

CHAPTER SUMMARY

Organic chemistry is the study of compounds of carbon. This is a separate branch of chemistry because of the large numbers of organic compounds and their occurrences and applications.

1.1 Elements and Compounds – Atoms and Molecules

Elements are the fundamental building units of substances. They are composed of tiny particles called **atoms**; atoms are the smallest particles of an element that retains the properties of that element. **Atoms** are composed of a positively charged **nucleus** that consists of **protons** (charge = +1, mass = 1) and **neutrons** (charge = 0, mass = 1). The nucleus is surrounded by negatively charged **electrons** that have negligible mass.

Elements combine to form **compounds**. A **molecule** is the smallest particle of a compound that retains the properties of the compound; atoms bond to one another to form a molecule.

1.2 Electron Configuration

A. Atomic Number and Atomic Mass

The **atomic number** of an atom is the number of protons in the nucleus; this is equal to the number of electrons surrounding the nucleus in a neutral atom. The **mass number** is the number of protons plus neutrons in the nucleus. **Isotopes** are atoms with the same number of electrons and protons but different numbers of neutrons; they have the same atomic number but different mass numbers. The **atomic mass** of an element is the weighted average of the naturally occurring isotopes.

B. Atomic Orbitals

The space electrons occupy around an atomic nucleus is described by **atomic orbitals**. The most common orbitals in organic chemistry are **s-orbitals**, spherical orbitals with the atomic nucleus located in the center, and dumbbell shaped **p-orbitals** in which the nucleus is between the lobes.

C. Filling Atomic Orbitals

Orbitals exist in **energy levels** or **shells** (numbered 1-7). An atomic orbital can be occupied by 0, 1, or 2 electrons. Atomic orbitals are filled according to the **Aufbau principle** beginning with the lowest energy orbitals and proceeding to higher energy ones. The **electron configuration** of an atom is described by the orbitals occupied in each shell and the number of electrons in each orbital.

D. Electron Configuration and the Periodic Table

The **periodic table of elements** is organized according to electron configuration. Elements are placed in **periods** that are related to the outermost shell of electrons and in **groups** that are related to the number of electrons in the outer shell. All elements in a group have the same number of outer shell electrons (the same as the group number) and the same electron configuration except for the shell number (for example in Group IV, C is $2s^2 2p^2$ and Si is $3s^2 3p^2$; both outer shells have four electrons).

E. Stable Octets

The elements in Group VIII are especially stable; their outer shell configuration is known as a **stable octet**.

1.3 Ionic Bonding and the Periodic Table

A. Ionic Bonding, Electronegativity, Electron Configuration, and the Periodic Table

Ionic bonding involves the complete transfer of electrons between two atoms of widely different electronegativities; charged **ions** are formed (one positive from the loss of electrons and one negative from the gain of electrons), both of which usually have a stable octet outer shell. The ionic bond results from the attraction between the **positive cation** and **negative anion**.

Electronegativity is defined as the attraction of an atom for its outer shell electrons. **Electronegative** elements have a strong attraction for electrons and form anions in chemical reactions; **electropositive** elements have relatively weak attractions for electrons and form cations.

B. Electron Dot Representation of Ions

The electrons in the outer shell of an anion are represented by dots surrounding the element's symbol. Anions have usually gained sufficient electrons to complete their outer shells. Cations have usually lost their outer shells, the next shell in becomes the new outer shell, a stable octet, and is not shown.

1.4 Covalent Bonding

A. Covalent Bonding, Electron Configuration, and the Periodic Table

Covalent bonds involve the sharing of electron pairs between atoms of similar electronegativities; in most cases one or both atoms obtain a stable octet outer shell of electrons. The most common valences in Groups I-IV of the periodic table result from the pairing of all outer shell electrons with outer shell electrons of other atoms; a stable octet results in Group IV, but Groups I-III have incomplete outer shells. The common valences of Groups V-VII result from the pairing of outer shell electrons with those of other atoms to form an octet. The predicted valences of Groups I-VII are 1,2,3,4,3,2,1 respectively. Electron dot formulas depict the outer shell of atoms in molecules showing **bonding** and **non-bonding electron pairs**.

B. Covalent Bonding in Organic Compounds

A **single bond** has one bonding pair of electrons; there are two bonding pairs (four electrons) in a **double bond** and three bonding pairs in a **triple bond**. The number of bonds formed by elements commonly found in organic compounds is: **C - 4; N - 3; O, S - 2; H - 1; F, Cl, Br, I - 1**. A carbon can have four single bonds, two double bonds, a double and two single bonds, or a triple and a single bond; all total four bonds. These bonds can be represented by electron dot or line bond formulas.

C. Drawing Electron Dot Formulas

In drawing **electron dot formulas**, one must use every atom in the **molecular formula** and satisfy the **valence** (the number of bonds formed) for each. A good procedure involves bonding together atoms with valences greater than one with single bonds, inserting double and triple bonds until all valences can be satisfied with the available monovalent atoms, and finally attaching the monovalent atoms.

D. The Structural Nature of Compounds

Ionic compounds are composed of positive and negative ions in a ratio that will provide an electrically neutral compound. The atoms of a covalent compound are attached to one another to form molecules. Dissolution of an ionic compound in water produces solvated ions whereas covalent compounds have solvated molecules.

E. Polyatomic Ions and Formal Charge

Polyatomic ions are charged species in which several atoms are connected by covalent bonds. The magnitude and location of the ion's charge is called the **formal charge**. The formal charge on an atom is equal to the group number of the atom on the periodic table minus the non-bonding electrons and half of the bonding electrons.

F. Polar Covalent Bonds

A **polar covalent bond** is composed of atoms with similar but not equal electronegativities. The more electronegative atom is **partially negative** and the other is **partially positive**.

1.5 An Orbital Approach to Covalent Bonding

A. Sigma and Pi Covalent Bonds

A covalent bond is formed by the overlap of two atomic orbitals each with one electron. There are two types: sigma and pi. A **sigma bond** involves the overlap of two atomic orbitals head-to-head in one position (such as two s-orbitals, an s and a p-orbital, or two p-orbitals). A **pi-bond** involves the overlap of parallel p-orbitals at both lobes.

B. Electron Configuration of Carbon

Bonding in carbon involves the promotion of a 2s electron to an empty 2p orbital thus creating four unpaired electrons, one in the 2s and one in each of the three 2p orbitals. This allows carbon to be tetravalent.

C. Shapes of Organic Molecules

The **shapes** of organic molecules are predicted using the following principle: atoms and non-bonding electron pairs attached to a common central atom are arranged as far apart in space as possible. If there are four surrounding groups, the shape is **tetrahedral**; with three, the groups protrude to the corners of a **triangle (trigonal)**; and with two, the region is **linear**.

D. Carbon with Four Bonded Atoms

A carbon with four bonded atoms is sp^3 -hybridized, tetrahedral, and has approximately 109° bond angles. The four atomic orbitals on carbon (an s and three p's) combine, through a process called **hybridization**, to form new orbitals with different geometric orientations. The four new sp^3 -orbitals are raindrop shaped and are oriented to the corners of a tetrahedron. All bonds to the carbon are sigma bonds.

E. Carbon Bonded to Three Atoms

A carbon with three bonded atoms is sp^2 -hybridized, trigonal, and has approximately 120° bond angles. There are three new sp^2 -hybrid orbitals directed to the corners of a triangle; these form sigma bonds with other atoms. The remaining p-orbital overlaps with a parallel p-orbital of an adjacent, sigma bonded atom to form a pi-bond and complete the double bond.

F. Carbon Bonded to Two Atoms

A carbon with two bonded atoms is sp -hybridized, linear, and has 180° bond angles. There are two new sp hybrid orbitals that are directed opposite to one another on a straight line; these form sigma bonds. The two remaining p-orbitals overlap with p-orbitals on a similarly hybridized atom to

form two pi-bonds and complete the triple bond. Alternatively, the two p-orbitals can overlap with counterparts on two adjacently bonded sp^2 -hybridized atoms forming two double bonds.

G. Bonding in Organic Compounds – A Summary

A carbon with four bonded groups is tetrahedral, sp^3 -hybridized, and has 109.5° bond angles. A carbon with three is trigonal, sp^2 -hybridized, and has 120° bond angles. A carbon with two bonded groups is linear, sp -hybridized, and has 180° bond angles.

A single bond is a sigma bond; a double bond is composed of one sigma bond and one pi-bond; a triple bond is one sigma and two pi-bonds.

Triple bonds are stronger than double bonds and double bonds are stronger than single bonds. The opposite order describes relative bond lengths.

1.6 Bonding to Oxygen and Nitrogen

An **oxygen** with two bonded atoms and two non-bonding electron pairs is sp^3 -hybridized and has two sigma bonds (single bonds). With only one bonded atom, the oxygen is sp^2 -hybridized and is involved in one sigma and one pi bond, a double bond. A **nitrogen** with three bonded atoms and one non-bonding electron pair is sp^3 -hybridized and has three sigma bonds (single bonds). With two bonded atoms the nitrogen is sp^2 -hybridized and involved in two single bonds (sigma) and a double bond (sigma and a pi). A nitrogen with only one bonded atom is sp -hybridized, has one single bond (sigma) and one triple bond (one sigma and two pi-bonds).

CONNECTIONS 1.1: Diamond, Graphite, and Buckyballs

SOLUTIONS TO PROBLEMS**1.1 Atomic and Mass Numbers**

Subtract the atomic number (the number of electrons; and protons) from the mass number (number of protons and neutrons) to get number of neutrons.

(a-b)	mass number	atomic number	electrons	protons	neutrons
^{12}C	12	6	6	6	6
^{13}C	13	6	6	6	7
^{35}Cl	35	17	17	17	18
^{37}Cl	37	17	17	17	20
(c) F	9, 19.0	S	16, 32.1	Al	13, 27.0

1.2 Electron Configuration

Na	$1s^2$	$2s^2 2p^6$	$3s^1$	Mg	$1s^2$	$2s^2 2p^6$	$3s^2$
Al	$1s^2$	$2s^2 2p^6$	$3s^2 3p^1$	Si	$1s^2$	$2s^2 2p^6$	$3s^2 3p^2$
P	$1s^2$	$2s^2 2p^6$	$3s^2 3p^3$	S	$1s^2$	$2s^2 2p^6$	$3s^2 3p^4$
Cl	$1s^2$	$2s^2 2p^6$	$3s^2 3p^5$	Ar	$1s^2$	$2s^2 2p^6$	$3s^2 3p^6$

1.3 Electron Configuration and the Periodic Table

Notice that the outer shells in all four periods are the same for each group except for the period number (1,2,3,4,5).

K	Ca	Ga	Ge	As	Se	Br	Kr
$4s^1$	$4s^2$	$4s^2 4p^1$	$4s^2 4p^2$	$4s^2 4p^3$	$4s^2 4p^4$	$4s^2 4p^5$	$4s^2 4p^6$
Rb	Sr	In	Sn	Sb	Te	I	Xe
$5s^1$	$5s^2$	$5s^2 5p^1$	$5s^2 5p^2$	$5s^2 5p^3$	$5s^2 5p^4$	$5s^2 5p^5$	$5s^2 5p^6$

1.4 Electron Configuration and the Periodic Table

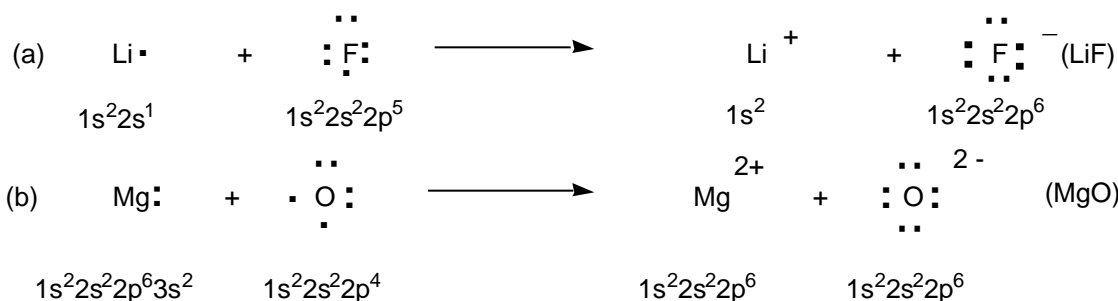
The number of outer shell electrons is the same as the group number to which the element belongs.

- (a) H, 1 (b) Al, 3 (c) C, 4 (d) N, 5 (e) S, 6 (f) Br, 7

1.5 Electron Configuration and the Periodic Table

He $1s^2$; Ne $2s^2 2p^6$; Ar $3s^2 3p^6$; Kr $4s^2 4p^6$; Xe $5s^2 5p^6$; Rn $6s^2 6p^6$

1.6 Ionic Bonding



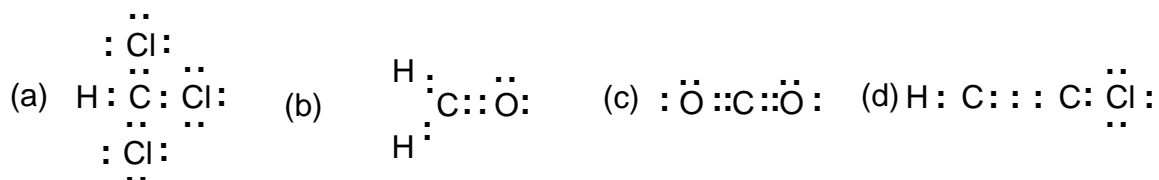
1.7 Ionic Bonding

- (a) NaF (b) Mg(OH)₂ (c) (NH₄)₂SO₄ (d) Li₂CO₃
 (e) CaO (f) CaCO₃ (g) NaNO₂ (h) KClO₃

1.8 Covalent Bonding: Valences

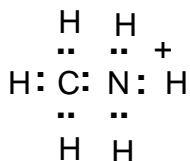
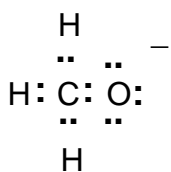
- (a) 3 (b) 4 (c) 4 (d) 3 (e) 2 (f) 2 (g) 1 (h) 1

1.9 Electron Dot Formulas



1.10 Electron Dot Formulas of Polyatomic Ions

A neutral atom will “own” the same number of electrons in its outer shell as its group number on the periodic table (that is half the bonding and all the non-bonding electrons). To determine the formal charge of an atom, subtract from the group number of that atom on the periodic table all the non-bonding electrons and half of the electrons in a bonding pair.



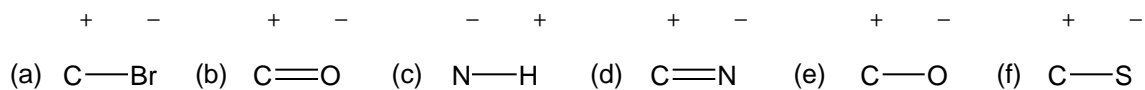
$$\text{C} \quad (4) - (0) - 1/2 (8) = 0$$

$$\text{H's} \quad (1) - (0) - 1/2 (2) = 0$$

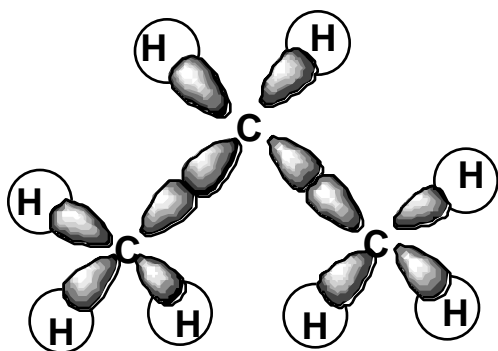
$$\text{O} \quad (6) - (6) - 1/2 (2) = -1$$

$$\text{N} \quad (5) - (0) - 1/2 (8) = +1$$

1.11 Polar Bonds

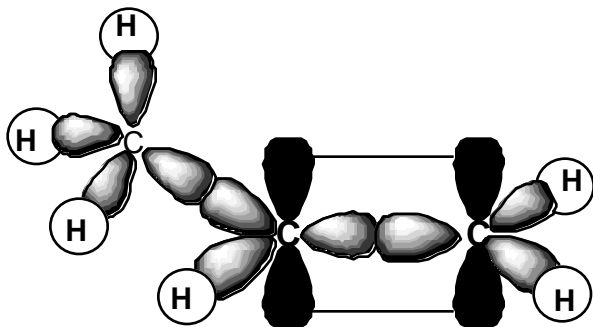


1.12 Bonding Picture of Propane



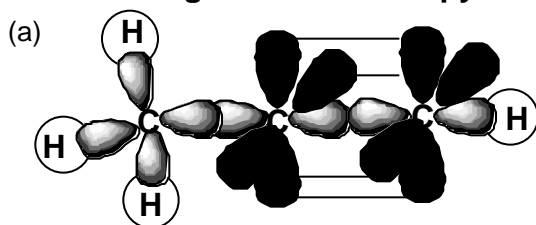
Each carbon is tetrahedral,
 sp^3 -hybridized,
 and has 109° bond angles

1.13 Bonding Picture of Propene



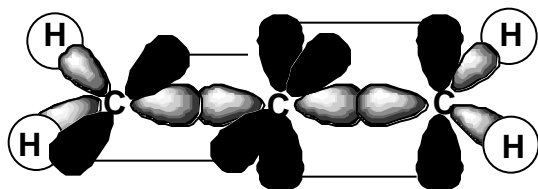
The carbons involved in the double bond are both trigonal, have 120° bond angles and are sp^2 -hybridized. The other carbon is tetrahedral, has 109° bond angles and is sp^3 -hybridized.

1.14 Bonding Pictures of Propyne and Propadiene



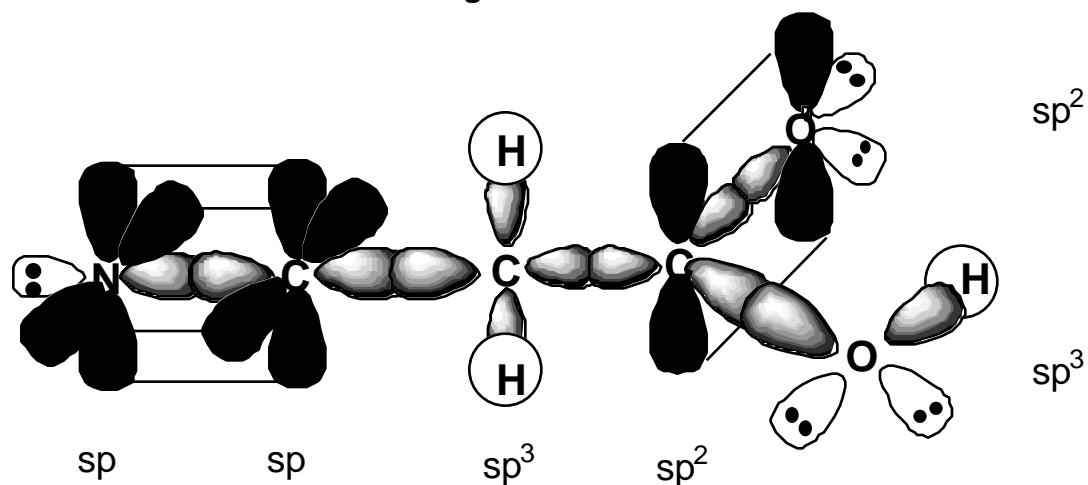
The two carbons involved in the triple bond are both sp -hybridized, display linear geometry, and have bond angles of 180° . The other carbon is sp^3 -hybridized, tetrahedral, and has 109° bond angles.

(b)



The middle carbon is involved in two double bonds, has two attached atoms sp -hybridization, a linear geometry, and bond angles of 180° . The two end carbons are connected to three atoms and are sp^2 -hybridized, trigonal, and have 120° bond angles.

1.15 Orbital Picture of Bonding



1.16 Atomic and Mass Numbers: Section 1.2A

See problem 1.1 for explanation.

- (a) ^{127}I 53 protons, 53 electrons, 74 neutrons;
 (b) ^{27}Al 13 protons, 13 electrons, 14 neutrons;
 (c) ^{58}Ni 28 protons, 28 electrons, 30 neutrons;
 (d) ^{208}Pb 82 protons, 82 electrons, 126 neutrons.

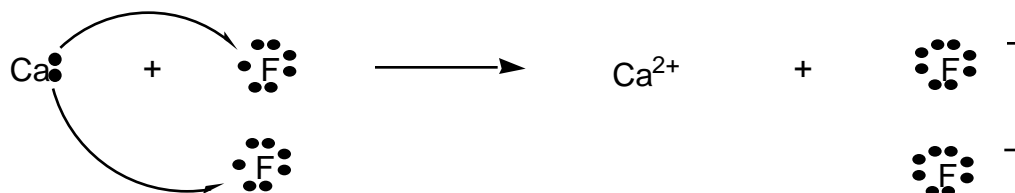
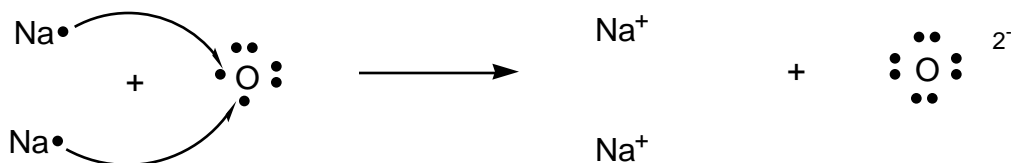
1.17 Electron Configurations : Section 1.2B-D

- (a) Na, $3s^1$; (b) Mg, $3s^2$; (c) B, $2s^2 2p^1$; (d) Ge, $4s^2 4p^2$;
 (e) P, $3s^2 3p^3$ (f) O, $2s^2 2p^4$; (g) I, $5s^2 5p^5$; (h) Kr, $4s^2 4p^6$

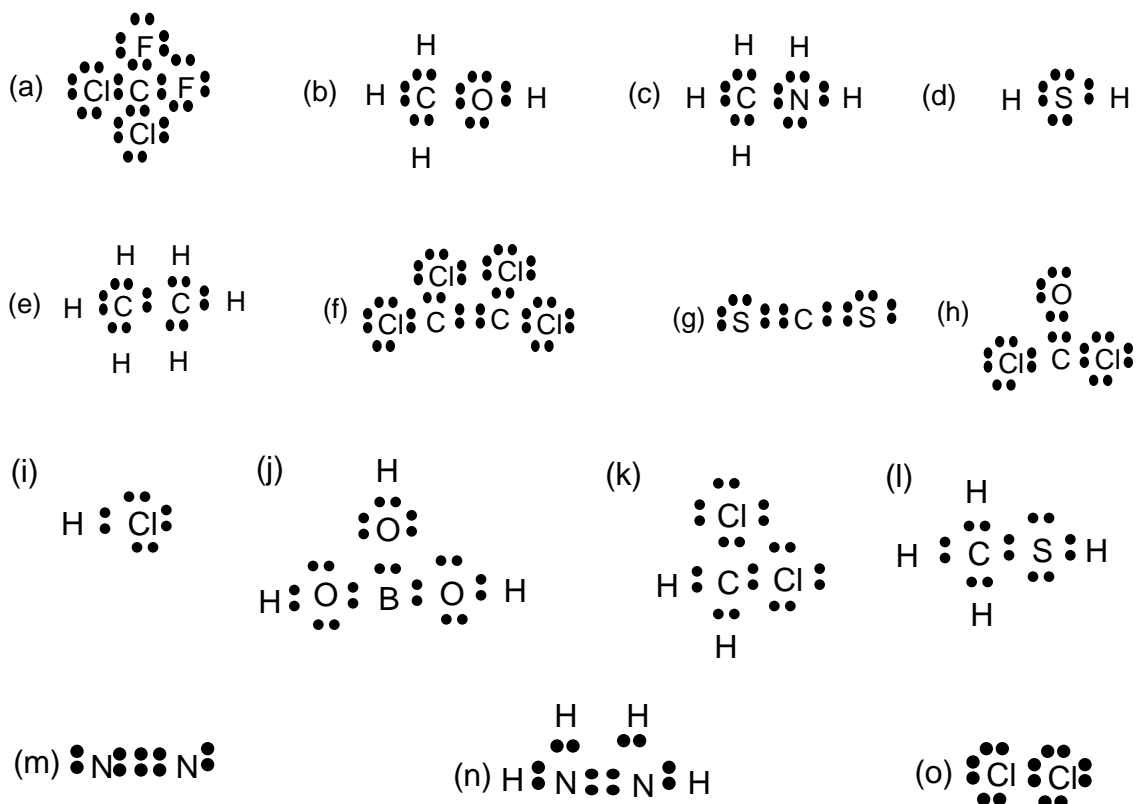
1.18 Electron Configurations: Section 1.2B-D

(a) Fr (b) Sn (c) Cl (d) Mg (e) B (f) Se (g) He (h) Xe (i) As

1.19 Ionic Reactions: Section 1.3

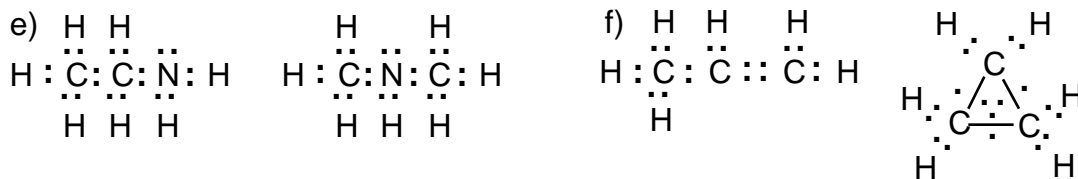
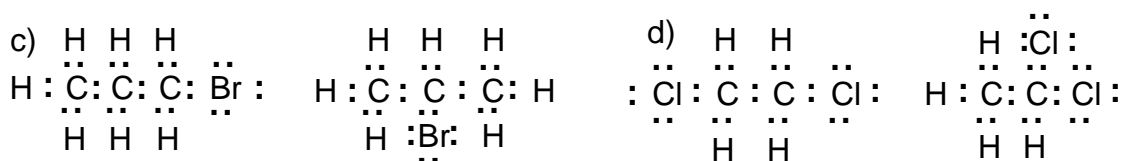
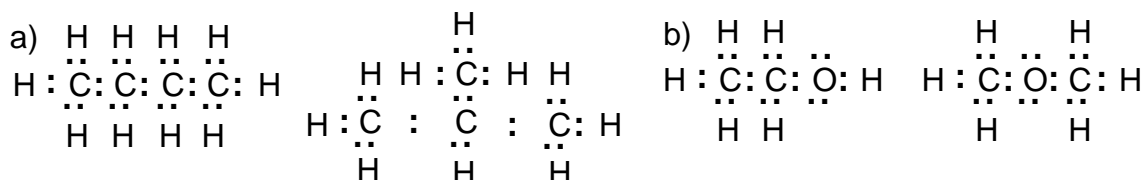
 (a) CaF_2

 (b) Na_2O


1.20 Electron Dot Formulas: Section 1.4A-C

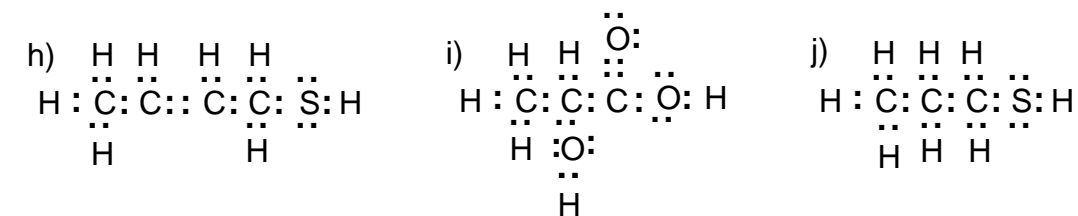
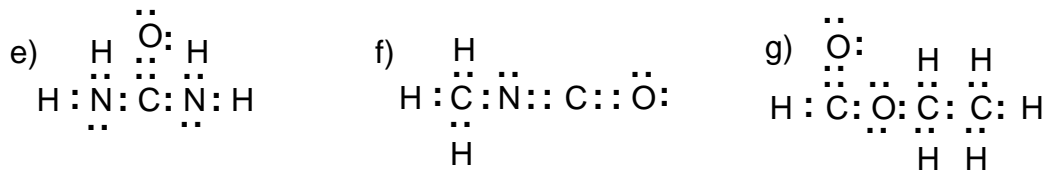
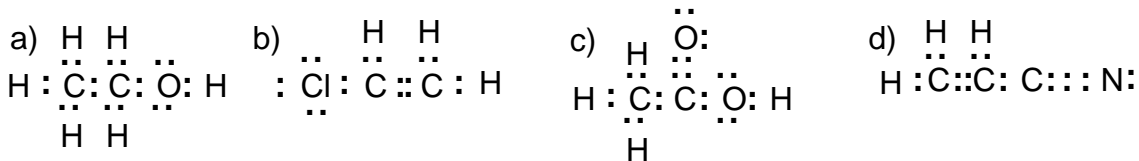




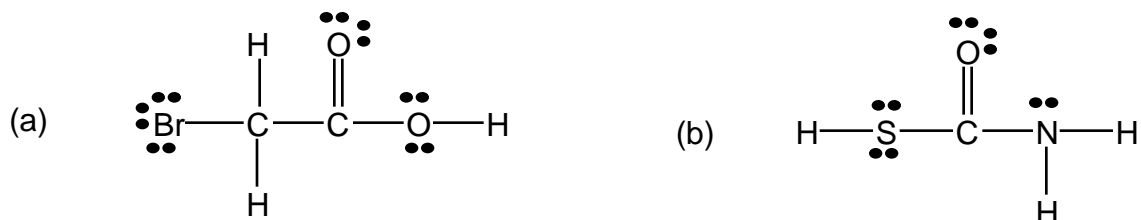
1.21 Electron Dot Formulas: Section 1.4A-C



1.22 Electron Dot Formulas: Section 1.4A-C

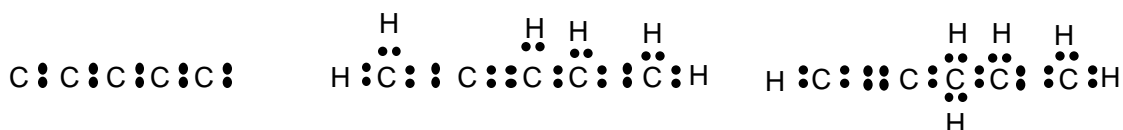


1.23 Electron Dot Formulas: Section 1.4A-C

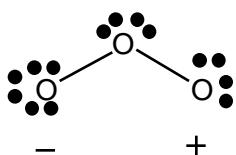


1.24 Electron Dot Formulas: Section 1.4A-C

Place five carbons in a row and connect them with single bonds. It would take 12 hydrogens to satisfy the valences of all these carbons if all the carbon-carbon bonds are single. For each double bond you insert, you need two less hydrogens; three double bonds are needed. For every triple bond you insert, you need four fewer hydrogens; one triple and one double bond will work for this formula.

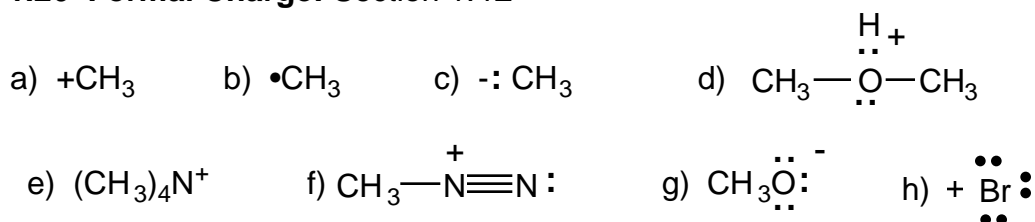


1.25 Electron Dot Formulas and Formal Charge: Section 1.4E

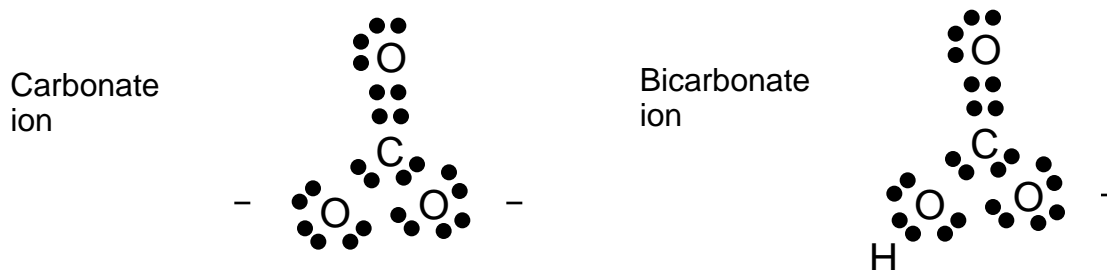


A neutral oxygen atom has six electrons. Ozone is neutral, has three oxygen atoms, and thus a total of 18 electrons. The negative oxygen has three non-bonding and one bonding pairs; the oxygen "owns" seven and is thus negative. The positive oxygen has two non-bonding pairs and one bonding pair; it "owns" five electrons and is thus positive.

1.26 Formal Charge: Section 1.4E

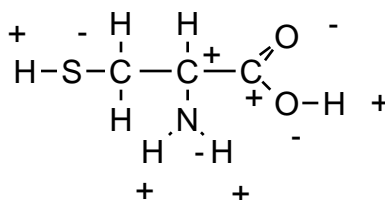


1.27 Electron Dot Formulas and Formal Charge: Section 1.4E



1.28 Polar Covalent Bonds: Section 1.4F

Most bonds in organic compounds are considered polar except carbon-hydrogen and carbon-carbon bonds.



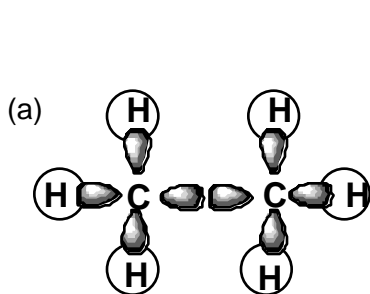
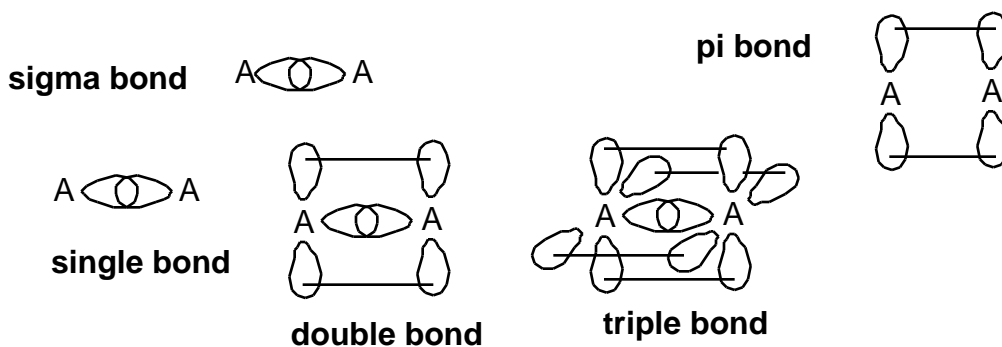
1.29-1.31 Bonding in Organic Compounds: Section 1.5

See section 1.5; there is a summary in 1.5G. Also see problems 1.12-1.15 and example 1.4.

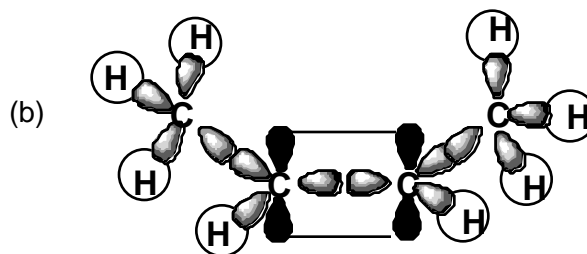
Problem 1.29: The carbons involved only in single bonds have four bonded groups and are sp^3 hybridized, tetrahedral, and have 109° bond angles. The carbons that have one double bond have three bonded groups and are sp^2 hybridized, trigonal, and have 120° bond angles. The carbons involved in triple bonds or two double bonds are sp hybridized, linear, and have 180° bond angles.

Problem 1.30: All single bonds are sigma bonds. A double bond is a sigma and a pi bond. A triple bond is constructed of a sigma and two pi bonds.

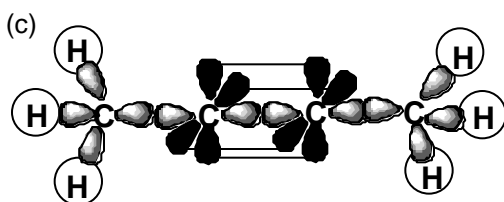
Problem 1.31: Bonding picture.



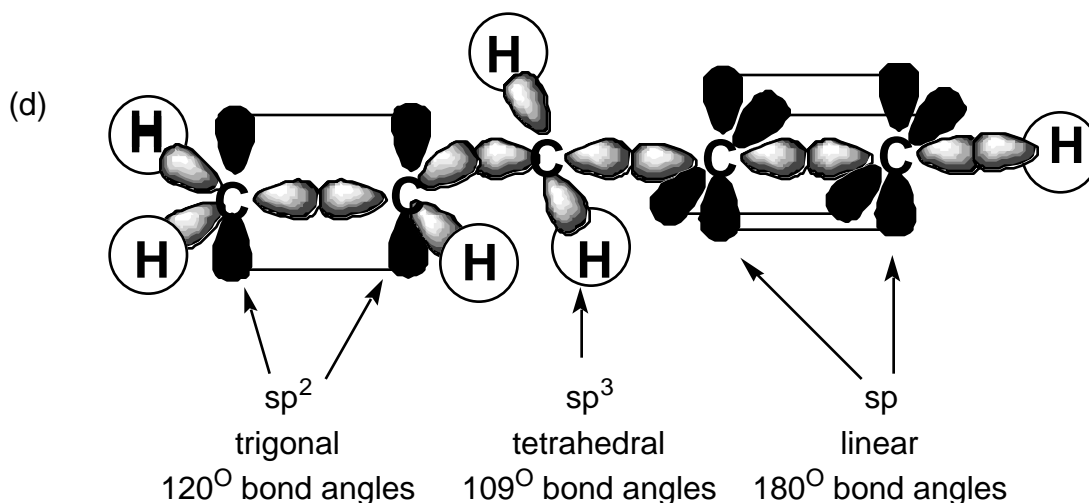
sp^3 , 109° , tetrahedral



Two end carbons: sp^3 , 109° , tetrahedral
Two middle carbons: sp^2 , 120° , trigonal



The two end carbons have four attached groups, are sp^3 -hybridized, tetrahedral, and have 109° bond angles. The two middle carbons have two attached groups, are sp -hybridized, linear and have 180° bond angles.



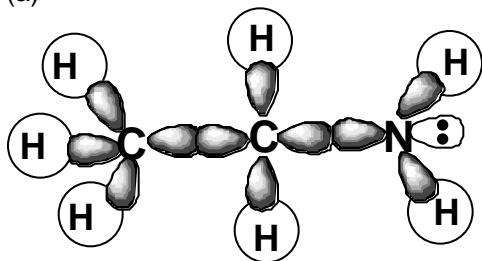
1.32-1.34 Bonding with Oxygen and Nitrogen: Section 1.6

Problem 1.32: Carbons, nitrogens, and oxygens involved only in single bonds have four groups that occupy space; four bonded groups with carbon, three bonded groups and a non-bonding electron pair with nitrogen, and two bonded groups and two non-bonding pairs with oxygen. All are sp^3 hybridized, tetrahedral, and have 109° bond angles. Carbons, nitrogens, and oxygens with one double bond have three groups that occupy space; these are three bonded groups for carbon, two bonded groups and a non-bonding pair for nitrogen and one bonded group and two non-bonding pairs for oxygen. All are sp^2 hybridized, trigonal, and have 120° bond angles. Carbons and nitrogens with a triple bond have only two groups that occupy space two bonded groups for carbon and one bonded group and a non-bonding electron pair for nitrogen. Both are: sp hybridized, linear, and have 180° bond angles.

Problem 1.33: Single bonds are sigma bonds; double bonds are one sigma and one pi bond. Triple bonds are one sigma and two pi bonds.

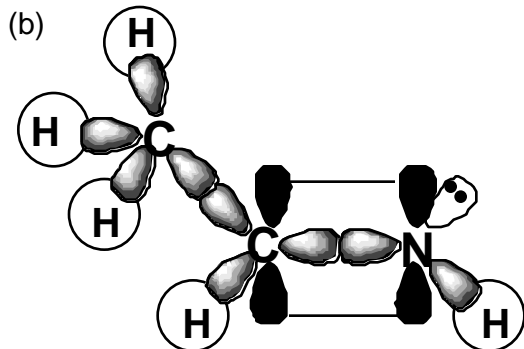
Problem 1.34: Bonding pictures.

(a)



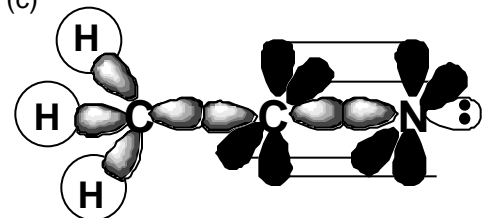
The carbons and nitrogen are sp^3 -hybridized, tetrahedral, and have bond angles that are approximately 109° .

(b)



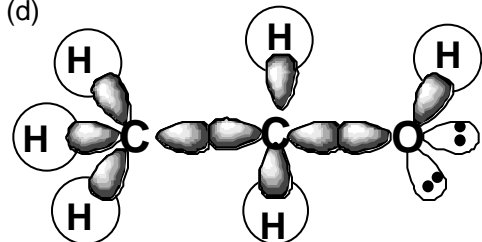
The carbon with three hydrogens is sp^3 -hybridized, tetrahedral and has 109° bond angles. The carbon and nitrogen in the triple bond are both sp^2 -hybridized, trigonal and have bond angles of 120° .

(c)



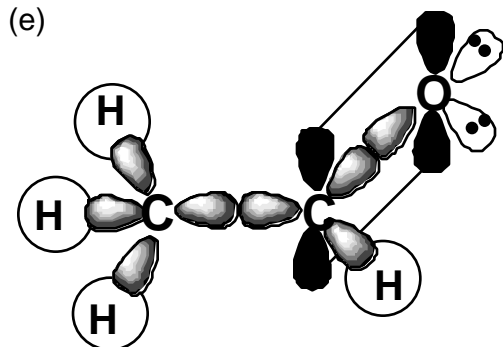
The carbon with three hydrogens is sp^3 hybridized, tetrahedral, and has 109° bond angles. The carbon and nitrogen in the triple bond are both sp -hybridized and linear; the carbon has 180° bond angles.

(d)



The carbons and oxygen each have four space-occupying groups; four bonded atoms for each carbon and two bonded atoms and two non-bonding electron pairs for the oxygen. These atoms are all sp^3 -hybridized, tetrahedral, and have approximate bond angles of 109° .

(e)



The carbon with three hydrogens is sp^3 -hybridized, tetrahedral, and has 109° bond angles. The carbon and oxygen in the double bond are both sp^2 -hybridized, trigonal, and have approximate bond angles of 120° .

1.35 Silicon: Section 1.4A-C

Silicon was a logical choice of an element for the Star Trek episode about a very different life form. Silicon is just below carbon in Group IV of the periodic table, has the same number of outer shell electrons, and has some properties that are similar. It can bond to itself (though not as extensively as carbon) and, like carbon, it is tetravalent.

1.36 Molecular Shape: Section 1.5

In NH_3 , nitrogen has four groups that occupy space, three bonding pairs (hydrogens) and one non-bonding pair of electrons. As such the preferred geometry is tetrahedral and the nitrogen is sp^3 hybridized.

$\text{N} \quad \text{s}^2 \text{p}^1 \text{p}^1 \text{p}^1$ hybridizes to $(\text{sp}^3)^2 (\text{sp}^3)^1 (\text{sp}^3)^1 (\text{sp}^3)^1$ in NH_3

Surrounding boron are three space occupying groups, the three fluorines. Boron does not have an octet of electrons. Therefore it assumes a trigonal shape and is sp^2 hybridized.

$\text{B} \quad \text{s}^1 \text{p}^1 \text{p}^1 \text{p}^0$ hybridizes to $(\text{sp}^2)^1 (\text{sp}^2)^1 (\text{sp}^2)^1 \text{p}^0$

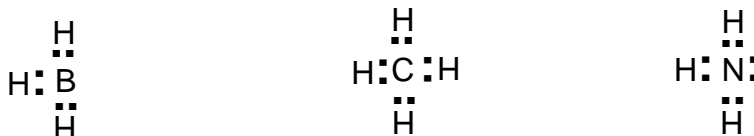
1.37 Bond Angles: Section 1.5

All four compounds have four pairs of electrons around the central atom. In CH_4 they are all bonding pairs and relatively confined to the carbon-hydrogen bonds. Methane is a classic example of a tetrahedral molecule with 109° bond angles. In ammonia, NH_3 , there are three bonding pairs of electrons and one non-bonding pair. The non-bonding pair tends to occupy more space and repel the bonding pairs thus slightly compressing the bond angles; the result is 107° bond angles. In water there are two non-bonding electron pairs. These spacious pairs repel each other and the two bonding pairs thus further compressing the bond angles to 105° .

1.38 Reactivity: Section 1.4A-C

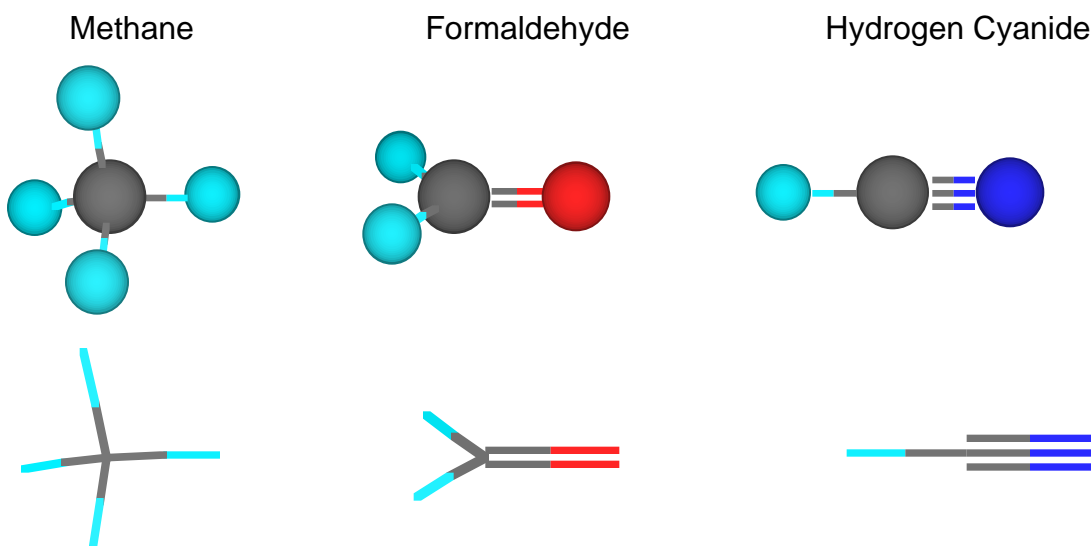
The carbon in CH_4 has a stable octet and all eight electrons are expressed as four bonding electron pairs. In NH_3 , the nitrogen has a stable octet but, since

nitrogen is in Group V and has five outer shell electrons, there is a non-bonding electron pair remaining following formation of three bonds. This pair of electrons is available for sharing with electron-deficient species unlike the bonding pairs of CH_4 . Boron is in Group III of the periodic table. Since it has only three outer shell electrons it forms three bonds. However, it does not achieve a stable octet. Consequently, it is attracted to species that have electron pairs available for bonding (such as the N in NH_3) because, in reacting, it can achieve a stable octet.



Activities with Molecular Models

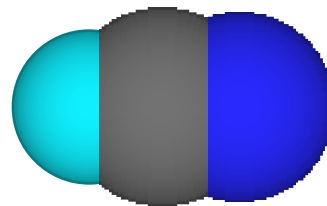
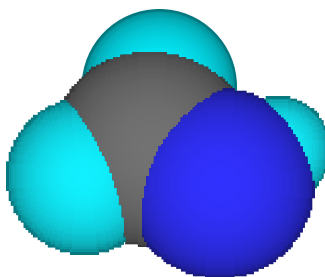
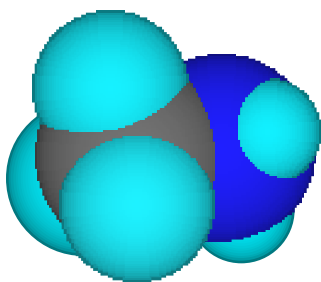
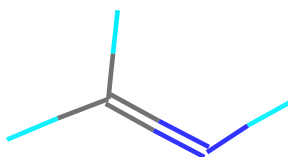
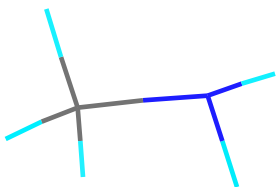
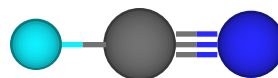
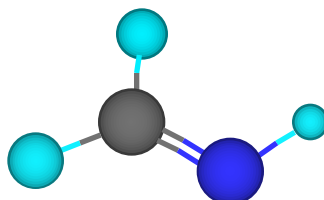
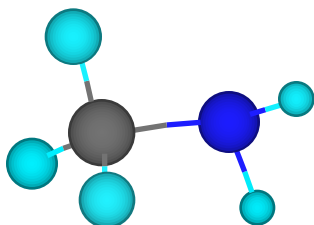
1. Make models of ethane (C_2H_6), ethene (C_2H_4), and ethyne (C_2H_2). These molecules illustrate sp^3 (tetrahedral), sp^2 (trigonal), and sp (linear) hybridizations respectively. Note the geometries and bond angles as you look at your models. (See textbook for models)
2. Make models of methane (CH_4), formaldehyde (CH_2O), and hydrogen cyanide (HCN). Observe the geometries and bond angles at each carbon.



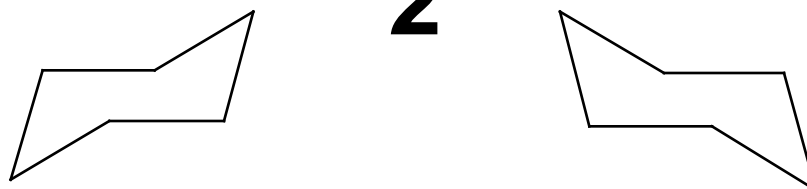
3. Make models of methanol (CH_4O) and formaldehyde (CH_2O). Note the geometries and bond angles of both the carbons and oxygens in these molecules.

(See textbook for models.)

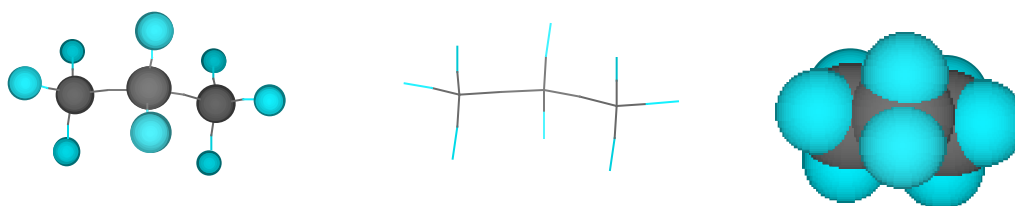
4. Make models of CH_5N , CH_3N , and HCN . Note the geometries and bond angles at both the carbons and the nitrogens.



2



**THE ALKANES:
STRUCTURE AND NOMENCLATURE
OF SIMPLE HYDROCARBONS**



CHAPTER SUMMARY

Organic compounds are classified according to common structural features that impart similar chemical and physical properties to the compounds within each group or family.

2.1 Hydrocarbons: An Introduction

Hydrocarbons are composed only of carbon and hydrogen and fall into two major classes - saturated and unsaturated. **Saturated hydrocarbons** or the **alkanes** are entirely constructed of single bonds and have the general formula C_nH_{2n+2} . **Unsaturated hydrocarbons** include the **alkenes** (C_nH_{2n}) in which there is at least one carbon-carbon double bond; the **alkynes** (C_nH_{2n-2}) where there is at least one carbon-carbon triple bond; and **aromatic hydrocarbons** which appear to have double bonds but actually have a special structure that is discussed in Chapter 6.

2.2 Molecular and Structural Formulas - Isomerism

Compounds are described by **molecular formulas** and **structural formulas**. **Molecular formulas** describe the kinds of atoms and numbers of

each in a molecule. **Structural formulas** describe the bonding arrangements of the atoms, that is, what atoms are bonded to one another and by what kinds of bonds. **Isomers** are compounds with the same molecular formula but different structural formulas. **Structural isomers (skeletal, positional, and functional)** differ in the bonding arrangement of atoms; different atoms are attached to one another. In **stereoisomerism** the same atoms are bonded to one another but their orientation in space differs; **conformational** and **geometric isomerism** are forms of stereoisomerism presented in this chapter.

2.3 Skeletal Isomerism in Alkanes

A. Isomers

Isomers are different compounds with the same molecular formula but different structural formulas. Skeletal isomers differ in the arrangement of the carbons in a set of isomers; there are differences in the carbon skeletons.

B. Drawing Structural Isomers

The rules and procedures for drawing structural isomers are the same used for drawing electron dot formulas. Every atom in the molecular formula must be used and each atom must have its valence satisfied. To draw a structure, bond all atoms with a valence greater than one with single bonds. Attach monovalent atoms to the polyvalent ones until all valences have been satisfied. If there are insufficient monovalent atoms in the formula to accomplish this, insert double bonds, triple bonds or draw cyclic structures until it is possible to satisfy all valences. To draw isomers, vary the arrangements of atoms and bonds to form different molecules.

C. Cycloalkanes

The simplest cycloalkanes have the general formula C_nH_{2n} ; they have two fewer hydrogens than the corresponding alkane and at least three of the carbons are arranged in a ring.

2.4 Representations of Structural Formulas

In Chapter 1, electron dot formulas were used to describe covalent compounds. More condensed representations involve replacing the electron dots with lines (one for a single bond, two for a double bond, three for a triple bond), grouping hydrogens on a carbon, grouping identical carbons, and using stick diagrams in which each corner represents a carbon with sufficient hydrogens to satisfy the valence.

2.5 Positional Isomerism

Positional isomers differ in the position of a noncarbon group or of a double bond or triple bond.

2.6 IUPAC Nomenclature of Alkanes

A. An Introduction to IUPAC Nomenclature

Many organic compounds have informal common names but the accepted way of naming compounds is by the **IUPAC system of nomenclature**.

B. Nomenclature of Continuous-Chain, Unbranched Alkanes:

The Basis for Organic Nomenclature

The base name of alkanes is derived from the Greek for the number of carbons in the **longest continuous carbon chain** (Table 2.1 of the text) followed by the suffix **ane**. The base name of cycloalkanes is based on the Greek for the number of carbons in the ring with the prefix **cyclo** and the suffix **ane**.

C. Nomenclature of Branched-Chain Alkanes

Branched-chain alkanes have a longer carbon chain, upon which the name is usually based, with attached shorter carbon chains. These shorter chains are called **alkyl groups** (Table 2.2 of the text) and are named by changing the **ane** (of the alkane name) to **yl**. The positions of alkyl groups are described with numbers; the longest carbon chain of an alkane is numbered starting at the end that gives the lowest number to the first substituent. Multiple numbers of identical alkyl groups are indicated with **di**, **tri**, **tetra**, etc.

D. Nomenclature of Halogenated Hydrocarbons (Alkyl Halides)

The prefixes **fluoro**, **chloro**, **bromo**, and **iodo** are used to indicate the presence of halogen in a molecule.

2.7 Conformational Isomerism

Conformational isomers are isomers in which the spatial relationship of atoms differs because of rotation around a carbon-carbon single bond. Because the rotation is unrestricted in most cases, conformational isomers are constantly interconverting and are not isolatable. There are two extreme conformations. In the **eclipsed conformation**, atoms on adjacent carbons are lined up with one another and are as close together as possible; this is the least stable

conformational arrangement. In the **staggered conformation**, atoms on adjacent atoms are staggered with one another and are as far apart as possible; this is the most stable conformational arrangement. Staggered and eclipsed forms are represented with **sawhorse diagrams** or **Newman projections**. Sawhorse diagrams are essentially stick structures highlighting the two carbons for which the conformations are being described. In a Newman projection the carbon-carbon bond is described by a circle with three bonds emanating from the center (the front carbon) and three from the perimeter (the back carbon).

2.8 Cycloalkanes - Conformational and Geometric Isomerism

A. Structure and Stability

Cycloalkanes are generally depicted with regular polygons though they actually exist in three-dimensional conformations. **Cyclopropane** and **cyclobutane** are less stable than other cycloalkanes since they are planar (cyclopropane) or nearly so (cyclobutane) and have internal bond angles significantly smaller (60° and 90° respectively) than the preferred tetrahedral angle (109°). The larger cycloalkanes are able to pucker out of planarity and assume tetrahedral angles.

B. Conformational Isomerism in Cyclohexane

Cyclohexane exists in two puckered conformations, the **boat and chair forms**, that have tetrahedral bond angles. The boat form is less stable and not preferred because of interactions between the two end or **flagpole** carbons and because the hydrogens on the other adjacent carbons are eclipsed. In the preferred chair form, atoms on adjacent carbons are staggered and there are no flagpole type interactions. There are two orientations of hydrogens in the chair conformation. **Axial hydrogens** are oriented directly above or below the "plane" of the ring in an alternating arrangement. **Equatorial hydrogens** protrude out along the perimeter of the ring.

C. Drawing the Cyclohexane Chair

In drawing the cyclohexane chair, keep in mind that there are four carbons in a plane. On one end there is a carbon oriented above the plane and on the other end there is a carbon oriented below the plane. Each carbon has an equatorial hydrogen oriented along the perimeter. There are three axial hydrogens on alternating carbons above the ring and three on the other carbons below the ring.

D. Conformational Isomerism in Substituted Cyclohexanes

In a monosubstituted cyclohexane, the substituent can be either in an equatorial or axial position. Equatorial positions are more spacious and in substituted cyclohexanes they are preferred. Cyclohexane rings flip between chair forms and establish an equilibrium. In the process of flipping, all equatorial positions become axial and all axial positions become equatorial. The equilibrium favors the chair in which substituents are equatorial. In monosubstituted cyclohexanes, the conformation in which the substituent is equatorial is favored. In disubstituted cyclohexanes where one group is axial and one equatorial, the equilibrium favors the chair form where the larger group occupies the more spacious equatorial position.

E. Geometric Isomerism in Cyclic Compounds

Disubstituted cycloalkanes exhibit geometric isomerism, a type of stereoisomerism. If both groups are on the same "side" of the ring (both up or both down) the isomer is termed cis. If they are on opposite "sides" (one up and one down) the isomer is trans.

2.9 Hydrocarbons: Relationship of Structure and Physical Properties

The **solid**, **liquid**, and **gas** states of a compound differ in arrangements of molecules, not in molecular structure. In the solid state the molecules are orderly arranged and immobile with maximum intermolecular attractions. In the liquid state, molecules are mobile but still there are intermolecular attractions. In the vapor phase molecules are mobile and ideally there are no intermolecular attractions. For these reasons, solids have a constant shape and volume, liquids have a constant volume and variable shape, and gases assume the size and shape of the container. **Physical properties** of hydrocarbons are related to structure.

A. Melting Point, Boiling Point, and Molecular Weight

Melting points and boiling points generally increase with molecular weight within a **homologous series** (a series of compounds in which each succeeding member differs from the previous one by a CH_2 group).

B. Melting Point, Boiling Point, and Molecular Structure

Branched chain hydrocarbons have less surface area and thus less opportunity for intermolecular attractions; as a result, their boiling points are lower than the straight chain isomers. However, their compact nature causes

them to fit more easily in a crystal lattice and thus they generally have higher melting points.

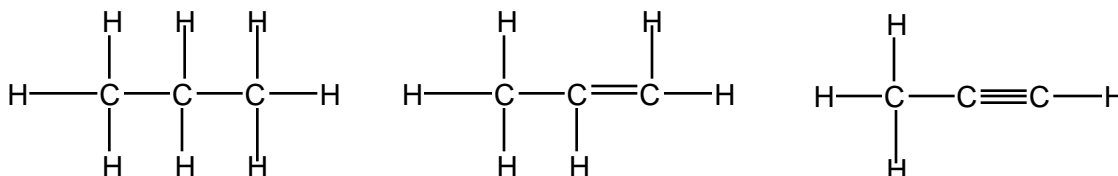
C. Solubility and Density

Hydrocarbons are **non-polar** and insoluble in water and, because they are less dense, they float on the surface of water.

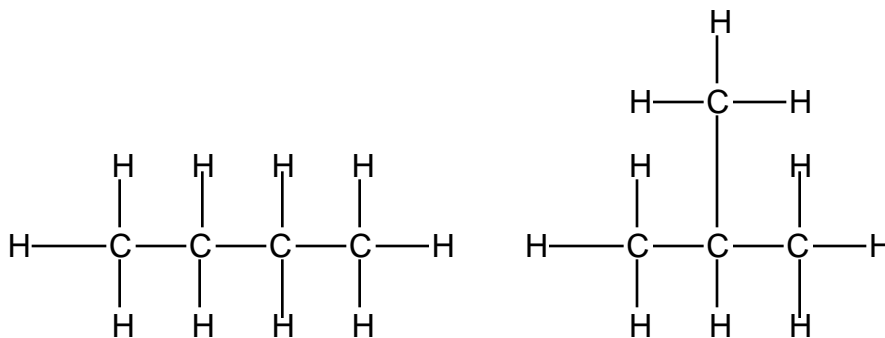
CONNECTIONS 2.1: Petroleum

SOLUTIONS TO PROBLEMS

2.1 Alkanes, Alkenes, and Alkynes



2.2 Skeletal Isomers



2.3 Skeletal Isomers

(a) All three of these structures are identical. In each, the longest continuous chain of carbon atoms is six with a CH₃ group attached to the second carbon from the end.

(b) The first and last structures are the same. In each, the longest continuous chain of carbons is six and there is a CH₃ group bonded to the third carbon from the end.

2.4 Skeletal Isomers

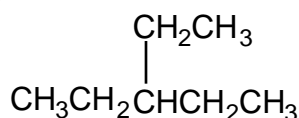
Start with a chain of seven carbons.



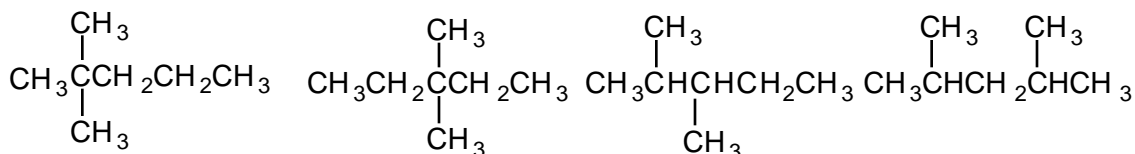
Now draw isomers with six carbons in the longest chain and vary the position of the one-carbon chain.



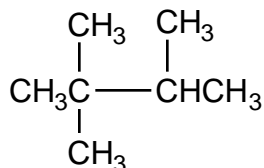
Now draw five carbon chains and place one two-carbon chain or two one-carbon chains on it. If the two-carbon side chain is placed on either the first or second carbon, it merely extends the longest chain. However, placing it on the third carbon gives us another isomer.



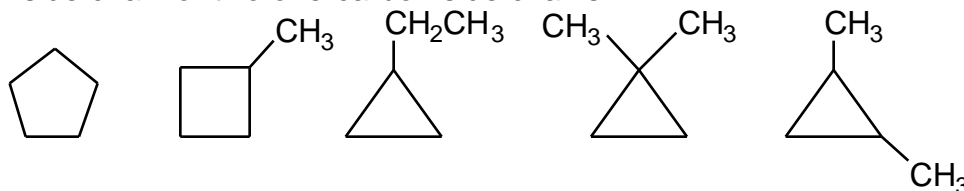
Now attach two one-carbon chains to the carbon skeleton.



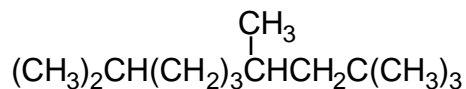
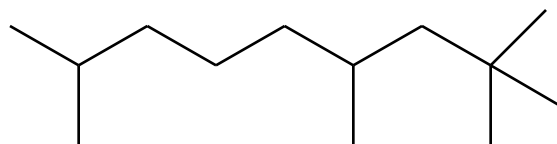
Finally, draw a four carbon chain with three one carbon side chains.

2.5 Skeletal Isomers of Cycloalkanes: Five cyclic compounds of C₅H₁₀.

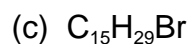
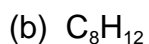
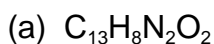
Start with a five-membered ring. Then use a four-membered ring with a one-carbon side chain. Finally, draw a three-membered ring with either one two-carbon side chain or two one-carbon side chains.



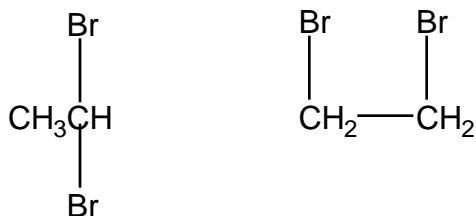
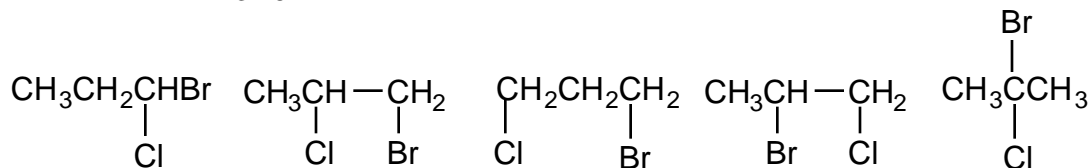
2.6 Representations of Structural Formulas



2.7 Molecular Formulas from Structural Formulas



2.8 Positional Isomers

Two isomers of $\text{C}_2\text{H}_4\text{Br}_2$ Five isomers of $\text{C}_3\text{H}_6\text{BrCl}$ 

2.9 IUPAC Nomenclature

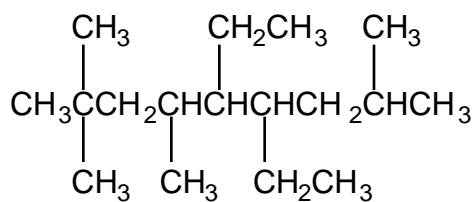
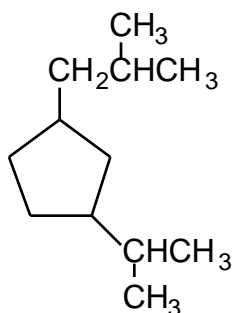
(a) Names of compounds in Example 2.1 as they appear:

hexane, 2-methylpentane, 3-methylpentane, 2,2-dimethylbutane, and 2,3-dimethylbutane.

(b) Names of nine isomers in Problem 2.4 as they appear:

heptane;
2-methylhexane and 3-methylhexane;
3-ethylpentane;
2,2-dimethylpentane; 3,3-dimethylpentane; 2,3-dimethylpentane;
and 2,4-dimethylpentane;
2,2,3-trimethylbutane

c. Structures from names



1-isobutyl-3-isopropylcyclopentane

5,6-diethyl-2,2,4,8-tetramethylnonane

2.10 Alkyl Halide Nomenclature

Names of compounds in section 2.5 as they appear.

1-bromobutane, 2-bromobutane,

1-bromo-2-methylpropane, and 2-bromo-2-methylpropane.

2.11 Alkyl Halide Nomenclature

(a) Names of compounds as they appear in problem 2.8a:

1,1-dibromoethane and 1,2-dibromoethane

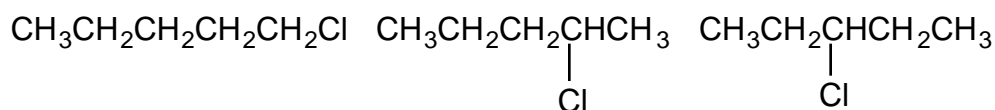
(b) Names of compounds as they appear in problem 2.8b..

1-bromo-1-chloropropane, 1-bromo-2-chloropropane,

1-bromo-3-chloropropane, 2-bromo-1-chloropropane, and

2-bromo-2-chloropropane

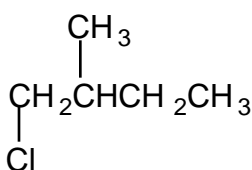
2.12 Skeletal and Positional Isomerism



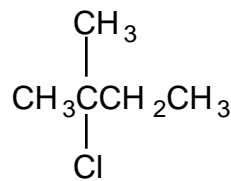
1-chloropentane

2-chloropentane

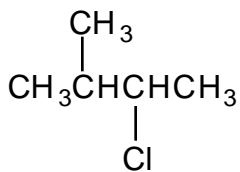
3-chloropentane



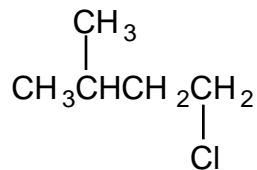
1-chloro-2-methylbutane



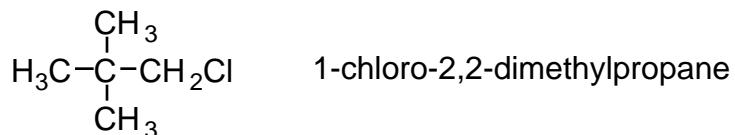
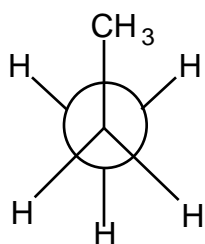
2-chloro-2-methylbutane



2-chloro-3-methylbutane

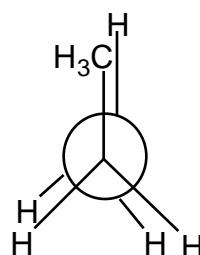


1-chloro-3-methylbutane

**2.13 Newman Projections of Propane**

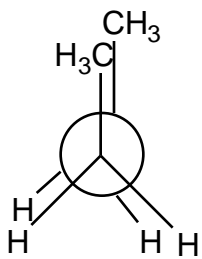
Staggered

Most Stable

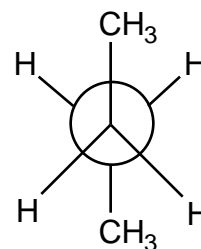
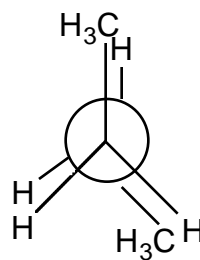
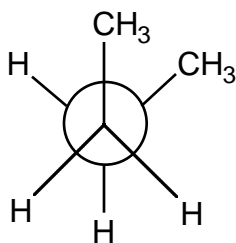


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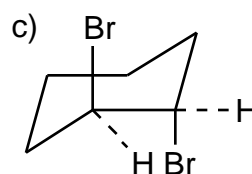
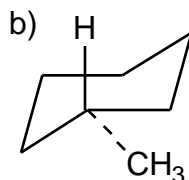
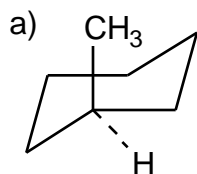
Least Stable

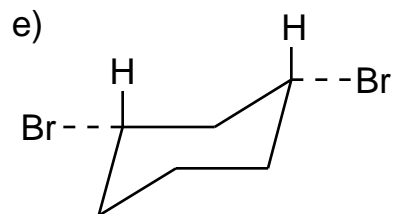
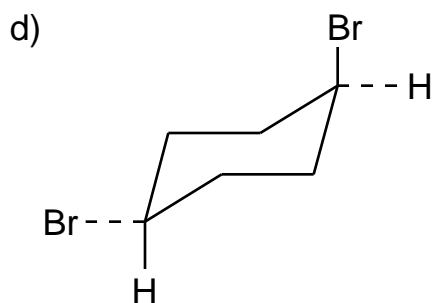
2.14 Conformational Isomers of Butane

Least Stable



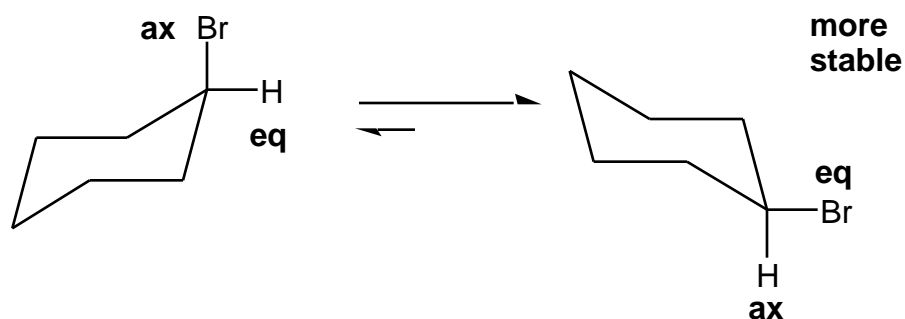
Most Stable

2.15 Cyclohexane Chair: Axial and Equatorial Positions

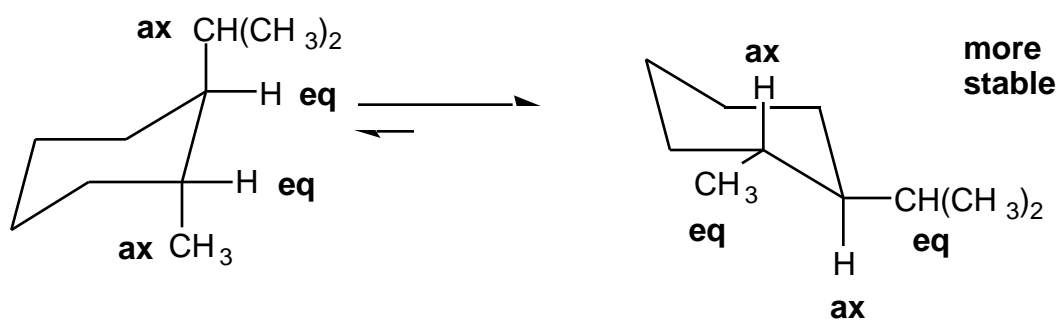


2.16 Equilibrium between Chair Forms

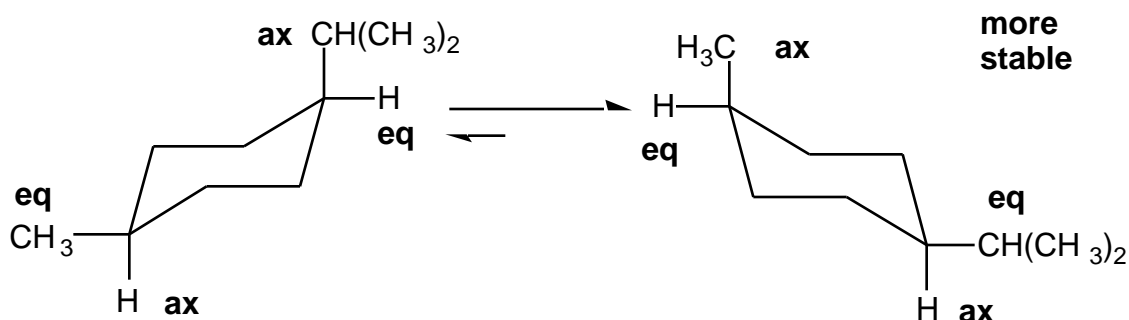
(a) The equatorial position is more spacious and the isomer more stable.



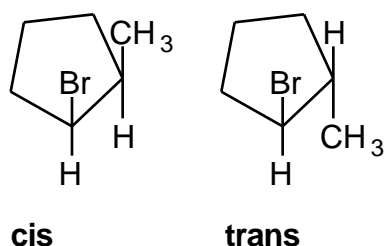
(b) The equatorial positions are more spacious and preferred in the equilibrium.



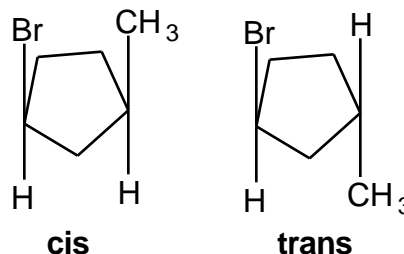
- (c) The equilibrium favors the isomer in which the larger isopropyl group is in the more spacious equatorial position.



2.17 Geometric Isomerism in Cyclic Compounds



1-bromo-2-methylcyclopentane



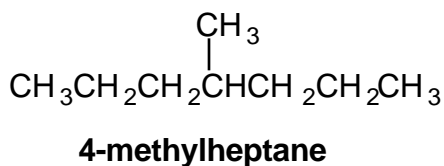
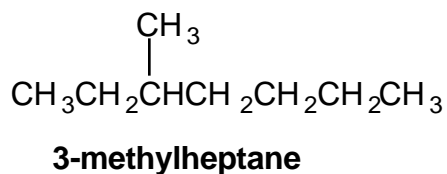
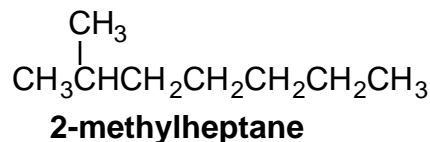
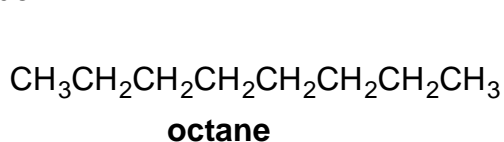
1-bromo-3-methylcyclopentane

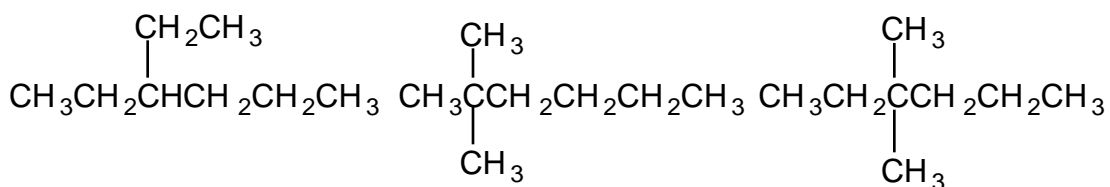
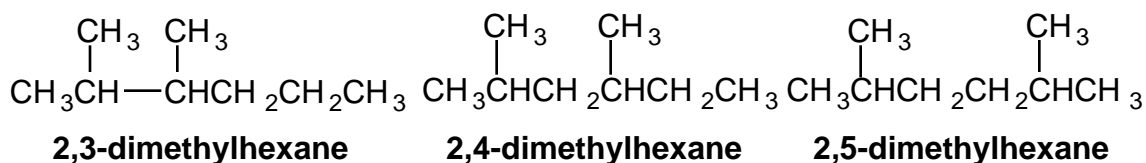
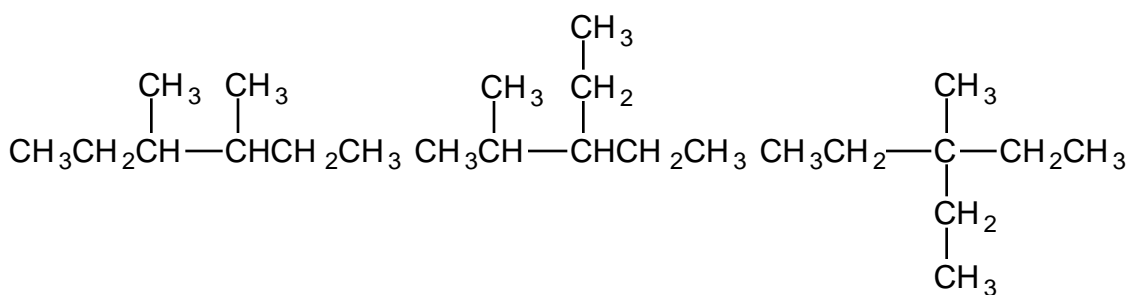
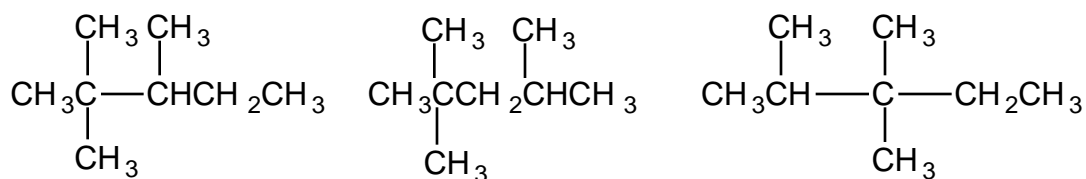
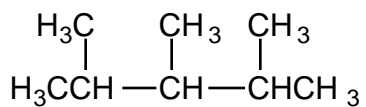
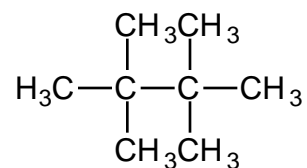
2.18 Molecular Weights

- (a) 16 (b) 46 (c) 342 (d) 264 ($11 \times 12 + 17 \times 1 + 2 \times 14 + 2 \times 16 + 32 + 23$)

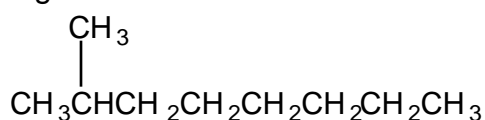
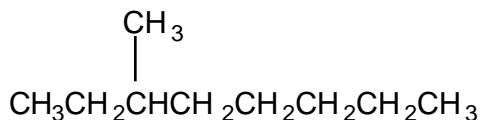
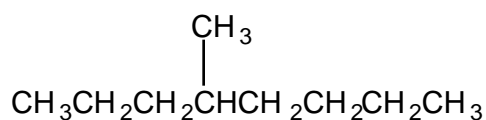
2.19 Skeletal Isomerism: Sections 2.3 and 2.6

(a) C_8H_{18} : Start with an eight-carbon chain. Then systematically make the longest chain one carbon shorter. Arrange the remaining carbons in each case on the chain in as many different ways as possible without extending the length of the base chain. The following isomers are drawn in a logical, systematic order.

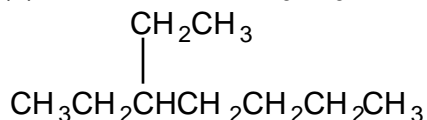
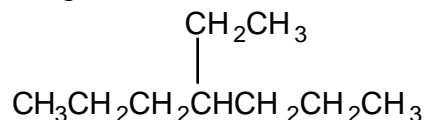
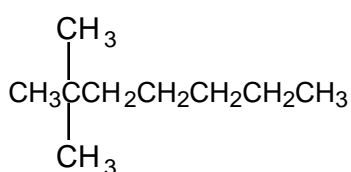
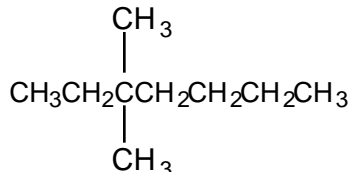
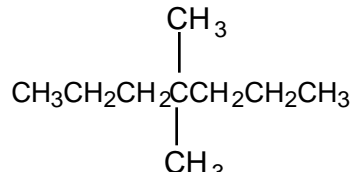
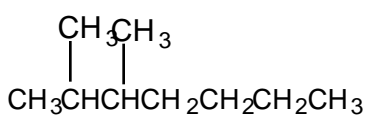
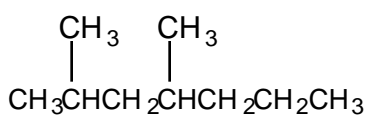
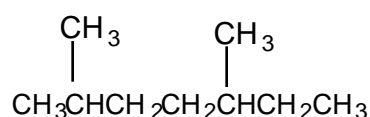
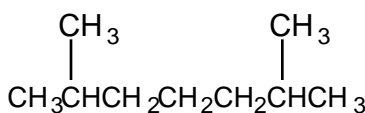
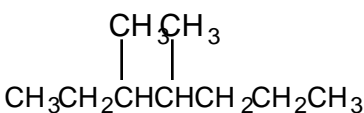
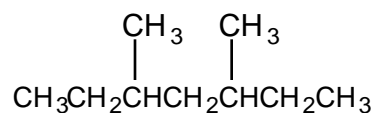


**3-ethylhexane****2,2-dimethylhexane****3,3-dimethylhexane****2,3-dimethylhexane****2,4-dimethylhexane****2,5-dimethylhexane****3,4-dimethylhexane****3-ethyl-2-methylpentane****3-ethyl-3-methylpentane****2,2,3-trimethylpentane****2,2,4-trimethylpentane****2,3,3-trimethylpentane****2,3,4-trimethylpentane****2,2,3,3-tetramethylbutane**

(b) three isomers of C_9H_{20} with eight carbons in the longest chain: write the longest chain straight across. Don't put anything on the chain that would make it longer.

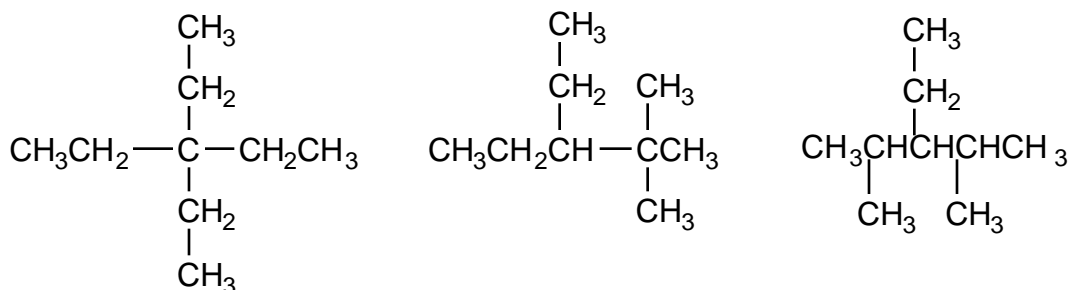
**2-methyloctane****3-methyloctane****4-methyloctane**

(c) 11 isomers of C_9H_{20} with seven carbons in the longest chain:

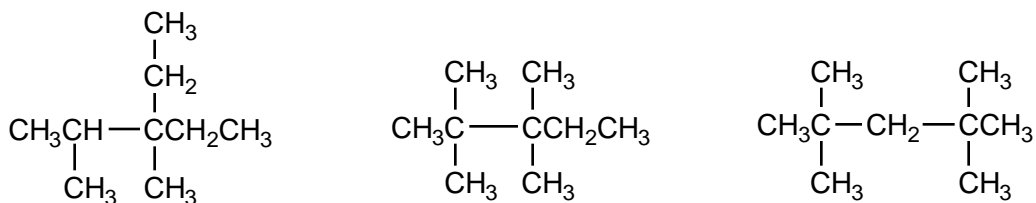
**3-ethylheptane****4-ethylheptane****2,2-dimethylheptane****3,3-dimethylheptane****4,4-dimethylheptane****2,3-dimethylheptane****2,4-dimethylheptane****2,5-dimethylheptane****2,6-dimethylheptane****3,4-dimethylheptane****3,5-dimethylheptane**

(d) Eight isomers of C_9H_{20} with five carbons in longest chain: Draw a five-carbon chain across the paper in a straight line. Arrange the remaining four

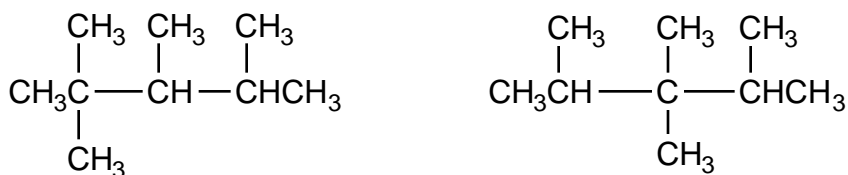
carbons in as many ways as possible without making the chain longer. The ways to consider arranging the remaining four carbons are: a) one four-carbon chain; b) a three- and a one-carbon chain, c) 2 two-carbon chains; d) 1 two- and 2 one-carbon chains; and e) 4 one-carbon chains. Variations a) and b) are not usable as there is no way to place a four- or three-carbon unit on a five-carbon chain without extending the longest chain.



3,3-diethylpentane 2,2-dimethyl-3-ethylpentane 2,4-dimethyl-3-ethylpentane



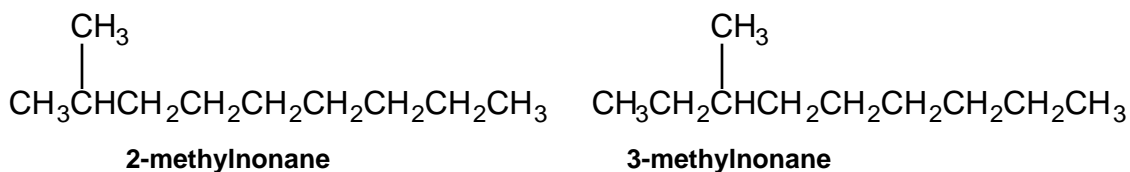
2,3-dimethyl-3-ethylpentane 2,2,3,3-tetramethylpentane 2,2,4,4-tetramethylpentane

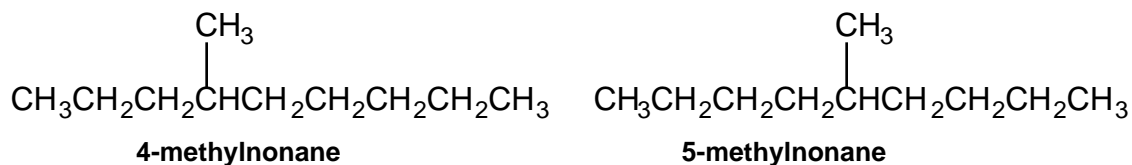


2,2,3,4-tetramethylpentane

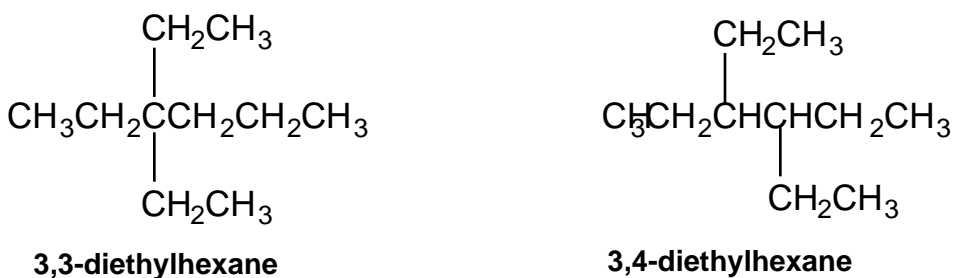
2,3,3,4-tetramethylpentane

(e) four isomers of $\text{C}_{10}\text{H}_{22}$ with nine carbons in the longest chain:

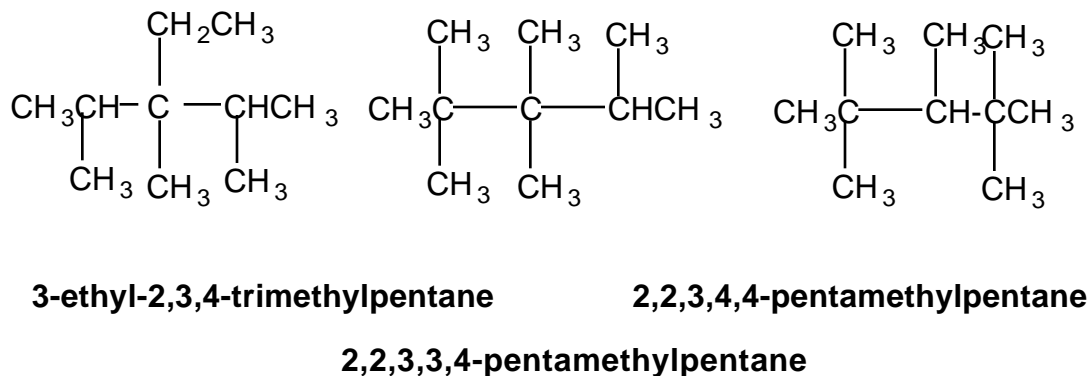
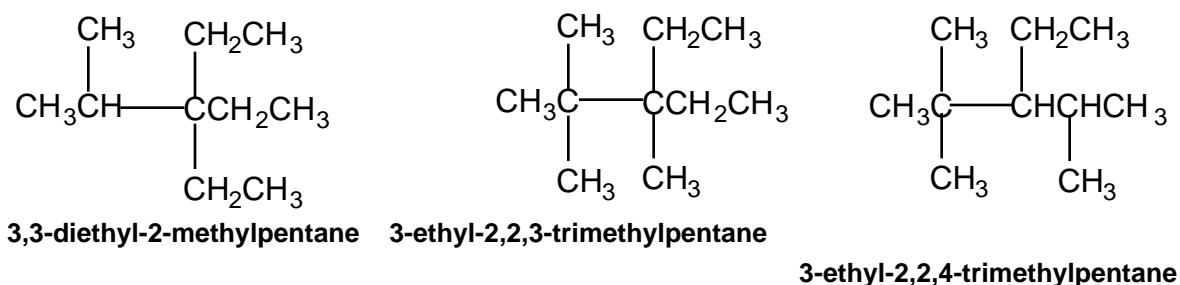




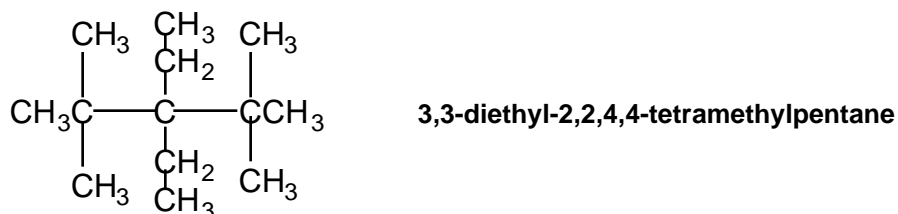
(f) two isomers of $\text{C}_{10}\text{H}_{22}$ with only two alkyl groups on a six carbon chain:



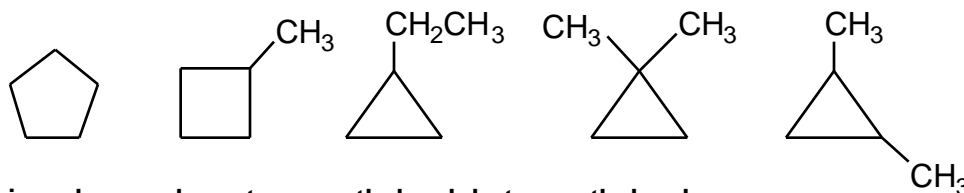
(g) six isomers of $\text{C}_{10}\text{H}_{22}$ with five carbons in the longest chain:



(h) the isomer of $C_{13}H_{28}$ with the shortest longest chain possible

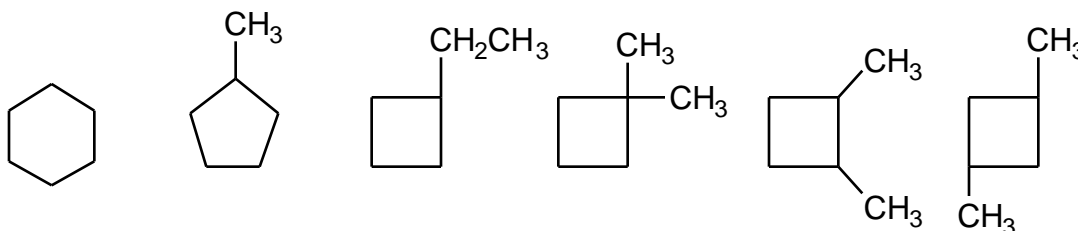


(i) five cyclic compounds of C_5H_{10}

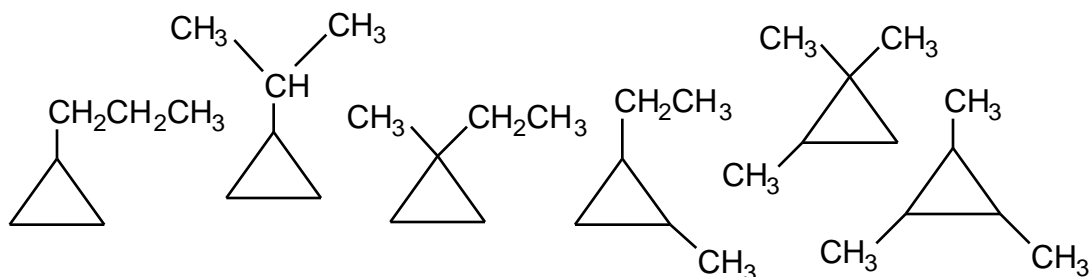


**Names in order: cyclopentane; methylcyclobutane; ethylcyclopropane
1,1-dimethylcyclopropane; 1,2-dimethylcyclopropane**

(j) twelve cyclic compounds of C_6H_{12}

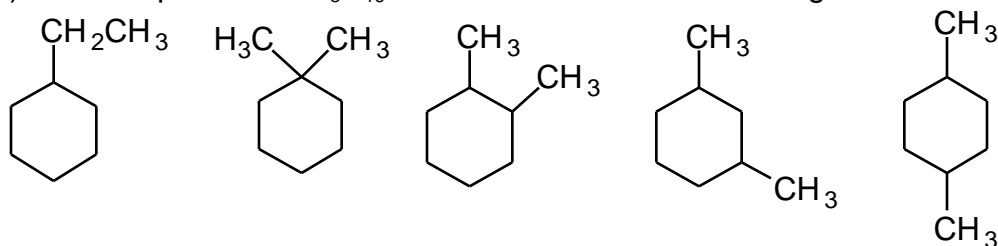


**Names in order: cyclohexane; methylcyclopentane; ethylcyclobutane;
1,1-dimethylcyclobutane; 1,2-dimethylcyclobutane; 1,3-dimethylcyclobutane.**



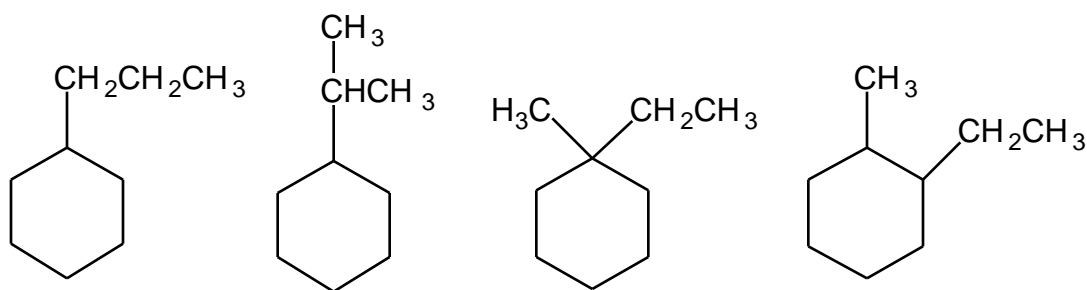
**Names in order: propylcyclopropane; isopropylcyclopropane;
1-ethyl-1-methylcyclopropane; 1-ethyl-2-methylcyclopropane;
1,1,2-trimethylcyclopropane; 1,2,3-trimethylcyclopropane.**

(k) five compounds of C_8H_{16} that have a six-membered ring

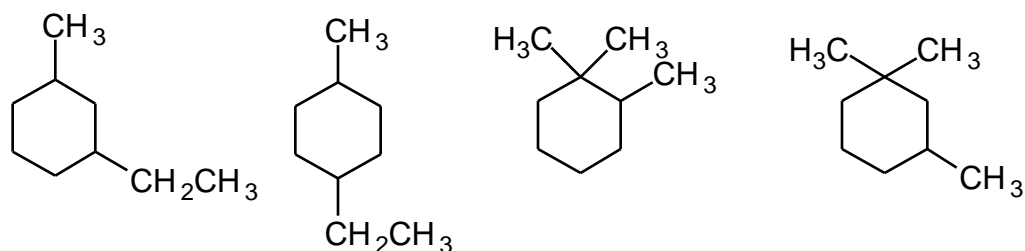


**Names in Order: ethylcyclohexane; 1,1-dimethylcyclohexane
1,2-dimethylcyclohexane; 1,3-dimethylcyclohexane;
1,4-dimethylcyclohexane**

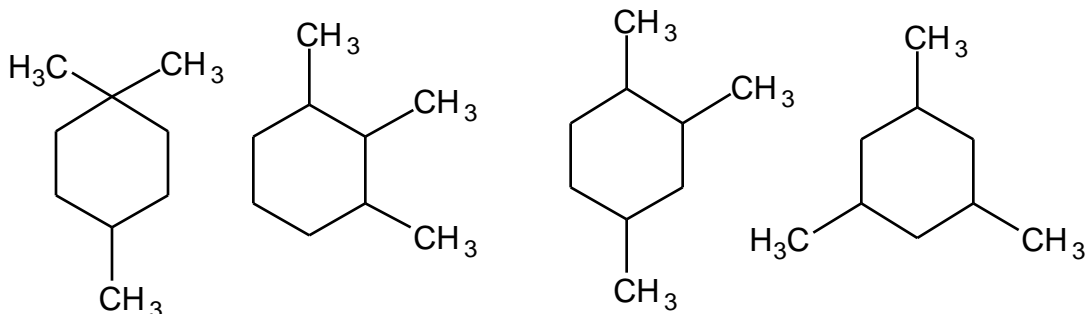
(l) 12 isomers of C_9H_{18} that have a six-membered ring



**Names in Order: propylcyclohexane; isopropylcyclohexane;
1-ethyl-1-methylcyclohexane; 1-ethyl-2-methylcyclohexane**



**Names in Order: 1-ethyl-3-methylcyclohexane;
1-ethyl-4-methylcyclohexane; 1,1,2-trimethylcyclohexane;
1,1,3-trimethylcyclohexane**



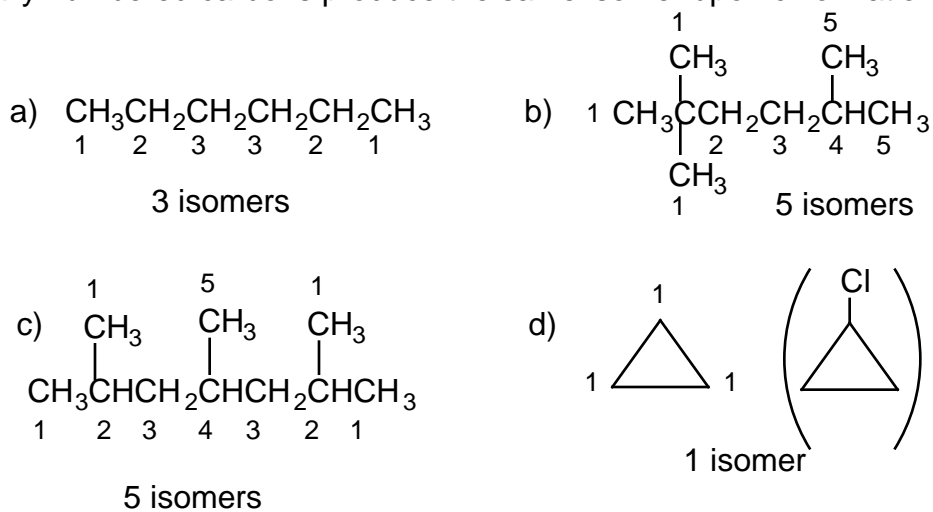
Names in Order: 1,1,4-trimethylcyclohexane;
1,2,3-trimethylcyclohexane; 1,2,4-trimethylcyclohexane;
1,3,5-trimethylcyclohexane

2.20 Nomenclature of Alkanes: Section 2.6

Names are included with structures in Problem 2.19.

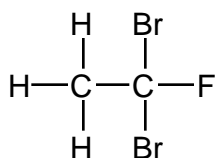
2.21 Positional Isomers: Section 2.5

Each carbon that can have a hydrogen replaced with a chlorine is numbered. Identically numbered carbons produce the same isomer upon chlorination.

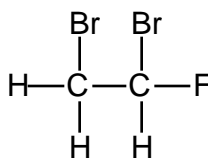


2.22 Skeletal and Positional Isomerism: Sections 2.3 and 2.5

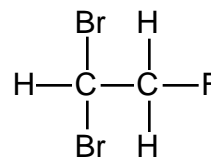
a) three isomers of $\text{C}_2\text{H}_3\text{Br}_2\text{F}$



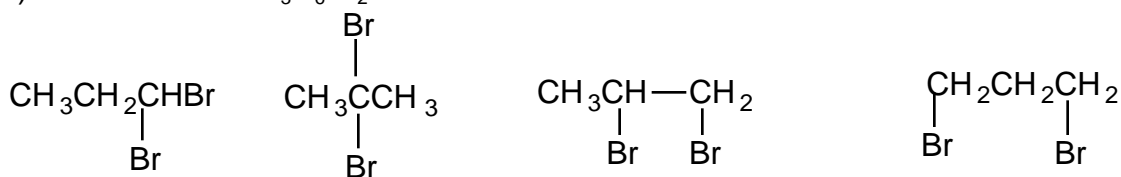
1,1-dibromo-1-fluoroethane



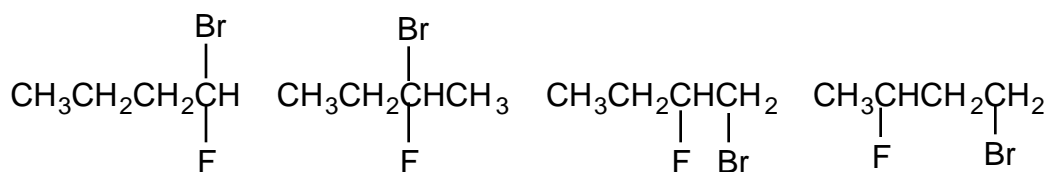
1,2-dibromo-1-fluoroethane



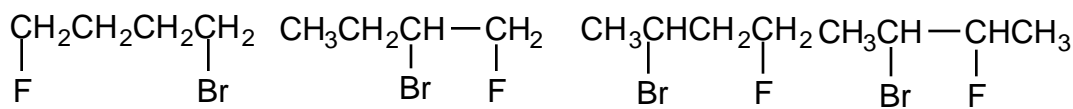
1,1-dibromo-2-fluoroethane

(b) four isomers of $C_3H_6Br_2$ 

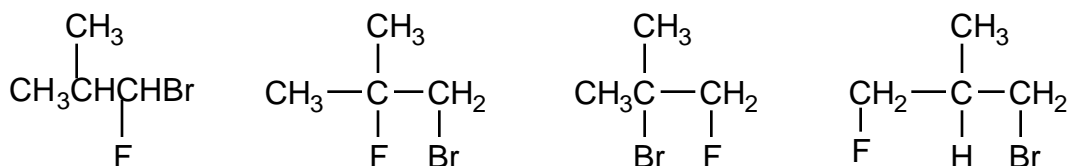
**Names in Order: 1,1-dibromopropane; 2,2-dibromopropane;
1,2-dibromopropane; 1,3-dibromopropane**

(c) twelve isomers of C_4H_8BrF 

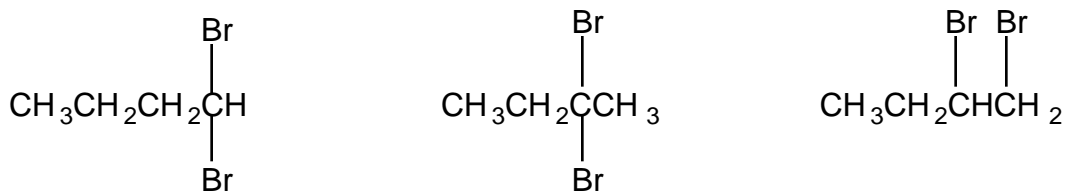
**Names in order: 1-bromo-1-fluorobutane; 2-bromo-2-fluorobutane;
1-bromo-2-fluorobutane; 1-bromo-3-fluorobutane**

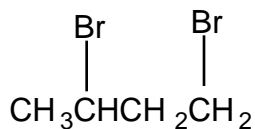
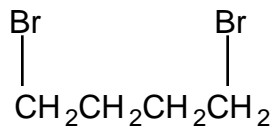
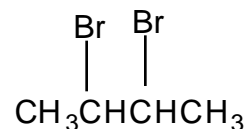


**Names in order: 1-bromo-4-fluorobutane; 2-bromo-1-fluorobutane;
3-bromo-1-fluorobutane; 2-bromo-3-fluorobutane**



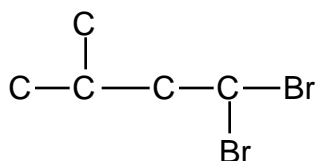
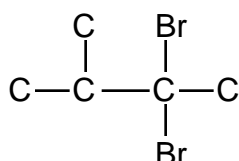
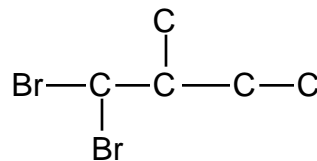
**Names in order: 1-bromo-1-fluoro-2-methylpropane; 1-bromo-2-fluoro-
2-methylpropane; 2-bromo-1-fluoro-2-methylpropane; 1-bromo-3-fluoro-
2-methylpropane**

(d) 6 isomers of $C_4H_8Br_2$ with four carbons in the longest chain**1,1-dibromobutane****2,2-dibromobutane****1,2-dibromobutane**

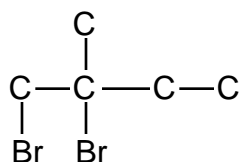
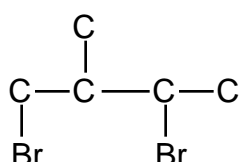
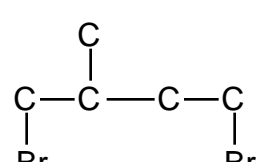
**1,3-dibromobutane****1,4-dibromobutane****2,3-dibromobutane**

(e) nine isomers of $\text{C}_5\text{H}_{10}\text{Br}_2$ with four carbons in the longest chain

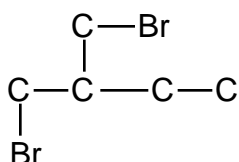
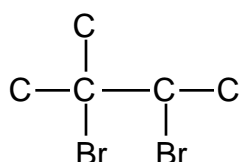
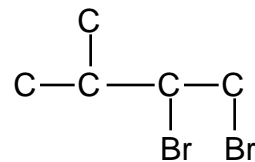
For simplicity let us just show the required carbon skeleton and move the two bromines around systematically. First, place two bromines on the same carbon.

**1,1-dibromo-3-methylbutane****1,1-dibromo-2-methylbutane****2,2-dibromo-3-methylbutane**

Now put a bromine on carbon-1 and vary the position of the other bromine.

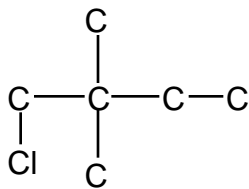
**1,2-dibromo-2-methylbutane****1,3-dibromo-2-methylbutane****1,4-dibromo-2-methylbutane**

Finally, draw isomers in which the bromines are on the middle two carbons and the two carbons on the other end.

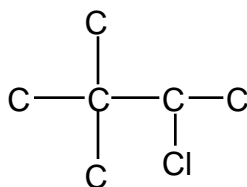
**1,3-dibromo-2-ethylpropane****1,2-dibromo-3-methylbutane****2,3-dibromo-2-methylbutane**

(f) five isomers of $C_6H_{13}Cl$ with four carbons in the longest chain.

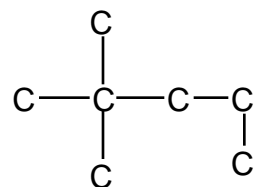
Again let us draw the carbon skeletons, there are two, and vary the position of the chlorine.



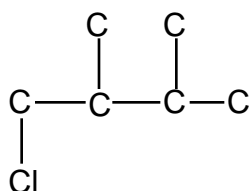
1-chloro-2,2-dimethylbutane



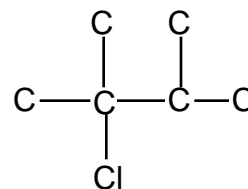
3-chloro-2,2-dimethylbutane



1-chloro-3,3-dimethylbutane



1-chloro-2,3-dimethylbutane



2-chloro-2,3-dimethylbutane

2.23 Nomenclature of Halogenated Alkanes: Section 2.6D

The names are with the structures in Problem 2.22.

2.24 Nomenclature of Alkanes: Section 2.6

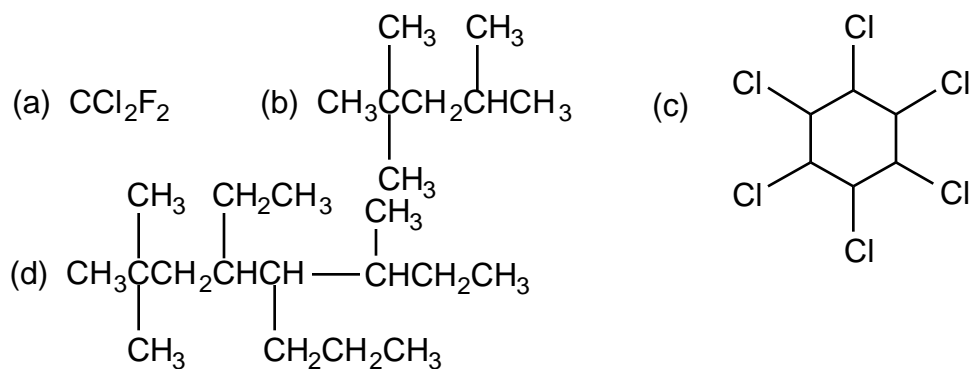
(a) propane (b) decane (c) octane

2.25 Nomenclature of Alkanes: Section 2.6

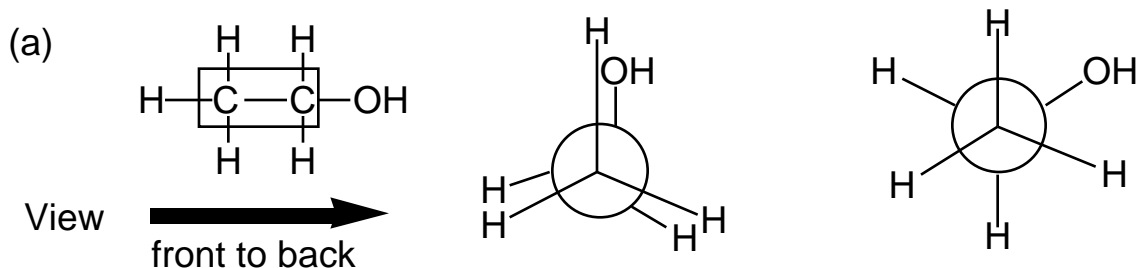
- (a) 4-methylnonane; (b) 5-propyldecane; (c) 2,5-dimethylhexane;
 (d) 4-ethyl-2-methylhexane; (e) 2,2,4,6-tetramethylheptane;
 (f) 6-propyl-2,4,4-trimethyldecane (longest chain is not written straight across the page); (g) 2-cyclobutylhexane; (h) 3,3,5,7-tetramethyldecane (note that the longest chain is not written straight across the page; the two fragments below are part of the longest chain.)
 (i) 2,2,3,3-tetramethylbutane; (j) ethylcyclopropane;
 (k) isopropylcyclopentane; (l) 1-butyl-4-t-butylcyclohexane;
 (m) 2,2-dimethylbutane; (n) 2,4-dimethylhexane;
 (o) 4-ethyl-2,2-dimethylhexane

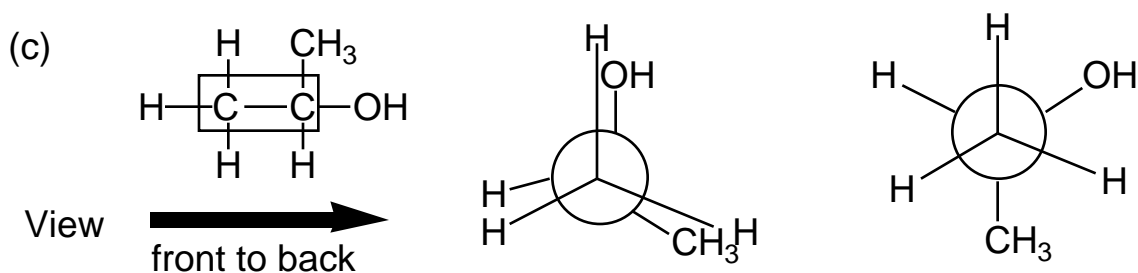
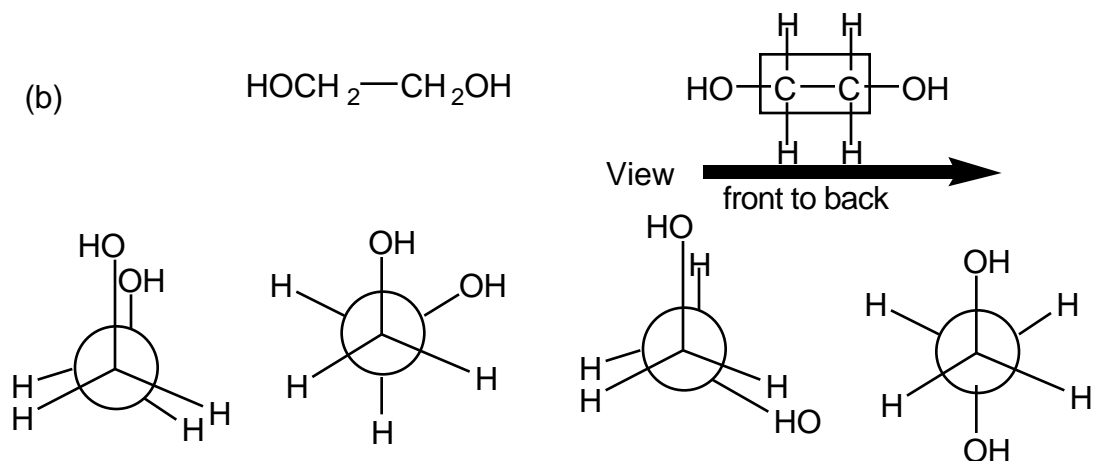
2.26 Nomenclature of Halogenated Alkanes: Section 2.6D

- (a) triiodomethane; (b) 2-bromo-3-methylbutane;
 (c) 1,3-dibromo-4-fluoro-2,4-dimethylpentane

2.27 IUPAC Nomenclature: Section 2.6**2.28 Conformational Isomers:** Section 2.7

In each case, draw the compound, determine what three groups are on each of the carbons to be placed in the Newman projection, draw the Newman projection with the bonds for the front carbon emanating from the center of the circle and those of the back carbon coming from the perimeter, and put the three groups on each carbon. Rotate between staggered and eclipsed conformations to get the extreme forms.

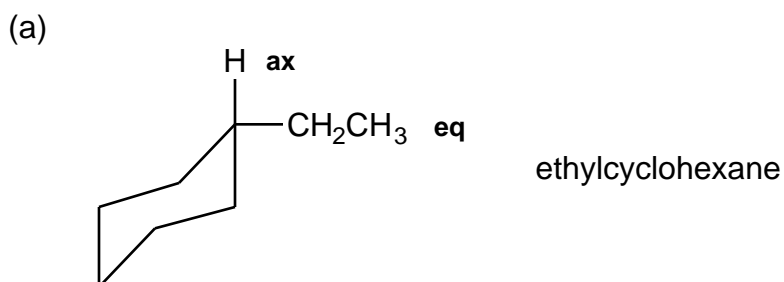




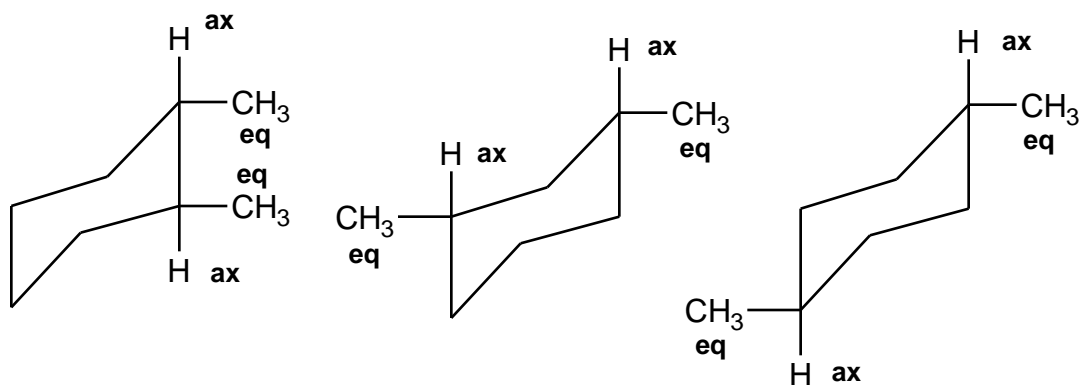
2.29 Conformational Isomerism in Substituted Cyclohexanes:

Section 2.8 B-D

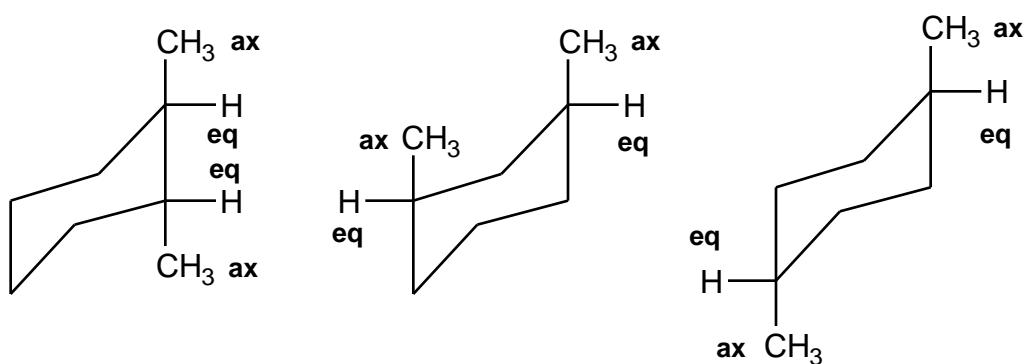
In doing these problems, remember that equatorial positions are roomier than axial positions and substituents occupy equatorial positions preferentially when possible. If there are two groups on the cyclohexane chair, the conformation in which the larger group is equatorial, or, if possible, both groups are equatorial, is preferred.



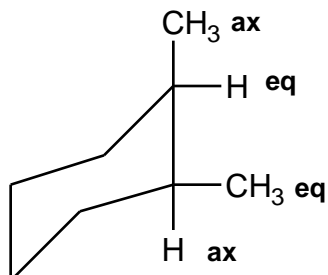
(b) most stable chair forms of 1,2-; 1,3-; and 1,4-dimethylcyclohexane



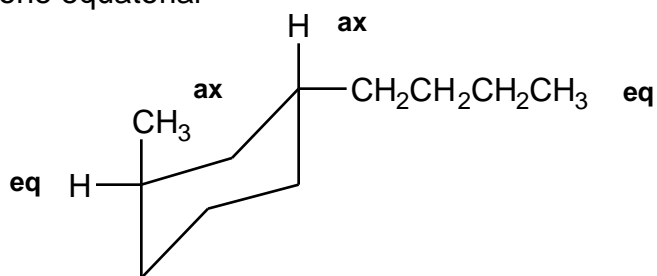
(c) least stable chair forms of compounds in part b



(d) 1,2-dimethylcyclohexane with one group axial and one equatorial



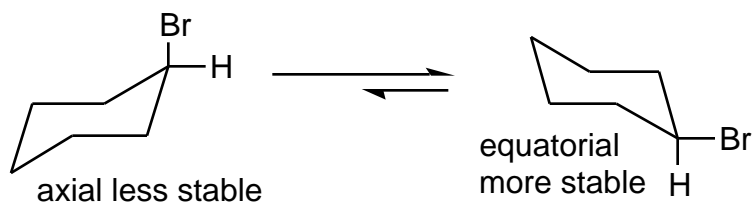
(e) most stable chair form of 1-butyl-3-methylcyclohexane with one group axial and one equatorial



the larger group
is in the roomier
equatorial
position

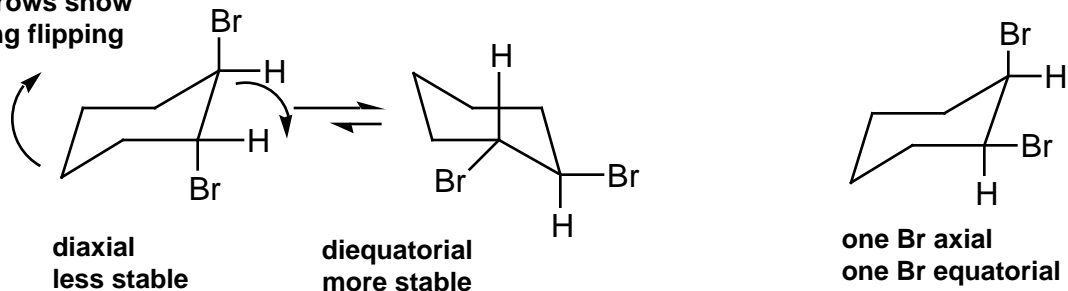
2.30 Conformational Isomerism in Substituted Cyclohexanes: Section 2.8

(a) bromocyclohexane

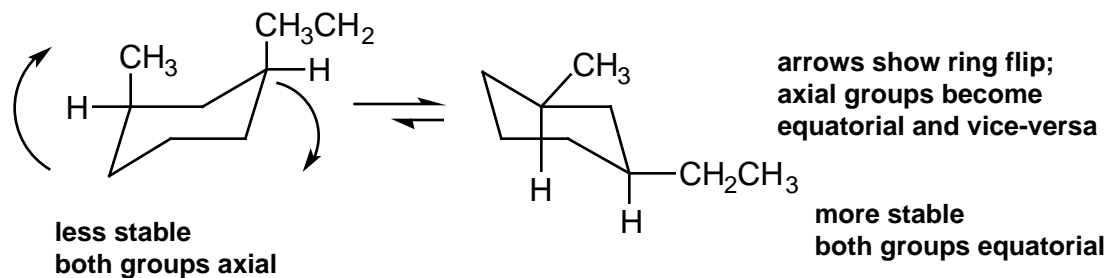


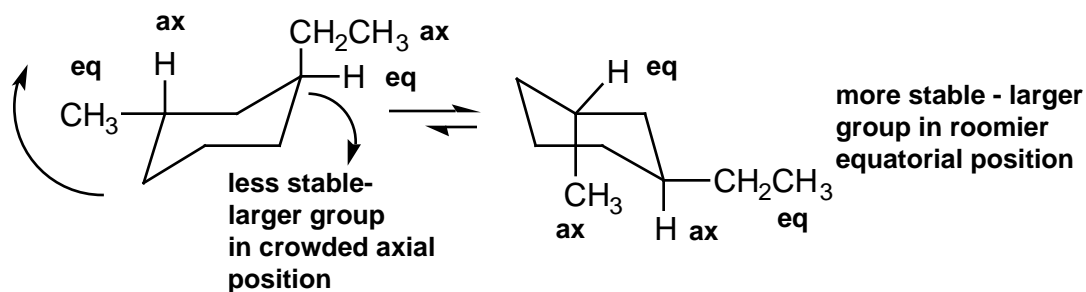
(b)

arrows show
ring flipping

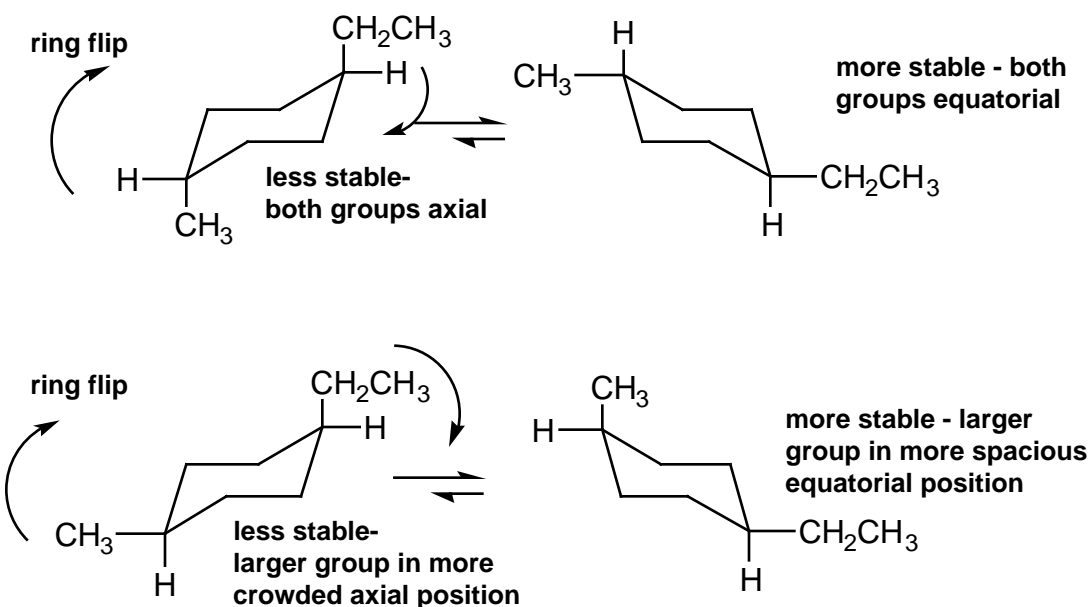


(c) 1-ethyl-3-methylcyclohexane

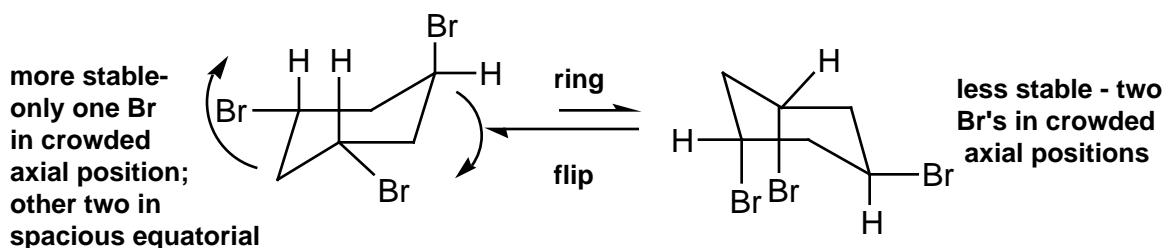




(d) 1-ethyl-4-methylcyclohexane

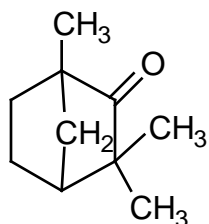


(e) 1,3,5-tribromocyclohexane

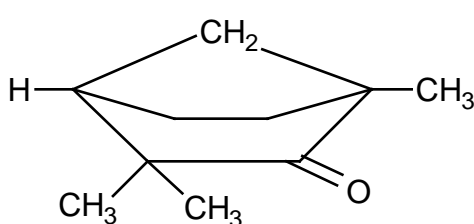
**2.31 Conformational Isomerism in Cyclohexane:** Section 2.8B

The structures show a one-carbon bridge between the first and fourth carbons of the ring. In the boat form, the first and fourth carbons are directed toward one another and are easily tied together by the single bonds to the —CH₂— bridge. However, in the chair form, these two carbons are so far removed from one

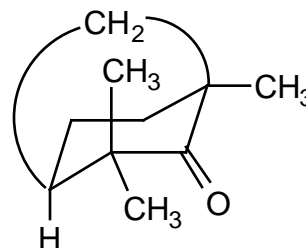
another that they cannot be bridged by a single carbon. The two single bonds are not long enough nor can they be conveniently directed in the necessary geometry.



Camphor

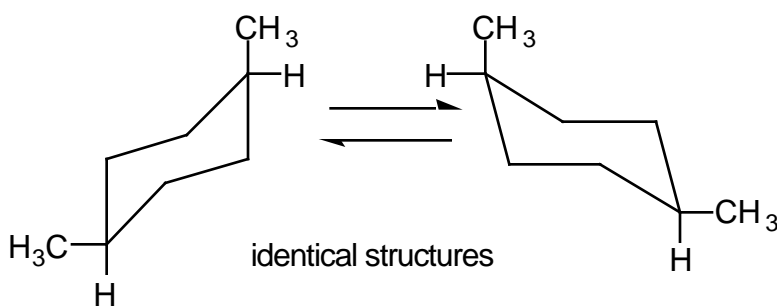


Boat Form

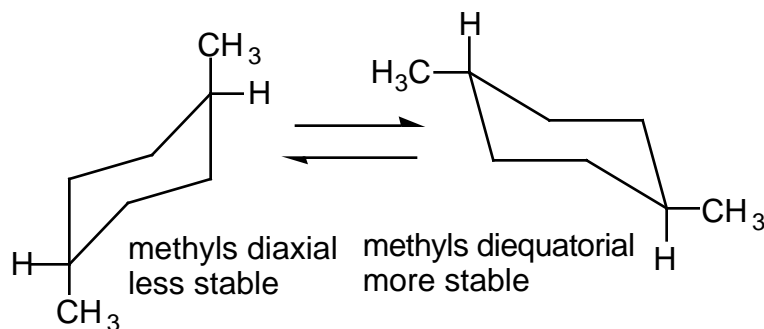


Chair Form

2.32 Conformational Isomerism



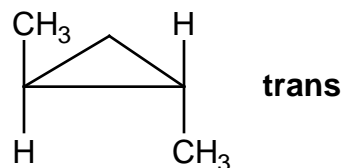
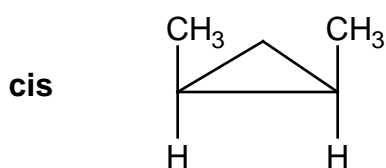
In the first compound, both conformers have one methyl axial and one equatorial. They are the same. You can bottle this isomer. It is the sole component of the equilibrium.



The diaxial conformer is in equilibrium with the diequatorial. The diequatorial is virtually the exclusive component of the equilibrium. The diaxial essentially cannot exist.

2.33 Geometric Isomerism: Section 2.8E

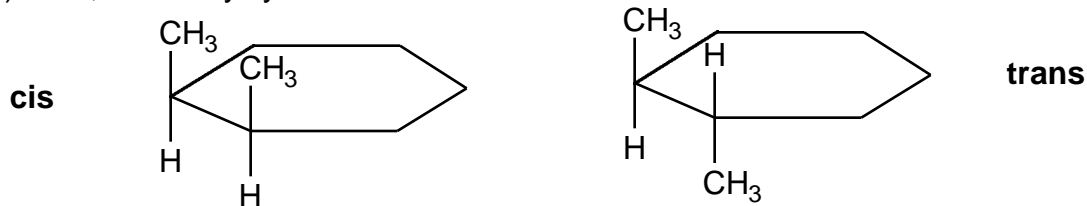
(a) 1,2-dimethylcyclopropane



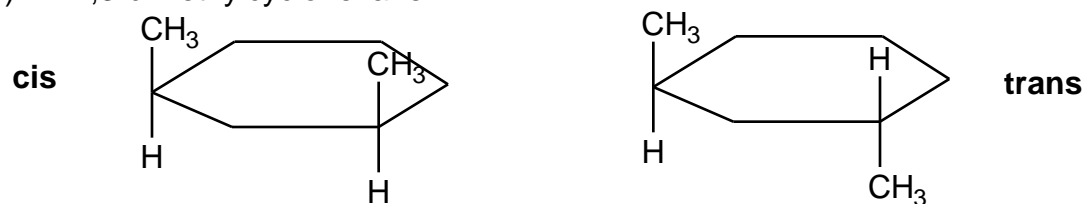
(b) 1-bromo-3-chlorocyclobutane

**2.34 Geometric Isomerism:** Section 2.8E

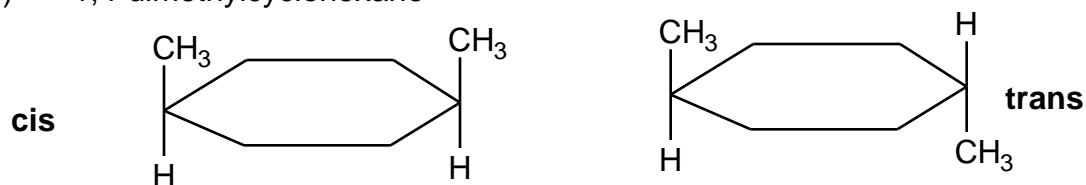
(a) 1,2-dimethylcyclohexane



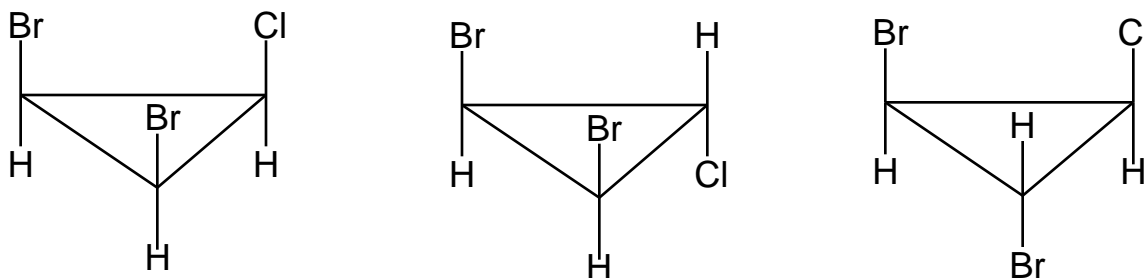
(b) 1,3-dimethylcyclohexane



(c) 1,4-dimethylcyclohexane

**2.35 Geometric Isomerism:** Section 2.8E

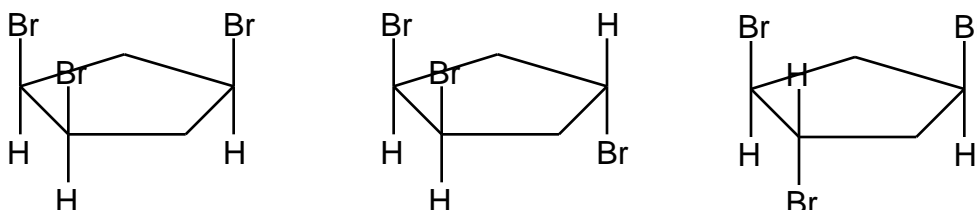
(a) 1,2-dibromo-3-chlorocyclopropane



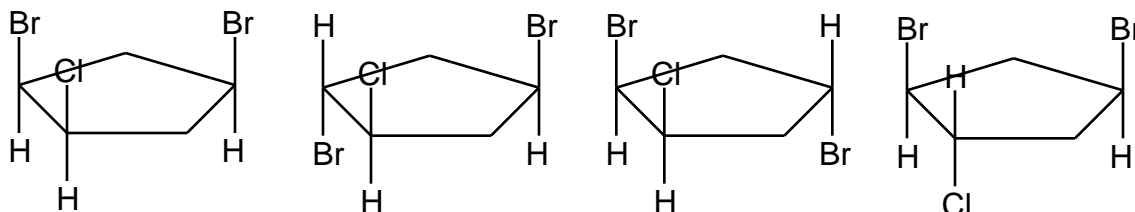
(b) 1,2,3-tribromocyclopropane



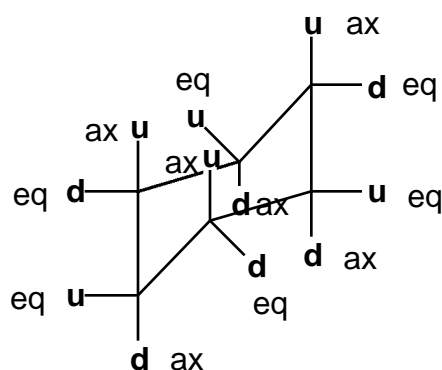
(c) 1,2,4-tribromocyclopentane



(d) 2-chloro-1,4-dibromocyclopentane

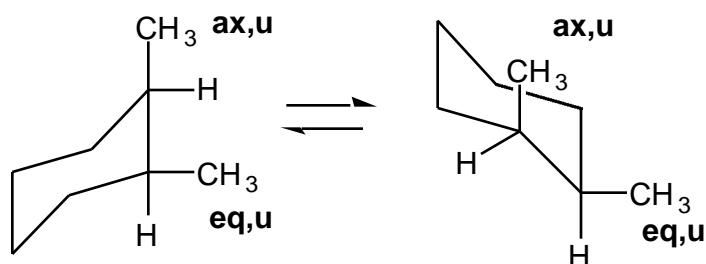
**2.36 Geometric Isomerism in the Cyclohexane Chair:** Section 2.8

To understand cis and trans on the cyclohexane chair, first draw the chair and insert bonds for the axial and equatorial positions (these are labeled in the diagram). Then note on each carbon, one bond can be considered up (**u**) and one down (**d**) relative to one another. In disubstituted cyclohexanes, if both groups are up or both down the isomer is cis. If they are up/down or down/up, the isomer is trans. Rationalize this with the chart in the textbook Problem 2.36. For example, in 1,2-disubstituted cyclohexanes, up/up or down/down is ax/eq or eq/ax and up/down or down/up is ax/ax or eq/eq.



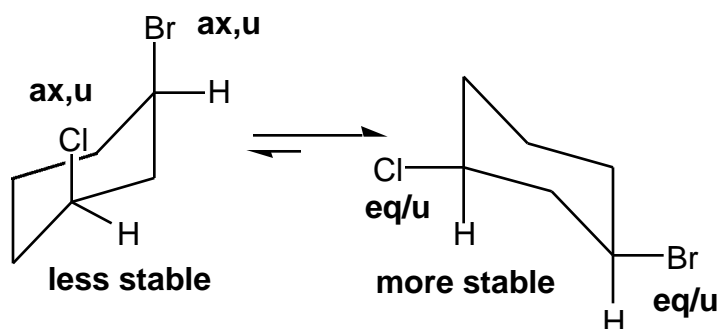
cis	u/u or d/d
trans	u/d or d/u

(a) cis 1,2-dimethylcyclohexane



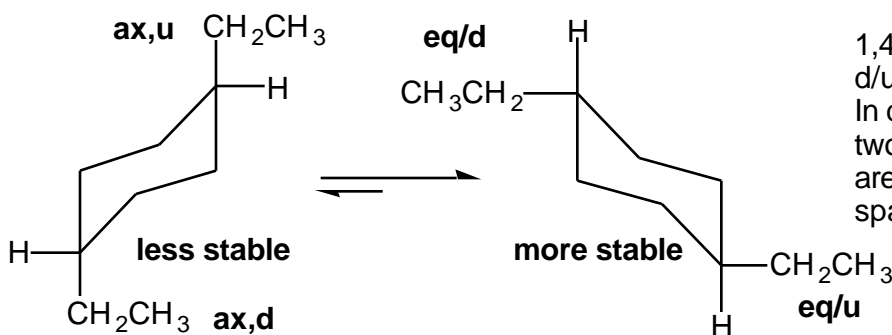
cis is up/up or down/down which is ax/eq or eq/ax in this case. The two conformations are essentially identical and of equal stability.

(b) cis 1-bromo-3-chlorocyclohexane



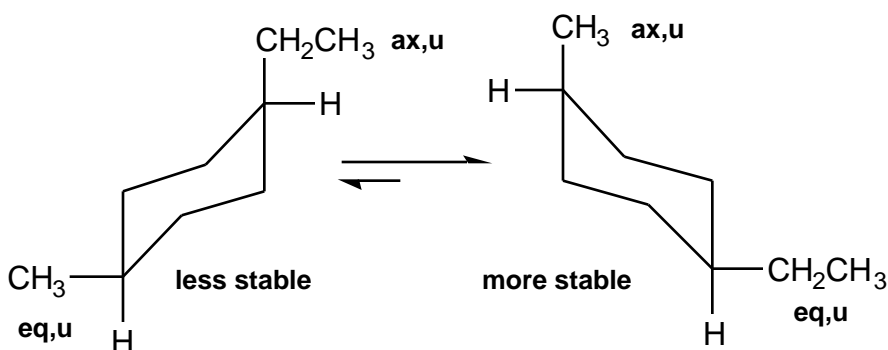
Cis is ax/ax or eq/eq in 1,3-disubstituted chairs since this is u/u or d/d. The eq/eq is more stable since the two large groups are in the more spacious equatorial positions.

