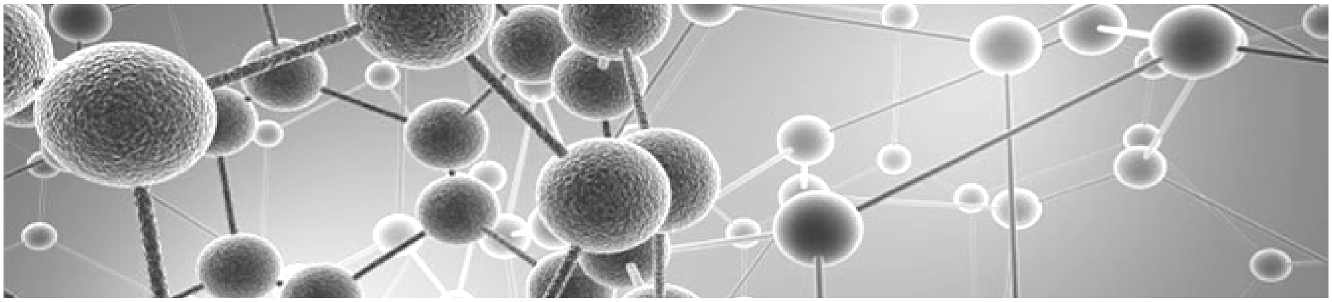
DAWSON COLLEGE

EXTRA CLASS NOTES FOR
ORGANIC CHEMISTRY
202-BZF-05



INSTRUCTOR:
YANN BROUILLETTE

Dear Students,

Thank you for choosing this complementary chemistry class. I hope you will find answers to some of the scientific questions you may ask yourself.

Be aware that these class notes were put together to ease the comprehension and facilitate the studying of the University level chemistry class entitled: Organic Chemistry 202-BZF-05.

You are still required to read the text book *Organic Chemistry 8th edition by Carey*, and do the suggested problems.

And remember, organic chemistry is like cooking… but don't lick your fingers!

Have a good session!

Your Instructor

Yann Brouillette, Ph. D.

Chapter 1:
Structures Determines Properties

1.6 Structural Formulas of Organic Molecules

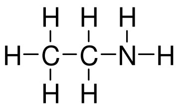
The **molecular formula** of a compound tells us which atoms and how many of each are present in the compound.
The order in which the atoms of a molecule are connected is called its **connectivity** (or constitution).
The connectivity of a molecule must be determined in order to write a **Lewis structure**. Most of the time carbon has four bonds, nitrogen has three, and oxygen two.

Writing Lewis Structures: Review

1. The molecular formula must be given
2. Based on the molecular formula, count the number of valence electrons.
3. Given the connectivity, connect bonded atoms by a shared electron pair bond represented by a dash (–).
4. Count the number of electrons in the bonds (twice the number of bonds), and subtract this from the total number of valence electrons. This will give you the number of electrons that still need to be added.
5. Add electrons in pairs so that as many atoms as possible have eight electrons (the octet rule). It is usually best to begin with the most electronegative atom (hydrogen is limited to two electrons; the duet rule). Under no circumstances can a second-row element such as C, N or O have more than eight valence electrons.
6. Calculate the formal charges.

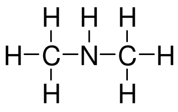
Isomers are different compounds that have the same molecular formula. Isomers can be either constitutional isomers or stereoisomers.

Constitutional isomers are isomers that differ in the order in which the atoms are connected (they are also called structural isomers). Example:



$H-\overset{H}{\underset{H}{C}}-\overset{H}{\underset{H}{C}}-\overset{H}{N}-H$

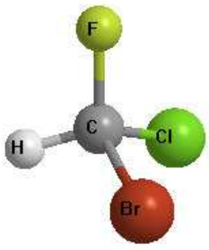
vs.



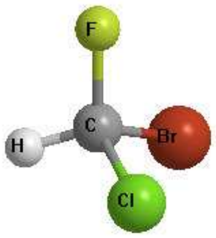
$H-\overset{H}{\underset{H}{C}}-\overset{H}{N}-\overset{H}{\underset{H}{C}}-H$

Both have the molecular formula C_2H_7N but the atoms are connected in a different order.

Stereoisomers are isomers that differ in the arrangement of atoms in space. (You need to know the geometry of the molecule to determine the type stereoisomer). Example:

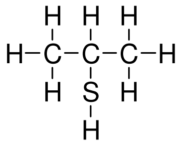


vs:

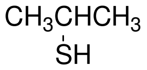


Writing Organic Structures

Condensed structural formulas are Lewis structures in which many (or all) covalent bonds and electron pairs are omitted. Subscripts are used to indicate the number of identical groups attached to a particular atom.



can be condensed to

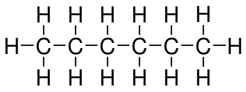


$\underset{\mathrm{SH}}{CH_3CHCH_3}$

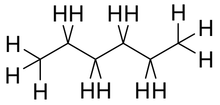
or $(CH_3)_2CHSH$

In Organic Chemistry, even simpler structural formulas are being used. These simplified representations are called **bond-line formulas** or **carbon skeleton diagrams**. They represent structure by showing bonds between carbons and atoms other than hydrogen. Atom symbols for Carbon (C) and Hydrogen (H) are omitted. Atoms other than carbon and hydrogen are called *heteroatoms* and are shown.

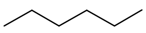
$CH_3(CH_2)_4CH_3$ is equal to



which becomes



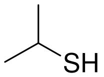
and is simplified to

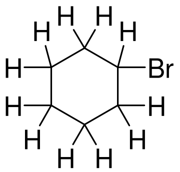


Note: Do not write CH_4 as a dot (•) nor CH_3CH_3 as a line (—).

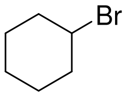
Examples:

$(CH_3)_2CHSH$ becomes

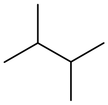




becomes



$(CH_3)_2CHCH(CH_3)_2$ becomes



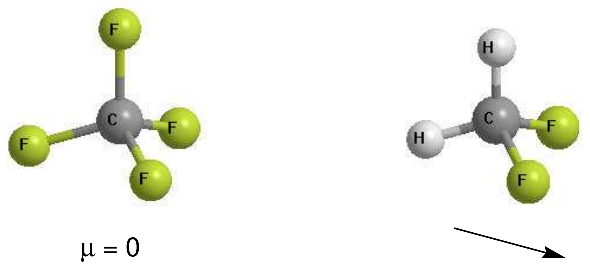
1.10 Molecular Dipole Moments

The molecular dipole moment is the resultant of all of the individual bond dipole moments of a molecule.

Some substances, such as carbon dioxide, have polar bonds, but no dipole moment because their geometry causes the individual C=O bond dipoles to cancel.

O=C=O (linear geometry) Dipole moment = 0

Another example is carbon tetrafluoride (left), with four polar C–F bonds and a tetrahedral shape, it has no net dipole moment. On the other hand, Difluoromethane (right), also with a tetrahedral shape, has a dipole moment, because the 2 C–H bond dipole do not cancel the 2 C–F bond dipoles.



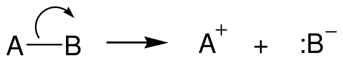
So from the Lewis structure of a molecule, we can use electronegativity to determine the polarity of bonds and combine that with the geometry of the molecule to predict whether the molecule has a dipole moment.

1.11 Curved arrows and Chemical Reactions

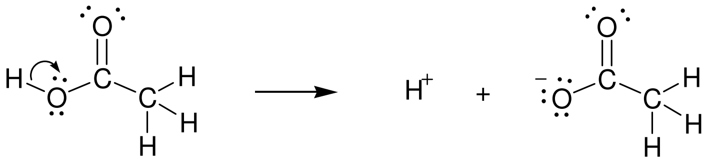
Curved arrows are used to track the flow of electrons in chemical reactions. The arrow begins where the electrons were originally and points to where they end up.

There are two kinds of curved arrows. A double-barbed arrow (↷) shows the movement of a pair of electrons, either a bonded pair or a lone pair. A single-barbed arrow (↷) shows the movement of one electron.

Consider the reaction shown below which shows the dissociation of A-B:



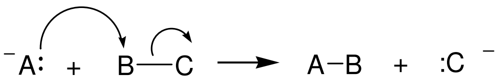
The curved arrow begins where the electrons are originally (in the bond) and points to atom B as their destination where they become an unshared pair of the anion B^-. The same process describes similar reactions.



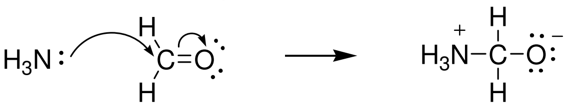
Note: The reactants do not always need to be a neutral compound (they can also be ions).

In all chemical reactions, charge as well as mass is conserved.

Many reactions combine bond making with bond breaking and require more than one curved arrow.



Curved-arrow notation is also applied to reactions in which double and triple bonds are made or broken. Only one component (one electron pair) of the double or triple bond is involved.



Note: Resist temptation to use curved arrows to show the movement of atoms. Curved arrows always show electron flow.

1.12 Acids and Bases: The Arrhenius View

Definitions of Acids and Bases:

Arrhenius

An acid ionizes in water to give protons. A base ionizes in water to give hydroxide ions.

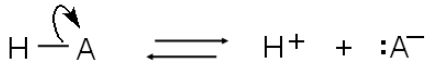
Brønsted-Lowry

An acid is a proton donor. A base is a proton acceptor.

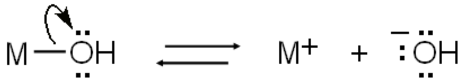
Lewis

An acid is an electron pair acceptor. A base is an electron pair donor.

An acid is a substance that ionizes to give protons when dissolved in water. Strong acids dissociate completely in water. Weak acids dissociate only partially.

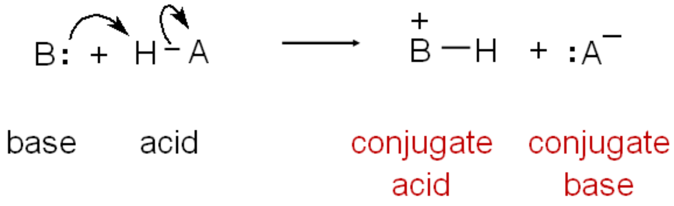


A base is a substance that ionizes to give hydroxide ions when dissolved in water. Strong bases dissociate completely in water. Weak bases dissociate only partially.



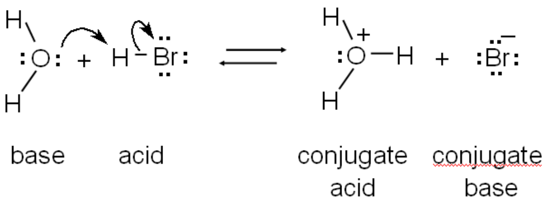
1.13 Acids and Bases: The Brønsted-Lowry View

In a Brønsted-Lowry Acid-Base Reaction, a proton is transferred from the acid to the base:



The base is converted to its conjugate acid, and the acid is converted to its conjugated base. (The only difference is the addition or subtraction of only one proton).

In the Brønsted-Lowry view, an acid doesn't dissociate in water; it transfers a proton to water. Water acts as a base. The systematic name for the conjugate acid of water (H_3O^+) is oxonium ion. Its common name is hydronium ion.



For an overview of Acidity constants (pK_a of Acids), please refer to Table 1.8 in your textbook.

1.14 What happened to pK_b?

In Organic Chemistry, a separate “basicity constant” K_b is unnecessary.

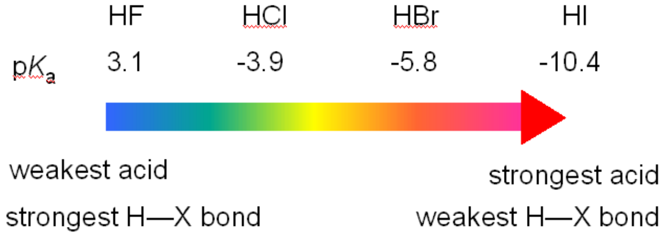
Assessing relative basicities requires only that we remember that the weaker the acid, the stronger the conjugate base and find the appropriate acid-base pair in the table. Because of the conjugate relationships in the Brønsted-Lowry approach, we can examine acid-base reactions by relying exclusively on p*K*a values.

1.15 How Structure Affects Acid Strength

The main ways in which structure affects acid strength depend on:

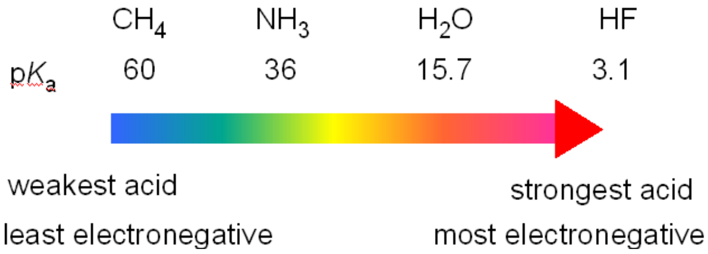
- The strength of the bond to the atom from which the proton is lost
- The electronegativity of the atom from which the proton is lost
- Electron delocalization in the conjugate base

Generally, **bond strength** decreases going down a group in the periodic table. Bond strength is the most important factor when considering acidity of protons bonded to atoms in same group of periodic table (as in HF, HCl, HBr, and HI).



As the halogen X becomes larger, the H—X bond becomes longer and weaker. Therefore, the acid strength increases.

Electronegativity is controlling factor when comparing acidity of protons bonded to atoms in the same row of the periodic table.

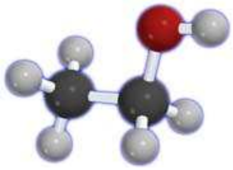


As the atom (A) to which H is bonded becomes more electronegative, the polarization $^{\delta+}H—A^{\delta-}$ becomes more pronounced and H is more easily transferred as H^+. (Another way of looking at it is that H becomes more positive as the atom to which it is attached becomes more electronegative).

In many acids the acidic proton is bonded to oxygen. Alcohols (RO—H) resemble water (HO—H) in their acidity. Example of acidity of alcohols:

	HO—H	CH_3O—H	CH_3CH_2O—H	$(CH_3)_2CHO$—H	$(CH_3)_3CHO$—H
	Water	Methanol	Ethanol	Isopropyl alcohol	*tert*-butyl alcohol
pK_a	15.7	15.2	16	17	18

Electronegative substituents can increase the acidity of alcohols by drawing electrons away from the —OH group. The comparison of ethanol with 2,2,2-Trifluoroethanol:



CH_3CH_2OH (pK_a: 16.0)

$C\mathbf{F_3}CH_2OH$ (pK_a: 11.3)

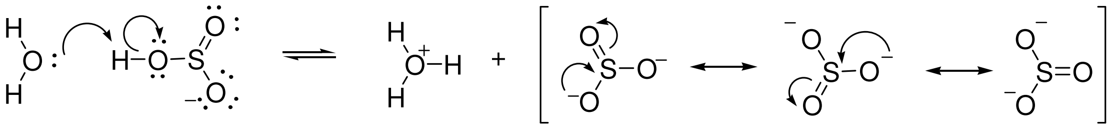
The electronegative fluorines attract electrons toward themselves and this attraction is transmitted through the bonds, increasing the positive character of the O—H proton. The greater the positive character of the O—H proton, the greater the acidity.

Structural effects that are transmitted through bonds are called inductive effects. Inductive effects arise by polarization of the electron distribution in the bonds between atoms. A substituent *induces* a polarization in the bonds between it and some remote site. The greater acidity of CF_3CH_2OH compared to CH_3CH_2OH is an example of an inductive effect.

Inductive effects depend on the electronegativity of the substituent and the number of bonds between it and the affected site. As the number of bonds between the two units increases, the inductive effect decreases.

Electron Delocalization in the conjugate base may help stabilize the negative charge of the conjugate base. Therefore, the proton is more free to leave, hence making it more acidic.

Ionization becomes more favorable if electron delocalization increases in going from right to left in the equation. Resonance is a convenient way to show electron delocalization.

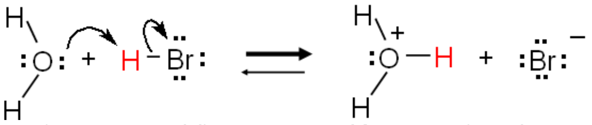


1.16 Acid-Base Equilibria

A reaction proceeds in the direction that converts the stronger acid and the stronger base to the weaker acid and the weaker base. A convenient way to represent an acid-base equilibrium is to put the strongest acid on the left hand side of the equation and the weaker acid is on the right.

$$\text{Stronger acid} + \text{Stronger base} \rightleftharpoons \text{Weaker acid} + \text{Weaker base}$$

Example of a Strong acid:

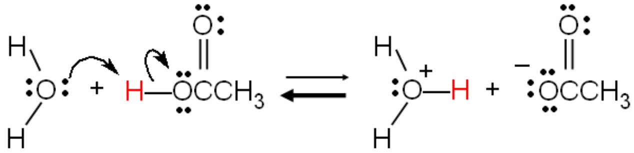


p*K*a = -5.8 (stronger acid)

p*K*a = -1.7 (weaker acid)

The equilibrium lies to the side of the weaker acid. (To the right)

Example of a Weak acid:



p*K*a = 4.7 (weaker acid) p*K*a = -1.7 (stronger acid)

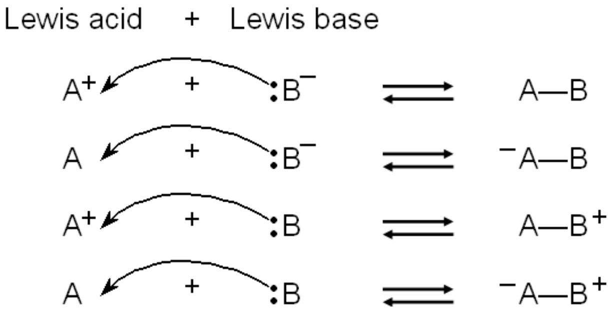
The equilibrium lies to the side of the weaker acid. (To the left)

Points to remember:

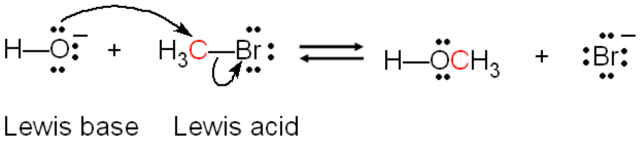
- A strong acid is one that is stronger than H_3O^+.
- A weak acid is one that is weaker than H_3O^+.
- A strong base is one that is stronger than HO^-.
- A weak base is one that is weaker than HO^-.
- The strongest acid present in significant quantities when a strong acid is dissolved in water is H_3O^+.
- The strongest acid present in significant quantities when a weak acid is dissolved in water is the weak acid itself.
- To predict the direction of acid-base reactions: the equilibrium lies to (points to) the side of the weaker acid. (which should be on the right)

1.17 Lewis Acids and Lewis Bases

The Lewis acid and the Lewis base can be either a neutral molecule or an ion.



The Lewis acid/Lewis base idea also includes certain substitution reactions in which one atom or group replaces another.



Lewis bases use an unshared pair to form a bond to some other atom and are also referred to as nucleophiles (“nucleus seekers”).

Lewis acids are electrophiles (“electrons seekers”).

Extra Problems:

1. Which of the following (Na^- , Mg^{2+} , O^{2-} , Mg^+) has (have) the same electron configuration as Ne?

   A) Na^- and O^{2-} B) Mg^{2+} and O^{2-} C) Mg^+ and O^{2-} D) only Mg^{2+}

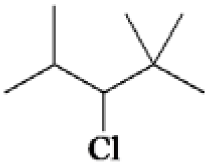
2. What is the charge on the phosphorus ion in Na_3P?
   A) -3 B) -1 C) +1 D) +3

3. Predict which bond is the most polar in ethanol, CH_3CH_2OH?
   A) C—C B) C—H C) C—O D) O—H

4. Which one of the following is the conjugate base of NH_3?
   A) NH_4^+ B) H^+ C) N^{3-} D) NH_2^-

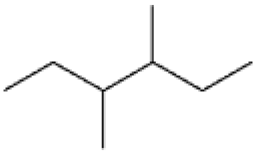
5. Which one of the following is the ionic compound formed between magnesium and chlorine?
   A) MgCl B) $MgCl_2$ C) Mg_2Cl_3 D) $MgCl_3$

6. Identify the condensed formula of the following structure:



A) $(CH_3)_2CHCHClCH(CH_3)_2$ C) $(CH_3)_2CHCHClC(CH_3)_3$
B) $CH_3CH(CH_3)CHClCH(CH_3)_2$ D) $(CH_3)_3CCHClCH(CH_3)_3$

7. What is the chemical formula of the following carbon skeleton diagram?

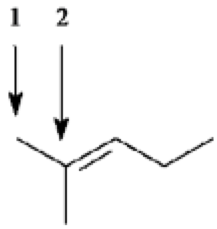


   A) C_8H_{14} B) C_8H_{16} C) C_8H_{18} D) C_8H_{20}

8. How many constitutional isomers of C4H9Br are possible?
   A) one B) two C) three D) four

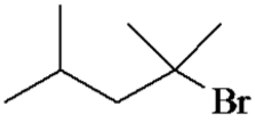
9. Which of the following molecules would you expect to have a dipole moment?
   I. CH2Cl2 II. CH3Cl III. CCl4
   A) only I B) only II C) I and II D) I, II, and III

10. How many hydrogen atoms are there on carbon atoms 1 and 2, respectively, in the structure below?



A) 4, 1 B) 4, 0 C) 3, 1 D) 3, 0

11. Which of the following best describes the relationship between the following two structures?



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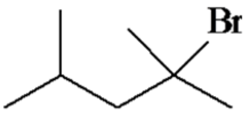
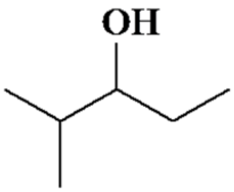


A) identical compounds
B) resonance structures
C) constitutional isomers
D) different compounds with different constitutions

12. Which of the following describes the relationship between the following two structures?



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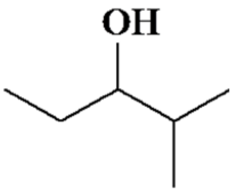
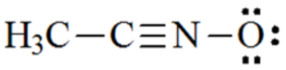


A) identical structures
B) resonance forms
C) constitutional isomers
D) different compounds with different compositions

13. The formal charges on the nitrogen and oxygen in the following structures are, respectively



$H_3C-C\equiv N-\ddot{\underset{\cdot\cdot}{O}}:$

A) +1, -1 B) 0, -1 C) +1, 0 D) 0, 0

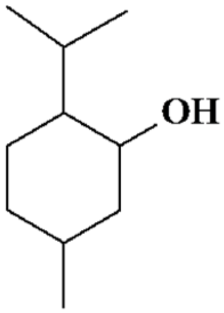
14. The hybridization of carbon atoms 1, 2, and 3 in the following are, respectively

$H_2C{=}CH{-}CH_3$

1 2 3

A) sp, sp, and sp^2 C) sp^2, sp^2, and sp^3
B) sp, sp, and sp^3 D) sp^2, sp^3, and sp^3

15. Give the molecular formula of the compound shown below:

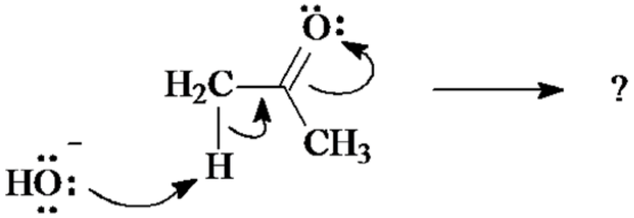


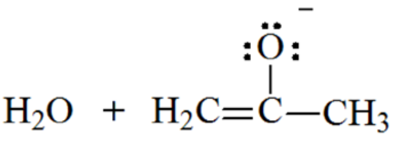
menthol (found in mint oils)

A) C8H16O B) C9H18O C) C10H18O D) C10H20O

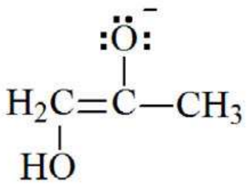
16. Which one of the following is the conjugate acid of ethanol?
A) $CH_3CH_2O^-$ B) $CH_3CH_2O^+$ C) $CH_3CH_2OH_2^+$ D) $CH_3CH_2OH_3^+$

17. Identify the species which results from the following movement of electron pairs.

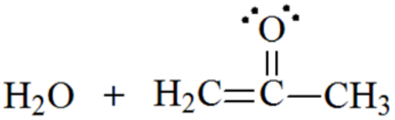


A) 

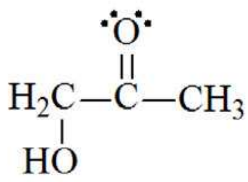
$H_2O + H_2C{=}\overset{:\ddot{O}:^-}{\overset{|}{C}}{-}CH_3$

C) 

$\underset{HO}{\overset{|}{H_2C}}{=}\overset{:\ddot{O}:^-}{\overset{|}{C}}{-}CH_3$

B) 

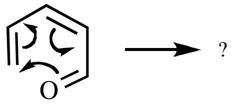
$H_2O + H_2C{=}\overset{\ddot{O}}{\overset{||}{C}}{-}CH_3$

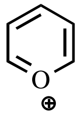
D) 

$\underset{HO}{\overset{|}{H_2C}}{-}\overset{\ddot{O}}{\overset{||}{C}}{-}CH_3$

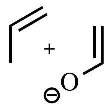
A) A B) B C) C D) D

18. What structure would result from these electron movement arrows?

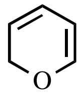




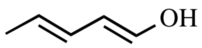
A



B



C

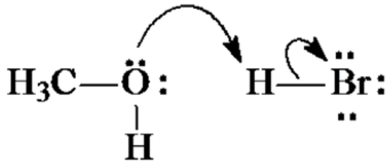


D

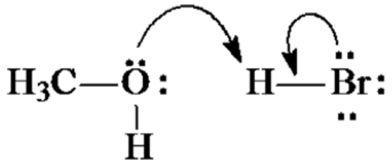
A) A B) B C) C D) D

19. Which one of the following mechanistically depicts the protonation of methanol by hydrogen bromide?

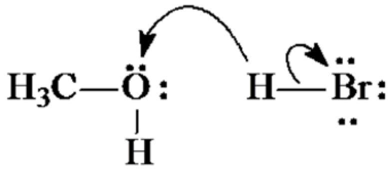
A)



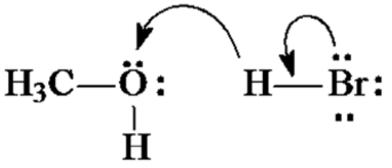
B)



C)



D)



A) A B) B C) C D) D

Answers: 1)B 2)A 3)D 4)D 5)B 6)C 7)C 8)D 9)C 10)D 11)A 12)A 13)A 14)C 15)D 16)C 17)A 18)C 19)A

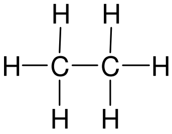
Chapter 2:
Alkanes and Cycloalkanes:
Introduction to Hydrocarbons

2.1 Classes of Hydrocarbons

Hydrocarbons are simple organic compound that contain only carbon and hydrogen.

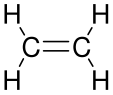
Hydrocarbons are divided into two main classes: aliphatic and aromatic.

- **Aliphatic** hydrocarbons (The word aliphatic was derived from the Greek word *aleiphar* meaning “fat”) include three major groups: alkane, alkene and alkyne.
    - Alkanes are hydrocarbons in which all of the bonds are *single* bonds.
    - Alkenes are hydrocarbons that contain a carbon-carbon *double* bond.
    - Alkynes are hydrocarbons that contain a carbon-carbon *triple* bond.



Ethane

(alkane)

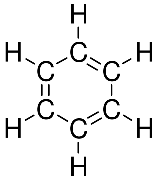


Ethene
or Ethylene
(alkene)

$H-C\equiv C-H$

Ethyne
or Acetylene
(alkyne)

- **Aromatic** hydrocarbons are also called arenes. Aromaticity is a chemical property in which a conjugated ring of unsaturated bonds, lone pairs or empty orbitals exhibit a stabilization stronger than would be expected due todelocalization and resonance. For the moment, the important point to remember is that the most common aromatic hydrocarbons are those that contain a benzene ring.



Benzene
(arene)

2.2 Electron Waves and Chemical Bonds

For a better understanding of covalent bonding, two additional theories will be introduced: The Valence Bond Model and the Molecular Orbital Model. Bonding in molecules can be explained on the basis of interactions between electron waves.

The Valence Bond Model bases the connection between two atoms on the overlap between half filled orbitals of the two atoms. The Molecular Orbital Model assembles a set of molecular orbitals by combining the atomic orbitals of <u>all</u> of the atoms in the molecule.

2.3 Bonding in H_2: The Valence Bond Model

Electron pair can be shared when half-filled orbital of one atom overlaps in phase with half-filled orbital of another.

A sigma bond (σ bond) is formed when orbitals overlap along the internuclear axis.

1. When the 1*s* orbitals of two separated hydrogen atoms are far apart, there is essentially no interaction. Each electron is associated with a single proton.
2. As the hydrogen atoms approach each other, their 1*s* orbitals begin to overlap and each electron begins to feel the attractive force of both protons.
3. When the hydrogen atoms are close enough so that appreciable overlap of the two 1*s* orbitals occurs, the concentration of electron density in the region between the two protons is more readily apparent.
4. A molecule of H_2 forms when the two hydrogen 1*s* orbitals have been replaced by a new orbital that encompasses both hydrogens and contains both electrons.

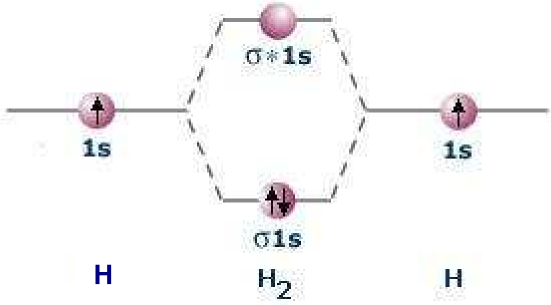
2.4 Bonding in H_2: The Molecular Orbital Model

The main idea is: electrons in a molecule occupy molecular orbitals (MOs) just as electrons in an atom occupy atomic orbitals (AOs).

The Molecular Orbital Method is illustrated by representing molecular orbitals as combinations of atomic orbitals (the Linear Combination of Atomic Orbitals-Molecular Orbital LCAO-MO). The additive combination generates a bonding orbital (sigma “ σ ” orbital), lower in energy than either of the original 1s orbitals. The subtractive combination generates an antibonding orbital (sigma star “ σ^* ” orbital), higher in energy than either of the original 1s orbitals.

There are two electrons per MO, just as two electrons per AO.

The MOs are expressed as combinations of AOs.



Anti-Bonding MO

Starting AOs

Bonding MO

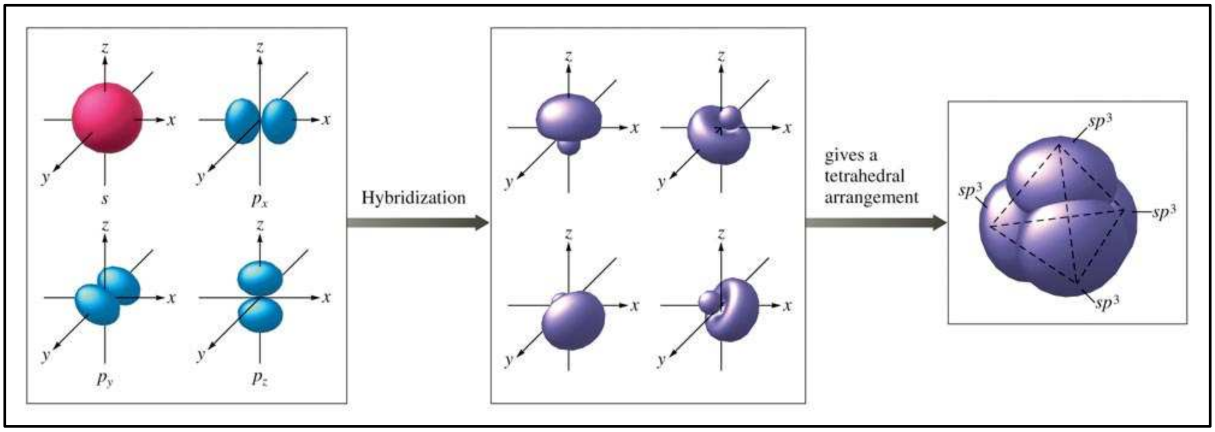
2.5 Introduction to Alkanes: Methane, Ethane, and Propane

Alkanes have the general molecular formula C_nH_{2n+2}. Simplest examples include:

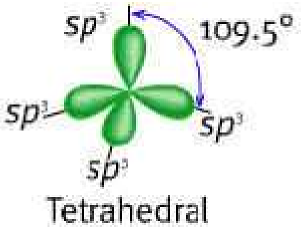
Methane	(CH_4)	CH_4	bp –160°C
Ethane	(C_2H_6)	CH_3CH_3	bp –89°C
Propane	(C_3H_8)	$CH_3CH_2CH_3$	bp –42°C

2.6 *sp^3* Hybridization and Bonding in Methane

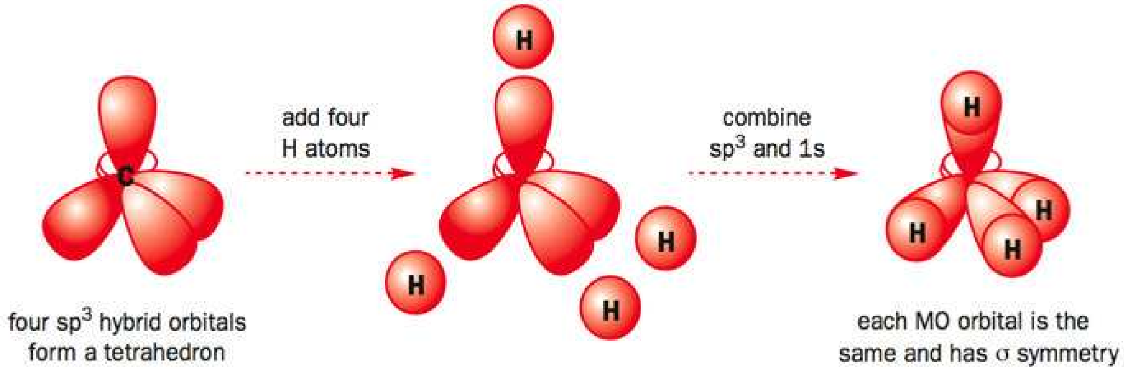
By mixing (or hybridizing) the 2*s*, 2p_x, 2p_y and 2p_z orbitals, four new orbitals are obtained. These four new orbitals are called sp^3 hybrid orbitals because they come from one *s* orbital and three *p* orbitals.



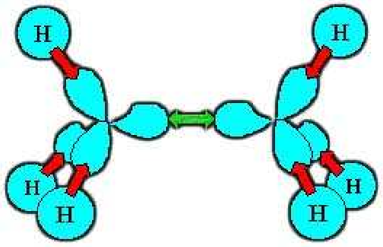
- All four sp^3 orbitals are of equal energy.
- The axes of the sp^3 orbitals point toward the corners of a tetrahedron.
- σ Bonds involving sp^3 hybrid orbitals of carbon are stronger than those involving unhybridized 2*s* or 2*p* orbitals.



When four Hydrogen atoms bind to a carbon atom, they form methane, which as a tetrahedral structure as shown below.



2.7 Bonding in Ethane



Ethane is formed by a carbon-carbon σ bond joining two CH_3 (methyl) groups. Each methyl group consists of an sp^3-hybridized carbon attached to three hydrogens by *sp^3*-1*s* σ bonds.

Each carbon has a tetrahedral geometry.

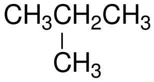
2.8 Isomeric Alkanes: The Butanes

Beginning with alkanes containing four carbon atoms (the butanes), constitutional isomers are possible. In the case of butanes (C_4H_{10}) two molecules have the same molecular formula but differ in connectivity.

n-Butane has four carbons joined together in a continuous chain. The *n* in *n*-butane stands for “normal” and means that the carbon chain is unbranched. On the other hand, isobutane has a branch carbon chain.

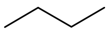
$CH_3CH_2CH_2CH_3$

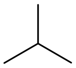
n-butane
(C_4H_{10})



$$\underset{\displaystyle CH_3}{CH_3\overset{}{C}H_2CH_3}$$

Isobutane
(C_4H_{10})





- All of the carbon atoms are sp^3 hybridized.
- All of the bonds are σ bonds.
- All the bond angles at carbon are close to tetrahedral.

This generalization holds for all alkanes regardless of the number of carbons they have.

2.9 Higher *n*-Alkanes

Formulas for higher *n*-alkanes can be abbreviated by indicating within parentheses the number of methylene groups in the chain.

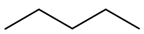
A **methylene** group is a CH_2 unit part of a chain (it cannot exist alone).
A **methine** group is a CH unit part of a chain (it cannot exist alone).

n-Alkanes have the general formula $CH_3(CH_2)_xCH_3$ and constitute a homologous series of compounds. A homologous series is one in which successive members differ by a methylene (—CH_2—) group.

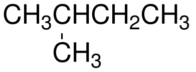
2.10 The C_5H_{12} Isomers

The number of isomeric alkanes increases as the number of carbons increase.
There is no simple way to predict how many isomers there are for a particular molecular formula.
It is also important to observe the molecule in 3D, to make sure that two molecules represented differently really are different.

n-pentane: $CH_3CH_2CH_2CH_2CH_3$ or $CH_3(CH_2)_3CH_3$ or

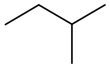


Isopentane:

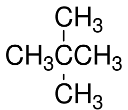


$$CH_3\underset{\displaystyle CH_3}{C}HCH_2CH_3$$

or $(CH_3)_2CHCH_2CH_3$ or

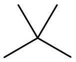


Neopentane:

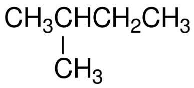


$$CH_3\overset{\displaystyle CH_3}{\underset{\displaystyle CH_3}{C}}CH_3$$

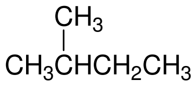
or $(CH_3)_4C$ or



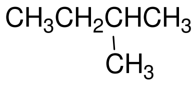
All these structures represent the same compound (isopentane). They are not isomers, they are identical compounds.



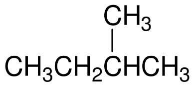
$\mathrm{CH_3\underset{CH_3}{\underset{|}{C}}HCH_2CH_3}$



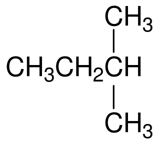
$\mathrm{CH_3\overset{CH_3}{\overset{|}{C}}HCH_2CH_3}$



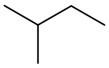
$\mathrm{CH_3CH_2\underset{CH_3}{\underset{|}{C}}HCH_3}$

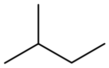


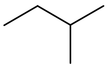
$\mathrm{CH_3CH_2\overset{CH_3}{\overset{|}{C}}HCH_3}$

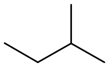


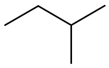
$\mathrm{CH_3CH_2\overset{CH_3}{\overset{|}{\underset{CH_3}{\underset{|}{C}}}}H}$











2.11 IUPAC Nomenclature of Unbranched Alkanes

Organic chemists have developed systematic ways to name compounds based on their structure. The most widely used approach is called the IUPAC rules. (IUPAC stands for International Union of Pure and Applied Chemistry).

Alkane names form the foundation of the IUPAC system; more complicated compounds are viewed as being derived from alkanes.

TABLE 2.2 IUPAC Names of Unbranched Alkanes

Number of carbon atoms	Name	Number of carbon atoms	Name	Number of carbon atoms	Name
1	Methane	11	Undecane	21	Henicosane
2	Ethane	12	Dodecane	22	Docosane
3	Propane	13	Tridecane	23	Tricosane
4	Butane	14	Tetradecane	24	Tetracosane
5	Pentane	15	Pentadecane	30	Triacontane
6	Hexane	16	Hexadecane	31	Hentriacontane
7	Heptane	17	Heptadecane	32	Dotriacontane
8	Octane	18	Octadecane	40	Tetracontane
9	Nonane	19	Nonadecane	50	Pentacontane
10	Decane	20	Icosane*	100	Hectane

Note: The *n*-prefix is not part of IUPAC name of any alkane. For example, *n*-butane is the "common name" for $CH_3CH_2CH_2CH_3$ and butane is the "IUPAC name" for the same molecule.

2.12 Applying the IUPAC Rules: The Names of the C_6H_{14} Isomers

IUPAC Rules for alkanes:

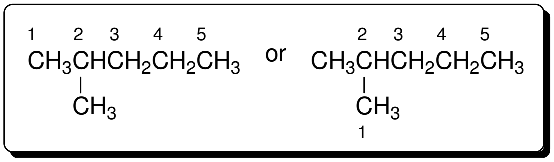
Step 1) Find the longest continuous carbon chain and use the IUPAC name of the unbranched alkane as the basis. The number of carbons must be linked together in an uninterrupted sequence.

Step 2) Identify the substituent groups attached to the parent chain.

Step 3) Number the chain from the end nearest the substituent, and identify the carbon to which the substituent is attached by number. In other words, number th longest continuous chain in the direction that gives the lowest number to the substituent group at the first point of branching.

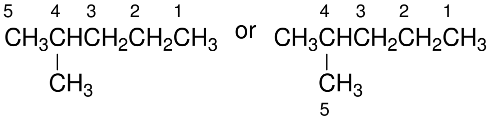
Step 4) The parent alkane is the last part of the name and is preceeded by the names of the substituent groups and their numerical locations (locants). Hyphens separate the locants from the words.

Example:



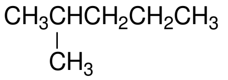
$\overset{1}{CH_3}\underset{\underset{CH_3}{|}}{\overset{2}{C}}H\overset{3}{CH_2}\overset{4}{CH_2}\overset{5}{CH_3}$ or $CH_3\underset{\underset{\underset{1}{CH_3}}{|}}{\overset{2}{C}}H\overset{3}{CH_2}\overset{4}{CH_2}\overset{5}{CH_3}$

not



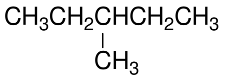
$\overset{5}{CH_3}\underset{\underset{CH_3}{|}}{\overset{4}{C}}H\overset{3}{CH_2}\overset{2}{CH_2}\overset{1}{CH_3}$ or $CH_3\underset{\underset{\underset{5}{CH_3}}{|}}{\overset{4}{C}}H\overset{3}{CH_2}\overset{2}{CH_2}\overset{1}{CH_3}$

Do not give two different names for the same molecule.



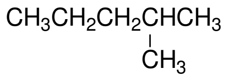
$CH_3\underset{\underset{CH_3}{|}}{C}HCH_2CH_2CH_3$

IUPAC name: 2-methylpentane



$CH_3CH_2\underset{\underset{CH_3}{|}}{C}HCH_2CH_3$

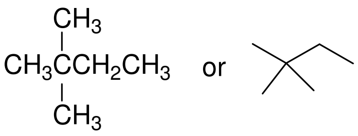
IUPAC name: 3-methylpentane



$CH_3CH_2CH_2\underset{\underset{CH_3}{|}}{C}HCH_3$

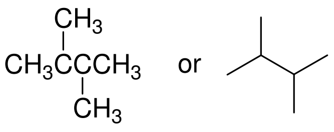
IUPAC name: 2-methylpentane

When the same substituent appears more than once, use replicating prefixes (di-, tri-, tetra-, etc.) according to the number of identical substituents attached to the main chain.



$CH_3\overset{\overset{CH_3}{|}}{\underset{\underset{CH_3}{|}}{C}}CH_2CH_3$

IUPAC name: 2,2-dimethylbutane



$CH_3\overset{\overset{CH_3}{|}}{C}\underset{\underset{CH_3}{|}}{C}CH_3$

IUPAC name: 2,3-dimethylbutane

2.13 Alkyl Groups

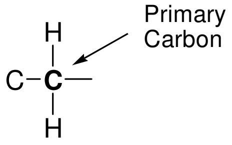
A methyl group (—CH_3) is an alkyl group derived from methane (CH_4). **Unbranched alkyl groups** in which the point of attachment is at the end of the chain are named in IUPAC nomenclature by replacing the *–ane* endings by *–yl.*

CH_3CH_2—	$CH_3(CH_2)_4CH_2$—	$CH_3(CH_2)_{14}CH_2$—
Ethyl group	**Hexyl** group	**Hexadecyl** group

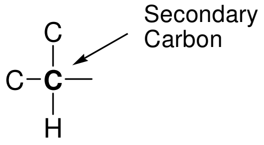
The dash line (—) at the end of the chain represents a potential point of attachment for some other atom.

Alkyl groups are designated as primary, secondary, or tertiary according to the degree of substitution of the carbon at the potential point of attachment.

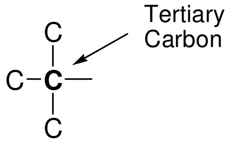
A **primary** carbon is directly attached to **one** other carbon.
A **secondary** carbon is directly attached to **two** other carbons.
A **tertiary** carbon is directly attached to **three** other carbons.
A **quaternary** carbon is directly attached to **four** other carbons.



Primary alkyl group



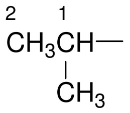
Secondary alkyl group



Tertiary alkyl group

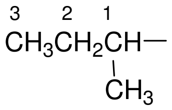
Branched alkyl groups are named by using the longest continuous chain **that begins at the point of attachment** as the base name.

So *iso*propyl (which is a common name) is actually a 1-methylethyl group.



$$\overset{2}{\mathrm{CH_3}}\underset{\mathrm{CH_3}}{\overset{1}{\mathrm{CH}}}\text{—}$$

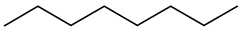
The same goes for *sec*-butyl (which is a common name); it is a 1-methylpropyl group.



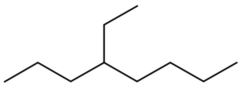
$$\overset{3}{\mathrm{CH_3}}\overset{2}{\mathrm{CH_2}}\underset{\mathrm{CH_3}}{\overset{1}{\mathrm{CH}}}\text{—}$$

2.14 IUPAC Names of Highly Branched Alkanes

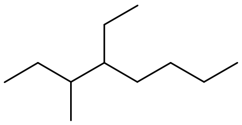
By combining the basic principles of IUPAC notation with the names of the various alkyl groups, we can develop systematic names for highly branched alkanes. Look at the example below to understand the steps of the process.



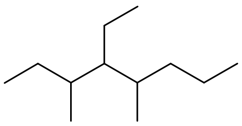
octane



4-Ethyloctane



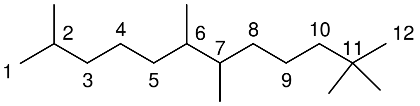
4-Ethyl-3-methyloctane



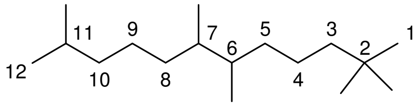
4-Ethyl-3,5-dimethyloctane

List the substituents in alphabetical order, but don't alphabetize di-, tri-, tetra-, etc.

An additional feature of IUPAC nomenclature that concerns the direction of numbering is the “first point of difference” rule. The chain must be numbered in the direction that gives the lower locant to the substituent at the first point of difference in the names.



2,6,7,11,11-pentamethyldodecane
NOT good

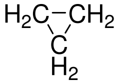


2,2,6,7,11-pentamethyldodecane
GOOD

2.15 Cycloalkane Nomenclature

Cycloalkanes are alkanes that contain a ring of three or more carbons.

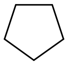
Cycloalkanes are named, under the IUPAC system, by adding the prefix cyclo- to the name of the unbranched alkane with the same number of carbons as the ring. They are characterized by the molecular formula C_nH_{2n}.



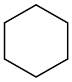
usually
represented
as

cyclopropane

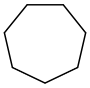
cyclobutane



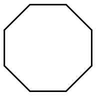
cyclopentane



cyclohexane

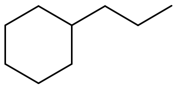


cycloheptane

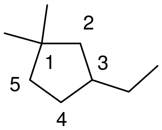


cyclooctane

Substituent groups are identified in the usual way. Their positions are specified by numbering the carbon atoms of the ring in the direction that gives the lowest number to the substituent at the first point of difference.

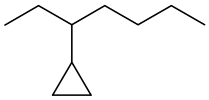


propylcyclohexane



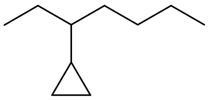
3-ethyl-1,1-dimethylcyclopentane

When the ring contains fewer carbon atoms than an alkyl group attached to it, the compound is named an alkane, and the ring is treated as a cycloalkyl substituent. But this rule is often not respected.



3-cyclopropylheptane

and
not



(heptan-3-yl)cyclopropane

2.16 Sources of Alkanes and Cycloalkanes

Main source: Petroleum.

2.17 Physical Properties of Alkanes and Cycloalkanes

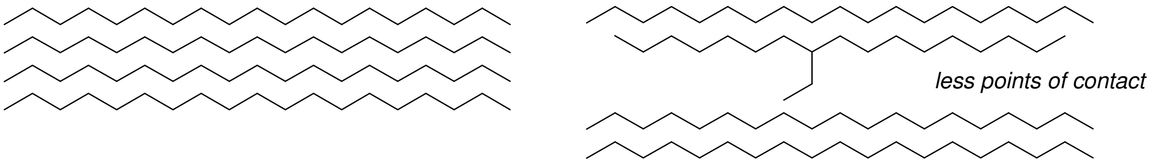
Boiling point - Melting point - Solubility in water

Boiling points are governed by strength of intermolecular attractive forces. Alkanes are nonpolar, so *dipole-dipole* and *dipole-induced dipole* forces are absent. Only forces of intermolecular attraction are *induced dipole-induced dipole* forces.

In order to vaporize a substance, enough energy must be added to overcome the intermolecular forces (the van der Waals forces).

Extended assemblies of *induced dipole-induced dipole* attractions can accumulate to give substantial intermolecular attractive forces. An alkane with a **higher molecular weight has** more atoms and electrons and, therefore, more opportunities for intermolecular attractions and **a higher boiling point than one with a lower molecular weight**.

On the other hand, branched alkanes have lower boiling points than their unbranched isomers. Isomers have, of course, the same number of atoms and electrons, but a molecule of a branched alkane has a smaller surface area than an unbranched one. The extended shape of an unbranched alkane permits more points of contact for intermolecular associations.



Induced dipole-induced dipole attractions are very weak forces individually, but there are so many in typical organic substances that they sum up to be important. They are the only forces of attraction possible between nonpolar molecules such as alkanes.

Melting points: The same induced dipole-induced dipole interactions that operate between molecules in the liquid, also operate in the solid form. Its just the degree of organization that is different.

Solubility in water: “Oil and water don’t mix”. Alkanes are virtually insoluble in water. The exclusion of nonpolar molecules, such as alkanes, from water is called the hydrophobic effect.

2.18 Chemical Properties: Combustion of Alkanes

Alkanes have a low level of reactivity. Essentially inert in acid-base reactions, they participate in oxidation-reduction reactions as the compound that undergoes oxidation.

Burning in the air (combustion) of hydrocarbons is exothermic and gives carbon dioxide and water as the products. The heat released on combustion of a substance is called its heat of combustion. The heat of combustion is equal to $-\Delta H°$ for the reaction written in the direction shown:

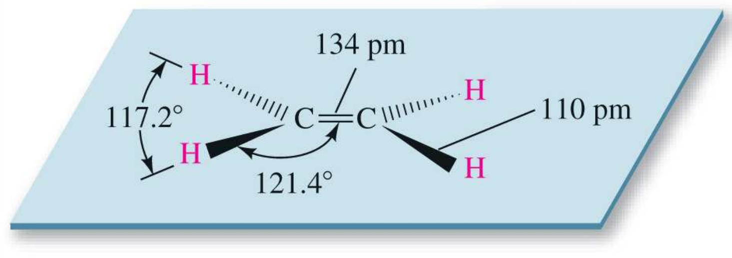
$$\Delta H° = \Delta H°\text{products} - \Delta H°\text{reactants}$$

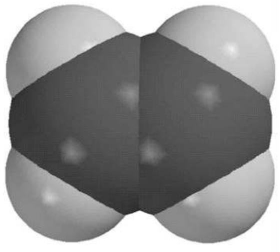
Where H° is the heat content, or enthalpy, of a compound in its standard state. In an exothermic process, the enthalpy of the products is less than that of the starting materials, and ΔH° is a negative number.

$$(CH_3)_2CHCH_2CH_2CH_2CH_3 + 11\ O_2 \rightarrow 7\ CO_2 + 8\ H_2O \qquad \Delta H° = 4812\ kJ$$

The heat evolved on burning an alkane increases with the number of carbon atoms.
The relative stability of isomers may be determined by comparing their respective heats of combustion.
The more stable of two isomers has the lower heat of combustion.

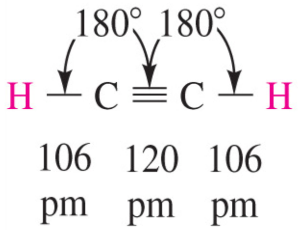
2.20 *sp*^{2} Hybridization and Bonding in Ethylene

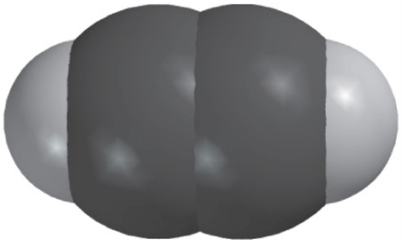




The carbon-carbon bond of ethylene is viewed as a combination of **a σ bond plus a π bond**. Each carbon is hybridized *sp*^{2} and forms a total of 3 σ bonds.

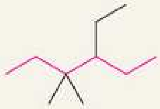
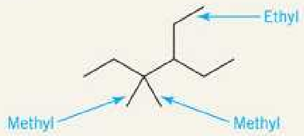
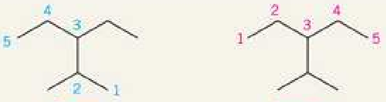
2.21 *sp* Hybridization and Bonding in Acetylene





The carbon-carbon bond of acetylene is viewed as a combination of **a σ bond plus two π bond**. Each carbon is hybridized *sp* and forms a total of 2 σ bonds.

TABLE 2.5 Summary of IUPAC Nomenclature of Alkanes and Cycloalkanes

Rule	Example
A. Alkanes **1.** Find the longest continuous chain of carbon atoms, and assign a basis name to the compound corresponding to the IUPAC name of the unbranched alkane having the same number of carbons.	The longest continuous chain in the alkane shown is six carbons.  This alkane is named as a derivative of hexane.
2. List the substituents attached to the longest continuous chain in alphabetical order. Use the prefixes *di-*, *tri-*, *tetra-*, and so on, when the same substituent appears more than once. Ignore these prefixes when alphabetizing.	The alkane bears two methyl groups and an ethyl group. It is an *ethyldimethylhexane*. 
3. Number from the end of the chain in the direction that gives the lower locant to a substituent at the first point of difference.	When numbering from left to right, the substituents appear at carbons 3, 3, and 4. When numbering from right to left the locants are 3, 4, and 4; therefore, number from left to right.  Correct Incorrect The correct name is *4-ethyl-3,3-dimethylhexane*.
4. When two different numbering schemes give equivalent sets of locants, choose the direction that gives the lower locant to the group that appears first in the name.	In the following example, the substituents are located at carbons 3 and 4 regardless of the direction in which the chain is numbered.  Correct Incorrect Ethyl precedes methyl in the name; therefore *3-ethyl-4-methylhexane* is correct.
5. When two chains are of equal length, choose the one with the greater number of substituents as the parent. (Although this requires naming more substituents, the substituents have simpler names.)	Two different chains contain five carbons in the alkane:  Correct Incorrect The correct name is *3-ethyl-2-methylpentane* (disubstituted chain), rather than 3-isopropylpentane (monosubstituted chain). *Continued*

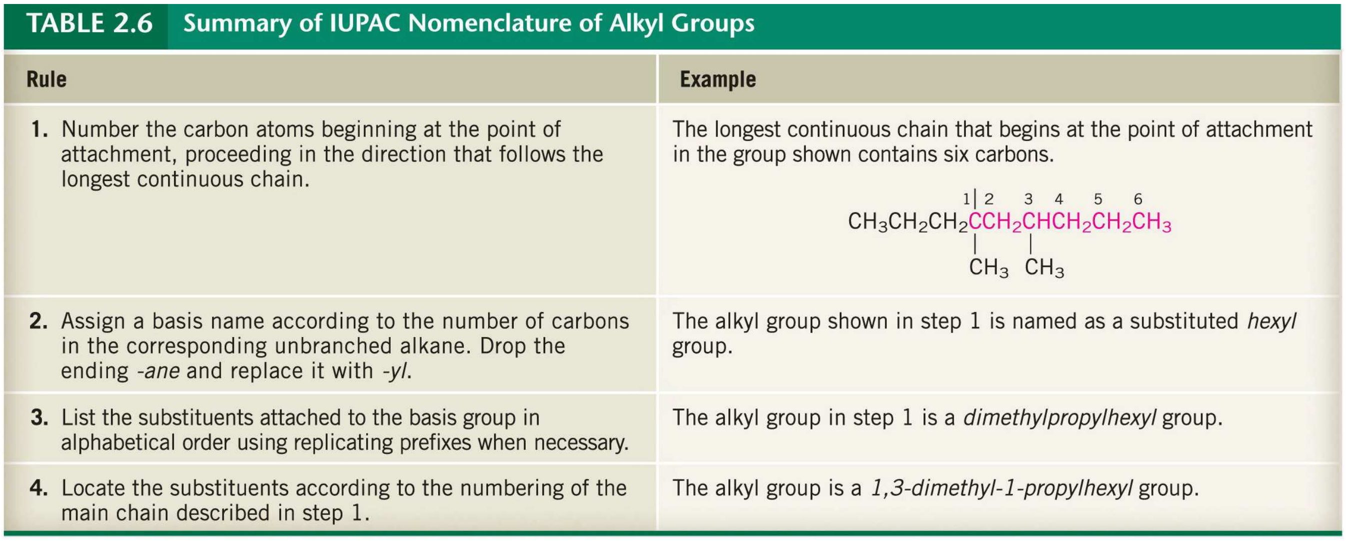


TABLE 2.6 Summary of IUPAC Nomenclature of Alkyl Groups

Rule	Example
1. Number the carbon atoms beginning at the point of attachment, proceeding in the direction that follows the longest continuous chain.	The longest continuous chain that begins at the point of attachment in the group shown contains six carbons. $\mathrm{CH_3CH_2CH_2\overset{1\,|}{\underset{CH_3}{C}}\overset{2}{C}H_2\overset{3}{\underset{CH_3}{C}}H\overset{4}{C}H_2\overset{5}{C}H_2\overset{6}{C}H_3}$
2. Assign a basis name according to the number of carbons in the corresponding unbranched alkane. Drop the ending *-ane* and replace it with *-yl*.	The alkyl group shown in step 1 is named as a substituted *hexyl* group.
3. List the substituents attached to the basis group in alphabetical order using replicating prefixes when necessary.	The alkyl group in step 1 is a *dimethylpropylhexyl* group.
4. Locate the substituents according to the numbering of the main chain described in step 1.	The alkyl group is a *1,3-dimethyl-1-propylhexyl* group.

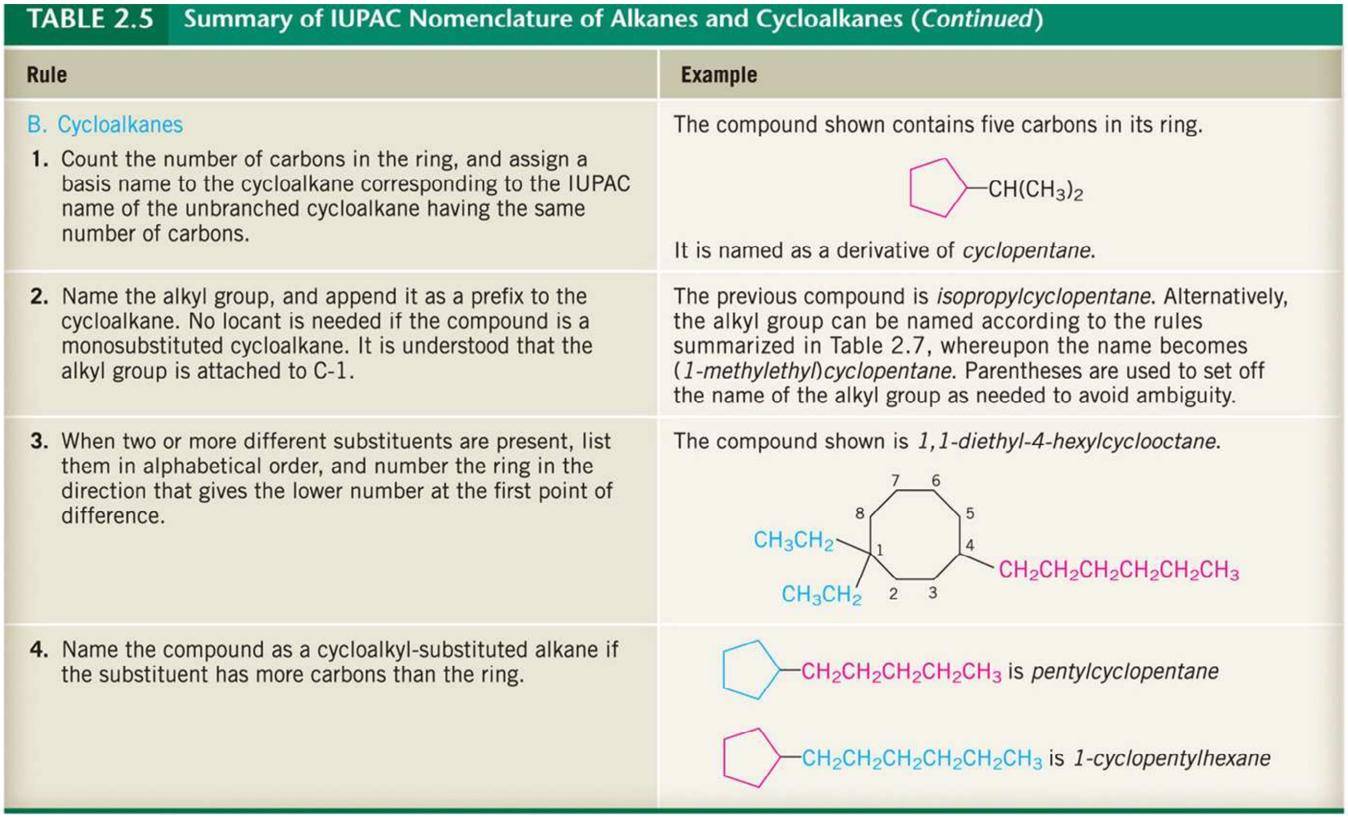


TABLE 2.5 Summary of IUPAC Nomenclature of Alkanes and Cycloalkanes (*Continued*)

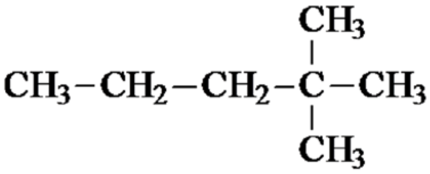
Rule	Example
B. Cycloalkanes **1.** Count the number of carbons in the ring, and assign a basis name to the cycloalkane corresponding to the IUPAC name of the unbranched cycloalkane having the same number of carbons.	The compound shown contains five carbons in its ring. —$\mathrm{CH(CH_3)_2}$ It is named as a derivative of *cyclopentane*.
2. Name the alkyl group, and append it as a prefix to the cycloalkane. No locant is needed if the compound is a monosubstituted cycloalkane. It is understood that the alkyl group is attached to C-1.	The previous compound is *isopropylcyclopentane*. Alternatively, the alkyl group can be named according to the rules summarized in Table 2.7, whereupon the name becomes (*1-methylethyl*)*cyclopentane*. Parentheses are used to set off the name of the alkyl group as needed to avoid ambiguity.
3. When two or more different substituents are present, list them in alphabetical order, and number the ring in the direction that gives the lower number at the first point of difference.	The compound shown is *1,1-diethyl-4-hexylcyclooctane*. $\mathrm{CH_3CH_2}$ $\mathrm{CH_3CH_2}$ 1 2 3 4 5 6 7 8 $\mathrm{CH_2CH_2CH_2CH_2CH_2CH_3}$
4. Name the compound as a cycloalkyl-substituted alkane if the substituent has more carbons than the ring.	—$\mathrm{CH_2CH_2CH_2CH_2CH_3}$ is *pentylcyclopentane* —$\mathrm{CH_2CH_2CH_2CH_2CH_2CH_3}$ is *1-cyclopentylhexane*

Extra Problems:

1. Alkanes are characterized by the general molecular formula:
   A) C_nH_{2n-2} B) C_nH_{2n} C) C_nH_{2n+2} D) C_nH_{2n+4}

2. Cycloalkanes are characterized by the general molecular formula:
   A) C_nH_{2n-2} B) C_nH_{2n} C) C_nH_{2n+2} D) C_nH_{2n+4}

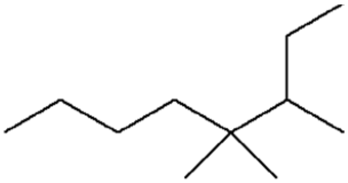
3. What is the IUPAC name of the following compound?



$$CH_3-CH_2-CH_2-\overset{\overset{\displaystyle CH_3}{|}}{\underset{\underset{\displaystyle CH_3}{|}}{C}}-CH_3$$

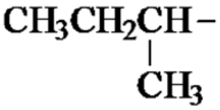
   A) 4,4-dimethylpentane C) 2,2-dimethylpentane
   B) 1-tert-butylpropane D) 1,1,1-trimethylbutane

4. The correct IUPAC name of the following compound is



   A) 2-ethyl-3,5-dimethylheptane. C) 3,4,4-trimethyloctane.
   B) 6-ethyl-5,5-dimethylheptane. D) 5,5,6-trimethyloctane.

