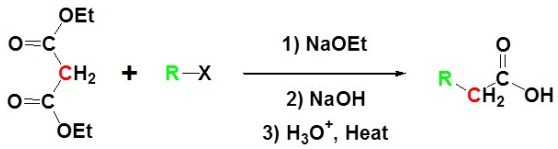
3) Tautomerization



All of the steps together form the Malonic ester synthesis.

$$RX \rightarrow RCH\text{-}_2CO_2H \tag{13.10.1}$$

Example



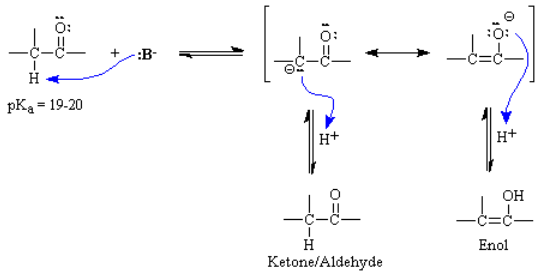
- Gamini Gunawardena from the OChemPal site (Utah Valley University)

13.10: Carboxylic Acids with a Carbonyl Group at the 3-Position can be Decarboxylated is shared under a not declared license and was authored, remixed, and/or curated by LibreTexts.

- **Malonic Ester Synthesis** is licensed CC BY-NC-SA 4.0.

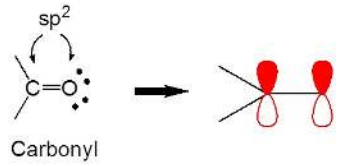
13.11: The Acidity of an α- Hydrogen

Alkyl hydrogen atoms bonded to a carbon atom in a a (alpha) position relative to a carbonyl group display unusual acidity. While the pK_a values for alkyl C-H bonds is typically on the order of 40-50, pK_a values for these alpha hydrogens is more on the order of 19-20. This can most easily be explained by resonance stabilization of the product carbanion, as illustrated in the diagram below.

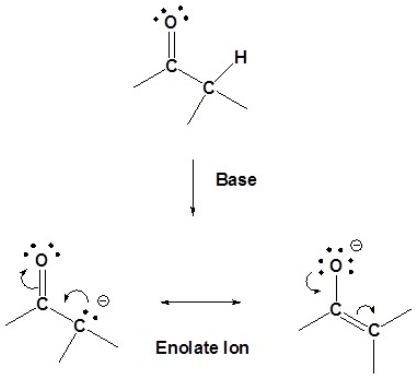


In the presence of a proton source, the product can either revert back into the starting ketone or aldehyde or can form a new product, the enol. The equilibrium reaction between the ketone or aldehyde and the enol form is commonly referred to as "keto-enol tautomerism". The ketone or aldehyde is generally strongly favored in this reaction.

Because carbonyl groups are sp^2 hybridized the carbon and oxygen both have unhybridized p orbitals which can overlap to form the C=O π bond.



The presence of these overlapping p orbitals gives α hydrogens (Hydrogens on carbons adjacent to carbonyls) special properties. In particular, α hydrogens are weakly acidic because the conjugate base, called an enolate, is stabilized though conjugation with the π orbitals of the carbonyl. The effect of the carbonyl is seen when comparing the pK_a for the α hydrogens of aldehydes (~16-18), ketones (~19-21), and esters (~23-25) to the pK_a of an alkane (~50).

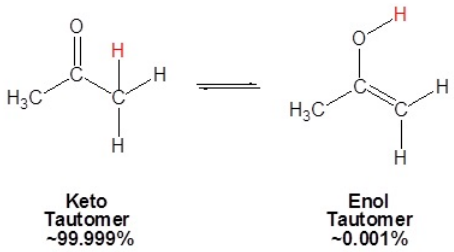


Of the two resonance structures of the enolate ion the one which places the negative charge on the oxygen is the most stable. This is because the negative change will be better stabilized by the greater electronegativity of the oxygen.

Keto-enol Tautomerism

Because of the acidity of α hydrogens carbonyls undergo keto-enol tautomerism. Tautomers are rapidly interconverted constitutional isomers, usually distinguished by a different bonding location for a labile hydrogen atom and a differently located double bond. The equilibrium between tautomers is not only rapid under normal conditions, but it often strongly favors one of the isomers (acetone, for example, is 99.999% keto tautomer). Even in such one-sided equilibria, evidence for the presence of the

minor tautomer comes from the chemical behavior of the compound. Tautomeric equilibria are catalyzed by traces of acids or bases that are generally present in most chemical samples.



Keto Tautomer ~99.999% **Enol Tautomer ~0.001%**

Contributors

Prof. Steven Farmer (Sonoma State University)

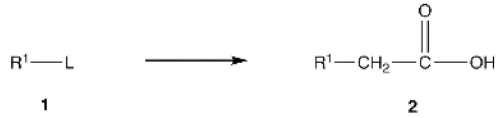
- Clarke Earley (Department of Chemistry, Kent State University Stark Campus)

13.11: The Acidity of an α- Hydrogen is shared under a not declared license and was authored, remixed, and/or curated by LibreTexts.

- **Acidity of Alpha Hydrogens & Keto-enol Tautomerism** by Clarke Earley, Steven Farmer is licensed CC BY 4.0.

13.12: The Malonic Ester Synthesis- A Way to Synthesize a Carboxylic Acid

Malonic ester is a reagent specifically used in a reaction which converts alkyl halides to carboxylic acids called the Malonic Ester Synthesis. Malonic ester synthesis is a synthetic procedure used to convert a compound that has the general structural formula 1 into a carboxylic acid that has the general structural formula 2.



- reaction 1:

  reaction 2:



  reaction 3:



  reaction 4:



  A more direct method to convert **3** into **4** is the reaction of **3** with the enolate ion **(5)** of ethyl acetate followed by hydrolysis of the resultant ester.



  However, the generation of **5** from ethyl acetate quantitatively in high yield is not an easy task because the reaction requires a very strong base, such as LDA, and must be carried out at very low temperature under strictly anhydrous conditions.



  Malonic ester synthesis provides a more convenient alternative to convert **3** to **4**.

Malonic ester synthesis can be adapted to synthesize compounds that have the general structural formula **6**.



R^3, R^4 = identical or different alkyl groups

eg:



reaction 1:



reaction 2:



reaction 1 (repeat):



reaction 2 (repeat):



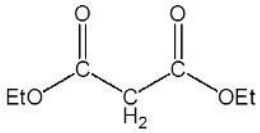
reaction 3:



reaction 4:



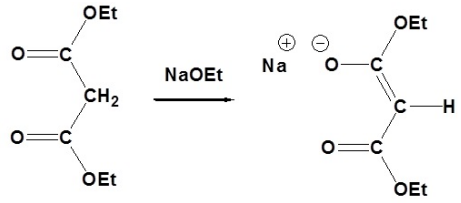
Malonic Ester Synthesis



Et = -CH_2CH_3

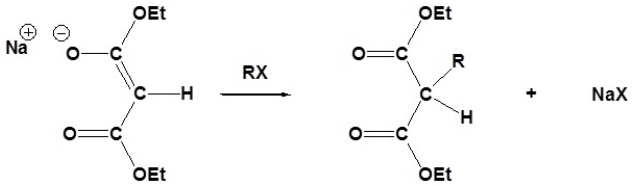
Malonic Ester

Due to the fact that Malonic ester's α hydrogens are adjacent to two carbonyls, they can be deprotonated by sodium ethoxide (NaOEt) to form Sodio Malonic Ester.

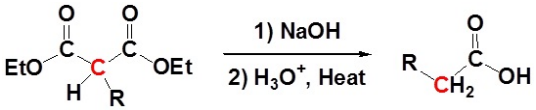


Malonic Ester **Sodio Malonic Ester**

Because Sodio Malonic Ester is an enolate, it can then be alkylated with alkyl halides.

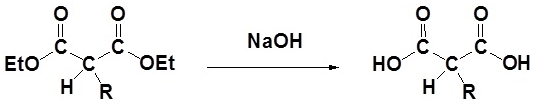


After alkylation the product can be converted to a dicarboxylic acid through saponification and subsequently one of the carboxylic acids can be removed through a decarboxylation step.

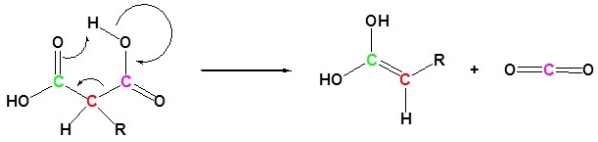


Mechanism

1) Saponification



2) Decarboxylation



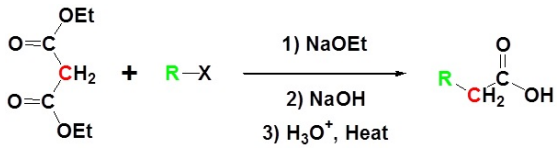
3) Tautomerization



All of the steps together form the Malonic ester synthesis.

$$RX \rightarrow RCH\text{-}_2CO_2H \tag{13.12.1}$$

Example



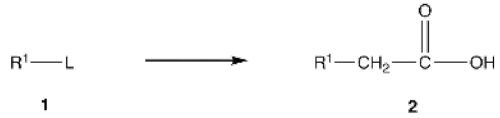
- Gamini Gunawardena from the OChemPal site (Utah Valley University)

13.12: The Malonic Ester Synthesis- A Way to Synthesize a Carboxylic Acid is shared under a not declared license and was authored, remixed, and/or curated by LibreTexts.

- **Malonic Ester Synthesis** is licensed CC BY-NC-SA 4.0.

13.13: The Acetoacetic Ester Synthesis- A Way to Synthesize a Methyl Ketone

Malonic ester is a reagent specifically used in a reaction which converts alkyl halides to carboxylic acids called the Malonic Ester Synthesis. Malonic ester synthesis is a synthetic procedure used to convert a compound that has the general structural formula 1 into a carboxylic acid that has the general structural formula 2.



- reaction 1:

  reaction 2:



  reaction 3:



  reaction 4:



  A more direct method to convert **3** into **4** is the reaction of **3** with the enolate ion **(5)** of ethyl acetate followed by hydrolysis of the resultant ester.



  However, the generation of **5** from ethyl acetate quantitatively in high yield is not an easy task because the reaction requires a very strong base, such as LDA, and must be carried out at very low temperature under strictly anhydrous conditions.



  Malonic ester synthesis provides a more convenient alternative to convert **3** to **4**.

Malonic ester synthesis can be adapted to synthesize compounds that have the general structural formula **6**.



R^3, R^4 = identical or different alkyl groups

eg:



reaction 1:



reaction 2:



reaction 1 (repeat):



reaction 2 (repeat):



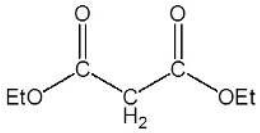
reaction 3:



reaction 4:



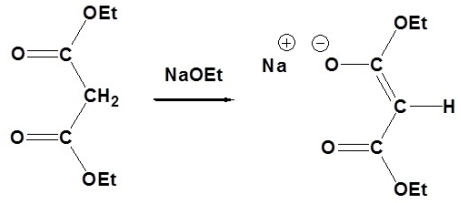
Malonic Ester Synthesis



Et = -CH_2CH_3

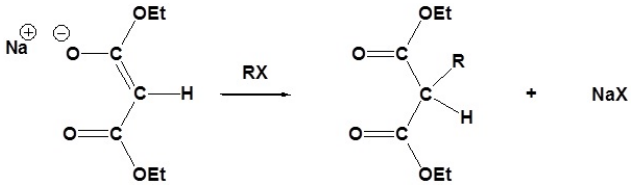
Malonic Ester

Due to the fact that Malonic ester's α hydrogens are adjacent to two carbonyls, they can be deprotonated by sodium ethoxide (NaOEt) to form Sodio Malonic Ester.

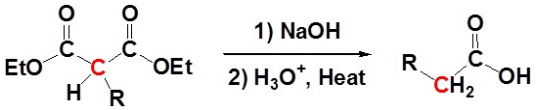


Malonic Ester **Sodio Malonic Ester**

Because Sodio Malonic Ester is an enolate, it can then be alkylated with alkyl halides.

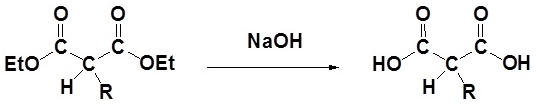


After alkylation the product can be converted to a dicarboxylic acid through saponification and subsequently one of the carboxylic acids can be removed through a decarboxylation step.

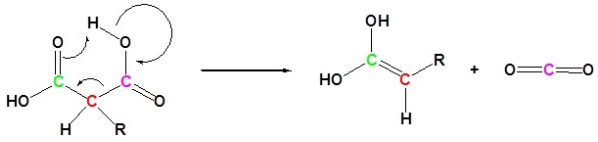


Mechanism

1) Saponification



2) Decarboxylation



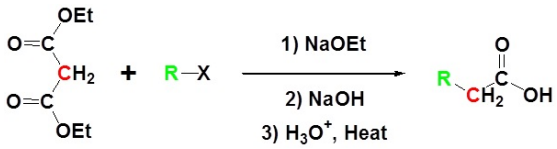
3) Tautomerization



All of the steps together form the Malonic ester synthesis.

$$RX \rightarrow RCH\text{-}_2CO_2H \tag{13.13.1}$$

Example



- Gamini Gunawardena from the OChemPal site (Utah Valley University)

13.13: The Acetoacetic Ester Synthesis- A Way to Synthesize a Methyl Ketone is shared under a not declared license and was authored, remixed, and/or curated by LibreTexts.

- **Malonic Ester Synthesis** is licensed CC BY-NC-SA 4.0.

13.14: Designing a Synthesis VII- Making New Carbon-Carbon Bonds

13.14: Designing a Synthesis VII- Making New Carbon-Carbon Bonds is shared under a not declared license and was authored, remixed, and/or curated by LibreTexts.

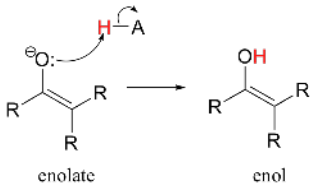
13.15: Reactions at the α-Carbon in Biological Systems

We come now to one of the most important mechanism types in metabolism: the carbon-carbon bond-forming 'aldol' condensation reaction.

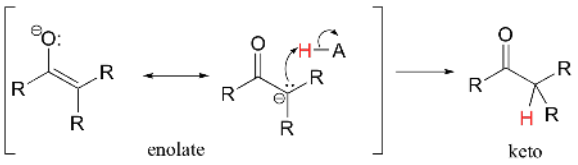
1. 13.3A: The general mechanism for an aldol reaction
2. 13.3B: Typical aldolase reactions - three variations on a theme
3. 13.3C: Going backwards: the retroaldol reaction
4. 13.3D: Going both ways: transaldolase

13.3A: The general mechanism for an aldol reaction

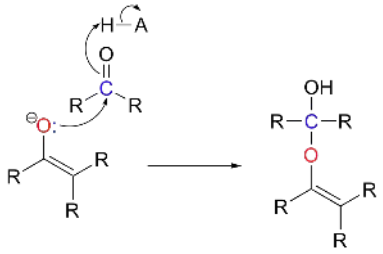
Consider the potential pathways available to a reactive enolate intermediate once the alpha-proton has been abstracted. The oxygen, which bears most of the negative charge, could act as a base, and the result would be an enol.



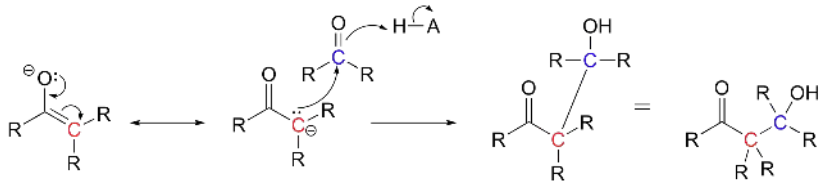
Alternatively, the enolate carbon, which bears a degree of negative charge, could act as a base, which is simply the reverse of the initial deprotonation step that formed the enolate in the first place.



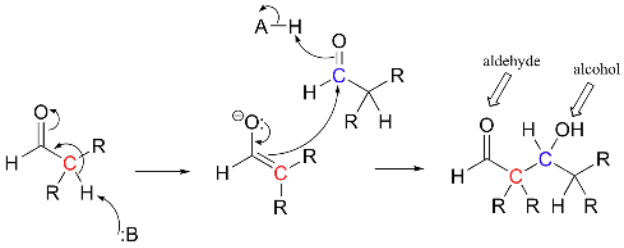
In both of these cases, the electron-poor species attacked by the enolate is an acidic proton. What if the electron-poor species - the electrophile - is not a proton but a carbonyl carbon? In other words, what if the enolate acts not as a base but rather as a *nucleophile* in a carbonyl addition (chapter 11) reaction? One possibility is that the enolate oxygen could be the nucleophile in a hemiketal-forming reaction:



Although you can find examples of this type of reaction in biochemistry, it is far more common for the enolate *carbon* to be the nucleophile, attacking an electrophilic carbonyl to form a new carbon-carbon bond.



Historically, the first examples of this mechanism type to be studied involved the non-enzymatic reaction of an aldehyde with itself (a so-called 'self-condensation' reaction, where 'condensation' means the formation of one larger molecule from two smaller ones).



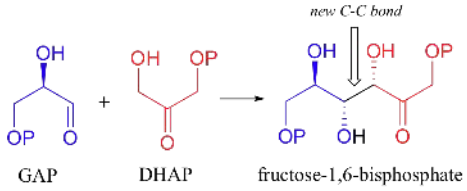
Because the resulting product contained both an **ald**ehyde and an alcoh**ol** functional group, the reaction was termed an 'aldol condensation', a name that has become standard for reactions of this type, whether or not an aldehyde is involved.

The enzymes that catalyze aldol reactions are called, not surprisingly, '**aldolases**'.

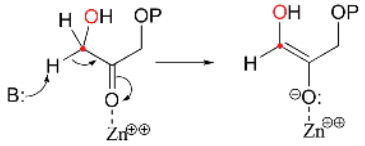
13.3B: Typical aldolase reactions - three variations on a theme

The first step in an aldolase reaction is the deprotonation of an alpha-carbon to generate a nucleophilic carbanion. Nature has evolved several distinct strategies to stabilize the intermediate that results. Some aldolases use a metal ion to stabilize the negative charge on an enolate intermediate, while others catalyze reactions that proceed through neutral Schiff base or enol intermediates.

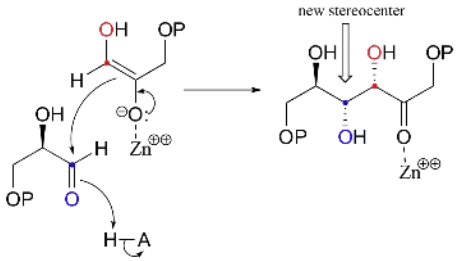
Let's examine first a reaction catalyzed by a so-called **'Class II' aldolase**, in which a metal cation - generally Zn^{2+} - bound in the active site serves to stabilize the negative charge on an enolate intermediate. Fructose 1,6-bisphosphate aldolase is an enzyme that participates in both the glycolytic (sugar burning) and gluconeogenesis (sugar building) biochemical pathways. For now, we will concentrate on its role in the gluconeogenesis pathway, but we will see it again later in its glycolytic role. The reaction catalyzed by fructose 1,6-bisphosphate aldolase is a condensation between two 3-carbon sugars, glyceraldehyde-3-phosphate (GAP) and dihydroxyacetone phosphate (DHAP), forming a six-carbon product (which leads, after three more enzymatic steps, to glucose).