(c) trans 1,4-diethylcyclohexane



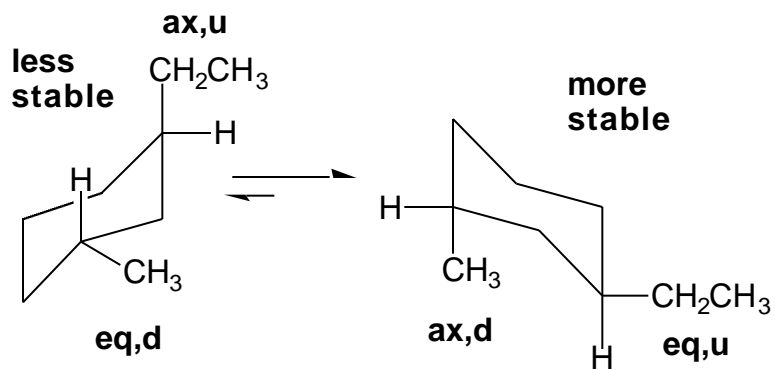
1,4 trans is u/d or d/u or di-ax or di-eq. In di-equatorial, the two large substituents are in the more spacious positions.

(d) cis 1-ethyl-4-methylcyclohexane



Cis is u/u or d/d which as shown is ax/eq or eq/ax for 1,4 disubstitution. The conformer in which the larger ethyl group is equatorial is the more stable since equatorial positions are more spacious.

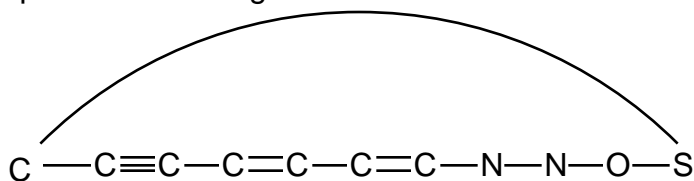
(e) trans 1-ethyl-3-methylcyclohexane



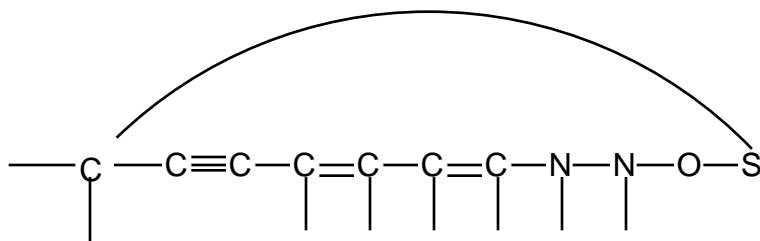
Trans is u/d as shown here. The more stable conformer has the larger ethyl group in the more spacious equatorial position and the smaller methyl group in the more crowded axial position.

2.37 Molecular Formulas

One approach to this problem is to bond continuously all the atoms with valences greater than one and insert the described rings and multiple bonds (the big arch represents one ring).



Now put lines on each atom corresponding to the number of monovalent atoms will be necessary to satisfy the valence. Note below you need eight monovalent elements.



There are two bromines in the molecule so you still need **six hydrogens** to provide a total of eight monovalent atoms.

2.38 Physical Properties: Section 2.9

(a) Boiling points increase with molecular weight within a homologous series. Both examples are alkanes; ethane has the greater molecular weight.

(b) These two compounds are isomers and have the same molecular weight. The unbranched isomer has greater surface area and thus there are more opportunities for intermolecular attraction. The greater the attractions between

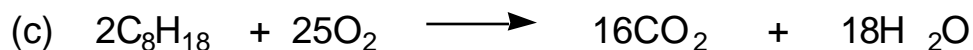
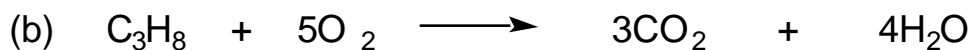
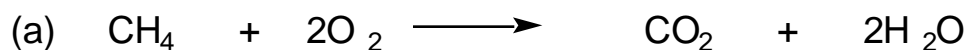
molecules, the more energy necessary to break these attractions and the higher is the boiling point. The branched isomer has less surface area and less intermolecular interactions as a result.

(c) CBr_4 has the higher molecular weight and thus the higher boiling point.

(d) Cyclohexane is more symmetrical and compact and consequently forms a more stable crystal lattice. Such a lattice requires more energy to disrupt and cyclohexane has a higher melting point.

(e) Melting points generally increase with molecular weight (all other factors being equal) since it requires more energy (higher temperatures) to give the heavier molecules enough motion to break out of a stationary crystal lattice.

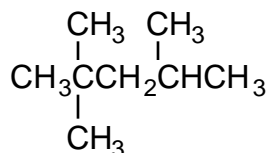
2.39 Combustion: Connection 2



2.40 Petroleum Fractions: Connection 2

(a) Gas - any hydrocarbon with 1-4 carbons; for example CH_4 , the main component of natural gas.

(b) Gasoline - any hydrocarbon with 5-10 carbons; for example



(c) Kerosene - any hydrocarbon with 11-18 carbons; for example $\text{CH}_3(\text{CH}_2)_{10}\text{CH}_3$

(d) Gas-Oil - any hydrocarbon with 15-18 carbons such as $\text{CH}_3(\text{CH}_2)_{16}\text{CH}_3$

(e) Wax-Oil - hydrocarbons with 18-20 carbons; $\text{CH}_3(\text{CH}_2)_{17}\text{CH}_3$

(f) Wax - high molecular weight hydrocarbons usually with 20 or more carbons; for example $\text{CH}_3(\text{CH}_2)_{22}\text{CH}_3$

Activities with Molecular Models

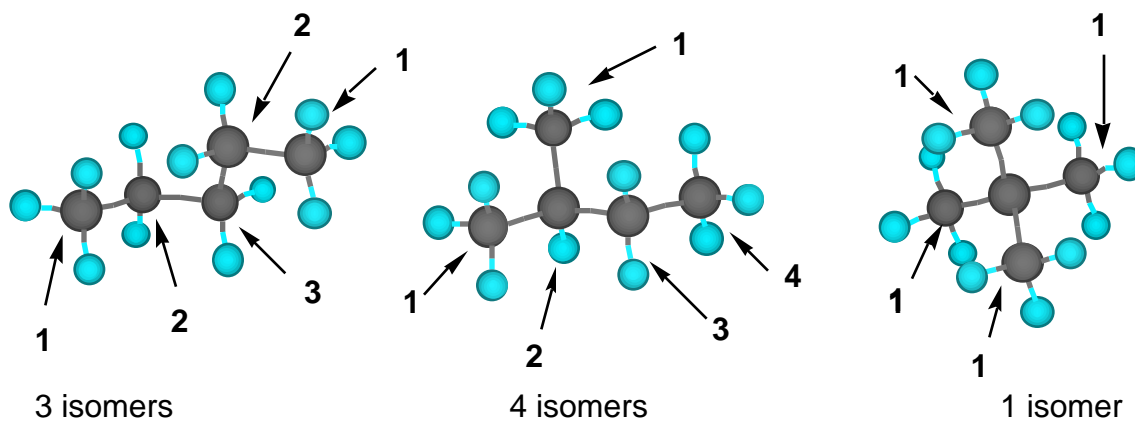
1. Make molecular models of the three skeletal isomers of C_5H_{12} . Note the tetrahedral geometry of each carbon. Also observe the increasing compactness of the molecules with branching.

The models are shown in question 2.

2. For each of the three isomers you made in exercise 1, see how many different places you can remove a hydrogen and attach a bromine. In each different case, you have made a positional isomer. How many can you make for each? Does symmetry within each molecule influence the number of possible positional isomers?

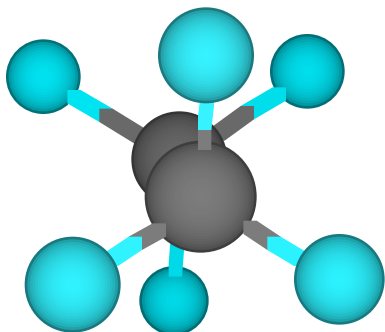
The following models have an arrow directed at each carbon that could exchange a hydrogen for a bromine. There are five such places in the first structure but only three of them will give different isomers. The two carbons labeled 1 will both give 1-bromopentane, for example. The two labeled 2 will both give 2-bromopentane, and the one labeled 3 will give 3-bromopentane.

Monobromination sites and number of isomers possible

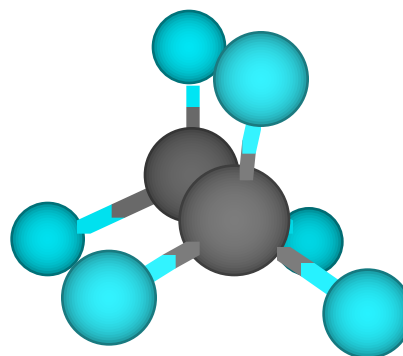


3. Make a model of ethane, C_2H_6 . Rotate the two carbons relative to each other around the carbon-carbon bond. Make the staggered and eclipsed conformations.

staggered



eclipsed

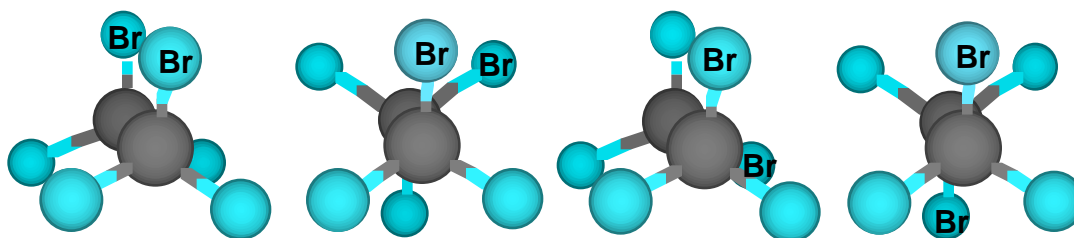


4. Using your models from exercise 3, remove one hydrogen and replace it with a bromine. Find the one staggered and one eclipsed conformation. Now replace a second hydrogen, on the other carbon, with a bromine. Find the two staggered and two eclipsed conformations.

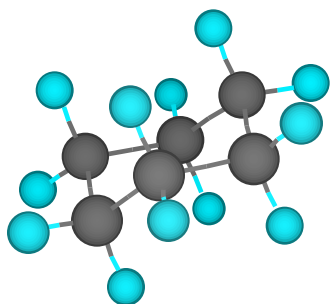
The Br symbol is put into one of the hydrogens on one carbon to show where you should place a bromine and what two conformations you will see.



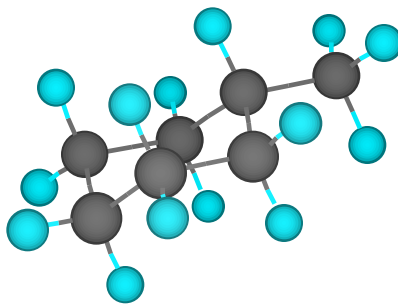
In the following models, there are two bromines, one on each carbon. In the first structure they are totally eclipsed. To get the other three models, the rear carbon is rotated to give staggered, eclipsed, and finally another staggered.



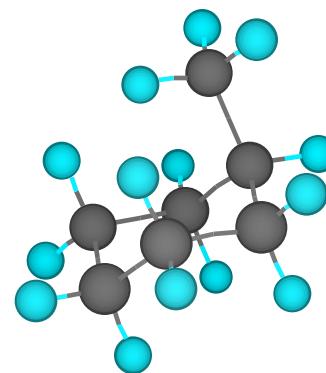
5. Make a model of the chair form of cyclohexane. Notice that each carbon-carbon bond is in a staggered conformation. Identify the axial and equatorial hydrogens.
6. Using the model from exercise 5, remove one axial hydrogen and place a methyl (CH_3) group in its place. Replace the hydrogen and put the methyl group in the place of an equatorial hydrogen.



Cyclohexane

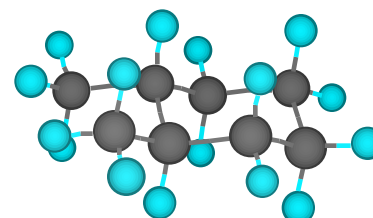
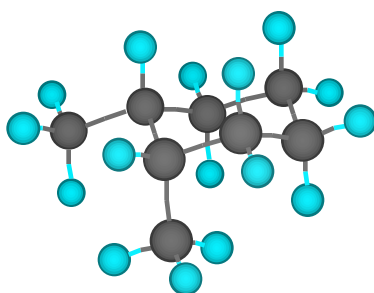
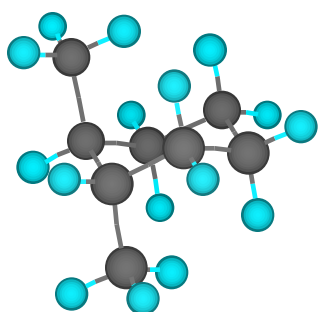


Methylcyclohexane (equatorial)
(more stable)

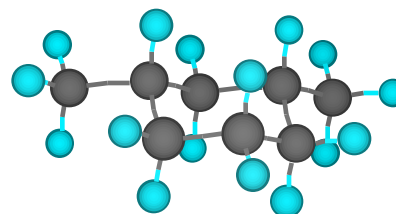
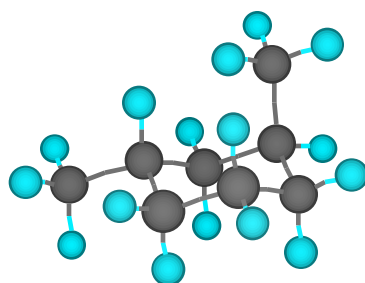
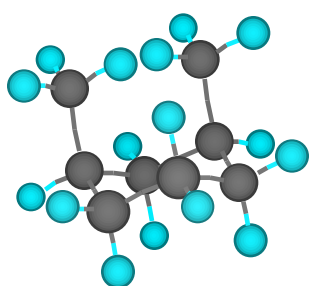


Methylcyclohexane (axial)

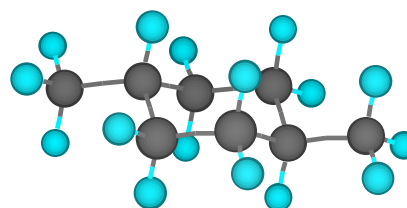
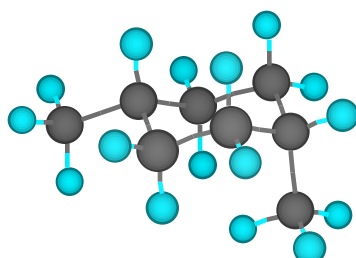
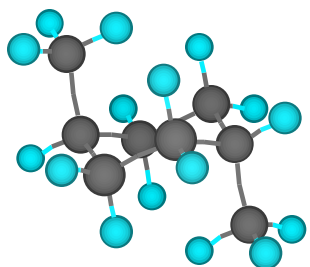
7. Using the model from exercise 6, make 1,2-dimethylcyclohexane with both methyl groups axial, one axial and one equatorial, and both equatorial.

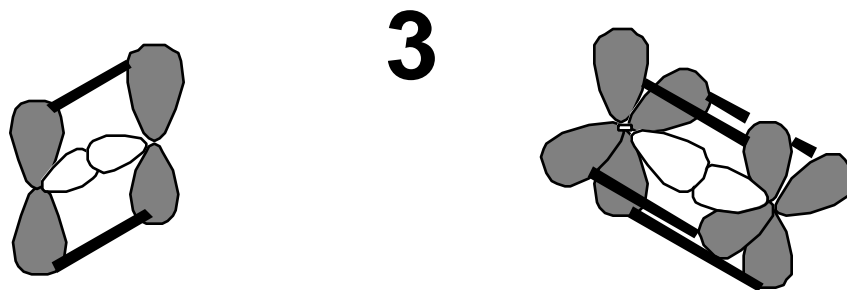


With 1,3-dimethylcyclohexane

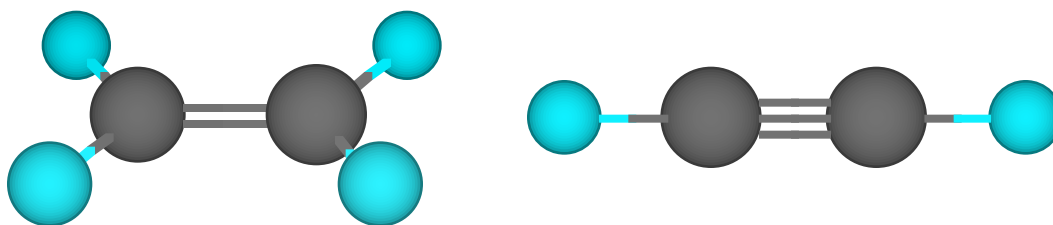


With 1,4-dimethylcyclohexane





Alkenes and Alkynes: Structure and Nomenclature



CHAPTER SUMMARY

3.1 Introduction to Alkenes and Alkynes

Alkenes are hydrocarbons in which there is at least one **carbon-carbon double bond**; **alkynes** have at least one **carbon-carbon triple bond**. Both are termed **unsaturated** because the carbons involved in the multiple bonds do not have the maximum number of bonded atoms possible (four for a carbon). Alkenes have the general formula C_nH_{2n} and alkynes are C_nH_{2n-2} .

3.2 Nomenclature of Alkenes and Alkynes

A. IUPAC Nomenclature

In **IUPAC nomenclature** double bonds are described with an **-ene** suffix attached to the name of the longest chain of carbons; the suffix is **-yne** for

alkynes. The carbon chain is numbered to give the lowest possible number to the multiple bond nearest the end of the longest chain; when there is a choice, double bonds take precedence.

B. Procedure for Naming Alkenes and Alkynes

(1) Name the longest continuous chain of carbons first making sure to select the chain so that it contains the double and triple bonds. (2) Use the suffix -ene for double bonds and -yne for triple bonds. (3) Number the chain giving preference to double or triple bonds (double over triple if necessary). (4) Name all other groups connected to the longest chain with prefixes.

C. Naming Compounds with Both Double and Triple Bonds

The suffix will have both -ene's and -ynes. Lowest numbers are given to multiple bonds with double bonds taking priority over triple when necessary.

D. Common Nomenclature

Simple alkenes are named by following the name of the corresponding alkyl group with ene, as in ethylene and propylene. Alkynes can be named as derivatives of the simplest alkyne, acetylene. Vinyl is the prefix designation for a two carbon alkene and allyl for a three carbon alkene.

CONNECTIONS 3.1 Oral Contraceptives

3.3 Skeletal, Positional, and Functional Isomerism in Alkenes and Alkynes

Alkenes and alkynes exhibit **skeletal isomerism** in which the carbon chain is varied and **positional isomerism** where the position of the multiple bond is different. **Functional isomers** differ in the class of compounds to which they belong. For example, functional isomers of an alkyne could be a diene, cycloalkene, or bicyclic alkane.

3.4 Functional Isomerism in Organic Chemistry

Common functional groups in organic chemistry include: **alkanes, alkenes, alkynes, aromatic hydrocarbons, carboxylic acids, aldehydes, ketones, alcohols, ethers, amines.**

CONNECTIONS 3.2 Chemical Communication in Nature**3.5 Geometric Isomerism in Alkenes****A. Cis-Trans Isomerism**

Alkenes in which there are two different groups on each of the double-bonded carbons are capable of exhibiting **geometric isomerism**. In the **cis isomer**, two identical or comparable groups are on the same side of the double bond and in the **trans isomer** they are on opposite sides. The **pi-bond** restricts rotation around the carbon-carbon double bond and prevents interconversion of the two isomeric forms. This is different from conformational isomerism in which staggered and eclipsed forms are interconvertible because of rotation around a carbon-carbon single bond. However, in both conformational and geometric isomerism, the more stable structures are those in which the larger groups are separated from one another. For this reason, the staggered conformations in conformational isomerism and the trans isomers (for simple alkenes) in geometric isomerism are the most stable.

CONNECTIONS 3.3 Geometric Isomerism and Vision**B. The E-Z System for Designating Configuration of Geometric Isomers**

In the **E-Z system**, the two groups on each of the two carbons are assigned a priority: higher priority, lower priority. If the two higher priority groups are on opposite sides of the double bond being considered, the isomer is **E**; if they are on the same side it is **Z**. Group priority is based on atomic number of the atom directly connected to the double bond carbons; the higher the atomic number, the higher the group priority.

3.6 Units of Unsaturation

One unit of unsaturation is expressed as a **double bond or a ring**. A **triple bond** is **two units of unsaturation**. To calculate units of unsaturation, compare the number of monovalent atoms to the number of carbons. Ignore oxygen. Ignore nitrogen, but subtract one hydrogen or monovalent atom from the formula for each nitrogen. At this point, if there are two times plus two as

many monovalent atoms as carbons, there are no units of unsaturation. For every two monovalent atoms fewer than this there is a unit of unsaturation.

SOLUTIONS TO PROBLEMS

3.1 General Molecular Formulas

Alkanes: C_nH_{2n+2} ; Cycloalkanes: C_nH_{2n} ; Alkenes: C_nH_{2n} ;

Alkynes: C_nH_{2n-2} Cycloalkenes: C_nH_{2n-2} ; Dienes: C_nH_{2n-2} ;

Cycloalkynes: C_nH_{2n-4}

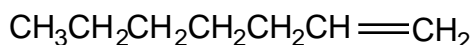
3.2 Nomenclature of Alkenes and Alkynes

(a) 1-heptene; (b) 2-heptyne; (c) 3-methylcyclohexene; (d) 2,4-heptadiene

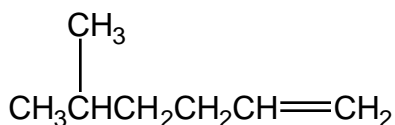
3.3 Nomenclature of Compounds with Both Double and Triple Bonds

(a) 2-hexen-4-yne; (b) 6-ethyl-4-octen-1-yne

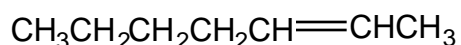
3.4 Skeletal, Positional, and Functional Isomerism



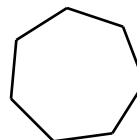
1-heptene



skeletal isomer

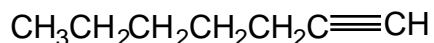


positional isomer

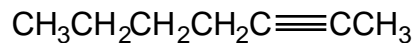


**functional isomer
(cycloalkane)**

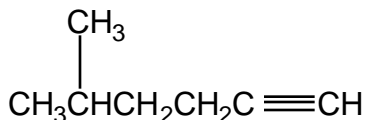
3.5 Skeletal, Positional, and Functional Isomerism



1-heptyne



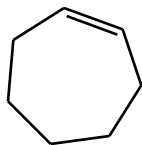
positional isomer



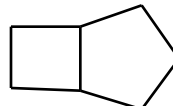
skeletal isomer



functional isomer (diene)

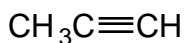


functional isomer (cycloalkene)

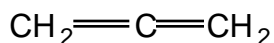


functional isomer (bicyclicalkane)

3.6 Functional Isomers



Propyne

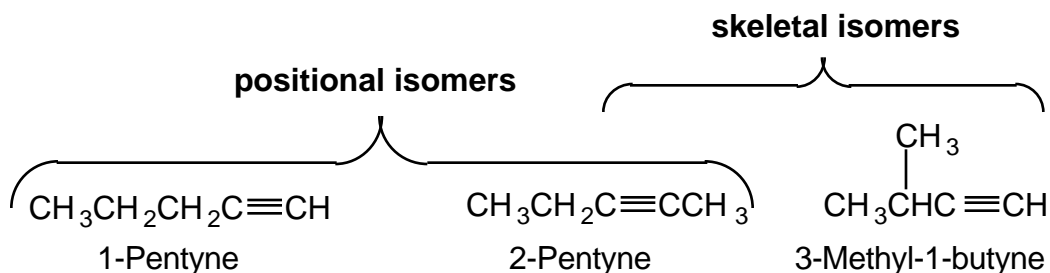


Propadiene



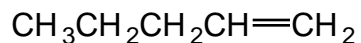
Cyclopropene

3.7 Skeletal and Positional Isomers

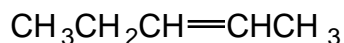


3.8 Skeletal and Positional Isomers

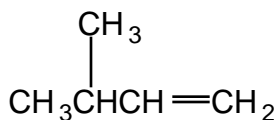
Each horizontal row of compounds represents a group of positional isomers. The top two compounds are skeletal isomers of the bottom three. Any cyclic compound such as cyclopentane would be a functional isomer as there would no longer be a double bond.



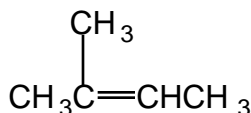
1-Pentene



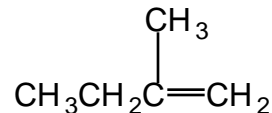
2-Pentene



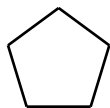
3-Methyl-1-butene



2-Methyl-2-butene



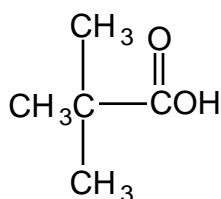
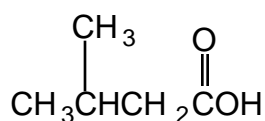
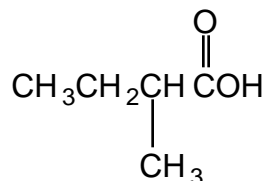
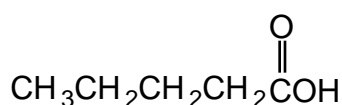
2-Methyl-1-butene



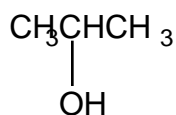
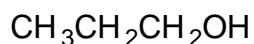
Cyclopentane is an example of a functional isomer. It is an alkane (cycloalkane) and not an alkene.

3.9 Functional Groups

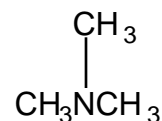
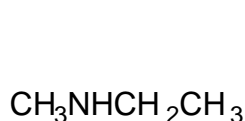
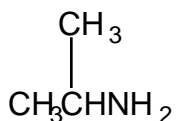
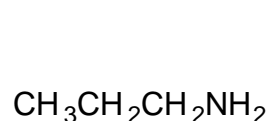
(a) four carboxylic acids with the formula $C_5H_{10}O_2$



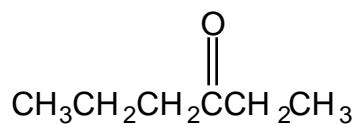
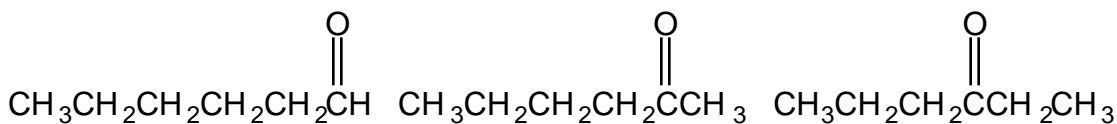
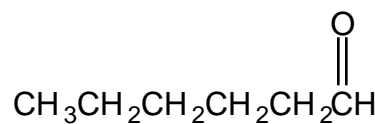
(b) two alcohols and one ether with the formula C_3H_8O



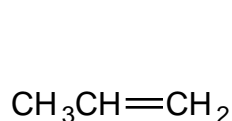
(c) four amines with the formula C_3H_9N



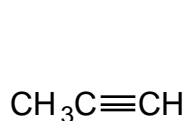
(d) three straight chain aldehydes and ketones with the formula



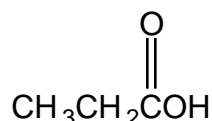
3.10 Functional Groups



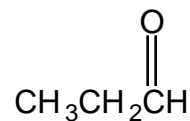
alkene



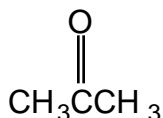
alkyne



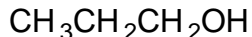
carboxylic acid



aldehyde



ketone



alcohol



amine

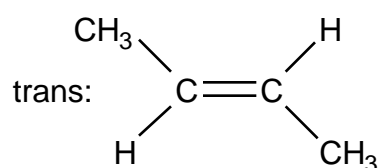
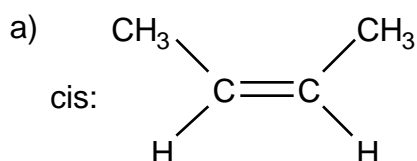


ether

3.11 Functional Groups

See Connections 3.2 in the text.

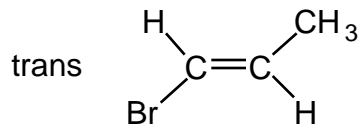
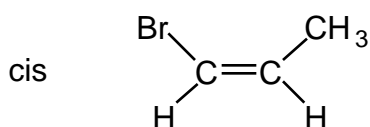
3.12 Geometric Isomerism



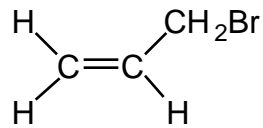
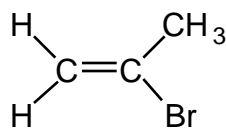
(b) For geometric isomerism, each carbon in the double bond must have two different attached groups. In 2-butene, each carbon has a hydrogen and methyl. In 1-butene, the first carbon has two identical groups, hydrogens, and thus cis-trans isomers do not exist.

3.13 Geometric Isomerism

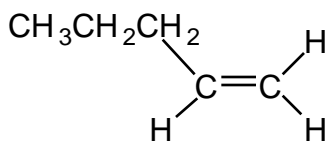
(a) 1-bromopropene has two different groups on each carbon involved in the double bond and exhibits geometric isomerism.



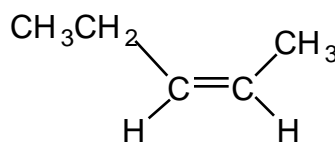
(2-bromopropene and 3-bromopropene each have two identical groups on one of the carbons and do not exhibit geometric isomerism.



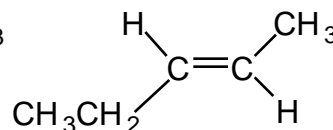
(b) 1-pentene has two hydrogens on one of the double bond carbons but 2-pentene has two different groups on each of these carbons.



1-pentene

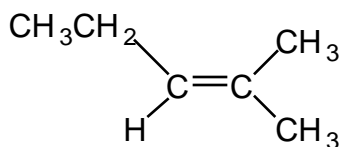


cis 2-pentene

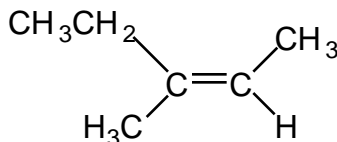


trans 2-pentene

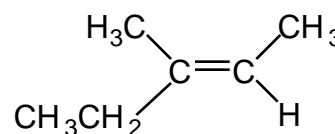
(c) In 2-methyl-2-pentene, there are two methyl groups on one of the double bond carbons and geometric isomerism is not possible. In 3-methyl-2-pentene, each carbon of the double bond has two different bonded groups. Notice that the cis and trans designations are made on the basis of the longest chain of carbon and whether it crosses the double bond in a cis or trans fashion.



2-methyl-2-pentene

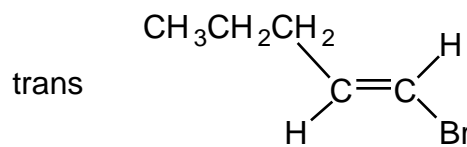
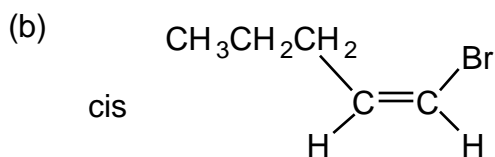
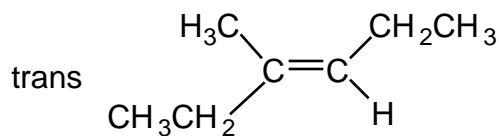
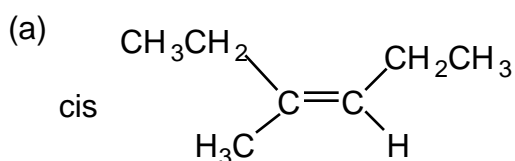


cis 3-methyl-2-pentene

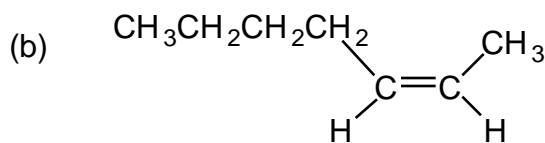
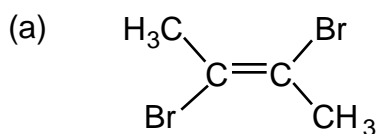


trans 2-methyl-2-pentene

3.14 Geometric Isomerism

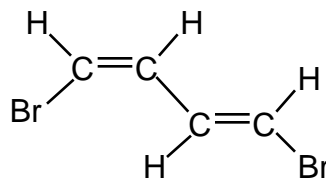


3.15 Geometric Isomerism



3.16 Geometric Isomerism

cis, trans 1,4-dibromo-1,3-butadiene



3.17 E-Z Designations

- (a) **Z** Each carbon in the double bond has a carbon and a hydrogen attached. In both cases the carbon is the higher priority and since they are on the same side the configuration is Z.
- (b) **Z** Cl is higher priority than H on the first carbon and Br is higher than C on the other. The higher priority groups are on the same side.
- (c) **E** Br is higher than C on the first carbon and C is higher than H on the other. The higher priority groups are on opposite sides.

3.18 Units of Unsaturation

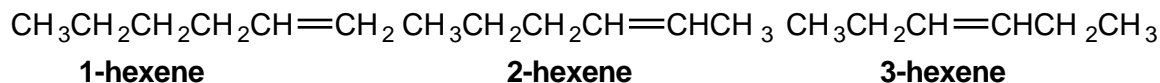
- (a) **4 units of unsaturation:** one triple bond (2) and two double bonds (one each)
- (b) **7 units of unsaturation:** five double bonds (one each) and two rings (one each). To determine how many rings, count how many cuts you would need to make to have no rings.
- (c) **3 units of unsaturation:** one ring (one) and one triple bond (two).

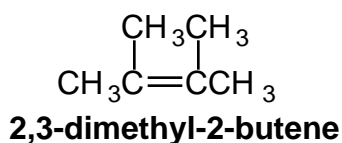
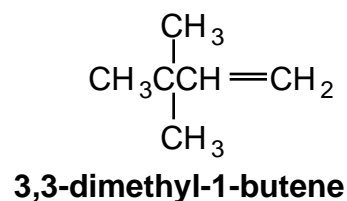
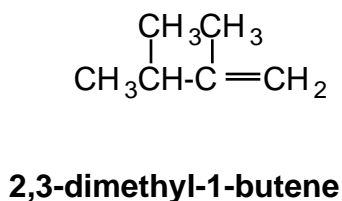
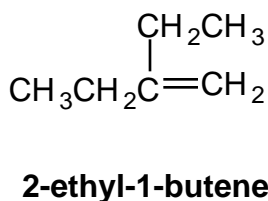
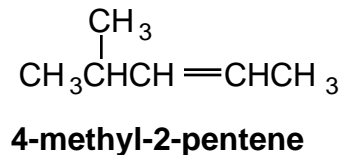
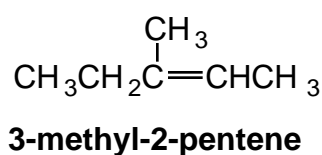
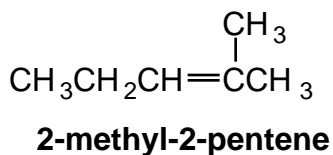
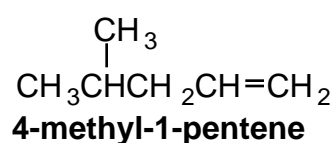
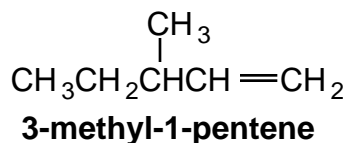
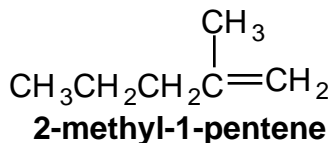
3.19 Units of Unsaturation

- (a) 1 (b) 2 (c) 4 (d) 5

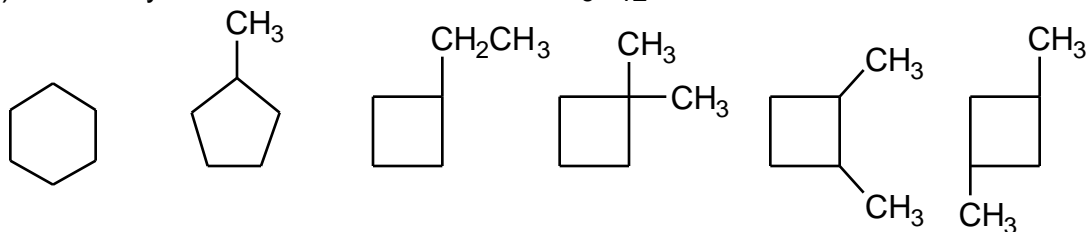
3.20 Skeletal and Positional Isomerism: Section 3.3

(a) thirteen alkenes with the formula C_6H_{12} that are skeletal or positional isomers. Note the systematic method for drawing the isomers.

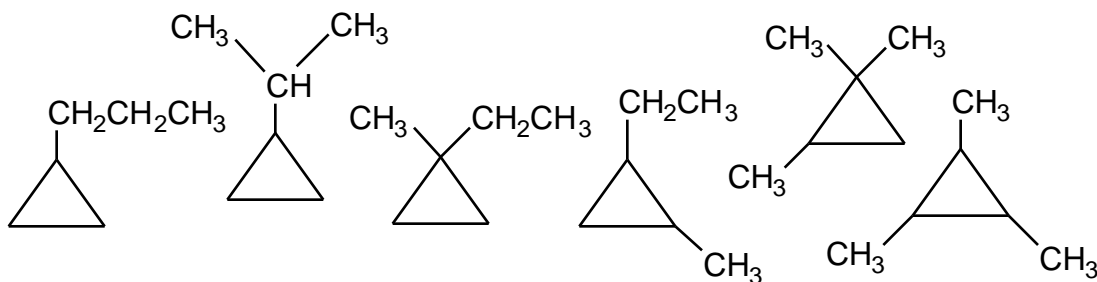




(b) twelve cycloalkanes with the formula C_6H_{12}

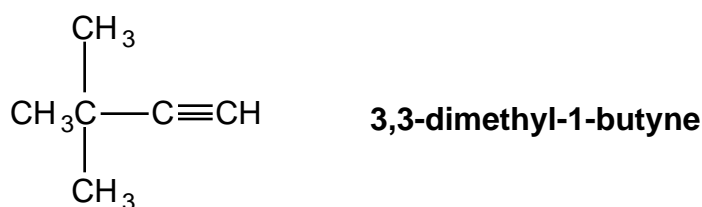
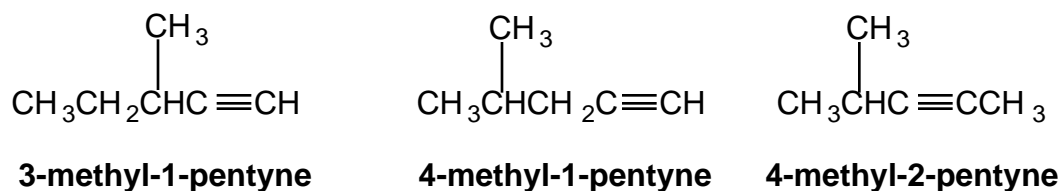
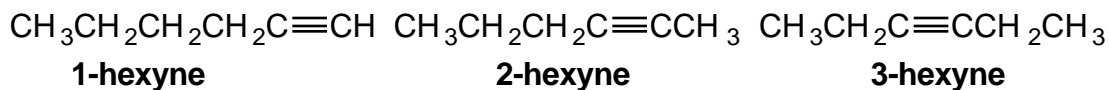


Names in order: cyclohexane; methylcyclopentane; ethylcyclobutane; 1,1-dimethylcyclobutane; 1,2-dimethylcyclobutane; 1,3-dimethylcyclobutane



Names in order: propylcyclopropane; isopropylcyclopropane; 1-ethyl-1-methylcyclopropane; 1-ethyl-2-methylcyclopropane; 1,1,2-trimethylcyclopropane; 1,2,3-trimethylcyclopropane

(c) the seven alkynes with the formula C₆H₁₀



3.21 Nomenclature of Alkenes, Alkynes, and Cycloalkanes

Section 3.2; Please see names in problem 3.20 solutions.

3.22 Nomenclature of Alkenes: Section 3.2

- (a) 1-heptene; (b) 3,4-dimethyl-3-heptene; (c) 4,4-dimethyl-2-pentene;
 (d) 4-ethyl-1-cyclopentene; (e) 2-cyclopropyl-5-propyl-3-octene;
 (f) 3,5-diethyl-8-methyl-3-nonene; (g) 2,4-octadiene;
 (h) 1,3,5,7-cyclooctatetraene; (i) 4,5-dibromo-2-methyl-2,4,6-nonatriene.

Let us illustrate the procedure with the last example:

- (i) 1. Nine carbons in the longest chain: **non**
 2. Three triple bonds: **nonatriene**
 3. Number the chain left to right; complete suffix: **2,4,6-nonatriene**
 4. Name all other groups with prefixes. The complete name is:
4,5-dibromo-2-methyl-2,4,6-nonatriene

3.23 Nomenclature of Alkynes: Section 3.2

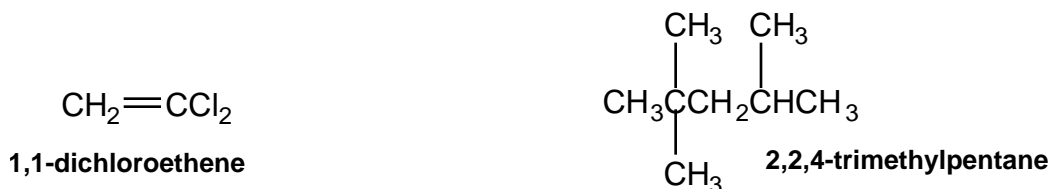
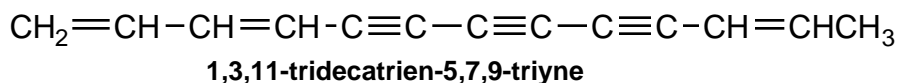
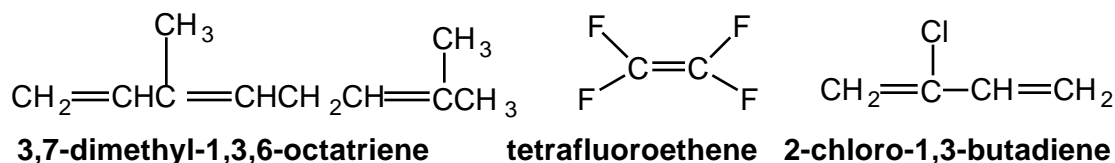
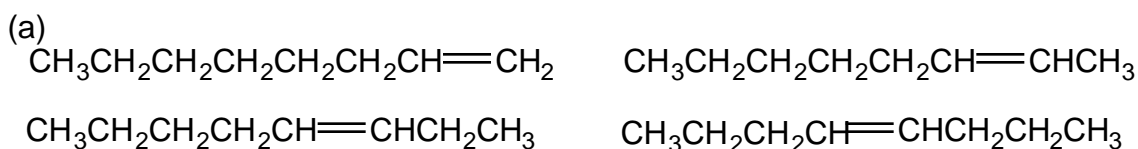
- (a) 1-butyne; (b) 2,2-dibromo-7-methyl-3-octyne; (c) 4-methyl-2-pentyne;
 (d) 3-ethyl-3-methyl-1-pentyne; (e) cyclooctyne;
 (f) 9-methyl-2,4,6-decatriyne

3.24 Nomenclature of Alkenes and Alkynes: Section 3.2

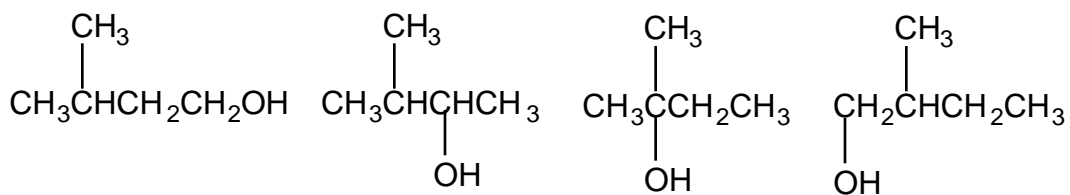
- (a) 2,9,9-trimethyl-2,5-decadiene; (b) 2,4,6,8-decatetrayne;
 (c) 4-hexen-1-yne; (d) 2-hexen-4-yne; (e) 2-methyl-1,3-decadien-5,7,9-triyne

A few comments: In (c) the triple bond is the first multiple bond reached in numbering and thus numbering is right to left. In (d) whichever way you number you encounter a multiple bond at carbon-2. In these cases, the double bond takes precedence and the numbering is left to right. The last problem is illustrated in detail below.

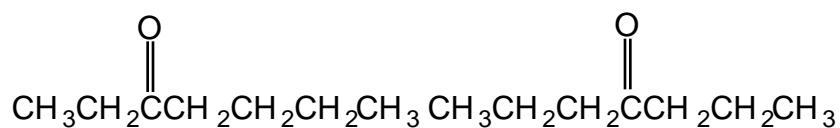
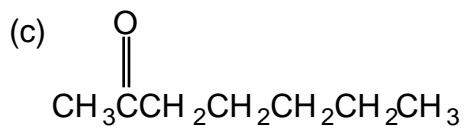
- (e)
1. The longest chain is ten carbons: **dec**
 2. There are two double bonds: **decadien**
and three triple bonds: **decadien triyne**
 3. Either way you number the chain, a multiple bond is at carbon-1;
give precedence to the double bond: **1,3-decadien-5,7,9-triyne**
 4. The methyl is named with a prefix; the complete name is:
2-methyl-1,3-decadien-5,7,9-triyne

3.25 IUPAC Nomenclature: Section 3.2**3.26 Positional Isomerism:** Section 3.3

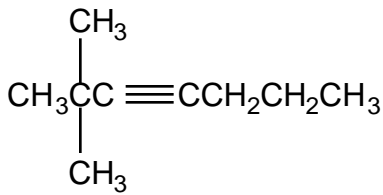
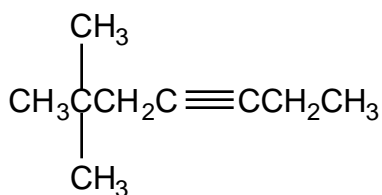
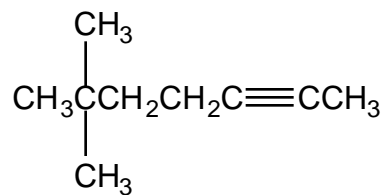
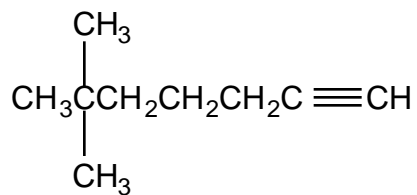
(b)



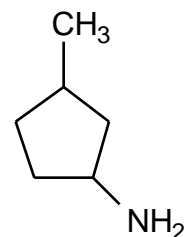
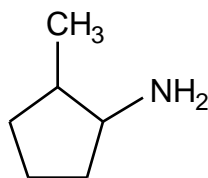
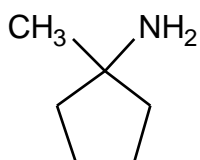
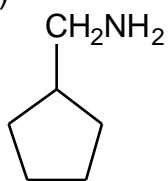
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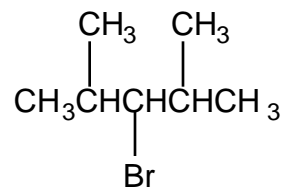
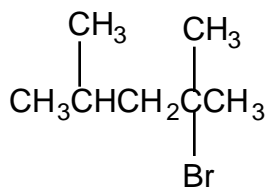
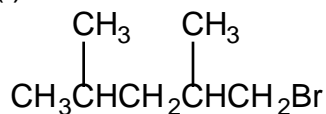
(d)



(e)

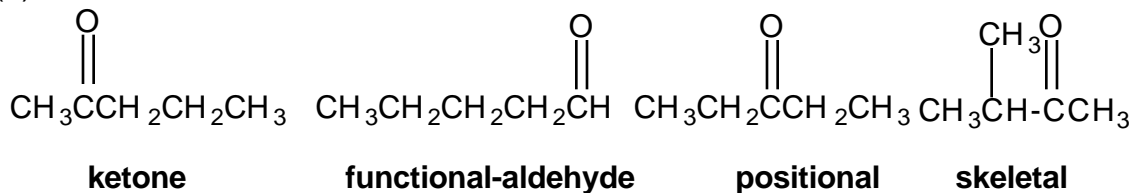


(f)

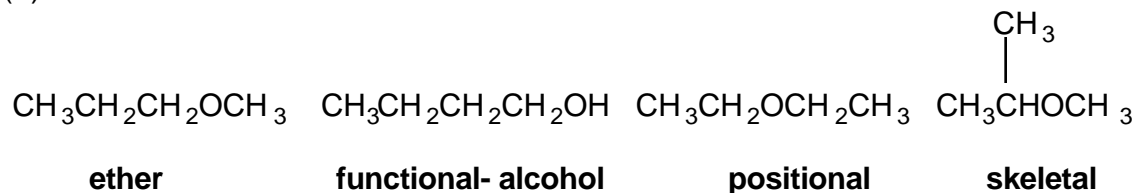


3.27-3.30 Functional, Positional, and Skeletal Isomerism

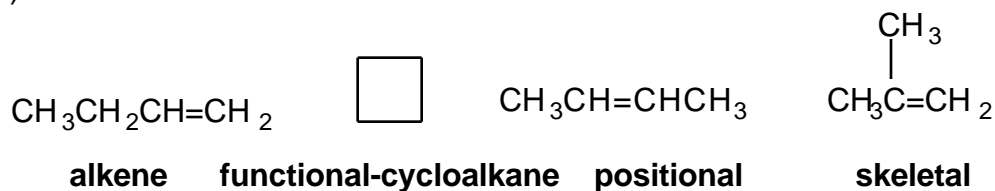
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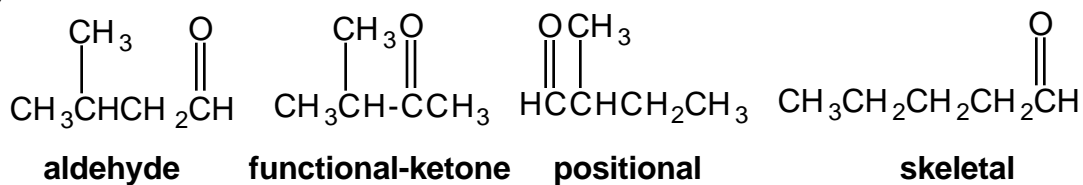
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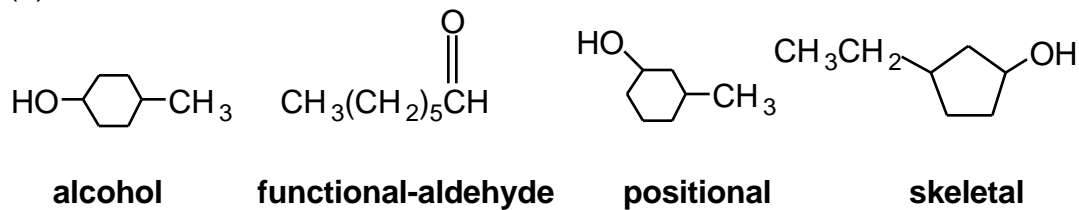
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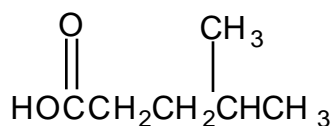
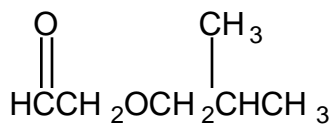
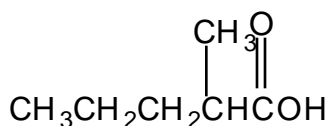
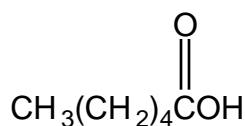
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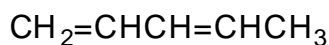
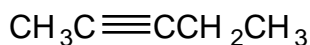
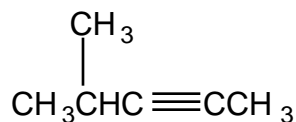
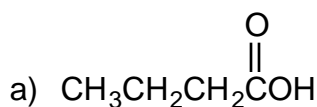
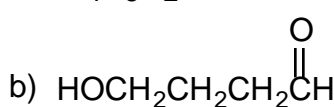
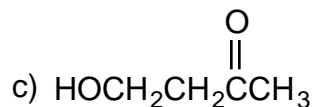
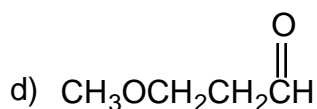
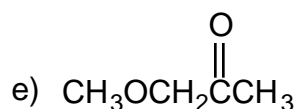
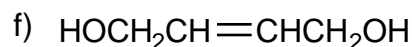
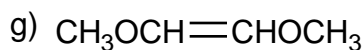
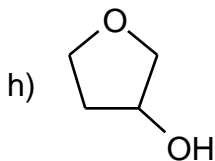
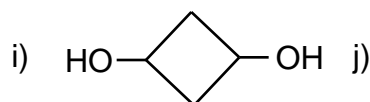
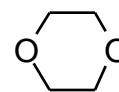
(e)



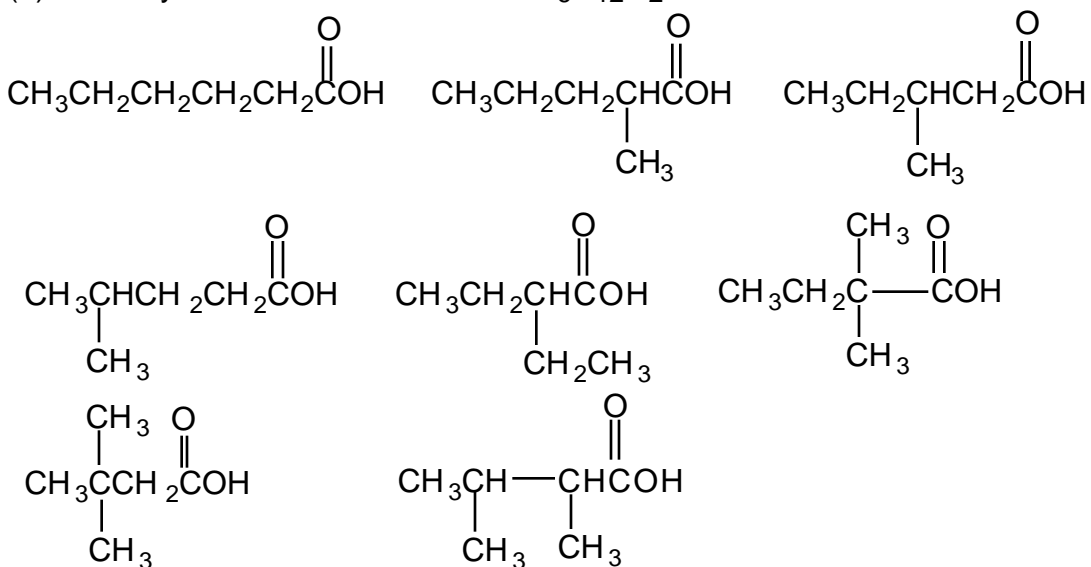
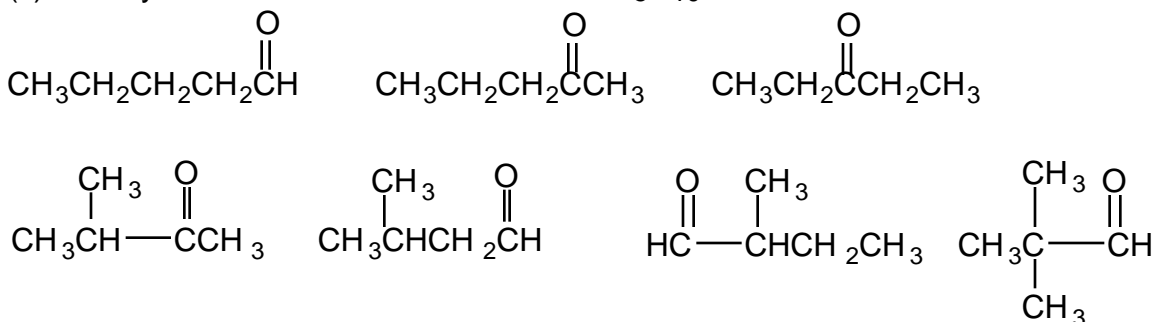
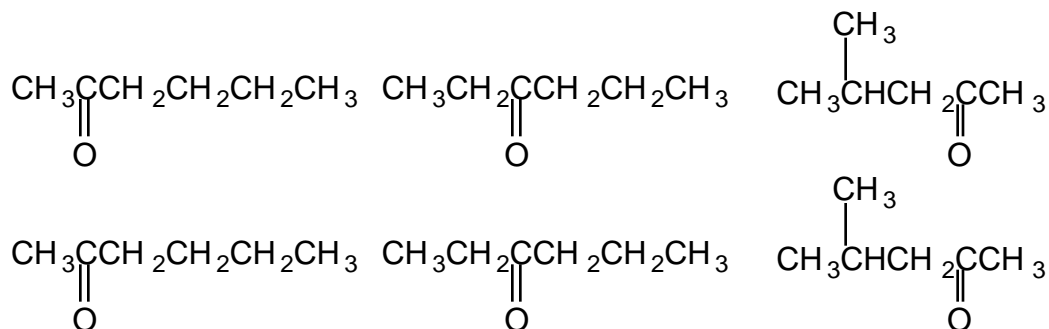
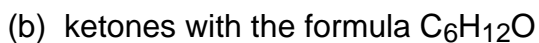
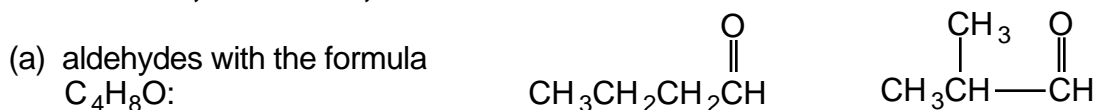
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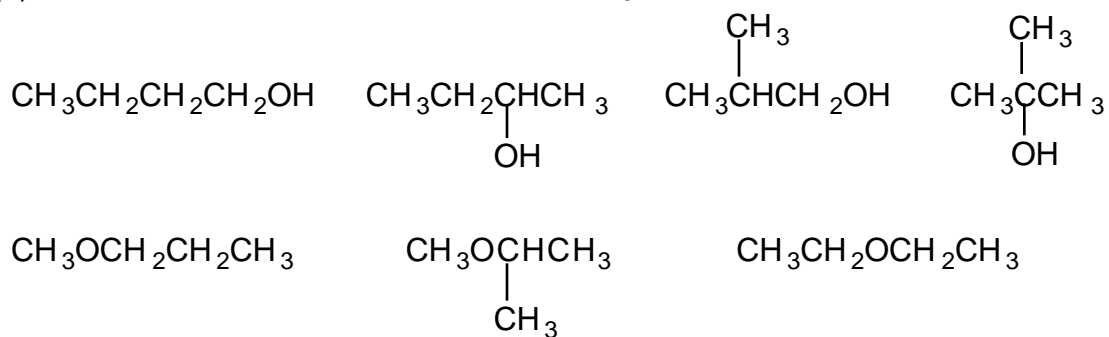
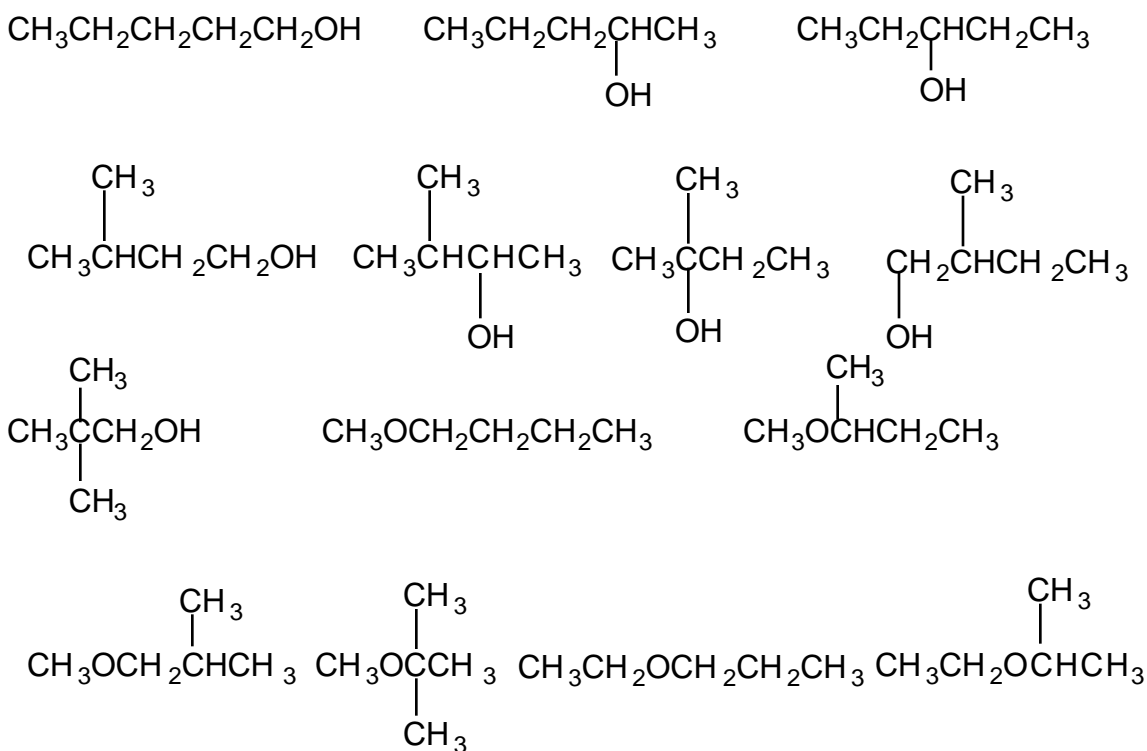
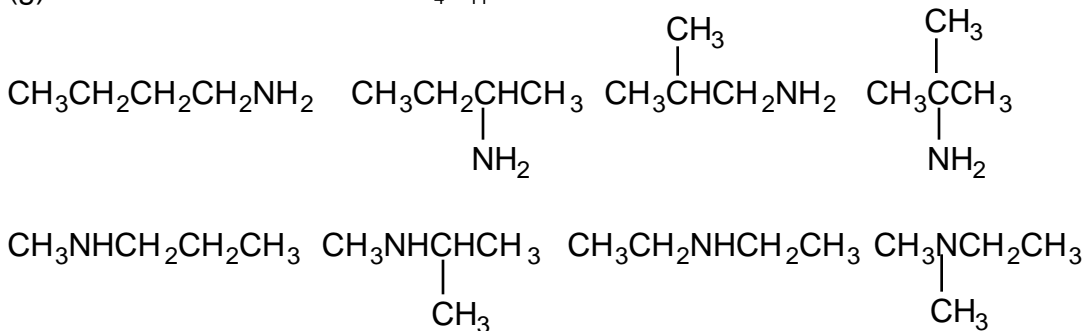
**carboxylic acid****functional: aldehyde/ether****positional****skeletal**

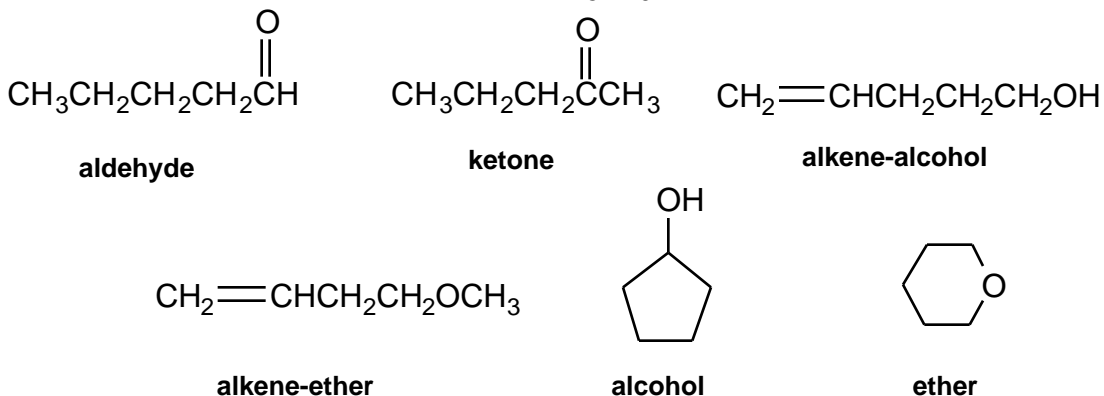
(g)

**alkyne****functional: alkene (diene)****positional****skeletal****3.31 Functional Isomers:** Section 3.4Functional isomers of $\text{C}_4\text{H}_8\text{O}_2$ **carboxylic acid****alcohol-aldehyde****alcohol-ketone****ether-aldehyde****ether-ketone****alkene-dialcohol****alkene-diether****alcohol-ether****dialcohol****diether**

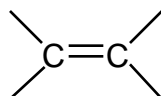
3.32 Skeletal, Positional, and Functional Isomers: Section 3.3



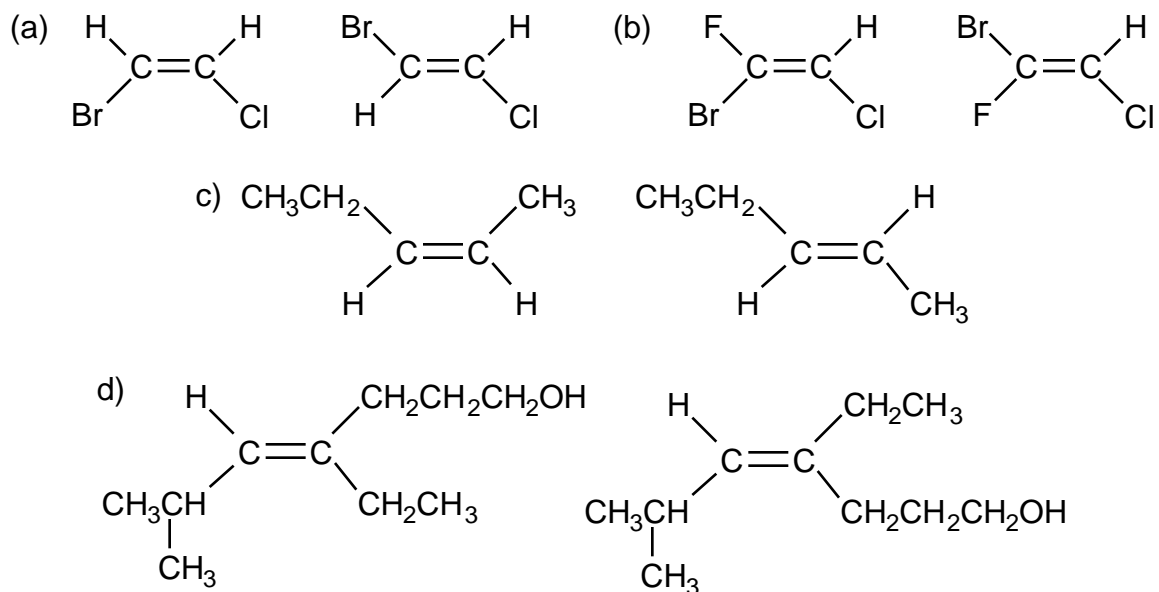
(e) alcohols or ethers with the formula $C_4H_{10}O$ (f) alcohols or ethers with the formula $C_5H_{12}O$ (g) amines with the formula $C_4H_{11}N$ 

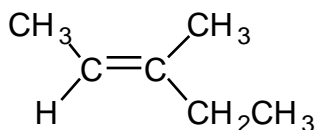
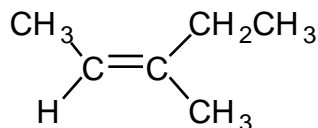
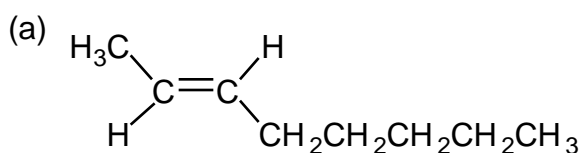
3.33 Functional Isomerism: Section 3.4Six functional isomers with the formula $C_5H_{10}O$ **3.34 Geometric Isomerism in Alkenes:** Section 3.5

To draw geometric isomers, first draw the two carbons of the double bond in the trigonal geometry.

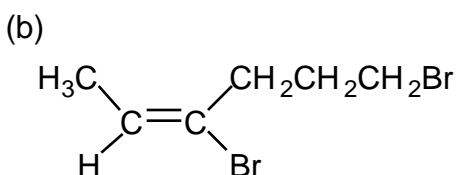


Identify the two groups on each carbon and attach them to the above template. This is one geometric isomer. Interchange the two groups on one of the carbons to obtain the other isomer.

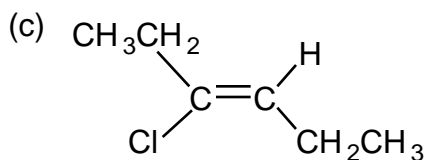


3.35 Geometric Isomerism: Section 3.5**trans or E****cis or Z****3.36 The E-Z Method for Expressing Configuration****E 2-octene**

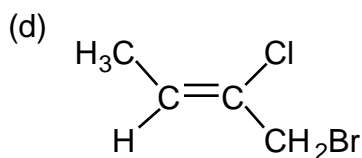
The alkyl groups are the higher priority on each ring and they are on opposite sides.

**E 3,6-dibromo-2-hexene:**

On the left carbon of the double bond, the methyl (C) is the higher priority group. The right carbon has a C and Br directly attached. The Br is of higher priority. The two higher priority groups are opposite.

**Z 3-chloro-3-hexene:**

On the left carbon, the chlorine is of higher priority than the carbon of the ethyl and on the right, the carbon of the ethyl is higher priority than the hydrogen. The two high priority groups are put on the same side.

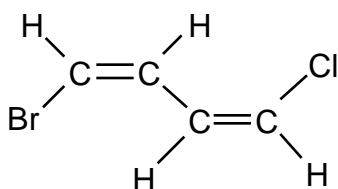
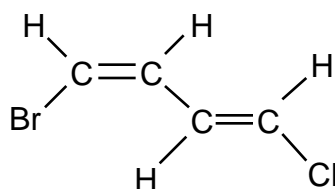
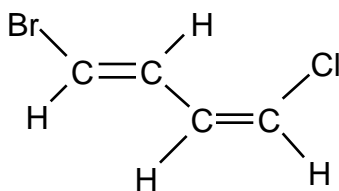
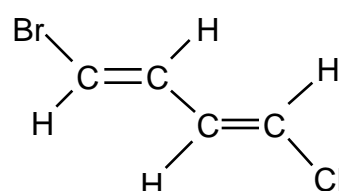
**Z 1-bromo-2-chloro-2-butene:**

On the left carbon of the double bond, the methyl group is of higher priority (C>H). Don't be fooled on the right; a Cl not a Br is directly attached. The Cl is of higher priority than CH₂Br. The Cl and CH₃ are placed on the same side for Z.

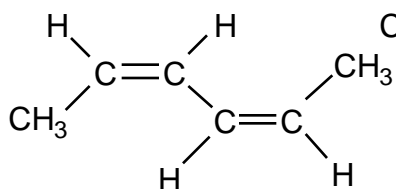
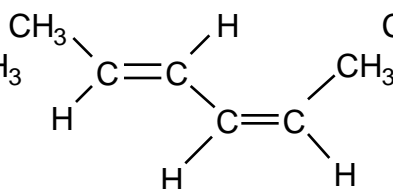
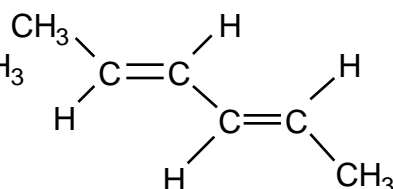
3.37 Geometric Isomerism in Alkenes: Section 3.5

Consider each double bond individually and be sure to draw the trigonal geometry carefully.

(a) This molecule is capable of exhibiting four geometric isomers since each double bond shows geometric isomerism and the molecule is not symmetrical.

**cis-cis****cis-trans****trans-cis****trans-trans**

(b) This molecule has two double bonds, both capable of geometric isomerism. However, each double bond has the same attached groups and the molecule is symmetrical. As a result the cis/trans and trans/cis isomers are the same and the total number of geometric isomers is only three.

**cis-cis****trans-cis or cis-trans****trans-trans**

(c) This compound has three double bonds capable of geometric isomerism and it is not symmetrical; there are eight possible isomers. All double bonds can be cis, all trans, two cis and one trans in three different ways, and one cis and two trans in three different ways.

cis cis cis

cis cis trans

cis trans trans

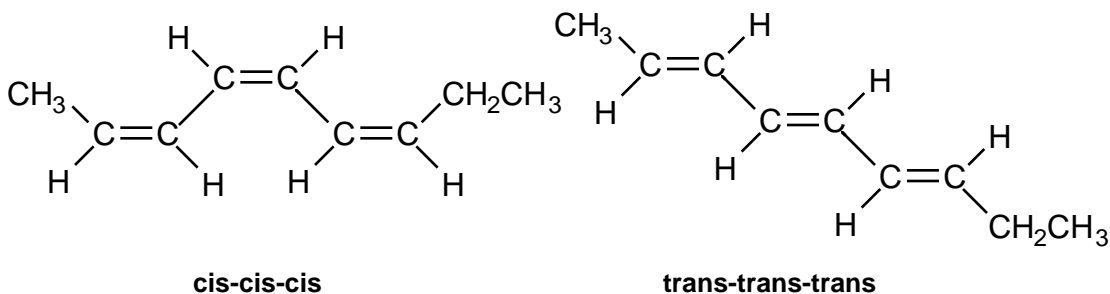
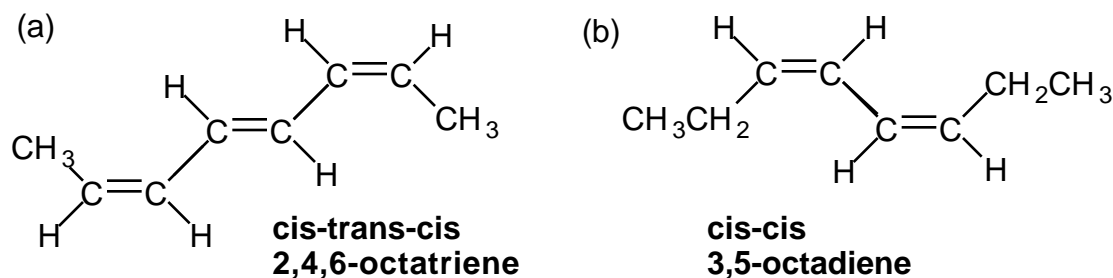
trans trans trans

cis trans cis

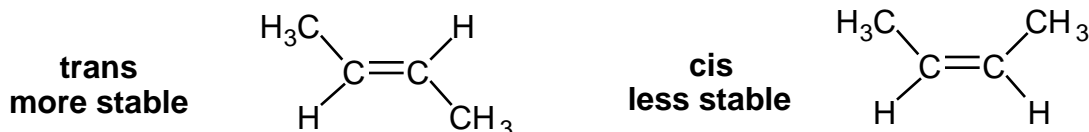
trans cis trans

trans cis cis

trans trans cis

**3.38 Geometric Isomerism:** Section 3.5**3.39 Geometric Isomerism:** Section 3.5

(a) The two methyl groups are the larger groups on each carbon and the more stable arrangement will have them separated as much as possible as in the trans isomer.

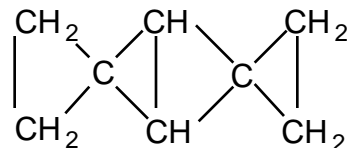
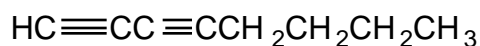


(b) In this case both compounds are cis and are less stable than their respective trans isomers. Comparing the two, however, the second one has much larger groups (t-butyl) than the first (methyl). The two t-butyl groups cis is a more strained situation than the two methyl groups cis.

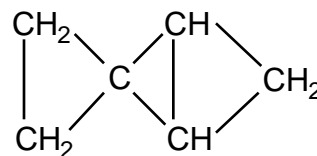
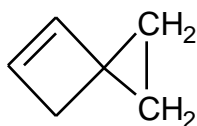
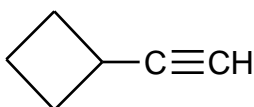
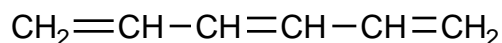
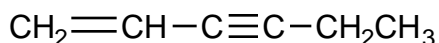


3.40 Expressing Units of Unsaturation: Section 3.6

(a) C_8H_{10} : With eight carbons this formula needs 18 hydrogens to be saturated. It has only 10, eight less than needed. For every two monovalent atoms short there is one unit of unsaturation, or four in this formula. Following are the requested compounds: one isomer with as many triple bonds as possible, one with as many double bonds as possible, and one with as many rings as possible.



(b) C_6H_8 : This formula has three units of unsaturation that can be expressed as one triple and one double bonds, three double bonds, one triple bond and one ring, two double bonds and a ring, one double bond and two rings, or three rings.

**(c) Expression of Four Units of Unsaturation**

Two triple bonds

One triple and two double bonds

One triple bond, one double bond, and one ring

One triple bond and two rings

Four double bonds

Three double bonds and one ring

Two double bonds and two rings

One double bond and three rings

Four rings

3.41 Units of Unsaturation: Section 3.6

(a) By several methods you can determine that for a hydrocarbon with 11 carbons there need to be $2n+2$ hydrogens (24 H's) for the compound to be

saturated. This formula is deficient 10 hydrogens and thus has 5 units of unsaturation. A triple bond is two units of unsaturation and a double bond or ring is one. This compound can have a maximum of two triple bonds (it must also have a ring or a double bond for the additional unit).

(b) A compound with five units of unsaturation can have a maximum of five double bonds since a double bond represents one unit.

(c) If a compound with five units of unsaturation has one triple bond (two units of unsaturation), it theoretically can have three rings since each ring represents one unit of unsaturation.

3.42 Units of Unsaturation: Section 3.6

(a) A compound with 13 carbons must have $2n+2$ or 28 monovalent atoms to be saturated. This one has a triple and double bond (three units of unsaturation) and thus needs only 22 monovalent atoms to satisfy valences. It has three bromines and thus needs 19 hydrogens.

(b) A compound with seven carbons and one oxygen needs 16 monovalent atoms to be saturated. With two double bonds, one triple bond, and one ring, this compound has five units of unsaturation and needs only six monovalent atoms to satisfy valences. Since it has five hydrogens already, it must have only one chlorine.

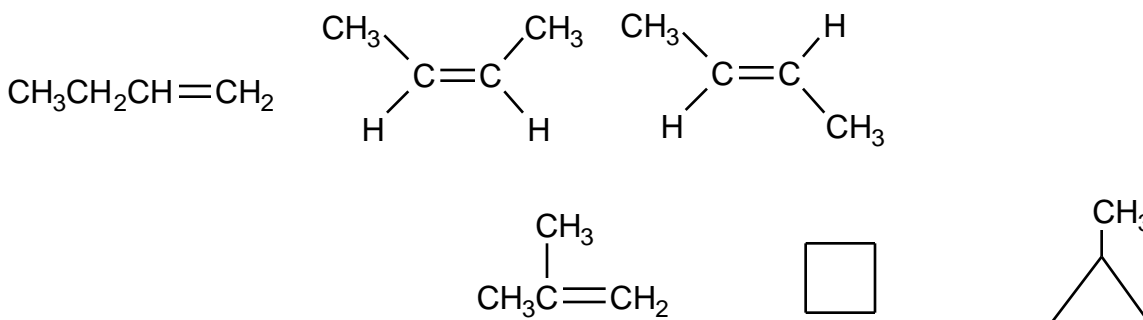
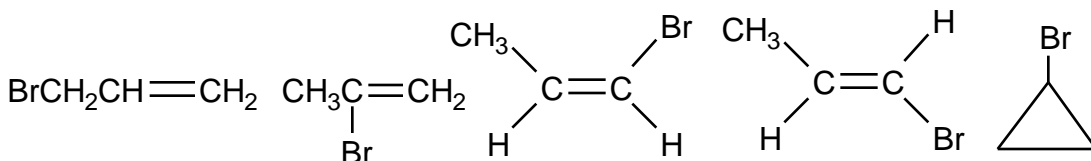
3.43 Units of Unsaturation: Section 3.6

In these problems you can easily see the double bonds (one unit of unsaturation) and the triple bonds (two units of unsaturation). To determine the number of rings (each ring is one unit), imagine that you are cutting the molecule with scissors. The number of rings is the minimum number of cuts you need to make to have no rings at all.

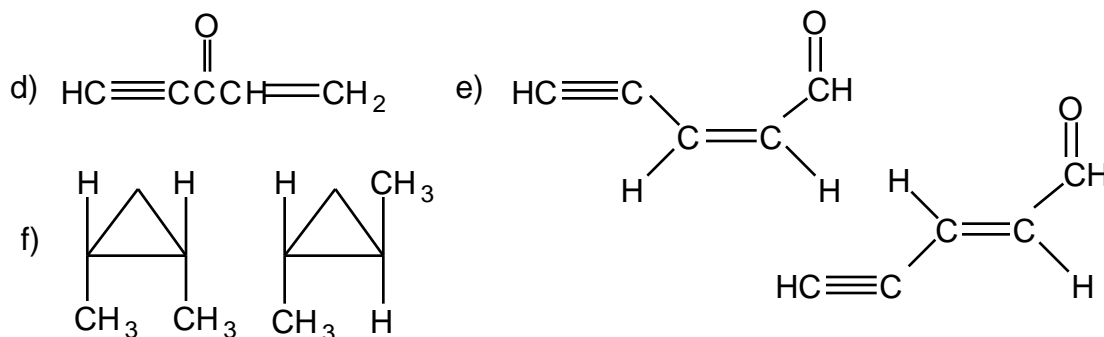
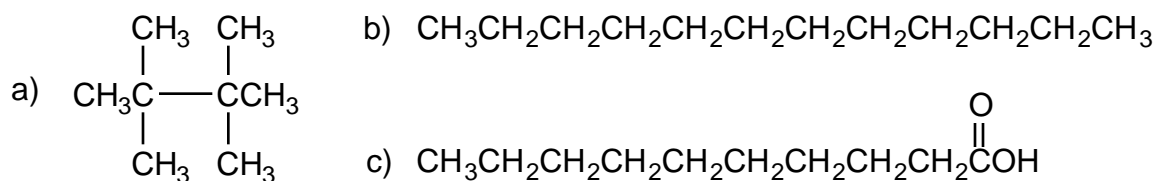
(a) four double bonds, one triple bond, and one ring: **seven units**

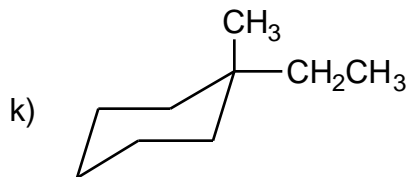
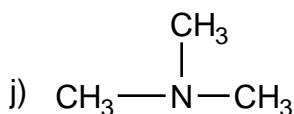
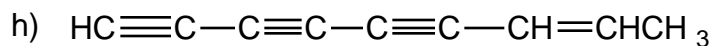
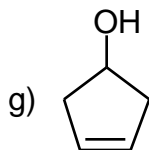
(b) three double bonds and three rings: **six units**

(c) seven double bonds and three rings: **ten units**

3.44 Isomers: Sections 3.3-3.5(a) six isomers of C_4H_8 (b) five isomers of C_3H_5Br **3.45 Types of Isomerism**

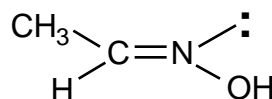
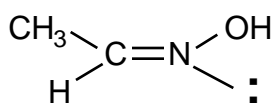
- (a) skeletal; (b) functional; (c) geometric; (d) positional;
 (e) skeletal; (f) functional; (g) conformational; (h) positional;
 (i) functional; (j) geometric; (k) conformational

3.46 Isomers



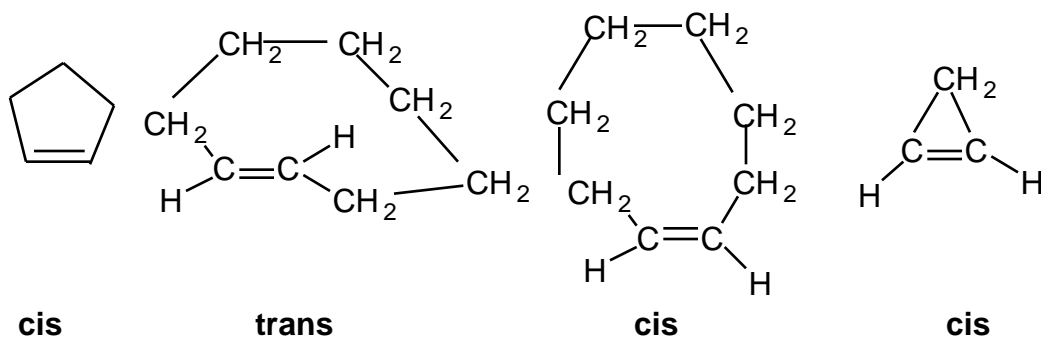
3.47 Geometric Isomerism: Section 3.5

This compound can exhibit geometric isomerism because the nitrogen is sp^2 hybridized and trigonal. The carbon has a methyl and a hydrogen and the nitrogen has an OH and an electron-pair.



3.48 Geometric Isomerism in Cycloalkenes

The flexibility to have a trans configuration in a ring does not occur until cyclooctene. As an extreme, consider the impossibility of having a trans configuration in cyclopropene.

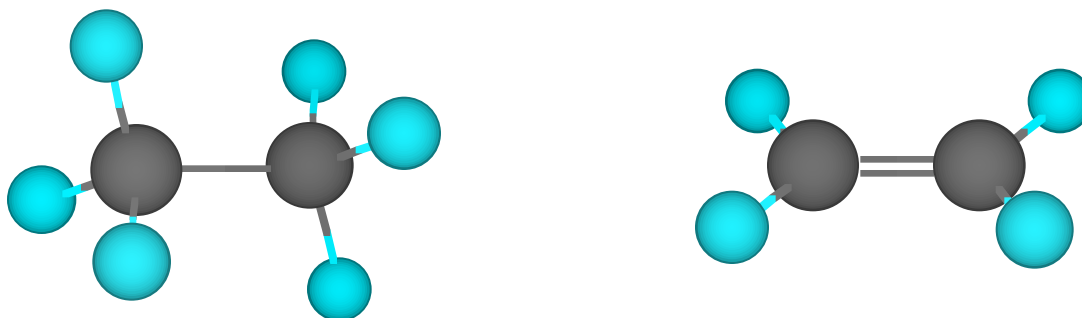


3.49 Geometric Isomerism in Cycloalkanes

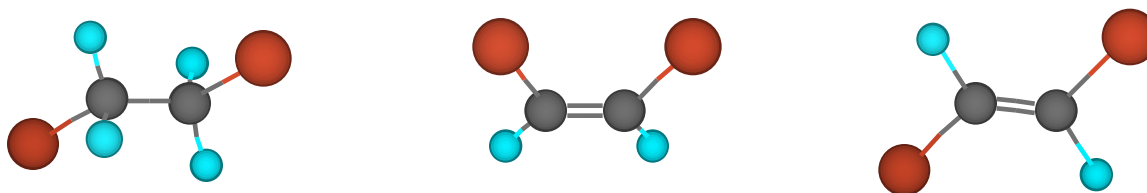
Because of the nature of a ring, the cis configuration is preferred. It isn't until eight membered rings that the trans can even exist. In larger rings it is easier for the trans configuration to exist without creating undue angle strain. Thus trans cyclodecene is more stable than trans cyclooctene.

Activities with Molecular Models

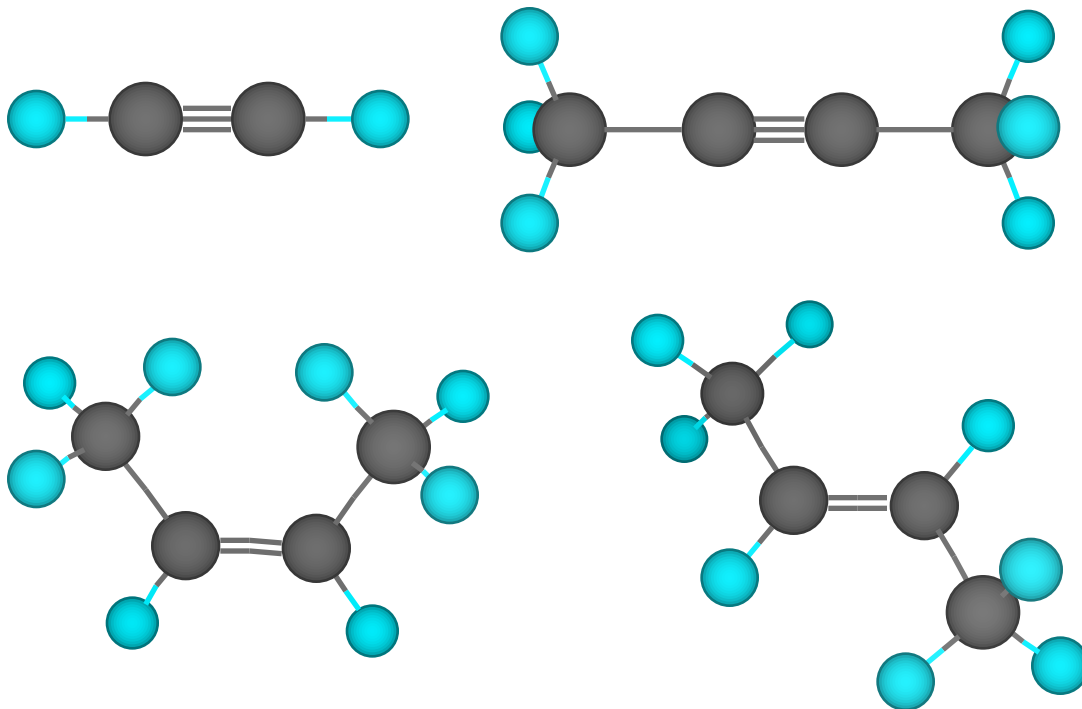
1. Make molecular models of ethane and ethene. Notice the tetrahedral shape and 109° bond angles around each carbon of ethane and the trigonal shape and 120° bond angles around each carbon of ethene. Also notice that you can rotate the single bond of ethane but not the double bond of ethene.



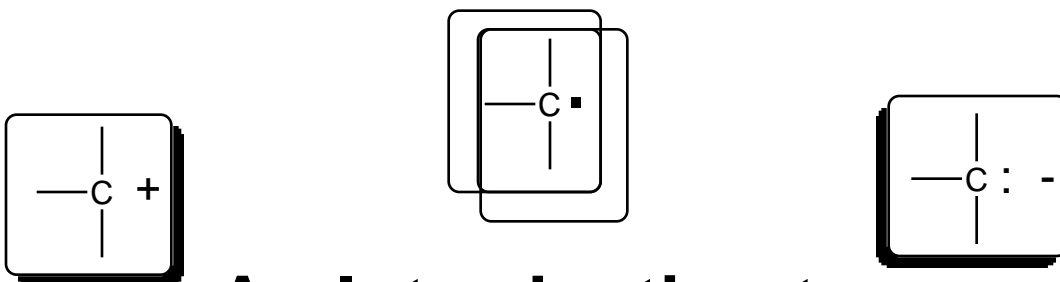
2. Using the models you made in exercise 1, replace a hydrogen on each carbon with a bromine. Notice in 1,2-dibromoethane that you can rotate around the carbon-carbon single bond to get all of the conformations and that they are interconvertible. However, notice that there is no rotation around the carbon-carbon double bond. If you put the two bromines on the same side you have the cis geometric isomer and if you put them on opposite sides you have trans. The cis and trans isomers are not interconvertible.



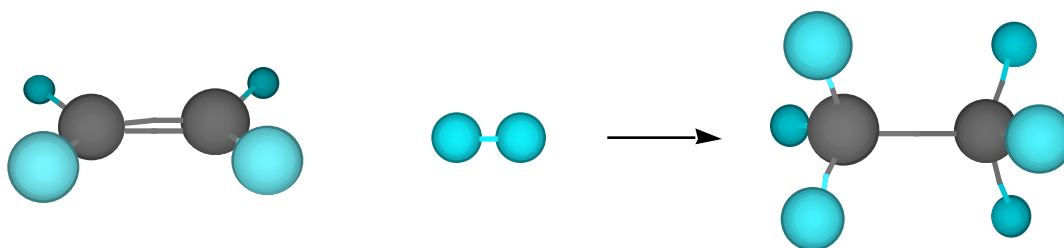
3. Make a model of ethyne. Now replace the hydrogens with methyl groups to get 2-butyne. Compare to 2-butene which exhibits cis-trans isomerism. Why does 2-butene show geometric isomerism but not 2-butyne?



4



An Introduction to Organic Reactions



CHAPTER SUMMARY

In the previous three chapters we have progressed from atoms and electrons to bonds and molecules to sophisticated structural representations and nomenclature of organic molecules. Chapter 4 uses this knowledge of organic structure to introduce organic chemical reactions.

4.1 General Principles of Organic Reactions

A. Types of Reactions: The Reaction Equation

A **reaction equation** describes what happens in a chemical reaction by displaying the reactants and products. It describes what bonds break in the reactants and what new bonds form in the products. There are three main types of organic reactions. In **substitution reactions**, an atom or group of atoms is replaced by another species. **Elimination reactions** involve the removal of a pair of atoms or groups from two adjacent atoms to form a

multiple bond. In **addition reactions** atoms or groups add to adjacent atoms involved in a multiple bond; the multiple bond is reduced.

B. Reaction Mechanisms

A **reaction mechanism** is a step-by-step description of how a reaction occurs. The reaction equation describes what happens; the mechanism describes how the reaction happens.

C. Reaction Mechanisms and Potential Energy Diagrams

Potential energy diagrams are used to depict energy changes during chemical reactions. The vertical axis of the diagram is potential energy and the horizontal axis describes reaction progress. Energy is required to break bonds and potential energy increases as bonds break in during the initial stages of a reaction. As new bonds form and a reaction comes to a conclusion, energy is released. The difference in energy between the starting materials and the products is called the **heat of reaction**. If the products are of lower energy than the reactants (more energy is released in bond formation than consumed in bond breaking), heat is evolved and the reaction is **exothermic**. The opposite is an **endothermic reaction**.

The process of bond cleavage or bond formation is called a **transition state** and appears as a maximum in the potential energy diagram curve. An **intermediate** is a short lived species formed in a multi-step reaction mechanism and is the result of a transition; it appears as a minimum on the reaction progress curve. The rate of a reaction depends on the difference in energy between that of the starting materials and an intermediate (or the products in a one step reaction); this is the **energy of activation**.

D. Reaction Intermediates

Multistep reaction mechanisms proceed through **reaction intermediates**. There are three major reaction intermediates involving carbon. A **carbocation** has a carbon with only three bonds, six outer-shell electrons and a positive charge. A **free radical** is a neutral carbon with only three bonds and seven outer shell electrons, one of which is unpaired. A **carbanion** has only three bonds but has eight outer shell electrons, one of which is a non-bonding pair, and a negative charge.

In chemical reactions, bonds break in the reactants and new bonds form in the products. In **homolytic** bond cleavage, the bonding electrons are evenly divided among the two parting atoms; neutral free radicals are the result. In **heterolytic** bond cleavage, the bonding electrons are unevenly

divided between the two parting atoms; charged species, such as carbocations and carbanions result.

4.2 Sites of Organic Reactions

Organic reactions usually occur at sites within molecules where there is a special availability or deficiency of electrons. **Electrophiles** are regions of a molecule or ion that are positive or deficient in electrons and which tend to attract electron-rich species and accept electrons in a chemical reaction. **Nucleophiles** are electron-rich, provide electrons in a chemical reaction, and tend to attract electron-deficient or positive species.

A. Multiple Bonds

Double and triple bonds are active reaction sites because they are rich in electrons and the electrons are accessible due to the nature of pi-bonds.

B. Polar Bonds

Because of the charge separation in **polar covalent bonds**, they are common reaction sites since they attract charged species.

C. Lewis Acids and Bases

Nucleophiles and electrophiles are also described as Lewis bases and acids. A **Lewis base** is a species that has a non-bonding pair of outer-shell electrons that can be shared in a chemical reaction. A **Lewis acid** is a substance that can accept a pair of electrons for sharing in a chemical reaction. Nitrogen compounds, such as **amines**, and oxygen derivatives, such as **alcohols and ethers**, are often Lewis bases because the nitrogen and oxygen have non-bonding electron pairs. **Hydrogen ion and simple boron and aluminum compounds** are examples of Lewis acids. **Carbocations** are Lewis acids and **carbanions** are Lewis bases.

D. Combination Reaction Sites

Again, the reaction sites are: multiple bonds (double and triple bonds); polar bonds; and Lewis acids (electrophiles) and Lewis bases (nucleophiles).

4.3 Getting Started

You might want to organize your study of organic reactions in the following way:

1. *General reaction equation:* Identify this as substitution, elimination, or addition.

2. *Predominant product:* Learn to determine this if more than one product is possible from a chemical reaction.
3. *Reaction mechanism:* Learn the step by step mechanism in a general way and understand whether it has carbocations, free radicals, or carbanions as intermediates.
4. *Specific examples:* Work specific example problems.

4.4 Halogenation of Alkanes: Chlorination and Bromination

A. General Reaction

Chlorination or bromination of alkanes is an example of a substitution reaction. A hydrogen on an alkane is replaced by a halogen; hydrogen halide is the by-product. The reaction is initiated by light or heat.

B. Chlorination of Methane: An Example of Halogenation

Chlorination of methane produces chloromethane, dichloromethane, trichloromethane, and tetrachloromethane.

C. Control of the Halogenation Reaction

To promote monohalogenation, a high ratio of alkane to halogen is used. Polyhalogenation is caused using a high ratio of halogen to alkane (at least as many moles of chlorine as hydrogens in the alkane to get complete chlorination. Even in monohalogenation, unsymmetrical alkanes yield multiple products whereas the symmetrical alkanes produce fewer monohalogenation products.

D. Mechanism of Halogenation

Halogenation proceeds by a **free-radical chain reaction** mechanism. In the **initiation step**, light or heat causes a halogen molecule to dissociate into free radicals. There are two **propagation steps**. In one the halogen free radical abstracts a hydrogen from the alkane leaving a carbon free radical. In the other, the carbon free radical reacts with a halogen molecule to form a carbon-halogen bond and a new halogen free radical. The two propagation steps alternate. The chain reaction can be slowed or halted by **chain termination steps** in which free radicals combine to form compounds without producing a new free radical to continue the chain reaction process.

CONNECTIONS 4.1: Chlorofluorocarbons and the Ozone Layer

CONNECTIONS 4.2: General Anesthetics

4.5 Preparation of Alkenes and Alkynes: Elimination Reactions

A. General Reaction Equation

Alkenes and alkynes are prepared by **elimination reactions** in which a carbon-carbon single bond is converted to a double or triple bond. In elimination reactions, atoms or groups are eliminated from adjacent carbons. Elimination once produces double bonds; twice produces triple bonds.

In **dehydrohalogenation reactions**, hydrogen and halogen are the atoms eliminated from adjacent carbons. Bases such as potassium hydroxide and sodium amide are the reagents. Both alkenes and alkynes can be synthesized by dehydrohalogenation.

In **dehydration reactions**, the elements of water, H and OH, are eliminated from adjacent carbon atoms; sulfuric acid is used as a catalyst. Generally the reaction is only effective in producing carbon-carbon double bonds.

B. Orientation of Elimination

The **Zaitsev rule** is used to predict the product of elimination when more than one product is possible. According to the Zaitsev rule, the most stable alkene is formed predominantly; this is the one in which the double bond is most highly substituted with alkyl groups.

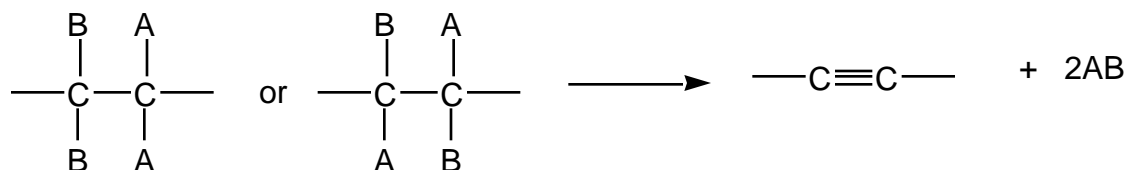
C. Mechanism of the Dehydration Reaction

The **dehydration reaction** proceeds via a **carbocation mechanism**. The three step mechanism starts with the protonation of the alcohol oxygen with a hydrogen ion from sulfuric acid by a Lewis acid-Lewis base reaction. Water departs in the second step leaving a carbocation intermediate. In the final step, a hydrogen ion leaves the adjacent carbon and the double bond forms.

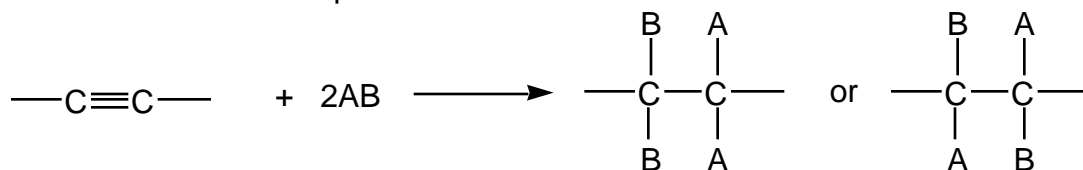
Use of Curved Arrows: Curved arrows are used to describe the movement of electrons in a reaction mechanism. The arrow starts with the electron(s) to be moved and ends at the atom or bond where they move. Full arrows are used to denote the movement of electron pairs and fish hook arrows are used to show the movement of single electrons.

SOLUTIONS TO PROBLEMS**4.1 Types of Reactions**

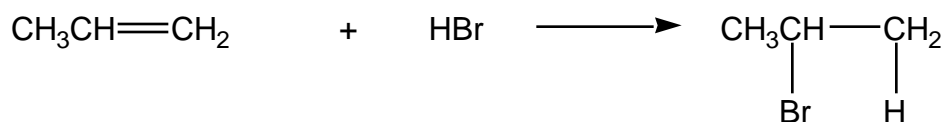
Double Elimination to Form a Triple Bond



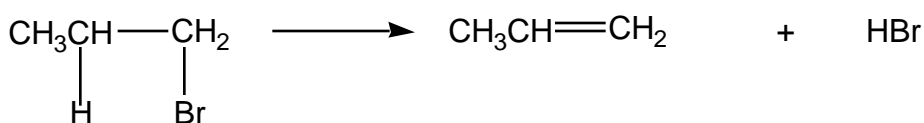
Double Addition to a Triple Bond

**4.2 Types of Reactions**

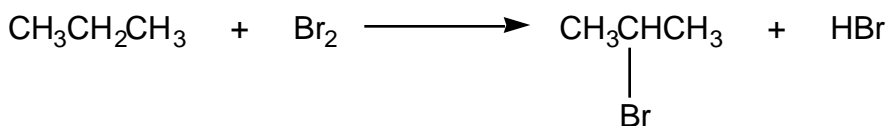
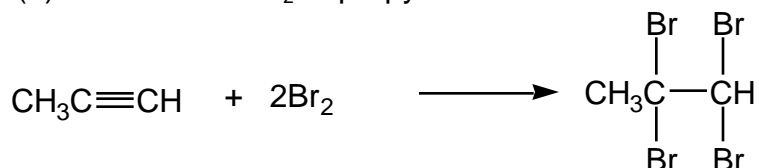
(a) Addition of HBr to propene



(b) Elimination of HBr from 1-bromopropane



(c) Substitution of bromine on propane

(d) Addition of 2Br₂ to propyne

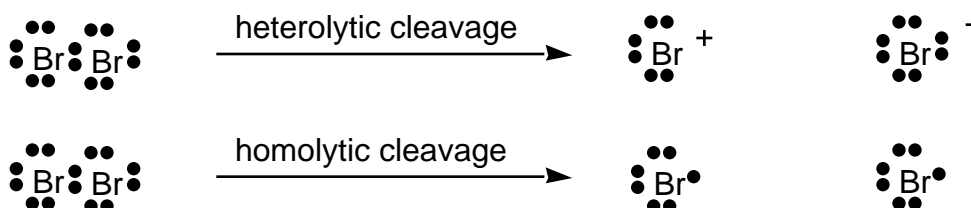
4.3 Types of Reactions

- (a) substitution; (b) elimination; (c) addition;
 (d) addition; (e) elimination; (f) substitution

4.4 Addition Reactions

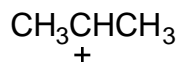
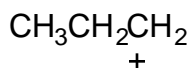
In the addition of HCl to propene, the hydrogen-chlorine bond breaks first. As the new carbon-hydrogen bond forms, the carbon-carbon double bond “breaks” and becomes a single bond. Finally, a new carbon-chlorine bond is formed.

4.5 Homolytic and Heterolytic Cleavage

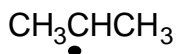
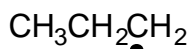


4.6 Reaction Intermediates

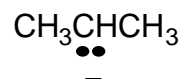
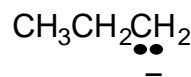
carbocations



free radicals



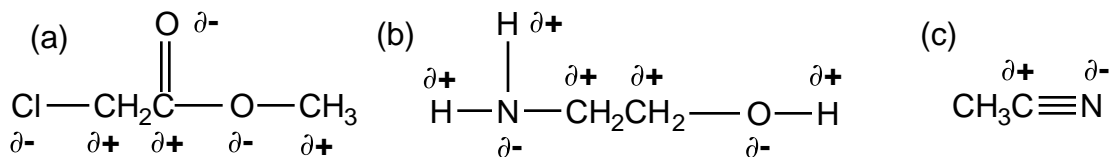
carbanions



4.7 Electrophiles and Nucleophiles

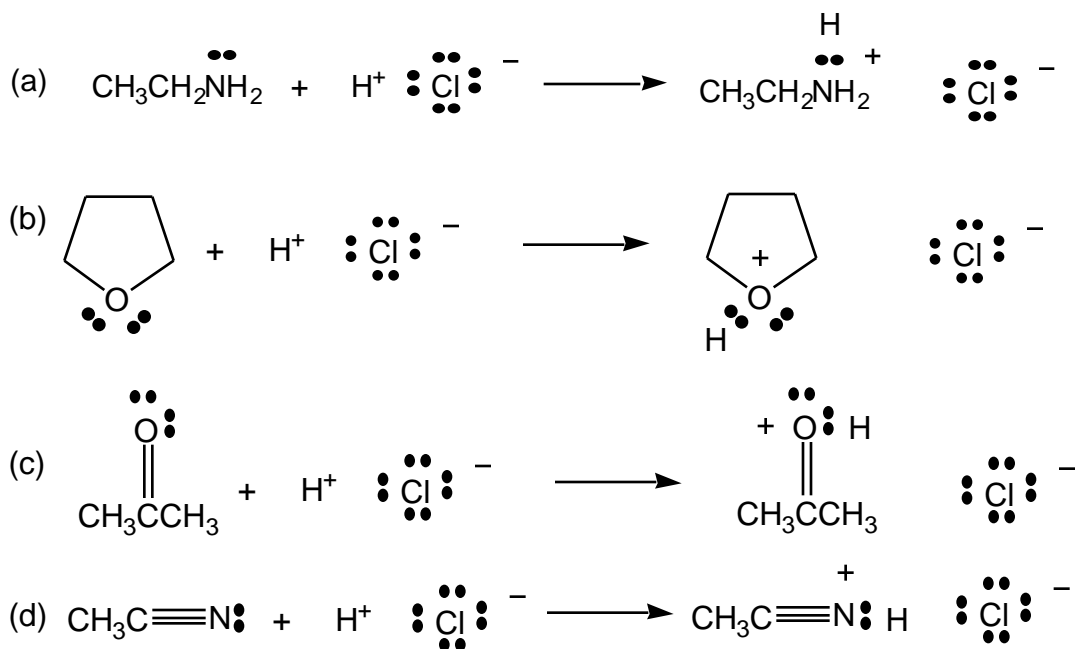
- (a) Electrophile: incomplete octet of electrons and positive charge.
 (b) Nucleophile: complete octet, non-bonding electron pairs, negative charge.
 (c) Nucleophile: complete octet, non-bonding electron pairs, negative charge.
 (d) Nucleophile: complete octet, non-bonding electron pairs, negative charge.
 (e) Electrophile: incomplete octet of electrons and positive charge.
 (f) Nucleophile: complete octet of electrons, non-bonding electron pair.

4.8 Polar Covalent Bonds



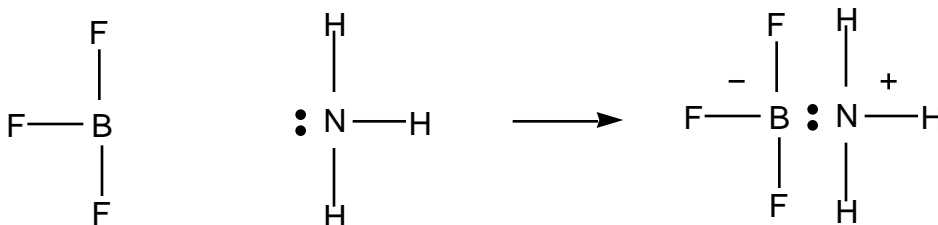
4.9 Lewis Acids and Bases

In all of the following cases, the Lewis base site is either a nitrogen with one non-bonding electron pair or an oxygen with two non-bonding electron pairs. The presence of a non-bonding pair that can be shared with a Lewis acid (hydrogen ion in these cases) makes the site a Lewis base.

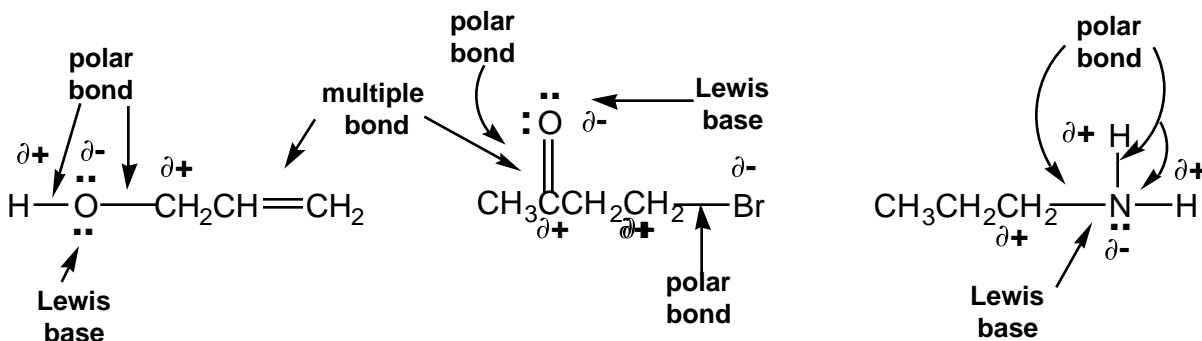


4.10 Lewis Acids and Bases

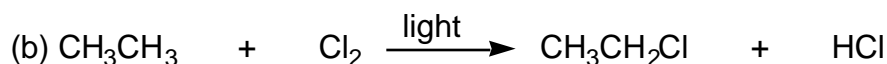
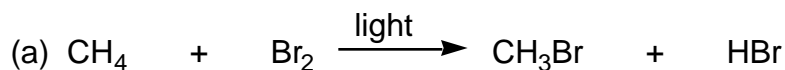
Boron trifluoride is a Lewis acid because boron has an incomplete octet of electrons in its outer shell. Ammonia is a Lewis base because it has a non-bonding electron pair in its complete octet outer shell.



4.11 Reaction Sites

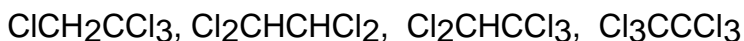


4.12 Halogenation of Alkanes



4.13 Chlorination of Ethane

After one hydrogen is replaced by a chlorine, that molecule can compete for chlorine with the ethane. This can continue to give products ranging from one hydrogen being replaced to all replaced by chlorine. HCl is the inorganic by-product.

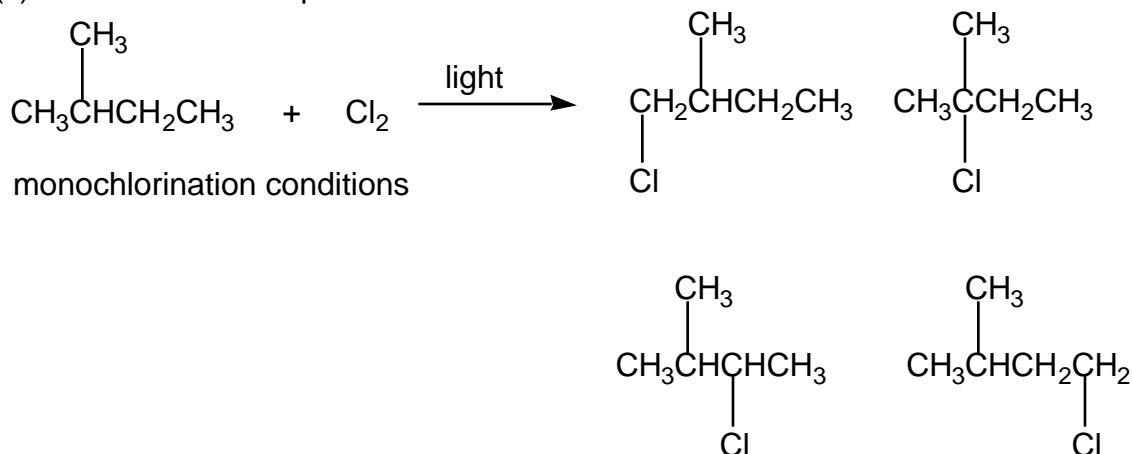
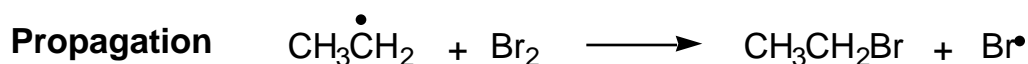
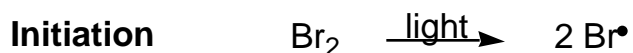
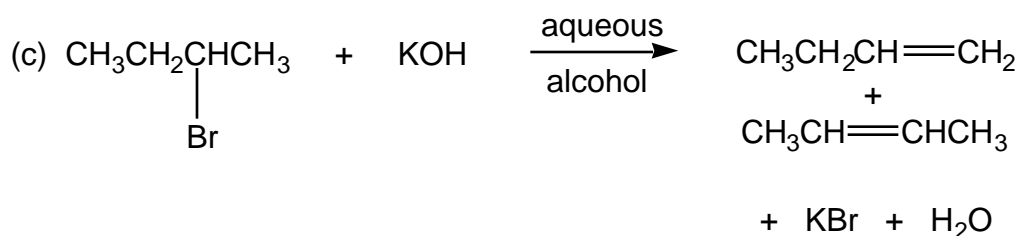
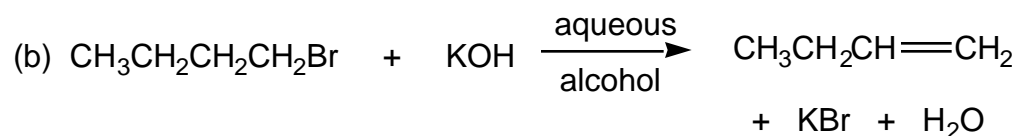
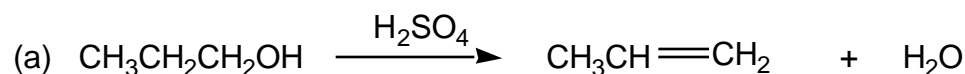
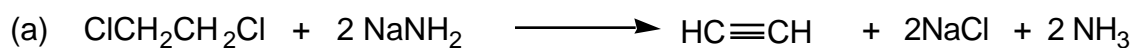


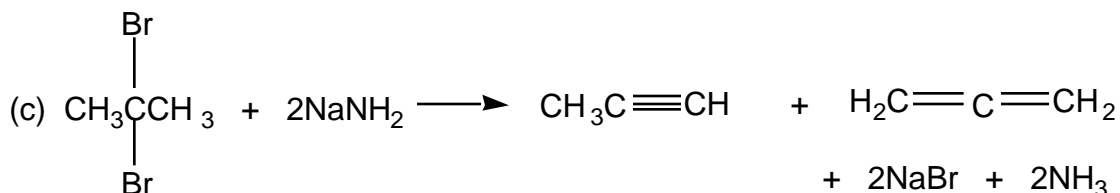
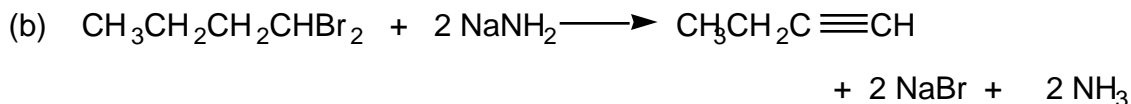
4.14 Control of Halogenation

(a) 2-Methylbutane has 12 hydrogens. To replace them all, the chlorine to alkane ratio must be at least 12:1.

(b) To promote monochlorination, the alkane should be in great excess so that an attacking chlorine is more likely to interact with an unchlorinated molecule compared to already chlorinated alkane. There will be unchlorinated alkane left at the conclusion of the reaction that can fairly easily be separated from the chlorination product.

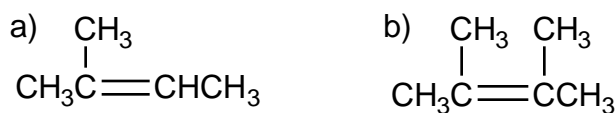
(c) Monochlorination products:

**4.15 Free-radical Chain Reaction Mechanism****4.16 Preparation of Alkenes****4.17 Preparation of Alkynes**

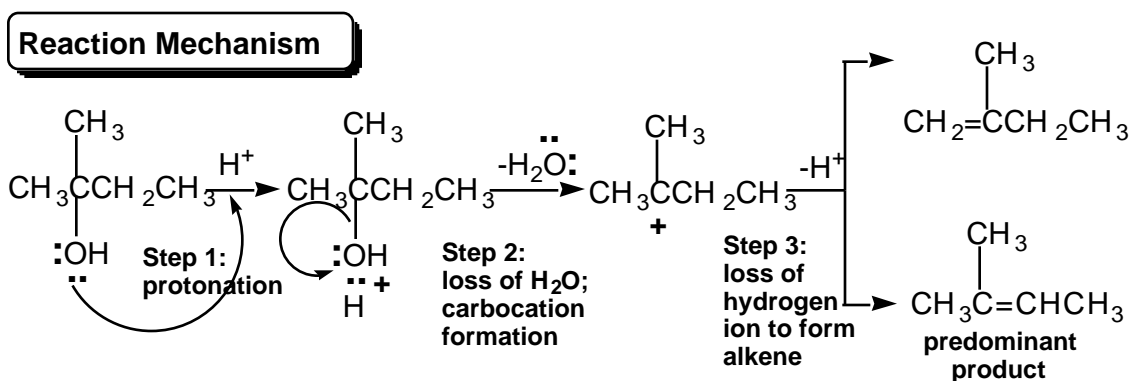
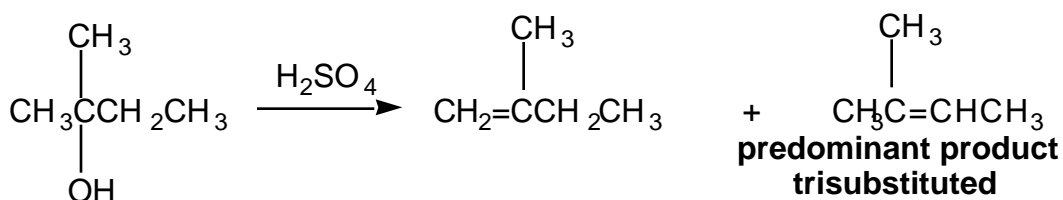


4.18 Orientation of Elimination: See Example 4.2

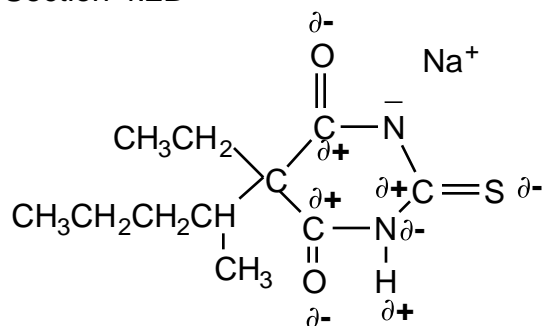
In (a), two alkenes are possible. Concentrate on the carbon with the OH. If the H on the carbon to the right eliminates, the product is monosubstituted; if the H on the carbon to the left is eliminated the major product, trisubstituted, is formed. In (b) a disubstituted alkene is formed if a hydrogen from the carbon to the left of the carbon-chlorine bond is eliminated. The product shown, which is tetrasubstituted, is formed if the H on the carbon to the right is eliminated.



4.19 Mechanism of Dehydration

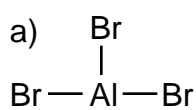


4.20 Polar Bonds: Section 4.2B

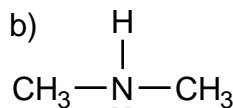


4.21 Lewis Acids and Bases: Section 4.2C

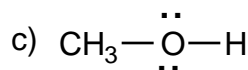
Lewis bases (b and c) have a lone pair of electrons, not used in bonding, which can be shared with a Lewis acid. Lewis acids usually have an incomplete outer shell (the Al and B in a and d) and thus can accept the non-bonding electron pair of a Lewis base.



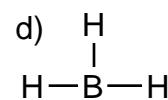
acid



base

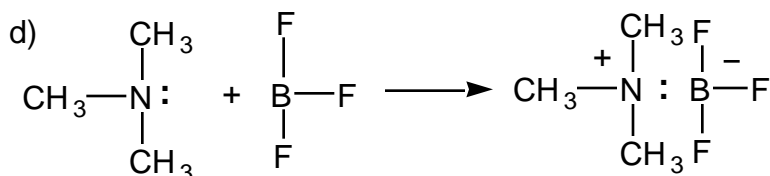
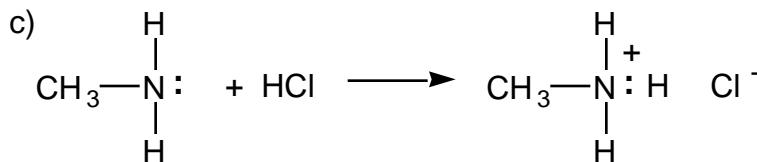
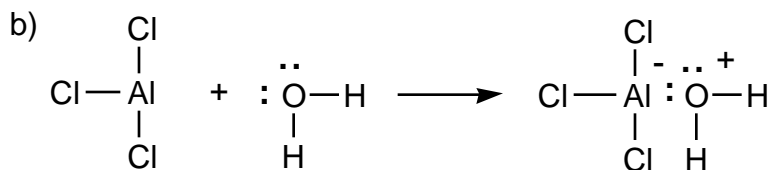
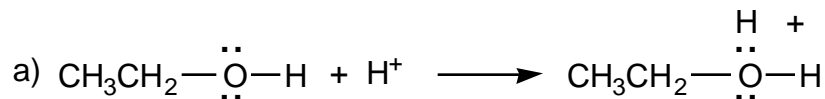


base

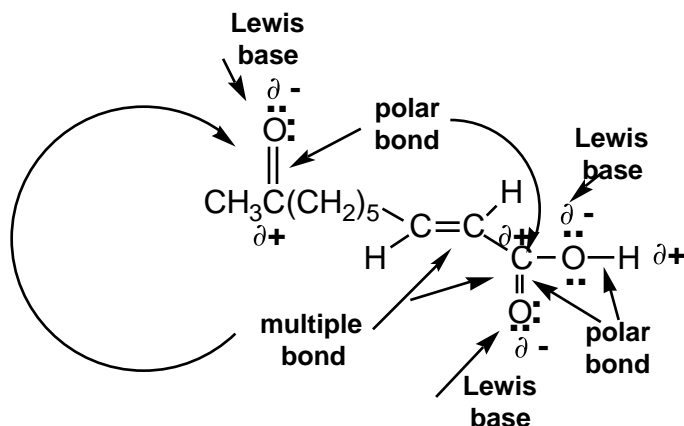


acid

4.22 Lewis Acids and Bases: Section 4.2C



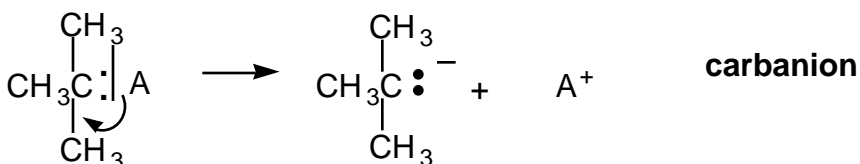
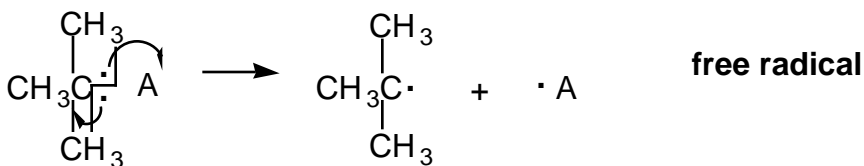
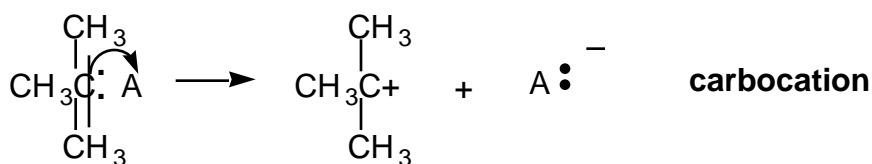
4.23 Reaction Sites: Section 4.2



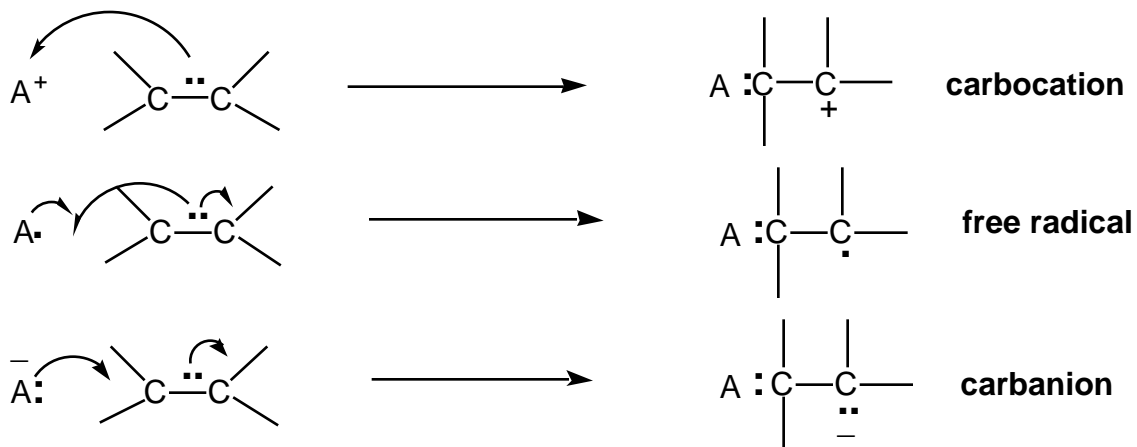
4.24 Electrophiles and Nucleophiles: Section 4.2

- (a) nucleophile - negative, non-bonding electron pairs; (b) electrophile - positive, incomplete octet; (c) nucleophile - non-bonding electron pairs; (d) nucleophile - non-bonding electron pair; (e) nucleophile - negative, non-bonding electron pairs; (f) electrophile - positive, carbocation with incomplete octet; (g) nucleophile - negative, non-bonding electron pair; (h) nucleophile - negative, non-bonding electron pairs.

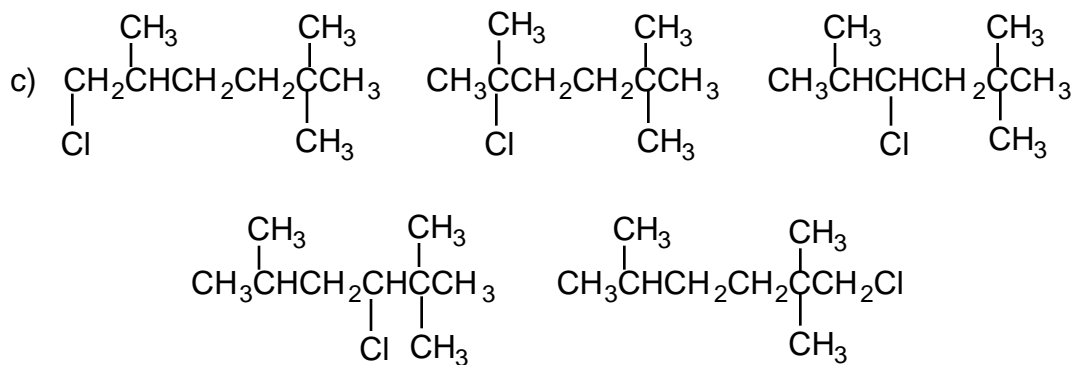
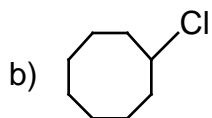
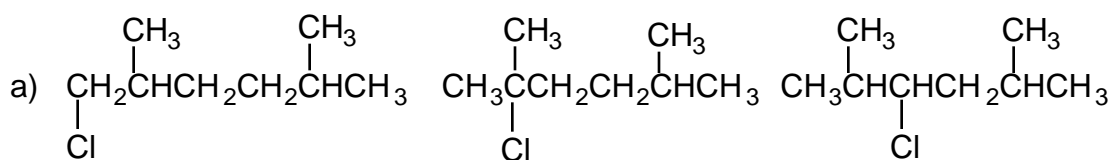
4.25 Reactive Intermediates: Section 4.1D



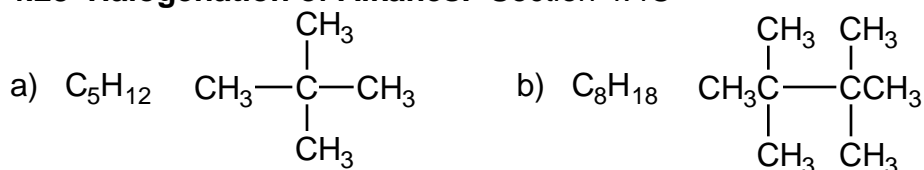
4.26 Reaction Intermediates: Section 4.1D



4.27 Halogenation of Alkanes: Section 4.4C

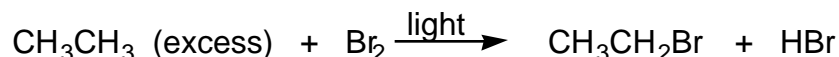


4.28 Halogenation of Alkanes: Section 4.4C

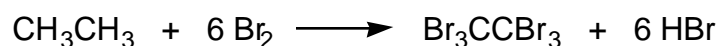
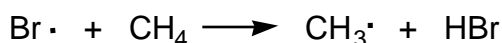


4.29 Halogenation of Alkanes: Section 4.4C

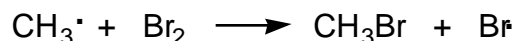
To obtain predominantly bromoethane, use a large excess of ethane relative to the bromine. Statistically, the bromine is more likely to encounter an ethane molecule than a bromoethane.



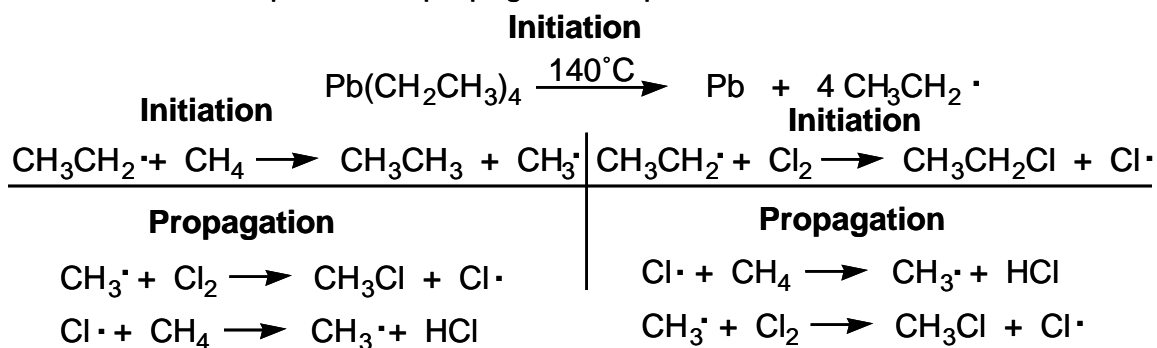
To obtain hexabromoethane, provide enough bromine (6 moles) to ensure that every hydrogen (six) can be replaced.

**4.30 Halogenation of Alkanes - Reaction Mechanism:** Section 4.4D

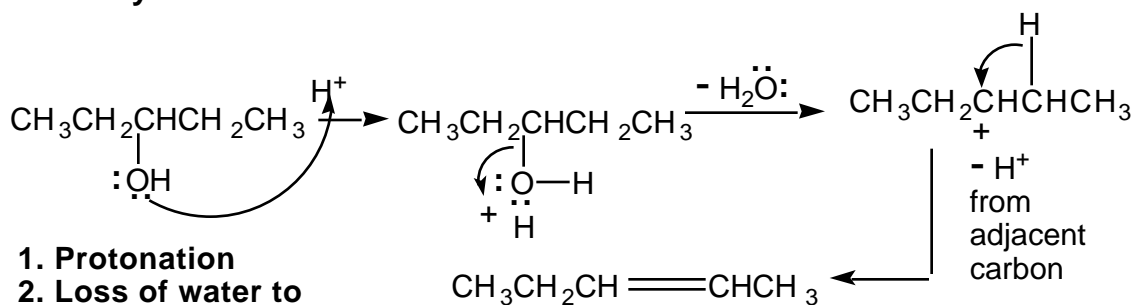
Propagation

**4.31 Halogenation of Alkanes - Reaction Mechanism** Section 4.4D

The ethyl radicals formed from the decomposition of tetraethyllead can react with methane to form methyl radicals or with chlorine to form chlorine radicals. Both of these are part of the propagation steps.



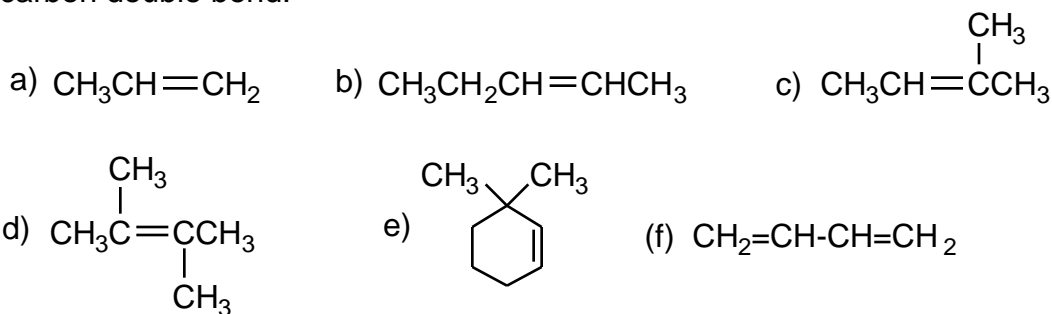
4.32 Dehydration of Alcohols: Section 4.5C



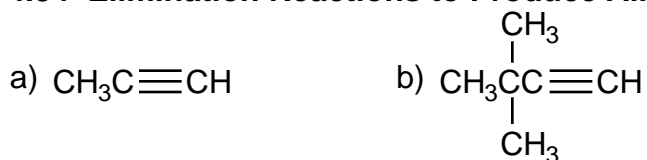
1. Protonation
2. Loss of water to form carbocation
3. Loss of proton to form alkene

4.33 Elimination Reactions to Produce Alkenes: Section 4.5A-B

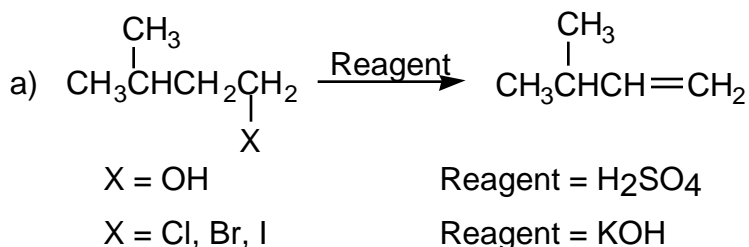
Examples a and c are dehydrohalogenation reactions and the others are dehydrations. The predominant product, when more than one product is possible, is the most highly substituted alkene. The most substituted alkene is the one with the most carbons directly connected to the carbons of the carbon-carbon double bond.



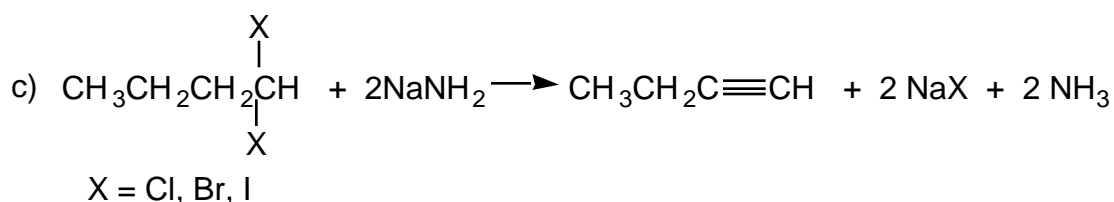
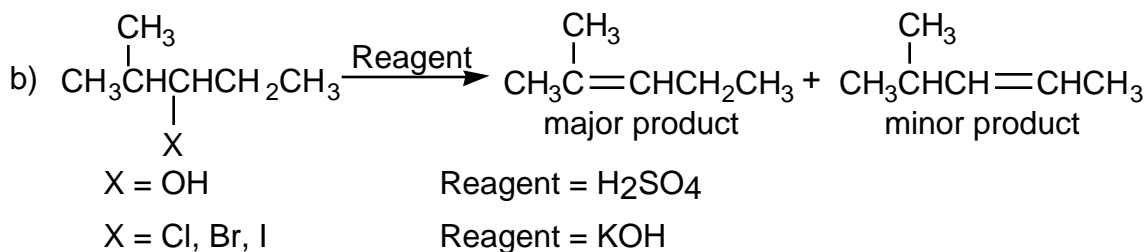
4.34 Elimination Reactions to Produce Alkynes: Section 4.5A-B



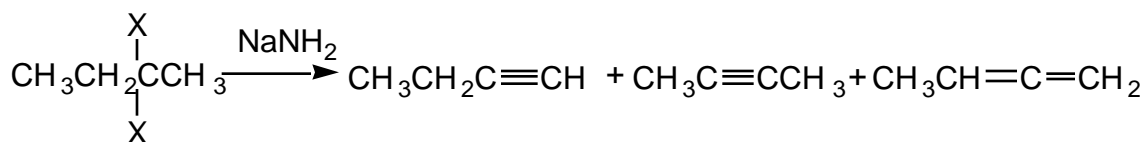
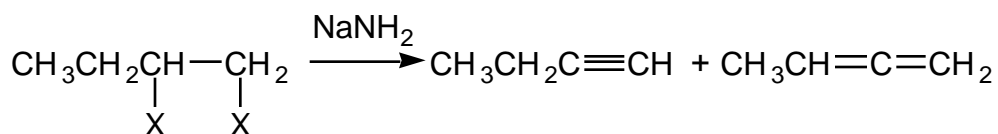
4.35 Preparation of Alkenes and Alkynes: Section 4.5A-B



The previous equation is the preferred method for preparing the desired product since having X on the next carbon would give the most substituted product predominantly.

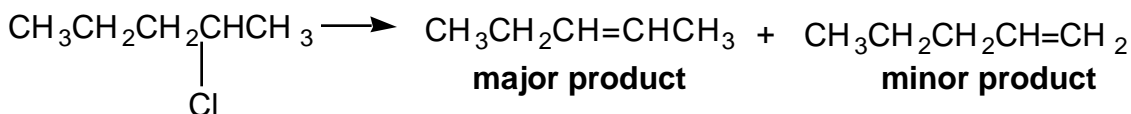
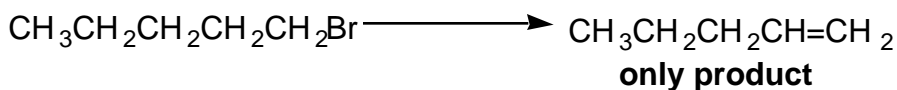


The other two possible dihalide starting materials are less desirable as they can give a diene product or 2-butyne as well as the desired 1-butyne.

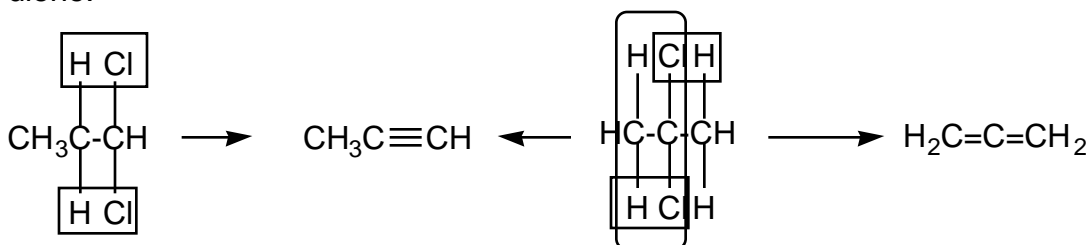


4.36 Preparation of Alkenes and Alkynes: Section 4.5A-B

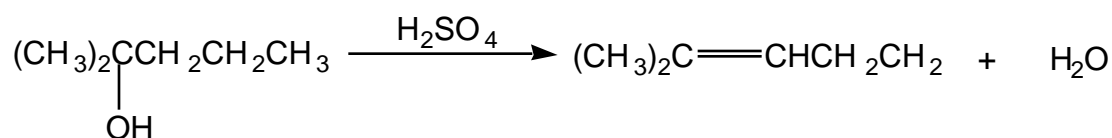
(a) Only one product is possible upon dehydrohalogenation of 1-bromopentane and it is not the desired product. Two products can form from 2-chloropentane; the most substituted is the desired 2-pentene and is formed predominantly.