5. The common name of the following group is

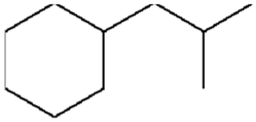


$$CH_3CH_2\underset{\underset{\displaystyle CH_3}{|}}{CH}-$$

   A) *n*-butyl. B) *sec*-butyl. C) isobutyl. D) *tert*-butyl.

6. Which one of the following is 2,2,5-trimethylhexane?
   A) $(CH_3)_2CHCH_2C(CH_3)_3$ C) $CH_3CH_2CH(CH_3)C(CH_3)_3$
   B) $(CH_3)_2CHCH_2CH_2C(CH_3)_3$ D) $(CH_3)_2CHCH_2\ CH_2CH_2C(CH_3)_3$

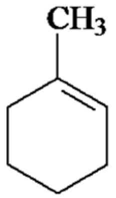
7. The correct name of the following compound is



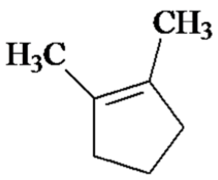
   A) (1-methylpropyl)cyclohexane. C) (2,2-dimethylethyl)cyclohexane.
   B) (2-methylpropyl)cyclohexane. D) (2,2-dimethylpropyl)cyclohexane.

8. The boiling point of isobutane (-10.2°C) is lower than n-butane (-0.4°C) because isobutane has
A) weaker intermolecular van der Waals forces.
B) stronger intermolecular van der Waals forces.
C) weaker dipole-dipole attractive forces.
D) stronger dipole-dipole attractive forces.

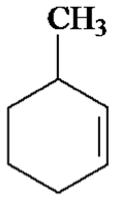
9. Which of the following are constitutional isomers?



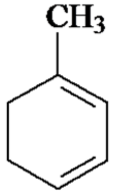
I



II



III

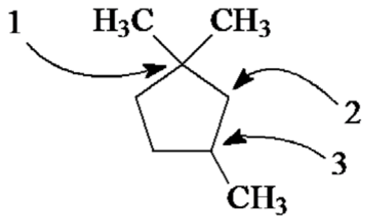


IV

A) I, II, and III
B) I, III, and IV
C) only I and III
D) all are constitutional isomers

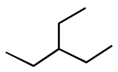
10. Arrange the following isomeric alkanes in order of increasing boiling point.
I. *n*-heptane
II. 2,3-dimethylpentane
III. 2,2,3-trimethylbutane
A) I < II < III B) II < III < I C) III < I < II D) III < II < I

11. Carbon atoms 1, 2, and 3 in the following structure are classified, respectively, as

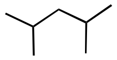


A) tertiary, primary, secondary.
B) quaternary, primary, tertiary.
C) quaternary, secondary, secondary .
D) quaternary, secondary, tertiary.

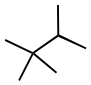
12. The lowest-boiling isomer of C7H16 would be



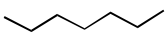
A



B



C



D

A) A B) B C) C D) D

Answers: 1)C 2)B 3)C 4)C 5)B 6)B 7)B 8)A 9)A 10)D 11)D 12)C

Chapter 3:
Alkanes and Cycloalkanes:
Conformation and cis-trans Stereoisomers

3.1 Conformational Analysis of Ethane

Conformations are different spatial arrangements of a molecule that are generated by rotation about single bonds

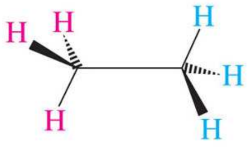
Conformational analysis is the study of how conformational factors affect the structure of a molecule and its properties.

Ethane is the simplest hydrocarbon that can have distinct conformations: staggered conformation and eclipsed conformation. The staggered and eclipsed conformations interconvert by rotation around the C-C bond, and do so very rapidly.

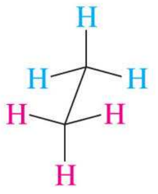
In the **staggered conformation**, each C—H bond of one carbon bisects an H—C—H angle of the other carbon.
In the **eclipsed conformation**, each C—H bond of one carbon is aligned with a C—H bond of the other carbon.

There are 3 useful drawing methods to represent these phenomenons: the wedge-and-dash, sawhorse and Newman projection drawings.

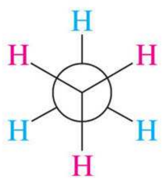
Staggered conformation of ethane



(*a*) Wedge-and-dash

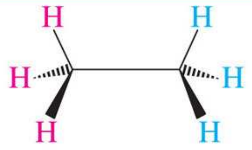


(*b*) Sawhorse

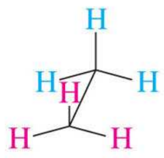


(*c*) Newman projection

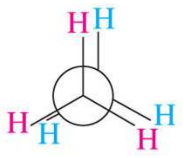
Eclipsed conformation of ethane



(*a*) Wedge-and-dash



(*b*) Sawhorse



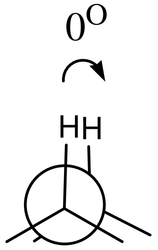
(*c*) Newman projection

In the **wedge-and-dash** drawings
— : represents a bond in the plane of the paper
▬ : represents a bond in front of the plane of the paper
┆┆┆ : represents a bond behind the plane of the paper

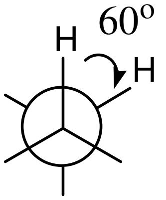
The **sawhorse** drawings show the conformation of a molecule without having to resort to different styles of bonds.

In the **Newman projection**, we sight down the C—C bond, and represent the front carbon by a point and the back carbon by a circle. Each carbon has three other bonds that are placed symmetrically around it.

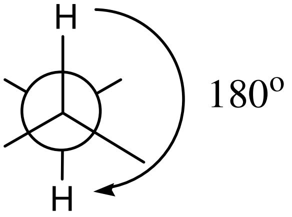
The torsion angle of the H—C—C—H unit in ethane is easily seen in a Newman projection.



Torsion angle: 0°
Eclipsed



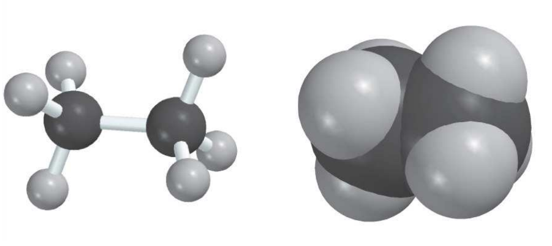
Torsion angle: 60°
Gauche



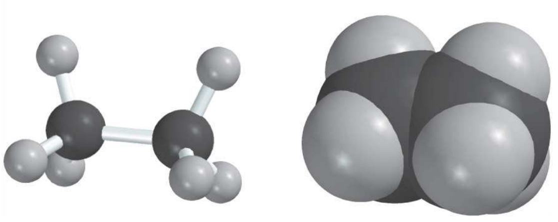
Torsion angle : 180°
Anti

When the torsion angle is approximately 60°, the spatial relationship is gauche.
When the torsion angle is 180°, the spatial relationship is anti.
(Staggered conformations have only gauche or anti relationships between bonds on adjacent atoms.)

Staggered conformation of ethane



Eclipsed conformation of ethane



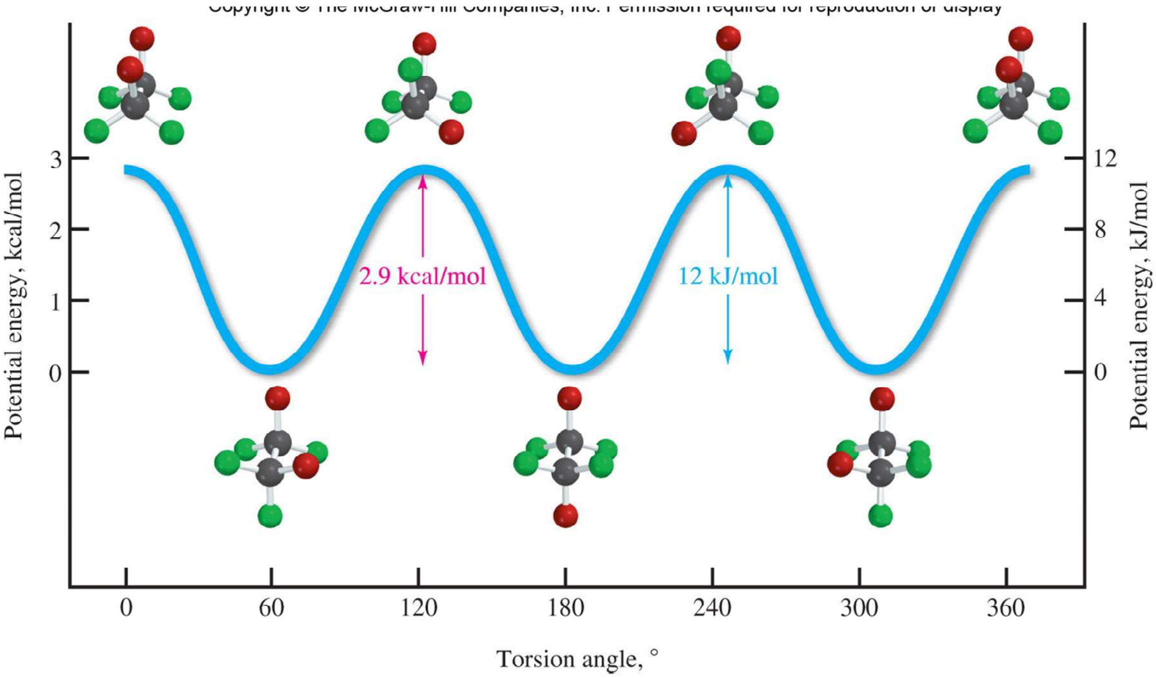
The staggered conformation is the most stable conformation; the eclipsed is the least stable conformation.

Repulsions between bonds on adjacent atoms destabilize the eclipsed conformation.

Better electron delocalization stabilizes the staggered conformation.

Conformations in which the torsion angles between adjacent bonds are other than 60° are said to have torsional strain. Eclipsed bonds produce the most torsional strain; staggered bond none.

Potential energy diagram for rotation about the carbon-carbon bond in ethane:



For one staggered conformation to get to the next, it must first pass through an eclipsed conformation and needs to gain 12kJ/mol of energy to reach it. This amount of energy is called the **Activation Energy** (E_{act}).

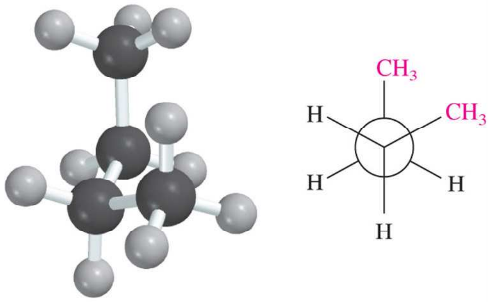
The point of maximum potential energy encountered by the reactants as they proceed to products is called the **transition state**.

Rotation around carbon-carbon bonds is one of the fastest processes in chemistry. Increase of temperature produces an increase in the rate of a typical chemical process.

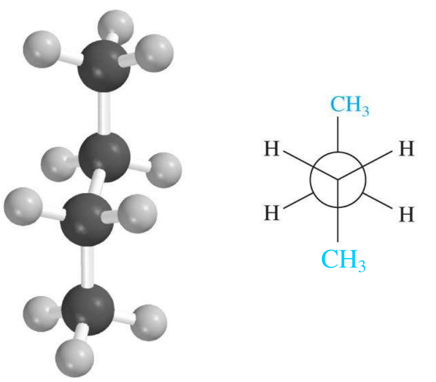
3.2 Conformational Analysis of Butane

The destabilization of a molecule that results when two of its atoms are too close to each other is called **van der Waals strain**, or **steric hindrance**, and contributes to the total steric strain. In the case of butane, van der Waals strain makes the gauche conformation less stable than the anti.

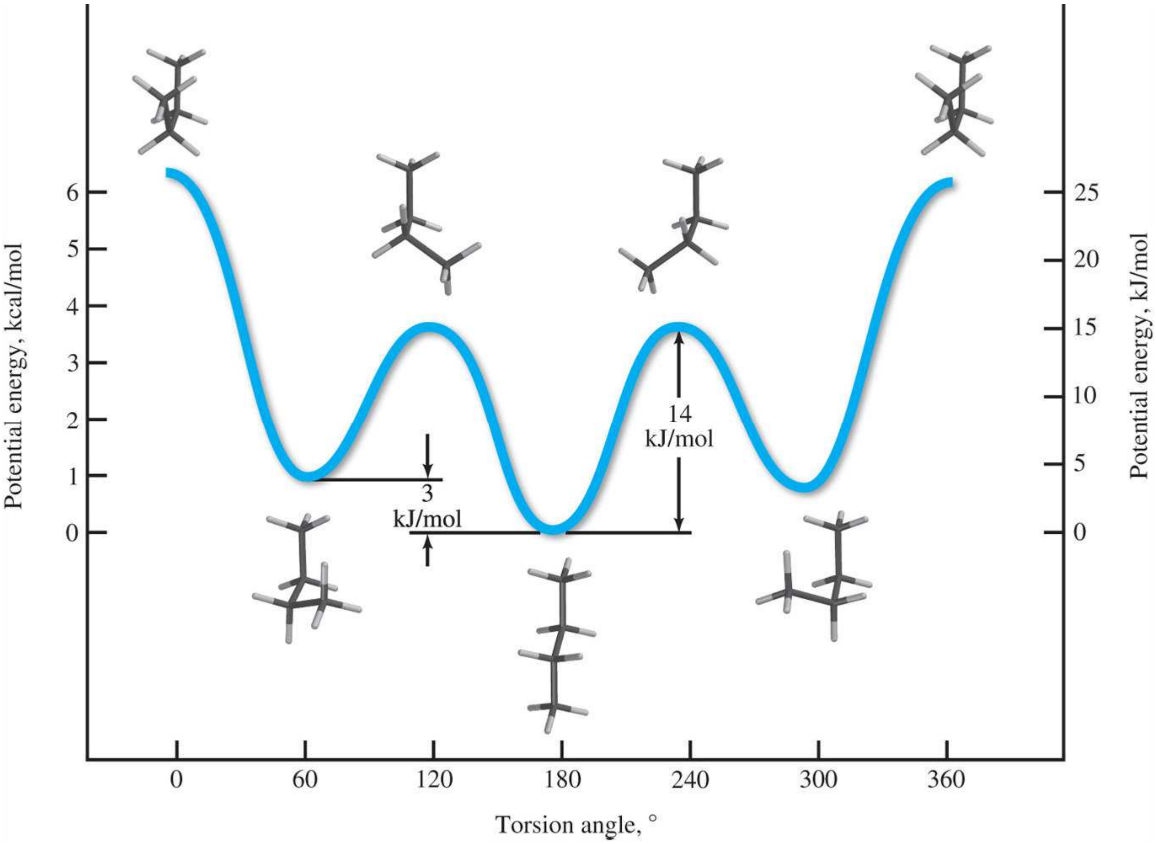
Gauche Conformation



Anti Conformation



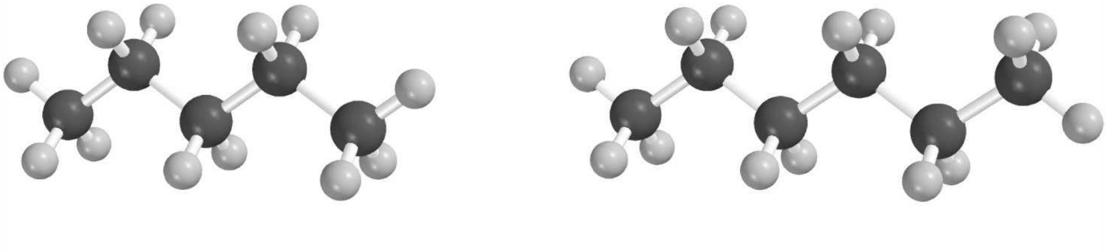
Potential energy diagram for the rotation around the central carbon-carbon bond in butane.



3.3 Conformations of Higher Alkanes

Higher alkanes having unbranched carbon chains are most stable in their all-anti conformations.

In depicting the conformations of higher alkanes it is often more helpful to look at them from the side rather than end-on as in Newman projection.


Pentane
Hexane

3.4 The Shapes of Cycloalkanes: Planar or Nonplanar?

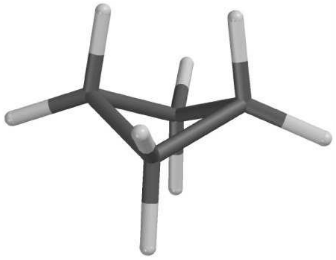
Angle strain is the strain a molecule has because one or more of its bond angles deviate from the ideal value. In the case of alkanes, the ideal value is 109.5°.

With the exception of cyclopropane, cycloalcanes are nonplanar.

3.5 Small Rings: Cyclopropane and Cyclobutane

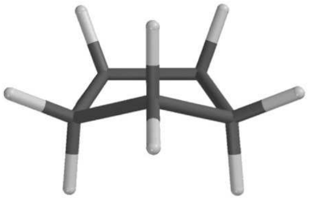
Cyclopropane is planar and destabilized by angle strain and torsional strain.
Cyclobutane is nonplanar and less strained than cyclopropane.

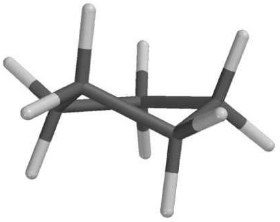

Cyclopropane


Cyclobutane

3.6 Cyclopentane

Cyclopentane has two nonplanar conformations that are of similar stability: the envelope and the half-chair.

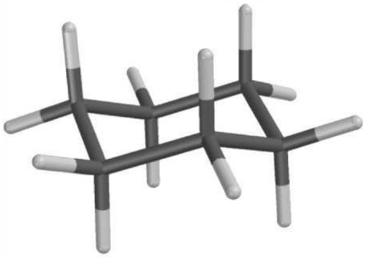

Envelope conformation of cyclopentane


Half-chair conformation of cyclopentane

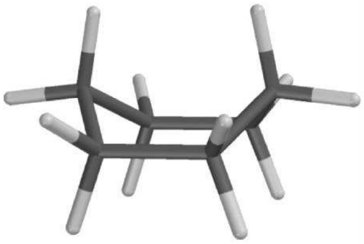
3.7 Conformations of Cyclohexane

Three conformations of cyclohexane have approximately tetrahedral angles at carbon: the chair, the boat, and the skew boat.

The chair conformation of cyclohexane is the most stable conformation and derivatives of cyclohexane almost always exist in the chair conformation.


Chair


Skew boat

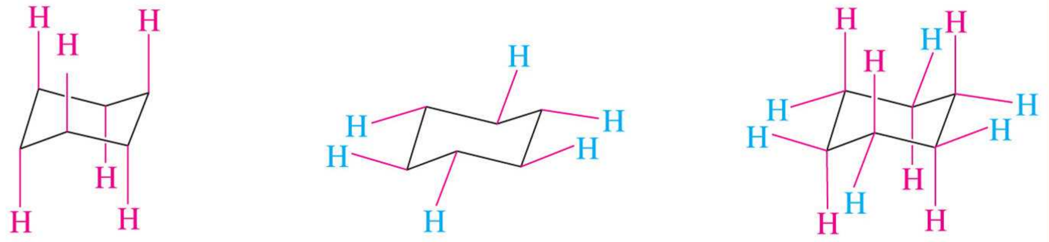

Boat

3.8 Axial and Equatorial Bonds in Cyclohexane

Hydrogens atoms in cyclohexane can be divided into two groups: the axial and equatorial.

Axial hydrogens have their bonds parallel to a vertical axe that passes through the ring's center.

Equatorial hydrogens are located along the equator of the molecule.



Axial C—H bonds

Equatorial C—H bonds

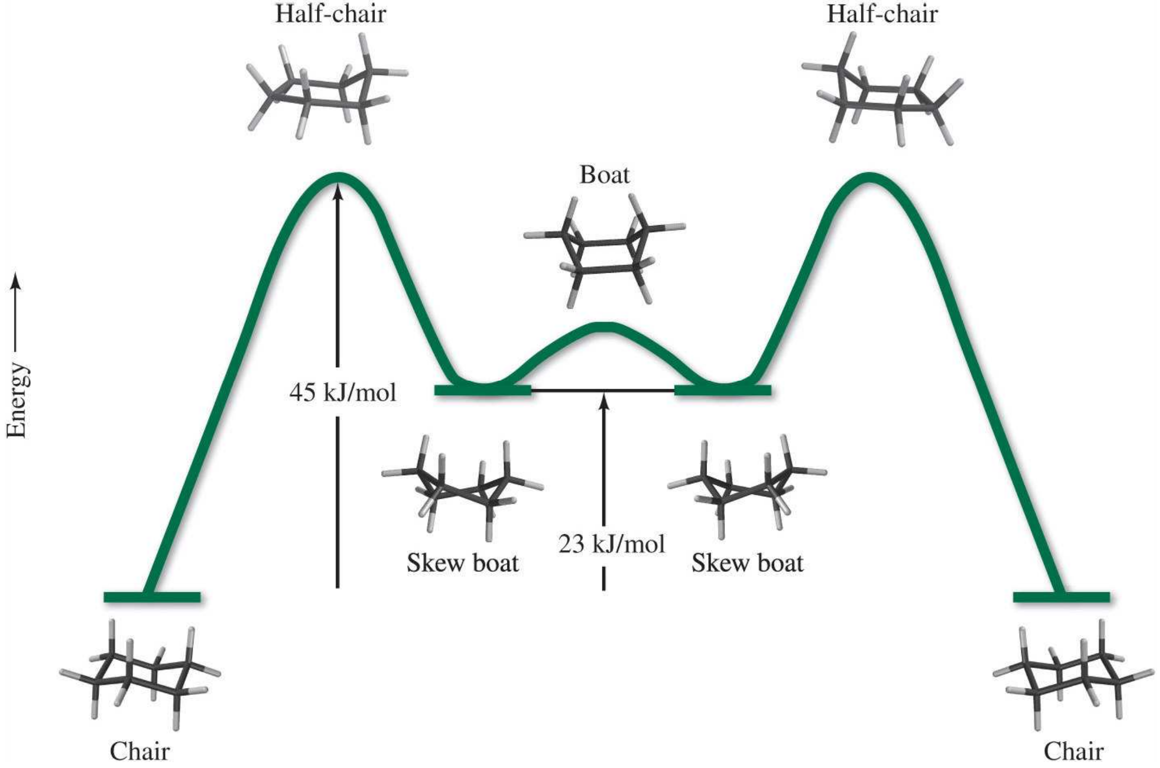
Axial and equatorial bonds together

3.9 Conformational Inversion in Cyclohexane

Alkanes are not locked into a single conformation. Rotation around the central carbon-carbon bond in butane occurs rapidly, interconverting anti and gauche conformations.

Cyclohexane is also conformationally mobile. Through a process known as **ring inversion**, **chair-chair interconversion**, or **ring flipping**, one chair conformation is converted to another chair. The skew boat must be seen as an intermediate in the ring flipping process.

The most important result of ring inversion is that any substituent that is axial in the original chair conformation becomes equatorial in the ring-flipped form and vice versa.



3.10 Conformational Analysis of Monosubstituted Cyclohexanes

The most stable conformation is chair.
A substituent is more stable when it is in an equatorial conformation.

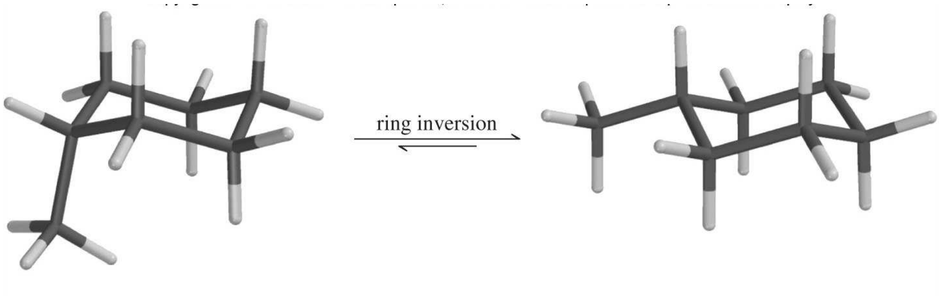
When two conformations of a molecule are in equilibrium with each other, the one with the lower free energy predominates. The reason equatorial methylcyclohexane is more stable than axial methylcyclohexane is because a methyl group is less crowded when it is equatorial than when it is axial.

An axial substituent is said to be crowded because of **1,3-diaxial repulsions** between itself and the other two axial substituents located on the same side of the ring.

Two chair conformation exist in rapid equilibrium, and the one in which the substituent is equatorial is more stable.

A branched alkyl group such as isopropyl exhibits a greater preference for the equatorial orientation than does methyl.

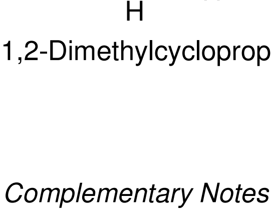
A tert-butyl group is so large that tert-butyl cyclohexane exists almost entirely in the conformation in which the tert-butyl group is equatorial.



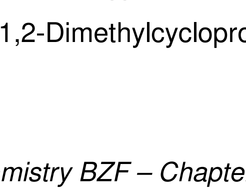
Methyl group axial (less stable) Methyl group equatorial (more stable)

3.11 Disubstituted Cycloalkanes: cis-trans Stereoisomers

When a cycloalkane bears two substituents on different carbons (methyl groups for example), these substituents may be on the same or on opposite sides of the ring. When substituents are on the same side, we say they are **cis** to each other. If they are on opposite sides, we say they are **trans** to each other.



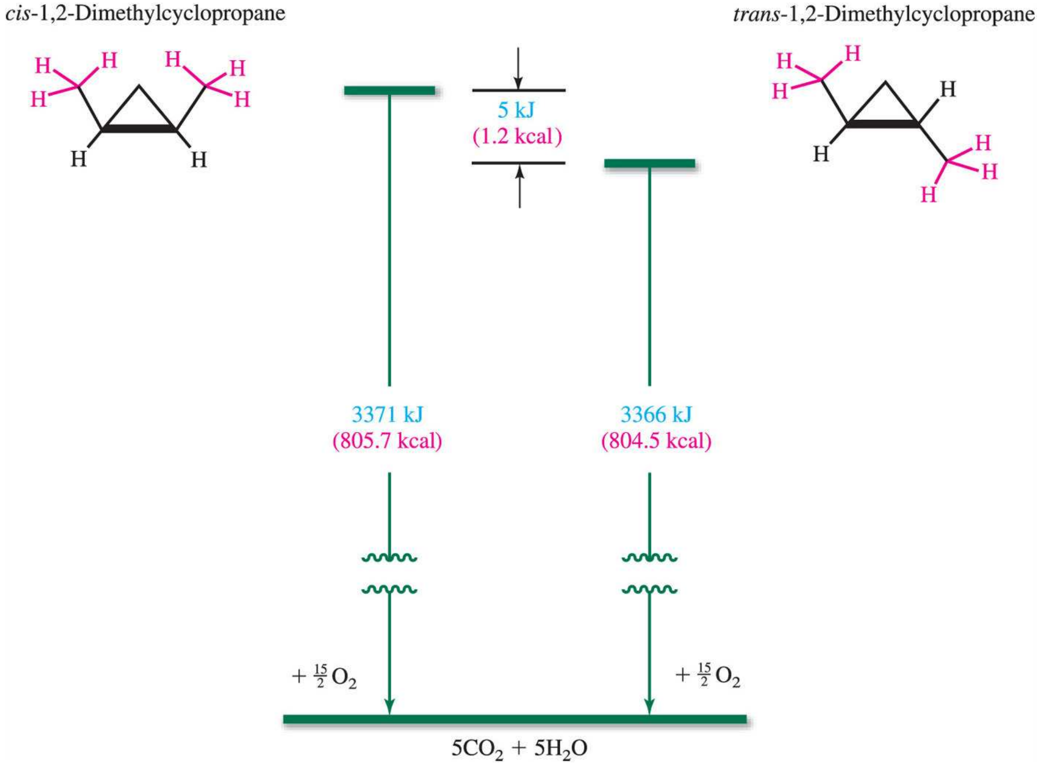
cis-1,2-Dimethylcyclopropane



trans-1,2-Dimethylcyclopropane

Recall that Stereoisomers are isomers that have same constitution but different arrangement of atoms in space. The cis and trans forms of 1,2-dimethylcyclopropane are stereoisomers.

The methyl groups on the same side of the ring in cis-1,2-dimethyl cyclopropane crowd each other and increase the potential energy of this stereoisomer. Steric hindrance between methyl groups is absent in trans-1,2-dimethylcyclopropane.



3.12 Conformational Analysis of Disubstituted Cyclohexanes

For an extensive view of all possibilities, please refer directly to the textbook.

The trans is more stable than the cis stereoisomer.

Cis-1,4-dimethylcyclohexane can adopt either of two equivalent chair conformations, each having one axial methyl group and one equatorial methyl group. The two are in rapid equilibrium with each other by ring flipping. The equatorial methyl group becomes axial, and the axial methyl group becomes equatorial.

Ring flipping does not alter the cis relationship between the methyl groups. Nor does it alter their up-versus down quality; substituents that are up in one conformation remain up in the ring flipped form.

The most stable conformation of trans-1,4-dimethylcyclohexane has both methyl groups in equatorial orientations.

In the same manner, the most stable conformation of cis-1,3-dimethylcyclohexane has both methyl groups equatorial.

If a disubstituted cyclohexane has two different substituents, then the most stable conformation is the chair that has the larger substituent in an equatorial orientation.

Conformations related by ring flipping are in rapid equilibrium with one another, but the distribution between them strongly favors those in which the bigger group (for example *tert*-butyl group) is equatorial.

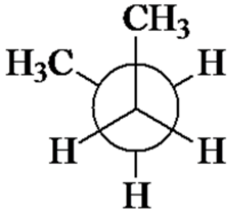
Conformational isomers are all stereoisomers. But not all stereoisomers are conformational isomers.

3.13 Medium and Large Rings

The same fundamental principles apply to medium and large rings as the ones that apply to smaller ones.

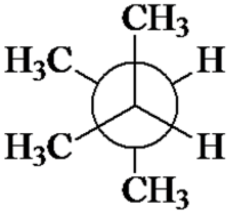
Extra Problems:

1. Identify the conformation of butane shown below.



A) anti B) gauche C) skewed D) eclipsed

2. What is the IUPAC name of the compound shown in the following Newman projection?



A)	1,1,2,2-tetramethylethane	C)	2,2,3,3-tetramethylbutane
B)	1,2-dimethylethane	D)	2,3-dimethylbutane

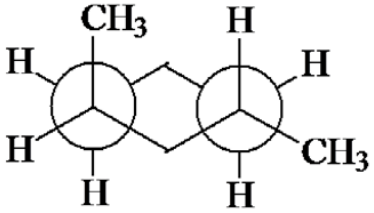
3. Which of the following can have *cis-trans* stereoisomers?

A)	1,1-dimethylcyclobutane	C)	1,1,3-trimethylcyclobutane
B)	1,3-dimethylcyclobutane	D)	1,1,3,3-tetramethylcylclobutane

4. The C—C—C bond angle in cyclopropane is

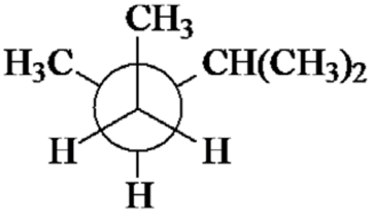
A) 60°. B) 90°. C) 109.5°. D) 120°.

5. The following structure is



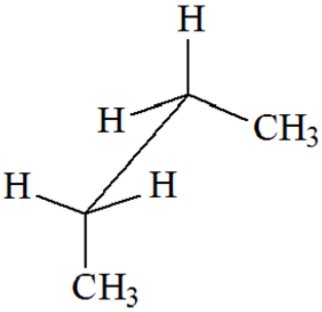
A) *cis*-1,3-dimethylcyclohexane.
B) *cis*-1,4-dimethylcyclohexane.
C) *trans*-1,3-dimethylcyclohexane.
D) *trans*-1,4-dimethylcyclohexane.

6. What is the IUPAC name of the compound shown below?



A) 1,2,3-trimethylbutane
B) 2,3-dimethylpentane
C) 2,3,4-trimethylpentane
D) 2-isopropylbutane

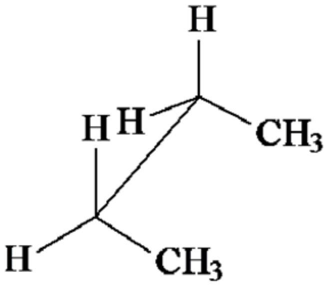
7. The sawhorse drawing of butane below is



A) a gauche conformation.
B) the anti conformation.
C) the least stable eclipsed conformation.
D) the most stable eclipsed conformation.

8. Which constitutional isomer of dimethylcyclohexane does not exhibit cis-trans isomerism?
A) 1,1-dimethylcyclohexane
B) 1,2-dimethylcyclohexane
C) 1,3-dimethylcyclohexane
D) 1,4-dimethylcyclohexane

9. The sawhorse drawing of butane below is the



A)	least stable staggered conformation.	C)	least stable eclipsed conformation.
B)	most stable staggered conformation.	D)	most stable eclipsed conformation.

10. What is the estimated dihedral angle between the two methyl groups on the structure shown below?

A) 30° B) 60° C) 90° D) 120°

11. The most stable conformation of *cis*-4-methyl-1-*tert*-butylcyclohexane is a chair conformation with
    A) both the -CH_3 and -$C(CH_3)_3$ equatorial.
    B) both the -CH_3 and -$C(CH_3)_3$ axial.
    C) the -CH_3 equatorial and the -$C(CH_3)_3$ axial.
    D) the -CH_3 axial and -$C(CH_3)_3$ equatorial.

12. The most stable chair conformation of cis-1-tert-butyl-3-methylcyclohexane has
A) both groups equatorial.
B) both groups axial.
C) the tert-butyl group equatorial and the methyl group axial.
D) the tert-butyl group axial and the methyl group equatorial.

Answers 1)B 2)D 3)B 4)A 5)C 6)B 7)A 8)A 9)C 10)B 11)D 12)A

Chapter 7:
Stereochemistry

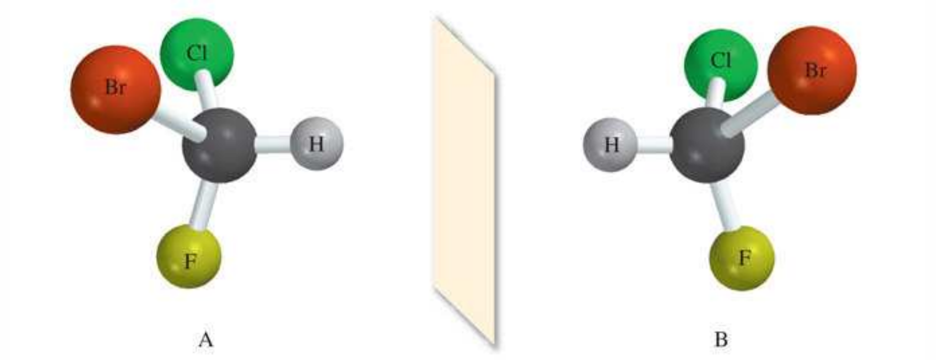
7.1 Molecular Chirality: Enantiomers

Stereoisomers are isomers that have the same constitution but differ in the spatial arrangement of their atoms.

Chirality: Related to the internal plane of symmetry of a molecule
A molecule is **chiral** if its two mirror image forms are not superimposable upon one another.
A molecule is **achiral** if its two mirror image forms are superimposable.

For example, your left hand and right hand are mirror images of each other, but can't be made to coincide point for point, palm to palm in 3D. They are chiral.

A molecular example is with Bromochlorofluoromethane ($BrClFCH_3$), which is chiral.



To test for superimposability, reorient B by turning it 180°. Then compare A and the new B (refered to as B'). The two do not match. A and B' cannot be superimposed on each other. Bromochlorofluoromethane is therefore a chiral molecule. We qualify the two mirror image forms as enantimoers of each other.

Enantiomers are classified as stereoisomers that are nonsuperimposable mirror images.

One cannot look at a single molecule in isolation and ask if it is an enantiomer any more than one can look at an individual human being and ask, "Is that person a cousin?".

A chiral molecule can have one and only one enantiomer.

7.2 The Chirality Center

A tetrahedral carbon atom with four different groups attached to it is called a chirality center. (You may also find in the literature the terms: chiral center, asymmetric center, stereocenter and stereogenic center which all mean the same thing).

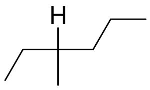
Carbons that are part of a double or triple bond cannot be chiral centers.

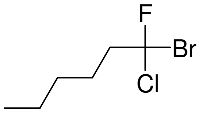
A molecule with a single chirality center is chiral.

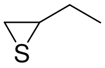
A chiral center can also be part of a ring.

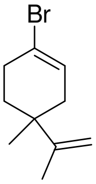
Even isotopes qualify as different substituents at a chirality center. (Deuterium ^2H = D and Tritium ^3H = T).

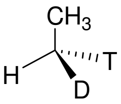
Examples of molecules containing one chiral center:









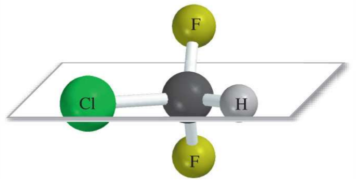


Everything that is disclosed in this section concerns molecules that have one and only one chirality center. A molecule with a single chirality center must be chiral. But a molecule with two or more chirality centers may be chiral or it may not (Sections 7.11-7.14).

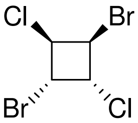
7.3 Symmetry in Achiral Structures

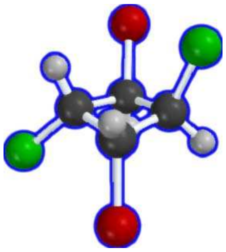
Any molecule with a plane of symmetry or a center of symmetry is superimposable on its mirror image and is achiral.

A **plane of symmetry** bisects a molecule into two mirror image halves (meaning that one half of the molecule is the mirror image of the other half).
Chlorodifluoromethane has a plane of symmetry.



A point in the center of the molecule is a **center of symmetry** if a line drawn from it to any element, when extended an equal distance in the opposite direction, encounters an identical element.





7.4 Optical Activity

Optical activity is the ability of a chiral substance to rotate the plane of polarized light and is measured using an instrument called the polarimeter.

A substance is optically active if it rotates the plane of polarized light. In order for a substance to exhibit optical activity, it must be chiral and one enantiomer must be present in excess of the other.

All achiral substances are optically inactive.

Enantiomeric forms of a chiral molecule cause a rotation of the plane of polarization in exactly equal amounts but in opposite directions. A solution containing equal quantities of enantiomers therefore exhibits no net rotations. Mixtures containing equal quantities of enantiomers are called **racemic mixtures**. Racemic mixtures are optically inactive.

When only one enantiomer is present, we say the substance is **optically pure**.

Optical purity = percent enantiomeric excess
= percent of one enantiomer – percent of the other enantiomer

For example, a material that is 50% optically pure contains 75% of one enantiomer and 25% of the other.

Rotation of the plane of polarized light in the clockwise sense is taken as positive (+), and rotation in the counterclockwise sense is taken as a negative (–) rotation. Older terms for positive and negative (–) rotations were dextrorotatory (*d*, to the right) and levorotatory (*l*, to the left).

A mixture of the 2 enantiomers of 2-hexanol, the (+)-2-hexanol and (–)-2-hexanol, is referred as (±)-2-hexanol.

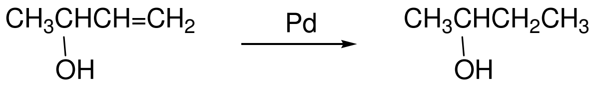
The direction and magnitude of the observed rotation α depends on how many molecules the light beam encounters. The **specific rotation** is a physical property of a substance and is abbreviated:

$$[\alpha]_D^T = 100\alpha / cl$$

Where a is the recorded value of rotation on the polarimeter
c is the concentration of the sample in grams per 100 mL of solution
l is the length of the polarimeter tube in decimeters
D is simply indicating the sodium D line
T is the temperature at which the value was taken

7.5 Absolute and Relative Configuration

Relative configuration compares the arrangement of atoms in space of one compound with those of another.
Absolute configuration is the precise arrangement of atoms in space.



$$\begin{array}{l}CH_3CHCH{=}CH_2\\ \quad\;\;|\\ \quad\;OH\end{array} \xrightarrow{Pd} \begin{array}{l}CH_3CHCH_2CH_3\\ \quad\;\;|\\ \quad\;OH\end{array}$$

[α] + 33.2°   [α] + 13.5°

No bonds are made or broken at the chirality center in this experiment. Therefore, when (+)-3-buten-2-ol and (+)-2-butanol have the same **sign** of rotation (the +), the arrangement of atoms in space is analogous. The two have the same relative configuration.

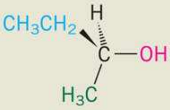
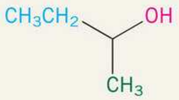
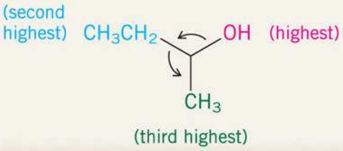
But in the absence of additional information, we can't tell which structure corresponds to (+)-3-buten-2-ol, and which one to (–)-3-buten-2-ol.

Also, not all compounds that have the same relative configuration have the same sign of rotation. (Not all R configuration have a + rotation).

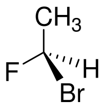
7.6 The Cahn-Ingold-Prelog *R-S* Notational System

In the *E-Z* system, substituents are ranked by atomic number according to a set of rules.

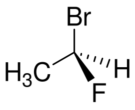
TABLE 7.1 Absolute Configuration According to the Cahn–Ingold–Prelog Notational System

Step number	**Example**
Given that the absolute configuration of (+)-2-butanol is  (+)-2-Butanol	
1. Identify the substituents at the chirality center, and rank them in order of decreasing precedence according to the system described in Section 5.4. Precedence is determined by atomic number, working outward from the point of attachment at the chirality center.	In order of decreasing precedence, the four substituents attached to the chirality center of 2-butanol are $HO— > CH_3CH_2— > CH_3— > H—$ (highest) (lowest)
2. Orient the molecule so that the lowest ranked atom or group points away from you. **3.** Draw the three highest ranked substituents as they appear to you when the molecule is oriented so that the lowest ranked group points away from you.	As represented in the wedge-and-dash drawing at the top of this table, the molecule is already appropriately oriented. Hydrogen is the lowest ranked atom attached to the chirality center and points away from us. 
4. If the order of decreasing precedence of the three highest ranked substituents appears in a clockwise sense, the absolute configuration is *R* (Latin *rectus,* "right," "correct"). If the order of decreasing precedence is counterclockwise, the absolute configuration is *S* (Latin *sinister,* "left").	The order of decreasing precedence is *counterclockwise.* The configuration at the chirality center is *S.* 

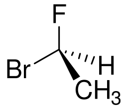
The R-S configurations are used to differentiate molecules. Make sure you recognize the different configurations using different representations. It is important to understand the possible rotations around a center atom.



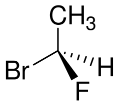
(*R*)-1-bromo-1-fluoroethane



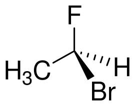
(*R*)-1-bromo-1-fluoroethane



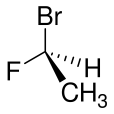
(*R*)-1-bromo-1-fluoroethane



(*S*)-1-bromo-1-fluoroethane



(*S*)-1-bromo-1-fluoroethane



(*S*)-1-bromo-1-fluoroethane

Compounds in which a chirality center is part of a ring are handled in an analogous fashion. To determine, for example, whether the configuration of (+)-4-methylcyclohexene is R or S, treat the right- and left-hand paths around the ring as if they were independent groups.

7.7 Fischer Projections

Purpose of Fischer projections is to show configuration at chirality center without necessity of drawing wedges and dashes or using models.

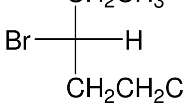
Rules for Fischer Projections

In the Fisher projections, the molecule is oriented so that the vertical bonds at the chirality center are directed away from you, and the horizontal bonds point towards you. The chirality center lies at the center of the cross.

Projection of molecule on page is a cross. When represented this way it is understood that horizontal bonds project outward, vertical bonds are back.

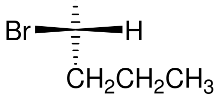
It is customary to orient the molecule so that the carbon chain is vertical with the lowest numbered carbon at the top.

The Fischer projection



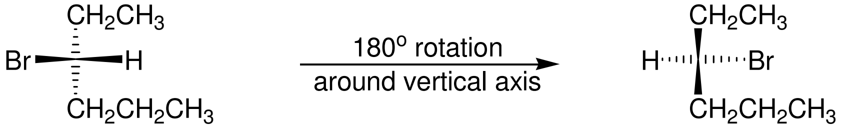
(*R*)-3-bromohexane

corresponds to

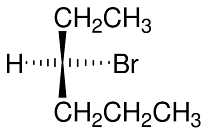


(*R*)-3-bromohexane

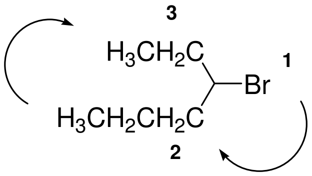
Make sure you always visualize your molecules in 3 dimensions.

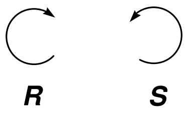


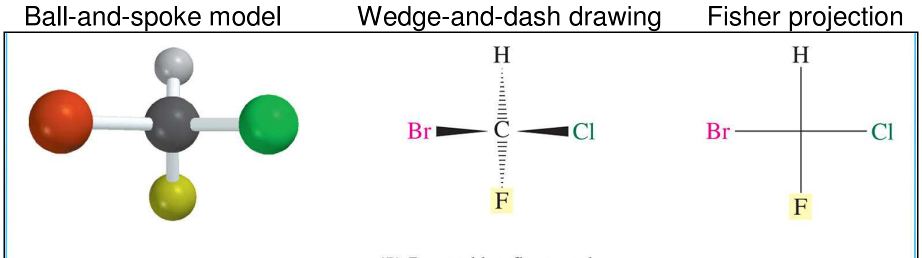
With H pointing away from us, the order of decreasing precedence (Br > $CH_2CH_2CH_3$ > CH_2CH_3) traces a clockwise path, verifying the configuration as *R*.



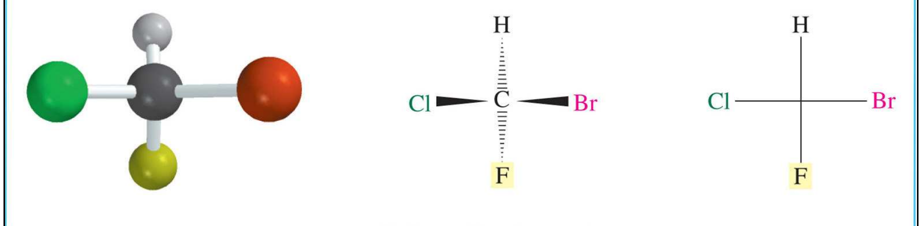
(*R*)-3-bromohexane







(*R*)-Bromochlorofluoromethane



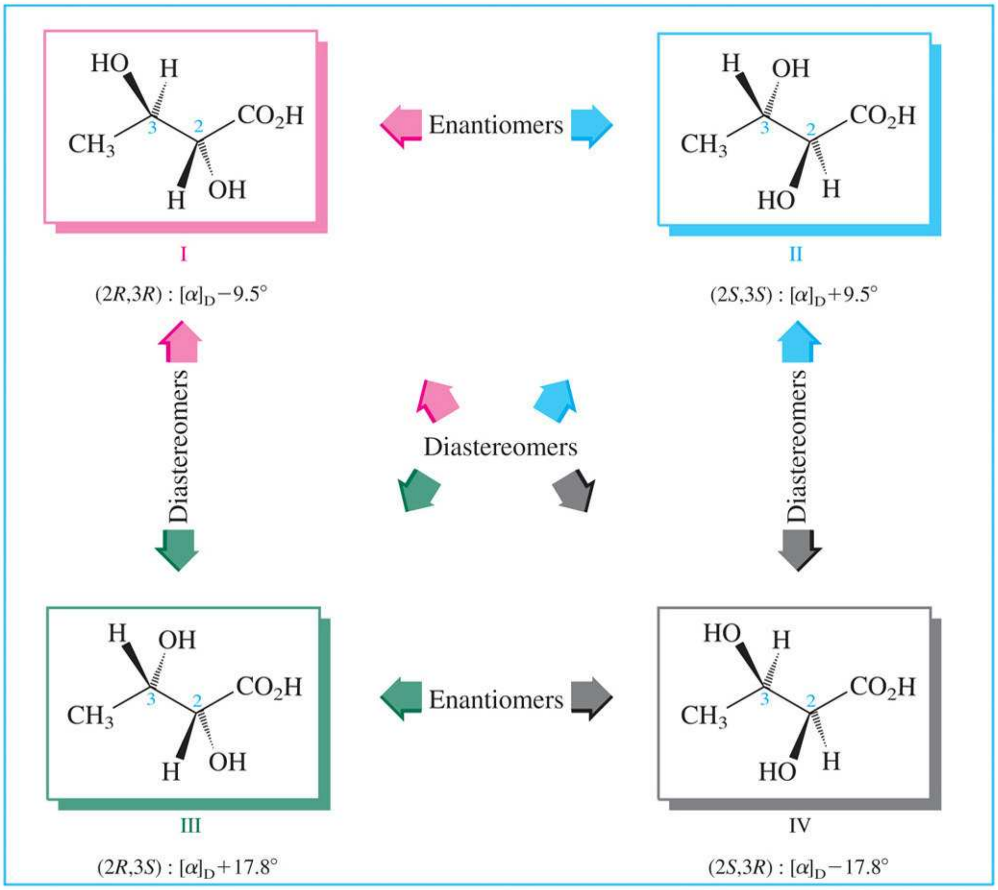
(*S*)-Bromochlorofluoromethane

7.8 Properties of Enantiomers

Both enantiomers of the same substance are identical in most of their physical properties (boiling point, melting point, etc.) The most prominent differences are biological ones such as taste, odor and medical effect, in which the substance interacts with a chiral receptor site.

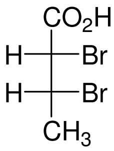
7.10 Chiral Molecules with Two Chirality Centers

Diastereoisomers are stereoisomers that are not mirror images (thus contain more than one chiral center).

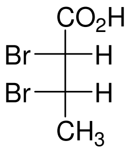


Organic chemists use an informal nomenclature system based on Fischer projections to distinguish between diastereomers. When the carbon chain is vertical and like substituents are on the same side of the Fisher projection, the molecule is described as **erythro** diastereomer.

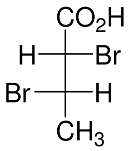
When like substituents are on opposite sides of the Fischer projection, the molecule is described as the **threo** diastereomer.



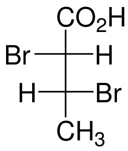
erythro



erythro



threo



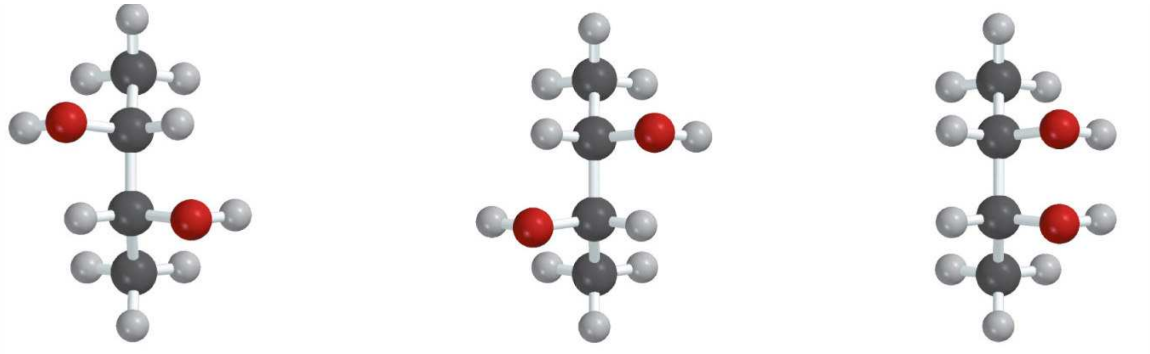
threo

Because diastereomers are not mirror images of each other, they can have quite different physical and chemical properties.

The *cis* and *trans* isomers of a particular compound are diastereomers of each other.

7.11 Achiral Molecules with Two Chirality Centers

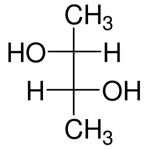
Achiral molecules that have chirality centers are called **meso forms**.



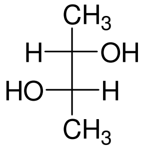
(2*R*,3*R*)-2,3-Butanediol (2*S*,3*S*)-2,3-Butanediol *meso*-2,3-Butanediol

The third structure has chiral centers but it is superposable on its mirror image. Therefore, this structure and its mirror image are the same. (2*S*,3*R*)-2,3-Butanediol and (2*R*,3*S*)-2,3-Butanediol are identical structures. It is therefore a meso form.

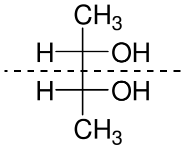
Fischer projections formulas can help us identify meso forms.



(2*R*,3*R*)-2,3-Butanediol



(2*S*,3*S*)-2,3-Butanediol



meso-2,3-Butanediol

When using Fischer projections for this purpose, however, be sure to remember what three-dimensional objects they stand for. One should not, for example, test for superimposition of the two chiral stereoisomers by a procedure that involves moving any part of a Fischer projection out of the plane of the paper in any step.

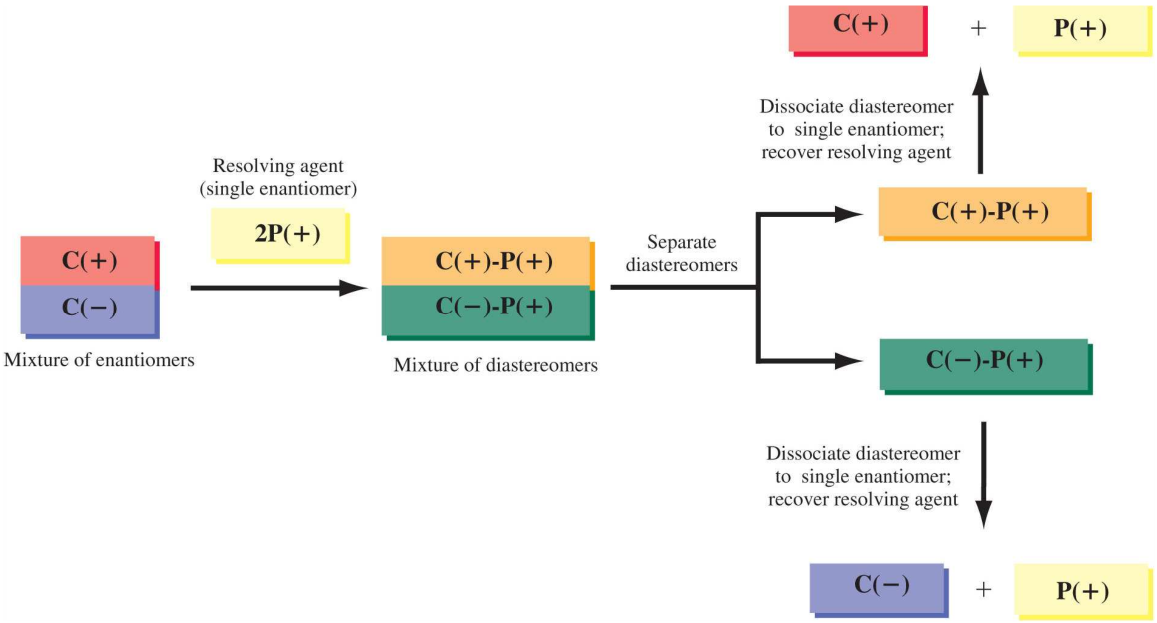
7.14 Resolution of Enantiomers

Resolution is the separation of a racemic mixture into its two enantiomeric forms.

It is normally carried out by converting the mixture of enantiomers to a mixture of diastereomers, separating the diastereomers, then regenerating the enantiomers.

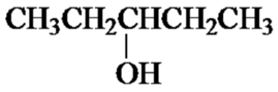
Since diastereomers can have different physical properties, they can serve as a means for their separation. The mixture of diastereomers is separated, usually by crytallization.

Kinetic resolution depends on the different rates of reaction of two enantiomers with a chiral reagent. A very effective form of kinetic resolution uses enzymes as catalysts to selectively bring about the reaction of one enantiomer in a racemic mixture (**enzymatic resolution**).



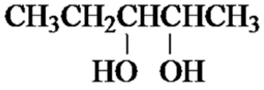
Extra Problems:

1. Which of the molecules below are chiral?



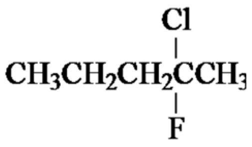
$CH_3CH_2\underset{\substack{|\\ OH}}{C}HCH_2CH_3$

I



$CH_3CH_2\underset{\substack{|\\ HO}}{C}H\underset{\substack{|\\ OH}}{C}HCH_3$

II



$CH_3CH_2CH_2\overset{\substack{Cl\\ |}}{\underset{\substack{|\\ F}}{C}}CH_3$

III

A) only II B) only III C) I and III D) II and III

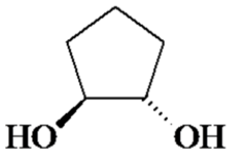
2. Which object below is achiral?
A) golf club (wood driver) B) baseball glove C) tennis shoe D) baseball bat

3. Which one of the following is a diastereomer of (R)-4-bromo-cis-2-hexene?
A) (S)-4-bromo-*cis*-2-hexene C) (R)-4-bromo-*trans*-2-hexene
B) (R)-5-bromo-*cis*-2-hexene D) (S)-5-bromo-*trans*-2-hexene

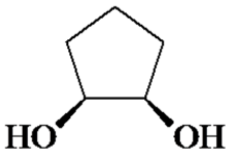
4. Which of the following statements is false?
A) Racemic mixtures are optically inactive.
B) Enantiomers have specific rotations which are equal, but have opposite signs.
C) Achiral molecules are optically inactive.
D) Meso compounds contain equal amounts of enantiomers.

5. Which one of the following groups has the highest rank as assigned by the Cahn-Ingold-Prelog system for stereogenic carbons?
A) –CH=CH2 B) –CH2OH C) –CH=O D) –CH2SH

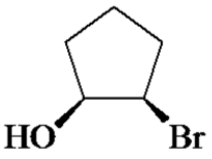
6. Which of the molecules below are chiral?



I



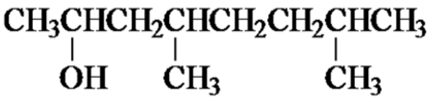
II



III

A) only I B) I and III C) II and III D) I, II, and III

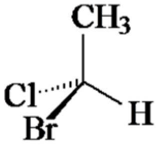
7. How many stereogenic centers are there in the following molecule?