In the first step of the condensation, an alpha-carbon on DHAP is deprotonated, leading to an enolate intermediate. The strategy used to stabilize this key intermediate is to coordinate the negatively-charged enolate oxygen to an enzyme-bound zinc cation.



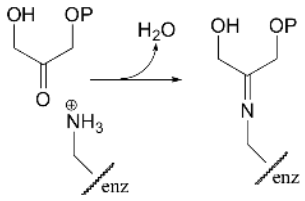
Next, the deprotonated a-carbon attacks the carbonyl carbon of GAP in a nucleophilic addition reaction, and protonation of the resulting alcohol leads directly to the fructose 1,6-bisphosphate product.



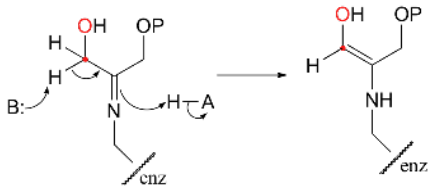
As with many other nucleophilic carbonyl addition reactions, a new stereocenter is created in this reaction, as a planar, achiral carbonyl group is converted to a tetrahedral, chiral alcohol. The enzyme-catalyzed reaction, not surprisingly, is completely

stereospecific: the DHAP substrate is positioned in the active site so as to attack the *re* (front)face of the GAP carbonyl group, leading to the *R* configuration at the new stereocenter.

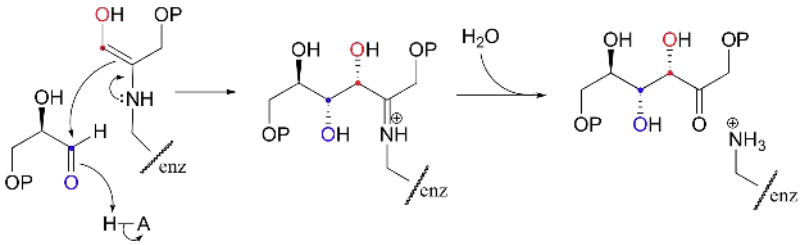
Interestingly, it appears that in bacteria, the fructose bisphosphate aldolase enzyme evolved separately from the corresponding enzyme in plants and animals. In plants and animals, the same aldol condensation reaction is carried out by a significantly different mechanism, in which the key intermediate is not a zinc-stabilized enolate but an enamine. The nucleophilic substrate (DHAP) is first linked to the enzyme through the formation of an imine (also known as a Schiff base, section 11.6) with a lysine residue in the active site.



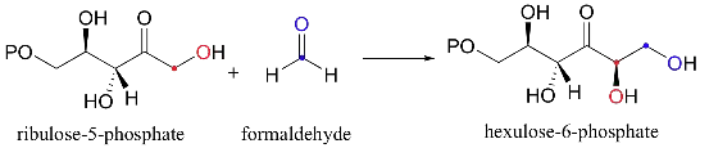
The alpha-proton is then abstracted by an active site base to form an enamine.



In the next step, the alpha-carbon attacks the carbonyl carbon of GAP, and the new carbon-carbon bond is formed. In order to release the product from the enzyme active site and free the enzyme to catalyze another reaction, the imine is hydrolyzed back to a ketone group.



There are many more examples of **'Class I' aldolase** reactions in which the key intermediate is a lysine-linked imine. Many bacteria are able to incorporate formaldehyde, a toxic compound, into carbohydrate metabolism by condensing it with ribulose monophosphate. The reaction proceeds through imine and enamine intermediates.



Template:ExampleStart

Exercise 13.5:

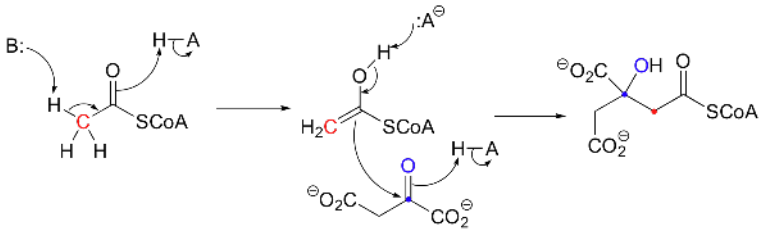
a) Propose a complete mechanism for the condensation reaction shown above.

b) Propose a complete mechanism for the conversion of hexulose-6-phosphate (formed from the condensation of ribulose-5-phosphate and formaldehyde) into fructose-6-phosphate.

Solution

Template:ExampleEnd

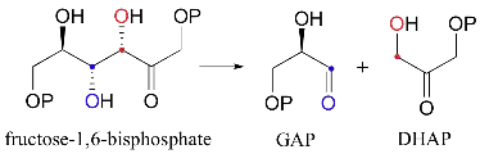
Along with aldehydes and ketones, esters and thioesters can act as the nucleophilic partner in aldol condensations. In the first step of the citric acid (Krebs) cycle, acetyl CoA condenses with oxaloacetate to form (S)-citryl CoA.



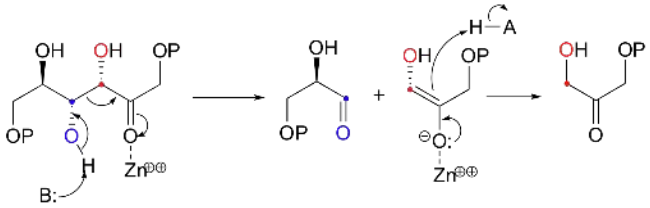
Notice that in this aldol reaction, the nucleophilic intermediate is stabilized by protonation, rather than by formation of an imine (as in the Class I aldolases) or by a metal ion (as in the Class II aldolases).

13.3C: Going backwards: the retroaldol reaction

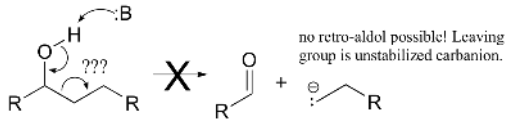
Although aldol reactions play a very important role in the formation of new carbon-carbon bonds in metabolic pathways, it is important to emphasize that they are also highly reversible: in most cases, the energy level of starting compounds and products are very close. This means that, depending on metabolic conditions, aldolases can also catalyze **retro-aldol** reactions (the reverse of aldol condensations, in which carbon-carbon bonds are *broken*). Recall that fructose 1,6-bisphosphate aldolase (section 13.3B) is active in the direction of sugar breakdown (glycolysis) as well as sugar synthesis (gluconeogenesis). In the glycolytic direction, the enzyme catalyzes - either by zinc cation or by imine/enamine mechanisms, depending on the organism - the retro-aldol cleavage of fructose bisphosphate into DHAP and GAP.



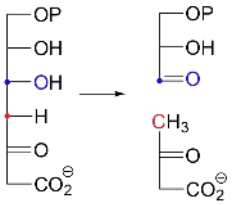
The mechanism is the exact reverse of the condensation reaction. Shown below is the mechanism for a Zn^{2+} - dependent (Type II) retroaldol cleavage. Notice that in the retroaldol reaction, the enolate intermediate is the *leaving group*, rather than the nucleophile.



The key thing to keep in mind when looking for a possible retro-aldol mechanism is that, when the carbon-carbon bond breaks, the electrons must have some place to go, where they will be stabilized by resonance. Generally, this means that there *must* be a carbonyl or imine group on the next carbon. If there is no adjacent carbonyl or imine group, the carbon-carbon bond is not free to break.



Here are two more examples of retro-aldol reactions. Bacterial carbohydrate metabolism involves this reversible, class I retro-aldol cleavage: (*Proc. Natl. Acad. Sci* **2001**, *98*, 3679).



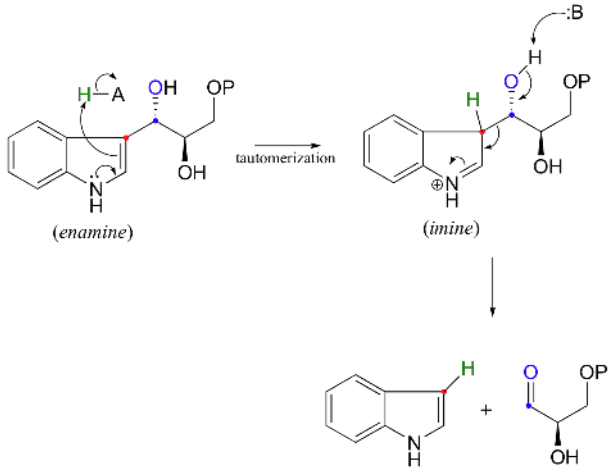
Template:ExampleStart

Exercise 13.6: Draw the structure of the enamine intermediate in the retroaldol reaction shown above.

Solution

Template:ExampleEnd

Another interesting example is the retro-aldol cleavage of indole-3-glycerol phosphate, a step in the biosynthesis of tryptophan.



Look carefully at this reaction - how is the leaving group stabilized? There is an imine group involved, but no participation by an enzymatic lysine. The imine is 'built into' the starting compound, available from the initial tautomerization of the cyclic enamine group in indole-3-glycerol phosphate.

Template:ExampleStart

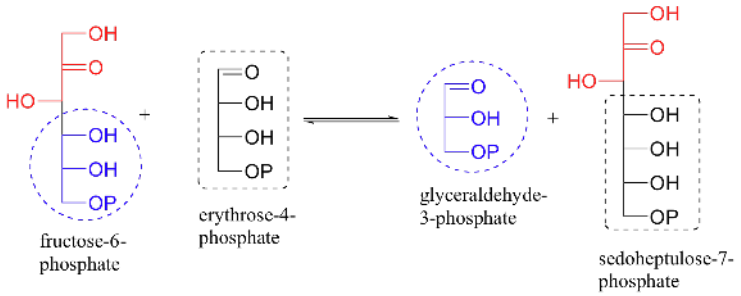
Exercise 13.7: Draw the reverse (aldol condensation) direction of the reaction above.

Solution

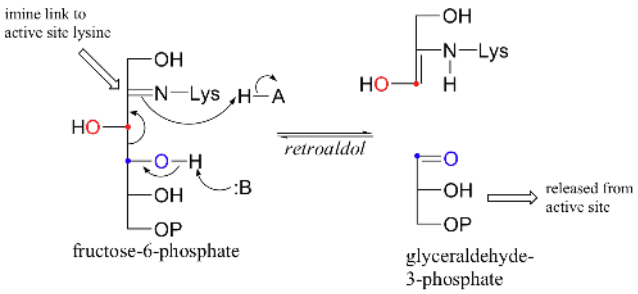
Template:ExampleEnd

13.3D: Going both ways: transaldolase

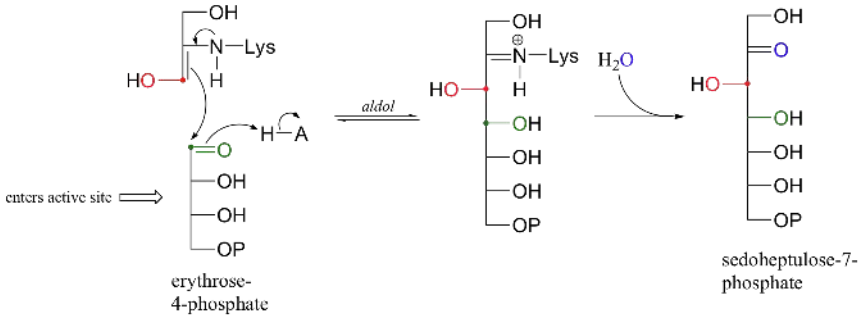
An enzyme called transaldolase, which is part of the 'pentose phosphate pathway' of carbohydrate metabolism, catalyzes an interesting combination of class I aldol and retro-aldol reactions. The overall reaction, which can proceed in either direction depending on metabolic requirements, converts 3- and 7-carbon sugars into 6- and 4-carbon sugars. Essentially, a 3-carbon unit breaks off from a ketone sugar (ketose) and then is condensed directly with an aldehyde sugar (aldose).



Let's follow the progress of the reaction in the left-to-right direction as depicted above. Because this is a class I aldolase, the first step is the formation of an imine linkage between the ketone carbon of fructose-6-phosphate (F6P) and a lysine group from the enzyme. The enzyme-substrate adduct then undergoes a retro-aldol step to free glyceralde-3-phosphate (GAP), which leaves the active site.



The second substrate, erythrose 4-phosphate (E4P), enters the active site, and an aldol condensation occurs between E4P and the 3-carbon fragment remaining from the cleavage of fructose-6-phosphate.



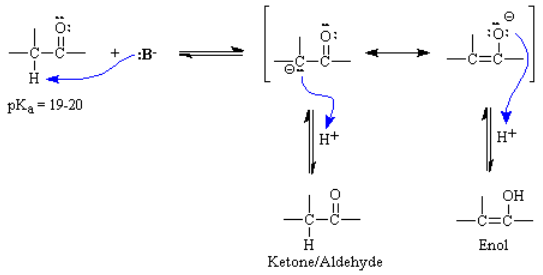
The final step is hydrolysis of the imine and subsequent dissociation of sedoheptulose 7-phosphate from the active site.

Organic Chemistry With a Biological Emphasis by Tim Soderberg (University of Minnesota, Morris)

13.15: Reactions at the α-Carbon in Biological Systems is shared under a not declared license and was authored, remixed, and/or curated by LibreTexts.

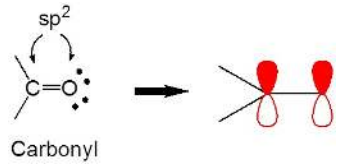
13.16: Keto-Enol Tautomers

Alkyl hydrogen atoms bonded to a carbon atom in a a (alpha) position relative to a carbonyl group display unusual acidity. While the pK_a values for alkyl C-H bonds is typically on the order of 40-50, pK_a values for these alpha hydrogens is more on the order of 19-20. This can most easily be explained by resonance stabilization of the product carbanion, as illustrated in the diagram below.

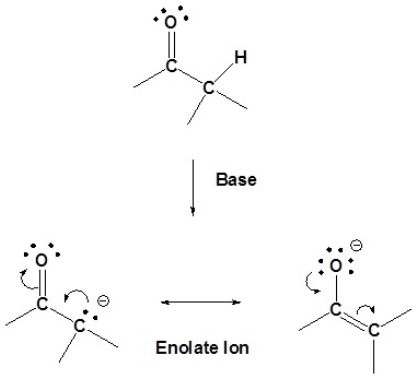


In the presence of a proton source, the product can either revert back into the starting ketone or aldehyde or can form a new product, the enol. The equilibrium reaction between the ketone or aldehyde and the enol form is commonly referred to as "keto-enol tautomerism". The ketone or aldehyde is generally strongly favored in this reaction.

Because carbonyl groups are sp^2 hybridized the carbon and oxygen both have unhybridized p orbitals which can overlap to form the C=O π bond.



The presence of these overlapping p orbitals gives α hydrogens (Hydrogens on carbons adjacent to carbonyls) special properties. In particular, α hydrogens are weakly acidic because the conjugate base, called an enolate, is stabilized though conjugation with the π orbitals of the carbonyl. The effect of the carbonyl is seen when comparing the pK_a for the α hydrogens of aldehydes (~16-18), ketones (~19-21), and esters (~23-25) to the pK_a of an alkane (~50).

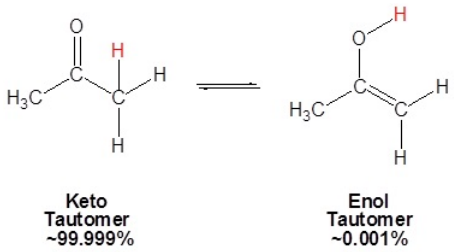


Of the two resonance structures of the enolate ion the one which places the negative charge on the oxygen is the most stable. This is because the negative change will be better stabilized by the greater electronegativity of the oxygen.

Keto-enol Tautomerism

Because of the acidity of α hydrogens carbonyls undergo keto-enol tautomerism. Tautomers are rapidly interconverted constitutional isomers, usually distinguished by a different bonding location for a labile hydrogen atom and a differently located double bond. The equilibrium between tautomers is not only rapid under normal conditions, but it often strongly favors one of the isomers (acetone, for example, is 99.999% keto tautomer). Even in such one-sided equilibria, evidence for the presence of the

minor tautomer comes from the chemical behavior of the compound. Tautomeric equilibria are catalyzed by traces of acids or bases that are generally present in most chemical samples.



Keto Tautomer ~99.999% **Enol Tautomer ~0.001%**

Contributors

Prof. Steven Farmer (Sonoma State University)

- Clarke Earley (Department of Chemistry, Kent State University Stark Campus)

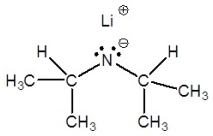
13.16: Keto-Enol Tautomers is shared under a not declared license and was authored, remixed, and/or curated by LibreTexts.

- **Acidity of Alpha Hydrogens & Keto-enol Tautomerism** by Clarke Earley, Steven Farmer is licensed CC BY 4.0.

13.17: Keto-Enol Interconversion

For alkylation reactions of enolate anions to be useful, these intermediates must be generated in high concentration in the absence of other strong nucleophiles and bases. The aqueous base conditions used for the aldol condensation are not suitable because the enolate anions of simple carbonyl compounds are formed in very low concentration, and hydroxide or alkoxide bases induce competing S_N2 and E2 reactions of alkyl halides. It is necessary, therefore, to achieve complete conversion of aldehyde or ketone reactants to their enolate conjugate bases by treatment with a very strong base ($pK_a > 25$) in a non-hydroxylic solvent before any alkyl halides are added to the reaction system. Some bases that have been used for enolate anion formation are: NaH (sodium hydride, $pK_a > 45$), $NaNH_2$ (sodium amide, $pK_a = 34$), and $LiN[CH(CH_3)_2]_2$ (lithium diisopropylamide, LDA, pK_a 36). Ether solvents like tetrahydrofuran (THF) are commonly used for enolate anion formation. With the exception of sodium hydride and sodium amide, most of these bases are soluble in THF. Certain other strong bases, such as alkyl lithium and Grignard reagents, cannot be used to make enolate anions because they rapidly and irreversibly add to carbonyl groups. Nevertheless, these very strong bases are useful in making soluble amide bases. In the preparation of lithium diisopropylamide (LDA), for example, the only other product is the gaseous alkane butane.