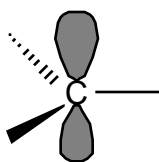
(b) 1,1-dichloropropane can only form propyne upon dehydrohalogenation. 2,2-dichloropropane could possibly eliminate in two different directions to give a diene.



(c) Either compound can produce the desired product. The first one can produce two alkenes whereas the second forms only one, the target compound.

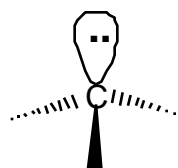


4.37 Carbocations: Section 4.1D



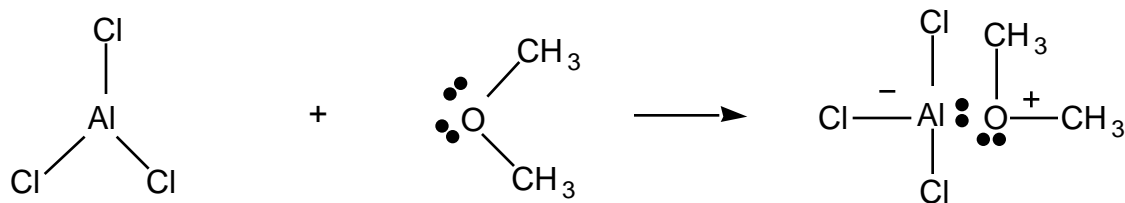
A carbocation has three bonded groups and is trigonal, sp^2 hybridized, and has 120° bond angles. The empty orbital is the unhybridized p-orbital.

4.38 Carbanions: Section 4.1D



In a carbanion, there are four space occupying groups - three bonded groups and the non-bonding electron pair. As a result, it is tetrahedral, sp^3 -hybridized, and has 109° bond angles. The non-bonding pair is in an sp^3 hybrid orbital.

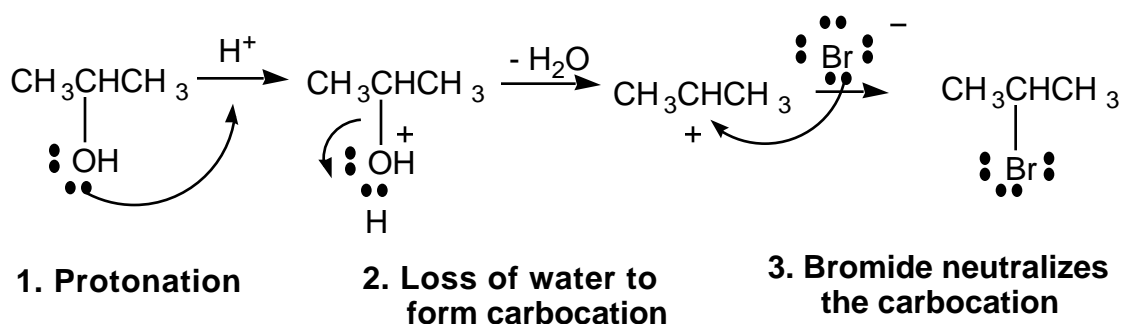
4.39 Lewis Acid, Lewis Base Reactions: Section 4.2C



Al: The aluminum in the AlCl_3 has three bonded groups and is thus trigonal, sp^2 -hybridized and has 120° bond angles. However, in the product the aluminum has four bonded groups and is tetrahedral, sp^3 -hybridized, and has 109° bond angles.

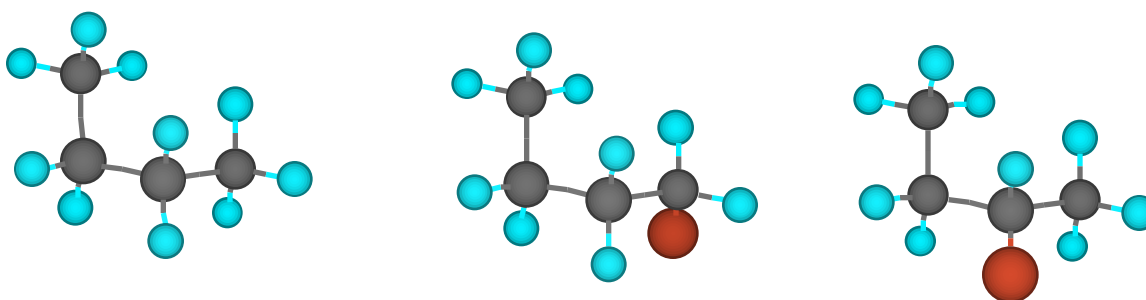
O: In the reactants, the oxygen has two bonded groups and two non-bonding pairs. In the product, it has three bonded groups and one non-bonding electron pair. In both cases it has four space-occupying groups and thus is tetrahedral, sp^3 -hybridized, and has 109° bond angles.

4.40 Reaction Mechanisms: Section 4.5C



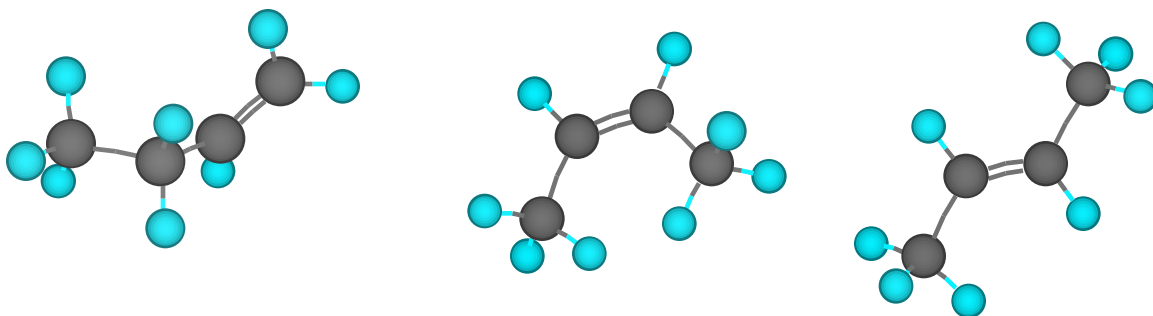
ACTIVITIES WITH MOLECULAR MODELS

1. Make a model of butane. How many different monobromination products are possible? Make a model of each.

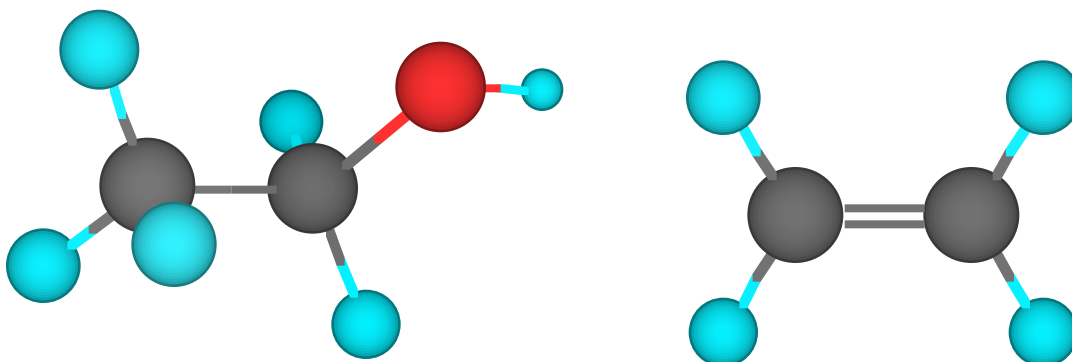


2. Using the models you made in exercise 1 of 1-bromo and 2-bromobutane, demonstrate the result of dehydrobromination. To do so, remove the bromine and a hydrogen from an adjacent carbon; insert a double bond between these two carbons. How many isomers are possible from each compound? Which is the more stable in the case where two are possible?

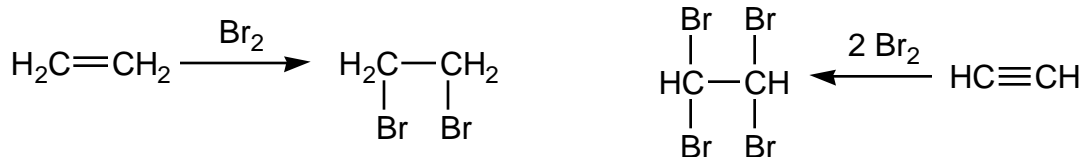
1-bromobutane gives the first product 1-butene as it is the only one possible from simple elimination. 2-bromobutane, you can see, can give the first product and the next two, the cis and trans forms of 2-butene. 2-butene is the more stable product and predominates over 1-butene.



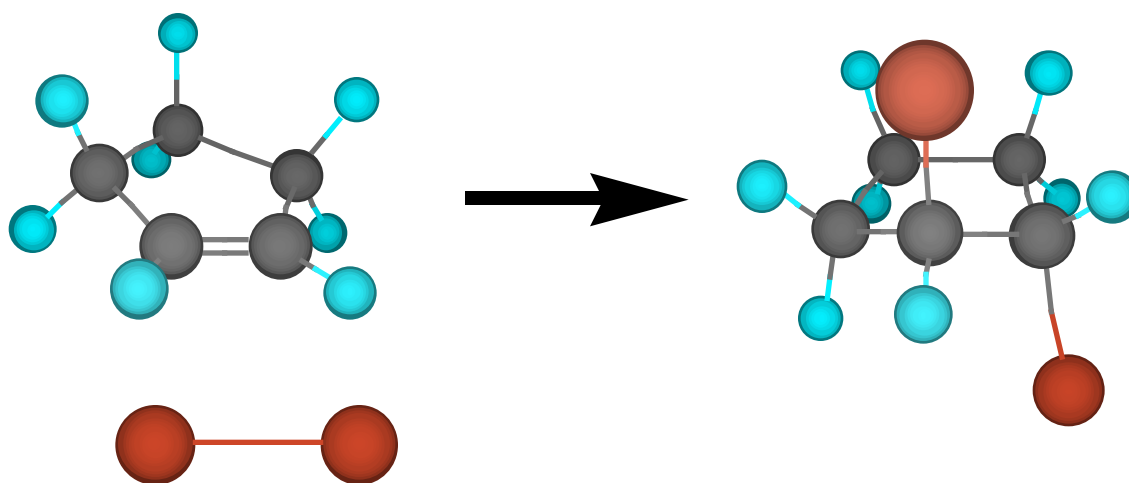
3. Make a model of ethanol and its dehydration product ethene.



5



Reactions of Alkenes and Alkynes



CHAPTER SUMMARY

Addition is the characteristic reaction of **alkenes and alkynes**. Since the carbons of a double or triple bond do not have the maximum number of attached atoms, they can add additional groups or atoms. **Double bonds** undergo addition once and **triple bonds** can undergo addition twice. The reactivity of alkenes and alkynes is due to the presence of **pi-bonds**. Unlike sigma bonds, pi-bonds are directed away from the carbons; the electrons are loosely held, very accessible, and quite attractive electron-deficient species (**electrophiles**) seeking an electron source.

5.1 Addition Reactions of Alkenes

A. General Reaction Equation for Addition to Alkenes

Alkenes add **hydrogen halides**, **halogens** (chlorine and bromine), **water** (sulfuric acid catalyst), and **hydrogen** (metal catalyst). One part of the adding reagent adds to each carbon of the double bond; the double bond becomes a single bond during the process.

B. Mechanism of Electrophilic Addition

With the exception of hydrogenation, the addition reactions of alkenes presented in this text occur by an **electrophilic addition mechanism**. The **electrophile** (H^+ or X^+) attacks the electron-rich pi-bond of the double bond. The pi electrons are used to form a single bond between the carbon and attacking species; the other carbon becomes a **carbocation**. The carbocation is then neutralized by halide ion or water; the addition is complete. In **bromination** reactions, the bromine adds in a **trans** fashion.

C. Orientation of Addition

When an **unsymmetrical reagent** adds to an **unsymmetrical alkene**, two addition products are possible. When the electrophile bonds, it can bond to either carbon of the carbon-carbon double bond to form two different carbocations. The more stable carbocation is favored and the addition product resulting from the more stable carbocation intermediate is the predominant product.

The order of **carbocation stability**: $3^\circ > 2^\circ > 1^\circ > \text{methyl}$. A **tertiary carbocation** has three bonded alkyl groups. **Secondary carbocations** have two alkyl groups bonded directly to the carbocation carbon and in **primary carbocations** there is only one. Since **alkyl groups** are **electron-releasing groups** they stabilize the positive carbocation. Tertiary carbocations have the greatest number of alkyl groups and are the most stable.

Reactions in which one product predominates are termed **regioselective** and those in which one is formed exclusively are **regiospecific**. The electrophilic addition reactions in this chapter are

usually regioselective and the rule for predicting the predominant product is known as **Markovnikov's rule**.

5.2 Addition Reactions of Alkynes

A. General Reaction Equation for Addition to Alkynes

Alkynes add hydrogen, hydrogen halides, and halogens (chlorine and bromine). They can add one mole of reagent to produce a double bond or two moles to form a single bond.

B. Mechanism of Catalytic Hydrogenation of Alkenes and Alkynes

Hydrogenation of alkenes and alkynes is accomplished in the presence of a metal catalyst which attracts both the hydrogen and hydrocarbon to its surface. As a result of the reactants being adsorbed onto the same surface, the reaction occurs with **cis addition**.

C. Electrophilic Addition Mechanism for Alkynes

The mechanism of **electrophilic addition** to alkynes is the same as with alkenes. **Orientation of addition** of unsymmetrical reagents to unsymmetrical alkynes is determined by the stability of the intermediate carbocation.

D. Addition of Water to Alkynes

Alkynes add water to form aldehydes and ketones.

5.3 Addition Polymers

A **polymer** is a giant molecule composed of a repeating structural unit called a **monomer**. **Addition polymers** result from the addition of alkene molecules to one another. The **polymerization** occurs by cationic, free-radical, and anionic reaction mechanisms. Examples of addition polymers include polyethylene, polystyrene, PVC, and Teflon.

A. Cationic Polymerization by Electrophilic Addition

In cationic polymerization, an electrophile (such as H^+) adds to the carbon-carbon double bond of a monomer to form the more stable carbocation. The reaction conditions are such that there is relatively little electrophile and corresponding carbocation neutralizing species. As a result, the carbocation attacks the double bond of another monomer molecule producing another carbocation that carries on the process until the growing chain is eventually neutralized.

B. Polymerization by a Free-Radical Chain Reaction

In this mechanism of polymerization, a small amount of free radicals is generated. These attack the carbon-carbon double bonds of monomer molecules, bond to one carbon, and produce the more stable free radical; this is the initiation step. Since few chains are initiated, the free radical attacks yet another monomer, adds to the double bond, and forms another free radical that, in turn, continues the process; this is propagation. Eventually two developing free radical chains may bond together and terminate the chain reaction.

CONNECTIONS 5.1 Serendipity in the Discovery of Polymers**CONNECTIONS 5.2 Recycling Plastics****5.4 Electrophilic Addition to Conjugated Dienes**

Conjugated dienes are compounds in which two carbon-carbon double bonds are separated by a single bond. Upon treatment with adding reagents, conjugated dienes undergo **1,2-addition**, in which the reagent adds to one of the double bonds and **1,4-addition** in which the reagent adds to the first and fourth carbons with the remaining double bond shifting between carbons 2 and 3. This is caused by the formation of an allylic intermediate such as an **allylic carbocation**. An allylic carbocation is one in which the carbocation carbon is attached directly to a carbon-carbon double bond. Such a carbocation engages in resonance allowing neutralization at the second and fourth carbons of the original conjugated diene.

Resonance forms are classical structures used to describe a more complex system; they do not actually exist. The species is more accurately described by a **resonance hybrid** which can be imagined as an average of the resonance forms. Resonance always stabilizes a system. Each atom in a resonance stabilized system has a p-orbital. Allylic carbocations are stabilized by delocalization of the positive charge.

5.5 Resonance Stabilization of Reactive Intermediates

Allylic carbocations, free radicals, and carbanions are resonance stabilized. In each case the stabilization is the result of delocalization of the positive or negative charge or the free radical. Resonance forms differ in the position of electrons and charge but not atoms. Every atom in an allylic carbocation, free radical, or carbanion possesses a p-orbital and the pi-electrons and charges or unpaired electrons are delocalized throughout these orbitals.

5.6 Natural and Synthetic Rubber

Natural rubber is produced from a milky-white colloidal latex found in the rubber tree. It is a polymeric terpene with isoprene being the recurring polymeric unit. Polyisoprene rubber can also be produced synthetically by the addition polymerization of isoprene by 1,4-addition. Other synthetic rubbers include SBR (styrene-butadiene rubber), polybutadiene, and neoprene. Rubber is strengthened, hardened, and made more elastic by a process called vulcanization in which sulfur bridges form links within the polymeric chains. These links become strained when the rubber is stretched and when released the rubber assumes its original conformation.

CONNECTIONS 5.3 Terpenes

5.7 Oxidation of Alkenes

A. Hydroxylation with Potassium Permanganate

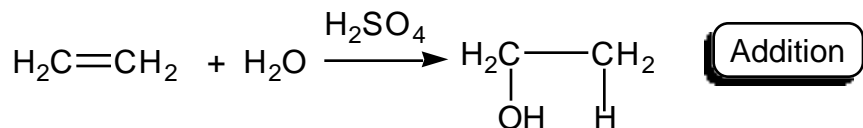
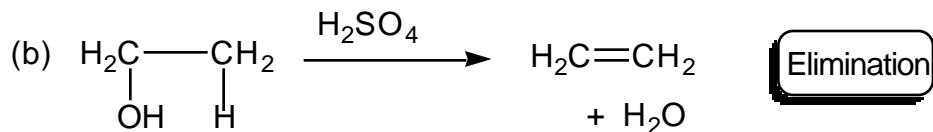
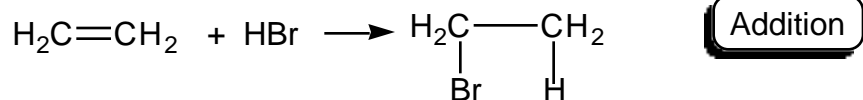
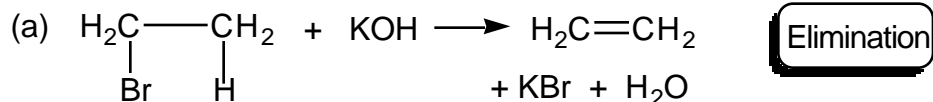
Treatment of alkenes with **potassium permanganate** produces 1,2-diols in a cis configuration.

B. Ozonolysis

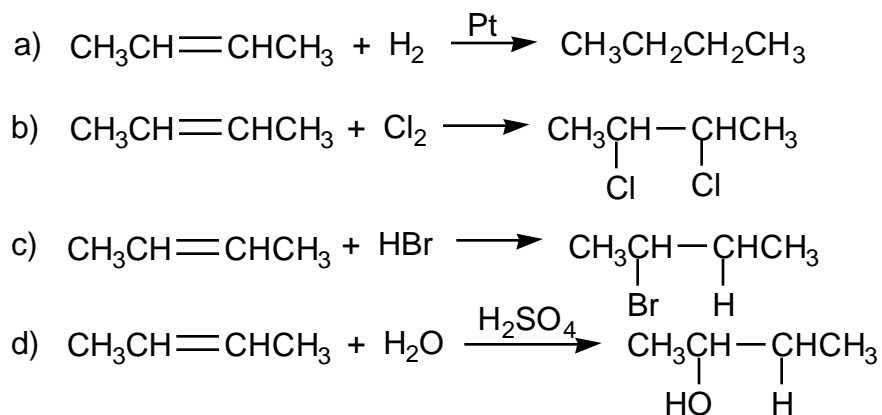
Ozonolysis cleaves the carbon-carbon double bond of an alkene to form aldehydes and ketones.

5.8 Acidity of Terminal Alkynes

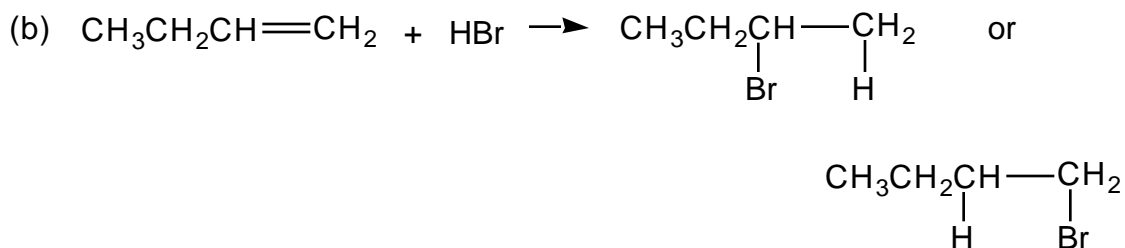
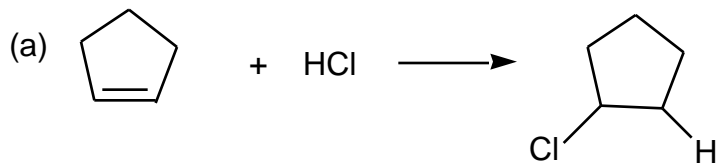
Terminal alkynes have weakly acidic hydrogens that can be abstracted by strong bases such as sodium amide.

CONNECTIONS 5.4 The Treatment of Atherosclerosis**SOLUTIONS TO PROBLEMS****5.1 Addition and Elimination Reactions**

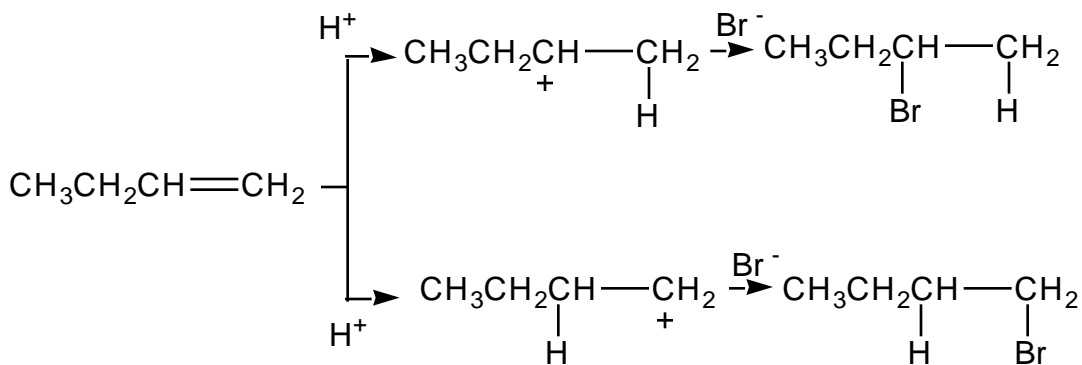
5.2 Addition Reactions of Alkenes



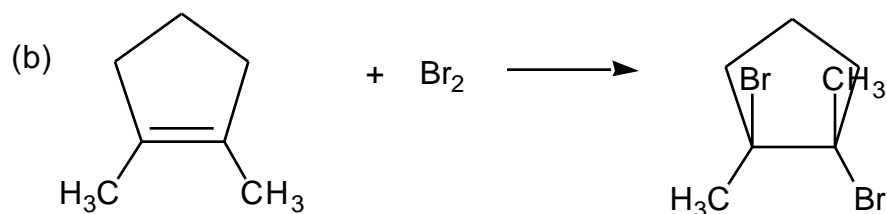
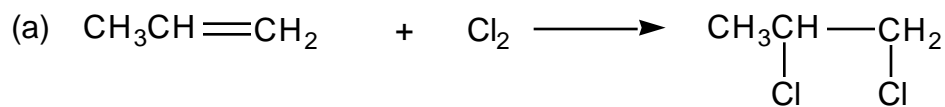
5.3 Addition Reactions



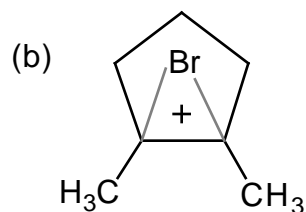
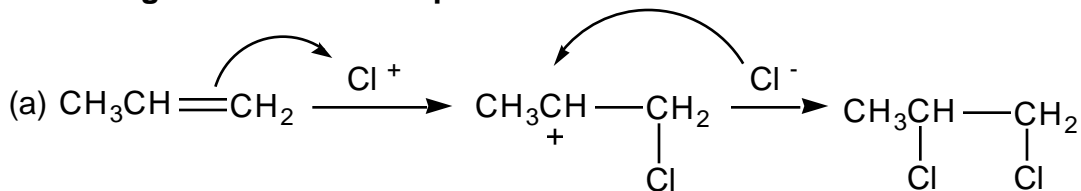
5.4 Electrophilic Addition Mechanism



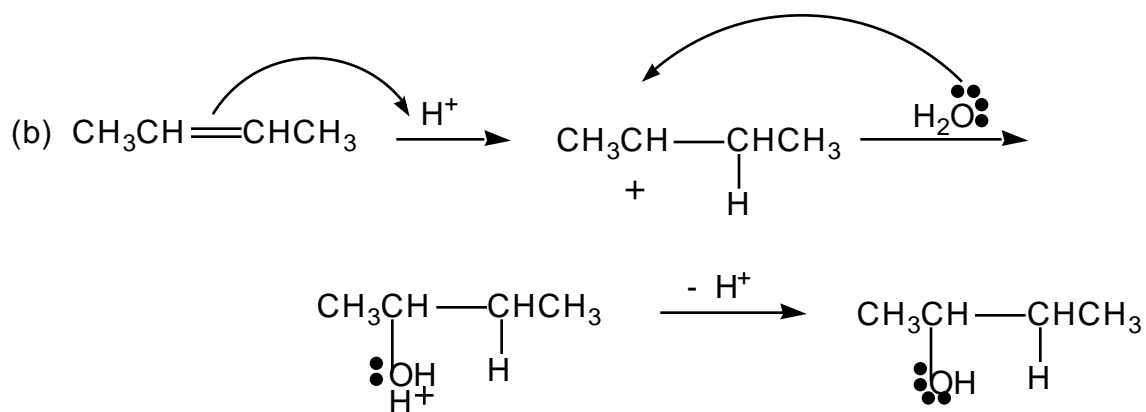
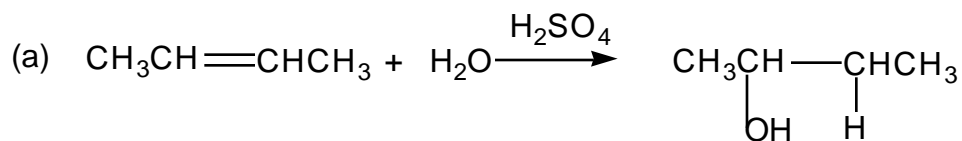
5.5 Halogenation of Alkenes



5.6 Halogenation: Electrophilic Addition

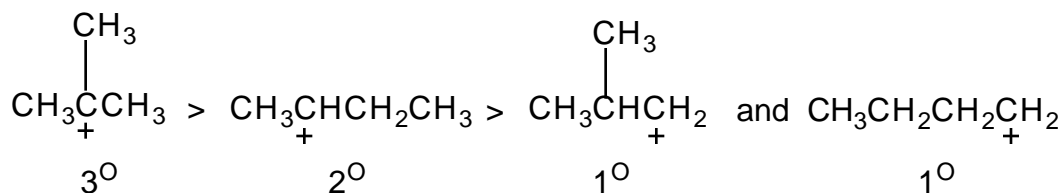


5.7 Hydration of Alkenes



5.8 Carbocations

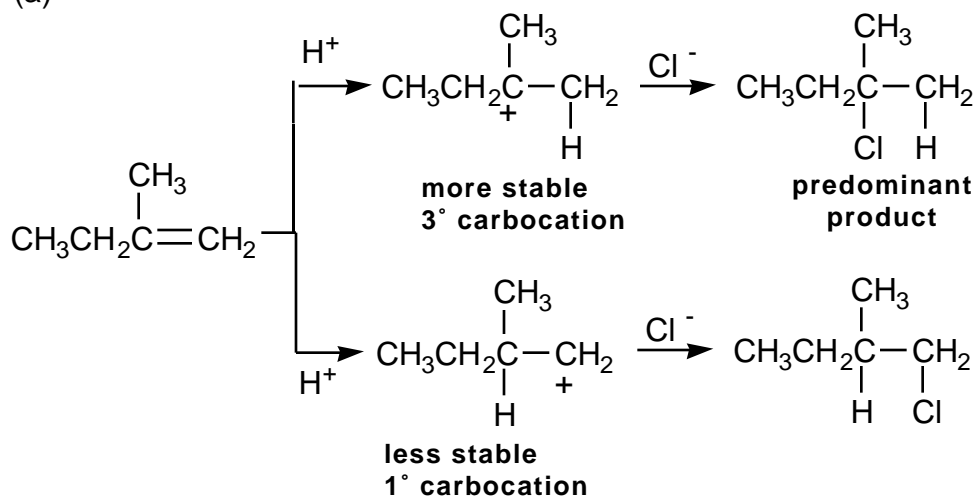
Arranged most to least stable:



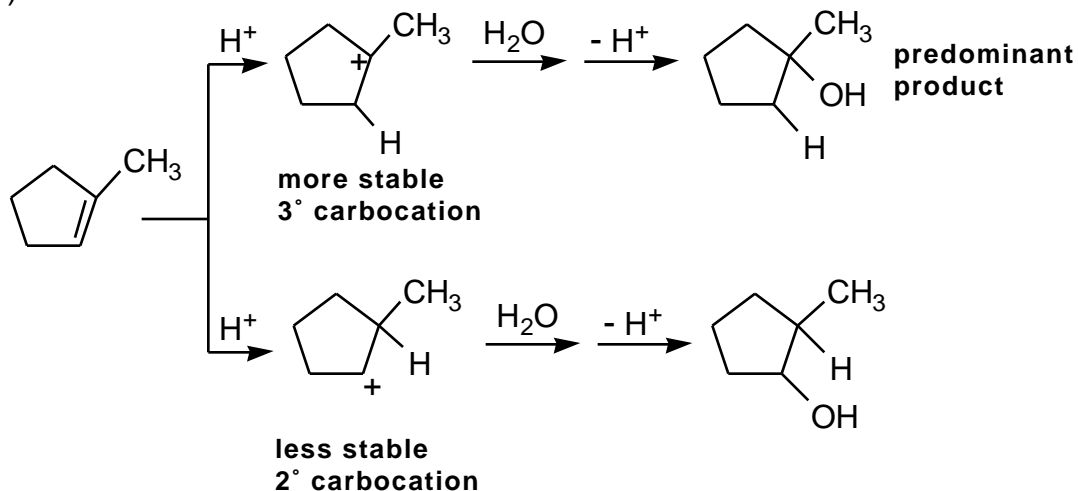
most stable

5.9 Orientation of Addition

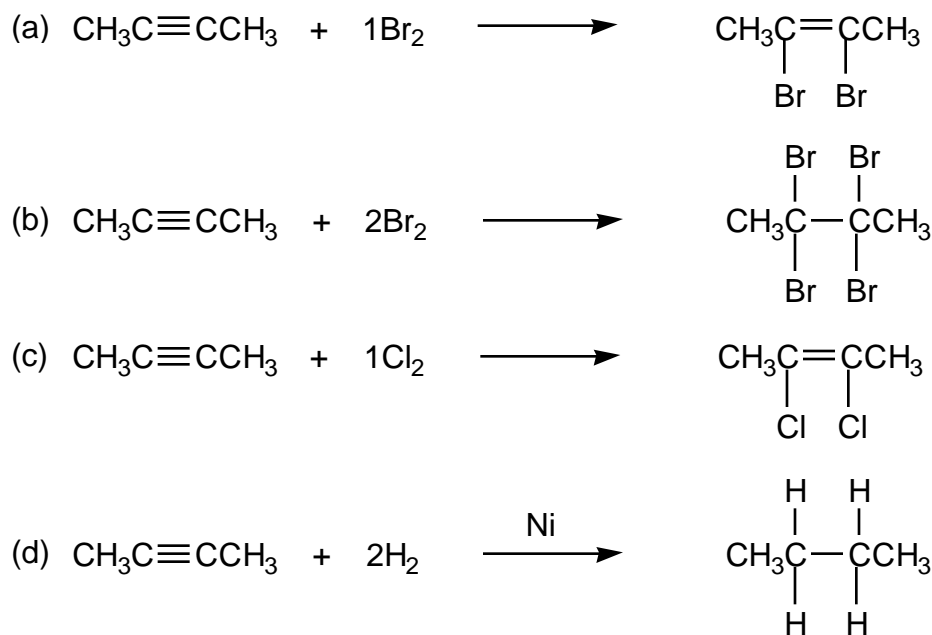
(a)



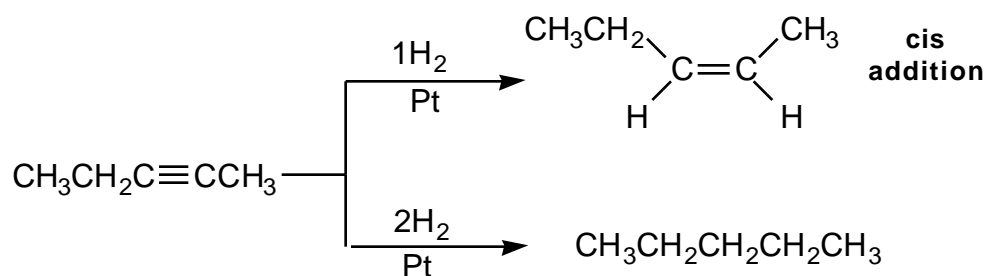
(b)



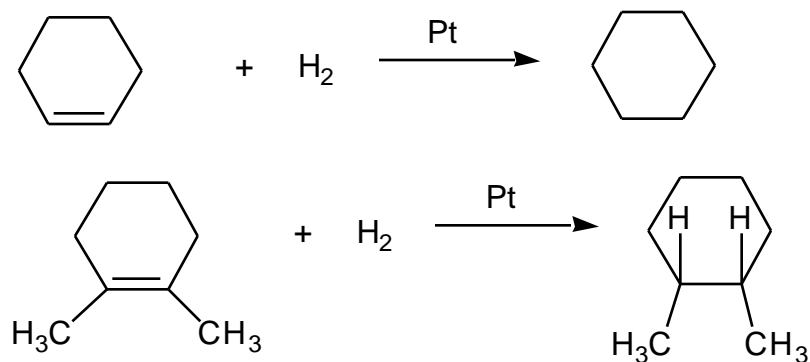
5.10 Addition Reactions of Alkynes



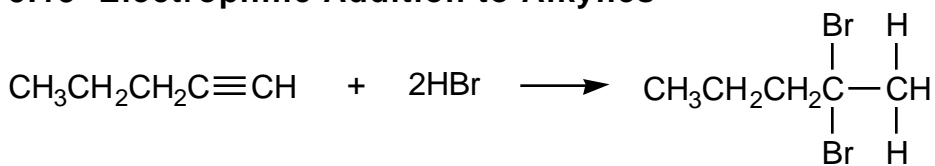
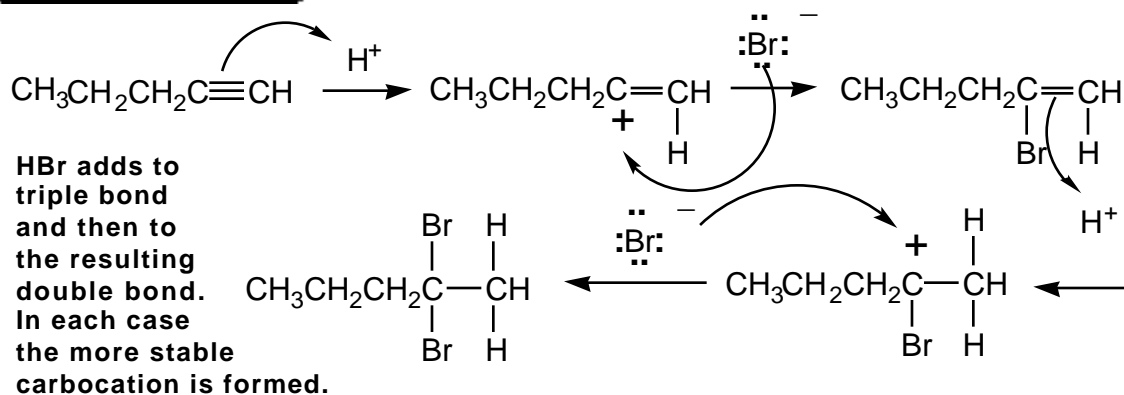
5.11 Hydrogenation of Alkynes



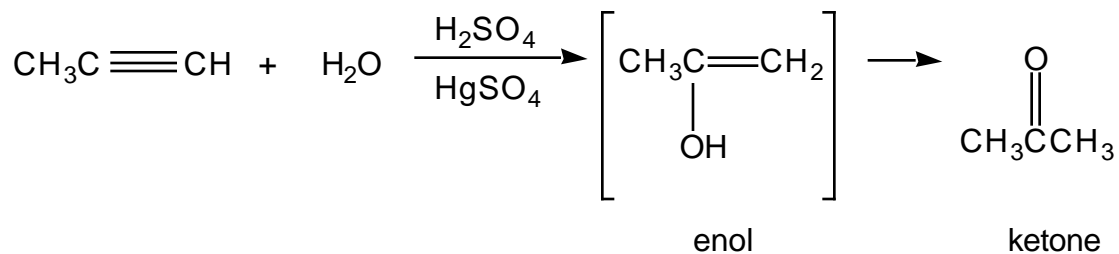
5.12 Hydrogenation of Alkenes



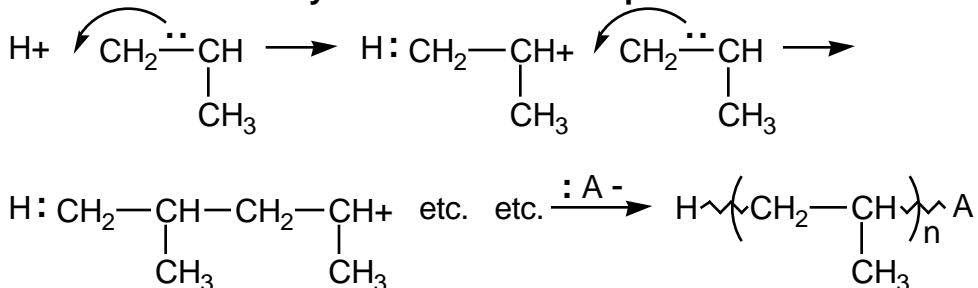
5.13 Electrophilic Addition to Alkynes


Reaction Mechanism


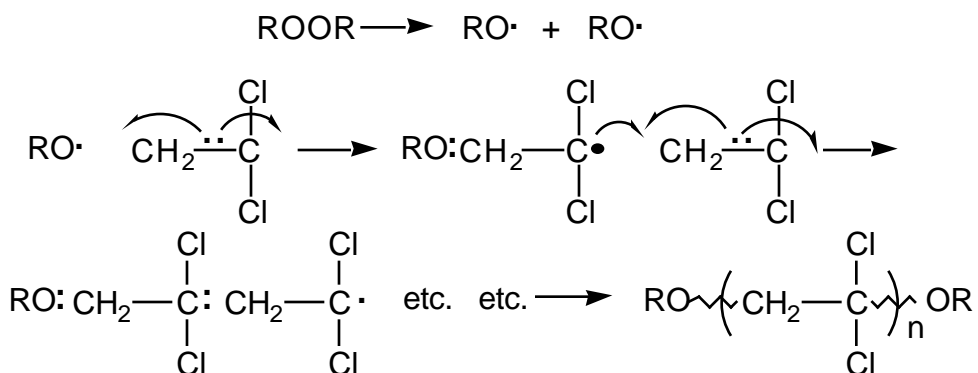
5.14 Hydration of Alkynes



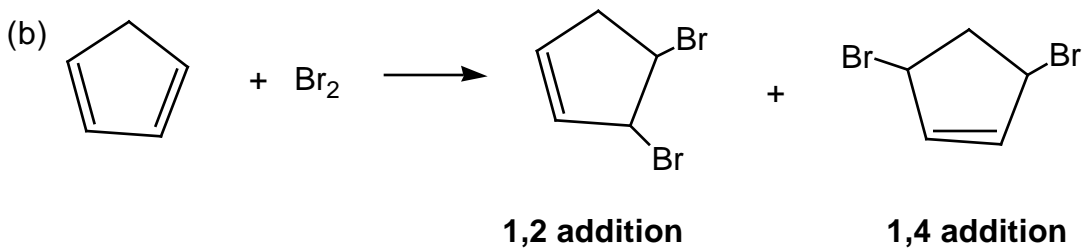
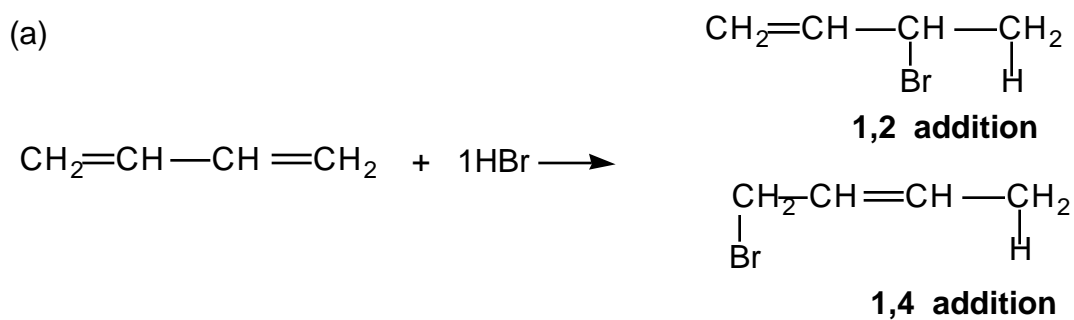
5.15 Cationic Polymerization of Propene



5.16 Free Radical Polymerization of 1,1-Dichloroethene



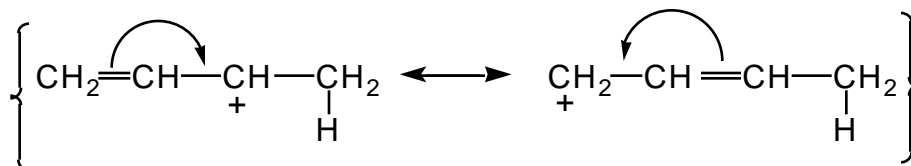
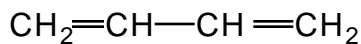
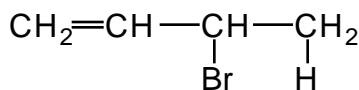
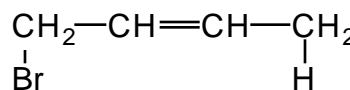
5.17 1,2 and 1,4 Addition



5.18 Electrophilic Addition Mechanism: 1,2 and 1,4 Addition

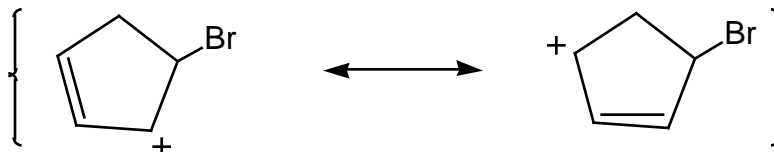
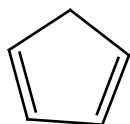
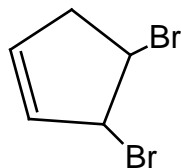
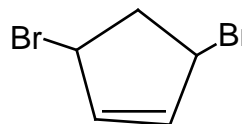
 (a) **Reaction Mechanism**
STEP 1: Electrophile, H^+

is attracted to pi-cloud and uses two pi-electrons to bond. More stable allylic carbocation results.

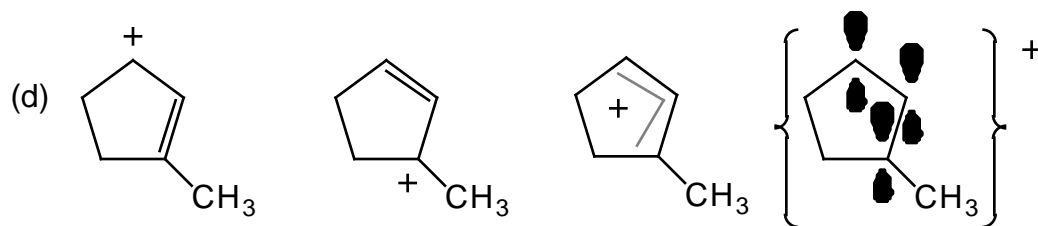
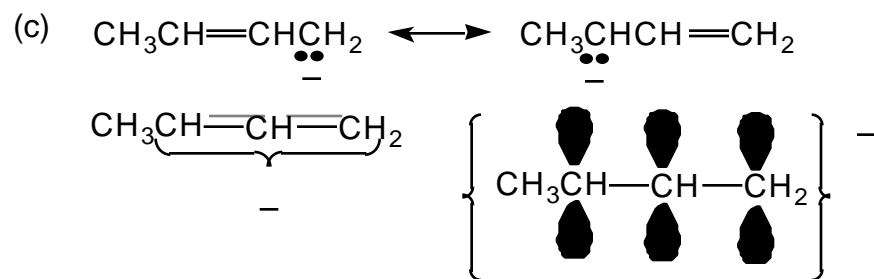
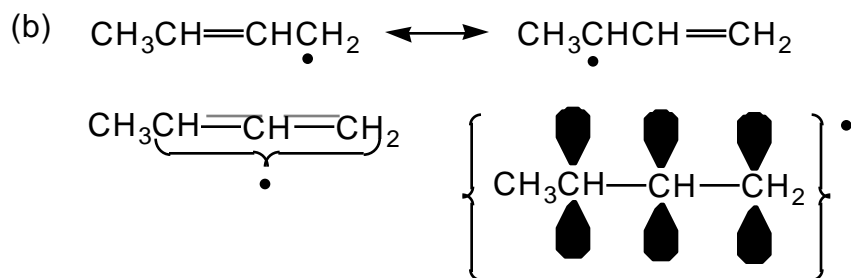
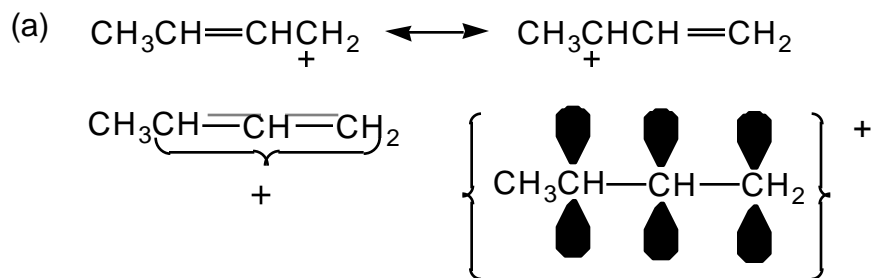

Resonance Forms
STEP 2: The allylic carbocation is resonance stabilized. Resonance forms show the two places it can be neutralized by bromide ion.

1,2 addition

1,4 addition

 (b) **Reaction Mechanism**
STEP 1: Electrophile, Br^+

is attracted to pi-cloud and uses two pi-electrons to bond. More stable allylic carbocation results.


Resonance Forms
STEP 2: The allylic carbocation is resonance stabilized. Resonance forms show the two places it can be neutralized by bromide ion.

1,2 addition

1,4 addition

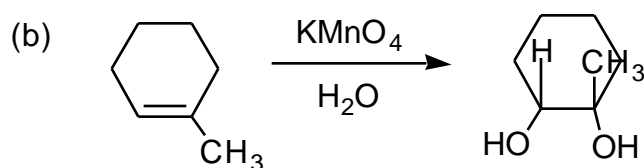
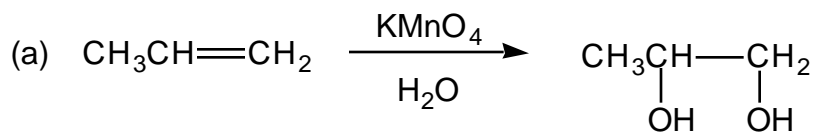
5.19 Resonance Forms, Hybrids, and Bonding Pictures



5.20 Terpenes

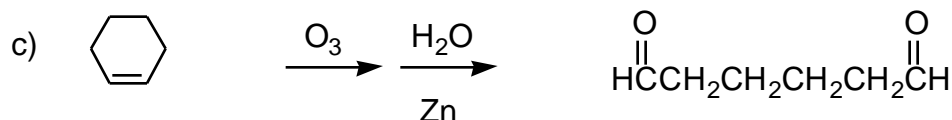
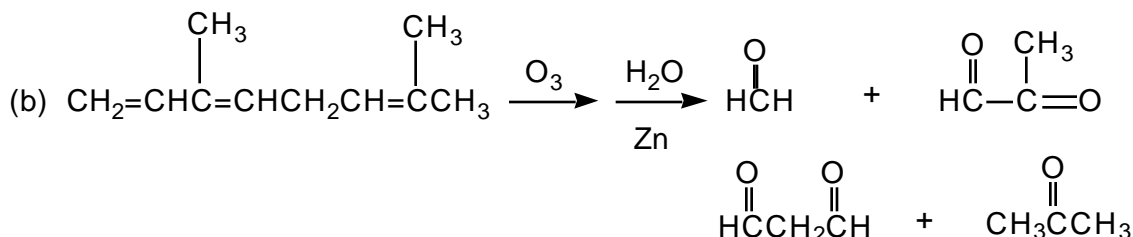
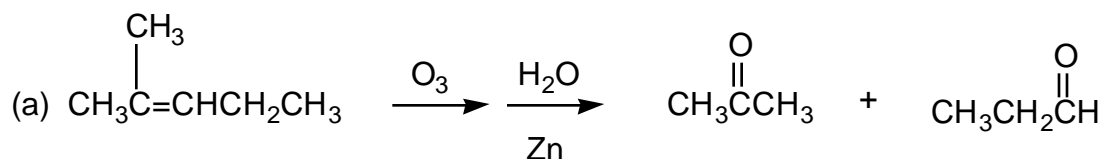
- (a) monocyclic monoterpene (b) acyclic monoterpene
 (c) bicyclic sesquiterpene (d) acyclic tetraterpene
 (e) tricyclic diterpene (f) monocyclic monoterpene
 (g) acyclic monoterpene

5.21 Reaction of Alkenes with Potassium Permanganate



5.22 Ozonolysis

Each double bond is cleaved; the carbons become carbon-oxygen double bonds.

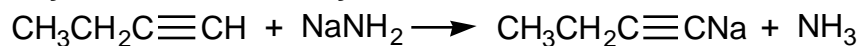


5.23 Ozonolysis

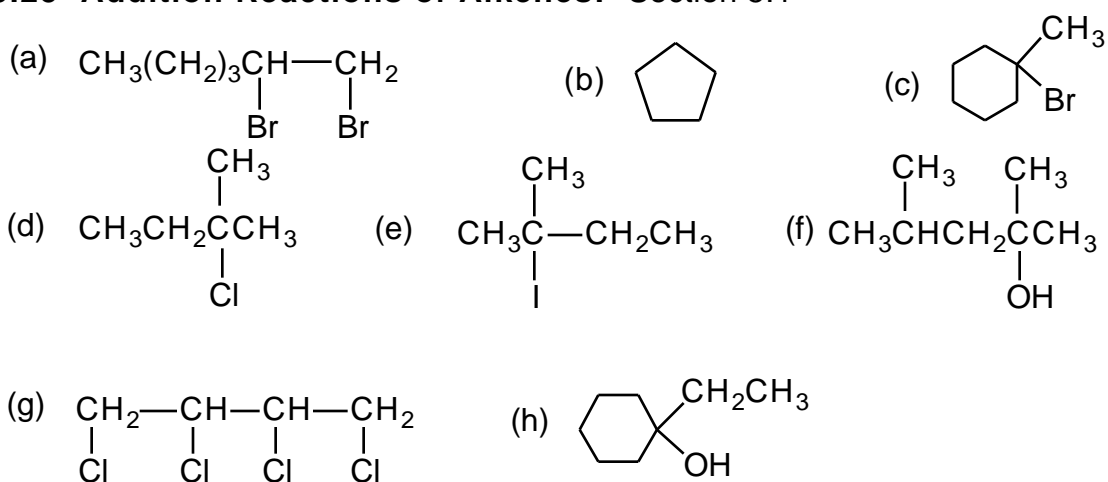
Wherever you see a carbon-oxygen double bond, there was originally a carbon-carbon double bond. Since there are only two carbon-oxygen double bonds, they must have been involved in the carbon-carbon double bond.



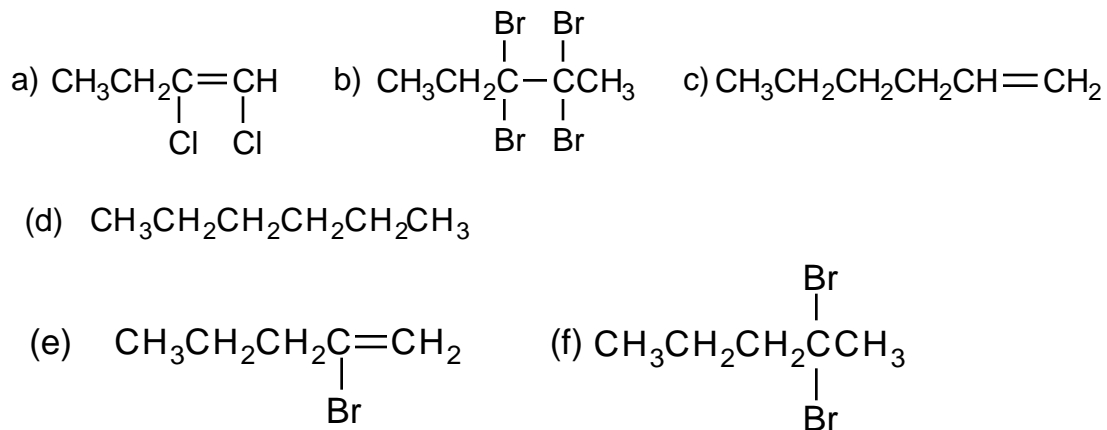
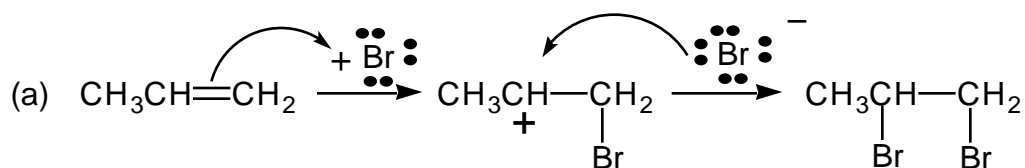
5.24 Acidity of Terminal Alkynes



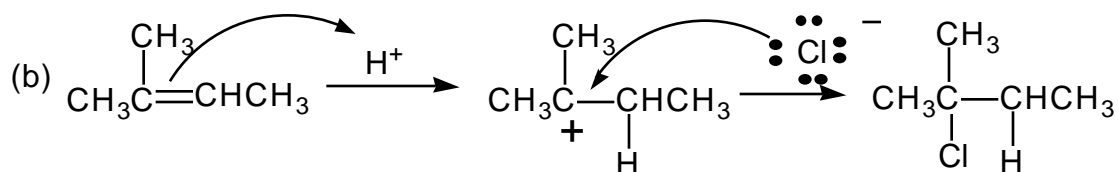
5.25 Addition Reactions of Alkenes: Section 5.1

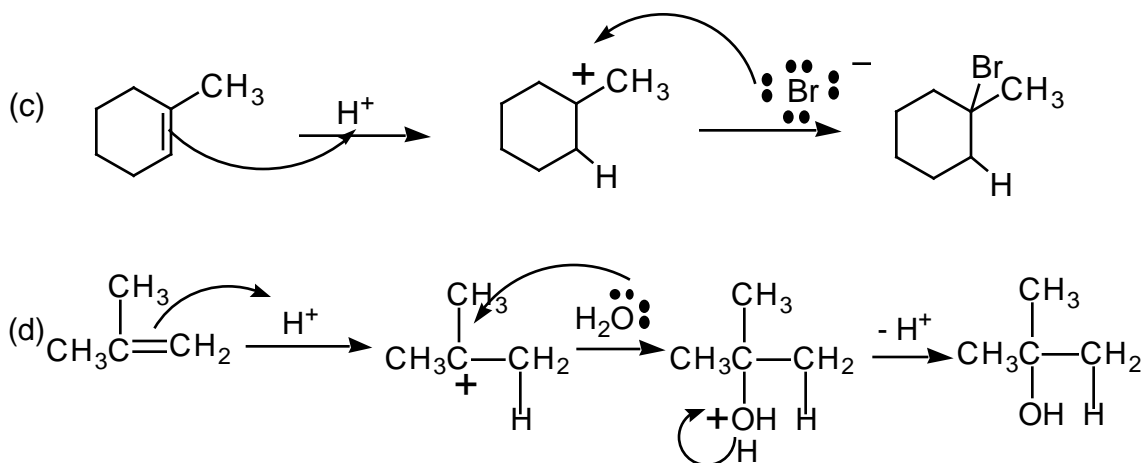


5.26 Addition Reactions of Alkynes: Section 5.2

5.27 Reaction Mechanisms - Electrophilic Addition to Alkenes:
Section 5.1B

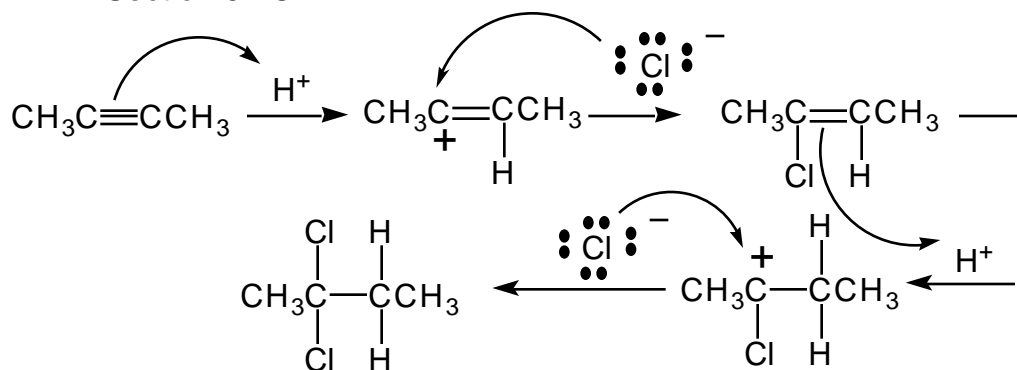
The carbocation in this case is actually a bromonium ion.





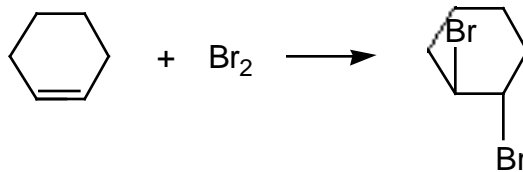
5.28 Reaction Mechanisms - Electrophilic Addition to Alkynes

Section 5.2C

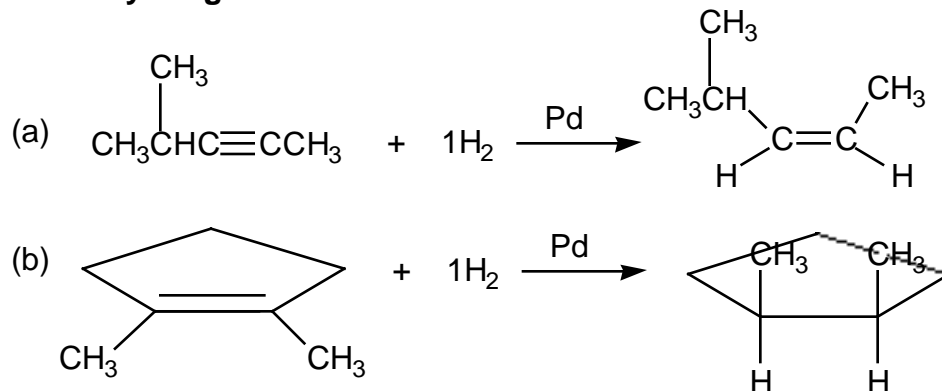


5.29 Bromination: Section 5.1B2

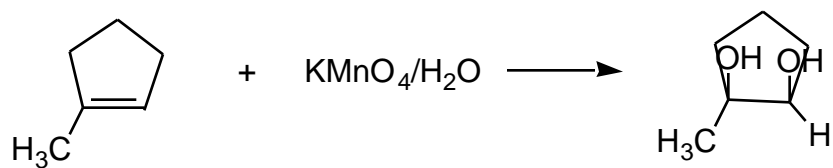
Bromination involves cis addition due to an intermediate bromonium ion.



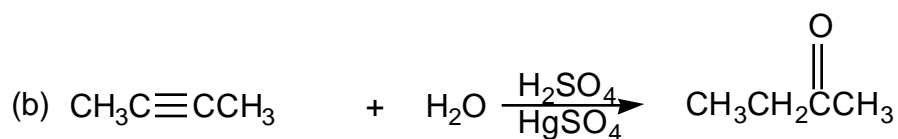
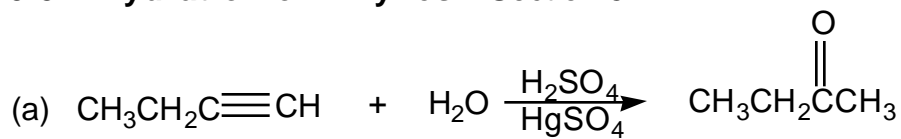
5.30 Hydrogenation: Section 5.2B



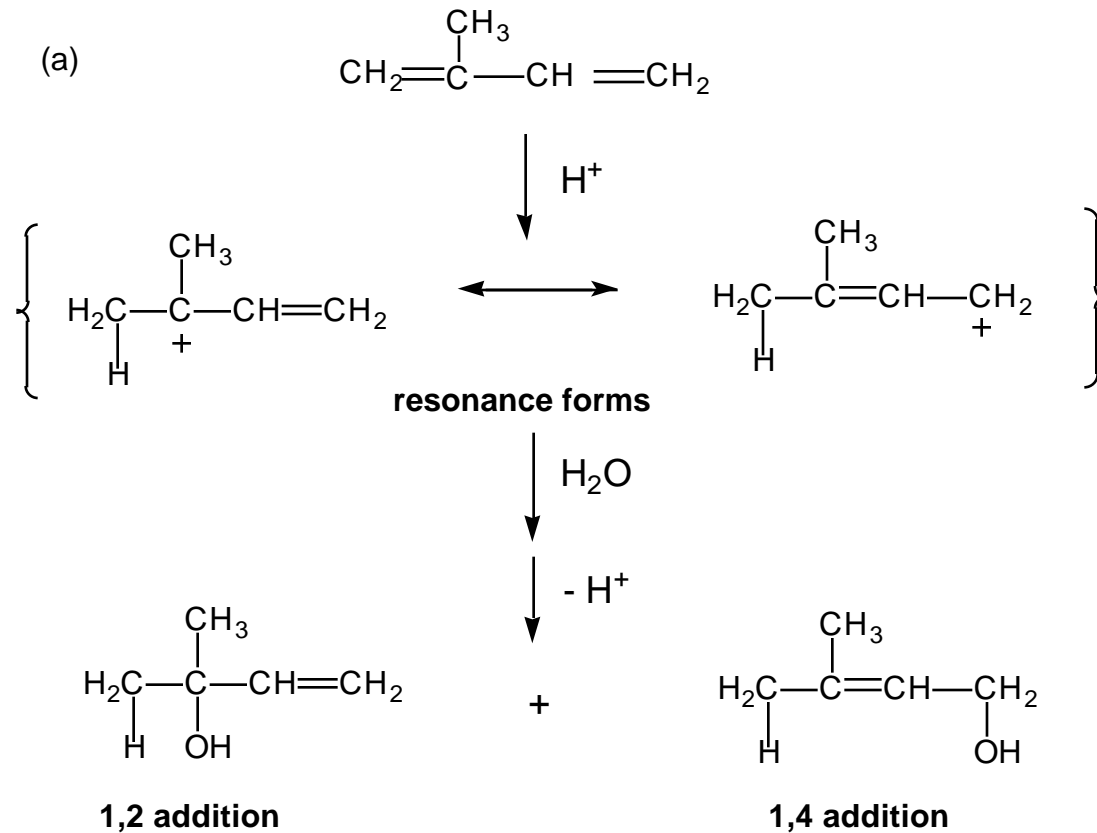
5.31 Reaction of Alkenes with Potassium Permanganate

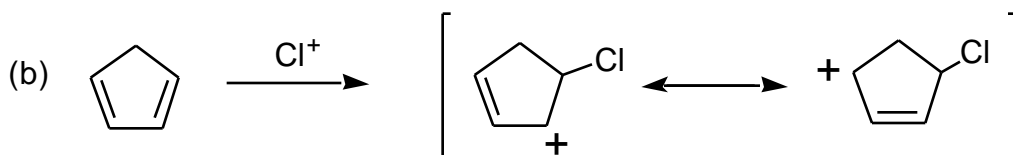


5.32 Hydration of Alkynes: Section 5.2D

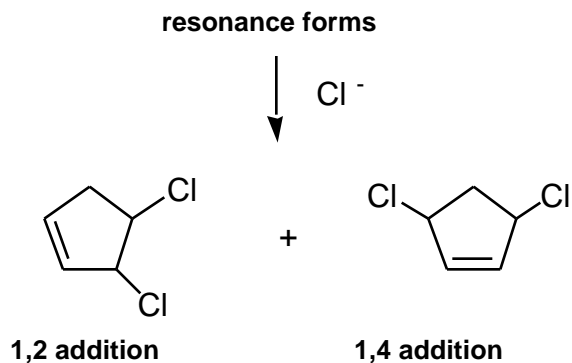


5.33 Electrophilic Addition to Conjugated Dienes: Section 5.4

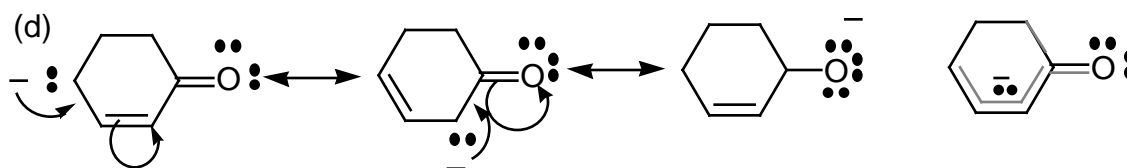
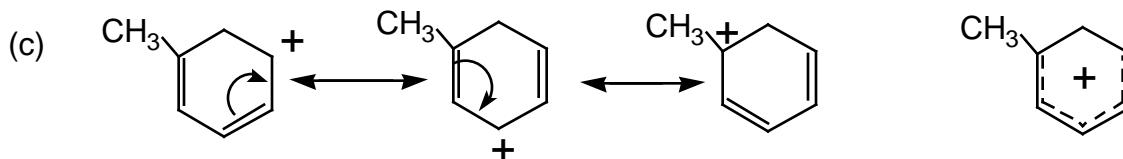
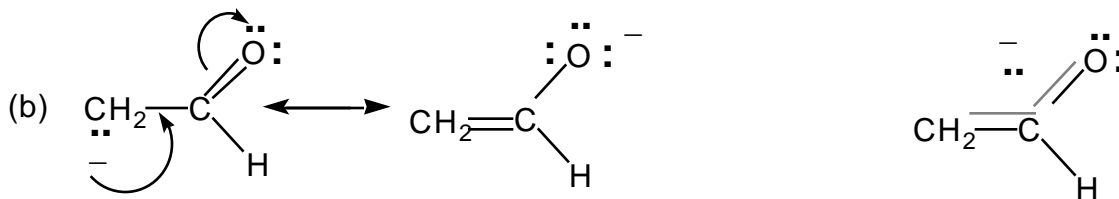
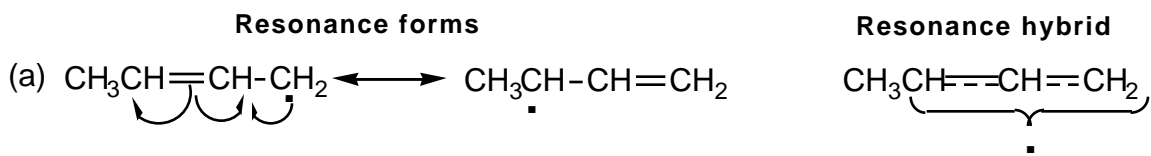




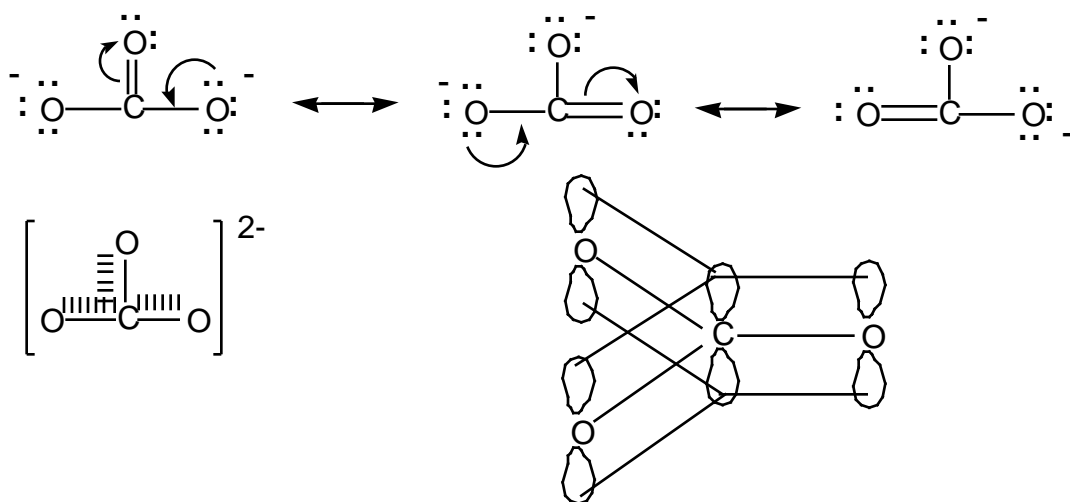
The electrophile attacks one of the double bonds to form an allylic carbocation that is described by two resonance forms. Neutralization forms two products.



5.34 Resonance Forms and Resonance Hybrids: Section 5.5



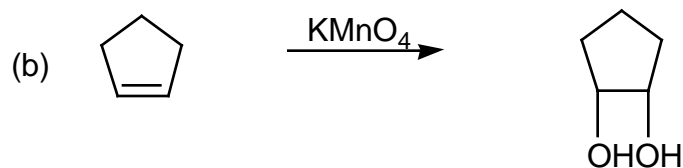
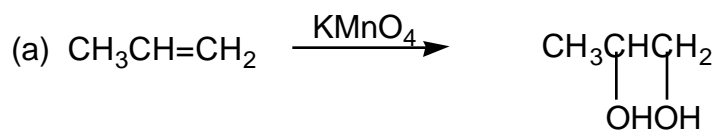
5.35 Resonance Forms and Resonance Hybrids: Section 5.5



5.36 Addition Polymers: Section 5.3

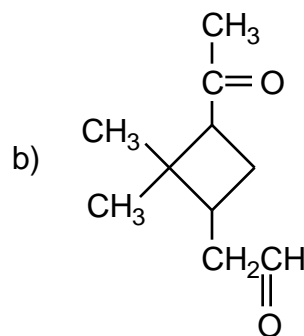
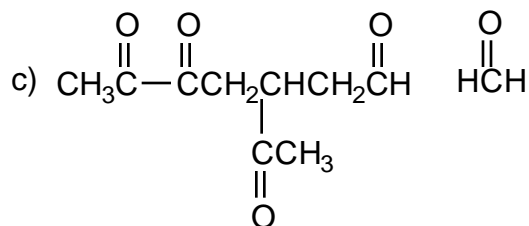
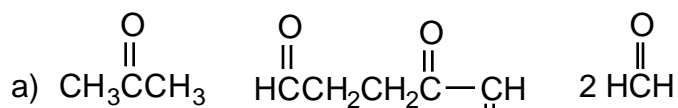


5.37 Oxidation of Alkenes: Section 5.7A



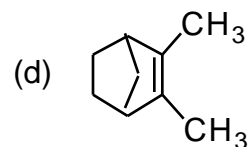
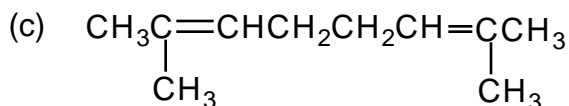
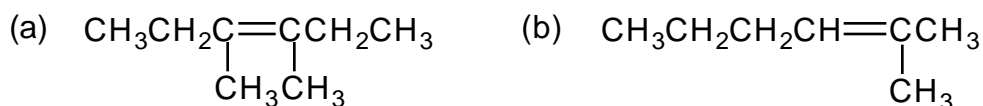
5.38 Ozonolysis: Section 5.7B

Each place there is a carbon-carbon double bond it cleaves and each carbon becomes a carbon-oxygen double bond.

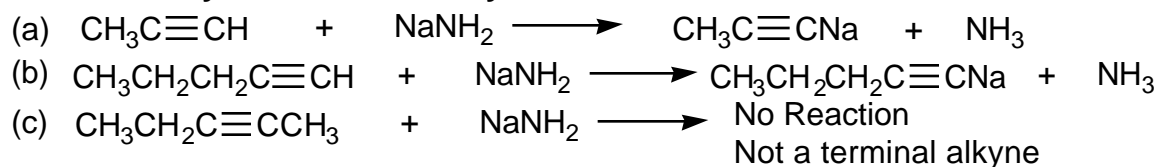


5.39 Ozonolysis: Section 5.7B

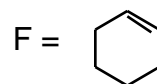
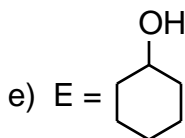
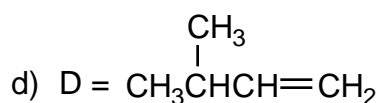
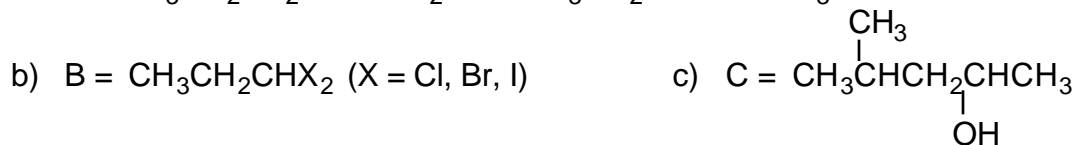
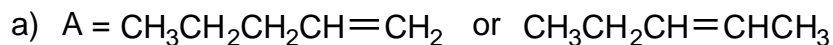
Since all of the examples are hydrocarbons, each place you see a carbon-oxygen double bond, you are looking at a carbon that originally was involved in a carbon-carbon double bond.

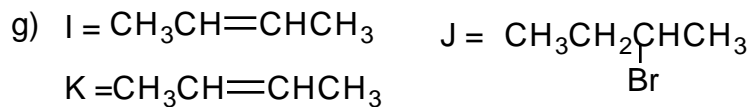
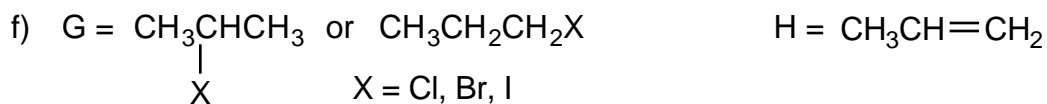


5.40 Acidity of Terminal Alkynes: Section 5.8

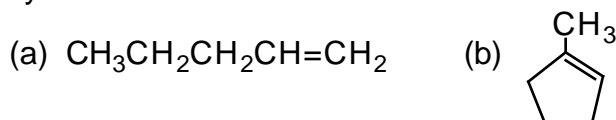
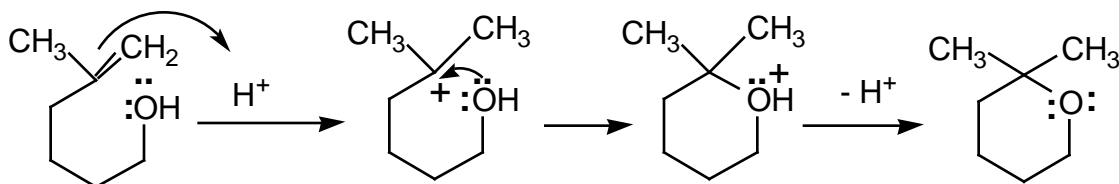


5.41 Synthesis: Sections 4.5, 5.1, 5.2

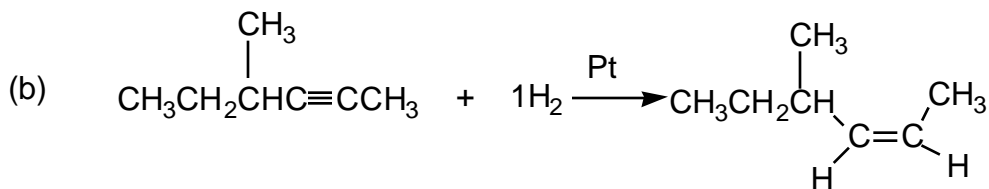
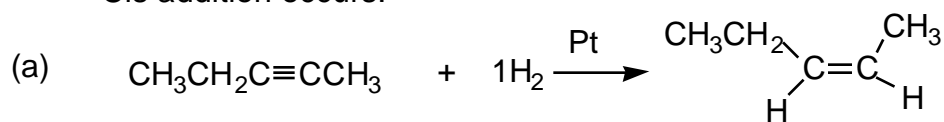
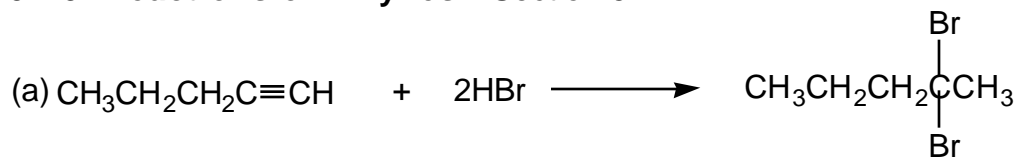


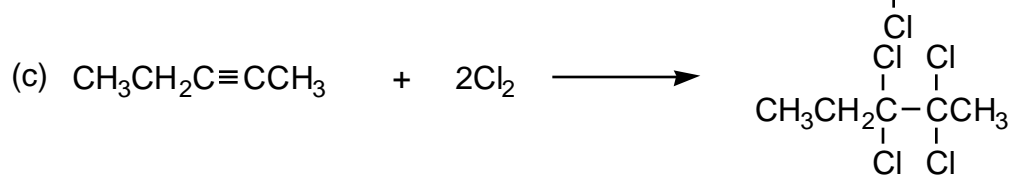
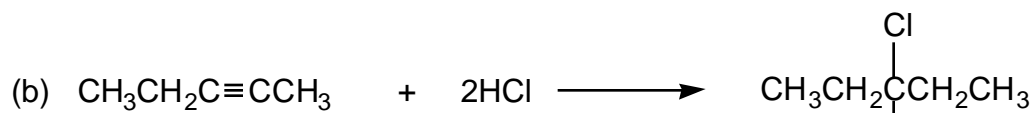
**5.42 Hydration:** Section 5.1

Pay attention to orientation of addition as explained in Section 5.1C.

**5.43 Reaction Mechanism:** Section 5.1**5.44 Hydrogenation:** Section 5.2B

Cis addition occurs.

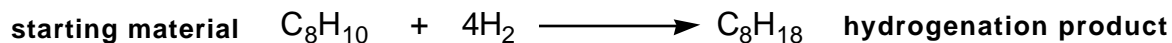
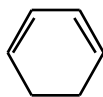
**5.45 Reactions of Alkynes:** Section 5.2

**5.46 Units of Unsaturation:** Sections 3.6, 5.1A.2, 5.2A

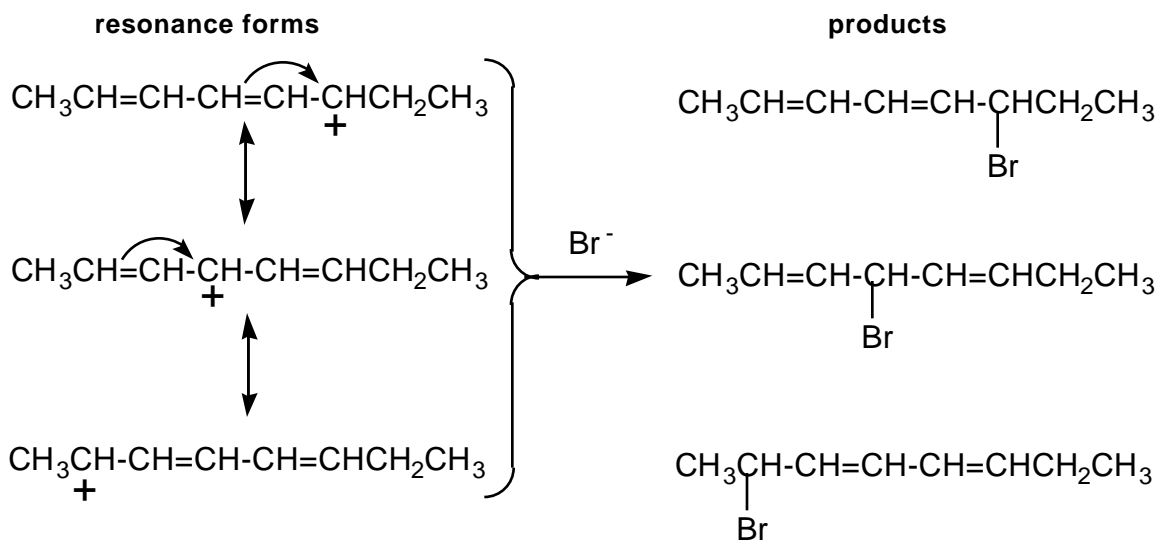
1-Buten-3-yne has one triple bond and one double bond. This represents three units of unsaturation. One mole of the compound will add three moles of bromine, one mole to the double bond and two to the triple bond.

5.47 Units of Unsaturation: Sections 3.6, 5.1A.4, 5.2A-B

Since the compound is non-cyclic all the units of unsaturation must be in the form of carbon-carbon double bonds or triple bonds. Four mole-equivalents of hydrogen are consumed so there must be four units of unsaturation: four double bonds, two triple bonds, or one triple and two double bonds.

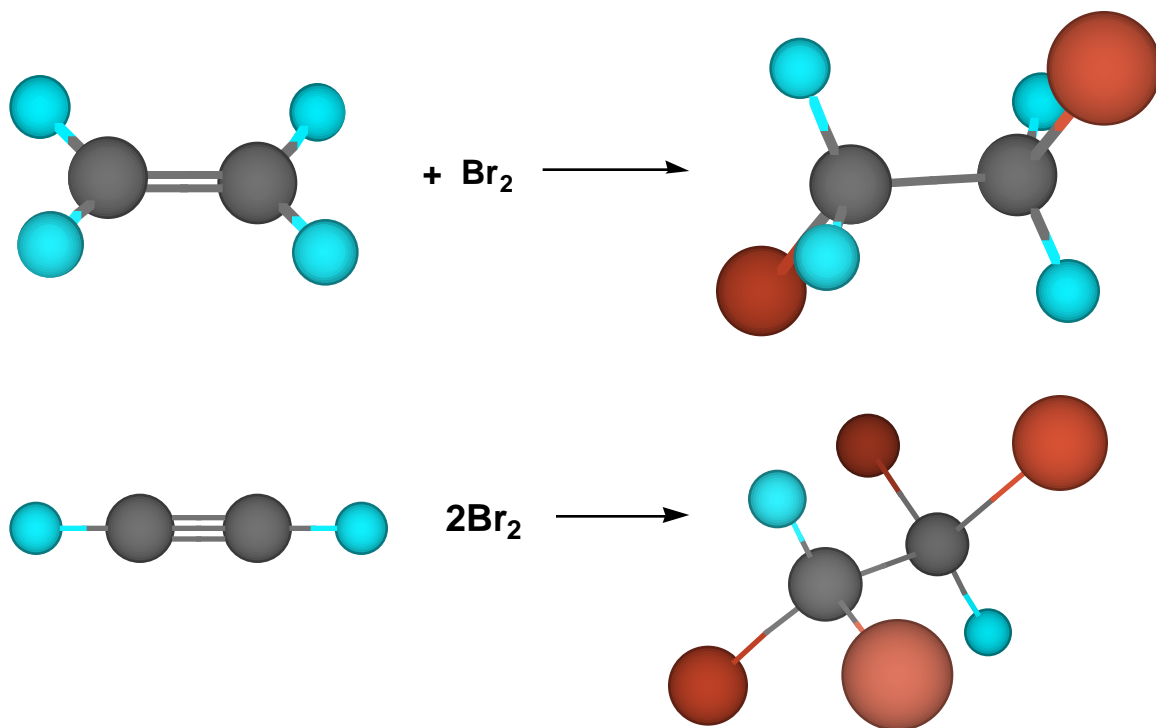
**5.48 1,4 Addition:** Section 5.4**5.49 Allylic Carbocations:** Section 5.4-5.5

The three resonance forms show where this resonance stabilized carbocation can be neutralized.

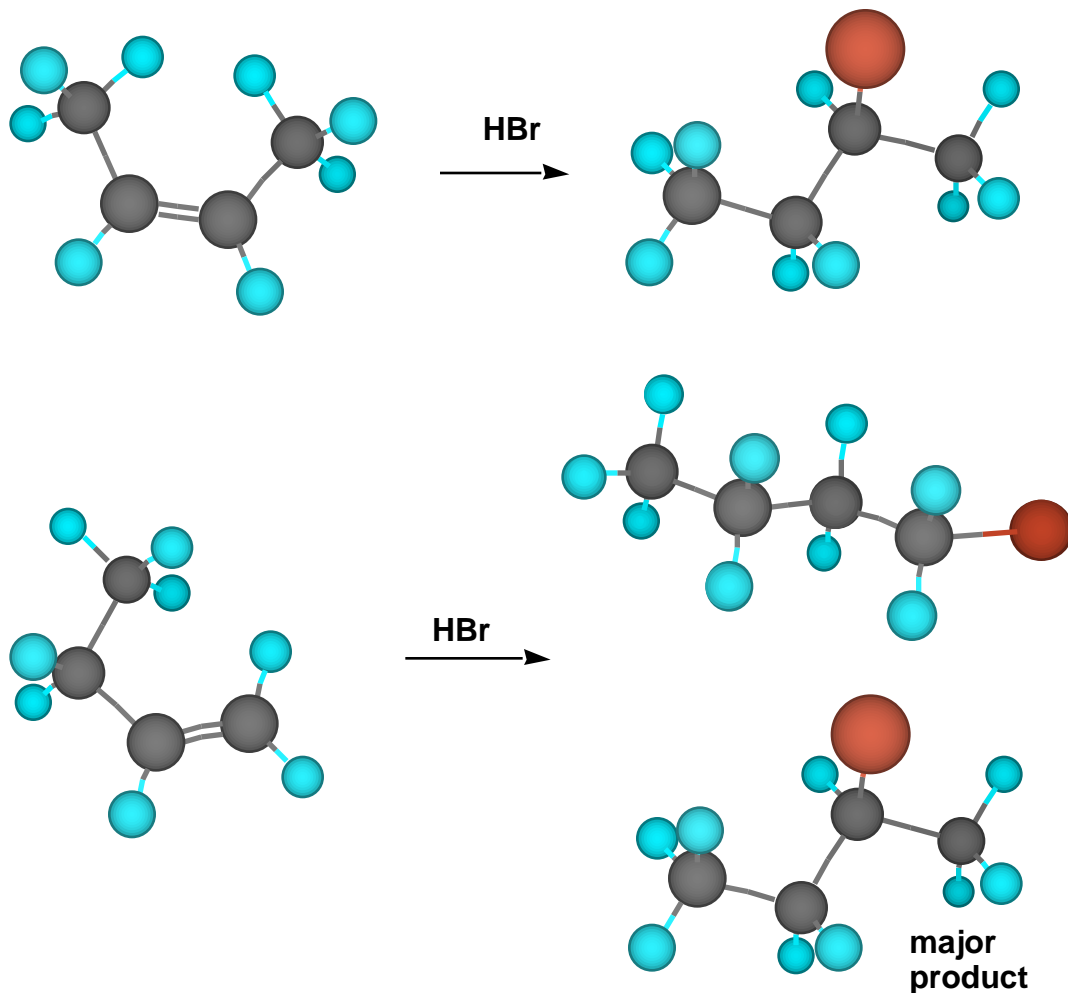


ACTIVITIES WITH MOLECULAR MODELS

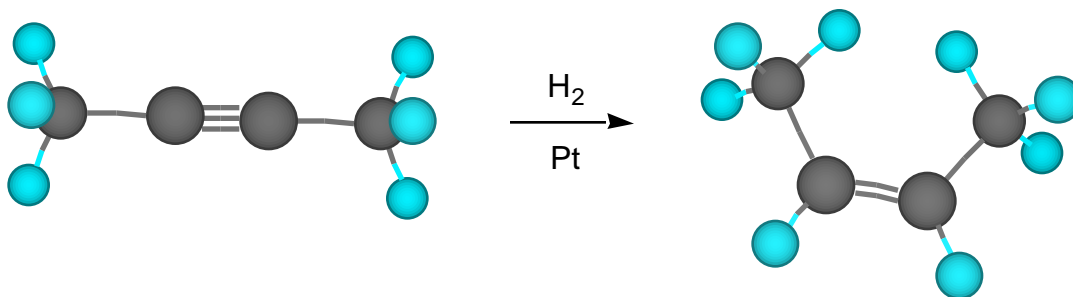
1. Make molecular models of ethene and ethyne. Now convert these to the products formed when bromine (Br_2) adds to the double bonds and triple bonds to form single bonds. How many bromines are needed to convert a double bond to a single bond and a triple bond to a single bond? How many bromines are in your products and to which carbons did they add?



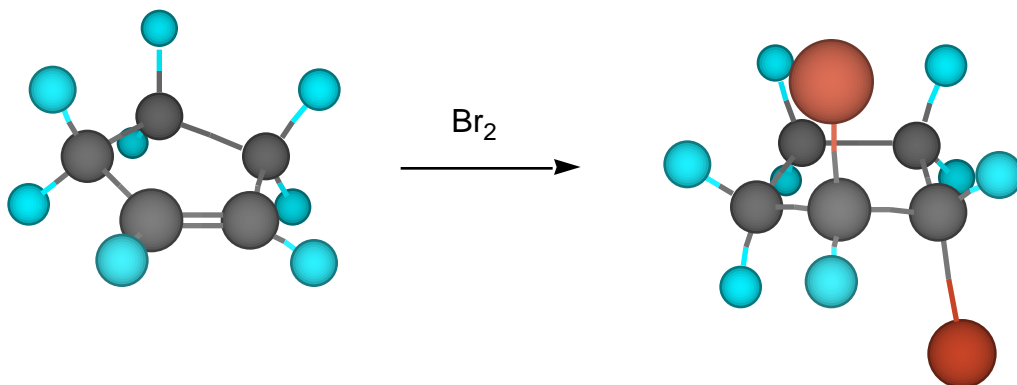
2. Make molecular models of 1-butene and 2-butene (cis or trans). Make models of the one product formed from the addition of HBr to 2-butene and the two products formed from 1-butene. Why is there a difference in the number of addition products. Which product predominates in the addition to 1-butene?



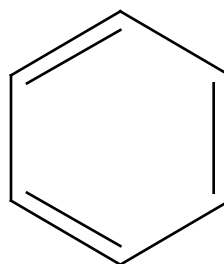
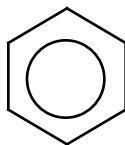
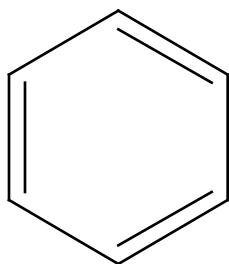
3. Make a model of 2-butyne and the product of cis addition of hydrogen.



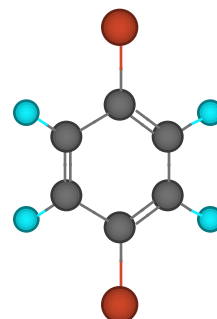
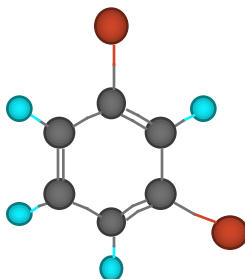
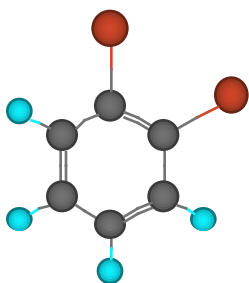
4. Make a model of cyclopentene and the product of trans addition of bromine.



6



Aromatic Compounds



CHAPTER SUMMARY

6.1 Introduction to Aromatic Compounds

Aromatic compounds are compounds that are similar to **benzene** in structure and chemical behavior. Benzene, C_6H_6 , is a cyclic compound commonly written as a hexagon with alternating double and single bonds.

6.2 Benzene: Structure and Bonding

A. Unusual Characteristics of Benzene

Benzene has two unusual features that are not necessarily apparent using classical molecular structures. First, it has an **unexpected stability**. This is evident in that benzene characteristically undergoes substitution reactions, in which the integrity of the benzene ring is maintained, rather than addition reactions that are characteristic of highly unsaturated compounds with double bonds. Even when addition reactions occur, as in the hydrogenation of benzene, the heat of reaction is significantly less than would be expected from hydrogenation of three carbon-carbon double bonds. The difference is known as the **resonance energy**.

Secondly, the carbon-carbon bond lengths are not as they appear in classical structures, three single and three double bonds; instead the bonds are all equal in length and intermediate between double and single bonds.

B. Bonding in Benzene

Benzene actually is a **resonance hybrid** of the two **resonance forms** written with alternating double and single bonds. The resonance hybrid is an average of the two and is often written with a circle inside the hexagon to denote bond lengths intermediate between double and single bonds. Each carbon in the benzene ring has a p-orbital. These parallel p-orbitals overlap continuously making all the carbon-carbon bonds identical.

C. Structure of Benzene - A Summary

Benzene is a flat six membered ring with the formula C_6H_6 . All six carbons are equivalent, all six hydrogens are equivalent, and all the carbon-carbon bonds are equivalent and intermediate in length between a single bond and double bond. Each carbon is trigonal, sp^2 -hybridized, and has 120° bond angles. There is a p-orbital on each carbon and the six overlap continuously around the ring.

CONNECTIONS 6.1 Cancer and Carcinogens

6.3 Nomenclature of Aromatic Systems

A. Aromatic Hydrocarbon Ring Systems

Naphthalene, anthracene, and phenanthrene are simple fused ring aromatic systems.

B. Monosubstituted Benzenes

Monosubstituted benzenes are named as derivatives of benzene or by common names such as **toluene, benzaldehyde, benzoic acid, benzenesulfonic acid, phenol, and aniline.**

C. Disubstituted Benzenes

Disubstituted benzenes can be named using **ortho** (1,2), **meta** (1,3), and **para** (1,4) designations; either the numbers or o, m, p are acceptable.

D. Polysubstituted Benzenes

When more than two groups are on a benzene ring, their positions must be numbered. If one of the groups is associated with a common name, the compound can be named as a derivative of the monosubstituted compound, numbering from the group designated in the common name.

E. Substituted Anilines

Substituents on the nitrogen of aniline are located by capital **N**.

F. Aromatic Compounds Designated by a Prefix

The prefix for benzene is **phenyl**. Benzene with a CH_2 group is **benzyl**.

CONNECTION 6.2 Gasoline

6.4 Electrophilic Aromatic Substitution

Because of its exceptional stability, benzene is resistant to chemical change and has substitution as its characteristic reaction. The special

electronic character of the system is preserved in substitution reactions whereas it would be destroyed with addition reactions. Because of its electron-rich pi electron system, benzene attracts electron-deficient species, electrophiles, that eventually replace a hydrogen on the ring.

A. Electrophilic Aromatic Substitution: The Reaction

The characteristic reaction of benzene and its derivatives is **electrophilic aromatic substitution**. In these reactions, a hydrogen on the benzene ring is replaced by a chlorine (**chlorination**), a bromine (**bromination**), an alkyl or acyl group (**Friedel-Crafts alkylation or acylation**), a nitro group (**nitration**), or a sulfonic acid group (**sulfonation**).

B. Electrophilic Aromatic Substitution: The Mechanism

Electrophilic aromatic substitution is a three-step process. First, a positive electrophile is generated. This is followed by two-step substitution. In the first step, the positive electrophile bonds to the benzene ring and produces a resonance stabilized carbocation. Then hydrogen ion is lost from the ring as the carbocation is neutralized and the benzene ring is regenerated.

C. Orientation of Substitution

Groups already present on a benzene ring direct the orientation of substitution of incoming groups. **Electron-donating groups** (hydroxy, alkoxy, amino, halogens and alkyl groups stabilize the intermediate carbocation and direct the incoming electrophile to the **ortho and para positions**; these groups are called **ortho, para directors**. **Electron-withdrawing groups** (carboxylic acid, aldehyde, ketone, cyano, nitro, and sulfonic acid) destabilize the carbocation and the incoming electrophile is directed to the **meta position**; these groups are called **meta directors**.

D. Activating and Deactivating Groups

Electron-donating groups increase the negative character of the ring and its attractiveness to electrophiles. As a result they increase reactivity and are called **activating groups**. Electron-withdrawing groups decrease

the negative character of the ring and are **deactivating groups**. The directing and activating or deactivating effects of substituents must be taken into account in devising synthesis schemes.

6.5 Oxidation of Alkylbenzenes

Alkyl side chains on benzene can be **oxidized** to **carboxylic acids** using potassium permanganate.

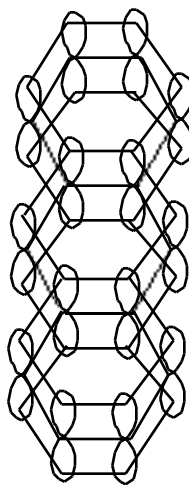
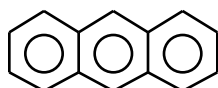
CONNECTIONS 6.3 Herbicides

SOLUTIONS TO PROBLEMS

6.1 Molecular Formulas of Aromatic Compounds

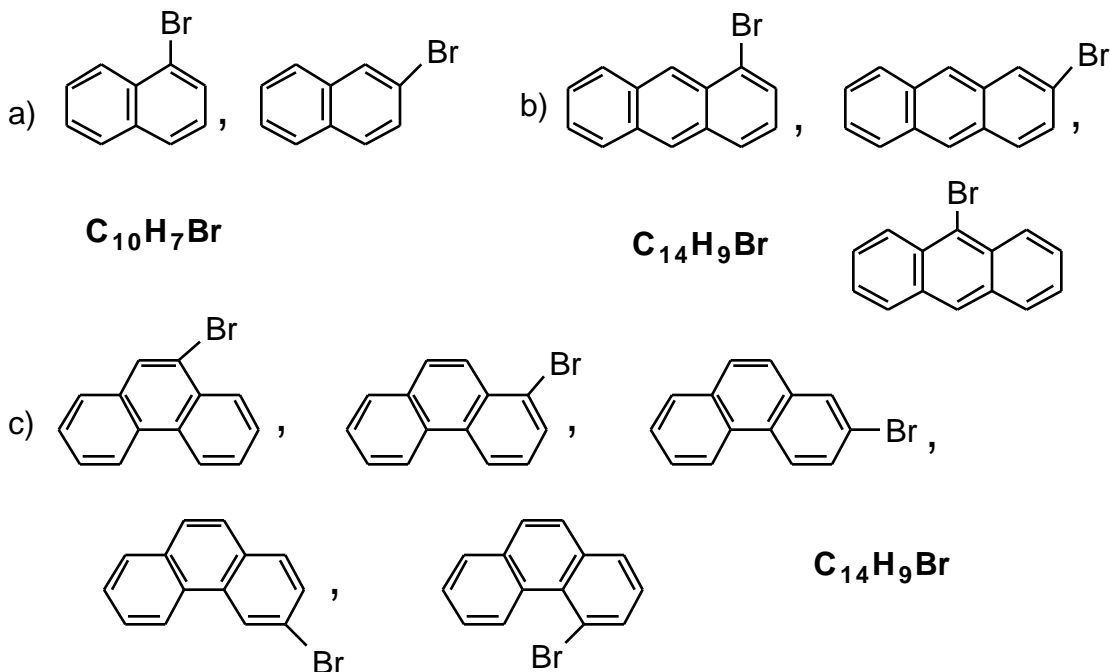
(a) C_6H_5Br ; (b) $C_{10}H_8$; (c) $C_{14}H_{10}$.

6.2 Bonding in Aromatic Compounds



6.3 Positional Isomers

Look very carefully. These compounds are very symmetrical and there are some carbons that do not have a hydrogen to replace.



6.4 Nomenclature of Monosubstituted Benzenes

(a) bromobenzene; (b) isopropylbenzene; (c) butylbenzene; (d) iodobenzene

6.5 Nomenclature of Disubstituted Benzenes

(a) m-ethylbenzaldehyde; (b) p-dibromobenzene;
 (c) o-chlorobenzenesulfonic acid; (d) m-nitroaniline

6.6 Nomenclature of Polysubstituted Benzenes

(a) 1-chloro-3-isopropyl-5-nitrobenzene; (b) 2,4-dibromobenzoic acid;
 (c) 2,3,4,5,6-pentachlorophenol; (d) 5-bromo-2-chloroaniline

6.7 Nomenclature of Substituted Anilines

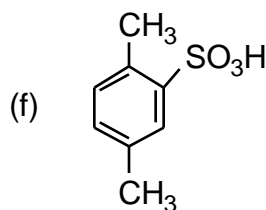
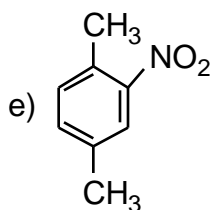
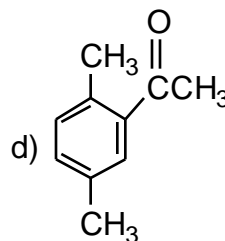
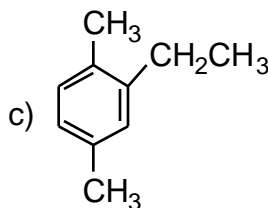
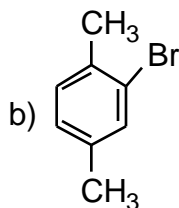
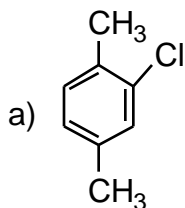
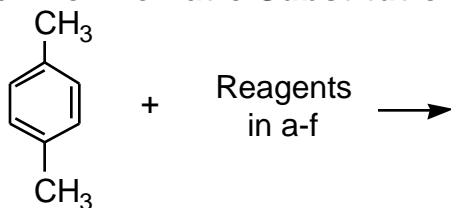
(a) N-butylaniline; (b) N-ethyl, N-methyl, para propylaniline;
 (c) 5-bromo-2-chloro-N,N-dimethylaniline

6.8 Nomenclature Using Prefixes for Aromatic Groups

(a) 4-methyl-2-phenylhexane; (b) 1,4-diphenyl-2-butyne;
 (c) p benzylbenzoic acid

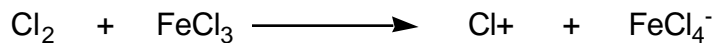
6.9 Electrophilic Aromatic Substitution

p-xylene

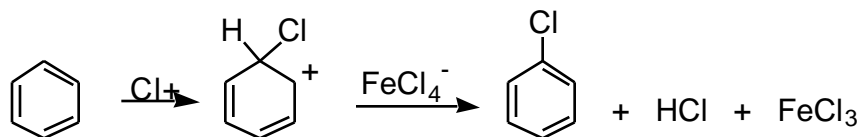


6.10 Electrophilic Aromatic Substitution - Chlorination

Generation of the Electrophile

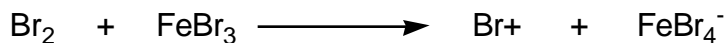


Two-Step Substitution

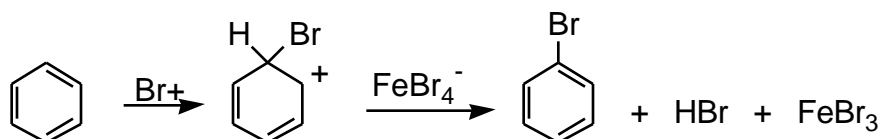


6.11 Electrophilic Aromatic Substitution - Bromination

Generation of the Electrophile



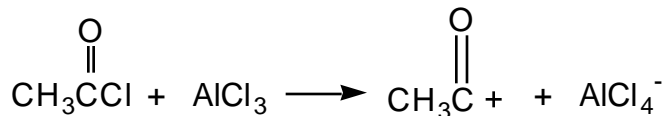
Two-Step Substitution



6.12 Electrophilic Aromatic Substitution - Alkylation and Acylation

(a) Acylation

Generation
of the
Electrophile

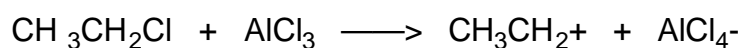


Two-step
Substitution

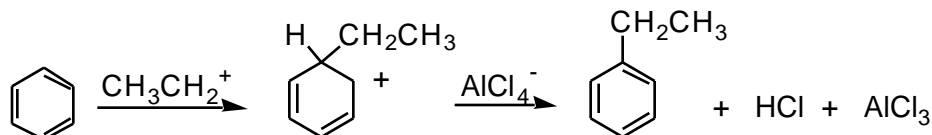


(b) Alkylation

Generation
of the
Electrophile

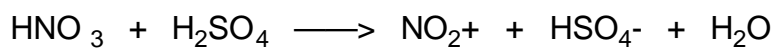


Two-step
Substitution

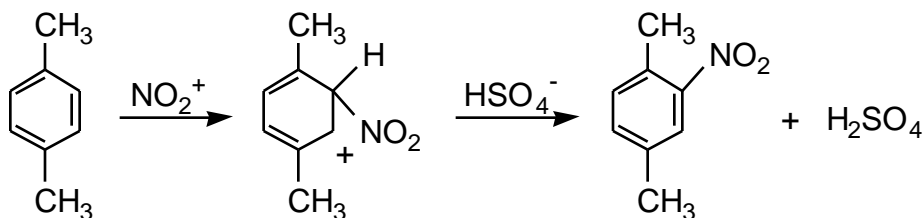


6.13 Electrophilic Aromatic Substitution - Nitration

Generation
of the
Electrophile

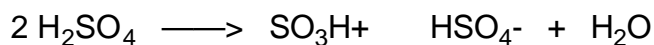


Two-step
Substitution

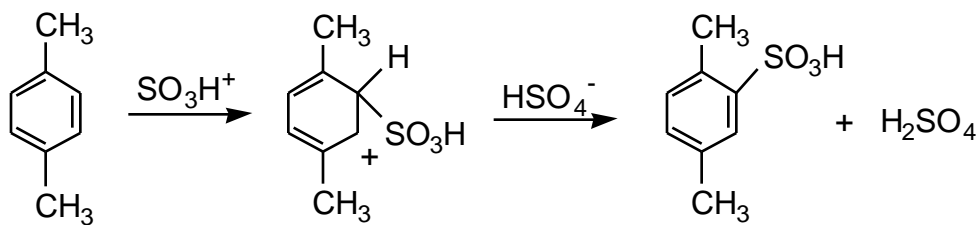


6.14 Electrophilic Aromatic Substitution - Sulfonation

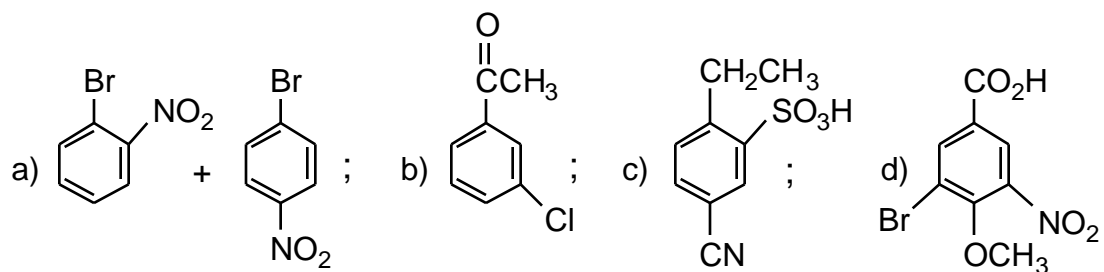
Generation
of the
Electrophile



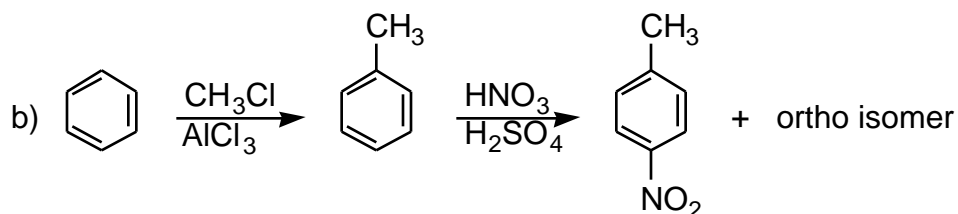
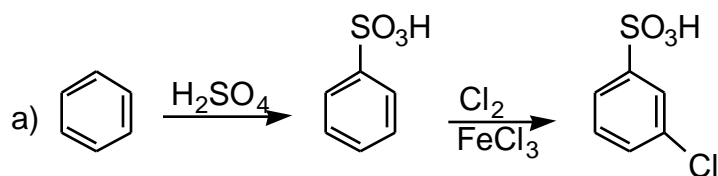
Two-step
Substitution



6.15 Electrophilic Aromatic Substitution Reactions



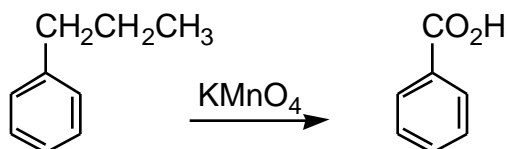
6.16 Synthesis Problems

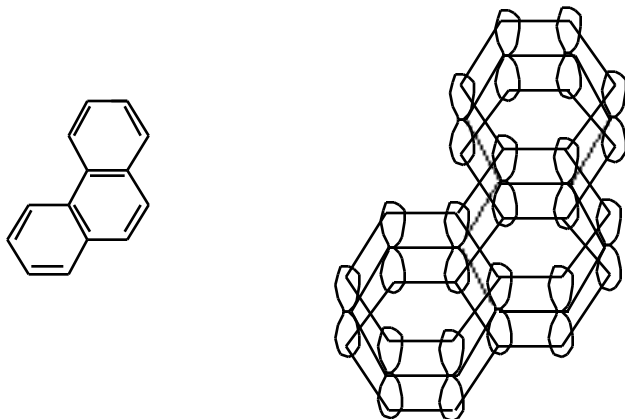


6.17 Activating and Deactivating Groups

- (a) methoxybenzene > benzene > chlorobenzene
 (b) phenol > p-nitrophenol > nitrobenzene
 (c) p-methylaniline > toluene > m-chlorotoluene

6.18 Oxidation of Alkylbenzenes



6.19 Bonding Pictures: Section 6.2B**6.20 Molecular Formulas:** Section 6.2

- (a) $C_{16}H_{10}$ (b) $C_{20}H_{12}$

6.21 Nomenclature of Mono and Disubstituted Benzenes:

Section 6.3B-C

- (a) fluorobenzene; (b) hexylbenzene; (c) t-butylbenzene;
 (d) o-dichlorobenzene; (e) m-dibromobenzene; (f) p-bromochlorobenzene;
 (g) m-iodobenzoic acid; (h) o-difluorobenzene (i) p-ethylbenzaldehyde;
 (j) o-nitrophenol;

6.22 Nomenclature of Polysubstituted Benzenes: Section 6.3D

- (a) 2,4-dichlorotoluene; (b) 3-bromo-5-methylaniline;
 (c) 2-ethyl-5-methylbenzenesulfonic acid; (d) 2,4,6-tribromophenol;
 (o) 3-bromo-2-chloro-5-nitroethylbenzene; (p) 1,3,5-trinitrobenzene

6.23 Nomenclature of Substituted Anilines: Section 6.3E

- (a) m-ethylaniline; (b) N-ethylaniline;
 (c) m-nitro-N,N-diethylaniline; (d) 3,5-dichloro-N-ethyl-N-methylaniline

6.24 Nomenclature Using Benzene as a Prefix: Section 6.3F

- (a) 2,4-dimethyl-2-phenylpentane; (b) p-benzylbenzaldehyde;
 (c) 5-ethyl-2-phenyl-2-heptene

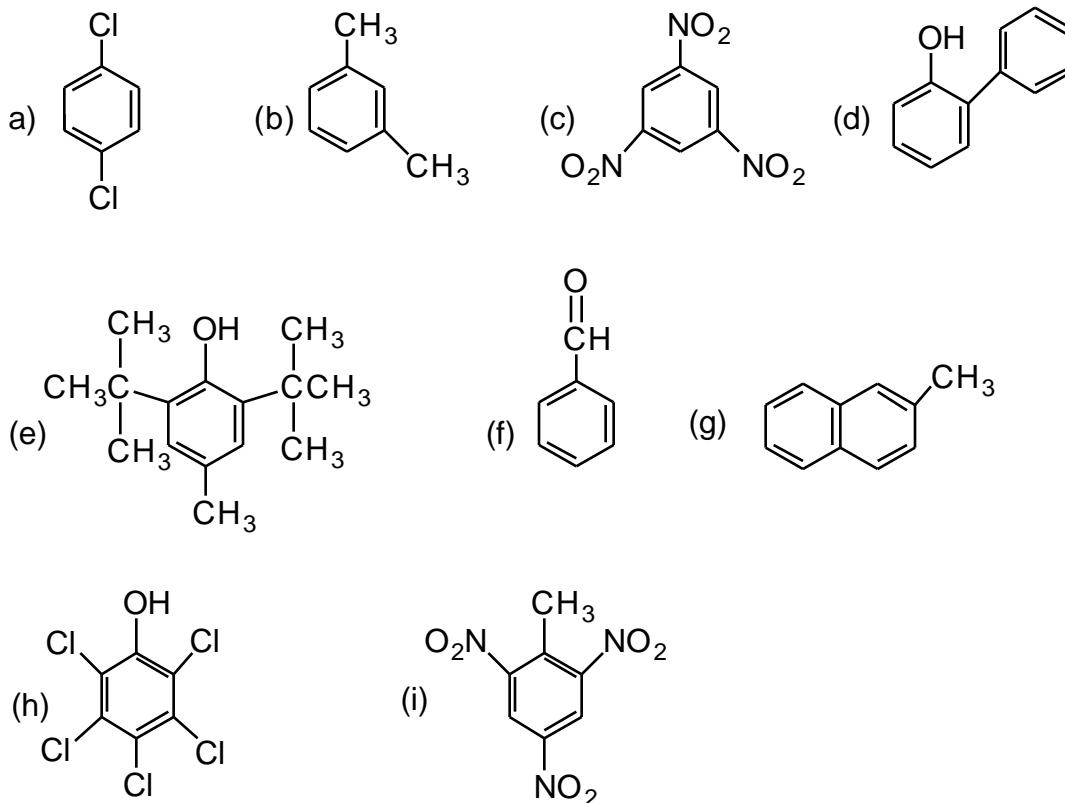
6.25 Nomenclature of Polynuclear Aromatic Compounds:

Section 6.3A

- (a) 1-bromo-5-fluoronaphthalene; (b) 1,4-dinitronaphthalene;

(c) 9-methylantracene; (d) 9-ethylphenanthrene

6.26 Nomenclature: Section 6.3

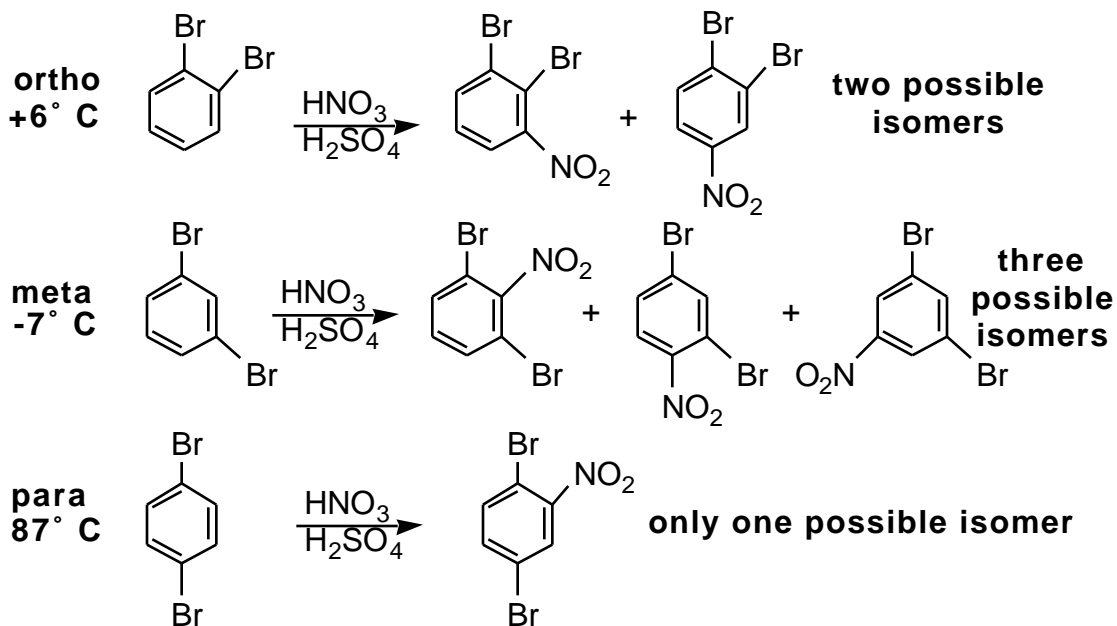


6.27 Positional Isomers: Section 6.3A

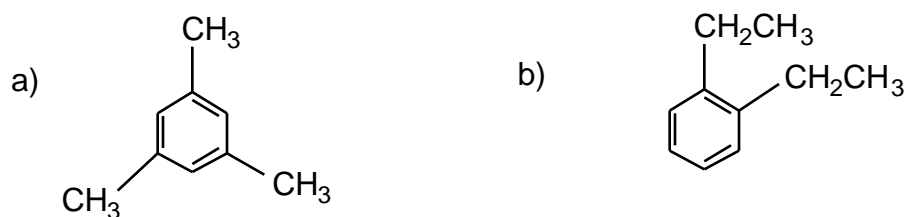
(a) 1,2,3-tribromobenzene; 1,2,4-tribromobenzene; 1,3,5-tribromobenzene
 (b) 3-chloro-1,2-dibromobenzene; 1-chloro-2,4-dibromobenzene;
 2-chloro-1,4-dibromobenzene; 2-chloro-1,3-dibromobenzene;
 4-chloro-1,2-dibromobenzene; 5-chloro-1,3-dibromobenzene
 (c) 1-bromo-2-chloro-3-fluorobenzene; 1-bromo-2-chloro-4-fluorobenzene;
 2-bromo-1-chloro-4-fluorobenzene; 2-bromo-1-chloro-3-fluorobenzene;
 4-bromo-2-chloro-1-fluorobenzene; 1-bromo-3-chloro-5-fluorobenzene;
 2-bromo-4-chloro-1-fluorobenzene; 1-bromo-3-chloro-2-fluorobenzene;
 1-bromo-4-chloro-2-fluorobenzene; 4-bromo-1-chloro-2-fluorobenzene;
 (d) 1,2; 1,3; 1,4; 1,5; 1,6; 1,7; 1,8; 2,3; 2,6; and 2,7-dibromonaphthalenes
 (e) 1,2; 1,3; 1,4; 1,10; 1,5; 1,6; 1,7; 1,8; 1,9; 2,3; 2,10; 2,6; 2,7; 2,9; and
 9,10 dinitroanthracenes

(f) 1,2; 1,3; 1,4; 1,5; 1,6; 1,7; 1,8; 1,9; 1,10; 2,3; 2,4; 2,5; 2,6; 2,7; 2,9; 2,10; 3,4; 3,5; 3,6; 3,9; 3,10; 4,5; 4,9; 4,10; and 9,10 dinitrophenanthrenes

6.28 Positional Isomers: Section 6.3

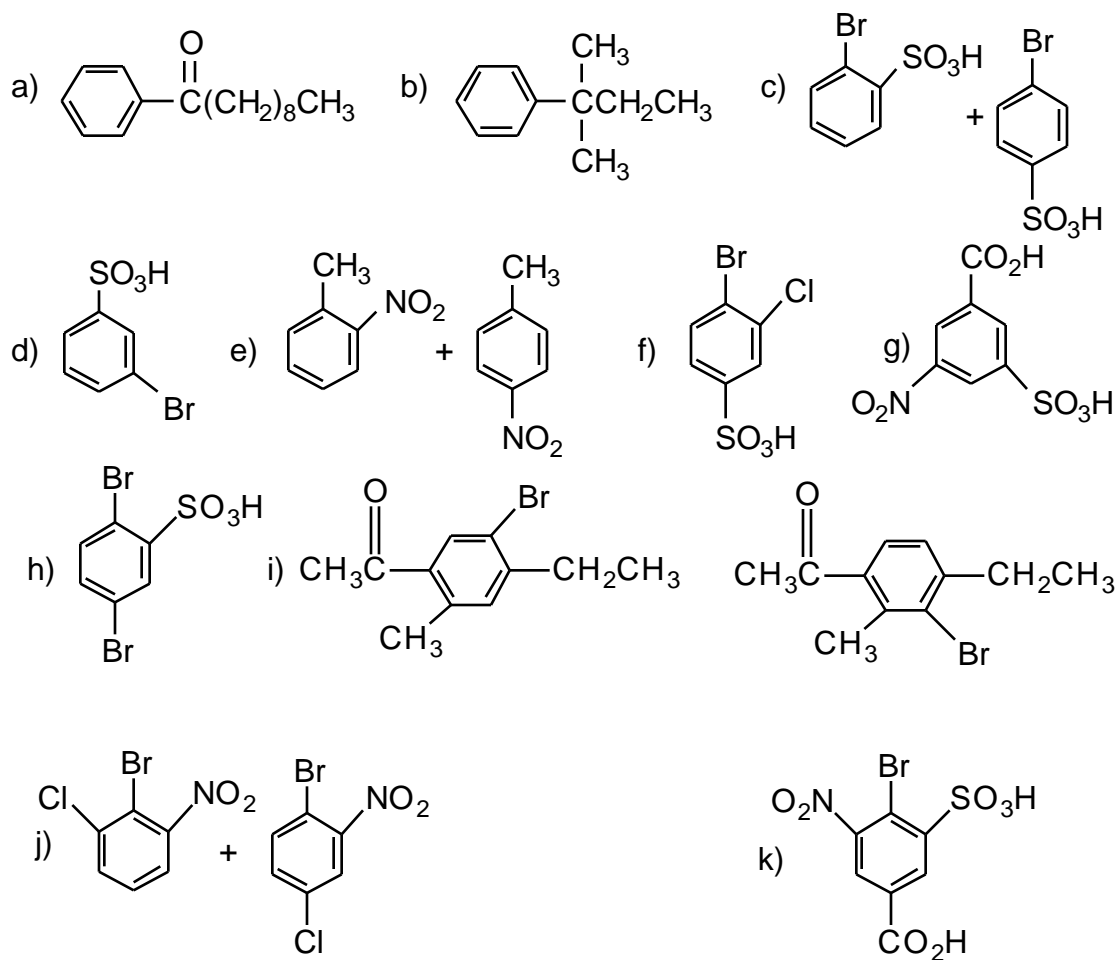


6.29 Positional Isomers: Section 6.3



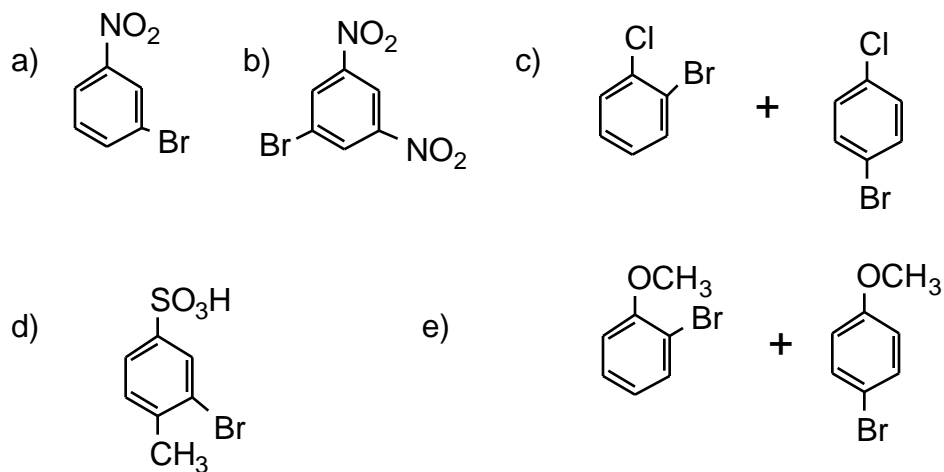
6.30 Reactions of Aromatic Compounds: Section 6.4

First look at the reagent and decide what is going to substitute for a hydrogen on the benzene ring - a halogen, alkyl, acyl, nitro, or sulfonic acid group. Then look at the groups on the ring and determine where they direct - ortho/ para or meta. Place the incoming group where it is directed by the existing groups. See Example 6.5 in the text.



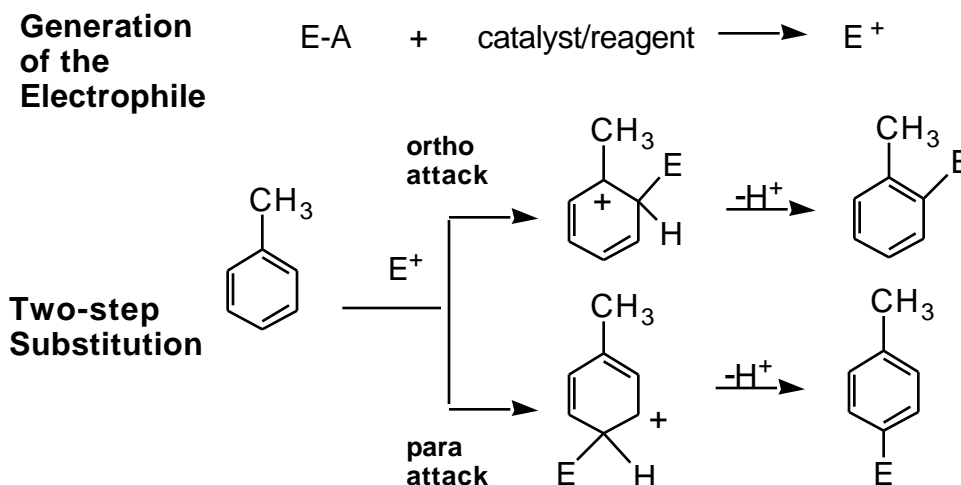
6.31 Reactions of Aromatic Compounds: Section 6.4

See explanation on problem 6.30.

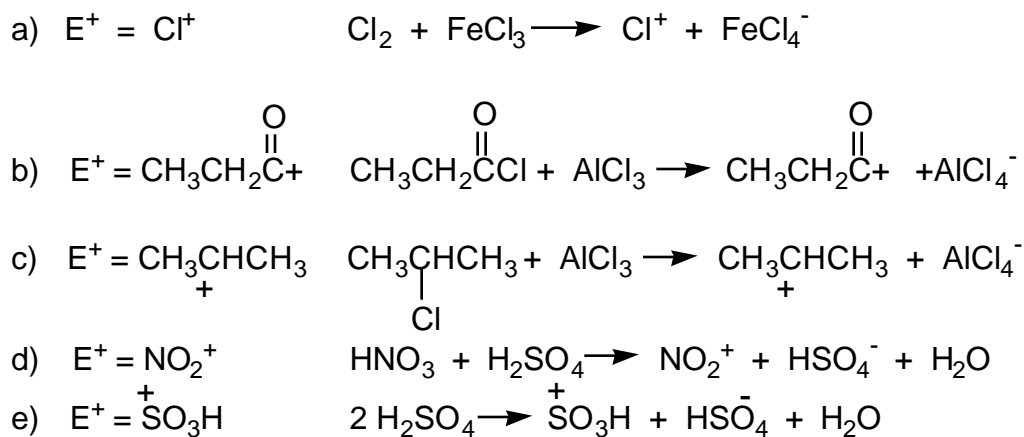


6.32 Reaction Mechanisms: Section 6.4B

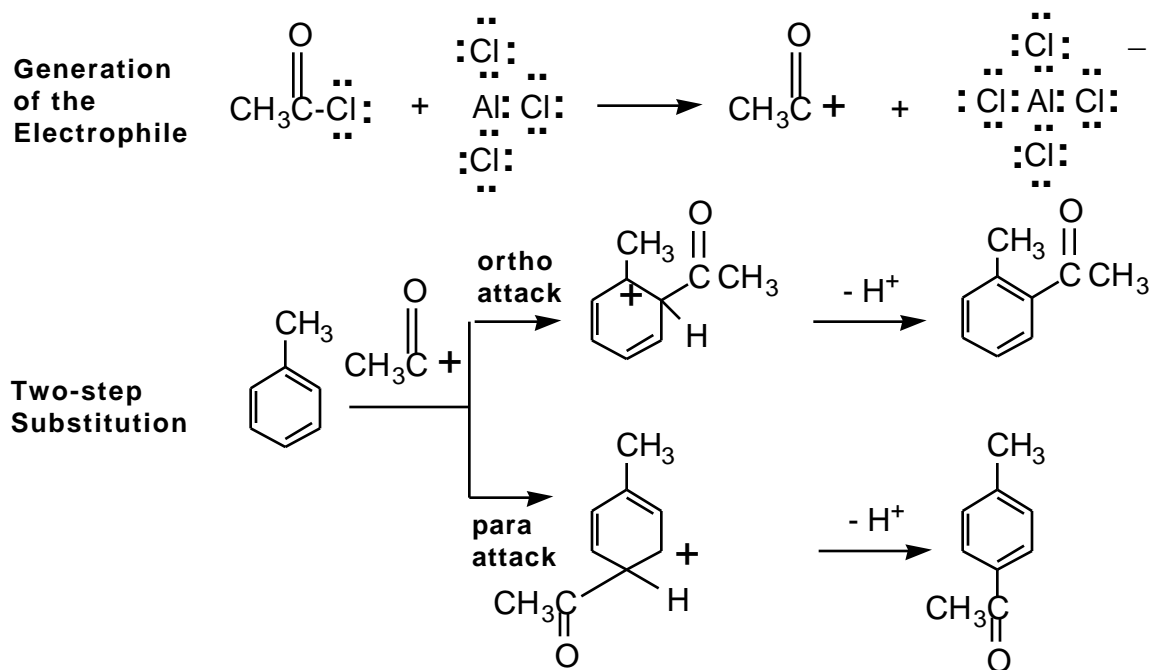
Following is the general mechanism for electrophilic aromatic substitution. First the electrophile is generated. Then two-step substitution occurs: the electrophile bonds to the ring forming a carbocation followed by elimination of a hydrogen ion to regenerate the benzene ring.



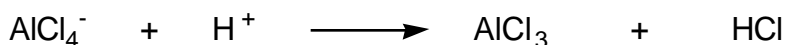
The mechanism is the same for all cases, only the electrophile differs. Following are the equations for generation of the electrophiles.



Below is a specific example using acylation, part (b).

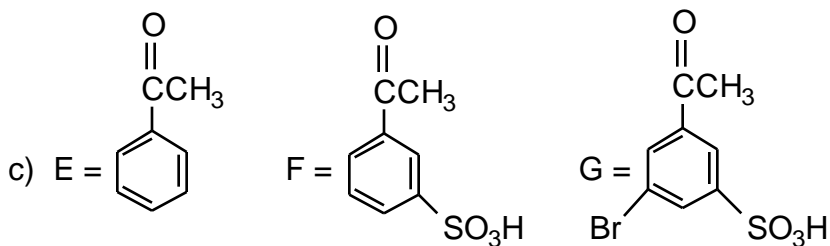
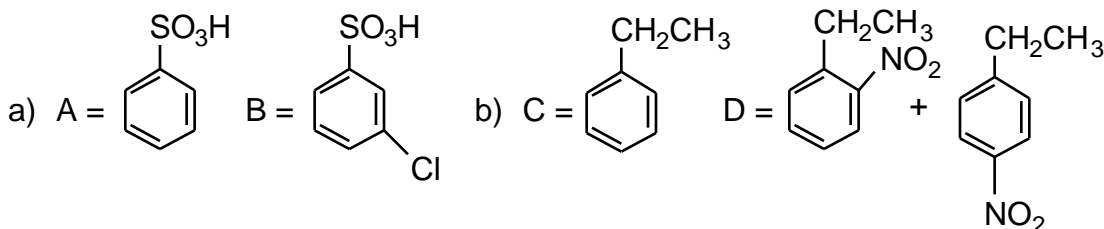


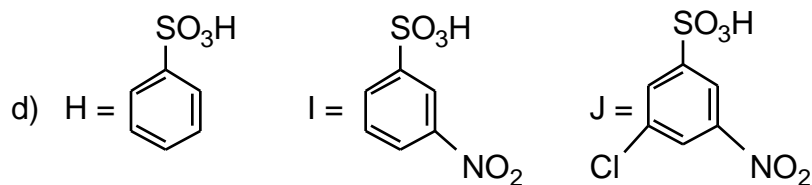
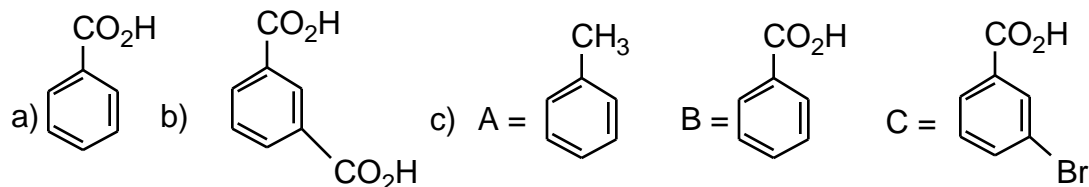
In this reaction, the catalyst is regenerated when hydrogen ion reacts with the aluminum tetrachloride anion.



6.33 Reactions of Aromatic Compounds: Section 6.4

To predict each product, first determine what group will be introduced on the benzene ring. If one or more groups are already on the ring, determine where they direct (o,p or m) and bond the incoming group accordingly.



**6.34 Oxidation of Alkylbenzenes:** Section 6.5**6.35 Synthesis:** Section 6.4 and 6.5

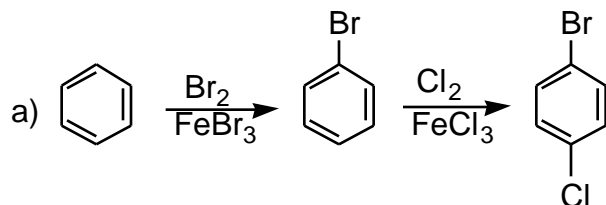
To make m-bromobenzoic acid from toluene one should first oxidize the methyl group to a carboxylic acid, which is a meta director, and then introduce the bromine. If the bromine is introduced first, it will go ortho and para since the methyl group is an ortho/para director.

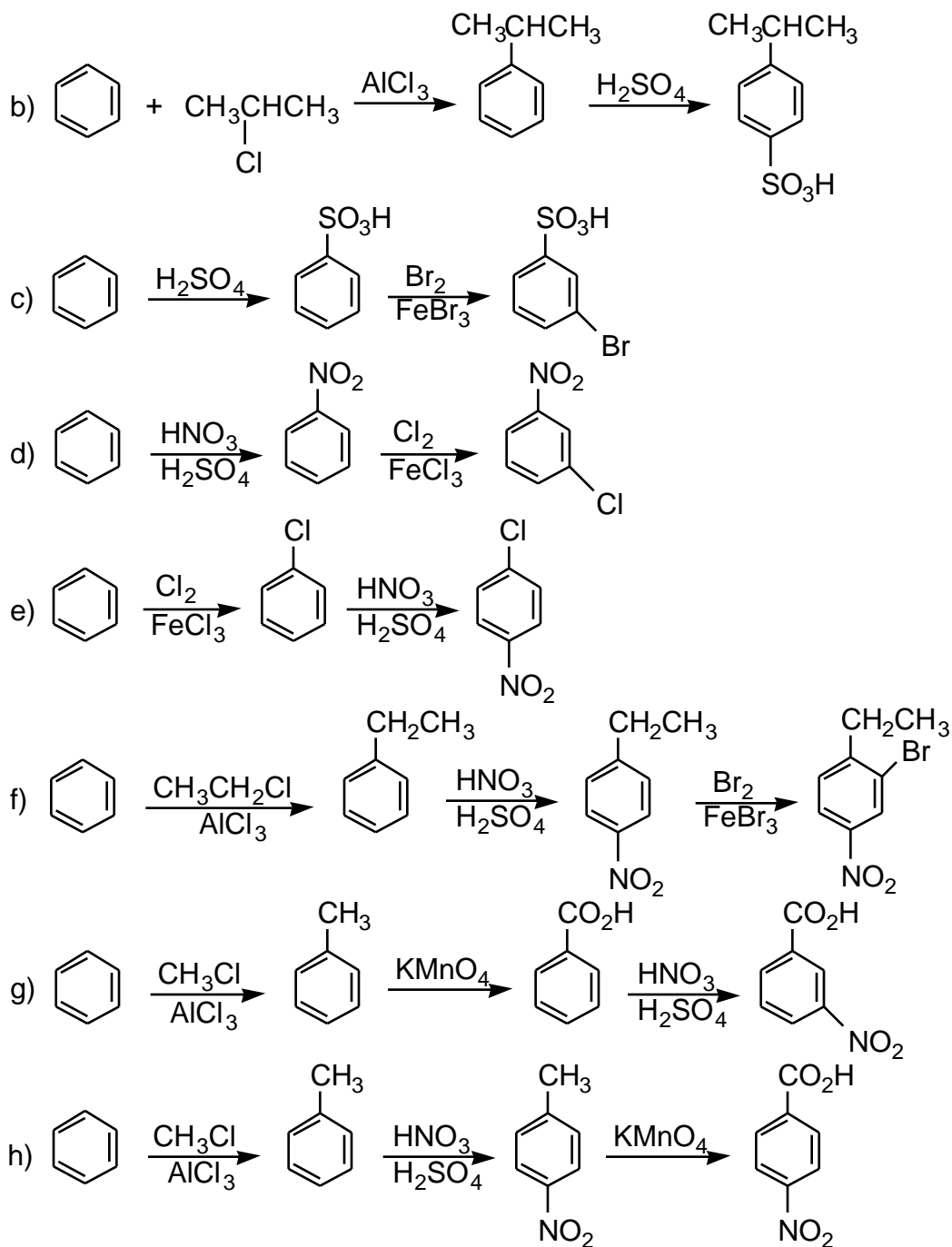
6.36 Synthesis: Section 6.4

The chlorine is an ortho/para director and the sulfonic acid group is a meta director. Since the desired product is p-chlorobenzenesulfonic acid, the chlorine should be introduced first so it can direct the sulfonic acid group para.

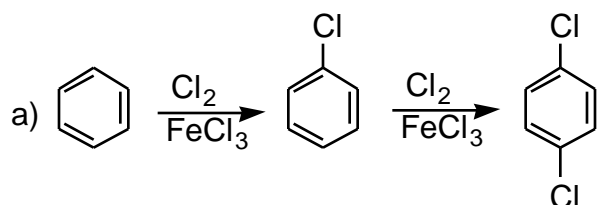
6.37 Synthesis: Sections 6.4-6.5

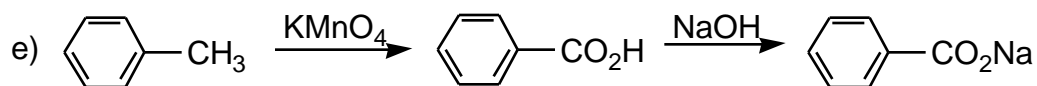
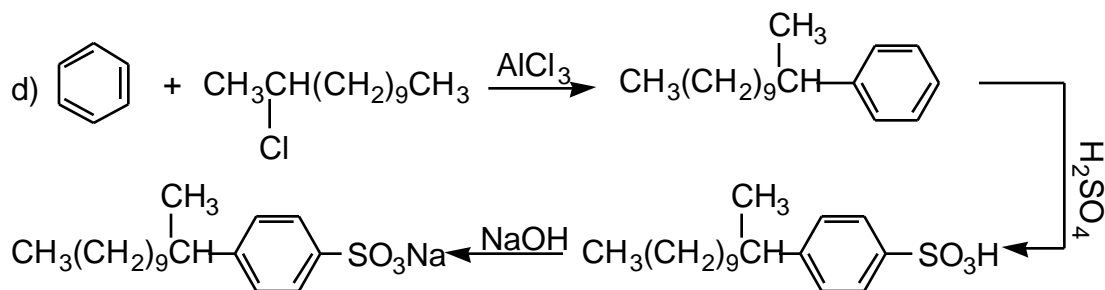
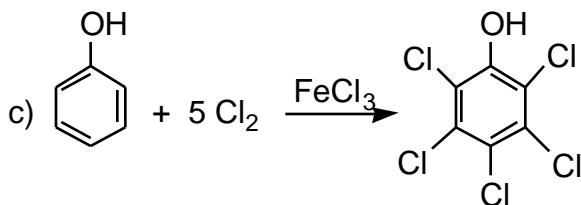
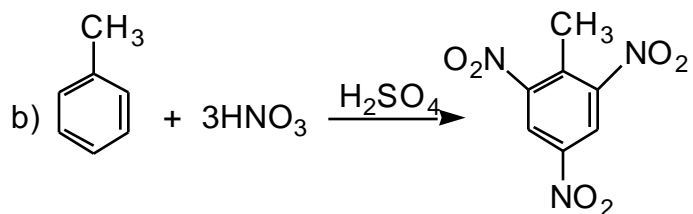
Draw the compound you are trying to synthesize. Determine the reagents needed to introduce each group. Then determine the order in which to introduce groups. For example, in a disubstituted benzene, cover one group with your finger. Does the remaining group direct so that the group you have covered would go where you want it?