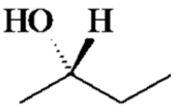
$CH_3CH(OH)CH_2CH(CH_3)CH_2CH_2CH(CH_3)CH_3$

A) only 1 B) two C) three D) four

8. Give the configurations, respectively, of the following two molecules.

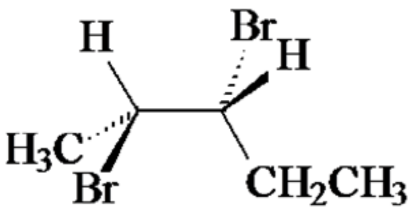


and



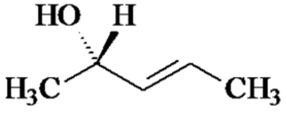
A) R and R B) R and S C) S and S D) S and R

9. What is the IUPAC name of the following compound?

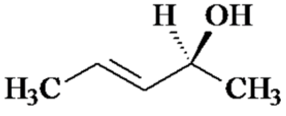


A)	(2S, 3S)-2,3-dibromopentane	C)	(2R, 3S)-2,3-dibromopentane
B)	(2S, 3R)-2,3-dibromopentane	D)	(2R, 3R)-2,3-dibromopentane

10. What is the relationship between the following two molecules?

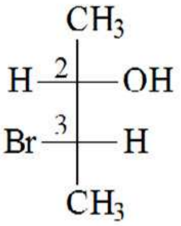


and



A) identical B) enantiomers C) diastereomers D) constitutional isomers

11. What are the configurations of carbons 2 and 3 in the Fischer projection below?

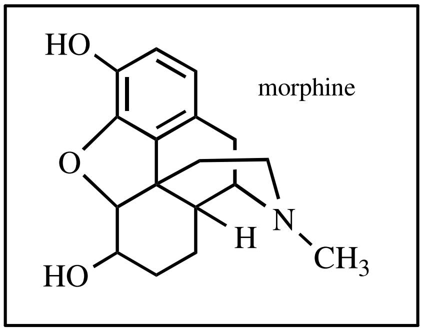


A) 2R, 3R B) 2R, 3S C) 2S, 3R D) 2S, 3S

12. A pure sample of (S)-phenylalanine has a specific rotation of +70°. A mixture of the two enantiomers of phenylalanine has a specific rotation of +7.0°. What are the percentages of the S and R enantiomers in the mixture?

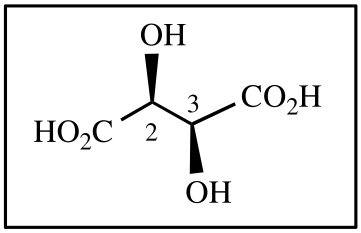
A)	95% S, 5% R	C)	55% S, 45% R
B)	90% S, 10% R	D)	52.5% S, 47.5% R

13. How many chiral centers are in this molecule?



A) 2 B) 4 C) 5 D) 6

14. What are the R/S assignments in this molecule? (assume the carbons are numbered as shown)



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

Ans: 1)D 2)D 3)C 4)D 5)D 6)B 7)B 8)B 9)D 10)A 11)D 12)C 13)C 14)B

Chapter 4:
Alcohols and Alkyl Halides

4.1 Functional Groups

A **Functional Group** is a structural *unit* in a molecule responsible for its characteristic behavior under a particular set of reaction conditions.

For example, the double bond is a functional group in an alkene, the triple bond is a functional group in an alkyne, and the benzene ring itself is a functional group in an arene.

Unsubstituted alkanes (RH) are not considered to have a functional group. In general, hydrogen atoms of alkanes are relatively unreactive and any other group attached to the hydrocarbon framework will be the functional group.

A **Reaction Mechanism** is **how** the structure of the reactant is transformed into the product.

In a reaction, ***R*** commonly stands for an alkyl group and ***X*** for a halogen atom.

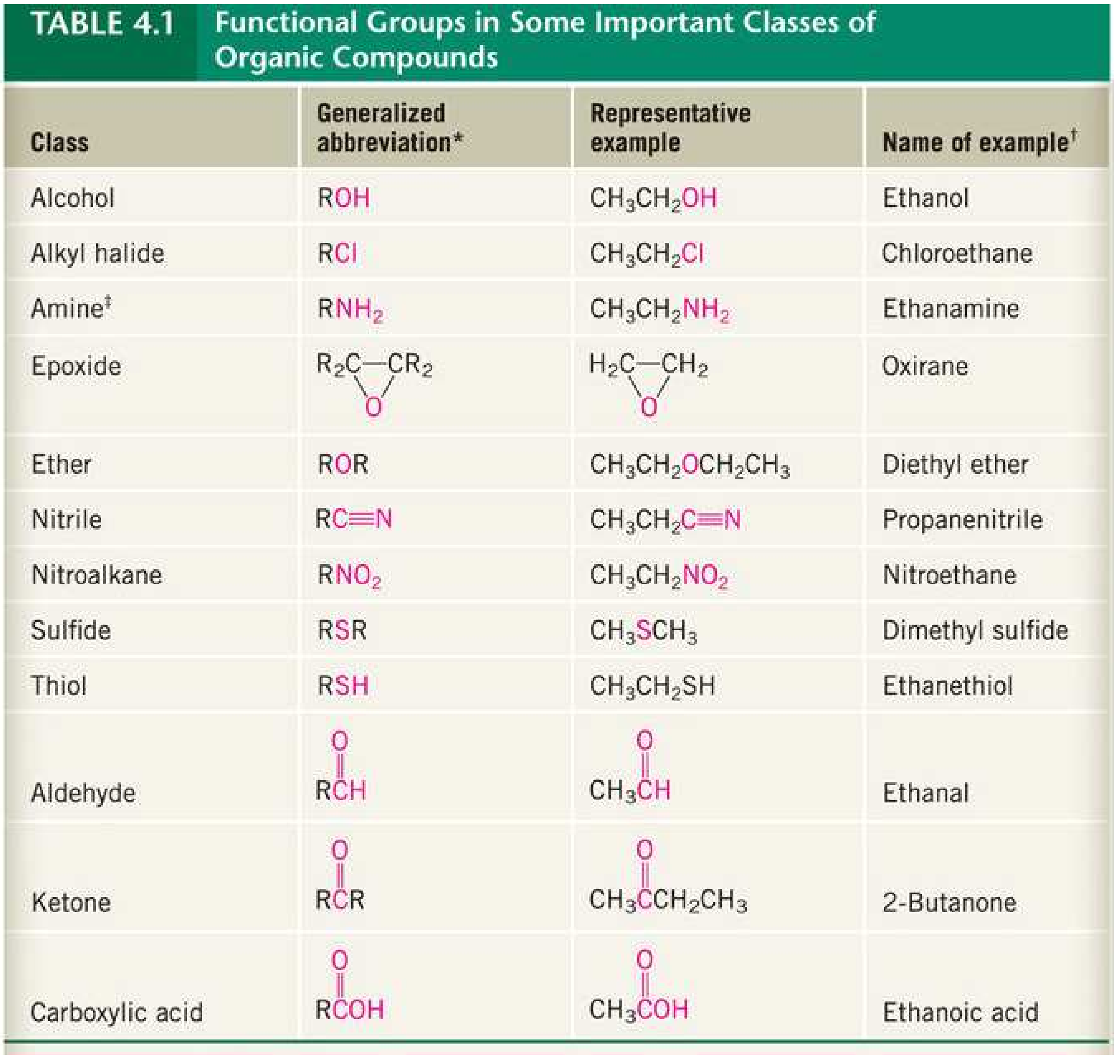
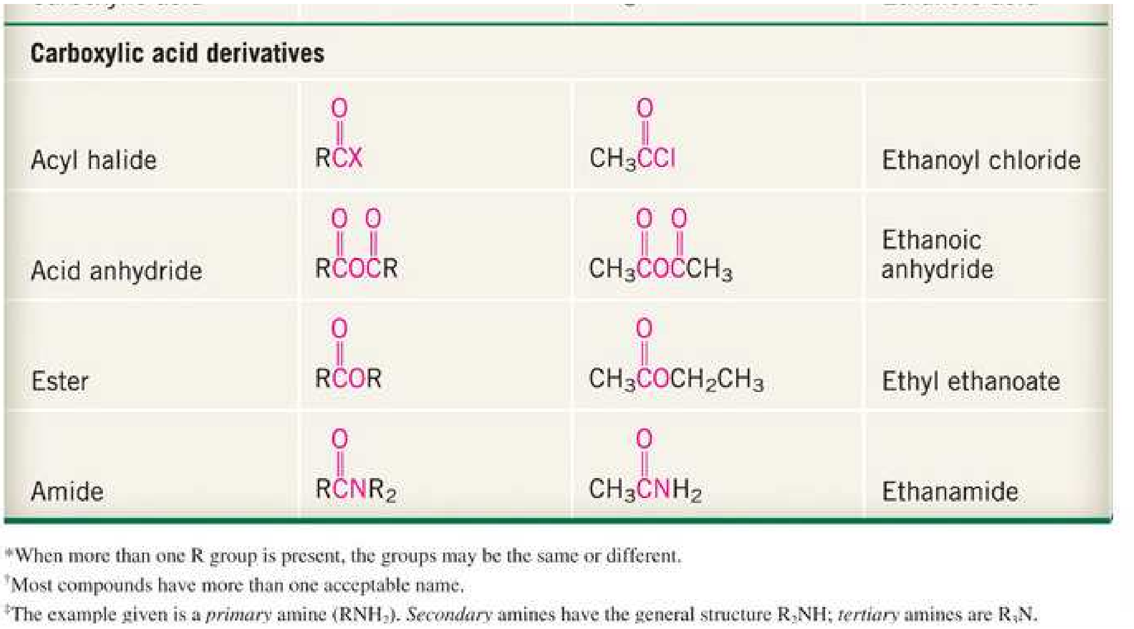


TABLE 4.1 Functional Groups in Some Important Classes of Organic Compounds

Class	Generalized abbreviation*	Representative example	Name of example[†]
Alcohol	ROH	CH_3CH_2OH	Ethanol
Alkyl halide	RCl	CH_3CH_2Cl	Chloroethane
Amine[‡]	RNH_2	$CH_3CH_2NH_2$	Ethanamine
Epoxide	$\underset{O}{R_2C{-}CR_2}$	$\underset{O}{H_2C{-}CH_2}$	Oxirane
Ether	ROR	$CH_3CH_2OCH_2CH_3$	Diethyl ether
Nitrile	$RC{\equiv}N$	$CH_3CH_2C{\equiv}N$	Propanenitrile
Nitroalkane	RNO_2	$CH_3CH_2NO_2$	Nitroethane
Sulfide	RSR	CH_3SCH_3	Dimethyl sulfide
Thiol	RSH	CH_3CH_2SH	Ethanethiol
Aldehyde	$R\overset{O}{\overset{\|}{C}}H$	$CH_3\overset{O}{\overset{\|}{C}}H$	Ethanal
Ketone	$R\overset{O}{\overset{\|}{C}}R$	$CH_3\overset{O}{\overset{\|}{C}}CH_2CH_3$	2-Butanone
Carboxylic acid	$R\overset{O}{\overset{\|}{C}}OH$	$CH_3\overset{O}{\overset{\|}{C}}OH$	Ethanoic acid



Carboxylic acid derivatives			
Acyl halide	$\overset{O}{\overset{\Vert}{RCX}}$	$CH_3\overset{O}{\overset{\Vert}{C}}Cl$	Ethanoyl chloride
Acid anhydride	$R\overset{O}{\overset{\Vert}{C}}O\overset{O}{\overset{\Vert}{C}}R$	$CH_3\overset{O}{\overset{\Vert}{C}}O\overset{O}{\overset{\Vert}{C}}CH_3$	Ethanoic anhydride
Ester	$R\overset{O}{\overset{\Vert}{C}}OR$	$CH_3\overset{O}{\overset{\Vert}{C}}OCH_2CH_3$	Ethyl ethanoate
Amide	$R\overset{O}{\overset{\Vert}{C}}NR_2$	$CH_3\overset{O}{\overset{\Vert}{C}}NH_2$	Ethanamide

*When more than one R group is present, the groups may be the same or different.

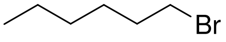
†Most compounds have more than one acceptable name.

‡The example given is a *primary* amine (RNH_2). *Secondary* amines have the general structure R_2NH; *tertiary* amines are R_3N.

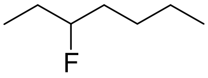
4.2 IUPAC Nomenclature of Alkyl Halides

There are several kinds of IUPAC nomenclature that can be applied to alcohols and alkyl halides. The two types that are most widely used are functional class nomenclature and substitutive

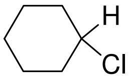
In **Functional Class Nomenclature** of Alkyl Halides, name the alkyl group and the halogen as separate words (alkyl + halide). The alkyl group is named on the basis of its longest continuous chain beginning at the carbon to which the halogen is attached.



Hexyl bromide

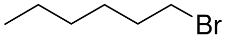


1-Ethylpentyl fluoride

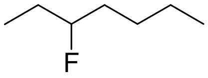


Cyclohexyl chloride

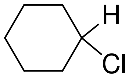
In **Substitutive Nomenclature** of Alkyl Halides, name the compound as halo-substituted alkanes. Number the longest chain containing the halogen in the direction that gives the lowest number to the substituted carbon.



1-Bromohexane

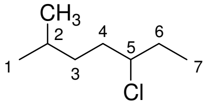


3-Fluoroheptane

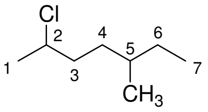


Chlorocyclohexane

When the carbon chain bears both a halogen and an alkyl substituent, the two are of equal rank when it comes to numbering the chain. Number the chain in the direction that gives the lowest number to the group (halogen or alkyl) that appears first.

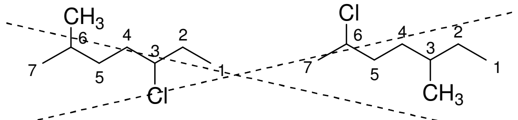


5-Chloro-2-methylheptane



2-Chloro-5-methylheptane

and not

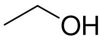
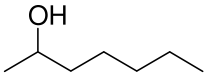
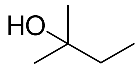


3-Chloro-6-methylheptane 6-chloro-3-methylheptane

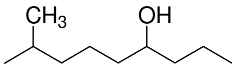
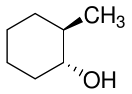
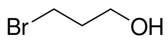
4.3 IUPAC Nomenclature of Alcohols

Functional Class Nomenclature of Alcohols names the alkyl group that bears the hydroxyl substituent (—OH) and adds "alcohol" as a separate word. The chain is always numbered beginning at the carbon to which the hydroxyl group is attached.

Substitutive Nomenclature of Alcohols names as "alkanols." Replace *-e* ending of alkane name with *-ol*. Number the chain in direction that gives lowest number to the carbon that bears the —OH group.

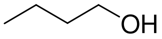
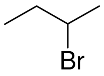
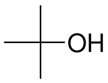
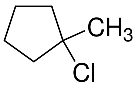
			
Functional Class:	Ethanol	1-Methylhexyl alcohol	1,1-dimethylpropyl alcohol
Substitutive:	Ethanol	Heptan-2-ol	2-methylbutan-2-ol

Hydroxyl groups outrank alkyl groups when it comes to numbering the chain. Number the chain in the direction that gives the lowest number to the carbon that bears the OH group. In the case of cyclic alcohol, the OH group is assumed to be attached to the C-1.

			
Functional Class:	8-methyl-4-nonanol	*trans*-2-Methylcyclohexanol	3-bromo-1-propanol
Substitutive:	8-methylnonan-4-ol	*trans*-2-Methylcyclohexan-1-ol	3-bromopropan-1-ol

4.4 Classes of Alcohols and Alkyl Halides

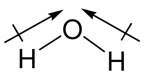
Alcohols and alkyl halides are classified as primary, secondary, or tertiary according to the "degree of substitution" of the carbon that bears the functional group. Degree of substitution is determined by counting the number of carbon atoms directly attached to the carbon that bears the halogen or hydroxyl group.

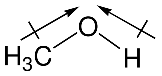
			
Butan-1-ol (Primary Alcohol) RCH_2G	2-Bromobutane (Secondary Alkyl Halide) R_2CHG	2-Methylpropan-2-ol (Tertiary Alcohol) R_3CG	1-chloro-1-methylcyclopentane (Tertiary Alcohol) R_3CG

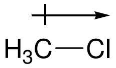
Where G is the functional group.

4.5 Bonding in Alcohols and Alkyl Halides

Alcohols and alkyl halides are polar and therefore have a dipole moment. Carbon-oxygen and carbon-halogen bond are polar covalent bonds, and carbon bears a partial positive charge in alcohols ($^{\delta+}\text{C—O}^{\delta-}$) and in alkyl halides ($^{\delta+}\text{C—X}^{\delta-}$).







4.6 Physical Properties of Alcohols and Alkyl Halides: Intermolecular Forces

The main physical properties we will be looking at are the Boiling point, Solubility in water and Density.

Highest **boiling point** results from strongest intermolecular attractive forces. Hydrogen bonding is stronger than other dipole-dipole attractions. In general, the boiling point of alkyl halides and alcohols increases with the number of carbon atoms, as it does with alkanes.

Since Cl is more polarizable than H. the greatest number of Cl atoms, the highest the boiling point. Fluorine is not very polarizable and induced dipole-induced dipole forces decrease with increasing fluorine substitution.

Alkyl halides are **insoluble in water**. Methanol, ethanol, isopropyl alcohol are completely miscible with water. The solubility of an alcohol in water decreases with increasing number of carbons (compound becomes more hydrocarbon-like).

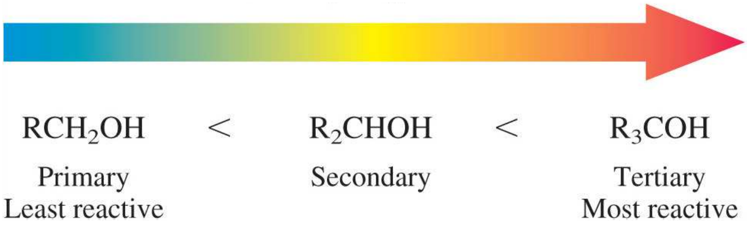
Most alkyl halides are **denser** than water. All liquid alcohols have densities of about 0.8 g/mL.

4.7 Preparation of Alkyl Halides from Alcohols and Hydrogen Halides

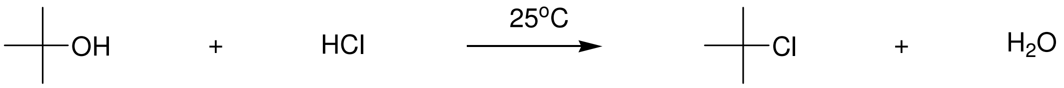
$$\underset{\text{Alcohol}}{R{-}OH} \quad + \quad \underset{\text{Hydrogen halide}}{H{-}X} \quad \rightarrow \quad \underset{\text{Alkyl halide}}{R{-}X} \quad + \quad \underset{\text{Water}}{H_2O}$$

The order of reactivity of the hydrogen halides parallels their acidity: HI > HBr > HCl >> HF.

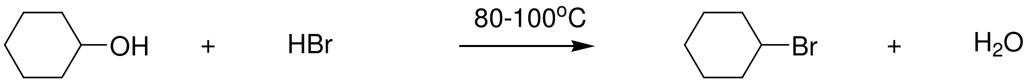
Among the various classes of alcohols, tertiary alcohols are observed to be the most reactive and primary alcohols the least reactive.



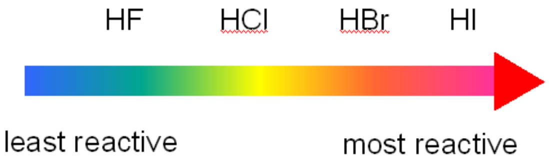
Tertiary alcohols are converted to alkyl chlorides in high yield within minutes on reaction with hydrogen chloride at room temperature and below.



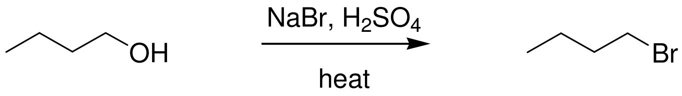
Secondary and primary alcohols do not react with HCl at fast rates. In these cases, the more reactive hydrogen halide HBr is used at elevated temperatures.



Hydrogen halide reactivity



The same kind of transformation may be carried out by heating an alcohol with sodium bromide and sulfuric acid.

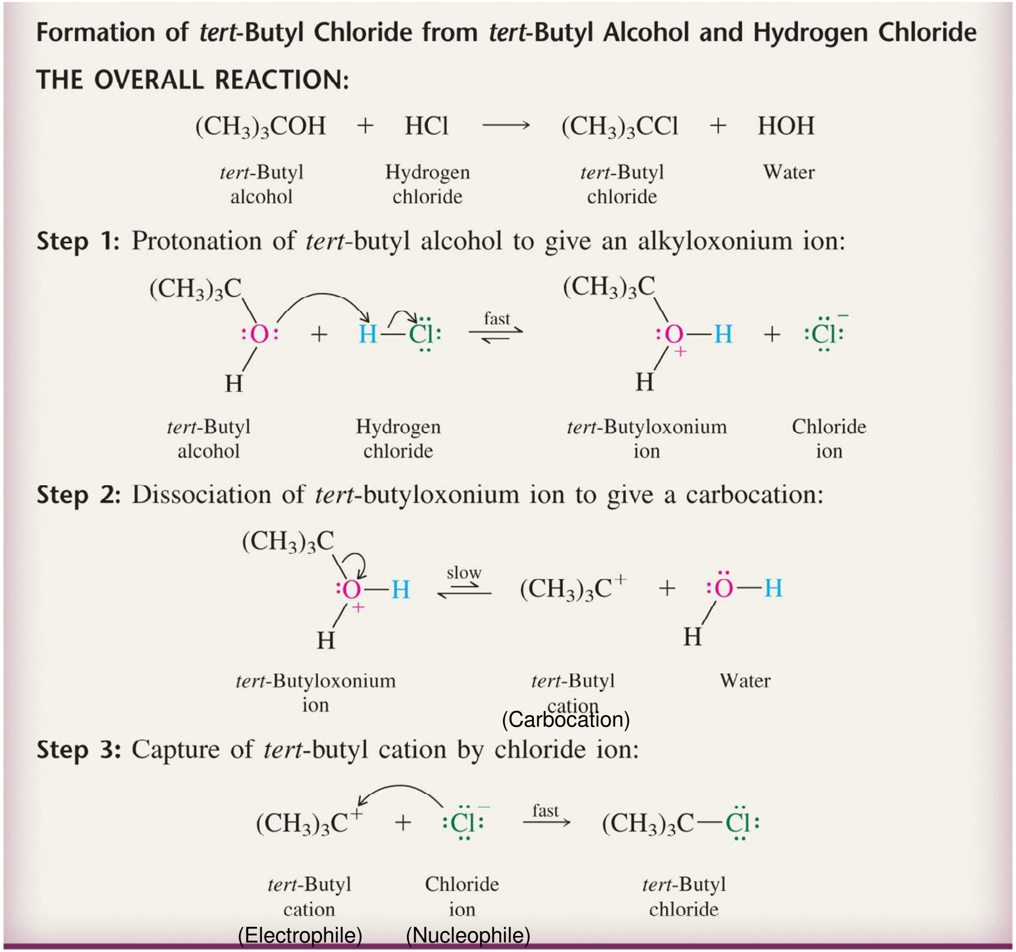


Note that reagents are indicated over the arrow, and water is usually omitted.

4.8 Mechanism of the Reaction of Alcohols with Hydrogen Halides: Hammond's Postulate

A **mechanism** describes how reactants are converted to products. Mechanisms are often written as a series of chemical equations showing the *elementary steps.* An elementary step is a reaction that proceeds by way of a single transition state. Mechanisms can be shown *likely* to be correct, but cannot be *proven* correct.

The reaction of an alcohol with a hydrogen halide is a **substitution**. A halogen replaces a hydroxyl group as a substituent on carbon, hence the name: substitution.



Formation of *tert*-Butyl Chloride from *tert*-Butyl Alcohol and Hydrogen Chloride

THE OVERALL REACTION:

$$(CH_3)_3COH + HCl \longrightarrow (CH_3)_3CCl + HOH$$

tert-Butyl alcohol	Hydrogen chloride	*tert*-Butyl chloride	Water

Step 1: Protonation of *tert*-butyl alcohol to give an alkyloxonium ion:

$$(CH_3)_3C\ddot{O}H + H-\ddot{Cl}: \xrightleftharpoons{\text{fast}} (CH_3)_3C\overset{+}{O}H_2 + :\ddot{Cl}:^-$$

tert-Butyl alcohol	Hydrogen chloride	*tert*-Butyloxonium ion	Chloride ion

Step 2: Dissociation of *tert*-butyloxonium ion to give a carbocation:

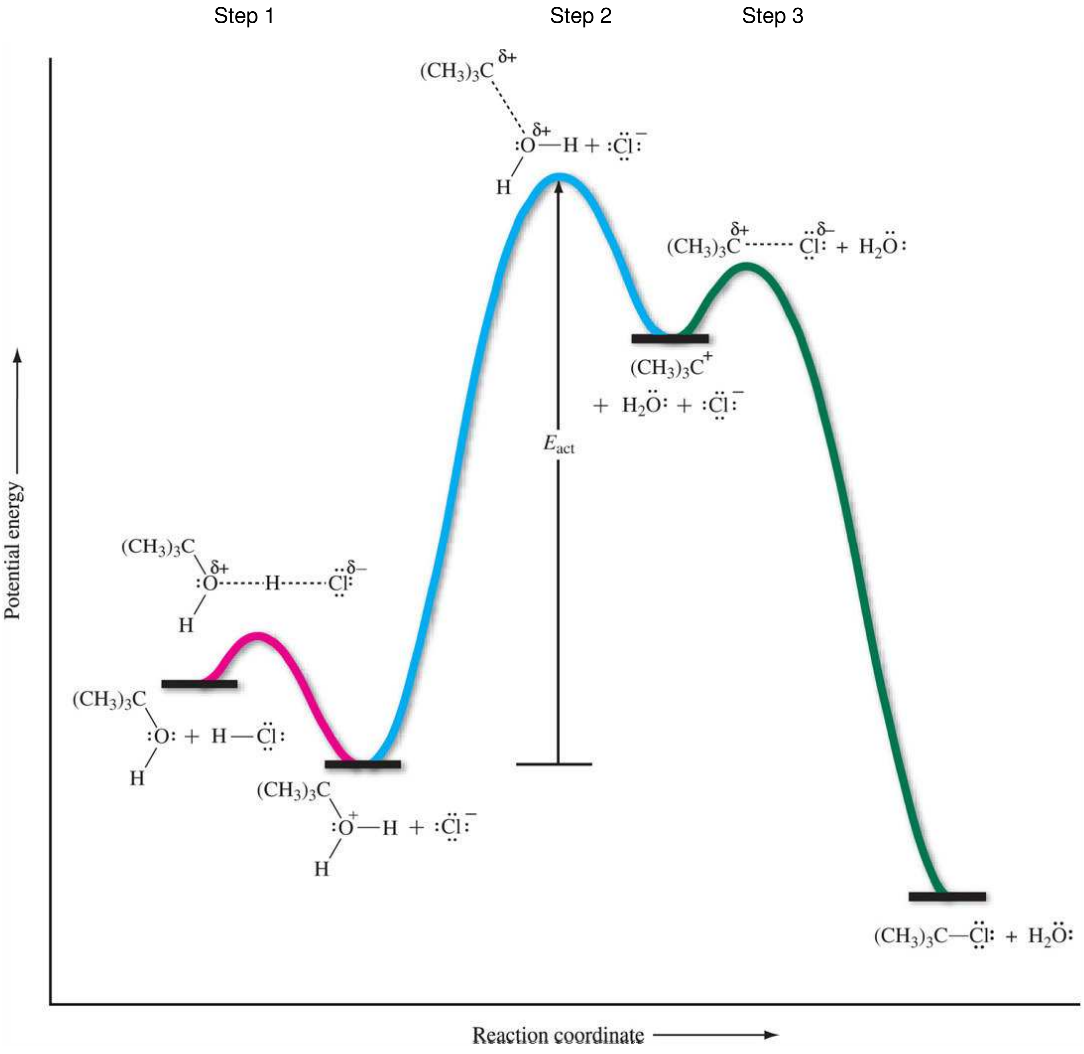
$$(CH_3)_3C\overset{+}{O}H_2 \xrightleftharpoons{\text{slow}} (CH_3)_3C^+ + :\ddot{O}H_2$$

tert-Butyloxonium ion	*tert*-Butyl cation (Carbocation)	Water

Step 3: Capture of *tert*-butyl cation by chloride ion:

$$(CH_3)_3C^+ + :\ddot{Cl}:^- \xrightarrow{\text{fast}} (CH_3)_3C-\ddot{Cl}:$$

tert-Butyl cation (Electrophile)	Chloride ion (Nucleophile)	*tert*-Butyl chloride



Dashed lines in transition states structures represent partial bonds, that is, bonds in the process of being made or broken.

Step 1: Proton Transfer

A strong acid such as HCl that ionizes completely when dissolved in water, also ionizes completely when dissolved in an alcohol. The first step is the formation of an alkyloxonium ion by proton transfer from the acid to the alcohol.

The **molecularity** of an elementary step is given by the number of species that undergo a chemical change in that step. Transfer of a proton from hydrogen chloride to *tert*-butyl alcohol is **bimolecular** because two molecules [HCl and $(CH_3)_3COH$] undergo chemical change.

The *tert*-butyloxonium ion formed in step 1 is an **intermediate**.

This step is known to be exothermic, so the products are placed lower in energy than the reactants. The activation energy (E_{act}) for proton transfer is low.

The species present at the transition state is not a stable structure and cannot be isolated.

Step 2: Carbocation Formation

A **carbocation** is an ion that contains a positively charged carbon.

Only one specie undergoes a chemical change in this step. Therefore it is a **unimolecular** step.

Whatever stabilizes carbocations will stabilize the transition state leading to them.

Because this step is endothermic, the products of it are placed higher in energy than the reactants.

Electrophiles ("electron-lovers" or "electron-seekers") are Lewis acids. They are electron-pair acceptors and react with Lewis bases (electron-pair donors).

Step 3: Carbocation Capture

The Lewis bases that react with electrophiles are called **nucleophiles** ("nucleus-seekers"). They have an unshared electron pair that they can use in covalent bond formation.

4.9 Potential Energy Diagrams for Multistep Reactions: The S_N1 Mechanism

The potential energy diagram for a multistep mechanism is simply a collection of the potential energy diagrams for the individual steps.

In the previous graph (p.53), the peaks correspond to transition states. The valleys correspond to the reactive intermediates.

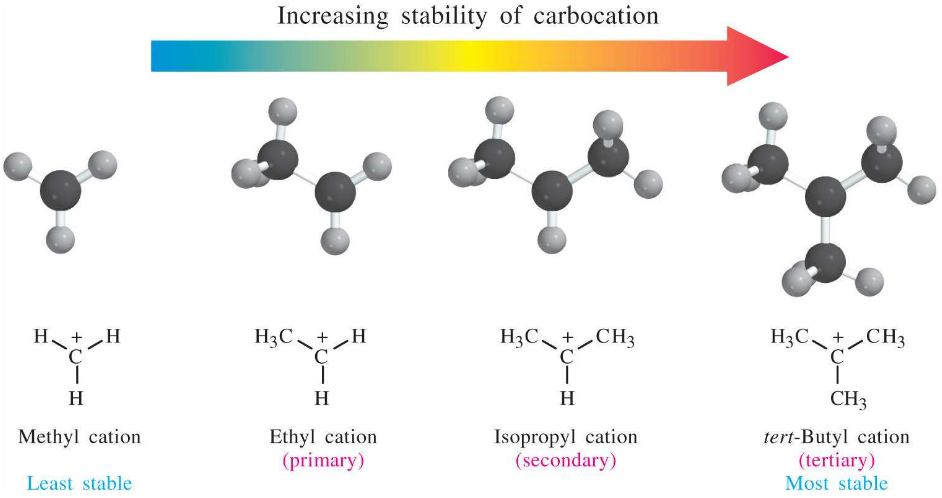
The slowest step is referred to as the rate-determining step.

S_N stands for substitution nucleophilic. It is followed by the number 1 or 2 according to wheter the rate-determining step is unimolecular or bimolecular.

The previous graph represented a S_N1 mechanism.

4.10 Structure, Bonding, and Stability of Carbocations

Alkyl groups directly attached to the positively charged carbon stabilize a carbocation.



Carbocations are classified according to the degree of substitution at the positively charged carbon.

Alkyl groups stabilize carbocations by releasing electron density to the positively charged carbon, thereby dispersing the positive charge.

There are two main ways the alkyl groups act as electron sources to stabilize carbocations:

- Inductive effect (by polarization of σ bonds)
- Hyperconjugation (electron delocalization is σ bonds via orbital overlap)

The positively charged carbon draws the electrons in its σ bonds toward itself and away from the atoms attached to it.

Electrons in a C—C bond are more polarisable than those in a C—H bond, so replacing hydrogens by alkyl groups reduces the net charge on the positively charged carbon.

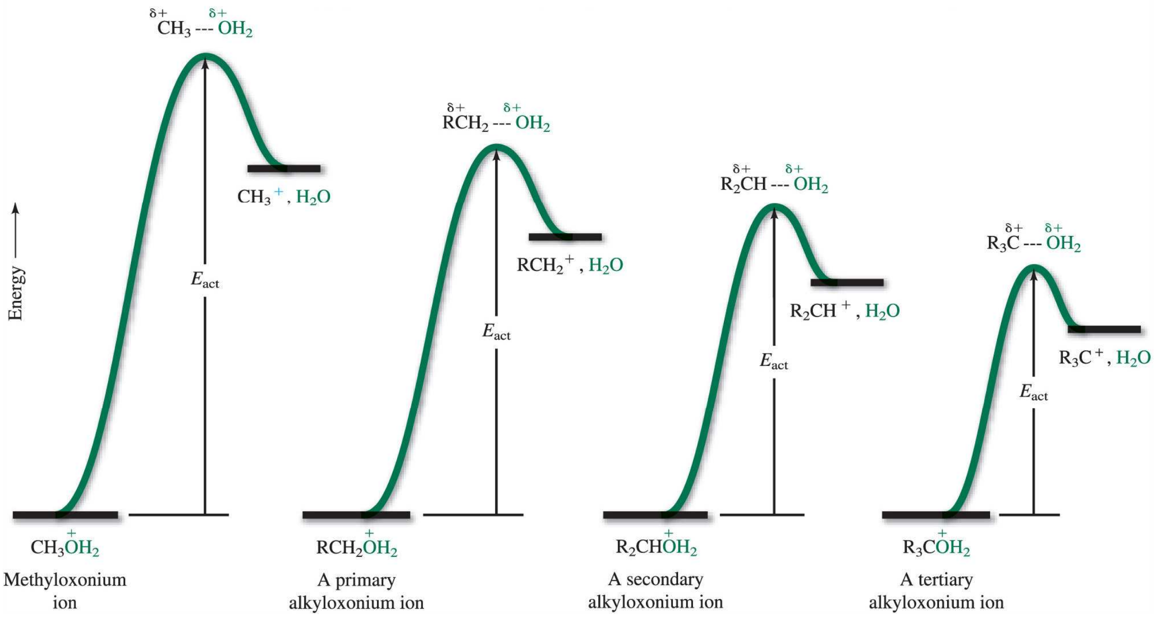
Alkyl groups are electron-releasing substituents with respect to their inductive effect. The more alkyl groups that are directly attached to the positively charged carbon, the more stable the carbocation.

4.11 Effect of Alcohol Structure on Reaction Rate

The more stable the carbocation, the faster it is formed.

Tertiary carbocations are more stable than secondary, which are more stable than primary, which are more stable than methyl.

Tertiary alcohols react faster than secondary, which react faster than primary, which react faster than methanol.

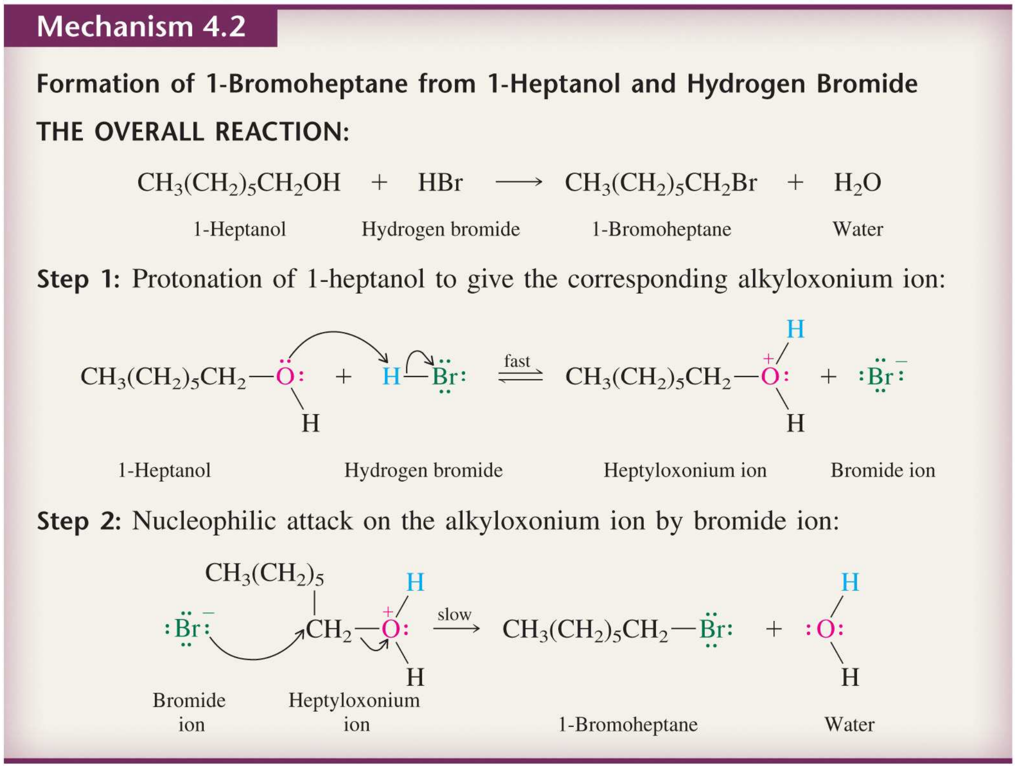


4.12 Reaction of Methyl and Primary Alcohols with Hydrogen Halides. The S_N2 Mechanism

Primary carbocations are too high in energy to allow S_N1 mechanism. Yet, primary alcohols are converted to alkyl halides.

They follow a different mechanism, one that avoids carbocation intermediates. Primary alcohols react by a **mechanism called S_N2** (substitution-nucleophilic-bimolecular).

The major difference between the S_N1 and S_N2 mechanisms is the second step. A mechanism is classified S_N2 when the nucleophilic substitution as a bimolecular rate-determining step. It is a bimolecular step because it involves both a nucleophile and an alkyloxonium ion.



Mechanism 4.2

Formation of 1-Bromoheptane from 1-Heptanol and Hydrogen Bromide

THE OVERALL REACTION:

$$\underset{\text{1-Heptanol}}{CH_3(CH_2)_5CH_2OH} + \underset{\text{Hydrogen bromide}}{HBr} \longrightarrow \underset{\text{1-Bromoheptane}}{CH_3(CH_2)_5CH_2Br} + \underset{\text{Water}}{H_2O}$$

Step 1: Protonation of 1-heptanol to give the corresponding alkyloxonium ion:

Step 2: Nucleophilic attack on the alkyloxonium ion by bromide ion:

Step 2 is slower than the proton transfer in step 1, so it is rate-determining.

Reaction rate is governed by the activation energy of the slowest step, regardless of how many steps there are.

4.14 Halogenation of Alkanes

Halogenation: Method for preparing alkyl halides.
Fluorination (with F_2), Chlorination (with Cl_2), Bromination (with Br_2) or Iodination (with I_2).

$$\underset{\text{Alkane}}{R{-}H} + \underset{\text{Halogen}}{X_2} \longrightarrow \underset{\text{Alkyl halide}}{R{-}X} + \underset{\text{Hydrogen halide}}{H{-}X}$$

4.15 Chlorination of Methane

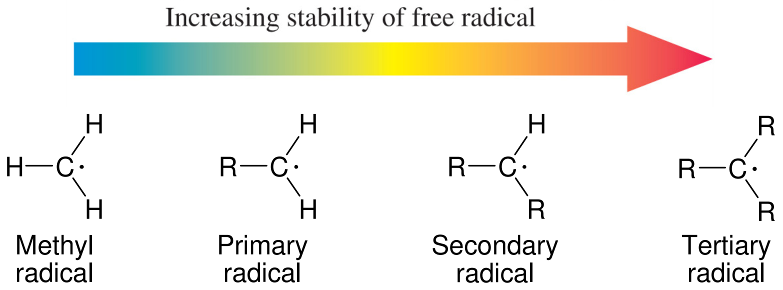
Carried out at high temperature (400-440 °C)

$$\begin{array}{llll} CH_4 & + Cl_2 & \rightarrow & CH_3Cl + HCl \\ CH_3Cl & + Cl_2 & \rightarrow & CH_2Cl_2 + HCl \\ CH_2Cl_2 & + Cl_2 & \rightarrow & CHCl_3 + HCl \\ CHCl_3 & + Cl_2 & \rightarrow & CCl_4 + HCl \end{array}$$

4.16 Structure and Stability of Free Radicals

Free radicals are species that contain unpaired electrons.

Alkyl radicals are classified as primary, secondary or tertiary according to the number of carbon atoms directly attached to the carbon that bears the unpaired electron.



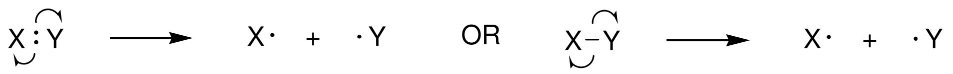
An alkyl radical is neutral and has one more electron that the corresponding carbocation.

More highly substituted radicals are more stable than less highly substituted ones, and the order of free-radical stability parallels that of carbocations.

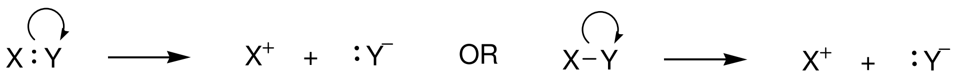
A chemical bond can be broken in two different ways—heterolytically or homolytically.

In a **homolytic bond cleavage**, the two electrons in the bond are divided equally between the two atoms. One electron goes with one atom, the second with the other atom.

The species formed by a homolytic bond cleavage of a neutral molecule are free radicals. The more stable the free-radical products, the weaker the bond, and the lower the bond-dissociation energy. The **bond-dissociation enthalpy** is the energy required for hemolytic bond cleavage.

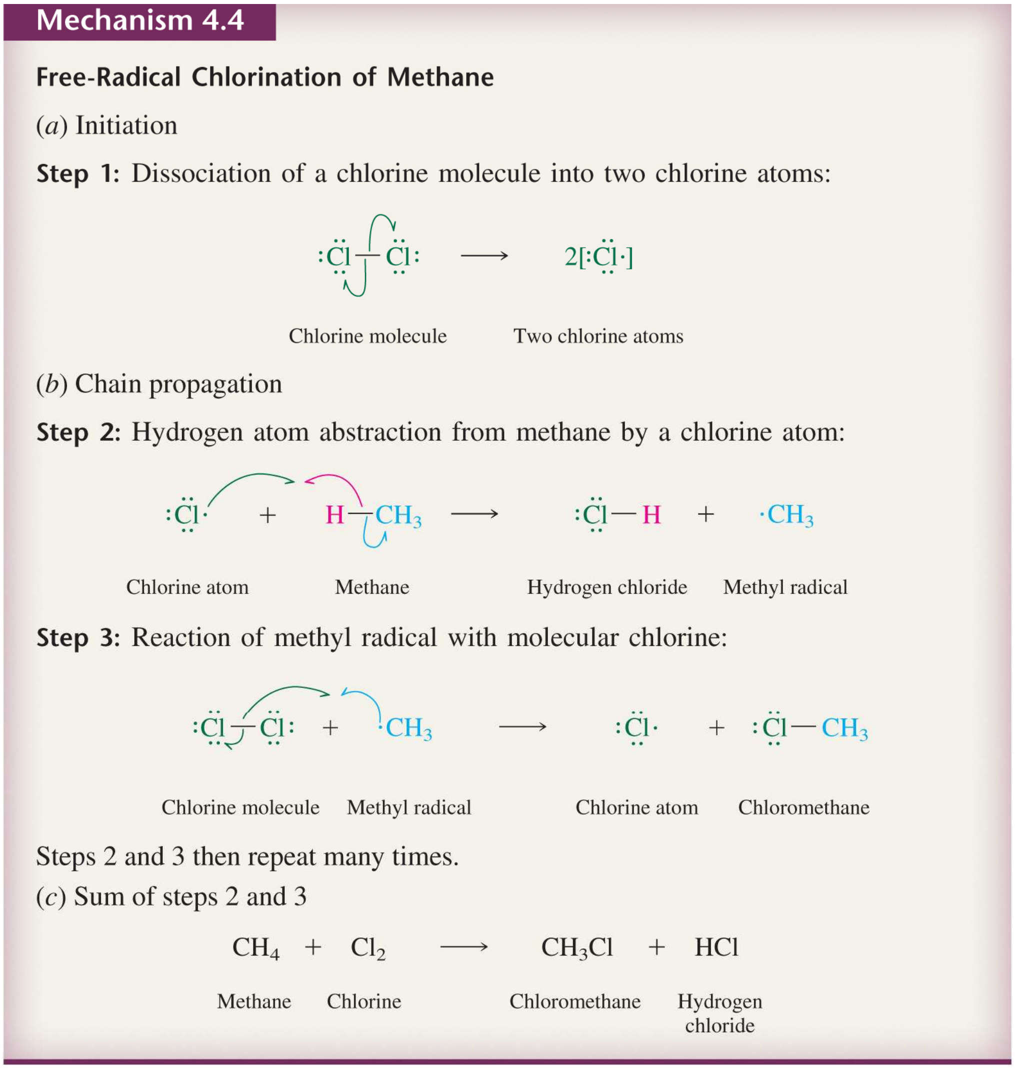


In a **heterolytic cleavage**, one atom retains both electrons.



Like carbocations, most free radicals are exceedingly reactive species; too reactive to be isolated.

4.17 Mechanism of Methane Chlorination



Mechanism 4.4

Free-Radical Chlorination of Methane

(*a*) Initiation

Step 1: Dissociation of a chlorine molecule into two chlorine atoms:

$$:\ddot{\underset{..}{Cl}}-\ddot{\underset{..}{Cl}}: \longrightarrow 2[:\ddot{\underset{..}{Cl}}\cdot]$$

Chlorine molecule — Two chlorine atoms

(*b*) Chain propagation

Step 2: Hydrogen atom abstraction from methane by a chlorine atom:

$$:\ddot{\underset{..}{Cl}}\cdot + H-CH_3 \longrightarrow :\ddot{\underset{..}{Cl}}-H + \cdot CH_3$$

Chlorine atom — Methane — Hydrogen chloride — Methyl radical

Step 3: Reaction of methyl radical with molecular chlorine:

$$:\ddot{\underset{..}{Cl}}-\ddot{\underset{..}{Cl}}: + \cdot CH_3 \longrightarrow :\ddot{\underset{..}{Cl}}\cdot + :\ddot{\underset{..}{Cl}}-CH_3$$

Chlorine molecule — Methyl radical — Chlorine atom — Chloromethane

Steps 2 and 3 then repeat many times.

(*c*) Sum of steps 2 and 3

$$CH_4 + Cl_2 \longrightarrow CH_3Cl + HCl$$

Methane — Chlorine — Chloromethane — Hydrogen chloride

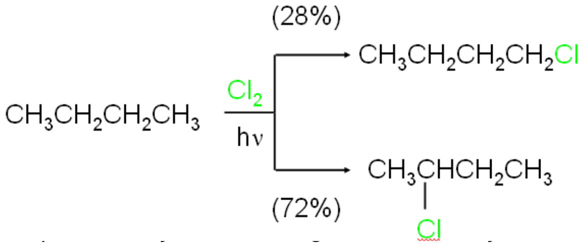
The chain reaction can be stopped by consuming free radicals (whenever two odd-electron species combine to give an even-electron product).

4.18 Halogenation of Higher Alkanes

Photochemical reactions are reactions that occur when light energy is absorbed by a molecule. Photochemical energy is indicated by writing “light” or “*hv*” above or below the arrow.

Chlorination of Alkanes

Chlorination of alkanes gives every possible monochloride derived from the original carbon skeleton. There is not much difference in the reactivity of the different hydrogens on the molecule.

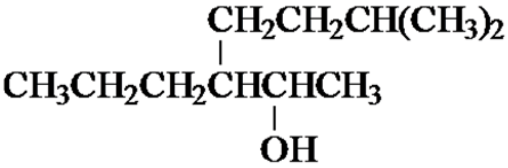


Chlorination of an alkane gives a mixture of every possible isomer having the same skeleton as the starting alkane. It is not very selective; a position (tertiary, secondary or primary) is not much favored compared to the other. It is useful for synthesis only when all hydrogens in a molecule are equivalent.

On the other hand, bromination is highly regioselective for substitution of tertiary hydrogens. It is a major synthetic application is in synthesis of tertiary alkyl bromides.

Extra Problems:

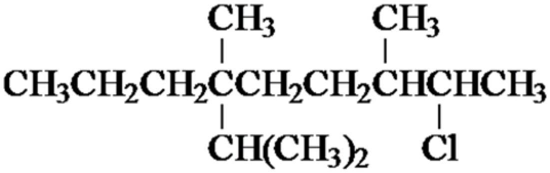
1. What is the IUPAC name of the compound below?



$CH_3CH_2CH_2CH(CH_2CH_2CH(CH_3)_2)CH(OH)CH_3$

A) 3-isobutyl-2-hexanol
B) 2-methyl-5-(1-hydroxyethyl)octane
C) 2-methyl-5-propyl-6-heptanol
D) 6-methyl-3-propyl-2-heptanol

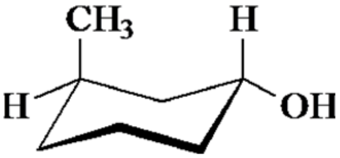
2. What is the IUPAC name of the compound below?



$CH_3CH_2CH_2C(CH_3)(CH(CH_3)_2)CH_2CH_2CH(CH_3)CH(Cl)CH_3$

A) 8-chloro-4-isopropyl-4,7-dimethylnonane
B) 2-chloro-6-isopropyl-3,6-dimethylnonane
C) 2-chloro-3,6,7-trimethyl-6-propyloctane
D) 6-*sec*-butyl-2-chloro-3,6-dimethyloctane

3. What is the IUPAC name of the following compound?



A) *cis*-3-methylcyclohexanol
B) *trans*-3-methylcyclohexanol
C) *cis*-5-methylcyclohexanol
D) *trans*-5-methylcyclohexanol

4. Which of the following is isobutyl alcohol?

A) $CH_3CH_2CH_2CH_2OH$
B) $CH_3CH_2CH(OH)CH_3$
C) $(CH_3)_2CHCH_2OH$
D) $(CH_3)_3COH$

5. What is the hybridization of the oxygen atom in alcohols?
   A) sp B) sp2 C) sp3

6. What is the nucleophile in the following substitution reaction?

   $(CH_3)_3COH + HBr \longrightarrow (CH_3)_3CBr + H_2O$

   A) $(CH_3)_3COH$

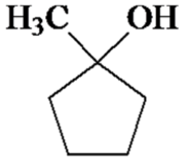
   B) $(CH_3)_3C^{\oplus}$

   C) $Br^{\ominus}$

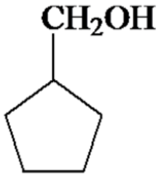
   D) $H^{\oplus}$

   A) A B) B C) C D) D

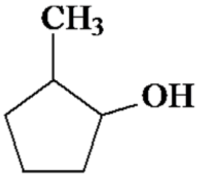
7. Arrange the following alcohols in order of their decreasing reactivity with HBr (most reactive first).



I



II



III

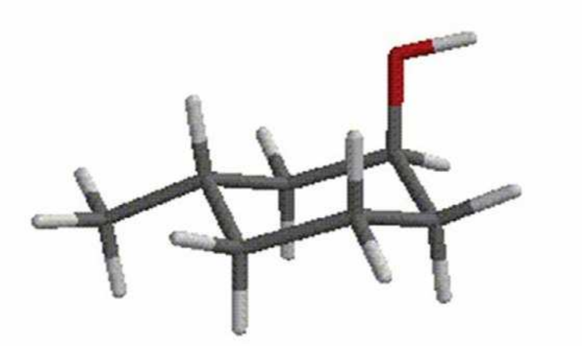
   A) I > II > III B) I > III > II C) III > I > II D) II > III > I

8. Which constitutional isomer of C_6H_{14} gives only two monochlorination products?
   A) 2-methylpentane
   B) 3-methylpentane
   C) 2,2-dimethylbutane
   D) 2,3-dimethylbutane

9. Which one of the following gives a single monochlorination product?
   A) 2,2-dimethylpropane
   B) 2,2-dimethylbutane
   C) 2,3-dimethylbutane
   D) 2-methylpropane

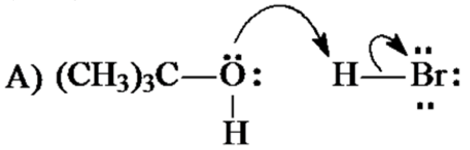
10. Which of the following hydrocarbons has the slowest reaction rate with Br_2 and light?
    A) CH_4 B) $CH_3CH_2CH_3$ C) $CH_3CH_2CH_2CH_3$ D) $(CH_3)_3CH$

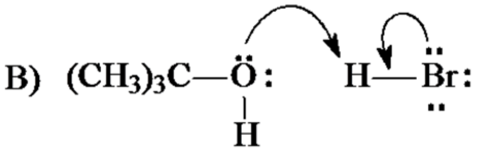
11. What is the name of the following compound?

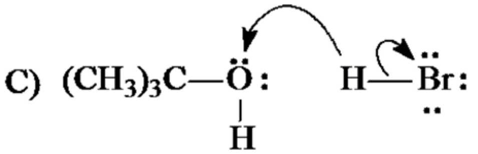


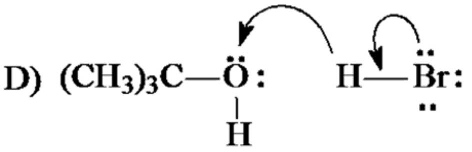
A)	*cis*-3-methylcyclohexanol	C)	*cis*-2-methylcyclopentanol
B)	*trans*-3-methylcyclohexanol	D)	*trans*-3-methylcyclopentanol

12. Which of the following mechanistically depicts the protonation of *tert*-butyl alcohol by hydrogen bromide?









A) A B) B C) C D) D

Ans: 1)D 2)B 3)B 4)C 5)C 6)C 7)B 8)D 9)A 10)A 11)B 12)A

Chapter 5:
Structure and Preparation of Alkenes: Elimination Reactions

Alkenes are hydrocarbons that contain a carbon-carbon double bond.

- Alkenes are also called "olefins".
- They are characterized by the molecular formula C_nH_{2n} (for one double bond).
- Alkenes are said to be "unsaturated".

5.1 Alkene Nomenclature (IUPAC)

1) Find the longest continuous chain that includes the double bond.
2) Replace the *-ane* ending of the unbranched alkane having the same number of carbons with *-ene*.
3) Number the chain in the direction that gives the lowest number to the doubly bonded carbon. The locant (or numerical position) of only one of the doubly bonded carbons is specified in the name; it is understood that the other doubly bonded carbon most follow in sequence.
4) If a substituent is present, identify its position by number.

The double bond takes precedence over alkyl groups and halogens when the chain is numbered.

Hydroxyl groups take precedence over the double bond when the chain is numbered. Compounds that contain both a double bond and a hydroxyl group use the combined suffix –*en* + -*ol*.

Examples:

$H_2C{=}CH_2$

Ethene
(common name: ethylene)

$H_3CHC{=}CH_2$

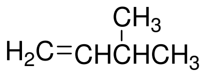
Prop-1-ene
(common name: propylene)

$H_2C{=}CHCH_2CH_3$

But-1-ene
or 1-butene

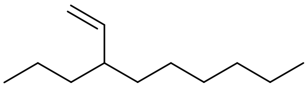
$H_3CHC{=}CHCH_3$

But-2-ene
or 2-Butene

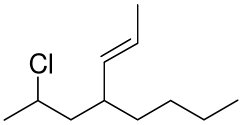


$H_2C{=}CH\overset{\overset{CH_3}{|}}{C}HCH_3$

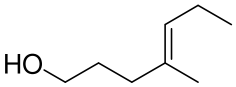
3-Methylbut-1-ene



3-Butylnon-1-ene
or 4-vinyldecane

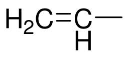


4-(2-Chloropropyl)oct-2-ene



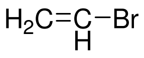
4-methylhept-4-en-1-ol

Alkenyl Groups:

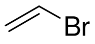

$H_2C{=}\underset{H}{C}{-}$

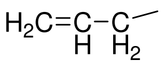
Vinyl

as in


$H_2C{=}\underset{H}{C}{-}Br$

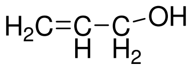
Vinyl bromide



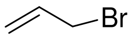

$H_2C{=}\underset{H}{C}{-}\underset{H_2}{C}{-}$

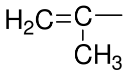
Allyl

as in


$H_2C{=}\underset{H}{C}{-}\underset{H_2}{C}{-}OH$

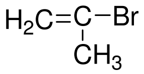
Allyl alcohol



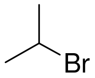

$H_2C{=}\underset{CH_3}{C}{-}$

Isopropenyl

as in


$H_2C{=}\underset{CH_3}{C}{-}Br$

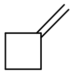
Isopropenyl bromide

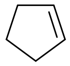


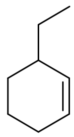
Cycloalkenes:

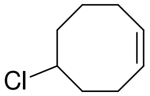
1) Replace the *-ane* ending of the cycloalkane having the same number of carbons with *-ene*.
2) Number *through* the double bond in the direction that gives the lower number to the first-appearing substituent.
3) When a CH_2 group is doubly bonded to a ring, the prefix *methylene* is added to the name of the ring.

Examples:


methylenecyclobutane

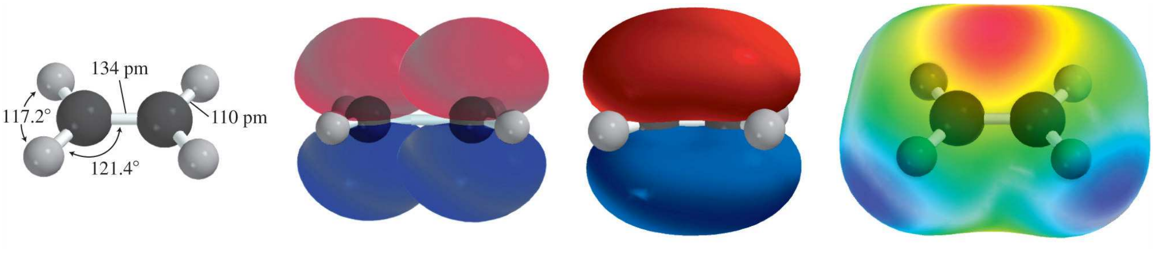

cyclopentene


3-ethylcyclohex-1-ene



5-chlorocyclooct-1-ene

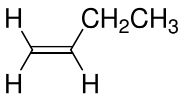
5.2 Structure and Bonding in Alkenes

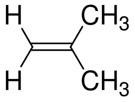


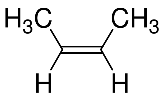
- Ethylene is planar.
- Each carbon is *sp*^{2} hybridized.
- The double bond consists of a σ bond and a π bond.
- The double bond in ethylene is stronger than the C—C single bond but is not twice as strong.

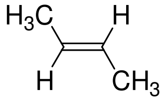
5.3 Isomerism in Alkenes

Ethylene is the only two-carbon alkene.
Propene is the only three-carbon alkene.
Alkenes with the molecular formula C_4H_8 have four isomers. (Recall that isomers are different compounds that have the same molecular formula).


but-1-ene


2-methylpropene


cis-but-2-ene


trans-but-2-ene

Free rotation around a double bond is not considered possible.

A ***cis* isomer** has identical (or analogous) substituents on same the same side of the double bond.
A ***trans* isomer** has identical (or analogous) substituents on opposite sides of the double bond.

Noticeably, cis-trans stereoisomerism in alkenes is not possible when one of the doubly bond carbons bears two identical substituents (such as but-1-ene and 2-methylpropene).

5.4 Naming Steroisomeric Alkenes by the E-Z Notational System

Cis and *trans* are ambiguous when analogous substituents are present on each side of the double bond.