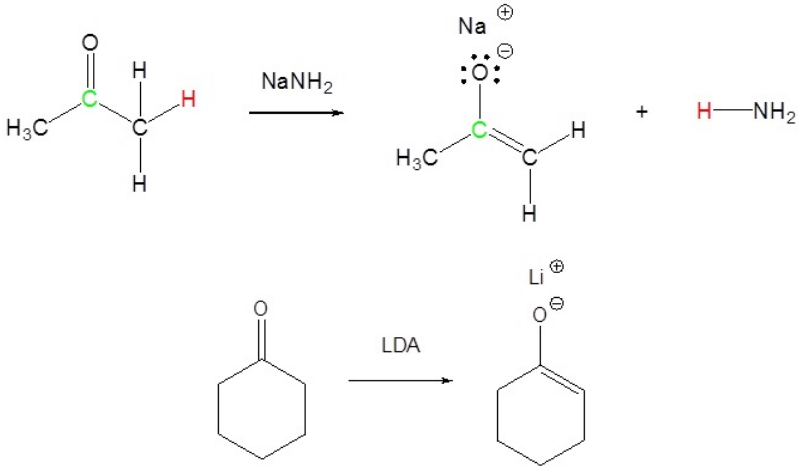
LDA



Sodium Amide

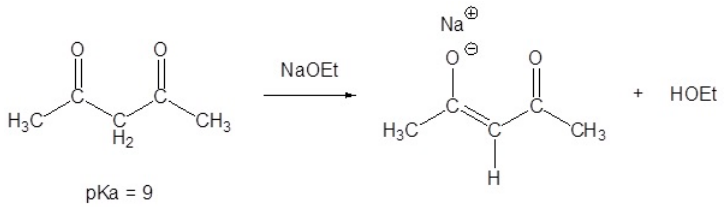
Because of its solubility in THF, LDA is a widely used base for enolate anion formation. In this application, one equivalent of diisopropylamine is produced along with the lithium enolate, but this normally does not interfere with the enolate reactions and is easily removed from the products by washing with aqueous acid. Although the reaction of carbonyl compounds with sodium hydride is heterogeneous and slow, sodium enolates are formed with the loss of hydrogen, and no other organic compounds are produced.

Examples

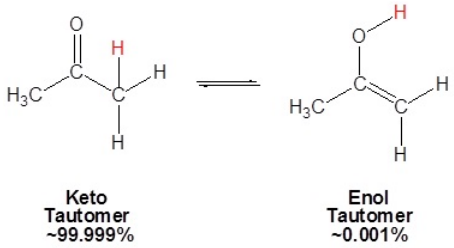


If the formed enolate is stabilized by more than one carbonyl it is possible to use a weaker base such as sodium ethoxide.

$NaOCH_2CH_3 = Na^+ {}^-OCH_2CH_3 = NaOEt$



Because of the acidity of α hydrogens, carbonyls undergo keto-enol tautomerism. Tautomers are rapidly interconverted constitutional isomers, usually distinguished by a different bonding location for a labile hydrogen atom and a differently located double bond. The equilibrium between tautomers is not only rapid under normal conditions, but it often strongly favors one of the isomers (acetone, for example, is 99.999% keto tautomer). Even in such one-sided equilibria, evidence for the presence of the minor tautomer comes from the chemical behavior of the compound. Tautomeric equilibria are catalyzed by traces of acids or bases that are generally present in most chemical samples.

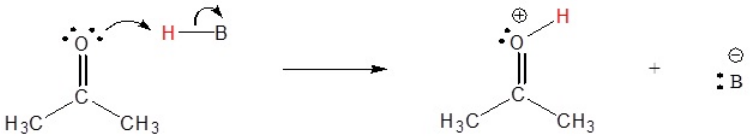


However under acidic and basic conditions the equilibrium can be shifted to the right

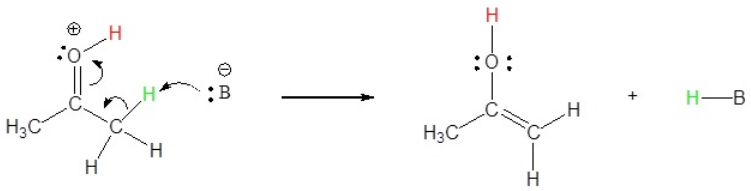
Mechanism for Enol Formation

Acid conditions

1) Protonation of the Carbonyl

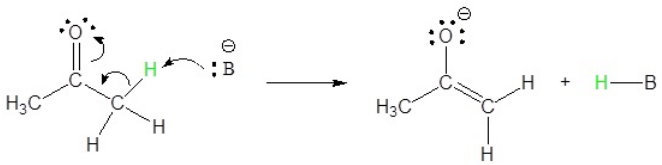


2) Enol formation

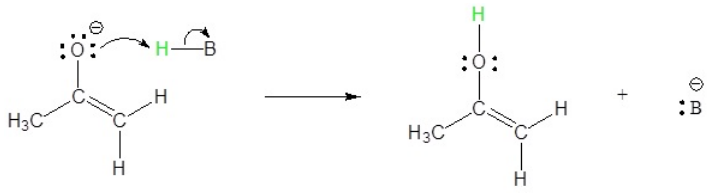


Basic conditions

1) Enolate formation



2) Protonation



Contributors

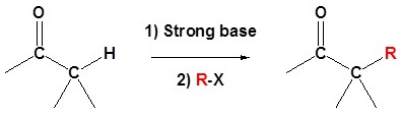
- William Reusch, Professor Emeritus (Michigan State U.), Virtual Textbook of Organic Chemistry
- Prof. Steven Farmer (Sonoma State University)

13.17: Keto-Enol Interconversion is shared under a not declared license and was authored, remixed, and/or curated by LibreTexts.

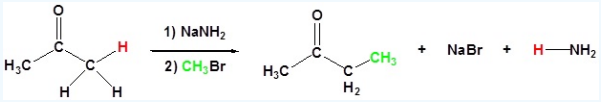
- **Synthesis of Enols and Enolates** is licensed CC BY-NC-SA 4.0.

13.18: How Enolate Ions and Enols React

Enolates can act as a nucleophile in S_n2 type reactions. The alpha alkylation reaction involves an α hydrogen being replaced with an alkyl group. This reaction is one of the more important for enolates because a carbon-carbon bond is formed. These alkylations are affected by the same limitations as S_n2 reactions previously discussed. Good leaving groups like chloride, bromide, iodide, tosylate, should be used. Also, secondary and tertiary leaving groups should not be used because of poor reactivity and possible competition with elimination reactions. Lastly, it is important to use a strong base, such as LDA or sodium amide, for this reaction. Using a weaker base such as hydroxide or an alkoxide leaves the possibility of multiple alkylation's occurring.

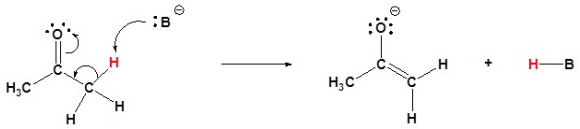


Example 13.18.1

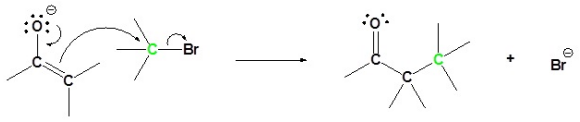


Mechanism

Stpe 1: Enolate formation

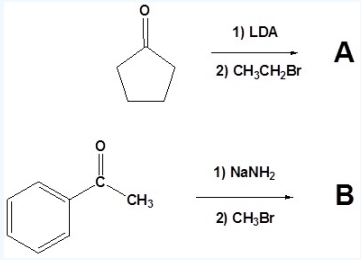


Step 2: S_n2 attack

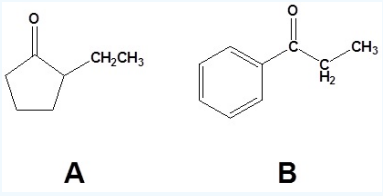


Example 13.18.2

Please write the structure of the product for the following reactions.



Solution



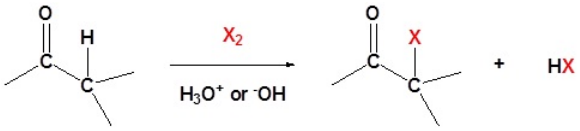
13.18: How Enolate Ions and Enols React is shared under a not declared license and was authored, remixed, and/or curated by LibreTexts.

- **Alpha Alkylation** by Steven Farmer is licensed CC BY 4.0.

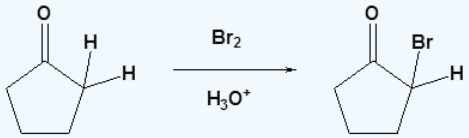
13.19: Halogenation of the α- Carbon and Aldehydes and Ketones

A carbonyl containing compound with α hydrogens can undergo a substitution reaction with halogens. This reaction comes about because of the tendency of carbonyl compounds to form enolates in basic condition and enols in acidic condition. In these cases even weak bases, such as the hydroxide anion, is sufficient enough to cause the reaction to occur because it is not necessary for a complete conversion to the enolate. For this reaction Cl_2, Br_2 or I_2 can be used as the halogens.

General reaction



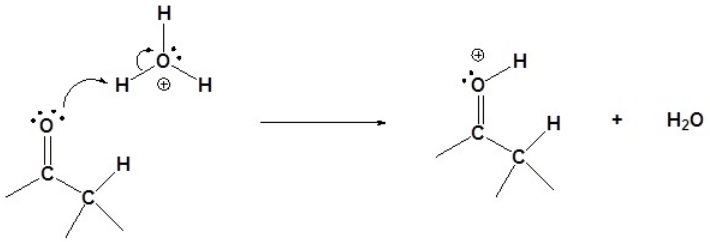
Example



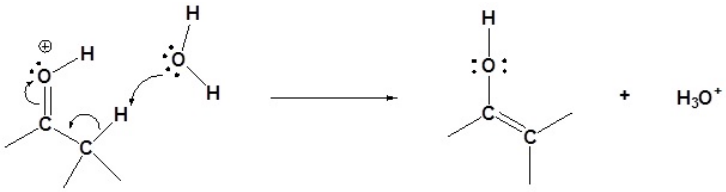
Acid Catalyzed Mechanism

Under acidic conditions the reaction occurs thought the formation of an enol which then reacts with the halogen.

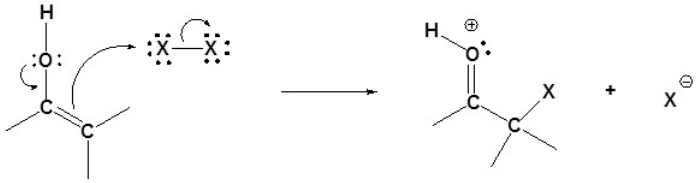
Step 1: Protonation of the carbonyl



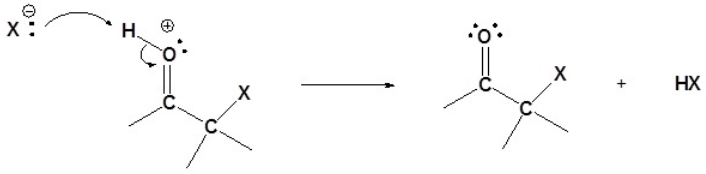
Step 2: Enol formation



Step 3: S_N2 attack



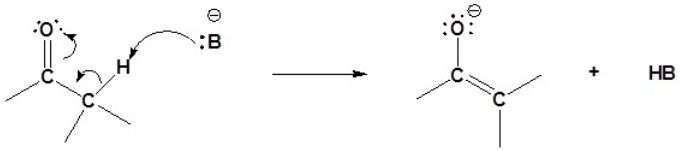
Step 4: Deprotonation



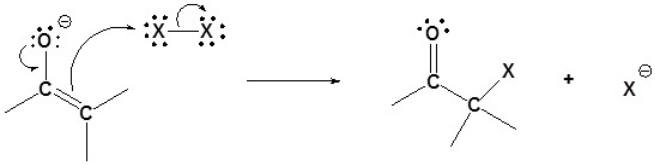
Base Catalyzed Mechanism

Under basic conditions the enolate forms and then reacts with the halogen. Note! This is base promoted and not base catalyzed because an entire equivalent of base is required.

Step 1: Enolate formation

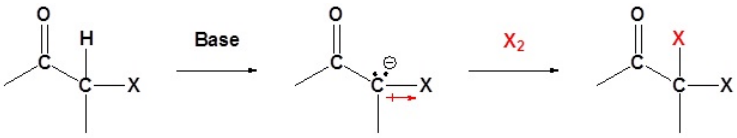


Step 2: S_N2 attack



Overreaction during base promoted α halogenation

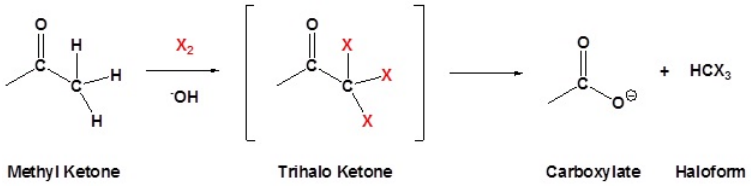
The fact that an electronegative halogen is placed on an α carbon means that the product of a base promoted α halogenation is actually more reactive than the starting material. The electron withdrawing effect of the halogen makes the α carbon even more acidic and therefor promotes further reaction. Because of this multiple halogenations can occur. This effect is exploited in the haloform reaction discussed later. If a monohalo product is required then acidic conditions are usually used.



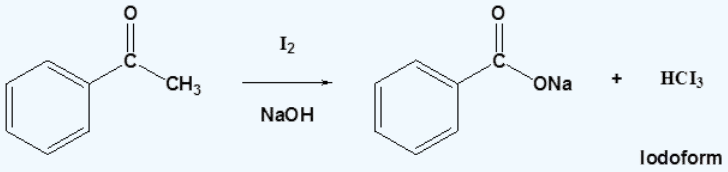
The Haloform Reaction

Methyl ketones typically undergo halogenation three times to give a trihalo ketone due to the increased reactivity of the halogenated product as discussed above. This trihalomethyl group is an effective leaving group due to the three electron withdrawing halogens and can be cleaved by a hydroxide anion to effect the haloform reaction. The product of this reaction is a carboxylate and a haloform molecule ($CHCl_3$, $CHBr_3$, CHI_3). Overall the haloform reaction represents an effective method for the conversion of methyl ketones to carboxylic acids. Typically, this reaction is performed using iodine because the subsequent iodoform (CHI_3) is a bright yellow precipitate which is easily filtered off.

General reaction

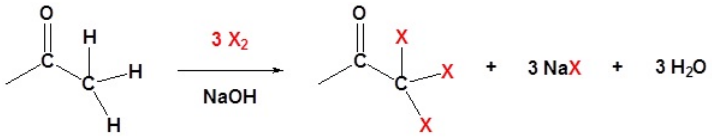


Example: The Haloform Reaction

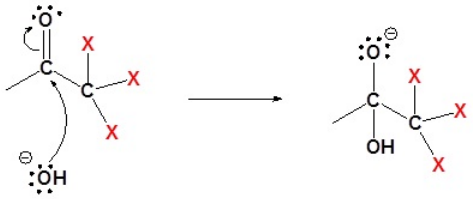


Mechanism

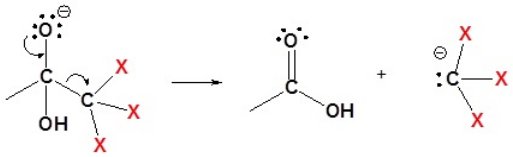
1) Formation of the trihalo species



2) Nulceophilic attack on the carbonyl carbon



3) Removal of the leaving group

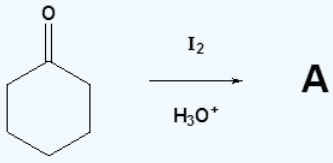


4) Deprotonation

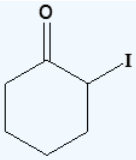


Exercise 13.19.1

Please draw the products of the following reactions



Answer



A

13.19: Halogenation of the α- Carbon and Aldehydes and Ketones is shared under a not declared license and was authored, remixed, and/or curated by LibreTexts.

- **Alpha Halogenation** by Steven Farmer is licensed CC BY 4.0.

SECTION OVERVIEW

13.20: Halogenation of the α- Carbon of Carboxylic Acids- The Hell-Volhard-Zelinski Reaction

Carbon is one of the most common elements on earth, and greatly influences everyday life. Common molecules containing carbon include carbon dioxide (CO_2) and methane (CH_4). Many scientists in a variety of fields study of carbon: biologists investigating the origins of life; oceanographers measuring the acidification of the oceans; and engineers developing diamond film tools. This article details the periodic properties of the carbon family and briefly discusses of the individual properties of carbon, silicon, germanium, tin, lead, and flerovium.

13.20: Halogenation of the α- Carbon of Carboxylic Acids- The Hell-Volhard-Zelinski Reaction is shared under a not declared license and was authored, remixed, and/or curated by LibreTexts.

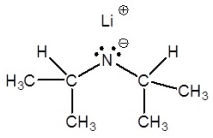
13.21: α- Halogenated Carbonyl Compounds Are Useful in Synthesis

13.21: α- Halogenated Carbonyl Compounds Are Useful in Synthesis is shared under a not declared license and was authored, remixed, and/or curated by LibreTexts.

13.22: Using LDA to Form an Enolate Ion

For alkylation reactions of enolate anions to be useful, these intermediates must be generated in high concentration in the absence of other strong nucleophiles and bases. The aqueous base conditions used for the aldol condensation are not suitable because the enolate anions of simple carbonyl compounds are formed in very low concentration, and hydroxide or alkoxide bases induce competing S_N2 and E2 reactions of alkyl halides. It is necessary, therefore, to achieve complete conversion of aldehyde or ketone reactants to their enolate conjugate bases by treatment with a very strong base ($pK_a > 25$) in a non-hydroxylic solvent before any alkyl halides are added to the reaction system. Some bases that have been used for enolate anion formation are: NaH (sodium hydride, $pK_a > 45$), $NaNH_2$ (sodium amide, $pK_a = 34$), and $LiN[CH(CH_3)_2]_2$ (lithium diisopropylamide, LDA, pK_a 36). Ether solvents like tetrahydrofuran (THF) are commonly used for enolate anion formation. With the exception of sodium hydride and sodium amide, most of these bases are soluble in THF. Certain other strong bases, such as alkyl lithium and Grignard reagents, cannot be used to make enolate anions because they rapidly and irreversibly add to carbonyl groups. Nevertheless, these very strong bases are useful in making soluble amide bases. In the preparation of lithium diisopropylamide (LDA), for example, the only other product is the gaseous alkane butane.





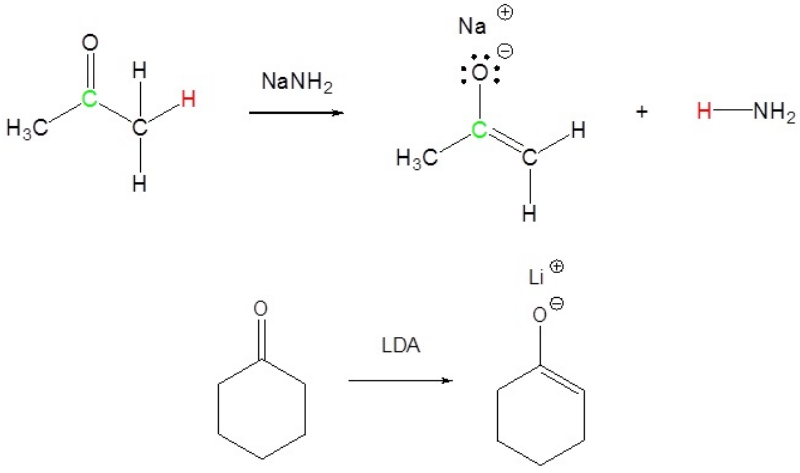
LDA



Sodium Amide

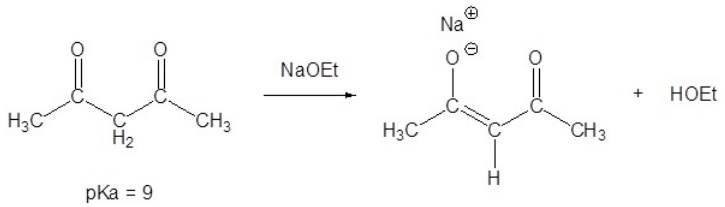
Because of its solubility in THF, LDA is a widely used base for enolate anion formation. In this application, one equivalent of diisopropylamine is produced along with the lithium enolate, but this normally does not interfere with the enolate reactions and is easily removed from the products by washing with aqueous acid. Although the reaction of carbonyl compounds with sodium hydride is heterogeneous and slow, sodium enolates are formed with the loss of hydrogen, and no other organic compounds are produced.