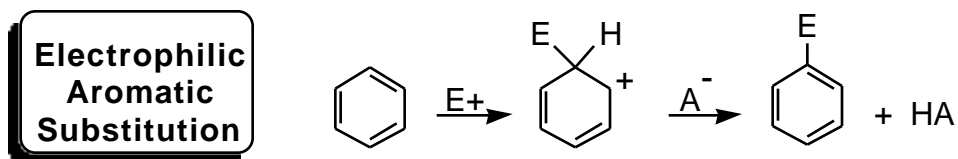
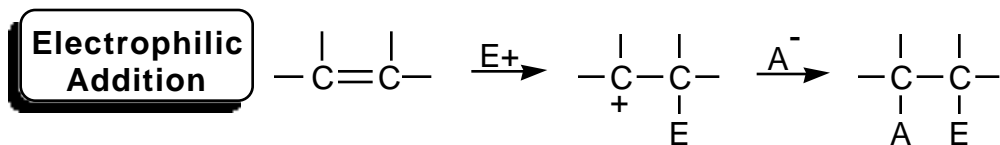


6.38 Synthesis: Sections 6.4-6.5

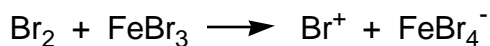
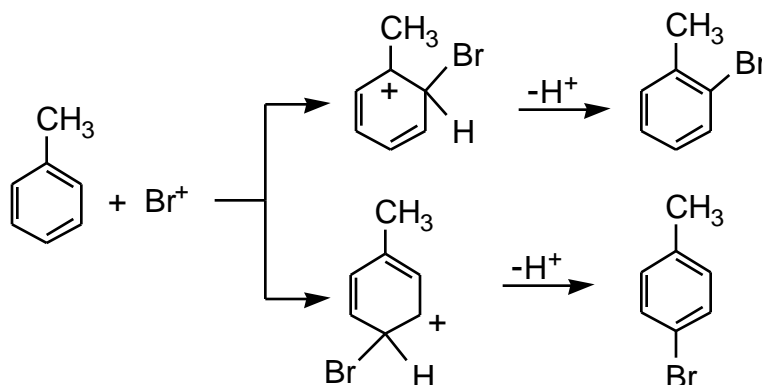




6.39 Reaction Mechanisms: Sections 5.1B and 6.4B



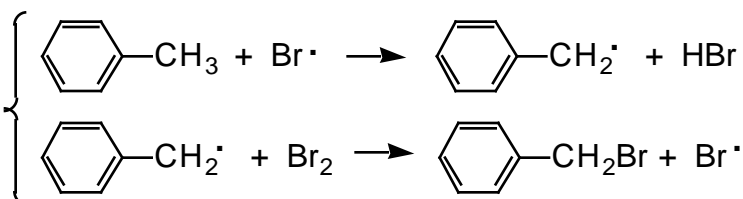
6.40 Reaction Mechanisms: Sections 4.4B and 6.4B.1

Electrophilic Aromatic SubstitutionGeneration
of the
ElectrophileTwo-step
Substitution**Free-radical Chain Bromination**

Initiation

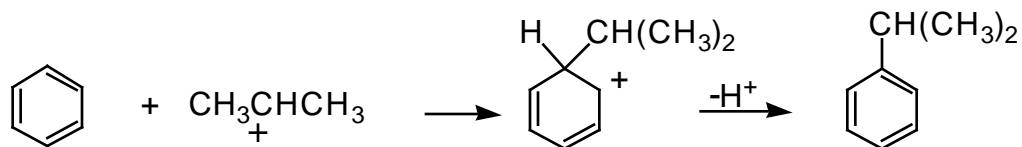


Propagation

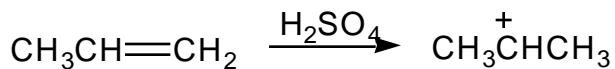
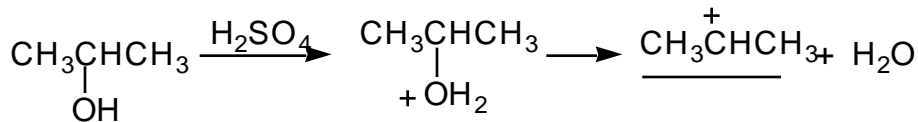
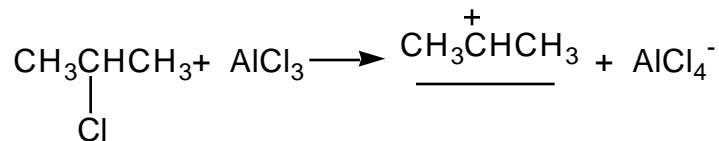


6.41 Reaction Mechanisms: Sections 4.5C, 5.1B, and 6.4B.2

The mechanism of electrophilic substitution for the synthesis of ethylbenzene is one of two-step substitution: the electrophile bonds and forms a carbocation which is neutralized upon elimination of hydrogen ion.



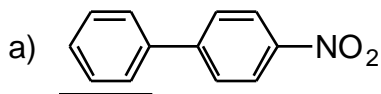
The difference in the three procedures described is in the way the electrophile is generated.



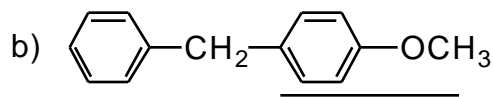
6.42 Activating and Deactivating Groups

- nitrobenzene < benzene < phenol
- chlorobenzene < benzene < aniline
- benzoic acid < p-methylbenzoic acid < p-xylene
- nitrobenzene < p-nitrotoluene < toluene < p-xylene

6.43 Activating and Deactivating Groups



The nitro group is deactivating; as a result, substitution occurs on the other ring.



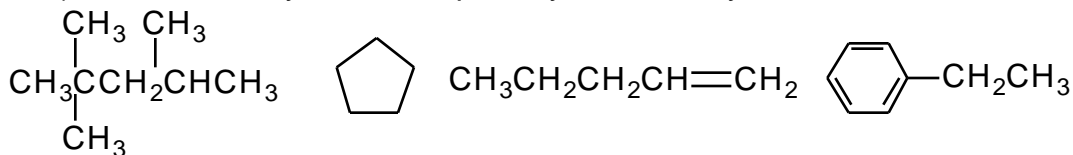
The methoxy group is activating and directs substitution to the ring it occupies.

6.44 Physical Properties: Section 2.9

- Ethylbenzene has a greater molecular weight.
- (b-d) The compound with the highest melting point in each case is the most symmetrical and consequently, forms a very strong and stable crystal lattice.

6.45 Gasoline: Connection 6.2

- 1)Hydrocarbons with 5-10 carbons
- 2)Branched hydrocarbon chains
- 3)Unsaturated, cyclic and especially aromatic hydrocarbons



Research
Octane
Number

100

101

91

107

6.46 Production of Gasoline: Connection 6.2

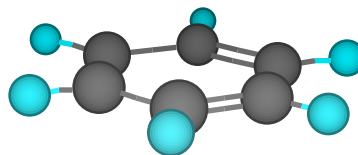
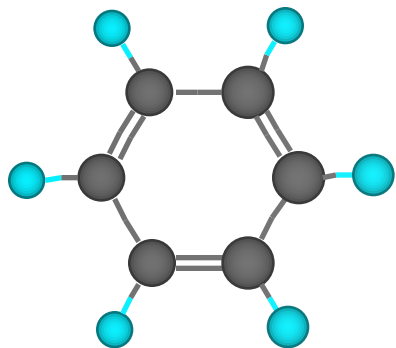
- a) Isomerization;
- b) Cracking;
- c) Isomerization or Aromatization;
- d) Alkylation or Polymerization;
- e) Alkylation;
- f) Aromatization

6.47 Basicity of Aniline

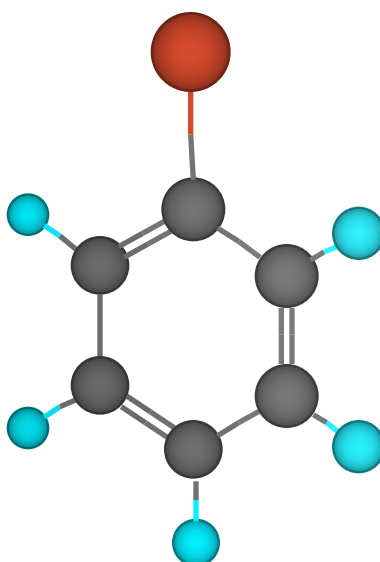
Any group that increases the availability of the electron pair of nitrogen will increase basicity and those that decrease availability will decrease basicity. Electron-withdrawing groups like nitro pull electrons from the ring and from the amine group whereas releasing groups do the opposite. Thus electron-withdrawing groups decrease basicity and electron-releasing groups increase basicity. Since resonance effects occur between positions in an ortho or para relationship, these groups will have greater effect if ortho or para rather than meta.

ACTIVITIES WITH MOLECULAR MODELS

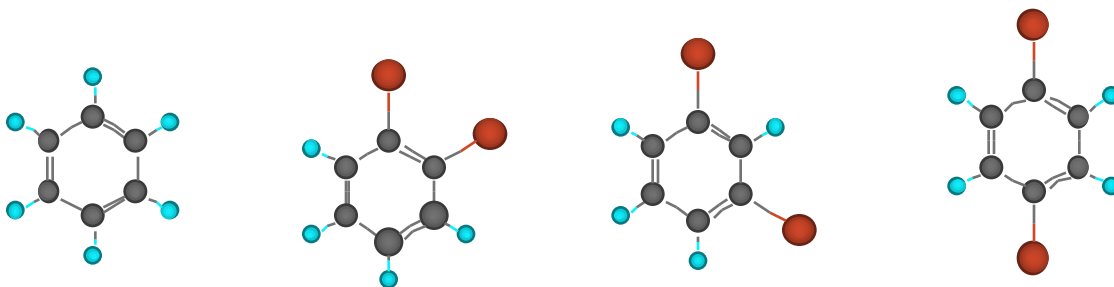
1. Make a molecular model of benzene if your model kit allows this to be done effectively. Note that the molecule is entirely planar, that all carbons are equivalent, that all hydrogens are equivalent, and that each carbon is trigonal with 120° bond angles.



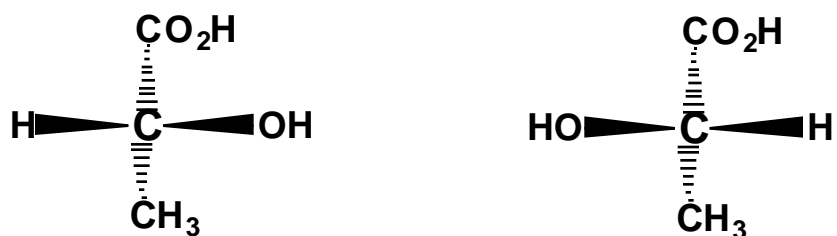
2. How many different places on a benzene ring can you replace one hydrogen with a bromine?



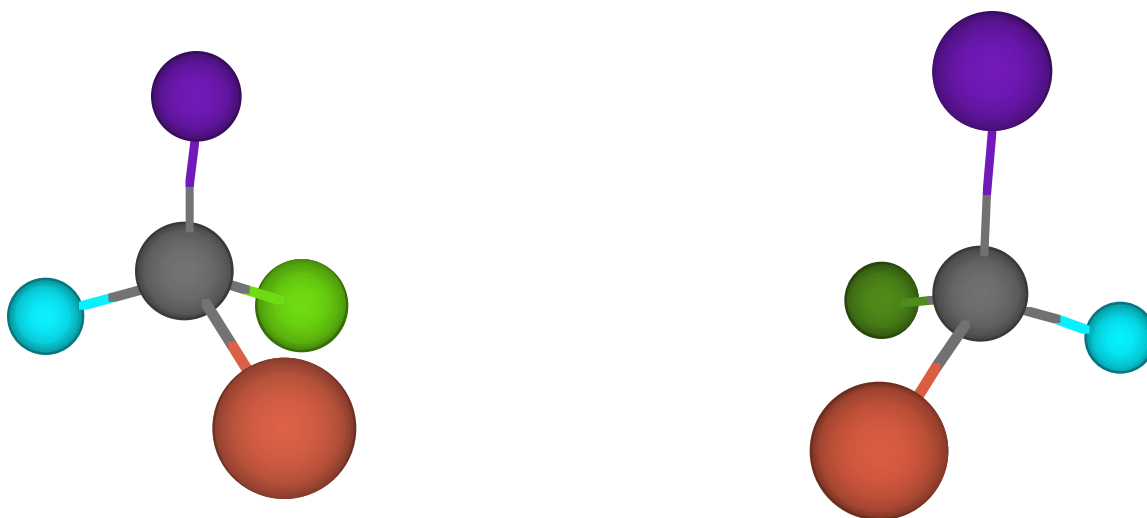
3. How many places on a benzene ring can you substitute two bromines for two hydrogens?



7



Stereochemistry



CHAPTER SUMMARY

7.1 Introduction

Isomers are compounds with identical molecular formulas but different structural formulas. **Structural or constitutional isomers** differ in the bonding arrangement of atoms; different atoms are attached to one another in the isomers. There are three types of structural isomers. **Skeletal isomers** differ in their carbon skeletons or chains. In **positional isomers**, the difference is in the position of a non-carbon group or multiple bond. **Functional isomers** belong to different groups or classes of organic

compounds. In **stereoisomerism** the same atoms are bonded to one another but their orientation in space differs; there are three types of stereoisomerism. **Geometric** or **cis-trans isomerism** refers to the orientation of groups around a double bond or on a ring. **Conformational isomers** differ in the extent of rotation around a carbon-carbon single bond. A third type, sometimes called **optical isomers**, are compounds that are identical in structure except where they are related as mirror images.

7.2 Stereoisomers with One Chiral Carbon Atom

A. Chiral Carbon Atoms, Enantiomers, and Racemic Mixtures

A carbon with four different bonded groups is called a **chiral carbon atom**, **chirality center**, or **stereocenter**. Because of its tetrahedral geometry, a chiral carbon atom can exist in either of two three-dimensional arrangements that are non-superimposable mirror images. **Enantiomers** are stereoisomers that are non-superimposable mirror images. All physical properties are identical for these two isomers except the direction of rotation of **plane polarized light**. One rotates plane polarized light to the right and is termed **dextrorotatory (d,+)**; the other rotates the light an equal amount in the opposite direction, to the left, and is termed **levorotatory (l,-)**. A compound that rotates plane polarized light is said to be **optically active** or **chiral**. A **chiral compound** or **optically active compound** is not superimposable on its mirror image. A **racemic mixture** is a 50/50 mixture of enantiomers; because the enantiomers cancel each others' rotation of plane polarized light, a racemic mixture is **optically inactive** (does not rotate plane polarized light).

B. Expressing the Configurations of Enantiomers in Three Dimensions

Enantiomers can be drawn using **wedges and dashes** to show the tetrahedral geometry or by using **Fischer projections** in which the tetrahedral nature is assumed. In both representations, horizontal bonds are coming out of the paper and vertical bonds are behind the paper.

C. Comparing Representations of Enantiomers

Drawings can be compared for superimposability or non-superimposability by **physically maneuvering** structures in a way to maintain the **configurational** relationships or **interchanging** groups on a chiral carbon atom. One interchange gives the mirror image, two maintains the original configuration but from a different perspective.

7.3 Measurement of Optical Activity - The Polarimeter

A. Plane Polarized Light

Light can be described as a wave vibrating perpendicular to its direction of propagation. Light vibrating in all possible planes is said to be unpolarized whereas that oscillating in only one plane is **plane polarized**.

B. The Polarimeter

A **polarimeter** is the instrument used to measure the rotation of plane polarized light by an optically active compound.

C. Specific Rotation

Specific rotation is a physical property of an optically active compound. The specific rotation of plane polarized light by an optically active compound is the observed rotation to the left, **levorotatory (l, -)** or to the right, **dextrorotatory (d,+)** divided by the length of the sample tube in decimeters and the concentration of the sample in g/cm³.

7.4 Stereoisomers with Two Chiral Carbon Atoms

Stereoisomers with **one chiral carbon** can only exist as a pair of enantiomers. More possibilities exist if there are two or more chiral carbons. Drawing stereoisomers of a formula should be done in a systematic fashion and in pairs of mirror images. These mirror images can be tested for superimposability. The maximum number of enantiomers possible for a compound is 2^n where n is the number of chiral carbons; this is known as the **van't Hoff rule**.

A. Molecules with Two Dissimilar Chiral Carbon Atoms: Enantiomers and Diastereomers

A compound with two dissimilar chiral carbon atoms has two possible pairs of enantiomers. The mirror image structures of one enantiomeric pair are diastereomers of those of the other enantiomeric pairs. **Diastereomers** are stereoisomers that are not mirror images. All physical properties of diastereomers are different including, usually, their rotation of plane polarized light.

B. Molecules with Two Similar Chiral Carbon Atoms: Enantiomers, Diastereomers, and Meso Compounds

A compound with two similar chiral carbon atoms has one pair of enantiomers and one meso compound. A **meso compound** has more than one chiral center and is superimposable on its mirror image; meso compounds are optically inactive. A meso compound is a diastereomer of each of the enantiomers. **Diastereomers** are stereoisomers that are not mirror images; all physical properties of diastereomers are usually different.

7.5 Stereoisomerism in Cyclic Compounds

Cyclic compounds can exhibit enantiomerism as well as geometric isomerism. A cyclic compound with two dissimilar chiral carbon atoms has two possible enantiomeric pairs. The cis isomer can exist as a pair of enantiomers and the trans isomer does the same. The two “cis” enantiomers are diastereomers of the two “trans” enantiomers. A cyclic compound with two similar chiral carbon atoms has a meso compound, the cis geometric isomer, and a pair of enantiomers, the trans geometric isomer. Again, the cis and trans isomers are related as diastereomers.

CONNECTIONS 7.1 Stereoisomerism in the Biological World

7.6 Specification of Configuration

A. R and S Designations of Chiral Carbon Atoms

The configuration of a chiral carbon can be described by the **R,S system**. The groups connected to the chiral carbon atom are assigned priorities. The molecule is then visualized so that the group of lowest

priority is directed away from the observer. The remaining three groups are in a plane and are visualized from highest to lowest priority. If in visualizing from the highest priority group to next highest, the eye moves **clockwise**, the configuration is **R**; if the eye moves **counterclockwise**, the configuration is **S**.

B. Determining Group Priorities

Priority depends on the atomic number of atoms directly attached to the chiral carbon atom. If two or more directly attached atoms are identical, one proceeds along the groups until differences are found. In double and triple bonds the groups are considered to be duplicated or triplicated.

C. Determining R and S Configurations

To determine R and S configurations it is necessary to orient the lowest priority group away from the observer. Using a Fischer projection for each chiral carbon with the lowest priority group going away from the observer is a convenient way to do this. To get the lowest priority group where you want it, you can use the rotation method or the interchange method (remember interchanges have to be made in pairs to retain the original configuration).

We have already seen in Chapter 3, Section 3.5B, the configuration of **geometric isomers** can be expressed using the **E,Z system**. If the two high priority groups are on the same side of the double bond, **E** is assigned; if they are on opposite sides, the configuration is **Z**.

7.7 Resolution of Enantiomers

Since enantiomers have identical physical properties they cannot be separated by physical means. They can be separated by **resolution through diastereomers**. In this method, enantiomers are converted to diastereomers by reaction with a pure optically active compound. Diastereomers have different physical properties and can be separated. After separation, the diastereomers are converted back to the original enantiomers.

7.8 Stereoisomerism and Chemical Reactions

Chiral carbon atoms can be generated during chemical reactions. If a single chiral carbon atom is generated in a compound that previously had no chiral carbon atoms, a pair of enantiomers results; they are formed in equal amounts. If a single chiral carbon is generated in a compound that already has a chiral carbon atom, a pair of diastereomers results; they are formed in unequal amounts.

If two chiral carbons are generated in a compound that previously had none, two general possibilities exist: (1) a single meso compound or a pair of enantiomers if the two chiral carbon atoms are similar; (2) a pair of enantiomers if the two chiral carbon atoms are dissimilar. If two chiral carbon atoms are generated in a compound that already has a chiral carbon atom, a pair of diastereomers is always the result.

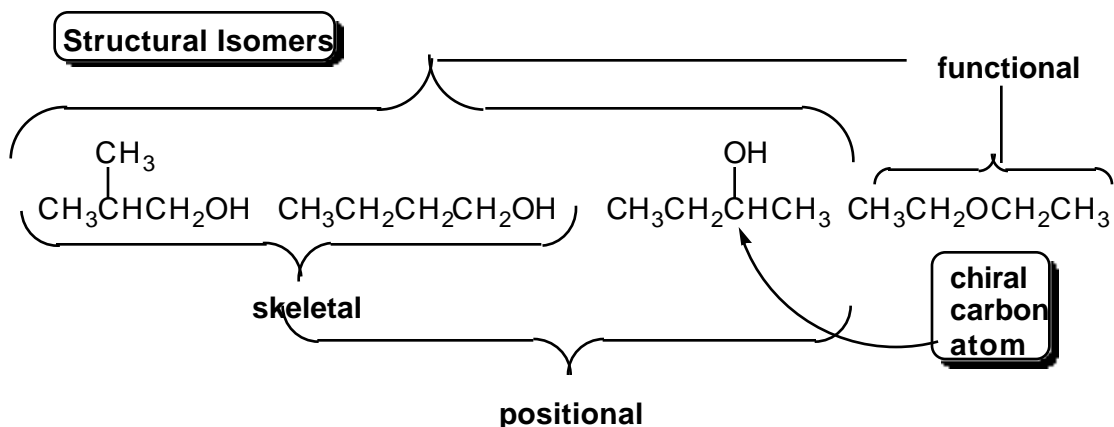
SOLUTIONS TO PROBLEMS

7.1 Chiral Objects

The answers to this question can vary in a few items depending on the type of item being considered or depending on one's concept of the item. Most are fairly straightforward, however.

Chiral Objects: a, c, d, f, h, j, k, m, n, o, r, s

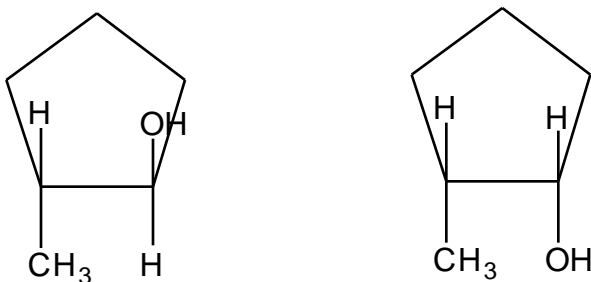
7.2 Structural Isomers



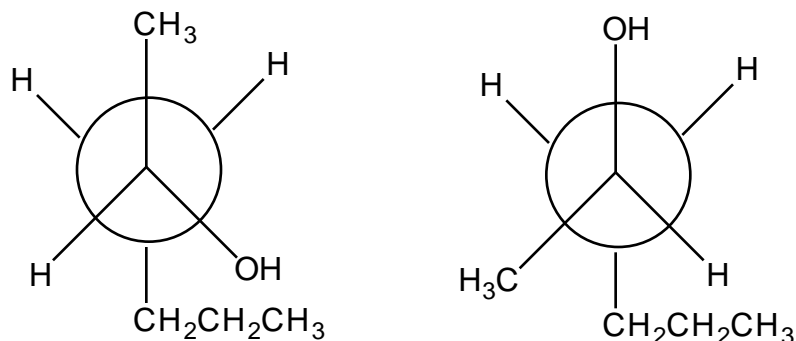
7.3 Isomerism

- (a) **skeletal** $\text{CH}_3\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{OH}$, $\text{CH}_3\overset{\text{CH}_3}{\text{C}}\text{HCH}_2\text{CH}_2\text{CH}_2\text{OH}$
- (b) **positional** $\text{CH}_3\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{OH}$, $\text{CH}_3\text{CH}_2\text{CH}_2\text{CH}_2\underset{\text{OH}}{\text{C}}\text{HCH}_3$
- (c) **functional** $\text{CH}_3\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{OH}$, $\text{CH}_3\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{OCH}_3$

(d) **geometric**



(e) **conformational**

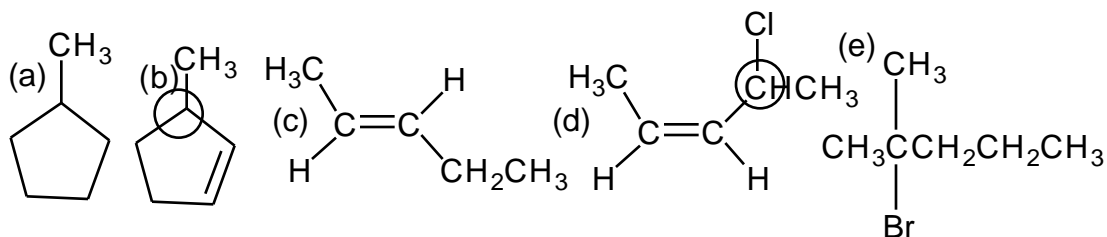


7.4 Chiral Carbon Atoms

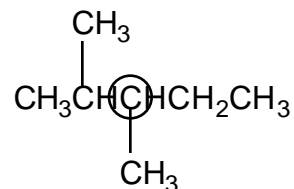
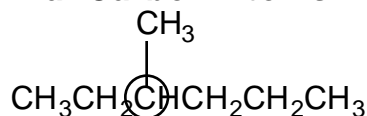
(a) the two carbons with the bromines; (b) carbons 3 and 5 (the two carbons with methyl groups); (c) there are no chiral carbon atoms in this structure; (d) the two carbons with the bromines.

7.5 Chiral Carbon Atoms and Enantiomers

Only (b) and (d) have chiral carbon atoms (circled) and have enantiomers.

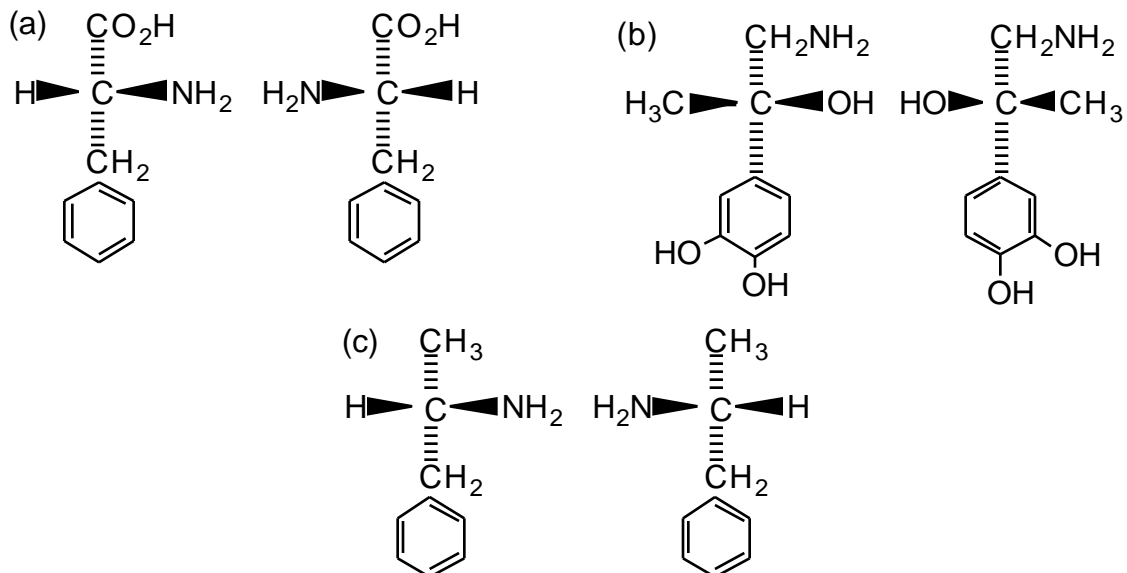


7.6 Chiral Carbon Atoms



7.7 Drawing Enantiomers

See Example 7.3 in the text for assistance.



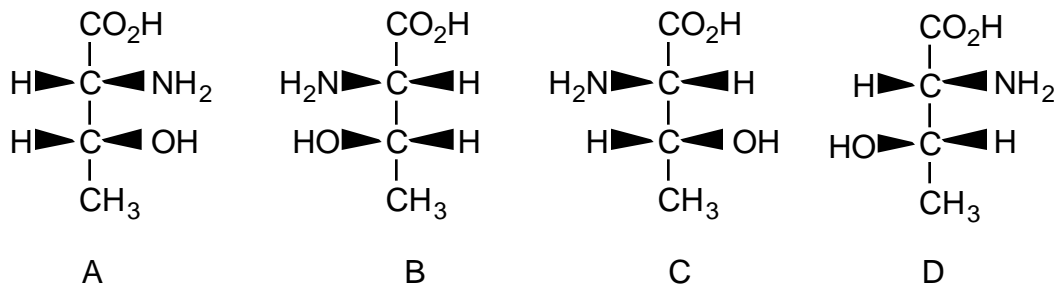
7.8 Maneuvering Stereoisomers

See Example 7.4 for assistance. Either physical maneuvering or interchanging of groups will work though the latter is probably faster and offers less chance of error.

Identical: c, d, e, **Mirror Image:** a, b, f, g, h

7.9 Stereoisomers of Threonine

Draw the optical isomers systematically and in pairs of mirror images. Start out drawing the wedge/dash representation you see in the structures below. Pick two groups, the acid and methyl in the example shown, and put one at the top and one at the bottom; they do not change positions. Now put the two hydrogens on one side and the other two groups on the other; draw the mirror image. Finally put the hydrogens on opposite sides; draw the mirror image. Compare the pairs of mirror images for superimposability. In this case, since the top and bottom of the molecule are different, there is no possibility of rotation to superimpose; there are two pairs of enantiomers.



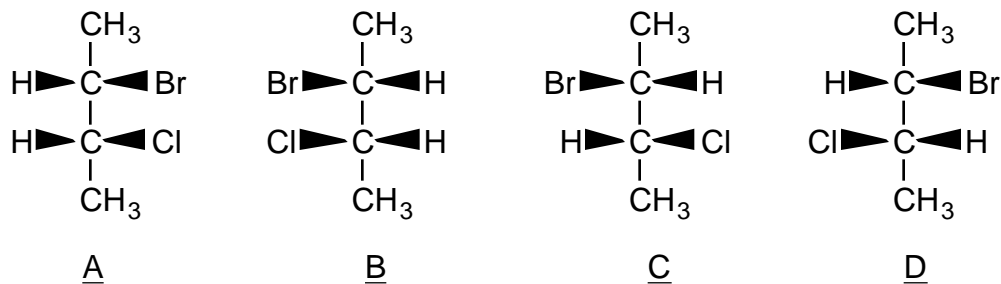
Enantiomers: AB, CD

Diastereomers: AC, AD, BC, BD

7.10 Drawing Stereoisomers

See problem 7.9 for a brief description of the systematic method for drawing optical isomers. Draw the isomers in pairs of mirror images.

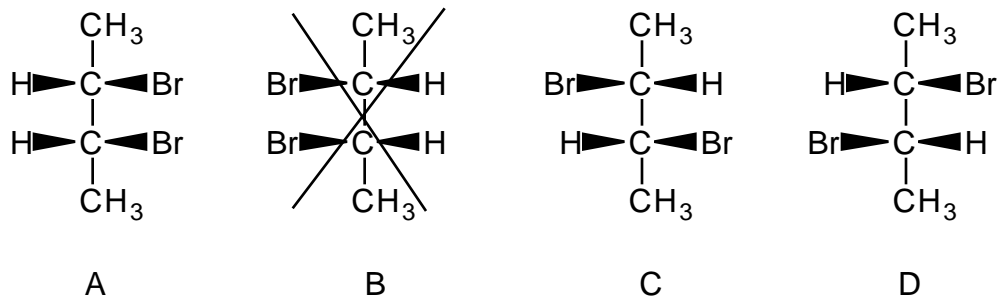
(a) The top half of the molecule is different from the bottom and thus there is no possibility of rotation to attempt superimposability of mirror images. There are two pairs of enantiomers.



Enantiomers: AB, CD

Diastereomers: AC, AD, BC, BD

(b) This molecule can be drawn so that the top and bottom halves are identically constituted thus allowing for 180° rotation to test for superimposability. There is one pair of enantiomers and one meso structure. B when rotated 180° is superimposable on A, its mirror image. Thus A is a meso structure. C and D are not superimposable and are enantiomers.



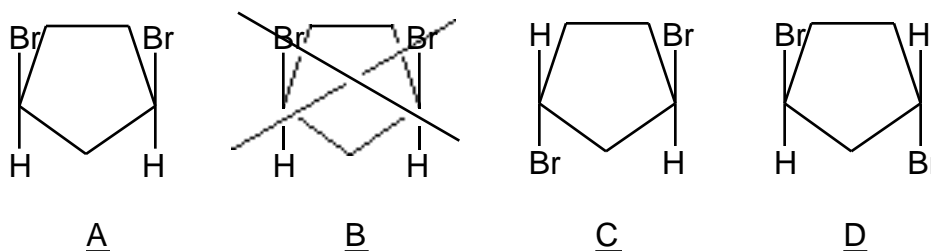
Meso structure: A

Enantiomers: CD

Diastereomers: AC and AD

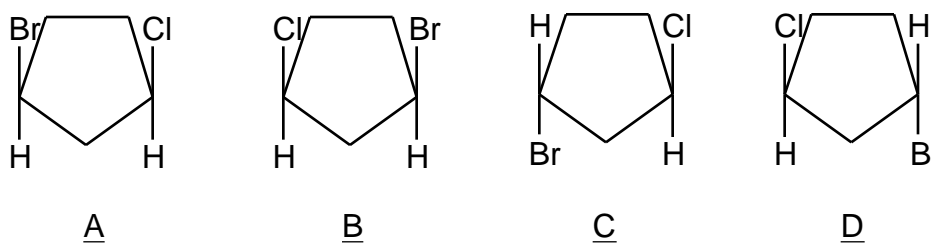
7.11 Stereoisomerism in Cyclic Compounds

(a) This compound has symmetry and is capable of having meso structures.



A=B; A is a meso **C and D are enantiomers**
Diastereomers: AC, AD

(b) There is no symmetry in this molecule and thus rotations to find superimposable mirror images will be fruitless.



Enantiomers: AB, CD **Diastereomers: AC, AD, BC, BD**

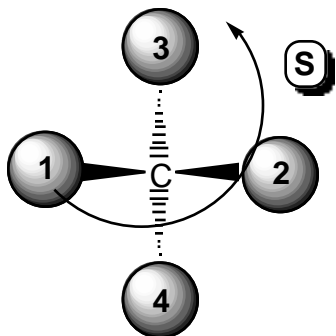
7.12 Specification of Configuration: Group Priorities

- (a) $I > Br > Cl > F$; (b) $Br > OCH_3 > CH_3 > H$;
 (c) $OH > CH_2OH > CH_2CH_2Br > CH_2CH_2CH_3$;
 (d) $Cl > SH > CO_2H > CH_2OH$

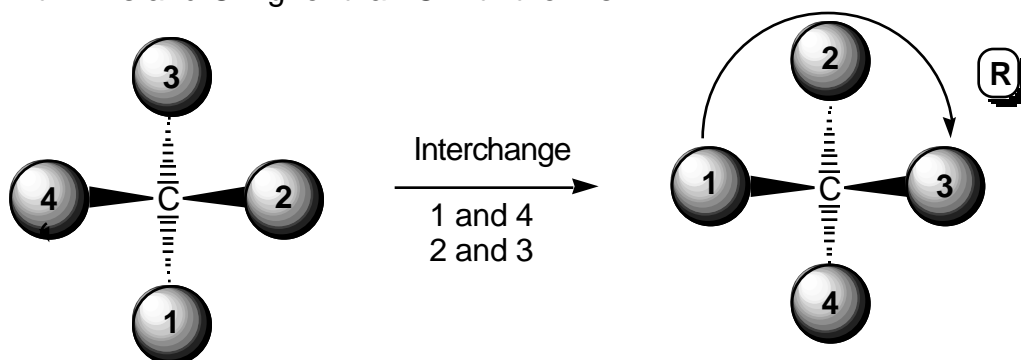
7.13 Specification of Configuration: R and S

The group priorities of the original drawing are shown and then they are interchanged (if necessary) in pairs to obtain the perspective with the lowest priority group oriented back.

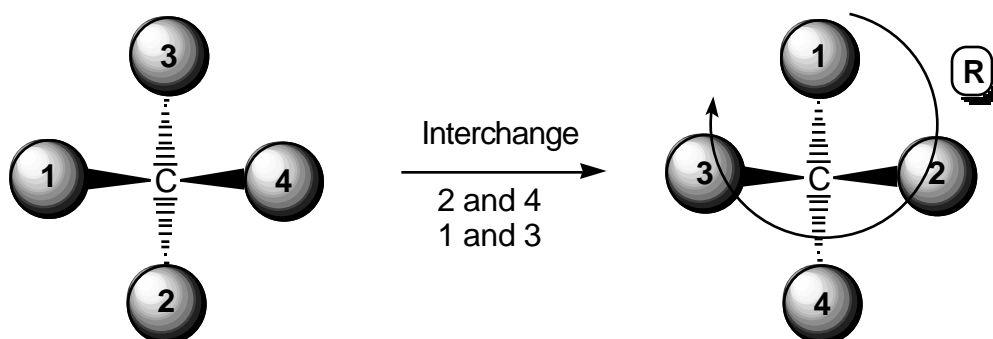
(a) Group priorities by atomic number of atoms directly connected to chiral carbon: $Br > F > C > H$.



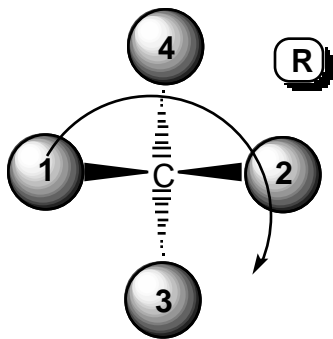
(b) Group priorities: N higher than the C's; C with 2H's and Br higher than C with 2H's and C higher than C with the H's.



(c) Group priorities: All C's, look at what is on the C's. #1 is a C with three C's because of triple bond; #2 is C with two C's and a H. We have to look at the second C on the next two because in each case the first C has a C and 2H's. #3 has 2H's and I and #4 has 3 oxygens; the I is of higher atomic number.

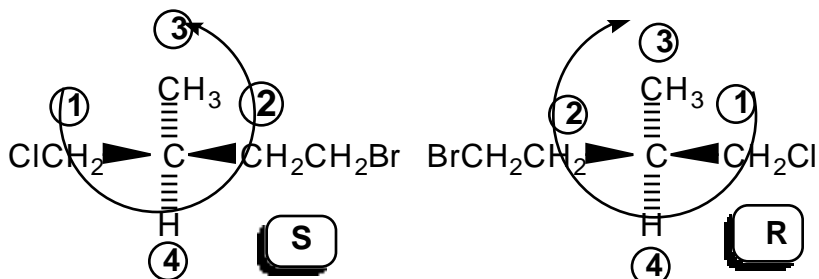


(d) Group priorities: #1 is O. The next three are all C's. #2 has O on C. #3 has C and 2H and #4 has 3H. No need to interchange as #4 is back.

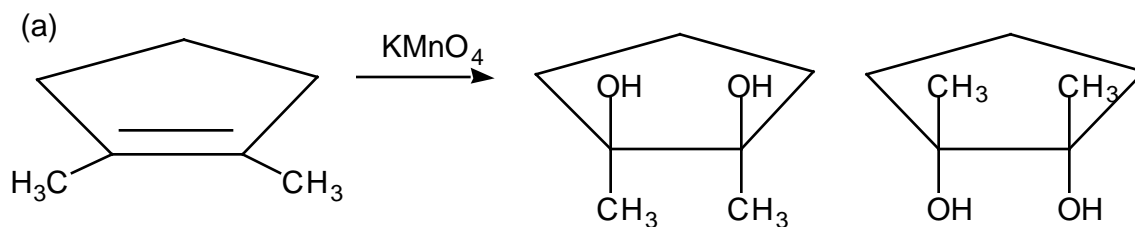


7.14 Specification of Configuration: R and S

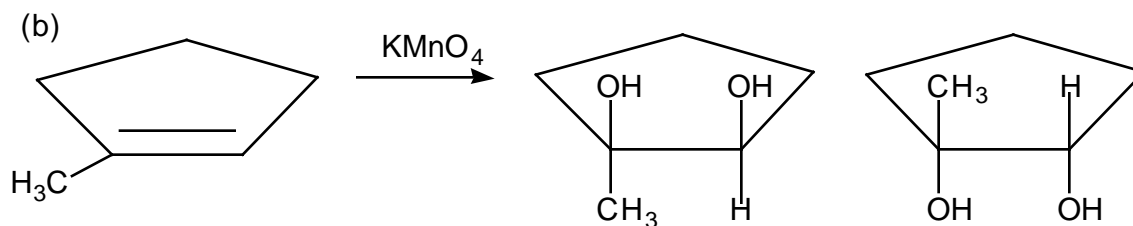
Group priorities: H is lowest atomic number and #4; the rest are C's. #1 C has a Cl. #2 has 2H and a C and #3 has 3H.



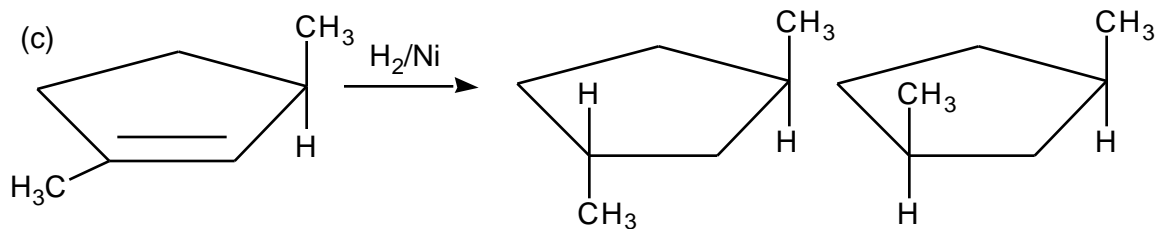
7.15 Stereoisomerism and Chemical Reactions



These two mirror image structures are identical.
Two chiral carbon atoms generated. **Meso structure**

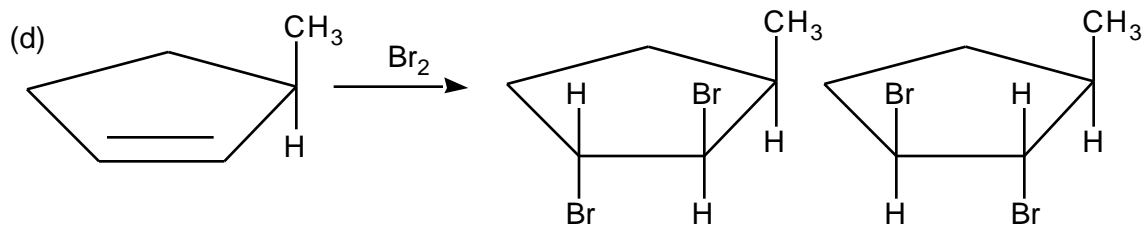


Two chiral carbons generated.
Pair of enantiomers



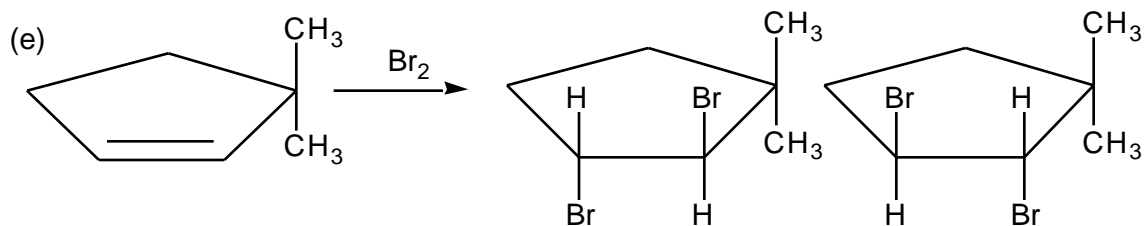
One chiral carbon generated; one present.
Structures are not mirror images.

Pair of diastereomers



Two chiral carbons generated; one present.
Structures are not mirror images.

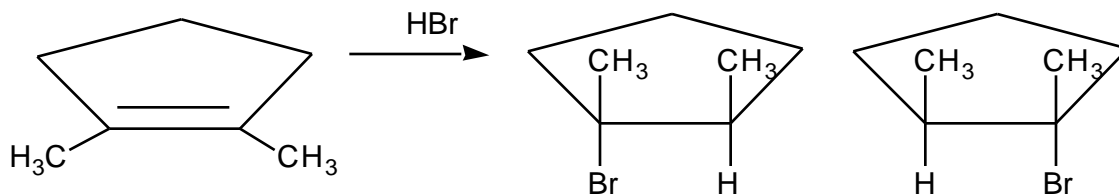
Pair of diastereomers



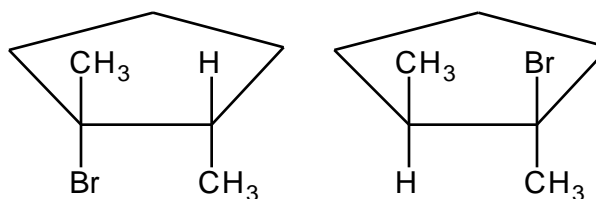
Two chiral carbons generated.
Structures are mirror images (flip either upside down).

Pair of enantiomers.

7.16 Stereoisomerism and Chemical Reactions

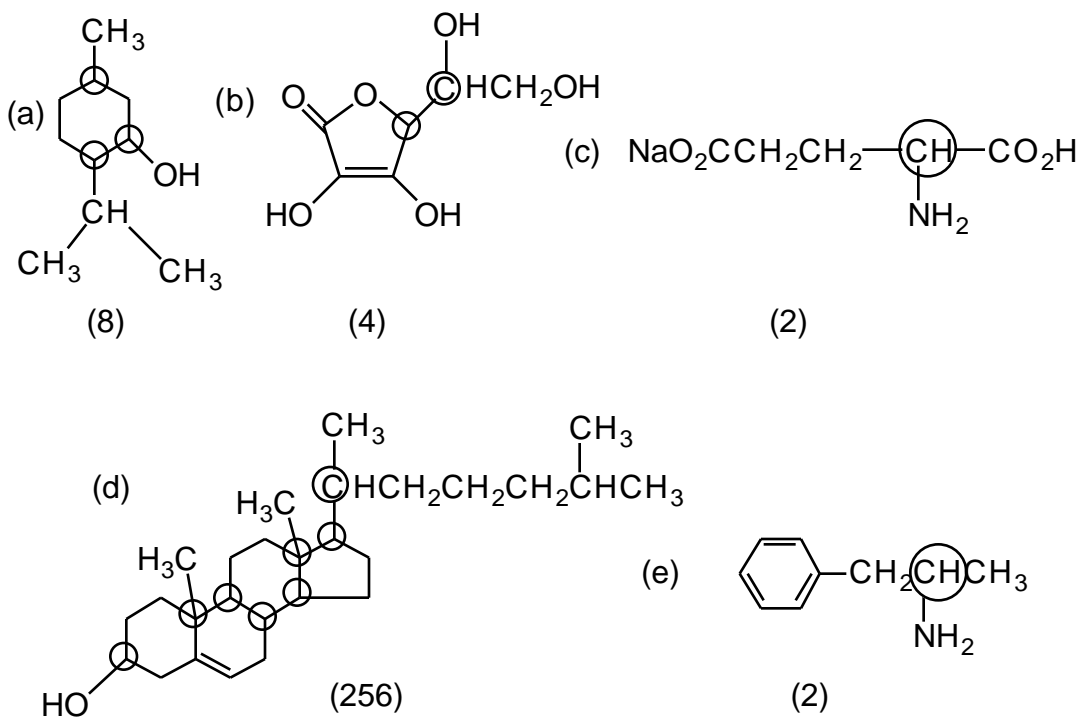


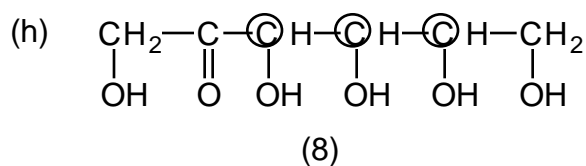
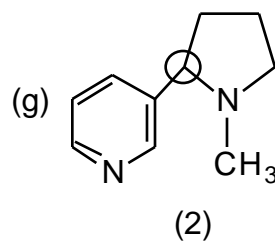
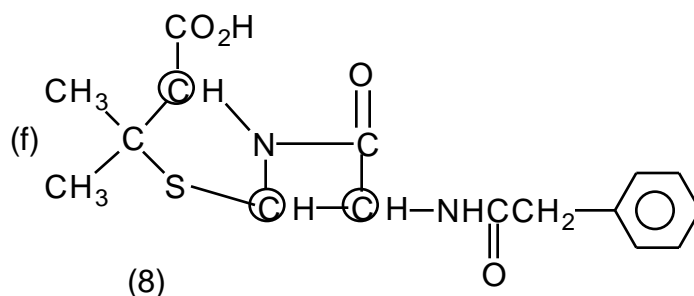
Two chiral carbons are generated.
Two pairs of enantiomers.
 (flip either of the bottom structures to see that they are mirror images.)



7.17 Chiral Carbons: Section 7.2

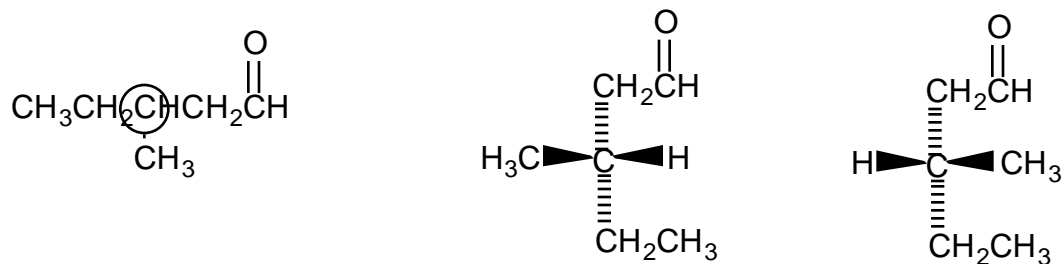
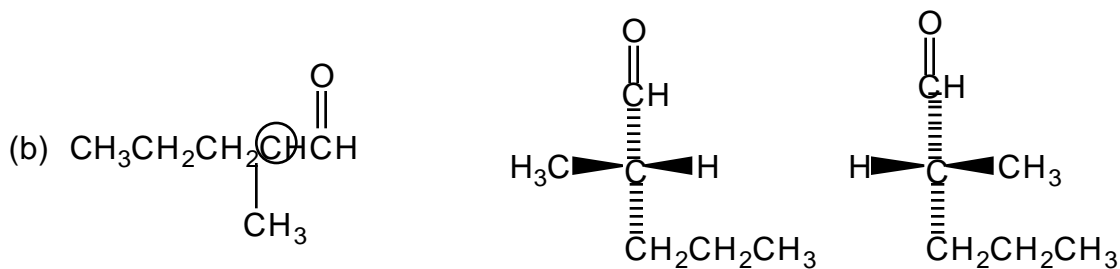
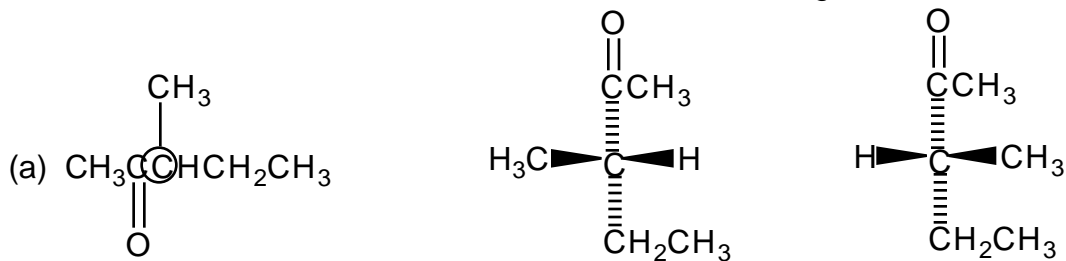
Chiral carbons have four different bonded groups; they are circled in the following compounds. The maximum number of possible optical isomers is 2^n where n is the number of chiral carbons (van't Hoff rule).

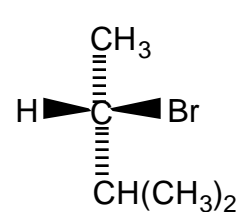
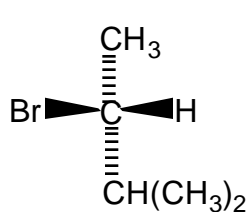
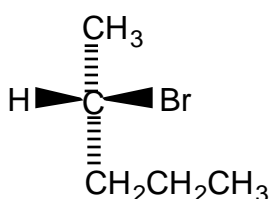
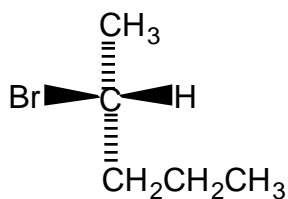
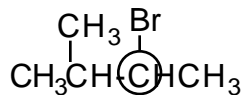
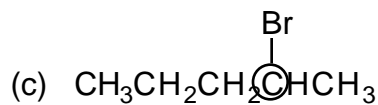
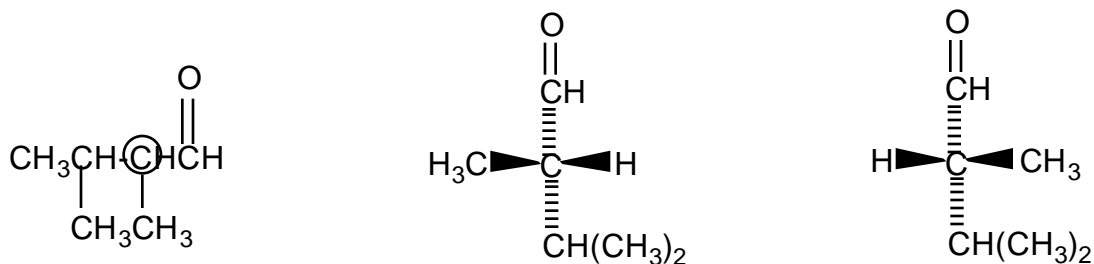




7.18-7.19 Chiral Carbons and Enantiomers: Sections 7.2

Chiral carbons are circled. Enantiomers shown with wedges/dashes.

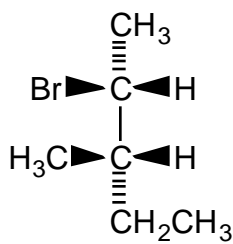
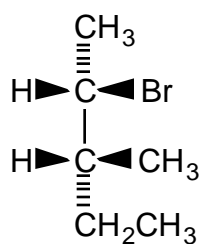




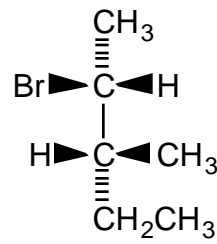
7.19 Enantiomers

Please see problem 7.18.

7.20 Enantiomers and Diastereomers: Section 7.4

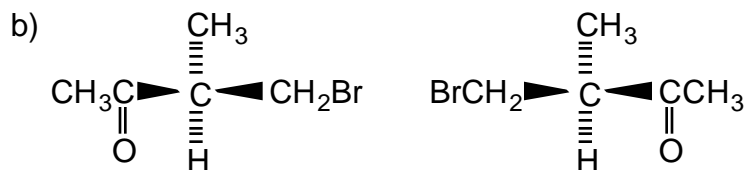
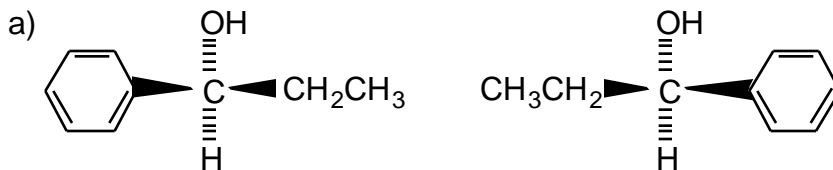


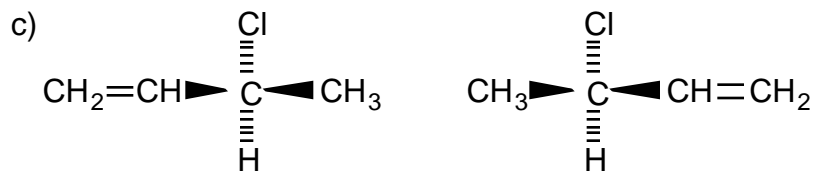
Enantiomers



Diastereomer

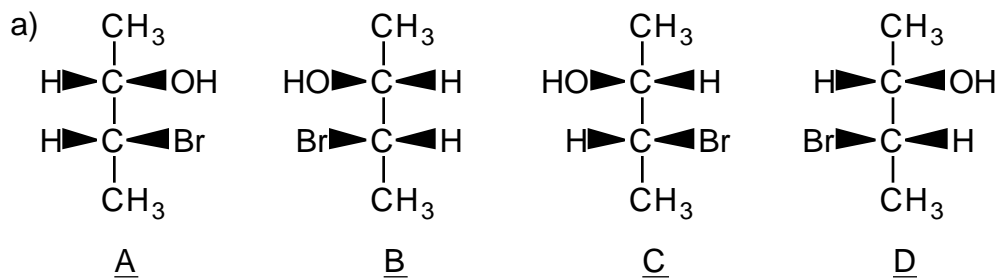
7.21 Enantiomers: Section 7.2A-B





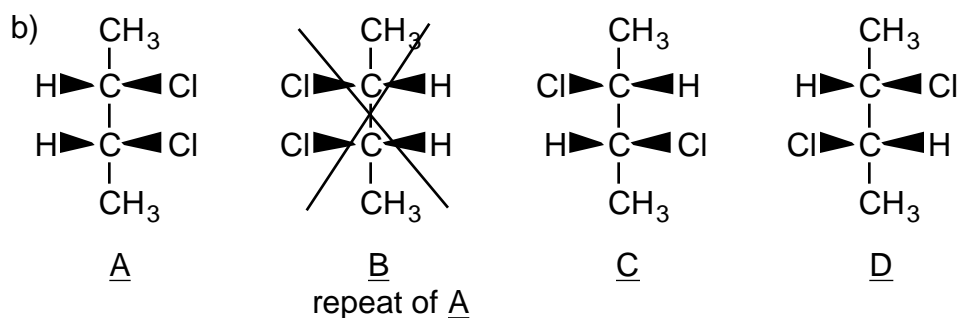
7.22 Stereoisomers: Section 7.4

In working the following problems, it is important to draw the isomers in pairs of mirror images and in an orderly fashion. It will be easiest in this way to identify enantiomers, diastereomers and meso compounds since their definitions involve mirror image relationships. Before working with these examples, be sure you are thoroughly familiar with the definitions in Table 7.2 and the examples explained in sections 7.4.



Enantiomers: AB, CD

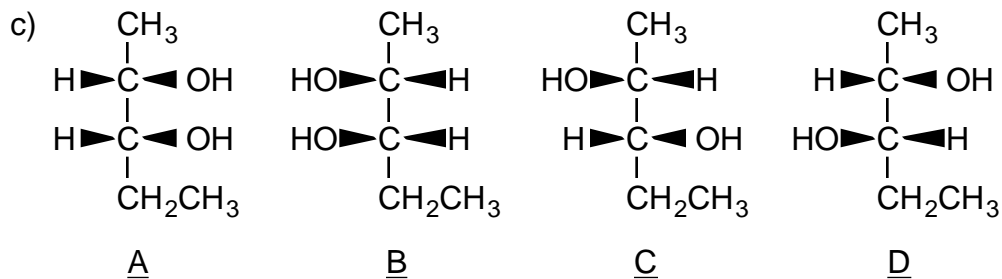
Diastereomers: AC, AD, BC, BD



Enantiomers: CD

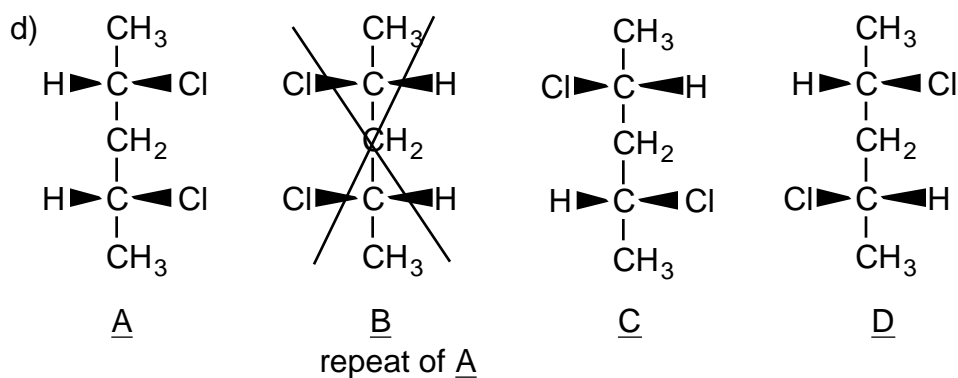
Meso: A

Diastereomers: AC, AD



Enantiomers: **AB, CD**

Diastereomers: **AC, AD, BC, BD**

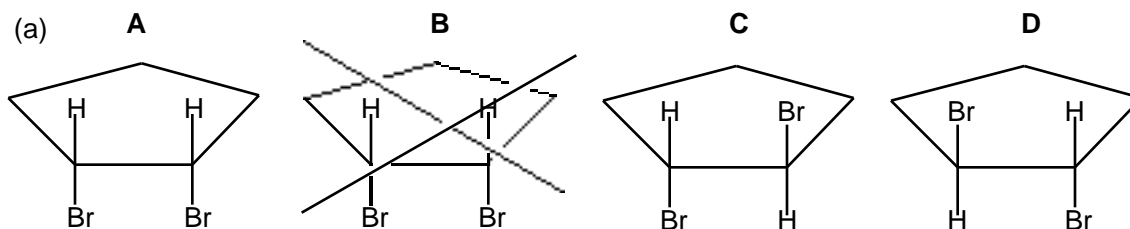


Enantiomers: **CD**

Meso: **A**

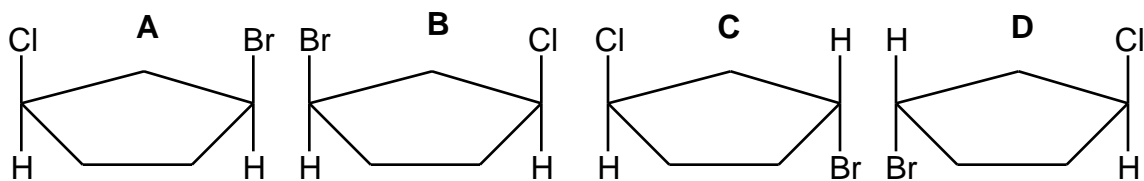
Diastereomers: **AC, AD**

7.23 Stereoisomerism in Cyclic Compounds: Section 7.5



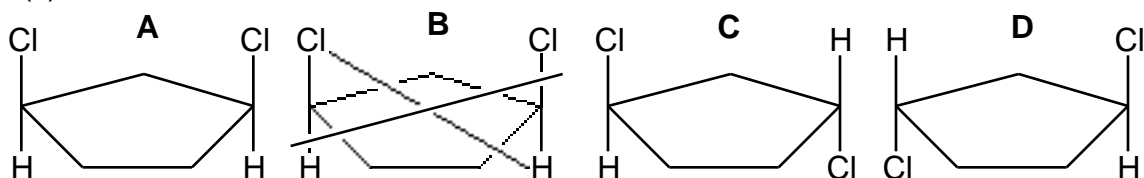
Meso: **A (B same as A)**; Enantiomers: **CD**; Diastereomers: **AC, AD**

(b)



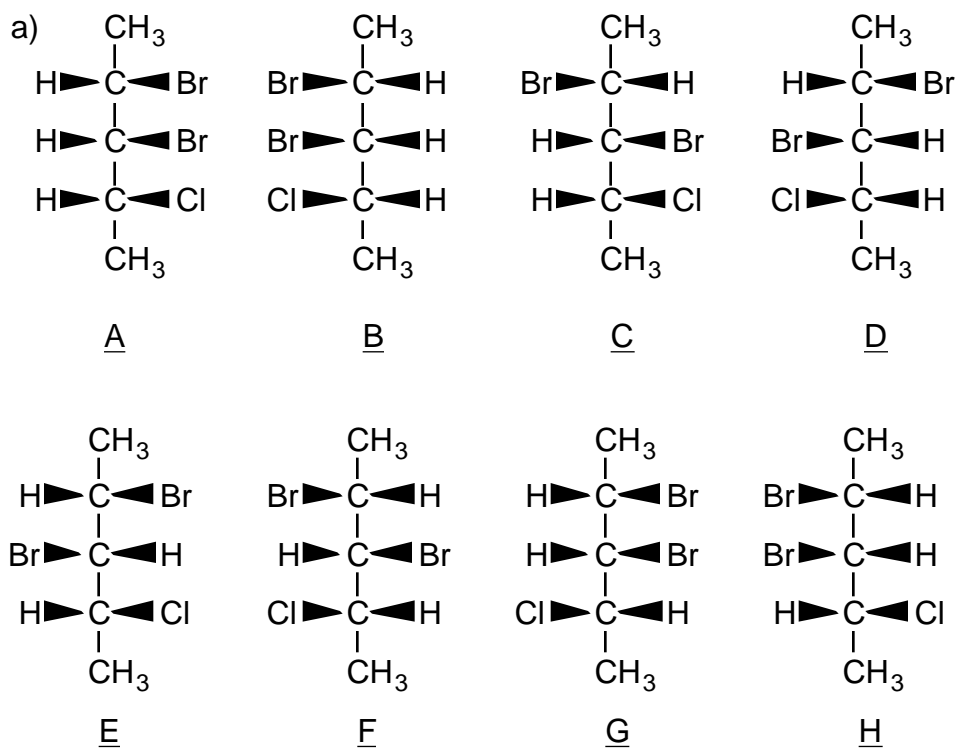
Enantiomers: AB, CD; **Diastereomers:** AC, AD, BC, BD

(c)



Meso: A (B same as A); **Enantiomers:** CD; **Diastereomers:** AC, AD

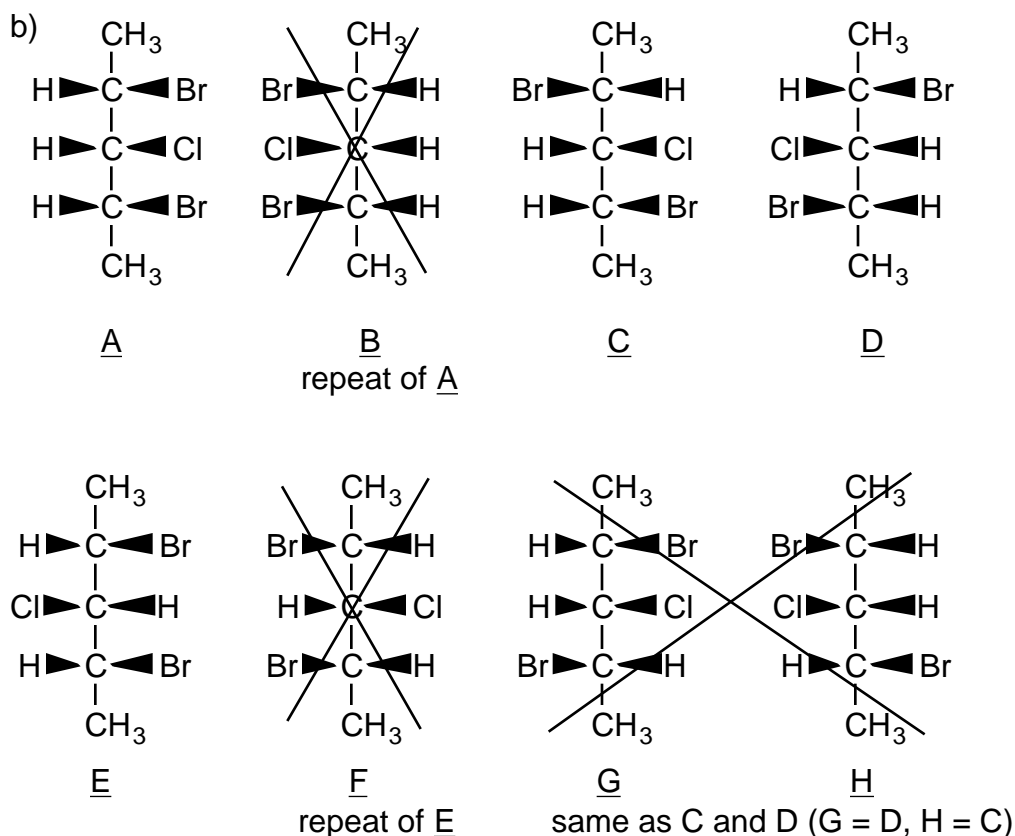
7.24 Stereoisomers: Section 7.4



enantiomers: AB, CD, EF, GH

meso: none

diastereomers: AC, AD, AE, AF, AG, AH, BC, BD, BE, BF, BG, BH, CE, CF, CG, CH, DE, DF, DG, DH, EG, EH, FG, FH



enantiomers: CD meso: A, E diastereomers: AC, AD, AE, CE, DE

In this example, the middle carbon is chiral but does not appear to be because of the symmetry of the molecule. However, the carbons above and below are both chiral. If they have different configurations then the middle carbon has four different attached groups and is a chiral carbon atom. Because of the symmetry, many of the eight structures you drew are identical.

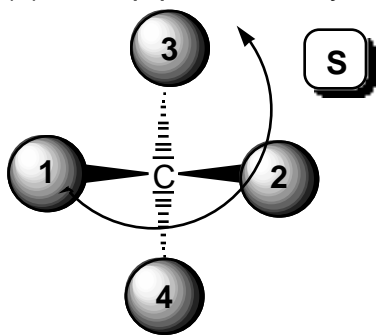
7.25 R,S Configurations: Section 7.6

- (a) $\text{Br} > \text{OCH}_3 > \text{CHO} > \text{H}$ (b) $\text{C}(\text{CH}_3)_3 > \text{CH}(\text{CH}_3)_2 > \text{CH}_2\text{CH}_3 > \text{CH}_3$
 (c) $\text{Br} > \text{F} > \text{CH}_2\text{Cl} > \text{CH}_2\text{CH}_2\text{I}$ (d) $\text{I} > \text{CH}_2\text{Br} > \text{CHCl}_2 > \text{CH}_3$
 (e) $\text{OCH}_3 > \text{NH}_2 > \text{CN} > \text{H}$

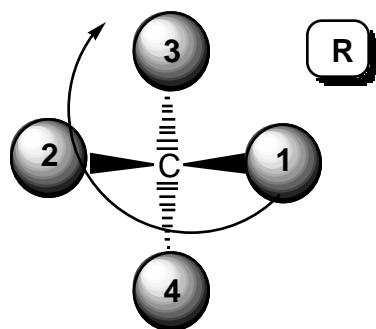
7.26 Specification of Configuration - R,S: Section 7.6

The group priorities of the original drawing are shown and then they are interchanged (if necessary) in pairs to obtain the perspective with the lowest priority group oriented back. For assistance, see Examples 7.5-7.7 for determining group priorities and Example 7.9 for assigning R or S.

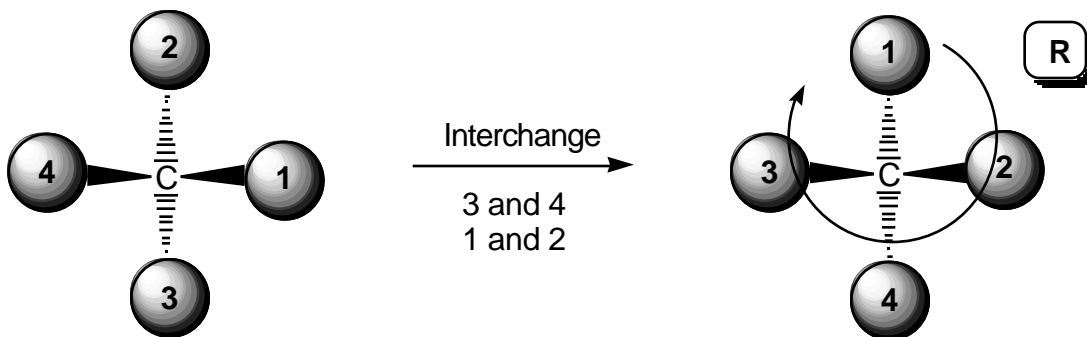
(a) Group priorities: By atomic number of directly attached atoms.



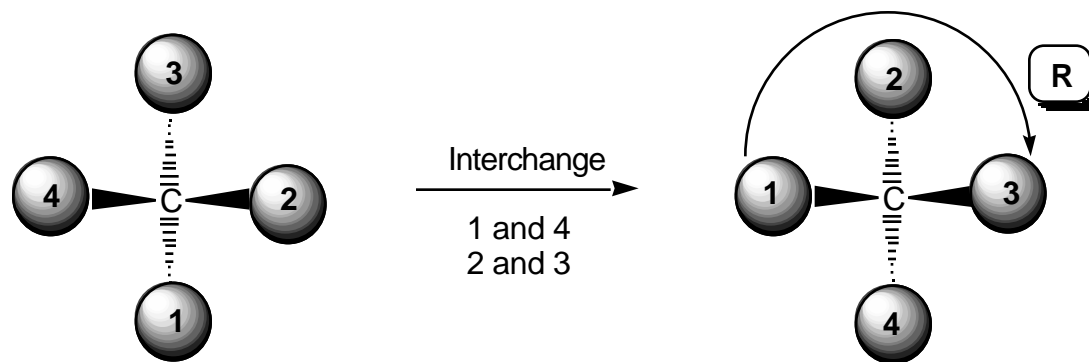
(b) Group priorities: O highest, H lowest of directly attached atoms. Carbon with C and 2H higher than carbon with 3H.



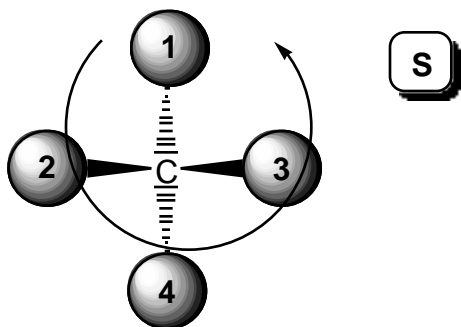
(c) Group priorities: Directly attached atoms all carbon. #1 is C with 2C,1H attached; all the others have one C and 2H. Looking at next carbons, #2 has a Cl; the other two have C and 2H. Looking at next carbons, #3 has a Br.



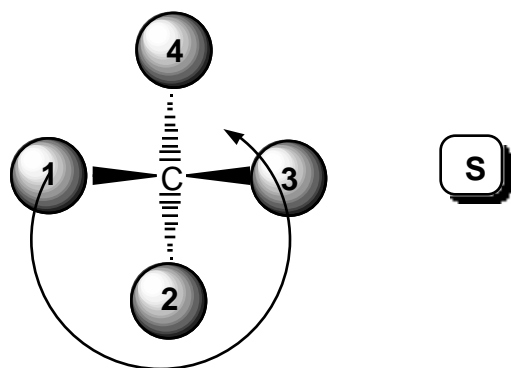
(d) Group Priorities: By atomic number of directly attached atoms.



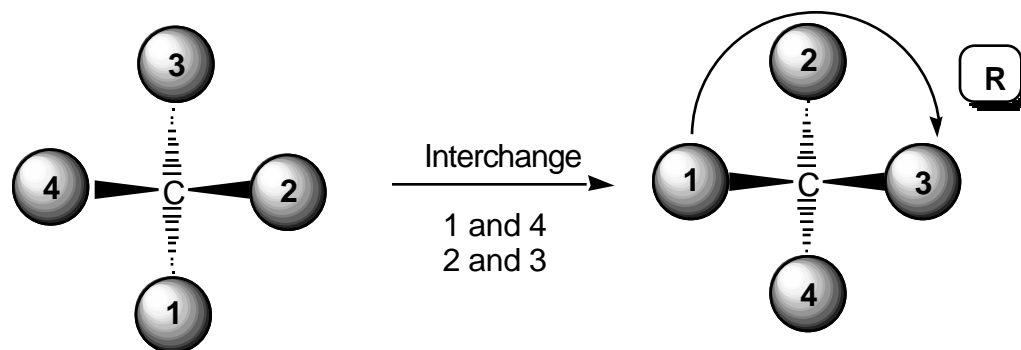
(e) Group priorities: H is #4; all other directly attached are carbon. Looking at the carbons, the highest atomic number attached group is Br and this is #1. The one with Cl is #2, and the one with three carbons is #3.



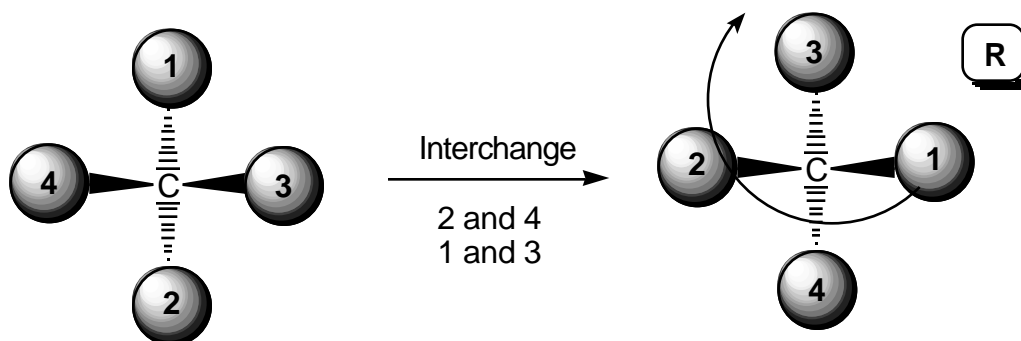
(f) Group priorities: Oxygen is first, the other directly attached atoms are carbons. The carbon with 3H is #4. The other two differ at the second carbon.



(g) Group priorities: N is the highest atomic number directly attached atom; H is the lowest. The C with the C and 2H is #2.



(h) Group priorities: Of directly attached atoms, Cl has highest atomic number followed by O, followed by C, followed by H.



7.27 Specification of Configuration - E, Z: Section 3.5B

- (a) **E** $\text{CH}_3 > \text{H}$ and $\text{Cl} > \text{CH}_3$
 (b) **Z** $(\text{CH}_3)_2\text{CH} > \text{CH}_2\text{CH}_2\text{CH}_3$ and $\text{SCH}_3 > \text{OCH}_2\text{CH}_3$
 (c) **Z** $\text{CH}_2\text{OH} > \text{CH}_3$ and $\text{Br} > \text{CH}_2\text{OH}$
 (d) **E** $\text{Br} > \text{H}$ and $\text{F} > \text{CH}_2\text{Cl}$
 (e) **E,Z** $\text{Br} > \text{H}$ and $\text{CH}=\text{CHBr} > \text{H}$ on both double bonds

7.28 Specification of Configuration - R,S,Z,E: Sections 3.5B and 7.6

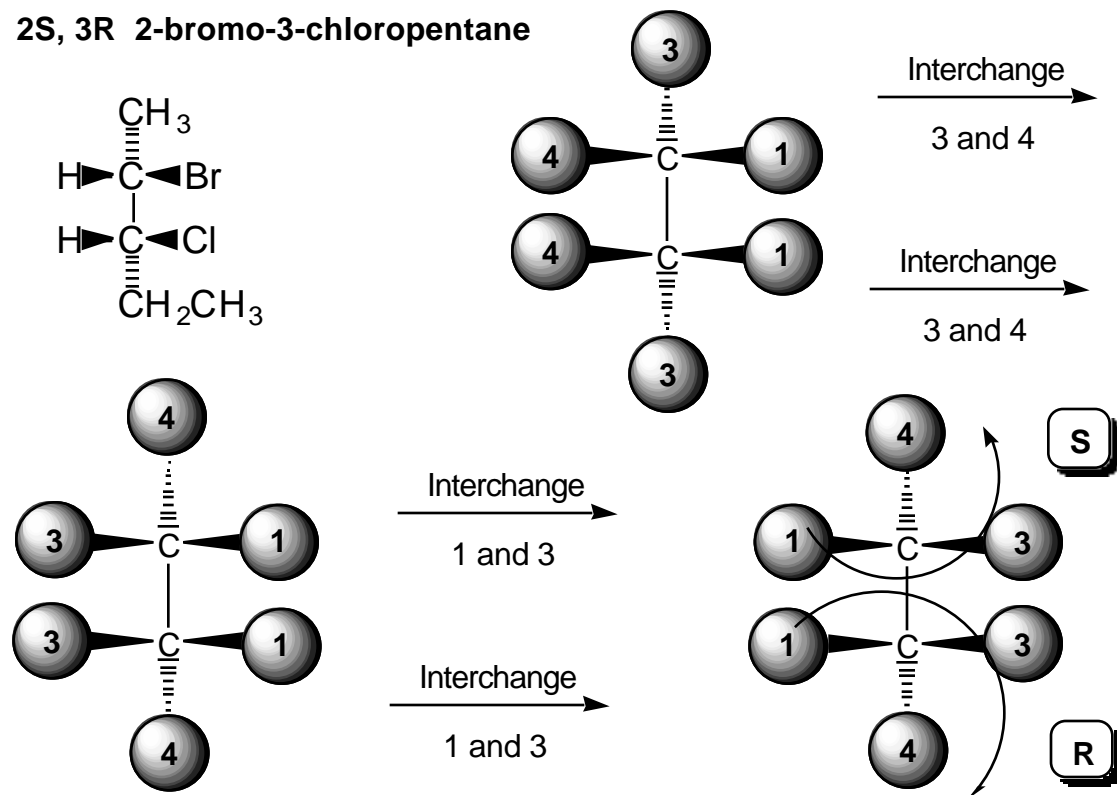
- R,Z** $\text{Br} > \text{CH}=\text{CHCH}_3 > \text{CH}_3 > \text{H}$ on chiral carbon
 $\text{CH}_3\text{CHBr} > \text{H}$ and $\text{CH}_3 > \text{H}$ on double bond

7.29 Specification of Configuration: Section 7.6

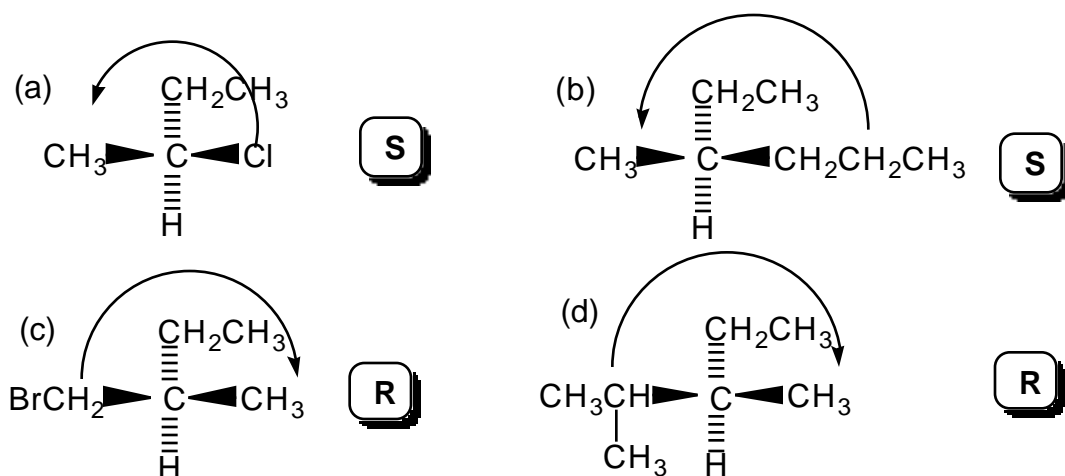
Lets put each chiral carbon atoms in a form that can easily be read. First on both the top and bottom chiral carbons interchange groups to get the hydrogens, the lowest priority group on each carbon, projecting behind the paper. Now interchange any other two groups to return to the original

configuration, but keep the hydrogens back. Note that in each case the other chiral carbon happens to be the second priority group. Since the low priority groups are behind the plane we can read the configuration directly.

2S, 3R 2-bromo-3-chloropentane

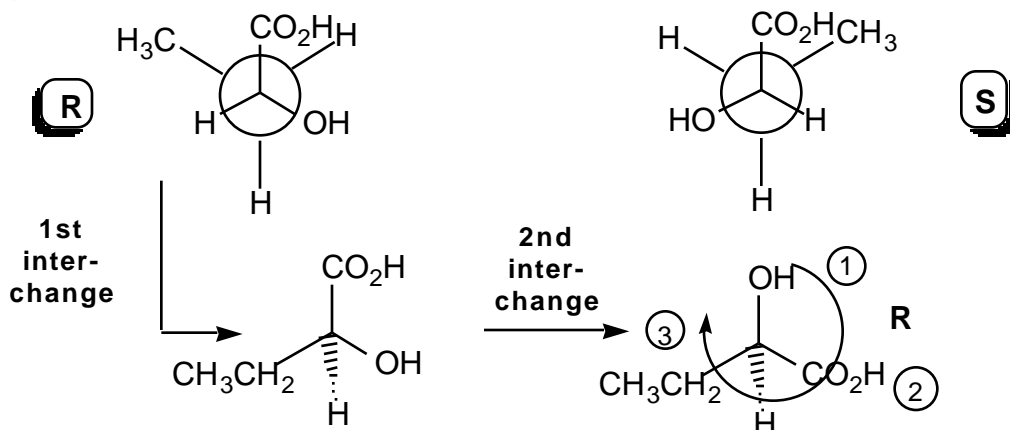


7.30 Specification of Configuration - R,S: Section 7.6



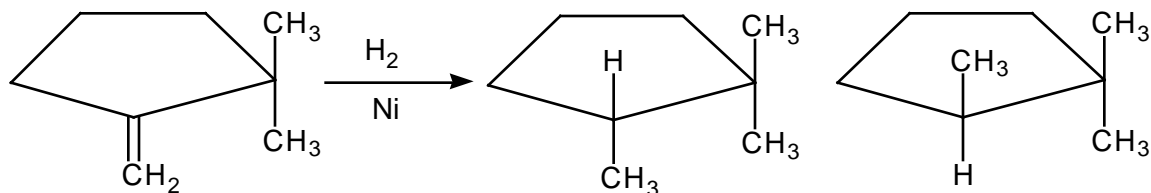
7.31 R,S Configurations: Section 7.6

To determine configuration is not as difficult as it might seem. Look at the Newman projection; you have three groups sticking out at you and one, the other carbon, projected behind. Exchange the back group, an ethyl, with the front hydrogen, the low priority group. Now you have hydroxy, acid, ethyl (this is the priority) in front. Exchange two other groups in front to restore the original configuration and determine R or S.



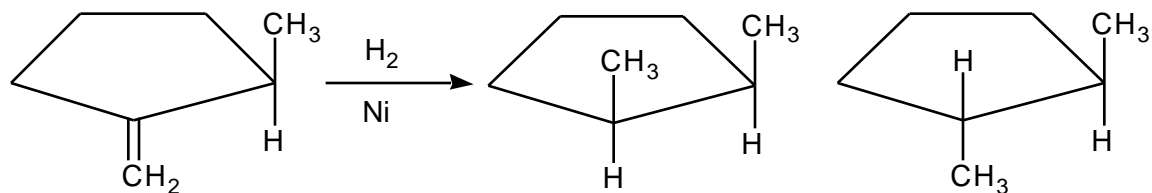
7.32 Stereoisomerism and Chemical Reactions: Section 7.8

In the first example a chiral carbon is generated in a compound that previously had none. The newly generated methyl can be above or below the ring but it makes no difference in terms of path of attack or stability of product. **A pair of enantiomers is formed in equal amounts.**

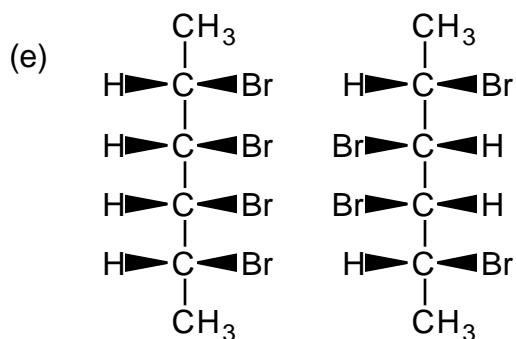
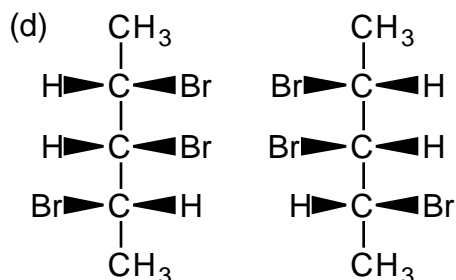
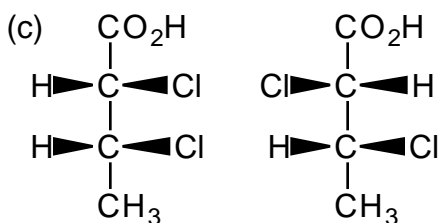
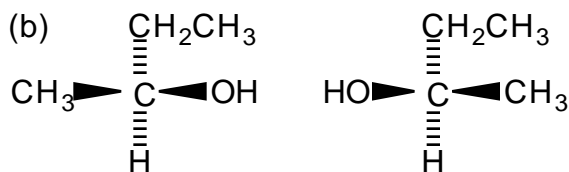
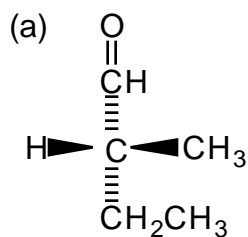


The second compound already has a chiral carbon atom. When the new one is generated, **a pair of diastereomers is formed in unequal amounts.** An examination of the diastereomers compared to the enantiomers can explain the production of enantiomers in equal amounts and diastereomers in unequal amounts. In one diastereomer, the newly generated methyl is on the same side of the ring as the existing methyl, a less stable cis arrangement. The two larger groups are on opposite sides in the other, a more stable trans arrangement. The products are of unequal stability and it is understandable they are formed in

unequal amounts. The enantiomers are of equal stability and formed in equal amounts. Identical paths of reaction in the first reaction and different ones in the second also support the difference in product ratio.



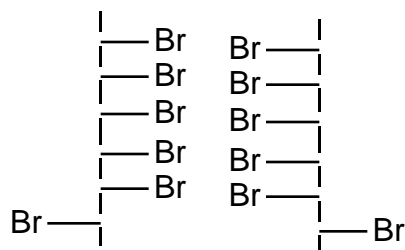
7.33 Stereoisomers: Sections 7.2, 7.4, 7.5



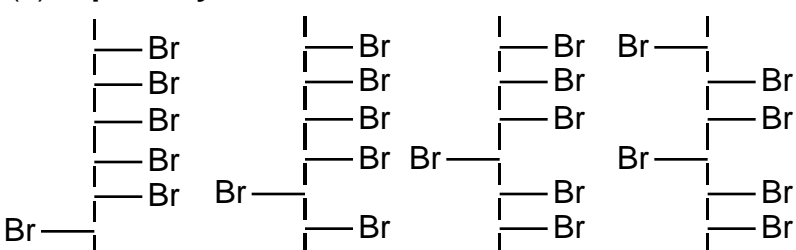
7.34 Stereoisomers: Section 7.4

The isomers are shown in simplified stick drawings. Since the top and bottom groups are identical, both methyl, they are not shown. Likewise, the hydrogens, (the other atoms on each of the chiral carbons) are not shown.

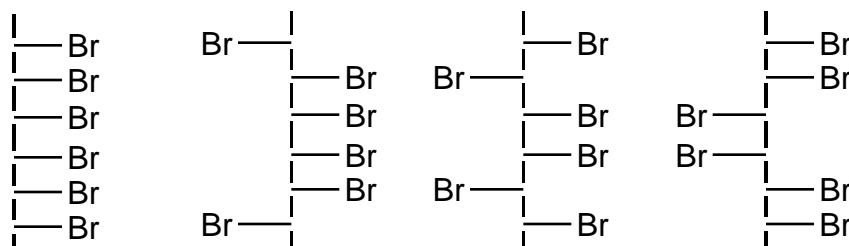
(a) Enantiomers



(b) Optically Active Diastereomers

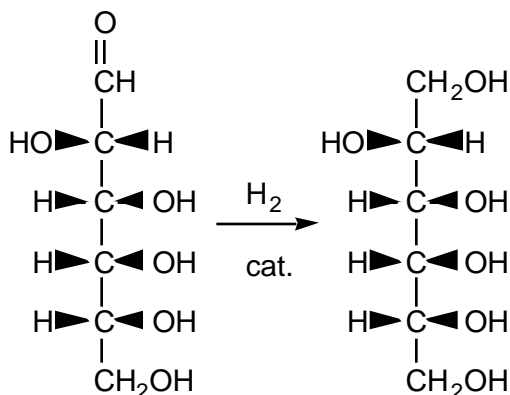


(c) Meso Compounds

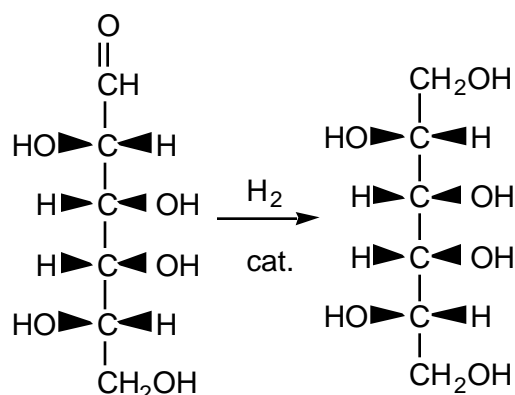
**7.35 Stereoisomerism and Chemical Reactions:** Section 7.4 and 7.8

(a) D-galactose is optically active. The top and bottom halves of the molecule are different so there is no possibility of rotating to test for superimposability on a mirror image. D-galactose is a pure enantiomer. However, the product of the reaction is a meso compound and not optically active. The aldehyde group on top was changed to an alcohol, the same as the bottom. If you draw the mirror image and rotate it 180° , you will find it is superimposable on the product shown.

(b)



Optically active product; the starting material is a diastereomer of galactose

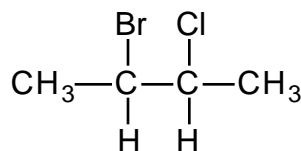


Optically inactive product: the starting material is the enantiomer of galactose. The product shown is the same as that formed from galactose.

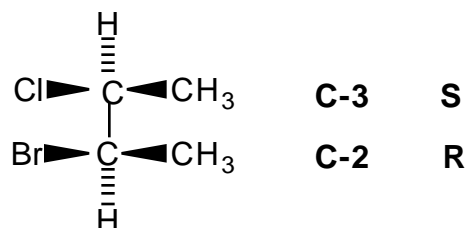
7.36 R,S Configurations: Section 7.6

(a)

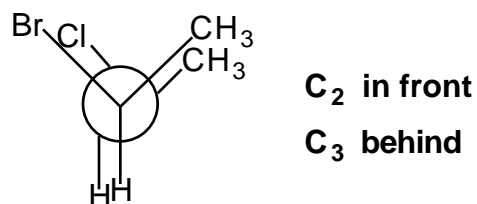
This is
2-bromo-3-chlorobutane



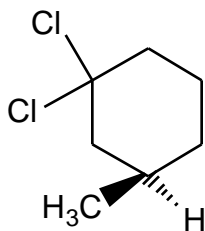
First draw the Fischer projection. For each chiral carbon, put the lowest priority group (H) behind the paper.



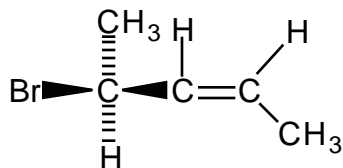
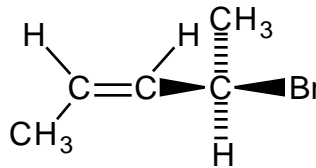
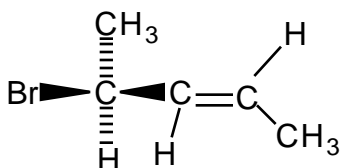
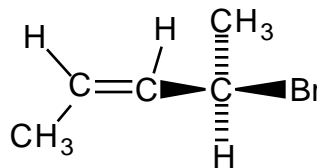
Now look up the C₂-C₃ bond of the eclipsed Fischer projection and translated it to a Newman projection.



(b)

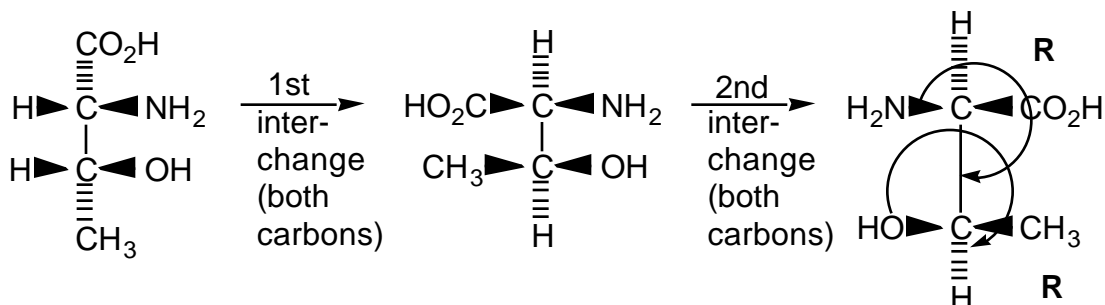


7.37 Stereoisomers:

S, cis**R, cis****S, trans****R, trans**

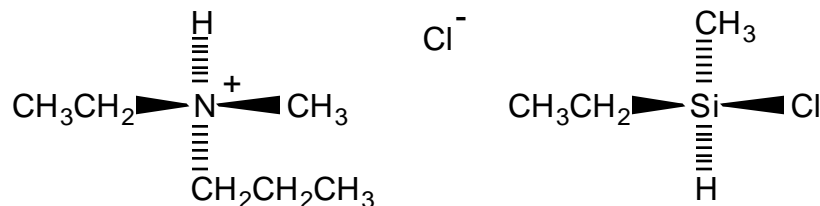
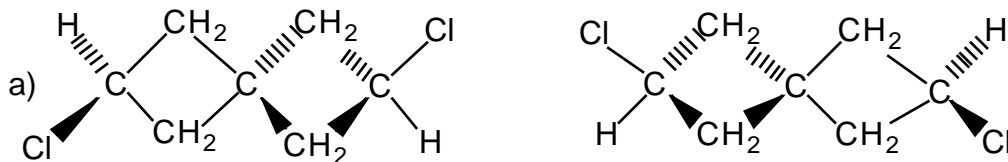
7.38 R and S Designations: Section 7.6

A way to do this problem is to move the lowest priority group on each carbon to a vertical bond going behind the paper by the interchange method and then interchange two other groups to get back to the original configuration. Then you can read the R,S directly. For example, let's use structure A in the answer to problem 7.9. This compound is 2R,3R.

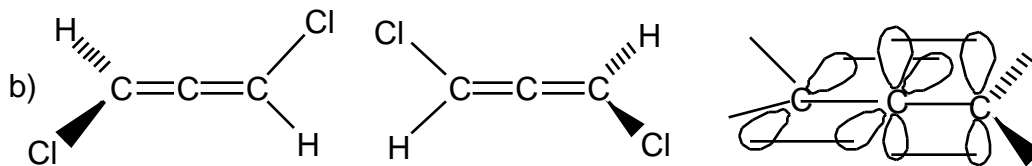


The configurations in Problem 7.9 are:

A	B	C	D
2R, 3R	2S, 3S	2S, 3R	2R, 3S

7.39 Optically Active Compounds without Chiral Carbons**7.40 Optically Active Compounds without Chiral Atoms**

The middle carbon is common to both rings. Since it is tetrahedral, one ring will be in the plane of the paper and other perpendicular (in and out of the paper). The H and Cl on the ring in and out of the paper are above and below the ring and thus in the plane of the paper. Those on the other ring are in front of and behind the paper plane. One cannot superimpose both rings and the Cl's (or H's) simultaneously.

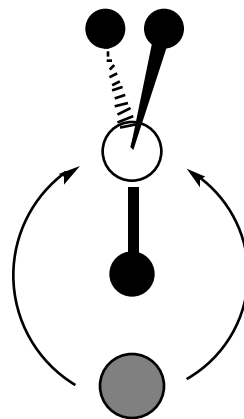
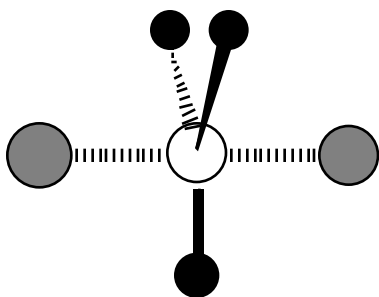


Since the middle carbon is involved in both double bonds, it has two p-orbitals which are perpendicular (90°) to each other. Thus the two pi-bonds are in perpendicular planes. Consequently, the H's and Cl's on each end are in perpendicular planes. No amount of rotating or turning the molecules will allow the simultaneous superimposition of both chlorines.

ACTIVITIES WITH MOLECULAR MODELS

Please see textbook.

8



Organic Halogen Compounds

CHAPTER SUMMARY

8.1 Introduction

Although organic halogen compounds are rarely found in nature, they do have a variety of commercial applications including use as insecticides, herbicides, dry-cleaning agents and degreasers, aerosol propellants and refrigerants, and important polymers.

8.2 Structure, Nomenclature, and Physical Properties

A. Structure and Properties

Alkyl halides are **organic halogen compounds** in which one or more hydrogens of a hydrocarbon have been replaced with a halogen. These compounds can be classified as **primary**, **secondary**, or **tertiary** depending on whether there are one, two, or three carbons respectively connected to the carbon bearing the halogen. In **aryl halides** the halogen is directly attached to a benzene or other aromatic hydrocarbon ring and in **benzylic halides**, the halogen is on a carbon directly

attached to a benzene ring. If the halogen is directly attached to a carbon-carbon double bond, it is termed **vinyl**, and if it is attached to a carbon directly attached to the double bond it is **allylic**.

Alkyl halides are generally **water insoluble** and have a **greater density** than water. Their **boiling points increase with molecular weight**; alkyl iodides have higher boiling points than the corresponding alkyl bromides which boil at higher temperatures than the chlorides

B. IUPAC Nomenclature

IUPAC nomenclature involves using the prefixes fluoro, chloro, bromo, and iodo to designate halogen in a molecule.

C. Common Nomenclature

A “salt-type” nomenclature is frequently used with alkyl halides in which the alkyl group’s name precedes the name of the halide. In addition, halogen derivatives of methane have familiar non-systematic names.

8.3 Preparations of Organic Halogen Compounds

A. Free-Radical Halogenation of Alkanes

B. Addition to Alkenes and Alkynes

C. Electrophilic Aromatic Substitution

D. Conversion of Alcohols to Alkyl Halides

CONNECTIONS 8.1 Drug Design

8.4 Nucleophilic Substitution

A. General Reaction

A characteristic reaction of alkyl halides is **nucleophilic substitution**. In this reaction, a **nucleophile (Lewis base)** replaces a halide ion, the **leaving group**. Chloride, bromide, and iodide are

effective leaving groups; common negative nucleophiles include OH^- , SH^- , NH_2^- , and their derivatives, as well as cyanide and acetylide ions.

B. Nucleophilic Substitution with Neutral Nucleophiles

Neutral nucleophiles include water, alcohols, and amines. These substances replace a leaving group such as halide ion; the product is a cationic salt that can be neutralized in some cases.

C. Introduction to Nucleophilic Substitution Reaction Mechanisms

There are two general nucleophilic substitution reaction mechanisms: (1) a one step process in which the nucleophile enters at the same time the leaving group exits ($\text{S}_{\text{N}}2$) and (2) a two step process in which the leaving group departs and then the nucleophile enters ($\text{S}_{\text{N}}1$).

D. The $\text{S}_{\text{N}}2$ Mechanism

The **$\text{S}_{\text{N}}2$ mechanism** is a one step process involving both the alkyl halide and nucleophile simultaneously. The nucleophile enters as the halide leaves, attacking the carbon from the side opposite to that from which the halide departs. The reaction is **bimolecular**; this means the reaction rate depends on the concentrations of both the alkyl halide and the nucleophile. The reaction involving optically active halides occurs with **inversion of configuration**.

E. The $\text{S}_{\text{N}}1$ Mechanism

The **$\text{S}_{\text{N}}1$ mechanism** is a two step process. In the first step the negative halide ion departs leaving a **carbocation intermediate**. In the second step the carbocation is neutralized by the nucleophile. $\text{S}_{\text{N}}1$ reactions commonly occur in neutral or acid conditions with neutral nucleophiles. The reaction rate is dependent on the slow step, carbocation formation from the alkyl halide, and is termed **unimolecular**. Reaction of an optically active alkyl halide by $\text{S}_{\text{N}}1$ results in the formation of a pair of enantiomers, an **optically inactive racemic mixture**, since the intermediate carbocation can be attacked from either side by the nucleophile.

F. Factors Influencing the Reaction Mechanism: **S_N2 versus S_N1**

Several factors influence whether a reaction will occur by an S_N1 or S_N2 mechanism: **carbocation stability, steric effects, strength of nucleophile, and the solvent**. **Tertiary halides** tend to react by the **S_N1** process because they can form the relatively stable tertiary carbocations and because the presence of three large alkyl groups sterically discourages attack by the nucleophile on the carbon-halogen bond. The **S_N2** reaction is favored for **primary halides** because it does not involve a carbocation intermediate (primary carbocations are unstable) and because primary halides do not offer as much steric hindrance to attack by a nucleophile as do the more bulky tertiary halides. **Strong nucleophiles** favor the **S_N2** mechanism and **polar solvents** promote **S_N1** reactions.

G. S_N1 and S_N2 : A Summary

1. *Reaction:* Both S_N1 and S_N2 reactions are simple substitution in which a nucleophile replaces a leaving group.
2. *Mechanism:* An S_N2 reaction proceeds by a one-step mechanism involving a five-centered transition state. An S_N1 reaction is a two-step process with a carbocation intermediate.
3. *Reaction Rates:* S_N2 reactions are bimolecular; the reaction rate depends on the concentrations of both the alkyl halide and the nucleophile. S_N1 reactions are unimolecular; the rate depends on the slowest of the two steps, the one in which the carbocation intermediate is formed.
4. *Stereochemistry:* S_N2 reactions involving optically active halides produce optically active products but with inversion of configuration of the chiral carbon atom bearing the halogen; attack by the nucleophile occurs on the opposite side from that the halide is leaving. S_N1 reactions proceed by a carbocation intermediate that can be attacked by the nucleophile from either side; a racemic mixture results.
5. *Structure and Reactivity:* S_N1 reactions are favored by bulky alkyl halides that form stable carbocations. Just the opposite is true for S_N2 reactions. Consequently, 3° halides usually react by an S_N1 mechanism, 1° by an S_N2 , and 2° by either depending on specific factors.

6. *Nucleophiles*: Strong nucleophiles favor S_N2 reactions.
7. *Solvent*: Polar solvents with unshared electron pairs such as water and alcohols favor S_N1 reactions.

8.5 Elimination Reactions of Alkyl Halides

Alkyl halides undergo **dehydrohalogenation** reactions in which **elimination** of a hydrogen and halogen from adjacent carbons produces a double bond.

A. The E_2 and E_1 Mechanisms

The elimination reaction mechanisms are analogous to those of nucleophilic substitution.

B. Comparison of E_2 and E_1 Reactions

The E_2 mechanism is a concerted one-step process in which a nucleophile abstracts a hydrogen ion from one carbon while the halide is leaving from an adjacent one. The E_1 mechanism is two-steps and involves a **carbocation intermediate** formed upon departure of the halide ion in the first step. E_2 reactions are **bimolecular** and the reaction rate depends on the concentrations of both the alkyl halide and nucleophile. E_1 reaction rates depend on the slowest step, formation of the carbocation, and are influenced only by the concentration of the alkyl halide; the reaction is **unimolecular**. E_2 reactions involve **anti elimination** and produce a specific alkene, either cis or trans. E_1 reactions involve an intermediate carbocation and thus give products of both **syn and anti elimination**.

8.6 Substitution versus Elimination

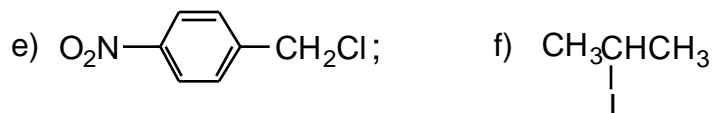
Nucleophilic substitution and elimination are competitive processes. Which prevails depends on a variety of factors. One important consideration is the stability of the alkene that would result from elimination. Since tertiary halides form the more stable highly substituted alkenes, they are more likely to react by elimination than primary halides.

SOLUTIONS TO PROBLEMS**8.1 Nomenclature**

- (a) 2-chloropentane; (b) 1,4-dibromo-2-butene; (c) p-difluorobenzene;
 (d) 1,1,1-trichloro-2,2-difluoroethane

8.2 Nomenclature

- (a) CBr_4 ; (b) CH_2Br_2 ; (c) CHI_3 ; (d) $\text{CH}_2=\text{CHBr}$;

**8.3 Nucleophilic Substitution**

CH_3I + reagents in a-i \longrightarrow

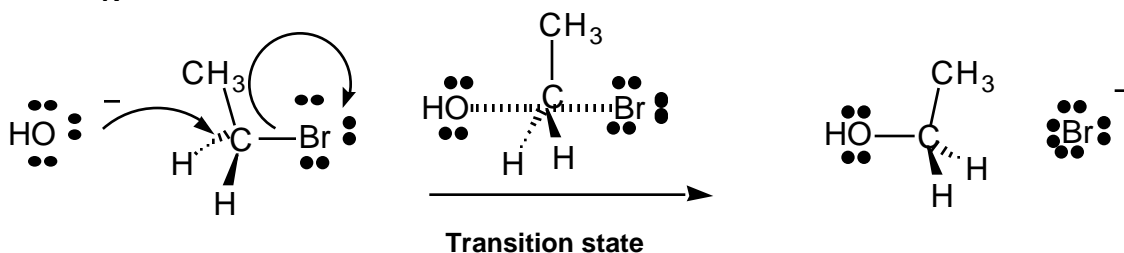
- (a) CH_3OH ; (b) $\text{CH}_3\text{OCH}_2\text{CH}_2\text{CH}_3$; (c) CH_3SH ; (d) CH_3SCH_3 ;
 (e) CH_3NH_2 ;
 f) $\text{CH}_3\text{NHCH}_2\text{CH}_3$; g) $\text{CH}_3\text{N}(\text{CH}_3)_2$; h) CH_3CN ; i) $\text{CH}_3\text{C}\equiv\text{CCH}_3$

8.4 Nucleophilic Substitution

- (a) $\text{CH}_3\text{CH}_2\text{CH}_2\text{Br} + \text{NaCN} \longrightarrow \text{CH}_3\text{CH}_2\text{CH}_2\text{CN} + \text{NaBr}$
 (b) $\text{CH}_3\text{CH}_2\text{CH}_2\text{CH}_2\text{Cl} + \text{NaOH} \longrightarrow \text{CH}_3\text{CH}_2\text{CH}_2\text{CH}_2\text{OH} + \text{NaCl}$
 (c) $\text{CH}_3\text{I} + \text{NaSCH}_3 \longrightarrow \text{CH}_3\text{SCH}_3 + \text{NaI}$

8.5 Nucleophilic Substitution

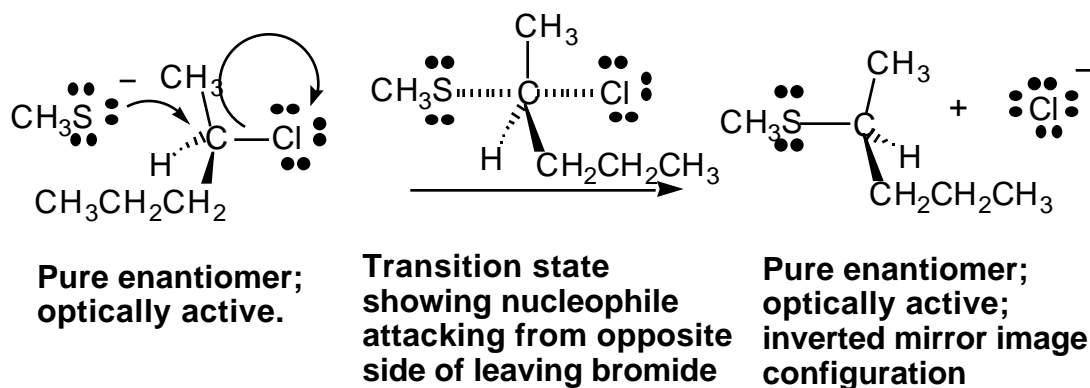
- (a) $\text{CH}_3\underset{\text{OH}}{\text{CH}}\text{CH}_2\text{CH}_3$ (b) $\text{CH}_3\underset{\text{OCH}_3}{\text{CH}}\text{CH}_2\text{CH}_3$ (c) $\text{CH}_3\underset{\text{N}(\text{CH}_3)_2}{\text{CH}}\text{CH}_2\text{CH}_3$

8.6 $\text{S}_\text{N}2$ Mechanism

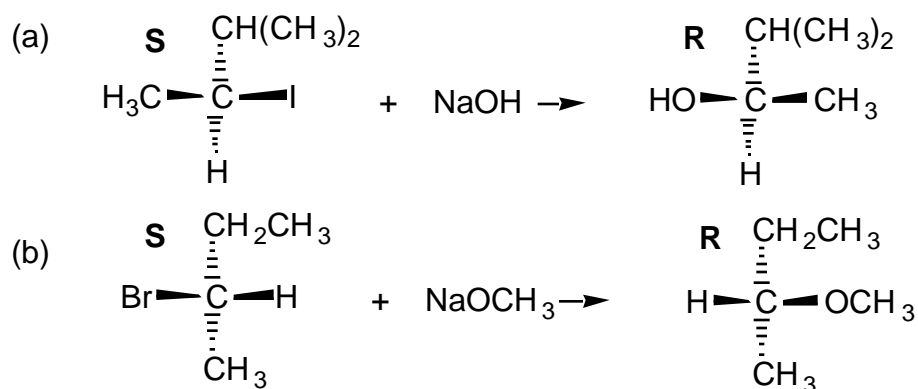
8.7 Reaction Rates

(a) 3x (b) 4x (c) 6x

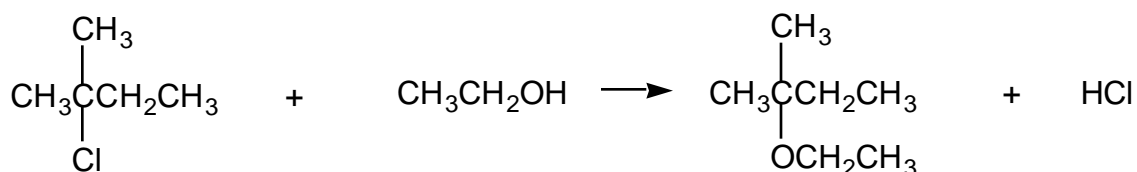
8.8 Reaction Rate Equations

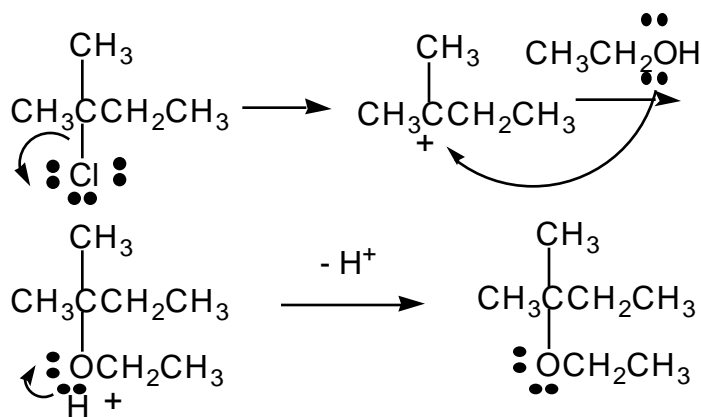
Rate = k (bromomethane) (NaOH) Rate = K (2-chloropentane) (NaSCH₃)8.9 S_N2 Mechanism with Stereochemistry

8.10-8.11 Inversion of Configuration



8.12 Nucleophilic Substitution



8.13 S_N1 Mechanism

8.14 Reaction Rate Equation

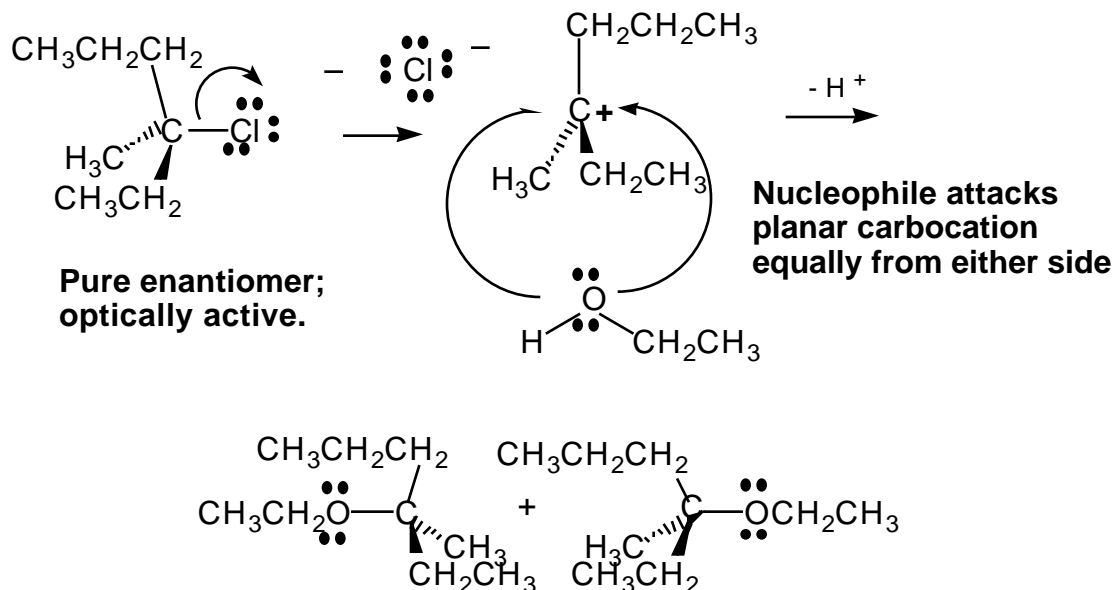
Rate = k (2-chloro-2-methylbutane)

8.15 Reaction Rates

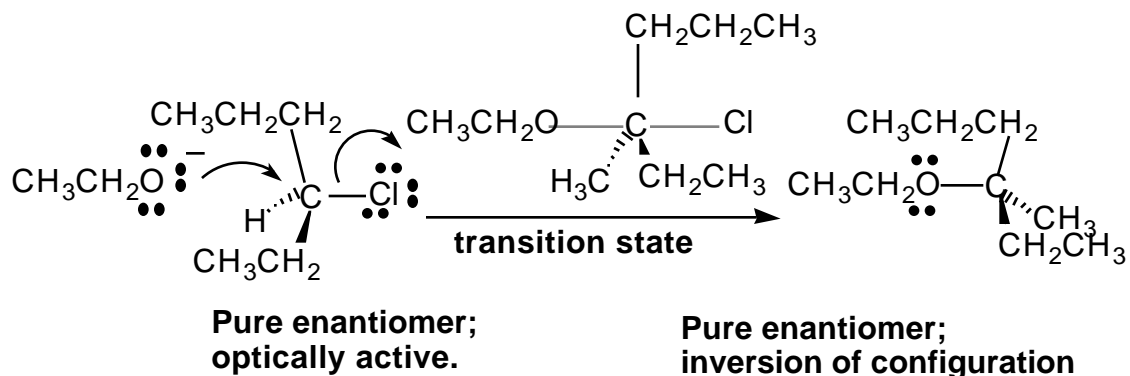
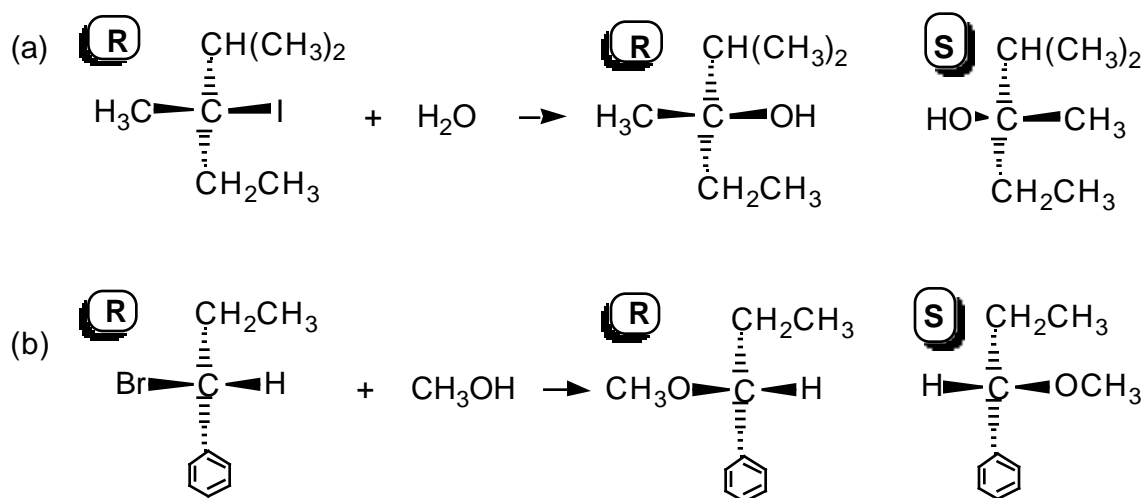
(a) no effect (b) 2x (c) 4x (d) 3x

8.16 S_N1 and S_N2 Reaction Mechanisms

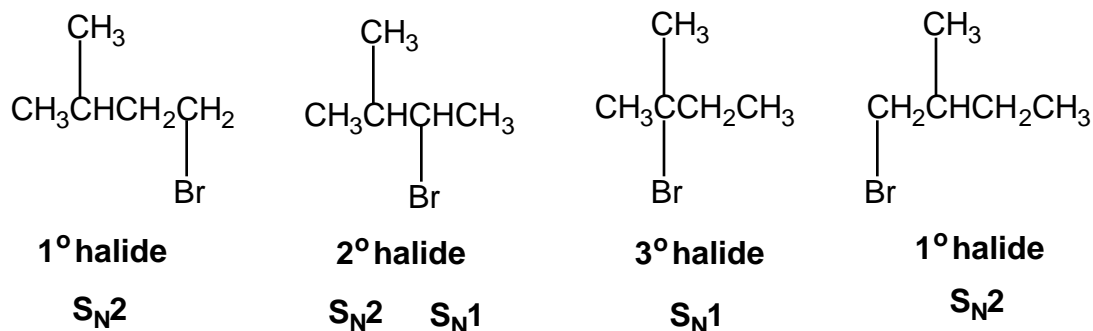
(a) S_N1



Both inversion and retention of configuration occur equally. A pair of enantiomers is the result. This is an optically inactive racemic mixture.

(b) S_N2 Mechanism8.17 -8.18 Racemization in S_N1 Reactions8.19 S_N1 Mechanism and Carbocation Stability

Tertiary carbocations are quite stable so tertiary halides tend to react by S_N1 mechanisms since the mechanism involves carbocation intermediates. Primary carbocations are unstable and primary halides react by the S_N2 mechanism in which there is no carbocation intermediate.



8.20 Steric Effects and S_N2 Mechanisms

The primary bromide, 1-bromobutane, is less crowded around the reacting carbon and thus more accessible to the incoming nucleophile. The S_N2 mechanism is likely to proceed faster in this case than with the more crowded secondary bromide.

8.21 Strength of Nucleophile

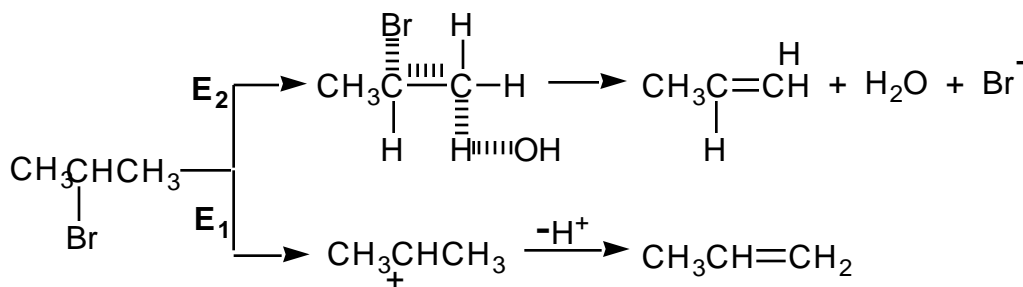
(a) CH₃O⁻ because it is negative; (b) NH₂⁻ because nitrogen is less electronegative than oxygen; (c) CH₃NH₂ because nitrogen is less electronegative than oxygen; (d) ⁻SH because it is negative and S is less electronegative than O; (e) CH₃CH₂SH because sulfur is less electronegative than oxygen.

8.22 Predicting Mechanisms

(a) S_N2: the reactants are a primary halide and a strong, negative nucleophile.

(b) S_N1: the reactants are a tertiary halide and a neutral nucleophile.

8.23 E₁ and E₂ Mechanisms



8.24 Rates of Elimination Reactions

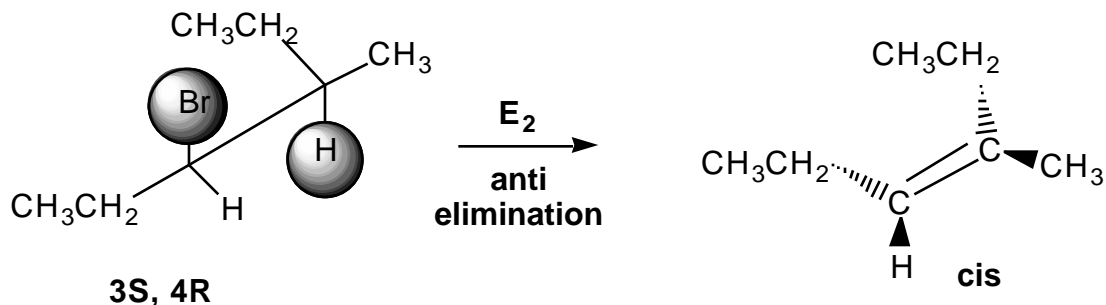
(a) double the reaction rate for both; (b) doubles the rate of E₂ but has no influence on E₁. (c) quadruples the rate of E₂ and doubles that of E₁; (d) increases E₂ 12 times and E₁ three times.

8.25 Rates of Substitution Reactions

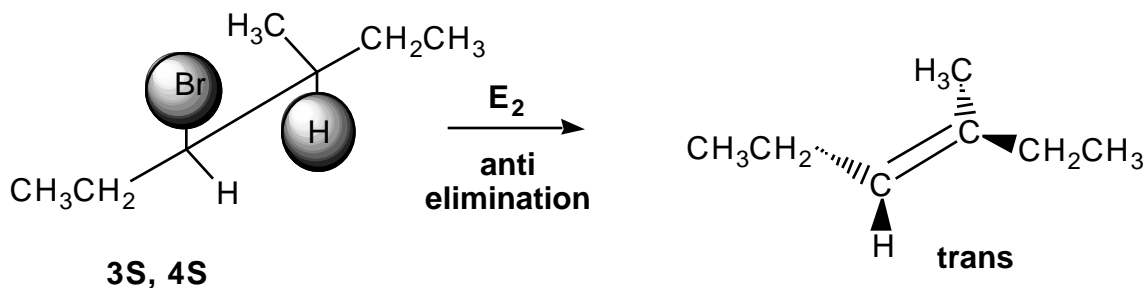
The answers are the same as those in problem 8.24.

8.26 Anti Elimination and E₂ Reactions

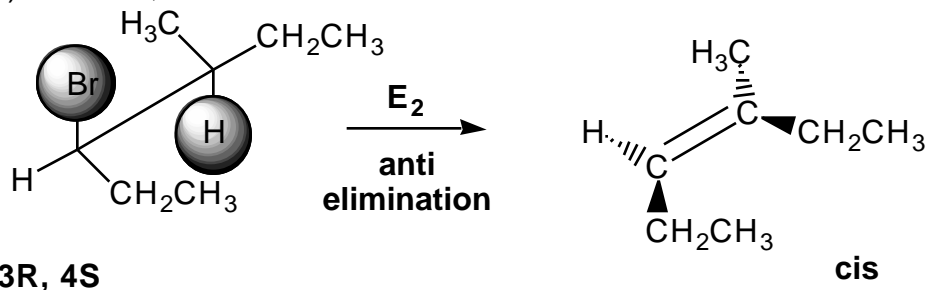
(a) Interchanging two groups on a chiral carbon produces the mirror image. Thus one interchange on the 3R carbon converts it to 3S.



(b) Interchanging two groups on the other carbon gives the mirror image configuration.

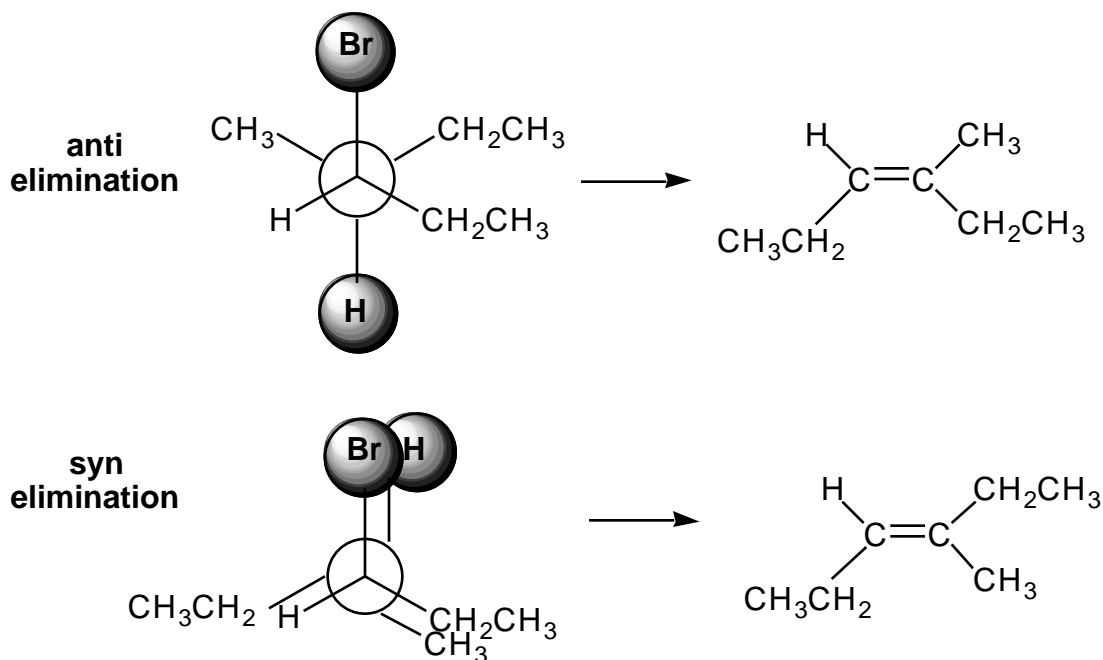
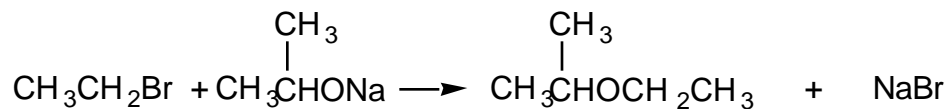


(c) from 3R, 4S

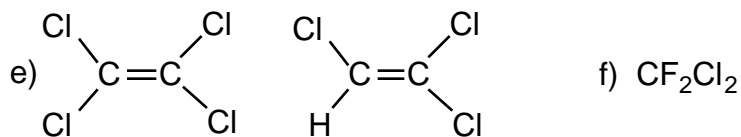
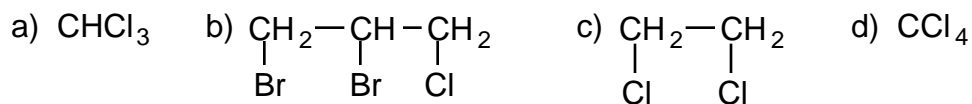


8.27 Syn and Anti Elimination

The E₂ reaction proceeds exclusively via anti elimination whereas the E₁ reaction is capable of both. Rotate the carbon-carbon bond to position for syn and anti elimination. Eliminate the H and Br as highlighted and then look down the axis from the front to back carbon and imagine a double bond has formed. Translate this into the products shown.

**8.28 Williamson Synthesis****8.29 IUPAC Nomenclature:** Section 8.2B

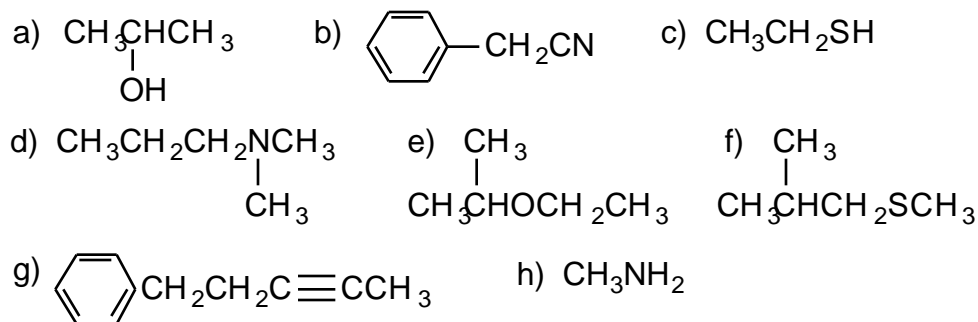
- (a) 3-bromopentane; (b) chloroethane; (c) 1-iodopropane;
 (d) 4,4-dimethyl-1,1,1-tribromopentane;
 (e) 2,4,6-trichloroheptane; (f) trans (or E) 5-bromo-6-methyl-2-heptene;
 (g) 5-iodo-2-hexyne; (h) meta bromochlorobenzene;

8.30 Nomenclature: Section 8.2B**8.31 Common Nomenclature:** Section 8.2C

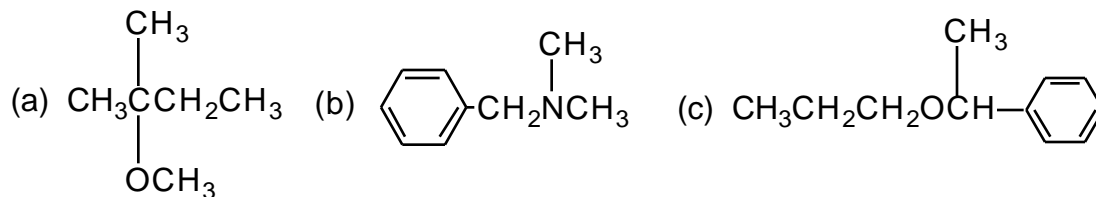
- (a) CH_3Br ; (b) CH_2Cl_2 ; (c) CHBr_3 ; (d) CF_4 ; (e) $\text{CH}_2=\text{CHCH}_2\text{I}$;

(f) $\text{CH}_2=\text{CHCl}$; (g) $\text{CH}_3\text{CHClCH}_2\text{CH}_3$; (h) $\text{CH}_3\text{CHBrCH}_3$

8.32 Nucleophilic Substitution: Section 8.4A

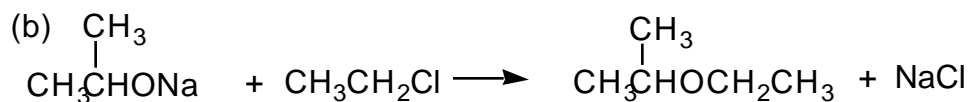
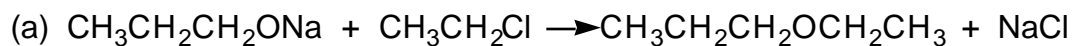


8.33 Nucleophilic Substitution: Section 8.4B



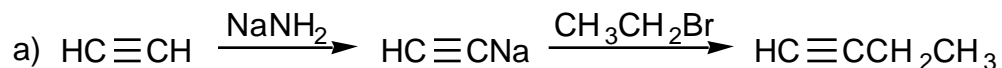
8.34 Williamson Synthesis of Ethers: Sections 8.4A and 8.6

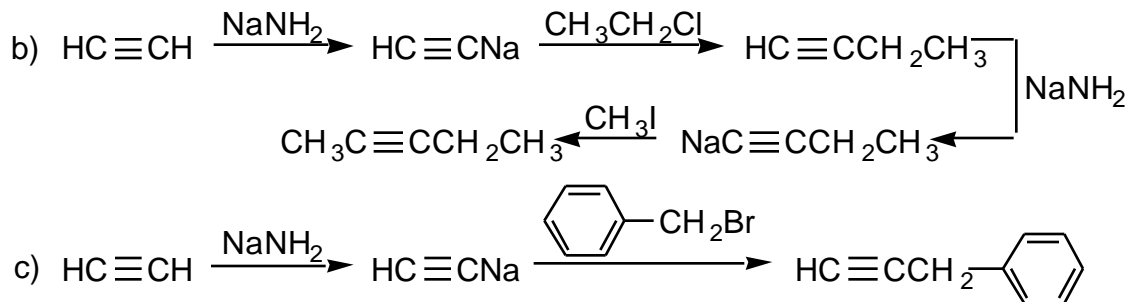
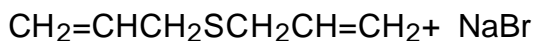
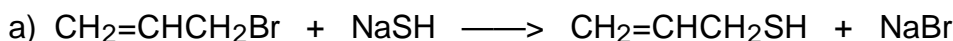
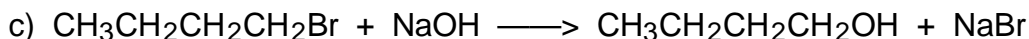
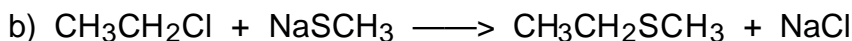
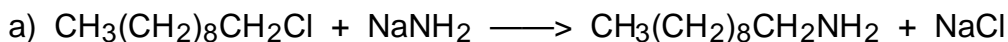
The halogen can be Cl, Br, or I.



8.35 Nucleophilic Substitution in Preparing Alkynes: Sections 5.8 and 8.4A

The halogen can be Cl, Br, or I.