So the IUPAC rule uses an atomic number criterion for ranking substituents.
E : higher ranked substituents on opposite sides
Z : higher ranked substituents on same side

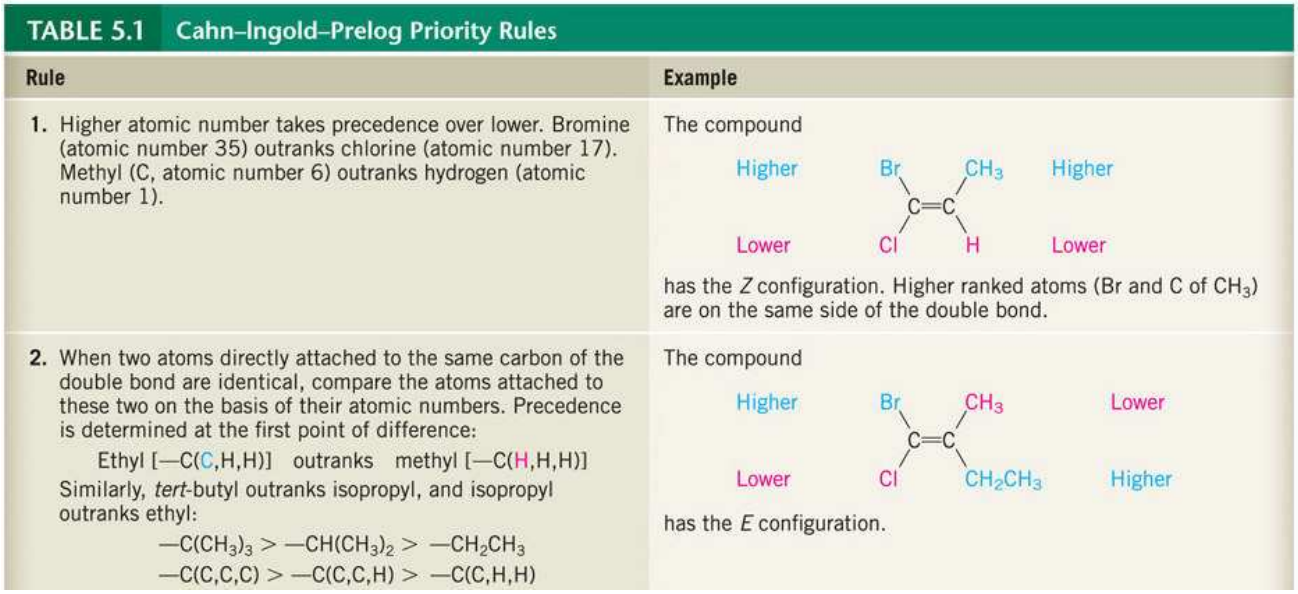
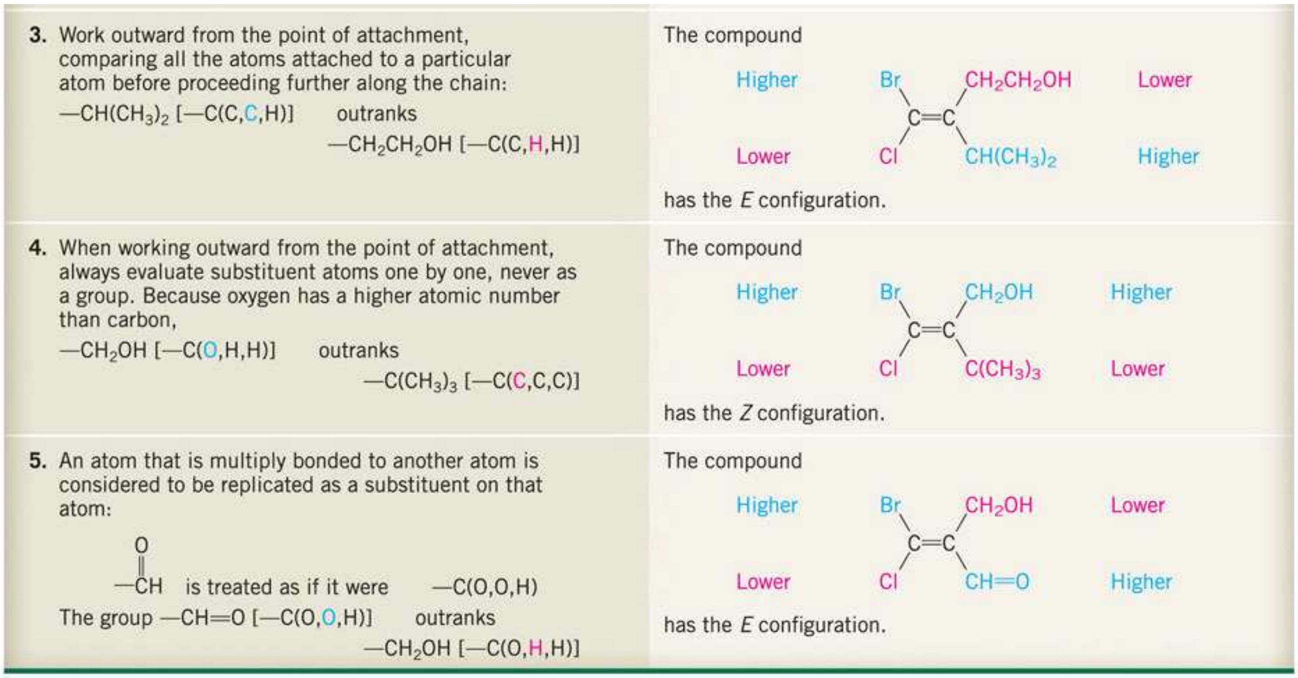


TABLE 5.1 Cahn–Ingold–Prelog Priority Rules

Rule	Example
1. Higher atomic number takes precedence over lower. Bromine (atomic number 35) outranks chlorine (atomic number 17). Methyl (C, atomic number 6) outranks hydrogen (atomic number 1).	The compound Higher Br CH$_3$ Higher C=C Lower Cl H Lower has the *Z* configuration. Higher ranked atoms (Br and C of CH_3) are on the same side of the double bond.
2. When two atoms directly attached to the same carbon of the double bond are identical, compare the atoms attached to these two on the basis of their atomic numbers. Precedence is determined at the first point of difference: Ethyl [—C(C,H,H)] outranks methyl [—C(H,H,H)] Similarly, *tert*-butyl outranks isopropyl, and isopropyl outranks ethyl: $—C(CH_3)_3 > —CH(CH_3)_2 > —CH_2CH_3$ —C(C,C,C) > —C(C,C,H) > —C(C,H,H)	The compound Higher Br CH$_3$ Lower C=C Lower Cl CH$_2$CH$_3$ Higher has the *E* configuration.



3. Work outward from the point of attachment, comparing all the atoms attached to a particular atom before proceeding further along the chain:

$-CH(CH_3)_2$ [$-C(C,C,H)$] outranks $-CH_2CH_2OH$ [$-C(C,H,H)$]

The compound

has the *E* configuration.

4. When working outward from the point of attachment, always evaluate substituent atoms one by one, never as a group. Because oxygen has a higher atomic number than carbon,

$-CH_2OH$ [$-C(O,H,H)$] outranks $-C(CH_3)_3$ [$-C(C,C,C)$]

The compound

has the *Z* configuration.

5. An atom that is multiply bonded to another atom is considered to be replicated as a substituent on that atom:

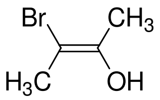
$-\overset{\overset{O}{\|}}{C}H$ is treated as if it were $-C(O,O,H)$

The group $-CH{=}O$ [$-C(O,O,H)$] outranks $-CH_2OH$ [$-C(O,H,H)$]

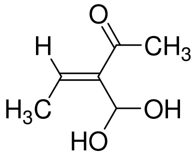
The compound

has the *E* configuration.

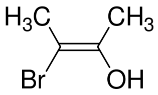
Example :



(*E*)-3-bromobut-2-en-2-ol



(*E*)-3-(dihydroxymethyl)pent-3-en-2-one



(*Z*)-3-bromobut-2-en-2-ol

5.5 Physical Properties of Alkenes

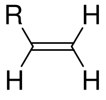
The lower molecular weight alkenes through C_4H_8 are gases at room temperature.

Alkenes are relatively nonpolar. The dipole moments of most alkenes are quite small.

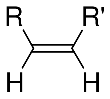
Alkyl substituents donate electrons to an sp^2-hybridized carbon to which they are attached slightly better than hydrogen does. Therefore, a methyl group donates electrons to the double bond.

5.6 Relative Stabilities of Alkenes

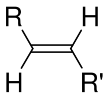
Double bonds are classified according to the number of carbons attached to them (degree of substitution).



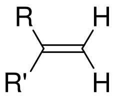
Monosubstituted



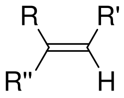
Disubstituted



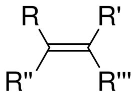
Disubstituted



Disubstituted



Trisubstituted



Tetrasubstituted

Factors governing alkene stability are:

Electronic Effect

- Alkyl groups are better electron-releasing substituents than hydrogen. Therefore they are better able to stabilize an alkene.
- Disubstituted alkenes are more stable than monosubstituted alkenes.
- In general, alkenes with more highly substituted double bonds are more stable than isomers with less substituted double bonds.

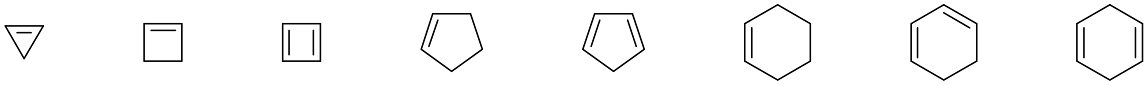
Steric Effect

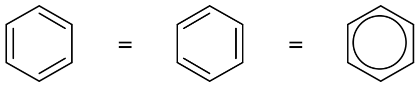
- Results when two or more atoms are close enough in space that a repulsion occurs between them.
- *Trans* alkenes are more stable than *cis* alkenes.

5.7 Cycloalkenes

Double bonds are accommodated by rings of all sizes.

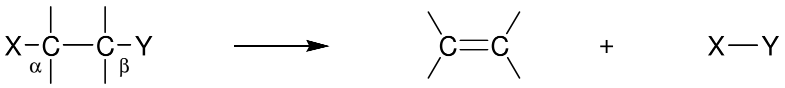
So far, cycloalkanes have been represented by structural formulas in which the double bonds are of the cis configuration. If the ring is large enough, a trans stereoisomer is also possible.





5.8 Preparation of Alkenes: Elimination Reactions

- Dehydrogenation of alkanes: X = Y = H
- Dehydration of alcohols: X = H; Y = OH
- Dehydrohalogenation of alkyl halides: X = H; Y = Br, etc.



$$\mathrm{X{-}\underset{\alpha}{C}{-}\underset{\beta}{C}{-}Y} \longrightarrow \mathrm{C{=}C} + \mathrm{X{-}Y}$$

Alkene formation requires that X and Y be substituents on adjacent carbon atoms. By making X the reference atom and identifying the carbon attached to it as the α (alpha) carbon, the Y atom is a substituent on the β (beta) carbon.
Carbon succeedingly more remote from the reference atom are designated χ (gamma), δ (delta) and so on until eventually ω (omega).
Beta (β) elimination reactions are also referred to as 1,2-eliminations.

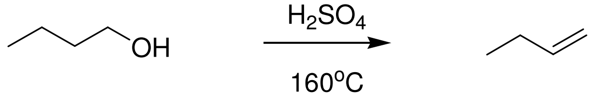
5.9 Dehydration of Alcohols

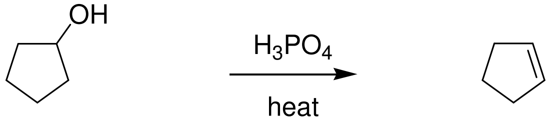
In the dehydration of alcohols, the H and OH are lost from adjacent carbons, and form water. An acid catalyst is necessary.

Sulfuric acid (H_2SO_4), Phosphoric acid (H_3PO_4) and Potassium hydrogen sulphate ($KHSO_4$) are the acids most often used in alcohol dehydrations.

Tertiary alcohols are more reactive than secondary alcohol, which are more reactive than primary alcohols.

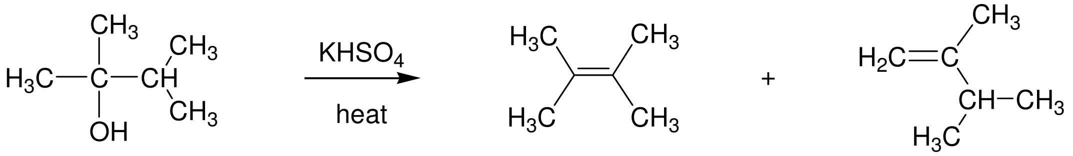
Examples:





5.10 Regioselectivity in Alcohol Dehydration: The Zaitsev Rule

A reaction that can proceed in more than one direction, but in which one direction predominates, is said to be regioselective.



2,3-dimethylbutan-2-ol

2,3-dimethylbut-2-ene
(major product)

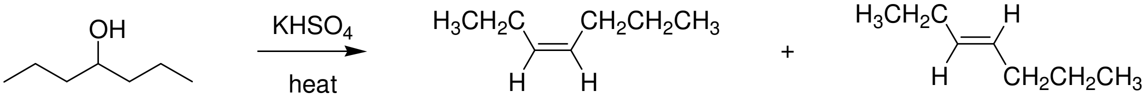
2,3-dimethylbut-1-ene
(minor product)

The Zaitsev Rule
When elimination can occur in more than one direction, the principal alkene is the one formed by loss of H from the β carbon having the fewest hydrogens.

β-Elimination reactions of alcohols yield the most highly substituted alkene as the major product.

5.11 Stereoselectivity in Alcohol Dehydration

In addition to being regioselective, alcohol dehydrations are stereoselective.
A **stereoselective reaction** is one in which a single starting material can yield two or more stereoisomeric products, but gives one of them in greater amounts than any other.



(*Z*)-hept-3-ene
(minor product)

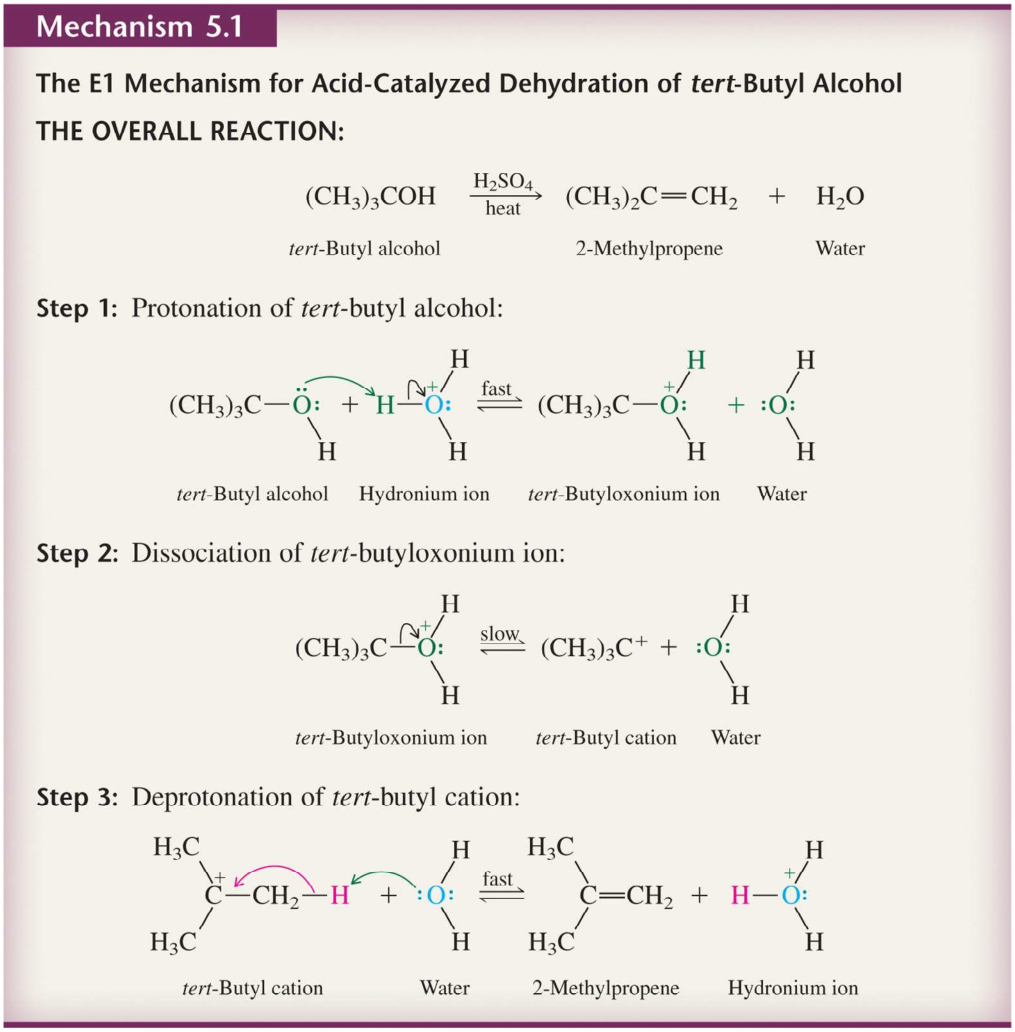
(*E*)-hept-3-ene
(major product)

5.12 The E1 and E2 Mechanisms of Alcohol Dehydration

The dehydration of alcohols and the reaction of alcohols with hydrogen halides share the following common features:

1) Both reactions are promoted by acids
2) The relative reactivity decreases in the order tertiary > secondary > primary

These similarities suggest that carbocations are intermediates in the acid-catalyzed dehydration of alcohols, just as they are in the reaction of alcohols with hydrogen halides.



Mechanism 5.1

The E1 Mechanism for Acid-Catalyzed Dehydration of *tert*-Butyl Alcohol

THE OVERALL REACTION:

$$(CH_3)_3COH \xrightarrow[\text{heat}]{H_2SO_4} (CH_3)_2C{=}CH_2 + H_2O$$

tert-Butyl alcohol — 2-Methylpropene — Water

Step 1: Protonation of *tert*-butyl alcohol:

tert-Butyl alcohol + Hydronium ion ⇌ (fast) *tert*-Butyloxonium ion + Water

Step 2: Dissociation of *tert*-butyloxonium ion:

$$(CH_3)_3C{-}\overset{+}{O}H_2 \xrightleftharpoons{\text{slow}} (CH_3)_3C^+ + H_2O$$

tert-Butyloxonium ion — *tert*-Butyl cation — Water

Step 3: Deprotonation of *tert*-butyl cation:

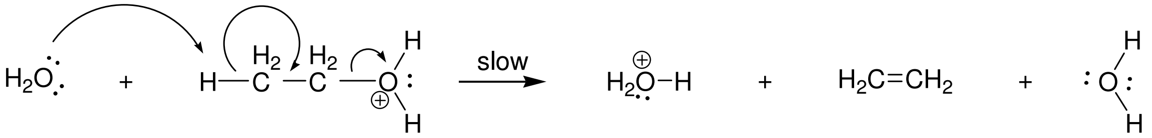
tert-Butyl cation + Water ⇌ (fast) 2-Methylpropene + Hydronium ion

Because rate-determining step is unimolecular, the overall dehydration process is referred to as a unimolecular elimination and is called the E1 mechanism.

In step 3, the carbocation acts as a Bronsted acid by transferring a proton to a Bronsted base (water).

Carbocations are strong acids; they are the conjugate acids of alkenes and readily lose a proton to form alkenes. Even weak bases such as water are sufficiently basic to abstract a proton from a carbocation.

As mentioned earlier, primary carbocations (from primary alcohol or other sources) are too high in energy to be reaction intermediates. In those cases, a different mechanism occurs.



Because rate-determining step involves two molecules (the alkyloxonium ion and water), the overall reaction is classified as bimolecular elimination, and is called the **E2 mechanism**

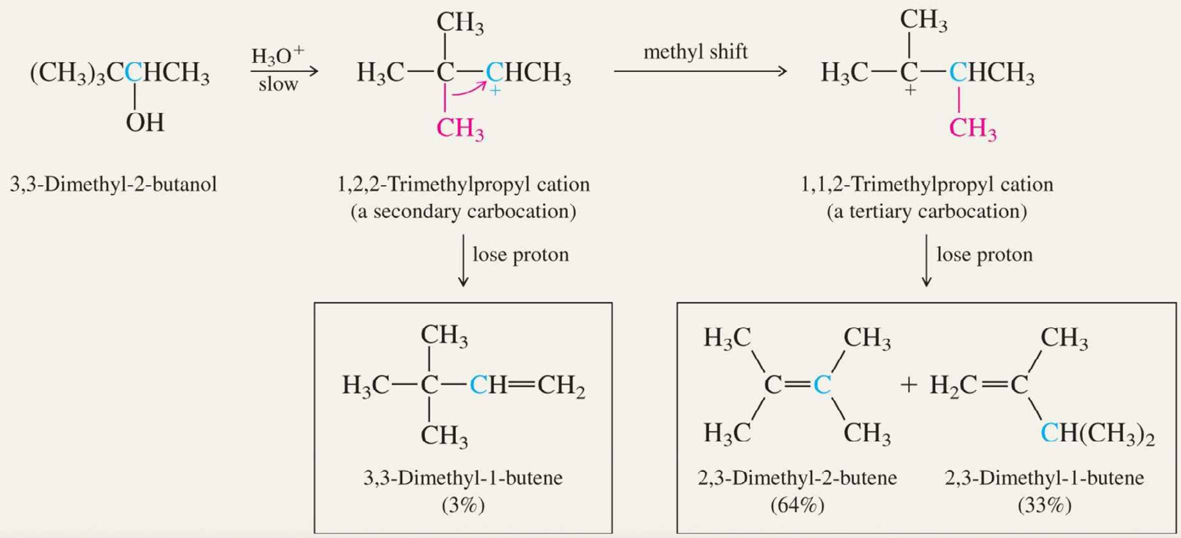
<u>Making sure everything is clear:</u>
In Chapter 4: Carbocations could be captured by halide anions to give alkyl halides.
In this chapter: Carbocation can lose a proton to form an alkene.
In the next section: Carbocations can undergo a rearrangement.

5.13 Rearrangements in Alcohol Dehydration

A rearrangement occurred when the alkene product does not have the same carbon skeleton as the starting alcohol.

Mechanism 5.2

Carbocation Rearrangement in Dehydration of 3,3-Dimethyl-2-butanol



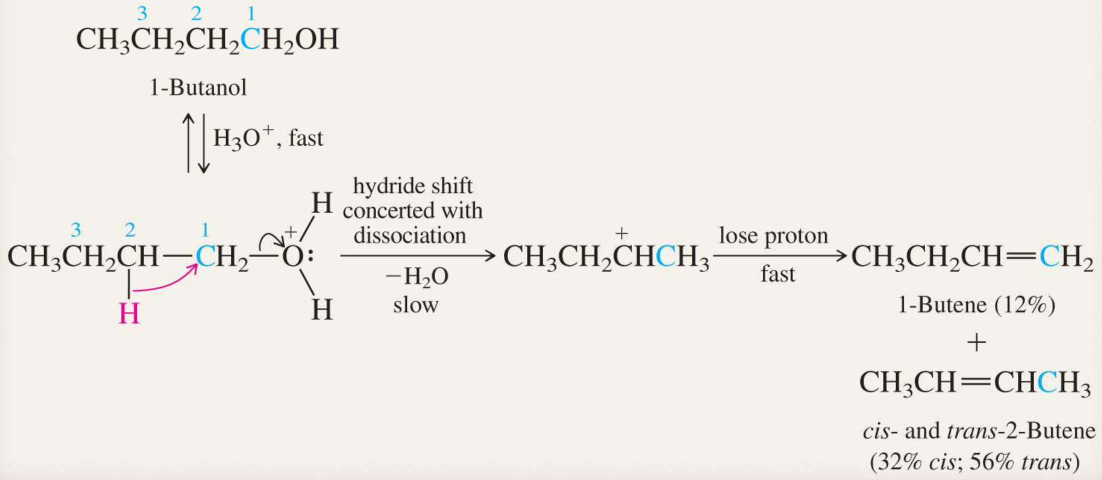
The rearranged alkenes arise by loss of a proton from the rearranged carbocation.

Tertiary carbocations are more stable than secondary carbocations. A rearrangement of a secondary to a tertiary carbocation is energetically favourable.

Once a carbocation is formed, anything that happens afterward happens rapidly.

Mechanism 5.3

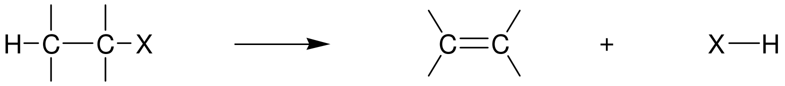
Hydride Shift in Dehydration of 1-Butanol



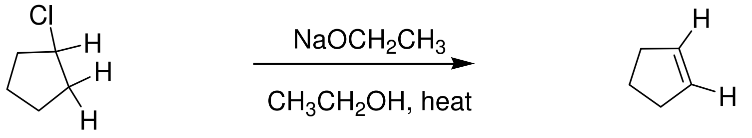
Alkyl groups other than methyl can also migrate to a positively charged carbon. Migration of hydrogen is called a hydride shift. They proceed in the direction that leads to a more stable carbocation.

5.14 Dehydrohalogenation of Alkyl Halides

Dehydrohalogenation is the loss of a hydrogen and a halogen from an alkyl halide. It is one of the most useful methods for preparing alkenes by b-elimination.



These reactions are carried out in the presence of a strong base, such as sodium ethoxide ($NaOCH_2CH_3$).

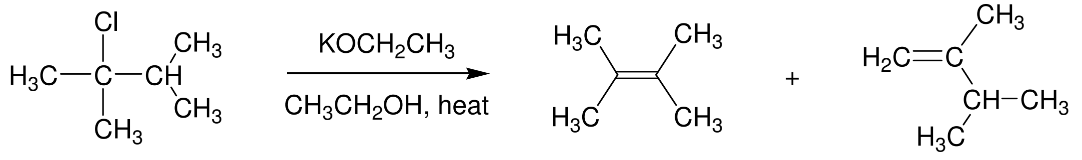


chlorocyclopentane

cyclopentene

Sodium methoxide ($NaOCH_3$), potassium hydroxide (KOH), potassium tert-butoxide ($KOC(CH_3)_3$) are also other suitable bases.

The regioselectivity of dehydrohalogenation of alkyl halides follows the Zaitsev's rule; more highly substituted double bond formation predominates.

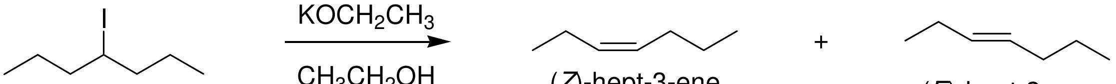


2-chloro-2,3-dimethylbutane

2,3-dimethylbut-2-ene (major)

2,3-dimethylbut-1-ene (minor)

In addition to being more regioselective, dehydrohalogenation of alkyl halides is stereoselective and favors formation of the more stable stereoisomer. Usually, as in the case of 5-iodoheptane, the *trans* (or *E*) alkene is formed in greater amounts than its *cis* (or *Z*) stereoisomer.

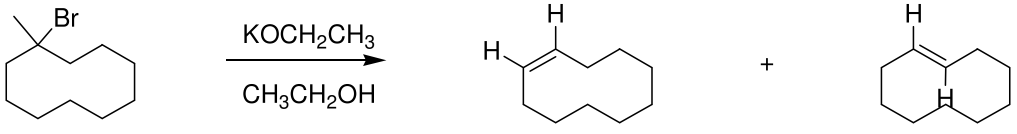


4-iodoheptane

(*Z*)-hept-3-ene

(*E*)-hept-3-ene

Dehydrohalogenation of cycloalkyl halides leads exclusively to *cis* cycloalkenes when the ring has fewer than ten carbons. As the ring becomes larger, it can accommodate either a *cis* or a *trans* double bond, and large-ring cycloalkyl halides give mixtures of *cis* and *trans* cycloalkenes.



1-bromo-1-methylcyclodecane

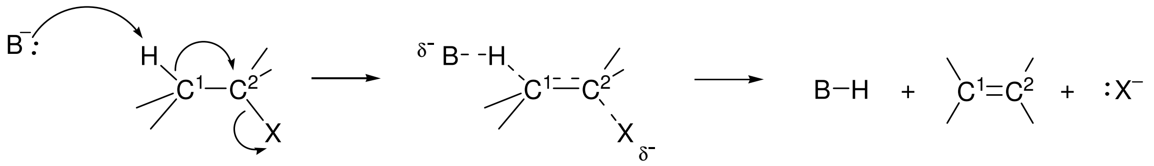
(*Z*)-cyclodecene

(*E*)-cyclodecene

5.15 The E2 Mechanism of Dehydrohalogenation of Alkyl Halides

Dehydrohalogenation of alkyl halides exhibits second-order kinetics (first order in alkyl halide and first order in base, so the rate = *k*[alkyl halide][base]) It implies that the rate-determining step involves both the base and the alkyl halide, so it is **bimolecular.**

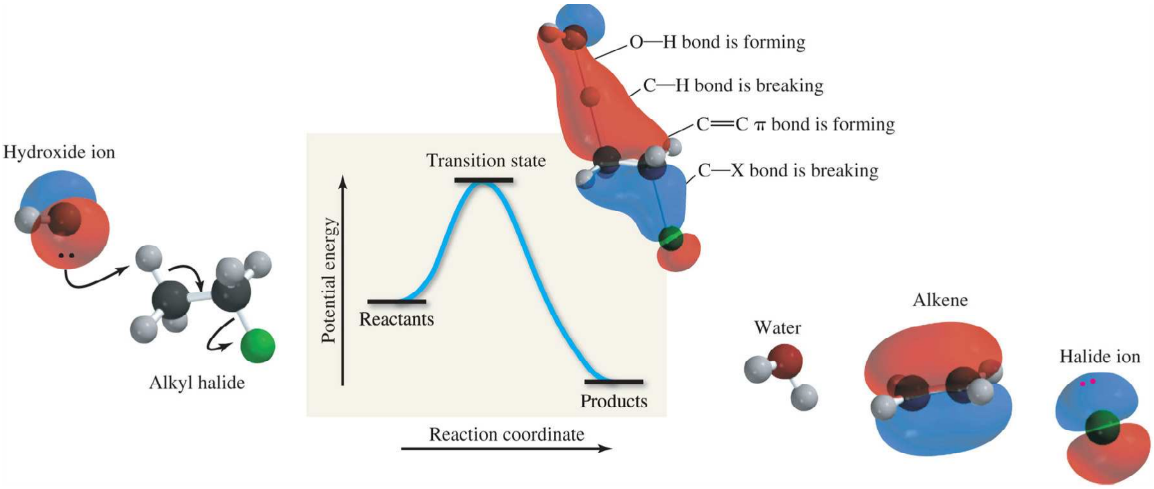
The rate of elimination depends on the halogen. That implies that carbon-halogen bond breaks in the rate-determining step.
The reactivity of alkyl halides increases with weaker C—X bond. Iodide is the best leaving group and fluoride is the poorest. (The weaker the carbon-halogen bond, the easier it is to break).



The four key elements of the E2 mechanism at the single transition step are:

B—H bond making
$C^1=C^2$ π bond formation
C^1—H bond breaking
C^2—X bond breaking

The E2 mechanism is followed whenever an alkyl halide (primary, secondary or tertiary) undergoes elimination in the presence of strong base.
The E2 mechanism is a concerted (one-step) bimolecular process in which the carbon-hydrogen and carbon-halogen bonds break in the same elementary step.

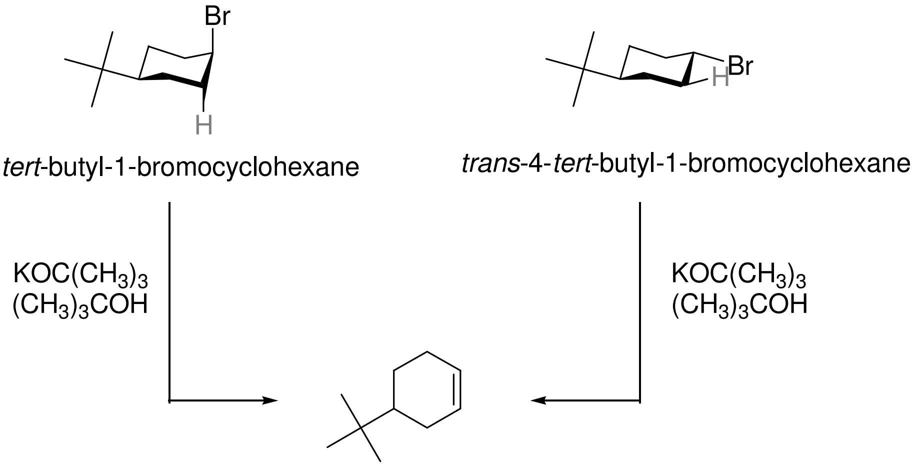


5.16 Anti Elimination in E2 Reactions: Stereoelectronic Effects

An effect on reactivity that has its origin in the spatial arrangement of orbitals (or bonds) is called a stereoelectronic effect.

The preference for an *anti coplanar* arrangement of H and the leaving group in the transition state for E2 dehydrohalogenation is an example of a stereoelectronic effect.

Example:



cis-4-*tert*-butyl-1-bromocyclohexane

trans-4-*tert*-butyl-1-bromocyclohexane

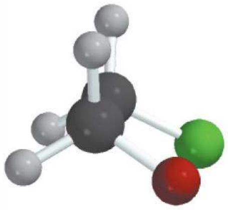
$KOC(CH_3)_3$
$(CH_3)_3COH$

$KOC(CH_3)_3$
$(CH_3)_3COH$

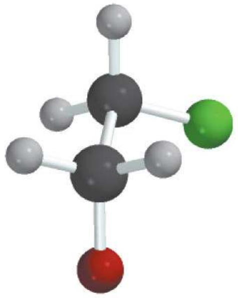
4-*tert*-butylcyclohexene

The *cis* isomer reacts over 500 times faster than the *trans*.
The two conformations that permit this are termed *syn coplanar* and *anti coplanar*.

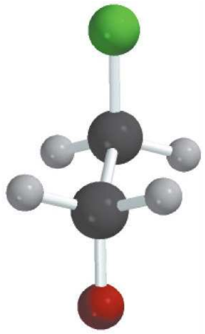
The different conformations for the H—C—C—X alignments:



Syn coplanar;
orbitals aligned but
bonds are eclipsed



Gauche;
orbitals not aligned for
double bond formation



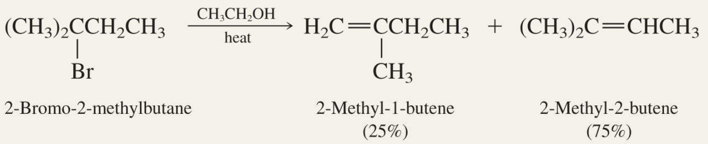
Anti coplanar;
orbitals aligned and
bonds are staggered

5.18 The E1 Mechanism of Dehydrohalogenation of Alkyl Halides

Mechanism 5.5

The E1 Mechanism for Dehydrohalogenation of 2-Bromo-2-methylbutane in Ethanol

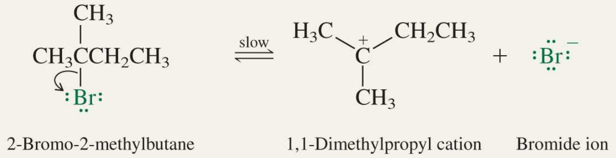
THE OVERALL REACTION:



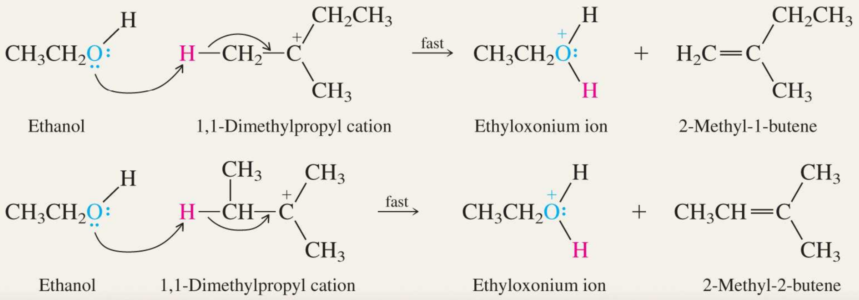
$$\underset{\text{Br}}{(CH_3)_2CCH_2CH_3} \xrightarrow[\text{heat}]{CH_3CH_2OH} \underset{CH_3}{H_2C{=}CCH_2CH_3} + (CH_3)_2C{=}CHCH_3$$

THE MECHANISM:

Step 1: Alkyl halide dissociates by heterolytic cleavage of carbon–halogen bond. (Ionization step)



Step 2: Ethanol acts as a base to remove a proton from the carbocation to give the alkene products. (Deprotonation step)



1. Alkyl halides can undergo elimination in absence of base.
2. A Carbocation is the intermediate.
3. The rate-determining step is unimolecular; ionization of alkyl halide.

Because the carbon-halogen bond breaks in the slow step, the rate of the reaction depends on the leaving group. Alkyl iodides have the weakest carbon-halogen bond and are the most reactive. Alkyl fluorides have the strongest carbon-halogen bond and are the least reactive.

Summary of Alkenes synthesis (textbook 7th edition p.215)

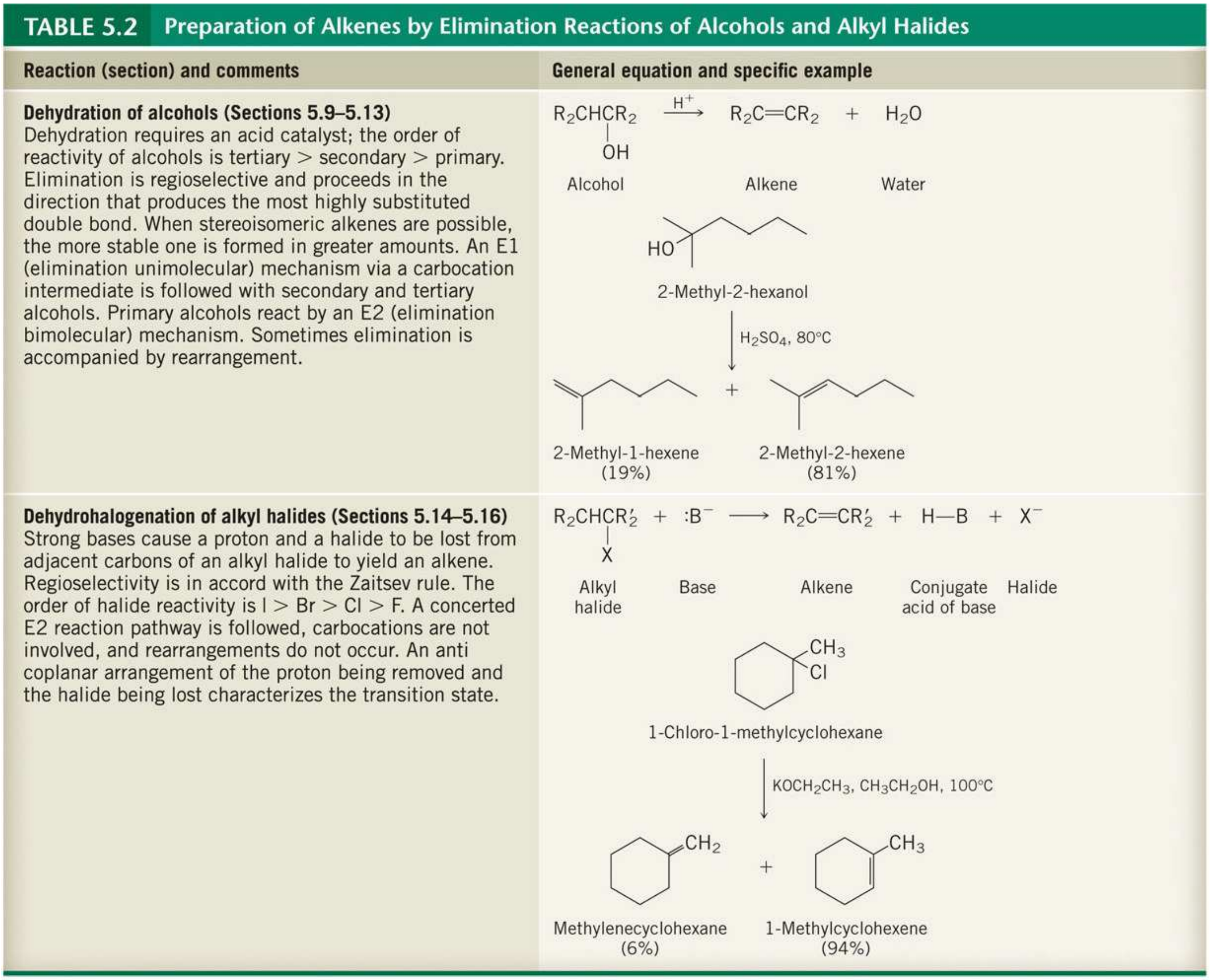
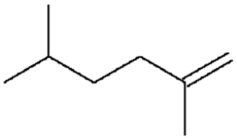


TABLE 5.2 Preparation of Alkenes by Elimination Reactions of Alcohols and Alkyl Halides

Reaction (section) and comments	General equation and specific example
Dehydration of alcohols (Sections 5.9–5.13) Dehydration requires an acid catalyst; the order of reactivity of alcohols is tertiary > secondary > primary. Elimination is regioselective and proceeds in the direction that produces the most highly substituted double bond. When stereoisomeric alkenes are possible, the more stable one is formed in greater amounts. An E1 (elimination unimolecular) mechanism via a carbocation intermediate is followed with secondary and tertiary alcohols. Primary alcohols react by an E2 (elimination bimolecular) mechanism. Sometimes elimination is accompanied by rearrangement.	$\underset{\text{OH}}{R_2CH\overset{\vert}{C}R_2} \xrightarrow{H^+} R_2C{=}CR_2 + H_2O$ Alcohol Alkene Water 2-Methyl-2-hexanol H_2SO_4, 80°C 2-Methyl-1-hexene (19%) + 2-Methyl-2-hexene (81%)
Dehydrohalogenation of alkyl halides (Sections 5.14–5.16) Strong bases cause a proton and a halide to be lost from adjacent carbons of an alkyl halide to yield an alkene. Regioselectivity is in accord with the Zaitsev rule. The order of halide reactivity is I > Br > Cl > F. A concerted E2 reaction pathway is followed, carbocations are not involved, and rearrangements do not occur. An anti coplanar arrangement of the proton being removed and the halide being lost characterizes the transition state.	$\underset{\text{X}}{R_2CH\overset{\vert}{C}R'_2} + :B^- \longrightarrow R_2C{=}CR'_2 + H{-}B + X^-$ Alkyl halide Base Alkene Conjugate acid of base Halide 1-Chloro-1-methylcyclohexane $KOCH_2CH_3$, CH_3CH_2OH, 100°C Methylenecyclohexane (6%) + 1-Methylcyclohexene (94%)

Extra Problems:

1. What is the IUPAC name of the following compound?



A) 2,5-dimethyl-1-hexene
B) 1,4-dimethyl-1-hexene
C) 2,5-dimethyl-2-hexene
D) 2,5-dimethyl-5-hexene

2. What is the IUPAC name of the following compound?

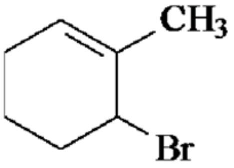
$(CH_3CH_2)_2C{=}CHCH_2CH_2CH_2CH(CH_3)_2$

A)	3-ethyl-8-methyl-3-nonene	C)	1,1-diethyl-6-methyl-3-heptene
B)	7-ethyl-2-methyl-6-nonene	D)	3-ethyl-7-isopropyl-3-octene

3. How many isomeric alkenes of formula C_4H_8, including stereoisomers, are possible?
   A) two B) three C) four D) five

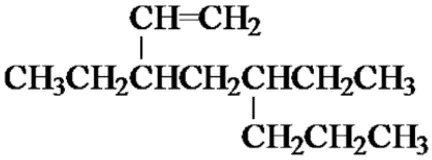
4. How many isomeric alkenes of formula C_5H_{10}, including stereoisomers, are possible?
   A) three B) four C) five D) six

5. What is the IUPAC name of the following compound?



A)	3-bromo-2-methylcyclohexene	C)	6-bromo-1-methylcyclohexene
B)	1-bromo-2-methyl-2-cyclohexene	D)	2-bromo-1-methylcyclohexene

6. What is the IUPAC name of the following compound?



$CH_3CH_2CH(CH{=}CH_2)CH_2CH(CH_2CH_2CH_3)CH_2CH_3$

A)	3-ethyl-propyl-1-heptene	C)	4,6-diethyl-1-octene
B)	ethyl-3-vinyloctane	D)	3,5-diethyl-1-octene

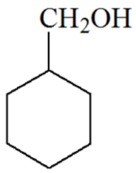
7. Which of the following alkenes exhibit E-Z isomerism?
   I. 1-chloropropene II. 2-chloropropene III. 3-chloropropene
   A) only I B) I and II C) II and III D) I and III

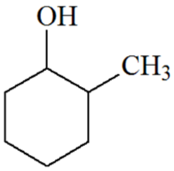
8. Which of the following C6H12 isomers has the highest heat of combustion?
   A) 1-hexene B) trans-3-hexene C) cis-3-hexene D) 2-methyl-2-pentene

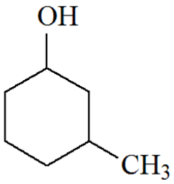
9. Identify the major organic product expected from the acid-catalyzed dehydration of 2-methyl-2-pentanol.

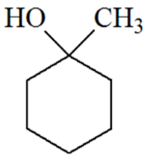
A)	2-methyl-1-pentene	C)	3-methyl-1-pentene
B)	2-methyl-2-pentene	D)	*cis*-3-methyl-2-pentene

10. Which alcohol below would undergo acid-catalyzed dehydration most readily?

A) 

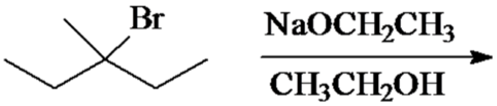
B) 

C) 

D) 

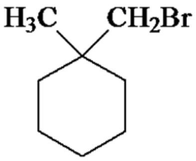
A) A B) B C) C D) D

11. How many isomeric alkenes are possible, including stereoisomers, in the following reaction?

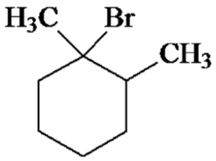


A) two B) three C) four D) five

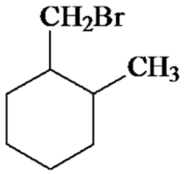
12. Which of the following cannot undergo an E2 reaction?



I



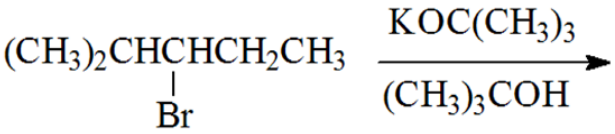
II



III

A) only I B) only II C) only III D) I and III

13. Including E-Z isomers, how many E2 products are possible in the following reaction?



$$(CH_3)_2CH\underset{\displaystyle Br}{\underset{|}{C}}HCH_2CH_3 \xrightarrow[(CH_3)_3COH]{KOC(CH_3)_3}$$

A) one B) two C) three D) four

14. Which of the following will give 2-methyl-1-butene as the only alkene product on treatment with KOC(CH3)3 in dimethyl sulfoxide?

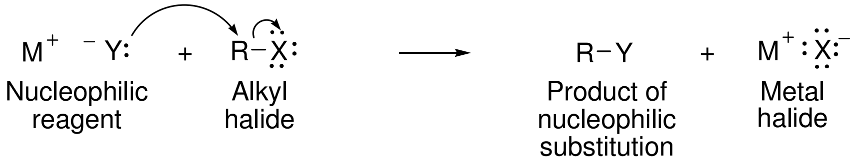
A) 2-bromo-3-methylbutane
B) 1-bromo-3-methylbutane
C) 2-bromo-2-methylbutane
D) 1-bromo-2-methylbutane

Answers: 1)A 2)A 3)C 4)D 5)C 6)D 7)A 8)A 9)B 10)D 11)B 12)A 13)C 14)D

Chapter 8:
Nucleophilic Substitution

A **Nucleophile** is a Lewis base (electron-pair donor).

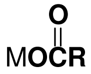
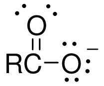
General equation of a Nucleophilic substitution with an alkyl halide:



8.1 Functional Group Transformation By Nucleophilic Substitution

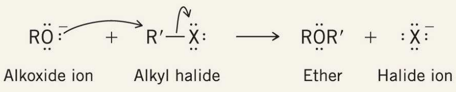
Nucleophilic substitution reactions of alkyl halides are related to elimination reactions in that the halogen acts as a leaving group on carbon and is lost as an ion. The carbon-halogen bond of the alkyl halide is broken heterolytically; the two electrons in that bond are lost *with* the leaving group.

The most encountered nucleophiles are anions, which are used as their salts (mostly Li^+, Na^+, K^+). The letter M is used to represent the metals. Some representative nucleophilic reagents are:

M**OR**	Metal **alkoxide**; source of the nucleophilic anion	$R\ddot{\underset{..}{O}}:^-$
 $M\overset{O}{\overset{\|}{C}}R$	Metal **carboxylate**; source of the nucleophilic anion	 $R\overset{:\ddot{O}}{\overset{\|}{C}}-\ddot{\underset{..}{O}}:^-$
M**SH**	Metal **hydrogen sulfide**; source of the nucleophilic anion	$H\ddot{\underset{..}{S}}:^-$
M**CN**	Metal **cyanide**; source of the nucleophilic anion	${}^-:C\equiv N:$
M**N$_3$**	Metal **azide**; source of the nucleophilic anion	${}^-\ddot{\underset{..}{N}}=\overset{+}{N}=\ddot{\underset{..}{N}}{}^-$

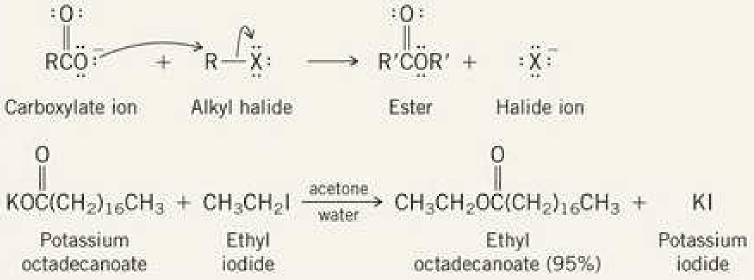
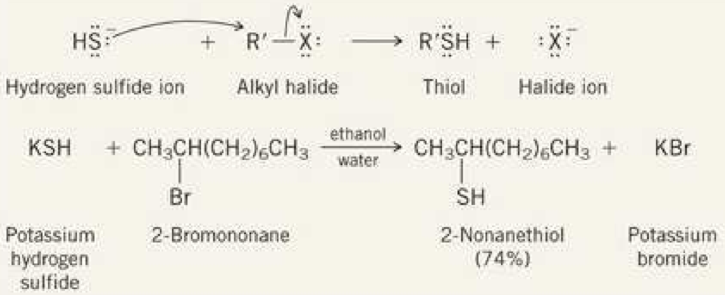
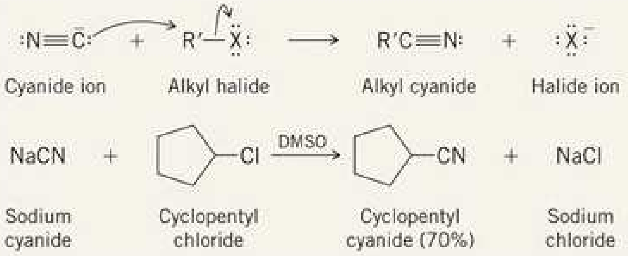
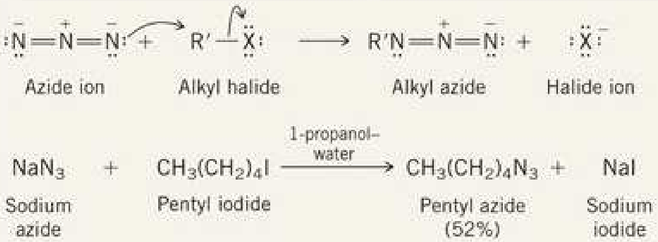
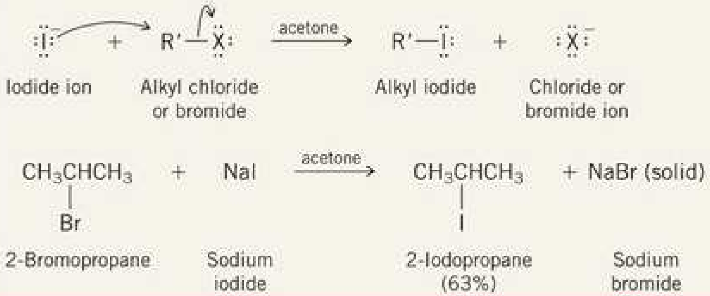
This chapter involves alkyl halides where the halogen is attached to an sp^3-hybridized carbon. Alkenyl halides and aryl halides, where the halogen is attached to an sp^2-hybridized carbon, are essentially unreactive under these conditions. Reactions are summarized in Table 8.1

TABLE 8.1 Representative Functional Group Transformations by Nucleophilic Substitution Reactions of Alkyl Halides

Nucleophile and comments	General equation and specific example
Alkoxide ion ($R\ddot{O}:^-$) The oxygen atom of a metal alkoxide is nucleophilic and replaces the halogen of an alkyl halide. The product is an *ether*.	 $R\ddot{\underset{..}{O}}:^- + R'-\ddot{\underset{..}{X}}: \longrightarrow R\ddot{\underset{..}{O}}R' + :\ddot{\underset{..}{X}}:^-$ Alkoxide ion · Alkyl halide · Ether · Halide ion $(CH_3)_2CHCH_2ONa + CH_3CH_2Br \xrightarrow{\text{isobutyl alcohol}} (CH_3)_2CHCH_2OCH_2CH_3 + NaBr$ Sodium isobutoxide · Ethyl bromide · Ethyl isobutyl ether (66%) · Sodium bromide

Continued

TABLE 8.1 Representative Functional Group Transformations by Nucleophilic Substitution Reactions of Alkyl Halides (*Continued*)

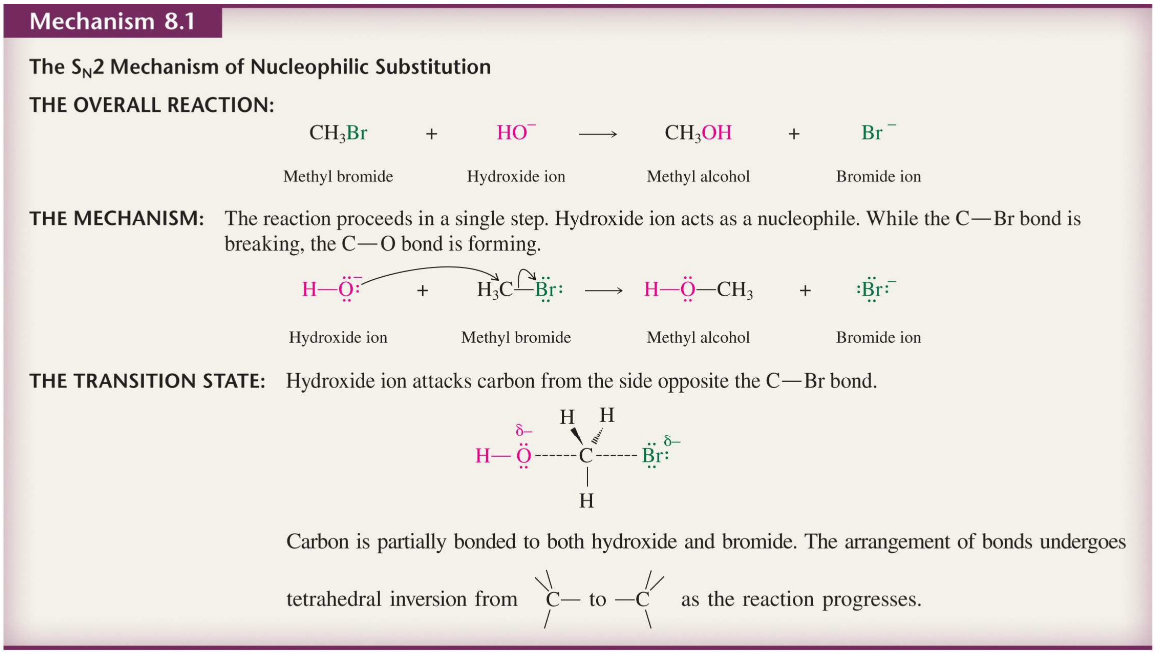
Nucleophile and comments	General equation and specific example
Carboxylate ion ($\mathrm{R\overset{O}{\overset{\|}{C}}{-}O^{-}}$) An *ester* is formed when the negatively charged oxygen of a carboxylate replaces the halogen of an alkyl halide.	 $\mathrm{R\overset{O}{\overset{\|}{C}}O^{-}} + \mathrm{R{-}X} \longrightarrow \mathrm{R'\overset{O}{\overset{\|}{C}}OR'} + \mathrm{X^{-}}$ Carboxylate ion, Alkyl halide, Ester, Halide ion $\mathrm{KO\overset{O}{\overset{\|}{C}}(CH_2)_{16}CH_3} + \mathrm{CH_3CH_2I} \xrightarrow[\text{water}]{\text{acetone}} \mathrm{CH_3CH_2O\overset{O}{\overset{\|}{C}}(CH_2)_{16}CH_3} + \mathrm{KI}$ Potassium octadecanoate, Ethyl iodide, Ethyl octadecanoate (95%), Potassium iodide
Hydrogen sulfide ion ($\mathrm{HS^{-}}$) Using hydrogen sulfide as a nucleophile permits the conversion of alkyl halides to compounds of the type RSH. These compounds are the sulfur analogs of alcohols and are known as *thiols.*	 $\mathrm{HS^{-}} + \mathrm{R'{-}X} \longrightarrow \mathrm{R'SH} + \mathrm{X^{-}}$ Hydrogen sulfide ion, Alkyl halide, Thiol, Halide ion $\mathrm{KSH} + \mathrm{CH_3\underset{Br}{\underset{\|}{C}}H(CH_2)_6CH_3} \xrightarrow[\text{water}]{\text{ethanol}} \mathrm{CH_3\underset{SH}{\underset{\|}{C}}H(CH_2)_6CH_3} + \mathrm{KBr}$ Potassium hydrogen sulfide, 2-Bromononane, 2-Nonanethiol (74%), Potassium bromide
Cyanide ion ($\mathrm{:\bar{C}{\equiv}N:}$) The negatively charged carbon atom of cyanide ion is usually the site of its nucleophilic character. Use of cyanide ion as a nucleophile permits the extension of a carbon chain by carbon–carbon bond formation. The product is an *alkyl cyanide,* or *nitrile.*	 $\mathrm{N{\equiv}C^{-}} + \mathrm{R'{-}X} \longrightarrow \mathrm{R'C{\equiv}N} + \mathrm{X^{-}}$ Cyanide ion, Alkyl halide, Alkyl cyanide, Halide ion NaCN + Cyclopentyl chloride $\xrightarrow{\text{DMSO}}$ Cyclopentyl cyanide + NaCl Sodium cyanide, Cyclopentyl chloride, Cyclopentyl cyanide (70%), Sodium chloride
Azide ion ($\mathrm{:\overset{-}{N}{=}\overset{+}{N}{=}\overset{-}{N}:}$) Sodium azide is a reagent used for carbon–nitrogen bond formation. The product is an *alkyl azide.*	 $\mathrm{\overset{-}{N}{=}\overset{+}{N}{=}\overset{-}{N}} + \mathrm{R'{-}X} \longrightarrow \mathrm{R'N{=}\overset{+}{N}{=}\overset{-}{N}} + \mathrm{X^{-}}$ Azide ion, Alkyl halide, Alkyl azide, Halide ion $\mathrm{NaN_3} + \mathrm{CH_3(CH_2)_4I} \xrightarrow{\text{1-propanol–water}} \mathrm{CH_3(CH_2)_4N_3} + \mathrm{NaI}$ Sodium azide, Pentyl iodide, Pentyl azide (52%), Sodium iodide
Iodide ion ($\mathrm{:I:^{-}}$) Alkyl chlorides and bromides are converted to *alkyl iodides* by treatment with sodium iodide in acetone. NaI is soluble in acetone, but NaCl and NaBr are insoluble and crystallize from the reaction mixture, making the reaction irreversible.	 $\mathrm{I^{-}} + \mathrm{R'{-}X} \xrightarrow{\text{acetone}} \mathrm{R'{-}I} + \mathrm{X^{-}}$ Iodide ion, Alkyl chloride or bromide, Alkyl iodide, Chloride or bromide ion $\mathrm{CH_3\underset{Br}{\underset{\|}{C}}HCH_3} + \mathrm{NaI} \xrightarrow{\text{acetone}} \mathrm{CH_3\underset{I}{\underset{\|}{C}}HCH_3} + \mathrm{NaBr\ (solid)}$ 2-Bromopropane, Sodium iodide, 2-Iodopropane (63%), Sodium bromide

8.2 Relative Reactivity of Halide Leaving Groups

Reactivity of halide leaving groups in nucleophilic substitution is the same as for elimination. Alkyl iodides undergo nucleophilic substitution at the fastest rate, alkyl fluorides the slowest.

8.3 The SN$_2$ Mechanism of Nucleophilic Substitution

A substitution nucleophilic bimolecular (S$_N$2) is a one-step concerted process in which both the alkyl halide and the nucleophile are involved at the transition state.



Mechanism 8.1

The S$_N$2 Mechanism of Nucleophilic Substitution

THE OVERALL REACTION:

$$CH_3Br + HO^- \longrightarrow CH_3OH + Br^-$$

Methyl bromide, Hydroxide ion, Methyl alcohol, Bromide ion

THE MECHANISM: The reaction proceeds in a single step. Hydroxide ion acts as a nucleophile. While the C—Br bond is breaking, the C—O bond is forming.

$$H{-}\ddot{O}{:}^- + H_3C{-}\ddot{B}r{:} \longrightarrow H{-}\ddot{O}{-}CH_3 + {:}\ddot{B}r{:}^-$$

Hydroxide ion, Methyl bromide, Methyl alcohol, Bromide ion

THE TRANSITION STATE: Hydroxide ion attacks carbon from the side opposite the C—Br bond.

Carbon is partially bonded to both hydroxide and bromide. The arrangement of bonds undergoes tetrahedral inversion from C— to —C as the reaction progresses.

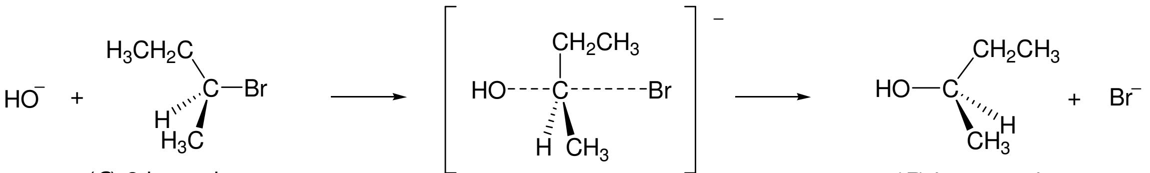
Two important factors of the mechanism are the kinetics and stereochemistry.

Kinetic studies measure the speed of a reaction. The rate determining step involves 2 molecules.

Stereochemistry studies the relative spatial arrangement of the atoms within the molecules before and after the reaction.

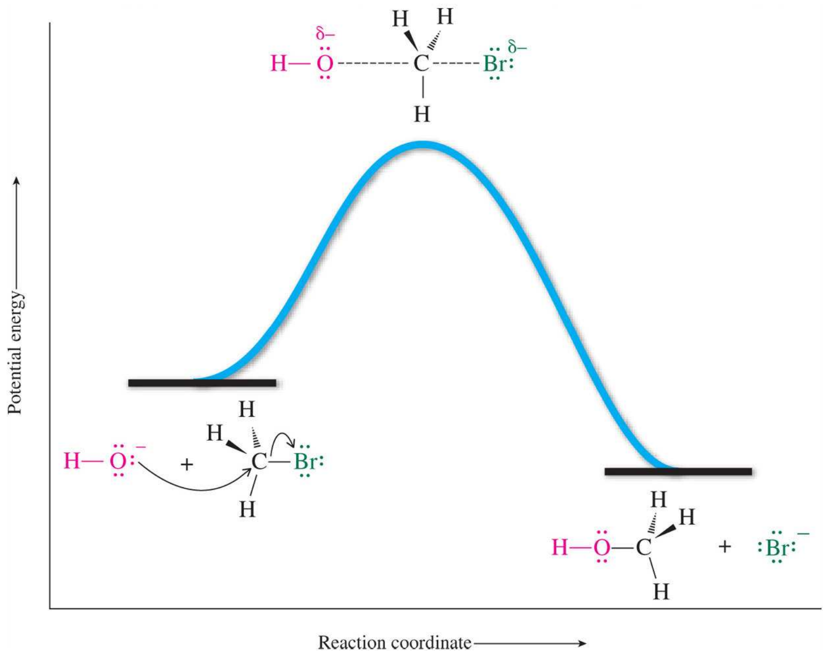
The nucleophile attacks the carbon from the side opposite to the bond of the leaving group. So S$_N$2 reactions proceed with inversion of configuration at the carbon that bears the leaving group. Therefore, the three-dimensional arrangement of the bonds in the product is opposite to that of the reactant.