Examples

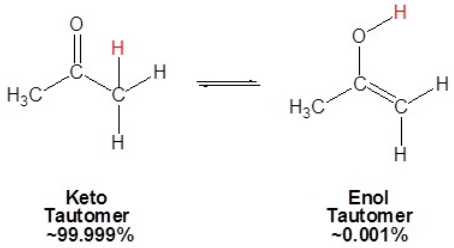


If the formed enolate is stabilized by more than one carbonyl it is possible to use a weaker base such as sodium ethoxide.

$NaOCH_2CH_3 = Na^+ {}^-OCH_2CH_3 = NaOEt$



Because of the acidity of α hydrogens, carbonyls undergo keto-enol tautomerism. Tautomers are rapidly interconverted constitutional isomers, usually distinguished by a different bonding location for a labile hydrogen atom and a differently located double bond. The equilibrium between tautomers is not only rapid under normal conditions, but it often strongly favors one of the isomers (acetone, for example, is 99.999% keto tautomer). Even in such one-sided equilibria, evidence for the presence of the minor tautomer comes from the chemical behavior of the compound. Tautomeric equilibria are catalyzed by traces of acids or bases that are generally present in most chemical samples.

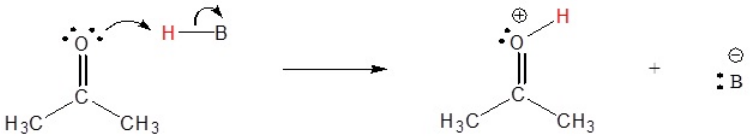


However under acidic and basic conditions the equilibrium can be shifted to the right

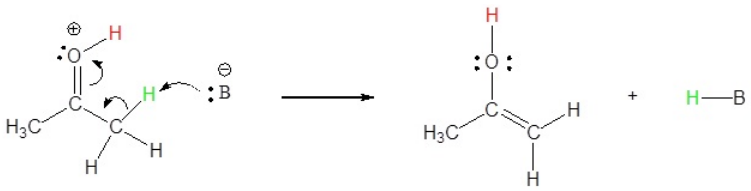
Mechanism for Enol Formation

Acid conditions

1) Protonation of the Carbonyl

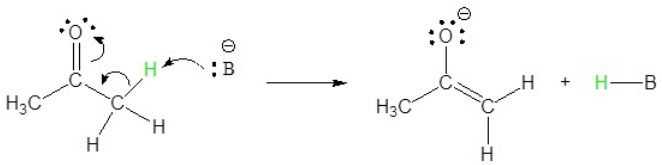


2) Enol formation

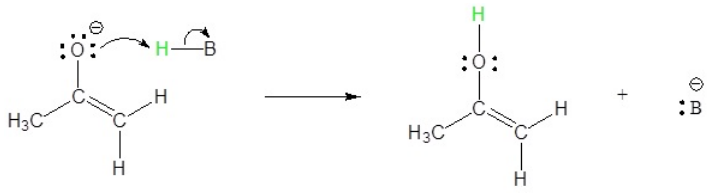


Basic conditions

1) Enolate formation



2) Protonation



Contributors

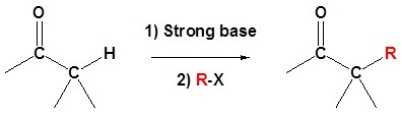
- William Reusch, Professor Emeritus (Michigan State U.), Virtual Textbook of Organic Chemistry
- Prof. Steven Farmer (Sonoma State University)

13.22: Using LDA to Form an Enolate Ion is shared under a not declared license and was authored, remixed, and/or curated by LibreTexts.

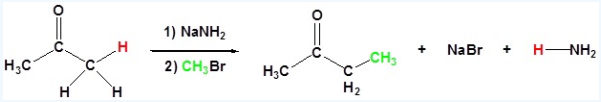
- **Synthesis of Enols and Enolates** is licensed CC BY-NC-SA 4.0.

13.23: Alkylating the α-Carbon of Carbonyl Compounds

Enolates can act as a nucleophile in S_n2 type reactions. The alpha alkylation reaction involves an α hydrogen being replaced with an alkyl group. This reaction is one of the more important for enolates because a carbon-carbon bond is formed. These alkylations are affected by the same limitations as S_n2 reactions previously discussed. Good leaving groups like chloride, bromide, iodide, tosylate, should be used. Also, secondary and tertiary leaving groups should not be used because of poor reactivity and possible competition with elimination reactions. Lastly, it is important to use a strong base, such as LDA or sodium amide, for this reaction. Using a weaker base such as hydroxide or an alkoxide leaves the possibility of multiple alkylation's occurring.

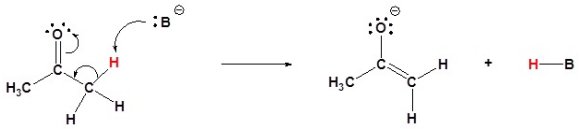


Example 13.23.1

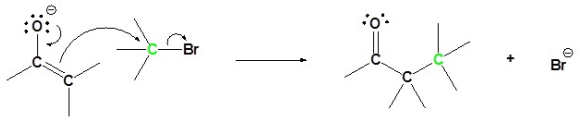


Mechanism

Stpe 1: Enolate formation

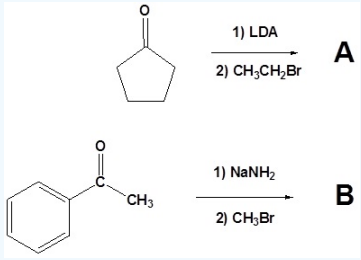


Step 2: S_n2 attack

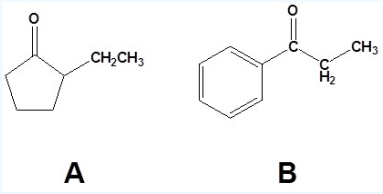


Example 13.23.2

Please write the structure of the product for the following reactions.



Solution



13.23: Alkylating the α-Carbon of Carbonyl Compounds is shared under a not declared license and was authored, remixed, and/or curated by LibreTexts.

- **Alpha Alkylation** by Steven Farmer is licensed CC BY 4.0.

CHAPTER OVERVIEW

14: Determing the Structure of Organic Compounds



Essential Organic Chemistry: 2nd Ed.
Bruice

Homework Problems
Homework Solutions

I II III IV V VI VII VIII IX X XI XII XIII XIV XV XVI XVII XVIII XIX XX XXI

Template:HideTOC

14: Determing the Structure of Organic Compounds is shared under a not declared license and was authored, remixed, and/or curated by LibreTexts.

CHAPTER OVERVIEW

15: The Organic Chemistry of Carbohydrates



Essential Organic Chemistry: 2nd Ed.
Bruice

Homework Problems
Homework Solutions

I II III IV V VI VII VIII IX X XI XII XIII XIV XV XVI XVII XVIII XIX XX XXI

Template:HideTOC

15.1: Classification of Carbohydrates
15.2: The D and L Notation
15.3: The Configurations of Aldoses
15.4: The Configurations of Ketoses
15.5: The Reactions of Monosaccharides in Basic Solutions
15.6: The Oxidation-Reduction Reactions of Monosaccharides
15.7: Monosaccharides form Crystalline Osazones
15.8: Lengthening the Chain- The Kiliani-Fischer Synthesis
15.9: Shortening the Chain- The Wohl Degradation
15.10: The Stereochemistry of Glucose- The Fischer Proof
15.11: Monosaccharides Form Cyclic Hemiacetals
15.12: Glucose is the Most Stable Aldohexose
15.13: Formation of Glycosides
15.14: The Anomeric Effect
15.15: Reducing and Nonreducing Sugars
15.16: Disaccharides
15.17: Polysaccharides
15.18: Some Naturally Occurring Products Derived from Carbohydrates
15.19: Carbohydrates on Cell Surfaces
15.20: Synthetic Sweeteners

15: The Organic Chemistry of Carbohydrates is shared under a not declared license and was authored, remixed, and/or curated by LibreTexts.

15.1: Classification of Carbohydrates

Carbohydrates

15.1: Classification of Carbohydrates is shared under a not declared license and was authored, remixed, and/or curated by LibreTexts.

15.2: The D and L Notation

Carbohydrates

15.2: The D and L Notation is shared under a not declared license and was authored, remixed, and/or curated by LibreTexts.

15.3: The Configurations of Aldoses

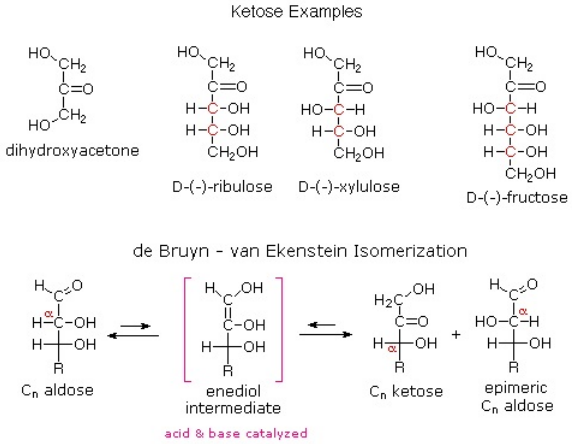
Carbohydrates

15.3: The Configurations of Aldoses is shared under a not declared license and was authored, remixed, and/or curated by LibreTexts.

15.4: The Configurations of Ketoses

If a monosaccharide has a carbonyl function on one of the inner atoms of the carbon chain it is classified as a ketose. Dihydroxyacetone may not be a sugar, but it is included as the ketose analog of glyceraldehyde. The carbonyl group is commonly found at C-2, as illustrated by the following examples (chiral centers are colored red). As expected, the carbonyl function of a ketose may be reduced by sodium borohydride, usually to a mixture of epimeric products. D-Fructose, the sweetest of the common natural sugars, is for example reduced to a mixture of D-glucitol (sorbitol) and D-mannitol, named after the aldohexoses from which they may also be obtained by analogous reduction. Mannitol is itself a common natural carbohydrate.

Although the ketoses are distinct isomers of the aldose monosaccharides, the chemistry of both classes is linked due to their facile interconversion in the presence of acid or base catalysts. This interconversion, and the corresponding epimerization at sites alpha to the carbonyl functions, occurs by way of an enediol tautomeric intermediate.



Because of base-catalyzed isomerizations of this kind, the Tollens' reagent is not useful for distinguishing aldoses from ketoses or for specific oxidation of aldoses to the corresponding aldonic acids. Oxidation by HOBr is preferred for the latter conversion.

Contributors

- Prof. Steven Farmer (Sonoma State University)
- William Reusch, Professor Emeritus (Michigan State U.), Virtual Textbook of Organic Chemistry

15.4: The Configurations of Ketoses is shared under a not declared license and was authored, remixed, and/or curated by LibreTexts.

- **Ketoses** is licensed CC BY-NC-SA 4.0.

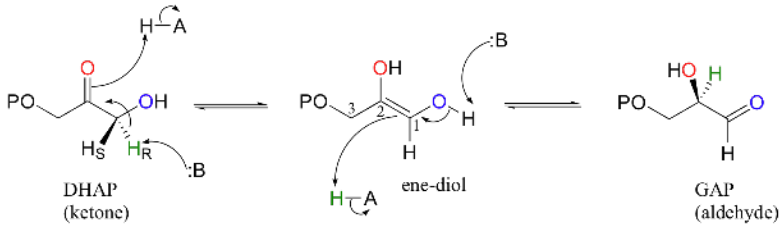
15.5: The Reactions of Monosaccharides in Basic Solutions

Enols, enolates, and enamines are reactive intermediates in many isomerization reactions. Isomerizations can involve either the interconversion of constitutional isomers, in which bond connectivity is altered, or of stereoisomers, where the stereochemical configuration is changed. Enzymes which interconvert constitutional isomers are called **isomerases**, while those which catalyze the interconversion of enantiomers and epimers are called **racemases** and **epimerases**, respectively.

13.2A: Carbonyl isomerization

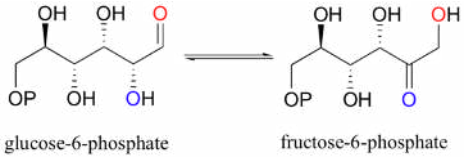
Two important chemical steps in the glycolytic pathway, catalyzed by the enzymes phosphoglucose isomerase and triose phosphate isomerase, involve successive keto-enol tautomerization steps. In both reactions, the location of a carbonyl group on a sugar molecule is shifted back and forth by a single carbon, as ketones are converted to aldehydes and back again - this is a conversion between two constitutional isomers.

Let's look first at the triosephosphate isomerase reaction, in the ketone to aldehyde direction. The ketone species, dihydroxyacetone phosphate (DHAP) is first converted to its enol tautomer with the assistance of an enzymatic acid/base pair (actually, this particular intermediate is known as an '**ene-*diol***' rather than an enol, because there are hydroxyl groups on both sides of the carbon-carbon double bond). The initial proton donor is positioned in the active site near the carbonyl carbon, and significantly lowers the pK_a of the alpha-proton.



The second step, leading to glyceraldehyde phosphate (GAP), is simply another tautomerization, this time in the reverse direction. However, because there happens to be a hydroxyl group on C_1, the carbonyl can form here as well as at C_2. Notice that DHAP is achiral while GAP is chiral, and that a new chiral center is introduced at C_2. The catalytic base abstracts the *pro-R* proton from *behind* the plane of the page, then gives the same proton back to C_2, again from behind the plane of the page.

In the phosphoglucose isomerase reaction, glucose-6-phosphate (an aldehyde sugar) and fructose-6-phosphate (a ketone sugar) are interconverted in a very similar fashion.

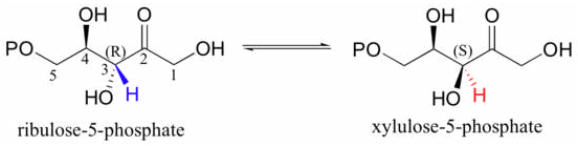


The enzyme ribose-5-phosphate isomerase (EC 5.3.1.6), which is active in both the Calvin cycle and the pentose phosphate pathway, catalyzes an analogous aldehyde-to-ketone isomerization between two five-carbon sugars.

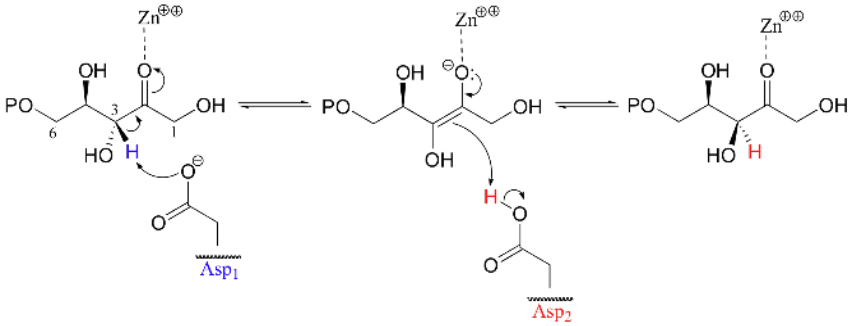
Template:exampleStart
Exercise 13.3: draw the ene-diol intermediate in the phosphoglucose isomerase reaction above.
Solution
Template:exampleEnd

13.2B: Stereoisomerization at chiral carbons

The enolate form of a carbonyl is a common intermediate in a type of stereoisomerization reaction known as an epimerization. Recall from section 3.7A that the term 'epimer' refers to a pair of diastereomers that differ at a single stereocenter. The five-carbon sugar phosphates ribulose-5-phosphate and xylulose-5-phosphate, for example, are epimers: they are identical except for their stereochemistry at C_3. A reaction in the Calvin cycle, which plants use to incorporate, or 'fix', the carbon atom from carbon dioxide into sugars, involves the interconversion of these two sugar phosphate epimers - in other words, inversion of configuration at C_3.



The reaction is simply a deprotonation at C_3 to form an enolate, followed by reprotonation to return to the ketone.



The key to epimerization is that *deprotonation and reprotonation occur at opposite sides of the planar, sp^2-hybridized intermediate*. In the epimerase reaction shown here, a coordinated pair of aspartate residues is located at opposite sides of the enzyme's active site. Asp_1, which is ionized at the start of the catalytic cycle, abstracts the C_3 proton from the *front* side of the plane of the page, converting C_3 from a chiral tetrahedral center to an achiral, planar group. When reprotonation occurs, it is Asp_2, on the *back* side of the plane of the page, which donates the proton, resulting in inversion of stereochemistry at C_3 (*J. Molec. Biol.* **2003**, *326*, 127-135).

Notice another thing about this epimerization reaction: the key intermediate is an enolate anion, stabilized by coordination to a zinc cation (a Lewis acid). Contrast this with the phosphoglucase isomerase reaction (section 13.2A), where stabilization of the key intermediate was achieved by proton donation to form a short-lived enol species.

There are many more examples of reactions in which the stereochemistry of an a-carbon in a carbonyl compound is inverted. The short polypeptides that form part of the peptidoglycan cell wall structure in bacteria contain some D-amino acids, which have the opposite stereochemistry at the a-carbon compared to the L-amino acids that are found almost exclusively in proteins. Enzymes called **amino acid racemases** catalyze the conversion between the L and D forms of these amino acids. While many amino acid racemases depend on the coenzyme pyridoxal phosphate to stabilize the key carbanion intermediate (we'll study these reactions in section 14.4B), others proceed through an enolate intermediate. Glutamate racemase, which converts L-glutamate to D-glutamate, is an example (*Biochemistry* **2001**, *40*, 6199). Although many mechanistic details are as yet unknown, it has been demonstrated that, at least for some of the cofactor-independent racemases, a pair of cysteine residues serves as the catalytic acid/base pair.

Template:exampleStart

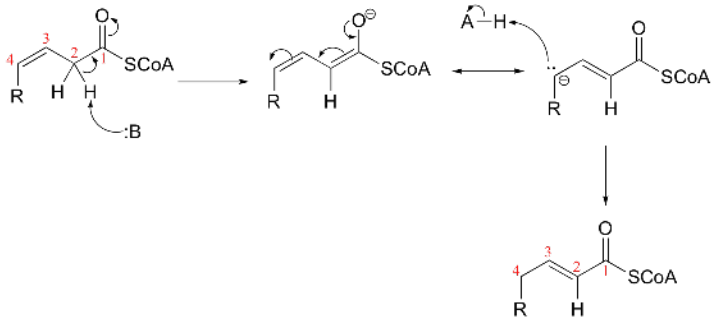
Exercise 13.4: Propose a likely mechanism for glutamate racemase, showing stereochemistry throughout.

Solution

Template:exampleEnd

13.2C: Alkene isomerization in the degradation of unsaturated fatty acids

The oxidation pathway for unsaturated fatty acids (in other words, fatty acids whose hydrocarbon chains contain one or more double bonds) involves the 'shuffling' of the position of carbon-carbon double bonds in the chain. This is accomplished by enoyl CoA isomerase, through an enolate intermediate. Here, the *cis* double bond between C_3 and C_4 is isomerized to a *trans* double bond between C_2 and C_3.