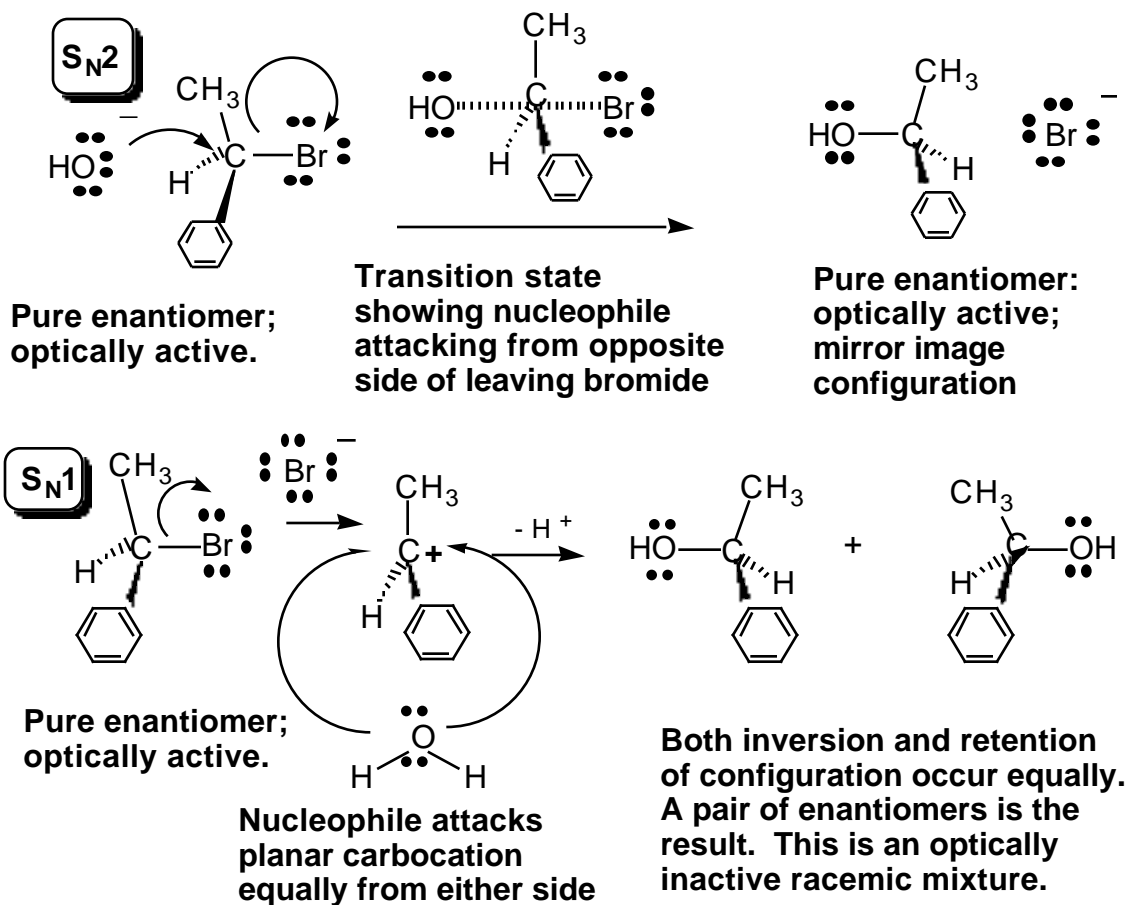


**8.36 Nucleophilic Substitution:** Section 8.4A**8.37 Synthesis:** Section 8.4A**8.38 S_N1 and S_N2 Mechanisms:** Section 8.4G

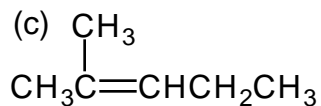
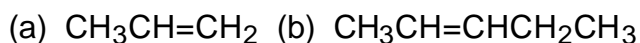
Characteristic	S _N 1	S _N 2
Rate Expression	Rate = k(RX)	Rate = k(RX)(Nu)
Reaction Intermediate	Carbocation (two steps)	None (one step)
Stereochemistry	Racemization: inversion and retention.	Inversion of configuration
Relative Reaction Rates of Alkyl Halides	3° > 2° > 1°	1° > 2° > 3°
Effect of Increasing Nucleophile Concentration	None, reaction rate is independent of the nucleophile	Reaction rate is increased
Effect of Increasing Alkyl Halide Concentration	Reaction rate is increased	Reaction rate is increased

Effect of Polar Solvent	Increases rate of reaction and likelihood of S_N1	Decreases rate and likelihood of S_N2
Effect of Non-Polar Solvent	Decreases rate and likelihood of S_N1	Increases rate and likelihood of S_N2
Effect of Bulky Groups at Reaction Center	Favors S_N1 as crowding decreased in carbocation	Disfavors S_N2 as transition state is more crowded (pentavalent)
Strength of the Nucleophile	Disfavors S_N1	Favors S_N2

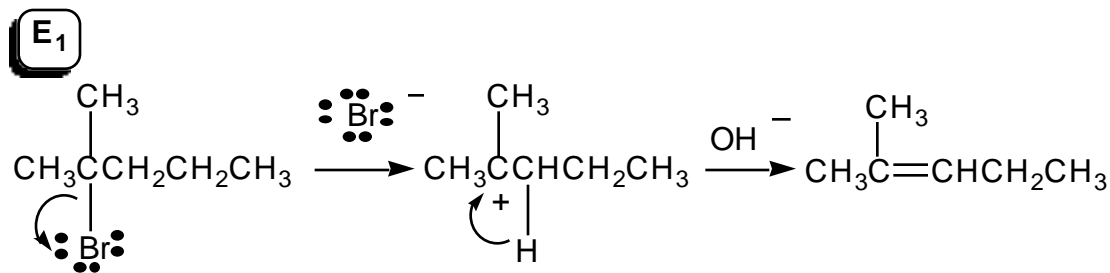
8.39 Nucleophilic Substitution Mechanisms: Section 8.4G



8.40 Elimination Reactions: Sections 4.5 and 8.5

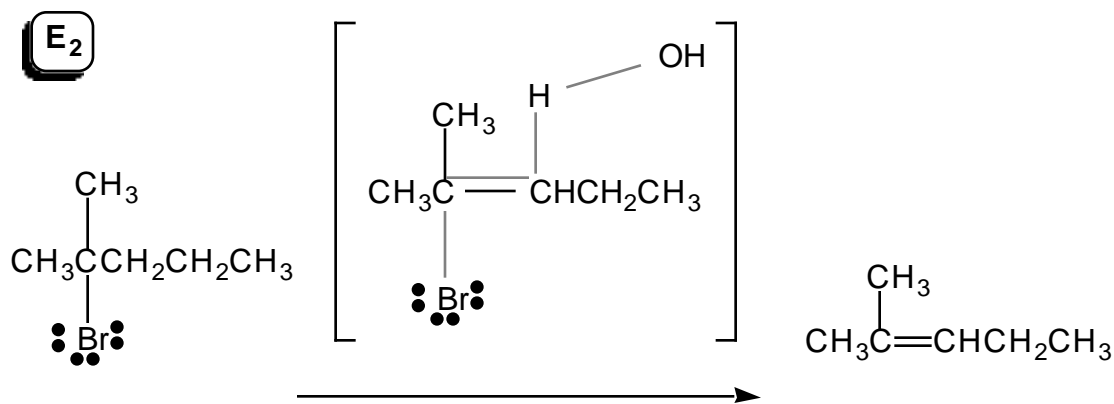


8.41 Elimination Reaction Mechanisms: Section 8.5

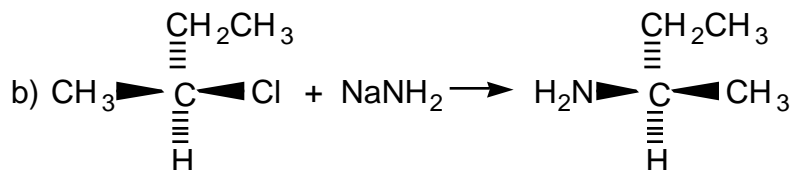
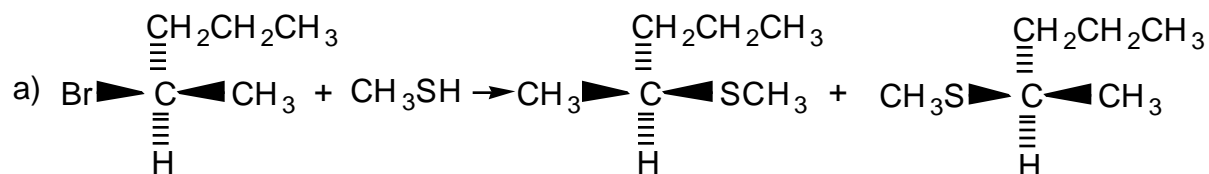


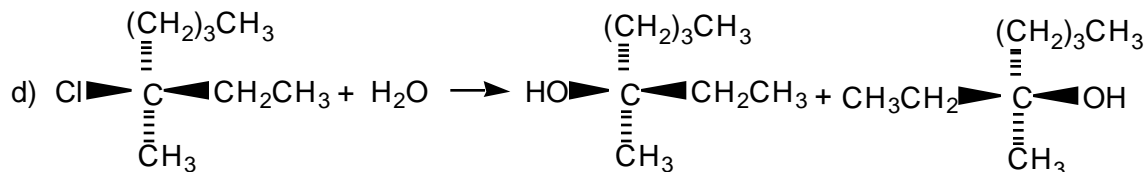
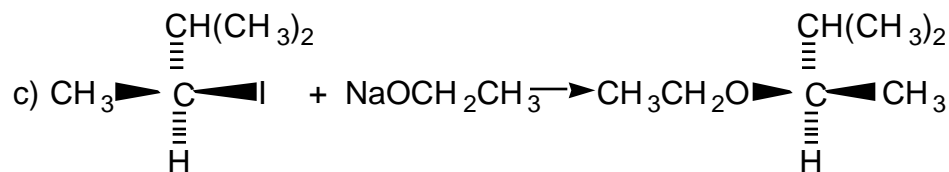
STEP 1: Bromide departs and is solvated by the aqueous ethanol solvent. A carbocation intermediate results.

STEP 2: Hydroxide abstracts the hydrogen ion to complete the elimination. The carbocation is neutralized, the double bond forms.



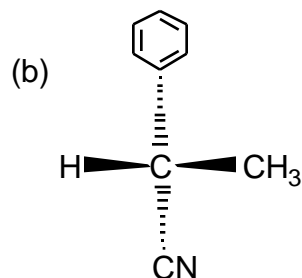
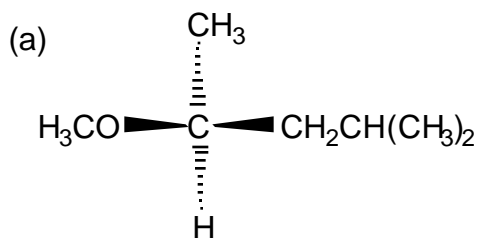
This is a concerted one-step mechanism in which bonds are breaking and new bonds forming all at once.

8.42 S_N1 and S_N2 Stereochemistry: Section 8.4 D.2 and E.2

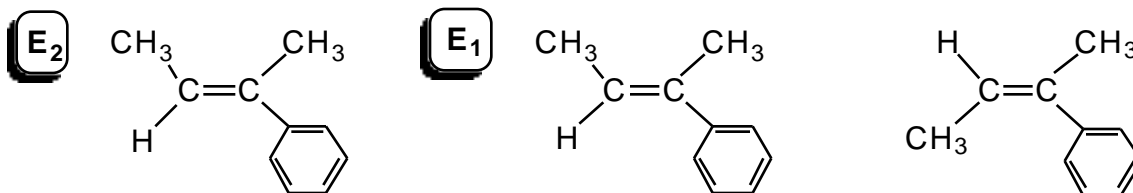


8.43 S_N1 and S_N2 Stereochemistry: Sections 8.4D.1 and E.1

S_N2 reactions proceed with inversion of configuration. Since both starting materials were optically active, the products are also optically active.



8.44 E₁ and E₂ Stereochemistry: Section 8.5

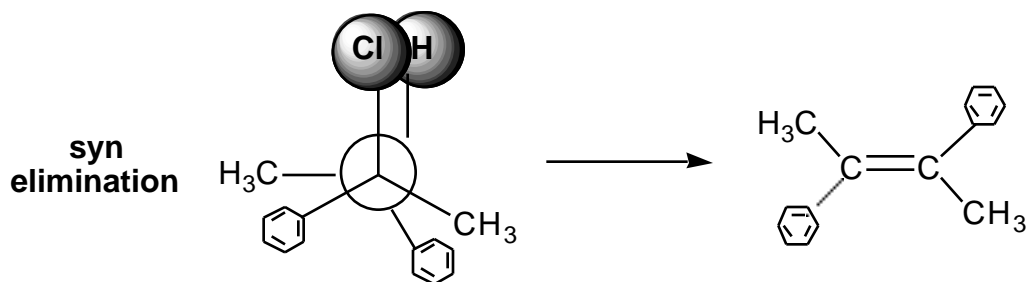
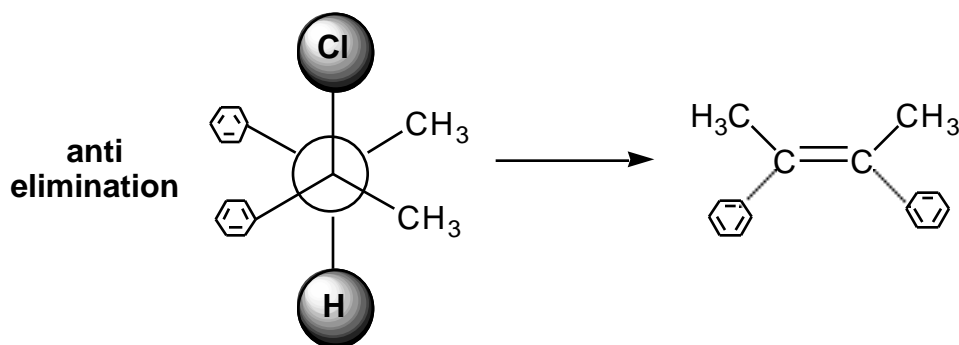
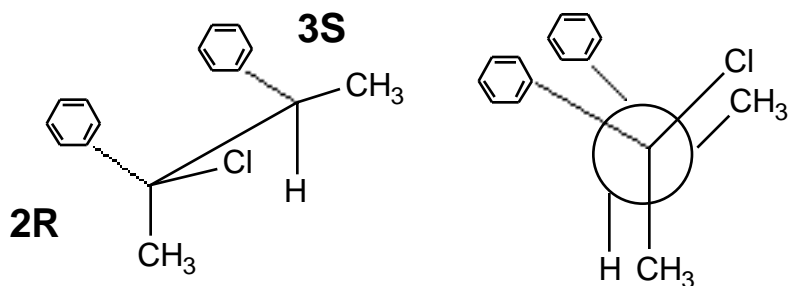
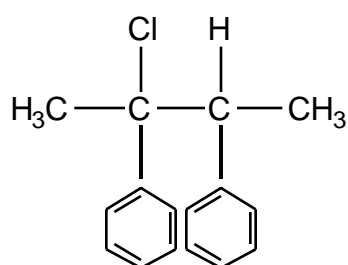


8.45 E₁ and E₂ Stereochemistry: Section 8.5

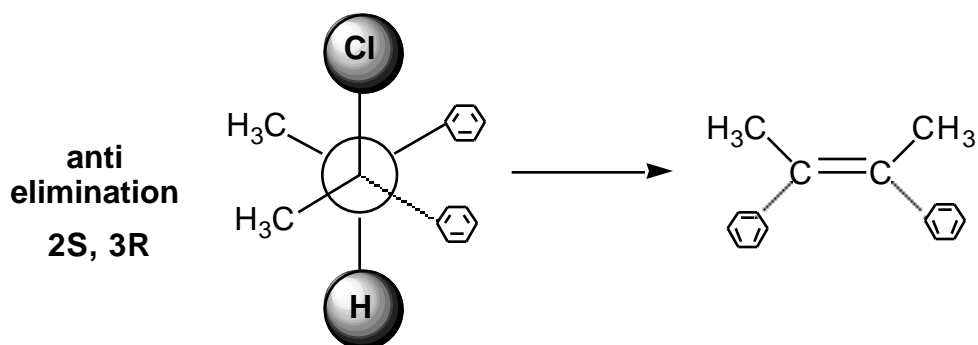
First draw the compound without stereochemistry. Then we will convert it to a Newman projection with the 2R, 3S configuration. This is most easily done by drawing an eclipsed Newman projection and putting the two low priority groups down and placing the others to conform to the stated configuration. Finally, rotate the Newmans to syn and anti elimination and draw the products.

E₂: anti elimination only

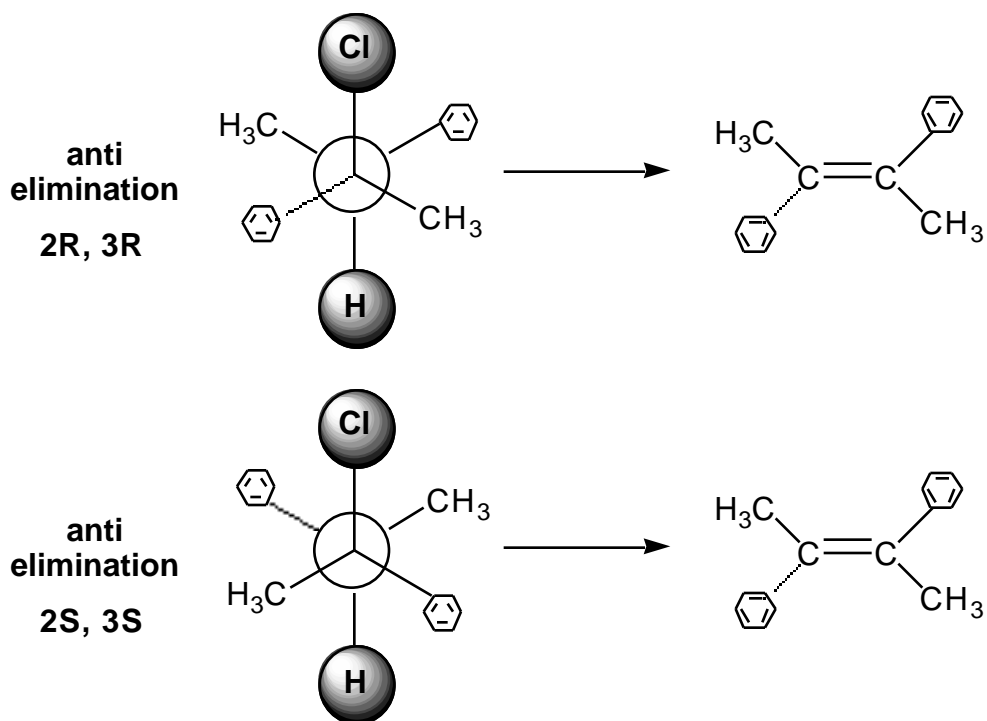
E₁: both syn and anti eliminations are possible



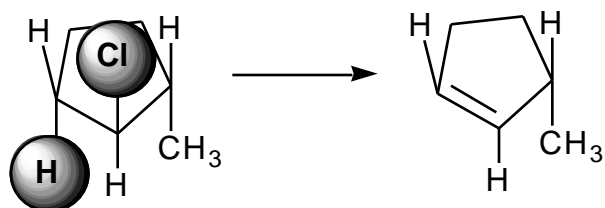
Another configuration that will produce the trans isomer.



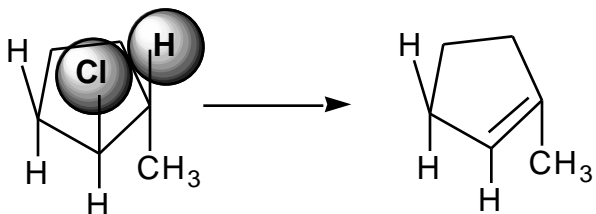
Two configurations that will produce the trans isomer.



8.46 E₁ and E₂ Stereochemistry: Sections 4.5B and 8.5



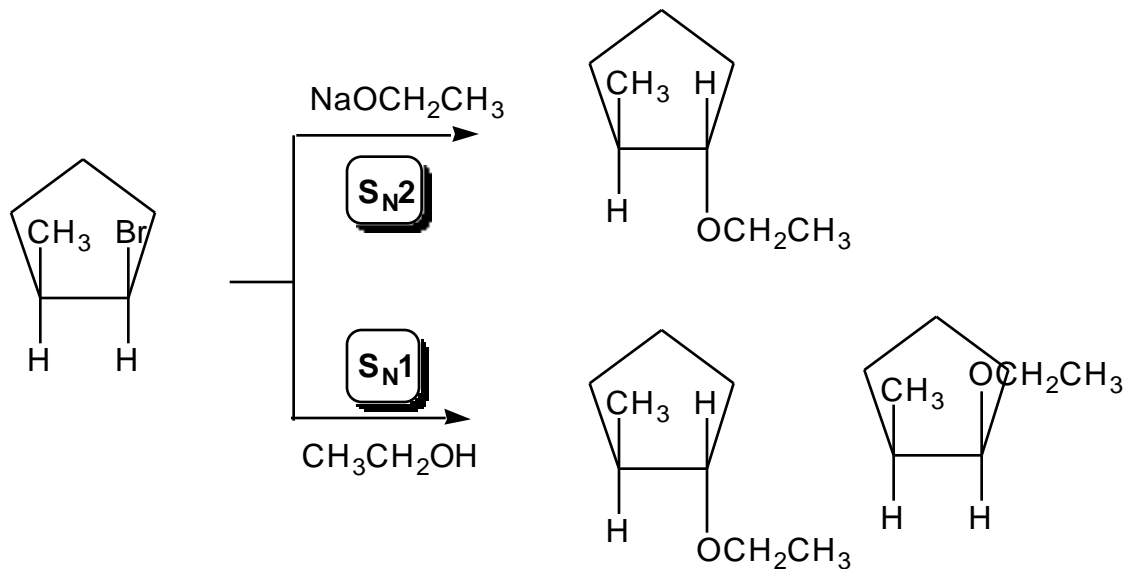
E₂ reactions proceed by anti elimination. The only anti possibility is shown and it does not give the most stable product (Saytzeff).



E₁ reactions proceed by syn or anti elimination. The syn shown gives the most stable alkene (Saytzeff).

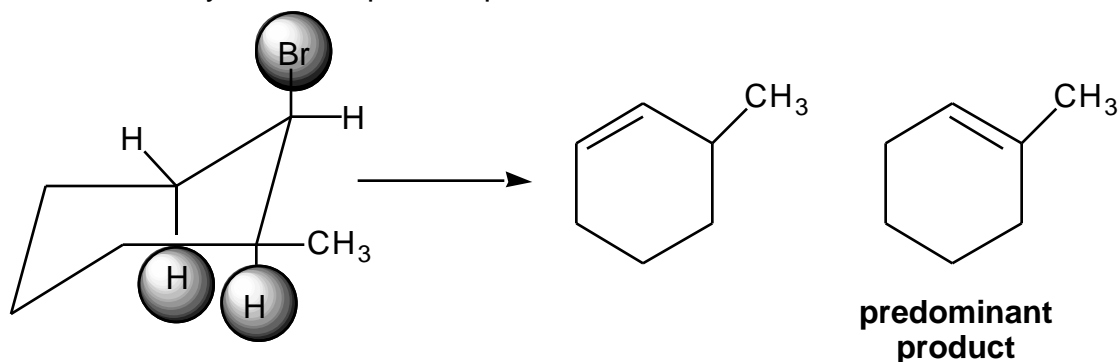
8.47 Nucleophilic Substitution Reactions: Section 8.4D.2

This first reaction is an S_N2 reaction as a result of the strong nucleophile. S_N2 reactions proceed with inversion of configuration so the product will be trans 1-ethoxy-2-methylcyclopentane. The S_N1 reaction involves a carbocation intermediate that can be attacked from either side and consequently the cis and trans products are formed.

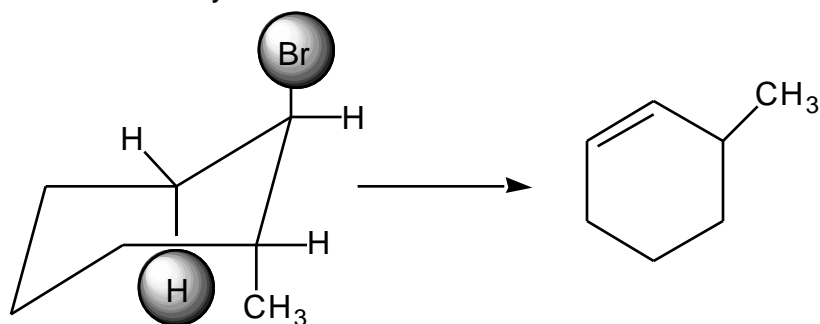


8.48 E₂ Elimination

(a) The chair shown has two possibilities for anti elimination. The more substituted Saytzeff Rule product predominates as it is more stable.



(b) The chair shown here has only one possibility for anti elimination and that product forms exclusively despite the fact that it is not the most substituted. You may notice that both groups are axial. Actually the diequatorial conformer is more stable and preferred but E₂ elimination occurs only on the small amount that exist at any one time in the diaxial conformation.



8.49 Nucleophilic Substitution Reactions: Section 8.4F



These are both primary halides and because they do not form stable carbocations and because they are relatively unhindered sterically, they react by $\text{S}_{\text{N}}2$.



The tertiary halide on the left is hindered to attack by a nucleophile but forms a stable carbocation. Consequently it reacts by $\text{S}_{\text{N}}1$. The other halide is secondary and can react by either mechanism.

8.50 Nucleophilic Substitution Reactions: Section 8.4F



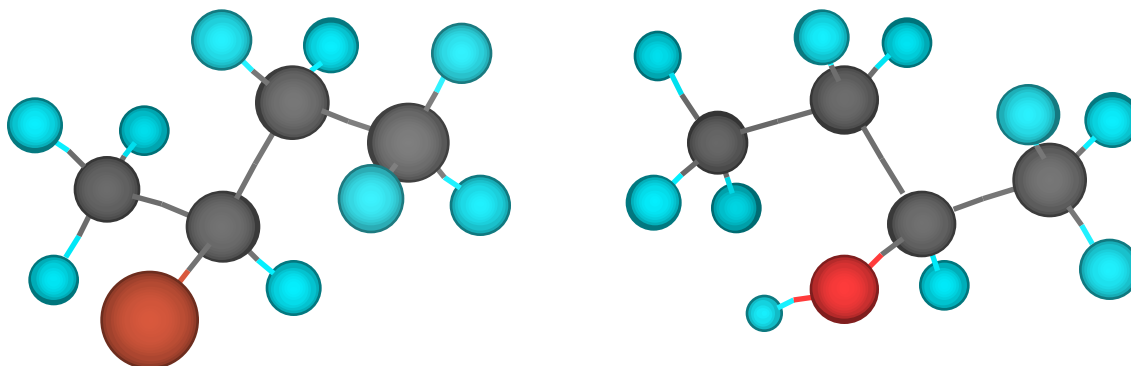
8.51 Substitution versus Elimination: Section 8.6



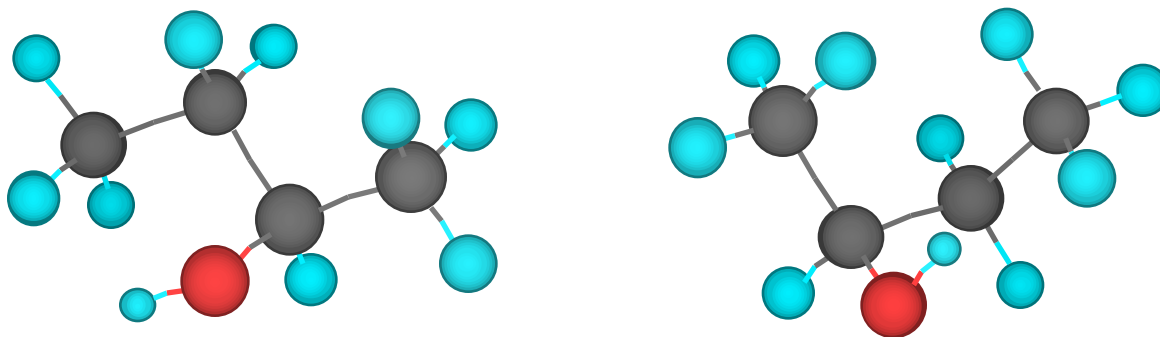
III is a tertiary halide and forms a highly substituted alkene. II forms a disubstituted alkene and I forms only a monosubstituted alkene. Elimination is favored when highly substituted stable alkenes are possible.

ACTIVITIES WITH MOLECULAR MODELS

1. Make a model of one of the enantiomers of 2-bromobutane. Make a model of the enantiomer that results from an S_N2 reaction in which the bromine is replaced by an OH. Make sure you have inversion of configuration. Look at the original enantiomer and visualize the OH coming in from the rear and displacing the bromine.



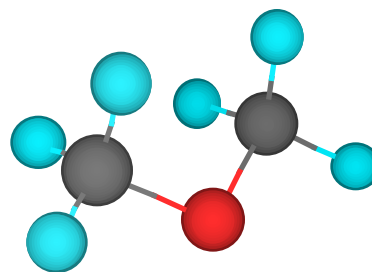
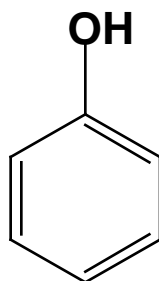
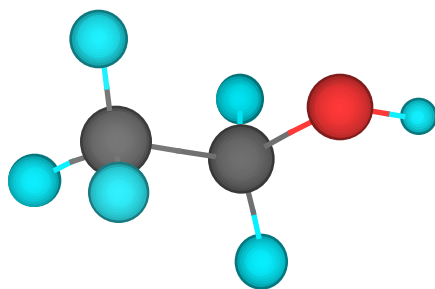
2. Now, using the 2-bromobutane enantiomer from exercise 1, make the models of the racemic mixture formed when the bromine is replaced by OH in an S_N1 reaction. Visualize the Br leaving first and the water attacking from either side of the carbocation to form the pair of enantiomers.



3. Make molecular models of the E_2 reactions described in section 8.5B.2. They may help you in understanding the stereochemistry.

Please see textbook.

9



Alcohols, Phenols, and Ethers

CHAPTER SUMMARY

9.1 Structure and Nomenclature

Alcohols, phenols, and ethers can be thought of as derivatives of water. Replacement of one hydrogen on water results in an **alcohol**, and replacement of both gives an **ether**. In **phenols**, one hydrogen of water is replaced by an aromatic ring. A **primary alcohol** has only one alkyl group attached to the carbon bearing the OH; a **secondary alcohol** has two and a **tertiary alcohol** has three.

A. IUPAC Nomenclature of Alcohols

The base name of an alcohol is derived from the Greek for the longest continuous carbon chain followed by the suffix **-ol**. If the alcohol is unsaturated, the double or triple bonds are designated with the suffixes -

en and **-yn** respectively. The carbon chain is numbered to give the lowest number to the alcohol group.

B. IUPAC Nomenclature of Ethers

The name of an ether is based on the longest carbon chain connected to the ether oxygen. The other alkyl group is named as an **alkoxy group**.

C. IUPAC Nomenclature of Phenols

Phenols are named according to the rules for a substituted benzene ring, except that the family name is phenol rather than benzene. Numbering of the ring begins with the hydroxyl group.

D. Common Nomenclature of Alcohols and Ethers

In common nomenclature, alcohols are often named with the alkyl group followed by alcohol (such as ethyl alcohol) and ethers are named using the names of the two alkyl groups followed by ether (such as diethyl ether).

9.2 Physical Properties - Hydrogen Bonding

Hydrogen bonding causes the boiling points of alcohols to be higher than those of compounds of similar molecular weight in other functional groups. Hydrogen bonding is an electrostatic attraction between the partially positive OH hydrogen of one molecule and a non-bonding electron-pair on the oxygen of another molecule. Because of hydrogen bonding, low molecular weight alcohols are water soluble. Hydrogen bonding occurs in molecules where hydrogen is bonded to a strongly electronegative element such as nitrogen, oxygen, or fluorine.

CONNECTIONS 9.1 Methyl, Ethyl, and Isopropyl Alcohols

9.3 Uses of Alcohols, Ethers, and Phenols

A. Alcohols

Methyl alcohol is used in industrial synthesis, as a solvent, and as a clean burning fuel. **Ethyl alcohol** is beverage alcohol; it is also used as a solvent and antiseptic. **Isopropyl alcohol** is rubbing alcohol.

B. Polyhydric Alcohols

Ethylene glycol is antifreeze and **glycerol** is a humectant. Glycerol can be converted into the explosive nitroglycerin.

C. Diethyl Ether

Diethyl ether is an important solvent and was once widely used as a general anesthetic.

D. Phenols

Phenol and many of its derivatives are used in over-the-counter medications as disinfectants and local anesthetics. They are also used as antioxidants, preservatives and photographic developers.

CONNECTIONS 9.2 Neurotransmitters - The Heart of the Matter**9.4 Preparations of Alcohols and Ethers****A. Hydration of Alkenes****B. Nucleophilic Substitution****C. Reduction of Aldehydes and Ketones****9.5 Reaction Sites in Alcohols, Phenols, and Ethers**

The **reaction sites** in alcohols, phenols, and ethers are the **polar bonds** (carbon-oxygen and oxygen-hydrogen) and the **lone pairs of electrons** on the oxygen. The unshared electron-pairs on alcohols and ethers make these compounds **Lewis bases**. Oxonium ions, in which the oxygen has three bonds and is positive, result from the protonation of alcohols and ethers. Most reactions of alcohols involve the **O-H bond, C-O bond, or both**.

9.6 Reactions Involving the O-H Bond of Alcohols and Phenols**A. Relative Acidities of Alcohols and Phenols**

The polar O-H bond of alcohols makes them weak acids. By the **Bronsted-Lowry** definition, acids are hydrogen ion donors and bases are hydrogen ion acceptors in chemical reactions. **Strong acids** are 100% ionized in water and **weak acids** are only partially ionized. Weak acids establish an equilibrium in water between their ionized and un-ionized forms. This equilibrium and the strength of an acid is described by the **acidity constant, K_a** . K_a is defined as the concentrations of the ionized forms of the acids (H_3O^+ and A^-) divided by the un-ionized form (HA). The stronger the acid, the greater will be the value of the acidity constant. Acid strengths are also expressed by **pK_a** , which is defined as the negative logarithm of K_a . Numerically smaller pK_a 's signify stronger acids and larger pK_a 's, weaker acids. Approximate pK_a 's include 50 for alkanes, 25 for terminal alkynes, 16 for alcohols, 10 for phenols, 5 for carboxylic acids, and -2 or so for strong inorganic acids.

The ion or molecule formed by the loss of a proton from an acid is the **conjugate base**. Strong acids form weak conjugate bases and weak acids form strong conjugate bases.

Phenols are one million to one billion times more acidic than alcohols and this is the characteristic property that distinguishes them. Phenols will react with the base sodium hydroxide but alcohols will not. The acidity of phenols is explained by **resonance stabilization** of the **phenoxide ion**; the negative charge is dispersed throughout the benzene ring as opposed to being concentrated on the oxygen as it is in the **alkoxide ion**. **Electron-withdrawing groups** on the benzene ring increase the acidity of phenols.

B. Reactions of Alcohols with Sodium Metal:

Reaction of the O-H Bond

Although alcohols will not react with sodium hydroxide as do phenols, they will react with sodium metal to form alkoxide ions and hydrogen gas.

C. Formation of Esters: Reaction of the O-H Bond

Alcohols will also react with organic and inorganic acids to form **esters**.

CONNECTIONS 9.3 Insecticides and Nerve Gases

9.7 Reactions of Alcohols and Ethers with Hydrogen Halides: Reaction of the C-O Bond by Nucleophilic Substitution

A. Reactions of Alcohols with Hydrogen Halides:

S_N1 and S_N2 Mechanisms

Alcohols react with hydrogen halides by nucleophilic substitution. The OH group is replaced by a halogen; water is the by-product. In the reaction mechanism, the first step involves formation of an **oxonium ion** by the Lewis acid-base reaction of the hydrogen ion of the hydrogen halide and alcohol oxygen. The rest of the reaction occurs by one of the nucleophilic substitution mechanisms depending on structure of the alcohol. In the **S_N2** reaction, the next step involves displacement of the water molecule by halide ion to form the final products. In the **S_N1** reaction, the water molecule departs leaving a carbocation that is neutralized by halide ion. The S_N2 reaction with an optically active alcohol proceeds with **inversion of configuration** whereas the S_N1 reaction produces **racemization**. Tertiary and secondary alcohols react by the S_N1 mechanism because they can form relatively stable intermediate carbocations; primary alcohols react by the S_N2 mechanism that does not require a carbocation. The relative rates of reaction are **$3^\circ > 2^\circ > 1^\circ$** .

B. Methods for Converting Alcohols to Alkyl Halides:

Reaction of the C-O Bond

Alcohols can also be converted to alkyl halides using **thionyl chloride** or **phosphorus trihalides**.

C. Reactions of Ethers with Hydrogen Halides:

S_N1 and S_N2 Mechanisms

Ethers react with hydrogen halides to form an alkyl halide and an alcohol. The alcohol in turn can react to form a second molecule of alkyl halide and water. Thus in the presence of two mole-equivalents of hydrogen halide, an ether produces two moles of alkyl halide and one of water. The reaction mechanism is analogous to that of alcohols and hydrogen halides. The ether is protonated first to form an oxonium ion. In

the **S_N2** reaction, the next step involves displacement of the alcohol molecule by halide ion to form the final products. In the **S_N1** reaction, the alcohol molecule departs leaving a carbocation that is neutralized by halide ion. Tertiary and secondary ethers react by the **S_N1** mechanism and primary and methyl ether carbons react by **S_N2**.

9.8 Dehydration of Alcohols by E₁ Elimination: Reaction of the C-O Bond

Alcohols dehydrate in the presence of strong acids such as sulfuric acid. The reaction proceeds via an **E₁ mechanism**. The alcohol oxygen is first protonated to give an oxonium ion which loses water to form a carbocation; subsequent loss of hydrogen ion forms the double bond. When more than one alkene is possible from a dehydration reaction, the more substituted one predominates.

9.9 Oxidation of Alcohols:

Reaction of the C-O and O-H Bonds

Primary alcohols oxidize to carboxylic acids; secondary alcohols oxidize to ketones with chromium trioxide or sodium dichromate. Tertiary alcohols do not oxidize under mild conditions. With **pyridinium chlorochromate (PCC)** the oxidation of primary alcohols can be stopped at **aldehydes**.

CONNECTIONS 9.4 Measuring Blood Alcohol

CONNECTIONS 9.5 Methanol and Ethylene Glycol Poisoning

9.10 Epoxides

Epoxides are three-membered cyclic ethers. The simplest, ethylene oxide is prepared from ethylene and oxygen. Epoxides are prepared more generally from alkenes using a peroxycarboxylic acid.

A. Reactions of Ethylene Oxide

The characteristic chemical property of epoxides is ring-opening reactions initiated by acid or base. Ethylene oxide undergoes such reactions with

water, alcohols, and amines to form commercially important products. The reaction is nucleophilic substitution.

B. Epoxy Resins

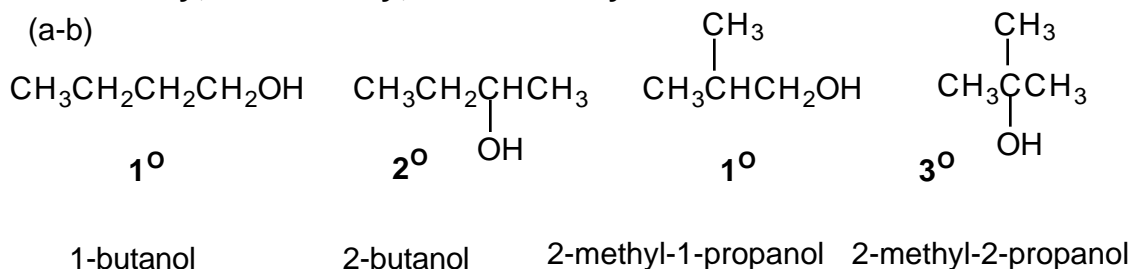
Epoxy resins are polymers with tremendous adhesive properties and are used to bind glass, porcelain, metal, and wood. The production involves a ring opening reaction on the epoxide epichlorohydrin as it reacts with bisphenol A.

9.11 Sulfur Analogues of Alcohols and Ethers

Thiols or alkyl hydrogen sulfides are sulfur analogues of alcohols and **sulfides** are sulfur analogues of ethers. Many of the lower molecular weight examples have strong odors and are naturally found in onions, garlic, and the spray of skunks.

SOLUTIONS TO PROBLEMS

9.1 Primary, Secondary, and Tertiary Alcohols



9.2 Nomenclature of Alcohols

(a) 4-methyl-2-cyclohexenol; (b) 5-bromo-3-hexynol

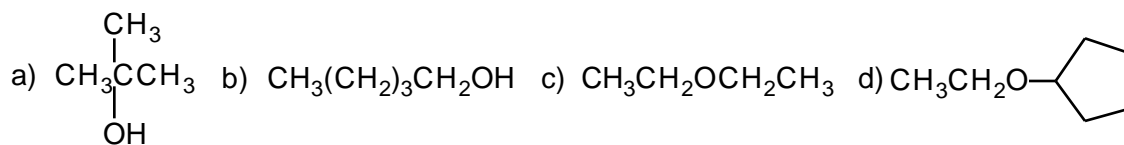
9.3 Nomenclature of Ethers

(a) 1-propoxyheptane; (b) dimethoxymethane; (c) 2-ethoxy-1-ethanol

9.4 Nomenclature of Phenols

(a) meta nitrophenol; (b) para butoxyphenol

9.5 Nomenclature of Alcohols, Phenols, and Ethers



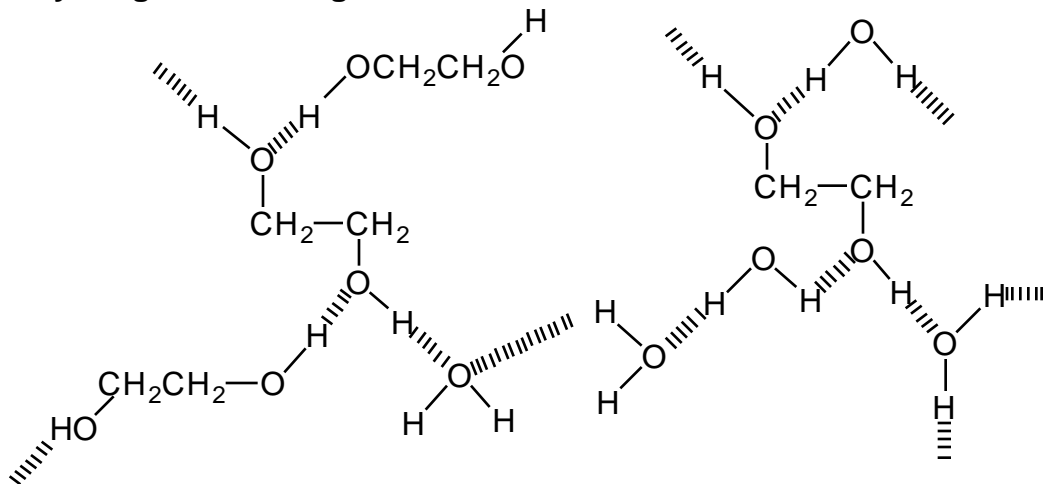
9.6 Physical Properties

Even though the molecular weights of these three compounds are similar, they have very different boiling points. Butane has the lowest boiling point because it is a non-polar compound (only carbon-carbon and carbon-hydrogen bonds) and thus has weak intermolecular attractions. Propanol has an O-H bond and is capable of hydrogen bonding, a phenomenon that causes strong intermolecular attractions and elevated boiling points. 1,2-Ethandiol has two O-H groups and thus greater opportunity for hydrogen bonding; as a result it has a drastically higher boiling point.

9.7 Physical Properties

Ethylbenzene, the third compound and gasoline component, has the lowest boiling point (136°C) because it has only carbon-carbon and carbon-hydrogen bonds and is non-polar. The first compound, rose oil, has the highest boiling point (221°C) because it has an O-H bond and is capable of hydrogen-bonding. The middle compound is an ether; though it is polar because of the C-O-C bonds, it is not capable of hydrogen-bonding and thus has an intermediate boiling point (171°C).

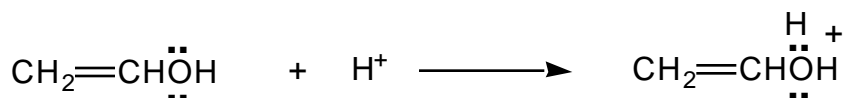
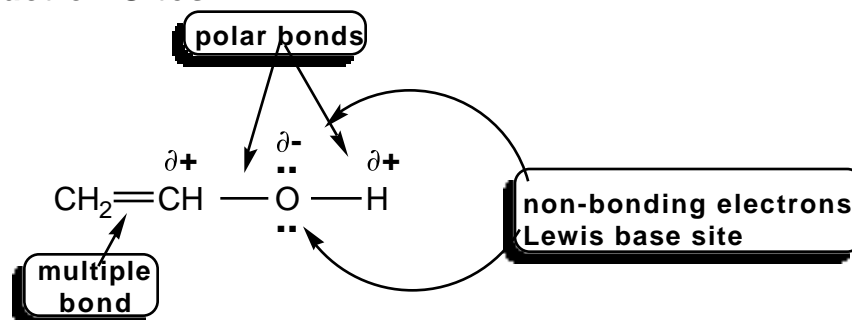
9.8 Hydrogen-Bonding



9.9 Physical Properties and Hydrogen-Bonding

The two compounds are isomers and have the same molecular weight. Butanoic acid has an OH group, is thus capable of hydrogen bonding and has the higher boiling point. Ethyl acetate cannot hydrogen bond..

9.10 Reaction Sites



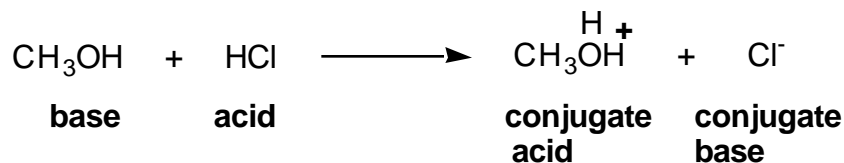
9.11 Relative Acidities

(a) pK_a 's: $11.8 < 6.2 < 3.4$

(b) K_a 's: $9.8 \times 10^{-12} < 6.7 \times 10^{-5} < 3.4 \times 10^{-3}$

(c) $\text{CH}_3\text{CH}_2\text{CH}_3 < \text{CH}_3\text{CH}_2\text{CH}_2\text{OH} < \text{CH}_3\text{CH}_2\text{CO}_2\text{H}$

9.12 Acids and Bases

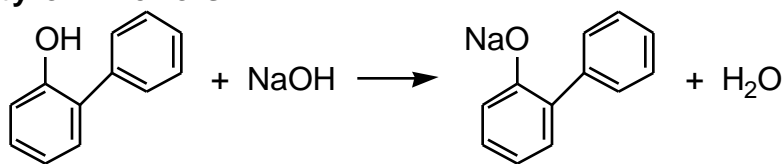


9.13 Relative Acidities

(a) No reaction: the conjugate acid that would be produced, $\text{CH}_3\text{CH}_2\text{OH}_2^+$, is stronger than the original acid, CH_4 . The conjugate base is likewise stronger than the original base. Thus the products of the theoretical neutralization would be more acidic and basic than the original compounds and immediately react to reform them.

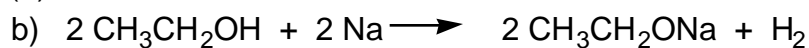
(b) Yes, neutralization would occur: HCl is a stronger acid than the conjugate acid, $\text{CH}_3\text{CO}_2\text{H}$. The conjugate base is weaker than the original base. Thus the two reactants shown are more reactive, i.e. more acidic and basic, than the theoretical products of the reaction.

9.14 Acidity of Phenols

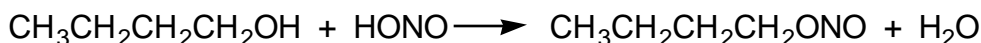


9.15 Reactions of the O-H Bond of Alcohols: Acidity

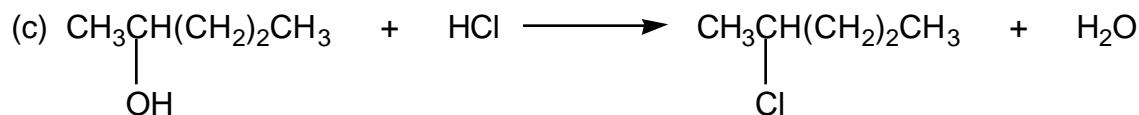
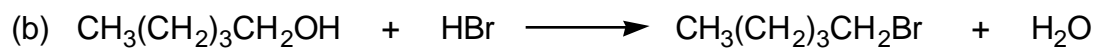
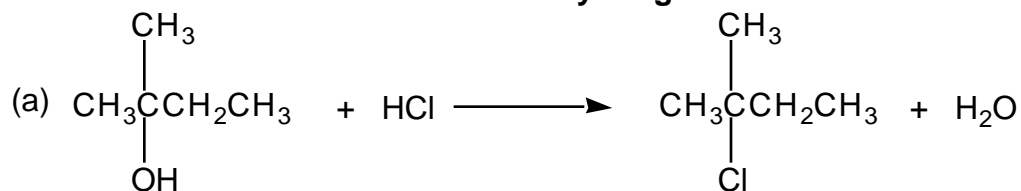
(a) No reaction with NaOH



9.16 Reactions of the O-H Bond of Alcohols: Ester Formation



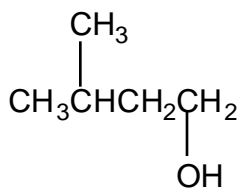
9.17 Reactions of Alcohols with Hydrogen Halides



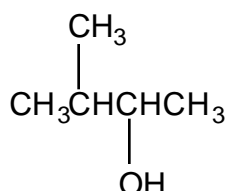
9.18 Reactions of Alcohols with Hydrogen Halides: Relative Rates

The compounds in Problem 9.17 show relative reactions rates in the following order: **a > c > b** since the relative rates of reaction of alcohols with hydrogen halides is **3° > 2° > 1°**. S_N2: (b); S_N1: (a) and (c).

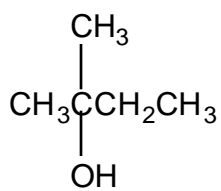
9.19 Lucas Reagent

Rate of Reaction with the Lucas Reagent

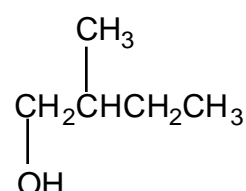
1° Alcohol one
hour with heat



2° Alcohol
5-15 minutes

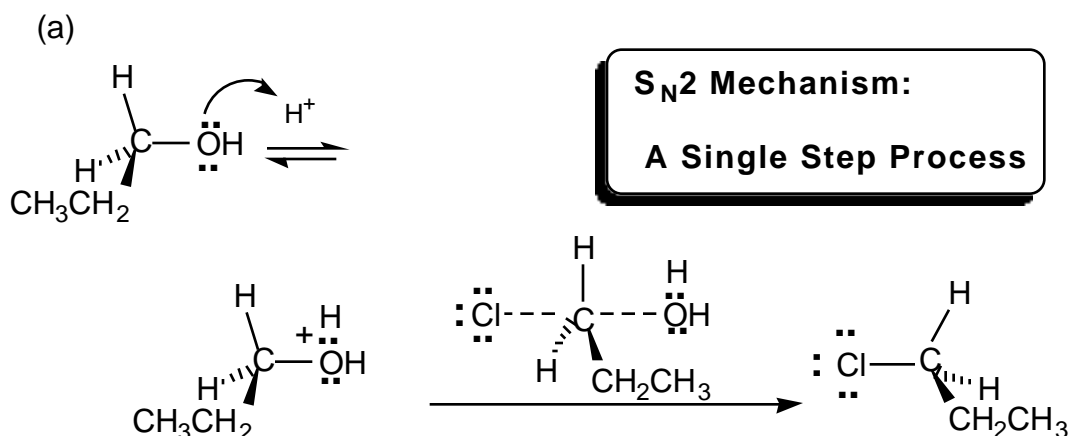


3° Alcohol
instantaneous



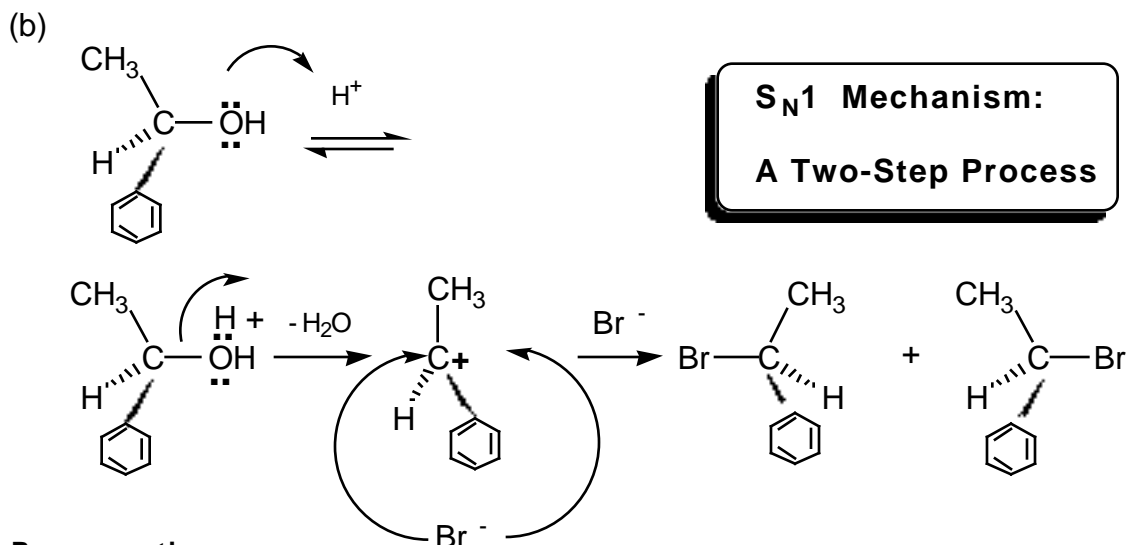
1° Alcohol one
hour with heat

9.20 Nucleophilic Substitution Mechanisms



Primary alcohol protonated to form primary oxonium ion. Oxonium ion is attacked by bromide.

Transition state showing bromide displacing water molecule from the opposite side to form final product.

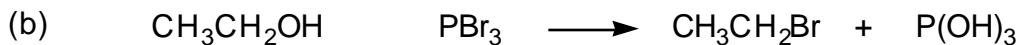
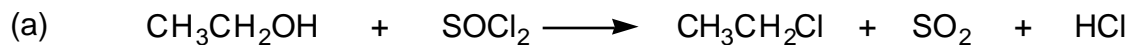


Pure enantiomer; optically active alcohol is protonated to optically active oxonium ion.

Nucleophile, Br⁻ attacks planar carbocation from either side.

Both inversion and retention of configuration occur equally. A pair of enantiomers results. This is an optically inactive racemic mixture.

9.21 Preparation of Alkyl Halides

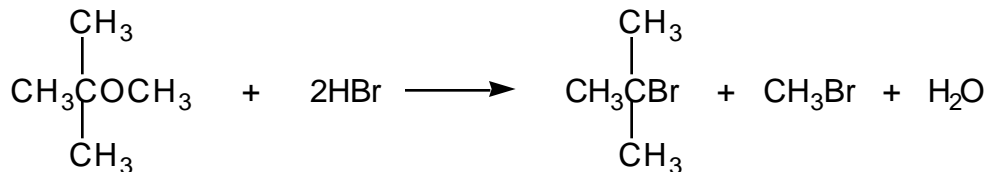
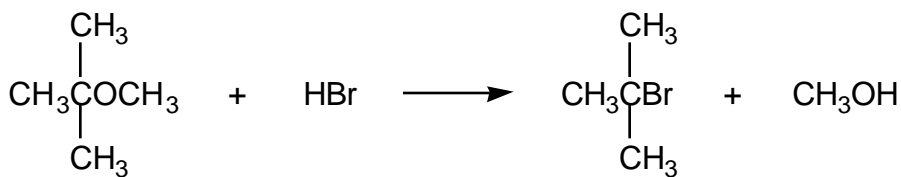
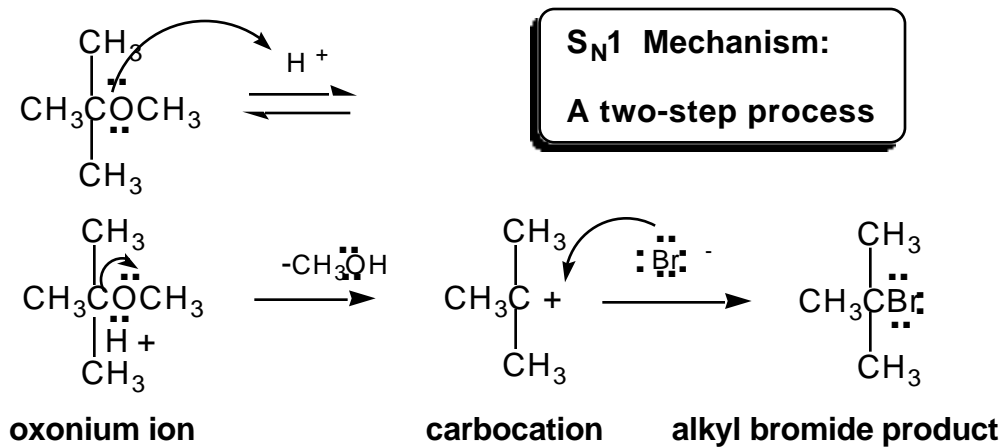


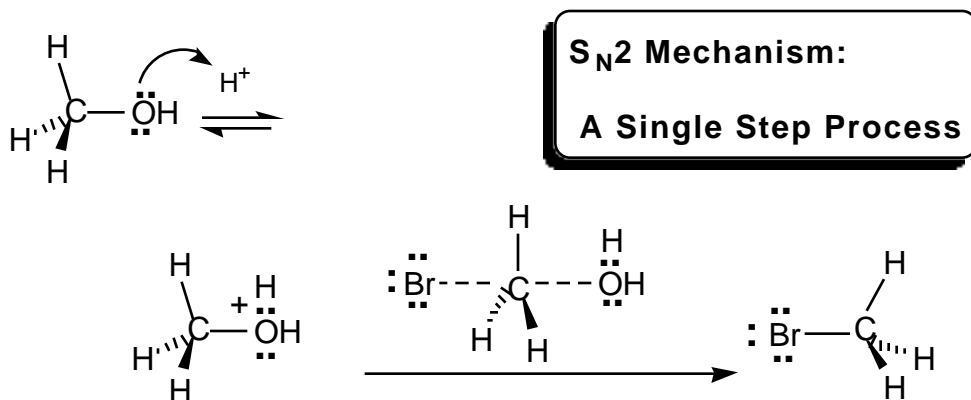
9.22 Preparation of Alkyl Halides

$\text{CH}_3\text{CH}_2\text{CH}_2\text{CH}_2\text{OH}$ can be converted to $\text{CH}_3\text{CH}_2\text{CH}_2\text{CH}_2\text{Cl}$

using the following reagents: (1) HCl with ZnCl_2
 (2) SOCl_2
 (3) PCl_3

9.23 Reaction of Ethers with Hydrogen Halides

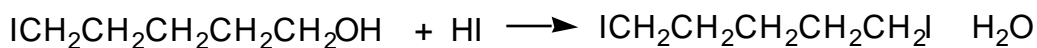
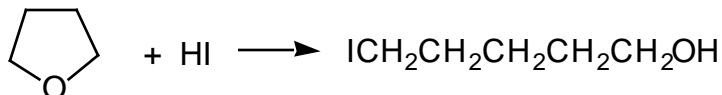
9.24 $\text{S}_{\text{N}}1$ Mechanism: Ethers and Hydrogen Halides



Primary alcohol protonated to form primary oxonium ion. Oxonium ion is attacked by bromide.

Transition state showing bromide displacing water molecule from the opposite side to form the final product.

9.25 Reactions of Ethers with Hydrogen Halides



9.26 E₁ and S_N1 Mechanisms

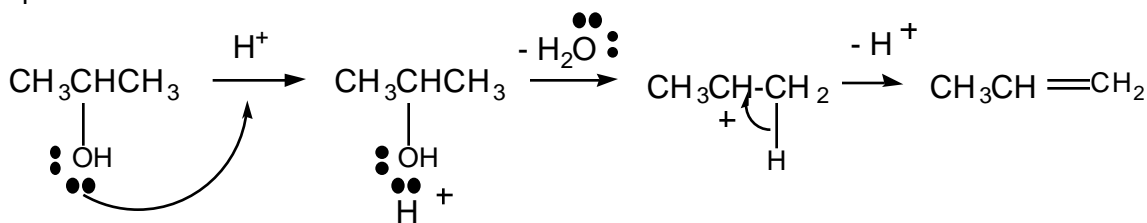
In all three mechanisms:

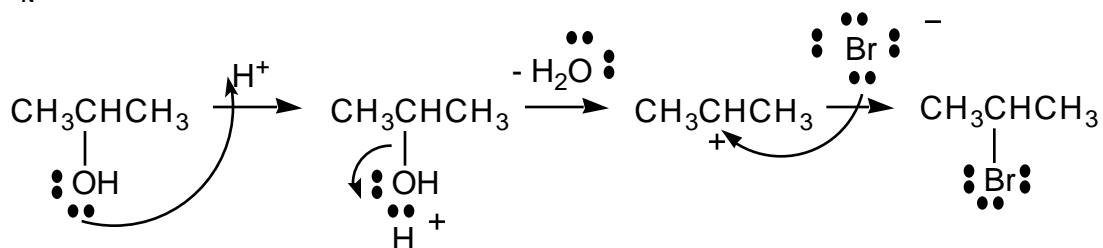
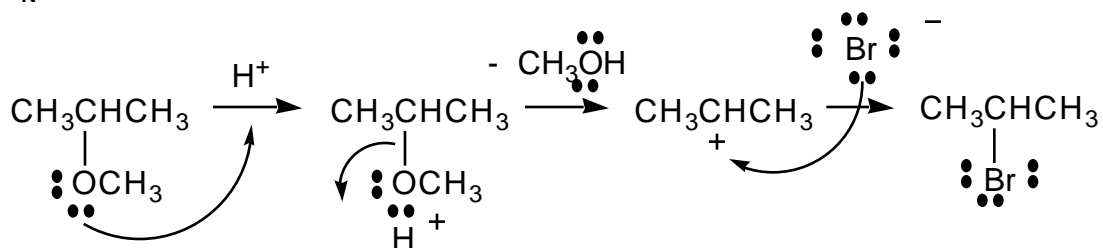
First step: alcohol or ether acts as Lewis base and reacts with hydrogen ion to form an oxonium ion.

Second step: water or methanol leaves and a carbocation is the result.

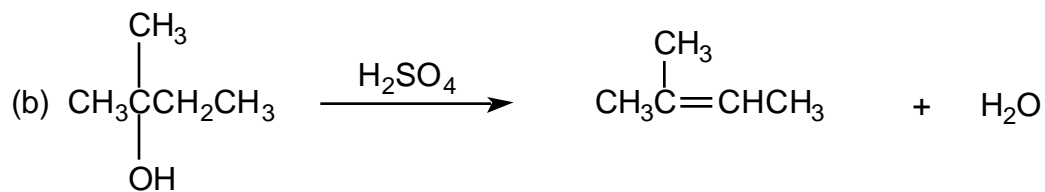
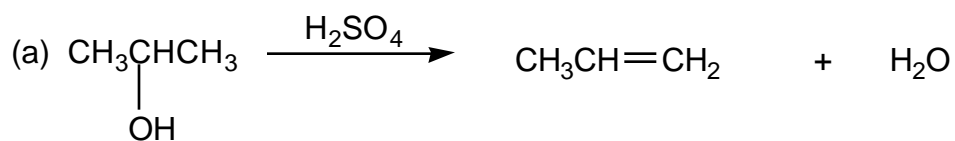
Third step: the carbocation can be neutralized by the loss of a hydrogen ion in the elimination reaction or by bromide in the substitution reactions.

E₁

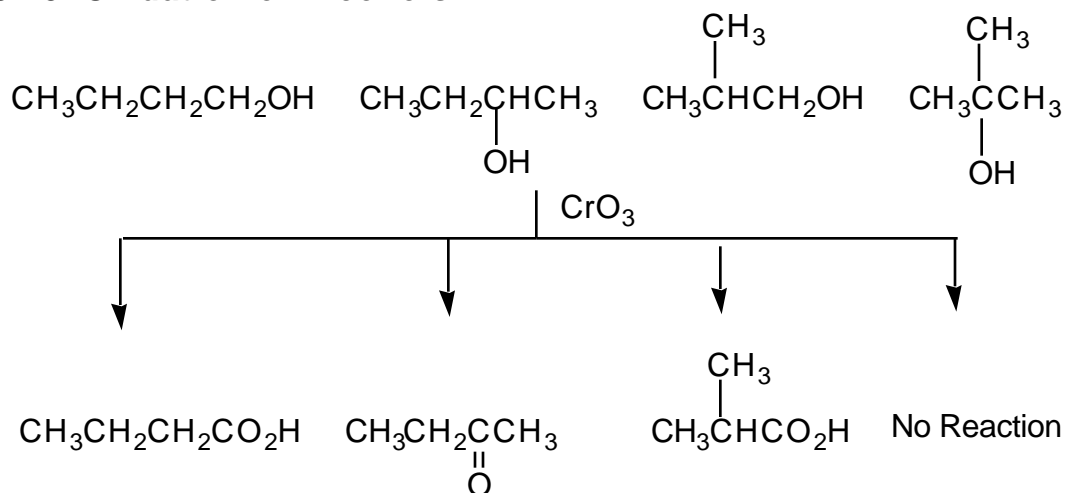


S_N1  S_N1 **9.27 Dehydration Reactions**

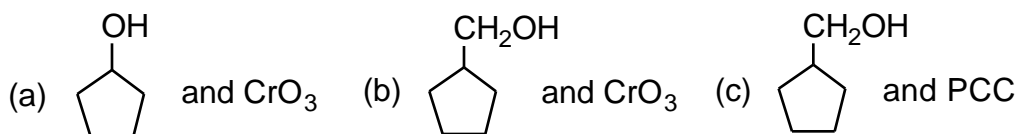
Focus your attention on the OH; remove it and a hydrogen from an adjacent carbon. The double bond forms between these two carbons. When more than one elimination product is possible, the most substituted alkene forms predominantly (Section 4.5B).



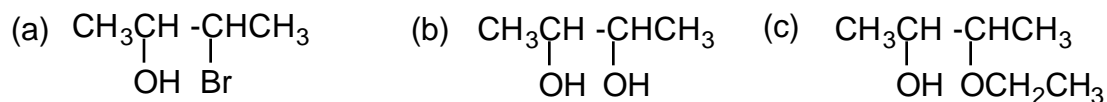
9.28 Oxidation of Alcohols



9.29 Oxidation of Alcohols

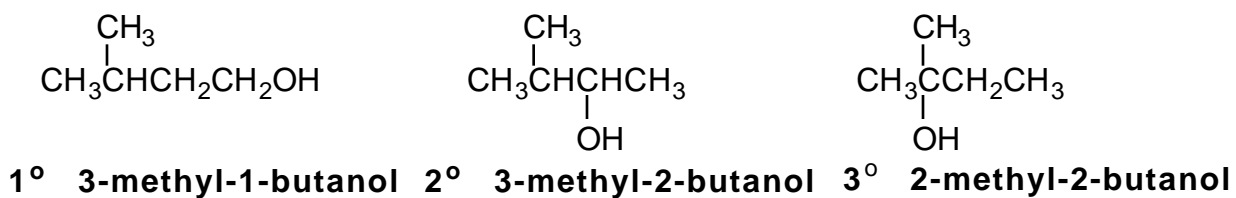
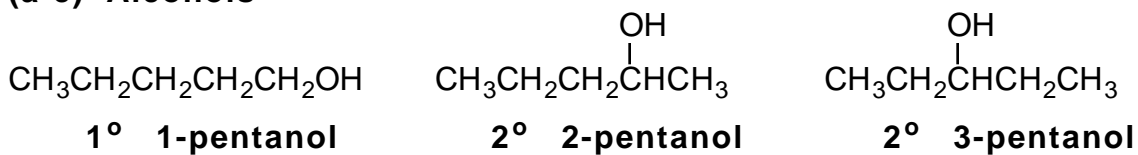


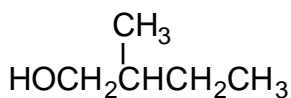
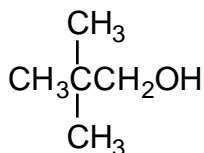
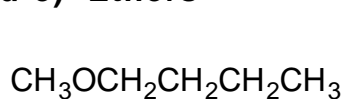
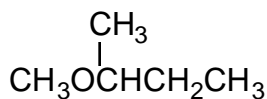
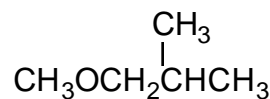
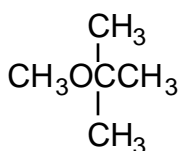
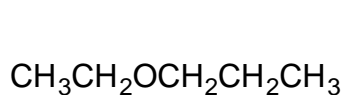
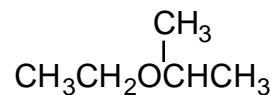
9.30 Reactions of Epoxides



9.31 Isomerism and Nomenclature: Section 9.1

(a-c) Alcohols



**1° 2-methyl-1-butanol****1° 2,2-dimethyl-1-propanol****(d-e) Ethers****1-methoxybutane****2-methoxybutane****1-methoxy-2-methylpropane****2-methoxy-2-methylpropane****1-ethoxypropane****2-ethoxypropane****9.32 IUPAC Nomenclature of Alcohols:** Section 9.1A

- (a) 1-nonanol; (b) 2-hexanol; (c) 2-methyl-2-butanol; (d) cyclopentanol;
 (e) 3,3-dimethyl-1-butanol; (f) 4-ethyl-4-methyl-1-cyclohexanol;
 (g) 2,2,3-trimethyl-3-pentanol; (h) 2,5-dimethyl-2-hexanol

9.33 IUPAC Nomenclature of Alcohols: Section 9.1A

- (a) 4,5-dibromo-3-hexanol; (b) 5-methyl-3-heptanol; (c) 1,5-pentandiol;
 (d) 1,3,5-cyclohexanetriol

9.34 IUPAC Nomenclature of Unsaturated Alcohols: Section 9.1A

- (a) 3-buten-2-ol; (b) 4-ethyl-2-hexyn-1-ol; (c) 2,4-hexadien-1,6-diol;
 (d) 3-cyclopenten-1-ol; (e) 2-phenyl-1-ethanol; (f) 1-hexyn-4-en-3-ol

9.35 IUPAC Nomenclature of Ethers: Section 9.1B

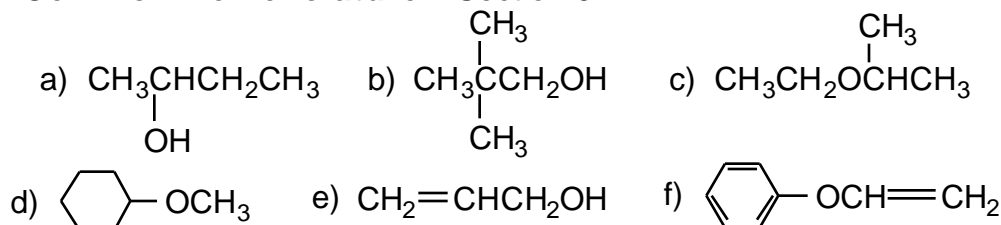
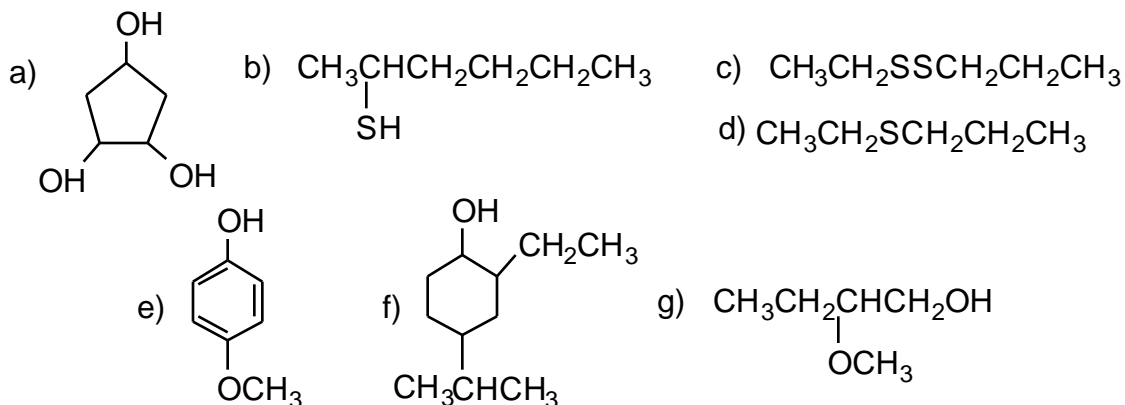
- (a) methoxyethane; (b) ethoxyethane; (c) 1-ethoxy-6-methoxyhexane;
 (d) propoxycyclopentane; (e) methoxycyclopropane

9.36 IUPAC Nomenclature of Ethers: Section 9.1B

- (a) tetramethoxymethane; (b) 3-methoxy-1-propanol; (c) 1-ethoxypropene;
 (d) 4-methoxy-2-buten-1-ol

9.37 IUPAC Nomenclature of Phenols: Section 9.1C

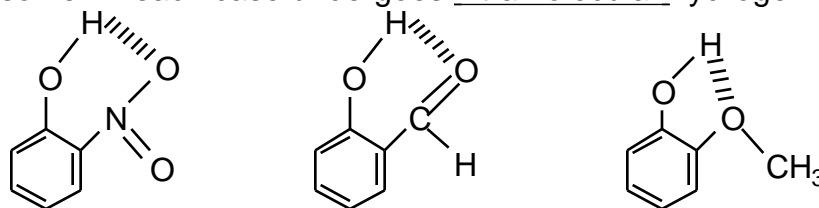
- (a) 2-methylphenol; (b) 3-bromophenol; (c) 4-ethylphenol;
 (ortho, meta, and para in a,b,c respectively is correct also)
 d) 4-methoxy-2-nitrophenol

9.38 Common Nomenclature: Section 9.1D**9.39 IUPAC Nomenclature:** Section 9.1**9.40 Physical Properties:** Sections 2.9 and 9.2

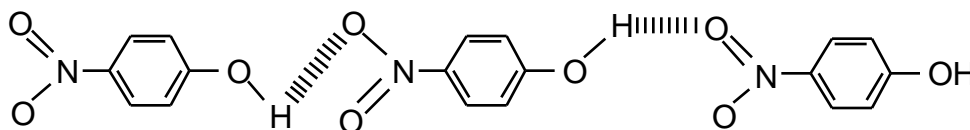
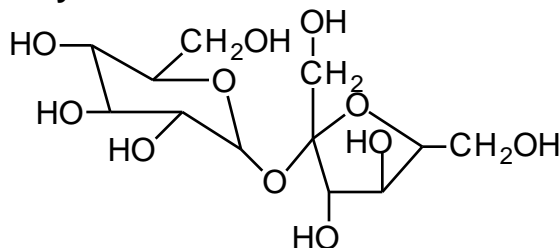
- (a) $\text{I} < \text{II} < \text{III}$ increasing molecular weight in homologous series
 (b) $\text{III} < \text{II} < \text{I}$ more OH groups and thus more hydrogen bonding
 (c) $\text{I} < \text{II} < \text{III}$ increasing number OH groups, increasing hydrogen bonding
 (d) $\text{III} < \text{II} < \text{I}$ increasing number OH groups, increasing hydrogen bonding
 (e) $\text{III} < \text{II} < \text{I}$ increasing number N-H bonds, increasing hydrogen bonding
 (f) $\text{II} < \text{I}$ no hydrogen bonding in II; I has OH and hydrogen bonding
 (g) $\text{III} < \text{II} < \text{I}$ OH bond more polar than NH; OH further polarized by C=O
 (h) $\text{II} < \text{I} < \text{III}$ II is non-polar; I is polar but no hydrogen bonding; III has OH and thus hydrogen bonding
 (i) $\text{III} < \text{I} < \text{II}$ II has strongest hydrogen bonding due to C=O next to OH; III has no hydrogen bonding.
 (j) $\text{I} < \text{II} < \text{III} < \text{IV} < \text{V} < \text{VI}$ increasing molecular weight

9.41 Physical Properties: Section 9.2

The ortho isomer in each case undergoes intramolecular hydrogen bonding.



Because of this, the attractions between molecules are diminished and boiling points are lower than might be expected. The relationship between the two substituents is not favorable for intramolecular hydrogen bonding in the para compounds, however. Thus, intermolecular hydrogen bonding occurs (as shown with p-nitrophenol) increasing attractions between molecules and thus the boiling points.

**9.42 Water Solubility:** Section 9.2

Sucrose has 12 carbons; there are OH groups on eight of them. This allows for tremendous hydrogen bonding with water and thus high water solubility.

9.43 Water Solubility: Section 9.2

(a) **hexanol < pentanol < ethanol:** increasing ratio of OH to hydrocarbon as boiling points increase.

(b) **pentane < heptanol < propanol:** pentane has no OH and cannot hydrogen bond to water; propanol has a higher ratio of OH to hydrocarbon than heptanol, is more like water and more water soluble.

(c) **hexane < hexanol < 1,2-ethanediol:** hexane has no OH and no hydrogen bonding; hexanol can hydrogen bond with water but has only one OH for all six carbons and has only slight water solubility; ethanediol has an OH on each carbon and is infinitely soluble in water.

(d) **pentane < ethoxyethane < butanol**: these compounds have similar molecular weights but the first two have no OH and thus no hydrogen bonding; the second is polar and has some slight water solubility and butanol has an OH and thus can hydrogen bond with water.

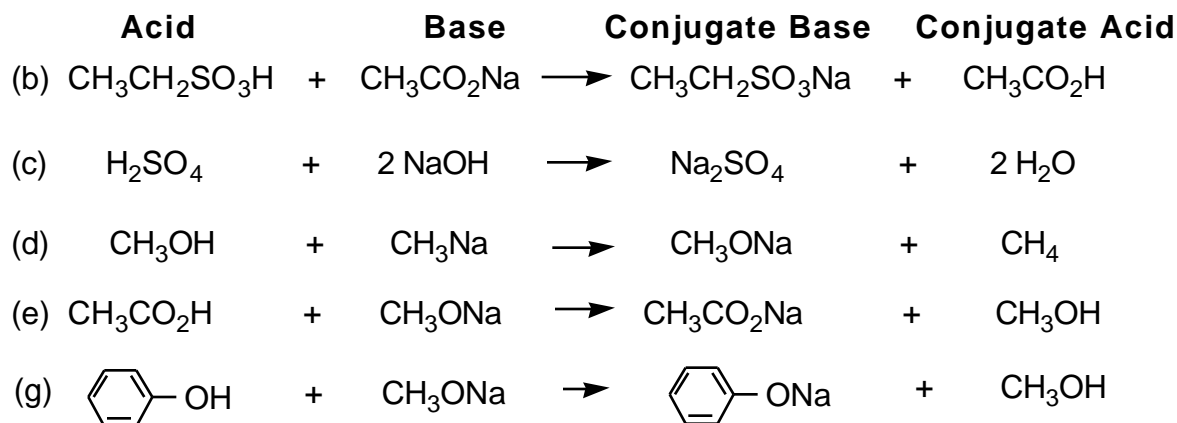
9.44 Acidity: Section 9.6A

(a) **No**: the conjugate acid and base are stronger than the original acid and base

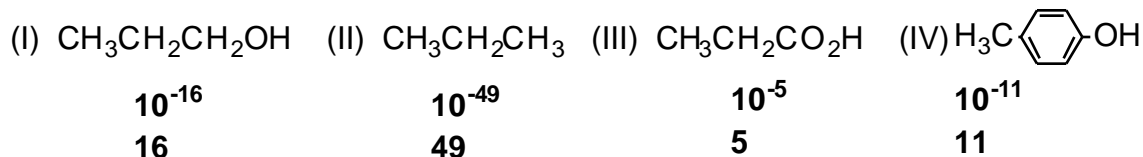
(b) **Yes**: the original acid and base are stronger than the conjugate forms

(c) **Yes**; (d) **Yes**; (e) **Yes**; (f) **No**; (g) **Yes**; (h) **No**

9.45 Acid Base Neutralization: Section 9.6A



9.46 Acidity Constants: Section 9.6A



Relative Acidities: II < I < IV < III

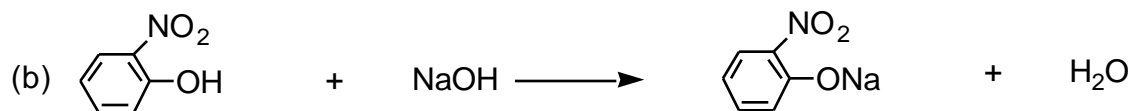
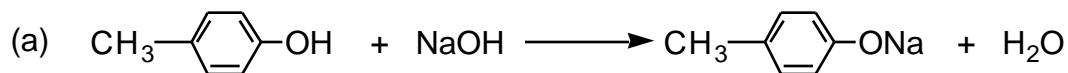
9.47 Acidity of Phenols: Section 9.6A.2

(a) **III < I < IV < II**: The methyl group is electron-releasing and decreases basicity; it is most effective ortho and para and probably a little more effective ortho due to proximity.

(b) **II < IV < I < III**: The acetyl group is electron-withdrawing and increases acidity; it is most effective ortho and para and probably a little more effective ortho due to proximity.

(c) $\text{II} < \text{IV} < \text{I} < \text{III}$: The methyl group decreases acidity and thus IV is more acidic than II. The nitro group increases acidity and III has more of them than does I.

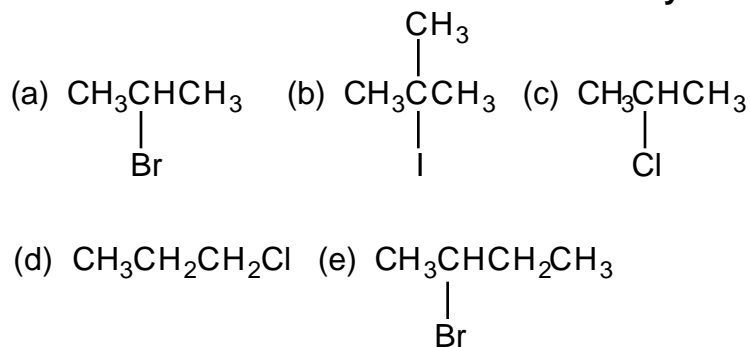
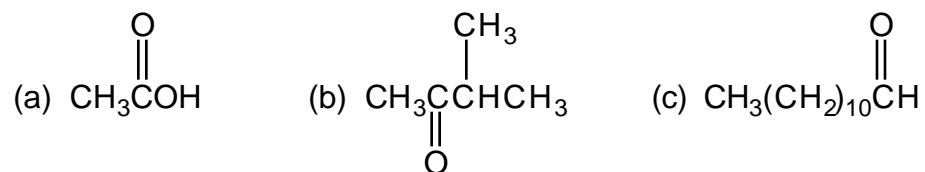
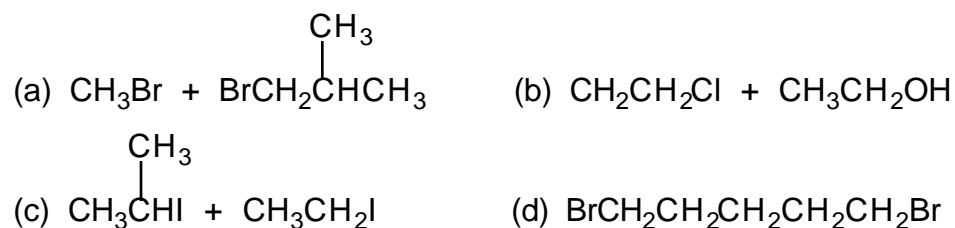
9.48 Acidity of Phenols: Section 9.6A.2



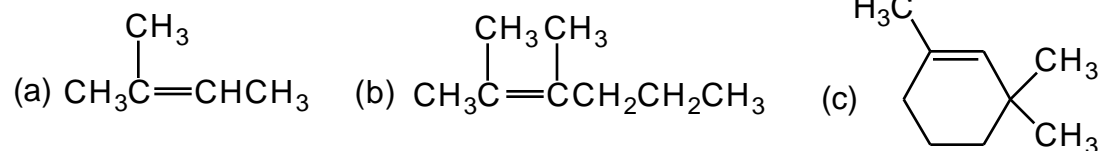
9.49 Reactions of Alcohols: Sections 9.5-9.9

Reagent

	I	II	III
	$\text{CH}_3\text{CH}_2\text{CH}_2\text{CH}_2\text{OH}$	$\text{CH}_3\underset{\text{OH}}{\text{CH}}\text{CH}_2\text{CH}_3$	$\text{CH}_3\overset{\text{CH}_3}{\underset{\text{OH}}{\text{C}}}\text{CH}_3$
a) Na	$\text{CH}_3\text{CH}_2\text{CH}_2\text{CH}_2\text{ONa}$	$\text{CH}_3\underset{\text{ONa}}{\text{CH}}\text{CH}_2\text{CH}_3$	$\text{CH}_3\overset{\text{CH}_3}{\underset{\text{ONa}}{\text{C}}}\text{CH}_3$
b) H_2SO_4	$\text{CH}_3\text{CH}_2\text{CH}=\text{CH}_2$	$\text{CH}_3\text{CH}=\text{CHCH}_3$	$\text{CH}_3\overset{\text{CH}_3}{\text{C}}=\text{CH}_2$
c) HCl/ZnCl_2	$\text{CH}_3\text{CH}_2\text{CH}_2\text{CH}_2\text{Cl}$	$\text{CH}_3\underset{\text{Cl}}{\text{CH}}\text{CH}_2\text{CH}_3$	$\text{CH}_3\overset{\text{CH}_3}{\underset{\text{Cl}}{\text{C}}}\text{CH}_3$
d) CrO_3/H^+	$\text{CH}_3\text{CH}_2\text{CH}_2\text{CO}_2\text{H}$	$\text{CH}_3\overset{\text{O}}{\parallel}{\text{C}}\text{CH}_2\text{CH}_3$	No Reaction
e) HNO_3	$\text{CH}_3\text{CH}_2\text{CH}_2\text{ONO}_2$	$\text{CH}_3\underset{\text{ONO}_2}{\text{CH}}\text{CH}_2\text{CH}_3$	$\text{CH}_3\overset{\text{CH}_3}{\underset{\text{ONO}_2}{\text{C}}}\text{CH}_3$

9.50 Reactions of Alcohols to Form Alkyl Halides: Section 9.7A-B**9.51 Oxidation of Alcohols:** Section 9.9**9.52 Reactions of Ethers:** Section 9.7C**9.53 Dehydration of Alcohols:** Sections 4.5B and 9.8

The predominant product is shown for each dehydration. Direct your attention to the OH group. Remove it and a hydrogen from an adjacent carbon. Draw a double bond between the two carbons. In cases where there is more than one adjacent carbon with hydrogens, remove the hydrogen from the one with the greatest number of alkyl groups (fewest number of hydrogens) to produce the most substituted alkene (the most stable).



9.54 Reactions of Alcohols with Hydrogen Halides: Section 9.7A

Refer to the structures in Problem 9.53. **Replace the OH groups with Br.**

9.55 Reactions of Epoxides: Section 9.10A

(a) HOCH₂CH₂OH (b) HOCH₂CH₂OCH₂CH₃ (c) HOCH₂CH₂N(CH₃)₂

(d) HOCH₂CH₂Br (e) BrCH₂CH₂Br

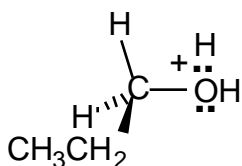
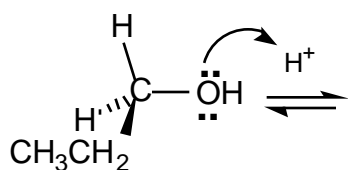
9.56 Reaction Mechanisms: Section 9.7A and C

Look at the carbon(s) directly bonded to the oxygens. If a carbon is primary, the mechanism of displacement is S_N2 because primary carbocations are unstable and the S_N2 reaction does not require a carbocation. If it is secondary or tertiary, the mechanism is S_N1. Secondary and tertiary carbocations are relatively stable and thus the S_N1 mechanism is possible.

(a) S_N2: primary alcohol; (b) S_N2 for both carbons: this is an ether where one carbon is methyl, one is primary; (c) S_N1: secondary alcohol; (d) S_N2 for the CH₃ carbon and S_N1 for the secondary carbon; (e) S_N2 for both carbons since both are primary.

9.57 Nucleophilic Substitution Mechanisms: Sections 9.7A and C

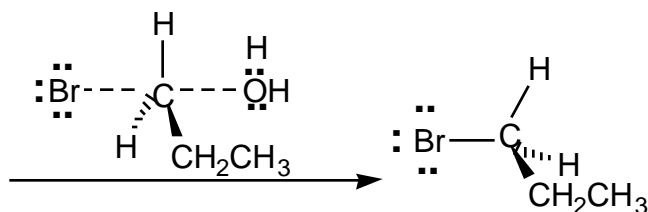
(a)



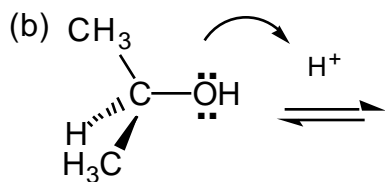
Primary alcohol protonated to form primary oxonium ion. Oxonium ion is attacked by bromide.

S_N2 Mechanism:

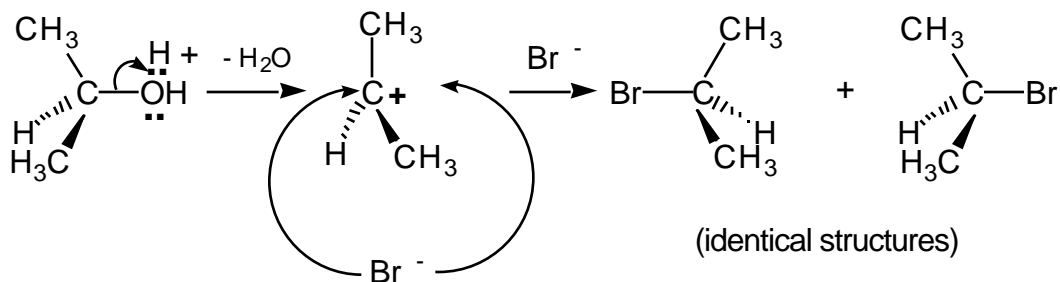
A Single Step Process



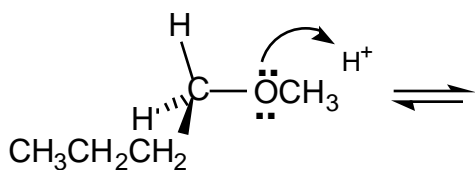
Transition state showing bromide displacing water molecule from the opposite side to form final product.



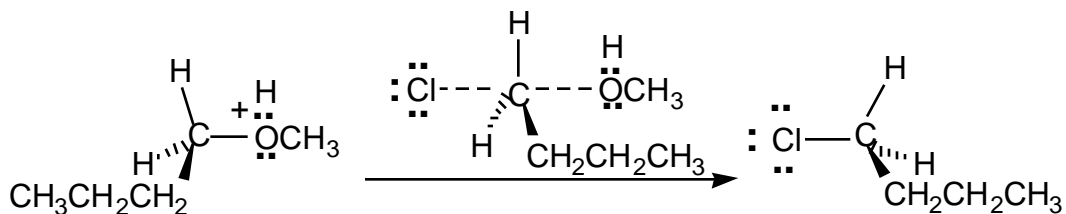
S_N1 Mechanism:
A Two-Step Process



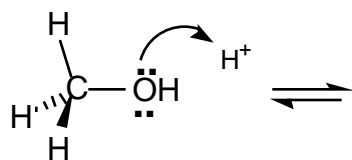
(c)



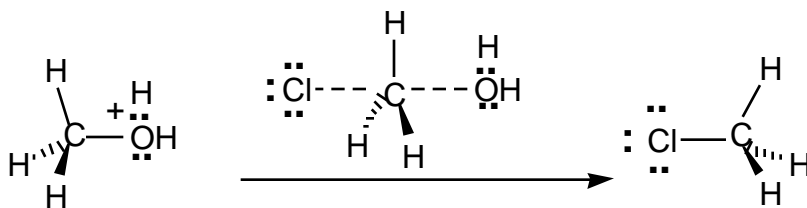
S_N2 Mechanism:
A Single Step Process

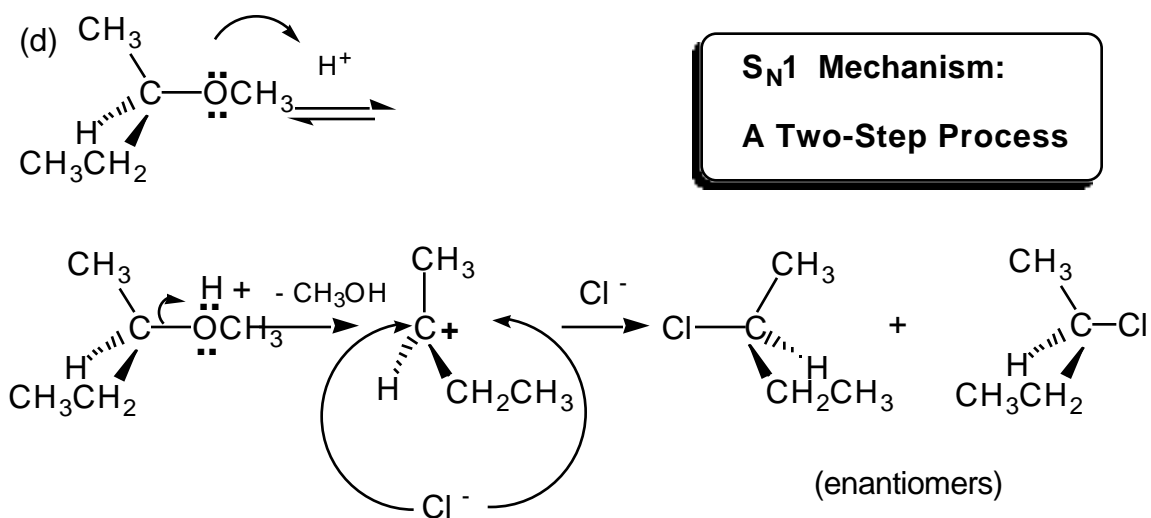


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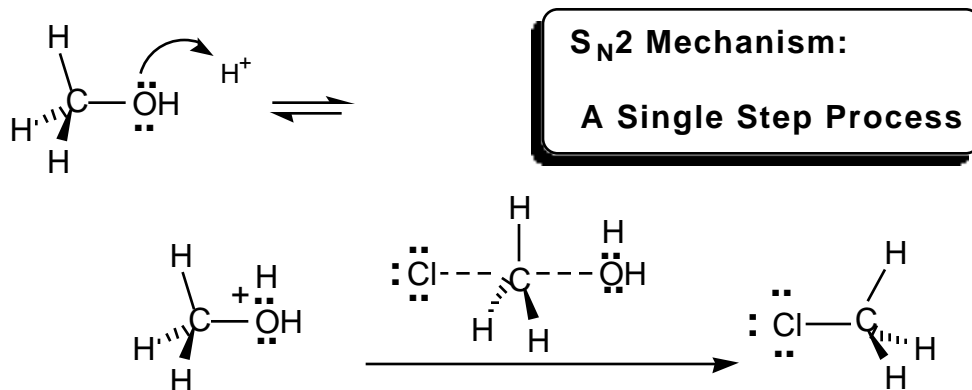


S_N2 Mechanism:
A Single Step Process

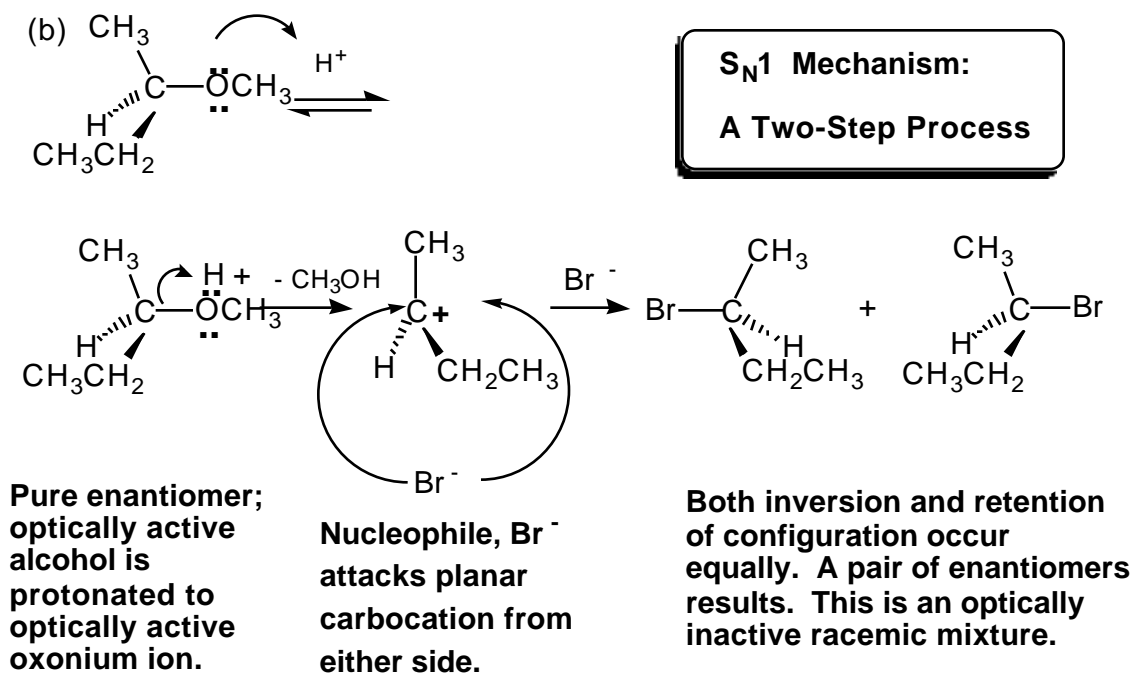
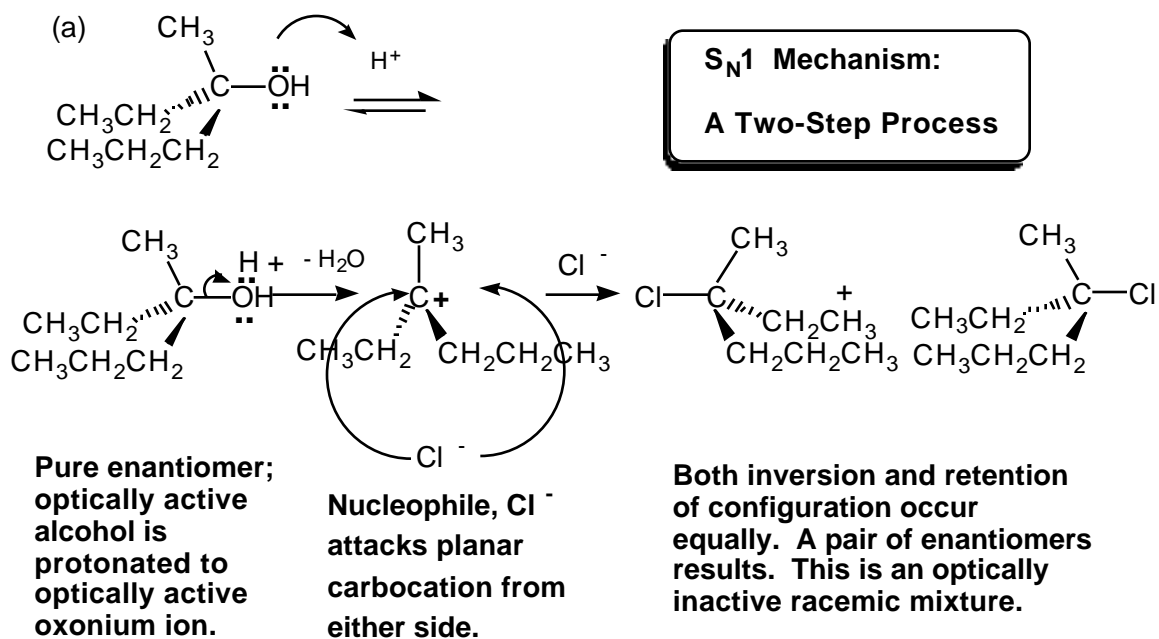




FOLLOWED BY

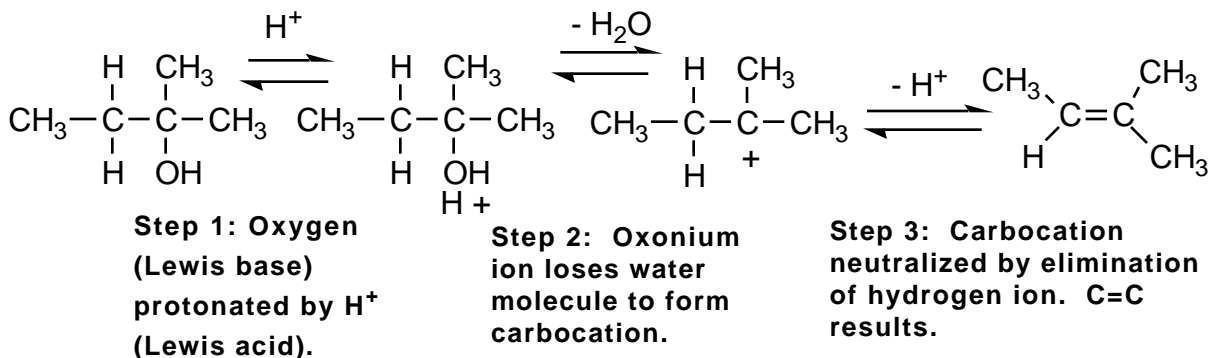
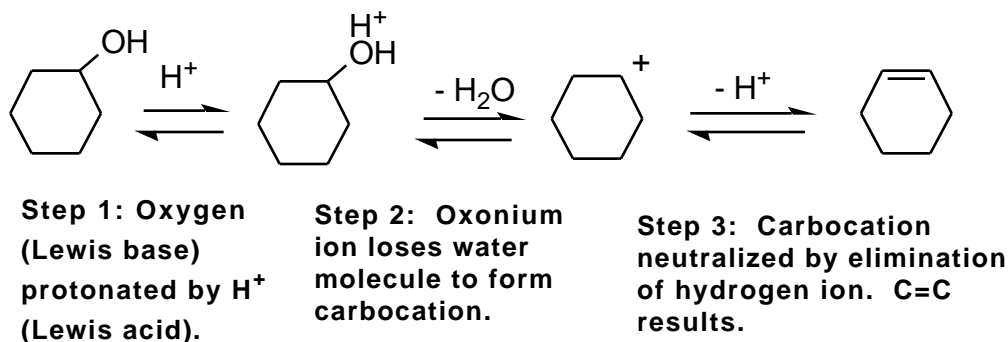


9.58 Nucleophilic Substitution Mechanisms: Section 9.7A and C



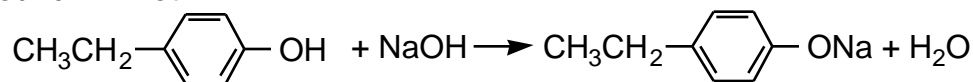
9.59 Dehydration Mechanism: Sections 4.5C and 9.8

(a)

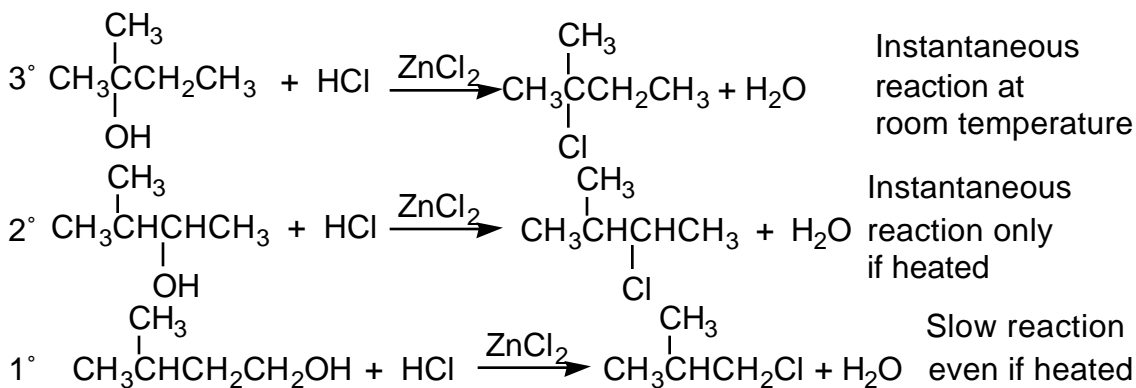
E₁ Mechanism for Dehydration of Alcohols**E₁ Mechanism for Dehydration of Alcohols**

9.60 Qualitative Analysis: Sections 9.6A.2 and 9.7A

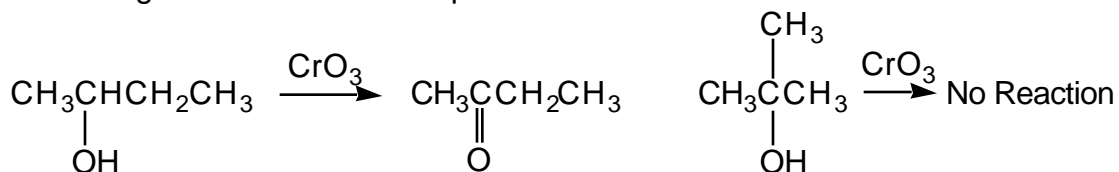
(a) p-Ethylphenol being a phenol is acidic and reacts with sodium hydroxide. Alcohols are not so acidic and do not react with sodium hydroxide. p-Ethylphenol will dissolve in a sodium hydroxide solution and the other compound will not.



(b) Treatment of each of these alcohols with the Lucas reagent will produce a turbid mixture as the alkyl halide is formed. However the reaction proceeds at different rates depending on the structure of the alcohol.

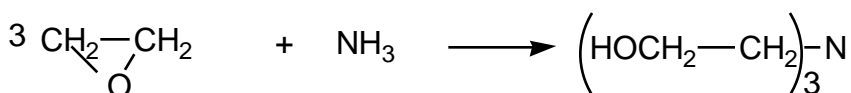


(c) The secondary alcohol is subject to oxidation but the tertiary alcohol is not. The positive reaction is observable as the yellow-orange oxidation reagent becomes green as the reaction proceeds.

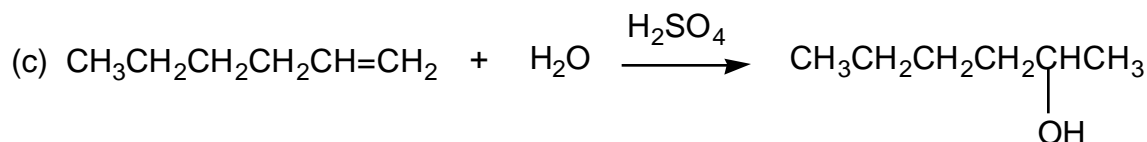
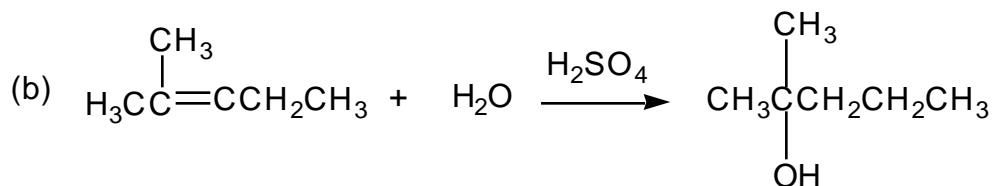
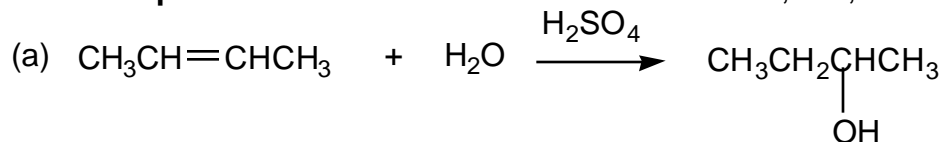


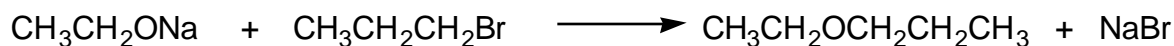
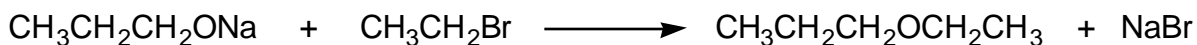
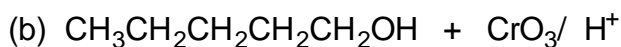
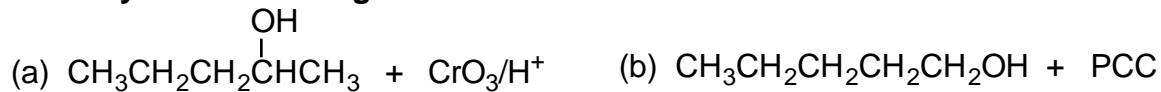
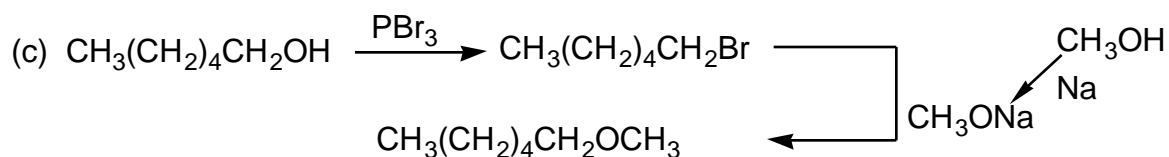
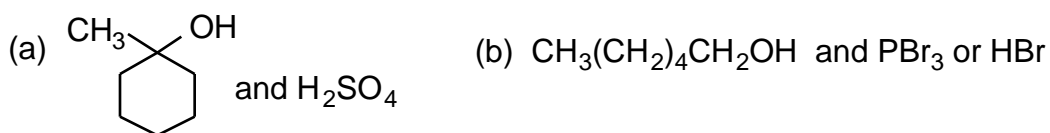
9.61 Epoxide Chemistry: Section 9.10

There are three N-H bonds to add across the epoxide ring.

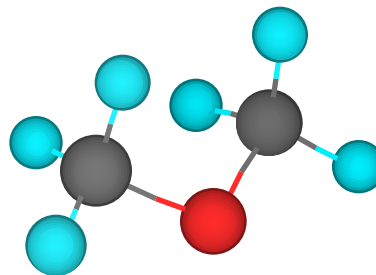
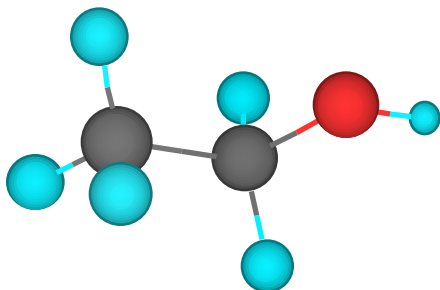


9.62 Preparations of Alcohols: Sections 5.1A.3, B.3, C and 9.4A



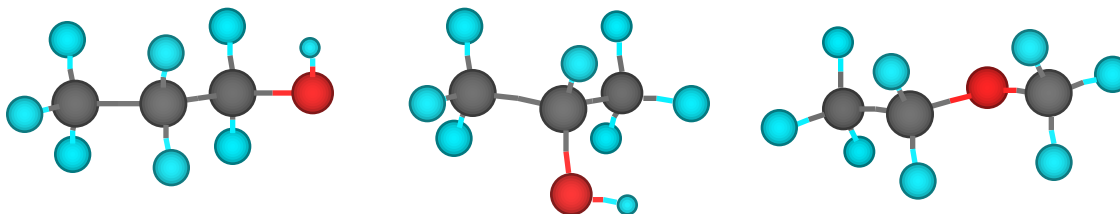
9.63 Williamson Synthesis of Ethers: Sections 8.4A, 8.6, and 9.4B**9.64 Synthesis Using Alcohols:** Section 9.9**9.65 Synthesis Using Alcohols:** Sections 9.7-9.8**ACTIVITIES WITH MOLECULAR MODELS**

1. Make molecular models of $\text{C}_2\text{H}_6\text{O}$, one alcohol and one ether.



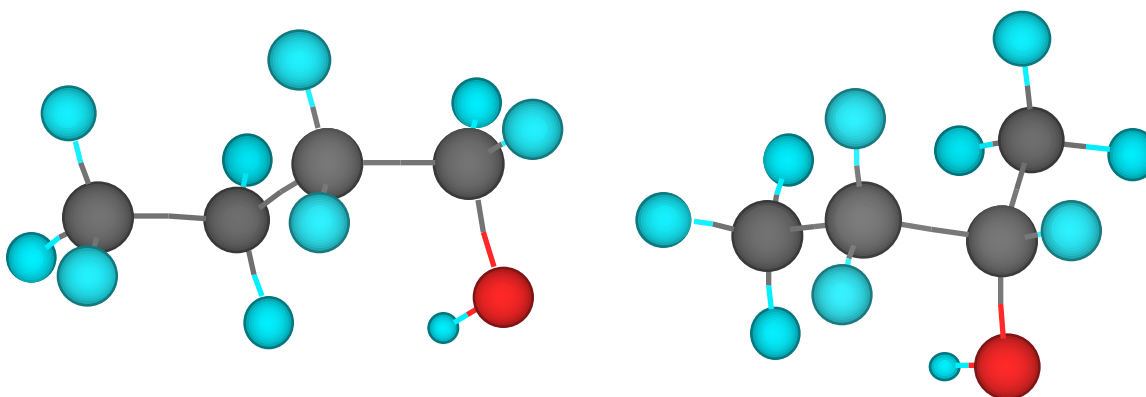
2. Make molecular models of the isomers of C_3H_6O , two alcohols and one ether. How many non-bonding electron pairs reside on the oxygen? What is the hybridization and geometric orientation of the carbons and the oxygen?

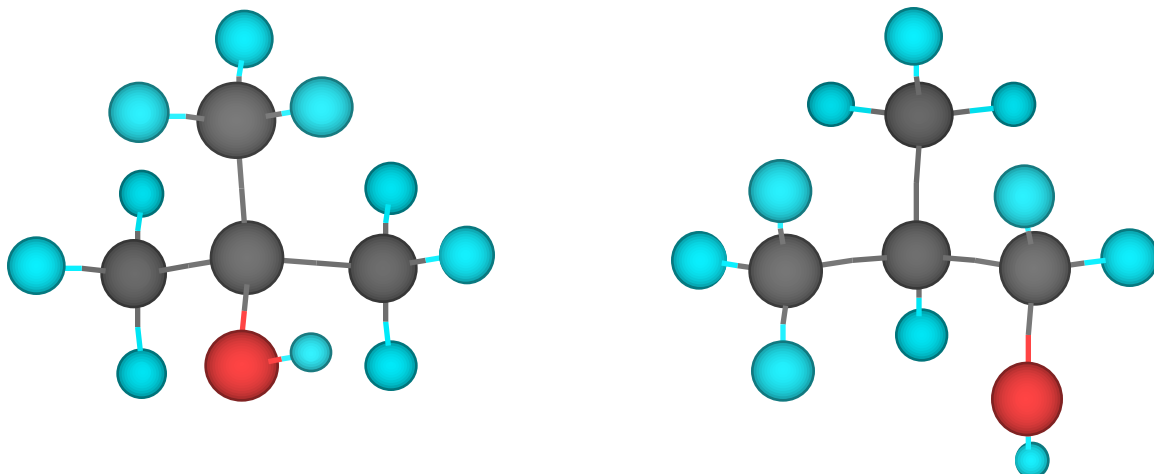
Each oxygen has two non-bonding electron pairs. The carbons and oxygens all have four bonding and non-bonding electron pairs total and are sp^3 hybridized with a tetrahedral geometry.



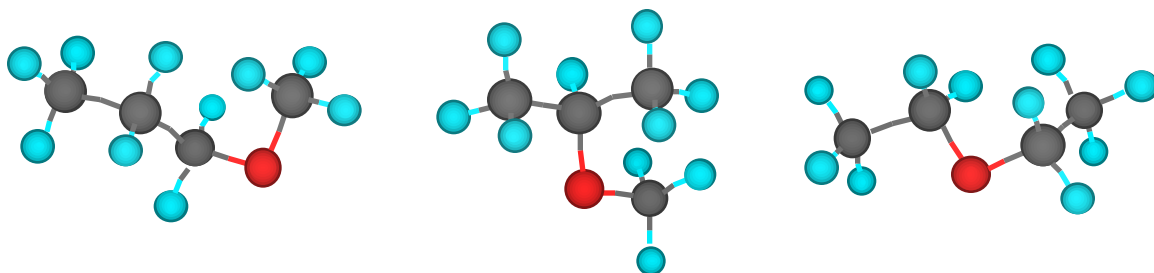
3. Make a model of one of the seven isomers of $C_4H_{10}O$ and then convert it into the other alcohols (four total) and ethers (three total). Draw each structure. Identify skeletal, positional, and functional isomers. Determine if the alcohols are primary, secondary, or tertiary.

The four structures below are alcohols. The first two are positional isomers of one another and the second two are also positional isomers of one another. The first two are skeletal isomers of the second two. The first and last alcohol are primary, the second is secondary, and the third is tertiary.

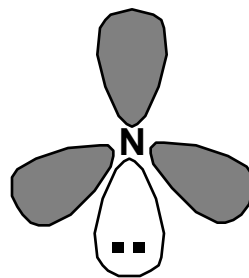
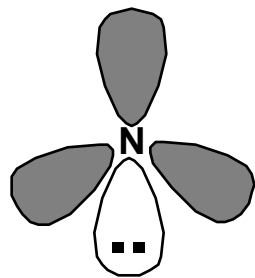




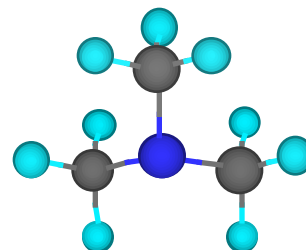
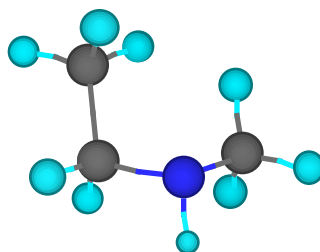
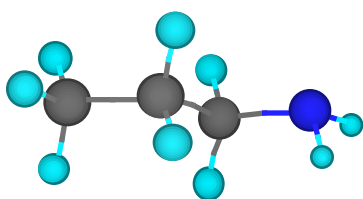
The following three compounds are all ethers and they are functional isomers of the previous four alcohols. The first two ethers are positional isomers of each other and the third is a skeletal isomer of the other two.



10



Amines



CHAPTER SUMMARY

10.1 Structure of Amines

Amines are derivatives of ammonia in which one or more hydrogens have been replaced by organic groups. Replacement of one hydrogen results in a **primary amine**. In a **secondary amine**, two hydrogens are replaced and in a **tertiary amine**, three hydrogens on ammonia are replaced. The nitrogen in alkyl amines is sp^3 hybridized, tetrahedral, and has bond angles of about 109° .

10.2 Nomenclature of Amines

A. Alkyl and Aromatic Amines

Common nomenclature of simple amines involves presenting the name of the alkyl group followed by the word amine (such as propylamine); this type of nomenclature is acceptable in IUPAC for simple amines. In **IUPAC nomenclature**, the name is based on the longest continuous chain of carbon atoms followed by the suffix -amine (such as 1-propanamine). Substituents on the carbon chain are located by a number; substituents on the nitrogen are located with N (such as N-methyl-1-propanamine). The simplest aromatic amine is **aniline**.

B. Unsaturated Amines

In **unsaturated amines**, the double bond or triple bond is named with the usual suffix (en and yn respectively) and located by a number.

CONNECTIONS 10.1 Nasal Decongestants, Diet Pills, and Stimulants

10.3 Physical Properties of Amines

Melting points and boiling points of amines generally increase with molecular weight. Because of **hydrogen bonding**, amines have higher than expected boiling points and lower molecular weight amines are water soluble. Amines with greater hydrogen bonding capacity have higher boiling points than those with similar molecular weight. Tertiary amines have no N-H bond and therefore cannot engage in hydrogen bonding; primary amines have two N-H bonds and secondary amines have two.

CONNECTIONS 10.2 Local Anesthetics and Cocaine

10.4 Basicity of Amines

A. Salt Formation

Basicity is the characteristic property of amines; the presence of a **non-bonding** electron pair on nitrogen makes amines **Lewis bases**.

Because of their basicity, amines react readily with strong mineral acids to form ammonium salts.

B. Expressing Relative Basicities of Amines: The Basicity Constant

Relative basicities are expressed using the **basicity constant, K_b** , which is defined as the concentrations of the ionized amine products in water (ammonium salt and hydroxide) divided by the concentration of the un-ionized amine. Larger K_b 's mean greater basicity. **pK_b** is the negative logarithm of K_b ; the smaller the pK_b the stronger the base.

C. Relationship of Structure and Basicity in Amines

1. **Electron-releasing groups** increase the availability of nitrogen's lone pair and, as a result, also increase the basicity of amines; **alkyl amines are more basic than ammonia.**

2. **Electron-withdrawing groups** decrease the availability of the non-bonding electron pair and decrease basicity; **amides are much less basic than ammonia.**

3. In aromatic amines, the non-bonding electron pair on nitrogen overlaps with the benzene pi-cloud by resonance; this decreases the availability of the lone pair and stabilizes the compound. As a result, **aromatic amines are considerably less basic than aliphatic amines.** Electron-donating groups on an aromatic amine increase availability of the non-bonding pair whereas electron-withdrawing groups decrease availability; as a result **electron-donating groups on an aromatic ring increase basicity and electron-withdrawing groups decrease basicity.** The effect of these groups is greatest at the ortho and para positions.

D. Expressing Basicity with Acidity Constants

Basicity can also be expressed with **acidity constants.** With amines, **K_a** defines the equilibrium in the direction of the ammonium salt ionizing to the free amine and hydronium ion in water. Since this is the opposite of the definition of K_b , small K_a 's and large pK_a 's mean strong basicity.

10.5 Amines as Nucleophiles: Alkylation by Nucleophilic Substitution

Alkylation involves treating ammonia or an amine with an alkyl halide. The amine, as a Lewis base with a non-bonding electron pair, is a good nucleophile and displaces the halide ion from the alkyl halide; the reaction is **nucleophilic substitution** with a neutral nucleophile. S_N2 reactions are common. Since alkylation tends to continue until four groups are bonded to the nitrogen, it has limited synthetic utility.

CONNECTIONS 10.3 Acetylcholine and Neuromuscular Blockade

10.6 Preparations of Amines by Reduction Reactions

A. Reduction of Aromatic Nitro Compounds

Amines can be synthesized by **reduction of nitro compounds** with hydrogen and platinum catalyst or with a tin and hydrochloric acid solution. Aromatic nitro compounds can be made by treating benzene or a benzene derivative with nitric and sulfuric acids.

B. Reduction of Nitriles

Nitriles can be reduced using hydrogen gas and nickel catalyst to produce amines.

C. Reduction of Amides

Lithium aluminum hydride is used to **reduce amides**. In both cases amines are the reduction products.

CONNECTIONS 10.4 Sulfa Drugs

10.7 Aromatic Diazonium Salts

A. Preparation

Upon treatment with sodium nitrite and hydrochloric acid at 0°C , primary aromatic amines can be converted to **aromatic diazonium salts**, an unstable species that is very useful in organic synthesis. Since a nitro group can be reduced to a primary amine, it is a synthetic precursor to a diazonium salt.

B. Replacement Reactions

Diazonium salts are quite useful in organic synthesis as the diazonium group can be easily replaced by fluorine, chlorine, bromine, iodine, cyanide, hydroxy, and hydrogen. In these **diazonium replacement reactions**, nitrogen gas is evolved.

C. Coupling Reactions

In **coupling reactions** of diazonium salts, nitrogen is retained and actually bonds to an activated aromatic ring in an **electrophilic aromatic substitution reaction**. This reaction is used to make **azo dyes**.

CONNECTIONS 10.5 Dyes and Dyeing

10.8 Heterocyclic Amines

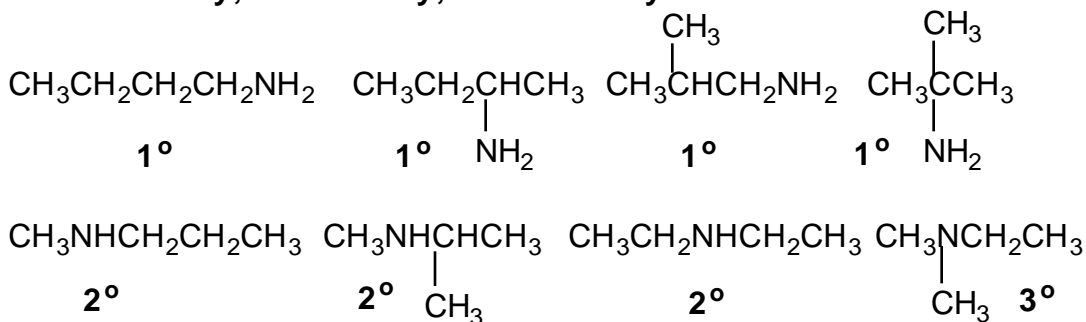
Heterocycles are cyclic compounds in which one or more of the ring atoms are not carbon.

A. Structure and Basicity of Heterocyclic Amines

Heterocyclic amines have nitrogen as one of the ring atoms. Although they are basic, their basicity can vary widely depending on structure and availability of nitrogen's non-bonding electron pair. Aromatic heterocyclic amines in which the nitrogen's non-bonding electron pair is part of the aromatic pi-cloud, the aromatic sextet, are much less basic than those in which it is not. If the nitrogen is involved in a "double bond", its lone pair is not in the pi cloud or part of the sextet.

B. Naturally Occurring Heterocyclic Amines: Alkaloids

Alkaloids are defined as plant-produced nitrogenous bases that have a physiological effect on humans. They are often classified according to the heterocyclic amine present in the structure. These include the following ring systems: pyrrolidine, pyrrole, piperidine, pyridine, quinoline, isoquinoline, indole, and purine.

SOLUTIONS TO PROBLEMS**10.1 Primary, Secondary, and Tertiary Amines****10.2 Nomenclature of Amines**

- (a) 1-nonanamine; (b) 2-hexanamine; (c) N,N-dimethyl-3-pentanamine;
 (d) N-ethyl-N-methyl-1-octanamine; (e) 2-ethyl-N-methylcyclohexanamine;
 (f) N-ethyl-N-methyl-3-nitroaniline

10.3 Nomenclature of Amines

Names of compounds in Problem 10.1 in order left to right.

First row: 1-butanamine; 2-butanamine; 2-methyl-1-propanamine;
 2-methyl-2-propanamine

Second row: N-methyl-1-propanamine; N-methyl-2-propanamine;
 N-ethylethanamine; N,N-dimethylethanamine.

10.4 Nomenclature of Amines

- (a) 2-penten-1-amine; (b) 5-methyl-3-hexyn-1-amine;
 (c) 2,4-hexadien-1,6-diamine; (d) N-methyl-3-penten-2-amine

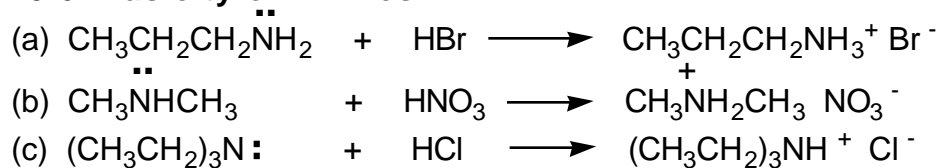
10.5 Physical Properties

(a) **ii < iii < i** These amines are isomers of one another. The differences in boiling point are determined by differences in hydrogen bonding capacity. ii is a tertiary amine with no N-H bonds and is incapable of hydrogen bonding. iii is a secondary amine with one N-H bond and i is a primary amine with two N-H bonds. The primary amine is most capable of hydrogen bonding and has the highest boiling point.

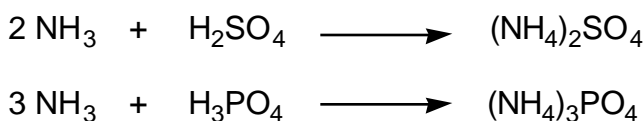
(b) **iii < iv < ii < i** These compounds have similar molecular weights. iii is non-polar and has no capacity for hydrogen bonding. iv and ii have N-H bonds

and can hydrogen bond; ii has a higher boiling point because it has two N-H bonds. i has an O-H bond and since this is much more polar than the N-H bonds, it hydrogen bonds more extensively and has the highest boiling point.

10.6 Basicity of Amines

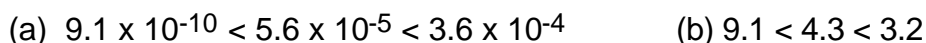


10.7 Ammonium Fertilizers



10.8 Basicity Constants

Constants are shown in increasing basicity.



10.9 Basicity Constants

(a) diethylamine; (b) triethylamine; (c) triethylamine; (d) p-methylaniline

10.10 Basicity of Amines

Arrangements are least basic to most basic.

(a) **ii < i < iii** Alkyl groups are electron-releasing and increase the availability of the lone pair of electrons on nitrogen. ii has no alkyl groups, i has one, and iii has two.

(b) **iii < ii < i** Carbon-oxygen double bonds are electron-withdrawing groups. They decrease the electron density around the nitrogen and lower the basicity. iii has two electron-withdrawing groups, ii has only one, and i has none.

(c) **v < iii < i < ii < iv** v has two electron-withdrawing groups, iii has one; these groups decrease lone pair availability and decrease basicity. i has neither releasing or withdrawing groups. ii has one electron-releasing group (alkyl) and iv has two; electron-releasing groups increase lone pair availability and increase basicity.

(d) $ii < iii < iv < v < i$ The amines with lowest basicity have an electron-withdrawing group (the carbon-oxygen double bond). The greater the distance of this group from the amine, the less effective. *v* has neither electron-releasing or electron-withdrawing groups, and *i* has an electron-releasing group which increases basicity.

10.11 Basicity of Amines

Arrangements are least basic to most basic.

(a) $i < ii < iii$ *i* and *ii* are both aromatic amines and are much less basic than *iii* which is an alkyl amine. Although *ii* is aromatic and not very basic, it does have a methyl group, an electron-releasing group, that increases basicity relative to the primary aromatic amine.

(b) $i < ii < iii$ The nitro group is electron-withdrawing and decreases basicity. It more effectively decreases basicity at ortho and para positions because of resonance; thus *ii* is more basic than *i*, because the nitro is meta in *ii* and cannot decrease basicity as effectively. *iii* has an electron-releasing group that increases basicity.

(c) $ii < i < iii$ *ii* has two withdrawing groups, *i* has one; electron-withdrawing groups decrease basicity. *iii* has an electron-releasing group that increases basicity.

(d) $ii < iii < i$ *ii* has an electron-withdrawing group attached directly to the nitrogen where it is most effective in decreasing lone pair availability and thus decreasing basicity. *iii* has an electron-withdrawing group but it is on the benzene ring, not right on the nitrogen. *i* has neither electron-releasing or withdrawing groups.

10.12 Expression of Basicity with Acidity Constants

Least to most basic for amines.

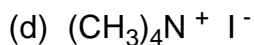
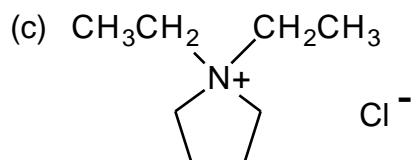
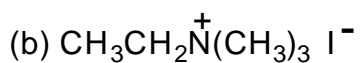
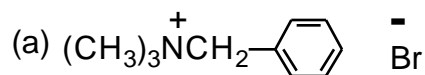
(a) $9.9 \times 10^{-10} < 8.3 \times 10^{-10} < 2.3 \times 10^{-11}$ (b) $5.25 < 9.81 < 10.74$

10.13 Expression of Acidity with Acidity Constants

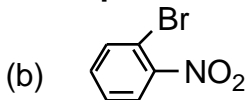
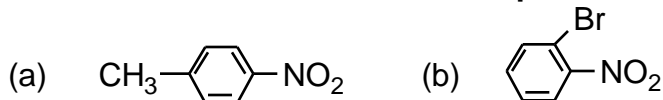
Least to most acidic for acids.

(a) $2.3 \times 10^{-11} < 8.3 \times 10^{-10} < 9.9 \times 10^{-10}$ (b) $10.74 < 9.81 < 5.25$

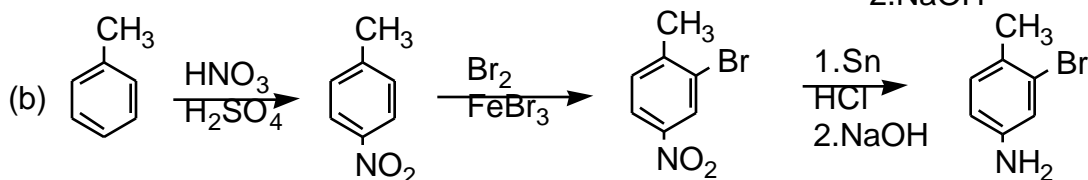
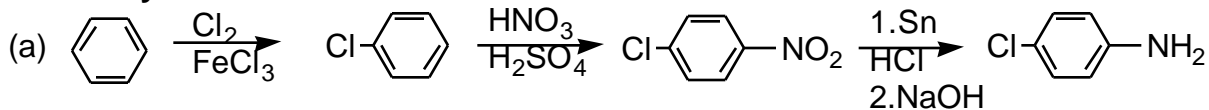
10.14 Alkylation of Amines by Nucleophilic Substitution



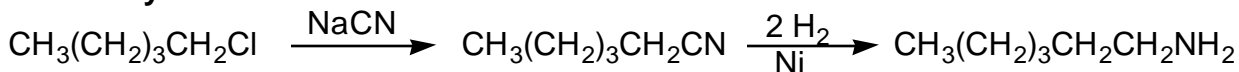
10.15 Reduction of Nitro Compounds



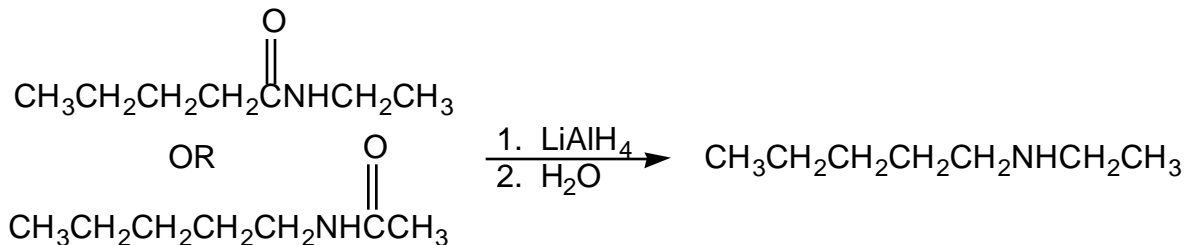
10.16 Synthesis of Amines



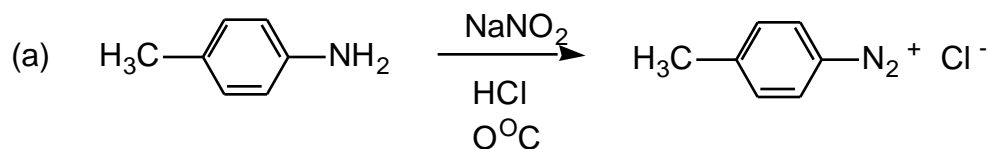
10.17 Synthesis of Amines

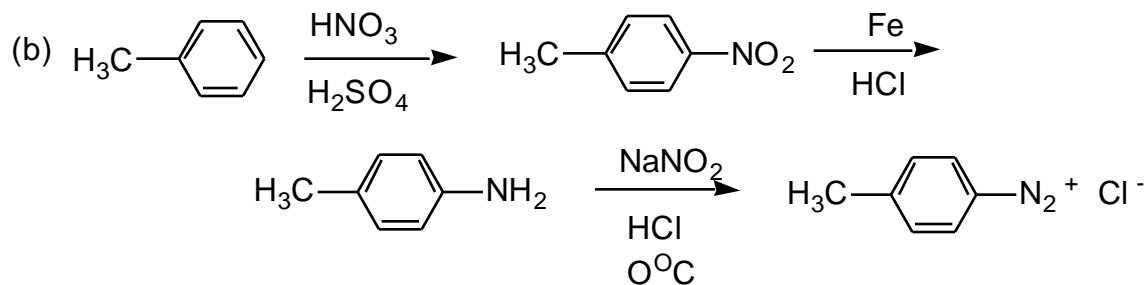


10.18 Reduction of Amides

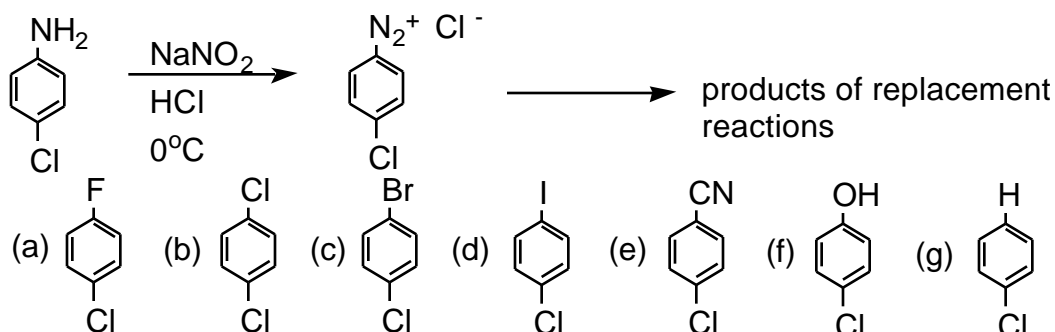


10.19 Preparation of Diazonium Salts

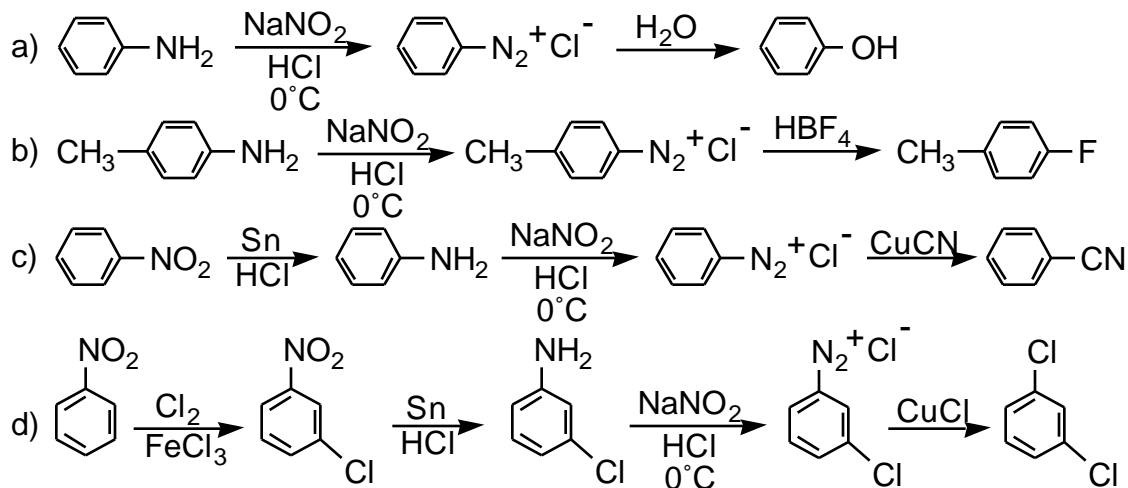




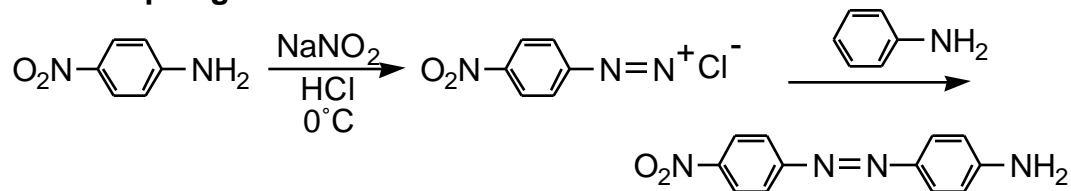
10.20 Diazonium Salt Replacement Reactions



10.21 Synthesis Using Diazonium Salts



10.22 Coupling Reactions of Diazonium Salts



10.23 Aromatic Heterocyclic Amines

Quinoline is aromatic. The ring system is planar and has a p-orbital on each carbon as a result of the "double bonds". There are a total of 6 pi electrons in the ring with the nitrogen. The non-bonding electron pair on nitrogen is not part of the aromatic sextet.

Indole is also aromatic. Two double bonds and the non-bonding electron pair of nitrogen comprise the aromatic sextet. There is a p-orbital on each carbon of the ring system as a result of the "double bonds". To allow aromaticity, the lone pair of electrons on nitrogen also exists in a p-orbital and is part of the aromatic sextet.

10.24 Aromatic Heterocyclic Amines

Isoquinoline is aromatic. The ring system is planar and has a p-orbital on each carbon as a result of the "double bonds". There are a total of 6 pi electrons in the ring with the nitrogen. The non-bonding electron pair on nitrogen is not part of the aromatic sextet.

Purine is also aromatic. Each ring is planar. Consider the five-membered ring first. Each atom has a p-orbital as a result of a "double bond" or, in the case of the NH, a p-orbital housing a non-bonding electron pair. There are six pi electrons, four from the "double bonds" and two from the lone pair of electrons on the NH. The lone pair of the other nitrogen is not part of the aromatic sextet. Now consider the six-membered ring. There are six pi electrons as a result of the three "double bonds" to complete the aromatic sextet. Neither of the nitrogens in this ring contributes its lone pair to the aromatic sextet.

10.25 IUPAC Nomenclature: Section 10.2A

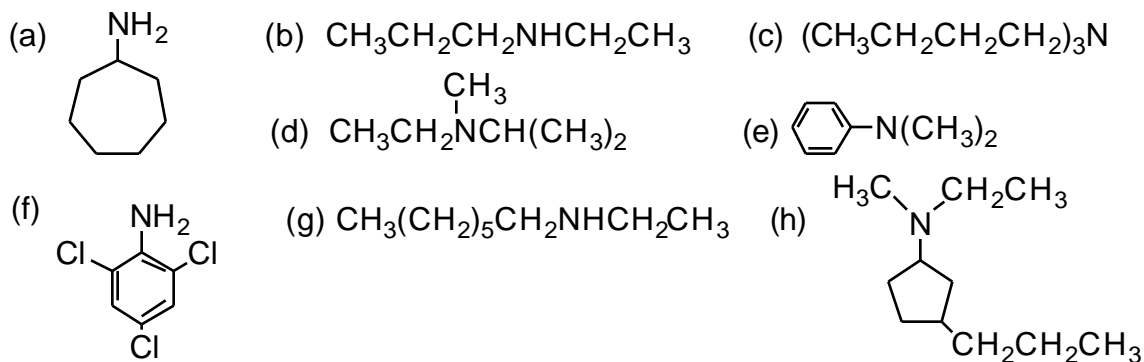
(a) 1-heptanamine; (b) 2-butanamine; (c) 1,8-octandiamine

10.26 IUPAC Nomenclature: Section 10.2A

(a) cyclohexanamine; (b) 4-methylcyclohexanamine;
(c) N-ethyl-4-methylcyclohexanamine; (d) p-methylaniline;
(e) N-ethyl-p-methylaniline; (f) N-ethyl-N-methylaniline;
(g) 2-bromo-N,N-diethyl-1-propanamine;
(h) 7,7-dimethyl-N,N-dipropyl-2-octanamine

10.27 IUPAC Nomenclature: Section 10.2B

- (a) 4-heptyn-1-amine; (b) 2-hexen-1-amine;
 (c) N-ethyl-2,4-hexadien-1-amine; (d) N,N-dimethyl-2-butyn-1-amine;
 (e) 3-cyclopenten-1-amine; (f) 3-methyl-3-cyclopenten-1-amine;
 (g) N,N-diethyl-3-methyl-3-cyclopenten-1-amine

10.28 IUPAC Nomenclature: Section 10.2A**10.29 Physical Properties:** Sections 2.9, 9.2, and 10.3

- (a) $\text{i} < \text{ii} < \text{iii} < \text{iv}$: increasing molecular weight in a homologous series
 (b) $\text{iii} < \text{i} < \text{ii}$: no hydrogen bonding in III; hydrogen bonding with OH is more effective than with NH because of increased bond polarity.
 (c) $\text{iii} < \text{ii} < \text{i}$: these compounds are isomers; the number of NH bonds increases from zero to two in this order and thus hydrogen bonding increases.
 (d) $\text{iii} < \text{ii} < \text{i}$: these compounds are isomers; the number of NH bonds increases from zero to two in this order and thus hydrogen bonding increases.

10.30 Physical Properties: Sections 2.9, 9.2, and 10.3

Methylamine has the lowest molecular weight and, though it has the most hydrogen bonding sites (two NH bonds), the low molecular weight gives it the lowest boiling point. Dimethylamine has one NH bond and can hydrogen bond and it is greater in molecular weight than methylamine. Although trimethylamine has the greatest molecular weight, it has no NH bonds and no hydrogen bonding; as a result it happens to fall in the middle. The boiling points of these compounds are close, they would be hard to predict, but they can be explained using hydrogen bonding and molecular weight.

10.31 Physical Properties: Section 2.9, 9.2, and 10.3

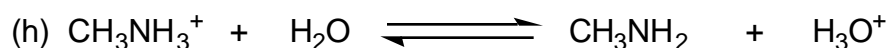
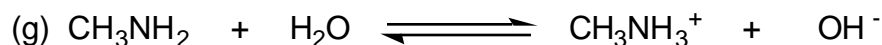
These compounds have similar molecular weights so that is not a factor. Pentane is non-polar and is incapable of hydrogen-bonding; this causes it to have the lowest boiling point. Butylamine has two NH bonds and diethylamine only one; the decreased ability to hydrogen bond gives diethylamine a lower boiling point. 1-butanol has an OH bond which is very polar and very effective in hydrogen bonding compared to amines; it has the highest boiling point as a result.

10.32 Basicity Constants: Section 10.4B

(a) $10^{-10} < 10^{-5} < 10^{-3}$; (b) $10 < 5 < 3$; (c) $11 < 6 < 3$; (d) $10^{-11} < 10^{-6} < 10^{-3}$

10.33 Acidity Constants: Sections 9.6A.1, 10.4D

(a) $10^{-12} < 10^{-8} < 10^{-3}$; (b) $10^{-3} < 10^{-8} < 10^{-12}$; (c) $12 < 8 < 3$;
 (d) $13 < 9 < 4$; (e) $4 < 9 < 13$; (f) $10^{-13} < 10^{-9} < 10^{-4}$

**10.34 Basicity of Amines:** Section 10.4C

(a) Propylamine is more basic than ammonia because the propyl group is an electron donating group and increases the electron availability around the nitrogen. (b) Diethylamine is more basic than ethylamine because it has two electron-donating groups (the ethyls) whereas ethylamine has only one; the electron-donating groups increase electron availability.