Example:



(*S*)-2-bromobutane

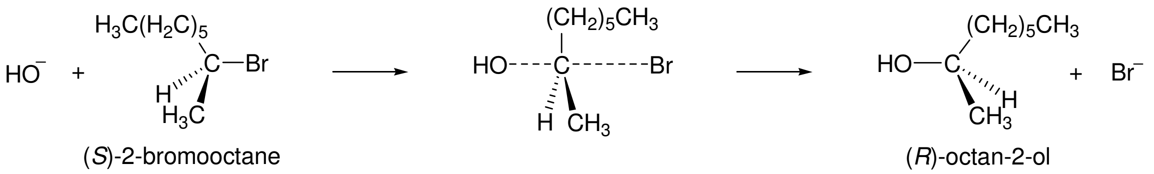
(*R*)-butan-2-ol



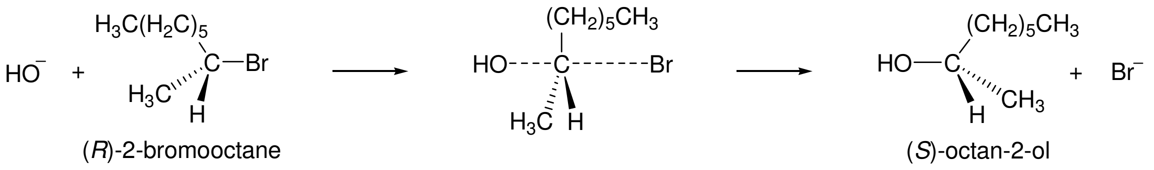
A **stereospecific reaction** is one in which stereoisomeric starting materials yield products that are stereoisomers of each other.

The reaction of 2-bromooctane with NaOH (in ethanol-water) is stereospecific.

(*S*)-2-Bromooctane → (*R*)-2-Octanol:



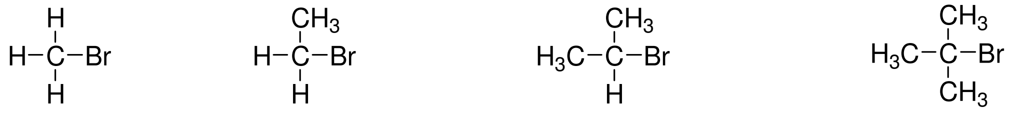
(*R*)-2-Bromooctane → (*S*)-2-Octanol:



8.4 Steric Effects and S_N2 Reaction Rates

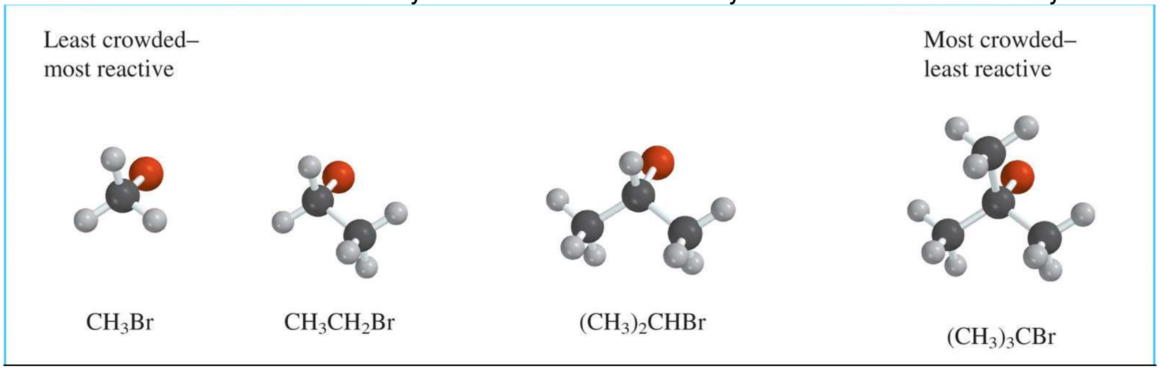
The rate of nucleophilic substitution by the S_N2 mechanism is governed by steric effects. Crowding at the carbon that bears the leaving group slows the rate of bimolecular nucleophilic substitution.

Steric hindrance occurs when the size of groups within a molecule prevents chemical reactions that are observed in related smaller molecules.



$\mathrm{H}-\overset{\mathrm{H}}{\underset{\mathrm{H}}{\mathrm{C}}}-\mathrm{Br}$ $\mathrm{H}-\overset{\mathrm{CH_3}}{\underset{\mathrm{H}}{\mathrm{C}}}-\mathrm{Br}$ $\mathrm{H_3C}-\overset{\mathrm{CH_3}}{\underset{\mathrm{H}}{\mathrm{C}}}-\mathrm{Br}$ $\mathrm{H_3C}-\overset{\mathrm{CH_3}}{\underset{\mathrm{CH_3}}{\mathrm{C}}}-\mathrm{Br}$

Primary Secondary Tertiary



Alkyl groups at the carbon atom adjacent to the point of nucleophilic attack also decrease the rate of the S_N2 reaction.

Fastest Slowest

$CH_3CH_2Br > CH_3CH_2CH_2Br > (CH_3)_2CHCH_2Br > (CH_3)_3CCH_2Br$

8.5 Nucleophiles and Nucleophilicity

The nucleophiles described in the previous sections have been anions (HO^-, HS^-, CH_3O^-, $N{\equiv}C^-$, etc.) However, not all nucleophiles are anions; many are neutral (H_2O, CH_3OH, NH_3, etc.)
All nucleophiles, however, are Lewis bases.

Many of the solvents in which nucleophilic substitutions are carried out are themselves nucleophiles. The term *solvolysis* refers to a nucleophilic substitution in which the nucleophile is the solvent.

Nucleophilicity (or nucleophilic strength) is a measure of the reactivity of a nucleophile. It measures how fast a Lewis base displaces a leaving group from a suitable substrate.

The connection between basicity and nucleophilicity holds when comparing atoms in the same row of the periodic table. Thus, HO^- is more basic and more nucleophilic than F^-, and NH_3 is more basic and more nucleophilic than H_2O. It does not hold when proceeding down a column in the periodic table. For example, I^- is the least basic of the halide ions but is the most nucleophilic. F^- is the most basic halide ion but the least nucleophilic.

TABLE 8.4 Nucleophilicity of Some Common Nucleophiles

Reactivity class	Nucleophile	Relative reactivity*
Very good nucleophiles	I^-, HS^-, RS^-	$>10^5$
Good nucleophiles	Br^-, HO^-, RO^-, CN^-, N_3^-	10^4
Fair nucleophiles	NH_3, Cl^-, F^-, RCO_2^-	10^3
Weak nucleophiles	H_2O, ROH	1
Very weak nucleophiles	RCO_2H	10^{-2}

Extra Problems:

1. Identify the nucleophile in the following reaction.

$$CH_3Br + NaOH \xrightarrow{H_2O} CH_3OH + NaBr$$

A) CH_3Br B) OH^- C) H_2O D) Br^-

2. Identify the leaving group in the following reaction.

$$CH_3CH_2Br + NaHS \xrightarrow{CH_3OH} CH_3CH_2SH + NaBr$$

A) CH_3CH_2Br B) HS^- C) Br^- D) CH_3OH

3. Which of the following cannot act as a nucleophile?
A) NH_3 B) H_2O C) I^- D) CH_4

4. In the S_N2 reaction, the "2" stands for
A) two reactants in the reaction.
B) two steps in the reaction.
C) two intermediates in the reaction.
D) bimolecular kinetics for the reaction.

5. Which of the following undergoes a substitution reaction with sodium cyanide in DMSO at the fastest rate?
A) CH_3CH_2F B) CH_3CH_2Cl C) CH_3CH_2Br D) CH_3CH_2I

6. Which of the following reacts the fastest by the S_N2 mechanism?
A) CH_3Br B) CH_3CH_2Br C) $(CH_3)_2CHBr$ D) $(CH_3)_3CBr$

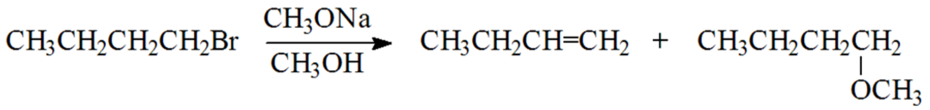
7. Identify the major product(s) in the reaction of (R)-2-bromopentane with sodium cyanide in DMSO?
A) (R)-2-cyanopentane
B) (S)-2-cyanopentane
C) racemic mixture of 2-cyanopentane
D) *trans*-2-pentene

8. What is the leaving group in the following reaction?

$$CH_3CH_2OH + HCl \longrightarrow CH_3CH_2Cl + H_2O$$

A) OH- B) H2O C) CH3CH2+ D) C1-

9. Identify the mechanistic pathways, respectively, for the products in the following reaction.



$$CH_3CH_2CH_2CH_2Br \xrightarrow[CH_3OH]{CH_3ONa} CH_3CH_2CH{=}CH_2 + CH_3CH_2CH_2\underset{\displaystyle OCH_3}{\underset{|}{CH_2}}$$

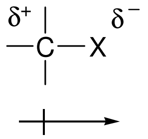
A) E1, SN1 B) E1, SN2 C) E2, SN1 D) E2, SN2

Answers: 1)B 2)C 3)D 4)D 5)D 6)A 7)B 8)B 9)D

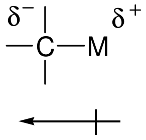
Chapter 14:
Organometallic Compounds

14.2 Carbon-Metal Bonds in Organometallic Compounds

Organometallic compounds are compounds that have a carbon-metal bond.



Halogen (X) is more electronegative than carbon



Metal (M) is less electronegative than carbon

An anion that contains a negatively charged carbon is referred to as a carbanion. Organometallic compounds have a carbanionic character.

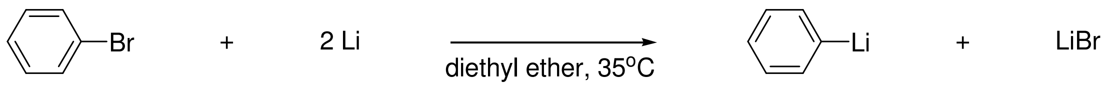
14.3 Preparation of Organolithium Compounds

Organolithium compounds are normally prepared by reaction of alkyl halides with lithium. It is an oxidation-reduction reaction where the carbon is reduced and the metal is oxidized.

RX	+	2M	$\longrightarrow$	RM	+	M^+X^-
Alkyl halide		Group 1 metal		Group 1 organometallic compound		Metal halide

Example:

$(CH_3)_3CCl$	+	2 Li	$\xrightarrow[\text{diethyl ether, -30}^{\circ}\text{C}]{}$	$(CH_3)_3CLi$	+	LiCl
tert-Butyl chloride		Lithium		*tert*-Butyllithium		lithium chloride



Bromobenzene Lithium Phenyllithium lithium bromide

The alkyl halide can be primary, secondary or tertiary. Alkyl iodides are the most reactive, followed by bromides, then chlorides. Fluorides are relatively unreactive.

Unlike elimination and nucleophilic substitution reactions, formation of organolithium compounds does not require that the halogen be bounded to *sp*^{3}-hybridized carbon.

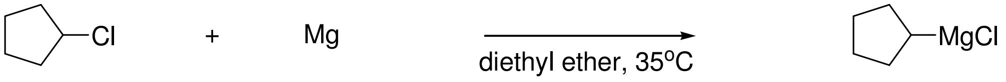
14.4 Preparation of Organomagnesium Compounds: Grignard Reagents

The Grignard reagents are named after the French chemist Victor Grignard who was a corecipient of the 1912 Nobel Prize in Chemistry.

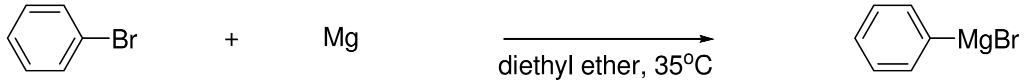
Grignard reagents are prepared from organic halides by reaction with magnesium.

RX	+	Mg	$\longrightarrow$	$RMgX$
Organic halide		Magnesium		Organomagnesium halide

Example:



Cyclopentyl chloride	Magnesium	diethyl ether, 35°C	Cyclopentylmagnesium chloride



Bromobenzene	Magnesium	diethyl ether, 35°C	Phenylmagnesium bromide

14.5 Organolithium and Organomagnesium Compounds as Brønsted Bases

Grignard reagents (M = MgX) and organolithium reagents (M = Li) are strong bases.

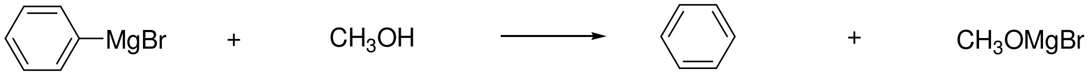
They react instantly with proton donors even as weakly acidic as water and alcohols. A proton is transferred from the hydroxyl group to the negatively polarized carbon of the organometallic compound to form a hydrocarbon.

$$R{-}M + H{-}\ddot{\underset{..}{O}}{-}R' \rightleftharpoons R{-}H + R'{-}\ddot{\underset{..}{O}}\!:^{-}\ M^{+}$$

Stronger base	Stronger acid	Weaker acid	Weaker base

Example:

$CH_3CH_2CH_2CH_2Li$	+	H_2O	$\longrightarrow$	$CH_3CH_2CH_2CH_3$	+	$LiOH$
Phenylmagnesium bromide		Water		Butane		Lithium hydroxide



Bromobenzene	Magnesium	Benzene	Methoxymagnesium bromide

Organolithium compounds and Grignard reagents act like carbanions and will abstract a proton from any substance more acidic than a hydrocarbon. Thus, N—H groups and terminal alkynes (RC≡C–H) are converted to their conjugate bases by proton transfer to organolithium and organomagnesium compounds.

Example:

CH_3Li	+	NH_3	$\rightleftharpoons$	CH_4	+	$LiNH_2$
Methyllithium (stronger base)		Ammonia (stronger acid: pKa = 36)		Methane (weaker acid: pKa = 60)		Lithium amide (weaker base)
CH_3CH_2MgBr	+	$HC\equiv CH$	$\rightleftharpoons$	CH_3CH_3	+	$HC\equiv CMgBr$
Ethylmagnesium bromide (stronger base)		Acetylene or Ethyne (stronger acid: pKa = 26)		Ethane (weaker acid: pKa = 62)		Ethynylmagnesium bromide (weaker base)

14.11 Alkane Synthesis Using Organocopper Reagents

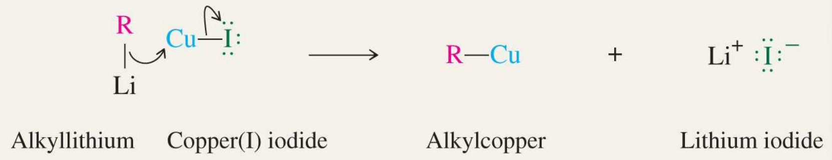
Lithium dialkylcuprates are also useful synthetic reagents.
They are prepared from two equivalents of an alkyllithiums and a copper(I) halide.

$2\ RLi$	+	CuX	$\xrightarrow[\text{diethyl ether or THF}]{}$	R_2CuLi	+	LiX
Alkyllithium		Cu(I) halide (X = Cl, Br, I)		Lithium dialkylcuprate		Lithium halide

Mechanism 14.1

Formation of a Lithium Dialkylcuprate (Gilman Reagent)

Step 1: One molar equivalent of an alkyllithium reagent displaces iodide from copper(I) iodide to give an alkylcopper(I) species.



Step 2: The second molar equivalent of the alkyllithium adds to the alkylcopper to give a negatively charged R_2Cu^- species called a *dialkylcuprate.* It is formed as its lithium salt, a lithium dialkylcuprate.

The reaction is carried out in diethyl ether or tetrahydrofuran solution. The lithium dialkylcuprate is soluble under these conditions and used directly.

Lithium dialkylcuprates and Lithium diarylcuprates react with alkyl halides to produce alkanes by carbon-carbon bond formation between the alkyl group of the alkyl halide and the alkyl group of the dialkylcuprate.

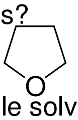
R_2CuLi	+	R'X	$\longrightarrow$	R−R'	+	RCu	+	LiX
Lithium dialkylcuprate		Alkyl halide		Alkane		Alkylcopper		Lithium halide

Example

$(CH_3CH_2)_2CuLi$	+	$CH_3(CH_2)_6CH_2I$	$\xrightarrow[\text{diethyl ether}]{}$	$CH_3(CH_2)_6CH_2CH_2CH_3$
Lithium diethylcuprate		1-Iodooctane		Decane

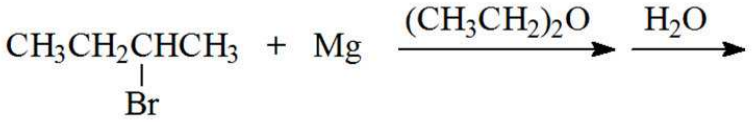
The reaction of cuprate reagents with alkyl halides follows the usual S_N2 order : CH_3 > primary > secondary > tertiary, and I > Br > Cl > F.

Extra Problems:

1. Which one of the following would not be a suitable solvent for Grignard reagents?
   A) $CH_3CH_2OCH_2CH_3$, diethyl ether
   C) tetrahydrofuran (THF) 

   B) CH_3CH_2OH, ethanol
   D) they would all be suitable solvents

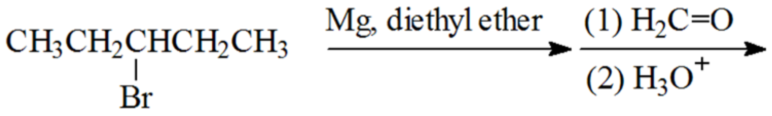
2. What are the products of the following sequence of reactions?



$$\underset{\displaystyle Br}{CH_3CH_2\overset{}{C}HCH_3} + Mg \xrightarrow{(CH_3CH_2)_2O} \xrightarrow{H_2O}$$

   A) 2-butanol and Mg(OH)Br
   B) 2-butanol and MgHBr
   C) butane and Mg(OH)Br
   D) butane and MgHBr

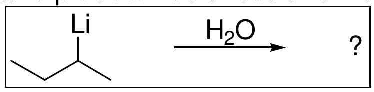
3. What is the major product of the following reaction?

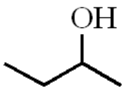


$$CH_3CH_2\underset{\displaystyle Br}{C}HCH_2CH_3 \xrightarrow{\text{Mg, diethyl ether}} \xrightarrow[(2)\ H_3O^+]{(1)\ H_2C{=}O}$$

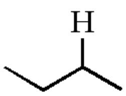
   A) 2-ethyl-1-pentanol
   B) 2-ethyl-1-butanol
   C) 3-pentanol
   D) 3-methyl-1-pentanol

4. What organic product would result from this reaction?





A



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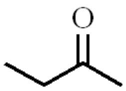
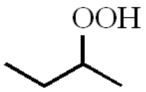


C



D

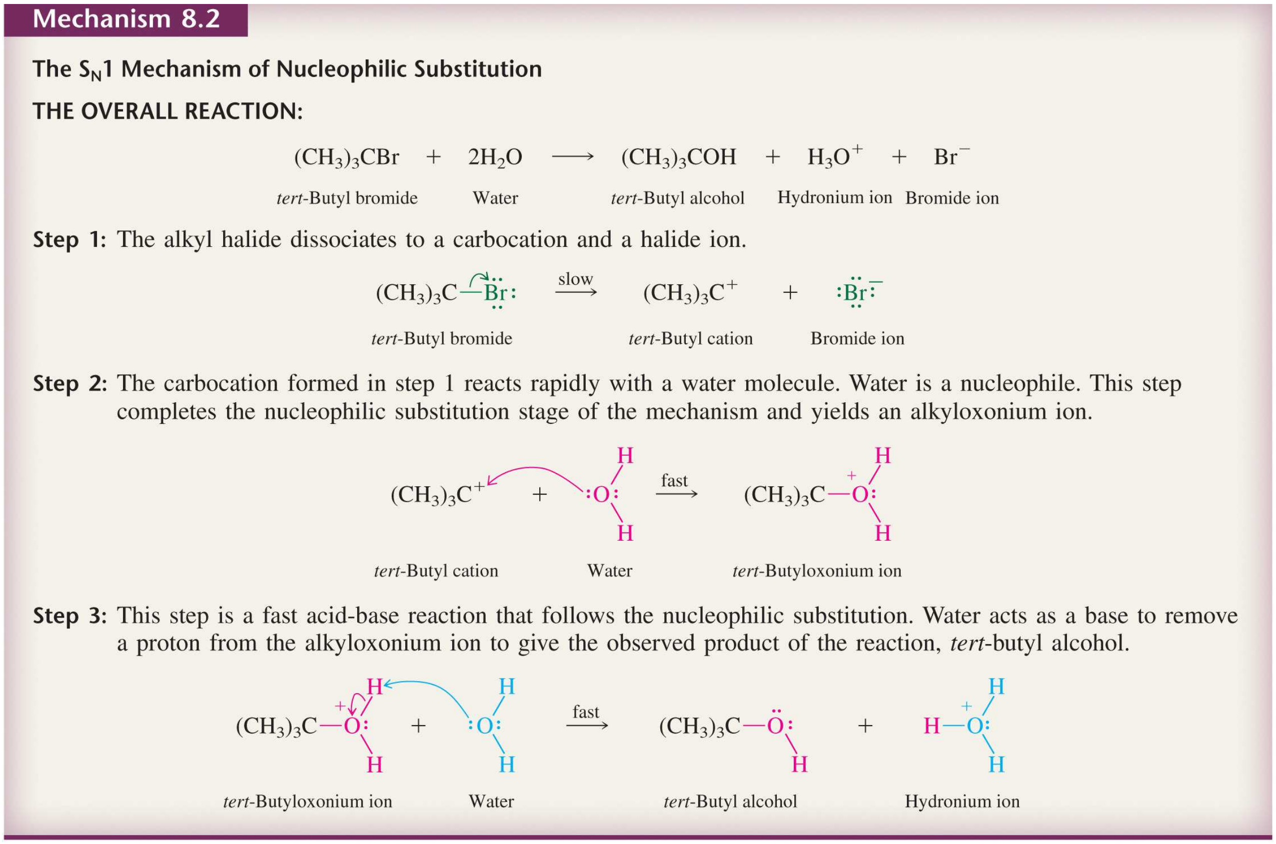
Answers: 1)B 2)C 3)B 4)B

Chapter 8 (Continue):
Nucleophilic Substitution

8.6 The S_N1 Mechanism of Nucleophilic Substitution

The first step in a substitution nucleophilic unimolecular (S_N1) is the dissociation of the alkyl halide to form a carbocation as the key intermediate.

The S_N1 mechanism is an ionization mechanism.



Mechanism 8.2

The S_N1 Mechanism of Nucleophilic Substitution

THE OVERALL REACTION:

$$(CH_3)_3CBr + 2H_2O \longrightarrow (CH_3)_3COH + H_3O^+ + Br^-$$

tert-Butyl bromide, Water, *tert*-Butyl alcohol, Hydronium ion, Bromide ion

Step 1: The alkyl halide dissociates to a carbocation and a halide ion.

$$(CH_3)_3C{-}\ddot{\underset{..}{Br}}: \xrightarrow{\text{slow}} (CH_3)_3C^+ + :\ddot{\underset{..}{Br}}:^-$$

tert-Butyl bromide, *tert*-Butyl cation, Bromide ion

Step 2: The carbocation formed in step 1 reacts rapidly with a water molecule. Water is a nucleophile. This step completes the nucleophilic substitution stage of the mechanism and yields an alkyloxonium ion.

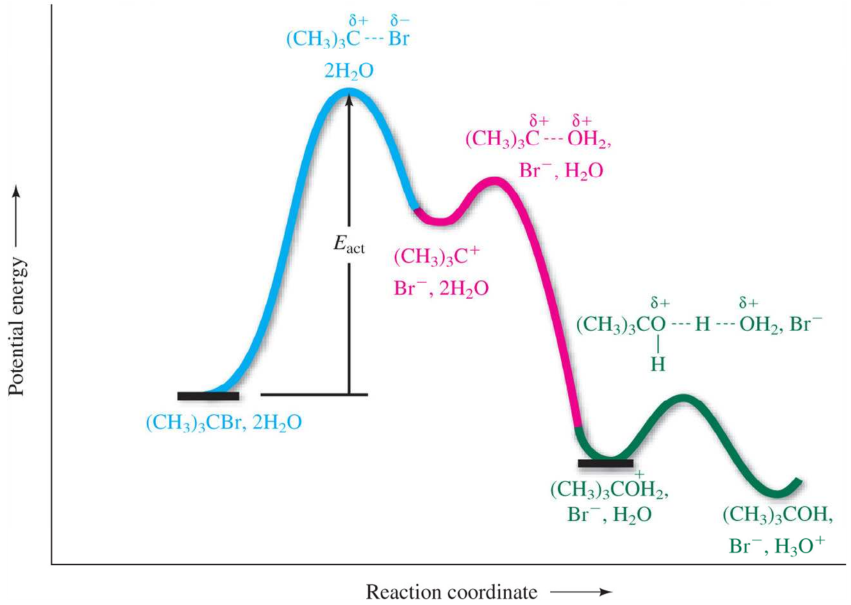
$$(CH_3)_3C^+ + :\ddot{O}H_2 \xrightarrow{\text{fast}} (CH_3)_3C{-}\overset{+}{O}H_2$$

tert-Butyl cation, Water, *tert*-Butyloxonium ion

Step 3: This step is a fast acid-base reaction that follows the nucleophilic substitution. Water acts as a base to remove a proton from the alkyloxonium ion to give the observed product of the reaction, *tert*-butyl alcohol.

$$(CH_3)_3C{-}\overset{+}{O}H_2 + :\ddot{O}H_2 \xrightarrow{\text{fast}} (CH_3)_3C{-}\ddot{O}H + H{-}\overset{+}{O}H_2$$

tert-Butyloxonium ion, Water, *tert*-Butyl alcohol, Hydronium ion



8.7 Carbocation Stability and S_N1 Reaction Rates

The relative reactivity of alkyl halides in S_N1 reactions is exactly the opposite of S_N2:

S_N1 reactivity: methyl < primary < secondary < tertiary
S_N2 reactivity: methyl > primary > secondary > tertiary

Methyl and primary carbocations are so high in energy that their intermediacy in nucleophilic susbstitutions is unlikely. In general, methyl and primary alkyl halides never react by the S_N1 mechanism. Tertiary alkyl halides never react by S_N2 mechanism.

8.8 Stereochemistry of S_N1 Reactions

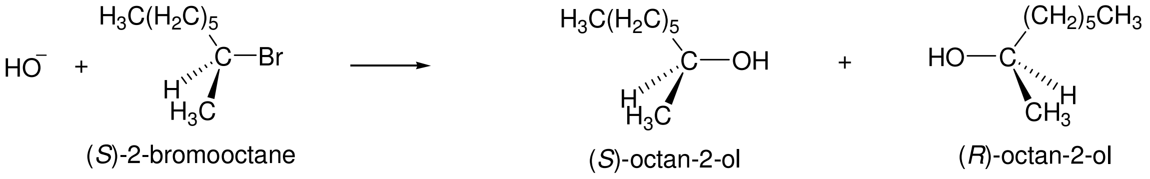
In general, Nucleophilic substitutions that exhibit first-order kinetic behavior are not stereospecific. In other words, the S_N1 mechanism is not very stereoselective.

Although S_N2 reactions are stereospecific and proceed with inversion of configuration at the chiral carbon, the situation is not as obvious for the S_N1.

When the leaving group departs from a chirality center of an optically active halide, the carbocation that results is *sp*^{2}-hybridized and is define in a plane of symmetry. The carbocation is now achiral. Both faces are available for attack by a nucleophile.

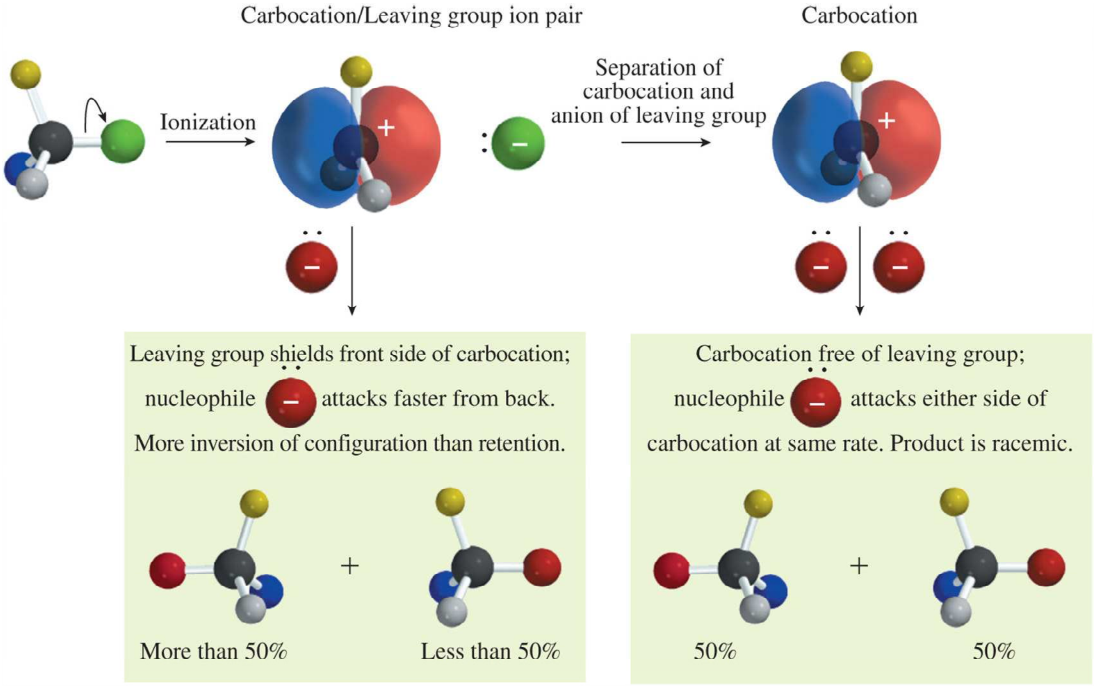
If a nucleophile can approach each face of the carbocation equally, the substitution by the S_N1 mechanism should give a 1:1 mixture of enantiomers, irrespective of wheter the starting alkyl halide is *R*, *S* or racemic. S_N1 reactions **should** give racemic products from optically active starting materials.

Example:



But in reality, there is still more inversion of configuration. Eventhough the leaving group (ion pair) completely dissociates from the carbocation, it still blocks the pathway for the nucleophile on that side.

In the previous example, there is still more (*R*)-octan-2-ol that is being produced (83%) in comparison to its enantiomer, the (*S*)-octan-2-ol (17%).



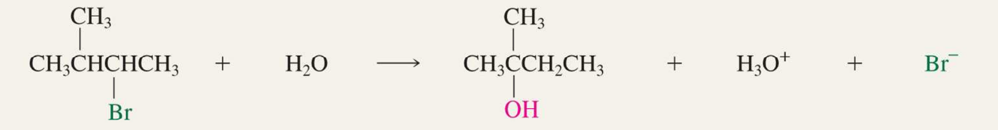
8.9 Carbocation Rearrangements in S_N1 Reactions

Since carbocations are intermediates in S_N1 reactions, rearrangements are possible.

Mechanism 8.3

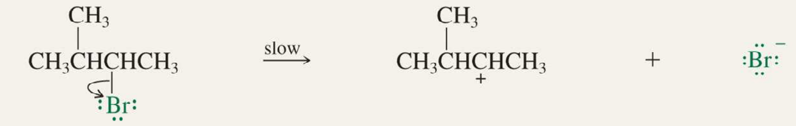
Carbocation Rearrangement in the S_N1 Hydrolysis of 2-Bromo-3-methylbutane

THE OVERALL REACTION:



2-Bromo-3-methylbutane Water 2-Methyl-2-butanol Hydronium ion Bromide ion

Step 1: The alkyl halide ionizes to give a carbocation and bromide ion. This is the rate-determining step.

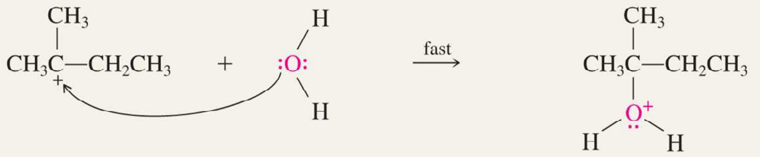


2-Bromo-3-methylbutane 1,2-Dimethylpropyl cation Bromide ion

Step 2: The carbocation formed in step 1 is secondary; it rearranges by a hydride shift to form a more stable tertiary carbocation.

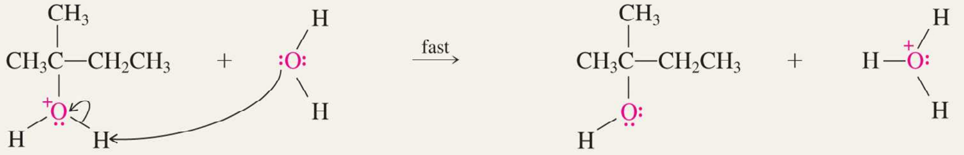
1,2-Dimethylpropyl cation 1,1-Dimethylpropyl cation

Step 3: The tertiary carbocation is attacked by water acting as a nucleophile.



1,1-Dimethylpropyl cation Water 1,1-Dimethylpropyloxonium ion

Step 4: Proton transfer from the alkyloxonium ion to water completes the process.



1,1-Dimethylpropyloxonium ion Water 2-Methyl-2-butanol Hydronium ion

8.10 Effect of Solvent on the Rate of Nucleophilic Substitution

The major effect of the solvent is on the rate of nucleophilic substitution, not on the nature of the products.

In general, S_N1 reaction rates increase in polar solvents. A non-polar solvent has little effect on the energy of the transition state of the S_N1 reaction. A polar solvent stabilizes the charge-separated transition state, lowers the activation energy, and increases the rate of reaction.

In general, S_N2 reaction rates increase in polar aprotic solvents. (Protic solvents have an —OH group that allows them to form hydrogen bonds to anionic nucleophiles. An aprotic solvent is one that does not have an —OH group.) Therefore, aprotic solvents do not solvate anions very strongly, leaving them much more able to express their nucleophilic character.

8.11 Substitution and Elimination as Competing Reactions

Alkyl halides can react with Lewis bases by nucleophilic substitution and/or elimination.

The structure of the alkyl halide and the basicity of the anion determine whether substitution or elimination will be the principal reaction observed.

Elimination versus Substitution

The major reaction of a secondary alkyl halide with an alkoxide ion (a stronger base than hydroxide) is elimination by the E_2 mechanism.

When is Substitution Favored?

Given that the major reaction of a secondary alkyl halide with an alkoxide ion is elimination by the E_2 mechanism, we can expect the proportion of substitution to increase with:

1) Decreased crowding at carbon that bears the leaving group increases substitution relative to elimination. But a crowded alkoxide base can favor Elimination even with a primary alkyl halide.

2) Decreased basicity of the nucleophile. Weakly basic nucleophile increases substitution relative to elimination.

Substitution by the S_N2 mechanism predominates only when the base is weaker than hydroxide or the alkyl halide is primary.

Tertiary alkyl halides are so sterically hindered that elimination is the major reaction with all anionic nucleophiles. Only in solvolysis reactions does substitution predominate over elimination with tertiary alkyl halides.

8.13 Looking back: reactions of Alcohols with Hydrogen Halides

The reactions of alcohols with hydrogen halides to give alkyl halides (Chapter 4) are nucleophilic substitution reactions of alkyloxonium ions in which water is the leaving group. Primary alcohols react by an S_N2-like displacement of water from the alkyloxonium ion by halide. Secondary and tertiary alcohols give alkyloxonium ions which form carbocations in an S_N1-like process. Rearrangements are possible with secondary alcohols, and substitution takes place with predominant, but not complete, inversion of configuration.

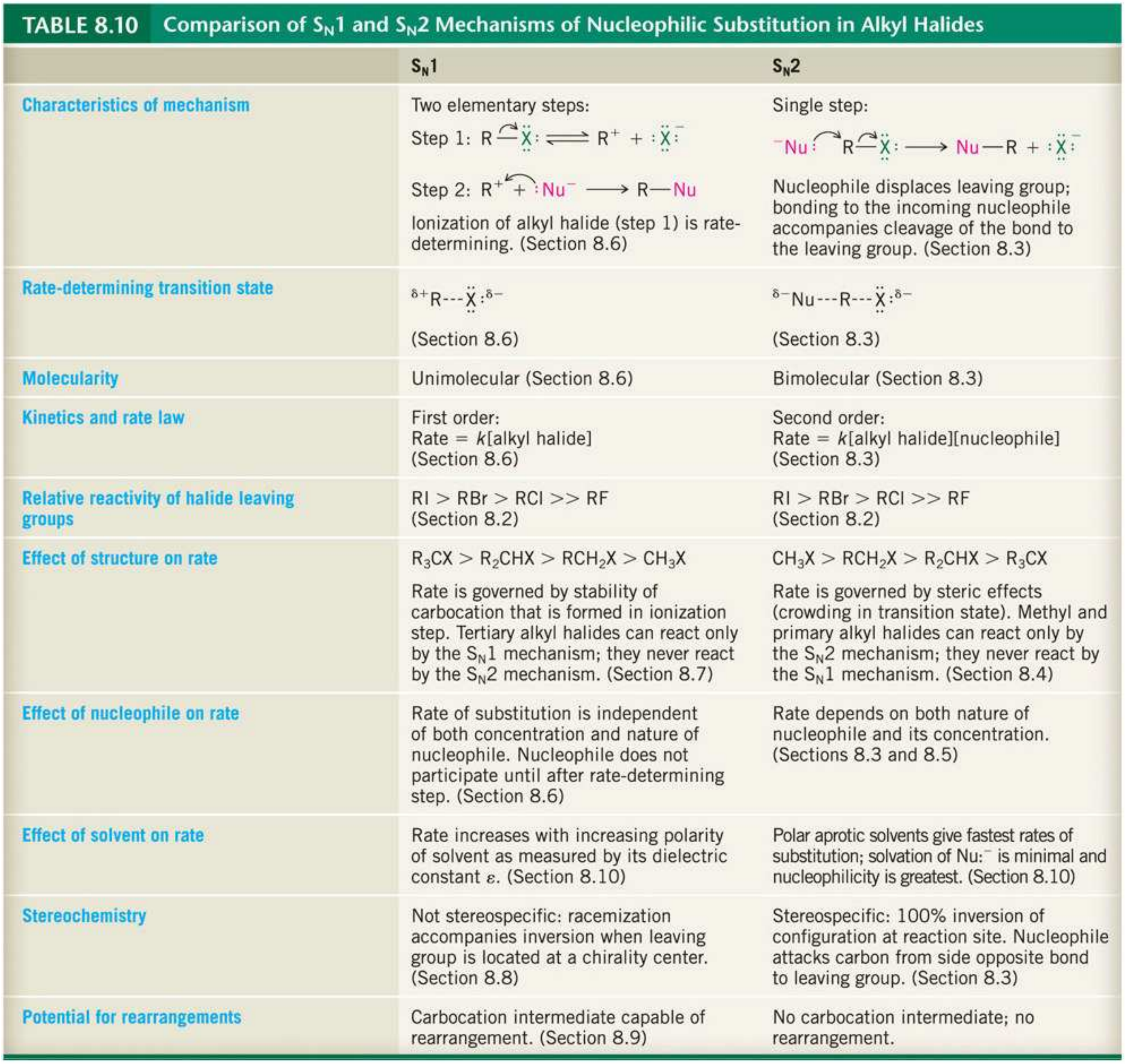


TABLE 8.10 Comparison of S_N1 and S_N2 Mechanisms of Nucleophilic Substitution in Alkyl Halides

	S_N1	S_N2
Characteristics of mechanism	Two elementary steps: Step 1: $R-\ddot{\underset{..}{X}}: \rightleftharpoons R^{+} + :\ddot{\underset{..}{X}}:^{-}$ Step 2: $R^{+} + :Nu^{-} \longrightarrow R-Nu$ Ionization of alkyl halide (step 1) is rate-determining. (Section 8.6)	Single step: $^{-}Nu: \; R-\ddot{\underset{..}{X}}: \longrightarrow Nu-R + :\ddot{\underset{..}{X}}:^{-}$ Nucleophile displaces leaving group; bonding to the incoming nucleophile accompanies cleavage of the bond to the leaving group. (Section 8.3)
Rate-determining transition state	$^{\delta+}R\text{---}\ddot{\underset{..}{X}}:^{\delta-}$ (Section 8.6)	$^{\delta-}Nu\text{---}R\text{---}\ddot{\underset{..}{X}}:^{\delta-}$ (Section 8.3)
Molecularity	Unimolecular (Section 8.6)	Bimolecular (Section 8.3)
Kinetics and rate law	First order: Rate = k[alkyl halide] (Section 8.6)	Second order: Rate = k[alkyl halide][nucleophile] (Section 8.3)
Relative reactivity of halide leaving groups	$RI > RBr > RCl >> RF$ (Section 8.2)	$RI > RBr > RCl >> RF$ (Section 8.2)
Effect of structure on rate	$R_3CX > R_2CHX > RCH_2X > CH_3X$ Rate is governed by stability of carbocation that is formed in ionization step. Tertiary alkyl halides can react only by the S_N1 mechanism; they never react by the S_N2 mechanism. (Section 8.7)	$CH_3X > RCH_2X > R_2CHX > R_3CX$ Rate is governed by steric effects (crowding in transition state). Methyl and primary alkyl halides can react only by the S_N2 mechanism; they never react by the S_N1 mechanism. (Section 8.4)
Effect of nucleophile on rate	Rate of substitution is independent of both concentration and nature of nucleophile. Nucleophile does not participate until after rate-determining step. (Section 8.6)	Rate depends on both nature of nucleophile and its concentration. (Sections 8.3 and 8.5)
Effect of solvent on rate	Rate increases with increasing polarity of solvent as measured by its dielectric constant ε. (Section 8.10)	Polar aprotic solvents give fastest rates of substitution; solvation of $Nu:^{-}$ is minimal and nucleophilicity is greatest. (Section 8.10)
Stereochemistry	Not stereospecific: racemization accompanies inversion when leaving group is located at a chirality center. (Section 8.8)	Stereospecific: 100% inversion of configuration at reaction site. Nucleophile attacks carbon from side opposite bond to leaving group. (Section 8.3)
Potential for rearrangements	Carbocation intermediate capable of rearrangement. (Section 8.9)	No carbocation intermediate; no rearrangement.

Extra Problems

1. Identify the nucleophile in the following reaction.

$$CH_3Br \;+\; NaOH \xrightarrow{H_2O} CH_3OH \;+\; NaBr$$

   A) CH_3Br B) OH^- C) H_2O D) Br^-

2. Identify the leaving group in the following reaction.

$$CH_3CH_2Br \;+\; NaHS \xrightarrow{CH_3OH} CH_3CH_2SH \;+\; NaBr$$

   A) CH_3CH_2Br B) HS^- C) Br^- D) CH_3OH

3. Which of the following cannot act as a nucleophile?
   A) NH_3 B) H_2O C) I^- D) CH_4

4. In the S_N2 reaction, the "2" stands for
   A) two reactants in the reaction.
   B) two steps in the reaction.
   C) two intermediates in the reaction.
   D) bimolecular kinetics for the reaction.

5. Which of the following undergoes a substitution reaction with sodium cyanide in DMSO at the fastest rate?
   A) CH_3CH_2F B) CH_3CH_2Cl C) CH_3CH_2Br D) CH_3CH_2I

6. Which of the following reacts the fastest by the S_N2 mechanism?
   A) CH_3Br B) CH_3CH_2Br C) $(CH_3)_2CHBr$ D) $(CH_3)_3CBr$

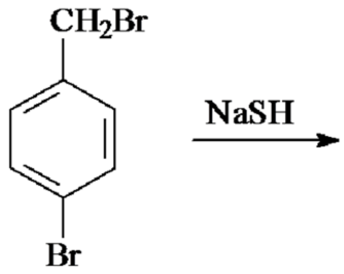
7. What is the leaving group in the following reaction?

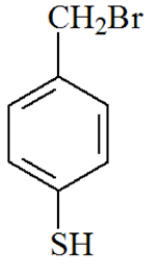
$$CH_3CH_2OH \;+\; HCl \longrightarrow CH_3CH_2Cl \;+\; H_2O$$

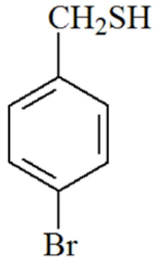
   A) OH- B) H2O C) CH3CH2+ D) C1-

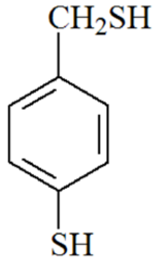
8. Starting with 1-hexene, which synthetic sequence below gives 2-cyanohexane?
   A) (1) H_2SO_4 (cat.), H_2O (2) NaCN
   B) (1) HBr/peroxide (2) NaCN
   C) (1) HBr (2) NaCN
   D) (1) Br_2, H_2O (2) NaCN

9. Give the product(s) of the following reaction?



A) 

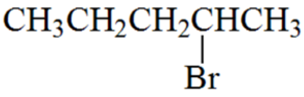
B) 

C) 

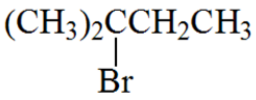
A) A   B) B   C) C   D) a mixture of A and B

10. Which of the following reacts fastest with methanol by the SN1 mechanism?

A) $CH_3CH_2CH_2CH_2CH_2Br$

B) 

$CH_3CH_2CH_2\underset{\displaystyle Br}{\underset{|}{C}}HCH_3$

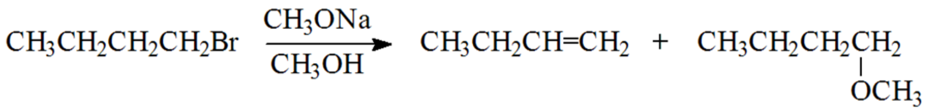
C) 

$(CH_3)_2\underset{\displaystyle Br}{\underset{|}{C}}CH_2CH_3$

D) $(CH_3)_3CCH_2Br$

A) A   B) B   C) C   D) D

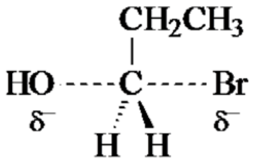
11. Identify the mechanistic pathways, respectively, for the products in the following reaction.



$$CH_3CH_2CH_2CH_2Br \xrightarrow[CH_3OH]{CH_3ONa} CH_3CH_2CH{=}CH_2 + CH_3CH_2CH_2\underset{\displaystyle OCH_3}{\underset{|}{C}}H_2$$

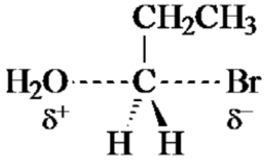
A) E1, S_N1 B) E1, S_N2 C) E2, S_N1 D) E2, S_N2

12. The species shown below represents the transition state for the



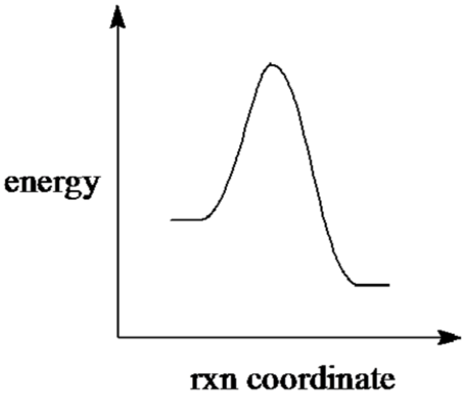
A) reaction of 1-propanol with HBr.
B) reaction of 1-bromopropane with OH^-.
C) elimination of HBr from 1-bromopropane.
D) addition of HBr to propene with peroxides.

13. The species shown below represents the transition state for the



A) reaction of 1-propanol with HBr.
B) reaction of 1-bromopropane with OH^-.
C) addition of HOBr to 1-propene.
D) addition of HBr to propene with peroxides.

14. Considering the S_N1, S_N2, E1, and E2 mechanisms, the energy diagram shown below corresponds to



A) only the S_N1 mechanism.
B) only the S_N2 mechanism.
C) both the S_N1 and E1 mechanisms.
D) both the S_N2 and E2 mechanisms.

Answers: 1)B 2)C 3)D 4)D 5)D 6)A 7)B 8)C 9)B 10)C 11)D 12)B 13)A 14)D

Chapter 6:
Addition Reactions with Alkenes

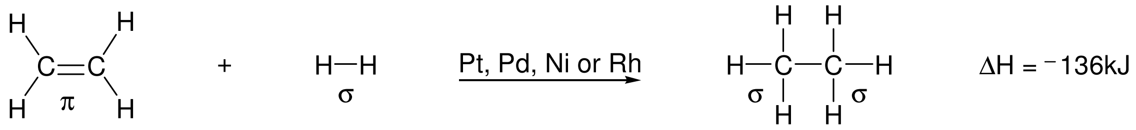
6.1 Hydrogenation of Alkenes

The characteristic reaction of alkenes is **addition** to the double bond.

Alkenes are **unsaturated hydrocarbons** because they have the capacity to react with substances that add to them. (In other words, Alkenes can still add two substituents instead of forming a double bond).

Alkanes are **saturated hydrocarbons** because they are incapable of undergoing addition reactions.

Hydrogenation is the addition of H_2 to a multiple bond.
Hydrogenation of all alkenes is exothermic (the heat of hydrogenation = $-\Delta H°$.)

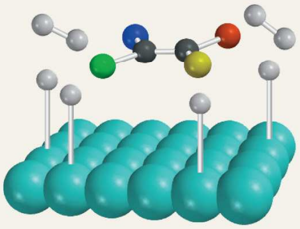


The uncatalyzed addition of hydrogen is very slow. The use of **catalysts** such as Platinum, Palladium, Nickel and Rhodium dramatically increases the reaction rate. The metal catalysts are insoluble and the reaction takes place at the interface between the two phases. They are called heterogeneous reactions.

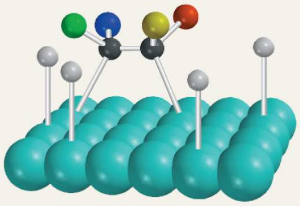
Mechanism 6.1

Hydrogenation of Alkenes

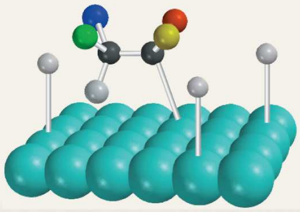
Step 1: Hydrogen molecules react with metal atoms at the catalyst surface. The relatively strong hydrogen–hydrogen σ bond is broken and replaced by two weak metal–hydrogen bonds.



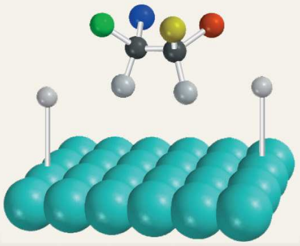
Step 2: The alkene reacts with the metal catalyst. The π component of the double bond between the two carbons is replaced by two relatively weak carbon–metal σ bonds.



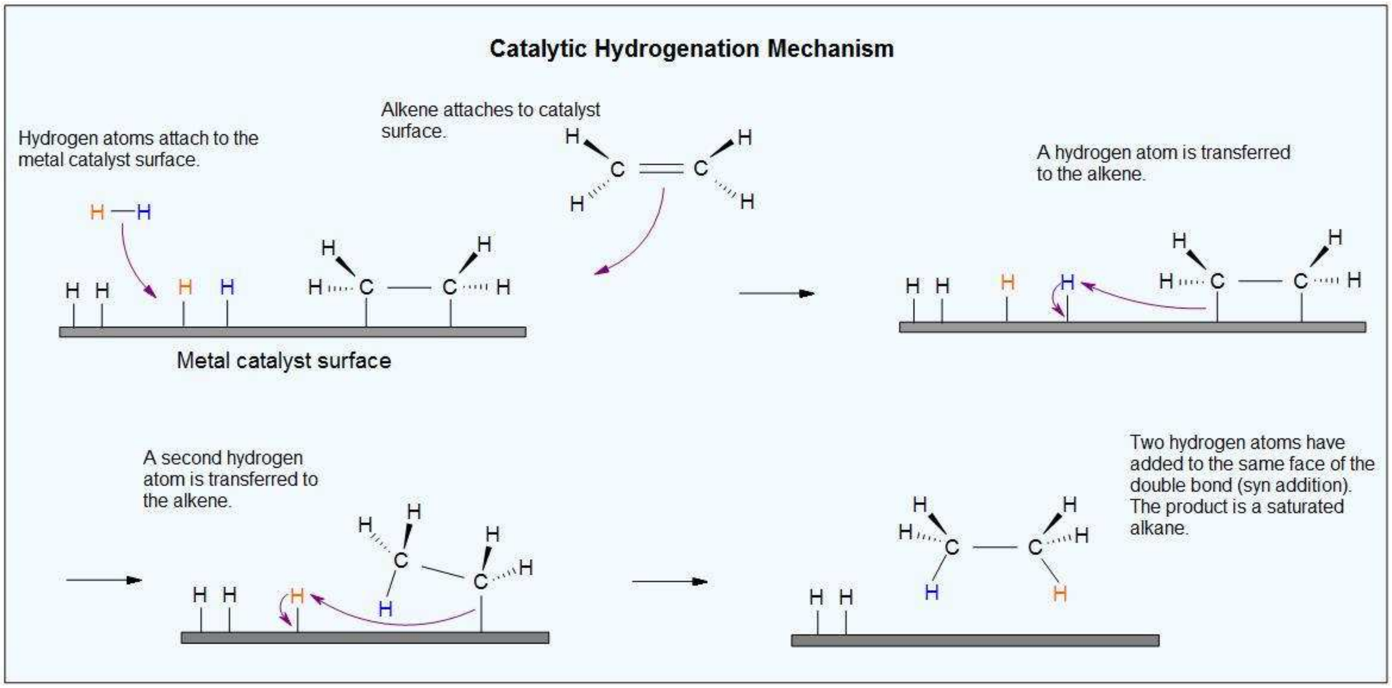
Step 3: A hydrogen atom is transferred from the catalyst surface to one of the carbons of the double bond.



Step 4: The second hydrogen atom is transferred, forming the alkane. The sites on the catalyst surface at which the reaction occurred are free to accept additional hydrogen and alkene molecules.



Different representations of the catalytic hydrogenation of ethylene:



6.2 Heats of Hydrogenation

Heats of hydrogenation can be used to measure relative stability of isomeric alkenes (estimate the stability of the double bond). The correlation with structure is the same as when heats of combustion were measured. The bigger the value for the heat of hydrogenation, the less stable the alkene.

Ethylene, which has no alkyl substituents to stabilize its double bond, has the highest heat of hydrogenation. The more the alkene is substituted, the more stable it is. Tetrasubstituted alkenes are more stable than monosubstituted alkenes. *Trans*-substituted alkenes are more stable than *cis*-substituted alkenes.

6.3 Stereochemistry of Alkene Hydrogenation

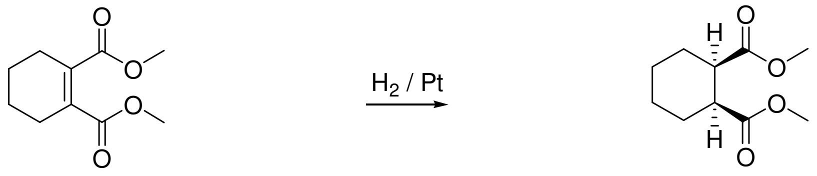
In alkene hydrogenation, the two hydrogen atoms both add to the same face of the double bond. It is called a syn addition of H.

The term **syn addition** describes the stereochemistry of reactions such as hydrogenation in which two atoms (or groups) add to the same face of a double bond. When atoms or groups add to opposite faces of the double bond, the process is called **anti addition**.

Remember that a reaction in which a single starting material can give two or more stereoisomeric products but yields one of them in greater amounts than the other (or even to the exclusion of the other) is said to be stereoselective.

Hydrogenation is stereoselective, corresponding to addition to less crowded face of the double bond.

Example:



dimethyl cyclohex-1-ene-1,2-dicarboxylate

(1*S*,2*R*)-dimethyl cyclohexane-1,2-dicarboxylate

6.4 Electrophilic Addition of Hydrogen Halides to Alkenes

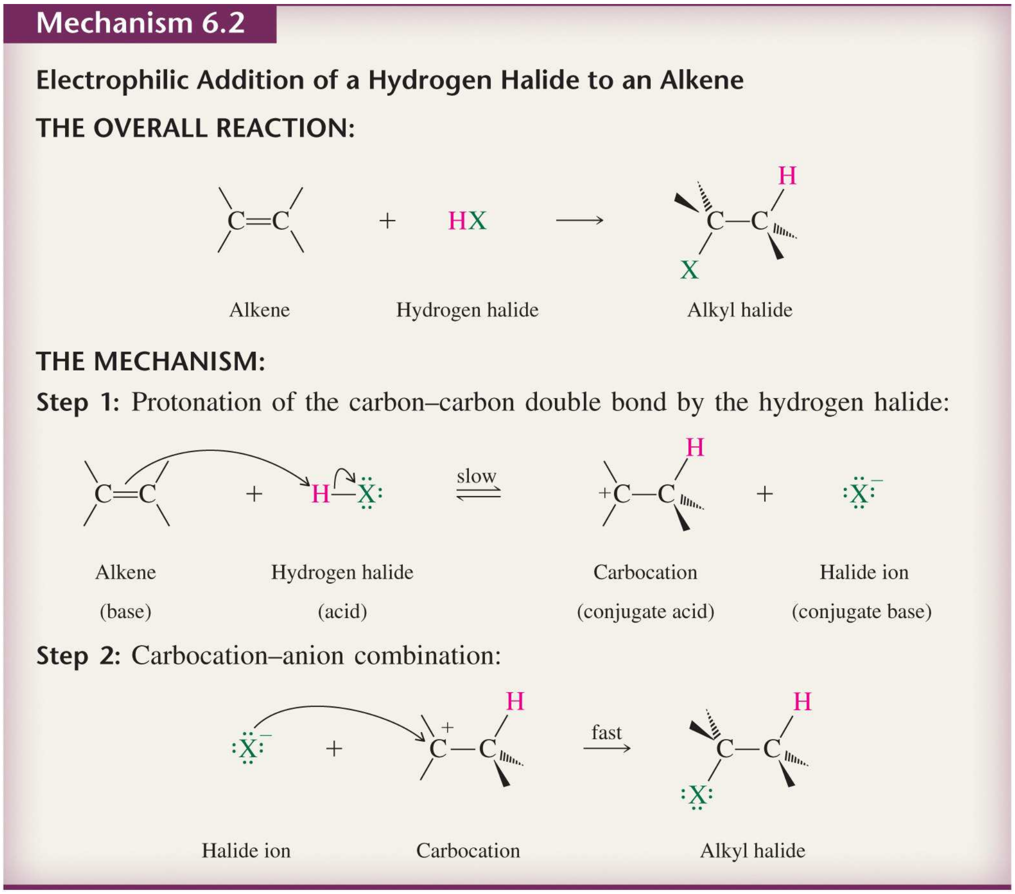
In many addition reactions the attacking reagent is a polar molecule; for example H—X.

Unlike acid-base reactions, proton transfer to carbon is almost always slow.

Electrophilic addition of hydrogen halides to alkenes proceeds by rate-determining formation of a carbocation intermediate.

Increasing reactivity of hydrogen halides in addition to alkenes proceeds in this way:

(slowest) HF << HCl < HBr < HI (fastest)



Mechanism 6.2

Electrophilic Addition of a Hydrogen Halide to an Alkene

THE OVERALL REACTION:

THE MECHANISM:

Step 1: Protonation of the carbon–carbon double bond by the hydrogen halide:

Step 2: Carbocation–anion combination:

This general mechanism is called **electrophilic addition**. It is not a substitution reaction because no substituent is getting replaced (remove) from the starting reagent.

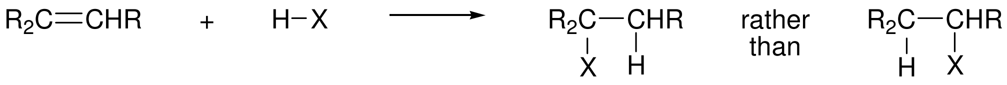
The characteristic chemical property of a C═C structural unit is susceptibility to attack by electrophiles. Electrons flow from the π component of the double bond toward the electrophile and ultimately become a shared-electron pair in a covalent bond.

6.5 Regioselectivity of Hydrogen Halide Addition: Markovnikov's Rule

Addition of hydrogen halide to unsymmetrical alkenes is so highly regioselective that it is considered regiospecific.

Markovnikov's Rule

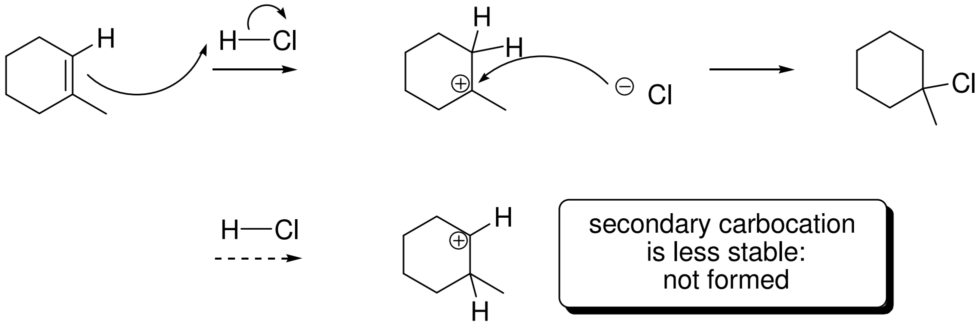
When an unsymmetrically substituted alkene reacts with a hydrogen halide, the hydrogen adds to the carbon that has the greater number of hydrogen substituents, and the halogen adds to the carbon that has the fewer hydrogen substituents.



$$R_2C{=}CHR \quad + \quad H{-}X \longrightarrow \underset{X}{R_2C}{-}\underset{H}{CHR} \quad \text{rather than} \quad \underset{H}{R_2C}{-}\underset{X}{CHR}$$

6.6 Mechanistic Basis for Markovnikov's Rule

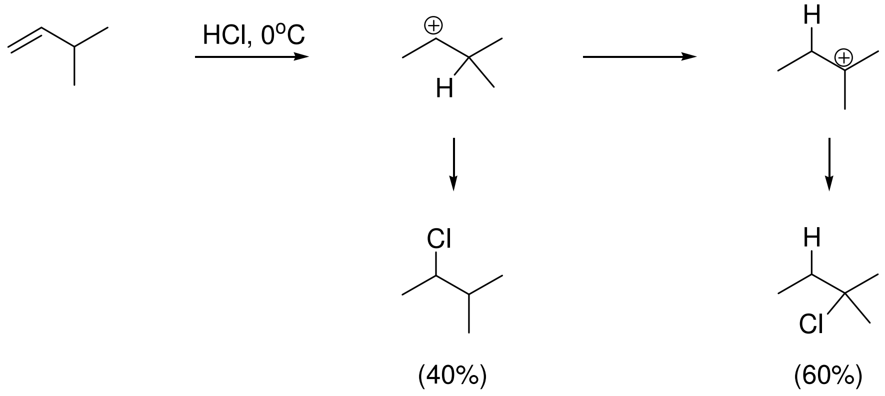
The protonation of double bond occurs in direction that gives more stable of two possible carbocations. The energy of activation is less and the reaction is faster for the reaction that proceeds through the more stable carbocation.



secondary carbocation
is less stable:
not formed

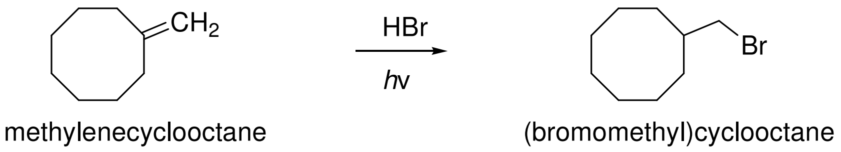
6.7 Carbocation Rearrangements in Hydrogen Halide Addition to Alkenes

Rearrangements sometimes occur due to carbocations intermediates.