The catalytic acid and base groups are glutamate and/or aspartate residues (*J. Biol Chem* **2001**, *276*, 13622).

In section 15.3A, we will see a different example of an alkene isomerization reaction mechanism in which the key intermediate is a carbocation, rather than an enolate.

Organic Chemistry With a Biological Emphasis by Tim Soderberg (University of Minnesota, Morris)

15.5: The Reactions of Monosaccharides in Basic Solutions is shared under a not declared license and was authored, remixed, and/or curated by LibreTexts.

15.6: The Oxidation-Reduction Reactions of Monosaccharides

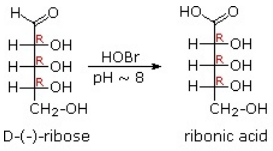
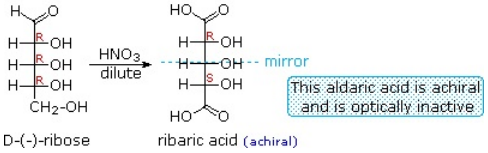
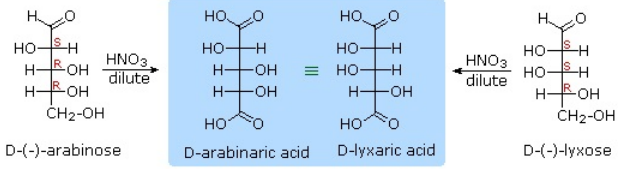
Overview

Emil Fischer made use of several key reactions in the course of his carbohydrate studies. These are described here, together with the information that each delivers.

Oxidation

As noted above, sugars may be classified as **reducing** or **non-reducing** based on their reactivity with **Tollens'**, **Benedict's** or **Fehling's** reagents. If a sugar is oxidized by these reagents it is called reducing, since the oxidant ($Ag^{(+)}$ or $Cu^{(+2)}$) is reduced in the reaction, as evidenced by formation of a silver mirror or precipitation of cuprous oxide. The Tollens' test is commonly used to detect aldehyde functions; and because of the facile interconversion of ketoses and aldoses under the basic conditions of this test, ketoses such as fructose also react and are classified as reducing sugars.

When the aldehyde function of an aldose is oxidized to a carboxylic acid the product is called an **aldonic acid**. Because of the 2º hydroxyl functions that are also present in these compounds, a mild oxidizing agent such as hypobromite must be used for this conversion (equation 1). If both ends of an aldose chain are oxidized to carboxylic acids the product is called an aldaric acid. By converting an aldose to its corresponding aldaric acid derivative, the ends of the chain become identical (this could also be accomplished by reducing the aldehyde to CH_2OH, as noted below). Such an operation will disclose any latent symmetry in the remaining molecule. Thus, ribose, xylose, allose and galactose yield achiral aldaric acids which are, of course, not optically active. The ribose oxidation is shown in equation 2 below.

1.	
2.	
3.	

Other aldose sugars may give identical chiral aldaric acid products, implying a unique configurational relationship. The examples of arabinose and lyxose shown in equation 3 above illustrate this result. Remember, a Fischer projection formula may be rotated by 180º in the plane of projection without changing its configuration.

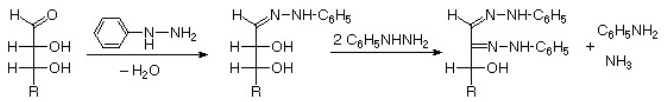
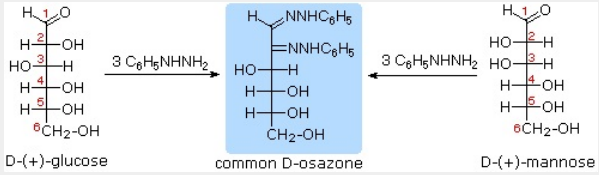
Reduction

Sodium borohydride reduction of an aldose makes the ends of the resulting **alditol** chain identical, $HOCH_2(CHOH)_nCH_2OH$, thereby accomplishing the same configurational change produced by oxidation to an aldaric acid. Thus, allitol and galactitol from

reduction of allose and galactose are achiral, and altrose and talose are reduced to the same chiral alditol. A summary of these redox reactions, and derivative nomenclature is given in the following table.

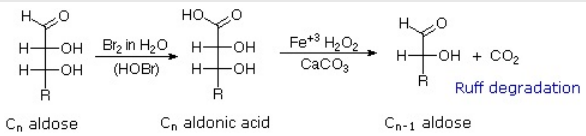
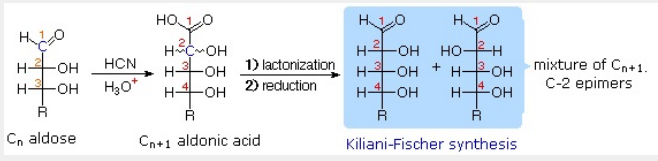
Derivatives of $HOCH_2(CHOH)_nCHO$		
HOBr Oxidation	——>	$HOCH_2(CHOH)_nCO_2H$ an Aldonic Acid
HNO_3 Oxidation	——>	$H_2OC(CHOH)_nCO_2H$ an Aldaric Acid
$NaBH_4$ Reduction	——>	$HOCH_2(CHOH)_nCH_2OH$ an Alditol

Osazone Formation

1.	
2.	

The osazone reaction was developed and used by Emil Fischer to identify aldose sugars differing in configuration only at the alpha-carbon. The upper equation shows the general form of the osazone reaction, which effects an alpha-carbon oxidation with formation of a bis-phenylhydrazone, known as an osazone. Application of the osazone reaction to D-glucose and D-mannose demonstrates that these compounds differ in configuration only at C-2.

Chain Shortening and Lengthening

1.	
2.	

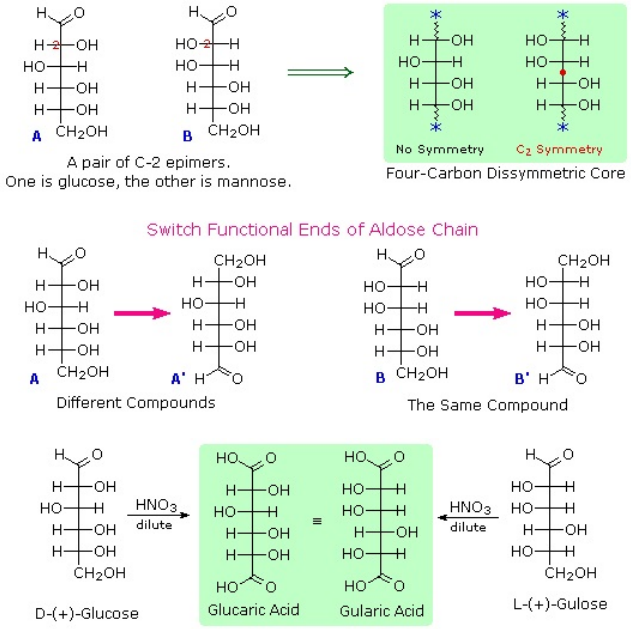
These two procedures permit an aldose of a given size to be related to homologous smaller and larger aldoses. The importance of these relationships may be seen in the array of aldose structures presented earlier, where the structural connections are given by the dashed blue lines. Thus Ruff degradation of the pentose arabinose gives the tetrose erythrose. Working in the opposite direction, a Kiliani-Fischer synthesis applied to arabinose gives a mixture of glucose and mannose. An alternative chain shortening procedure known as the Wohl degradation is essentially the reverse of the Kiliani-Fischer synthesis.

Fischer's train of logic in assigning the configuration of D-glucose

1. Ribose and arabinose (two well known pentoses) both gave erythrose on Ruff degradation. As expected, Kiliani-Fischer synthesis applied to erythrose gave a mixture of ribose and arabinose.

2. Oxidation of erythrose gave an achiral (optically inactive) aldaric acid. This defines the configuration of erythrose.
3. Oxidation of ribose gave an achiral (optically inactive) aldaric acid. This defines the configuration of both ribose and arabinose.
4. Ruff shortening of glucose gave arabinose, and Kiliani-Fischer synthesis applied to arabinose gave a mixture of glucose and mannose.
5. Glucose and mannose are therefore epimers at C-2, a fact confirmed by the common product from their osazone reactions.
6. A pair of structures for these epimers can be written, but which is glucose and which is mannose?

To determine which of these epimers was glucose, Fischer made use of the inherent C2 symmetry in the four-carbon dissymmetric core of one epimer **(B)**. This is shown in the following diagram by a red dot where the symmetry axis passes through the projection formula. Because of this symmetry, if the aldehyde and 1º-alcohol functions at the ends of the chain are exchanged, epimer **B** would be unchanged; whereas A would be converted to a different compound.



Fischer looked for and discovered a second aldohexose that represented the end group exchange for the epimer lacking the latent C2 symmetry **(A)**. This compound was L-(+)-gulose, and its exchange relationship to D-(+)-glucose was demonstrated by oxidation to a common aldaric acid product. The remaining epimer is therefore mannose.

Contributors

Prof. Steven Farmer (Sonoma State University)

William Reusch, Professor Emeritus (Michigan State U.), Virtual Textbook of Organic Chemistry

15.6: The Oxidation-Reduction Reactions of Monosaccharides is shared under a not declared license and was authored, remixed, and/or curated by LibreTexts.

- **Important Reactions** by William Reusch is licensed CC BY-NC-SA 4.0.

15.7: Monosaccharides form Crystalline Osazones

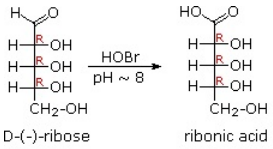
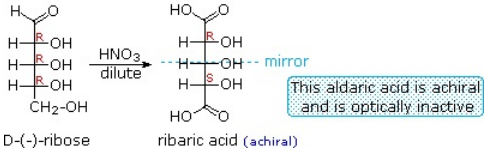
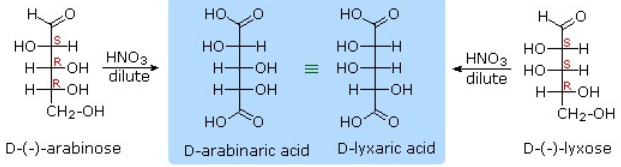
Overview

Emil Fischer made use of several key reactions in the course of his carbohydrate studies. These are described here, together with the information that each delivers.

Oxidation

As noted above, sugars may be classified as **reducing** or **non-reducing** based on their reactivity with **Tollens'**, **Benedict's** or **Fehling's** reagents. If a sugar is oxidized by these reagents it is called reducing, since the oxidant ($Ag^{(+)}$ or $Cu^{(+2)}$) is reduced in the reaction, as evidenced by formation of a silver mirror or precipitation of cuprous oxide. The Tollens' test is commonly used to detect aldehyde functions; and because of the facile interconversion of ketoses and aldoses under the basic conditions of this test, ketoses such as fructose also react and are classified as reducing sugars.

When the aldehyde function of an aldose is oxidized to a carboxylic acid the product is called an **aldonic acid**. Because of the 2º hydroxyl functions that are also present in these compounds, a mild oxidizing agent such as hypobromite must be used for this conversion (equation 1). If both ends of an aldose chain are oxidized to carboxylic acids the product is called an aldaric acid. By converting an aldose to its corresponding aldaric acid derivative, the ends of the chain become identical (this could also be accomplished by reducing the aldehyde to CH_2OH, as noted below). Such an operation will disclose any latent symmetry in the remaining molecule. Thus, ribose, xylose, allose and galactose yield achiral aldaric acids which are, of course, not optically active. The ribose oxidation is shown in equation 2 below.

1.	
2.	
3.	

Other aldose sugars may give identical chiral aldaric acid products, implying a unique configurational relationship. The examples of arabinose and lyxose shown in equation 3 above illustrate this result. Remember, a Fischer projection formula may be rotated by 180º in the plane of projection without changing its configuration.

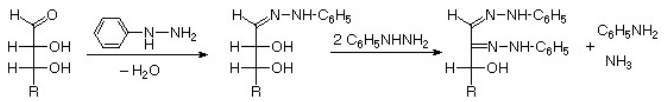
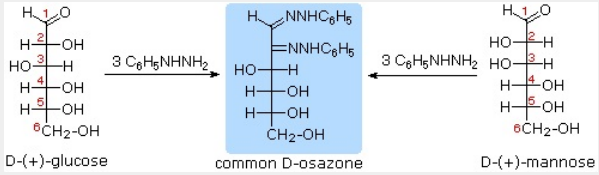
Reduction

Sodium borohydride reduction of an aldose makes the ends of the resulting **alditol** chain identical, $HOCH_2(CHOH)_nCH_2OH$, thereby accomplishing the same configurational change produced by oxidation to an aldaric acid. Thus, allitol and galactitol from

reduction of allose and galactose are achiral, and altrose and talose are reduced to the same chiral alditol. A summary of these redox reactions, and derivative nomenclature is given in the following table.

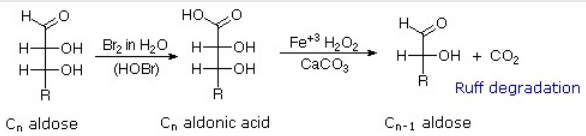
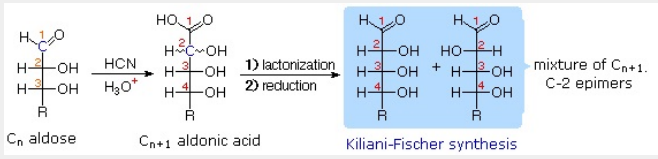
Derivatives of $HOCH_2(CHOH)_nCHO$		
HOBr Oxidation	——>	$HOCH_2(CHOH)_nCO_2H$ an Aldonic Acid
HNO_3 Oxidation	——>	$H_2OC(CHOH)_nCO_2H$ an Aldaric Acid
$NaBH_4$ Reduction	——>	$HOCH_2(CHOH)_nCH_2OH$ an Alditol

Osazone Formation

1.	
2.	

The osazone reaction was developed and used by Emil Fischer to identify aldose sugars differing in configuration only at the alpha-carbon. The upper equation shows the general form of the osazone reaction, which effects an alpha-carbon oxidation with formation of a bis-phenylhydrazone, known as an osazone. Application of the osazone reaction to D-glucose and D-mannose demonstrates that these compounds differ in configuration only at C-2.

Chain Shortening and Lengthening

1.	
2.	

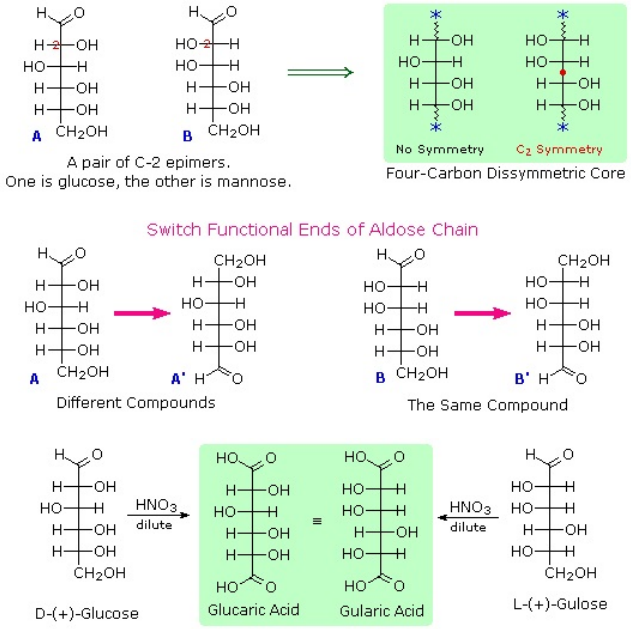
These two procedures permit an aldose of a given size to be related to homologous smaller and larger aldoses. The importance of these relationships may be seen in the array of aldose structures presented earlier, where the structural connections are given by the dashed blue lines. Thus Ruff degradation of the pentose arabinose gives the tetrose erythrose. Working in the opposite direction, a Kiliani-Fischer synthesis applied to arabinose gives a mixture of glucose and mannose. An alternative chain shortening procedure known as the Wohl degradation is essentially the reverse of the Kiliani-Fischer synthesis.

Fischer's train of logic in assigning the configuration of D-glucose

1. Ribose and arabinose (two well known pentoses) both gave erythrose on Ruff degradation. As expected, Kiliani-Fischer synthesis applied to erythrose gave a mixture of ribose and arabinose.

2. Oxidation of erythrose gave an achiral (optically inactive) aldaric acid. This defines the configuration of erythrose.
3. Oxidation of ribose gave an achiral (optically inactive) aldaric acid. This defines the configuration of both ribose and arabinose.
4. Ruff shortening of glucose gave arabinose, and Kiliani-Fischer synthesis applied to arabinose gave a mixture of glucose and mannose.
5. Glucose and mannose are therefore epimers at C-2, a fact confirmed by the common product from their osazone reactions.
6. A pair of structures for these epimers can be written, but which is glucose and which is mannose?

To determine which of these epimers was glucose, Fischer made use of the inherent C2 symmetry in the four-carbon dissymmetric core of one epimer **(B)**. This is shown in the following diagram by a red dot where the symmetry axis passes through the projection formula. Because of this symmetry, if the aldehyde and 1º-alcohol functions at the ends of the chain are exchanged, epimer **B** would be unchanged; whereas A would be converted to a different compound.



Fischer looked for and discovered a second aldohexose that represented the end group exchange for the epimer lacking the latent C2 symmetry **(A)**. This compound was L-(+)-gulose, and its exchange relationship to D-(+)-glucose was demonstrated by oxidation to a common aldaric acid product. The remaining epimer is therefore mannose.

Contributors

Prof. Steven Farmer (Sonoma State University)

William Reusch, Professor Emeritus (Michigan State U.), Virtual Textbook of Organic Chemistry

15.7: Monosaccharides form Crystalline Osazones is shared under a not declared license and was authored, remixed, and/or curated by LibreTexts.

- **Important Reactions** by William Reusch is licensed CC BY-NC-SA 4.0.

15.8: Lengthening the Chain- The Kiliani-Fischer Synthesis

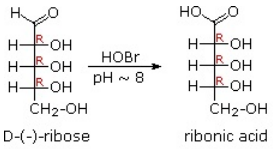
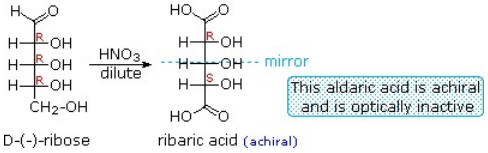
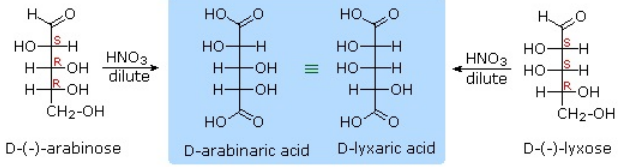
Overview

Emil Fischer made use of several key reactions in the course of his carbohydrate studies. These are described here, together with the information that each delivers.

Oxidation

As noted above, sugars may be classified as **reducing** or **non-reducing** based on their reactivity with **Tollens'**, **Benedict's** or **Fehling's** reagents. If a sugar is oxidized by these reagents it is called reducing, since the oxidant ($Ag^{(+)}$ or $Cu^{(+2)}$) is reduced in the reaction, as evidenced by formation of a silver mirror or precipitation of cuprous oxide. The Tollens' test is commonly used to detect aldehyde functions; and because of the facile interconversion of ketoses and aldoses under the basic conditions of this test, ketoses such as fructose also react and are classified as reducing sugars.