(c) Aniline is an aromatic amine. Its non-bonding electron pairs are pulled into the benzene ring by resonance making them less available to acids. This makes it much less basic than cyclohexylamine which is an alkylamine.

(d) Both are aromatic amines and are a lot less basic than alkyl amines. However, the N-methylaniline has an electron-donating group on the nitrogen (methyl) which increases electron availability and thus basicity.

(e) In N-phenylaniline, there are two benzene rings attached to the nitrogen. The non-bonding electron pair on nitrogen is drawn into both and this makes the compound less basic than aniline in which there is only one benzene ring.

(f) Chlorine is an electron-withdrawing group. As such it makes the non-bonding electron pair on nitrogen less available. As a result, aniline is more basic.

(g) Nitro groups are electron-withdrawing groups; they decrease electron availability and basicity. There are two nitro groups on 2,4-dinitroaniline so it is less basic than p-nitroaniline where there is only one.

(h) Chlorine withdraws electrons and decreases basicity; 2-chloropropanamine is less basic than propanamine for this reason.

(i) Both of these compounds have a chlorine which is an electron-withdrawing group and decreases basicity. In 3-chloropropanamine the chlorine is further away from the amine group than in 2-chloropropanamine and, because of this, it has a diminished effect. Thus 3-chloropropanamine is more basic.

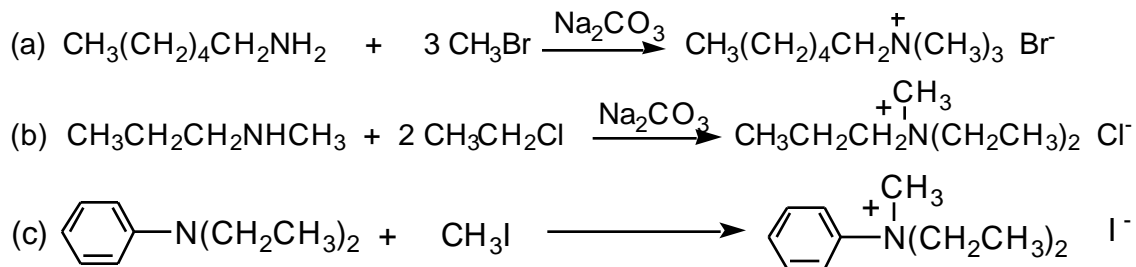
10.35 Acidity and Basicity of Phenol and Aniline: Sections 9.6A.2, and 10.4C.3

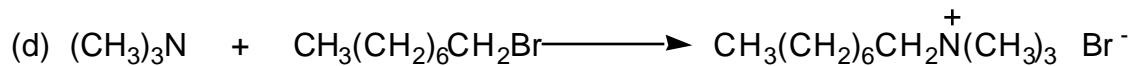
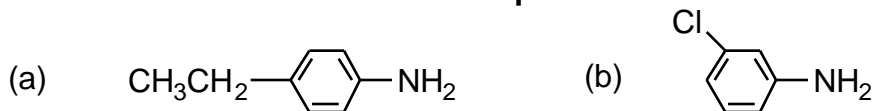
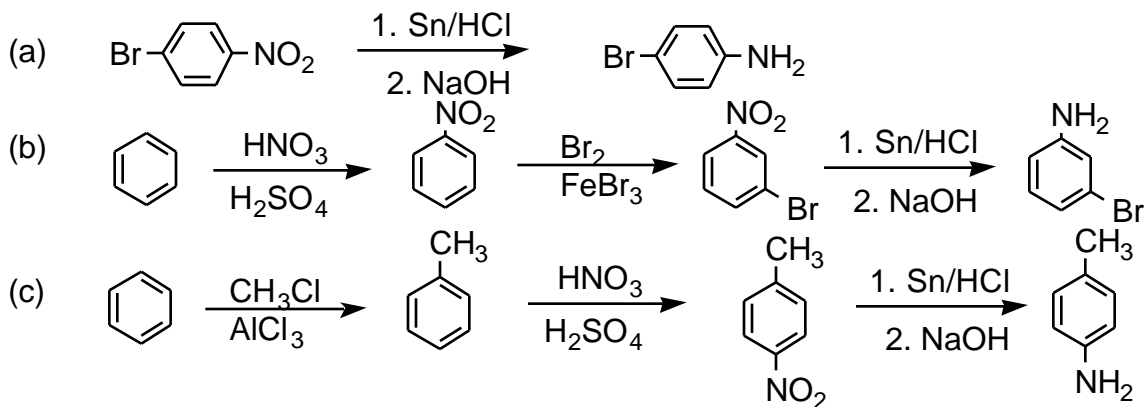
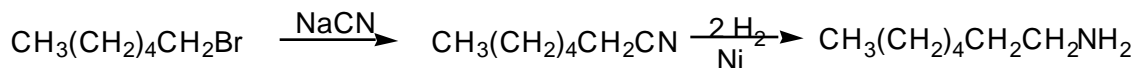
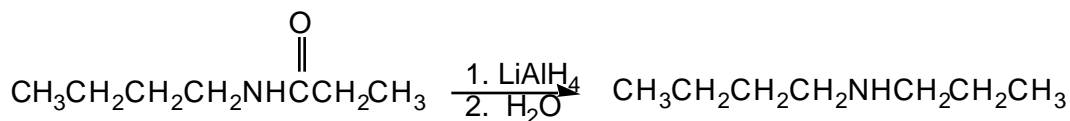
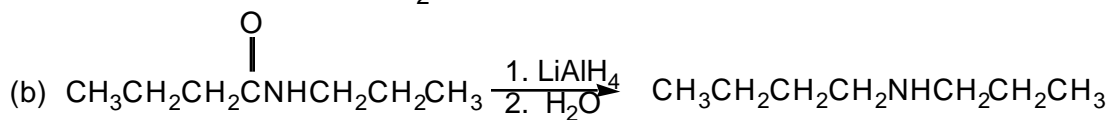
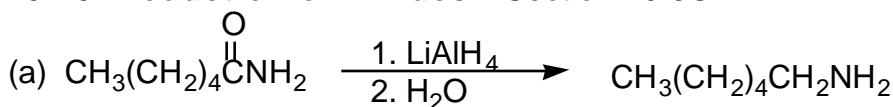
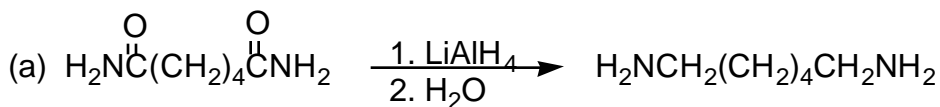
Phenols are more acidic than alcohols because one of the non-bonding electron pairs on oxygen is drawn into the benzene ring by resonance. This stabilizes the phenoxide ion that is formed upon ionization and thus the acidity of phenol is enhanced by the phenomenon. This same withdrawal of electrons by the benzene ring stabilizes aniline and decreases the availability of the non-bonding electron pair on nitrogen. Both effects decrease the basicity of aniline relative to alkyl amines.

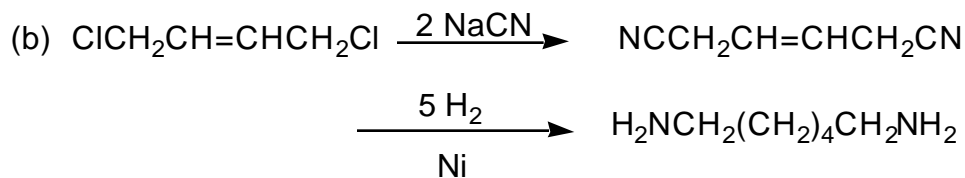
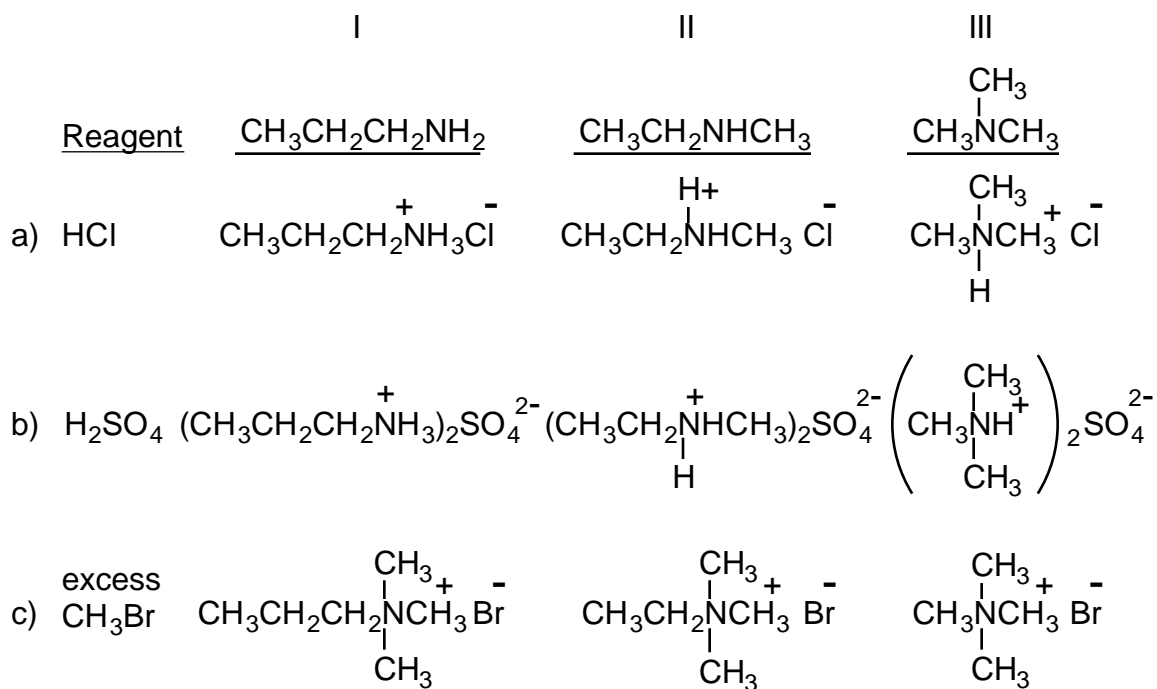
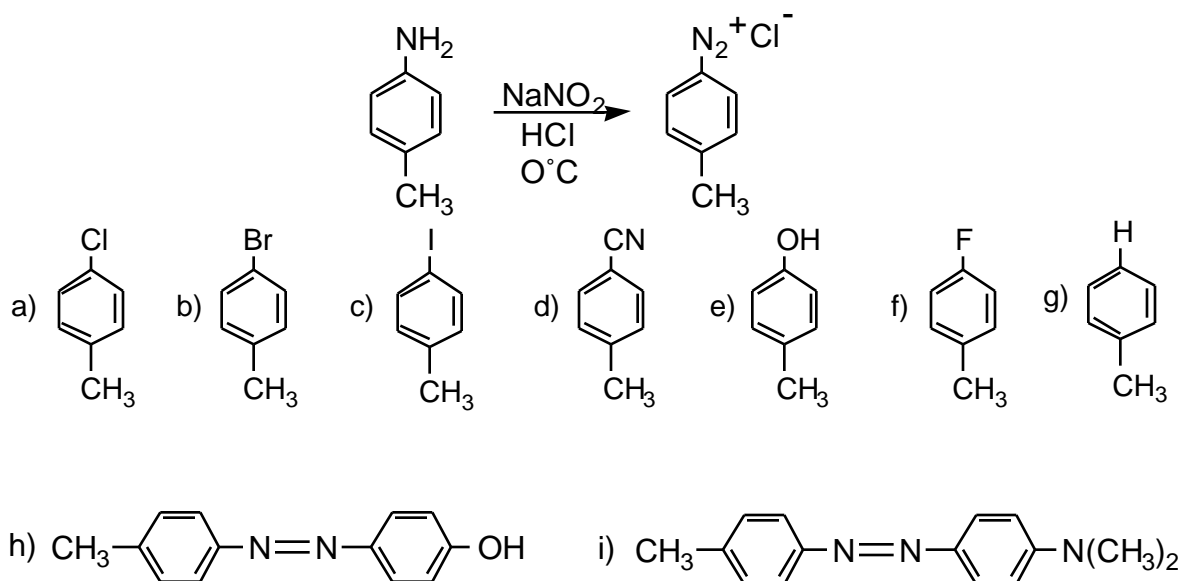
The withdrawal of electrons into the benzene ring makes both aniline and phenol more electron-rich. In electrophilic aromatic substitution, the ring is attacked by a positive electrophile; the more negative the ring, the more readily it reacts with an electrophile.

Please see the textbook references for the resonance structures and hybrids described.

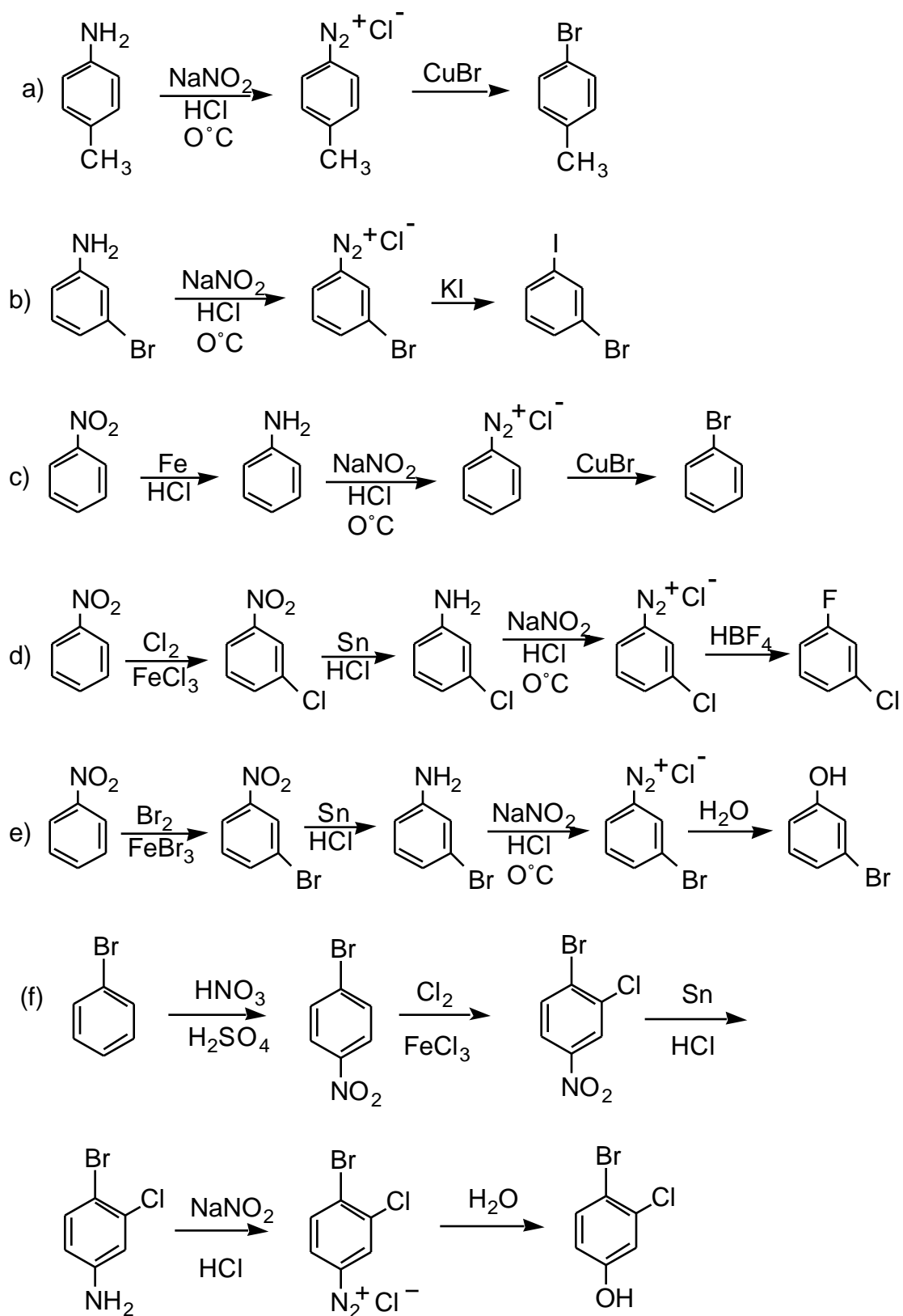
10.36 Alkylation of Amines: Section 10.5

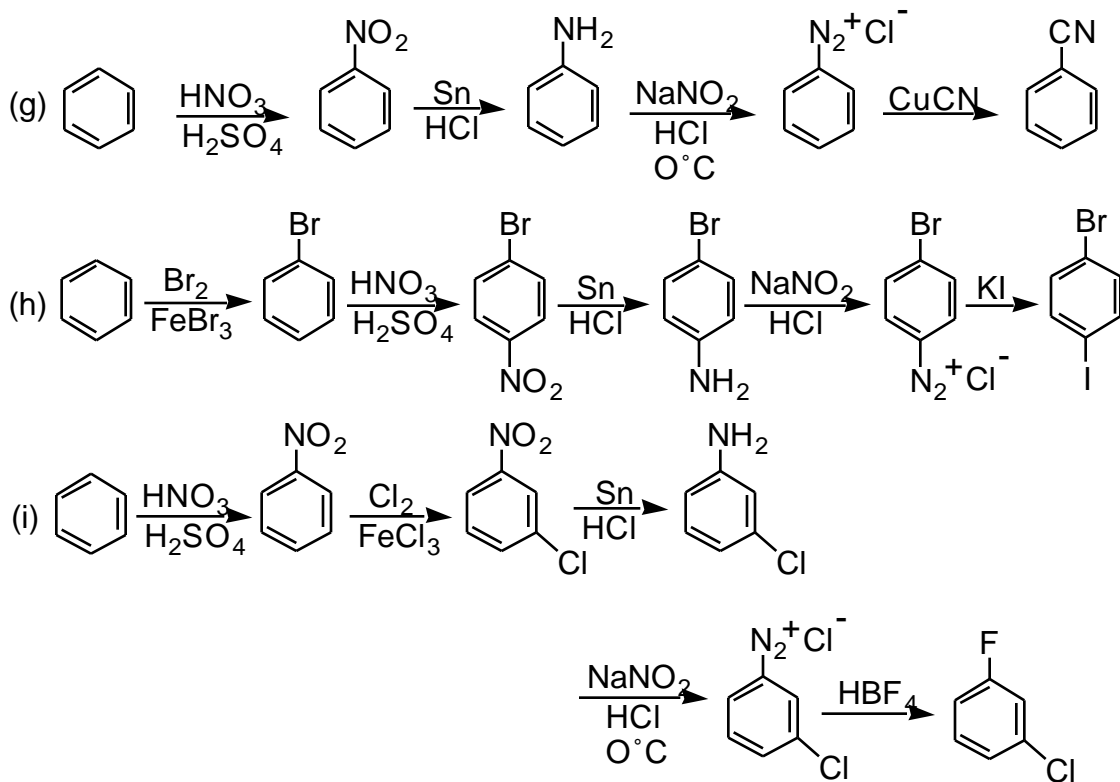



10.37 Reduction of Nitro Compounds: Section 10.6A

10.38 Reduction of Nitro Compounds: Sections 6.4 and 10.6A

10.39 Reduction of Nitriles: Sections 8.4 and 10.6

10.40 Reduction of Amides: Section 10.6C

10.41 Reductions to form Amines: Section 10.6


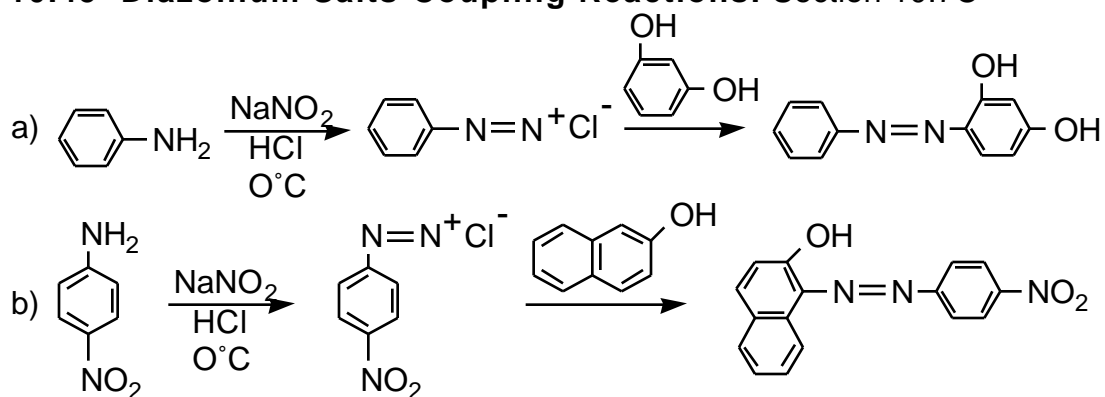

10.42 Reactions of Amines: Sections 10.5A and 10.6

10.43 Reactions of Diazonium Salts: Section 10.7


10.44 Syntheses Using Diazonium Salts: Sections 6.4 and 10.7





10.45 Diazonium Salts-Coupling Reactions: Section 10.7C



10.46 Basicity of Aromatic Amines: Section 10.8A

Both compounds need six pi-electrons in the ring system and a p-orbital on each ring atom to be aromatic. In each case there are two double bonds which provide four pi-electrons and four p-orbitals. The final p-orbital and two pi-electrons are provided by a nitrogen in each case. Visualize the nitrogen not involved in a double bond as housing its non-bonding electron pair in a p-orbital that overlaps with the others in the ring. Because of this overlap, this non-bonding electron pair is not as available to acids and the basicity is

drastically diminished. If an acid base reaction occurred, this electron pair would be used and the aromaticity destroyed, another factor that causes diminished basicity. In imidazole, there is a second nitrogen, the one involved in the double bond. Its non-bonding electron pair is not part of the pi-system as the double bond provides the p-orbital at that location and there already exists the aromatic sextet of electrons. Consequently, this electron-pair is much more available than that of the other nitrogen or the pair on the nitrogen in pyrrole and imidazole is four million times more basic than pyrrole.

10.47 Aromaticity of Heterocyclic Compounds: Section 10.8A

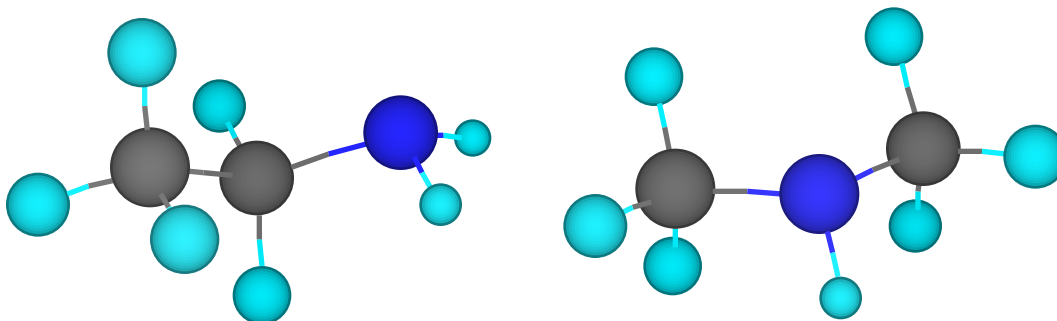
Both compounds are cyclic, planar, have a p-orbital on each ring atom, and have six pi-electrons. Four of the electrons and four of the p-orbitals come from the double bonds. The last p-orbital and the final two pi-electrons are a result of one of the non-bonding electron pairs on oxygen and sulfur existing in a p-orbital that overlaps with the others and completes the aromatic system.

10.48 Dyes: Connections 10.5

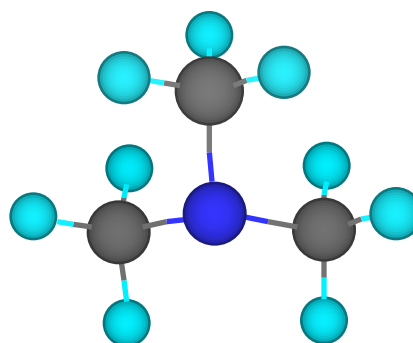
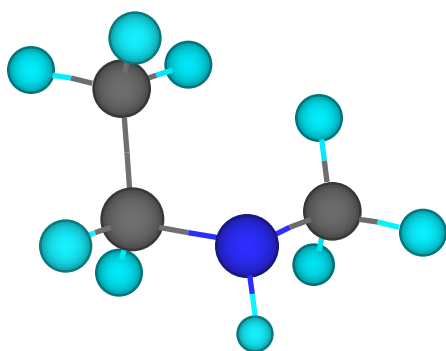
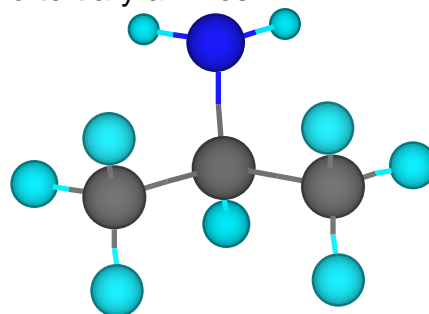
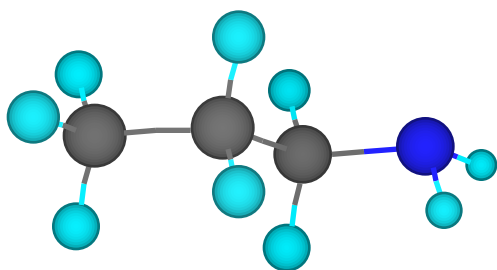
Chromophore and auxochrome groups are listed early in the Connections essay. Look for these along with extensive conjugation in the structures of dyes presented.

ACTIVITIES WITH MOLECULAR MODELS

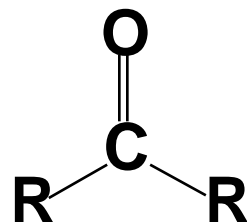
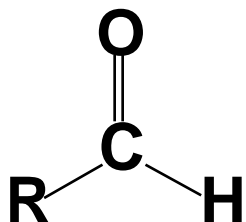
1. Make models of a primary and a secondary amine of C_2H_7N .



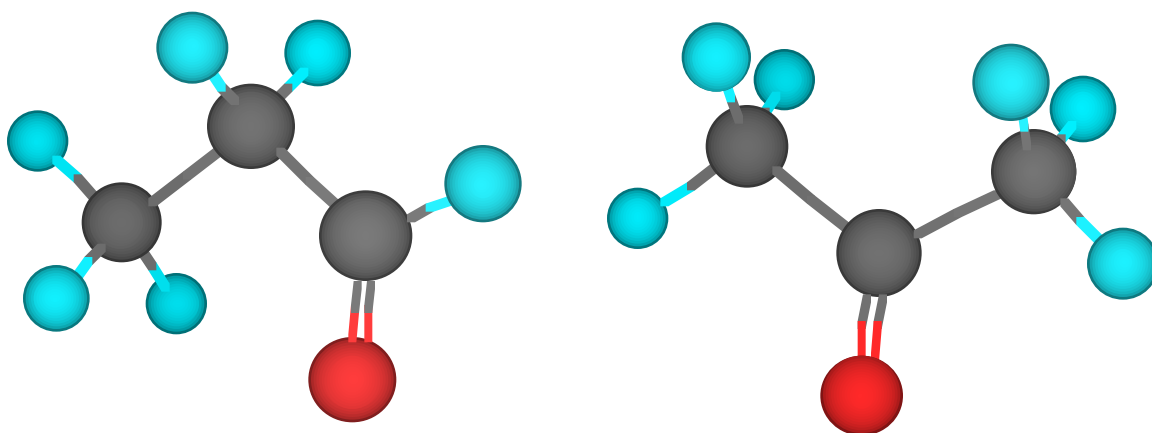
2. Make models of the four isomers of C_3H_9N . What is the hybridization of each carbon and the nitrogen? How many non-bonding electron pairs are on the nitrogen? Identify primary, secondary and tertiary amines.



11



ALDEHYDES AND KETONES



CHAPTER SUMMARY

11.1 Structure of Aldehydes and Ketones

Aldehydes and **ketones** both have a **carbonyl group** (carbon-oxygen double bond); aldehydes have at least one carbon bonded to the carbonyl group, whereas in ketones the carbonyl is bonded to two carbons.

11.2 Nomenclature of Aldehydes and Ketones

A. IUPAC Nomenclature of Aldehydes and Ketones

In IUPAC nomenclature, the suffix for aldehydes is **-al** and for ketones, **-one**. The prefix for both is **oxo**.

B. Polyfunctional Aldehydes and Ketones

In polyfunctional compounds, the group highest in the following sequence is designated with a suffix and the others with prefixes: **aldehyde > ketone > alcohol > amine**.

C. Unsaturated and Polyfunctional Aldehydes and Ketones

In naming, first determine the longest continuous carbon chain; insert the suffix *an*, *en*, or *yn* to designate all single bonds or one or more double bonds or triple bonds respectively; use the suffix ending for the functional group highest in the above sequence; name all other groups with prefixes; number the carbon chain to give the lowest number to the functional group.

D. Common Nomenclature

The first four aldehydes have trivial names: formaldehyde, acetaldehyde, propionaldehyde, and butyraldehyde. The simplest ketone is acetone. Others are named by expressing the name of each alkyl group, followed by ketone.

CONNECTIONS 11.1 Formaldehyde and Synthetic Polymers

11.3 Some Preparations of Aldehydes and Ketones

A. Hydration of Alkynes

B. Ozonolysis of Alkenes

C. Friedel-Crafts Reaction

D. Oxidation of Alcohols

11.4 Oxidation of Aldehydes: Tollens' "Silver Mirror" Test

Aldehydes and ketones are chemically distinguished by oxidation. Aldehydes are easily oxidized and ketones are not. In the **Tollens' "silver mirror" test** aldehydes are oxidized to carboxylic acids and ketones are not oxidized. A silver mirror plates on the side of the test tube as silver ion is reduced to silver metal.

11.5 Addition Reactions of Aldehydes and Ketones

A. General Considerations

The carbonyl group of aldehydes and ketones is reactive because it is polar, there is a pi bond, there are two non-bonding electron-pairs on oxygen, and it has a flat, open structure that makes it accessible to other reagents. Because of its polarity, the carbonyl group attracts nucleophiles to the partially positive carbon and electrophiles to the electron-rich oxygen. Among nucleophiles commonly used in reactions with aldehydes and ketones are the hydride ion, carbanions, water, alcohols, and amines. Because aldehydes have only one alkyl group compared to two for ketones (alkyl groups are large relative to hydrogen and hinder nucleophilic attack), they tend to be more reactive than ketones.

Addition is the characteristic reaction of aldehydes and ketones. When unsymmetrical reagents add, the positive part bonds to the partially negative carbonyl oxygen and the negative part bonds to the partially positive carbon. The reactions are not as simple as those of alkenes since the product of straight addition is often unstable and either exists in equilibrium with the original aldehyde or ketone or reacts further to form a more stable substance. Hydrogen and hydrogen cyanide usually form stable addition products. The addition products from water and hydrogen halides are in equilibrium with the original aldehyde or ketone; the equilibrium usually favors the starting materials. Most other adding reagents form an intermediate addition product that further reacts to form a stable substance.

B. Mechanisms of Nucleophilic Addition Reactions of Aldehydes and Ketones

Nucleophilic addition is the characteristic mechanism for addition reactions of aldehydes and ketones. It can be **base-initiated** in which a negative or neutral nucleophile attacks the carbonyl carbon generating a negative carbonyl oxygen that is subsequently neutralized. In the **acid-initiated mechanism**, hydrogen ion bonds to the carbonyl oxygen; a carbocation results which is neutralized by the nucleophile.

C. Addition of Hydrogen Cyanide

Hydrogen cyanide adds to aldehydes and ketones to form a simple addition product called a **cyanohydrin**. The mechanism is **base-initiated nucleophilic addition** with cyanide as the nucleophile.

D. Reduction to Alcohols: Catalytic Hydrogenation

Aldehydes and ketones undergo **catalytic hydrogenation** using hydrogen gas under pressure and a metal catalyst such as nickel. Primary alcohols result from the hydrogenation of aldehydes and secondary alcohols are prepared from ketones.

E. Reduction to Alcohols with Sodium Borohydride and Lithium Aluminum Hydride

Aldehydes and ketones can be **reduced** using **sodium borohydride or lithium aluminum hydride**. The reaction is **base-initiated** with hydride ion as the nucleophile. One mole of sodium borohydride or lithium aluminum hydride reduces four moles of aldehyde or ketone; the reaction mixture is then acidified to produce the neutral alcohol.

F. Grignard Addition - Preparation of Alcohols

Grignard reagents are prepared from the reaction of alkyl halides with magnesium in ether solvent. The alkyl group assumes a negative character and is a nucleophile. When presented with an aldehyde or ketone, the Grignard attacks the carbonyl carbon in a **base-initiated nucleophilic addition**. Neutralization of the negative intermediate results in the preparation of an alcohol. Grignard reagents react with formaldehyde to form primary alcohols, with other aldehydes to form secondary alcohols, and with ketones to produce tertiary alcohols. In

devising a Grignard synthesis, one must realize that one alkyl group of the target alcohol comes from the Grignard reagent and the other hydrogens or alkyl groups come from the chosen aldehyde or ketone.

G. Alcohol Addition - Acetal Formation

Aldehydes and ketones react with alcohols by **acid-initiated nucleophilic addition** to form **hemiacetals** which are usually unstable. Reaction with a second mole of alcohol produces a **acetal**. **Carbohydrates** usually exist in hemiacetal or acetal forms.

H. Addition of Amines

Primary amines react with aldehydes and ketones to form **imines** by nucleophilic addition. Many of the products are crystalline derivatives which have been used to characterize the original carbonyl compounds.

11.6 Reactions Involving Alpha Hydrogens

A. Acidity of Alpha Hydrogens

Alpha hydrogens are hydrogens on carbons directly attached to a carbonyl group. They are **weakly acidic** and can be abstracted by base to form a **carbanion**. The carbanion is called an **enolate ion** and is resonance stabilized. Neutralization of the enolate ion results in an **enol**, a compound in which an alcohol group is directly bonded to a carbon involved in a carbon-carbon double bond. The enol is in equilibrium with the original aldehyde or ketone in an equilibrium referred to as **keto-enol tautomerism**. The equilibrium usually favors the keto form.

B. The Aldol Condensation

The **aldol condensation** involves the reaction of two molecules of an aldehyde or ketone that has alpha hydrogens. Abstraction of an alpha hydrogen by base produces a carbanion which attacks the carbonyl carbon of the other molecule by **base-initiated nucleophilic addition**; an alcohol group is formed. Often the alcohol dehydrates to form the final product, an unsaturated aldehyde or ketone. In a **crossed aldol condensation**, a carbonyl compound with alpha hydrogens reacts with one without alpha hydrogens.

SOLUTIONS TO PROBLEMS**11.1 Nomenclature of Aldehydes and Ketones**

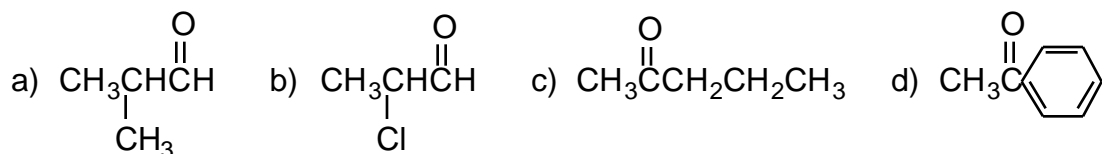
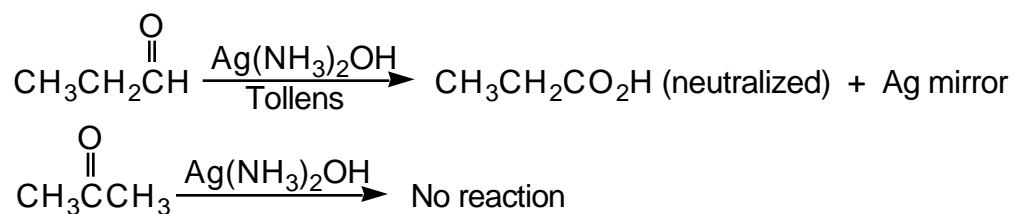
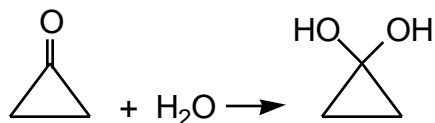
- (a) 4,4-dimethylpentanal (b) 2-octanone; (c) cyclohexanone;
 (d) 4-bromo-2-pentanone

11.2 Nomenclature of Multifunctional Aldehydes and Ketones

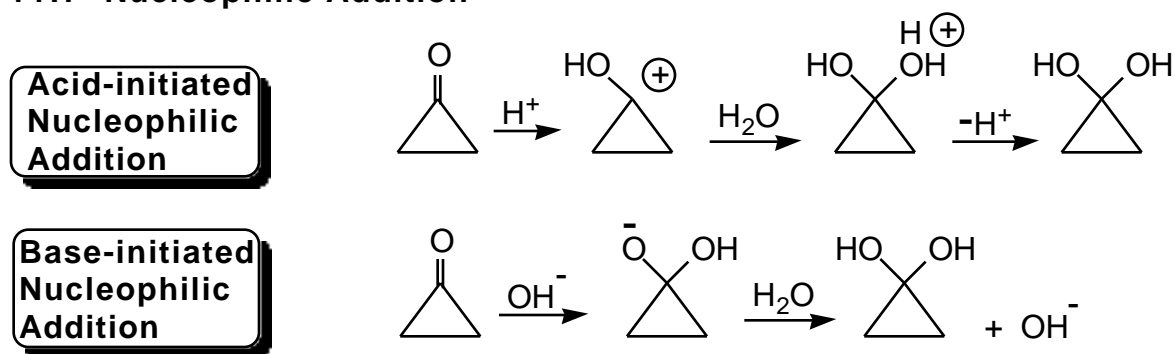
- (a) 1,3,5-cyclohexanetrione; (b) 5-hydroxyhexanal; (c) 7-bromo--3-hydroxy-7-methyl-5-oxooctanal; (d) 6-amino-4-hydroxy-2-heptanone

11.3 Nomenclature of Unsaturated Aldehydes and Ketones

- (a) 3-butyral; (b) 3-cyclopenten-1-one; (c) 7-hydroxy-2-methyl-4-oxo-5-octenal

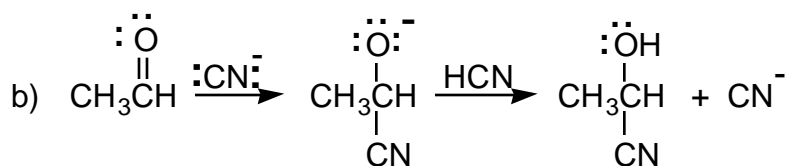
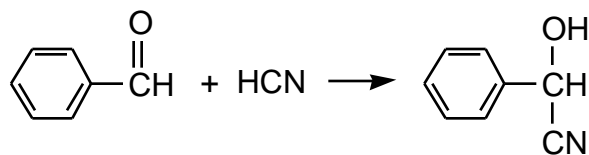
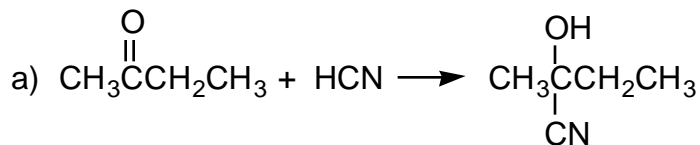
11.4 Common Nomenclature of Aldehydes and Ketones**11.5 Oxidation of Aldehydes****11.6 Addition of Water to Aldehydes and Ketones**

11.7 Nucleophilic Addition

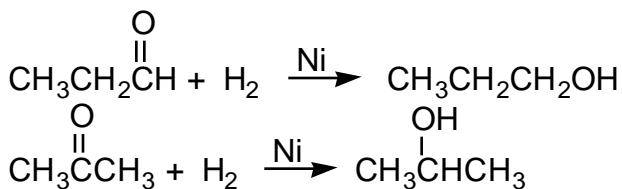


11.8 Addition of HCN to Aldehydes and Ketones

The reaction actually is performed using NaCN followed with acid as shown in the mechanism.

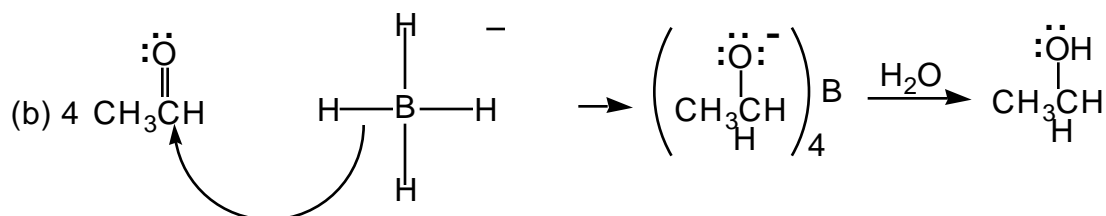
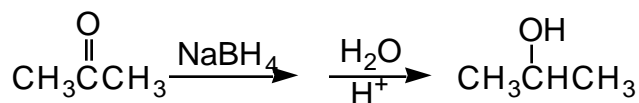
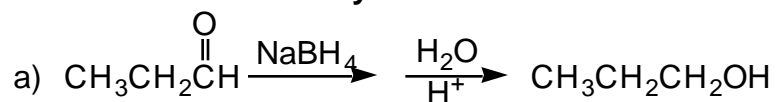


11.9 Catalytic Hydrogenation

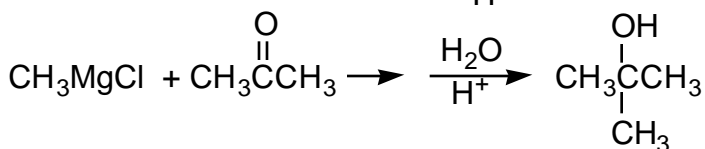
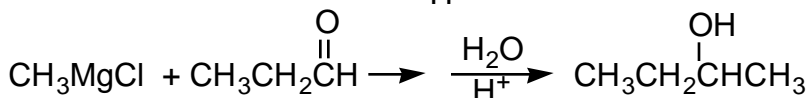
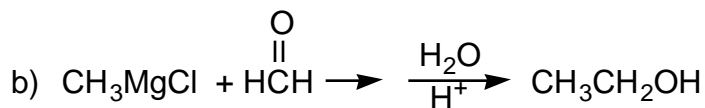
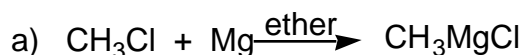


Tertiary alcohols cannot be prepared in this way because a C=O can't have three alkyl groups attached to the carbon. There is no possible aldehyde or ketone precursor.

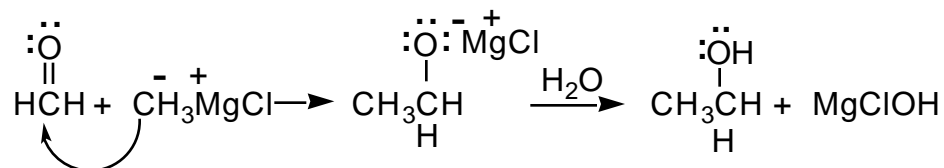
11.10 Sodium Borohydride Reductions



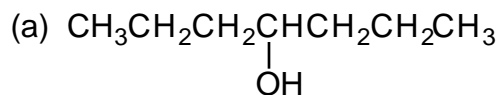
11.11 Grignard Preparation of Alcohols



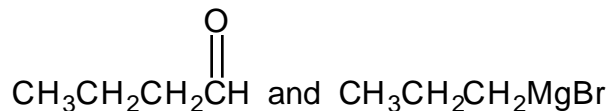
11.12 Grignard Reaction Mechanism

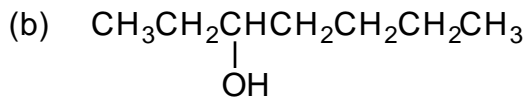


11.13 Grignard Preparation of Alcohols

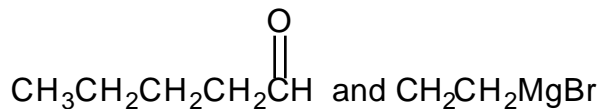
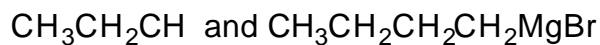


The two alkyl groups connected to the alcohol carbon are identical so there is only one possible synthesis.

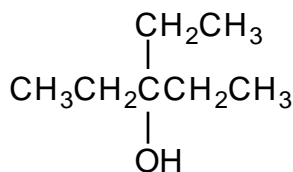




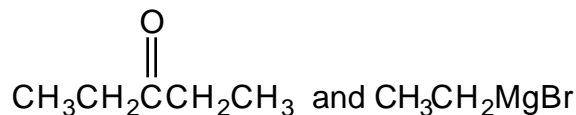
The two alkyl groups connected to the alcohol carbon are different so there are two possible syntheses.



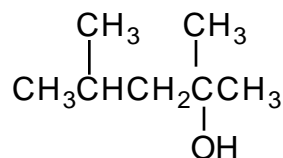
(c)



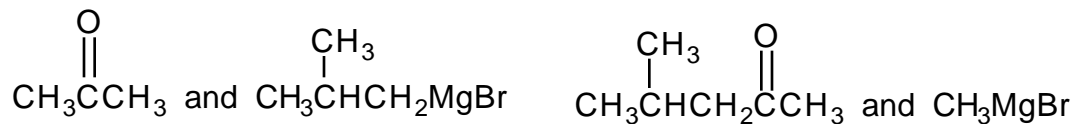
All three alkyl groups connected to the alcohol carbon are identical so there is only one possible synthesis.



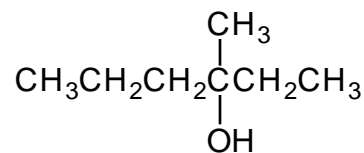
(d)



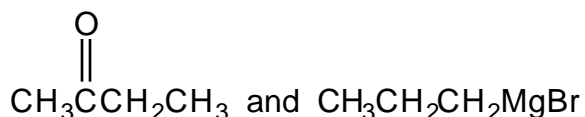
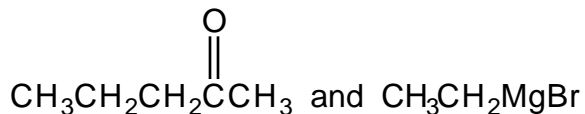
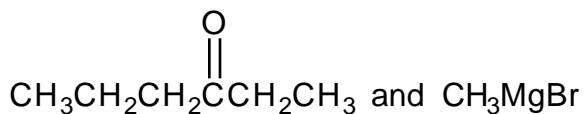
Since two of the three alkyl groups connected to the alcohol carbon are identical (there are only two different alkyl groups), there are two syntheses.



(e)

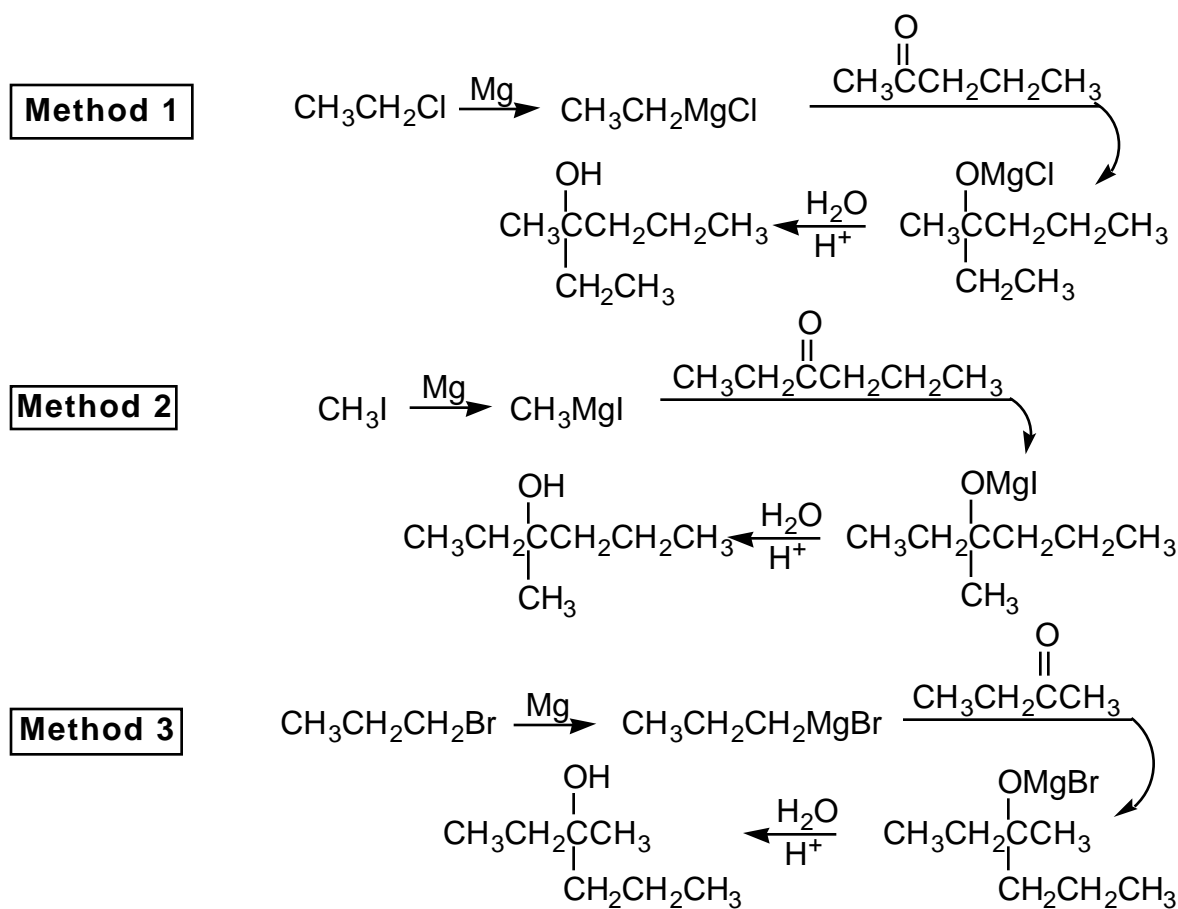


There are three different alkyl groups attached to the alcohol carbon and thus three different syntheses.

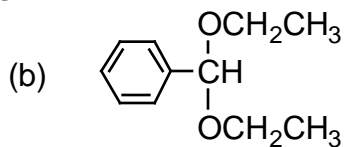
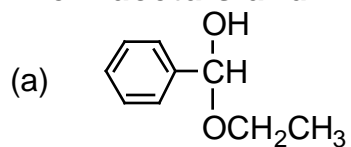


See next problem for a more detailed look at the syntheses of this alcohol.

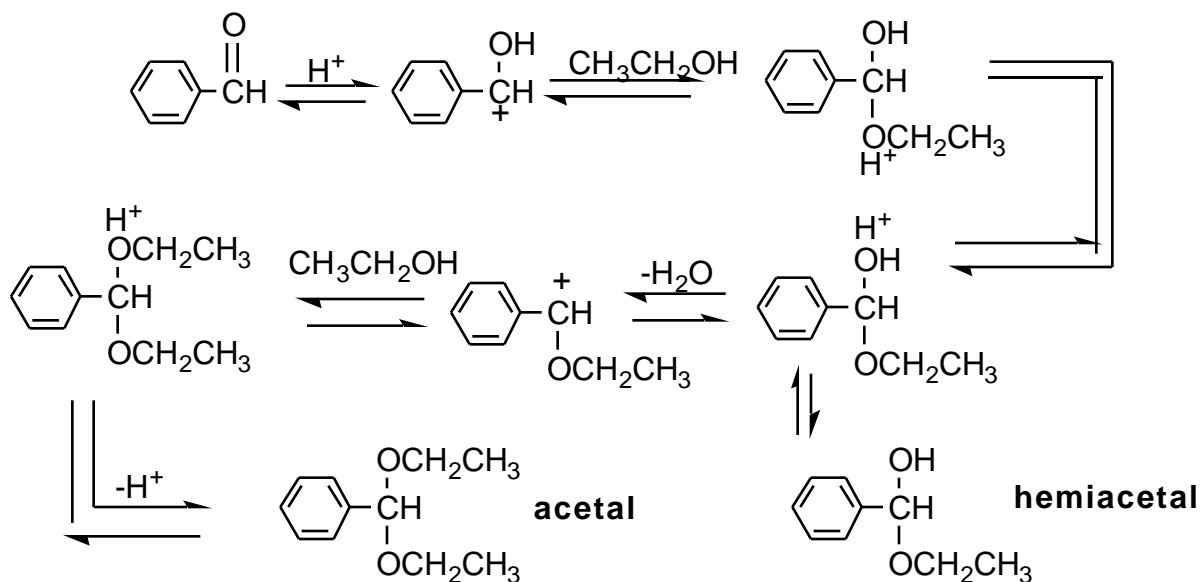
11.14 Grignard Preparation of Alcohols



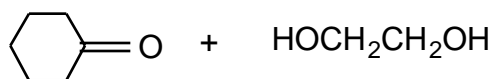
11.15 Hemiacetals and Acetals



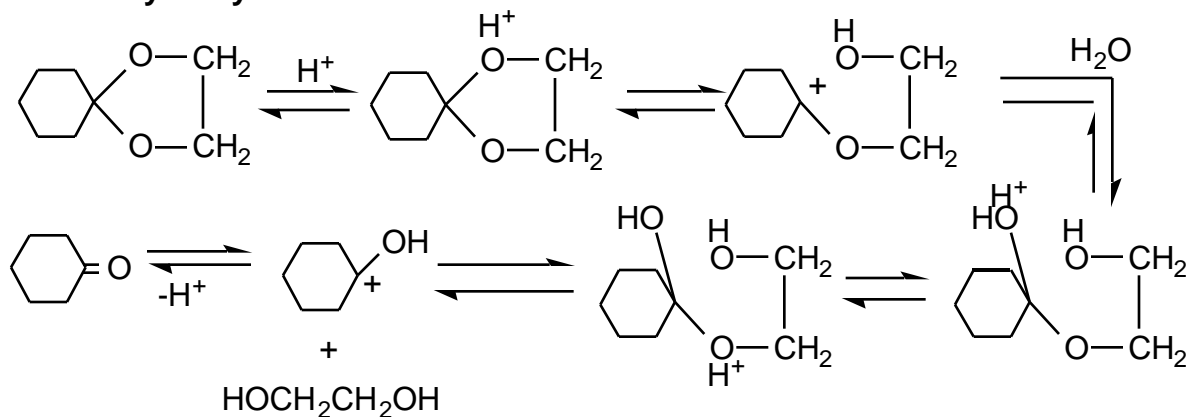
11.16 Hemiacetal and Acetal Formation Reaction Mechanism



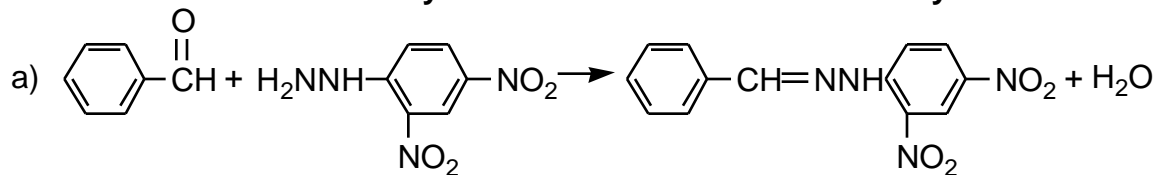
11.17 Acetal Formation

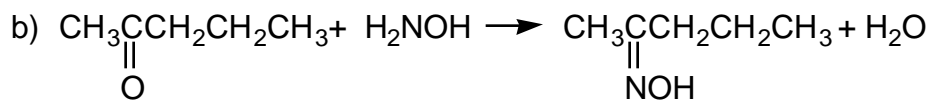
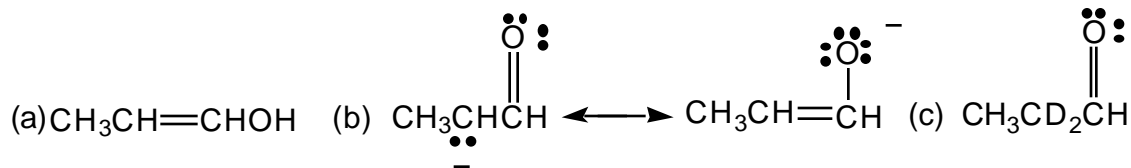
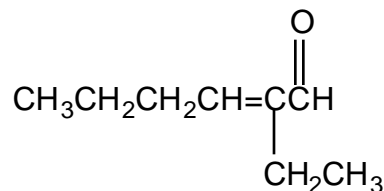


11.18 Hydrolysis of Acetals

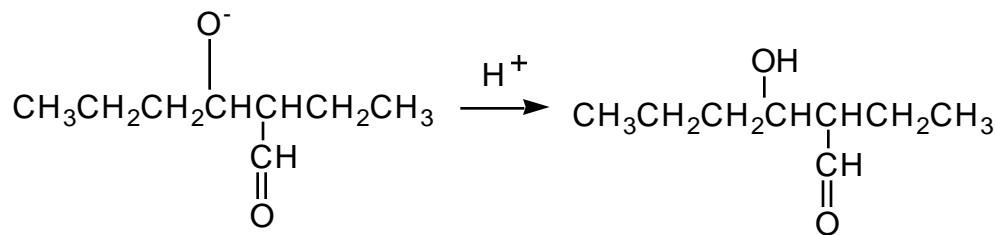
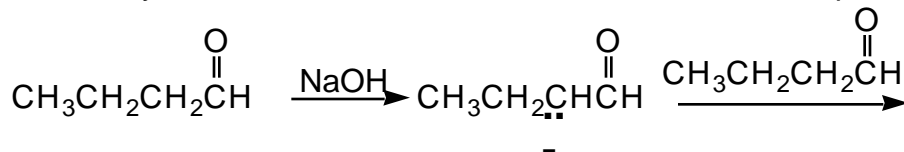
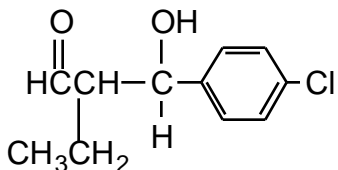
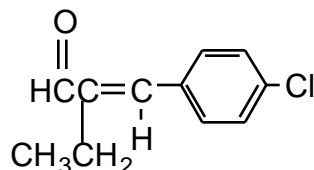


11.19 Reaction of Aldehydes and Ketones with Primary Amines

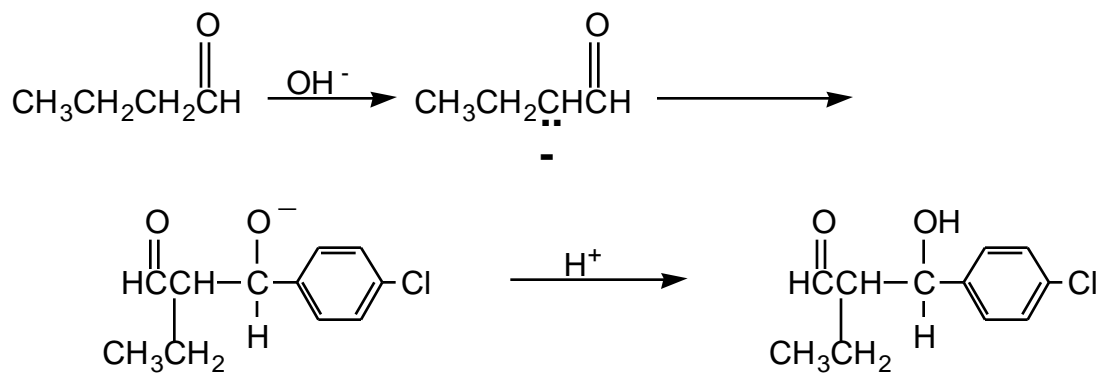


**11.20 Keto and Enol Forms****11.21 Aldol Condensation****11.22 Aldol Condensation Mechanism**

Only the aldol mechanism is shown; not the subsequent dehydration.

**11.23 Crossed Aldol Condensation****Aldol Product****Dehydration Product****11.24 Mechanism of Aldol Condensation**

Only the aldol condensation mechanism is shown, not the dehydration.

**11.25 IUPAC Nomenclature of Aldehydes:** Section 11.2A

- (a) decanal; (b) 4-methylpentanal; (c) 5-ethyl-3-methylheptanal;
 (d) p-methylbenzaldehyde; (e) 1,6-hexandial

11.26 IUPAC Nomenclature of Ketones: Section 11.2A

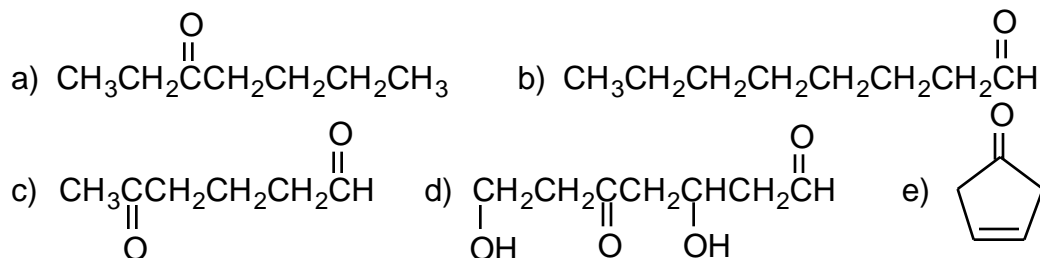
- (a) 3-heptanone; (b) 2-methyl-4-heptanone; (c) 4-methylcyclohexanone;
 (d) 2,4,6-heptantrione; (e) 4,5-dibromo-1,3-cyclopentandione

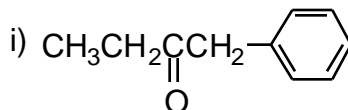
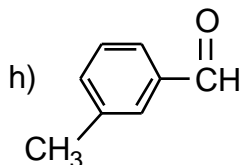
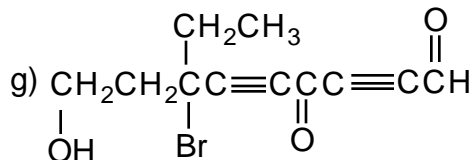
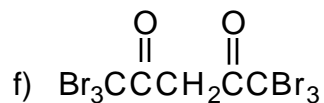
11.27 IUPAC Nomenclature of Aldehydes and Ketones: Section 11.2B

- (a) propanal; (b) 3-pentanone; (c) 3,5-dihydroxyhexanal;
 (d) 4-amino-2-pentanone; (e) 5-hydroxy-3-oxohexanal;
 (f) 4-hydroxy-2,6-octandione; (g) 3-amino-5-methylhexanal;
 (i) 4-hydroxycyclohexanone

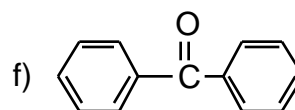
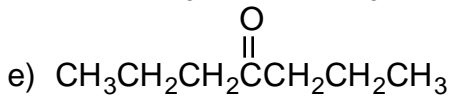
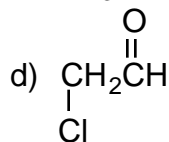
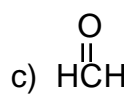
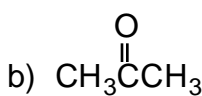
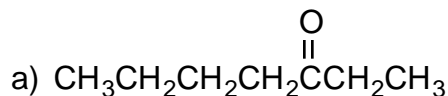
11.28 IUPAC Nomenclature of Aldehydes and Ketones: Section 11.2C

- (a) 3-butenal; (b) 1-hydroxy-3-butyn-2-one; (c) 2,4-hexadienal;
 (d) 6-amino-3-oxo-4,7-octadienal; (e) 3-hepten-2,5-dione;
 (f) 4-oxo-2-hexen-5-ynal

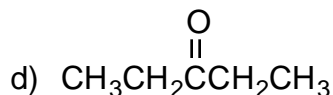
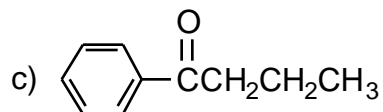
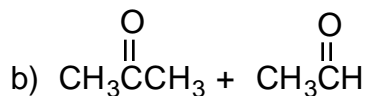
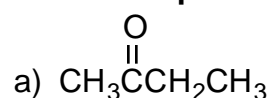
11.29 IUPAC Nomenclature: Section 11.2



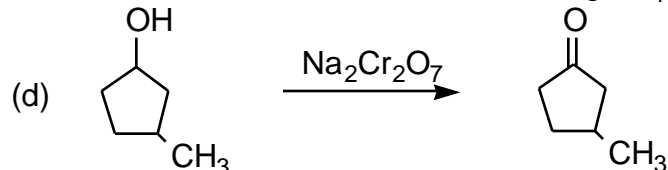
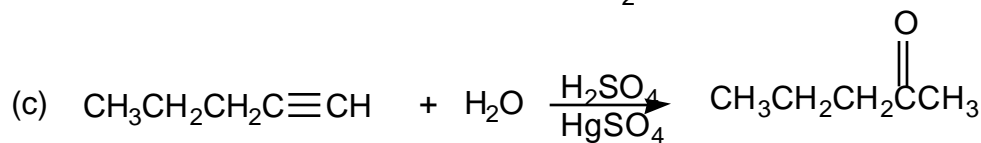
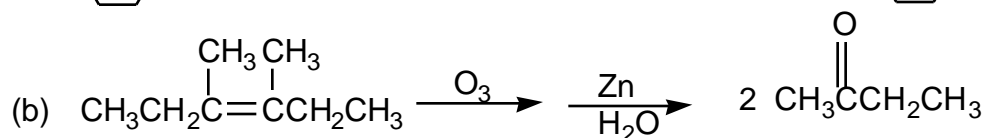
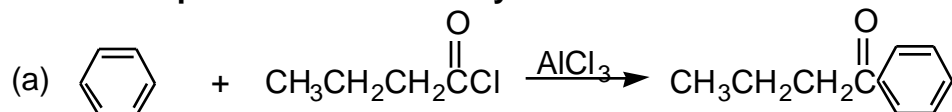
11.30 Common Nomenclature: Section 11.2D

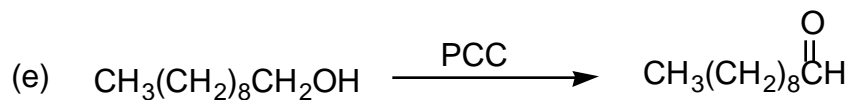


11.31 Preparations of Aldehydes and Ketones: Section 11.3

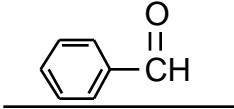
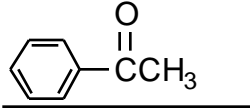
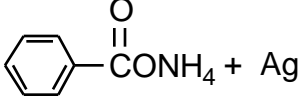
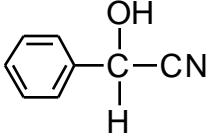
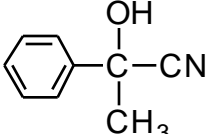

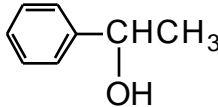

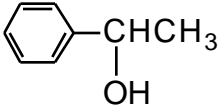
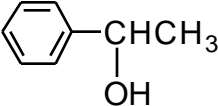
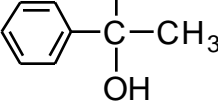
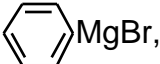
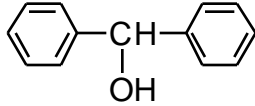
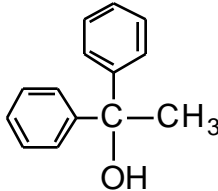
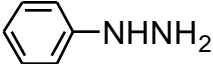
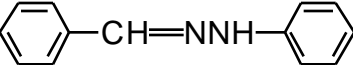
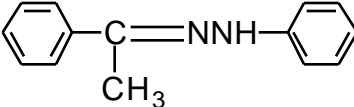
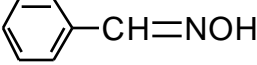
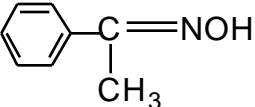
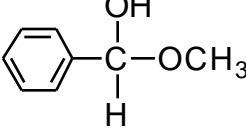
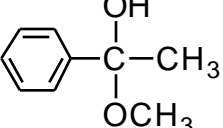


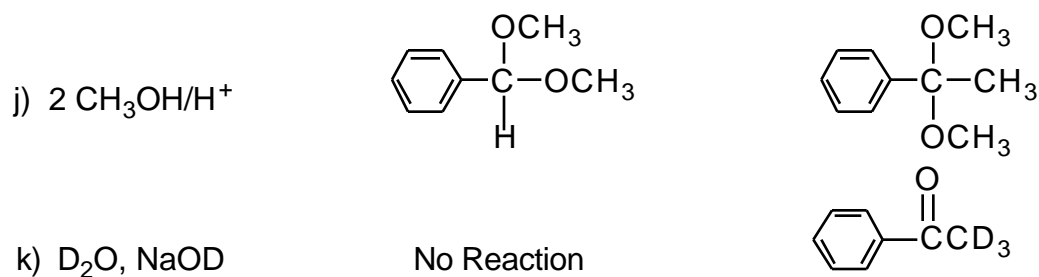
11.32 Preparations of Aldehydes and Ketones: Section 11.3



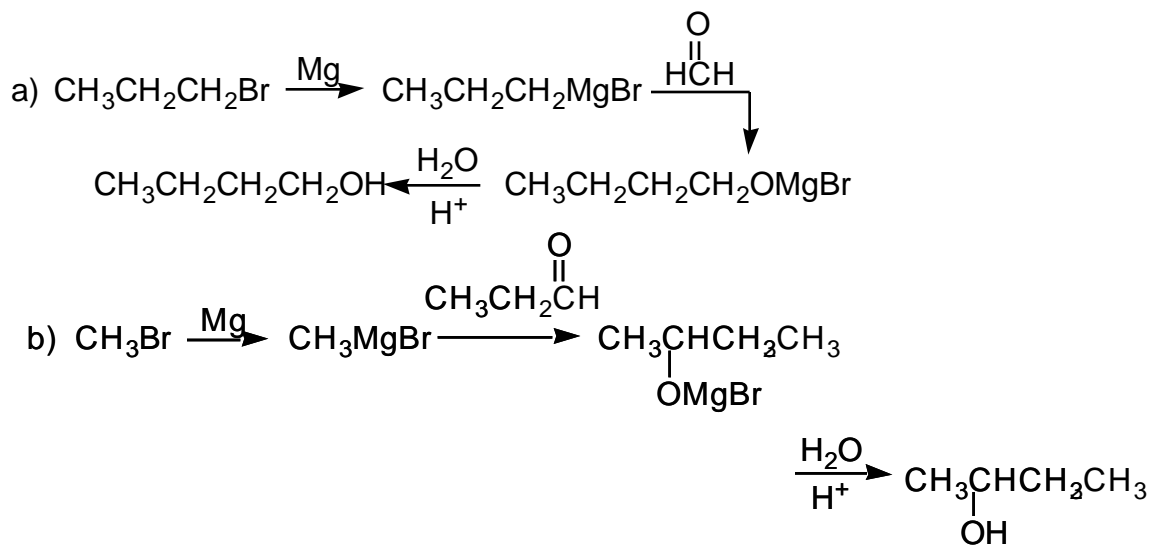


11.33 Reactions of Aldehydes and Ketones: Section 11.5-11.6

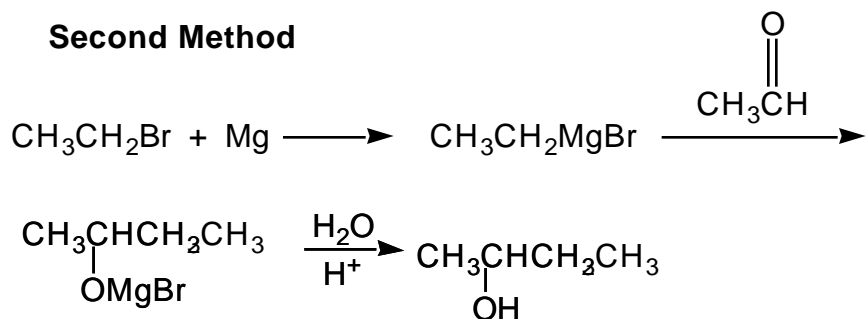
Reagent	I. Products from	II. Products from
		
a) Tollens' Reagent $\text{Ag}(\text{NH}_3)_2\text{OH}$	 + Ag	No reaction
b) HCN		
c) H_2/Ni		
d) NaBH_4 , then H_2O		
e) CH_3MgCl , then H_2O		
f)  then H_2O		
g) 		
h) H_2NOH		
i) $\text{CH}_3\text{OH}/\text{H}^+$		

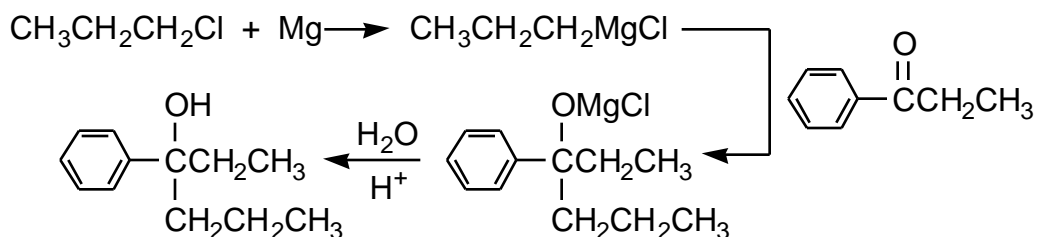
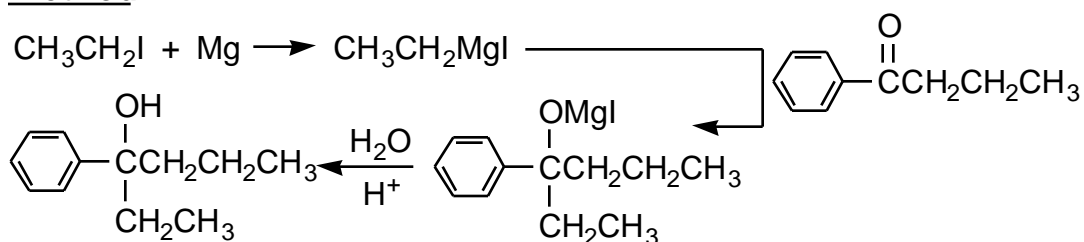
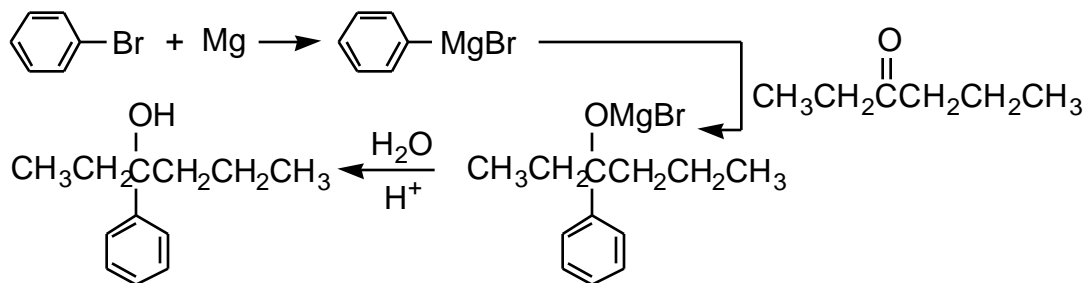
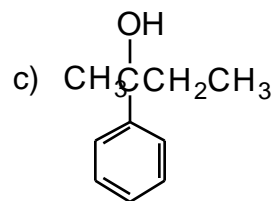
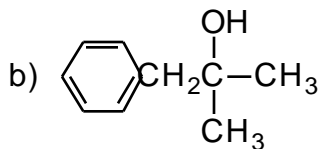
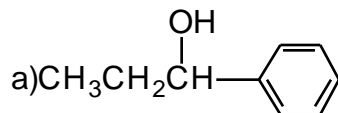


11.34 Grignard Synthesis of Alcohols: Section 11.5F.3

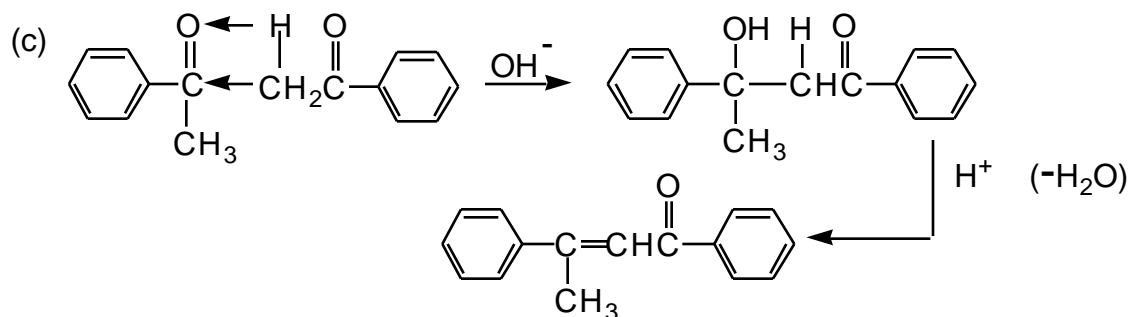
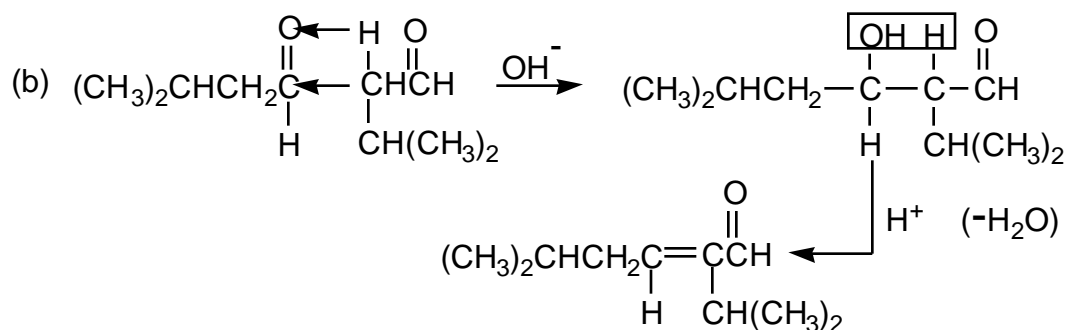
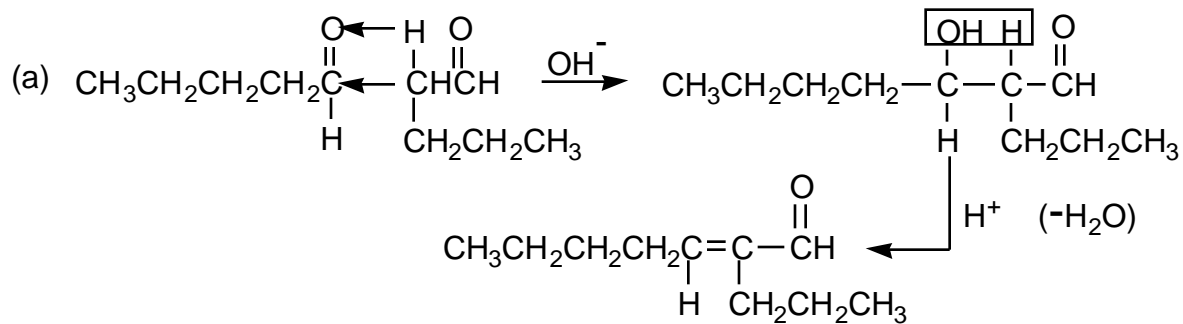


Second Method

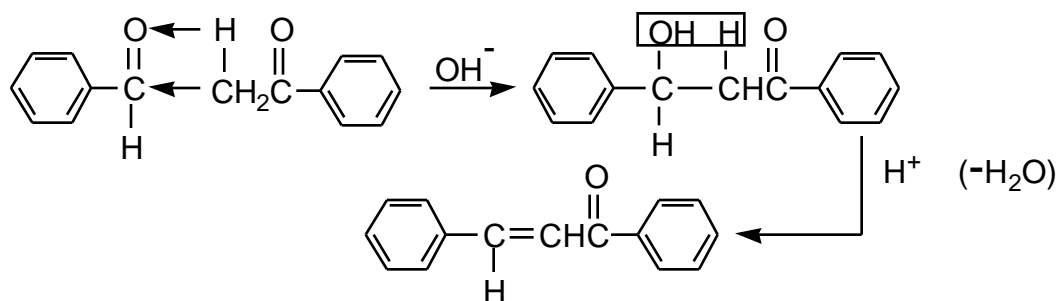


c) **Method 1****Method 2****Method 3****11.35 Grignard Synthesis of Alcohols: Section 11.5F**

11.36 Aldol Condensation: Section 11.6B

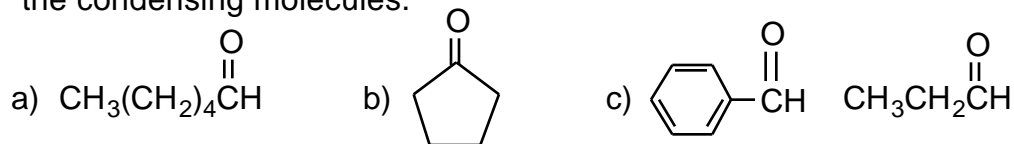
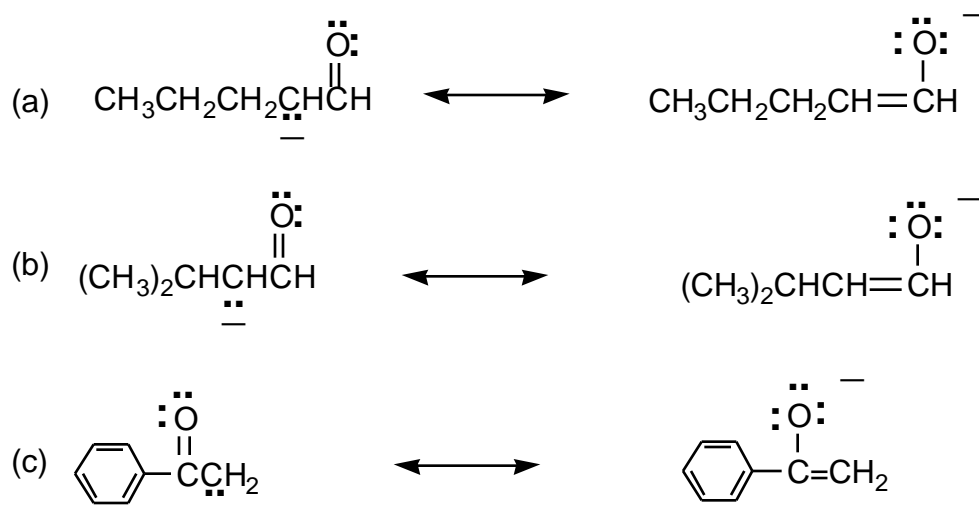
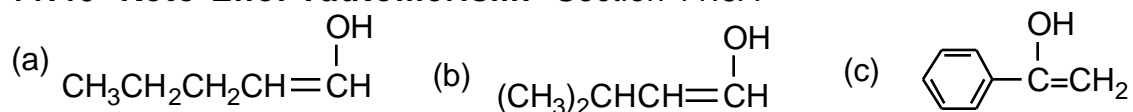
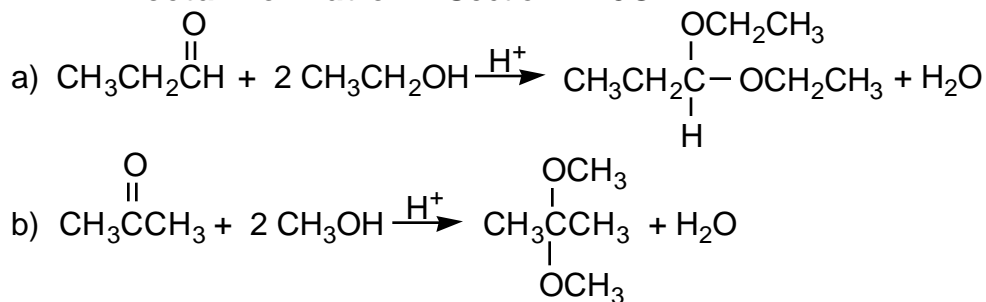


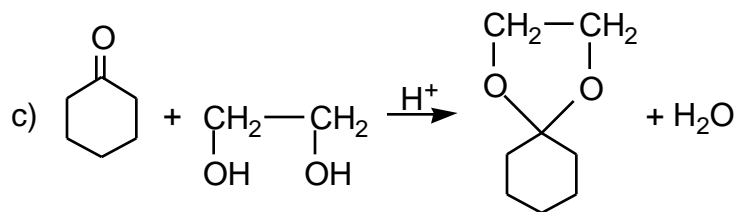
11.37 Crossed Aldol Condensation: Section 11.6B.3



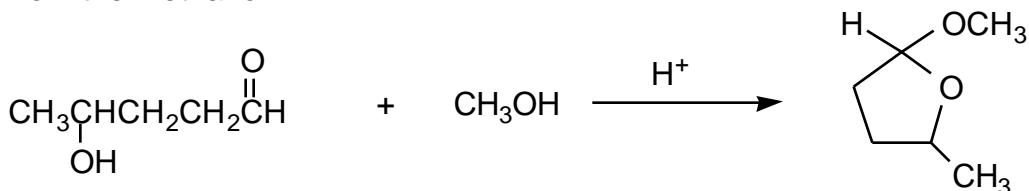
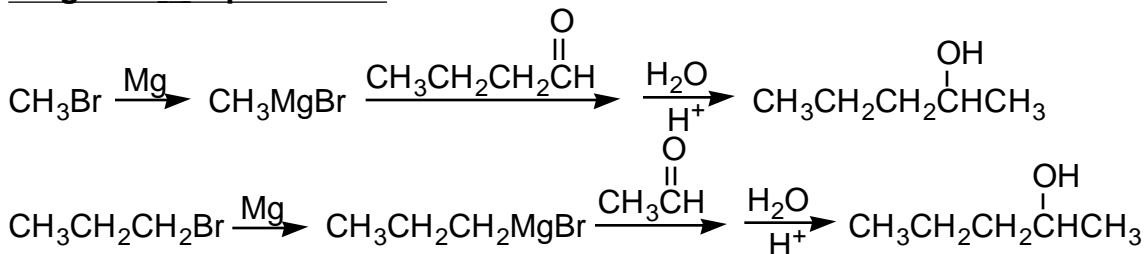
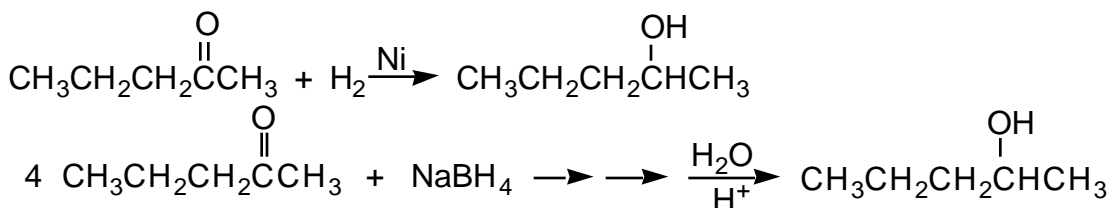
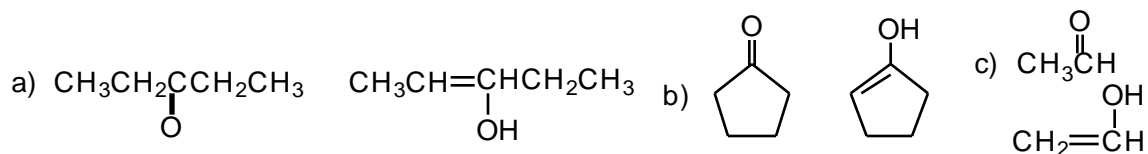
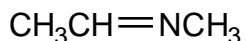
11.38 Aldol Condensation: Section 11.6B

The starting aldehydes or ketones are shown. These substances are exposed to base, NaOH, to effect reaction. The carbon-carbon double bond in the product shown in the text is the point of connection between the condensing molecules.

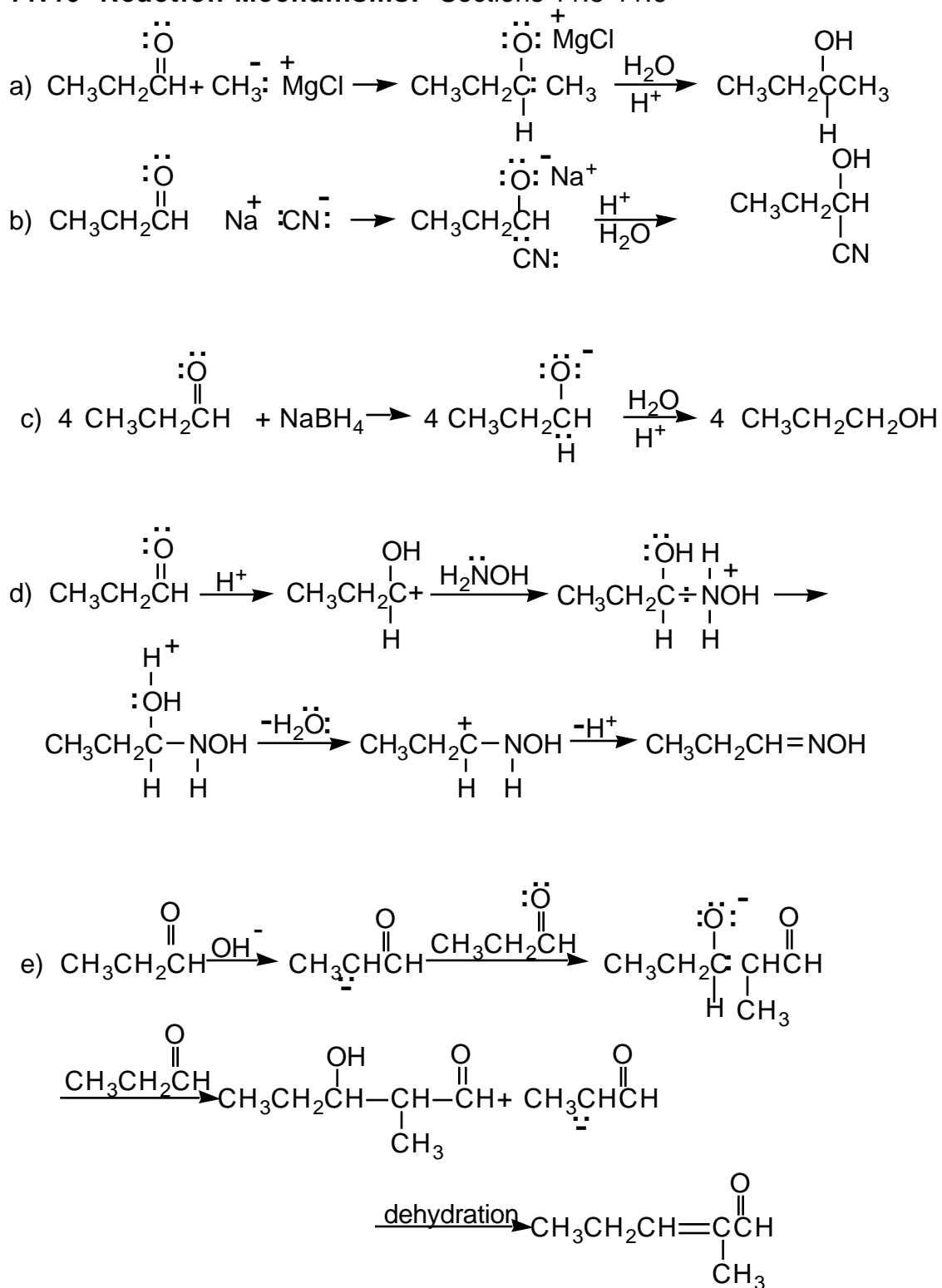
**11.39 Enolate Ions:** Section 11.6A**11.40 Keto-Enol Tautomerism:** Section 11.6A**11.41 Acetal Formation:** Section 11.5G

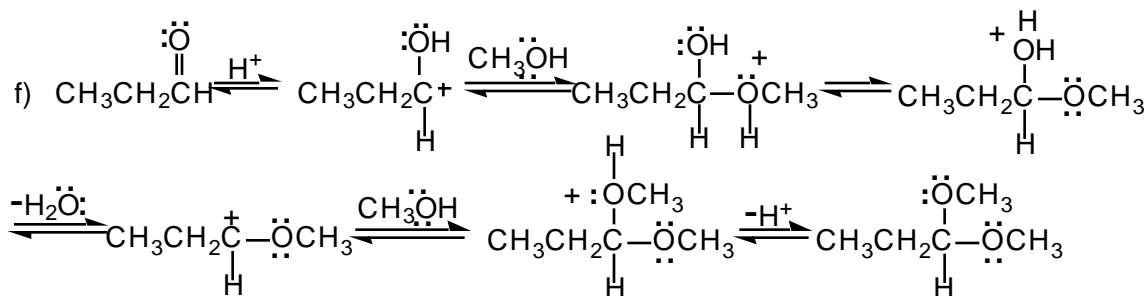
**11.42 Acetal Formation:** Section 11.5G

One mole of alcohol comes internally from the alcohol group on the hydroxy aldehyde. This causes the cyclic structure. The second mole comes from the methanol.

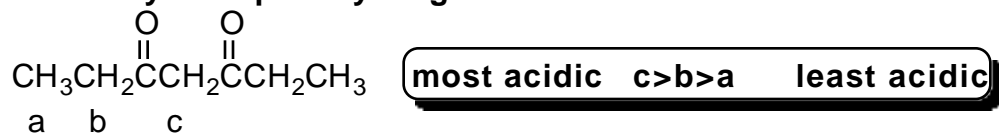
**11.43 Preparation of Alcohols:** Sections 11.5D-F**Grignard Preparations****Reductions****11.44 Keto-Enol Tautomerism:** Section 11.6A**11.45 Tautomerism:** Section 11.6A

11.46 Reaction Mechanisms: Sections 11.5-11.6



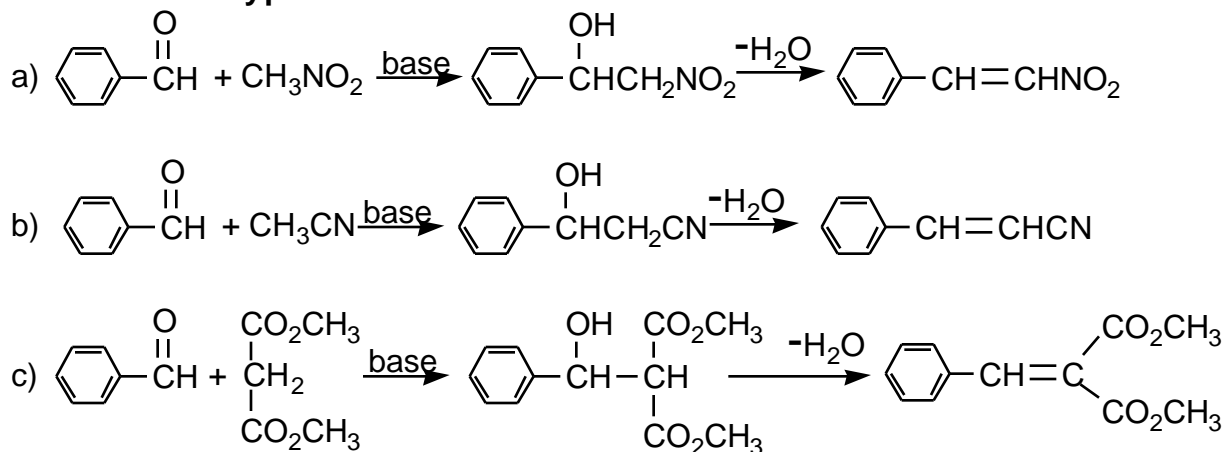


11.47 Acidity of Alpha Hydrogens: Section 11.6A



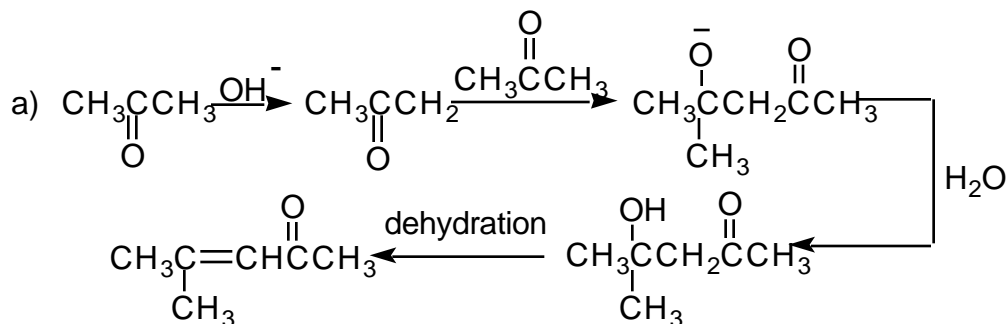
Hydrogen c is next to two electron withdrawing groups, carbonyl groups, and is the most acidic; b is adjacent to one and a is not adjacent to any.

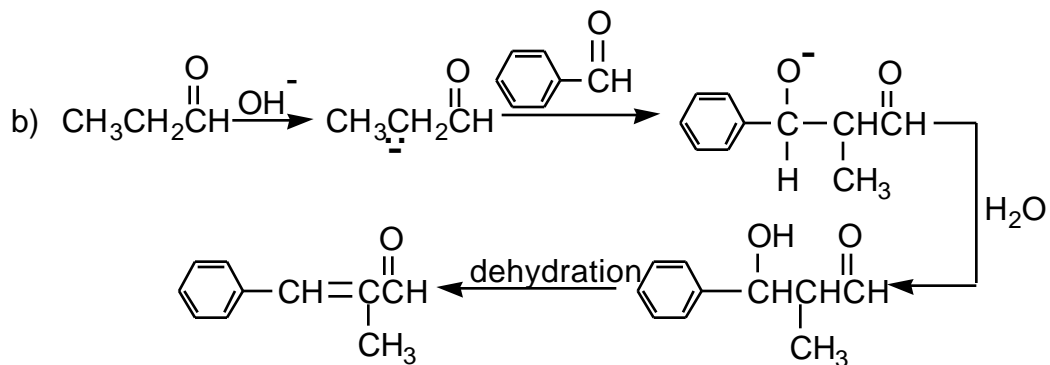
11.48 Aldol-Type Condensations: Section 11.6B



11.49 Reaction Mechanisms of Aldol-Type Condensations:

Section 11.6

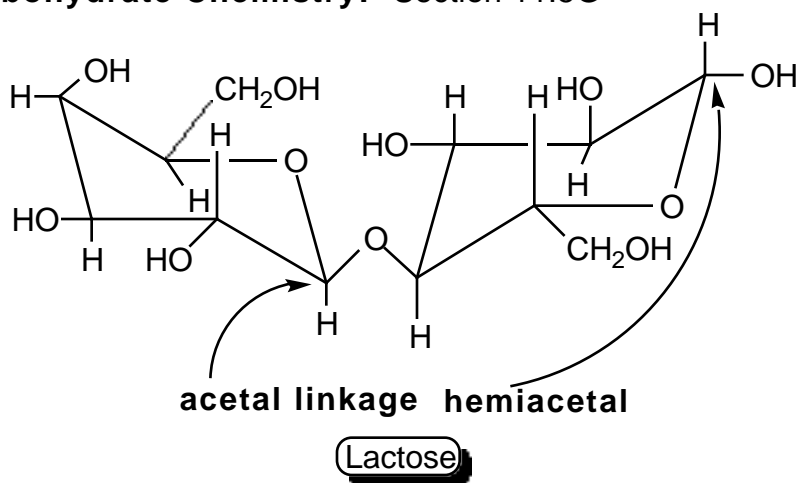




11.50 Organic Qualitative Analysis

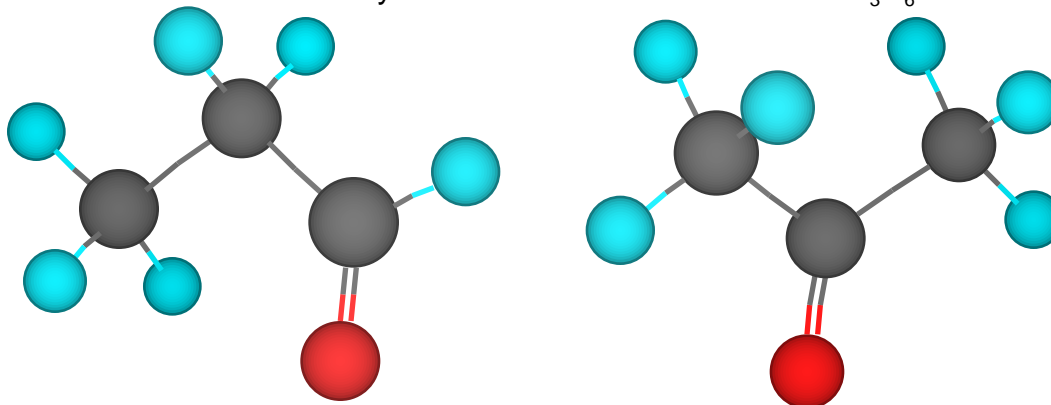
- a) Propanal is an aldehyde and will give a positive silver mirror test when treated with Tollens' reagent. Propanone is a ketone and does not oxidize.
- b) Propanone is a ketone and will give a positive 2,4 DNP test. A colored precipitate will form when 2,4-dinitrophenylhydrazine is mixed with propanone. 2-Propanol is an alcohol and will not react with 2,4-DNP.
- c) Butanal and butanone being an aldehyde and ketone respectively give a positive 2,4-DNP test. Butanol is an alcohol and will not react with the 2,4-DNP reagent since the test is specific for carbonyl compounds. Butanal can be distinguished from butanone with Tollens' test which is specific for aldehydes.

11.51 Carbohydrate Chemistry: Section 11.5G

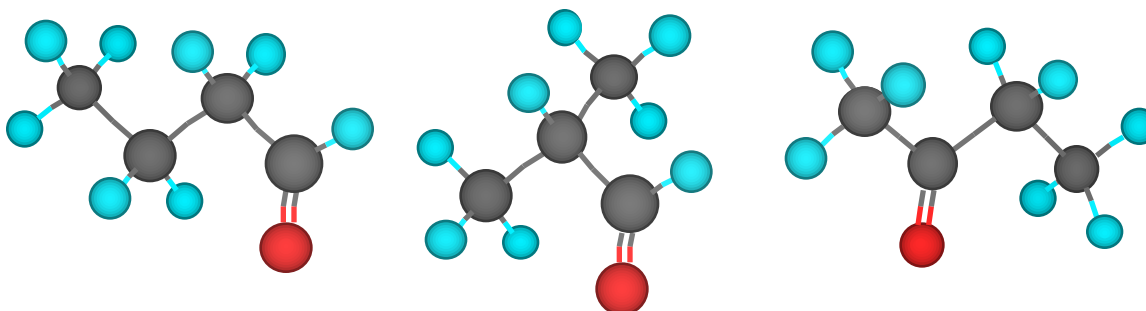


ACTIVITIES WITH MOLECULAR MODELS

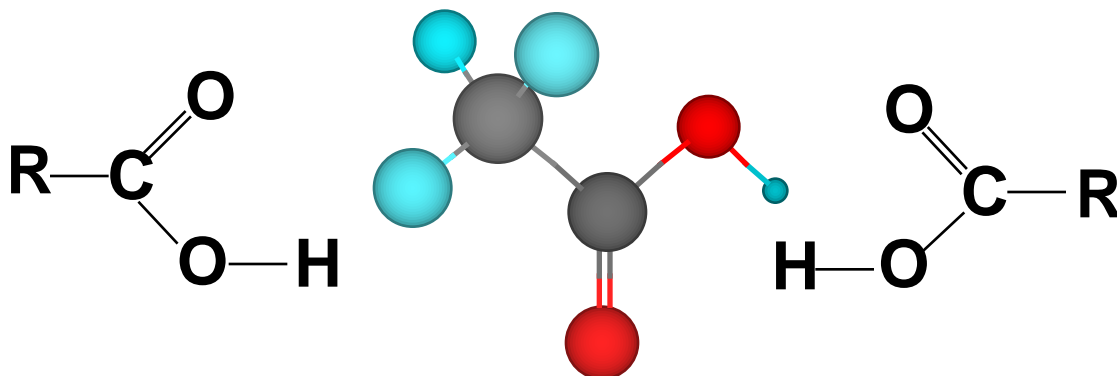
1. Make models of the aldehyde and ketone with the formula C_3H_6O .



2. Make models of the three isomers of C_4H_8O . Identify aldehydes and ketones. How many non-bonding electron pairs are on the oxygen of each model? What are the hybridizations of the carbons and the oxygen?



12



CARBOXYLIC ACIDS

CHAPTER SUMMARY

12.1 Structure of Carboxylic Acids

Carboxylic acids are structurally characterized by the **carboxyl group**, a carbon-oxygen double bond with a directly attached OH group. This is a very reactive functional group because (1) there are three polar bonds, the carbon-oxygen double and single bonds and the oxygen-hydrogen bond; (2) the double bond has electrons in a pi-bond; and (3) there are two unshared electron pairs on each oxygen. Carboxylic acids have an unpleasant odor and taste; they are found widely in nature.

12.2 Nomenclature of Carboxylic Acids

A. Simple Carboxylic Acids

Carboxylic acids are almost always named using a suffix. The suffix **oic acid** is attached to the name for the longest continuous carbon chain. If the acid group is attached to a ring the suffix **carboxylic acid** is used.

B. Polyfunctional Carboxylic Acids

Of the functional groups, carboxylic acids are the highest priority and named with a suffix; the other functional groups - aldehydes, ketones, alcohols and amines are named with prefixes if in a molecule where a carboxylic acid has received the suffix designation.

C. General Procedure for Naming Organic Compounds

A general procedure for naming organic compounds is given in this chapter since this is the last major functional group covered. **The procedure for naming organic compounds is:**

- (1) Name the longest continuous carbon chain.
- (2) Name carbon-carbon double and triple bonds with suffixes en and yn respectively; if all carbon-carbon bonds are single, use an.
- (3) Name the highest priority functional group with a suffix (acid > aldehyde > ketone > alcohol > amine) and the others with prefixes.
- (4) Number the carbon chain giving preference to the functional group named by a suffix, then multiple bonds (carbon-carbon double bonds take priority over triple bonds when making a choice is necessary), then groups named with prefixes.
- (5) Name all other groups with prefixes and number them.

D. Common Names of Carboxylic Acids

Carboxylic acids are also named with common names that often describe a familiar source or property of the compound.

12.3 Physical Properties of Carboxylic Acids

The boiling points of carboxylic acids are high relative to other classes of compounds due to **hydrogen bonding**; carboxylic acid molecules can hydrogen bond in two places and as a result often exist as dimers. Lower molecular weight carboxylic acids are water soluble.

12.4 Acidity of Carboxylic Acids

A. Reactions of Acids with Base: Salt Formation

Acidity is the characteristic property of carboxylic acids; they react with strong bases like sodium hydroxide and weaker bases such as sodium bicarbonate. The ability to be neutralized by sodium bicarbonate distinguishes carboxylic acids from phenols.

B. Explanation for the Acidity of Carboxylic Acids

The acidity of carboxylic acids is the result of **resonance stabilization** in the **carboxylate anion** formed upon ionization or neutralization of the acid.

C. Structure and Relative Acidities of Carboxylic Acids

The acidity of carboxylic acids is described by the **acidity constant**, K_a , and its negative logarithm, pK_a . Large K_a 's and small pK_a 's denote high acidities. Acid strength is influenced by substituents on the carboxylic acid molecule. **Electron-withdrawing groups** disperse the negative character of the carboxylate ion and increase acidity whereas **electron-releasing groups** intensify the negative charge and decrease acidity. The **strength, number, and proximity** of electron-withdrawing groups can have dramatic effects on relative acidities.

D. Nomenclature of the Salts of Carboxylic Acids

Salts of carboxylic acids are named by changing the **oic acid** suffix of the acid to **ate** and preceding it by the name of the **cation**.

CONNECTIONS 12.1 Food Preservatives**12.5 Preparations of Carboxylic Acids****A. Oxidation of Alkylbenzenes****B. Oxidation of Primary Alcohols****C. Hydrolysis of Nitriles****D. Carbonation of Grignard Reagents**

SOLUTIONS TO PROBLEMS**12.1 IUPAC Nomenclature**

- (a) heptanoic acid; (b) 4,4,4-tribromobutanoic acid; (c) 1,5-pentandioic acid; (d) cyclohexanecarboxylic acid (e) m-methylbenzoic acid; (f) 3-chlorocyclobutanecarboxylic acid

12.2 IUPAC Nomenclature

- (a) 2-hydroxypropanoic acid; (b) 1-cyclopentenecarboxylic acid; (c) 3-hexyn-1,6-dioic acid

12.3 IUPAC Nomenclature

- (a) 4-amino-2-pentenoic acid; (b) 4-hydroxy-2,5-cyclohexadien-1-carboxylic acid; (c) 3,5-dioxohexanoic acid

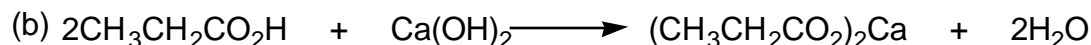
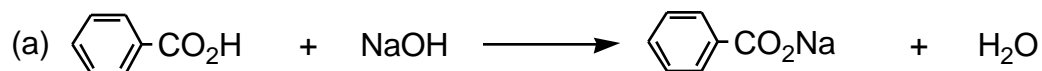
12.4 Boiling Points of Carboxylic Acids

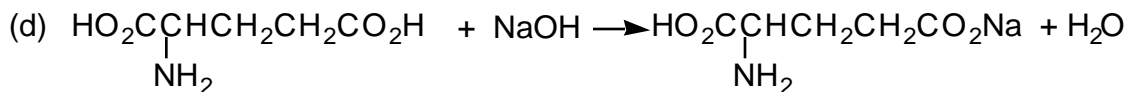
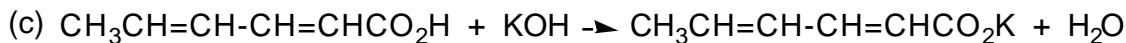
The compounds decrease in boiling point in the order given as capacity for hydrogen bonding decreases in this order. The first one has two carboxylic acid groups and thus two sites for hydrogen bonding. The second has only one carboxylic acid group and there are none, no O-H bonds at all, in the third.

12.5 Water Solubility of Carboxylic Acids

most soluble ethanoic acid > pentanoic acid > decanoic acid **least soluble**
(all proportions) (3.7g/100g) (0.2g/100g)

As the molecular weight of the acids increase the proportion of non-polar hydrocarbon to polar carboxyl group increases. As a result, the solubility in the polar solvent, water, decreases.

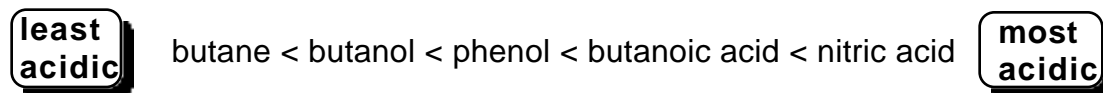
12.6 Neutralization of Carboxylic Acids



12.7 Relative Acidities of Carboxylic Acids and Phenols

Both phenols and carboxylic acids are neutralized by the strong base sodium hydroxide. Since both are water soluble, there would be no obvious visible difference with this reagent, even if there were a difference in extent of reaction. However, phenols are a lot less acidic than carboxylic acids and will not react with the weak base sodium bicarbonate. If one adds sodium bicarbonate to aqueous solutions of these compounds, bubbles of carbon dioxide will be visible as the bicarbonate and propanoic acid neutralize one another. Since the phenol does not react, no CO_2 evolution will be observed.

12.8 Relative Acidities

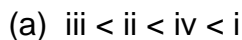


12.9 Relative Acidities

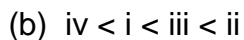
Numerically larger acidity constants mean greater acidity. However, smaller pK_a 's denote greater acidity.



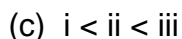
12.10 Relative Acidities



All of these compounds have three electron withdrawing groups on the carbon next to the carboxylic acid. Relative acidity depends on the strength of the groups. Electronegativity of halogens is $\text{F} > \text{Cl} > \text{Br} > \text{I}$.



Relative acidities depend on the number and proximity of electron withdrawing groups. The most acidic, ii, has two chlorines on the carbon directly adjacent to the acid group. In iii, one of the two chlorines has been moved one carbon away. In i, both chlorines are two carbons away from the acid and in iv, there is only one chlorine and it is as far from the acid as it can be.



The most acidic, iii, has two acid groups; each acts as an electron-withdrawing group on the other and increases acidity. ii has neither electron-withdrawing or electron-releasing groups, and i has one electron-releasing group which decreases acidity.

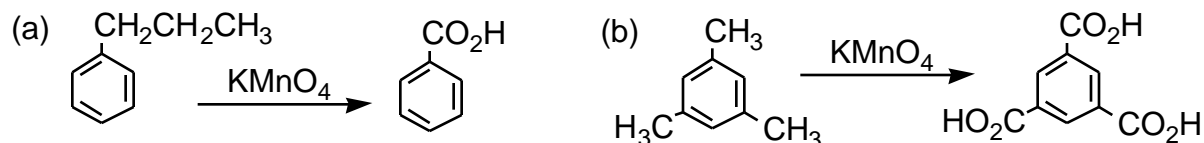
(d) meta < para < ortho

Each has one electron-withdrawing group. Because of resonance, the ortho and para chloro's increase acidity more than meta. In addition, the ortho is closer and thus this is the most acidic.

12.11 Nomenclature of Carboxylic Acid Salts

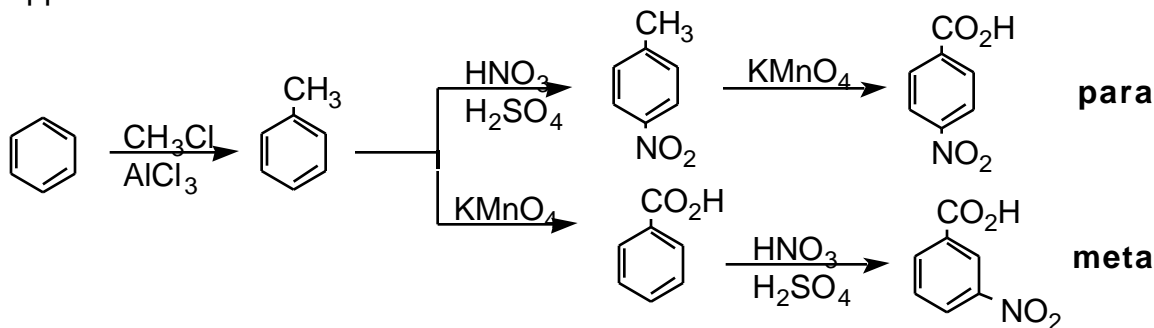
- (a) Sodium ethanoate; (b) calcium propanoate; (c) potassium 2-butenate
(d) ammonium p-bromobenzoate

12.12 Preparations of Carboxylic Acids

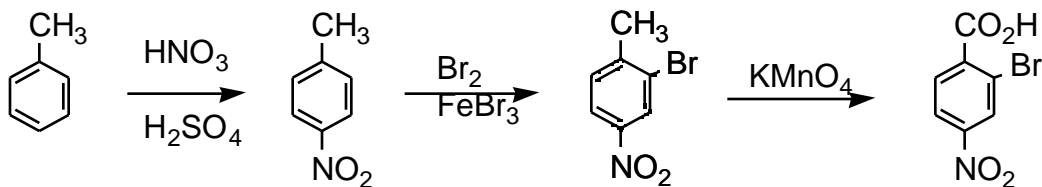
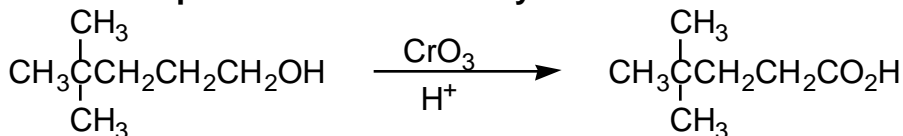
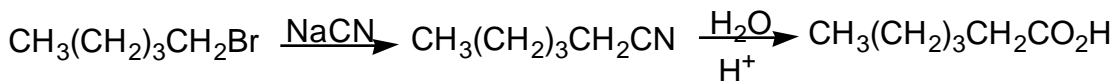
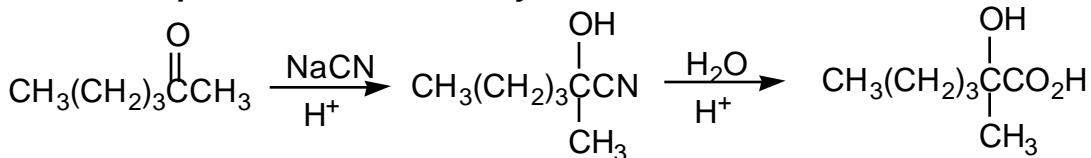
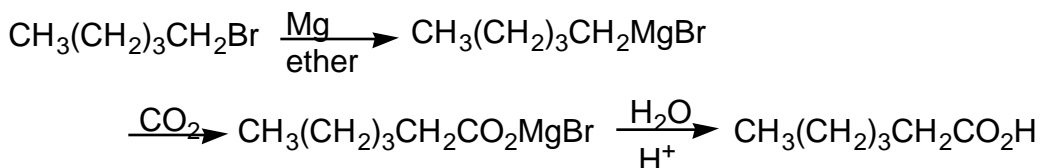


12.13 Preparations of Carboxylic Acids

(a) The important thing to remember here is that the methyl group is an ortho-para director whereas the carboxylic acid group directs meta. For the para isomer one would oxidize the methyl after introducing the nitro group; just the opposite would be done to obtain the meta isomer.



(b) Directive effects are important. The methyl directs the nitro para. The methyl and nitro both direct to the desired position for the bromine. Oxidation gives the requested compound.

**12.14 Preparations of Carboxylic Acids****12.15 Preparations of Carboxylic Acids****12.16 Preparations of Carboxylic Acids****12.17 Preparations of Carboxylic Acids****12.18 Nomenclature of Carboxylic Acids:** Section 12.2A

- (a) nonanoic acid; (b) pentanoic acid; (c) 4-methylpentanoic acid;
 (d) 3-ethyl-5-methylhexanoic acid; (e) 1,4-butandioic acid
 (f) 2,2,2-trichloroethanoic acid

12.19 Nomenclature of Carboxylic Acids: Section 12.2A

- (a) cycloheptanecarboxylic acid; (b) cyclobutane -1,3-dicarboxylic acid;
 (c) 3-ethylcyclopentanecarboxylic acid

12.20 Nomenclature of Carboxylic Acids: Section 12.2A

- (a) 2,4-dichlorobenzoic acid; (b) p-nitrobenzoic acid;
 (c) m-methylbenzoic acid

12.21 Nomenclature of Polyfunctional Carboxylic Acids: Section 12.2B

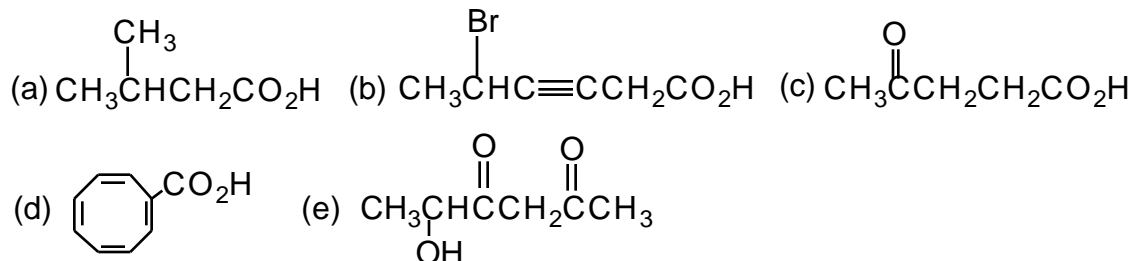
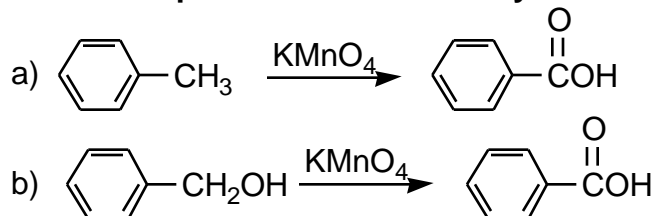
- (a) 2-hexenoic acid; (b) 5-hydroxyhexanoic acid;
 (c) 4-oxocyclohexanecarboxylic acid; (d) 1-cyclobutenecarboxylic acid;
 (e) 2-buten-1,4-dioic acid; (f) 3,5-dioxohexanoic acid;
 (g) 2,4-hexadienoic acid; (h) 4-oxo-2-pentynoic acid;
 (i) 4-amino-2-butenic acid

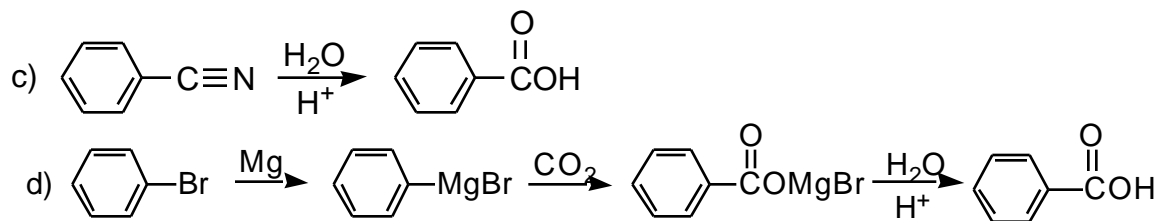
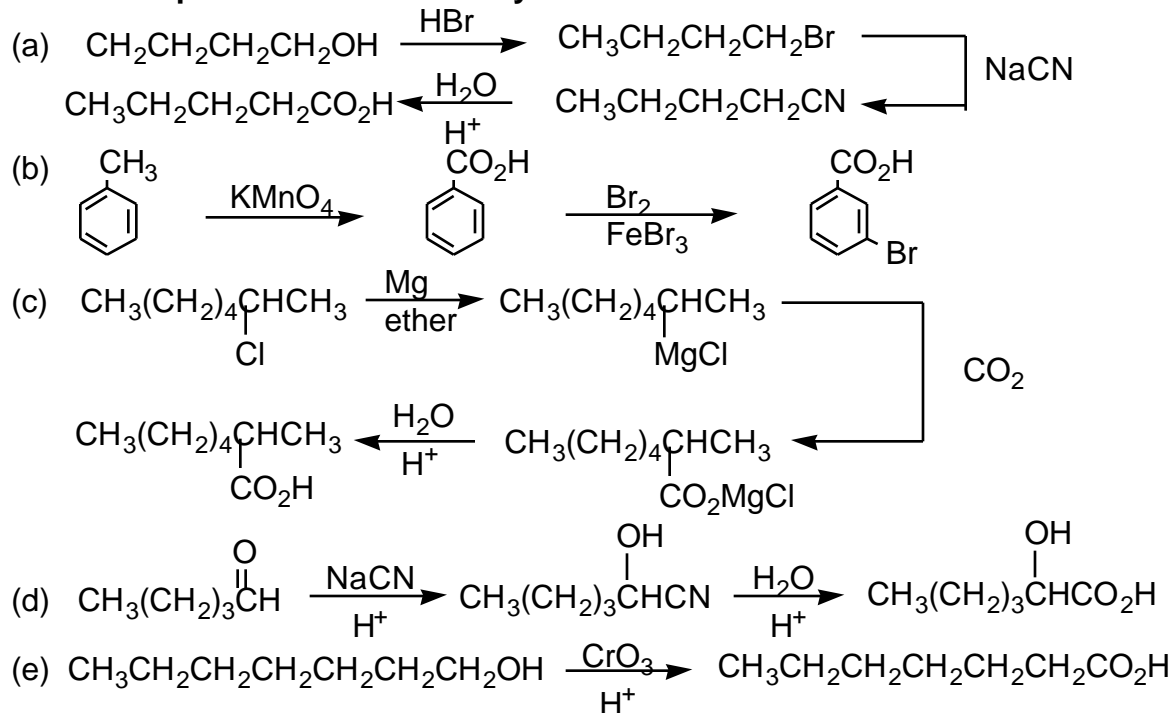
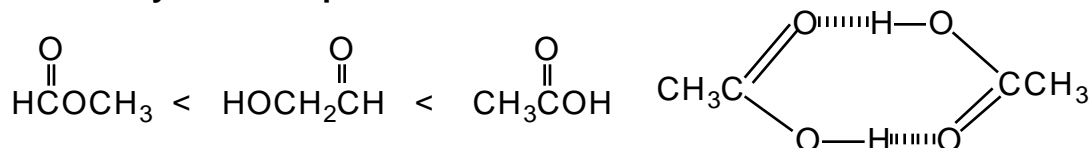
12.22 Nomenclature of Organic Compounds: Section 12.2C

- (a) 2-butenal; (b) 6-amino-2,4-hexandien-1-ol; (c) 3-hydroxy-2,4-pentandione;
 (d) 3-hexyn-2,5-dione; (e) 4-hydroxy-2-cyclohexen-1-one;
 (f) N,N-dimethyl-2-cyclopentenamine; (g) 4-hydroxy-2-heptenoic acid;
 (h) 8-bromo-7-hydroxy-2-octen-5-yn-4-one

12.23 Nomenclature of Carboxylic Acid Salts: Section 12.4D

- (a) sodium butanoate; (b) calcium ethanoate;
 (c) potassium 4,4,4-tribromobutanoate; (d) ammonium 2,4-dibromobenzoate;
 (e) sodium cyclopentanecarboxylate; (f) sodium 4-oxo-2-pentenoate

12.24 IUPAC Nomenclature: Section 12.2**12.25 Preparations of Carboxylic Acids:** Section 12.5

**12.26 Preparations of Carboxylic Acids:** Section 12.5**12.27 Physical Properties:** Section 12.3

The lowest boiling compound has no O-H bonds and cannot hydrogen bond. In the compound with the highest boiling point, the O-H bond is polarized by the C=O making the hydrogen bonding even stronger. Also in ethanoic acid, two molecules can orient so that hydrogen bonding can occur in two positions.

12.28 Physical Properties: Section 12.3

The dramatic difference in boiling points between chloroethane and ethanoic acid is a result of the ability of ethanoic acid to hydrogen bond. Bromoethane has a higher boiling point than chloroethane because bromoethane has a higher molecular weight. However, this increase in molecular weight doesn't

come close to offsetting the hydrogen bonding ability of ethanoic acid in influencing boiling points.

12.29 Acidity: Section 12.4B-C

Least Acidic \longrightarrow **Most Acidic**

- a) 4 < 2 < 3 < 1 b) 3 < 2 < 1 c) 2 < 4 < 1 < 3
 d) 4 < 1 < 3 < 2 e) 3 < 2 < 1 f) 3 < 1 < 4 < 2

(a) The electronegativity of the halogens is $F > Cl > Br$; the acidity is in the same direction because electron-withdrawing groups increase acidity. The #4 compound doesn't have an electron-withdrawing group and is least acidic.

(b) The carbon oxygen double bond is an electron-withdrawing group and will increase acidity. The closer to the acid group, the more effective and acidity is in this direction.

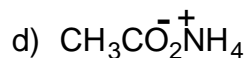
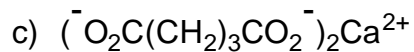
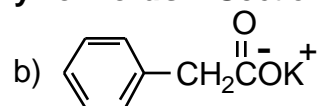
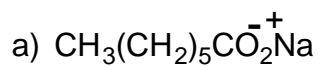
(c) Each compound has two bromines; these are electron-withdrawing groups and will increase acidity. The proximity of the bromines to the acid group is the determining factor. In the least acidic they are on carbons 3 and 4; in the next, carbons 2 and 4; in the next, carbons 2 and 3; and in the most acidic, both are on carbon 2.

(d) Chlorine is electron-withdrawing and will increase acidity. On a benzene ring the effect will be greatest with the chlorine is ortho or para to the acid group. In the least acidic, there is only one chlorine and it is meta; the compound with just one chlorine, but para, is next. The other two compounds have two chlorines. In each one is para and the other is either meta or ortho; the ortho is more effective and this is the most acidic.

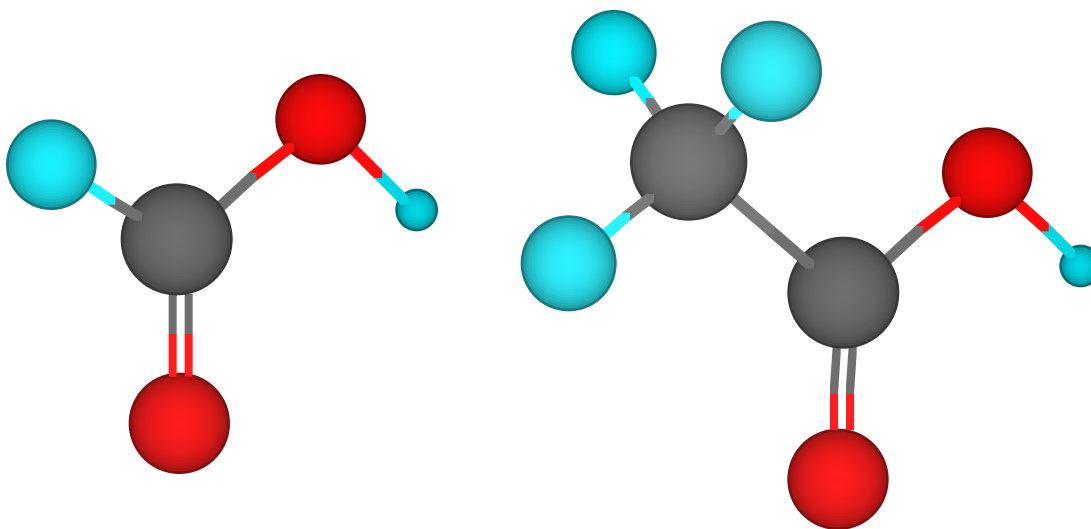
(e) These are dicarboxylic acids. Acid groups are electron-withdrawing so each can increase the acidity of the other. The determining factor here is how close they are to one another.

(f) These are four different classes of organic compounds. Alkanes are not acidic. Alcohols are very slightly acidic but no so much as phenols in which the anion formed from ionization is resonance stabilized. Carboxylic acids are the most acidic because of the electron-withdrawing carbon-oxygen double bond and the resonance stabilization of the anion.

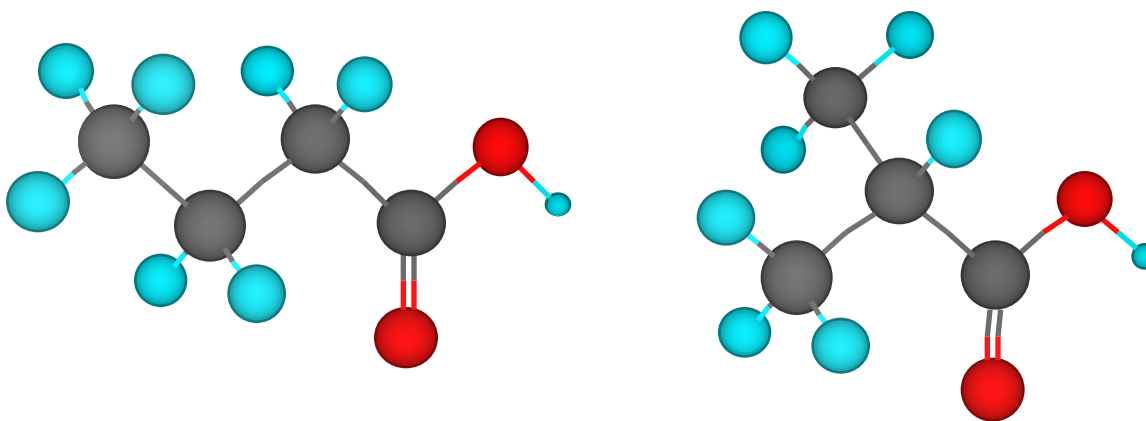
12.32 Neutralization Reactions of Carboxylic Acids: Section 12.4A

**ACTIVITIES WITH MOLECULAR MODELS**

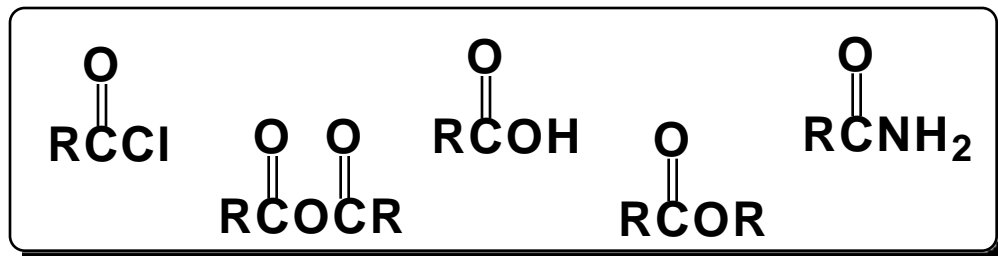
1. Make molecular models of formic acid, a component of the sting of ants, and acetic acid, which is 5% of most vinegars.



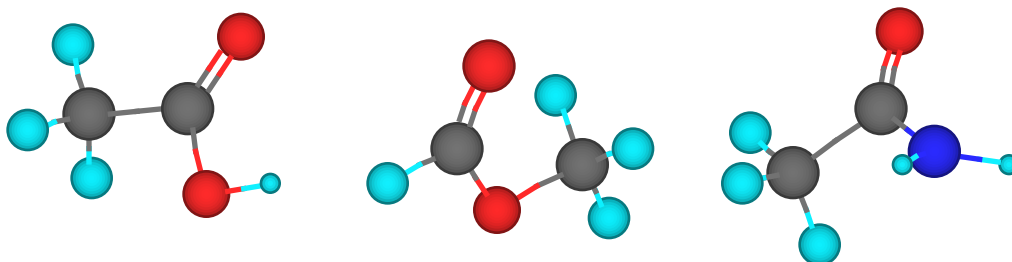
2. There are two carboxylic acids with the formula of $\text{C}_4\text{H}_8\text{O}_2$. Make molecular models of each.



13



DERIVATIVES OF CARBOXYLIC ACIDS



CHAPTER SUMMARY

13.1 Structure and Nomenclature of Carboxylic Acid Derivatives

A. Structure

Carboxylic acids and their derivatives can be expressed as variations of a single formula in which an electronegative atom - oxygen, nitrogen, or halogen - is attached to a carbon-oxygen double bond. The fundamental acid derivatives and their electronegative groups are: **acid chlorides**, Cl; **acid anhydrides**, O₂CR; **carboxylic acids**, OH; **esters**, OR; and **amides**, NH₂, NHR, or NR₂. Acid chlorides and

anhydrides are very reactive and are used in synthetic organic chemistry; the others are found abundantly in nature.

The reactivity of carboxylic acids and their derivatives is a result of **polar bonds, non-bonding electron pairs and the carbon-oxygen double bond**. The C=O can attract both **nucleophiles** and **electrophiles**.

B. Nomenclature of Carboxylic Acid Derivatives

Carboxylic acids are named by adding the suffix **oic acid** to the base name. **Acid chlorides** are named by changing the **ic acid** of the parent carboxylic acid to **yl chloride**. The suffix **acid** is changed to **anhydride** to name **acid anhydrides**. **Esters** are named like acid salts by changing **ic acid** to **ate** and preceding the name by the name of the **alkyl group**. To name **amides**, the **oic acid** is changed to **amide**.

CONNECTIONS 13.1 Aspirin and Other Analgesics

13.2 Nucleophilic Acyl Substitution Reactions

A. The Reaction

A characteristic reaction of carboxylic acid derivatives is **nucleophilic acyl substitution**. In this reaction a negative or neutral nucleophile replaces a leaving group to form a substitution product. The **leaving groups** and **nucleophiles** are the groups that define the various acid derivatives; as a result, the reaction usually involves the conversion of one acid derivative into another. The **order of reactivity** of acid derivatives is: **acid chloride > anhydride > acid or ester > amide**. In general, reaction of any of these derivatives with water produces acids; with alcohols, esters result; and with amines, amides are formed.

B. The Reaction Mechanism

Nucleophilic acyl substitution can be **initiated by a negative or neutral nucleophile** attacking the partially positive carbonyl carbon. In this two-step mechanism, a **tetrahedral intermediate** is formed; loss of the leaving group produces the new acid derivative. Alternatively,

the reaction can be **acid catalyzed**. In this mechanism, a hydrogen ion bonds to the carbonyl oxygen to form a carbocation. The nucleophile bonds to the carbocation to form the **tetrahedral intermediate**; when the leaving group departs the new acid derivative is formed.

13.3 Nucleophilic Acyl Substitution Reactions of Acid Chlorides

A. Synthesis of Acid Chlorides

Carboxylic acid chlorides are synthesized by treating a carboxylic acid with thionyl chloride.

B. Reactions of Acid Chlorides

Acid chlorides react with sodium salts of carboxylic acids to form anhydrides, with alcohols to form esters, with water to form acids, and with amines to form amides.

C. Nucleophilic Acyl Substitution Mechanism

These reactions generally proceed by a nucleophile initiated mechanism. An acid salt, water, alcohol, ammonia, or amine attacks to form a tetrahedral intermediate. The new derivative is formed upon departure of the chloride (as HCl).

13.4 Nucleophilic Acyl Substitution Reactions of Acid Anhydrides

A. Synthesis of Acid Anhydrides

Acid anhydrides are synthesized from acid chlorides and carboxylic acid salts.

B. Reactions of Acid Anhydrides

Anhydrides react with alcohols to form esters, with water to form carboxylic acids, and with amines to form amides.

C. Nucleophilic Acyl Substitution Mechanism

The reaction mechanism is usually nucleophile initiated. A Lewis base - alcohol, water, ammonia, or amine - attacks the carbonyl carbon to

form a tetrahedral intermediate. Elimination of a molecule of carboxylic acid produces the new acid derivative.

13.5 Nucleophilic Substitution Reactions of Carboxylic Acids

A. Reactions of Carboxylic Acids

Carboxylic acids react with thionyl chloride to form acid chlorides. Reaction with alcohols gives esters, and with amines, amides are formed.

B. Nucleophilic Acyl Substitution Mechanism

Many nucleophilic acyl substitution reactions of carboxylic acids are acid-initiated. For example, in esterification, the carbonyl group is protonated, alcohol attacks to form the tetrahedral intermediate, proton transfers occur, and water leaves.

13.6 Nucleophilic Acyl Substitution Reactions of Esters

A. Reactions of Esters

Esters can be converted to acids with water; reaction with an alcohol produces a new ester by a process called **transesterification**. Esters react with amines to form amides.

B. Nucleophilic Acyl Substitution Mechanism

Esters react by both acid and nucleophile initiated mechanisms. Hydrolysis of esters by acid catalysis is exactly the reverse of the mechanism for the acid-catalyzed esterification of a carboxylic acid. Base-catalyzed hydrolysis of esters is called saponification. Hydroxide attacks to form a tetrahedral intermediate. Loss of alkoxide ion then occurs. The alkoxide neutralizes the resulting carboxylic acid to form the salt.

C. Synthesis of Esters by Nucleophilic Acyl Substitution

To determine the materials for ester synthesis, look at the carbon oxygen double bond. On one side is a single bond to an oxygen. Mentally break this bond and put a hydrogen on the oxygen; this is the

alcohol to use. On the carbonyl carbon place an OH, Cl, or O₂CR to determine the acid or acid derivative to use in the ester synthesis.

13.7 Nucleophilic Acyl Substitution Reactions of Amides

Amides are the least reactive of the carboxylic acid derivatives; they can be prepared from any of the other acid derivatives. **Hydrolysis**, either acid- or base-catalyzed, to form acids is the only nucleophilic acyl substitution reaction.

13.8 Polyamides and Polyesters

Polyamides such as Nylon are formed from dicarboxylic acids and diamines. **Polyesters** such as Dacron are formed from the reaction of dicarboxylic acids or diesters with dialcohols.

13.9 Nucleophilic Addition Reactions of Carboxylic Acid Derivatives

A. Reduction with Lithium Aluminum Hydride

Carboxylic acid derivatives can also undergo **nucleophilic addition** reactions. By a combination of nucleophilic acyl substitution and nucleophilic addition, all of the acid derivatives except amides can be reduced to primary alcohols using **lithium aluminum hydride**. The first hydride ion displaces the leaving group; the resulting aldehyde is reduced to the primary alcohol. Reduction of amides produces amines.

B. Reaction with Grignard Reagents

Esters and acid chlorides react with **Grignard reagents** to form tertiary alcohols. The first mole of Grignard displaces the alkoxide or chloride leaving group to form a ketone. The ketone undergoes nucleophilic addition to form the tertiary alcohol.

13.10 Reactions of Acid Derivatives Involving Carbanions

A. Malonic Ester Synthesis

Certain acid derivatives are capable of reactions involving intermediate carbanions. The **malonic ester synthesis** is used to synthesize substituted acetic acids. The reaction involves abstraction of

alpha hydrogens to form resonance stabilized carbanions; these carbanions become the nucleophiles in reactions with alkyl halides.

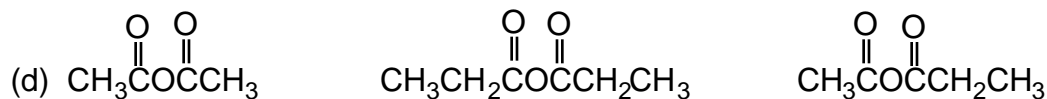
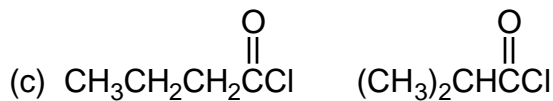
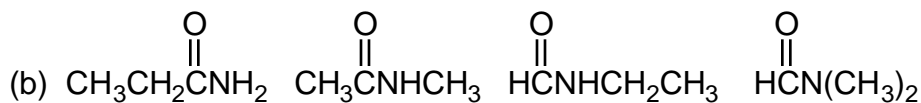
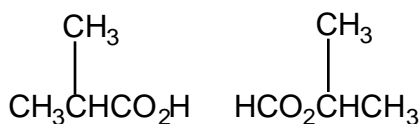
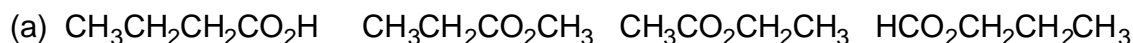
B. Claisen Condensation

The **Claisen condensation** is a carbanion reaction in which the carbanion produced by alpha hydrogen abstraction on an ester displaces the alkoxy group of another ester molecule; the reaction produces keto esters.