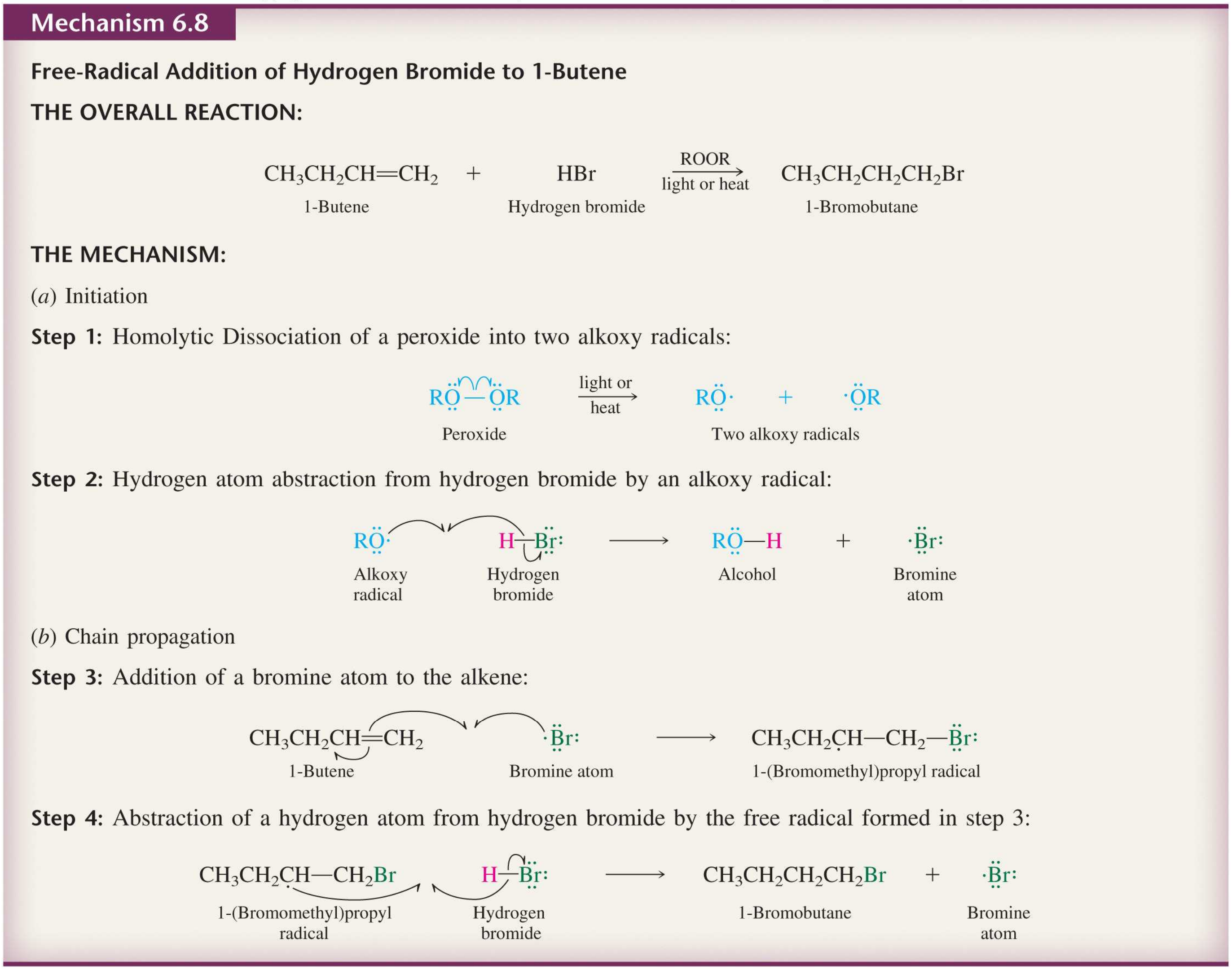


6.8 Free-Radical Addition of Hydrogen Bromide to Alkenes

Hydrogen bromide is unique among the hydrogen halides in that it can add to alkenes either by electrophilic of free radical addition. Under photochemical conditions or in the presence of peroxides (the peroxide effect), free radical addition is observed, and HBr adds to the double bond with a regioselectivity opposite to Markovnikov's rule.



methylenecyclooctane (bromomethyl)cyclooctane



Mechanism 6.8

Free-Radical Addition of Hydrogen Bromide to 1-Butene

THE OVERALL REACTION:

$$CH_3CH_2CH{=}CH_2 + HBr \xrightarrow[\text{light or heat}]{\text{ROOR}} CH_3CH_2CH_2CH_2Br$$

1-Butene Hydrogen bromide 1-Bromobutane

THE MECHANISM:

(*a*) Initiation

Step 1: Homolytic Dissociation of a peroxide into two alkoxy radicals:

$$R\ddot{\underset{..}{O}}-\ddot{\underset{..}{O}}R \xrightarrow[\text{heat}]{\text{light or}} R\ddot{\underset{..}{O}}\cdot + \cdot\ddot{\underset{..}{O}}R$$

Peroxide Two alkoxy radicals

Step 2: Hydrogen atom abstraction from hydrogen bromide by an alkoxy radical:

$$R\ddot{\underset{..}{O}}\cdot \quad H-\ddot{\underset{..}{Br}}: \longrightarrow R\ddot{\underset{..}{O}}-H + \cdot\ddot{\underset{..}{Br}}:$$

Alkoxy radical Hydrogen bromide Alcohol Bromine atom

(*b*) Chain propagation

Step 3: Addition of a bromine atom to the alkene:

$$CH_3CH_2CH{=}CH_2 \quad \cdot\ddot{\underset{..}{Br}}: \longrightarrow CH_3CH_2\dot{C}H-CH_2-\ddot{\underset{..}{Br}}:$$

1-Butene Bromine atom 1-(Bromomethyl)propyl radical

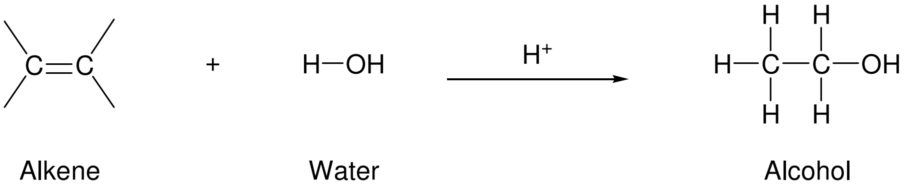
Step 4: Abstraction of a hydrogen atom from hydrogen bromide by the free radical formed in step 3:

$$CH_3CH_2\dot{C}H-CH_2Br \quad H-\ddot{\underset{..}{Br}}: \longrightarrow CH_3CH_2CH_2CH_2Br + \cdot\ddot{\underset{..}{Br}}:$$

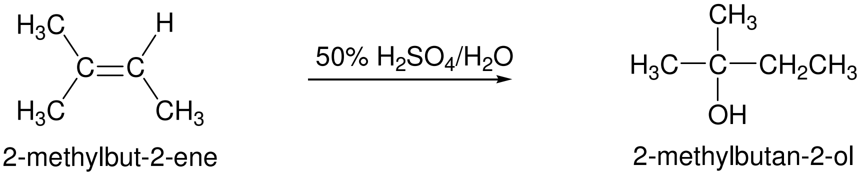
1-(Bromomethyl)propyl radical Hydrogen bromide 1-Bromobutane Bromine atom

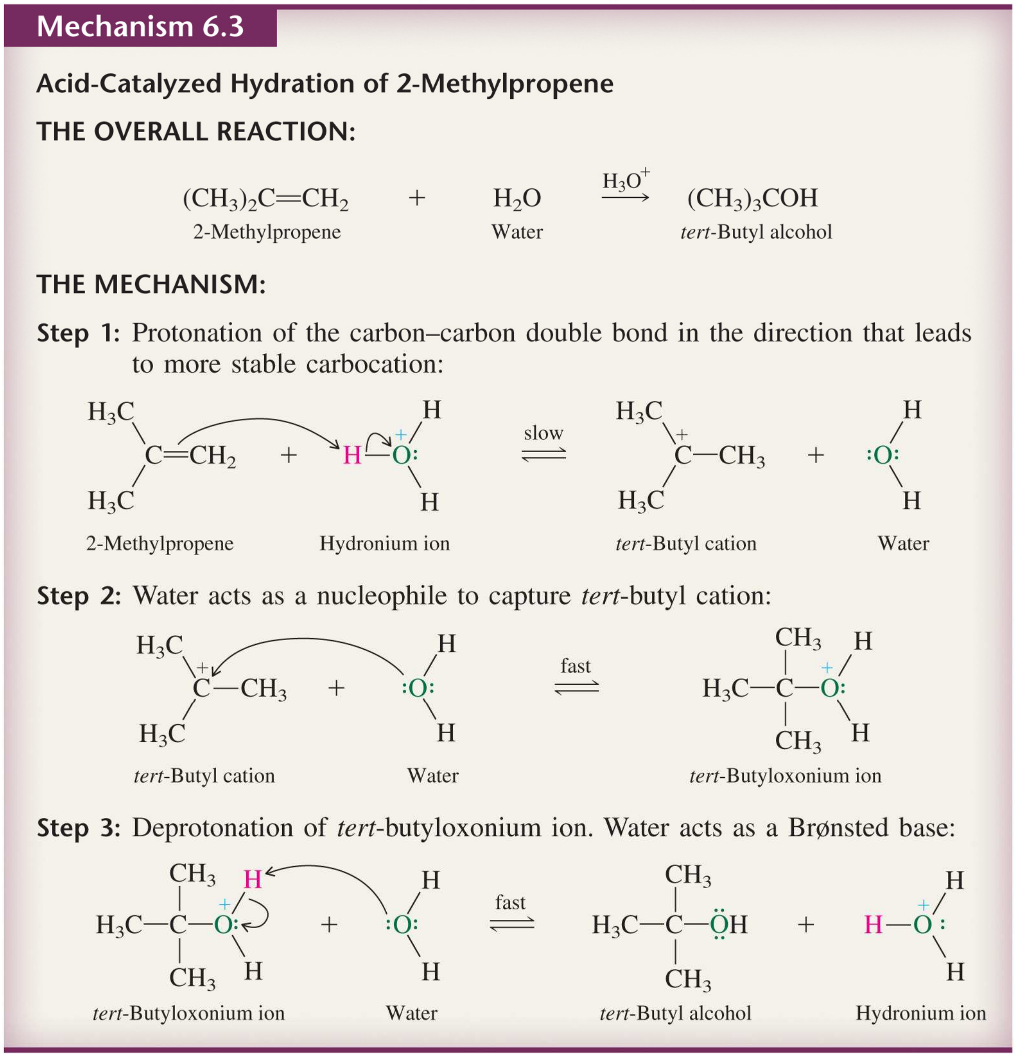
6.10 Acid-Catalyzed Hydration of Alkenes

Another method for the hydration of alkenes is by reaction with water under conditions of acid catalysis.



Markovnikov's rule is followed.





Mechanism 6.3

Acid-Catalyzed Hydration of 2-Methylpropene

THE OVERALL REACTION:

$$(CH_3)_2C{=}CH_2 + H_2O \xrightarrow{H_3O^+} (CH_3)_3COH$$

2-Methylpropene — Water — *tert*-Butyl alcohol

THE MECHANISM:

Step 1: Protonation of the carbon–carbon double bond in the direction that leads to more stable carbocation:

Step 2: Water acts as a nucleophile to capture *tert*-butyl cation:

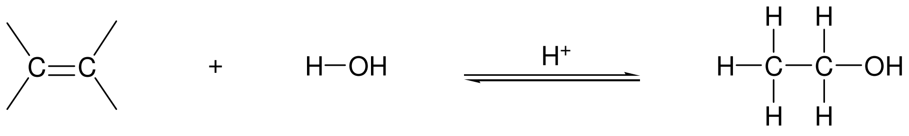
Step 3: Deprotonation of *tert*-butyloxonium ion. Water acts as a Brønsted base:

The acid-catalyzed hydration of an alkene and the acid-catalyzed dehydration of an alcohol are the reverse of each other.

Microscopic Reversibility Principle:
In an equilibrium process, the same intermediates and transition states are encountered in the forward direction and the reverse, but in the opposite order.

Mechanism 6.3 is the reverse of *Mechanism 5.1* (Class Notes p. 54).

6.11 Thermodynamics of Addition-Elimination Equlibria



Since we can prepare alcohols from alkenes, and alkenes from alcohols, **Le Châtelier's principle** helps us predict qualitatively how an equilibrium will respond to changes in experimental conditions.

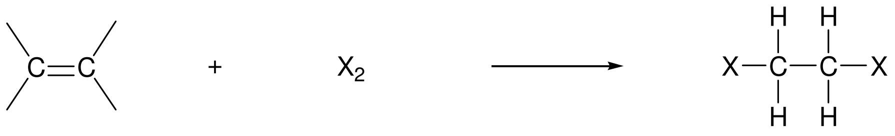
Le Châtelier's principle states that a system at equilibrium adjusts so to minimize any stress applied to it.

For the hydration-dehydration equilibria, the key stress is water.

Adding water pushes the equilibrium toward more product (alcohol).

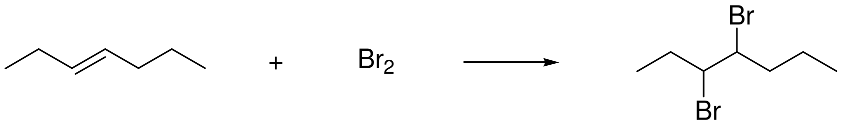
Removing water pushes the equilibrium toward more reactant (alkene).

6.15 Addition of Halogens to Alkenes



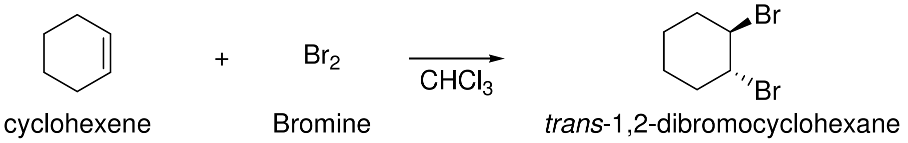
Halogens normally react with alkenes by electrophilic addition.
The products of these reactions are called vicinal dihalides. Two substituents (in this case the halogens) are vicinal if they are attached to adjacent carbons.

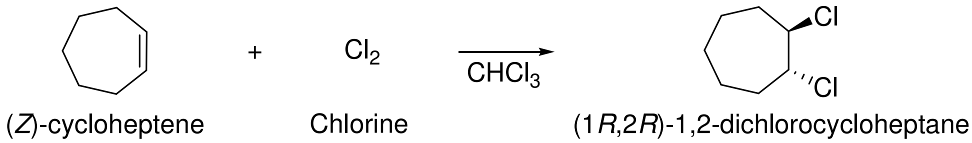
The scope is limited to Cl_2 and Br_2.
F_2 addition proceeds with explosive violence.
I_2 addition is endothermic: vicinal diiodides dissociate to an alkene and I_2. (Easily reversible reaction).



6.16 Stereochemistry of Halogen Addition

Anti addition is observed; the two bromine atoms of Br_2 or the two atoms of the Cl_2 add to opposite faces of the double bond.

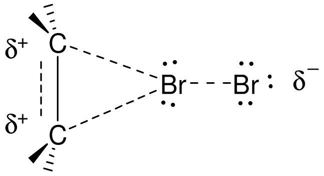




6.17 Mechanism of Halogen Addition to Alkenes: Halonium Ions

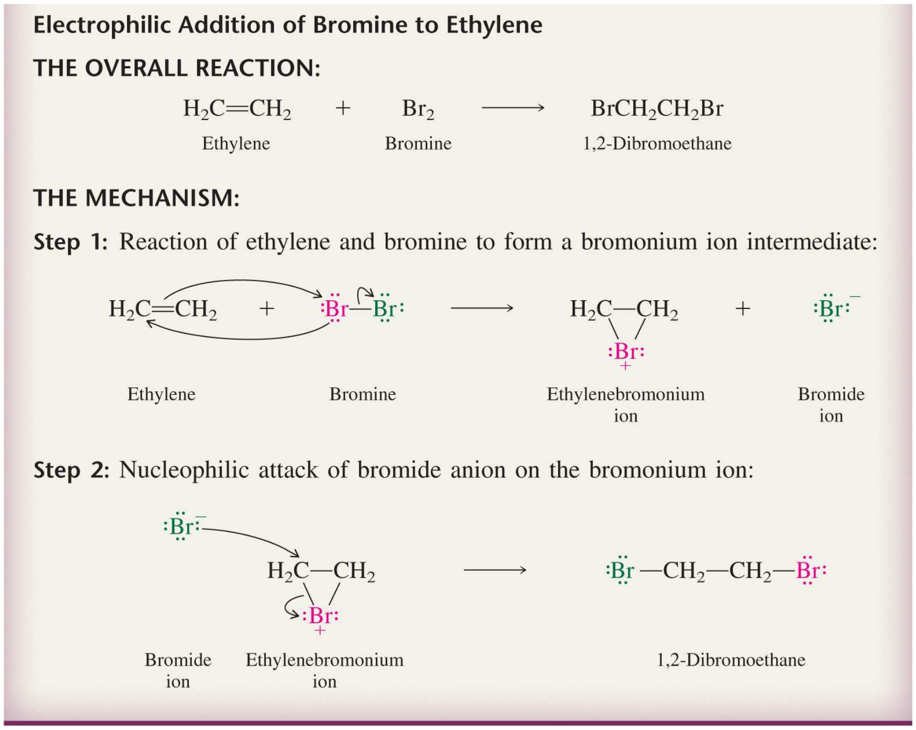
The Mechanism is an electrophilic addition. Br_2 is not polar, but it is polarizable.
Two steps of the mechanism:

(1) formation of bromonium ion (positive charge residing on bromine, not carbon)
(2) nucleophilic attack on bromonium ion by bromide (from opposite side).



Transition state for bromonium ion formation from an alkene and bromine

More highly substituted double bonds react faster. Alkyl groups on the double bond make it more "electron rich." They release electrons, stabilize the transition state for bromonium ion formation, and increase the reaction rate.



Electrophilic Addition of Bromine to Ethylene

THE OVERALL REACTION:

$$H_2C{=}CH_2 + Br_2 \longrightarrow BrCH_2CH_2Br$$

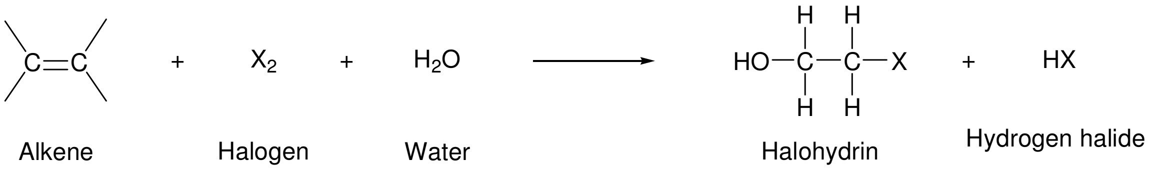
THE MECHANISM:

Step 1: Reaction of ethylene and bromine to form a bromonium ion intermediate:

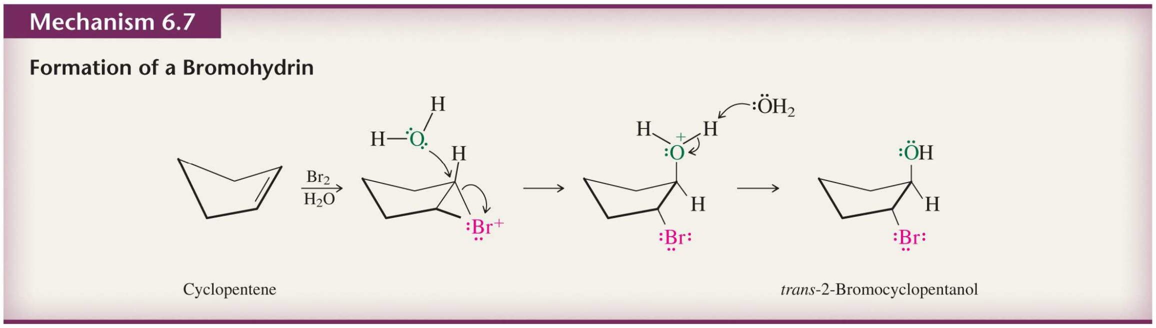
Step 2: Nucleophilic attack of bromide anion on the bromonium ion:

6.18 Conversion of Alkenes to Vicinal Halohydrins

In **aqueous solution**, chlorine and bromine react with alkenes to form vicinal halohydrins, compounds that have a halogen and a hydroxyl group on adjacent carbons.

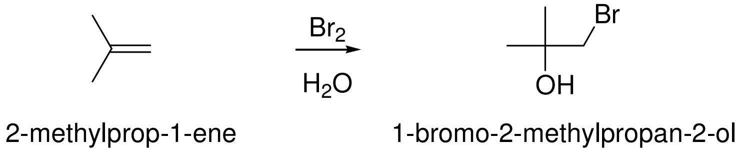


Anti addition occurs. The halogen and the hydroxyl group add to the opposite faces of the double bond.


Mechanism 6.7

Formation of a Bromohydrin

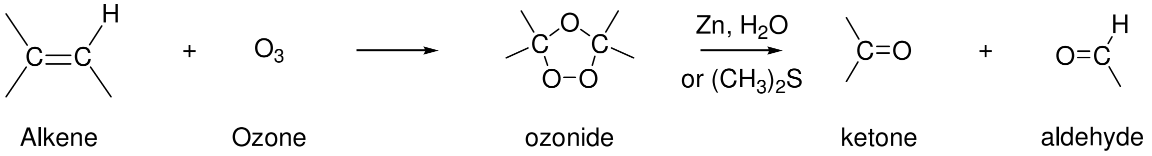
The regioselectivity of addition is established by the water attack on the more highly substituted carbon.



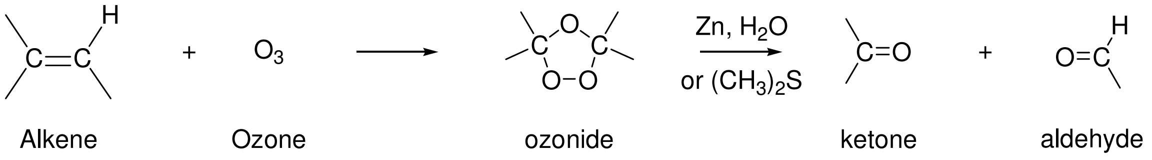
6.20 Ozonolysis of Alkenes

The first step is the reaction of the alkene with ozone (O_3).The product is an *ozonide*
The second step is reduction of the ozonide, carried out in the presence of Zn in water, or dimethyl sulfide $(CH_3)_2S$.

Two aldehydes and two ketones, or an aldehyde and a ketone are the general products formed.



Alkenes Ozonolysis Mechanism (for your information, not exam material)



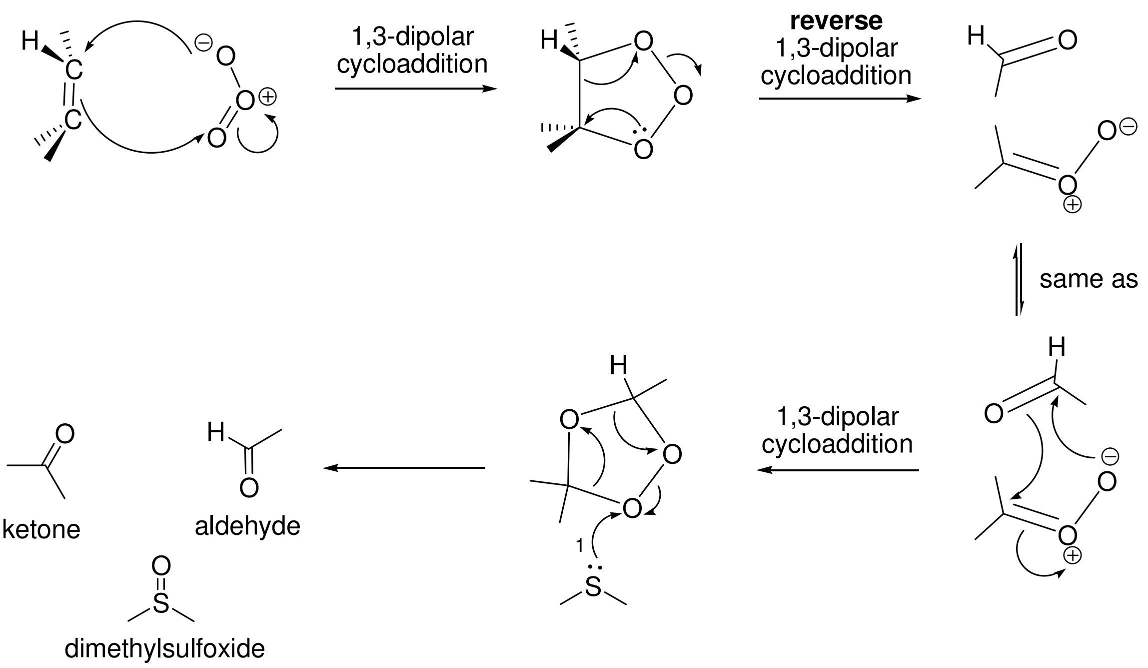
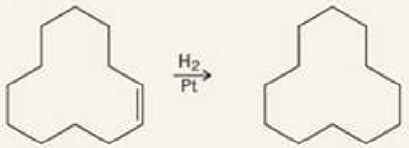
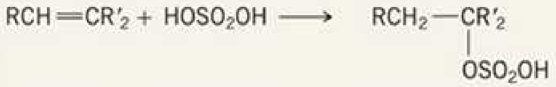
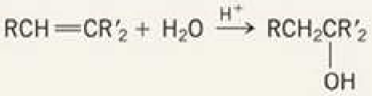
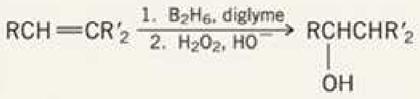


TABLE 6.6 Addition Reactions of Alkenes

Reaction (section) and comments	General equation and specific example
Catalytic hydrogenation (Sections 6.1–6.3) Alkenes react with hydrogen in the presence of a platinum, palladium, rhodium, or nickel catalyst to form the corresponding alkane.	$R_2C{=}CR_2 + H_2 \xrightarrow{\text{Pt, Pd, Rh, or Ni}} R_2CHCHR_2$ Alkene Hydrogen Alkane  *cis*-Cyclododecene Cyclododecane (100%)
Addition of hydrogen halides (Sections 6.4–6.7) A proton and a halogen add to the double bond of an alkene to yield an alkyl halide. Addition proceeds in accordance with Markovnikov's rule; hydrogen adds to the carbon that has the greater number of hydrogens, halide to the carbon that has the fewer hydrogens.	 $RCH{=}CR'_2 + HX \longrightarrow RCH_2{-}\underset{X}{CR'_2}$ Alkene Hydrogen halide Alkyl halide  Methylenecyclohexane Hydrogen chloride 1-Chloro-1-methylcyclohexane (75–80%)
Addition of sulfuric acid (Section 6.8) Alkenes react with sulfuric acid to form alkyl hydrogen sulfates. A proton and a hydrogen sulfate ion add to the double bond in accordance with Markovnikov's rule. Alkenes that yield tertiary carbocations on protonation tend to polymerize in concentrated sulfuric acid (Section 6.21).	 $RCH{=}CR'_2 + HOSO_2OH \longrightarrow RCH_2{-}\underset{OSO_2OH}{CR'_2}$ Alkene Sulfuric acid Alkyl hydrogen sulfate  $H_2C{=}CHCH_2CH_3 + HOSO_2OH \longrightarrow H_3C{-}\underset{OSO_2OH}{CH}CH_2CH_3$ 1-Butene Sulfuric acid *sec*-Butyl hydrogen sulfate
Acid-catalyzed hydration (Section 6.9) Addition of water to the double bond of an alkene takes place in aqueous acid. Addition occurs according to Markovnikov's rule. A carbocation is an intermediate and is captured by a molecule of water acting as a nucleophile.	 $RCH{=}CR'_2 + H_2O \xrightarrow{H^+} RCH_2\underset{OH}{CR'_2}$ Alkene Water Alcohol $H_2C{=}C(CH_3)_2 \xrightarrow{50\%\ H_2SO_4/H_2O} (CH_3)_3COH$ 2-Methylpropene *tert*-Butyl alcohol (55–58%)
Hydroboration-oxidation (Sections 6.11–6.13) This two-step sequence achieves hydration of alkenes in a stereospecific syn manner, with a regioselectivity opposite to Markovnikov's rule. An organoborane is formed by electrophilic addition of diborane to an alkene. Oxidation of the organoborane intermediate with hydrogen peroxide completes the process. Rearrangements do not occur.	 $RCH{=}CR'_2 \xrightarrow[\text{2. } H_2O_2,\ HO^-]{\text{1. } B_2H_6\text{, diglyme}} R\underset{OH}{CH}CHR'_2$ Alkene Alcohol $(CH_3)_2CHCH_2CH{=}CH_2 \xrightarrow[\text{2. } H_2O_2,\ HO^-]{\text{1. } H_3B\cdot THF} (CH_3)_2CHCH_2CH_2CH_2OH$ 4-Methyl-1-pentene 4-Methyl-1-pentanol (80%)

Continued

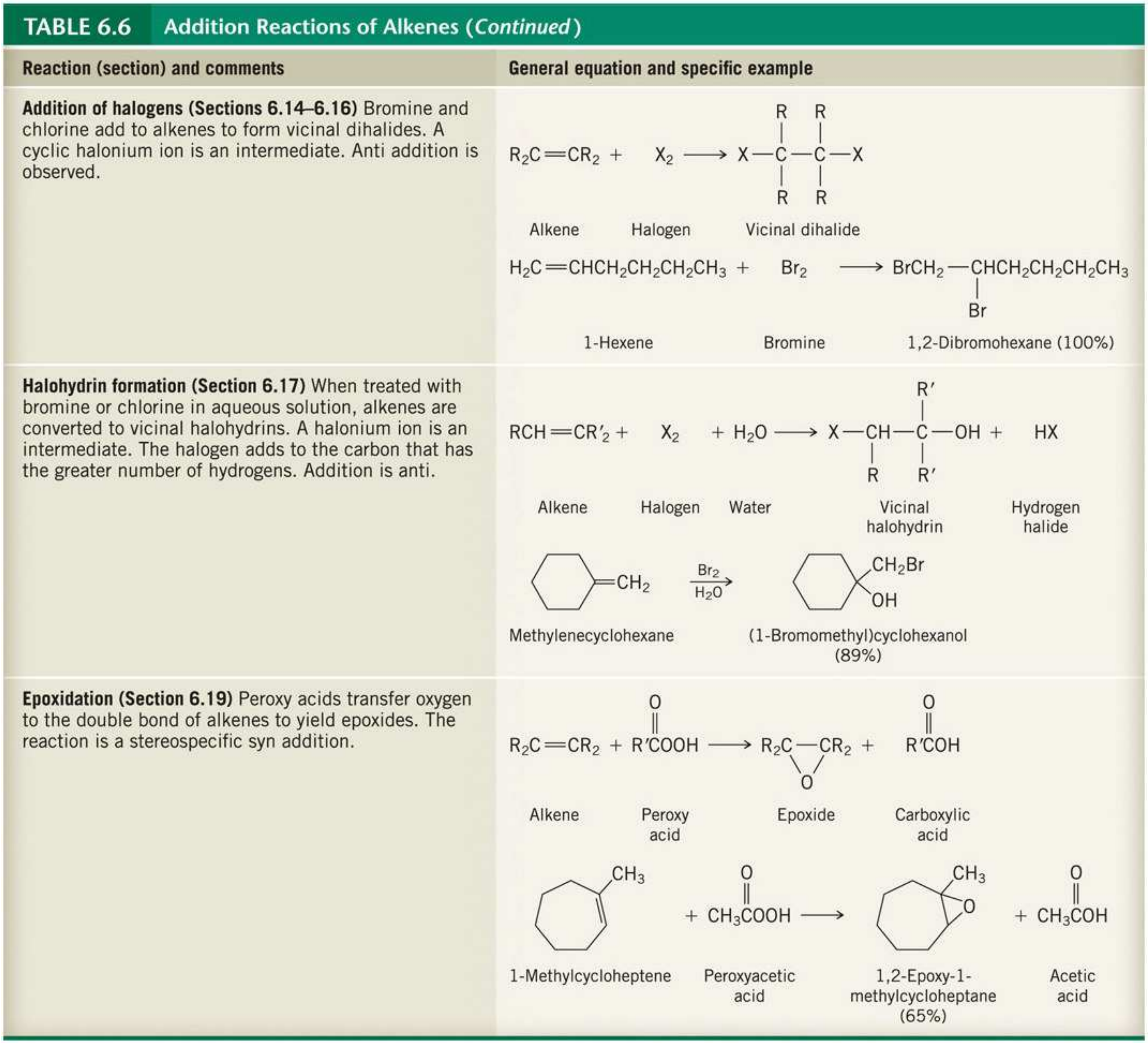


TABLE 6.6 Addition Reactions of Alkenes (*Continued*)

Reaction (section) and comments	General equation and specific example
Addition of halogens (Sections 6.14–6.16) Bromine and chlorine add to alkenes to form vicinal dihalides. A cyclic halonium ion is an intermediate. Anti addition is observed.	$R_2C{=}CR_2 + X_2 \longrightarrow X{-}CR_2{-}CR_2{-}X$ Alkene, Halogen, Vicinal dihalide $H_2C{=}CHCH_2CH_2CH_2CH_3 + Br_2 \longrightarrow BrCH_2{-}\underset{\mid \atop Br}{C}HCH_2CH_2CH_2CH_3$ 1-Hexene, Bromine, 1,2-Dibromohexane (100%)
Halohydrin formation (Section 6.17) When treated with bromine or chlorine in aqueous solution, alkenes are converted to vicinal halohydrins. A halonium ion is an intermediate. The halogen adds to the carbon that has the greater number of hydrogens. Addition is anti.	$RCH{=}CR'_2 + X_2 + H_2O \longrightarrow X{-}\underset{\mid \atop R}{C}H{-}\overset{R' \atop \mid}{\underset{\mid \atop R'}{C}}{-}OH + HX$ Alkene, Halogen, Water, Vicinal halohydrin, Hydrogen halide Methylenecyclohexane $\xrightarrow[H_2O]{Br_2}$ (1-Bromomethyl)cyclohexanol (89%)
Epoxidation (Section 6.19) Peroxy acids transfer oxygen to the double bond of alkenes to yield epoxides. The reaction is a stereospecific syn addition.	$R_2C{=}CR_2 + R'\overset{O \atop \parallel}{C}OOH \longrightarrow R_2C{-}CR_2\ (\text{O bridge}) + R'\overset{O \atop \parallel}{C}OH$ Alkene, Peroxy acid, Epoxide, Carboxylic acid 1-Methylcycloheptene $+ CH_3\overset{O \atop \parallel}{C}OOH \longrightarrow$ 1,2-Epoxy-1-methylcycloheptane (65%) $+ CH_3\overset{O \atop \parallel}{C}OH$ Peroxyacetic acid, Acetic acid

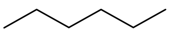
13.25 Molecular Formula as a Clue to Structure

A compound's molecular formula gives information about the number of double bonds and rings it contains.

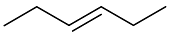
A saturated compound has a molecular formula C_nH_{2n+2}.

A mono unsaturated compound, due to the presence of one double bond or one ring, has a molecular formula C_nH_{2n}

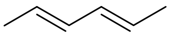
A poly unsaturated compound has two hydrogens less per unit of insaturation, in comparison with the unsaturated hydrocarbon.



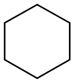
C_6H_{14}



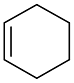
C_6H_{12}



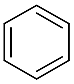
C_6H_{10}



C_6H_{12}



C_6H_{10}



C_6H_6

Extra Problems

1. Which one of the following is not a metal catalyst for the hydrogenation of an alkene?
   A) Pd B) Pt C) Na D) Ni

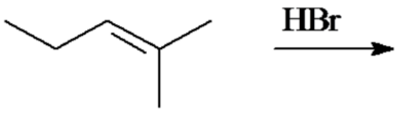
2. What is(are) the product(s) in the Pd-catalyzed hydrogenation of 1,2-dimethylcyclopentene?
   A) *trans*-1,2-dimethylcyclopentane
   B) *cis*-1,2-dimethylcyclopentane
   C) a mixture of *trans* and *cis*-1,2-dimethylcyclopentane
   D) 1,1-dimethylcyclopentane

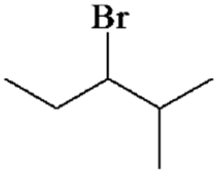
3. Which of the following alkenes is expected to have the highest heat of hydrogenation?
   A) 1-pentene B) *trans*-2-pentene C) *cis*-2-pentene D) 2-methyl-2-butene

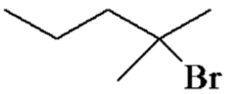
4. Which alkene below is thermodynamically the most stable?
   A) 1-hexene B) *trans*-3-hexene C) *cis*-3-hexene D) 2-methyl-2-pentene

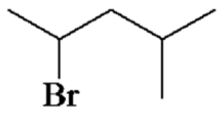
5. The stereochemical pathway for the hydrogenation of an alkene with a metal catalyst, such as platinum, occurs *via*
   A) syn addition.
   B) anti addition.
   C) Markovnikov addition.
   D) anti-Markovnikov addition.

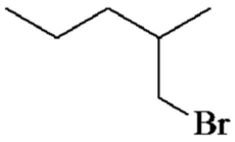
6. What is the major product of the following reaction?



A)


B)


C)


D)


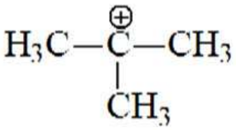
7. What is the major product of the following reaction?

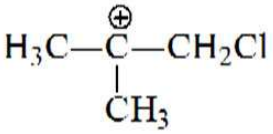
$$CH_3CH_2CH_2CH{=}C(CH_3)_2 \quad + \quad Br_2 \quad \longrightarrow$$

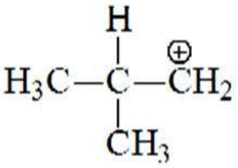
   A) 1,2-dibromo-2-methylhexane
   B) 2,2-dibromo-2-methylhexane
   C) 2,3-dibromo-2-methylhexane
   D) 2,4-dibromo-2-methylhexane

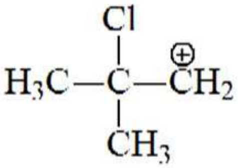
8. What is the intermediate in the following reaction?

$(CH_3)_2C{=}CH_2 \quad + \quad HCl \longrightarrow$

A) 
$H_3C-\underset{CH_3}{\overset{\oplus}{C}}-CH_3$

C) 
$H_3C-\underset{CH_3}{\overset{\oplus}{C}}-CH_2Cl$

B) 
$H_3C-\underset{CH_3}{\overset{H}{C}}-\overset{\oplus}{C}H_2$

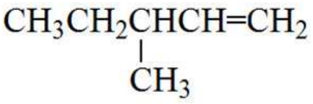
D) 
$H_3C-\underset{CH_3}{\overset{Cl}{C}}-\overset{\oplus}{C}H_2$

9. Addition of HCl to 3-methyl-1-pentene gives two products. One of these is 2-chloro-3-methylpentane. What is the other product?

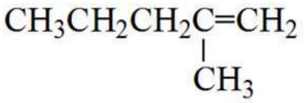
A)	1-chloro-3-methylpentane	C)	3-chloro-2-methylpentane
B)	3-chloro-3-methylpentane	D)	2-chloro-2-methylpentane

10. Which of the following alkenes gives 1-bromo-2-methyl-2-pentanol upon reaction with Br_2/H_2O?

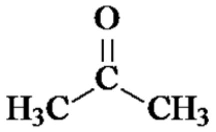
A) $CH_3CH{=}CHCH(CH_3)_2$

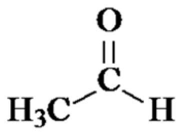
B) 
$CH_3CH_2\underset{CH_3}{CH}CH{=}CH_2$

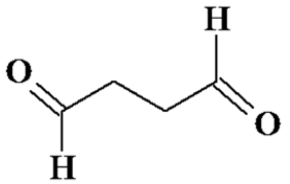
C) $CH_3CH_2CH{=}C(CH_3)_2$

D) 
$CH_3CH_2CH_2\underset{CH_3}{C}{=}CH_2$

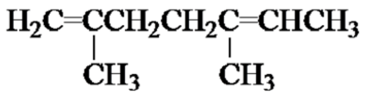
11. A compound is treated with ozone followed by zinc in water to give the following three products. Which structure below best fits the data?



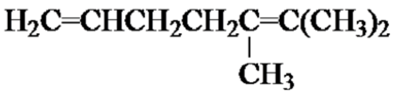




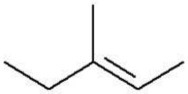
A) $CH_3CH{=}CH(CH_2)_3CH{=}C(CH_3)_2$

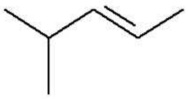
C) 
$H_2C{=}\underset{CH_3}{C}CH_2CH_2\underset{CH_3}{C}{=}CHCH_3$

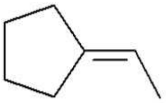
B) $(CH_3)_2C{=}CHCH_2CH_2CH{=}CHCH_3$

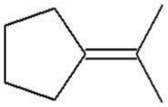
D) 
$H_2C{=}CHCH_2CH_2\underset{CH_3}{C}{=}C(CH_3)_2$

12. Which of the following gives acetone, $(CH_3)_2C{=}O$, as one of the products of its ozonolysis?

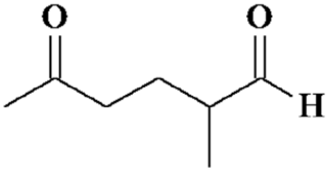
A) 

B) 

C) 

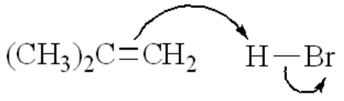
D) 

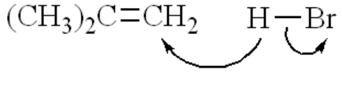
13. A compound, $C_7H_{13}Cl$, is reacted with sodium ethoxide and gives a single elimination product, C_7H_{12}. Treatment with ozone followed by zinc and water gives the compound below. Identify the original compound.

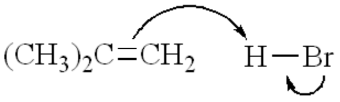


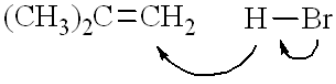
A)	2-chloro-1,1-dimethylcyclopentane	C)	4-chloro-1,2-dimethylcyclopentane
B)	1-chloro-1,2-dimethylcyclopentane	D)	2-chloro-1,3-dimethylcyclopentane

14. Which of the following correctly depicts the mechanistic first step in the addition of HBr to 2-methylpropene?

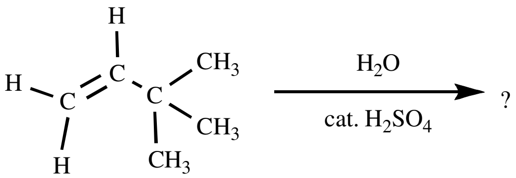
A) 
$(CH_3)_2C{=}CH_2 \quad H{-}Br$

C) 
$(CH_3)_2C{=}CH_2 \quad H{-}Br$

B) 
$(CH_3)_2C{=}CH_2 \quad H{-}Br$

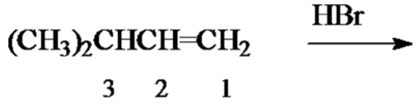
D) 
$(CH_3)_2C{=}CH_2 \quad H{-}Br$

15. What major product would you expect from this reaction?



A)	3,3-dimethyl-2-butanol	C)	2,3-dimethyl-2-butanol
B)	3,3-dimethyl-1-butanol	D)	2,2-dimethyl-3-butanol

16. The rearrangement which occurs in the following reaction can be described as a



$$\underset{3\ \ 2\ \ 1}{(CH_3)_2CHCH{=}CH_2} \xrightarrow{HBr}$$

A)	hydride shift from C-2 to C-1.	C)	proton shift from C-2 to C-1.
B)	hydride shift from C-3 to C-2.	D)	methyl group shift from C-3 to C-2.

Answers: 1)C 2)B 3)A 4)D 5)A 6)B 7)C 8)A 9)B 10)D 11)B 12)D 13)D 14)A 15)C 16)B

Chapter 9:
Alkynes

Hydrocarbons that contain a carbon-carbon triple bond are called alkynes. Mono-unsaturated noncyclic alkynes have the molecular formula C_nH_{2n-2}.

Compounds of the type RC≡CH are the most acidic of all hydrocarbons.

9.1 Sources of alkynes

Industrial preparation of acetylene is by dehydrogenation of ethylene. The cost of energy makes acetylene a more expensive industrial chemical than ethylene.

$$H_3C{-}CH_3 \xrightarrow{800^{o}C} H_2C{=}CH_2 \quad + \; H_2 \xrightarrow{1150^{o}C} HC{\equiv}CH \quad + \; H_2$$

Some alkynes occur naturally.

9.2 Nomenclature

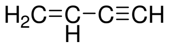
Ethyne (or most commonly called Acetylene; HC≡CH) is the simplest alkyne. Both are acceptable IUPAC names. Compounds that have their triple bond at the end of a carbon chain (RC≡CH) are called monosubstituted alkynes or terminal alkynes.

Higher alkynes are named in much the same way as alkenes, with the exception of using an -*yne* suffix instead of -*ene*. They have the same priority than alkenes as a functional group.

If a compound contains both a double bond and a triple bond, the chain is numbered so as to give the first multiple bond the lowest number, irrespective of whether it is a double bond or triple bond. An *en* suffix for the double bond precedes *yne* and is separated from it by the *yne* locant.

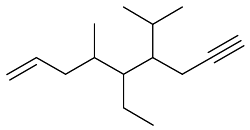
The —C≡H substituent is designated as an ethynyl group.

Examples:

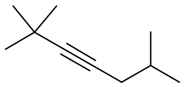


$H_2C{=}\underset{H}{C}{-}C{\equiv}CH$

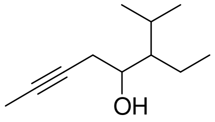
but-1-en-3-yne



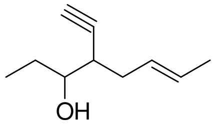
5-ethyl-6-isopropyl-4-methylnon-1-en-8-yne



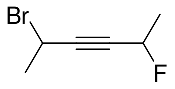
2,2,6-trimethylhept-3-yne



3-ethyl-2-methyloct-6-yn-4-ol



(*E*)-4-ethynyloct-6-en-3-ol



2-bromo-5-fluorohex-3-yne

9.3 Physical Properties of Alkynes

The physical properties of alkynes are similar to those of alkanes and alkenes.
Low density and low water-solubility. They are slightly more polar and generally have slightly higher boiling points than the corresponding alkanes and alkenes

9.4 Structure and Bonding in Alkynes: *sp* Hybridization

Triple bonds are linear.
The carbon-carbon triple bond has *sp* hybridization.
The hydrogens in C–H bonds behave as if they are attached to an increasingly more electronegative carbon in the series ethane < ethene < ethyne.

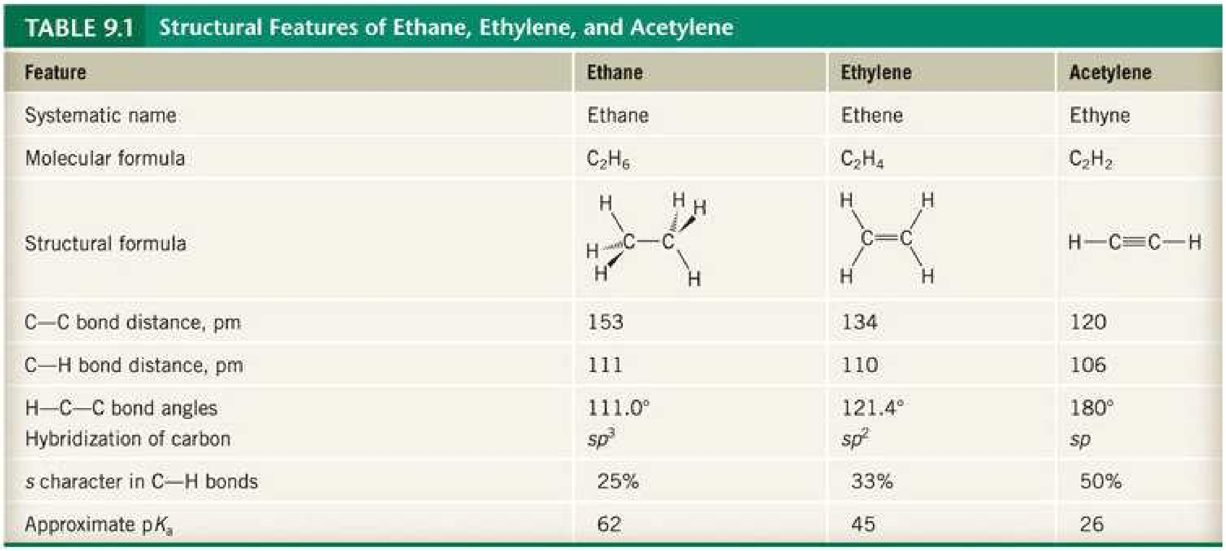


TABLE 9.1 Structural Features of Ethane, Ethylene, and Acetylene

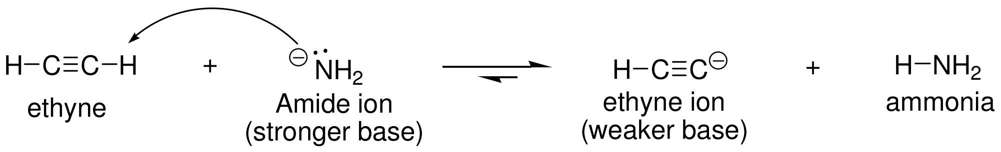
Feature	Ethane	Ethylene	Acetylene
Systematic name	Ethane	Ethene	Ethyne
Molecular formula	C_2H_6	C_2H_4	C_2H_2
Structural formula			H—C≡C—H
C—C bond distance, pm	153	134	120
C—H bond distance, pm	111	110	106
H—C—C bond angles Hybridization of carbon	111.0° sp^3	121.4° sp^2	180° sp
s character in C—H bonds	25%	33%	50%
Approximate pK_a	62	45	26

9.5 Acidity of Acetylene and Terminal Alkynes

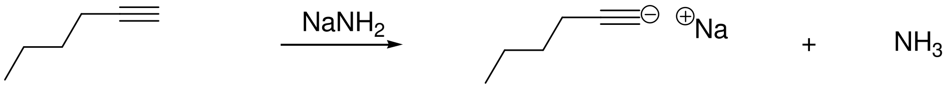
In general, the C—H bonds of hydrocarbons show little tendency to ionize, so hydrocarbons are exceedingly weak acids. Nonetheless, alkynes are not nearly as weak as alkanes or alkenes.

The conjugate base of a hydrocarbon is called a carbanion.

The amide ion is a much stronger base than the acetylide ion and converts acetylene to its conjugate base quantitatively.



Example:



Anions of acetylene and terminal alkynes are nucleophilic and react with methyl and primary alkyl halides to form carbon-carbon bonds by nucleophilic substitution.

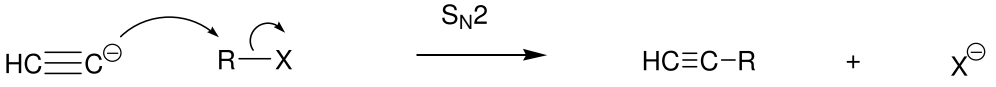
9.6 Preparation of Alkynes by Alkylation of Acetylene and Terminal Alkynes

There are two main methods for the preparation of alkynes:

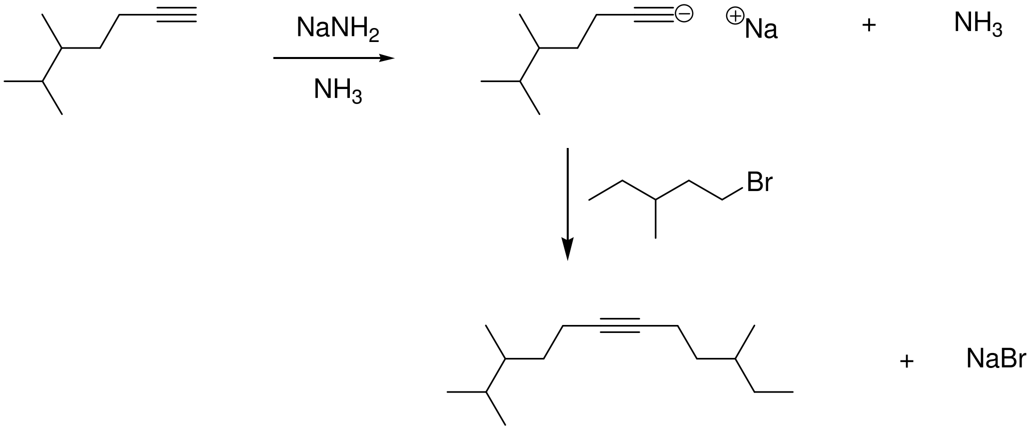
- Carbon-carbon bond formation (alkylation of acetylene and terminal alkynes)
- Functional-group transformations (elimination)

Reactions that attach alkyl groups to molecular fragments are called alkylation reactions.

In the alkylation of acetylene and terminal alkynes, the alkylating agent is an alkyl halide, and the reaction is nucleophilic substitution. The nucleophile is sodium acetylide or the sodium salt of a terminal (monosubstituted) alkyne.

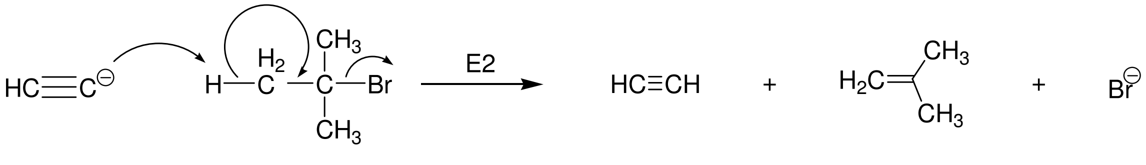


Example:



Acetylide anions are very basic, and react with secondary and tertiary alkyl halides by elimination.

Example:

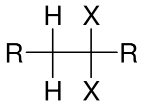


The desired S_N2 substitution pathway is observed only with methyl and primary alkyl halides.

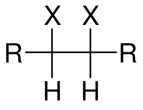
9.7 Preparation of Alkynes by Elimination Reactions

Preparation of alkynes by double dehydrohalogenation of dihaloalkanes.

The two types of dihalide:
- Geminal dihalide: Both halogens are on the same carbon
- Vicinal dihalide: The halogens are on adjacent carbons

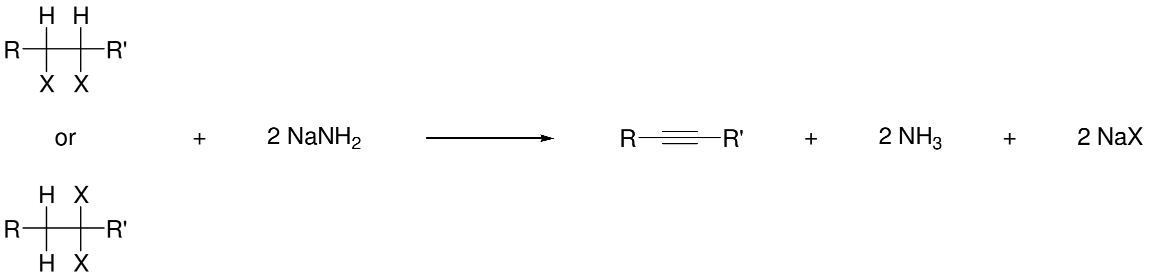


geminal dihalide



vicinal dihalide

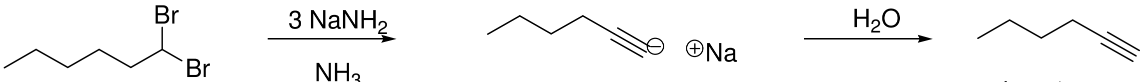
Double dehydrohalogenation of a geminal dihalide or vicinal dihalde:



The most frequent applications of these procedures lie in the preparation of terminal alkynes. Since the terminal alkyne product is acidic enough to transfer a proton to amide anion, one equivalent of base in addition to the two equivalents required for double dehydrohalogenation is needed.

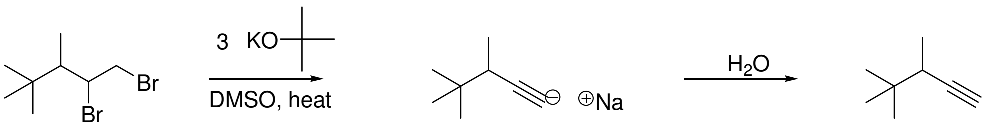
Adding water or acid after the reaction is complete converts the sodium salt to the corresponding alkyne.

Examples:



1,1-dibromohexane

hex-1-yne

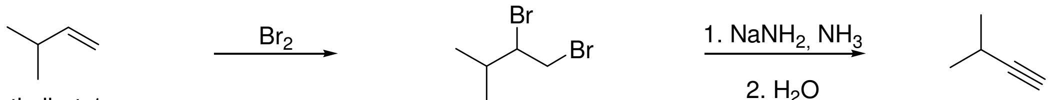


1,2-dibromo-3,4,4-trimethylpentane

3,4,4-trimethylpent-1-yne

The reaction can also be carried out with potassium tert-butoxide in dimethylsulfoxide (DMSO) and heat.

A glimpse at multi step synthesis:



3-methylbut-1-ene → 1,2-dibromo-3-methylbutane → 3-methylbut-1-yne

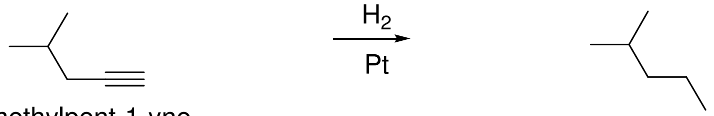
9.8 Reactions of Alkynes

- Hydrogenation (Section 9.9)
- Metal-Ammonia Reduction (Section 9.10)
- Addition of Hydrogen Halides (Section 9.11)
- Addition of Halogens (Section 9.13)
- Ozonolysis (Section 9.14)

9.9 Hydrogenation of Alkynes

In the presence of finely divided platinum, palladium, nickel or rhodium, two molar equivalents of hydrogen add to the triple bond of an alkyne to yield an alkane.
Like the hydrogenation of alkenes, hydrogenation of alkynes is a syn addition; *cis* alkenes are intermediates in the hydrogenation of alkynes to alkanes.

Example :

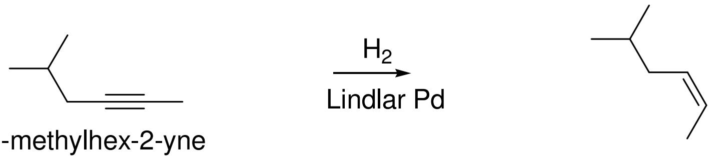


4-methylpent-1-yne

2-methylpentane

Hydrogenation of alkynes with **Lindlar catalyst** stops at the alkene step. Hydrogenation of alkynes with internal triple bonds gives only *cis* alkenes.

Example:



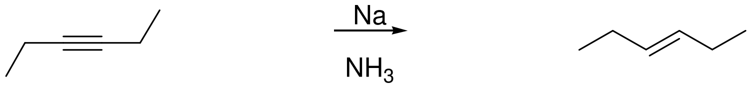
5-methylhex-2-yne

(*Z*)-5-methylhex-2-ene

9.10 Metal-Ammonia Reduction of Alkynes

Another way to convert alkynes to alkenes is by reduction with sodium (or lithium or potassium) in ammonia. This partial reduction of alkynes froms trans-alkenes.

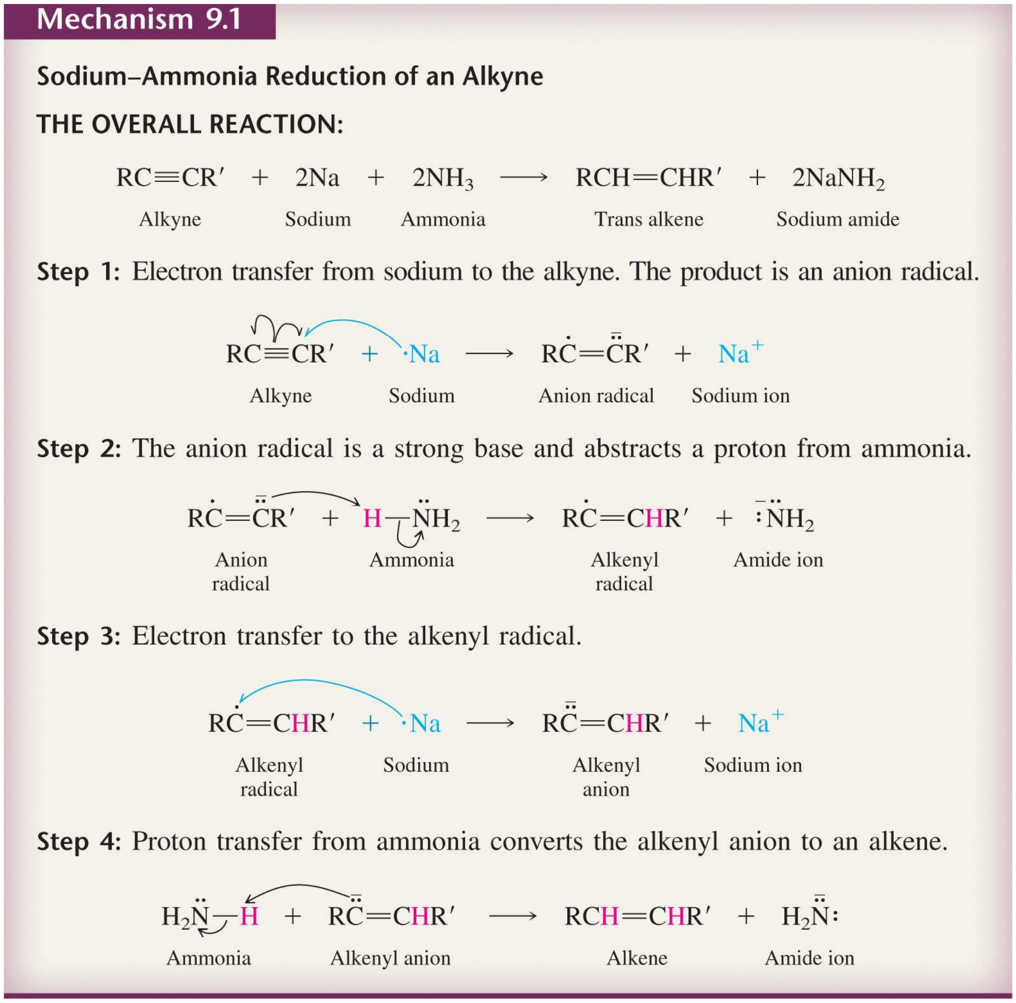
Example:



hex-3-yne

(*E*)-hex-3-ene

Note: The reagent Na and Na^+ are different and yield different products.