When the aldehyde function of an aldose is oxidized to a carboxylic acid the product is called an **aldonic acid**. Because of the 2º hydroxyl functions that are also present in these compounds, a mild oxidizing agent such as hypobromite must be used for this conversion (equation 1). If both ends of an aldose chain are oxidized to carboxylic acids the product is called an aldaric acid. By converting an aldose to its corresponding aldaric acid derivative, the ends of the chain become identical (this could also be accomplished by reducing the aldehyde to CH_2OH, as noted below). Such an operation will disclose any latent symmetry in the remaining molecule. Thus, ribose, xylose, allose and galactose yield achiral aldaric acids which are, of course, not optically active. The ribose oxidation is shown in equation 2 below.

1.	
2.	
3.	

Other aldose sugars may give identical chiral aldaric acid products, implying a unique configurational relationship. The examples of arabinose and lyxose shown in equation 3 above illustrate this result. Remember, a Fischer projection formula may be rotated by 180º in the plane of projection without changing its configuration.

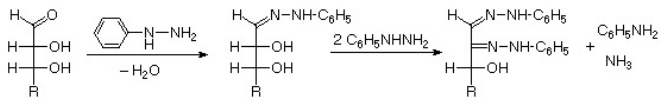
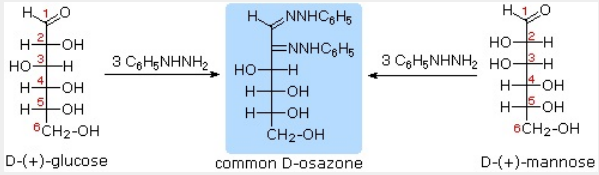
Reduction

Sodium borohydride reduction of an aldose makes the ends of the resulting **alditol** chain identical, $HOCH_2(CHOH)_nCH_2OH$, thereby accomplishing the same configurational change produced by oxidation to an aldaric acid. Thus, allitol and galactitol from

reduction of allose and galactose are achiral, and altrose and talose are reduced to the same chiral alditol. A summary of these redox reactions, and derivative nomenclature is given in the following table.

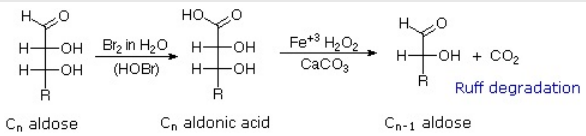
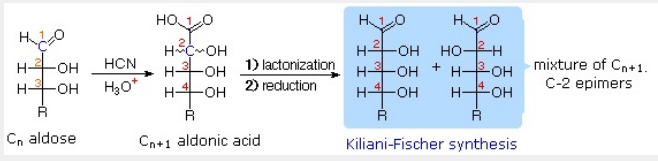
Derivatives of $HOCH_2(CHOH)_nCHO$		
HOBr Oxidation	——>	$HOCH_2(CHOH)_nCO_2H$ an Aldonic Acid
HNO_3 Oxidation	——>	$H_2OC(CHOH)_nCO_2H$ an Aldaric Acid
$NaBH_4$ Reduction	——>	$HOCH_2(CHOH)_nCH_2OH$ an Alditol

Osazone Formation

1.	
2.	

The osazone reaction was developed and used by Emil Fischer to identify aldose sugars differing in configuration only at the alpha-carbon. The upper equation shows the general form of the osazone reaction, which effects an alpha-carbon oxidation with formation of a bis-phenylhydrazone, known as an osazone. Application of the osazone reaction to D-glucose and D-mannose demonstrates that these compounds differ in configuration only at C-2.

Chain Shortening and Lengthening

1.	
2.	

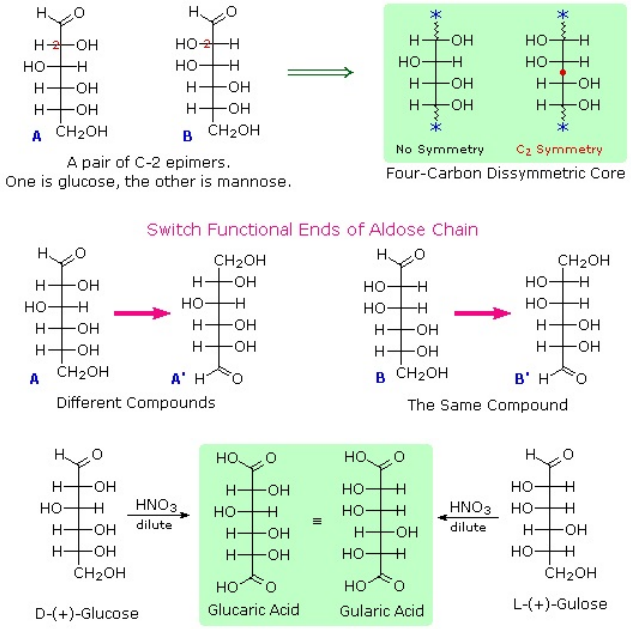
These two procedures permit an aldose of a given size to be related to homologous smaller and larger aldoses. The importance of these relationships may be seen in the array of aldose structures presented earlier, where the structural connections are given by the dashed blue lines. Thus Ruff degradation of the pentose arabinose gives the tetrose erythrose. Working in the opposite direction, a Kiliani-Fischer synthesis applied to arabinose gives a mixture of glucose and mannose. An alternative chain shortening procedure known as the Wohl degradation is essentially the reverse of the Kiliani-Fischer synthesis.

Fischer's train of logic in assigning the configuration of D-glucose

1. Ribose and arabinose (two well known pentoses) both gave erythrose on Ruff degradation. As expected, Kiliani-Fischer synthesis applied to erythrose gave a mixture of ribose and arabinose.

2. Oxidation of erythrose gave an achiral (optically inactive) aldaric acid. This defines the configuration of erythrose.
3. Oxidation of ribose gave an achiral (optically inactive) aldaric acid. This defines the configuration of both ribose and arabinose.
4. Ruff shortening of glucose gave arabinose, and Kiliani-Fischer synthesis applied to arabinose gave a mixture of glucose and mannose.
5. Glucose and mannose are therefore epimers at C-2, a fact confirmed by the common product from their osazone reactions.
6. A pair of structures for these epimers can be written, but which is glucose and which is mannose?

To determine which of these epimers was glucose, Fischer made use of the inherent C2 symmetry in the four-carbon dissymmetric core of one epimer **(B)**. This is shown in the following diagram by a red dot where the symmetry axis passes through the projection formula. Because of this symmetry, if the aldehyde and 1º-alcohol functions at the ends of the chain are exchanged, epimer **B** would be unchanged; whereas A would be converted to a different compound.



Fischer looked for and discovered a second aldohexose that represented the end group exchange for the epimer lacking the latent C2 symmetry **(A)**. This compound was L-(+)-gulose, and its exchange relationship to D-(+)-glucose was demonstrated by oxidation to a common aldaric acid product. The remaining epimer is therefore mannose.

Contributors

Prof. Steven Farmer (Sonoma State University)

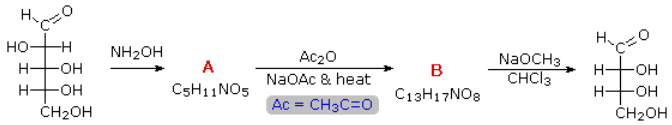
William Reusch, Professor Emeritus (Michigan State U.), Virtual Textbook of Organic Chemistry

15.8: Lengthening the Chain- The Kiliani-Fischer Synthesis is shared under a not declared license and was authored, remixed, and/or curated by LibreTexts.

- **Important Reactions** by William Reusch is licensed CC BY-NC-SA 4.0.

15.9: Shortening the Chain- The Wohl Degradation

The ability to shorten (degrade) an aldose chain by one carbon was an importanat tool in the structure elucidation of carbohydrates. This was commonly accomplished by the Ruff procedure. An interesting alternative technique, known as the **Wohl degradation** has also been used. The following equation illustrates the application of this procedure to the aldopentose, arabinose. Based on your knowledge of carbonyl chemistry, and considering that the Wohl degradation is in essence the reverse of the Kiliani-Fischer synthesis, you should be able to draw structural formulas for intermediates **A** and **B**. Using the zig-zag chain tool, draw suitable formulas in the drawing window on the left **without specifying substituent configurations**. When you are finished, check your answer by pressing the appropriate **Check Intermediate**button. A help screen is available for the drawing window.



Contributors

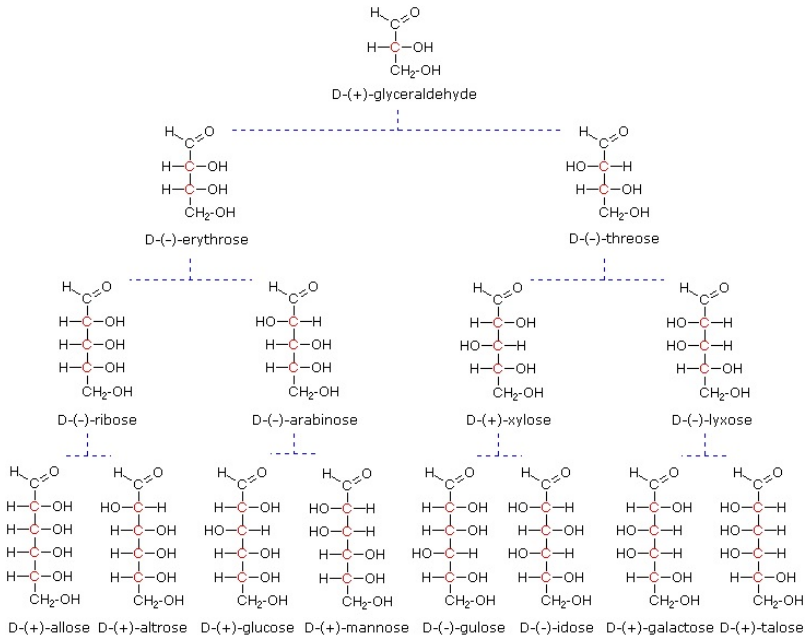
- William Reusch, Professor Emeritus (Michigan State U.), Virtual Textbook of Organic Chemistry

15.9: Shortening the Chain- The Wohl Degradation is shared under a not declared license and was authored, remixed, and/or curated by LibreTexts.

15.10: The Stereochemistry of Glucose- The Fischer Proof

The four chiral centers in glucose indicate there may be as many as sixteen (2^4) stereoisomers having this constitution. These would exist as eight diastereomeric pairs of enantiomers, and the initial challenge was to determine which of the eight corresponded to glucose. This challenge was accepted and met in 1891 by the German chemist Emil Fischer. His successful negotiation of the stereochemical maze presented by the aldohexoses was a logical tour de force, and it is fitting that he received the 1902 Nobel Prize for chemistry for this accomplishment. One of the first tasks faced by Fischer was to devise a method of representing the configuration of each chiral center in an unambiguous manner. To this end, he invented a simple technique for drawing chains of chiral centers, that we now call the Fischer projection formula.

At the time Fischer undertook the glucose project it was not possible to establish the **absolute configuration** of an enantiomer. Consequently, Fischer made an arbitrary choice for (+)-glucose and established a network of related aldose configurations that he called the **D**-family. The mirror images of these configurations were then designated the **L**-family of aldoses. To illustrate using present day knowledge, Fischer projection formulas and names for the D-aldose family (three to six-carbon atoms) are shown below, with the asymmetric carbon atoms (chiral centers) colored red.



The last chiral center in an aldose chain (farthest from the aldehyde group) was chosen by Fischer as the D / L designator site. If the hydroxyl group in the projection formula pointed to the right, it was defined as a member of the D-family. A left directed hydroxyl group (the mirror image) then represented the L-family. Fischer's initial assignment of the D-configuration had a 50:50 chance of being right, but all his subsequent conclusions concerning the relative configurations of various aldoses were soundly based. In 1951 x-ray fluorescence studies of (+)-tartaric acid, carried out in the Netherlands by Johannes Martin Bijvoet (pronounced "buy foot"), proved that Fischer's choice was correct.

It is important to recognize that the sign of a compound's specific rotation (an experimental number) does not correlate with its configuration (D or L). It is a simple matter to measure an optical rotation with a polarimeter. Determining an absolute configuration usually requires chemical interconversion with known compounds by stereospecific reaction paths.

Contributors

Prof. Steven Farmer (Sonoma State University)

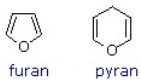
William Reusch, Professor Emeritus (Michigan State U.), Virtual Textbook of Organic Chemistry

15.10: The Stereochemistry of Glucose- The Fischer Proof is shared under a not declared license and was authored, remixed, and/or curated by LibreTexts.

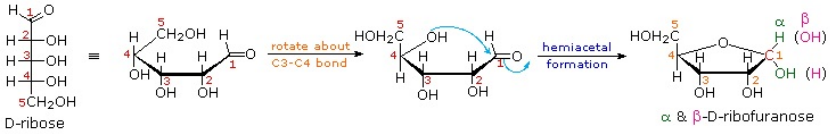
- **The Configuration of Glucose and Other Sugars** by William Reusch is licensed CC BY-NC-SA 4.0.

15.11: Monosaccharides Form Cyclic Hemiacetals

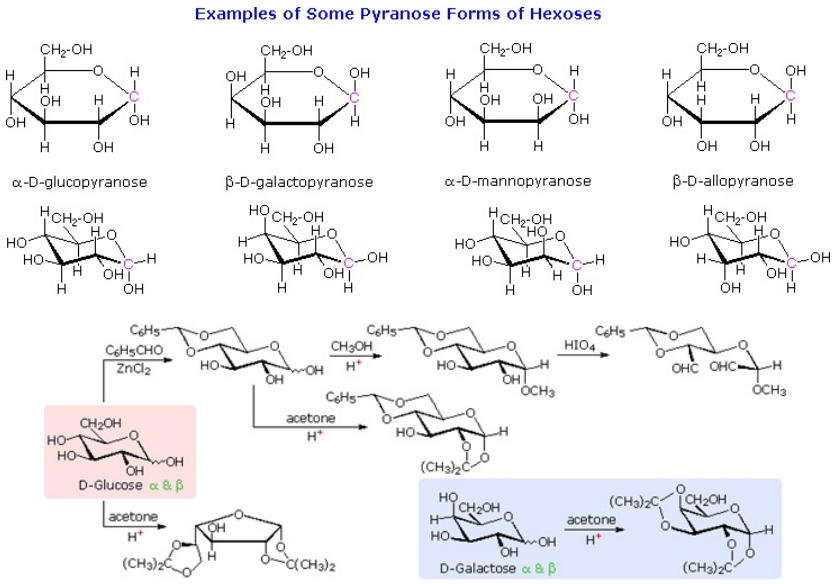
As noted above, the preferred structural form of many monosaccharides may be that of a cyclic hemiacetal. Five and six-membered rings are favored over other ring sizes because of their low angle and eclipsing strain. Cyclic structures of this kind are termed furanose (five-membered) or pyranose (six-membered), reflecting the ring size relationship to the common heterocyclic compounds furan and pyran shown on the right.



Ribose, an important aldopentose, commonly adopts a furanose structure, as shown in the following illustration. By convention for the D-family, the five-membered furanose ring is drawn in an edgewise projection with the ring oxygen positioned away from the viewer. The anomeric carbon atom (colored red here) is placed on the right. The upper bond to this carbon is defined as beta, the lower bond then is alpha.



The cyclic pyranose forms of various monosaccharides are often drawn in a flat projection known as a Haworth formula, after the British chemist, Norman Haworth. As with the furanose ring, the anomeric carbon is placed on the right with the ring oxygen to the back of the edgewise view. In the D-family, the alpha and beta bonds have the same orientation defined for the furanose ring (beta is up & alpha is down). These Haworth formulas are convenient for displaying stereochemical relationships, but do not represent the true shape of the molecules. We know that these molecules are actually puckered in a fashion we call a chair conformation. Examples of four typical pyranose structures are shown below, both as Section 3.8: Fischer and Haworth projections and as the more representative chair conformers. The anomeric carbons are colored red.



The size of the cyclic hemiacetal ring adopted by a given sugar is not constant, but may vary with substituents and other structural features. Aldolhexoses usually form pyranose rings and their pentose homologs tend to prefer the furanose form, but there are many counter examples. The formation of acetal derivatives illustrates how subtle changes may alter this selectivity. A pyranose structure for D-glucose is drawn in the rose-shaded box on the left. Acetal derivatives have been prepared by acid-catalyzed reactions with benzaldehyde and acetone. As a rule, benzaldehyde forms six-membered cyclic acetals, whereas acetone prefers to form five-membered acetals. The top equation shows the formation and some reactions of the 4,6-O-benzylidene acetal, a commonly employed protective group. A methyl glycoside derivative of this compound (see below) leaves the C-2 and C-3 hydroxyl groups

exposed to reactions such as the periodic acid cleavage, shown as the last step. The formation of an isopropylidene acetal at C-1 and C-2, center structure, leaves the C-3 hydroxyl as the only unprotected function. Selective oxidation to a ketone is then possible. Finally, direct di-O-isopropylidene derivatization of glucose by reaction with excess acetone results in a change to a furanose structure in which the C-3 hydroxyl is again unprotected. However, the same reaction with D-galactose, shown in the blue-shaded box, produces a pyranose product in which the C-6 hydroxyl is unprotected. Both derivatives do not react with Tollens' reagent. This difference in behavior is attributed to the cis-orientation of the C-3 and C-4 hydroxyl groups in galactose, which permits formation of a less strained five-membered cyclic acetal, compared with the trans-C-3 and C-4 hydroxyl groups in glucose. Derivatizations of this kind permit selective reactions to be conducted at different locations in these highly functionalized molecules.

Contributors

- Prof. Steven Farmer (Sonoma State University)
- William Reusch, Professor Emeritus (Michigan State U.), Virtual Textbook of Organic Chemistry

15.11: Monosaccharides Form Cyclic Hemiacetals is shared under a not declared license and was authored, remixed, and/or curated by LibreTexts.

- **Cyclic Forms of Monosaccharides** is licensed CC BY-NC-SA 4.0.

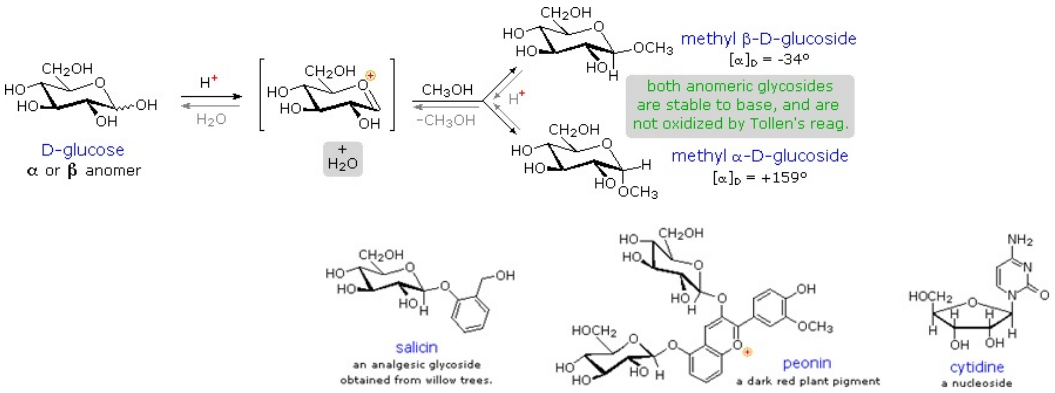
15.12: Glucose is the Most Stable Aldohexose

15.12: Glucose is the Most Stable Aldohexose is shared under a not declared license and was authored, remixed, and/or curated by LibreTexts.