CONNECTIONS 13.2 Barbiturates

SOLUTIONS TO PROBLEMS

13.1 Structures of Acid Derivatives



13.2 Nomenclature of Acid Chlorides

(a) pentanoyl chloride; (b) 2-propenoyl chloride; (c) p-nitrobenzoyl chloride

13.3 Nomenclature of Acid Anhydrides

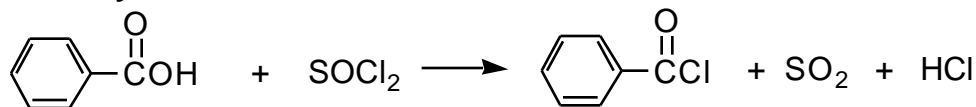
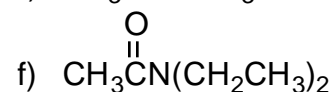
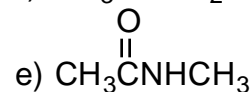
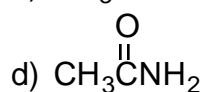
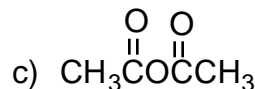
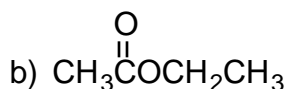
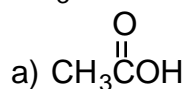
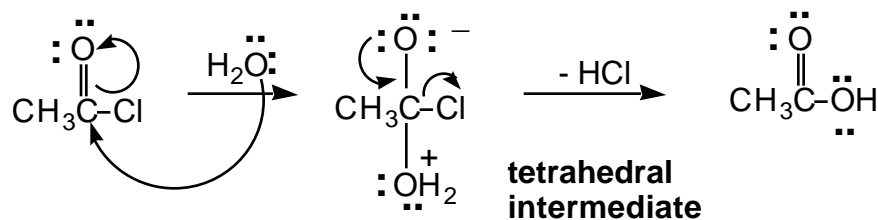
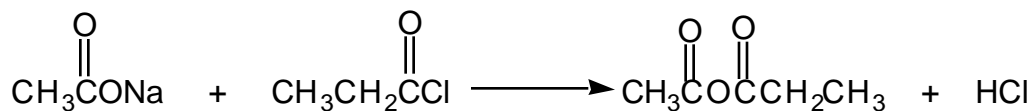
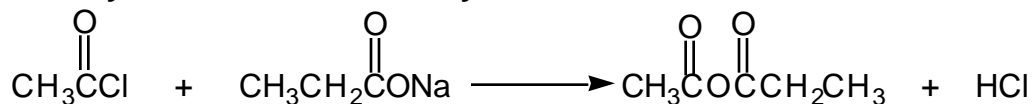
(a) ethanoic anhydride; (b) pentanoic anhydride;
(c) ethanoic pentanoic anhydride

13.4 Nomenclature of Esters

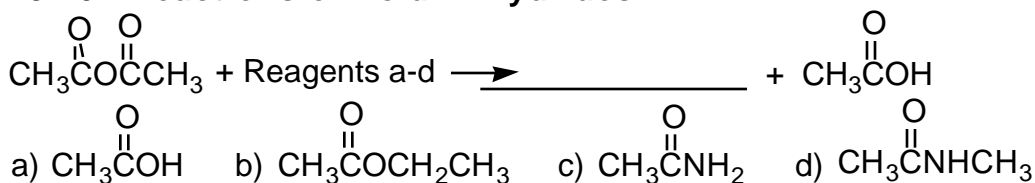
(a) methyl ethanoate; (b) ethyl 2-propenoate; (c) isopropyl m-chlorobenzoate

13.5 Nomenclature of Amides

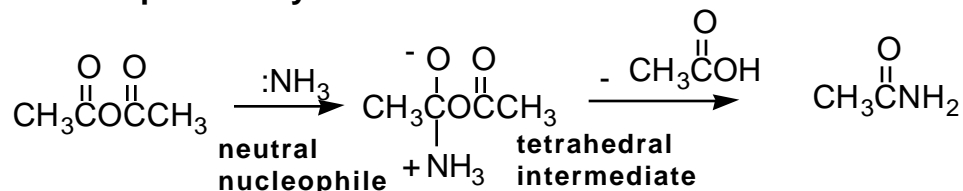
(a) ethanamide; (b) 2-propenamide; (c) p-bromo-N-methylbenzamide;
 (d) N-methylethanamide; (e) N,N-dimethyl-2-propenamide;
 (f) p-bromo-N-ethyl-N-methylbenzamide

13.6 Synthesis of Acid Chlorides**13.7 Reactions of Acid Chlorides****13.8 Nucleophilic Acyl Substitution Mechanism****13.9 Synthesis of Acid Anhydrides**

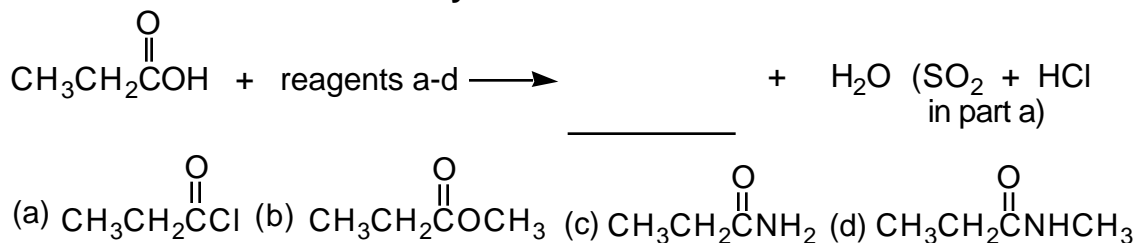
13.10 Reactions of Acid Anhydrides



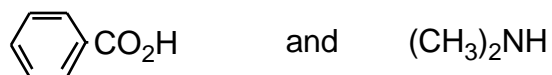
13.11 Nucleophilic Acyl Substitution Mechanism



13.12 Reactions of Carboxylic Acids

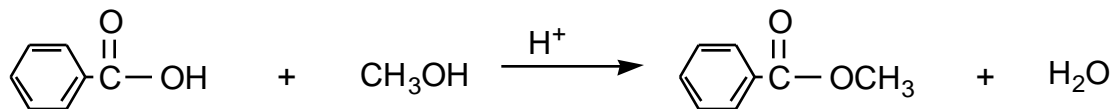


13.13 Preparations of Amines from Carboxylic Acids

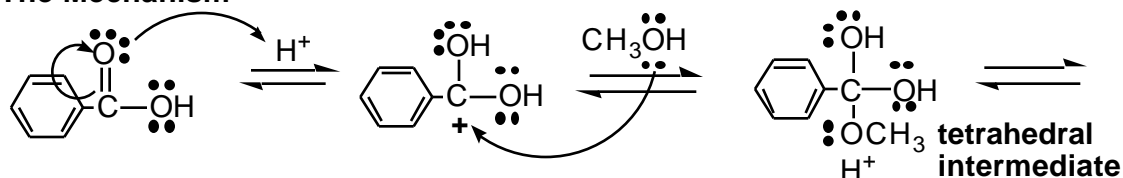


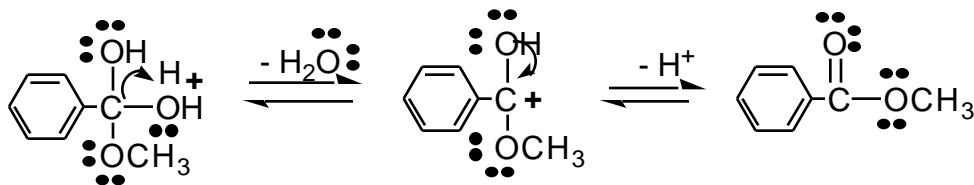
13.14 Acid Catalyzed Esterification Mechanism

The Reaction

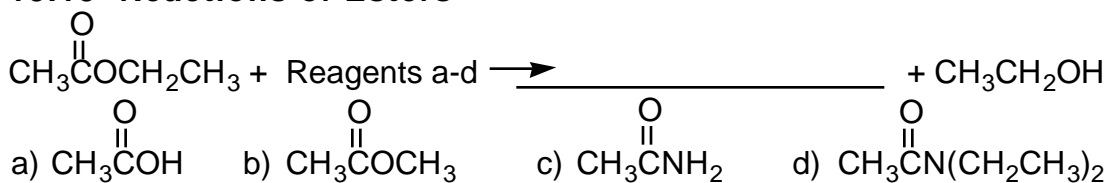


The Mechanism



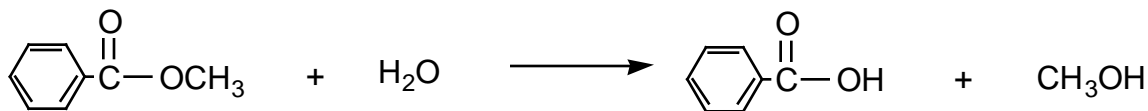


13.15 Reactions of Esters



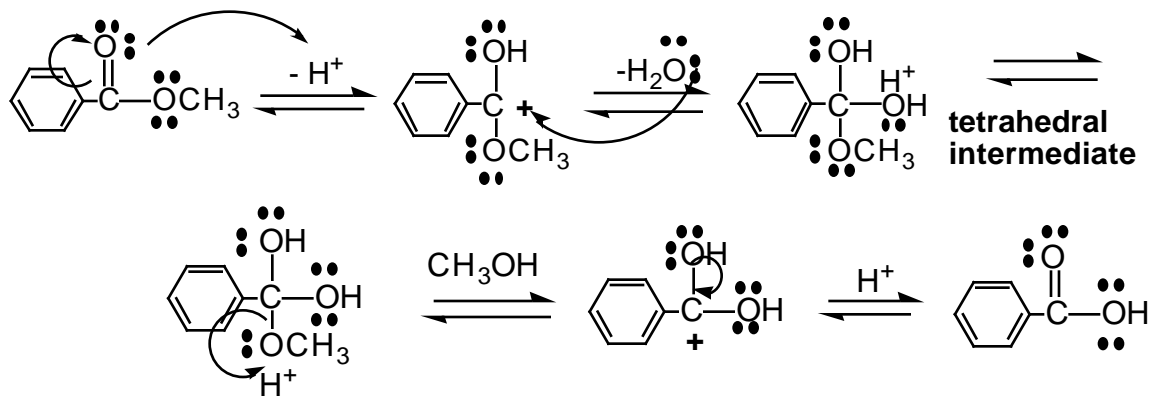
13.16 Acid and Base Catalyzed Ester Hydrolysis

The Reaction

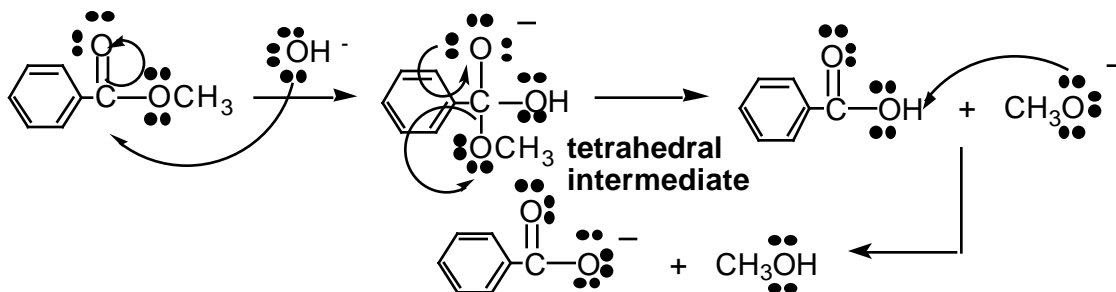


(a) Acid Catalyzed Hydrolysis

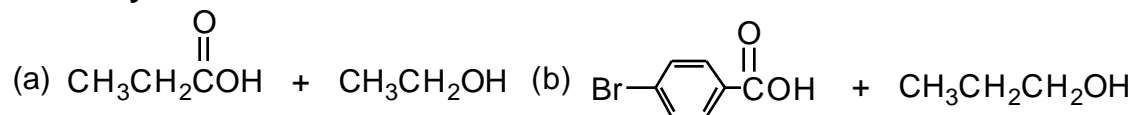
Note that this mechanism is the opposite of the esterification shown in problem 13.14. Both processes are equilibria.



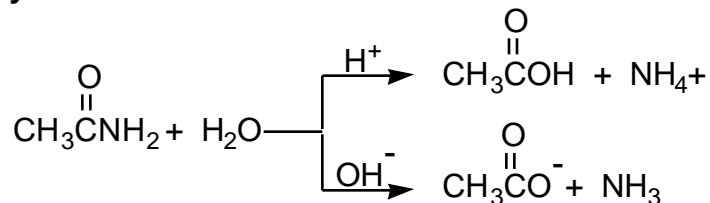
(b) Base Catalyzed Hydrolysis: Saponification



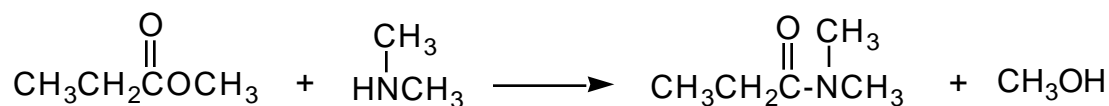
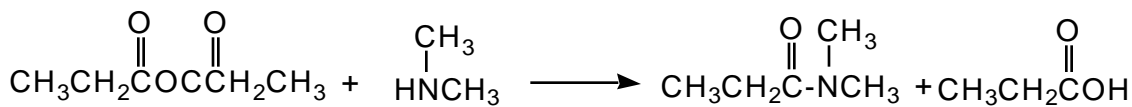
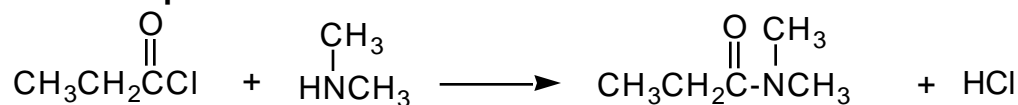
13.17 Synthesis of Esters



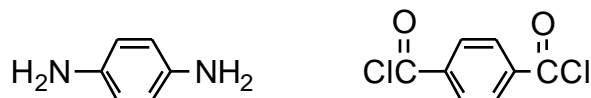
13.18 Hydrolysis of Amides



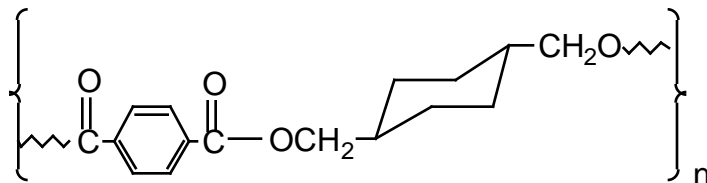
13.19 Preparations of Amides



13.20 Polyamides

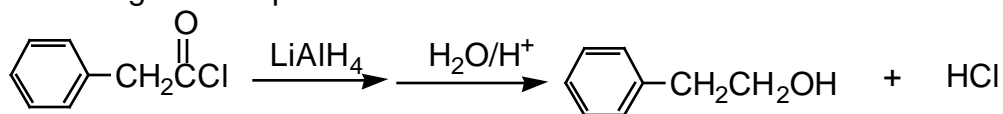


13.21 Polyesters

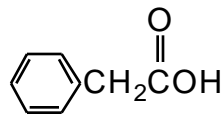
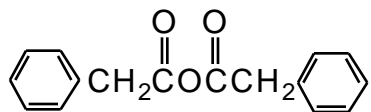


13.22 Reduction of Acid Chlorides with Lithium Aluminum Hydride

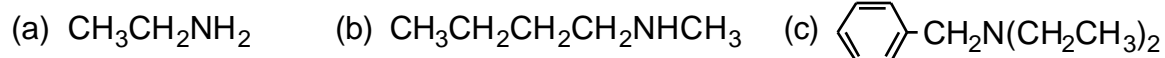
Following is the equation for reduction of an acid chloride.



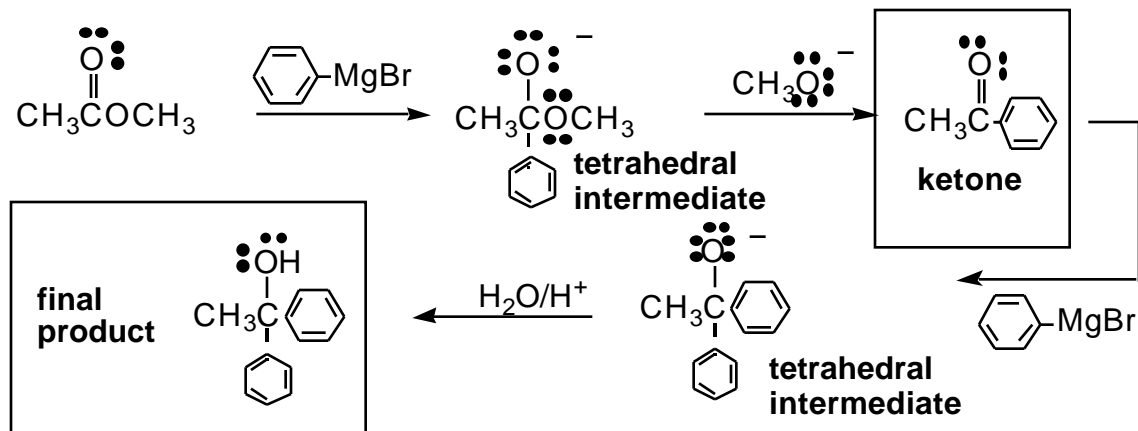
Lithium aluminum hydride will reduce the following acid anhydride and carboxylic acid to the same alcohol product.



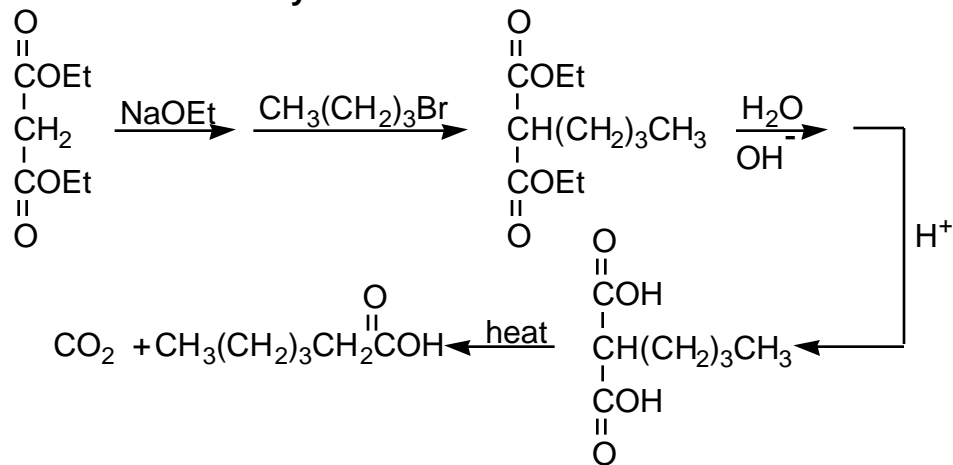
13.23 LiAlH_4 Reduction of Amides to Amines



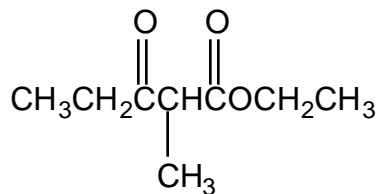
13.24 Reaction of Grignard Reagents with Esters



13.25 Malonic Ester Synthesis



13.26 Claisen Condensation



13.27 Nomenclature of Carboxylic Acids: Section 12.2



(d) 4-oxopentanoic acid; (e) 2-aminoethanoic acid; (f) 6-hydroxy-2,4-heptadienoic acid; (g) m-bromobenzoic acid; (h) cyclopentanecarboxylic acid; (i) 1,6-hexandioic acid

13.28 Nomenclature of Acid Chlorides: Section 13.1B.1

(a) butanoyl chloride; (b) 2-butenoyl chloride; (c) 3-oxopentanoyl chloride; (d) p-chlorobenzoyl chloride

13.29 Nomenclature of Acid Anhydrides: Section 13.1B.2

(a) butanoic anhydride; (b) propanoic anhydride; (c) butanoic propanoic anhydride

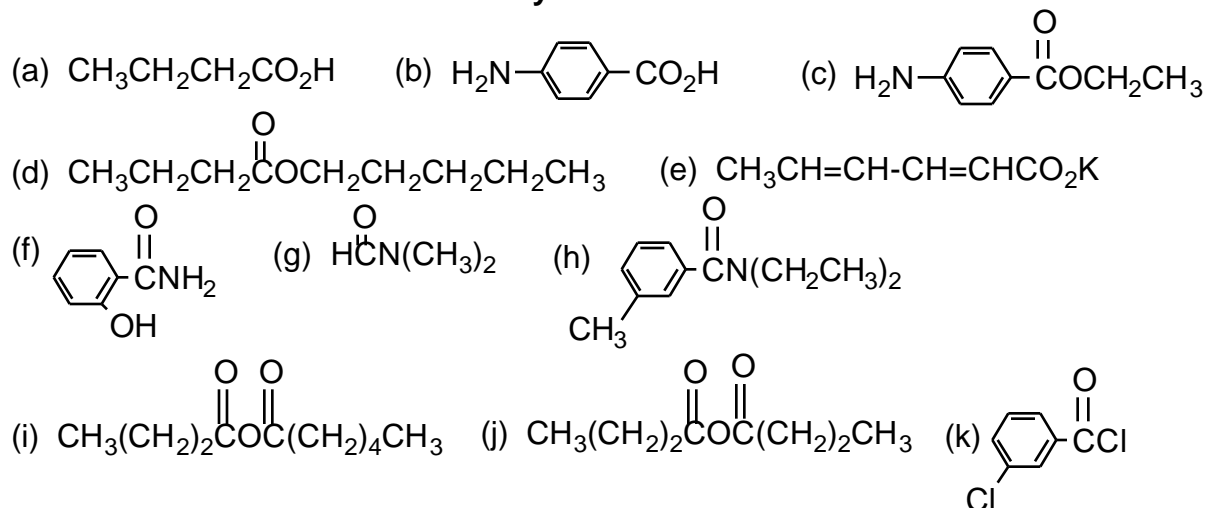
13.30 Nomenclature of Esters: Section 13.1B.3

(a) methyl pentanoate; (b) ethyl butanoate; (c) propyl propanoate; (d) butyl ethanoate; (e) pentyl methanoate; (f) isopropyl propanoate; (g) methyl p-nitrobenzoate; (h) butyl 2,4-hexadienoate

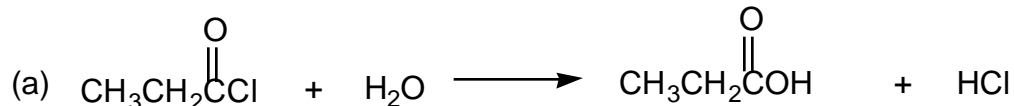
13.31 Nomenclature of Amides: Section 13.1B.4

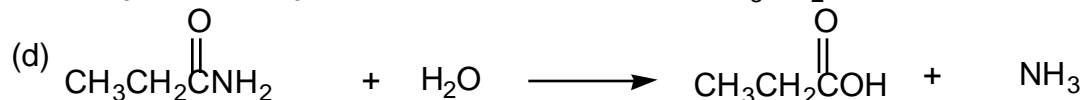
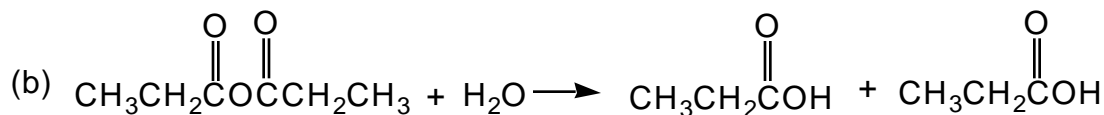
(a) pentanamide; (b) N-methylbutanamide; (c) N-ethylpropanamide; (d) N,N-dimethylpropanamide; (e) N-ethyl-N-methylethanamide; (f) N,N-diethyl-o-methylbenzamide; (g) 4-hydroxy-N-propyl-2-pentanamide

13.32 Nomenclature of Carboxylic Acid Derivatives: Section 13.1

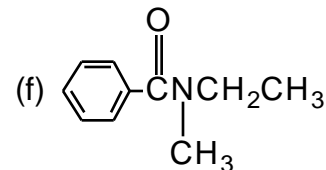
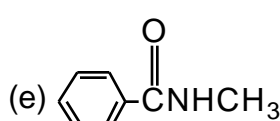
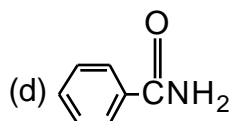
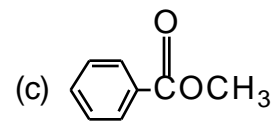
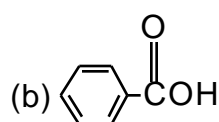
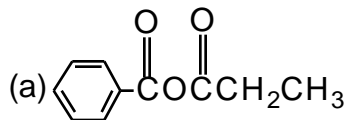


13.33 Reactions of Acid Derivatives: Section 13.3-13.7

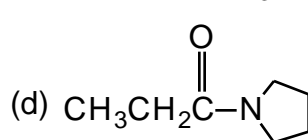
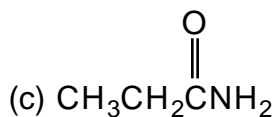
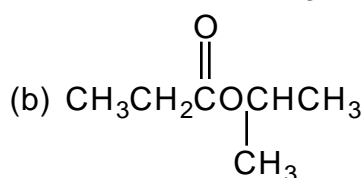
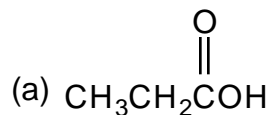


**13.34 Reactions of Acid Chlorides:** Section 13.3

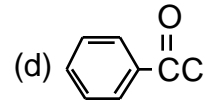
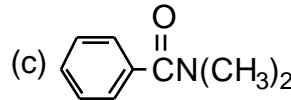
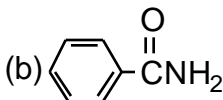
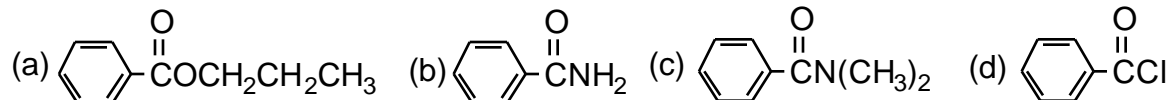
The by-product in all of these reactions is HCl except in (a) where it is NaCl.

**13.35 Reactions of Acid Anhydrides:** Section 13.4

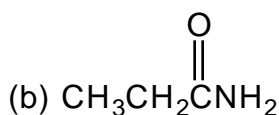
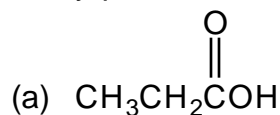
The by-product of each of these reactions is $\text{CH}_3\text{CH}_2\text{CO}_2\text{H}$.

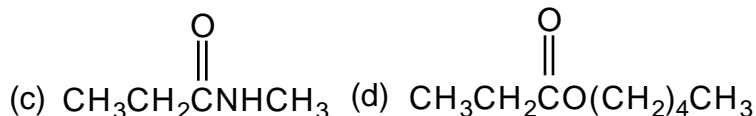
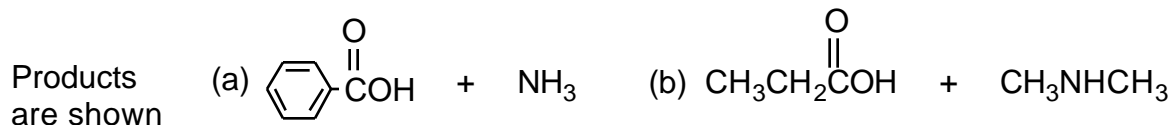
**13.36 Reactions of Carboxylic Acids**

The by-product of these reactions is water except in (d) where it is $\text{SO}_2 + \text{HCl}$.

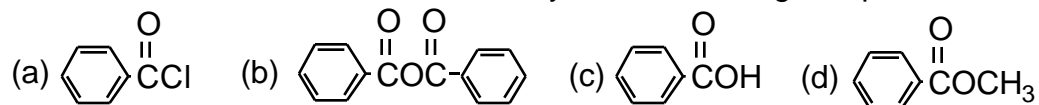
**13.37 Reactions of Esters:** Section 13.6

The by-product of all of these reactions is methanol, CH_3OH .

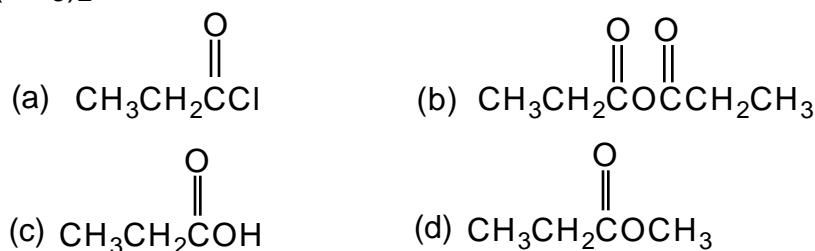


**13.38 Reactions of Amides:** Section 13.7**13.39 Preparations of Amides:** Section 13.7

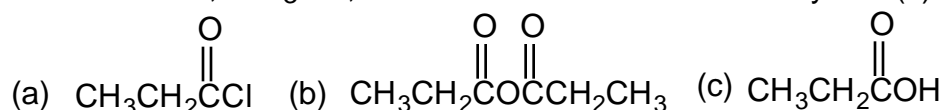
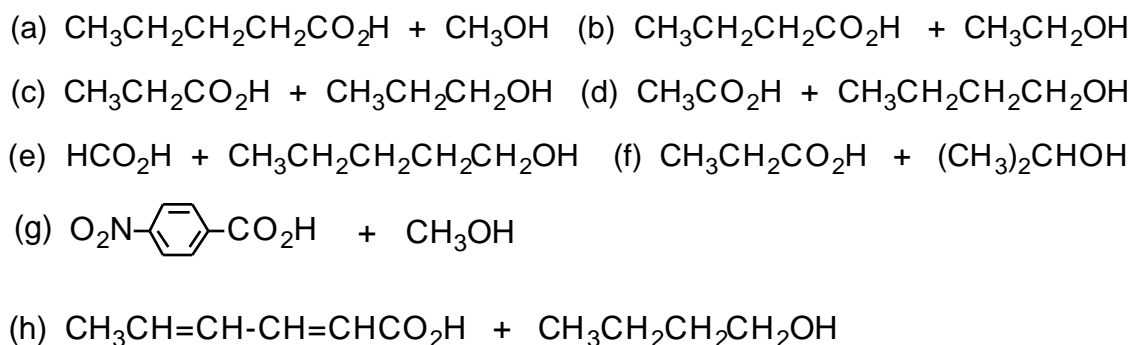
To make the amide in 13.38a treat any of the following compounds with NH_3 .

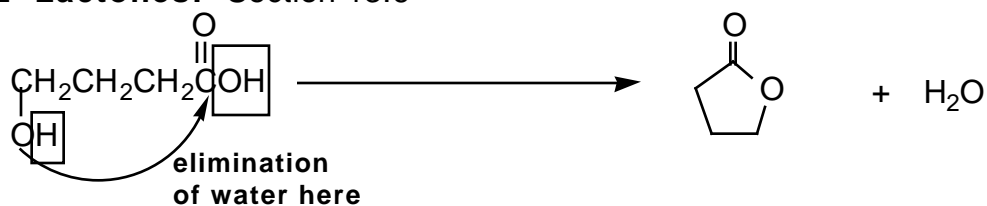
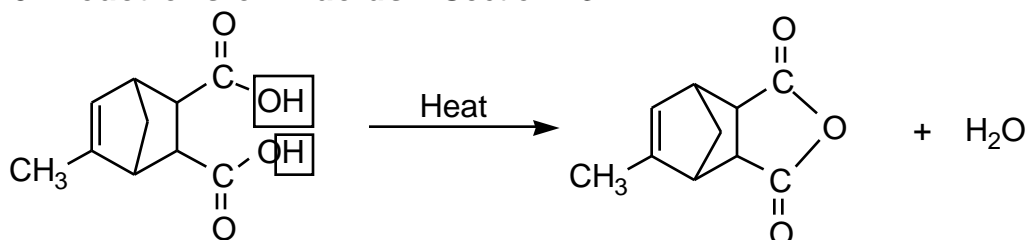


To make the amide in 13.38b treat any of the following compounds with $(\text{CH}_3)_2\text{NH}$.

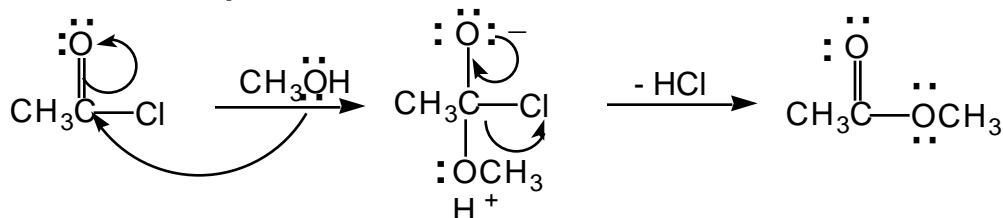
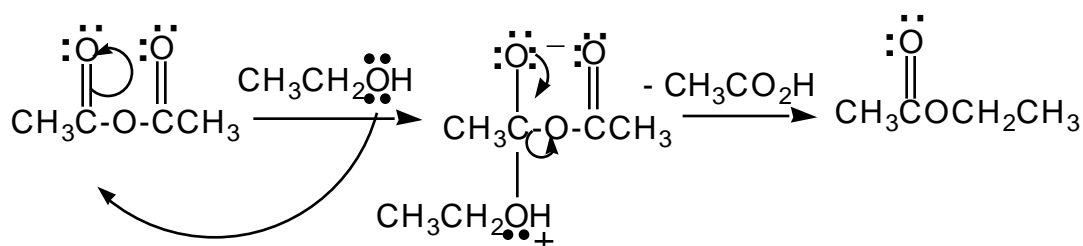
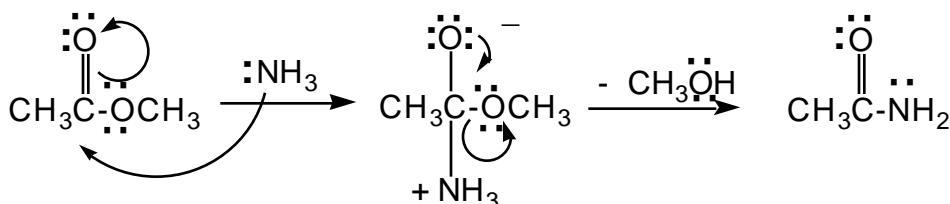
**13.40 Preparations of Esters:** Section 13.6

To prepare the ester in problem 13.37, treat any of the following compounds with methanol, CH_3OH , or with methanol and acid catalyst in (c).

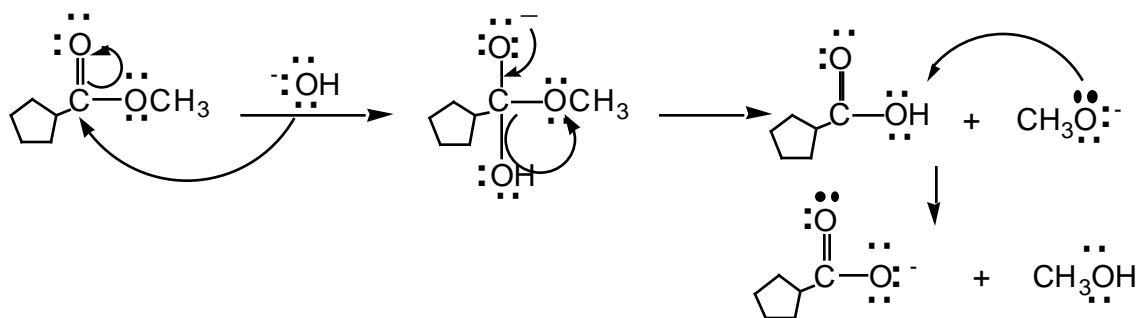
**13.41 Preparations of Esters:** Section 13.6C

13.42 Lactones: Section 13.6**13.43 Reactions of Diacids:** Section 13.4**13.44 Nucleophilic Acyl Substitution Mechanisms:**

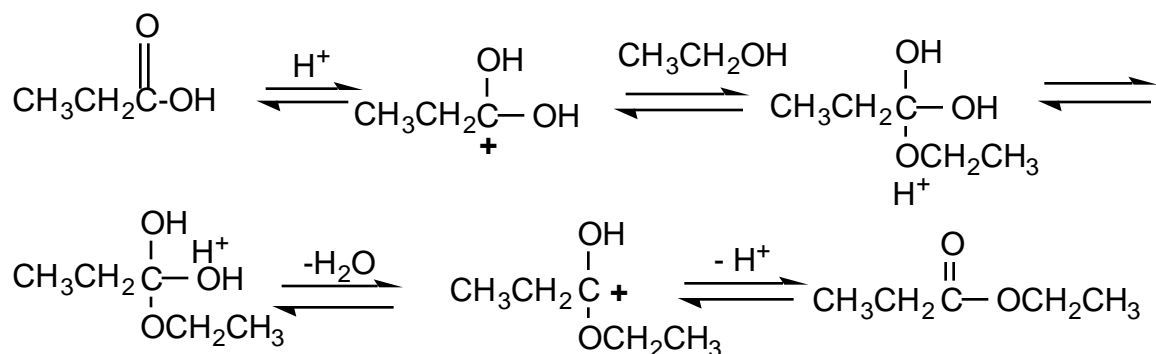
Sections 13.2-13.7

(a) Neutral Nucleophile Initiated**(b) Neutral Nucleophile Initiated****(c) Neutral Nucleophile Initiated**

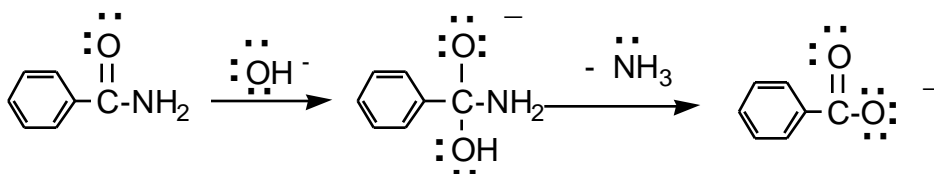
(d) Negative Nucleophile Initiated: Saponification



(e) Acid Catalyzed Esterification



(f) Negative Nucleophile Initiated


 13.45 Reactions with $LiAlH_4$: Section 13.9A

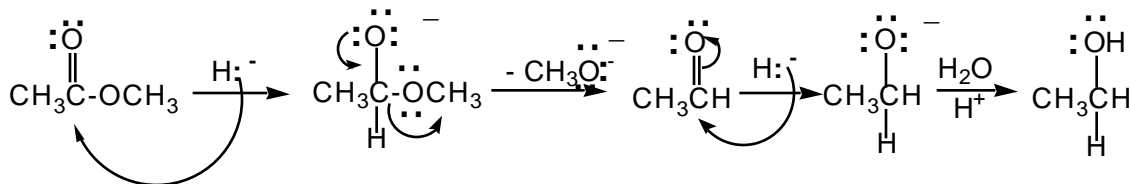
- (a) C1CCCC1CO (b) OCC1=CC=C(CO)C=C1 (c) CCCCCCCCCCCCCO
 (d) CCCCCCN (e) CCN(C)CC1=CC=C(C)C=C1

13.46 Acid Derivatives and Grignard Reagents: Section 13.9B

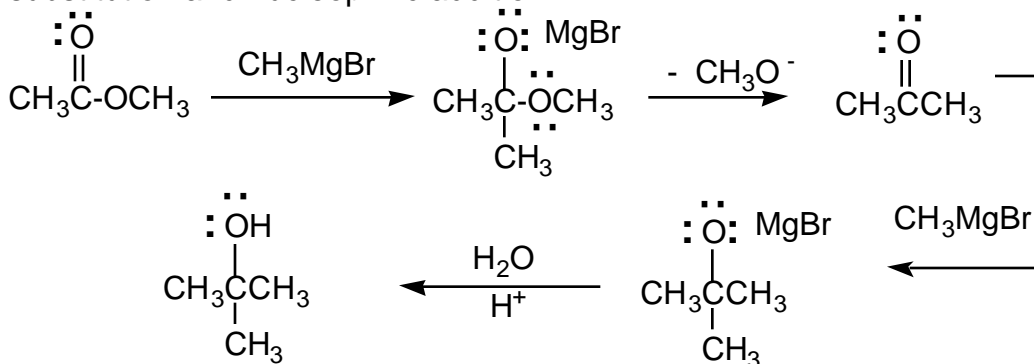
- (a) CCCC(O)CC (b) O=C(c1ccccc1)c2ccc(Cl)cc2 (c) OCCCOCC(O)c1ccccc1

13.47 Nucleophilic Addition Mechanisms: Section 13.9

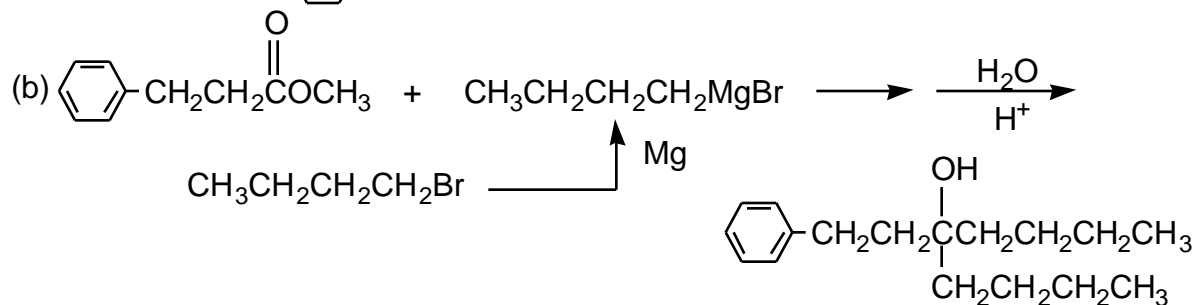
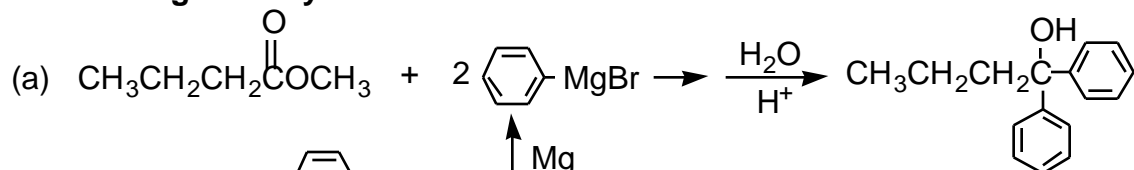
(a) This mechanism shows the reaction of hydride as a negative nucleophile but does not show the coordination of intermediates with aluminum.



(b) As with the previous mechanism, this one involves nucleophilic acyl substitution and nucleophilic addition.

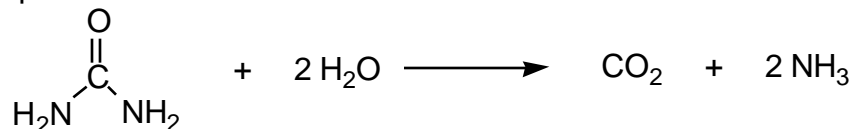


13.48 Grignard Synthesis of Alcohols: Section 13.9B



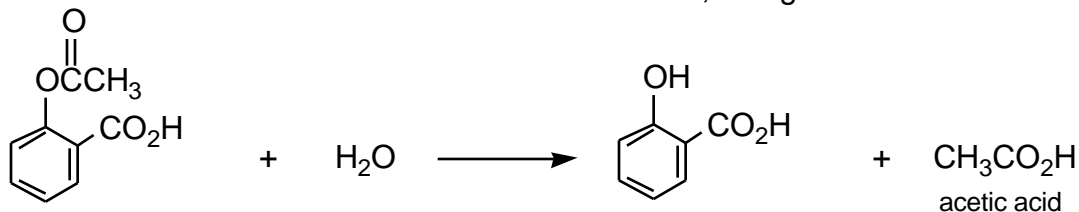
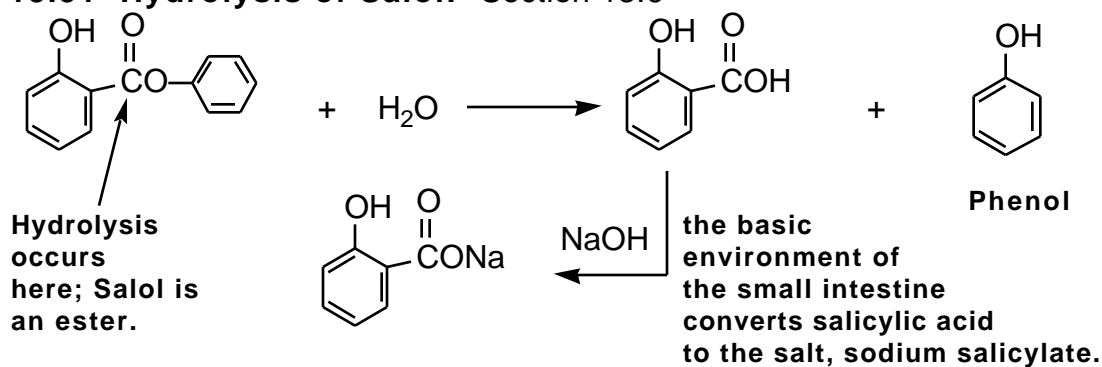
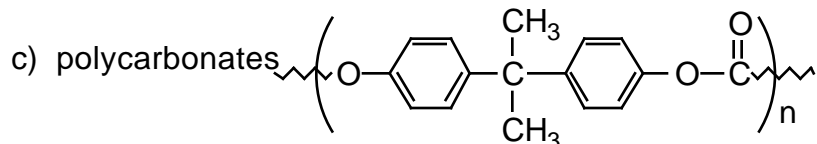
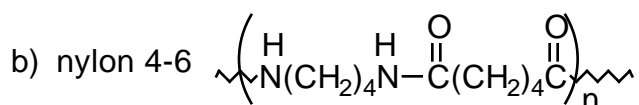
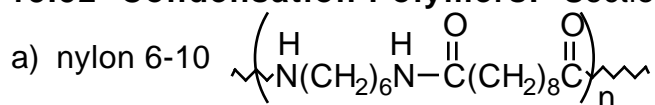
13.49 Hydrolysis of Urea: Section 13.7

Urea is an amide (actually a diamide) and is subject to hydrolysis by water, the "solvent" in urine. Water is the nucleophile in the substitution and the result can be visualized as carbonic acid and ammonia. The carbonic acid is unstable and decomposes to carbon dioxide.

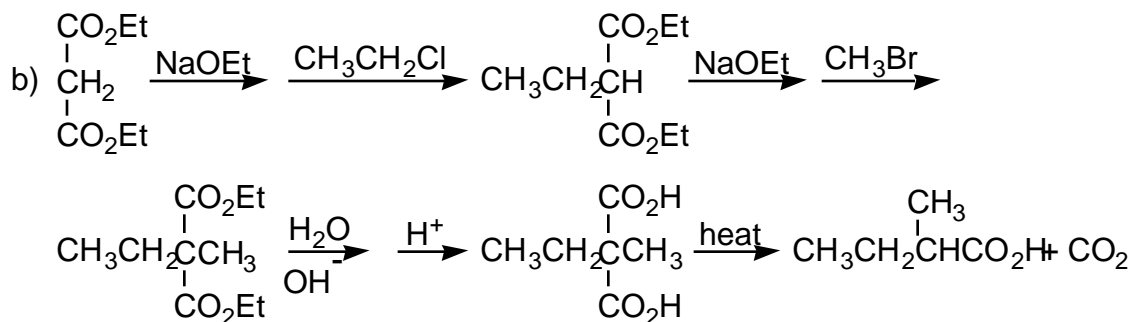
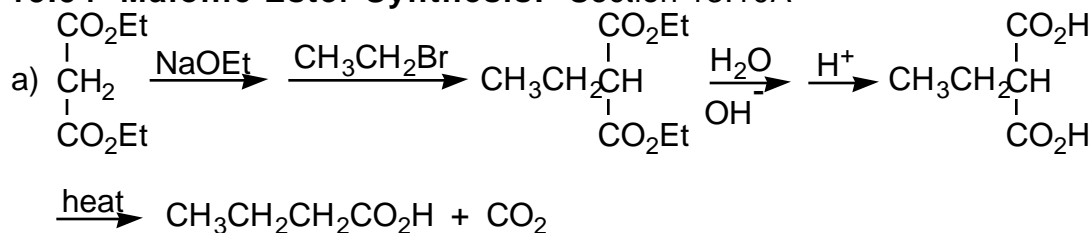
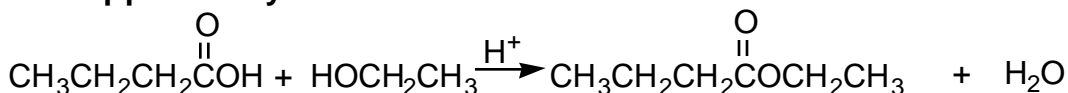
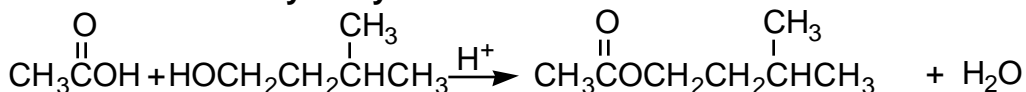
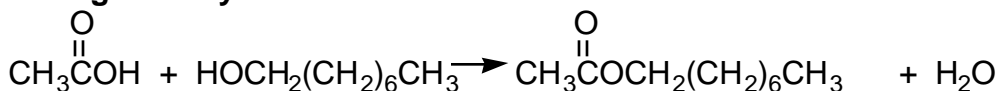
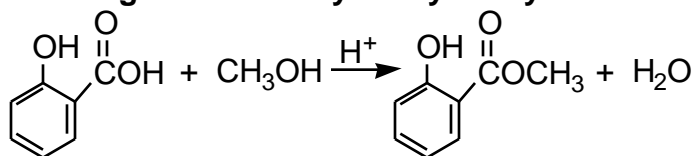
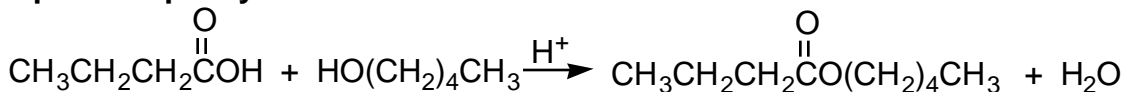
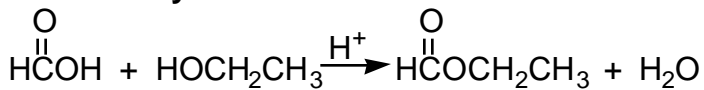


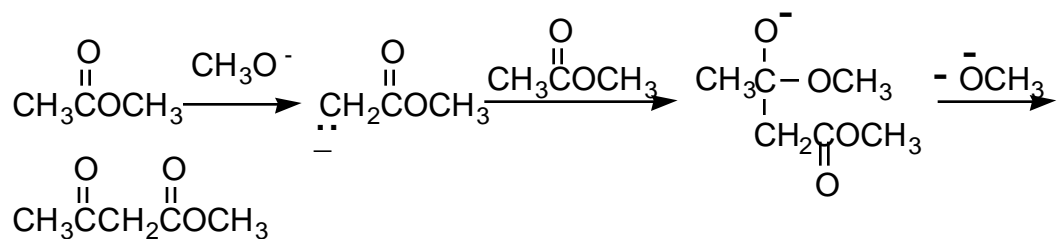
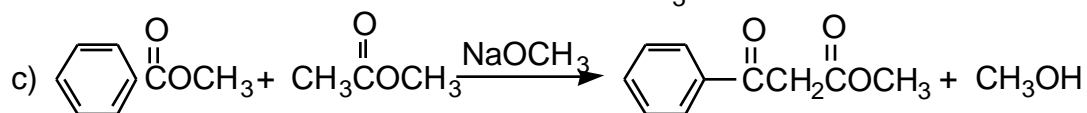
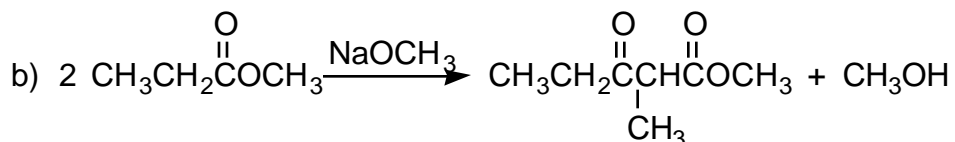
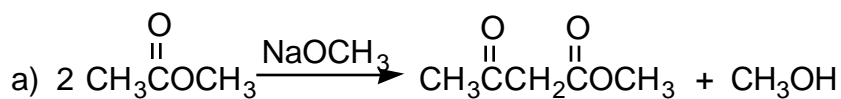
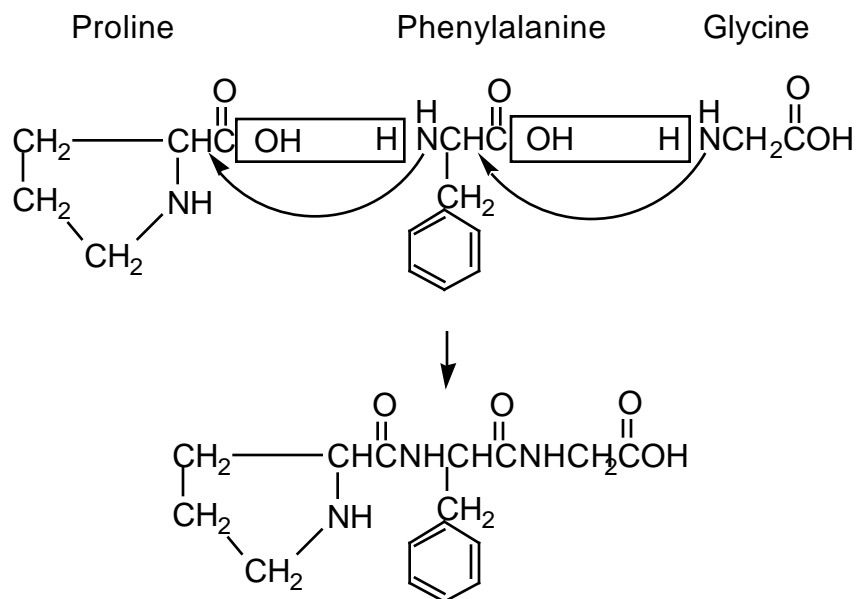
13.50 Decomposition of Aspirin: Section 13.6

Aspirin is an ester. In the presence of moisture, such as a humid climate, under prolonged conditions, it can hydrolyze by nucleophilic acyl substitution to an acid and alcohol. The acid formed is acetic acid, vinegar acid.

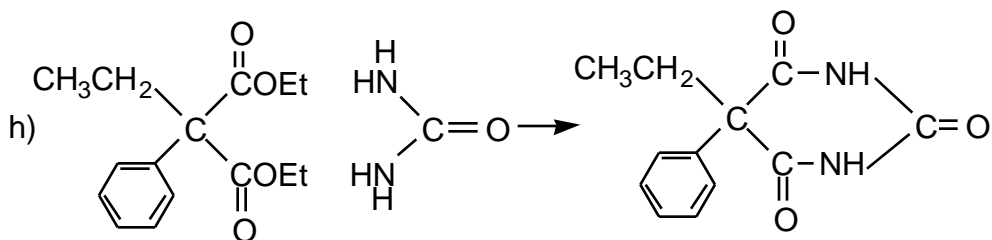
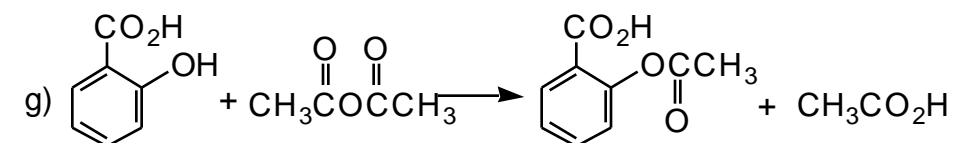
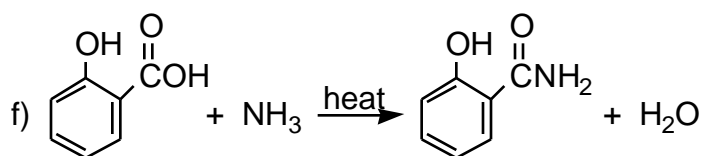
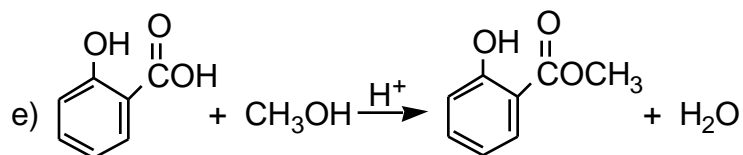
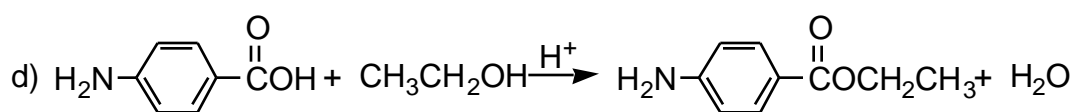
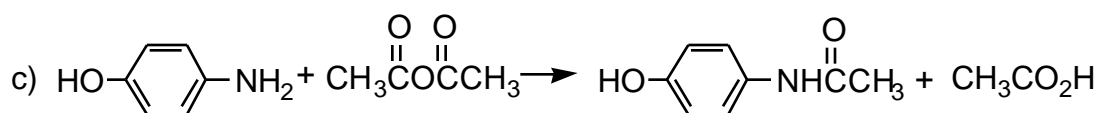
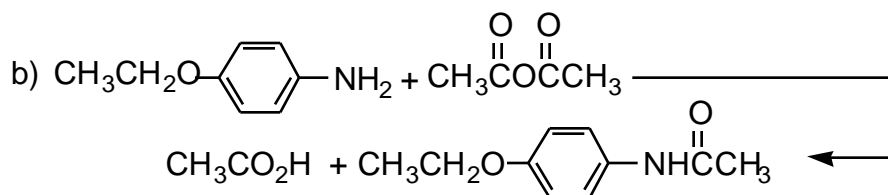
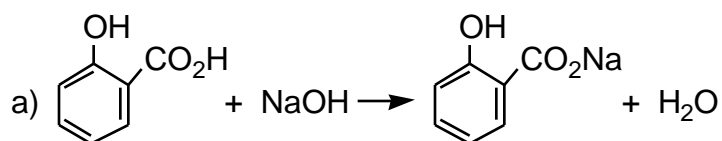
**13.51 Hydrolysis of Salol:** Section 13.6**13.52 Condensation Polymers:** Section 13.8**13.53 Polyurethanes:** Section 13.8

These polymers appear to be structurally both polyamides and polyesters.

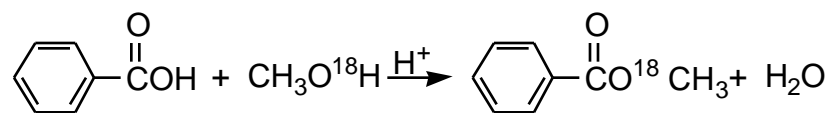
13.54 Malonic Ester Synthesis: Section 13.10A**13.55 Familiar Esters:** Sections 13.1B.3 and 13.6C**Pineapple: ethyl butanoate****Banana: 3-methylbutyl ethanoate****Orange: octyl ethanoate****Wintergreen: methyl o-hydroxybenzoate****Apricot: pentyl butanoate****Rum: ethyl methanoate**

13.56 Claisen Condensation: Section 13.10B**13.57 Claisen Condensation:** Section 13.10B**13.58 Proteins**

13.59 Preparation of Medicinal Compounds: Chapters 12 and 13



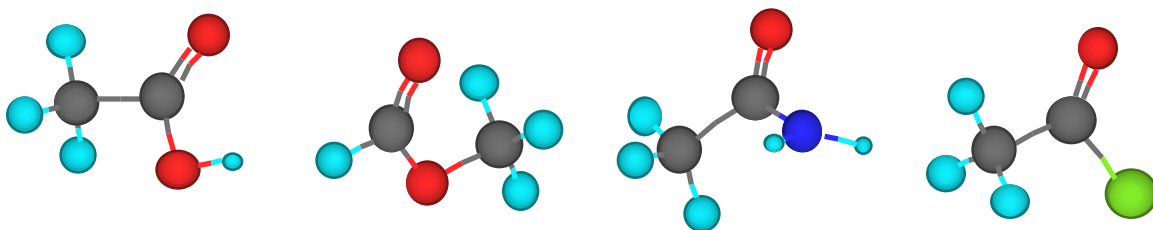
13.60 Reaction Mechanisms: Section 13.6B



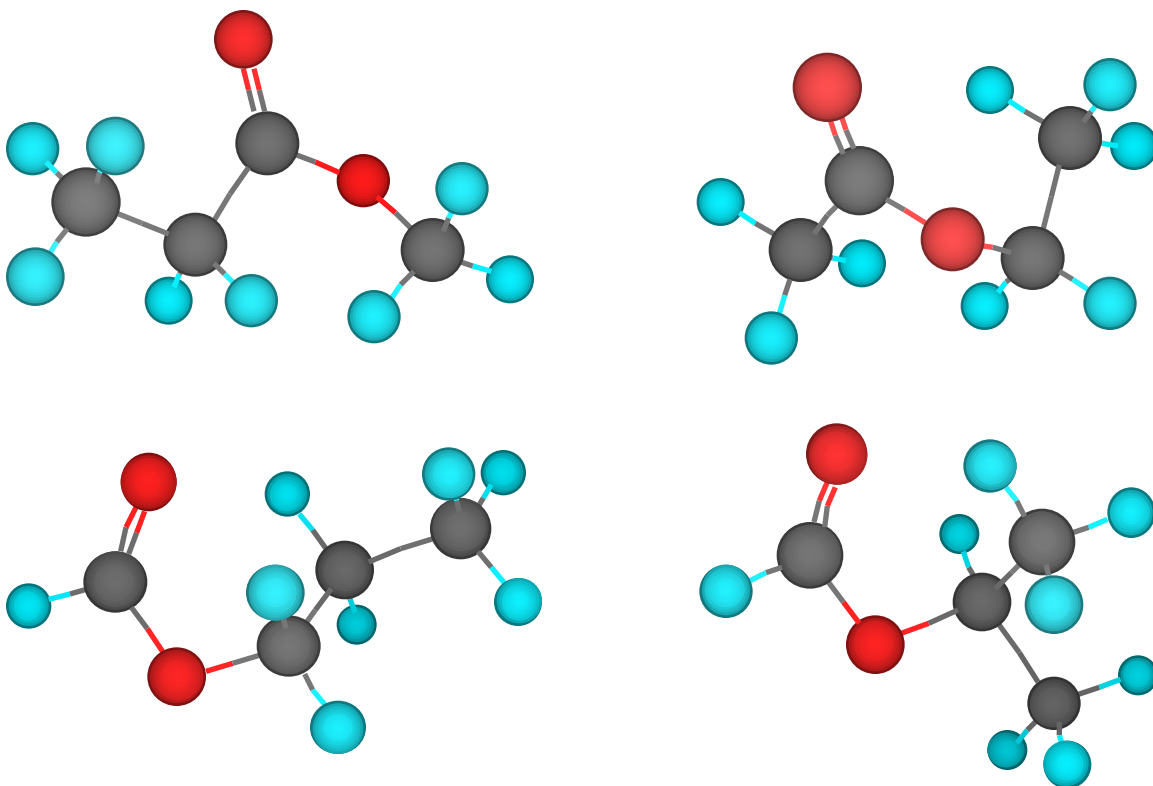
In the starting materials, the methanol has the labeled oxygen. Since the ester oxygen has the labeled oxygen in the ester product, the oxygen of the ester must have come from the alcohol.

ACTIVITIES WITH MOLECULAR MODELS

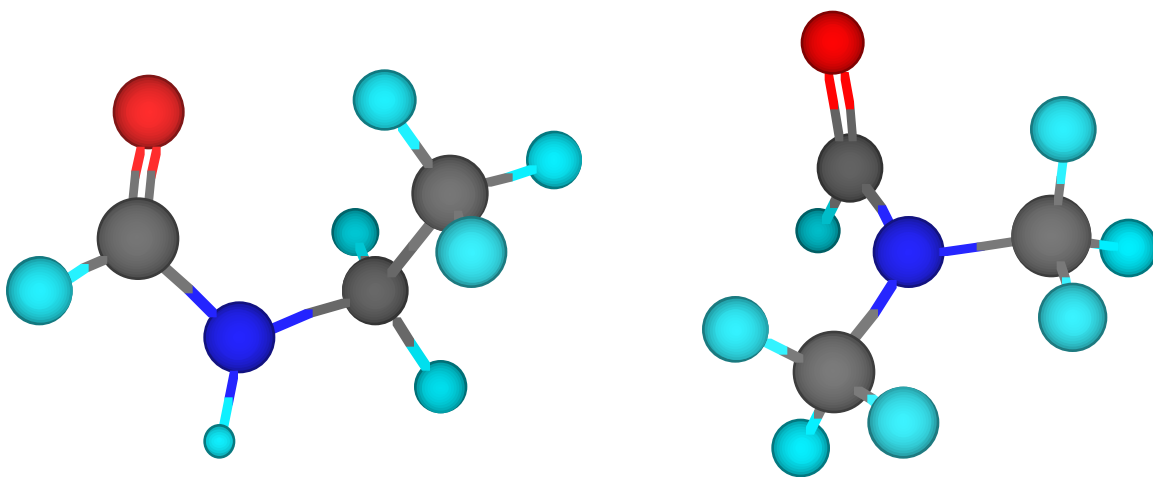
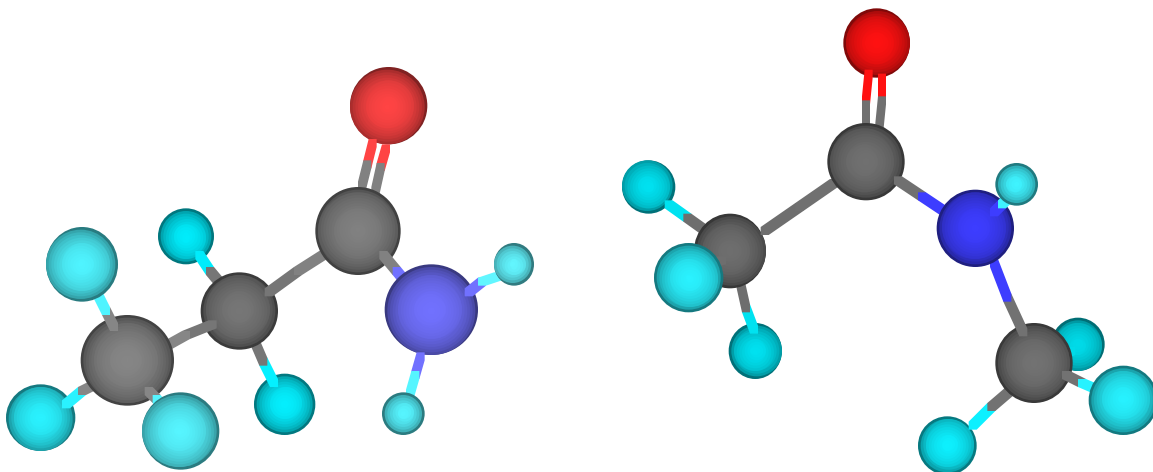
1. Make molecular models of the simplest acid, ester, amide, and acid chloride with only two carbons.



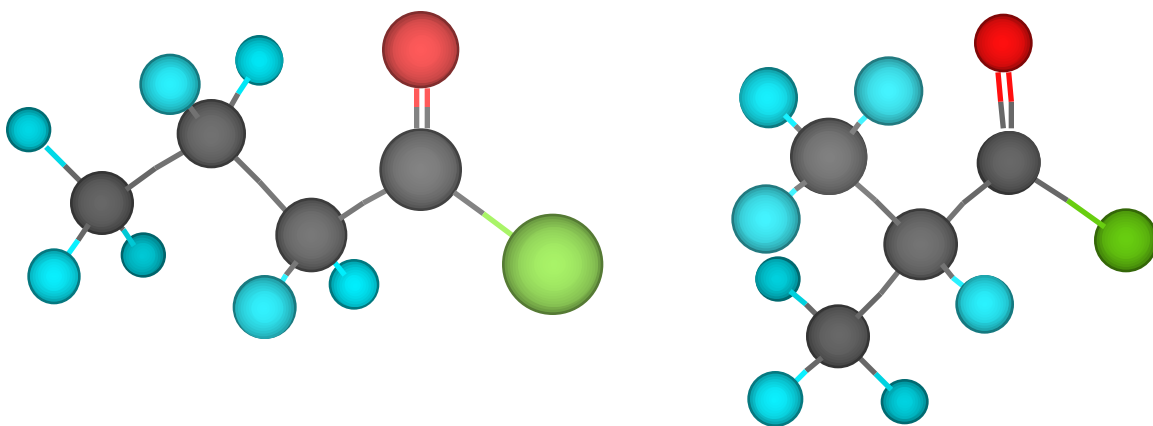
2. Make models of the four esters with the formula $\text{C}_4\text{H}_8\text{O}_2$.



3. Make models of the four amides with the formula C_3H_7NO .

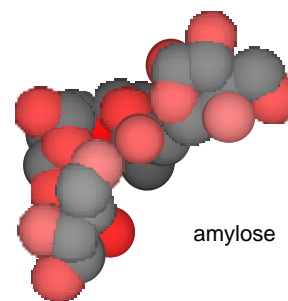
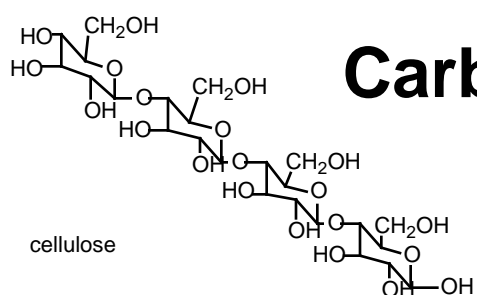


4. Make models of the two acid chlorides with the formula C_4H_7OCl .



14

Carbohydrates



CHAPTER SUMMARY

14.1 Chemical Nature of Carbohydrates - Polyhydroxy Aldehydes and Ketones

Carbohydrates are a class of organic biopolymers which consist of polyhydroxy aldehydes and ketones, their derivatives and polymers. Other terms for carbohydrates include sugars and saccharides. A single monomer unit is called a **monosaccharide**; several units are referred to as an **oligosaccharide**; larger polymers are called **polysaccharides**. The simplest carbohydrates are glyceraldehyde and dihydroxyacetone.

14.2 Nomenclature of Carbohydrates

The nomenclature of carbohydrates usually includes the suffix **-ose**. Monosaccharides may also be identified according to the nature of the carbonyl functional group (**aldose** or **ketose**), the number of carbons in the molecule (**tri-**, **tetr-**, **pent-** ose) or a combination of these two. Monosaccharides also have common names such as **ribose**, **glucose**, **galactose**, and **fructose** (four of the most common monosaccharides found in nature).

14.3 Structures of Monosaccharides

A. D,L - Aldoses: Open Chain Structures

Monosaccharides have one or more chiral carbon centers and can thereby form **enantiomers** and **diastereomers**. Most common monosaccharides are in the **D-family**. This means that, using D-glyceraldehyde as a starting point, other chiral carbons can be inserted between the carbonyl group and the D- carbon, producing families of

diastereomers. If two monosaccharides differ in their structures by the configuration at only one chiral center, then they are called **epimers**.

CONNECTIONS 14.1 Diabetes

B. Ketoses

Ketoses are the functional isomers of the aldoses. A family of ketose structures can be generated in the same manner as aldoses.

C. Fischer Projections

The method of drawing saccharides in a vertical orientation with the most highly oxidized carbon at the top is called a **Fischer Projection**. It does not represent the real, three-dimensional structure of the molecule.

D. Cyclic Structures - Hemiacetal Formation

The carbonyl and alcohol groups within the same monosaccharide may react together if the carbon chain is long enough. The result is a **cyclic hemiacetal**. A new chiral center is formed at the carbon which was previously the carbonyl. The two optical isomers that can result are called **anomers**. Five- and six-membered cyclic structures predominate with the alcohol oxygen as the last member of the ring. These are referred to as **furanoses** and **pyranoses**, respectively. Cyclic structures exist in equilibrium with the open-chain form.

Haworth Formulas show the cyclic nature of monosaccharides with the -OH and -CH₂OH groups oriented up and down around a planar ring, that is, above and below the plane of the ring. **Conformational structures** more accurately illustrate the three-dimensional nature of cyclic monosaccharides, especially in the chair conformation of six-membered rings. The -OH and -CH₂OH groups are oriented in axial and equatorial positions around the ring and correspond to the up and down placement in a Haworth Formula. Anomeric isomers are designated as α - if the -OH group is down or axial or as β - if up or equatorial.

14.4 Some Reactions of Monosaccharides

A. Oxidation of Carbohydrates (Reducing Sugars)

The easy oxidation of the aldehyde group using a mild oxidizing agent such as copper (II) and silver (I) can detect the presence of carbohydrate. The carbohydrates are referred to as **reducing sugars**. This type of test cannot distinguish between aldoses and ketoses,

however, because the alkaline conditions of the reaction lead to tautomerization of the ketone and immediate oxidation.

B. Reduction of Monosaccharides

The carbonyl group can be reduced to produce **sugar alcohols** such as sorbitol and mannitol.

C. Esterification

Also the alcohol groups may be esterified with a variety of acids including phosphoric acid. These **esters** are found extensively in metabolism.

CONNECTIONS 14.2 Prevention of Disease and Detoxification

14.5 Disaccharides and Polysaccharides

A. Glycosidic Linkages or Bonds

A reaction between one of the many alcohol groups on a monosaccharide with the hemiacetal group of an adjacent monosaccharide molecule to form an acetal is the method by which carbohydrates polymerize into disaccharides (sucrose and lactose), oligosaccharides, and polysaccharides such as starch, cellulose and glycogen. The α or β configuration of the anomeric carbon will be locked into position by this polymerization process. Not only does the diether linkage, called a **glycosidic bond**, resist oxidation by weak oxidizing agents (becoming **nonreducing sugars**) but it also is metabolically stable. Stereo-specific hydrolysis agents, known as enzymes, are required to cleave the glycoside.

B. Disaccharides

The most common disaccharides are lactose and sucrose. Lactose is found in milk and sucrose is table sugar from sugar cane and beets. Lactose is a reducing sugar while sucrose is not. Bacteria in animal mouths can use sucrose not only as food but also to form a cement which bonds the bacteria to the teeth - plaque.

CONNECTIONS 14.3 Low-Calorie Sweeteners

C. Polysaccharides

Starch, glycogen and cellulose are all polyglucose but differ in the nature of the glycosidic bonds, α versus β , and the positions of attachment.

Also the functions of these polysaccharides differ as do their commercial uses.

Nature produces variations in the functional groups of polysaccharides which gives rise to a diversity of overall structure and function. A good example is the A, B, O -blood type variation found in humans.

CONNECTIONS 14.4 Nitrocellulose and Rayon

Connections 14.4 summarizes the history and manufacture of the semi-synthetic materials rayon and nitrocellulose, both made from naturally occurring cellulose.

SOLUTIONS TO PROBLEMS

14.1 Nomenclature of Carbohydrates: Section 14.2

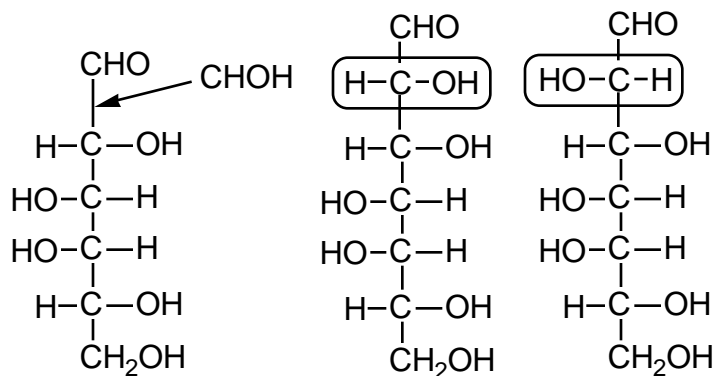
Allose is an aldohexose while xylose is an aldopentose.

14.2 Structures of Monosaccharides: Section 14.3

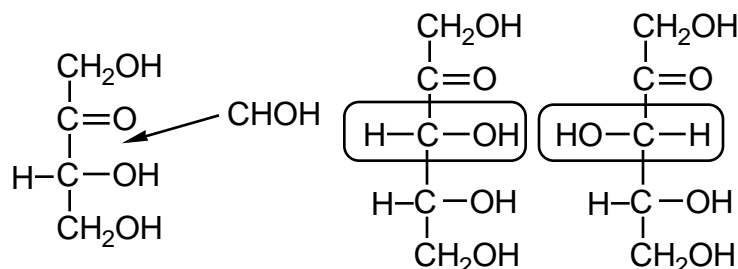
Epimers have a different configuration at only one chiral carbon center. Epimers of D-glucose would be D-allose, D-mannose, and D-galactose.

Diastereomers have different configurations at more than one chiral carbon center. Therefore any of the non-epimers of D-glucose would be diastereomers.

14.3 Structures of Monosaccharides: Section 14.3

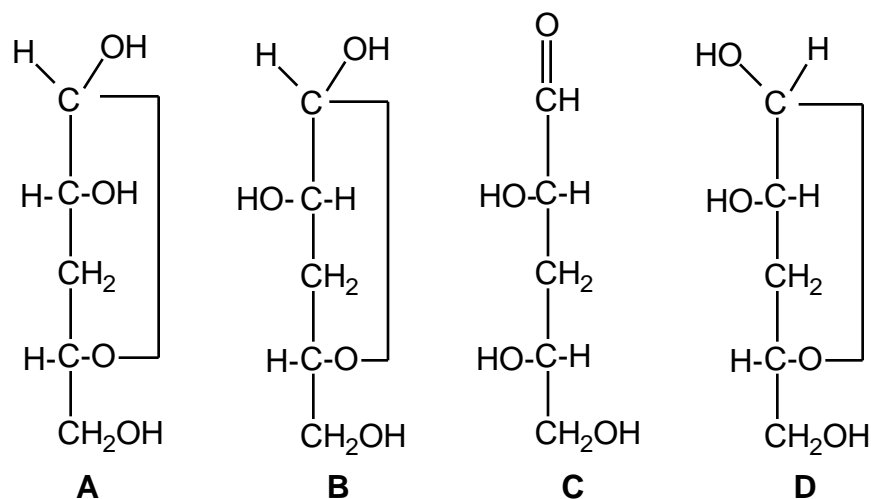


14.4 Structures of Monosaccharides: Section 14.1



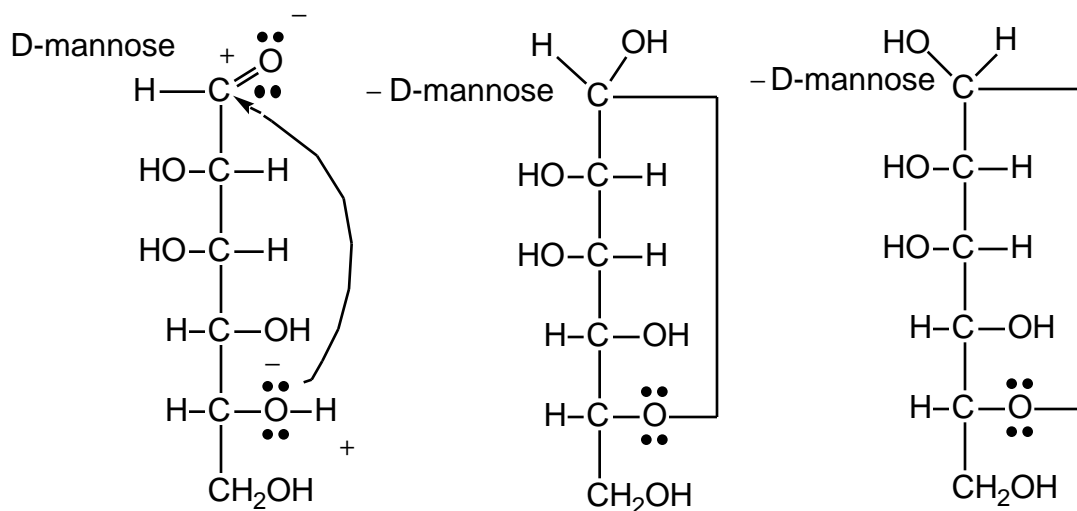
There are only two ketopentoses derived from D-erythrulose. They are epimers.

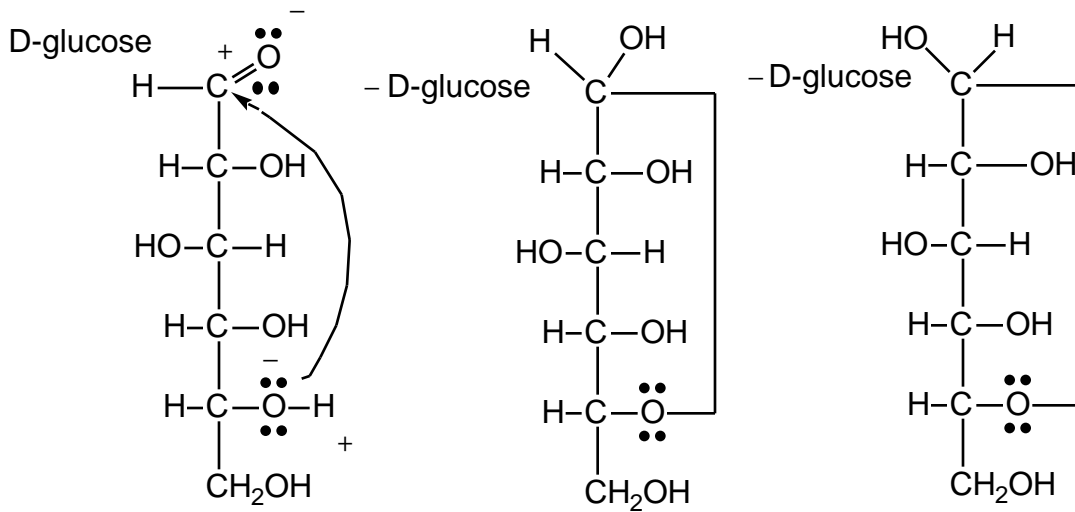
14.5 Structures of Monosaccharides: Section 14.3



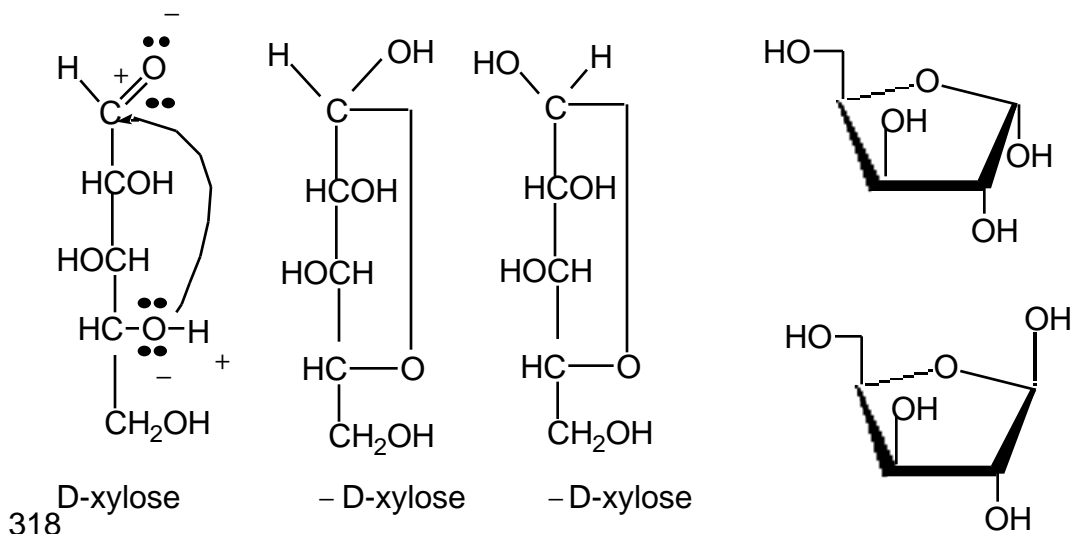
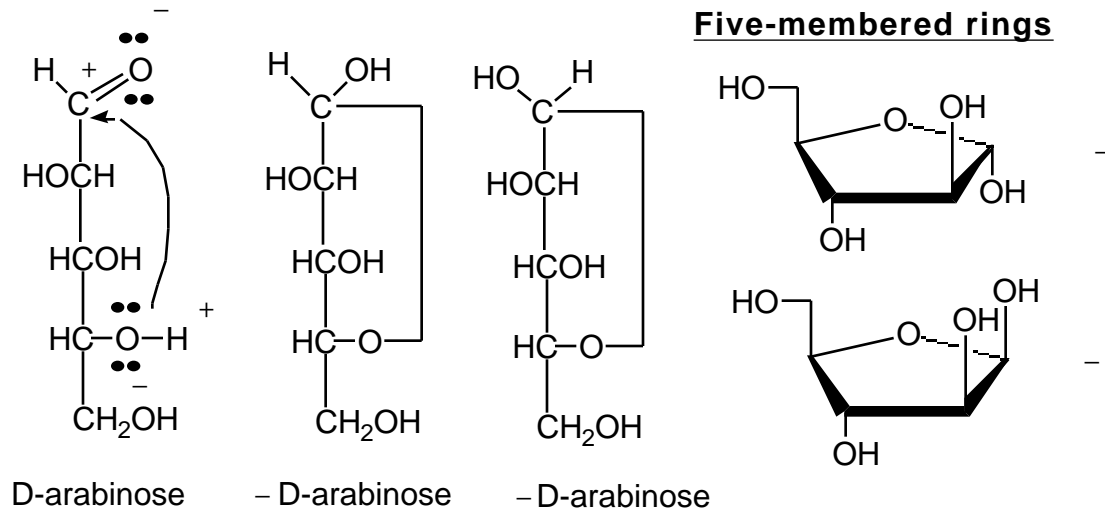
The epimers are **A & B**; the anomers are **B & D**; the diastereomers are **A & B**, **A & D**, **B & D**. Compound **C** could be an enantiomer to the open-chain form of **A**. In its current form, however, it doesn't have the same number of chiral carbon centers as do the other compounds.

14.6 Structures of Monosaccharides: Section 14.3D

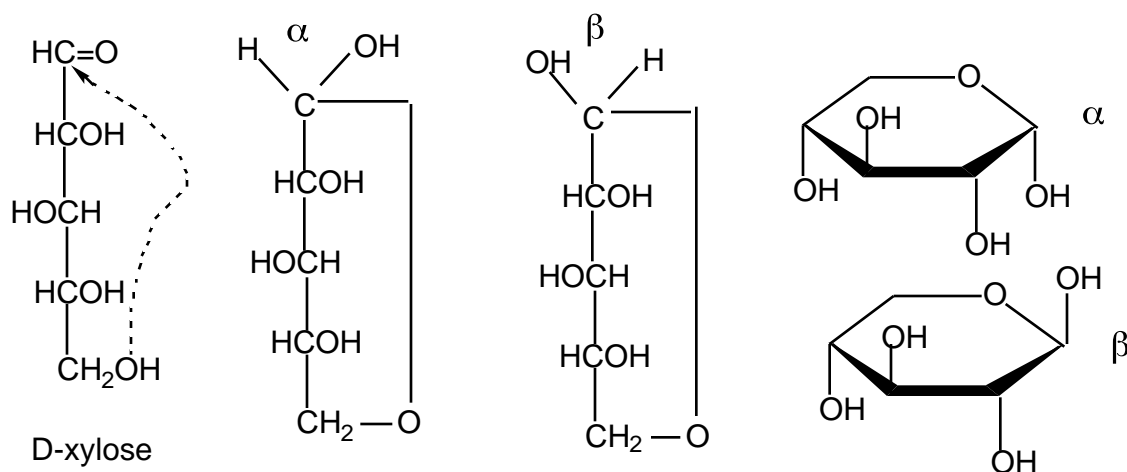
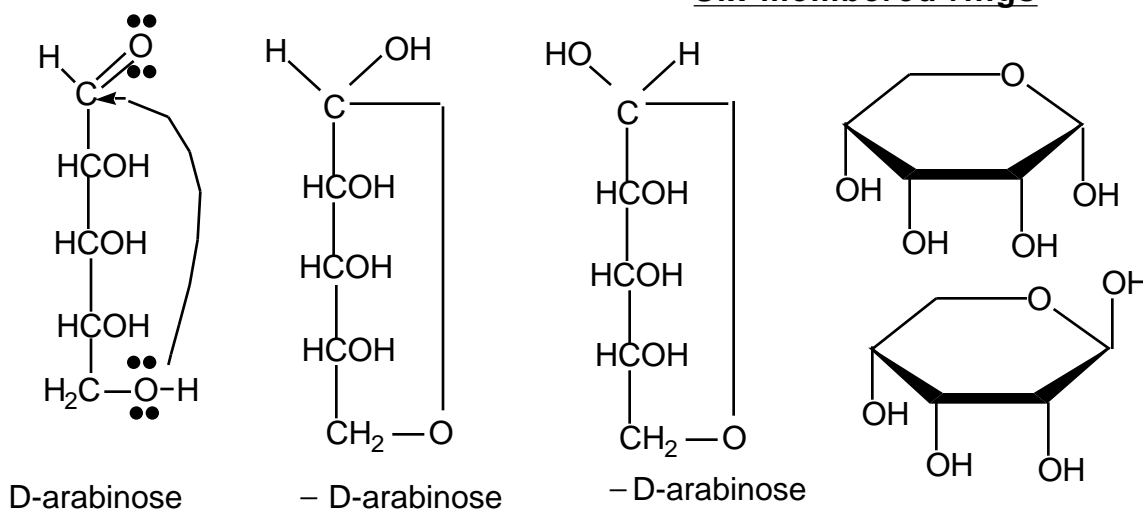




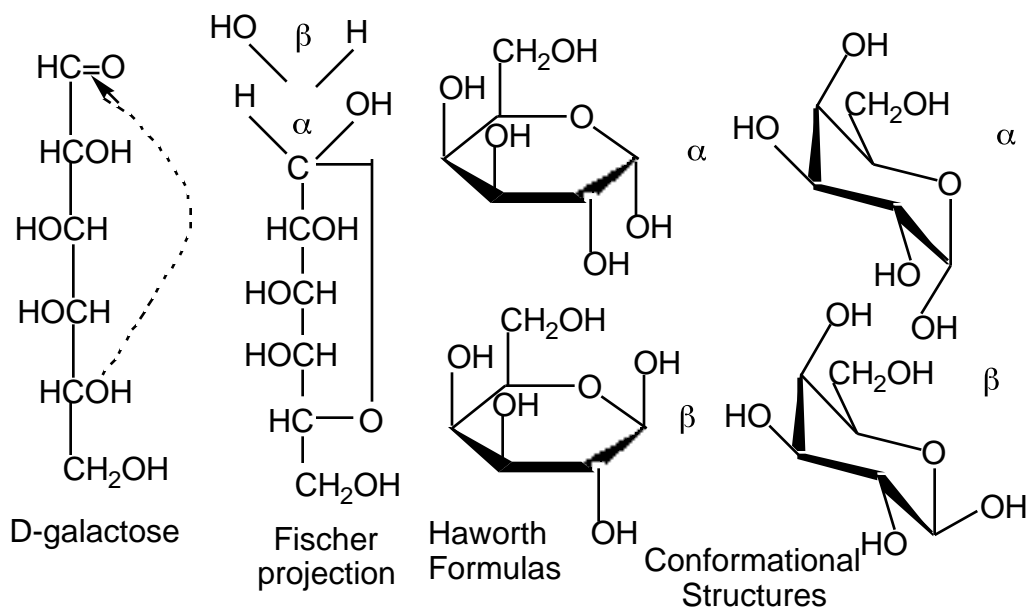
14.7 Structures of Monosaccharides: Section 14.3D



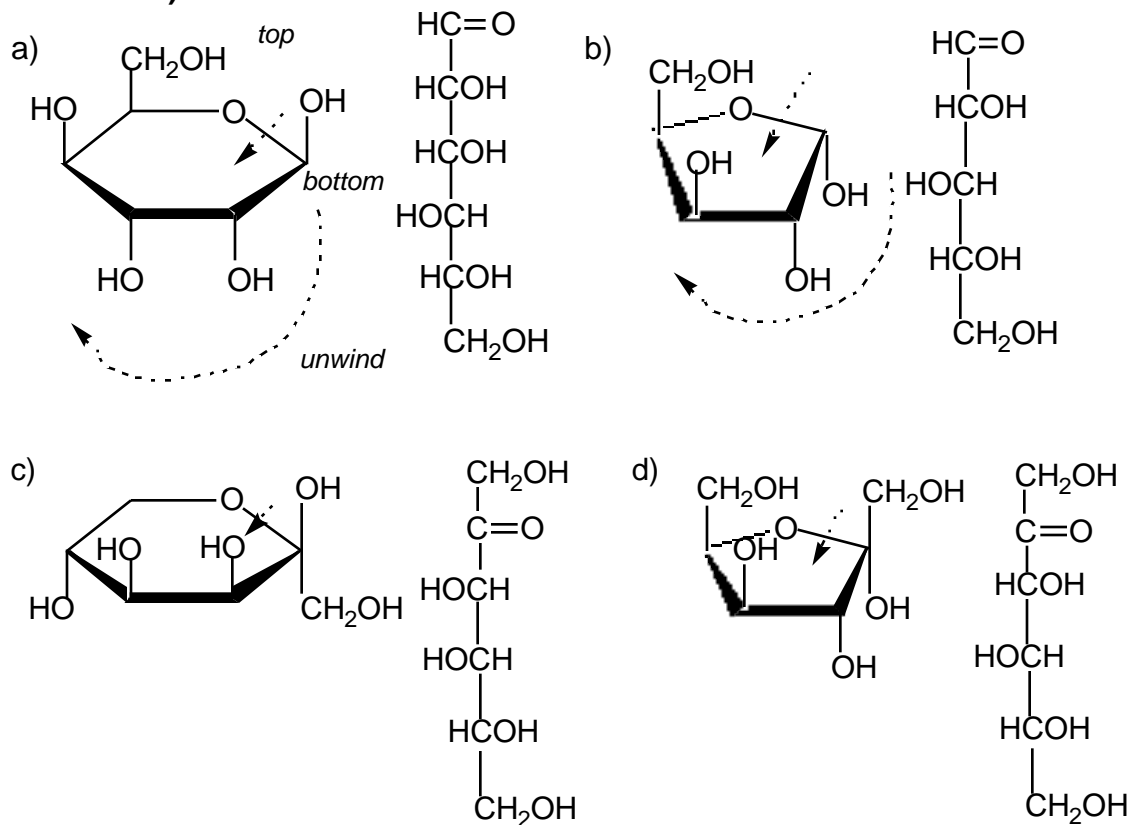
Six-membered rings



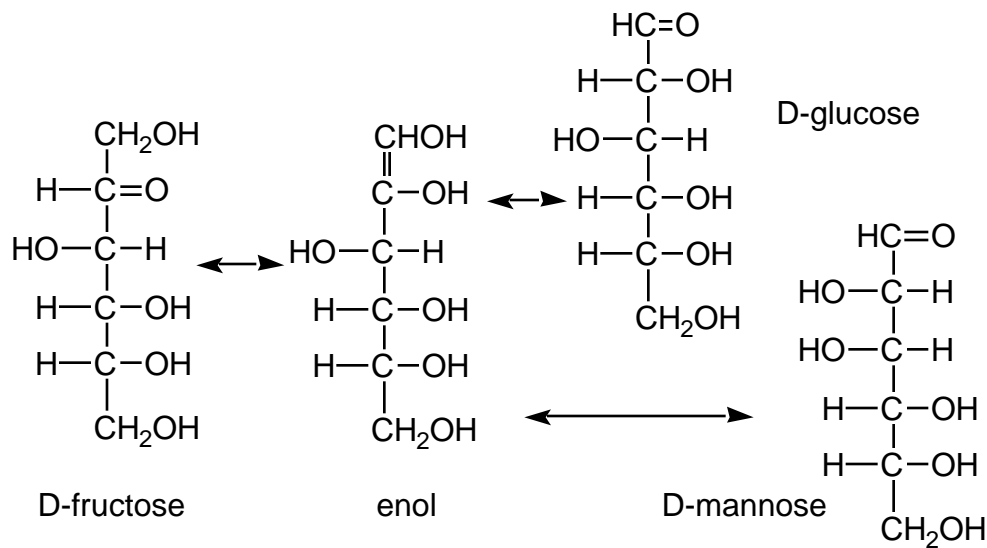
14.8 Structures of Monosaccharides (Cyclic and Open-chain Structures): Section 14.3

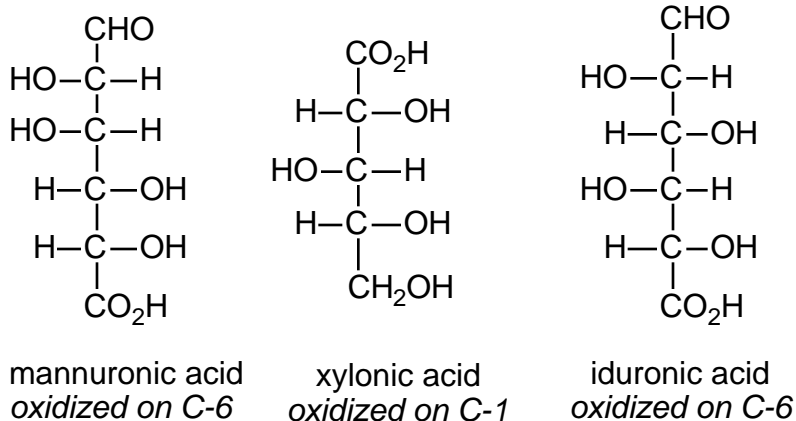
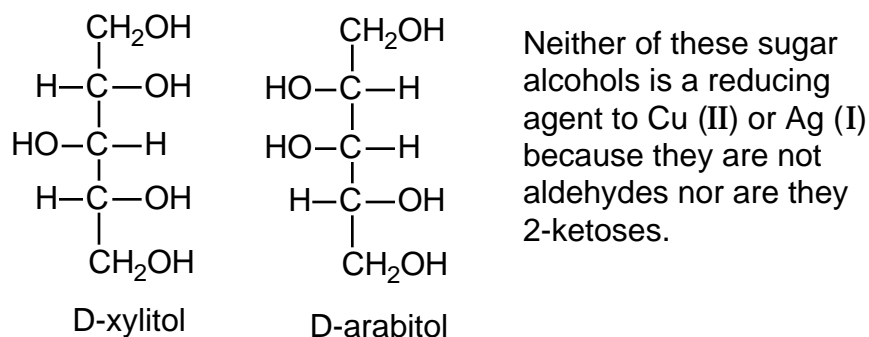
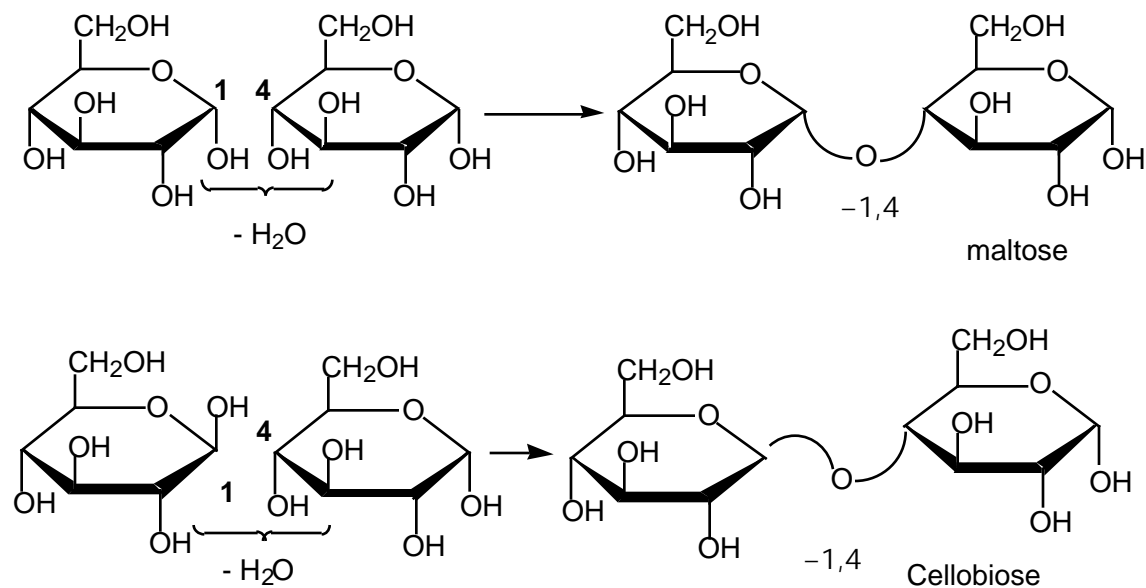


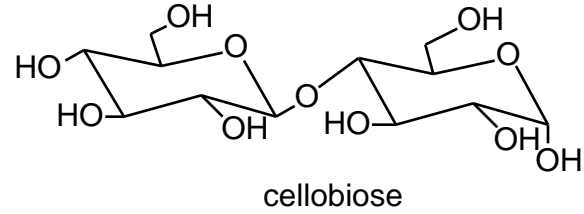
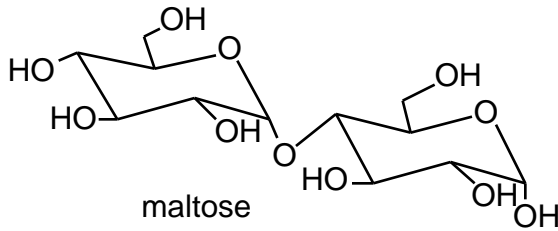
14.9 Structures of Monosaccharides (Cyclic and Open-chain Structures): Section 14.3



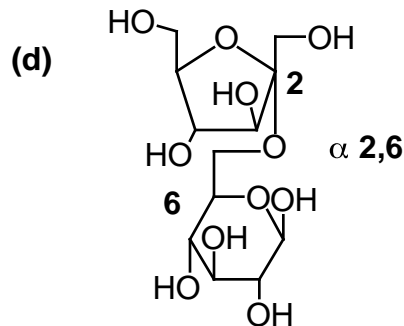
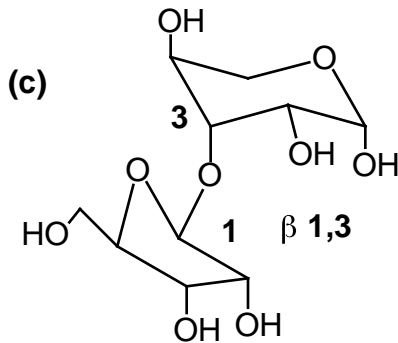
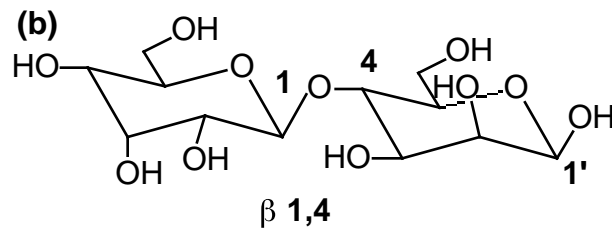
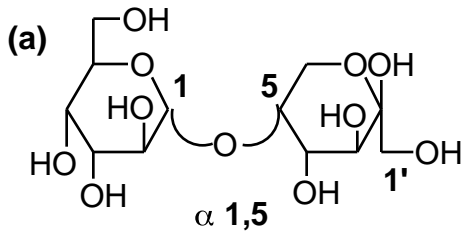
14.10 Some Reactions of Monosaccharides: Section 14.4



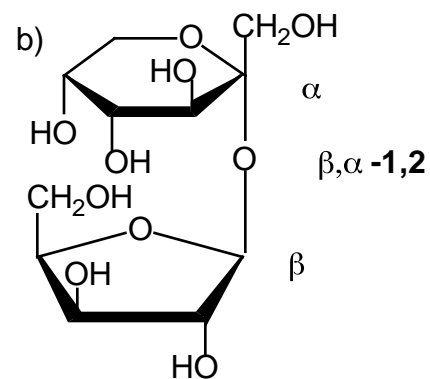
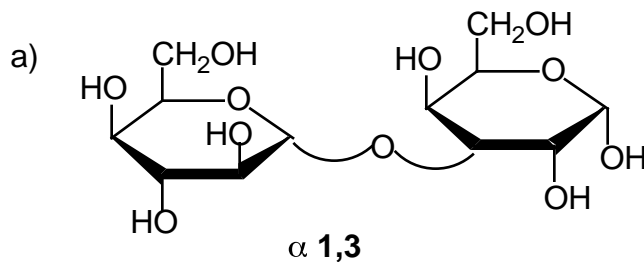
14.11 Some Reactions of Monosaccharides (Oxidation): Section 14.4**14.12 Some Reactions of Monosaccharides (Reduction):** Section 14.4B**14.13 Disaccharides and Polysaccharides:** Section 14.5



14.14 Disaccharides and Polysaccharides (Glycosidic Linkages or Bonds): Section 14.5A



14.15 Disaccharides and Polysaccharides: Sections 14.5



14.16 Disaccharides and Polysaccharides: Sections 14.5

Besides the acetal and alcohol groups, chitin contains an amide. This group is neither acidic nor basic.

Heparin contains alcohol and acetal groups as well as acidic sulfonic acid and carboxyl groups.

14.17 Terms

- a) A hexose is a six-carbon sugar while a pentose has five carbons.
- b) An aldose has an aldehyde (RCH=O) functional group while a ketose has a ketone (RCOR).
- c) A reducing sugar has an alcohol and ether functional groups on the same carbon. A nonreducing sugar is a diether.
- d) Monosaccharides are small, single carbohydrate units, usually containing five or six carbons. Polysaccharides are polymers of monosaccharides linked by glycosidic bonds.
- e) α - and β -D-glucose are anomers, that is, they are both the cyclic forms of glucose with opposite configurations for the -OH group attached to the new chiral center, the former carbonyl group.
- f) Fischer projections are structures drawn vertically with the most oxidized carbon appearing at the top. They are not related spatially to real structures. Haworth formulas are cyclic carbohydrate structures in the form of cyclopentane and cyclohexane-type rings.
- g) Amylose is the "linear" form of starch in which all of the glucose units are linked -1,4 while amylopectin is branched, its main chain of glucose units linked through an -1,4 glycosidic bond with -1,6 bonded-branches about every 25 monomer units.
- h) Glycogen is a polymer of glucose with a main chain having -1,4 glycosidic bonds and -1,6 branches every 8-10 units. Cellulose is polyglucose linked -1,4 .
- i) Type 1 diabetes involves the absence or near absence of insulin to regulate body glucose concentrations. Type 2 diabetes is a more complicated condition in which insulin is usually present but not functioning properly.

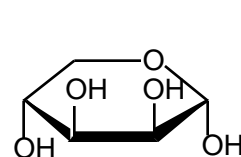
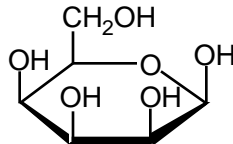
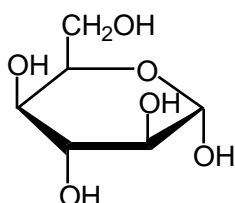
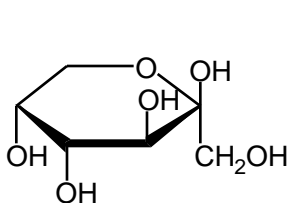
- j) Viscose rayon is a form of cellulose which has been processed by derivatization and reconstitution while acetate rayon is derivatized cellulose.
- k) Fehling's test uses Cu (II) as a weak oxidizing agent while Tollen's test uses Ag (I).

14.18 Structure: Sections 14.3, 14.4 and 14.5

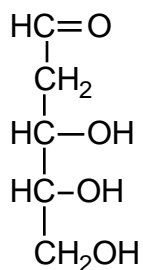
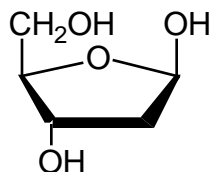
- a) Cellobiose and maltose are both dimers of glucose and both are reducing sugars. Cellobiose has a β -1,4 glycosidic bond while maltose has an α -1,4 bond.
- b) Galactose and glucose, linked β -1,4, are the units in the reducing sugar lactose. Sucrose is nonreducing because of the α -1,2 glycosidic bond between fructose and glucose.
- c) β -D-glucose and β -D-galactose are epimers differing in the configuration about C-4. Both are reducing sugars.
- d) β -D-glucose and β -D-fructose are reducing sugars and functional isomers of each other.
- e) β -D-xylose and β -D-ribose are both aldopentoses and reducing sugars. They differ in configuration at C-1 of the cyclic form as well as at C-3.
- f) Maltose has two glucose units linked α -1,4 while lactose is composed of galactose and glucose linked β -1,4; both are reducing.
- g) Cellulose is a linear polyglucose linked β -1,4 while starch consists of amylose (polyglucose α -1,4) and amylopectin (α -1,4 with α -1,6 branches). Both have reducing ends but not much would be seen with Fehling's or Tollen's tests because of the large molecular weight of both polymers.

14.19 Structure: Section 14.4

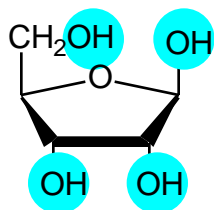
- a) β -D-fructose b) β -D-idose c) β -D-talose d) β -D-lyxose



14.20 Structure: Section 14.3

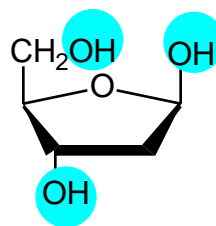
2-deoxyribose
open-chain form2-deoxyribose
Haworth form

14.21 Reactions: Section 14.4



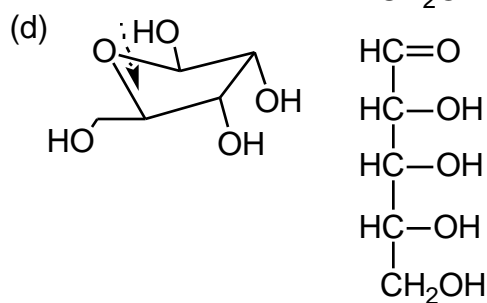
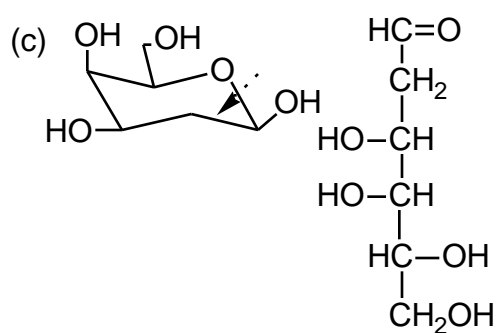
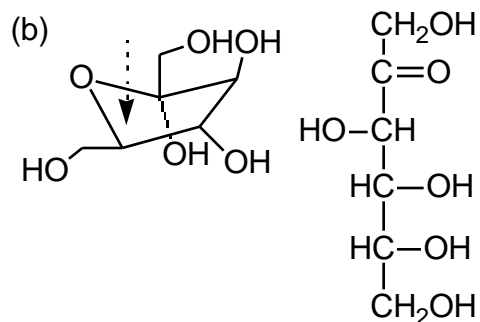
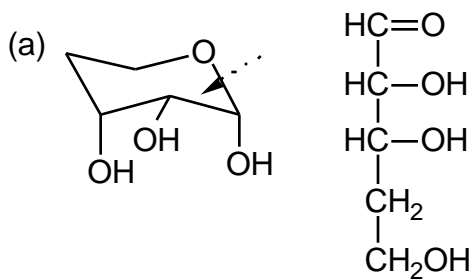
ribose

Ribose has 4 alcohol groups which can be esterified, while 2-deoxyribose has 3.



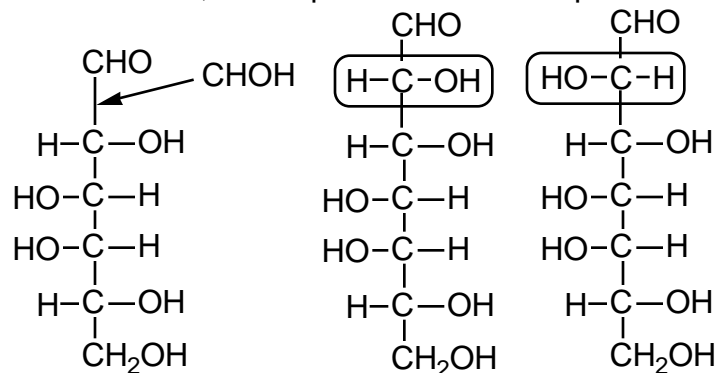
2-deoxyribose

14.22 Structure: Section 14.3



14.23 Optical Isomers: Section 14.3

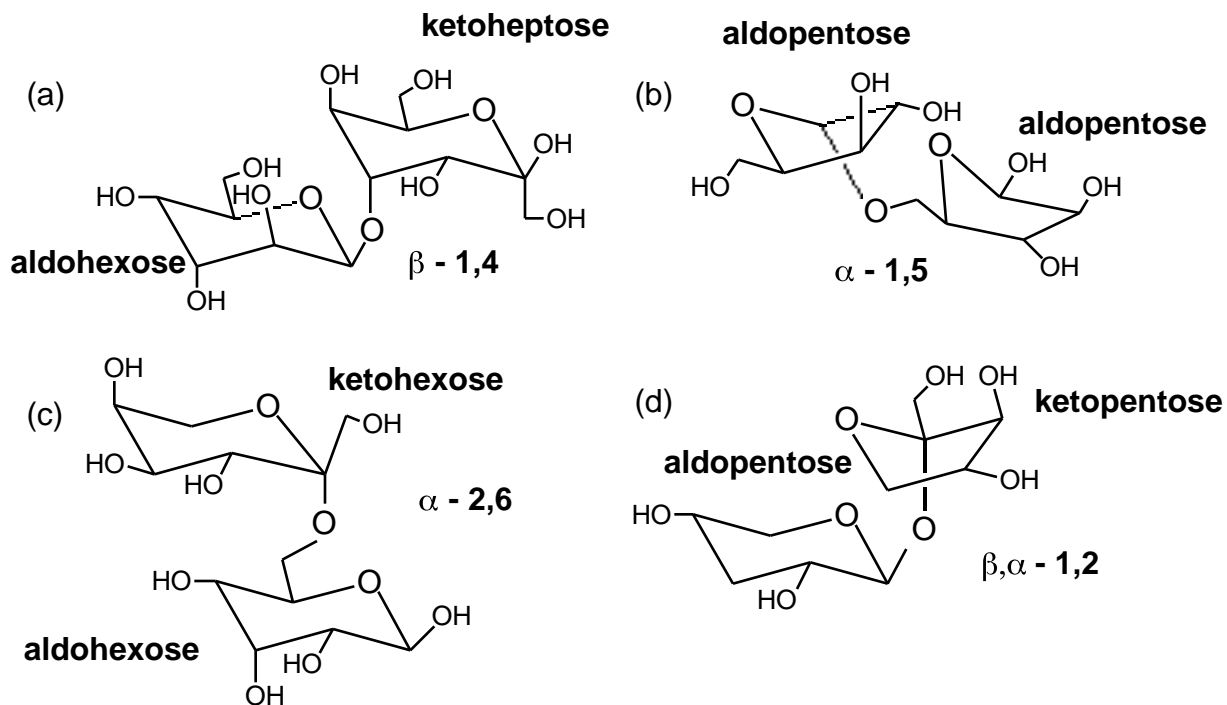
There are two chiral carbons; four optical isomers are possible.



a/b are identical because you can rotate **b** in the plane of the page and it will superimpose on **a**. **a** is also obviously meso and is therefore not optically active. **c/d** are enantiomers. **a** is a diastereomer of **c** and **d**.

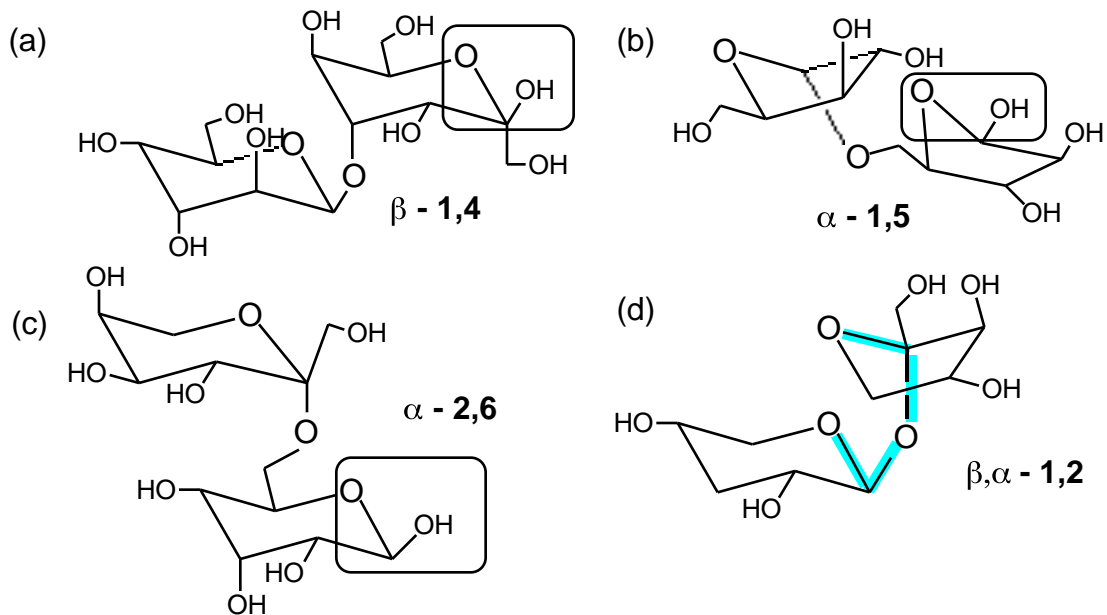
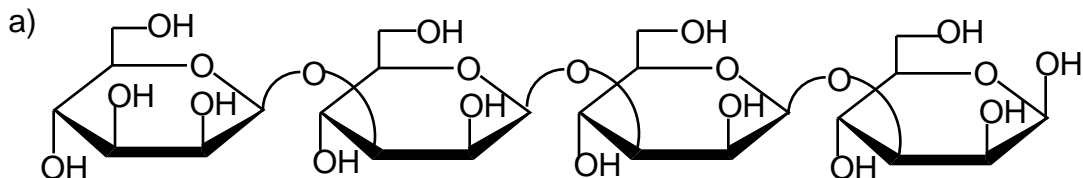
14.24 Reactions: Section 14.4

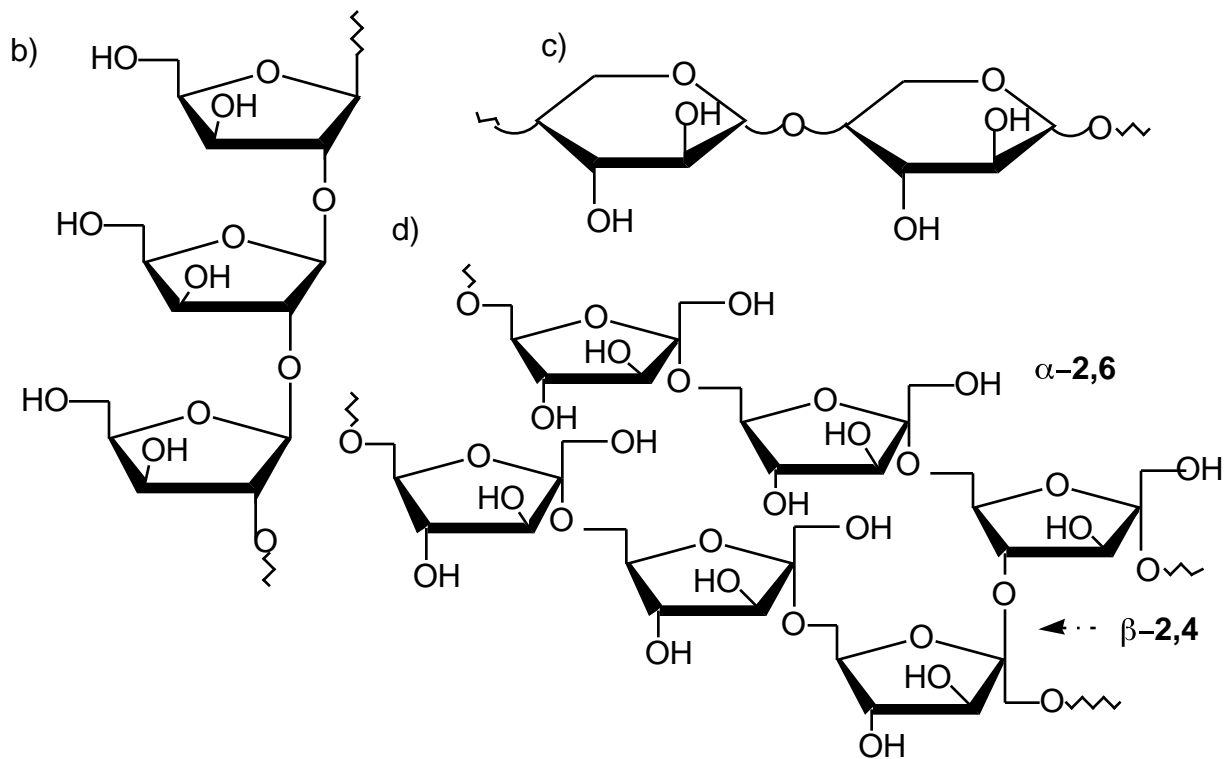
In the presence of acid, which also assumes an aqueous solution, the α and β forms of D-glucose will rapidly come into equilibrium with the open-chain aldehyde. Both the α and β anomers can react with methanol to form the methyl acetal.

14.25 Structure: Section 14.5

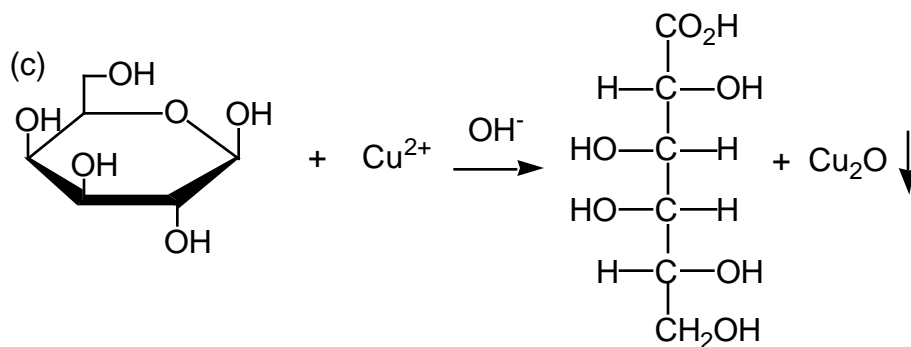
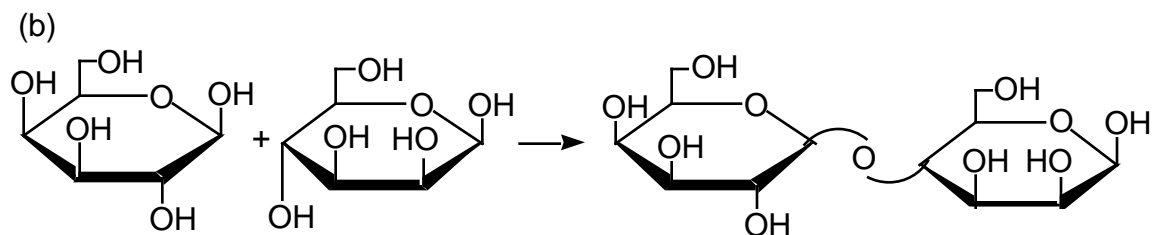
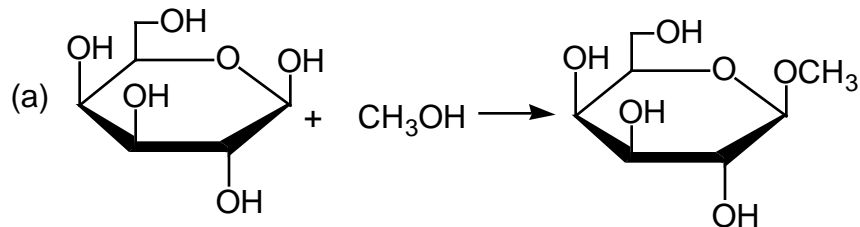
14.26 Reactions: Section 14.4

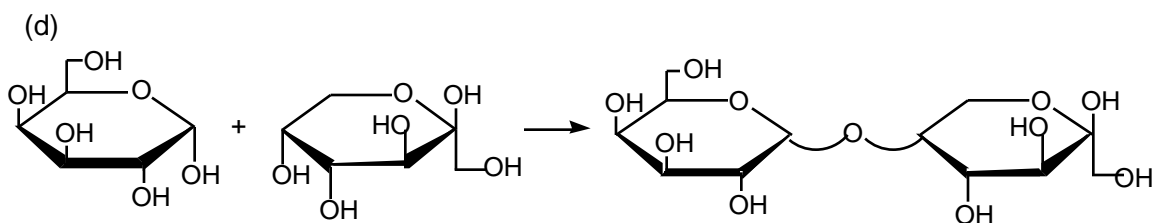
In the previous question, the first three, a,b,c, are reducing sugars. The d structure has both saccharides involved in an acetal-ketal linkage.

**14.27 Structure:** Section 14.5



14.28 Reactions: Sections 14.4 and 14.5

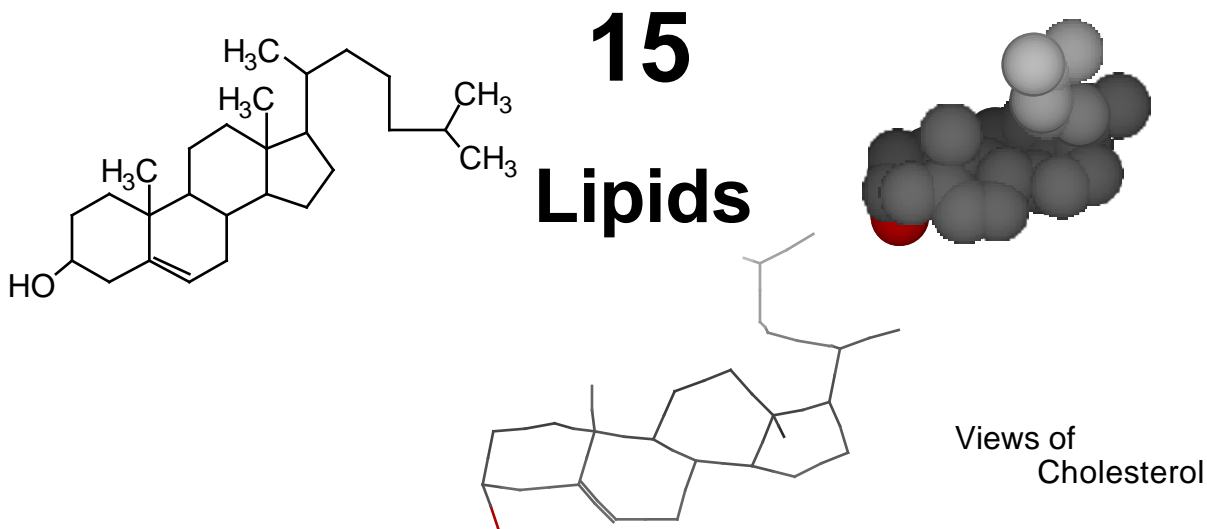


**14.29 Reactions:** Section 14.4

Fructose can tautomerize to glucose under the alkaline conditions of both the Fehling and Tollens tests. Therefore both fructose and glucose will test positive.

14.30 Reactions: Section 14.4

Since Fehling's test gives a positive result for any aldose or 2-ketose, it is evidence that there could be a sugar in urine but would not be a definitive test for glucose per se.



CHAPTER SUMMARY

15.1 The Nature of Lipids

Lipids can best be defined as biomolecules which are **soluble to a great extent in nonpolar solvents**. In contrast to carbohydrates, proteins and nucleic acids, lipids do not have polymeric forms. By virtue of their **hydrophobic nature** they aggregate into large complexes, held together to a significant degree by nonpolar interactions.

The structures of lipids are quite varied: triacylglycerols (fats and oils), waxes, phospholipids, sphingolipids, steroids, eicosanoids, fat soluble vitamins, and pigments. Some lipids are **simple** in structure while others are more **complex**. Among these molecules are those which are esters in nature and therefore **saponifiable** in aqueous base. Others are **nonsaponifiable**. Many are **completely nonpolar** while others are **amphipathic**, that is, they have a polar/nonpolar nature.

15.2 Waxes - Simple Esters of Long-Chain Alcohols and Acids

Waxes are functionally the simplest of the lipids and are probably the most nonpolar.

15.3 Fats and Oils - Triesters of Glycerol

Fats and oils are triesters of glycerol and long-chain fatty acids. The fatty acids are usually **10-24 carbons** in length; they can be

saturated or **cis-unsaturated**. Saturated triacylglycerols have high melting points and are commonly called fats. Cis-unsaturation leads to a dramatic lowering of melting point and the presence of a liquid, or oil, at room temperature. **Short-hand notations** can be written for the fatty acids which indicate the number of carbons/ number of double bonds/ positions of double bonds from the carboxyl end of the molecule; for example, linoleic acid would be C_{18:2}^{9, 12}. Another way to describe unsaturated fatty acids denotes the position of the first double bond from the alkyl end of the molecule; for example, linoleic acid would be 6.

CONNECTIONS 15.1 Errors in the Metabolism of Fatty Acids - Lorenzo's Oil

15.4 Reactions of Fats and Oils

A. Addition Reactions

The double bonds are subject to addition reactions such as **iodination** and **hydrogenation**.

The conversion of the double bonds in oils to single bonds leads to an increase in viscosity. Margarine is the product of hydrogenation of naturally occurring oils.

B. Oxidation Reactions

Oxidative cleavage at double bonds, the process of rancidification, is undesirable in foods because of the bad taste of the oxidation products. Oxidation can also lead to **polymerization** or cross-linking of fatty acid chains. This exothermic process is useful in terms of setting a finish on paints and dangerous if it occurs with combustible materials in an enclosed space.

C. Saponification

The ester bonds in fats and oils can be hydrolyzed in the presence of base to produce **soaps** which are the sodium salts of fatty acids. Soap making is an ancient process which has changed little over millenia.

15.5 Soaps and Detergents

A. Structure of Soaps

A soap molecule has a nonpolar, alkyl end and a polar, salt end. Because of this dual polarity, it is called amphipathic. This

hydrophobic/hydrophilic nature is essential to the function of such molecules.

B. Mechanism of Soap Action

The **cleaning action of soap** involves lowering the surface tension of water by disrupting hydrogen bonds at the surface and the formation of micelles within the volume of water present. **Micelles** are aggregations of soap molecules arranged so that the hydrophobic “tails” are oriented towards each other away from the water solvent and the hydrophilic “heads” are pointed into the water.

C. Detergents

Detergents are amphipathic molecules which have enhanced solubility and biodegradability properties compared to soaps. Instead of having a sodium salt in the polar portion of the molecule, other ionic and polar groups are used giving rise to what are called "cationic", "anionic" and "nonionic" detergents.

15.6 Biolipids - Structures and Functions

A. Triacylglycerols

Triacylglycerols, or **TAGs**, are a major source of food energy for higher animals. The metabolism of TAGs gives us about 2.5 times the amount of chemical energy as does the metabolism of carbohydrates.

B. Phospholipids

This class of amphipathic lipids is very similar in structure to TAGs, but the polar portion is an ester of phosphoric acid. Schematically, **phospholipids** have this polar head plus two nonpolar tails.

C. Sphingolipids

While the overall structural scheme of a polar head and two nonpolar tails is also found in **sphingolipids**, this class of amphipathic lipids has its own unique set of distinguishing structures.

The main function of these two subclasses is to produce the semipermeable **lipid bilayer membrane** structure of the cell. The current model of a cell membrane is referred to as **fluid mosaic**. Proteins and cholesterol are also incorporated with the bilayer for purposes of stability, permeability, and cell recognition.

D. Steroids

A fused multiple-ring system is the structural framework for **steroids**. **Cholesterol** is the nonpolar, nonsaponifiable progenitor of the metabolic and gonadal hormones such as cortisol, testosterone and estrogen as well as the bile acids used for the intestinal absorption of fats and oils. Many toxins fit into this lipid subclass.

CONNECTIONS 15.2 RU-486**E. Eicosanoids**

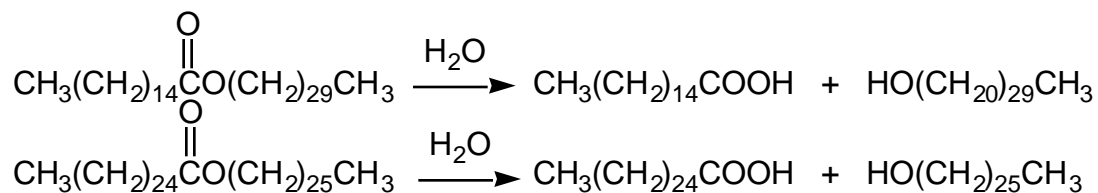
Eicosanoids in the form of prostaglandins, prostacyclins, thromboxanes, and leukotrienes are short-lived metabolites of fatty acids which affect a variety of tissues in the body.

F. Vitamins

Vitamins A, D, E, and K are called the **fat-soluble vitamins** and must be part of the diet for health and vigor.

G. Pigments

Many **pigments** found in algae, bacteria and plants, such as chlorophyll, are lipid in nature. These molecules help to convert light energy to metabolic energy by systems of conjugated bonds.

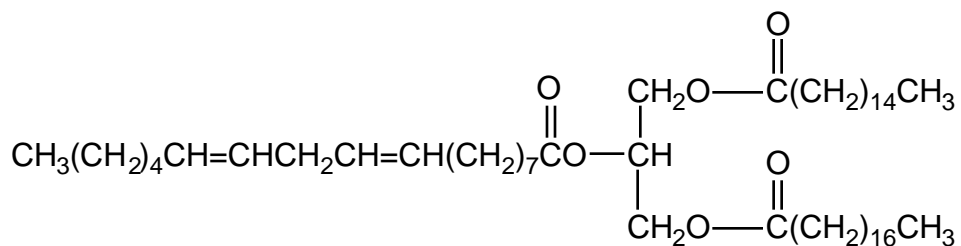
SOLUTIONS TO PROBLEMS**15.1 Structure and Reactions:** Sections 15.2, 15.3**15.2 Structure of Lipids**

Fats and oils are simple, nonpolar and saponifiable.

15.3 Structures: Section 15.3

- $\text{CH}_3(\text{CH}_2)_{17}\text{CH}=\text{CH}(\text{CH}_2)_7\text{COOH}$
- $\text{CH}_3(\text{CH}_2)_{15}\text{CH}=\text{CHCH}_2\text{CH}_2\text{CH}=\text{CH}(\text{CH}_2)_3\text{COOH}$
- $\text{CH}_3(\text{CH}_2)_4\text{CH}=\text{CHCH}_2\text{CH}=\text{CHCH}_2\text{CH}=\text{CHCH}_2\text{CH}=\text{CH}(\text{CH}_2)_7\text{COOH}$

15.4 Structure: Section 15.3



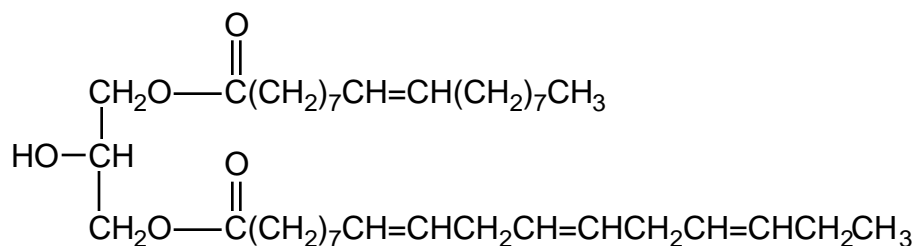
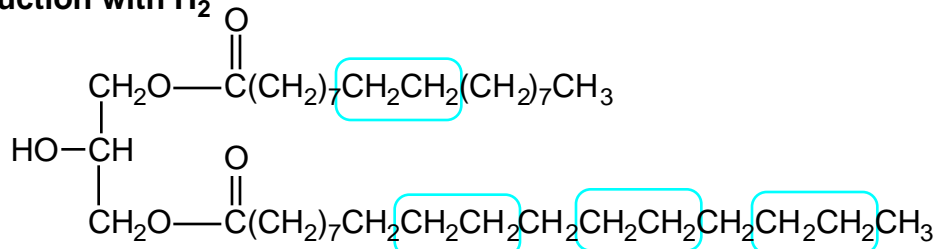
15.5 Structure: Section 15.3

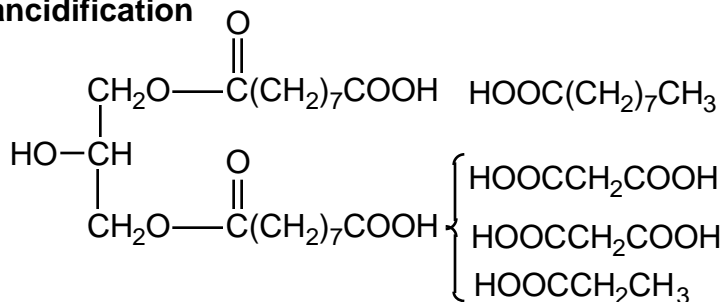
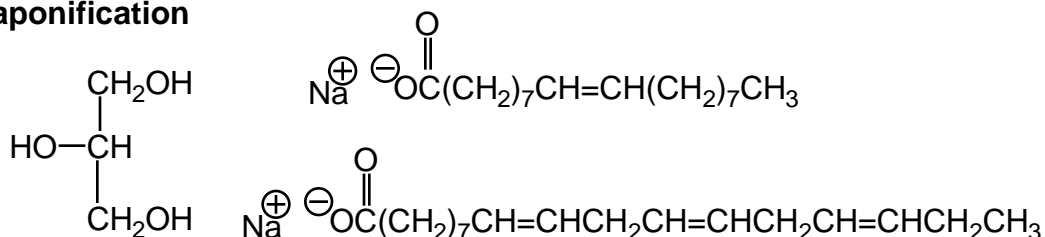
$\text{CH}_3(\text{CH}_2)_7\text{CH}=\text{CH}(\text{CH}_2)_{11}\text{COOH}$ is erucic acid.

15.6 Reactions: Section 15.4

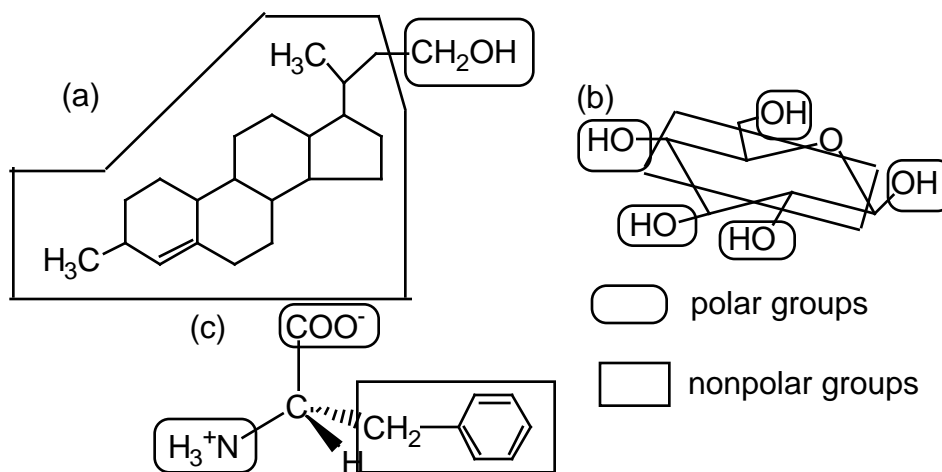
- a) Trimyristin is saturated and therefore has an I_2 number of zero. Triolein would have one double bond per fatty acid and 3 moles of I_2 would react with it. Glyceryl oleopalmitostearate has only one double bond (oleo). The order would be trimyristin < glyceryl oleopalmitostearate < triolein.
- b) Stearic < oleic < linoleic < linolenic

15.7 Soaps and Detergents: Section 15.5

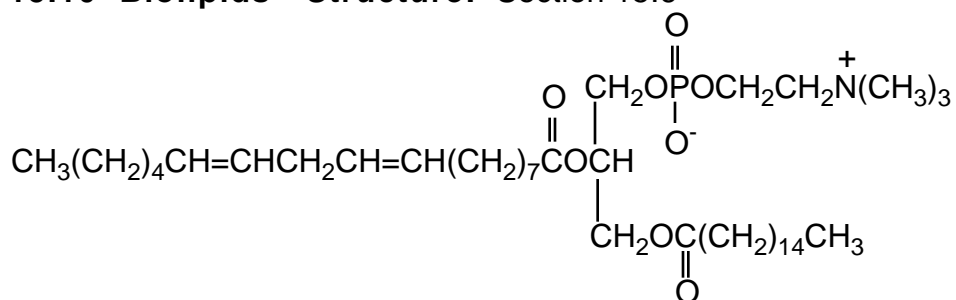
Reduction with H_2 

Rancidification**Saponification****15.8 Reactions:** Section 15.4

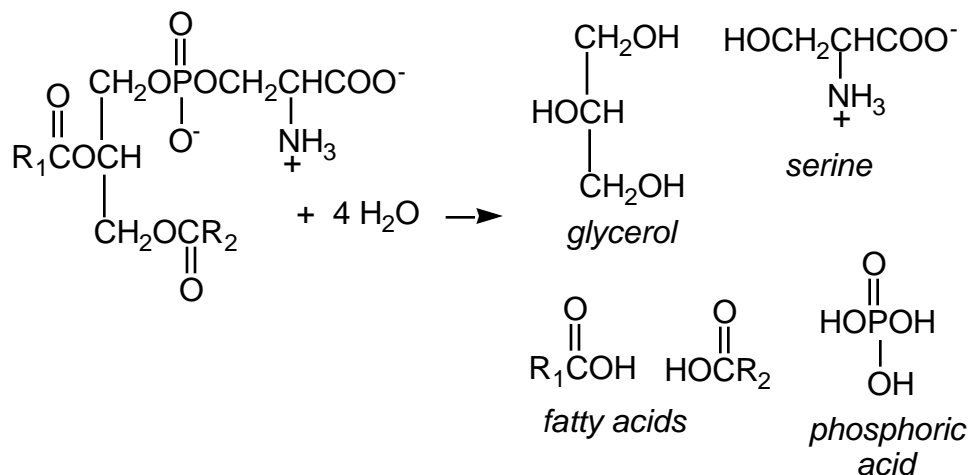
Margarines are semisynthetic and are not naturally-occurring. They are "organic" in the chemical meaning of the word, that is, they contain carbon. However, in the popular consumer vocabulary, since they are processed, they are not "organic" or natural.