Mechanism 9.1

Sodium–Ammonia Reduction of an Alkyne

THE OVERALL REACTION:

$$\underset{\text{Alkyne}}{RC{\equiv}CR'} + \underset{\text{Sodium}}{2Na} + \underset{\text{Ammonia}}{2NH_3} \longrightarrow \underset{\text{Trans alkene}}{RCH{=}CHR'} + \underset{\text{Sodium amide}}{2NaNH_2}$$

Step 1: Electron transfer from sodium to the alkyne. The product is an anion radical.

$$\underset{\text{Alkyne}}{RC{\equiv}CR'} + \underset{\text{Sodium}}{\cdot Na} \longrightarrow \underset{\text{Anion radical}}{R\dot{C}{=}\overset{-}{\ddot{C}}R'} + \underset{\text{Sodium ion}}{Na^+}$$

Step 2: The anion radical is a strong base and abstracts a proton from ammonia.

$$\underset{\text{Anion radical}}{R\dot{C}{=}\overset{-}{\ddot{C}}R'} + \underset{\text{Ammonia}}{H{-}\ddot{N}H_2} \longrightarrow \underset{\text{Alkenyl radical}}{R\dot{C}{=}CHR'} + \underset{\text{Amide ion}}{:\overset{-}{\ddot{N}}H_2}$$

Step 3: Electron transfer to the alkenyl radical.

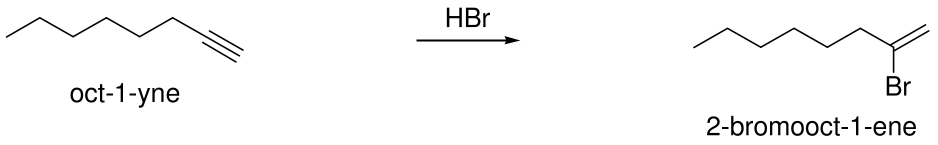
$$\underset{\text{Alkenyl radical}}{R\dot{C}{=}CHR'} + \underset{\text{Sodium}}{\cdot Na} \longrightarrow \underset{\text{Alkenyl anion}}{R\overset{-}{\ddot{C}}{=}CHR'} + \underset{\text{Sodium ion}}{Na^+}$$

Step 4: Proton transfer from ammonia converts the alkenyl anion to an alkene.

$$\underset{\text{Ammonia}}{H_2\ddot{N}{-}H} + \underset{\text{Alkenyl anion}}{R\overset{-}{\ddot{C}}{=}CHR'} \longrightarrow \underset{\text{Alkene}}{RCH{=}CHR'} + \underset{\text{Amide ion}}{H_2\overset{-}{\ddot{N}}:}$$

9.11 Addition of Hydrogen Halides to Alkynes

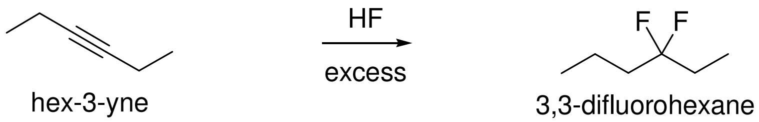
The regioselectivity of hydrogen halides addition follows Markovnikov's rule. A proton adds to the carbon that has the greater number of hydrogens, and halide adds to the carbon with the fewer hydrogens.



oct-1-yne

2-bromooct-1-ene

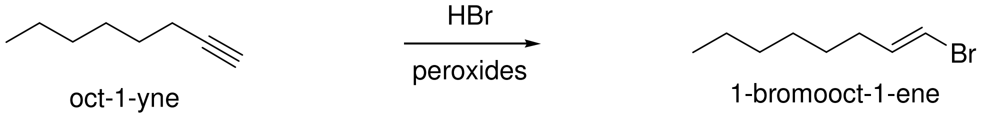
In the presence of excess hydrogen halide, geminal dihalides are formed by sequential addition of two molecules of hydrogen halide to the carbon-carbon triple bond. Both protons become bonded to the same carbon and both halogens to the adjacent carbon.



hex-3-yne

3,3-difluorohexane

Hydrogen bromide (but not hydrogen chloride or hydrogen iodide) adds to alkynes by a free-radical mechanism when peroxides are present in the reaction mixture; a regioselectivity opposite to Markovnikov's rule.

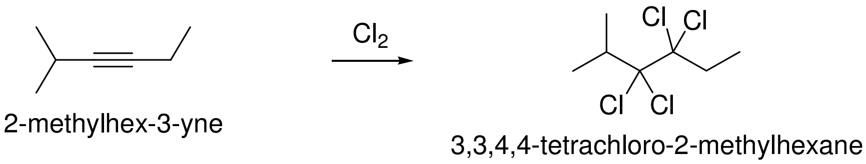


oct-1-yne

1-bromooct-1-ene

9.13 Addition of Halogens to Alkynes

Alkynes react with chlorine and bromine to yield tetrahaloalkanes.
Two molecules of the halogen add to the triple bond.

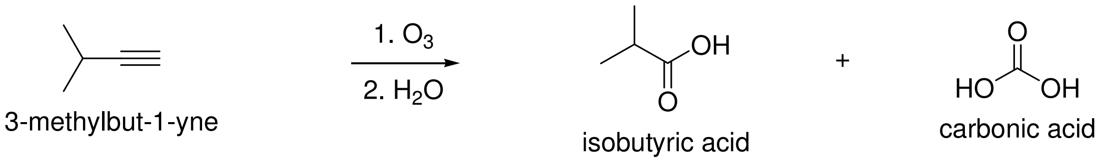


2-methylhex-3-yne

3,3,4,4-tetrachloro-2-methylhexane

9.14 Ozonolysis of Alkynes

Two carboxylic acids are produced when alkynes are subjected to ozonolysis.



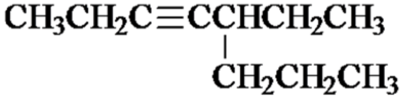
3-methylbut-1-yne

isobutyric acid

carbonic acid

Extra Problems:

1. What is the IUPAC name of the following compound?

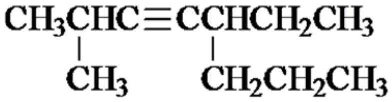


$$\mathrm{CH_3CH_2C{\equiv}C\underset{\underset{\displaystyle CH_2CH_2CH_3}{|}}{C}HCH_2CH_3}$$

A) 5-propyl-3-heptyne　　C) 5-ethyl-3-octyne
B) 5-isopropyl-3-heptyne　　D) 4-ethyl-5-octyne

2. Which of the following gives only one organic product on ozonolysis?
A) 2-hexyne B) 3-hexyne C) 2-heptyne D) 3-heptyne

3. What is the IUPAC name of the following compound?



$$\mathrm{CH_3\underset{\underset{\displaystyle CH_3}{|}}{C}HC{\equiv}C\underset{\underset{\displaystyle CH_2CH_2CH_3}{|}}{C}HCH_2CH_3}$$

A) 2-methyl-5-propyl-3-heptyne　　C) 5-ethyl-2-methyl-3-octyne
B) 1-isopropyl-3-propyl-1-pentyne　　D) 4-ethyl-7-methyl-5-octyne

4. Select the best base to quantitatively remove a proton from acetylene.
A) $NaNH_2$ B) NH_3 C) NaOH D) $NaOCH_2CH_3$

5. Predict the major product(s) in the reactions below.

$$\mathrm{HC{\equiv}CH} \xrightarrow[\text{2) } CH_3Br]{\text{1) } NaNH_2} \xrightarrow[\text{2) 1-iodohexane}]{\text{1) } NaNH_2}$$

A) 1-nonyne B) 2-nonyne C) cis-2-nonene D) trans-2-nonene

6. Which sequence of reactions works best in synthesizing *cis*-3-nonene?

A) (1) 1-butyne, $NaNH_2$
(2) 1-bromopentane
(3) Na, NH_3

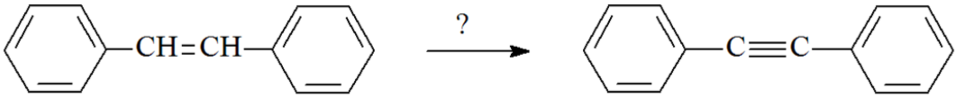
B) (1) 1-butyne, $NaNH_2$
(2) 1-bromopentane
(3) H_2, Lindlar Pd

C) (1) 1-pentyne, $NaNH_2$
(2) 1-bromobutane
(3) H_2O, $H_2SO_4/HgSO_4$

D) (1) 1-pentyne, $NaNH_2$
(2) 1-bromobutane
(3) 2 HCl
(4) $NaNH_2$

7. Which of the following reagents would be used to convert 2-pentyne to *cis*-2-pentene?
A) $NaNH_2$, NH_3 B) Na, NH_3 C) H_2, Lindlar Pd D) H_2O, $HgSO_4/H_2SO_4$

8. Which sequence of reactions below works best in carrying out the following conversion?



A) (1) HBr (2) excess $NaNH_2$
B) (1) Br_2 (2) excess $NaNH_2$
C) (1) Br_2, H_2O (2) excess $NaNH_2$
D) (1) H_2O, H_2SO_4(cat.) (2) excess $NaNH_2$

9. Which of the following is the correct IUPAC name of the product for the reaction shown below?

$$CH_3C{\equiv}CCH_2CH_2CH(CH_3)_2 \xrightarrow{\text{Na, NH}_3}$$

A)	*cis*-2-methyl-5-heptene	C)	*cis*-6-methyl-2-heptene
B)	*trans*-2-methyl-5-heptene	D)	*trans*-6-methyl-2-heptene

10. How would you carry out the following conversion?

$$(CH_3)_2CHC{\equiv}CH \xrightarrow{?} (CH_3)_2CHCH_2CH_2Br$$

A) (1) H_2/Lindlar Pd (2) HBr
B) (1) H_2/Lindlar Pd (2) HBr, peroxides
C) (1) HBr (1 eq) (2) H_2/Pd
D) (1) Br_2 (1 eq) (2) H_2/Pd

A) A B) B C) C D) D

11. What is the major product of the reaction shown below?

$$CH_3CH_2C{\equiv}CH \xrightarrow{\text{2 HCl}}$$

A)	1,1-dichlorobutane	C)	2,2-dichlorobutane
B)	1,2-dichlorobutane	D)	1,12,2-tetrachlorobutane

12. Ozonolysis of an alkyne gave the two compounds shown below. What is the IUPAC name of the original alkyne?

$CH_3CH_2CH_2CO_2H$ and $(CH_3)_3CCO_2H$

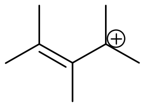
A)	2,2-dimethyl-3-octyne	C)	2,2-dimethyl-3-heptyne
B)	3,3-dimethyl-4-octyne	D)	6,6-dimethyl-3-heptyne

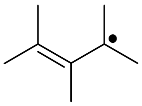
Answers: 1)C 2)B 3)C 4)A 5)B 6)B 7)C 8)B 9)D 10)B 11)C 12)C

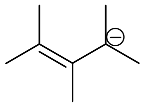
Chapter 10:
Conjugation in Alkadienes and Allylic Systems

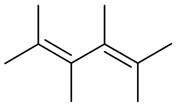
A double bond can affect the properties of a second functional unit to which it is directly attached.

Conjugate systems are two (or more) functionalities joined together. It is a conjugation.


Allylic carbocation


Allylic free radical

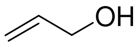

Allylic anion

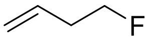

Conjugated diene

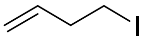
Conjugation permits two functional units within a molecule to display a kind of reactivity that is qualitatively different from that of either unit alone.

10.1 The Allyl Group

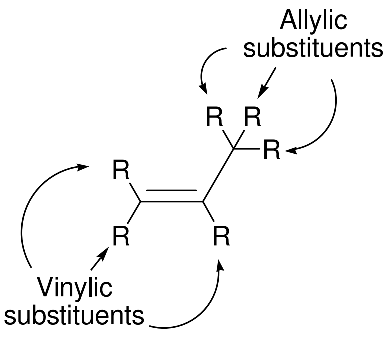
The group $H_2C{=}CHCH_2{-}$ is known as allyl.


Allyl alcohol
(prop-2-en-1-ol)


Allyl fluoride
(4-fluorobut-1-ene)

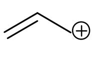

Allyl iodide
(4-iodobut-1-ene)

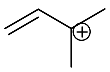
The ***sp³* hybridized carbon** of a $C{=}C{-}C$ unit is classified as an **allylic carbon** and atoms or groups attached to it are allylic substituents. The two ***sp²*-hybridized** carbons are **vinylic** and atoms or groups attached to them are vinylic substituents.

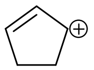


10.2 Allylic Carbocations

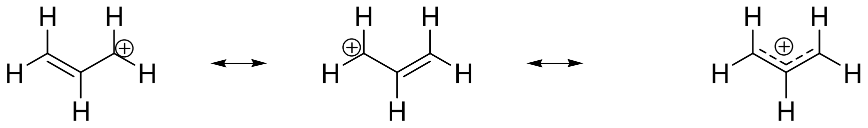
Allylic carbocations are carbocations in which an allylic carbon bears the positive charge. Allyl cation is the simplest allylic carbocation.


Allyl cation


1,1-Dimethylallyl cation


2-Cyclopentenyl cation

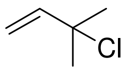
Allylic carbocations are more stable than simple alkyl cations because the C═C group acts as an electron-donating substituent to the positively charged carbon. We can represent this electron donation in resonance terms as:



The double bond is conjugated to the positively charged carbon. The two resonance forms of allyl cation are equivalent, and the positive charge is shared equally by the carbons at each end.

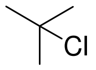
In an ion where one allylic carbon is secondary and the other is primary, the one that is secondary bears more of the positive charge.

10.3 S_N1 Reactions of Allylic Halides



3-chloro-3-methylbut-1-ene

vs.



2-chloro-2-methylpropane

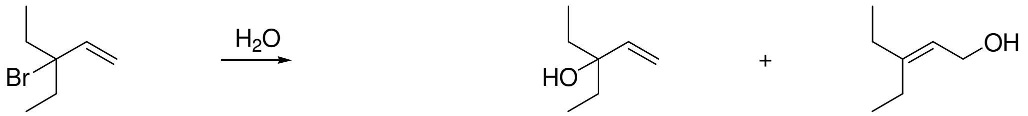
In comparing 3-chloro-3-methylbut-1-ene with 2-chloro-2-methylpropane, the allylic chloride is more reactive, because it ionizes more rapidly and forms a more stable carbocation. This greater stability is attributed to allylic resonance.

On the other hand, both carbons can undergo the nucleophilic substitution.

The nucleophile bonds to the carbon that bears more of the positive charge; therefore, the tertiary substituted carbon is the major product.

Be sure you understand that we are not dealing with an equilibrium between two isomeric carbocations. There is only one carbocation.

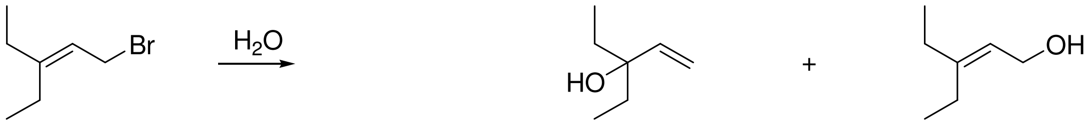
Example:



3-bromo-3-ethylpent-1-ene

3-ethylpent-1-en-3-ol (major)

3-ethylpent-2-en-1-ol



3-bromo-3-ethylpent-1-ene

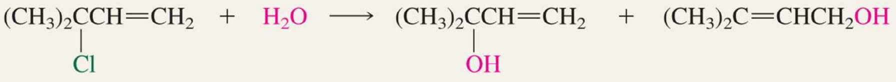
3-ethylpent-1-en-3-ol (major)

3-ethylpent-2-en-1-ol

Mechanism 10.1

Hydrolysis of an Allylic Halide (3-Chloro-3-methyl-1-butene)

THE OVERALL REACTION:



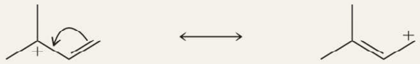
$$(CH_3)_2\underset{\mid \atop Cl}{C}CH{=}CH_2 + H_2O \longrightarrow (CH_3)_2\underset{\mid \atop OH}{C}CH{=}CH_2 + (CH_3)_2C{=}CHCH_2OH$$

3-Chloro-3-methyl-1-butene Water 2-Methyl-3-buten-2-ol 3-Methyl-2-buten-1-ol

Step 1: The alkyl halide ionizes to give a carbocation. This step is rate-determining.

3-Chloro-3-methyl-1-butene Chloride ion 1,1-Dimethylallyl cation

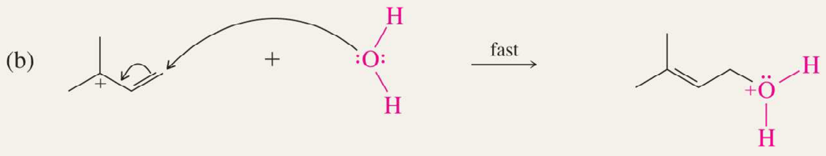
The positive charge in the 1,1-dimethylallyl cation is shared between two allylic carbons.



Major contributor Minor contributor

Step 2: The carbocation (shown in its most stable resonance form) reacts with water. Water acts as a nucleophile; its oxygen can bond to either the tertiary carbon (a) or the primary carbon (b).

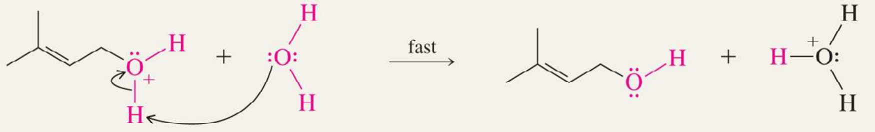
Water 1,1-Dimethylallyl cation (major contributor) 1,1-Dimethylallyloxonium ion



1,1-Dimethylallyl cation (major contributor) Water 3,3-Dimethylallyloxonium ion

Step 3: The alkyloxonium ions formed in step 2 are converted to the corresponding alcohols by proton transfer. Water is the proton acceptor.

Water 1,1-Dimethylallyloxonium ion Hydronium ion 2-Methyl-3-buten-2-ol



3,3-Dimethylallyloxonium ion Water 3-Methyl-2-buten-1-ol Hydronium ion

10.4 S_N2 Reactions of Allylic Halides

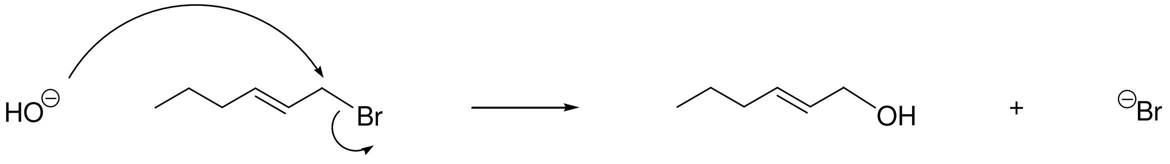
Allylic halides also undergo S_N2 reactions faster than simple primary alkyl halides.

Two factors:

Steric:
The trigonal carbon (hybridized sp^2) is less crowded than the tetrahedral carbon (hybridized sp^3).

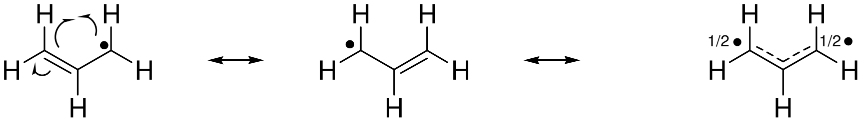
Electronic:
Electron delocalization lowers the energy, which means lower activation energy.

With secondary and tertiary allylic halides or under solvolysis conditions, S_N1 reactions can compete with S_N2, and a mixture of direct displacement and allylic rearrangement products results.



10.5 Allylic Free Radicals

Allylic free radicals are also stabilized by electron delocalization.



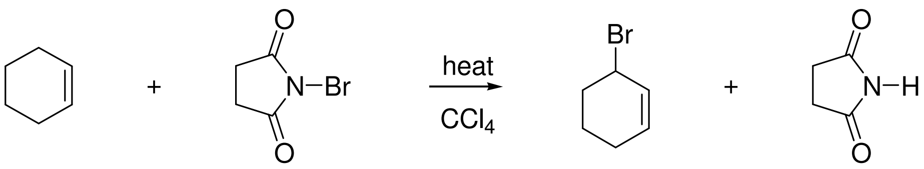
Allyl radical is a conjugated system in which three electrons are delocalized over three carbons. The resonance structures indicate that the unpaired electron has an equal probability of being found at C-1 or C-3. C-2 shares none of the unpaired electrons. In other words, the unpaired electron in allyl radical "divides its time" equally between the C-1 and C-3.

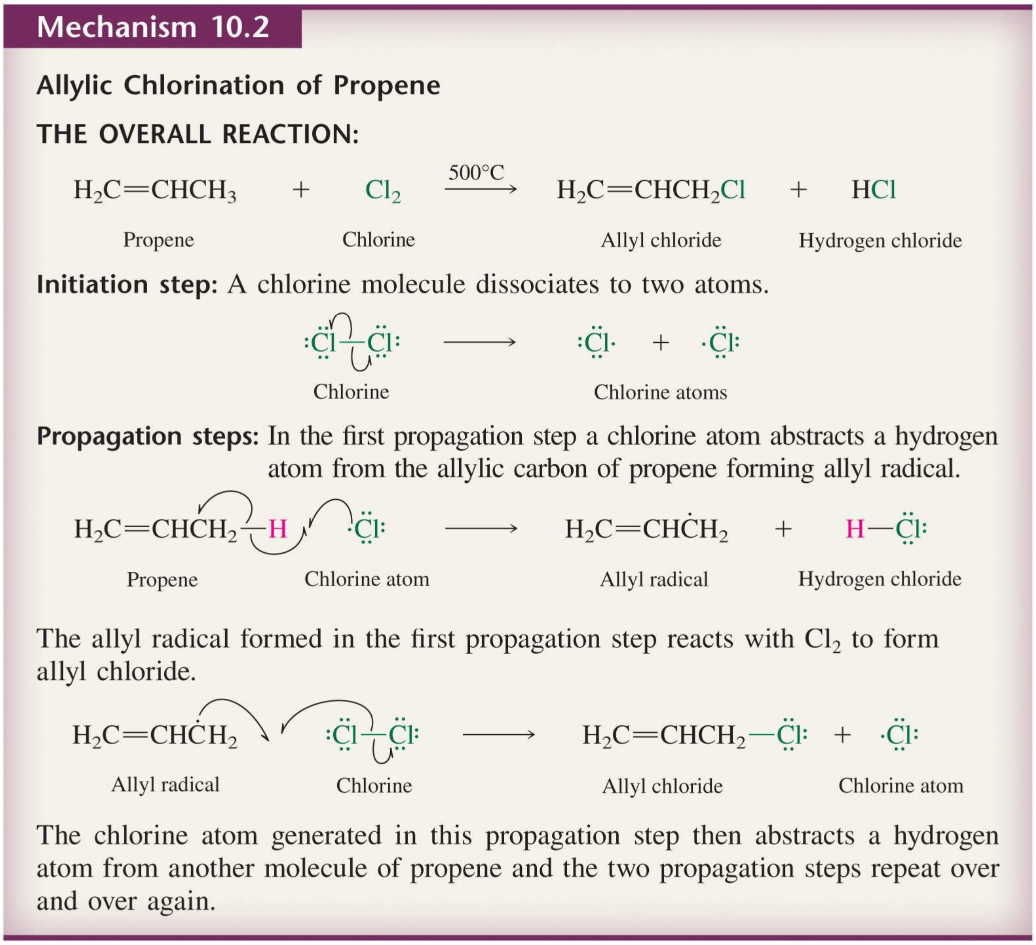
10.6 Allylic Halogenation

Although alkenes typically react with chlorine and bromine by addition to the double bond at room temperature, substitution becomes competitive at higher temperatures, especially when the concentration of the halogen is low.

When substitution does occur, it is highly selective for the allylic position.

N-Bromosuccinimide (NBS) provides a low concentration of molecular bromine, which reacts with alkenes by a mechanism analogous to that of other free radical halogenation.





Mechanism 10.2

Allylic Chlorination of Propene

THE OVERALL REACTION:

$$H_2C{=}CHCH_3 + Cl_2 \xrightarrow{500°C} H_2C{=}CHCH_2Cl + HCl$$

Propene Chlorine Allyl chloride Hydrogen chloride

Initiation step: A chlorine molecule dissociates to two atoms.

$$:\ddot{\underset{..}{Cl}}-\ddot{\underset{..}{Cl}}: \longrightarrow :\ddot{\underset{..}{Cl}}\cdot + \cdot\ddot{\underset{..}{Cl}}:$$

Chlorine Chlorine atoms

Propagation steps: In the first propagation step a chlorine atom abstracts a hydrogen atom from the allylic carbon of propene forming allyl radical.

$$H_2C{=}CHCH_2-H \quad \cdot\ddot{\underset{..}{Cl}}: \longrightarrow H_2C{=}CH\dot{C}H_2 + H-\ddot{\underset{..}{Cl}}:$$

Propene Chlorine atom Allyl radical Hydrogen chloride

The allyl radical formed in the first propagation step reacts with Cl_2 to form allyl chloride.

$$H_2C{=}CH\dot{C}H_2 \quad :\ddot{\underset{..}{Cl}}-\ddot{\underset{..}{Cl}}: \longrightarrow H_2C{=}CHCH_2-\ddot{\underset{..}{Cl}}: + \cdot\ddot{\underset{..}{Cl}}:$$

Allyl radical Chlorine Allyl chloride Chlorine atom

The chlorine atom generated in this propagation step then abstracts a hydrogen atom from another molecule of propene and the two propagation steps repeat over and over again.

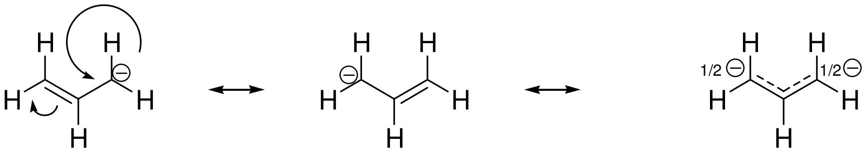
All the allylic hydrogens in the starting alkene must be equivalent.

Both resonance forms of the allylic radical must be equivalent.

If two resonance forms are not equivalent; it will give mixture of isomeric allylic halide.

10.7 Allylic Anions

Like allyl cation and allyl radical, allyl anion is planar and stabilized by electron delocalization.



Propene is significantly more acidic than propane. The allyl anion is a weaker base and holds its unshared electron pair more strongly than propyl anion.

The charge is delocalized to both terminal carbons, stabilizing the conjugate base.

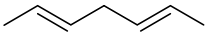
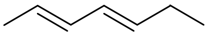
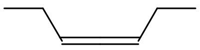
10.8 Classes of Dienes

A hydrocarbon that contains two double bonds is called an alkadiene, and the relationship between the double bonds is described as isolated, conjugated, or cumulated.

Isolated diene: Two carbon-carbon double bonds separated by one (or more) *sp*^{3}-hybridized carbon.

Conjugated diene: Two carbon-carbon double bonds connected to each other by a single bond.

Cumulated dienes: Two carbon-carbon double bonds in which one carbon is common to the two double bonds.

Isolated diene		(2*E*,5*E*)-hepta-2,5-diene
Conjugated diene		(2*E*,4*E*)-hepta-2,4-diene
Cumulated diene		hepta-3,4-diene

Nomenclature:

Alkadienes are named according to the IUPAC rules by replacing the –ane ending of an alkane with –adiene and locating the position of each double bond by number.

Compounds with three carbon-carbon double bonds are called alkatrienes and named accordingly, etc.

10.9 Relative Stabilities of Dienes

The increased stability due to conjugation is called the delocalization energy, resonance energy or conjugation energy.

Thus the order of alkadiene stability is:

Cumulated diene (least stable) < Isolated diene < Conjugated diene (most stable)

10.10 Bonding in Conjugated Dienes

The factor most responsible for the increased stability of conjugated double bonds is the greater delocalization of their π electrons compared with the π electrons of isolated double bonds.

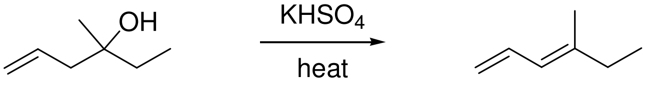
In isolated dienes, an *sp*^{3}-hybridized carbon isolates the two π orbitals, preventing the exchange of electrons between them.

In a conjugated diene, the π electrons are delocalized over four carbons.

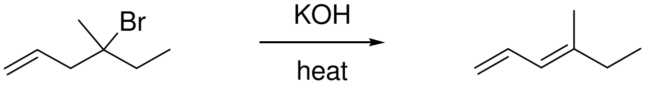
Delocalization of electrons lowers the energy and gives a more stable molecule.

10.12 Preparation of Dienes

Dehydration of Alcohols



Dehydrohalogenation of Alkyl Halides



Dienes with isolated double bonds can be formed when the structure of the alkyl halide doesn’t permit the formation of a conjugated diene.

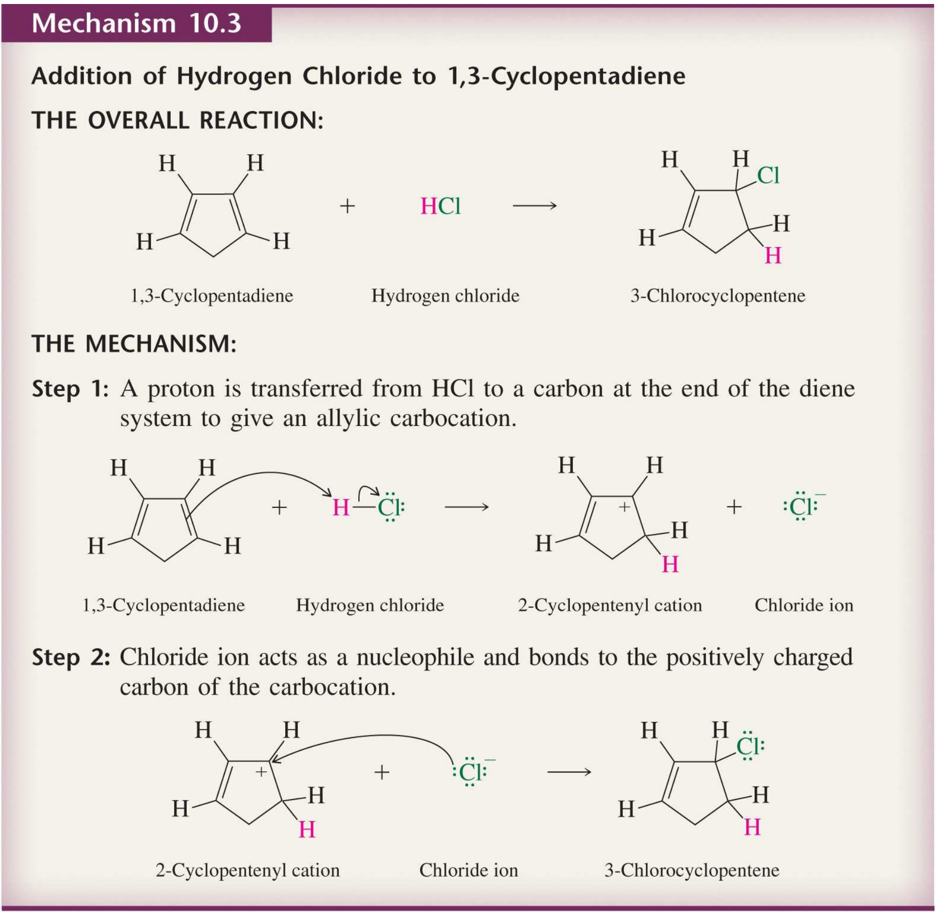
Reactions of Dienes:

- Isolated dienes: double bonds react independently of one another.
- Cumulated dienes: specialized topic: (not discussed further in this class).
- Conjugated dienes: reactivity pattern requires us to think of conjugated diene system as a functional group of its own.

10.13 Addition of Hydrogen Halides to Conjugated Dienes

Our study of chemical reactions of alkadienes will be limited to those of conjugated dienes. (The reactions of isolated dienes are essentially the same as those of individual alkenes. The reactions of allenes are – like their preparation – so specialized that their treatment is better suited to an advanced course in organic chemistry).

Electrophilic addition is the characteristic rection of alkenes. Conjugated dienes undergo addition with the same electrophiles that react with alkenes, and by the same mechanisms.



Mechanism 10.3

Addition of Hydrogen Chloride to 1,3-Cyclopentadiene

THE OVERALL REACTION:

1,3-Cyclopentadiene + HCl ⟶ 3-Chlorocyclopentene

1,3-Cyclopentadiene Hydrogen chloride 3-Chlorocyclopentene

THE MECHANISM:

Step 1: A proton is transferred from HCl to a carbon at the end of the diene system to give an allylic carbocation.

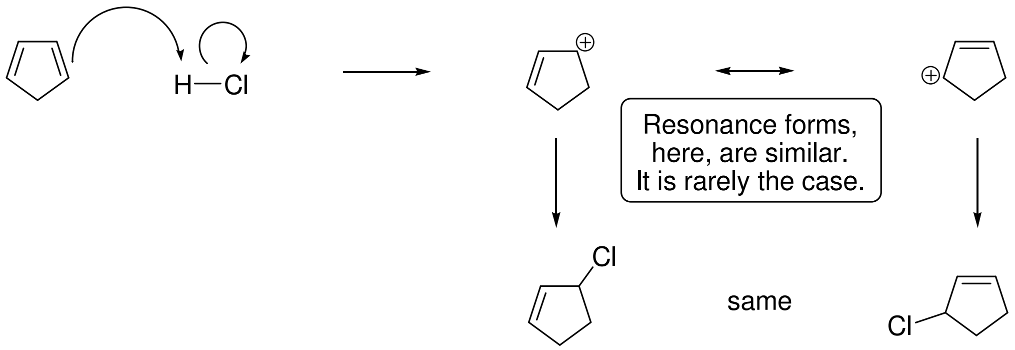
1,3-Cyclopentadiene Hydrogen chloride 2-Cyclopentenyl cation Chloride ion

Step 2: Chloride ion acts as a nucleophile and bonds to the positively charged carbon of the carbocation.

2-Cyclopentenyl cation Chloride ion 3-Chlorocyclopentene

Electrophilic Addition to Conjugated Dienes:

- The regioselectivity is governed by the stability of the resulting carbocation.
- Protonation occurs at the end of the diene unit because an allylic carbocation results.



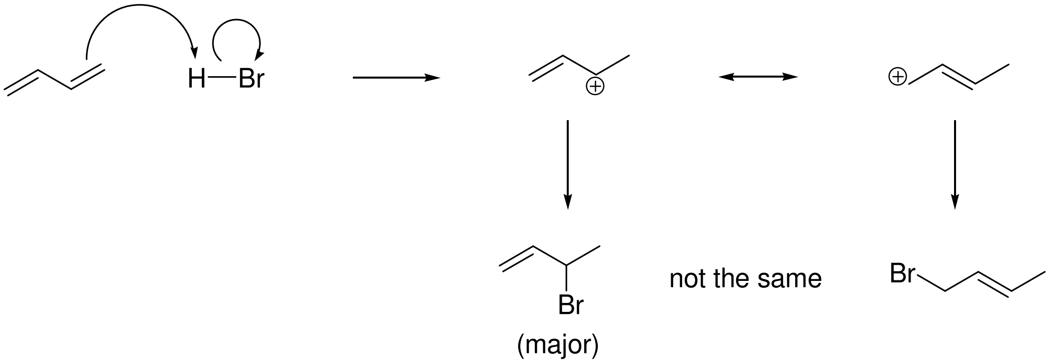
Resonance forms, here, are similar. It is rarely the case.

1,2-Addition versus 1,4-Addition:

1,2-Addition : Product corresponding to the addition of a proton to the C-1 and halogen to the C-2 of the conjugated diene. (Also called direct addition).

1,4-Addition: Product corresponding to the addition of a proton to the C-1 and halogen to the C-4 of the conjugated diene. (Also called conjugate addition).

- Electrophilic addition occurs.
- The 1,2 and 1,4-addition are both observed.
- The product ratio depends on the reaction temperature.



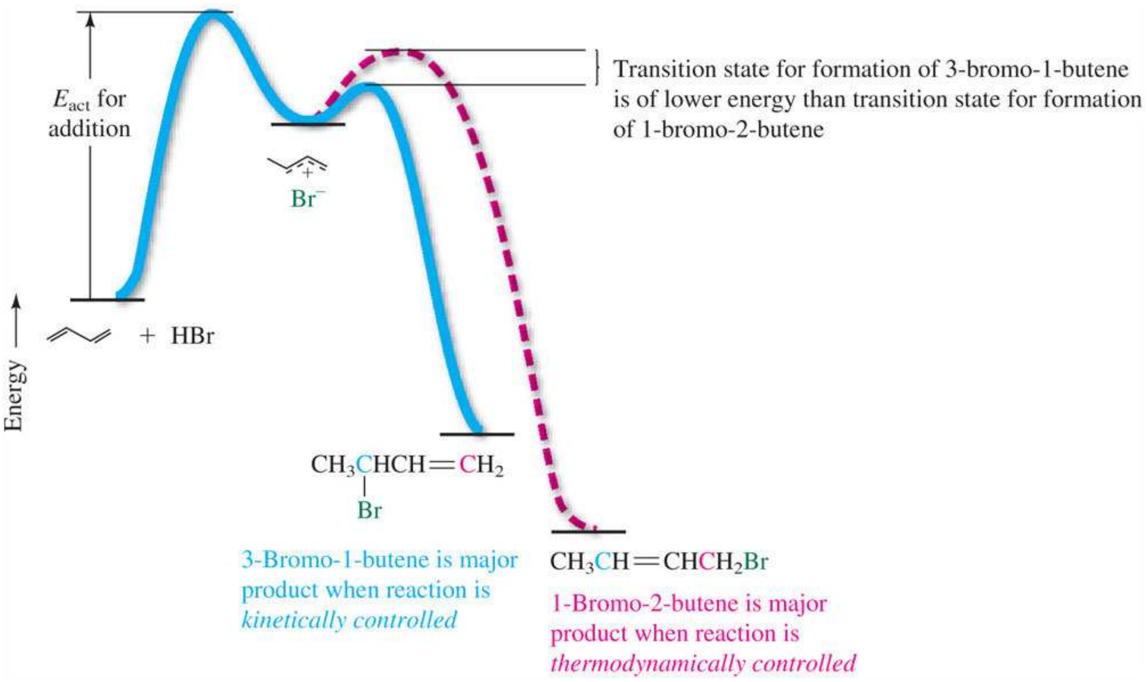
3-Bromo-1-butene (left) *is formed faster* than 1-bromo-2-butene (right) because allylic carbocations react with nucleophiles preferentially at the carbon that bears the greater share of positive charge.

On the other hand, 1-Bromo-2-butene *is more stable* than 3-bromo-1-butene because it has a more highly substituted double bond.

The two products equilibrate (are produced in equivalent ratios) at 25℃. Below that temperature, 3-Bromo-1-butene is predominant, and above that temperature, 1-Bromo-2-butene is predominant.

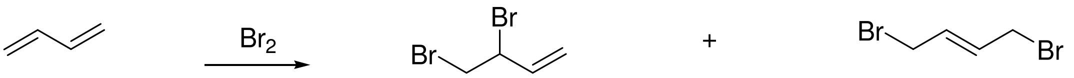
Kinetic Control versus Thermodynamic Control

Kinetic control: The major product is the one formed at the fastest rate.
Thermodynamic control: The major product is the one that is the most stable.



10.14 Halogen Addition to Dienes

Mixtures of 1,2- and 1,4-addition products are obtained when 1,3-butadiene reacts with chlorine or bromine.



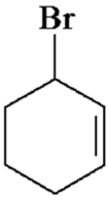
1,2-addition product

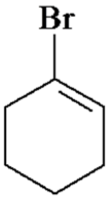
1,4-addition product
(major)

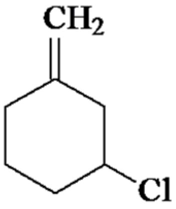
The tendency for the 1,4-addition is favored.
The *E* double bond products are produced almost exclusively.

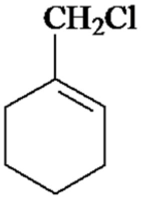
Extra Problems:

1. Identify the allylic halide(s).


I


II


III

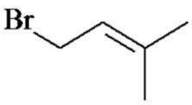

IV

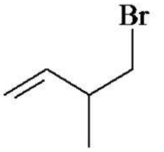
   A) only II B) I and II C) I and IV D) I, III, and IV

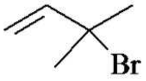
2. How many vinylic hydrogens are there in 1-ethylcyclohexene?
   A) one B) two C) three D) four

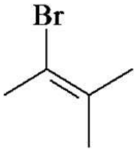
3. What is(are) the expected product(s) of the following reaction? Notice that there is heat.

$$H_2C{=}CHCH(CH_3)_2 \xrightarrow[\text{heat}]{\text{NBS, CCl}_4}$$


I

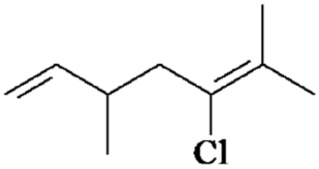

II


III


IV

   A) only II B) only III C) I and III D) II and IV

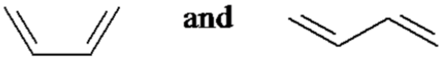
4. What is the IUPAC name of the following diene?



   A) 3-chloro-2,5-dimethyl-2,6-heptadiene
   B) 3-chloro-2,5-dimethyl-1,5-heptadiene
   C) 5-chloro-3,5-dimethyl-1,6-heptadiene
   D) 5-chloro-3,6-dimethyl-1,5-heptadiene

5. Which of the following are conjugated dienes?
   I. 1,2-octadiene II. 1,3-octadiene III. 2,5-octadiene IV. 1,7-octadiene
   A) only I B) only II C) I and II D) II and III

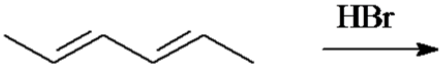
6. What is the relationship between the *s*-cis and *s*-trans forms of 1,3-butadiene?

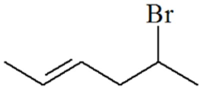


A) constitutional isomers
B) different conformations of the same compound
C) diastereomers
D) resonance forms

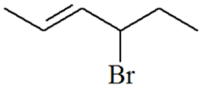
7. Addition of one equivalent of HBr to 1,3-cyclohexadiene gives
A) bromocyclohexane.
B) 3-bromocyclohexene.
C) 4-bromocyclohexene.
D) 3-bromocyclhexene and 4-bromocyclohexene.

8. Which of the following is the 1,4-addition product in the reaction shown below?

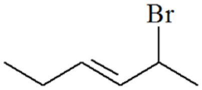




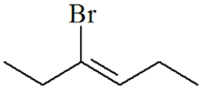
A)



B)

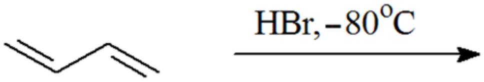


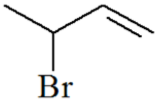
C)



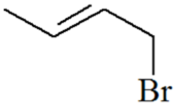
D)

9. What is the kinetically controlled product in the following reaction?

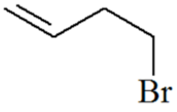




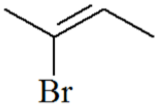
A)



B)



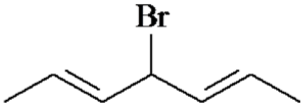
C)



D)

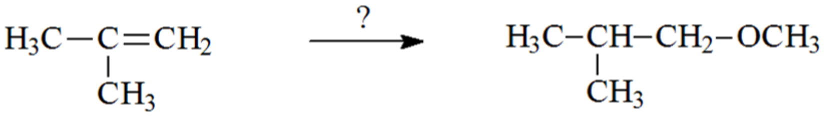
A) A B) B C) C D) D

10. Give the total number of resonance forms of the carbocation which results from the S_N1 ionization of the compound shown below.



A) no resonance forms - a single Lewis structure B) two C) three D) four

11. Which reaction sequence below would work best (and with highest overall yield) in the following conversion?



$$\underset{\displaystyle CH_3}{H_3C-\underset{|}{C}=CH_2} \xrightarrow{?} H_3C-\underset{\underset{\displaystyle CH_3}{|}}{CH}-CH_2-OCH_3$$

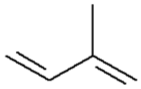
A) (1) H_2/Pt
(2) Br_2, light
(3) $CH_3O^-Na^+$

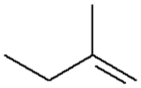
B) (1) NBS, CCl_4, heat
(2) $CH_3O^-Na^+$
(3) H_2/Pt

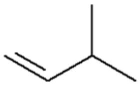
C) (1) NBS, CCl_4, heat
(2) H_2/Pt
(3) $CH_3O^-Na^+$

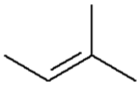
D) (1) HBr, peroxides
(2) CH_3OH, heat

12. Which one of the following gives only a single allylic bromide on heating with NBS in carbon tetrachloride?

A) 

B) 

C) 

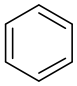
D) 

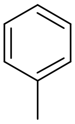
Answers: 1)C 2)A 3)C 4)D 5)B 6)B 7)B 8)C 9)A 10)C 11)B 12)A

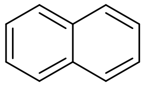
Chapter 11:
Arenes and Aromaticity

Arenes are hydrocarbons based on the benzene ring as a structural unit. They are also referred to as aromatic hydrocarbons.

Arenes are much more stable than simple conjugated trienes. A conjugated system that closes on itself can have properties that are much different from those of open-chain polyenes.


benzene


toluene


naphthalene

11.1 Benzene

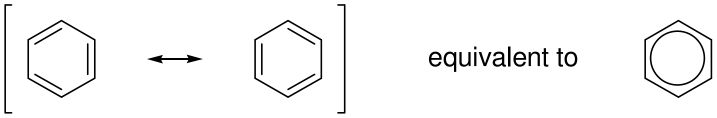
Although benzene and toluene are not particularly fragrant compounds themselves, their origins in aromatic plant extracts led them (and related compounds) to be classified as **aromatic** hydrocarbons.

Alkanes, alkenes and alkynes belong to another class called the **aliphatic** hydrocarbons.

11.2 The Structure of Benzene
11.3 A resonance Picture of Bonding in Benzene
11.5 An Orbital Hybridization View of Bonding in Benzene

Like alkenes and alkynes, arenes are unsaturated.

The low reactivity of benzene and its derivatives reflects their special stability. Benzene is not a cyclohexatriene, nor is it a pair of rapidly equilibrating cyclohexatriene isomers.



- Benzene is planar.
- All the bond angles are of 120°.
- Every carbon is hybridized sp^2.
- The six p electrons of benzene are delocalized over all six carbons.
- The carbon-carbon bond distances in benzene are all identical and have intermediate values between typical single-bond and double-bond lengths.

11.4 The Stability of Benzene

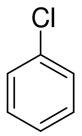
Hydrogenation of benzene is more difficult than hydrogenation of alkenes and alkynes.

The resonance energy of benzene is a measure of how much more stable benzene is than would be predicted on the basis of a pair of rapidly interconverting 1,3,5-cyclohexatrienes.

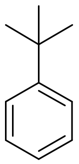
Because of its very large increment of resonance energy, benzene (and related compounds) constitute a separate category of compounds (the aromatics).

11.7 Substituted Derivatives of Benzene and Their Nomenclature

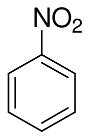
All compounds that contain a benzene ring are aromatic.



Chlorobenzene



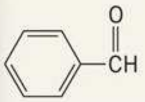
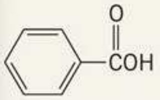
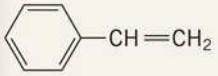
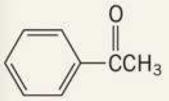
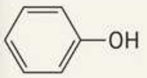
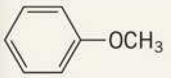
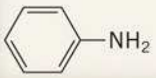
tert-Butylbenzene



Nitrobenzene

Many simple monosubstituted derivatives of benzene have common names of long standing that have retained in the IUPAC system.

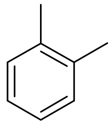
TABLE 11.1 Names of Some Frequently Encountered Derivatives of Benzene

Structure	Systematic name	Common name*
	Benzenecarbaldehyde	Benzaldehyde
	Benzenecarboxylic acid	Benzoic acid
	Vinylbenzene	Styrene
	Methyl phenyl ketone	Acetophenone
	Benzenol	Phenol
	Methoxybenzene	Anisole
	Benzenamine	Aniline

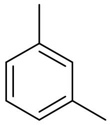
Dimethyl derivatives of benzene are called **xylenes**. There are three xylene isomers, the ortho (o)-, meta (m)- and para (p)- substituted derivatives.

The prefix ***ortho* (*o*)** signifies a 1,2-disubstituted benzene ring.
The prefix ***meta* (*m*)** signifies a 1,3-disubstituted benzene ring.
The prefix ***para* (*p*)** signifies a 1,4-disubstituted benzene ring.

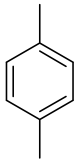
These prefixes are used mainly to relate one substituent to another on the ring.



o-xylene
(1,2-dimethylbenzene)



m-xylene
(1,3-dimethylbenzene)

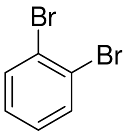


p-xylene
(1,4-dimethylbenzene)

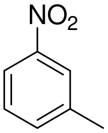
Rules governing Arenes nomenclature

1) Benzene is considered as the parent and comes last in the name.
2) Substituents are listed in alphabetical order.
3) Number the ring in the direction that gives lowest locant at the first point of difference.

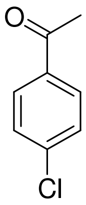
Example:



o-Dibromobenzene
(1,2-dibromobenzene)

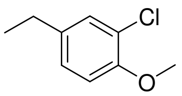


m-nitrotoluene
(1-methyl-3-nitrobenzene)

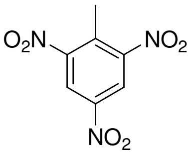


p-Chloroacetophenone
(1-(4-chlorophenyl)ethanone)

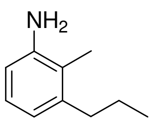
The *o*, *m* and *p* prefixes are not used when three or more substituents are present on benzene; numerical locants must be used instead.



4-ethyl-2-Fluoro**anisole**
(2-chloro-4-ethyl-1-methoxybenzene)



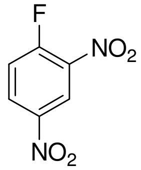
2,4,6-Trinitro**toluene**
2-methyl-1,3,5-(trinitrobenzene)
TNT



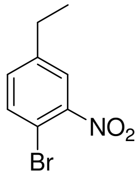
2-Methyl-3-propyl**aniline**
(2-methyl-3-propylbenzenamine)

The base name of the benzene derivative determines the carbon at which numbering begins: anisole has its methoxy group at C-1, toluene its methyl group at C-1, and aniline its amino group at C-1 (refer to Table 1.1).
The direction of numbering is chosen to give the next substituted position its lowest number irrespective of what substituent it bears.
The order of appearance of substituents in the name is alphabetical.

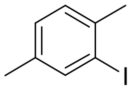
When no other base name than benzene is appropriate, positions are numbered to give the lowest locant to the first point of difference.



1-Fluoro-2,4-dinitrobenzene

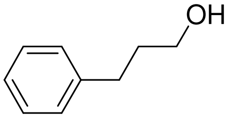


1-Bromo-4-ethyl-2-nitrobenzene

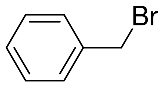


2-Iodo-1,4-dimethylbenzene

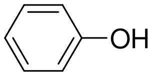
When the benzene ring is named as a substituent, the word phenyl is used. It stands for C_6H_5—. An arene named as a substituent is called an aryl group. A benzyl group is $C_6H_5CH_2$—.



3-phenylpropan-1-ol



Benzyl bromide



phenol

11.9 Physical Properties of Arenes

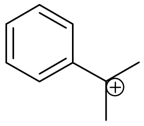
Arenes (aromatic hydrocarbons) resemble other hydrocarbons. They are:
- nonpolar
- insoluble in water
- less dense than water
- intermolecular forces are weak and limited to van der Waals attractions

11.10 Reactions of Arenes: A Preview

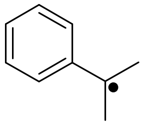
1. Some reactions involve the ring.
   a) Reduction
      Catalytic hydrogenation (Section 11.3) *do not need to know*
      Birch reduction (Section 11.10) *do not need to know*
   b) Electrophilic aromatic substitution (Chapter 12)
   c) Nucleophilic aromatic substitution (Chapter 12)

2. In other reactions the ring is a substituent. (Sections 11.11-11.16)

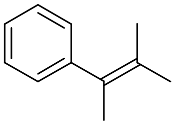
The benzylic carbon is analogous to allylic carbon.



Benzylic carbocation



Benzylic Radical



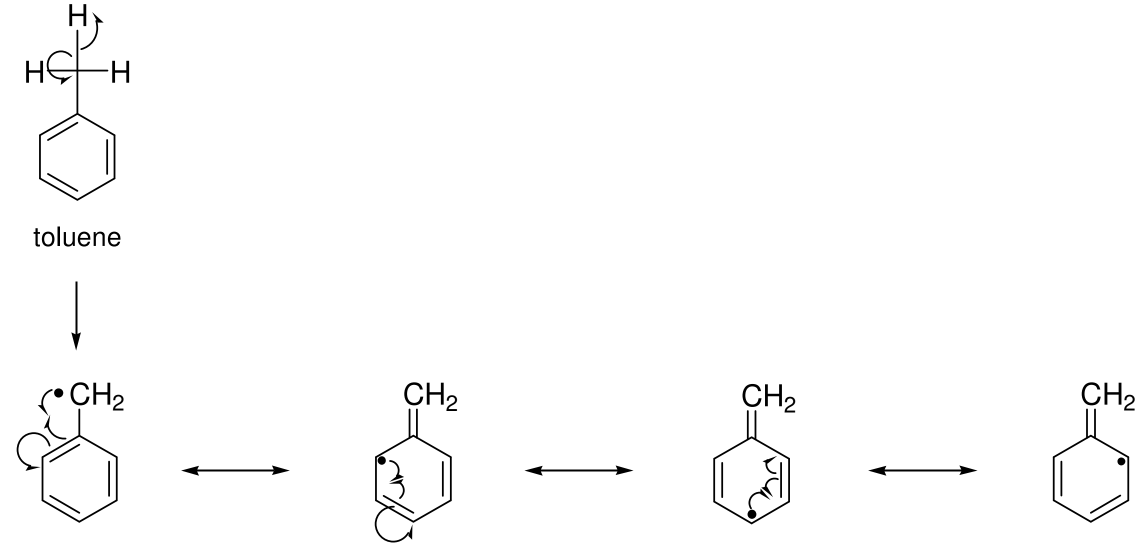
Alkenylbenzene

11.12 Free-Radical Halogenation of Alkylbenzenes

The benzylic position in alkylbenzenes is analogous to the allylic position in alkenes. Thus a benzylic C—H bond (like an allylic one) is weaker than a C—H bond of an alkane.

Electron delocalization stabilizes benzyl radical and weakens the benzylic C—H bond.

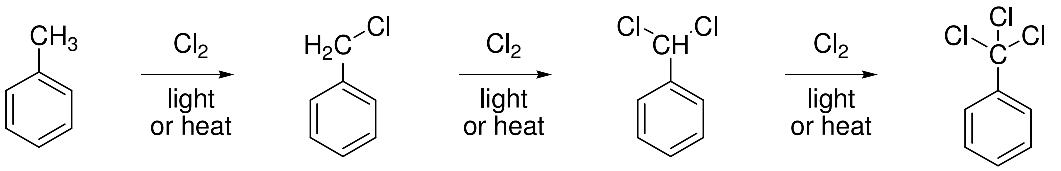
The unpaired electron in benzyl radical is shared due to delocalization of the unpaired electron.



toluene

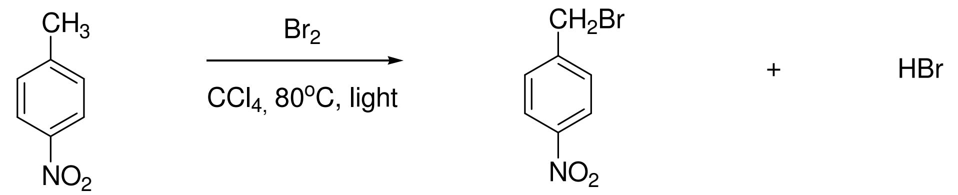
benzyl radical

The **free-radical chlorination of toluene** is a industrial process highly regioselective for the benzylic position. Similarly, dichlorination and trichlorination are also selective for the benzylic carbon.
The propagation steps in the formation of benzyl chloride involve benzyl radical as an intermediate.



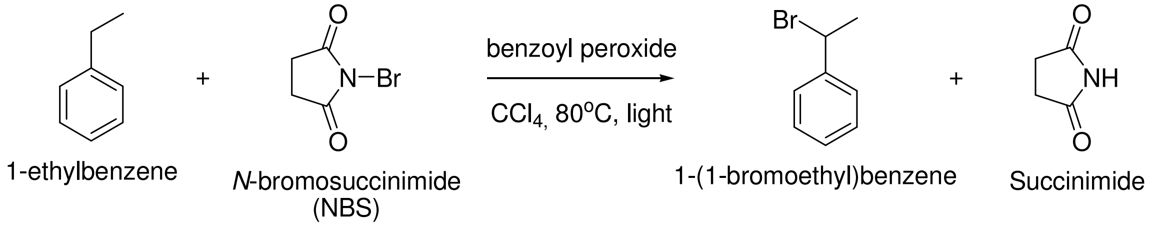
toluene benzyl chloride (dichloromethyl)benzene (trichloromethyl)benzene

Benzylic bromination is used in the laboratory to introduce a halogen at the benzylic position. It is also carried out under conditions of photochemical initiation.



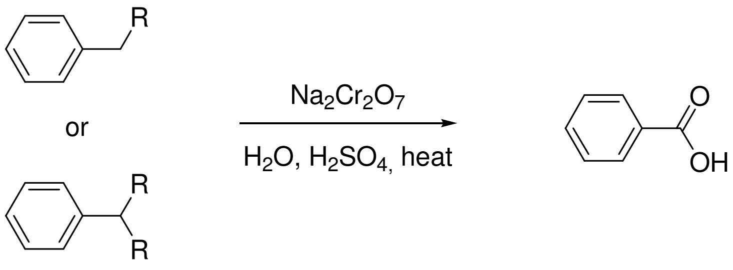
p-nitrotoluene *p*-nitrobenzylbromide

N-Bromosuccinimide (NBS) is also a convenient reagent for benzylic bromination.

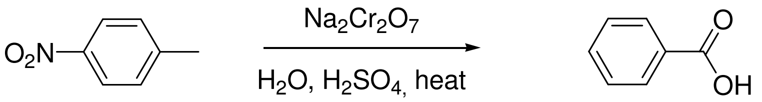


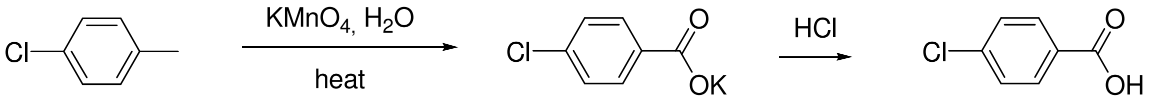
11.13 Oxidation of Alkylbenzenes

Alkyl side chain on a benzene ring is oxidized when heated with chromic acid ($Na_2Cr_2O_7$). The oxidizing agent Potassium permanganate ($KMnO_4$) reacts similarly.



R = Alkyl substituents

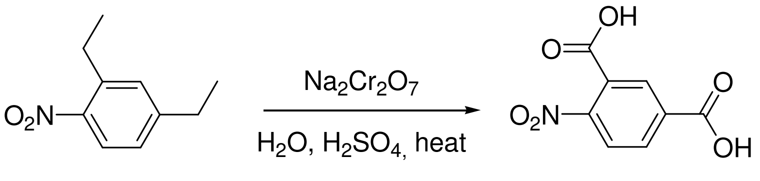


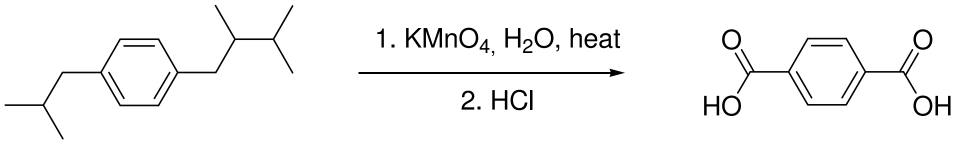


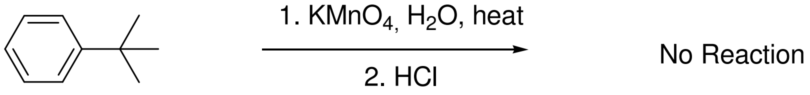
When two alkyl groups are present on the ring, both are oxidized.

An alkyl group, regardless of its chain length, is converted to a carboxylic group (—CO_2H) attached directly to the ring.

A trisubstituted carbon substituent (—CR_3) attached to the ring does not undergo oxididation under these conditions, because it lacks benzylic hydrogens.





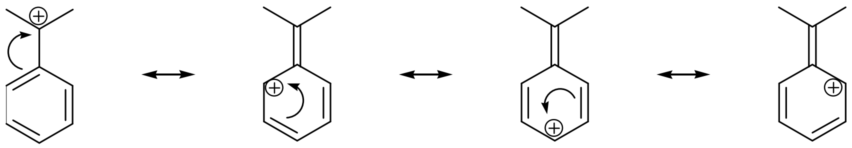


11.14 S_N1 Reactions of Benzylic Halides

Benzylic halides undergo nucleophilic substitution faster than simple alkyl halide.

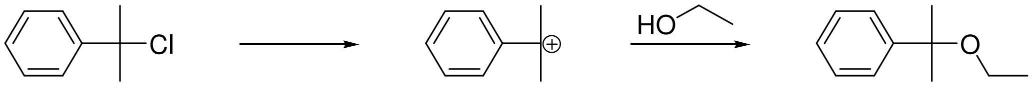
A phenyl substituent stabilizes a carbocation more than a methyl group.