15.13: Formation of Glycosides

Acetal derivatives formed when a monosaccharide reacts with an alcohol in the presence of an acid catalyst are called glycosides. This reaction is illustrated for glucose and methanol in the diagram below. In naming of glycosides, the "ose" suffix of the sugar name is replaced by "oside", and the alcohol group name is placed first. As is generally true for most acetals, glycoside formation involves the loss of an equivalent of water. The diether product is stable to base and alkaline oxidants such as Tollen's reagent. Since acid-catalyzed aldolization is reversible, glycosides may be hydrolyzed back to their alcohol and sugar components by aqueous acid.

The anomeric methyl glucosides are formed in an equilibrium ratio of 66% alpha to 34% beta. From the structures in the previous diagram, we see that pyranose rings prefer chair conformations in which the largest number of substituents are equatorial. In the case of glucose, the substituents on the beta-anomer are all equatorial, whereas the C-1 substituent in the alpha-anomer changes to axial. Since substituents on cyclohexane rings prefer an equatorial location over axial (methoxycyclohexane is 75% equatorial), the preference for alpha-glycopyranoside formation is unexpected, and is referred to as the anomeric effect.



Glycosides abound in biological systems. By attaching a sugar moiety to a lipid or benzenoid structure, the solubility and other properties of the compound may be changed substantially. Because of the important modifying influence of such derivatization, numerous enzyme systems, known as glycosidases, have evolved for the attachment and removal of sugars from alcohols, phenols and amines. Chemists refer to the sugar component of natural glycosides as the glycon and the alcohol component as the aglycon.

Two examples of naturally occurring glycosides and one example of an amino derivative are displayed above. Salicin, one of the oldest herbal remedies known, was the model for the synthetic analgesic aspirin. A large class of hydroxylated, aromatic oxonium cations called anthocyanins provide the red, purple and blue colors of many flowers, fruits and some vegetables. Peonin is one example of this class of natural pigments, which exhibit a pronounced pH color dependence. The oxonium moiety is only stable in acidic environments, and the color changes or disappears when base is added. The complex changes that occur when wine is fermented and stored are in part associated with glycosides of anthocyanins. Finally, amino derivatives of ribose, such as cytidine play important roles in biological phosphorylating agents, coenzymes and information transport and storage materials.

Contributors

Prof. Steven Farmer (Sonoma State University)

William Reusch, Professor Emeritus (Michigan State U.), Virtual Textbook of Organic Chemistry

15.13: Formation of Glycosides is shared under a not declared license and was authored, remixed, and/or curated by LibreTexts.

- **Glycosides** is licensed CC BY-NC-SA 4.0.

15.14: The Anomeric Effect

15.14: The Anomeric Effect is shared under a not declared license and was authored, remixed, and/or curated by LibreTexts.

15.15: Reducing and Nonreducing Sugars

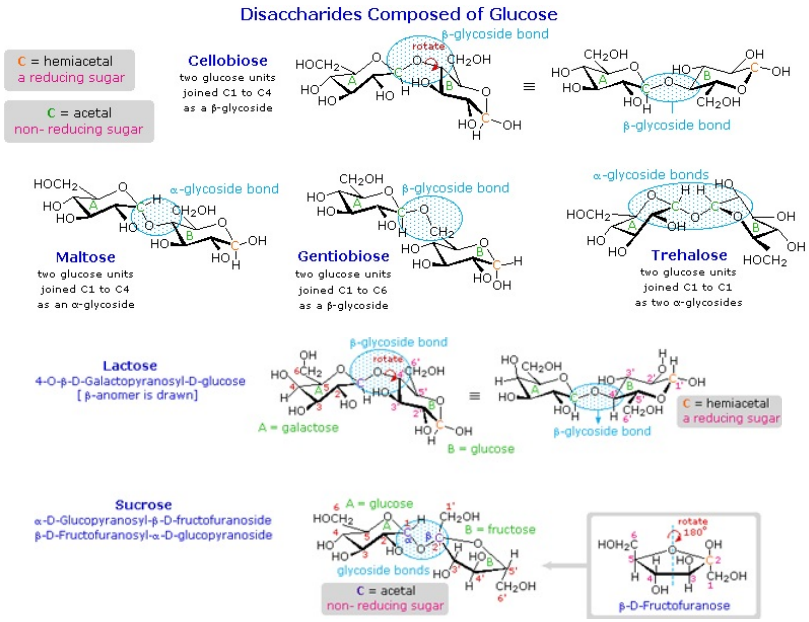
15.15: Reducing and Nonreducing Sugars is shared under a not declared license and was authored, remixed, and/or curated by LibreTexts.

15.16: Disaccharides

When the alcohol component of a glycoside is provided by a hydroxyl function on another monosaccharide, the compound is called a disaccharide. Four examples of disaccharides composed of two glucose units are shown in the following diagram. The individual glucopyranose rings are labeled A and B, and the glycoside bonding is circled in light blue. Notice that the glycoside bond may be alpha, as in maltose and trehalose, or beta as in cellobiose and gentiobiose. Acid-catalyzed hydrolysis of these disaccharides yields glucose as the only product. Enzyme-catalyzed hydrolysis is selective for a specific glycoside bond, so an alpha-glycosidase cleaves maltose and trehalose to glucose, but does not cleave cellobiose or gentiobiose. A beta-glycosidase has the opposite activity.

In order to draw a representative structure for cellobiose, one of the glucopyranose rings must be rotated by 180º, but this feature is often omitted in favor of retaining the usual perspective for the individual rings. The bonding between the glucopyranose rings in cellobiose and maltose is from the anomeric carbon in ring A to the C-4 hydroxyl group on ring B. This leaves the anomeric carbon in ring B free, so cellobiose and maltose both may assume alpha and beta anomers at that site (the beta form is shown in the diagram). Gentiobiose has a beta-glycoside link, originating at C-1 in ring A and terminating at C-6 in ring B. Its alpha-anomer is drawn in the diagram. Because cellobiose, maltose and gentiobiose are hemiacetals they are all reducing sugars (oxidized by Tollen's reagent). Trehalose, a disaccharide found in certain mushrooms, is a bis-acetal, and is therefore a non-reducing sugar. A systematic nomenclature for disaccharides exists, but as the following examples illustrate, these are often lengthy.

- Cellobiose : 4-O-β-D-Glucopyranosyl-D-glucose (the beta-anomer is drawn)
- Maltose : 4-O-α-D-Glucopyranosyl-D-glucose (the beta-anomer is drawn)
- Gentiobiose : 6-O-β-D-Glucopyranosyl-D-glucose (the alpha-anomer is drawn)
- Trehalose : α-D-Glucopyranosyl-α-D-glucopyranoside



Although all the disaccharides shown here are made up of two glucopyranose rings, their properties differ in interesting ways. Maltose, sometimes called malt sugar, comes from the hydrolysis of starch. It is about one third as sweet as cane sugar (sucrose), is easily digested by humans, and is fermented by yeast. Cellobiose is obtained by the hydrolysis of cellulose. It has virtually no taste, is indigestible by humans, and is not fermented by yeast. Some bacteria have beta-glucosidase enzymes that hydrolyze the glycosidic bonds in cellobiose and cellulose. The presence of such bacteria in the digestive tracts of cows and termites permits these animals to use cellulose as a food. Finally, it may be noted that trehalose has a distinctly sweet taste, but gentiobiose is bitter.

Disaccharides made up of other sugars are known, but glucose is often one of the components. Two important examples of such mixed disaccharides are displayed above. Lactose, also known as milk sugar, is a galactose-glucose compound joined as a beta-glycoside. It is a reducing sugar because of the hemiacetal function remaining in the glucose moiety. Many adults, particularly

those from regions where milk is not a dietary staple, have a metabolic intolerance for lactose. Infants have a digestive enzyme which cleaves the beta-glycoside bond in lactose, but production of this enzyme stops with weaning. Cheese is less subject to the lactose intolerance problem, since most of the lactose is removed with the whey. Sucrose, or cane sugar, is our most commonly used sweetening agent. It is a non-reducing disaccharide composed of glucose and fructose joined at the anomeric carbon of each by glycoside bonds (one alpha and one beta). In the formula shown here the fructose ring has been rotated 180º from its conventional perspective.

Contributors

Prof. Steven Farmer (Sonoma State University)

William Reusch, Professor Emeritus (Michigan State U.), Virtual Textbook of Organic Chemistry

---

15.16: Disaccharides is shared under a not declared license and was authored, remixed, and/or curated by LibreTexts.

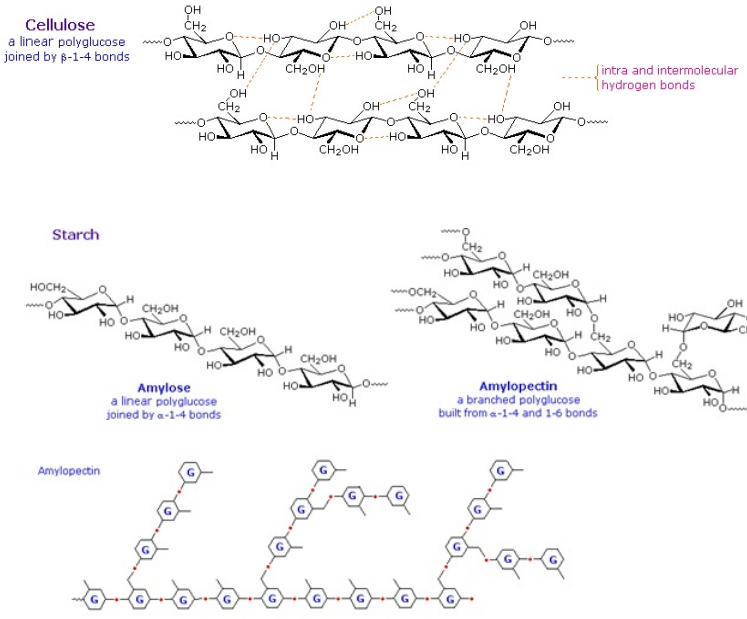
- **Disaccharides** is licensed CC BY-NC-SA 4.0.

15.17: Polysaccharides

As the name implies, polysaccharides are large high-molecular weight molecules constructed by joining monosaccharide units together by glycosidic bonds. They are sometimes called glycans. The most important compounds in this class, cellulose, starch and glycogen are all polymers of glucose. This is easily demonstrated by acid-catalyzed hydrolysis to the monosaccharide. Since partial hydrolysis of cellulose gives varying amounts of cellobiose, we conclude the glucose units in this macromolecule are joined by beta-glycoside bonds between C-1 and C-4 sites of adjacent sugars. Partial hydrolysis of starch and glycogen produces the disaccharide maltose together with low molecular weight dextrans, polysaccharides in which glucose molecules are joined by alpha-glycoside links between C-1 and C-6, as well as the alpha C-1 to C-4 links found in maltose. Polysaccharides built from other monosaccharides (e.g. mannose, galactose, xylose and arabinose) are also known, but will not be discussed here.

Over half of the total organic carbon in the earth's biosphere is in cellulose. Cotton fibers are essentially pure cellulose, and the wood of bushes and trees is about 50% cellulose. As a polymer of glucose, cellulose has the formula $(C_6H_{10}O_5)_n$ where n ranges from 500 to 5,000, depending on the source of the polymer. The glucose units in cellulose are linked in a linear fashion, as shown in the drawing below. The beta-glycoside bonds permit these chains to stretch out, and this conformation is stabilized by intramolecular hydrogen bonds. A parallel orientation of adjacent chains is also favored by intermolecular hydrogen bonds. Although an individual hydrogen bond is relatively weak, many such bonds acting together can impart great stability to certain conformations of large molecules. Most animals cannot digest cellulose as a food, and in the diets of humans this part of our vegetable intake functions as roughage and is eliminated largely unchanged. Some animals (the cow and termites, for example) harbor intestinal microorganisms that breakdown cellulose into monosaccharide nutrients by the use of beta-glycosidase enzymes.

Cellulose is commonly accompanied by a lower molecular weight, branched, amorphous polymer called *hemicellulose*. In contrast to cellulose, hemicellulose is structurally weak and is easily hydrolyzed by dilute acid or base. Also, many enzymes catalyze its hydrolysis. Hemicelluloses are composed of many D-pentose sugars, with xylose being the major component. Mannose and mannuronic acid are often present, as well as galactose and galacturonic acid.



Starch is a polymer of glucose, found in roots, rhizomes, seeds, stems, tubers and corms of plants, as microscopic granules having characteristic shapes and sizes. Most animals, including humans, depend on these plant starches for nourishment. The structure of starch is more complex than that of cellulose. The intact granules are insoluble in cold water, but grinding or swelling them in warm water causes them to burst.

The released starch consists of two fractions. About 20% is a water soluble material called amylose. Molecules of amylose are linear chains of several thousand glucose units joined by alpha C-1 to C-4 glycoside bonds. Amylose solutions are actually

dispersions of hydrated helical micelles. The majority of the starch is a much higher molecular weight substance, consisting of nearly a million glucose units, and called amylopectin. Molecules of amylopectin are branched networks built from C-1 to C-4 and C-1 to C-6 glycoside links, and are essentially water insoluble. Representative structural formulas for amylose and amylopectin are shown above. The branching in this diagram is exaggerated, since on average, branches only occur every twenty five glucose units.

Hydrolysis of starch, usually by enzymatic reactions, produces a syrupy liquid consisting largely of glucose. When cornstarch is the feedstock, this product is known as corn syrup. It is widely used to soften texture, add volume, prohibit crystallization and enhance the flavor of foods. Glycogen is the glucose storage polymer used by animals. It has a structure similar to amylopectin, but is even more highly branched (about every tenth glucose unit). The degree of branching in these polysaccharides may be measured by enzymatic or chemical analysis.

Contributors

Prof. Steven Farmer (Sonoma State University)

William Reusch, Professor Emeritus (Michigan State U.), Virtual Textbook of Organic Chemistry

---

15.17: Polysaccharides is shared under a not declared license and was authored, remixed, and/or curated by LibreTexts.

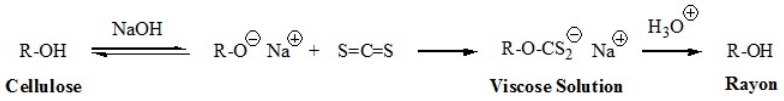
- **Polysaccharides** is licensed CC BY-NC-SA 4.0.

15.18: Some Naturally Occurring Products Derived from Carbohydrates

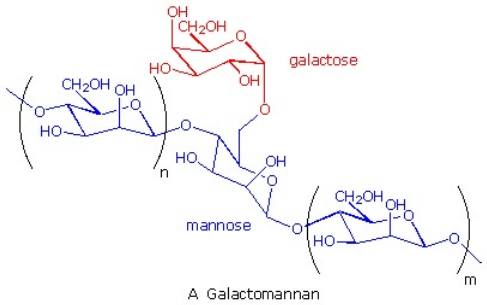
Cotton, probably the most useful natural fiber, is nearly pure cellulose. The manufacture of textiles from cotton involves physical manipulation of the raw material by carding, combing and spinning selected fibers. For fabrics the best cotton has long fibers, and short fibers or cotton dust are removed. Crude cellulose is also available from wood pulp by dissolving the lignan matrix surrounding it. These less desirable cellulose sources are widely used for making paper.

In order to expand the ways in which cellulose can be put to practical use, chemists have devised techniques for preparing solutions of cellulose derivatives that can be spun into fibers, spread into a film or cast in various solid forms. A key factor in these transformations are the three free hydroxyl groups on each glucose unit in the cellulose chain, --$[C_6H_7O(OH)_3]_n$--. Esterification of these functions leads to polymeric products having very different properties compared with cellulose itself.

- **Cellulose Nitrate**, first prepared over 150 years ago by treating cellulose with nitric acid, is the earliest synthetic polymer to see general use. The fully nitrated compound, --$[C_6H_7O(ONO_2)_3]_n$--, called guncotton, is explosively flammable and is a component of smokeless powder. Partially nitrated cellulose is called pyroxylin. Pyroxylin is soluble in ether and at one time was used for photographic film and lacquers. The high flammability of pyroxylin caused many tragic cinema fires during its period of use. Furthermore, slow hydrolysis of pyroxylin yields nitric acid, a process that contributes to the deterioration of early motion picture films in storage.
- **Cellulose Acetate**, --$[C_6H_7O(OAc)_3]_n$--, is less flammable than pyroxylin, and has replaced it in most applications. It is prepared by reaction of cellulose with acetic anhydride and an acid catalyst. The properties of the product vary with the degree of acetylation. Some chain shortening occurs unavoidably in the preparations. An acetone solution of cellulose acetate may be forced through a spinneret to generate filaments, called acetate rayon, that can be woven into fabrics.
- **Viscose Rayon**, is prepared by formation of an alkali soluble xanthate derivative that can be spun into a fiber that reforms the cellulose polymer by acid quenching. The following general equation illustrates these transformations. The product fiber is called **viscose rayon**.



Many complex polysaccharides are found in nature. The galactomannans, consisting of a mannose backbone with galactose side groups, are an interesting and useful example. A (1-4)-linked beta-D-mannose chain is adorned with 1-6-linked alpha-D-galactose units, as shown in the diagram below. The ratio of galactose to mannose usually ranges from 1:2 to 1:4. An important source of this substance is the guar bean, grown principally in northwestern India, and Pakistan. Altough guar protein is not of nutritional value to humans (guar means 'cow food' in Hindi), the bean is important as a source of guar gum, a galactomannan which forms a gel in water. The food industry uses this material as a stabilizer in ice cream, cream cheese and salad dressings.



A Galactomannan

Recently, guar gum has becomes an essential ingredient for mining oil and natural gas in a process called hydraulic fracturing. The demand for guar has increased to such a degree that the poor farmers in northwestern India have had their lives transformed by unexpected wealth.

Contributors

Prof. Steven Farmer (Sonoma State University)

William Reusch, Professor Emeritus (Michigan State U.), Virtual Textbook of Organic Chemistry

---

15.18: Some Naturally Occurring Products Derived from Carbohydrates is shared under a not declared license and was authored, remixed, and/or curated by LibreTexts.

- **Synthetic Modification of Cellulose** is licensed CC BY-NC-SA 4.0.

15.19: Carbohydrates on Cell Surfaces

15.19: Carbohydrates on Cell Surfaces is shared under a not declared license and was authored, remixed, and/or curated by LibreTexts.

15.20: Synthetic Sweeteners

Saccharin

15.20: Synthetic Sweeteners is shared under a not declared license and was authored, remixed, and/or curated by LibreTexts.