15.9 Nature of Lipids: Section 15.1

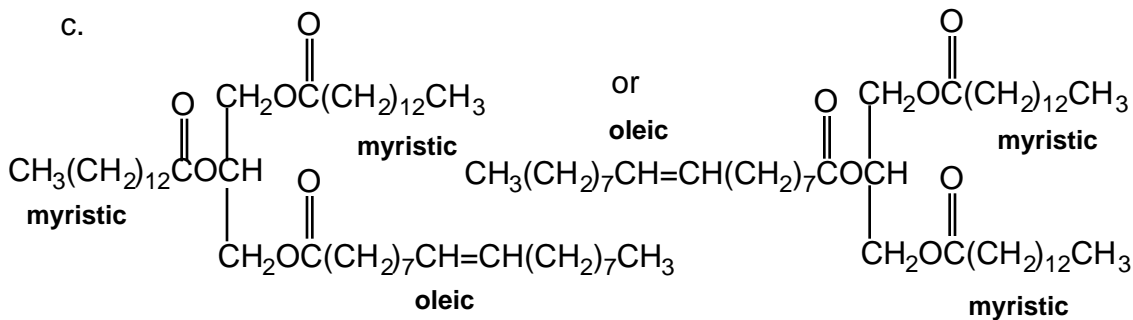
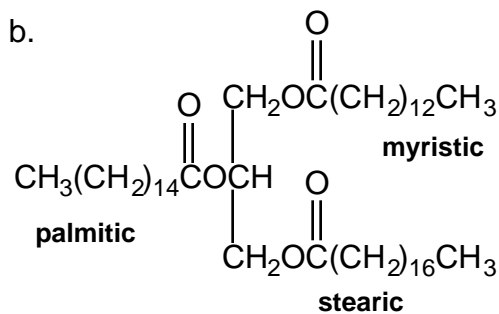
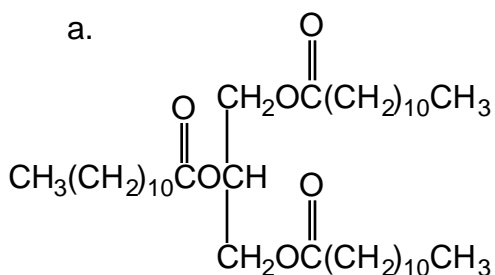
15.10 Biolipids - Structure: Section 15.6



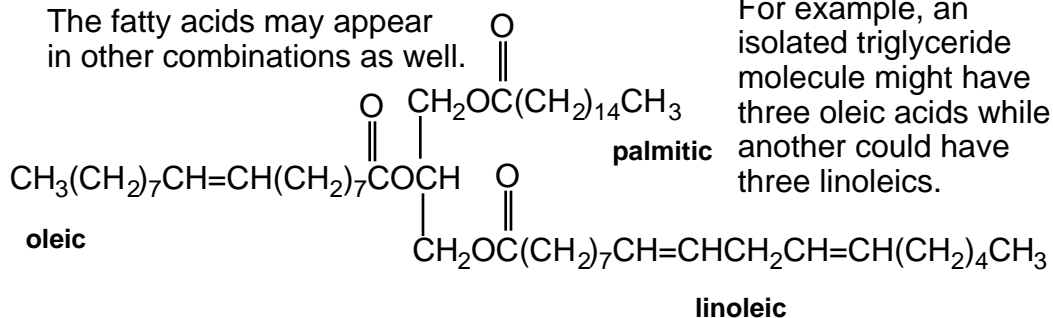
15.11 Biolipids - Structure: Section 15.6



15.12 Structures of Fats and Oils: Section 15.3



- d. The fatty acids may appear in other combinations as well.



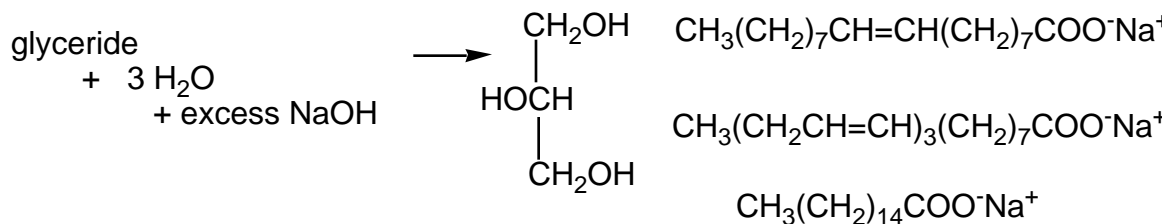
For example, an isolated triglyceride molecule might have three oleic acids while another could have three linoleics.

- e. Same as for part d.

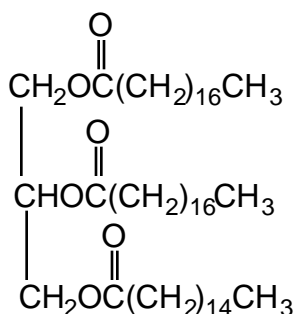
15.13 Reactions of Fats and Oils: Section 15.4

The following products will be formed with the glyceride in question:

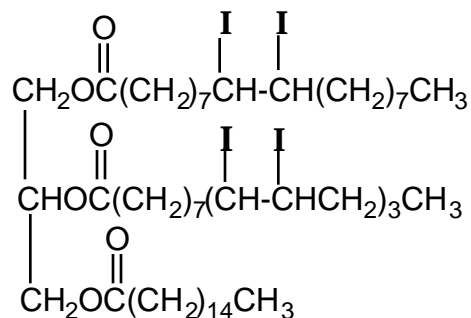
- a.



- b. hydrogenation



- c. I₂/CCl₄



15.14 Reactions of Soaps: Section 15.4

- a) $2 \text{CH}_3(\text{CH}_2)_{16}\text{COO}^-\text{Na}^+ + \text{Mg}^{2+} \longrightarrow (\text{CH}_3(\text{CH}_2)_{16}\text{COO}^-)_2\text{Mg}^{2+} + 2 \text{Na}^+$
 b) $3 \text{CH}_3(\text{CH}_2)_{16}\text{COO}^-\text{Na}^+ + \text{Fe}^{3+} \longrightarrow (\text{CH}_3(\text{CH}_2)_{16}\text{COO}^-)_3\text{Fe}^{3+} + 3 \text{Na}^+$
 c) $\text{CH}_3(\text{CH}_2)_{16}\text{COO}^-\text{Na}^+ + \text{H}^+ \longrightarrow \text{CH}_3(\text{CH}_2)_{16}\text{COOH} + \text{Na}^+$

15.13 Structure of Fatty Acids: Section 15.3

- a) $\text{CH}_3(\text{CH}_2)_5\text{CH}=\text{CH}(\text{CH}_2)_9\text{COOH}$ This is neither 3 nor 6. It is 7.

b) $\text{CH}_3(\text{CH}_2\text{CH}=\text{CH})_6(\text{CH}_2)_2\text{COOH}$ This is an 3.

15.17 Structure of Fatty Acids: Section 15.3

a) $\text{CH}_3(\text{CH}_2)_3(\text{CH}_2\text{CH}=\text{CH})_4(\text{CH}_2)_7\text{COOH}$

The first double bond would appear at position 9 from the carboxyl end.

b) $\text{CH}_3(\text{CH}_2)_3(\text{CH}_2\text{CH}=\text{CH})_5(\text{CH}_2)_{10}\text{COOH}$

The first double bond would appear at position 12 from the carboxyl end.

c) $\text{CH}_3(\text{CH}_2)_3(\text{CH}_2\text{CH}=\text{CH})_3(\text{CH}_2)_{12}\text{COOH}$

The first double bond would appear at position 14 from the carboxyl end.

15.17 Structures of Soaps and Detergents: Section 15.4

a) $\text{CH}_3(\text{CH}_2)_{14}\text{CO}_2^-\text{Na}^+$ would be an effective soap because it is the sodium salt of a long chain fatty acid.

b) $(\text{CH}_3(\text{CH}_2)_{16}\text{CO}_2^-)_2\text{Ca}^{2+}$ would be insoluble in water and so would not be effective as a soap.

c) $\text{CH}_3\text{CH}_2\text{CO}_2^-\text{Na}^+$ does not have a long nonpolar carbon chain and therefore could not make good micelles. It would not be an effective soap.

d) $\text{CH}_3(\text{CH}_2)_{14}\text{CH}_2\text{N}(\text{CH}_3)_3^+\text{Cl}^-$ would be a good detergent because it is a soluble ammonium salt with a long carbon chain.

e) $\text{CH}_3(\text{CH}_2)_{16}\text{CH}_3$ has no polar region, is not amphipathic, and therefore cannot have soap action.

f) $\text{CH}_3(\text{CH}_2)_{14}\text{CO}_2\text{H}$ is a neutral molecule. The protonated carboxyl end is not polar enough to counteract the long hydrocarbon chain.

g) $\text{CH}_3(\text{CH}_2)_{14}\text{CH}_2\text{OSO}_3^-\text{Na}^+$ should be a good detergent.

15.18 Properties of Soaps and Detergents: Section 15.4

a)	b)	c)
$\text{CH}_3(\text{CH}_2)_{14}\text{COO}^-\text{Na}^+$ <i>nonpolar</i>	$\text{CH}_3(\text{CH}_2)_{14}\text{CH}_2\text{N}(\text{CH}_3)_3^+\text{Cl}^-$ <i>nonpolar</i>	$\text{CH}_3(\text{CH}_2)_{14}\text{CH}_2\text{OSO}_3^-\text{Na}^+$ <i>nonpolar</i>
	<i>polar</i>	<i>polar</i>
		<i>polar</i>

15.19 Consumer Chemistry

This should be carried out in the grocery and/or drug stores.

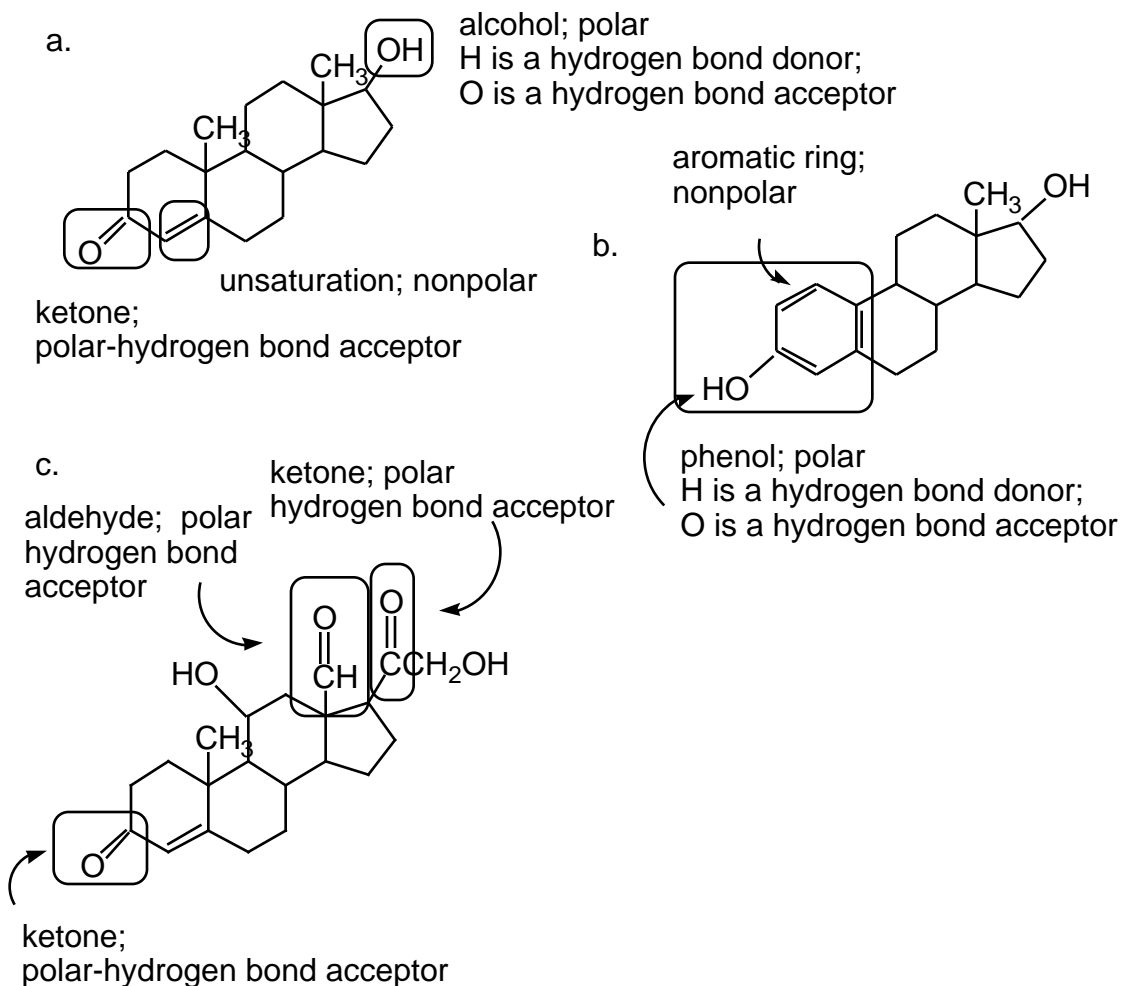
15.20 Properties of Fats and Oils: Section 15.3

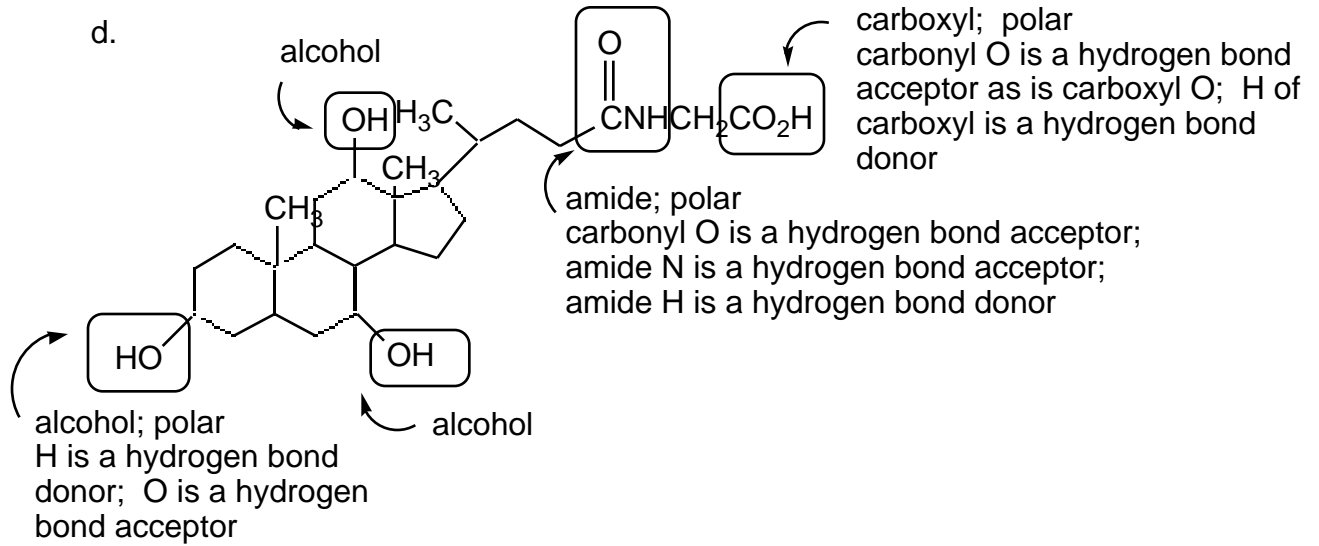
The melting point of a triglyceride decreases with an increase in double bonds or unsaturation. The iodine number is a measure of unsaturation. Therefore the higher the iodine number, the lower the melting point.

15.21 Structure: Section 15.4

Detergents, phospholipids and sphingolipids are alike in that they are amphipathic molecules. In a polar solvent like water they will aggregate so that their nonpolar portions are away from the solvent.

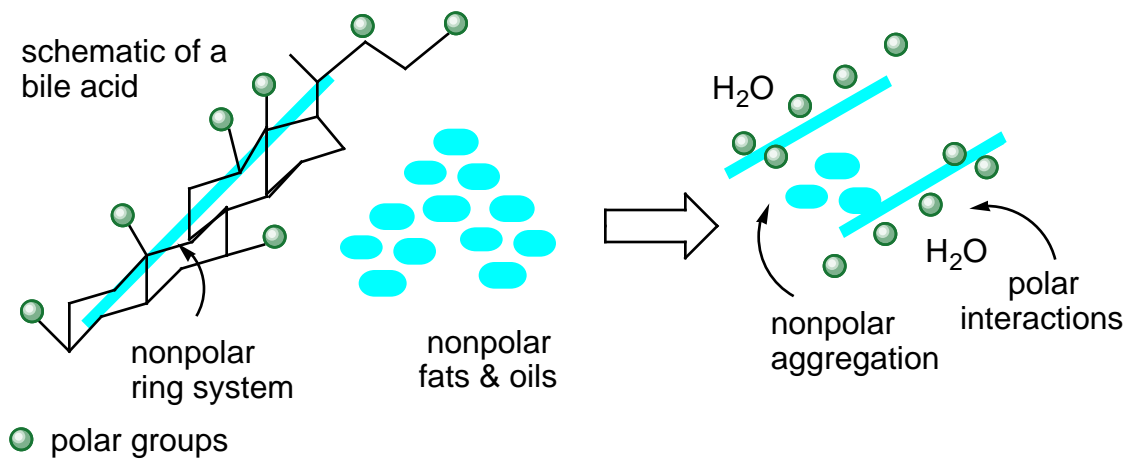
They differ because phospholipids and sphingolipids have two nonpolar "tails" while detergents usually have only one. While detergents form micelles with one layer of molecules shaped into a sphere, the other two types form lipid bilayers such that a polar solvent can appear within and outside of the structure.

15.22 Structure of Biolipids: Section 15.6



15.23 Functions of Biolipids: Section 15.6

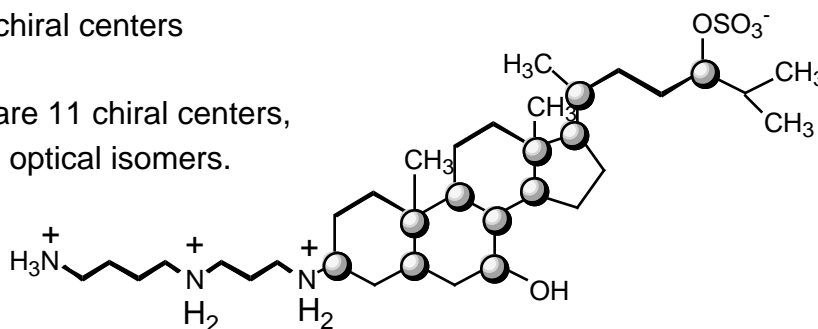
The acidic carboxyl and sulfonic acid portions of the bile acids are polar as are the alcohol groups rimming the steroid nucleus. The fused ring system is nonpolar. Therefore the bile acids are amphipathic and could form micelles which could engulf fats and oils in the intestines.

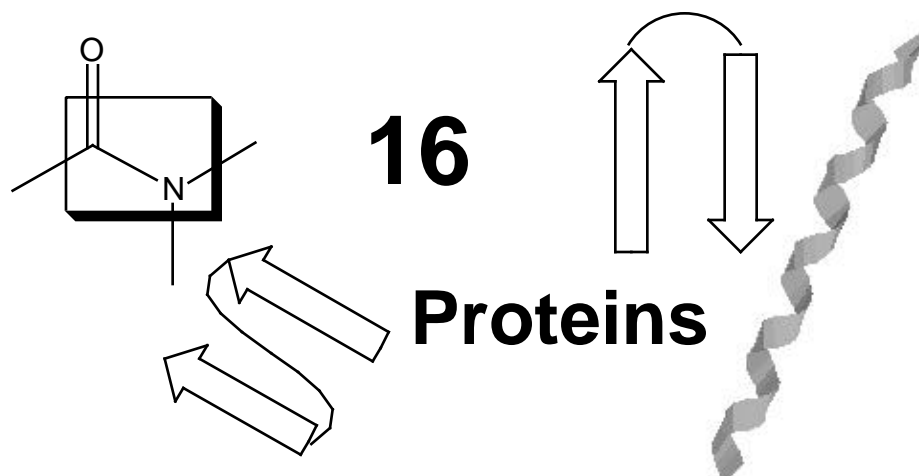


15.24 Structure of Biolipids: Section 15.6

● chiral centers

There are 11 chiral centers,
 2×10^3 optical isomers.





CHAPTER SUMMARY

Proteins are polymers of amino acids. With **20 different fundamental amino acids** as building blocks, an extraordinarily large variety of proteins can be biosynthesized under the direction of the genetic code.

16.1 Structure of Amino Acids

A. Fundamental Structure - An Amine and An Acid

As the term amino acid describes, each monomer has an **amine group** and a **carboxylic acid group** attached to a prochiral carbon. In addition **side chains** can also be present. These range from a simple hydrogen to long carbon chains with functional groups.

B. Ionization of Amino Acids

The amine and carboxyl groups exhibit typical **acid-base behavior** which is pH-dependent. At low pH both groups are protonated: the amine group has a plus (+) charge and the carboxyl is neutral (0). As the pH rises the carboxyl loses its proton becoming negatively charged (-). At higher pH values the amine (+) deprotonates to produce a neutral amine (0). The result of this sequential deprotonation is a series of charged forms ranging from + to 0 to -. If the side chains are capable of acid-base reactions, **the number of possible charged forms depends upon the number and types of amino acids present, the pH, and the pK_a of each ionizable group.** This is true of proteins as well as amino acids. The pH at which the molecule has a net

charge of zero, the **zwitterion form**, is called the **pI** or isoelectric (isoelectronic) state. The pI can be calculated by taking the average of the two pK_a values on either side of the zwitterion form. At a pH lower than the pI the molecule will be in a net + charged form while at a pH greater than the pI it will be in a net - charged form. Charged forms can be separated in an electric field, a process known as **electrophoresis**.

C. The Common Amino Acids

There are 20 common amino acids which can be grouped by the nature of the R side chain. Our groups are acidic, basic, alkyl, polar, aromatic, sulfur-containing, and cyclic.

16.2 The Peptide Bond: Formation of Polypeptides and Proteins

Polypeptides and proteins are the products of amide, or **peptide, bond** formation between the amine group of one amino acid and the carboxyl of another.

16.3 The Hierarchy of Protein Structure

A. Primary Protein Structure - The Sequence of Amino Acids

The sequence of amino acids in the polymer, from the free amino- or N-terminus to the free carboxyl- or C-terminus, is called the **primary (1⁰) structure** of a protein. This sequence is dictated by the genetic code.

B. Secondary Protein Structure - Helices and Pleated Sheets

A peptide bond has partial double bond character that makes it planar; the geometry is usually trans. As the polypeptide chain grows, the peptide bond can participate in hydrogen bonding - amide hydrogen to carbonyl oxygen. Because of the geometry of the peptide bond, this hydrogen bonding goes on between amino acids which are distant from each other. Organized, folded **secondary (2⁰) structures** are formed. The **alpha helix** and **beta pleated sheet** are the two most common secondary structures. In the alpha helix hydrogen bonding usually occurs between the peptide bonds of four amino acids distant from each other. Beta structure involves the polypeptide chain in its fully extended form coming back on itself to hydrogen bond side-to-side. The two polypeptide strands in beta structures may be **parallel** or **antiparallel** to each other.

Secondary structures are, in turn, organized into **domains**, or supersecondary structures.

Collagen, which is the most abundant protein of the body, has unique primary and secondary structures. A high glycine and proline content leads to fairly rigid, kinked strands which can intertwine in a triple helical structure held together by hydrogen bonding between strands. The collagen helices aggregate to form skin, bone and connective tissue.

C. Protein Tertiary Structure

Side chains of the amino acids participate in **tertiary (3⁰) structure**, that is, they stabilize the overall conformation of the protein molecule. The forces which hold tertiary structure together include covalent (**disulfide bridges**) and noncovalent (**hydrogen bonding, salt bridge, hydrophobic interactions**). Shapes of tertiary structure subunits can be **globular** or **fibrous**.

D. Quaternary Protein Structure - Association of Subunits

Many proteins have more than one folded subunit, linked by the same types of noncovalent forces which hold 3⁰ structure together. All of the subunits are needed for the protein to function properly. This is known as **quaternary (4⁰) structure**.

E. Complex Proteins - Proteins Plus

All of the interactions mentioned above are integral parts of the **simple** structure of a protein. In addition proteins may have cofactors such as metal ions, carbohydrates or lipids, and/or organic molecules associated with them. This makes the proteins **complex**. **Myoglobin** and **hemoglobin** are examples of related complex proteins. Myoglobin has a single globular protein subunit complexed with an organic heterocyclic system known as **heme**. The heme in turn holds an iron (II) ion which can bind molecular oxygen, O₂. All of these components contribute to the function of myoglobin: the storage of oxygen in muscle tissue. Hemoglobin is related to myoglobin both structurally and functionally. It contains four myoglobin-type subunits each of which has an iron(II)-heme complex that can bind O₂. However, the four subunits interact cooperatively in order to transport oxygen in the blood from the lungs to the cells.

CONNECTIONS 16.1 Sickle Cell Anemia - A Biochemical Disease**F. Denaturation**

The forces which hold a protein molecule together can be disrupted by changes in temperature and pH as well as by organic solvents and mechanical manipulation. This is known as **denaturation**.

CONNECTIONS 16.2 Mad Cow Disease**16.4 Functions of Proteins**

With the great structural versatility available, proteins exhibit a phenomenal breadth of function. Catalysis, protection and regulation were but three discussed in this chapter.

A. Enzymes - Biological Catalysts

Enzymes are proteins which act as **catalysts** to the complex reactions that occur in the metabolism of living organisms. These reactions include oxidation-reduction, the formation and breaking of carbon-carbon, carbon-nitrogen, and other bonds, hydrolysis, synthesis, group transfer, and isomerization. An enzyme functions by presenting an interactive, three dimensional environment to the reactants (**substrates**). This allows the reaction to be **stereospecific, rapid, and selective**, that is, producing few, if any, spurious by-products. The **active site** of an enzyme has a **substrate binding subsite** and a group of amino acids which effect catalysis, the **catalytic site**. Nonprotein components are common partners in a cooperative catalytic process.

B. Enzyme Control

The actions of enzymes can be controlled and/or modified by species known as **inhibitors** or an enzyme may be activated/inactivated by **covalent modification**. Most enzymes have precursor forms which are inactive. These are known as **zymogens**.

C. Antibodies - Immune System Protection

The complex protective network of higher organisms is called the **immune system**. One part consists of **glycoproteins** (carbohydrate-protein) called **antibodies**. Antibodies bind to foreign substances, **antigens**, and help to mark and destroy the invader. This assault is a key component to the process of **immunization** in which the immune system is trained to respond aggressively to unwanted toxins, bacteria,

and viruses. The specificity of antibodies has proven invaluable in diagnostics and has high potential for targeted medications.

CONNECTIONS 16.3 Testing for Drugs, Pregnancy, and AIDS

D. Polypeptide and Protein Hormones - Metabolic Regulation

The regulation of metabolism is in part due to polypeptide and protein **hormones**, the products of the endocrine system. With the development of recombinant DNA techniques, specific protein hormones can now be made using bacteria and yeast. There has been ongoing discussion and controversy concerning the genetic manipulation of proteins for medical and commercial purposes.

CONNECTIONS 16.4 Growth Hormone

16.5 Determination of Protein Structure

There exists a general consensus that **the primary structure of a protein eventually determines its tertiary structure**. Therefore it is extremely important to be able to study a protein's primary structure.

A. Amino Acid Composition

Amino acid content is found by complete hydrolysis of the peptide bonds, separation of the constituent amino acids by column chromatography, and quantitation using reagents such as **ninhydrin** or **dansyl chloride**. However, this gives us no information about the N- to C-sequence.

B. Sequence of Amino Acids - Determination of Primary Structure

Sequential analysis can be accomplished by using the Edman technique. Treatment of an intact polypeptide with **phenylisothiocyanate** derivatizes the N- amino acid leaving the rest of the peptide intact for further **Edman degradation**. Large chains must be **fragmented** into shorter peptides, more easy to work with chemically. Cleavage of peptide bonds at specific amino acid residues is accomplished using enzymes such as **trypsin** (Lys, Arg), **chymotrypsin** (aromatics), and **carboxypeptidase** (C-terminus amino acids).

16.6 Organic Synthesis of Polypeptides

A. General Considerations

Polypeptides can be produced synthetically by reactions common to organic chemistry. Since both the amine and carboxyl groups are functionally active, a general procedure of functional group blocking, activation of other groups, and coupling of amino acids is carried out.

B. Solid-State Synthesis

An organized series of synthesis reactions can conveniently be carried out using the **solid state**, that is, columns to which the growing polypeptide chain is attached while various reagents are washed through.

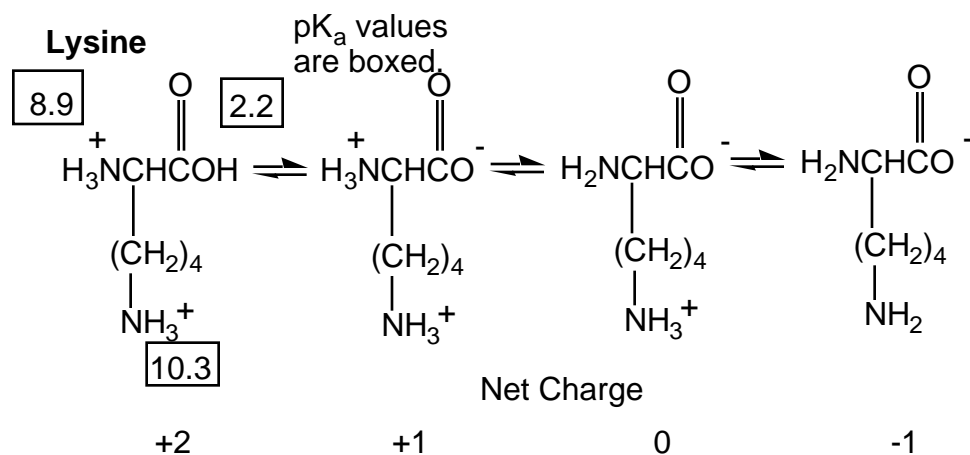
An understanding of proteins is essential for appreciating the link between organic chemistry and biochemistry.

SOLUTIONS TO PROBLEMS

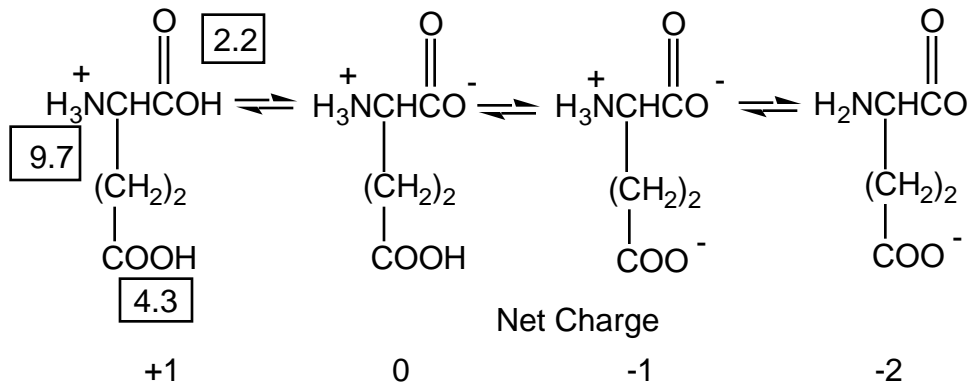
16.1 Amino Acid Structure: Ionization Section 16.1B

Arginine, lysine, and histidine have (+1) to (0) ionization transitions, while aspartic acid, glutamic acid, cysteine, and tyrosine have (0) to (-1) transitions.

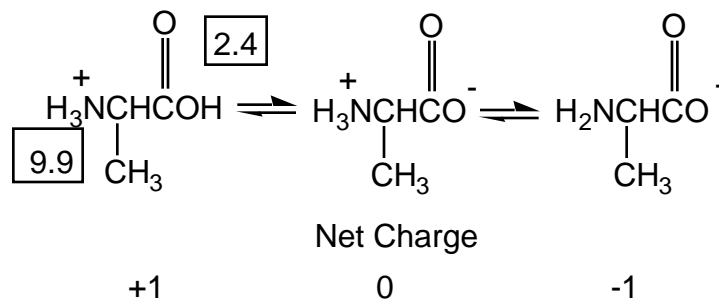
16.2 Ionized Forms of Amino Acids: Section 16.1



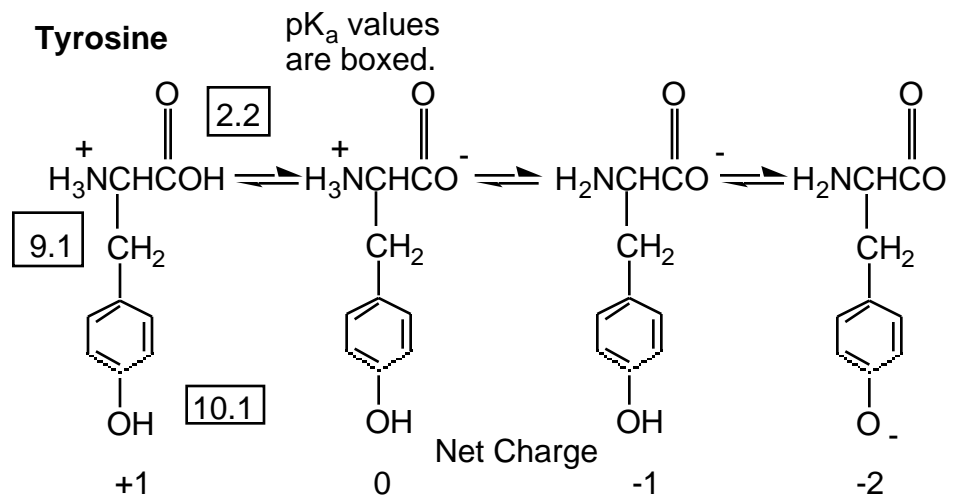
Glutamic Acid



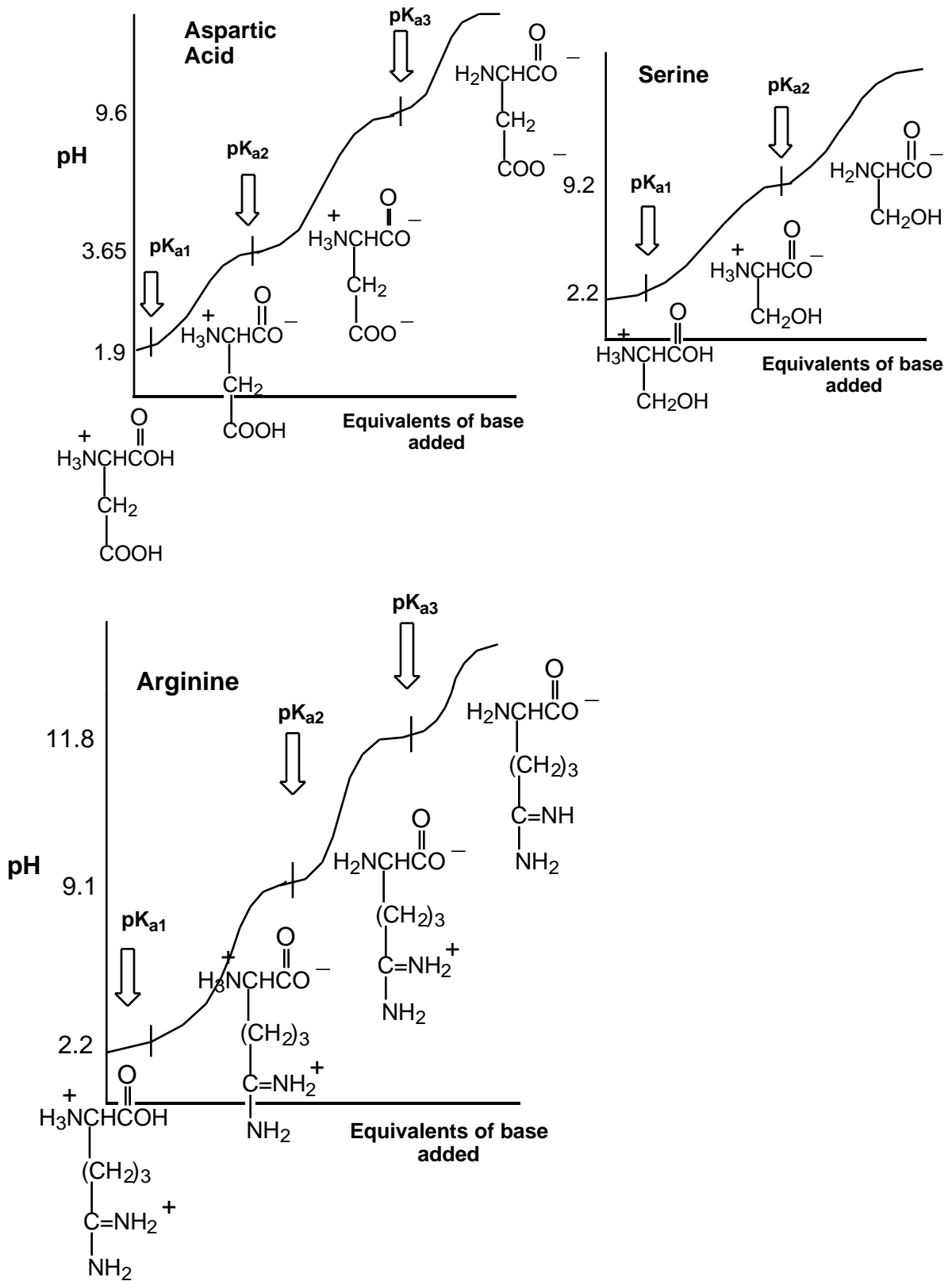
Alanine



Tyrosine



16.3 Acid-Base Behavior of Amino Acids: Section 16.1B

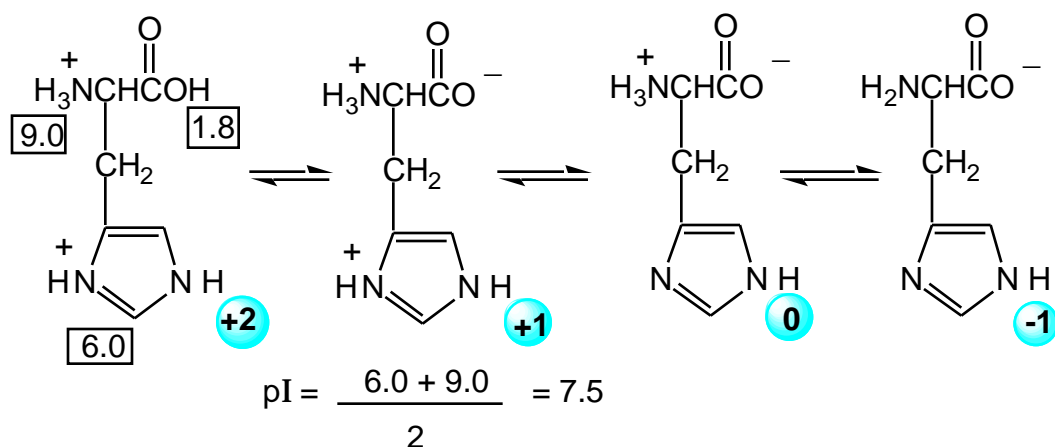


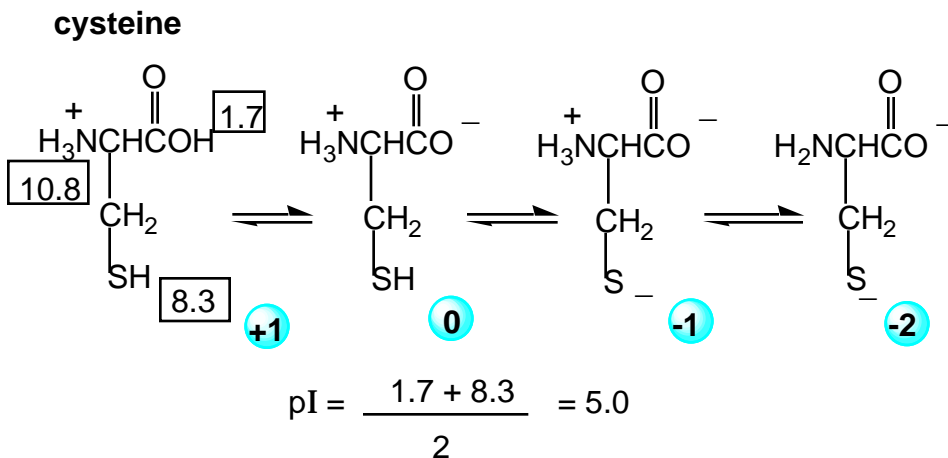
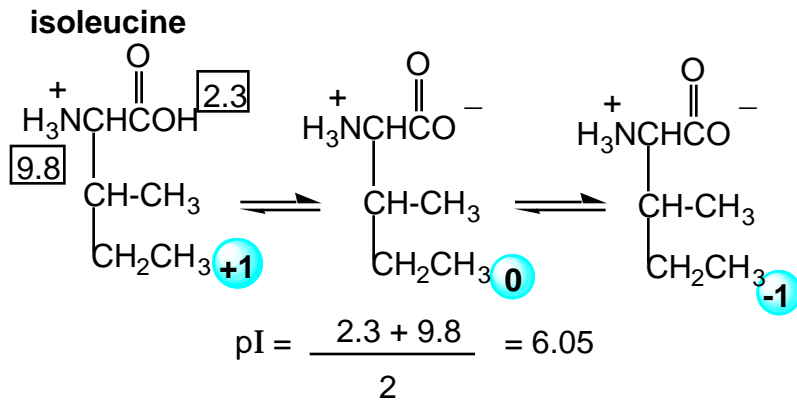
16.4 Ionization of Amino Acids: Section 16.1

group	pK _a	charge change	charge at pH 8.7	movement
glutamic acid				net -1
-COOH	2.2	0 → -1	-1	towards
-NH ₂	9.7	+1 → 0	+1	(+) pole
R	4.3	0 → -1	-1	
arginine				net +1
-COOH	2.2	0 → -1	-1	towards
-NH ₂	9.1	+1 → 0	+1	(-) pole
R	11.8	+1 → 0	+1	
threonine				net 0
-COOH	2.2	0 → -1	-1	no
-NH ₂	9.1	+1 → 0	+1	movement
R	-			
tyrosine				net 0
-COOH	2.2	0 → -1	-1	no
-NH ₂	9.1	+1 → 0	+1	movement
R	10.1	0 → -1	0	
histidine				net 0
-COOH	1.8	0 → -1	-1	no
-NH ₂	9.0	+1 → 0	+1	movement
R	6.0	+1 → 0	0	

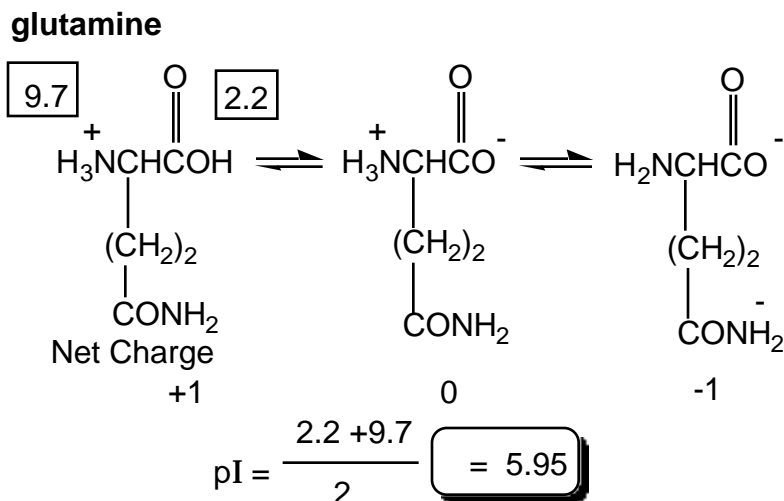
16.5 Ionization of Amino Acids: Section 16.1

histidine



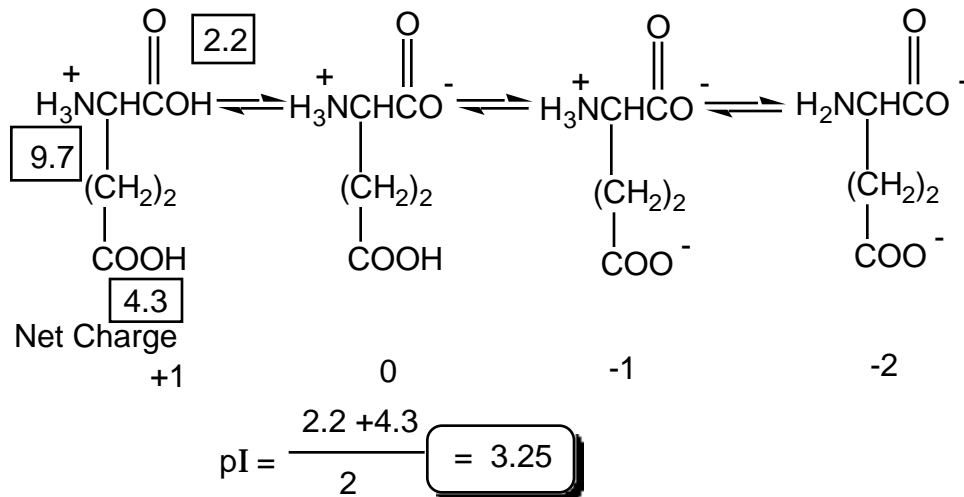


16.6 Ionization of Amino Acids: Section 16.1



The pI for Gln is higher than that for Glu due to the loss of ionizability of the side chain carboxyl group.

glutamic acid



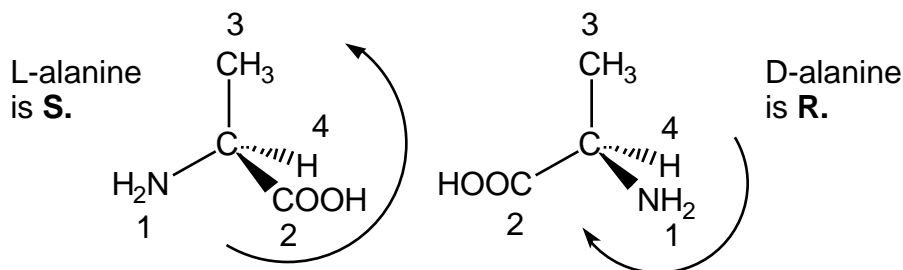
16.7 Ionization of Amino Acids: Section 16.1

See problems 16.4 and 16.5 for ionization information.

Histidine would most likely be in the 0 or zwitterion form at pH 6.8.

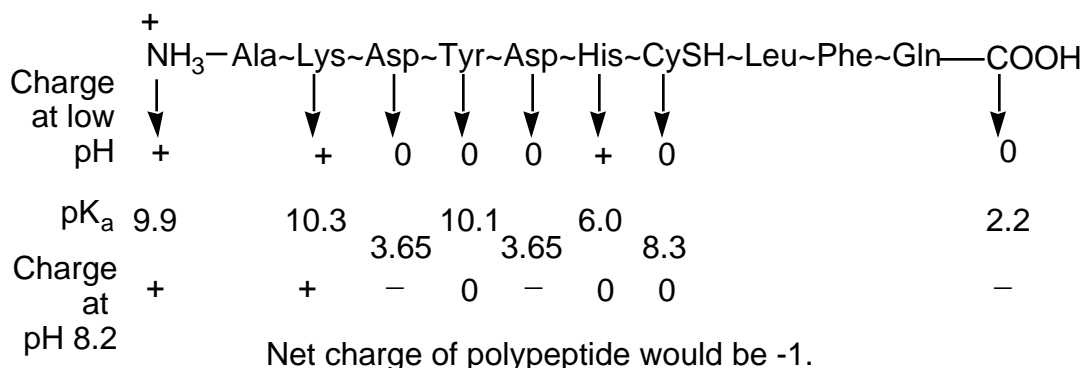
Tyrosine should be in its -2 form at pH 13.4.

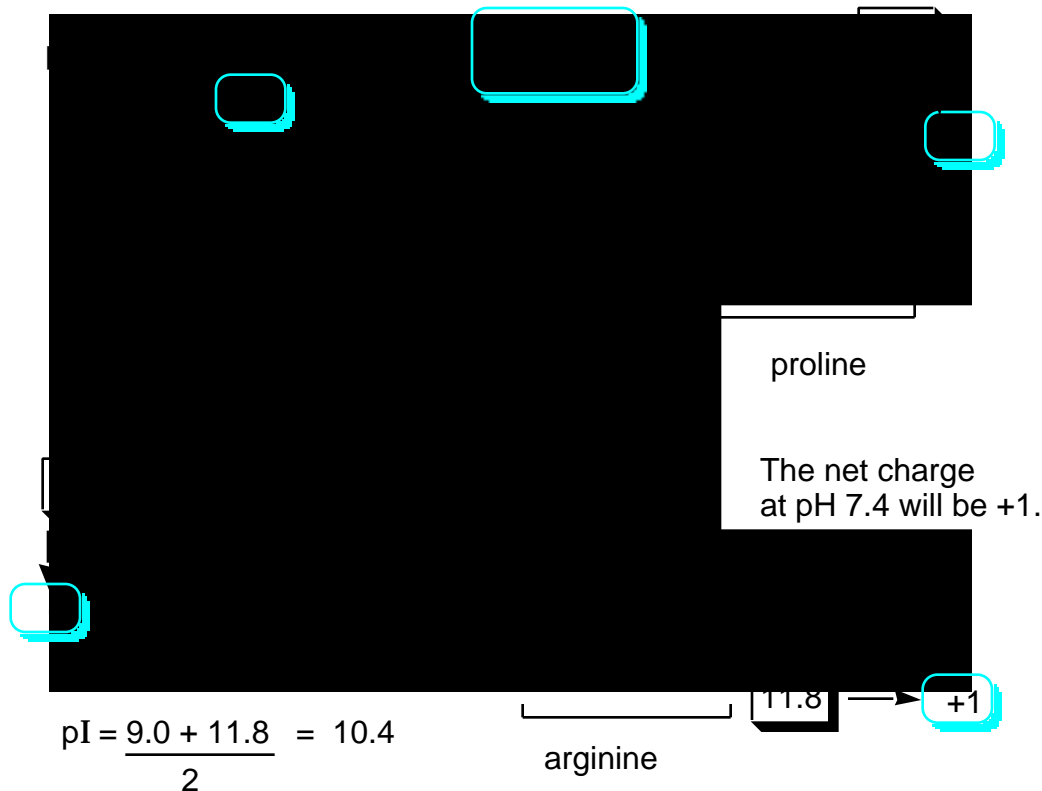
16.8 Chirality of Amino Acids: Section 16.1



16.9 Chirality of Amino Acids: Section 16.1 Glycine is optically inactive because it has two hydrogens on the alpha carbon (C-2). Four different groups are required for optical activity.

16.10 Polypeptides: Structure



16.11 Ionization of Polypeptides: Sections 16.1 and 16.2**16.12 Hierarchy of Protein Structure:** Section 16.3B

At pH 7.4 polyaspartic acid would have a large net negative charge on its side chains while polylysine would have a large net positive charge. This would cause repulsion of the R groups and lead to helix destabilization.

16.13 Hierarchy of Protein Structure: Section 16.3B

Polythreonine has an alcohol group and a methyl group on the beta carbon. Polyisoleucine has a methyl and an ethyl group on this carbon. The presence of groups which can hydrogen bond or which introduce bulk close to the polypeptide backbone seem to be impediments to the formation of helical segments.

16.14 Hierarchy of Protein Structure: Section 16.3B

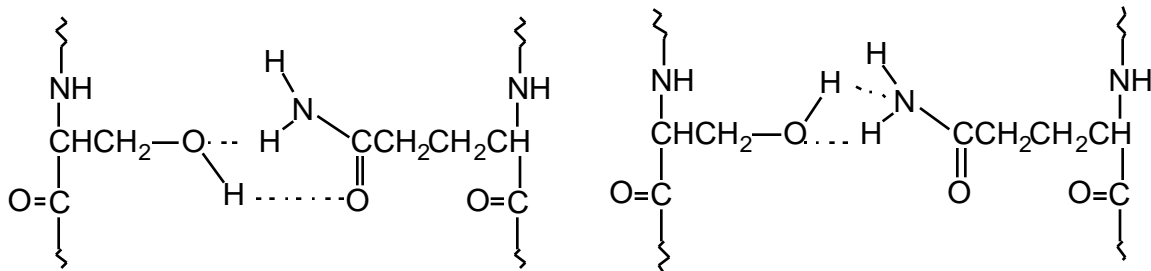
Leu, Ala, Ser, and Tyr would be "comfortable" in alpha helices because they have either small side chains (Ala and Ser) or extended alkyl groups (Leu) or a planar structure (Tyr).

Ala, Ser, and Gly could work in a beta sheet structure because of their small or nonexistent side chains which could allow the stacking of beta chains.

Pro with its ring structure would not fit into either of the conventional secondary structures but rather would be a place where one secondary structure could transition into another. Gly, with its ability for free rotation, could also be found at bends and breaks in regular secondary structure.

Lys has a charged, nitrogen-containing side chain under most pH conditions. It could exist in an alpha helix if there weren't any other positively charged groups in the area. Also at pHs above the pK_a of the R group, Lys would be "happy" in a helix.

16.15 Hierarchy of Protein Structure: Section 16.3C

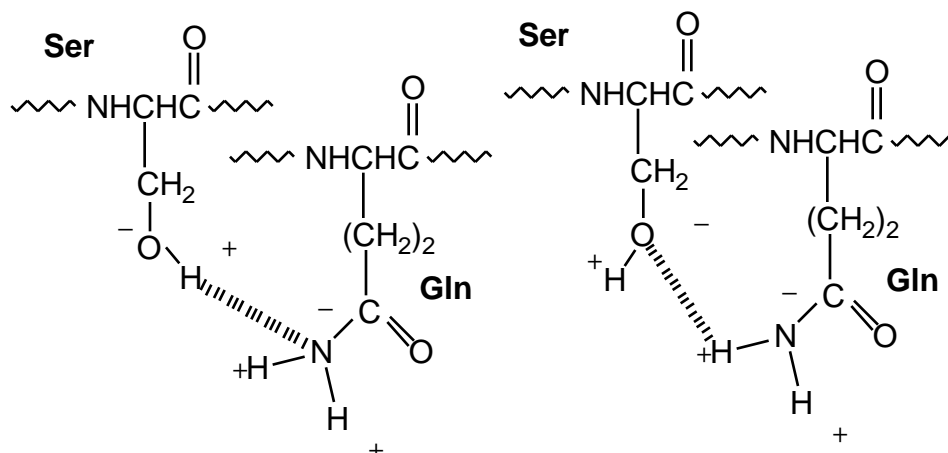


16.16 Hierarchy of Protein Structure: Section 16.3C

- a) Thr and H₂O - hydrogen bonding
- b) Asn and Trp - hydrogen bonding
- c) Asp and Glu - repulsive forces
- d) His and Val - hydrophobic interactions if above pH 6.0

16.17 Hierarchy of Protein Structure: Section 16.3F

Since the interior of a water soluble protein has a large degree of hydrophobicity or nonpolarity, nonpolar O₂ and N₂ could stabilize the denaturation of a protein by exposing the nonpolar interior to the air.

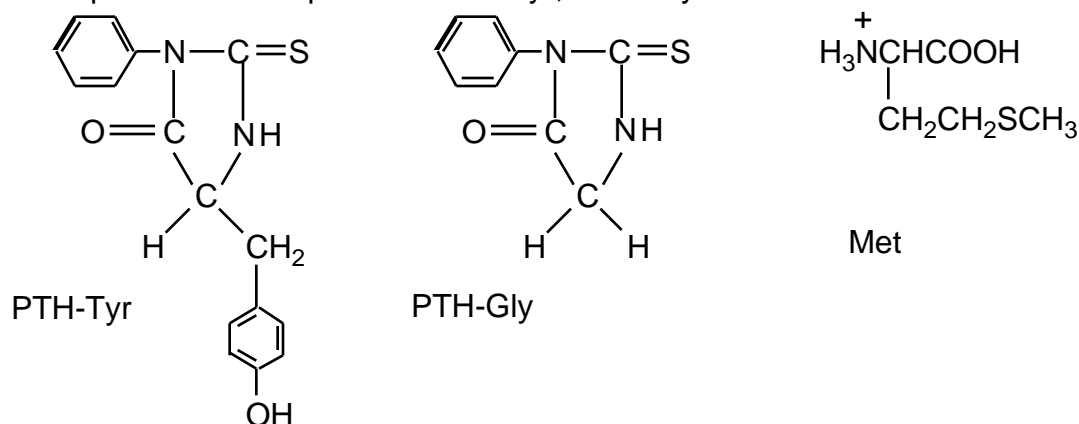


16.18 Hierarchy of Protein Structure: Section 16.3

Salt bridges and ion-dipole interactions would be upset by lowering the pH of a protein solution.

16.19 Determination of Protein Structure: Section 16.5B

Two more cycles of degradation on the polypeptide remaining in Example 16.3 would produce PTH-Tyr, PTH-Gly and free Met.

**16.20 Determination of Protein Structure:** Section 16.5B

The theoretical yield for a five-step N-terminal sequential degradation would be

- Step 1: 85%
 Step 2: $(0.85) * 85\% = 72.25\%$
 Step 3: $(0.85) * 72.25\% = 61.4\%$
 Step 4: $(0.85) * 61.4\% = 52.2\%$
 Step 5: $(0.85) * 52.2\% = 44.4\%$

16.21 Determination of Protein Structure: Section 16.5B

Chymotrypsin digestion of the polypeptide in Example 16.4 would have produced the fragments: Gly ~ His ~ Lys ~ Gly ~ Phe and free Ile.

Trypsin digestion followed by chymotrypsin would produce the following three fragments: Gly ~ His ~ Lys, Gly ~ Phe and free Ile.

16.22 The Organic Synthesis of Polypeptides: Section 16.6

For the hypothetical amino acids - A, B, C, and D - 4! or 24 possible combinations exist.

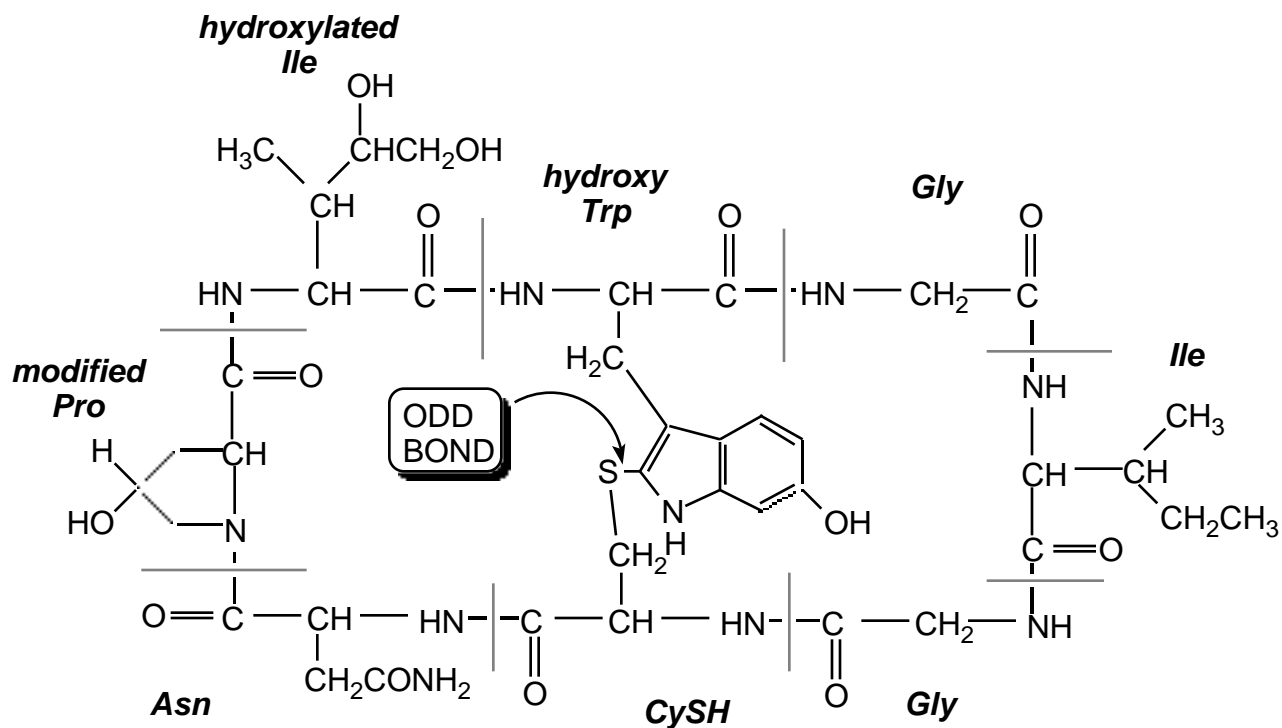
ABCD	ADBC	BCDA	BACD
ABDC	ADCB	BCAD	BADC
ACDB		BDAC	
ACBD		BDCA	

CDAB	DABC
CDBA	DACB
CABD	DBCA
CADB	DBAC
CBDA	DCAB
CBAD	DCBA

16.23 Structure: Section 16.1

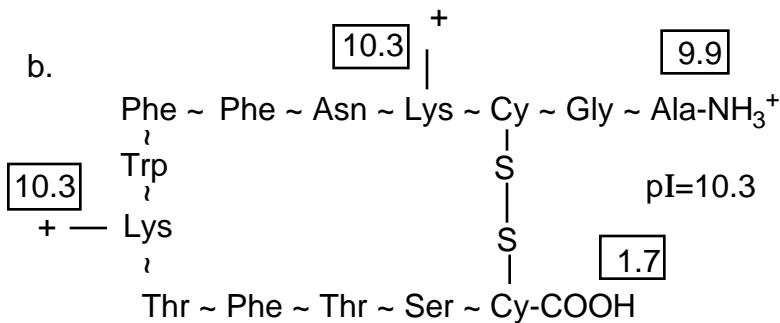
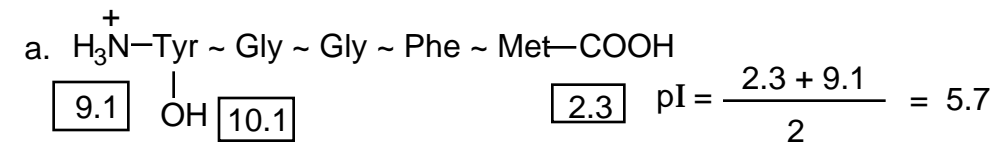
- | | |
|-----------------------------|--|
| a) glycine | e) proline |
| b) tyrosine | f) serine, threonine,
asparagine, glutamine,
histidine, tryptophan, tyrosine |
| c) cysteine | g) threonine, isoleucine |
| d) all except Gly, Thr, Ile | |

16.24 Structure: Section 16.2



16.25 Structure: Sections 16.1 and 16.5

The amino acids, from N- to C-termini are: Glu, Ile, Thr, Lys.

16.26 Structure: Section 16.1

At low pH this polypeptide has a +3 charge.

At pH > 1.7 it will be +2; at pH > 9.9 it will be +1.

The next two ionizable groups are both lysines. The average of their pK_a s will be 10.3.

16.27 Structure: Sections 16.1 and 16.2

To associate with the negatively charged nucleic acids, histones would have a net positive charge, that is, they are basic. The basic amino acids are lysine and arginine with some contributions from histidine, depending upon the pH.

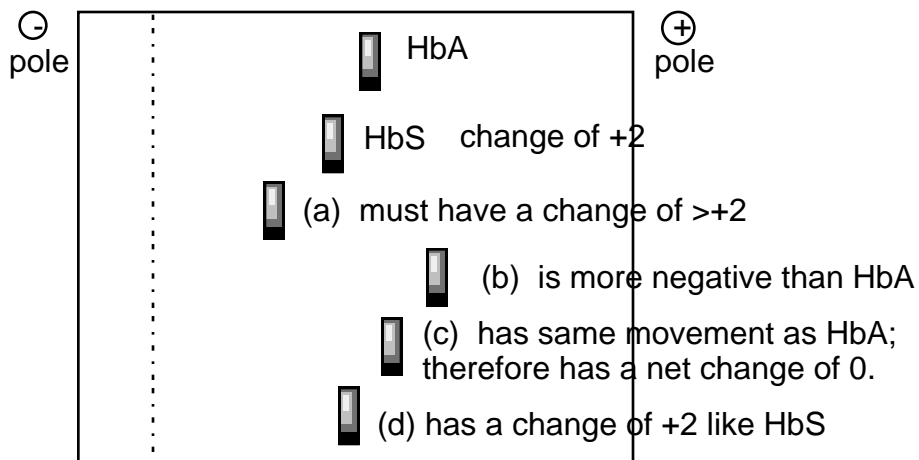
16.28 Structure: Sections 16.1, 16.2, and 16.4

Keep in mind that each hemoglobin molecule has two α and two β chains.

Using normal hemoglobin, HbA, as a starting point, find the change in charge which occurs with the change in amino acid.

Changes in Primary Sequence

Hb variant	chain	position from N-terminus	AA in HbA	AA in variant	Charge alteration
S		6	Glu	Val	change of +2
C		6	Glu	Lys	change of +4
Chesapeake		92	Arg	Leu	change of -2
Hasharon		47	Asp	His	change of +2
Koln		98	Val	Met	no change



a) is Hb C; b) is Hb Chesapeake; c) is Hb Köln; d) is Hb Hasharon.

16.29 Hierarchy of Protein Structure: Section 16.3

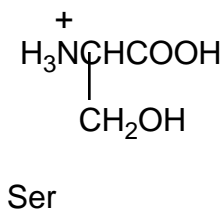
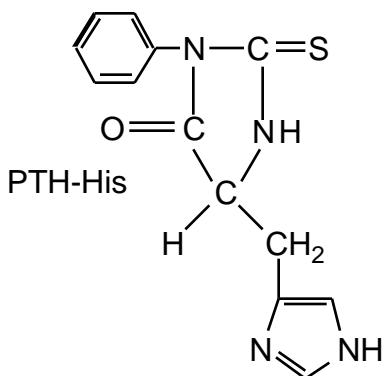
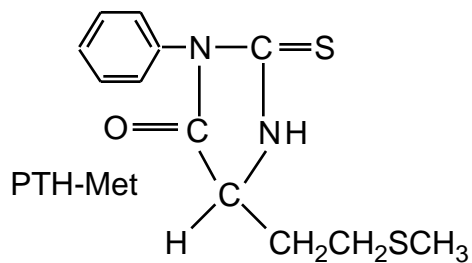
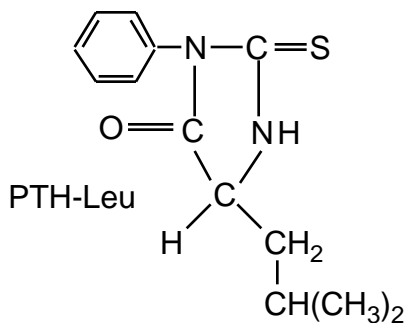
a) 4⁰ b) 3⁰,4⁰ c) 2⁰,3⁰,4⁰ d) 1⁰ e) 3⁰,4⁰ f) 3⁰

16.30 Hierarchy of Protein Structure: Section 16.3

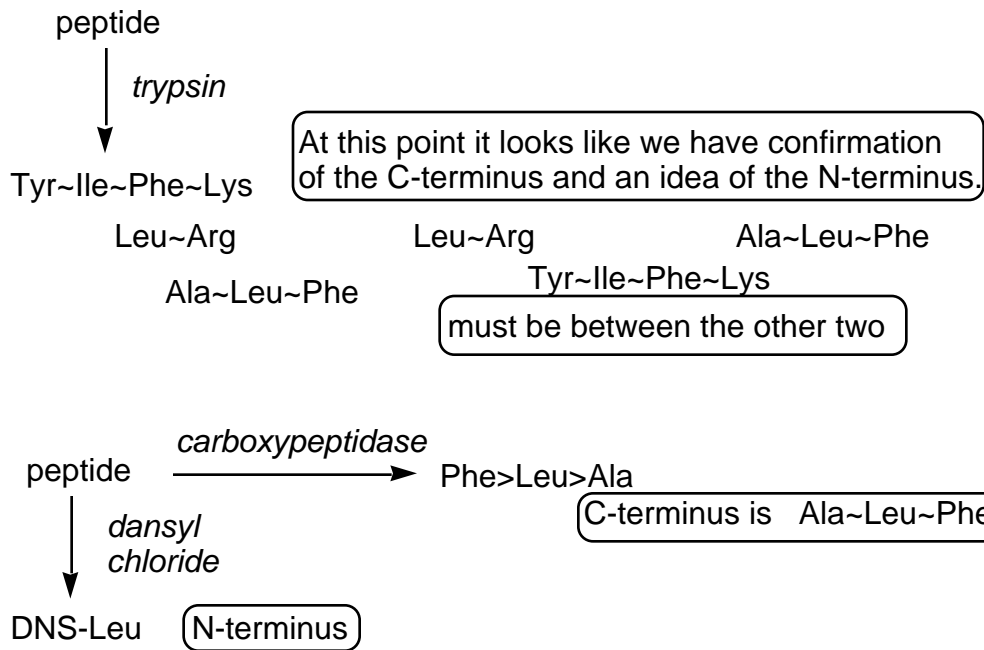
- a) hydrogen bonding
- b) hydrophobic interactions
- c) salt bridges
- d) none

16.31 Determination of Protein Structure: Section 16.5

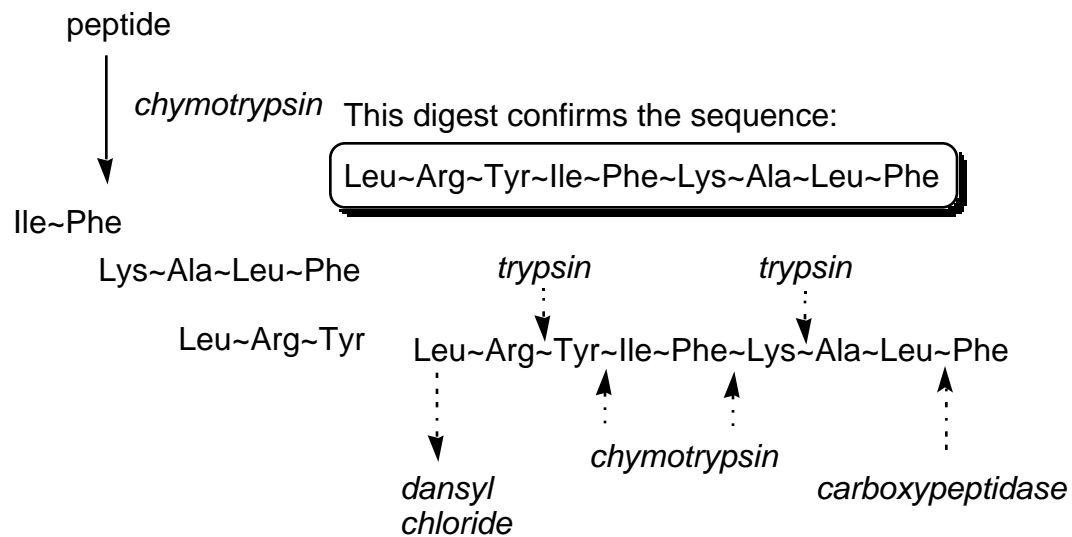
Three cycles of the Edman degradation would produce three PTH - amino acids and a free amino acid.

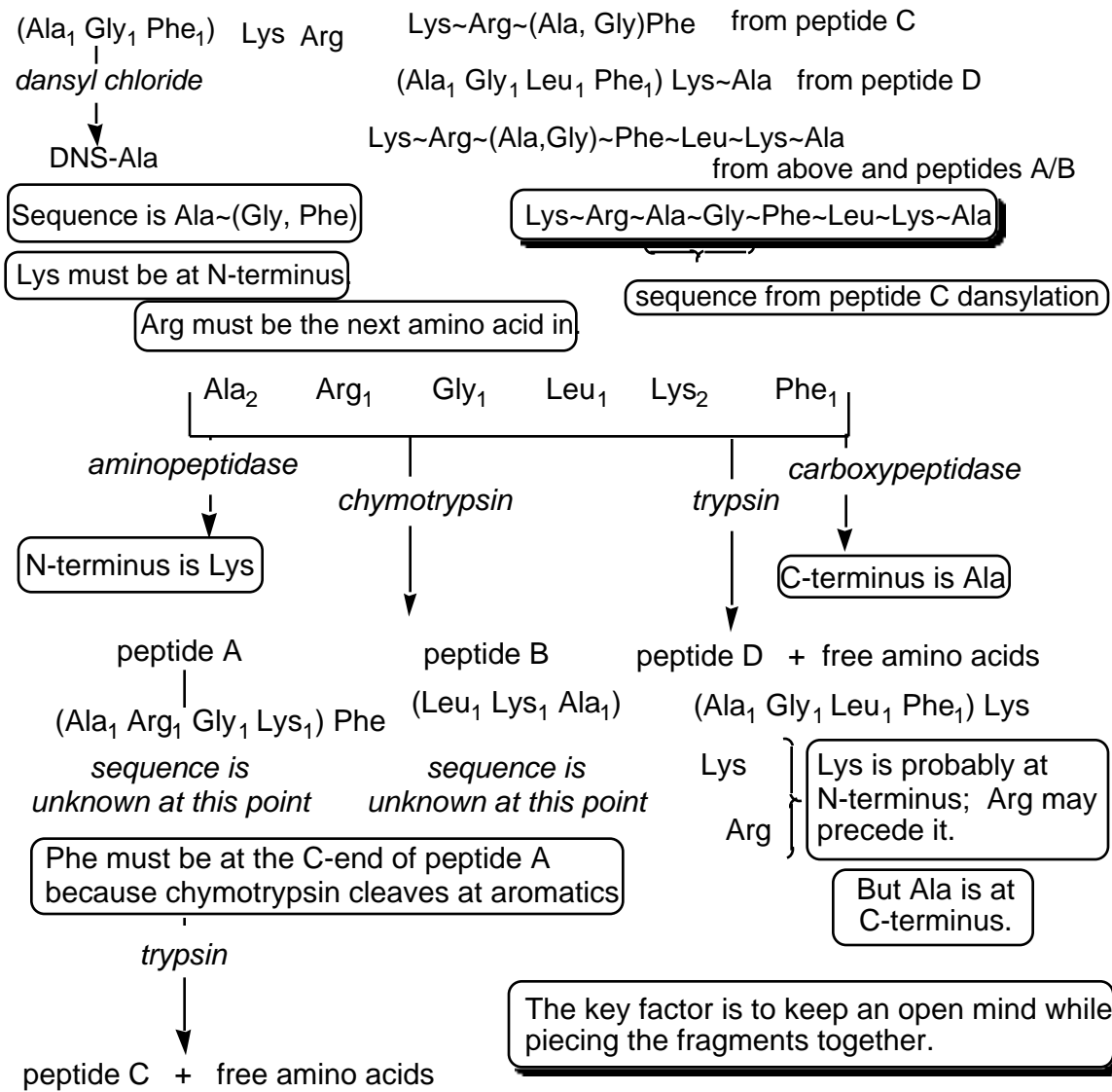


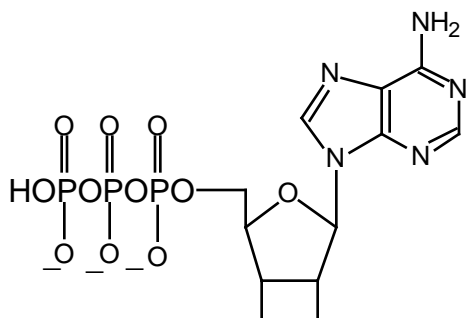
16.32 Determination of Protein Structure: Section 16.5



16.33 Determination of Protein Structure: Section 16.5





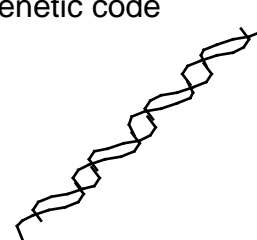


17

recombinant DNA

genetic code

viruses



AIDS

Nucleic Acids

CHAPTER SUMMARY

17.1 The Chemical Structure of Nucleic Acids

Nucleic acids are the biopolymers which constitute our genes. The monomer unit is called a **nucleotide**. A nucleotide is composed of a **heterocyclic base**, either a **purine** or **pyrimidine**, a **ribose** or **deoxyribose** sugar unit, and a **phosphate** group.

The two types of nucleic acids are **DNA (deoxyribonucleic acid)** and **RNA (ribonucleic acid)**. These differ in their chemical makeup in the sugar group: deoxyribose in DNA and ribose in RNA; and in the heterocyclic bases: **DNA has adenine(A), guanine(G), thymine(T), and cytosine(C) while RNA has uracil(U) in place of thymine.** The primary structures of DNA and RNA polymers have phosphodiester bridges between (deoxy)ribose units to form a sugar-phosphate backbone. The bases are covalently bound from the hemiacetal group of the sugar to a ring nitrogen. Nucleic acid polymers are usually written from the 5' end (of the sugar unit) to the 3' end, left to right. Often the backbone is represented simply as a horizontal line with the bases protruding. The acidity of the polyprotic phosphate imparts a negative charge and hydrophilicity to the sugar-phosphate backbone at physiological pH. The polymerization of just a few nucleotides produces an **oligonucleotide** while many comprise a **polynucleotide** and a very large number, a nucleic acid.

The secondary structure of nucleic acids involves **hydrogen bonding** between the heterocyclic bases. A and T can form two hydrogen bonds ($A \cdots T$) as can A and U ($A \cdots U$) while G and C form three ($G \cdots C$).

17.2 Other Structures Involving Nucleotides

A. Energy Intermediates

Mononucleotides and dinucleotides are important in metabolism. Adenosine tri-, di- and mono-phosphates, **ATP**, **ADP** and **AMP**, are energy intermediates.

B. Chemical Messengers

Cyclic adenosine monophosphate (**cAMP**) acts as an intermediary in transferring a chemical signal from outside a cell to the metabolic processes inside a cell.

C. Redox Factors - Nucleotide Vitamins

Nicotinamide(niacinamide) adenine dinucleotide, **NAD⁺**, and the flavin mono- and di- nucleotides (**FMN**, **FAD**) exist in oxidized and reduced forms. This makes them invaluable cofactors in enzymatically catalyzed oxidation-reduction reactions.

17.3 The Hierarchy of Nucleic Acid Structure

A. DNA Structure: The Double Helix

In DNA two polynucleotide strands hydrogen bond to each other through their bases in an **antiparallel** fashion. Bond angles in the sugar-phosphate backbone cause the double strand to twist into a helix. This is the classical **double helix structure of DNA** as postulated by Watson, Crick and Wilkinson. DNA is complexed with basic proteins called **histones** forming supercoiled coils. RNA can appear as a double helix but is usually found as a single strand (ss) taking on a variety of secondary structures depending upon its function.

B. RNA Structure

RNA has a polymeric structure similar to that of DNA with the substitution of a uracil for thymine. The overall structure of RNA can be single or double-stranded and RNA performs a variety of functions having to do with the transcription and translation of the DNA genetic code into functional proteins.

17.4 The Genetic Code

The main function of DNA is to **store genetic information in its nucleotide sequence**. The genetic code consists of base triplets (**codons**) most of which correspond to one of the 20 fundamental amino acids in proteins.

A. DNA Replication

Replication or duplication of DNA is a **semiconservative** process which depends upon **base pairing**, that is, hydrogen bonding. The double helical DNA partially unwinds and cellular nucleotide triphosphates pair with the exposed bases. Enzymes effect the polymerization process with the result being two DNA helices, each with a parent strand and a daughter strand.

CONNECTIONS 17.1 The Human Genome Project

B. Transcription and Translation

The **transcription**(copying in mRNA reciprocal code) **and translation**(using the mRNA to place amino acids in the proper sequence) of the DNA code to protein products proceeds through a complicated series of steps first involving the formation of a **messenger RNA (mRNA)** having a base sequence complementary to that of the parent DNA strand. The mRNA then associates with **ribosomal RNA (rRNA)** - protein complexes. **Transfer RNA (tRNA)** molecules bearing specific amino acids are then base-paired with the mRNA. Many enzyme-catalyzed reactions later, a protein product is formed.

A higher order (eukaryotic) gene contains both coding (**exon**) sequences and intervening (**intron**) or noncoding sequences. Therefore the transcription and translation process is also one of cutting and splicing the exon sequences for the production of a functional protein.

17.5 Characteristics of Transcription and Translation

Among the key characteristics of DNA code interpretation are that the code is nearly universal, is degenerate, has no coding overlaps, is fairly reliable, and consumes energy.

17.6 Mutation of DNA

Although the replication and transcription/translation processes occur with high fidelity, occasionally **mutations** can occur. These can lead to death,

predisposition to disease, congenital malformations or syndromes, or evolutionary progress.

CONNECTIONS 17.2 Acquired Immune Deficiency Syndrome: AIDS

17.7 Viruses

Viruses are species consisting of nucleic acids, usually ssRNA, encased in a **protein coat** and require a host organism for their replication. Once a virus invades a host cell, it uses its own **reverse transcriptase** enzyme to encode its genome into the host DNA thereby ensuring its survival. **AIDS, acquired immune deficiency syndrome**, is produced by a **retrovirus** that attacks the immune system.

17.8 Oncogenes

Oncogenes are those genes which are believed responsible for uncontrolled, cancerous cell growth. Cancer can be due to the production of growth factors or the inhibition of growth suppressors.

17.9 Recombinant DNA and Biotechnology

Manipulation of the genetic code through **recombinant DNA** allows molecular biologists to modify and transfer genes both for the study of disease and the production of new cellular characteristics.

CONNECTIONS 17.3 DNA Fingerprinting

SOLUTIONS TO PROBLEMS

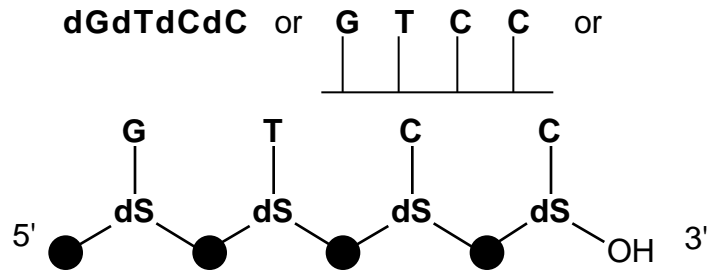
17.1 Structure: Section 17.1, Chapters 15, 16, 17

	Carbohydrates	Lipids	Proteins	Nucleic Acids
Functional Groups	<ul style="list-style-type: none"> ●aldehydes ●ketones ●alcohols 	<ul style="list-style-type: none"> ●alkyl groups and rings ●carboxylic and phosphoric acids and esters 	<ul style="list-style-type: none"> ●amines ●carboxylic acids ●amides 	<ul style="list-style-type: none"> ●carbohydrate ●heterocyclic bases ●phosphate esters
Macro Structure	<ul style="list-style-type: none"> ●polymers of saccharides 	<ul style="list-style-type: none"> ●no polymers ●aggregates 	<ul style="list-style-type: none"> ●polymers of amino acids 	<ul style="list-style-type: none"> ●polymers of nucleotides (base, sugar, phosphate)

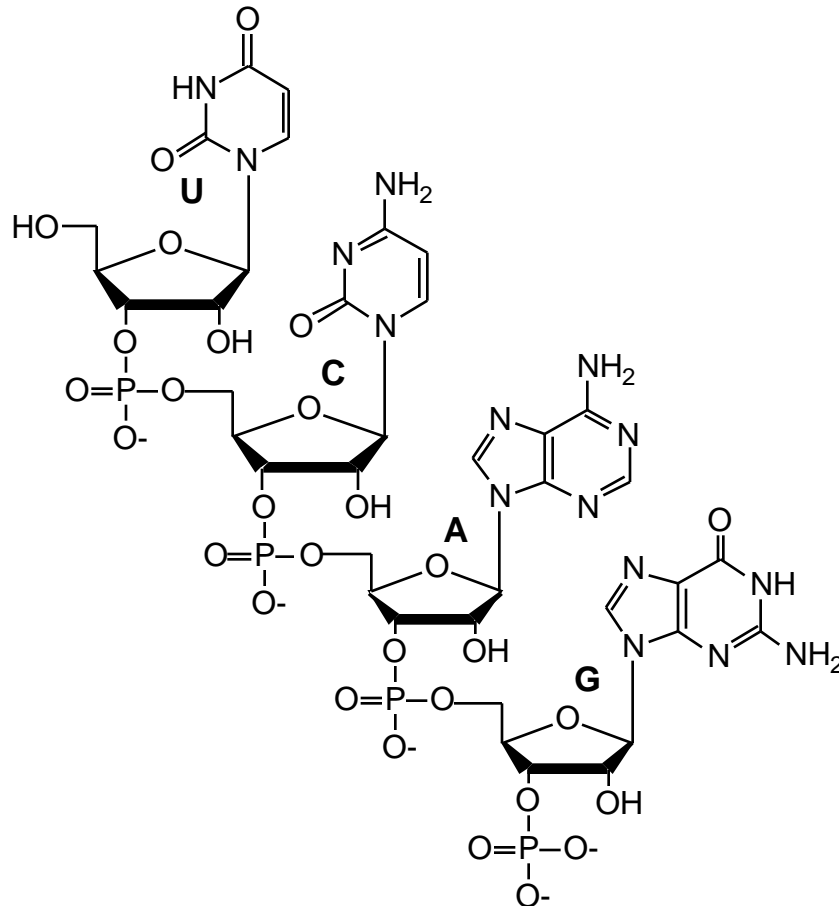
17.3 Polynucleotide Structure: Section 17.1

Following the example in Section 17.1 in the text

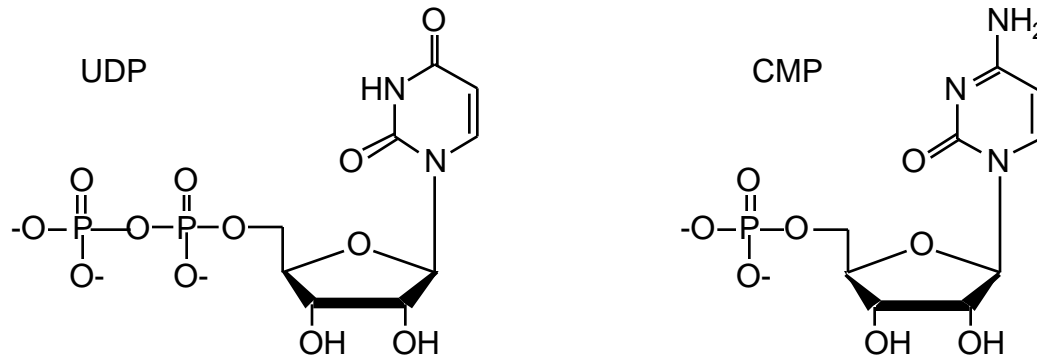
GTCC could also be represented schematically as



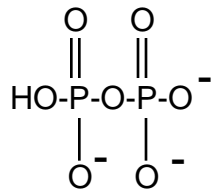
17.3 Structure: Section 17.2



17.4 Structure: Section 17.2



17.5 Structure: Section 17.2



17.6 Structure: Section 17.3

Histones should contain basic amino acids such as lysine and arginine. These amino acids have a (+) charge at physiological pH and would interact with the negatively (-) charged phosphates as well as with the electronegative oxygens in the sugar alcohol groups.

17.7 The Genetic Code: Section 17.4

The sequence of DNA, 5' to 3', should start at band 1 and be

G T T C G G A T

17.8 The Genetic Code: Section 17.4

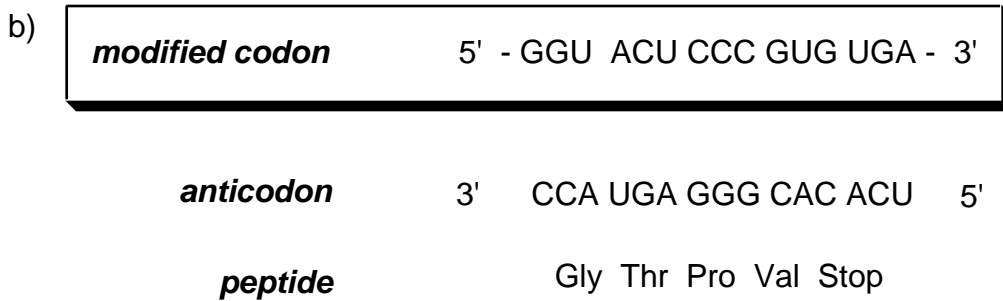
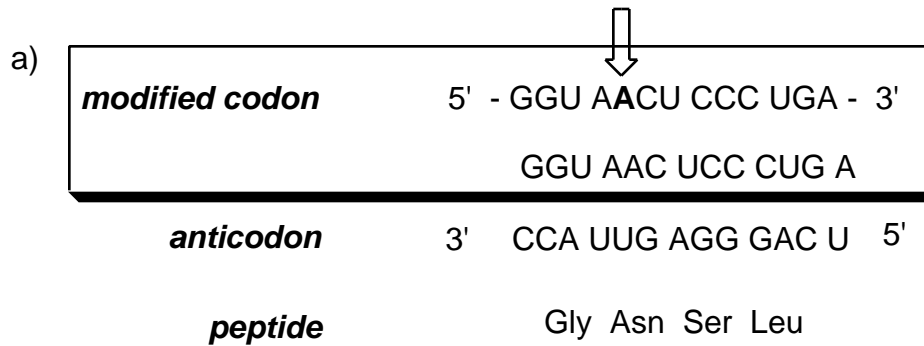
<i>coding (sense) strand</i>	5'	GGT ACT CCC TGA	3'
<i>antisense strand</i>	3'	CCA TGA GGG ACT	5'

<i>codon</i>	5' - GGU ACU CCC UGA - 3'
--------------	---------------------------

<i>anticodon</i>	3'	CCA UGA GGG ACU	5'
------------------	----	-----------------	----

<i>peptide</i>	Gly Thr Pro Stop
----------------	------------------

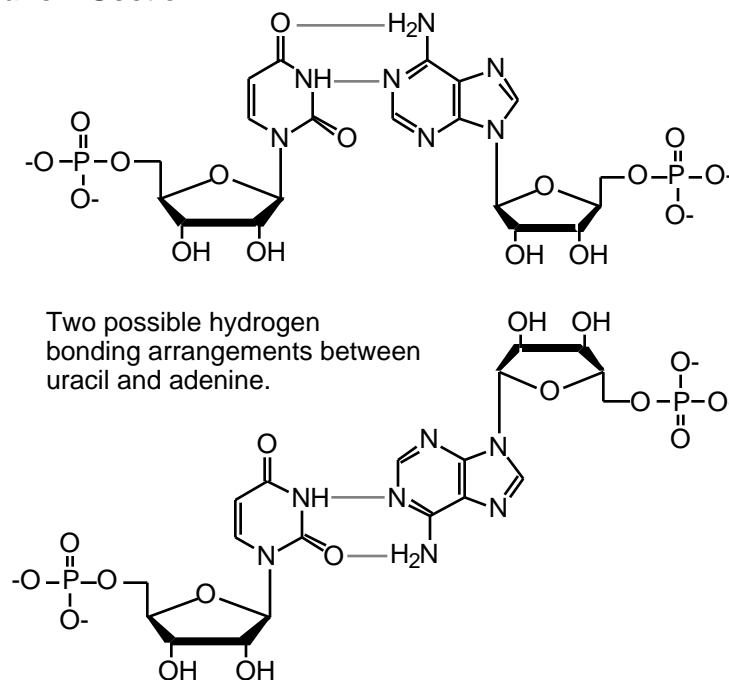
17.9 The Genetic Code: Section 17.4



17.10 Structure: Section 17.1

DNA uses adenine, thymine, cytosine, and guanine as bases; RNA uses uracil rather than thymine. DNA has deoxyribose; RNA has ribose. DNA usually can be found as a double helix; RNA is commonly found single stranded and nonhelical.

17.11 Structure: Section 17.1



17.12 Genetic Code: Section 17.4

sense DNA 5' G T A A C G T C G C T T 3'

antisense DNA 3' C A T T G C A G C G A A 5'

mRNA 5' G U A A C G U C G C U U 3'

mRNA as triplet code(codon) GUA ACG UCG CUU

tRNA (anticodon) CAU UG C AGC GAA

peptide Val Thr Ser Leu

17.13 Structure: Section 17.1

One mole of the polynucleotide sequence in problem 17.12 would produce the following upon hydrolysis:

- 3 moles G
- 4 moles T
- 2 moles A
- 3 moles C
- 12 moles deoxyribose
- 12 moles phosphate

17.14 Structure: Section 17.1

$$10^6 \text{ nucleotides} \left(\frac{\text{helix turn}}{10 \text{ nucleotides}} \right) \left(\frac{34 \overset{\text{O}}{\text{\AA}}}{\text{helix turn}} \right) \left(\frac{10^{-10} \text{ meters}}{\overset{\text{O}}{\text{\AA}}} \right) = 3.4 \times 10^{-4} \text{ meters}$$

17.15 Energy-Related Nucleotides: Section 17.2

<u>Species</u>	<u>Bases</u>	<u>Number of moles</u>		
		Ribose	Phosphate	
ATP	adenine	1	1	3
FAD	flavin	1	2	2
	adenine	1		
NADH	nicotinamide	1	2	2
	adenine	1		
FMN	flavin	1	1	1

17.16 Genetic Code: Section 17.4

Glucagon would require a minimum of $(37 \times 3) + 6$ (start/stop) nucleotides, that is, 117 nucleotides.

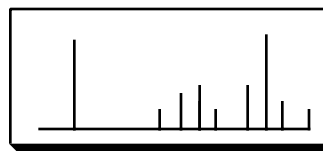
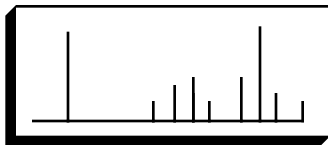
17.17 Genetic Code: Section 17.4

For hemoglobin E the amino acid substitutions are lysine for glutamic acid. The codons for Lys are AAA and AAG while those for Glu are GAA and GAG. The difference is A - G in the first nucleotide of the triplet. Both of these bases are purines and would fit about the same in the helix of DNA. The hydrogen bonding patterns are different, with A involved in 2 while G is involved in 3, but hydrogen bonding to a lesser extent could still occur.

For hemoglobin M_{Boston} the tyrosine would come from UAU and UAC codons while the normal hemoglobin's histidine is derived from CAU and CAC. Again we see the substitution of U for C (T for C in the parent DNA). Both are pyrimidines. U (T) usually forms 2 hydrogen bonding pairs while C forms 3.

Mutations could change the bases in the DNA complementary strand such that only 2 hydrogen bonds were available and in the correct orientation. Such a change would cause the aberrant base to be paired during replication.

18



Spectroscopy

CHAPTER SUMMARY

18.1 Spectroscopy

Spectroscopy involves instrumental methods for determining the structure of organic compounds by measuring and interpreting their interaction with electromagnetic radiation. Radiation can cause a measurable transformation or perturbation in molecules such as molecular rotation, bond vibration, promotion of electrons to higher energy levels, or even permanent disruption of the molecule.

Energy is described in wavelengths or frequency. The **wavelength** is the distance between two maxima in an energy wave. **Frequency** is the number of waves per unit distance or cycles per second. The energy of an electromagnetic radiation is directly proportional to frequency (the greater the frequency, the greater the energy), and inversely proportional to wavelength (the shorter the wavelength, the greater the energy).

Spectroscopy is possible because molecules absorb exactly the wavelength of energy necessary for a particular permutation and the absorption of these wavelengths is often characteristic of a particular structural feature. It is not possible either to accumulate radiation of lower energies to attain the total needed for a molecular transition or to extract it from higher energy radiation; it must be the exact wavelength or frequency corresponding to the energy of the transition. A **spectrometer** is an instrument that measures the absorption of energy by a chemical compound.

18.2 Infrared Spectroscopy

In **infrared spectroscopy**, the interaction of compounds with infrared radiation in the 2-15 micrometer wavelength range or frequencies in the 5000 cm^{-1} to 670 cm^{-1} range is measured. This relatively weak radiation causes vibration of bonds in the molecule including stretching, scissoring, bending, rocking, twisting, or wagging. Infrared spectroscopy is useful in identifying functional groups in molecules; this is especially evident in the 1400-3500 cm^{-1} region where the characterizing bonds in alkenes, alkynes, aldehydes, ketones, alcohols, and acids stretch. The remainder of the spectrum, in conjunction with the functional group region, gives a "fingerprint" that is often unique for a compound.

18.3 Ultraviolet-Visible Spectroscopy

Ultraviolet-visible spectroscopy utilizes the 200-750 nanometer region of the electromagnetic spectrum. Radiation of these wavelengths causes the promotion to higher energy levels of loosely held electrons such as non-bonding electrons or electrons involved in pi-bonds. For absorption in this particular region there must be conjugation of double bonds.

18.4 Nuclear Magnetic Resonance: ^1H NMR

In **nuclear magnetic resonance spectroscopy**, energy in the radiofrequency range causes the nuclei some atoms such as ^1H and ^{13}C to flip from alignment of their magnetic moments with an external magnetic field to non-alignment. There are three important aspects to **^1H or proton nuclear magnetic resonance**: chemical shift, integration, and splitting.

A. Chemical Shift

The number of different signals that appear in a proton NMR spectrum is often equal to the number of different hydrogens in a molecule. The location of a signal is characteristic of hydrogens in specific chemical environments and is described by **chemical shift**; chemical shift is measured in delta units and in proton NMR, most signals

come between 0 and 15. Chemical shifts are compared to **tetramethylsilane (TMS)** which has a shift defined as zero.

B. Integration

The area under an NMR peak can be determined by **integration**. Comparison of the integration (areas) of the signals on an NMR spectrum gives the ratio of hydrogen types in a molecule; if the molecular formula is known, the actual number of each type of hydrogen can be determined.

C. Splitting

Splitting is caused by the influence of the magnetic fields generated by hydrogens on adjacent carbons on the total magnetic field felt by a proton. The number of peaks into which a signal is split is one more than the total number of hydrogens on directly adjacent carbons.

D. Summary of Proton NMR

To interpret the proton NMR of a compound, the following procedure is useful. First, using integration write a possible fragment for each peak in the spectrum; for example if the area of a peak is 3, write down CH_3 as an initial idea. Arrange additional atoms in reasonable and simple units. Using the chemical shift and splitting, start putting the pieces of the puzzle together until a complete compound has been constructed that is consistent with chemical shift, integration, and splitting.

18.5 Carbon-13 NMR

Carbon-13 NMR requires sophisticated instrumentation since ^{13}C is only 1.1% of naturally occurring carbon. ^{13}C NMR is useful in the following ways. (1) The number of peaks in a spectrum is the number of non-equivalent carbons in the molecule. (2) The chemical shift provides information about the structural environment of each carbon. The range in ^{13}C NMR is more than 200 delta units. (3) The number of peaks into which a signal is split is one more than the number of hydrogens bonded to that carbon.

CONNECTIONS 14.1: MRI: Magnetic Resonance Imaging

18.6 Mass Spectrometry

Using **mass spectrometry** it is possible to determine the molecular weight and molecular formula of a compound. The structure of the compound is determined by breaking the molecule into smaller identifiable fragments with an electron beam, separating the fragments by mass in a magnetic field, and piecing the identified fragments back together, like a puzzle. The most intense peak in a mass spectrum is called the **base peak**. The peak equal to the molecular weight of the compound is called the **molecular ion**. Any peaks less than the molecular ion are called **fragment ions**.

A. Molecular Formula Determination

The molecular formula of a compound is determined using the ratios of natural occurring isotopes of an element. For example, carbon-13 is 1.1% of natural carbon. For every carbon in the molecular ion (M), the M+1 peak is 1.1% of M. For chlorine, the M+2 peak is 33% of M for each chlorine; for bromine it is almost 100% for each bromine; and for sulfur the M+2 peak is 4.5% of M for each sulfur. If the molecular ion has an odd mass number, there are an odd number of nitrogens in the molecule.

B. Fragmentation Patterns

When a molecule fragments upon exposure to a beam of electrons, the most common **fragment ions** are those that are most stable; they generally follow carbocation stability principles. Fragmentation does not occur in abundance at double and triple bonds. By understanding the most likely fragmentation points, the structures of fragment ions can be deduced from their masses and pieced together to determine the structure of the original molecule.

SOLUTIONS TO PROBLEMS

18.1 Infrared Spectroscopy

(a) The reactant has a carbon-nitrogen triple bond that stretches at 2210-2260 cm^{-1} . This unit is transformed to a carboxylic acid in the product that show C=O stretching at 1660-1780 cm^{-1} and a broad O-H stretch at 2500-3300 cm^{-1} .

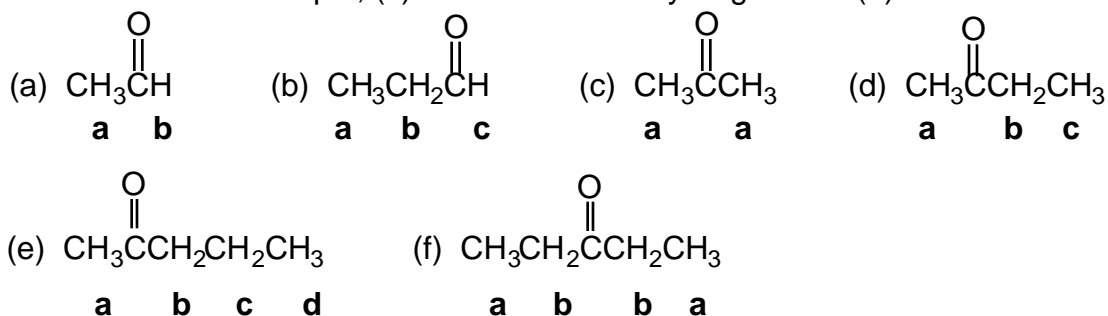
- (b) Cyclopentene has a C=C that stretches at 1600-1675 cm^{-1} ; cyclopentane does not.
- (c) The aldehyde has a C=O stretch at 1660-1780 cm^{-1} and a special C-H stretch as a sharp spike at 2700-2820 cm^{-1} . These are replaced by the O-H that stretches at 3400-3650 cm^{-1} .
- (d) The reactant is a primary amine and shows a doublet of N-H stretches at 3300-3500 cm^{-1} . The product is a tertiary amine and does not have an N-H bond.

18.2 UV-Visible Spectroscopy

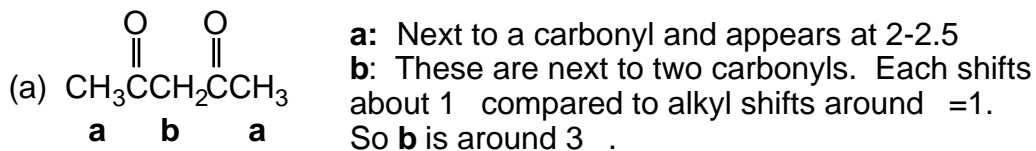
- (a) 1,3-Cyclohexadiene can be distinguished because the double bonds are conjugated as opposed to those in 1,4-cyclohexadiene that are not conjugated.
- (b) Propanone has a C=O but in propenal the C=O is conjugated with a C=C and thus distinguishable.
- (c) Look up these two compounds and those in part d in the index of your text. Carvone is distinguishable because it has a ketone group conjugated with a carbon-carbon double bond. Menthol has no double bonds at all.
- (d) Both of these compounds have lots of double bonds but in squalene, none are conjugated whereas in Vitamin A, all are conjugated with one another.

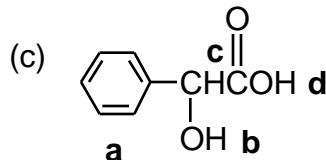
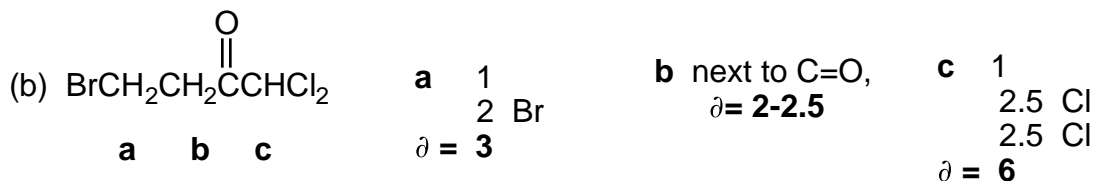
18.3 Proton NMR: Equivalent and Non-Equivalent Hydrogens

In each of the molecules, each different type of hydrogen is given a letter. Hydrogens in identical environments within a single molecule are given the same letter. For example, (c) has one kind of hydrogen and (e) has four.



18.4 Proton NMR: Chemical Shift





a: These are aromatic hydrogens and generally come in the $\delta = 7-8$ range.

b: Alcohol hydrogens are variable and cannot be accurately predicted.

c: If this hydrogen were next to nothing it would be an alkane and come around $\delta = 1$. But it is next to three groups that shift it in addition to the normal $\delta = 1$. The benzene shifts it another 1.4, the C=O shifts it another 1, and the oxygen shifts it another 2.4-3.4, lets say 2.9. So the approximate chemical shift will be $1+1.4+1+2.9$ or $\delta = 6.3$.

d: Carboxylic acid hydrogens come in the $\delta = 9-12$ region.

18.5 Proton NMR: Integration

(1) First add up the integration values: $149+58+91=298$

(2) There are 10 hydrogens causing this total integration. Divide 298 by 10; each hydrogen is worth 29.8 integration units.

(3) Since a hydrogen is worth 29.8 integration units, if we divide 29.8 into the integration units for each signal, we will obtain the number of hydrogens in each signal.

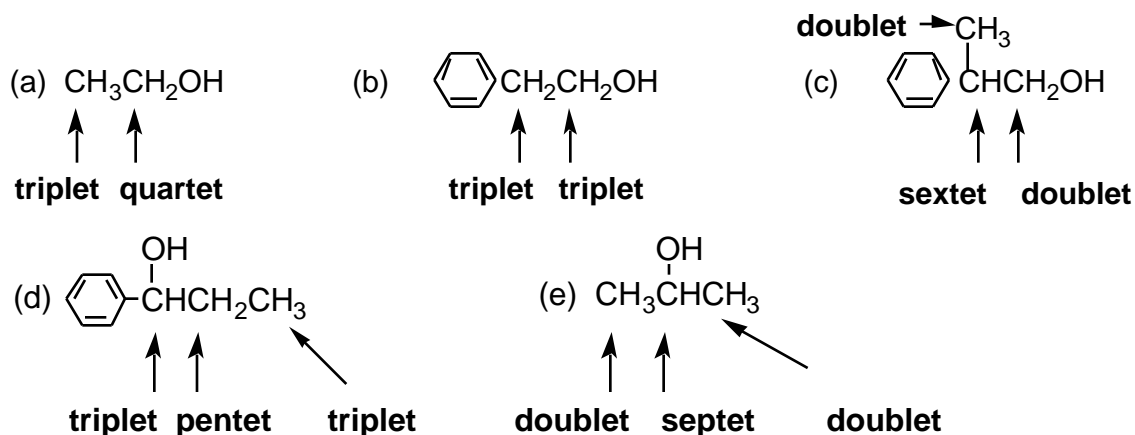
$\delta = 7$: 149 units divided by 29.8 units/H gives us 5 hydrogens.

$\delta = 2.3$: 58 units divided by 29.8 units/H rounds off to 2 hydrogens.

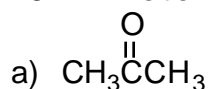
$\delta = 1.1$: 91 units divided by 29.8 units/H gives us the nearest whole number, 3 hydrogens.

18.6 Proton NMR: Splitting

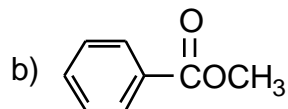
The number of peaks into which a signal is split is one more than the total number of hydrogens on directly adjacent carbons.



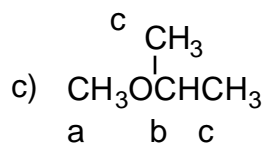
18.7 Proton NMR



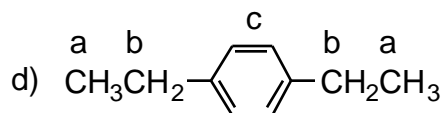
There is only one signal in the NMR and this compound has only one type of hydrogen. The other compound has three types of hydrogens and would have three signals.



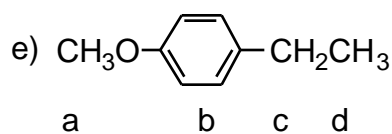
Each compound has only two types of hydrogens which appear as singlets. The difference is in the chemical shift of the methyl group. Here it is connected to oxygen and comes at $\delta = 3.9$. In the other compound it is connected to a carbonyl and would appear at $\delta = 2-2.5$.



This compound has three types of hydrogens as shown and three signals: a at 3.1, b at 3.5, and c at 1.1. The other compound has only two types of hydrogens and would have only two signals one of which would be a triplet and the other a quartet.



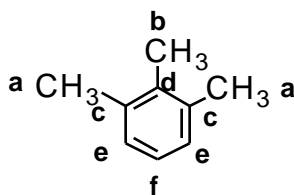
This is the only compound that gives three signals; the others give two. In addition, this compound shows splitting whereas the others give only singlets. a is at 1.3, b at 2.7, and c at 7.2.



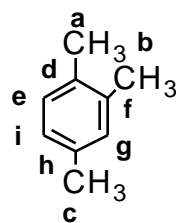
a is at $\delta = 3.7$, b at 7.0, c at 2.6, and d at 1.2. The third compound gives only three peaks with no splitting and can be eliminated. The first two each give four peaks with identical splitting patterns. The difference is in the chemical shifts. The

methyl singlet (a) comes at 3.7 in this compound as it is connected to an oxygen. In the other compound it is connected to the benzene ring and would come at 2.3-2.9. Likewise, the CH_2 quartet comes at 2.6 here since it is connected to the benzene ring. In the other compound, it is bonded to oxygen and would come at 3.3-5.

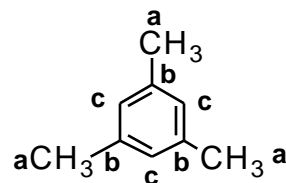
18.8 Carbon-13 NMR



6 types of carbons
6 NMR signals



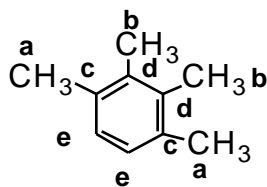
9 types of carbons
9 NMR signals



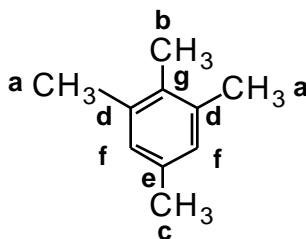
3 types of carbons
3 NMR signals

The carbons in the benzene ring appear at 138 and 127.

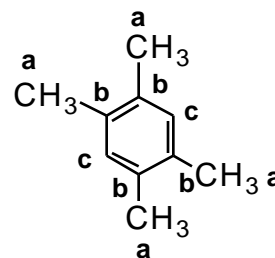
18.9 Carbon-13 NMR



5 types of carbons
5 signals
135,134,127,21,16



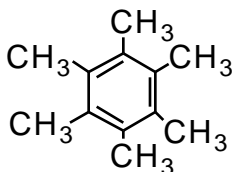
7 types of carbons
7 signals
136,134,132,128,21,20,15



3 types of carbons
3 signals
134,131,19

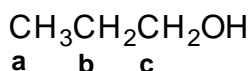
The methyl groups carbons are the signals in the range of 15-21; the chemical shifts around 127-136 are aromatic carbons.

18.10 Carbon-13 NMR

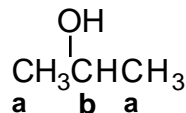


In hexamethylbenzene, the six methyl carbons are equivalent and the six benzene carbons are equivalent. As a result, there are only two carbon-13 NMR signals in the spectrum.

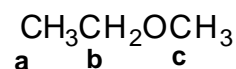
18.11 Carbon-13 NMR with Splitting

 C_3H_8O isomers

3 signals
a: quartet
b: triplet
c: triplet



2 signals
a: quartet
b: doublet



3 signals
a: quartet
b: triplet
c: quartet

18.12 Mass Spectrometry: Molecular Formulas

(a) Number of C's = $M+1/M \times 0.11 = 7.7/1.1 = 7$

Seven carbons contribute 84 to the molecular ion so there must be 12 hydrogens to give a mass of 96. The formula is C_7H_{12} .

(b) Number of C's = $M+1/M \times 0.11 = 3.3/1.1 = 3$

The M+2 peak is 33% of M for every Cl so there is one Cl.

The mass of three carbons and one chlorine is $36 + 35 = 71$.

We need 21 more mass units. They can't all be hydrogen. There must be one oxygen (16) and five hydrogens. The molecular formula is C_3H_5OCl .

(c) Number of C's = $M+1/M \times 0.11 = 6.6/1.1 = 6$

The M+2 peak is 98% of M for each Br so there must be one Br. The six carbons (72) and one bromine (79) add to 151. There must be five hydrogens to get to the mass of 156. The molecular formula is C_6H_5Br .

(d) Number of C's = $M+1/M \times 0.11 = 3.3/0.11 \times 49 = 6$

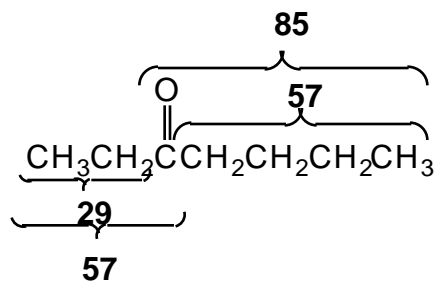
The M + 2 peak is 98% of M for every Br. Since it is twice the size of the M peak there must be two bromines. The six carbons (72) and two bromines (158) add to 230. Thus there must be four hydrogens to get to the mass of 234. The formula is $C_6H_4Br_2$.

(e) Number of C's = $M+1/M \times 0.11 = 2.2/1.1 = 2$

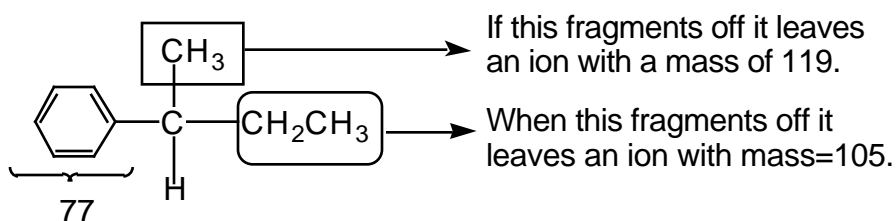
The M + 2 peak is 4.5% of M for each sulfur. There must be a sulfur. Since M has an odd mass there must be an odd number of nitrogens. The two carbons (24), one sulfur (32) and one nitrogen (14) add to 70. We can't have three nitrogens as the mass would then be 98. The atoms we already have cannot accommodate 21 hydrogens. There must be one oxygen (16); the total mass is now 86. There must be five hydrogens. The formula is C_2H_5NSO .

18.13 Mass Spectrometry

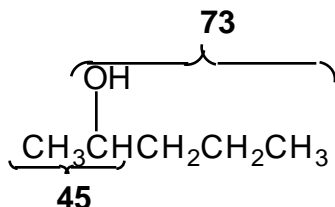
(a) Ketones fragment on either side of the carbonyl. The smallest peak is the smallest alkyl group and the largest is the largest acyl group.



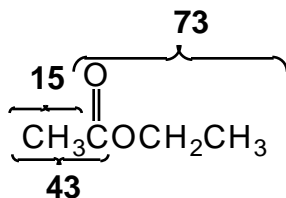
(b) Monosubstituted benzenes give a peak at 77 for the ring (C_6H_5). The other fragmentations are at the carbon connected to the ring leaving benzylic carbocations.



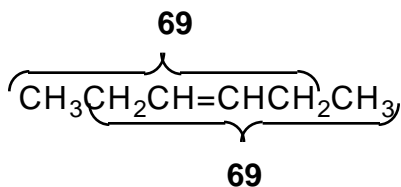
(c) Alcohols cleave at the alcohol carbon.


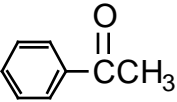
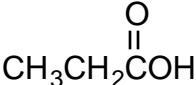
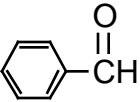


(d) Esters give three major peaks on either side of the carbon-oxygen double bond. The smallest peak is the alkyl group connected to the $\text{C}=\text{O}$ and the largest is the ester function.



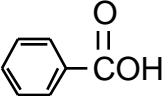
(e) Alkenes cleave at the carbon attached to the double bond to leave behind an allylic carbocation. In this case, since there is only one peak of this type, the alkene must be symmetrical.


18.14 Infrared Spectroscopy: Section 18.2

- a)  cyclohexene has a C=C stretch around 1600-1670 cm⁻¹ and cyclohexane does not.
- b)  both compounds have characteristic benzene peaks but this compound has a C=O stretch around 1660-1780 cm⁻¹.
- c) CH₃C≡CH as an alkyne, this compound has a triple bond stretch at 2100-2260 cm⁻¹ and a C-H (triple bond carbon) stretch around 3300 cm⁻¹
- d)  both compounds have the carbonyl, C=O stretch but this one also has the O-H stretch for the carboxylic acid as a broad band 2500-3300 cm⁻¹
- e) CH₃CH₂CH₂NH₂ this is a primary amine and has an N-H stretch appearing as a doublet around 3300-3500 cm⁻¹
- CH₃NHCH₂CH₃ as a secondary amine, the N-H stretch appears as a singlet around 3300-3500 cm⁻¹
- (CH₃)₃N this is a tertiary amine, there is no N-H stretch
- f) CH₃CH₂C≡N the carbon-nitrogen triple bond stretch is at 2210-2260 cm⁻¹
- g)  both compounds are similar in that they have carbonyl groups and benzene rings; this one has the C-H bond of the aldehyde group that stretches at 2700-2820 cm⁻¹

h) $\text{CH}_3\text{CH}_2\text{OH}$ there is the characteristic O-H stretch around $3400\text{-}3650\text{ cm}^{-1}$ in the alcohol but absent in the ether.

i) CH_3NO_2 the NO_2 group gives two strong bands at $1500\text{-}1570\text{ cm}^{-1}$ and $1300\text{-}1370\text{ cm}^{-1}$

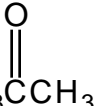

j)  both have carbonyl and benzene signals but the acid has a broad O-H stretch between 2500 and 3300 cm^{-1}

k) $\text{CH}_3\text{CH}_2\text{NHCH}_3$ N-H stretch as single peak at $3300\text{-}3500\text{ cm}^{-1}$

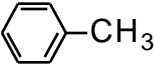
18.15 ^1H Nuclear Magnetic Resonance: Section 18.4

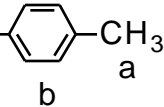
Approximate NMR data follows.

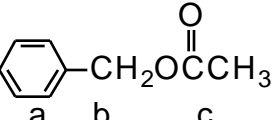
(a) CH_4 = 0.9 singlet (b) CH_3OCH_3 = 3.3-5 singlet

(c)  = 2-2.5 singlet (d)  = 7-8 singlet (e) CH_3Br = 2.7-3.8

(f) CHBr_3 = 4.5-6 (g) CH_3OH = 3-3.5 singlet, 3H and variable singlet, 1H

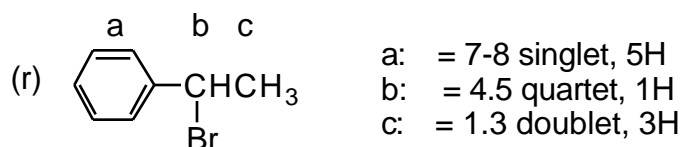
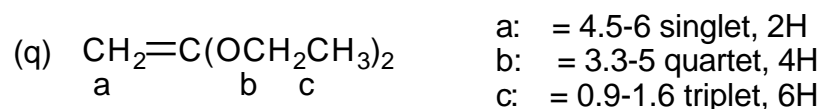
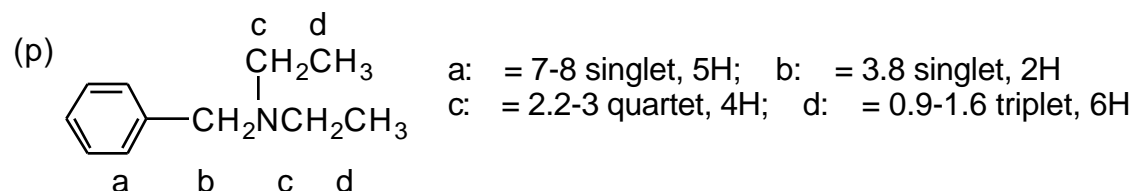
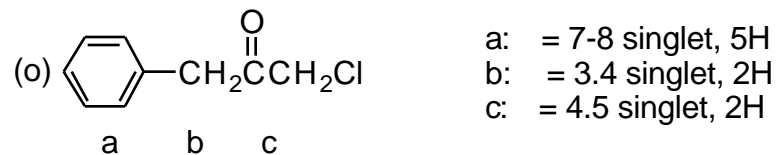
(h)  a: = 7-8 singlet, 5H
b: = 2.3-2.9 singlet, 3H

(i)  a: = 2.3-2.9 singlet, 6H
b: = 7-8 singlet, 4H

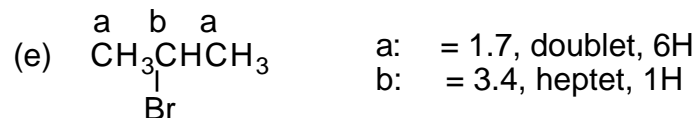
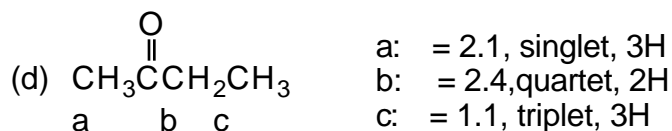
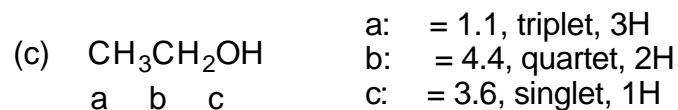
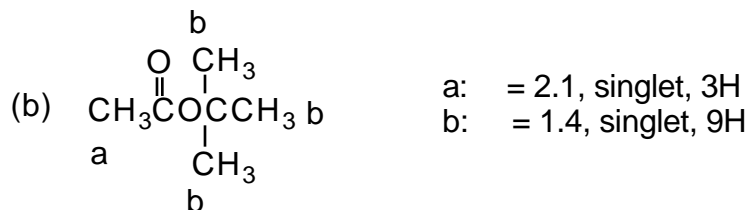
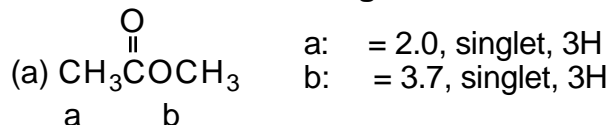
(j)  a: 7-8 singlet, 5H
b: 5.5 singlet, 2H
c: 2.3 singlet, 3H

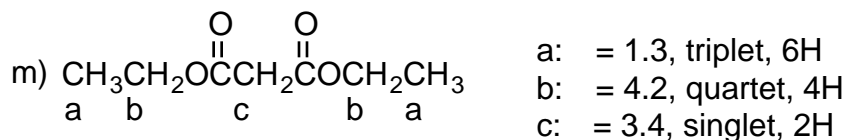
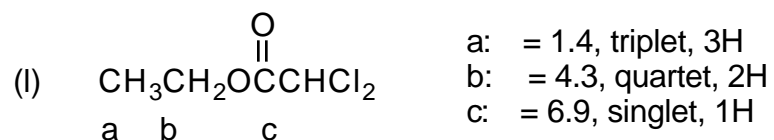
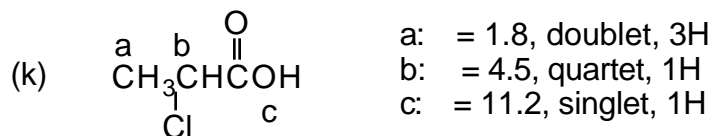
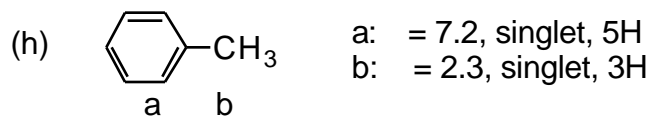
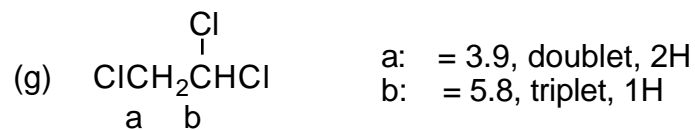
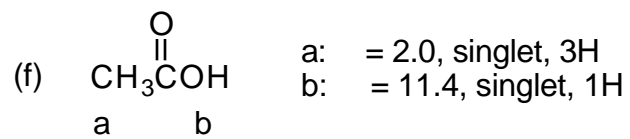
(k) $\text{Cl}_2\text{CHCH}_2\text{Cl}$ a: = 5.5-6.6 triplet b: = 2.3-2.6 doublet (l) CH_3CHBr_2 a: = 1.3 doublet, 3H b: = 5.2 quartet, 1H

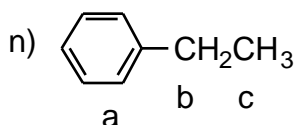
(m) $(\text{CH}_3)_2\text{CHOCH}(\text{CH}_3)_2$ a: = 1.3 doublet, 12H
b: = 3.3-5 heptet, 2H



18.16 ^1H Nuclear Magnetic Resonance: Section 18.4







a: = 7.2, singlet, 5H

b: = 2.7, quartet, 2H

c: = 1.3, triplet, 3H

18.17 Carbon-13 NMR Without Splitting: Section 18.5

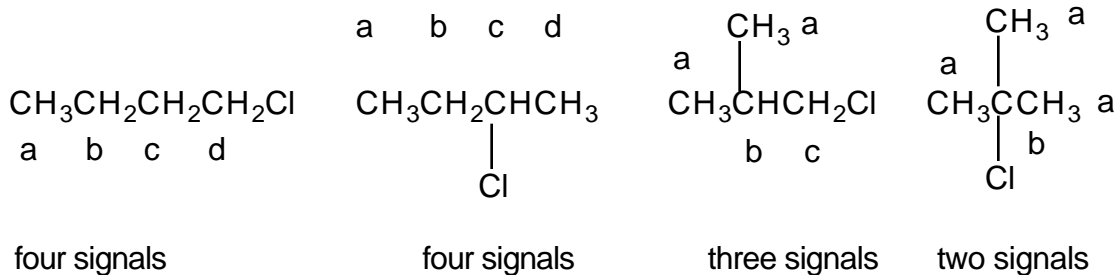
(a) C_3H_7Br

$CH_3CH_2CH_2Br$ This compound has three different types of carbons and is the one with three signals at 36, 26, and 13.

$CH_3\underset{Br}{\underset{|}{CH}}CH_3$ The two methyl carbons are equivalent here so there are only two different types of carbons and two signals, 45 and 28.

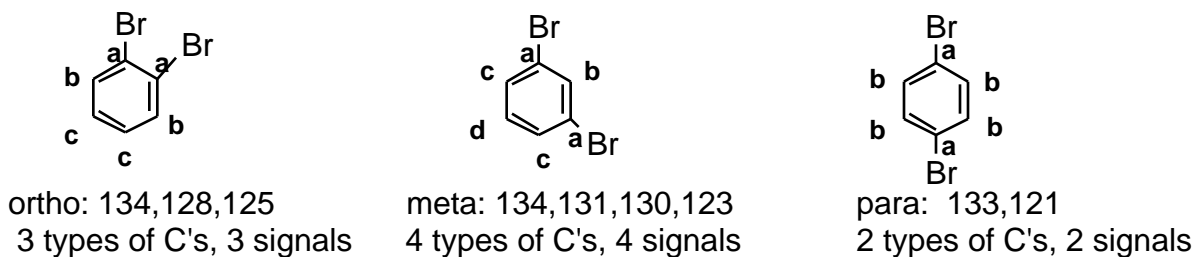
(b) C_4H_9Cl

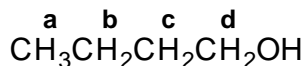
Following are the four isomers and the number of C-13 signals.



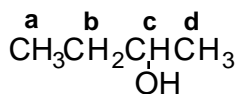
(c) Dibromobenzenes

Each isomer has a different number of different types of carbons and thus can easily be identified by C-13 NMR.

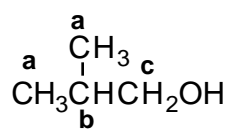


(d) $C_4H_{10}O$ isomers

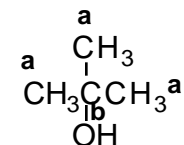
4 types of C
4 signals



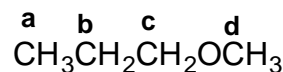
4 types of C
4 signals



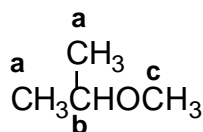
3 types of C
3 signals



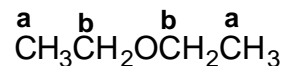
2 types of C
2 signals



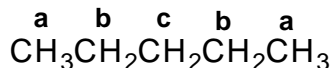
4 types of C
4 signals



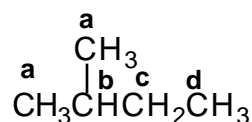
3 types of C
3 signals



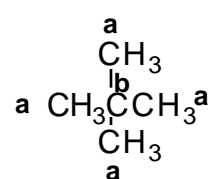
2 types of C
2 signals

(e) C_5H_{12} isomers

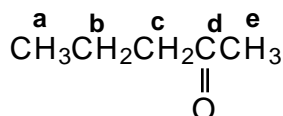
3 types of carbons
3 signals



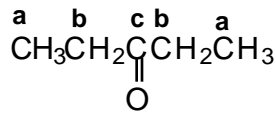
4 types of carbons
4 signals



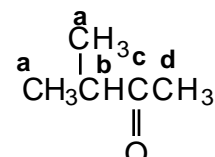
2 types of carbons
2 signals

(f) $C_5H_{10}O$ ketones

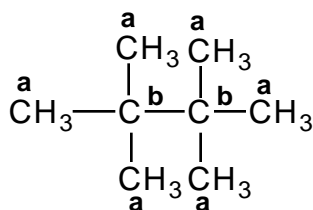
5 types of carbons
5 signals



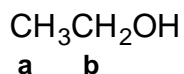
3 types of carbons
3 signals: 212,35,8



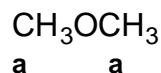
4 types of carbons
4 signals

(g) C_8H_{18} isomer

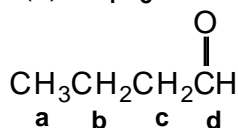
This is the most symmetrical of the 18 isomers. There are only two kinds of carbons and thus only two signals in the carbon-13 NMR spectrum. (There is only one kind of hydrogen and only one peak in the proton NMR spectrum.)

18.18 ^{13}C NMR with Splitting: Section 18.5(a) $\text{C}_2\text{H}_6\text{O}$ isomers

There are two kinds of carbons and two signals. a is a quartet since there are three attached hydrogens and b is a triplet since there are two hydrogens

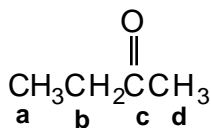


There is only one kind of carbon and thus only one signal. Since the carbons have three attached hydrogens the one signal appears as a quartet

(b) $\text{C}_4\text{H}_8\text{O}$ 

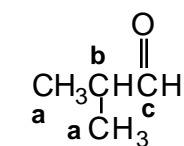
4 signals

a: quartet b: triplet
c: triplet d: doublet



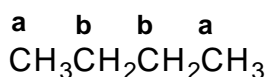
4 signals

a: quartet b: triplet
c: singlet d: quartet



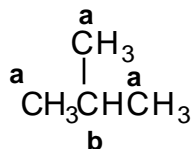
3 signals

a: quartet b: doublet
c: doublet

(c) C_4H_{10} 

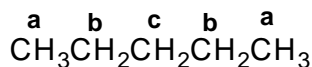
2 signals

a: quartet b: triplet



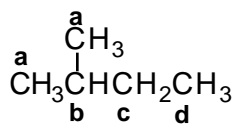
2 signals

a: quartet b: doublet

(e) C_5H_{12} isomers

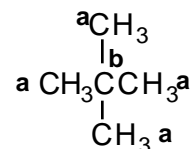
3 signals

a: quartet b: triplet
c: triplet



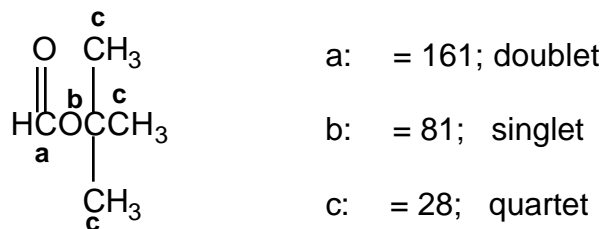
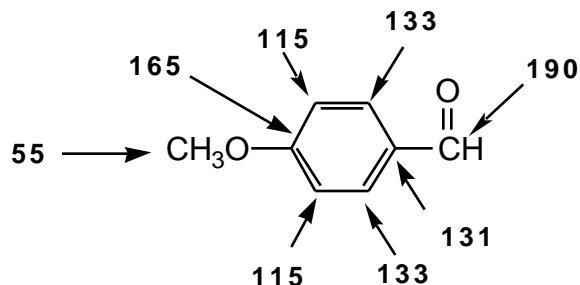
4 signals

a: quartet b: doublet
c: triplet d: quartet



2 signals

a: quartet
b: singlet

18.19 ^{13}C NMR: Section 18.518.20 ^{13}C NMR: Section 18.5

18.21 Mass Spectrometry: Section 18.6

a) C_8H_{18} No. of carbons = $\frac{M + 1}{0.011 \times M} = \frac{8.8}{0.011 \times 100} = 8$

b) $\text{C}_2\text{H}_5\text{Cl}$ No. of carbons = $\frac{M + 1}{0.011 \times M} = \frac{2.2}{0.011 \times 100} = 2$
The $M + 2$ peak is 33% of M indicating one chlorine.
 $M = 2 \text{ C's (24)} + 1 \text{ Cl (35)} + 5 \text{ H (5)} = 64$

c) $\text{C}_3\text{H}_5\text{BrO}$ No. of carbons = $\frac{M + 1}{0.011 \times M} = \frac{1.3}{0.011 \times 40} = 3$

The $M + 2$ peak is almost equal to the M indicating the presence of one bromine (or three chlorines).

$$M = 3 \text{ C's (36)} + 1 \text{ Br (79)} + 1 \text{ O (16)} + 5 \text{ H (5)} = 136$$

d) CH_4S No. of carbons = $\frac{M + 1}{0.011 \times M} = \frac{1.1}{0.011 \times 100} = 1$

The $M + 2$ peak is 4.5% of M indicating one sulfur.

$$M = 1 \text{ C (12)} + 1 \text{ S (32)} + 4 \text{ H (4)} = 48$$

e) $\text{C}_2\text{H}_2\text{Cl}_2$ No. of carbons = $\frac{M + 1}{0.011 \times M} = \frac{1.8}{0.011 \times 80} = 2$

$$\frac{M + 2}{M} = \frac{54}{80} = 0.675$$

The M + 2 peak is 0.675 of M peak indicating the presence of two chlorines.

$$M = 2 \text{ C's (24)} + 2 \text{ Cl's (70)} + 2 \text{ H (2)} = 96$$

f) **C₆H₄Br₂** $\frac{\text{No. of carbons}}{M} = \frac{M + 1}{0.011 \times M} = \frac{3.3}{0.011 \times 50} = 6$

$$\frac{M + 2}{M} = \frac{99}{50} = 1.98$$

The M + 2 peak is twice M indicating the presence of two bromines.

$$M = 6 \text{ C's (72)} + 2 \text{ Br's (158)} + 4 \text{ H (4)} = 234$$

g) **C₃H₉N** $\frac{\text{No. of carbons}}{M} = \frac{M + 1}{0.011 \times M} = \frac{2.5}{0.011 \times 75} = 3$

The M peak is odd indicating the presence of an odd number of nitrogens.

$$M = 3 \text{ C's (36)} + 1 \text{ N (14)} + 9 \text{ H (9)} = 59$$

h) **C₇H₅OCl** $\frac{\text{No. of carbons}}{M} = \frac{M + 1}{0.011 \times M} = \frac{2.3}{0.011 \times 30} = 7$

$$\frac{M + 2}{M} = \frac{10}{30} = 0.33$$

The M + 2 is one third of M indicating one chlorine.

$$M = 7 \text{ C's (84)} + 1 \text{ Cl (35)} + 1 \text{ O (16)} + 5 \text{ H (5)} = 140$$

i) **C₂H₄S₂** $\frac{\text{No. of carbons}}{M} = \frac{M + 1}{0.011 \times M} = \frac{1.5}{0.011 \times 70} = 2$

$$\frac{M + 2}{M} = \frac{6.3}{70} \times 100\% = 9\%$$

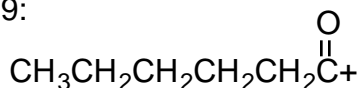
M + 2 is 9% of M indicating two sulfurs (4.5% of M for each).

$$M = 2 \text{ C's (24)} + 2 \text{ S's (64)} + 4 \text{ H (4)} = 92$$

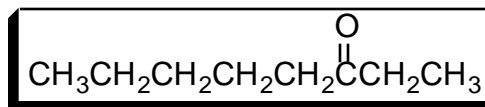
18.22 Mass Spectrometry: Section 18.6

(a) The shortest alkyl group is 29: CH_3CH_2^+

The longest acyl group is 99:



The ketone is:



57 is $\text{CH}_3\text{CH}_2\overset{\text{O}}{\parallel}\text{C}^+$ and 71 is $\text{CH}_3\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2^+$

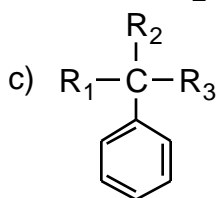
b) $\text{R}_1\text{CH}_2\text{CH}=\text{CHCH}_2\text{R}_2$ Alkenes fragment by losing R_1 and R_2 .

$98 - 83 = 15$ indicating one R is a CH_3

$98 - 69 = 29$ indicating other R is an CH_2CH_3

The alkene is $\text{CH}_3\text{CH}_2\text{CH}=\text{CHCH}_2\text{CH}_2\text{CH}_3$ -->

$+\text{CH}_2\text{CH}=\text{CHCH}_2\text{CH}_2\text{CH}_3$ 83 $\text{CH}_3\text{CH}_2\text{CH}=\text{CHCH}_2^+$ 69

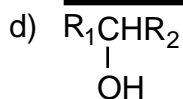
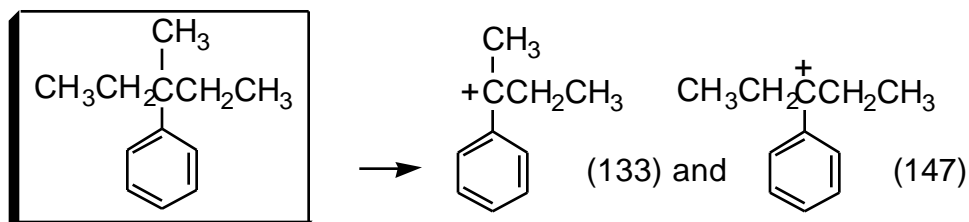


Aromatic compounds of this type fragment by losing R_1 , R_2 , and R_3 to form benzylic carbocations.

$162 - 147 = 15$ indicating that at least one R is CH_3

$162 - 133 = 29$ indicating that at least one R is CH_3CH_2

Since there are 12 carbons, the following must be the compound.

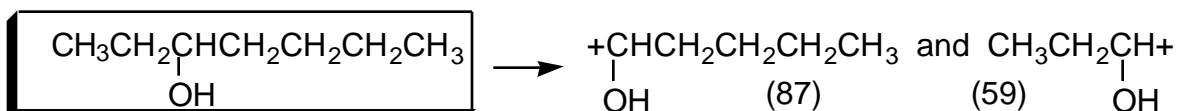


Alcohols fragment by loss of alkyl groups, R_1 and R_2 .

$116 - 87 = 29$ indicating one group is CH_3CH_2 .

$116 - 59 = 57$ indicating one group is $\text{CH}_3\text{CH}_2\text{CH}_2\text{CH}_2$.

The alcohol is:

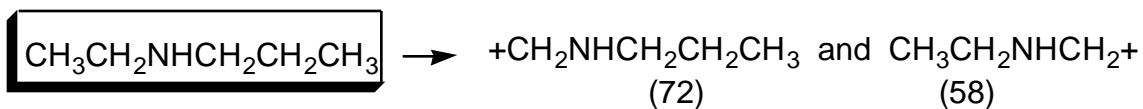


e) $\text{R}_1\text{CH}_2\text{NHCH}_2\text{R}_2$ Amines fragment by loss of alkyl groups (R_1 , R_2).

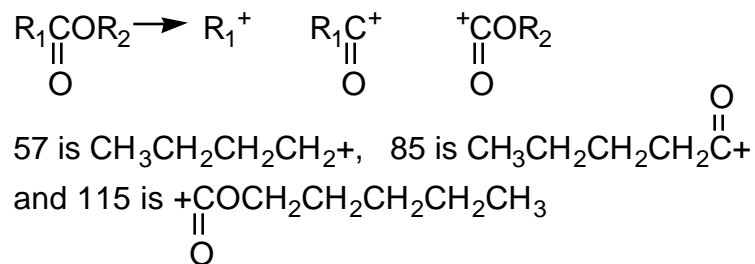
$87 - 72 = 15$ indicating one R is CH_3 -

87 - 58 = 29 indicating other R is CH₃CH₂-

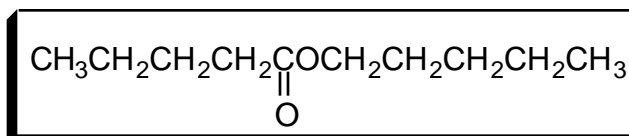
The amine is:



f) Esters fragment as follows:



The ester is:



18.23 Mass Spectrometry: Section 18.6