Index

Glossary

Sample Word 1 | Sample Definition 1

Detailed Licensing

Overview

Title: Chemistry 2300 (Budhi)

Webpages: 238

All licenses found:

- Undeclared: 100% (238 pages)

By Page

- Chemistry 2300 (Budhi) - *Undeclared*
  - Front Matter - *Undeclared*
    - TitlePage - *Undeclared*
    - InfoPage - *Undeclared*
    - Table of Contents - *Undeclared*
    - Licensing - *Undeclared*
  - 1: Electronic Structure and Covalent Bonding - *Undeclared*
    - 1.1: The Structure of an Atom - *Undeclared*
    - 1.2: How Electrons in an Atom are Distributed - *Undeclared*
    - 1.3: Ionic and Covalent Bonds - *Undeclared*
    - 1.4: How the Structure of a Compound is Represented - *Undeclared*
    - 1.5: Atomic Orbitals - *Undeclared*
    - 1.6: How atoms form Covalent Bonds - *Undeclared*
    - 1.7: How Single Bonds Are Formed in Organic Compounds - *Undeclared*
    - 1.8: How a Double Bond is Formed- The Bonds in Ethene - *Undeclared*
    - 1.9: How a Triple Bond is Formed- The Bonds in Ethyne - *Undeclared*
    - 1.10: Bonding in the Methyl Cation, the Methyl Radical, and the Methyl Anion - *Undeclared*
    - 1.11: The Bonds in Water - *Undeclared*
    - 1.12: The Bonds in Ammonia and in the Ammonium Ion - *Undeclared*
    - 1.13: The Bond in a Hydrogen Halide - *Undeclared*
    - 1.14: Summary- Hybridization, Bond Lengths, Bond Strengths, and Bond Angles - *Undeclared*
    - 1.15: The Dipole Moments of Molecules - *Undeclared*
    - 1.16: An Introduction to Acids and Bases - *Undeclared*
    - 1.17: pka and pH - *Undeclared*
    - 1.18: 1.18 Organic Acids and Bases - *Undeclared*
    - 1.19: How to Predict the Outcome of an Acid-Base Reaction - *Undeclared*
    - 1.20: How to Determine the Position of Equilibrium - *Undeclared*
    - 1.21: How the Structure of an Acid Affects its pka Value - *Undeclared*
    - 1.22: How Substituents Affect the Strength of an Acid - *Undeclared*
    - 1.23: An Introduction to Delocalized Electrons - *Undeclared*
    - 1.24: A Summary of the Factors that Determine Acid Strength - *Undeclared*
    - 1.25: How pH Affects the Structure of an Organic Compound - *Undeclared*
    - 1.26: Buffer Solutions - *Undeclared*
    - 1.27: Lewis Acids and Bases - *Undeclared*
  - 2: Acids and Bases - *Undeclared*
    - 2.1: An Introduction to Acids and Bases - *Undeclared*
    - 2.2: pka and pH - *Undeclared*
    - 2.3: Organic Acids and Bases - *Undeclared*
    - 2.4: How to Predict the Outcome of an Acid-Base Reaction - *Undeclared*
    - 2.5: How to Determine the Position of Equilibrium - *Undeclared*
    - 2.6: How the Structure of an Acid Affects its pka Value - *Undeclared*
    - 2.7: How pH Affects the Structure of an Organic Compound - *Undeclared*
    - 2.8: Buffer Solutions - *Undeclared*
    - 2.9: Lewis Acids and Bases - *Undeclared*
  - 3: An Introduction to Organic Compounds- Nomenclature, Physical Properties, and Representation of Structure - *Undeclared*
    - 3.1: How Alkyl Substituents Are Named - *Undeclared*
    - 3.2: The Nomenclature of Alkanes - *Undeclared*
    - 3.3: The Nomenclature of Cycloalkanes • Skeletal Structures - *Undeclared*
    - 3.4: The Nomenclature of Alkyl Halides - *Undeclared*

- 3.5: The Structures of Alkyl Halides, Alcohols, Ethers, and Amines - *Undeclared*
- 3.6: The Physical Properties of Alkanes, Alkyl Halides, Alcohols, Ethers, and Amines - *Undeclared*
- 3.7: Rotation Occurs About Carbon-Carbon Single Bonds - *Undeclared*
- 3.8: Some Cycloalkanes Have Angle Strain - *Undeclared*
- 3.9: Conformers of Cyclohexane - *Undeclared*
- 3.10: Conformers of Monosubstituted Cyclohexanes - *Undeclared*
- 3.11: Conformers of Disubstituted Cyclohexanes - *Undeclared*
- 3.12: Fused Cyclohexane Rings - *Undeclared*

- 4: Alkenes- Structure, Nomenclature, and an Introduction to Reactivity - *Undeclared*
  - 4.1: Molecular Formulas and the Degree of Unsaturation - *Undeclared*
  - 4.2: The Nomenclature of Alkenes - *Undeclared*
  - 4.3: The Structures of Alkenes - *Undeclared*
  - 4.4: Alkenes Can Have Cis and Trans Isomers - *Undeclared*
  - 4.5: Naming Alkenes Using the E Z System - *Undeclared*
  - 4.6: How Alkenes React (Curved Arrows Show the Flow of Electrons) - *Undeclared*
  - 4.7: A Reaction Coordinate Diagram Describes the Energy Changes That Take Place During a Reaction - *Undeclared*
- 5: The Reactions of Alkenes and Alkynes- An Introduction to Multistep Synthesis - *Undeclared*
  - 5.1: The Addition of a Hydrogen Halide to an Alkene - *Undeclared*
  - 5.2: Carbocation Stability Depends on the Number of Alkyl Groups Attached to the Positively Charged Carbon - *Undeclared*
  - 5.3: Electrophilic Addition Reactions Are Regioselective - *Undeclared*
  - 5.4: The Addition of Water to an Alkene - *Undeclared*
  - 5.5: The Addition of an Alcohol to an Alkene - *Undeclared*
  - 5.6: The Nomenclature of Alkynes - *Undeclared*
  - 5.7: The Structure of Alkynes - *Undeclared*
  - 5.8: The Physical Properties of Unsaturated Hydrocarbons - *Undeclared*
  - 5.9: The Addition of Hydrogen Halides and Addition of Halogens to an Alkyne - *Undeclared*
  - 5.10: The Addition of Hydrogen to Alkenes and Alkynes - *Undeclared*
  - 5.11: A Hydrogen Bonded to an sp Carbon is "Acidic" - *Undeclared*
  - 5.12: Synthesis Using Acetylide Ions - *Undeclared*
  - 5.13: An Introduction to Multistep Synthesis - *Undeclared*
- 6: Isomers and Stereochemistry - *Undeclared*
  - 6.1: Cis-Trans Isomers Result from Restricted Rotation - *Undeclared*
  - 6.2: A Chiral Object Has a Nonsuperimposable Mirror Image - *Undeclared*
  - 6.3: An Asymmetric Center Is a Cause of Chirality in a Molecule - *Undeclared*
  - 6.4: Isomers with One Asymmetric Center - *Undeclared*
  - 6.5: Asymmetric Centers and Stereocenters - *Undeclared*
  - 6.6: How to Draw Enantiomers - *Undeclared*
  - 6.7: Naming Enantiomers by the R,S System - *Undeclared*
  - 6.8: Chiral Compounds Are Optically Active - *Undeclared*
  - 6.9: How Specific Rotation is Measured - *Undeclared*
  - 6.10: Enantiomeric Excess - *Undeclared*
  - 6.11: Isomers with More than One Asymmetric Center - *Undeclared*
  - 6.12: Meso Compounds Have Asymmetric Centers but Are Optically Inactive - *Undeclared*
  - 6.13: How to Name Isomers with More than One Asymmetric Center - *Undeclared*
  - 6.14: Reactions of Compounds that Contain an Asymmetric Center - *Undeclared*
  - 6.15: Using Reactions that Do Not Break Bonds to an Asymmetric Center to Determine Relative Configurations - *Undeclared*
  - 6.16: How Enantiomers Can Be Separated - *Undeclared*
  - 6.17: Nitrogen and Phosphorus Atoms Can Be Asymmetric Centers - *Undeclared*
  - 6.18: Stereochemistry of Reactions- Regioselective, Stereoselective, and Stereospecific Reactions - *Undeclared*
  - 6.19: The Stereochemistry of Electrophilic addition Reactions of Alkenes - *Undeclared*
  - 6.20: The Stereochemistry of Enzyme-Catalyzed Reactions - *Undeclared*
  - 6.21: Enantiomers Can Be Distinguished by Biological Molecules - *Undeclared*
- 7: Delocalized Electrons and Their Effect on Stability, Reactivity, and pKa (Ultraviolet and Visible

Spectroscopy) - *Undeclared*
- 7.1: Delocalized Electrons Explain Benzene's Structure - *Undeclared*
- 7.2: The Bonding in Benzene - *Undeclared*
- 7.3: Resonance Contributors and the Resonance Hybrid - *Undeclared*
- 7.4: How to Draw Resonance Contributors - *Undeclared*
- 7.5: The Predicted Stabilities of Resonance Contributors - *Undeclared*
- 7.6: Delocalized Energy Is the Additional Stability Delocalized Electrons Give to a Compound - *Undeclared*
- 7.7: Examples That Show How Delocalized Electrons Affect Stability - *Undeclared*
- 7.8: A Molecular Orbital Description of Stability - *Undeclared*
- 7.9: How Delocalized Electrons Affect pKa Values - *Undeclared*
- 7.10: Delocalized Electrons Can Affect the Product of a Reaction - *Undeclared*
- 7.11: Thermodynamic Versus Kinetic Control of Reactions - *Undeclared*
- 7.12: The Diels-Adler Reaction Is a 1,4-Addition Reaction - *Undeclared*

8: Aromaticity- Reactions of Benzene and Substituted Benzenes - *Undeclared*
- 8.1: The Two Criteria for Aromaticity - *Undeclared*
- 8.2: Applying the Criteria for Aromaticity - *Undeclared*
- 8.3: Aromatic Heterocyclic Compounds - *Undeclared*
- 8.4: The Nomenclature of Monosubstituted Benzenes - *Undeclared*
- 8.5: How Benzene Reacts - *Undeclared*
- 8.6: The General Mechanism for Electrophilic Aromatic Substitution Reactions - *Undeclared*
- 8.7: Halogenation of Benzene - *Undeclared*
- 8.8: Nitration of Benzene - *Undeclared*
- 8.9: Sulfonation of Benzene - *Undeclared*
- 8.10: The Friedel-Crafts Acylation of Benzene - *Undeclared*
- 8.11: The Friedel-Crafts Alkylation of Benzene - *Undeclared*
- 8.12: The Nomenclature of Disubstituted and Polysubstituted Benzenes - *Undeclared*
- 8.13: The Effect of Substituents on Reactivity - *Undeclared*
- 8.14: The Effect of Substituents on Orientation - *Undeclared*
- 8.15: The Effect of Substituents on pKa - *Undeclared*

9: Substitution and Elimination Reactions of Alkyl Halides - *Undeclared*
- 9.1: How Alkyl Halides React - *Undeclared*
- 9.2: The Mechanism For an \(S_N2\) Reaction - *Undeclared*
- 9.3: Factors That Affect \(S_N2\) Reactions - *Undeclared*
- 9.4: The Mechanism for an \(S_N1\) Reaction - *Undeclared*
- 9.5: Factors That Affect \(S_N1\) Reactions - *Undeclared*
- 9.6: Comparing the \(S_N2\) and \(S_N1\) Reactions of Alkyl Halides - *Undeclared*
- 9.7: Elimination Reaction of Alkyl Halides - *Undeclared*
- 9.8: Products of Elimination Reactions - *Undeclared*
- 9.9: Comparing the E2 and E1 Reactions of Alkyl Halides - *Undeclared*
- 9.10: Does an Alkyl Halide Undergo SN2, E2 Reactions or SN1 Reactions? - *Undeclared*
- 9.11: Does an Alkyl Halide Undergo SN2/E2 Reactions or SN1/E1 Reactions? - *Undeclared*
- 9.12: Solvent Effects - *Undeclared*
- 9.13: Using Substitution Reactions to Synthesize Organic Compounds - *Undeclared*
- 9.14: Biological Methylating Reagents - *Undeclared*

10: Reactions of Alcohols, Amines, Ethers, and Epoxides - *Undeclared*
- 10.1: Nomenclature of Alcohols - *Undeclared*
- 10.2: Substitution Reactions of Alcohols - *Undeclared*
- 10.3: Elimination Reactions of Alcohols- Dehydration - *Undeclared*
- 10.4: Oxidation of Alcohols - *Undeclared*
- 10.5: Amines Do Not Undergo Substitution or Elimination Reactions - *Undeclared*
- 10.6: Nomenclature of Ethers - *Undeclared*
- 10.7: Nucleophilic Substitution Reactions of Ethers - *Undeclared*
- 10.8: Nucleophilic Substitution Reactions of Epoxides - *Undeclared*
- 10.9: Using Carbocation Stability to Determine the Carcinogenicity of an Arene Oxide - *Undeclared*

11: Carbonyl Compounds I- Reactions of Carboxylic Acids and Carboxylic Derivatives - *Undeclared*
- 11.1: The Nomenclature of Carboxylic Acids and Carboxylic Acid Derivatives - *Undeclared*

- 11.2: The Structures of Carboxylic Acids and Carboxylic Acid Derivatives - *Undeclared*
- 11.3: The Physical Properties of Carbonyl Compounds - *Undeclared*
- 11.4: Carboxylic Acids and Carboxylic Acid Derivatives found in Nature - *Undeclared*
- 11.5: How Carboxylic Acids and Carboxylic Acids Compounds React - *Undeclared*
- 11.6: Relative Reactivities of Carboxylic Acids and Carboxylic Acid Derivatives - *Undeclared*
- 11.7: Reactions of Acyl Halides - *Undeclared*
- 11.8: Reactions of Esters - *Undeclared*
- 11.9: Acid-Catalyzed Ester Hydrolysis - *Undeclared*
- 11.10: Soaps, Detergents, and Micelles - *Undeclared*
- 11.11: Reactions of Carboxylic Acids - *Undeclared*
- 11.12: Reactions of Amides - *Undeclared*
- 11.13: Acid-Catalyzed Amide Hydrolysis - *Undeclared*
- 11.14: The Synthesis of Carboxylic Acid Derivatives - *Undeclared*
- 11.15: Nitriles - *Undeclared*

12: Carbonyl Compounds II- Reactions of Aldehydes and Ketones • More Reactions of Carboxylic Acid Derivatives - *Undeclared*

- 12.1: The Nomenclature of Aldehydes and Ketones - *Undeclared*
- 12.2: The Relative Reactivities of Carbonyl Compounds - *Undeclared*
- 12.3: How Aldehydes and Ketones React - *Undeclared*
- 12.4: Gringard Reagents - *Undeclared*
- 12.5: Reactions of Carbonyl Compounds with Hydride Ion - *Undeclared*
- 12.6: Reactions of Aldehydes and Ketones with Amines - *Undeclared*
- 12.7: Reactions of Aldehydes and Ketones with Water - *Undeclared*
- 12.8: Reactions of Aldehydes and Ketones with Alcohols - *Undeclared*
- 12.9: Nucleophilic Addition to α, β- Unsaturated Carboxylic Acid Derivatives - *Undeclared*
- 12.10: Nucleophilic Addition to α, β- Unsaturated Carbonyl Compounds - *Undeclared*
- 12.11: Protecting Groups - *Undeclared*
- 12.12: Addition of Sulfur Nucleophiles - *Undeclared*
- 12.13: The Wittig Reaction Forms an Alkene - *Undeclared*
- 12.14: Stereochemistry of Nucleophilic Addition Reactions- Re and Si Faces - *Undeclared*
- 12.15: Designing a Synthesis VI- Disconnections, Synthons, and Synthetic Equivalents - *Undeclared*
- 12.16: Enzyme-Catalyzed Additions to α, β-Unsaturated Carbonyl Compounds - *Undeclared*

13: Carbonyl Compounds III- Reactions at the α- Carbon - *Undeclared*

- 13.1: Alkylation and Acylation of the α-Carbon Using an Enamine Intermediate - *Undeclared*
- 13.2: Alkylation of the β-Carbon- The Michael Reaction - *Undeclared*
- 13.3: An Aldol Addition Forms β-Hydroxaldehydes or β-Hydroxyketones - *Undeclared*
- 13.4: Dehydration of Aldol Addition Products Form α, β-Unsaturated Aldehydes and Ketones - *Undeclared*
- 13.5: The Crossed Aldol Addition - *Undeclared*
- 13.6: A Claisen Condensation Forms a β-Keto Ester - *Undeclared*
- 13.7: Other Crossen Condensations - *Undeclared*
- 13.8: Intramolecular Condensation and Addition Reactions - *Undeclared*
- 13.9: The Robinson Annulation - *Undeclared*
- 13.10: Carboxylic Acids with a Carbonyl Group at the 3-Position can be Decarboxylated - *Undeclared*
- 13.11: The Acidity of an α- Hydrogen - *Undeclared*
- 13.12: The Malonic Ester Synthesis- A Way to Synthesize a Carboxylic Acid - *Undeclared*
- 13.13: The Acetoacetic Ester Synthesis- A Way to Synthesize a Methyl Ketone - *Undeclared*
- 13.14: Designing a Synthesis VII- Making New Carbon-Carbon Bonds - *Undeclared*
- 13.15: Reactions at the α-Carbon in Biological Systems - *Undeclared*
- 13.16: Keto-Enol Tautomers - *Undeclared*
- 13.17: Keto-Enol Interconversion - *Undeclared*
- 13.18: How Enolate Ions and Enols React - *Undeclared*
- 13.19: Halogenation of the α- Carbon and Aldehydes and Ketones - *Undeclared*
- 13.20: Halogenation of the α- Carbon of Carboxylic Acids- The Hell-Volhard-Zelinski Reaction - *Undeclared*
- 13.21: α- Halogenated Carbonyl Compounds Are Useful in Synthesis - *Undeclared*
- 13.22: Using LDA to Form an Enolate Ion - *Undeclared*
- 13.23: Alkylating the α-Carbon of Carbonyl Compounds - *Undeclared*

- 14: Determing the Structure of Organic Compounds - *Undeclared*
- 15: The Organic Chemistry of Carbohydrates - *Undeclared*
  - 15.1: Classification of Carbohydrates - *Undeclared*
  - 15.2: The D and L Notation - *Undeclared*
  - 15.3: The Configurations of Aldoses - *Undeclared*
  - 15.4: The Configurations of Ketoses - *Undeclared*
  - 15.5: The Reactions of Monosaccharides in Basic Solutions - *Undeclared*
  - 15.6: The Oxidation-Reduction Reactions of Monosaccharides - *Undeclared*
  - 15.7: Monosaccharides form Crystalline Osazones - *Undeclared*
  - 15.8: Lengthening the Chain- The Kiliani-Fischer Synthesis - *Undeclared*
  - 15.9: Shortening the Chain- The Wohl Degradation - *Undeclared*
  - 15.10: The Stereochemistry of Glucose- The Fischer Proof - *Undeclared*
  - 15.11: Monosaccharides Form Cyclic Hemiacetals - *Undeclared*
  - 15.12: Glucose is the Most Stable Aldohexose - *Undeclared*
  - 15.13: Formation of Glycosides - *Undeclared*
  - 15.14: The Anomeric Effect - *Undeclared*
  - 15.15: Reducing and Nonreducing Sugars - *Undeclared*
  - 15.16: Disaccharides - *Undeclared*
  - 15.17: Polysaccharides - *Undeclared*
  - 15.18: Some Naturally Occurring Products Derived from Carbohydrates - *Undeclared*
  - 15.19: Carbohydrates on Cell Surfaces - *Undeclared*
  - 15.20: Synthetic Sweeteners - *Undeclared*
- Back Matter - *Undeclared*
  - Index - *Undeclared*
  - Glossary - *Undeclared*
  - Detailed Licensing - *Undeclared*