Resonance structures indicate the positive charge is shared by the benzylic carbon and the ring carbons ortho and para to it.



Dispersal of the charge does not result in nucleophilic attack at more than one carbon. There is no "benzylic rearrangement" analogous to allylic rearrangement. Substitution does not occur on the ring.

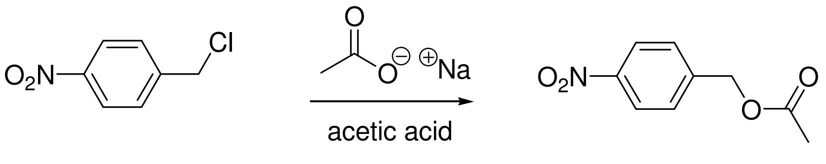
When conditions are chosen to favour S_N1 substitution over E2 elimination (solvolysis, weakly basic nucleophile), benzylic halides give a single substitution product (only one possible product).



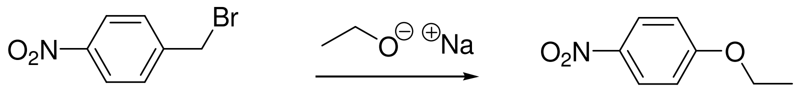
11.14 S_N2 Reactions of Benzylic Halides

Like allylic halide, substitution is faster than a normal primary halide.

Primary benzylic halides are ideal substrates for S_N2 reactions. In addition to being very reactive, they are unable to undergo competing E2 elimination.

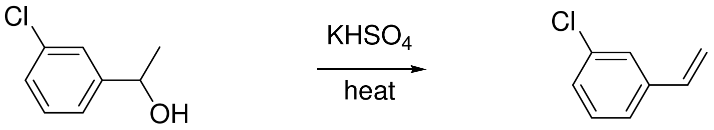


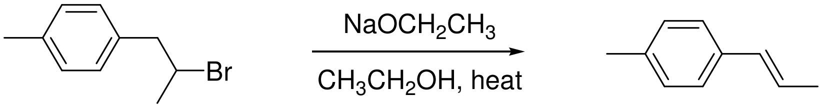
Benzylic halides that are secondary resemble secondary alkyl halides in that they undergo substitution only when the nucleophile is weakly basic. If the nucleophile is a strong base such as sodium ethoxide, elimination by the E2 mechanism is faster than substitution.



11.16 Preparation of Alkenylbenzenes

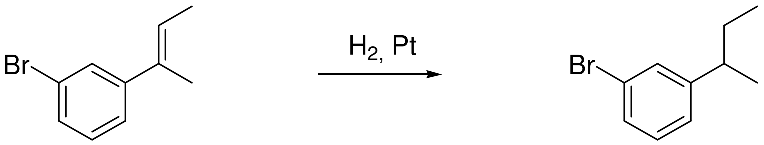
Acid-catalysed dehydration of benzylic alcohols is a useful route to alkenylbenzenes.
So too is dehydrohalogenation under E2 conditions.

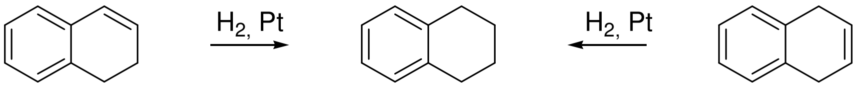




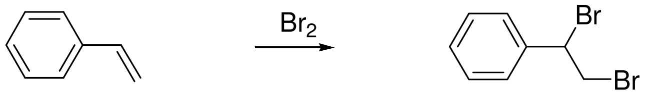
11.17 Addition Reactions of Alkenylbenzenes

Hydrogenation of the side-chain double bond of an alkenylbenzene is much easier than hydrogenation of the aromatic ring and leaves the ring unaffected.

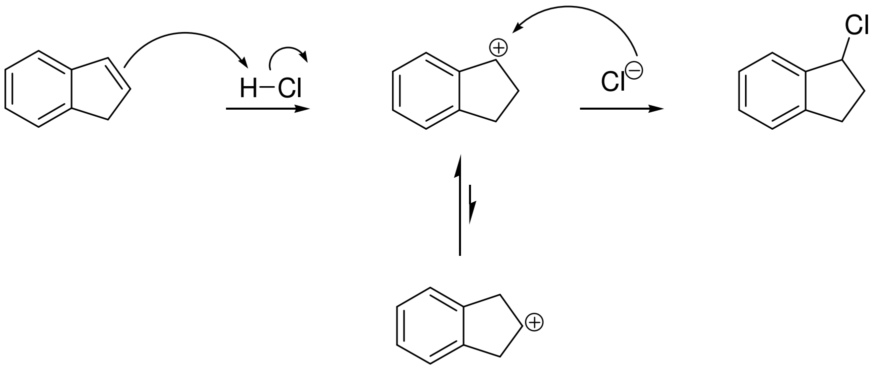




Addition reactions to the double bond are typical of alkenes when treated with electrophilic reagents.



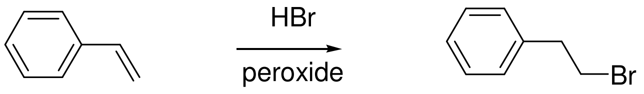
The regioselectivity of the electrophilic addition is governed by the ability of an aromatic ring to stabilize an adjacent carbocation. Only a single chloride is formed.



Only the benzylic chloride is formed because protonation of the double bond occurs in the direction tha gives a carbocation that is both secondary and benzylic.

Protonation in the opposite direction also gives a secondary carbocation, but this carbocation is not benzylic.

In the presence of peroxides, hydrogen bromide adds to the double bond of styrene with a regioselectivity opposite to Markov's rule. The reaction is a free-radical addition, and the regiochemistry is governed prefential formation of the more stable radical.



11.20 Hückel's Rule:

The additional factor that influences aromaticity is the number of π electrons.

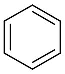
Rule: Among planar, monocyclic, **completely conjugated polyenes**, only those with $4n + 2$ π electrons possess special stability (are aromatic).

Hydrocarbons with $(4n + 2) = 2, 6, 10, 14 \ldots$ π electrons will be aromatic.

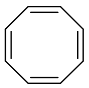
Hydrocarbons with $(4n) = 4, 8, 12, 16 \ldots$ π electrons will be antiaromatic.

Each double bond contributes two π electrons (é).
A negatively charged carbon contributes two π electrons (é).
A positively charged carbon contributes none.

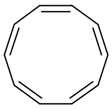
4 π é
anti-aromatic



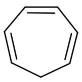
6 π é
aromatic



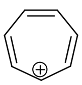
8 π é
anti-aromatic



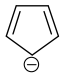
10 π é
aromatic



non-aromatic
lacks cyclic conjugation

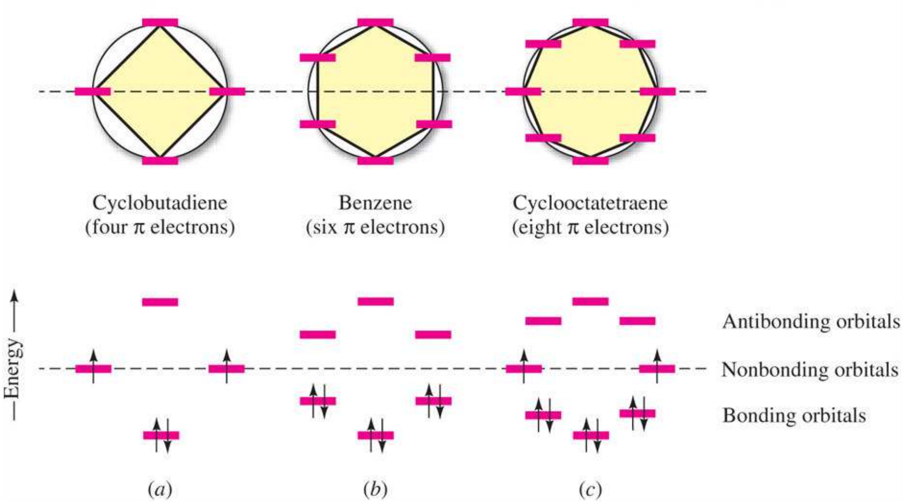


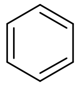
6 π é
aromatic



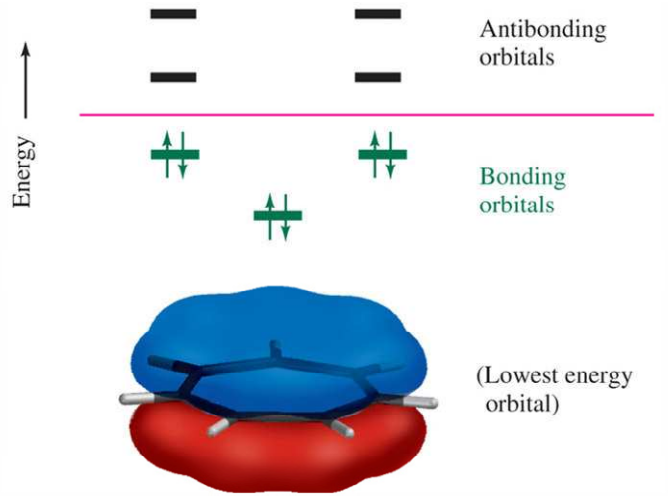
6 π é
aromatic

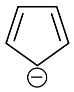
Frost Circle:



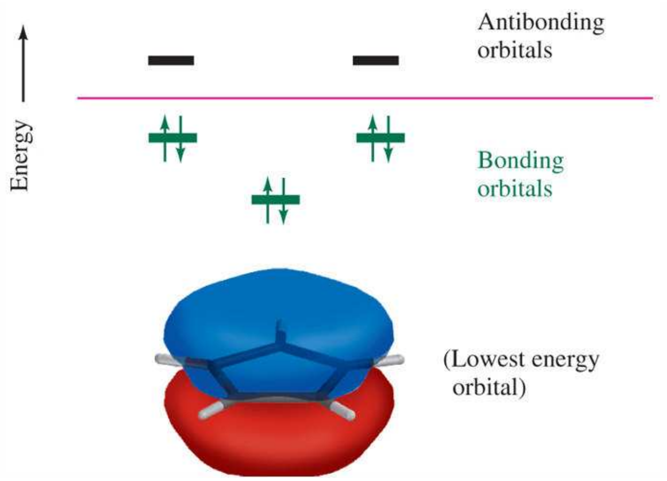


6 π é
aromatic





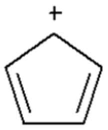
6 π é
aromatic



Extra Problems

1. How many isomeric tribromobenzenes are possible?
   A) one B) two C) three D) four

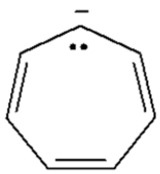
2. Which of the following ions are aromatic species?



I

II

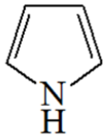
III



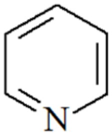
IV

   A) I and III B) II and III C) II and IV D) III and IV

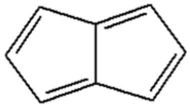
3. Identify the aromatic compounds.



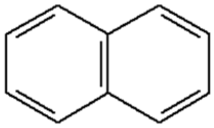
I



II



III



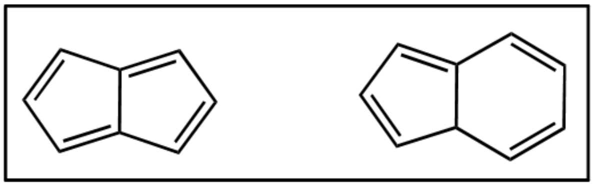
IV

   A) I and II B) III and IV C) I, II, and IV D) all of them

4. Which of the following reacts at the fastest rate when heated with N-bromosuccinimide (NBS) and benzoyl peroxide in carbon tetrachloride at 80oC?
   A) toluene
   B) ethylbenzene
   C) isopropylbenzene (cumene)
   D) *tert*-butylbenzene

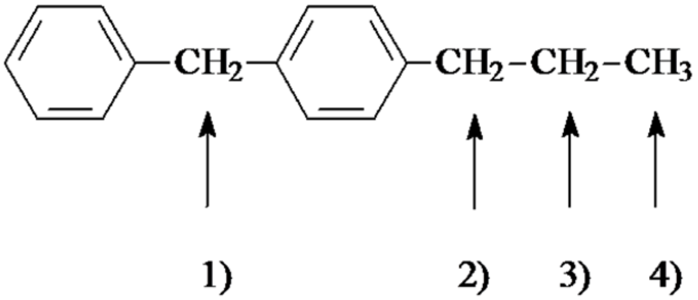
5. Side chain oxidations of alkylbenzenes with $Na_2Cr_2O_7$ and H_2SO_4/H_2O will not work if the alkyl side chain has
   A) only one carbon.
   B) four or more carbons.
   C) benzylic hydrogens.
   D) no benzylic hydrogens.

6. From left to right, these two compounds are



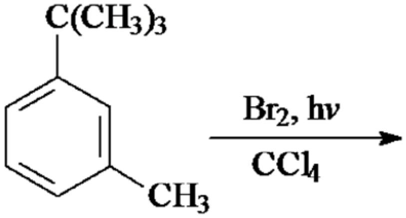
   A) aromatic and antiaromatic
   B) antiaromatic and non-aromatic
   C) antiaromatic and aromatic
   D) both are antiaromatic

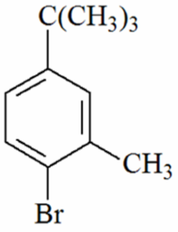
7. Which hydrogen atom would be most easily extracted by a bromine atom?



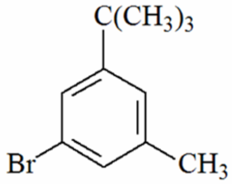
A) 1 B) 2 C) 3 D) 4

8. What is the product of the reaction shown below?

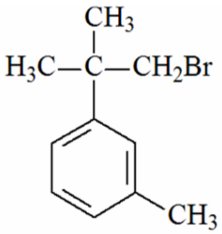




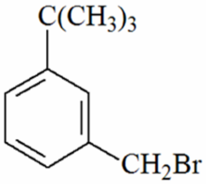
I.



II.



III.



IV.

A) I B) II C) III D) IV

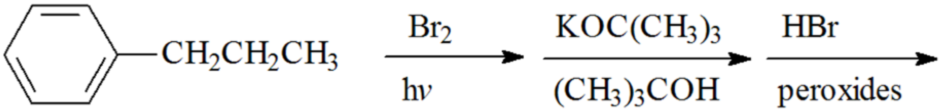
9. A compound X, C_8H_{10}, is oxidized to benzoic acid with potassium dichromate, $K_2Cr_2O_7$, in sulfuric acid. What is compound X?
A) *para*-xylene B) propylbenzene C) styrene D) ethylbenzene

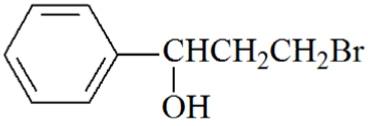
10. Acid-catalyzed dehydration of *cis*-2-phenylcyclopentanol gives

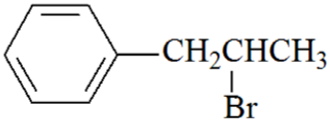
A) 1-phenylcyclopentene.	C) 4-phenylcyclopentene.
B) phenylcyclopentane.	D) 1-phenylcyclopentanol.

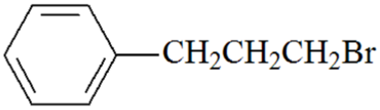
11. How many isomeric tetrachlorobenzenes are there?
A) two B) three C) four D) five

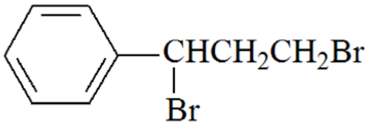
12. Propylbenzene is subjected to the sequence of reactions below. What is the final product?



A) 

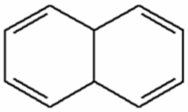
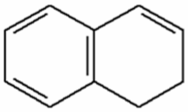
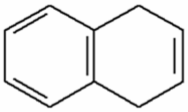
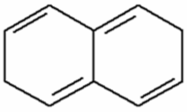
B) 

C) 

D) 

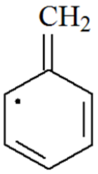
A) A B) B C) C D) D

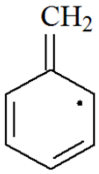
13. Which of the following has the lowest heat of reaction on catalytic hydrogenation? (4 moles of H_2 per mole of hydrocarbon)

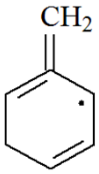
A) 
B) 
C) 
D) 

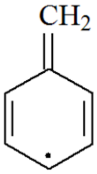
A) A B) B C) C D) D

14. Which one of following is <u>not</u> a resonance form of the benzyl free radical?

A) 

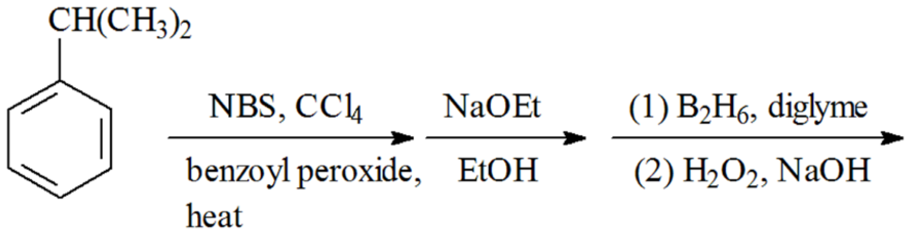
B) 

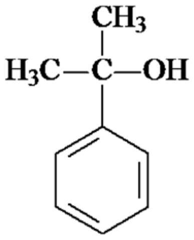
C) 

D) 

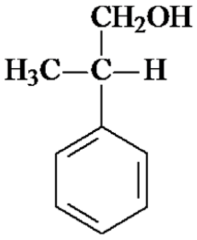
A) A B) B C) C D) D

15. Which of the following is the product from the reaction sequence shown below?

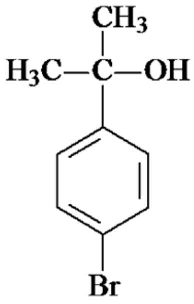




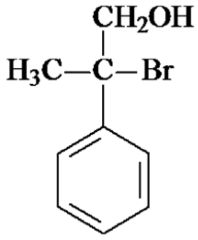
I



II



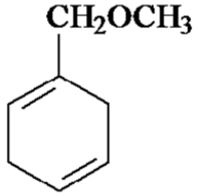
III



IV

A) I B) II C) III D) IV

16. Starting with toluene, which sequence of reactions below works best to prepare the following cyclohexadiene compound?



A) toluene $\xrightarrow[\text{CH}_3\text{OH}]{\text{Na, NH}_3}$ $\xrightarrow[\text{CCl}_4]{\text{NBS, heat}}$ $\xrightarrow[\text{CH}_3\text{OH}]{\text{NaOCH}_3}$

B) toluene $\xrightarrow[\text{CCl}_4]{\text{NBS, heat}}$ $\xrightarrow[\text{CH}_3\text{OH}]{\text{NaOCH}_3}$ $\xrightarrow[\text{CH}_3\text{OH}]{\text{Na, NH}_3}$

C) toluene $\xrightarrow[\text{CH}_3\text{OH}]{\text{NaOCH}_3}$ $\xrightarrow[\text{CH}_3\text{OH}]{\text{Na, NH}_3}$ $\xrightarrow[\text{CCl}_4]{\text{NBS, heat}}$

D) all the above would be good syntheses

A) A B) B C) C D) D

Answers: 1)C 2)B 3)C 4)C 5)D 6)B 7)A 8)D 9)D 10)A 11)B 12)B 13)B 14)C 15)B 16)B

Chapter 12:
Reactions of Arenes:
Electrophilic and Nucleophilic Aromatic Substitution

This chapter examines aromatic ring as a functional group.

The reagents that react with the aromatic ring of benzene and its derivatives are electrophiles.

When electrophiles reacted with alkenes, an addition reaction is observed.
When electrophiles react with the aromatic ring of benzene and its derivatives (arenes), a substitution reaction is observed.

Arenes have the general formula ArH, where Ar stands for the aryl group.

$$\underset{\text{Arene}}{\text{Ar—H}} \quad + \quad \underset{\text{Electrophilic Reagent}}{\text{E—Y}} \longrightarrow \underset{\text{Product of electrophilic aromatic substitution}}{\text{Ar—H} \quad + \quad \text{E—Y}}$$

12.1 Representative Electrophilic Aromatic Substitution Reactions of Benzene

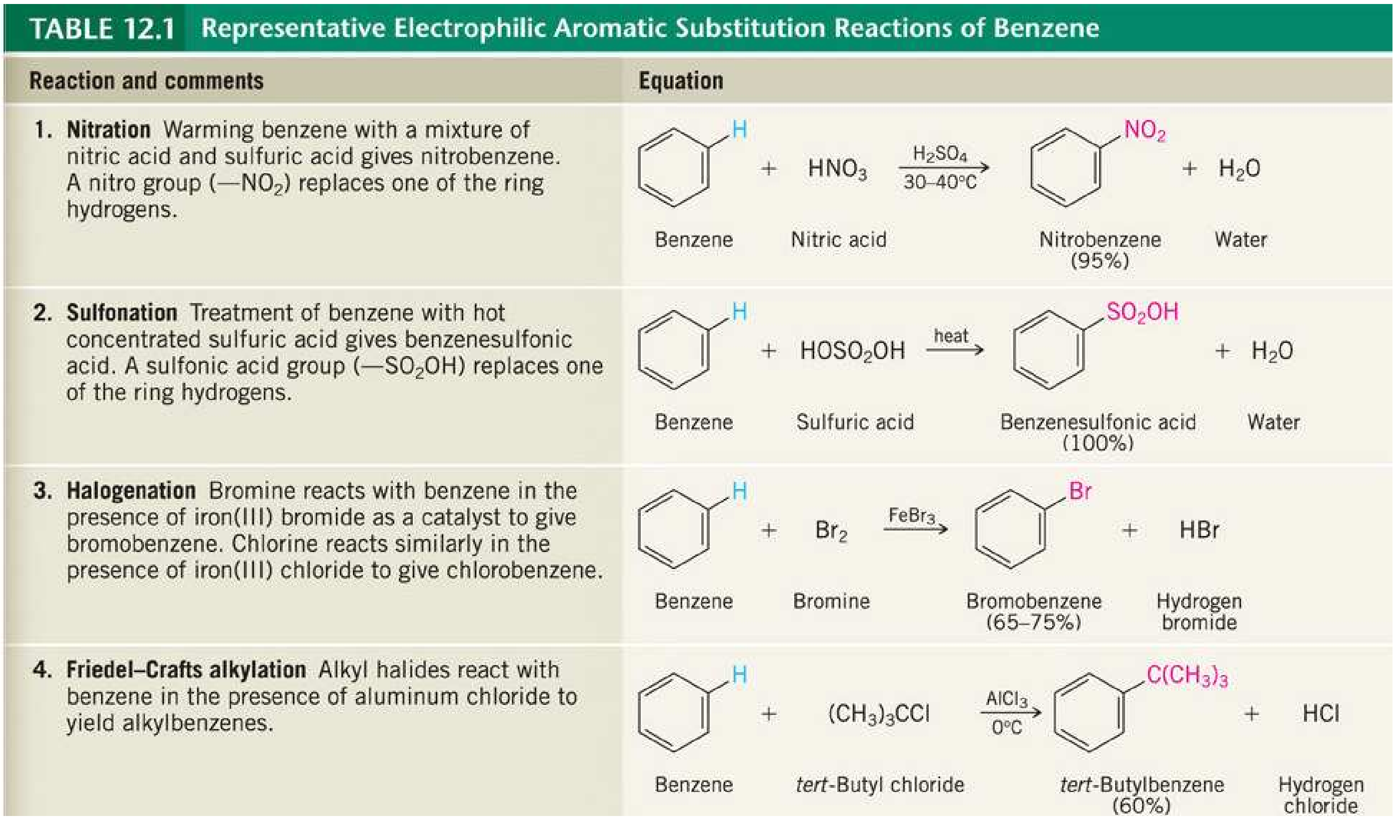


TABLE 12.1 Representative Electrophilic Aromatic Substitution Reactions of Benzene

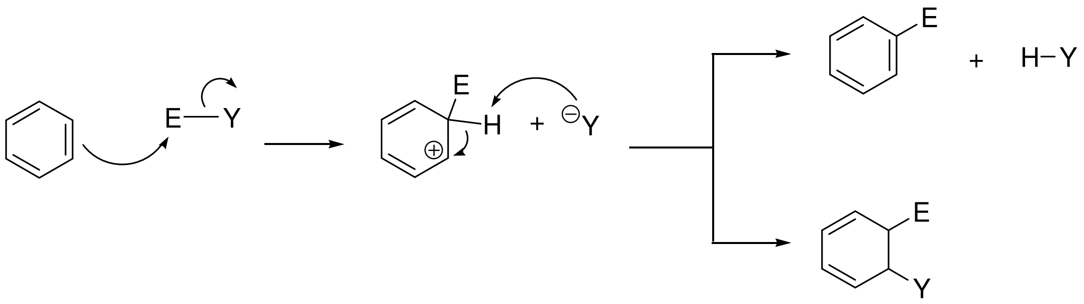
Reaction and comments	Equation
1. **Nitration** Warming benzene with a mixture of nitric acid and sulfuric acid gives nitrobenzene. A nitro group (—NO_2) replaces one of the ring hydrogens.	Benzene (H) + HNO_3 (Nitric acid) $\xrightarrow[30\text{–}40°C]{H_2SO_4}$ Nitrobenzene (NO_2) (95%) + H_2O (Water)
2. **Sulfonation** Treatment of benzene with hot concentrated sulfuric acid gives benzenesulfonic acid. A sulfonic acid group (—SO_2OH) replaces one of the ring hydrogens.	Benzene (H) + $HOSO_2OH$ (Sulfuric acid) $\xrightarrow{heat}$ Benzenesulfonic acid (SO_2OH) (100%) + H_2O (Water)
3. **Halogenation** Bromine reacts with benzene in the presence of iron(III) bromide as a catalyst to give bromobenzene. Chlorine reacts similarly in the presence of iron(III) chloride to give chlorobenzene.	Benzene (H) + Br_2 (Bromine) $\xrightarrow{FeBr_3}$ Bromobenzene (Br) (65–75%) + HBr (Hydrogen bromide)
4. **Friedel–Crafts alkylation** Alkyl halides react with benzene in the presence of aluminum chloride to yield alkylbenzenes.	Benzene (H) + $(CH_3)_3CCl$ (*tert*-Butyl chloride) $\xrightarrow[0°C]{AlCl_3}$ *tert*-Butylbenzene ($C(CH_3)_3$) (60%) + HCl (Hydrogen chloride)

12.2 Mechanistic Principles of Electrophilic Aromatic Substitution

In the first step, an electrophile accepts an electron pair from the π system of benzene to form a carbocation (an arenium ion).

Once formed, the cyclohexadienyl cation rapidly loses a proton, restoring the aromaticity of the ring. The product of electrophilic aromatic substitution is then obtained.

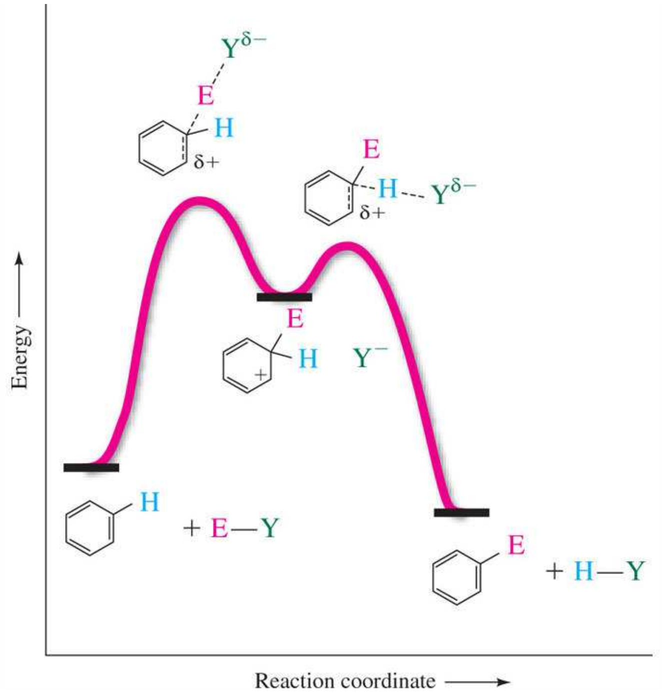
Product of electrophilic aromatic substitution



Not aromatic: NOT FORMED

Substitution occurs preferentially because there is a substantial driving force favoring rearomatization.

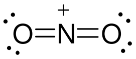
Many of the electrophilic reagents that react rapidly with alkenes do not react at all with benzene. Others react only in the presence of catalysts that increase their electrophilicity.



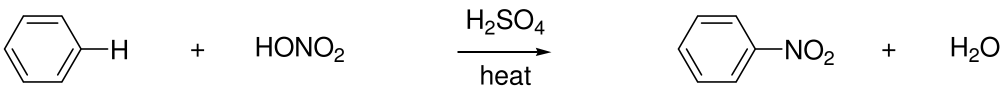
Your role as a future awesome chemist is to identify the electrophile in nitration, sulfonation, halogenation, Friedel-Crafts alkylation and Friedel-Crafts acylation. According to the mechanism, you can predict the major product formed.

12.3 Nitration of Benzene

The Electrophile (E^+) in this reaction is the nitronium ion:



$O=\overset{+}{N}=O$

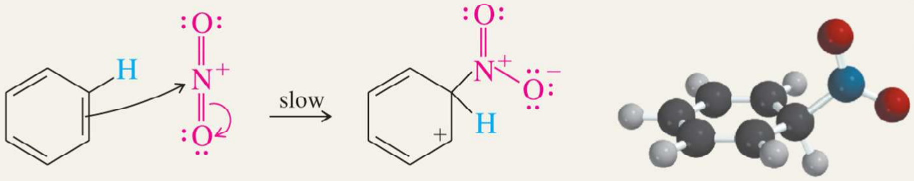


Nitric acid **Nitrobenzene**

Mechanism 12.1

Nitration of Benzene

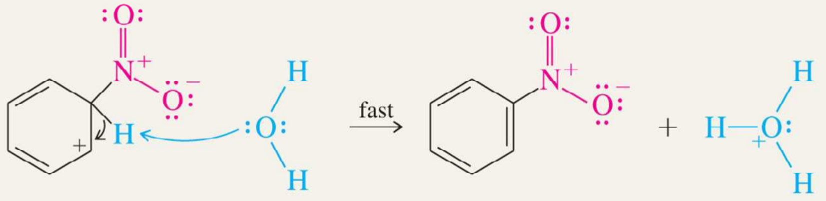
Step 1: Reaction of nitronium cation with the π system of the aromatic ring. (The molecular model depicts the cyclohexadienyl cation intermediate.)



Benzene and nitronium ion

Cyclohexadienyl cation intermediate

Step 2: Loss of a proton from the cyclohexadienyl cation.



Cyclohexadienyl cation intermediate

Water

Nitrobenzene

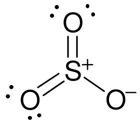
Hydronium ion

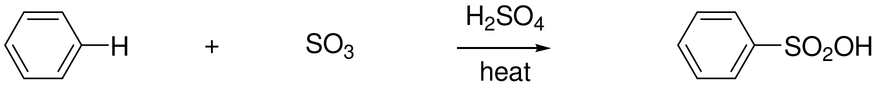
In the first step: Formation of the cation intermediate.

In the second step: Aromaticity of the ring is restored.

12.4 Sulfonation of Benzene

Several electrophiles are present, but the major one is sulfur trioxide:





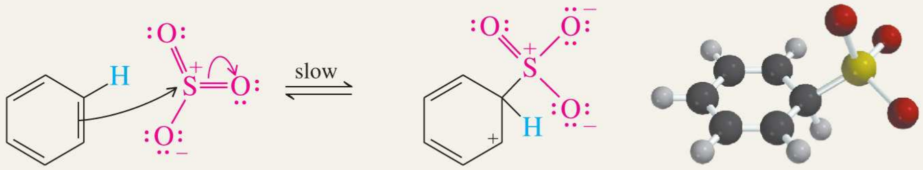
Sulfur trioxode

Benzenesulfonic acid

Mechanism 12.2

Sulfonation of Benzene

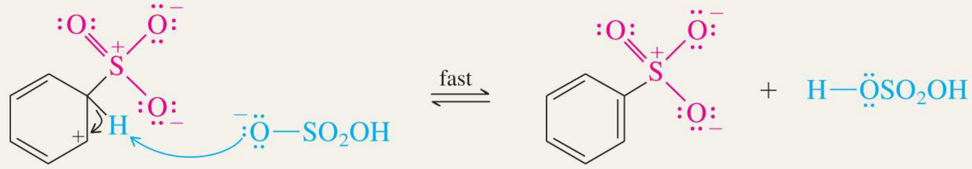
Step 1: Sulfur trioxide reacts with benzene in the rate-determining step. (The molecular model depicts the cyclohexadienyl cation intermediate.)



Benzene and sulfur trioxide

Cyclohexadienyl cation intermediate

Step 2: A proton is abstracted from the sp^3-hybridized carbon of the intermediate to restore the aromaticity of the ring. The species shown that abstracts the proton is a hydrogen sulfate ion formed by ionization of sulfuric acid.



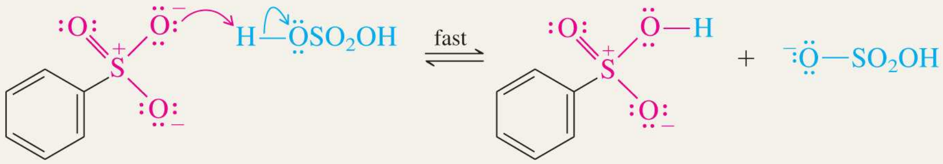
Cyclohexadienyl cation intermediate

Hydrogen sulfate ion

Benzenesulfonate ion

Sulfuric acid

Step 3: A rapid proton transfer from the oxygen of sulfuric acid to the oxygen of benzenesulfonate completes the process.



Benzenesulfonate ion

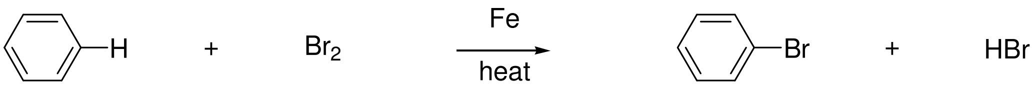
Sulfuric acid

Benzenesulfonic acid

Hydrogen sulfate ion

12.5 Halogenation of Benzene

Bromine is too weak to react with benzene, although it adds rapidly to alkenes. A catalyst is needed.



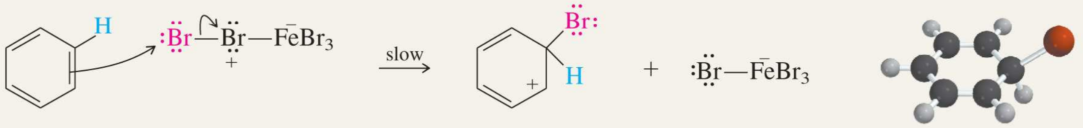
Bromine **Bromobenzene**

Iron (III) bromide, $FeBr_3$, is formed by the reaction of Iron with bromine. It is a weak Lewis acid that combines with bromine furthermore to form a Lewis acid/Lewis base complex that makes bromine more electrophilic.

Mechanism 12.3

Bromination of Benzene

Step 1: The bromine–iron(III) bromide complex is the active electrophile that reacts with benzene. Two of the π electrons of benzene are used to form a bond to bromine and give a cyclohexadienyl cation intermediate. (The molecular model depicts the cyclohexadienyl cation intermediate.)

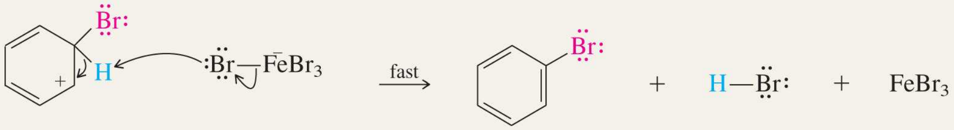


Benzene and bromine–iron(III) bromide complex

Cyclohexadienyl cation intermediate

Tetrabromoferrate ion

Step 2: Loss of a proton from the cyclohexadienyl cation yields bromobenzene.



Cyclohexadienyl cation intermediate

Tetrabromoferrate ion

Bromobenzene

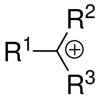
Hydrogen bromide

Iron(III) bromide

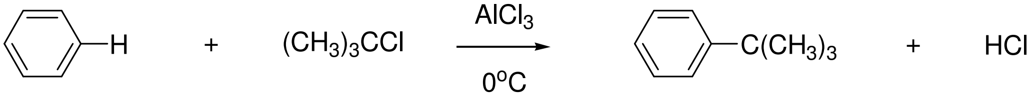
Chlorination is similar to the bromination of this type.

12.6 Friedel-Crafts Alkylation of Benzene

The electrophile in these reactions are carbocations:



Alkyl halides react with benzene in the presence of aluminium chloride to yield alkyl benzenes.



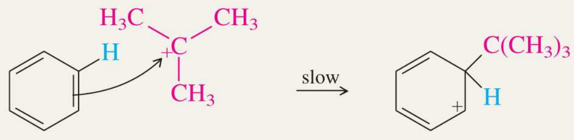
Alkyl halide **tert-Butylbenzene**

Alkyl halides alone are insufficiently electrophilic to react with benzene. Aluminium chloride serves as a Lewis acid catalyst to convert tertiary and secondary alkyl halides to carbocations, which then alkylate the aromatic ring. In other words, they act as a Lewis acid to promote ionization of the alkyl halide.

Mechanism 12.4

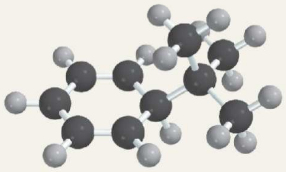
Friedel–Crafts Alkylation

Step 1: Once generated by the reaction of *tert*-butyl chloride and aluminum chloride, *tert*-butyl cation is attacked by the π electrons of benzene, and a carbon-carbon bond is formed. (The molecular model depicts the cyclohexadienyl cation intermediate.)

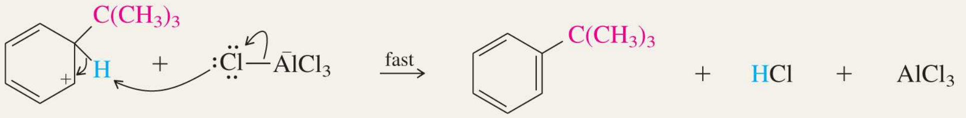


Benzene and *tert*-butyl cation

Cyclohexadienyl cation intermediate



Step 2: Loss of a proton from the cyclohexadienyl cation intermediate yields *tert*-butylbenzene.



Cyclohexadienyl cation intermediate

Tetrachloroaluminate ion

tert-Butylbenzene

Hydrogen chloride

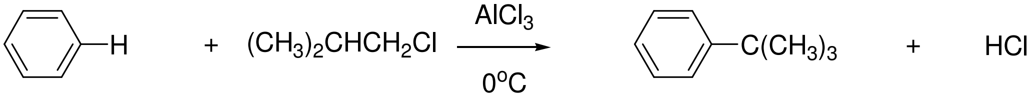
Aluminum chloride

First step: reaction with the carbocation
Second step: Aromatization

Tertiary and secondary alkyl halides react by the mechanism depicted above.
Methyl and ethyl halides do not form carbocations, but do alkylate benzene under Friedel-Crafts conditions.

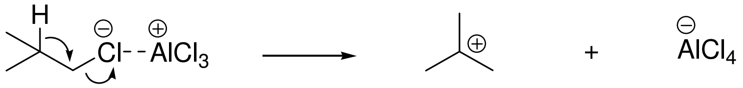
Rearrangements can occur, especially when primary alkyl halides are used.

Example of a rearrangements in the Friedel-Crafts alkylation of arenes:



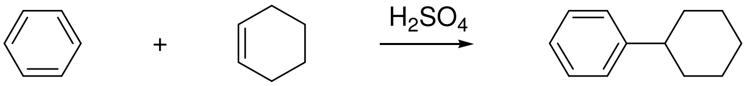
Isobutyl chloride **tert-Butylbenzene**

A hydride migration occurs:



Alkenes, which can be converted to carbocations by protonation, can be used to alkylate benzene.

Other example of Friedel-Crafts alkylation (without use of $AlCl_3$):



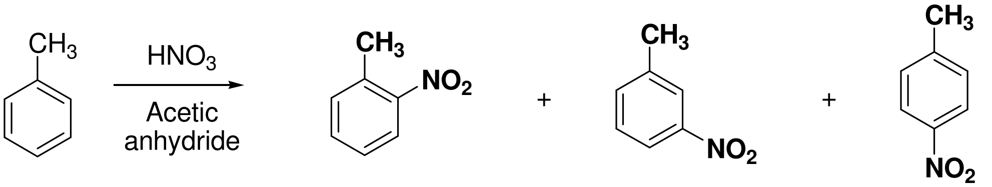
12.9 Rate and Regioselectivity in Electrophilic Aromatic Substitution

Substituents on an aromatic ring can influence both the **rate** and **regioselectivity** of electrophilic aromatic substitution (EAS).

Substituents are classified as **activating** or **deactivating** according to whether they cause electrophilic aromatic substitution to occur more rapidly or less rapidly than benzene.

With respect to regioselectivity, substituents are either ***ortho*****,** ***para*****-directing** or ***meta*****-directing**.

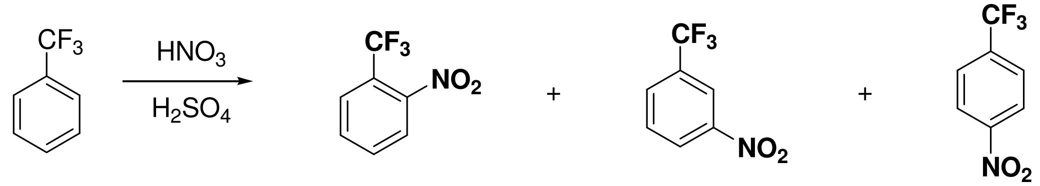
Three products are possible from nitration of toluene:



o-Nitrobenzene (63%) *m*-Nitrobenzene (3%) *p*-Nitrobenzene (34%)

Because substitution in toluene occurs primarily at positions *ortho* and *para* to methyl, we designate a methyl substituent as an *ortho*, *para*-director.

Three products are also possible from nitration of (trifluoromethyl)benzene :



o-Nitro(trifluoromethyl) benzene (6%)

m-Nitro(trifluoromethyl) benzene (91%)

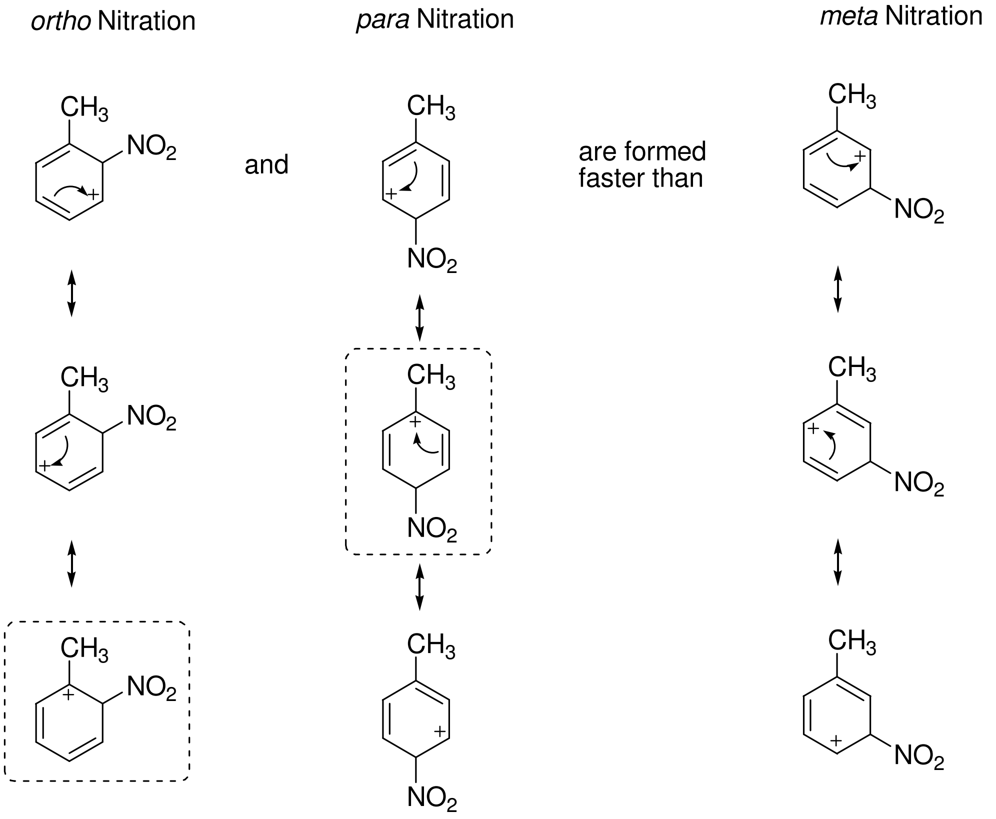
p-Nitro(trifluoromethyl) benzene (3%)

Because substitution in (trifluoromethyl)benzene occurs primarily at positions *meta* to trifluoromethyl, we designate a trifluoromethyl substituent as a *meta* -director.

12.10 Rate and Regioselectivity in the Nitration of Toluene

The carbocation stability controls the regioselectivity.

Carbocations that give *o*- and *p*-nitrotoluene are more stable (hence formed faster) than the one that gives *m*-nitrotoluene.



Resonance contributes to a tertiary carbocation

Resonance **does not** contribute to a tertiary carbocation

Interpretation of the Nitration of Toluene:

- The rate-determining intermediates for *ortho* and *para* nitration each have a resonance form that is a tertiary carbocation. All of the resonance forms for the rate-determining intermediate in *meta* nitration are secondary carbocations.

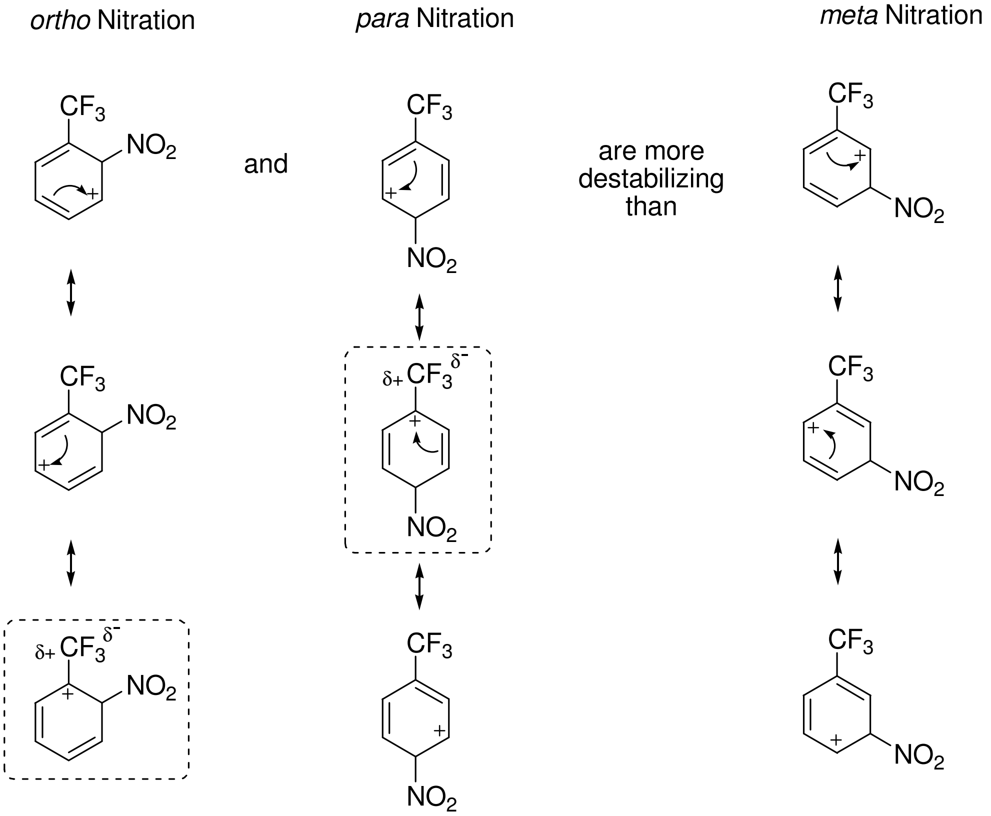
- Tertiary carbocations, being more stable, are formed faster than secondary ones. Therefore, the intermediates for attack at the *ortho* and *para* positions are formed faster than the intermediate for attack at the *meta* position. This explains why the major products are *o*- and *p*-nitrotoluene.

A methyl group is an activating substituent because it stabilizes the carbocation intermediate formed in the rate-determining step more than hydrogen does.

Methyl and other alkyl groups are referred to as **electron-donating (or electron-releasing) groups**, and activates all the available ring carbons toward electrophilic substitution (*ortho* and *para* more than *meta*).

12.11 Rate and Regioselectivity in the Nitration of (Trifluoromethyl)benzene

Because F is so electronegative, the carbon of a CF_3 group bears a partial positive charge. CF_3 is a powerful **electron-withdrawing group**. It destabilizes a carbocation. In other words, it is not favorable to have a carbocation next to the carbon bearing a partial positive charge.



Positive charge on carbon bearing CF_3 group = unstable

No destabilizing resonance form

Interpretation of the nitration of (Trifluoromethyl)benzene:

The rate-determining intermediates for *ortho* and *para* nitration each have a resonance form in which the positive charge is on a carbon that bears a CF_3 group. Such a resonance structure is strongly destabilized. The intermediate in *meta* nitration avoids such a structure. It is the least unstable of three unstable intermediates and is the one from which most of the product is formed.

12.12 Substituent Effects in Electrophilic Aromatic Substitution: Activating Substituents

Generalizations:

1. All **activating substituents are *ortho-para* directors**.
2. Halogen substituents are slightly deactivating, but *ortho-para* directing.
3. Strongly deactivating substituents are *meta* directors.

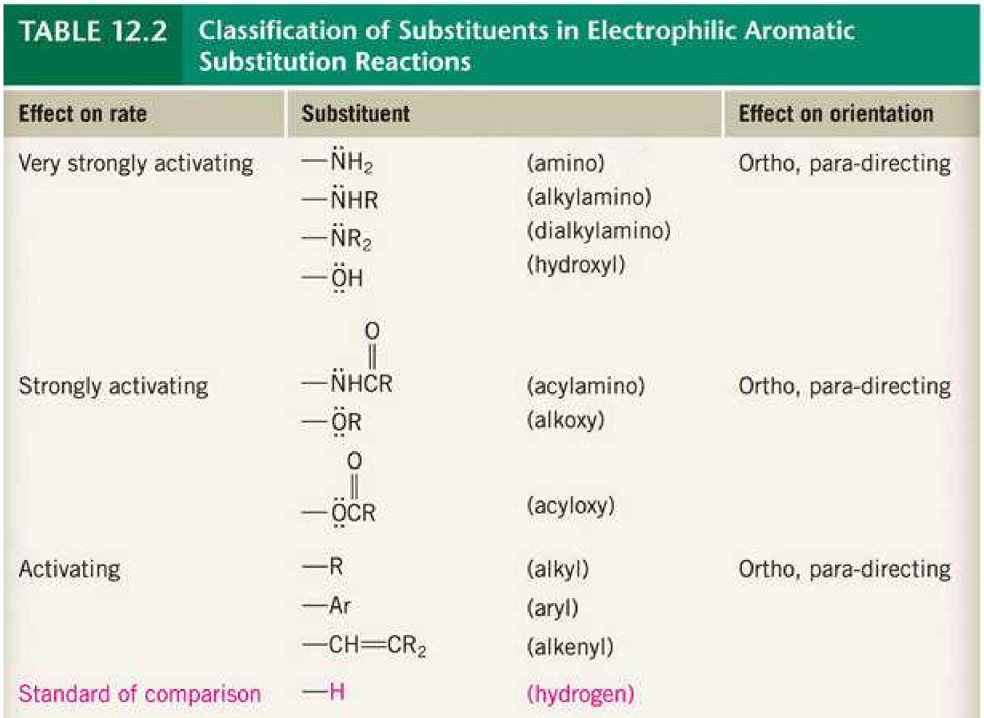
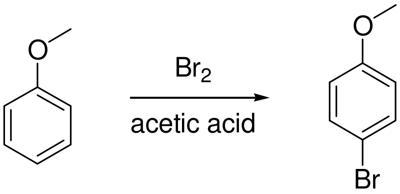


TABLE 12.2 **Classification of Substituents in Electrophilic Aromatic Substitution Reactions**

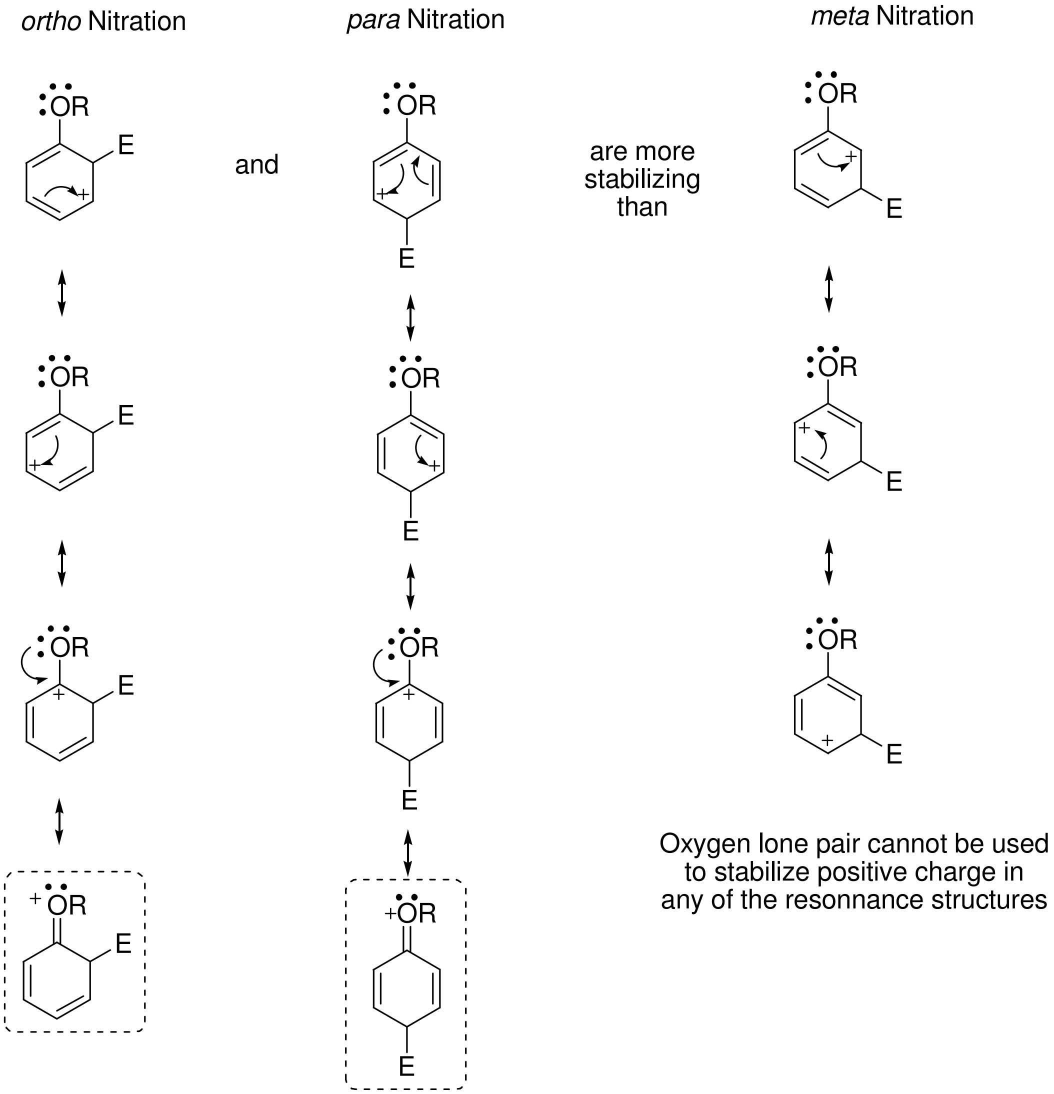
Effect on rate	Substituent		Effect on orientation
Very strongly activating	$-\ddot{N}H_2$	(amino)	Ortho, para-directing
	$-\ddot{N}HR$	(alkylamino)	
	$-\ddot{N}R_2$	(dialkylamino)	
	$-\ddot{\underset{\cdot\cdot}{O}}H$	(hydroxyl)	
Strongly activating	$-\ddot{N}H\overset{\overset{O}{\|}}{C}R$	(acylamino)	Ortho, para-directing
	$-\ddot{\underset{\cdot\cdot}{O}}R$	(alkoxy)	
	$-\ddot{\underset{\cdot\cdot}{O}}\overset{\overset{O}{\|}}{C}R$	(acyloxy)	
Activating	$-R$	(alkyl)	Ortho, para-directing
	$-Ar$	(aryl)	
	$-CH{=}CR_2$	(alkenyl)	
Standard of comparison	$-H$	(hydrogen)	

Hydroxyl, alkoxyl and acyloxy groups activate the ring to such an extent that bromination occurs rapidly even in the absence of a catalyst.

For example, the bromination of Anisole does not require $FeBr_3$ as catalyst:



Electron-donating groups with a lone pair on the atom directly attached to the ring are *ortho-para* directing and strongly activating.



Oxygen lone pair cannot be used to stabilize positive charge in any of the resonnance structures

Oxygen lone pair participates in the most stable resonance contributor

Nitrogen-containing substituents related to the amino group are even better electron-releasing groups and more strongly activating than the corresponding oxygen-containing substituents.

12.13 Substituent Effects in Electrophilic Aromatic Substitution: Strongly Deactivating Substituents

Electron-withdrawing Groups (EWG) destabilize intermediates for *ortho* and *para* substitution.

Deactivating substituents **are *meta* directors**.

Many EWG have a carbonyl group attached directly to the ring.

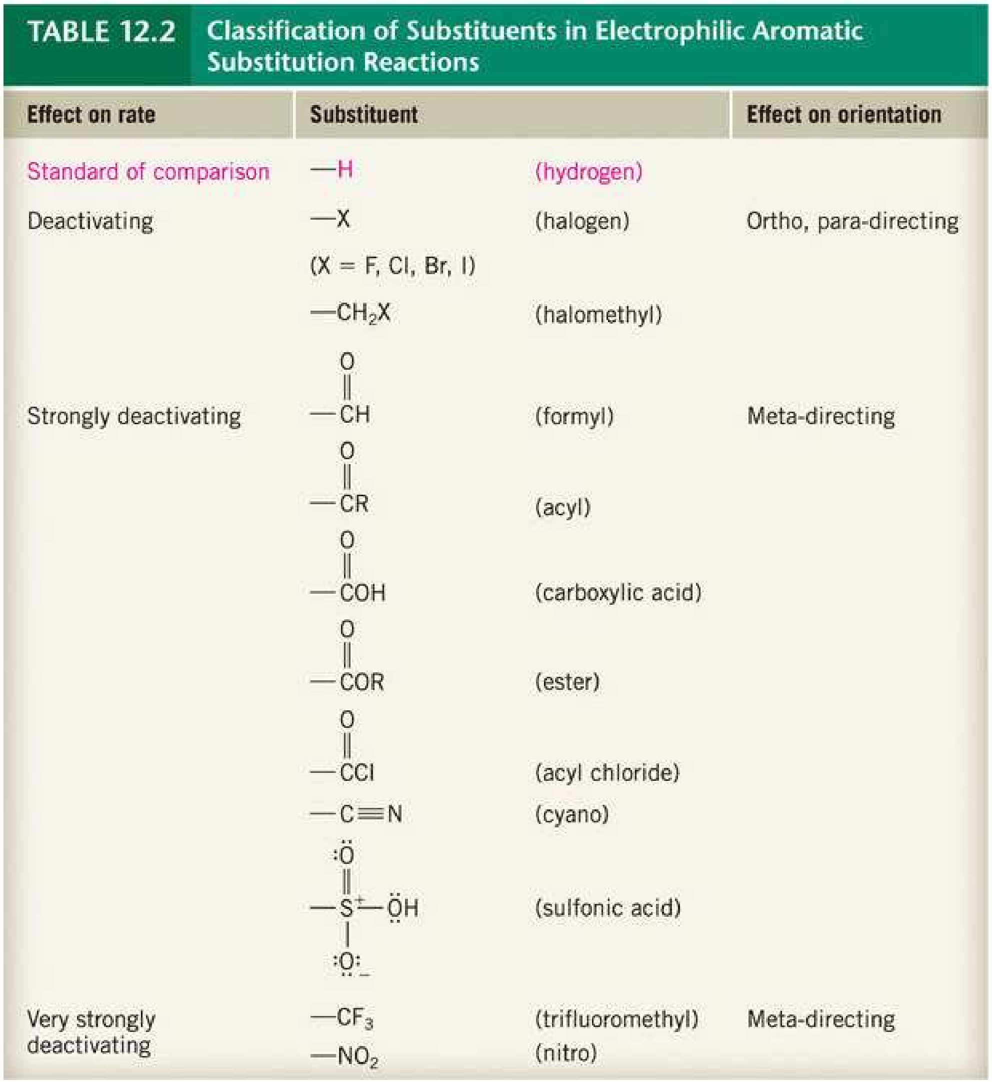


TABLE 12.2 Classification of Substituents in Electrophilic Aromatic Substitution Reactions

Effect on rate	Substituent		Effect on orientation
Standard of comparison	$-\mathrm{H}$	(hydrogen)	
Deactivating	$-\mathrm{X}$	(halogen)	Ortho, para-directing
	(X = F, Cl, Br, I)		
	$-\mathrm{CH_2X}$	(halomethyl)	
Strongly deactivating	$-\overset{\overset{\mathrm{O}}{\Vert}}{\mathrm{C}}\mathrm{H}$	(formyl)	Meta-directing
	$-\overset{\overset{\mathrm{O}}{\Vert}}{\mathrm{C}}\mathrm{R}$	(acyl)	
	$-\overset{\overset{\mathrm{O}}{\Vert}}{\mathrm{C}}\mathrm{OH}$	(carboxylic acid)	
	$-\overset{\overset{\mathrm{O}}{\Vert}}{\mathrm{C}}\mathrm{OR}$	(ester)	
	$-\overset{\overset{\mathrm{O}}{\Vert}}{\mathrm{C}}\mathrm{Cl}$	(acyl chloride)	
	$-\mathrm{C}\equiv\mathrm{N}$	(cyano)	
	$-\underset{\underset{:\ddot{\mathrm{O}}:^{-}}{\vert}}{\overset{\overset{:\ddot{\mathrm{O}}}{\Vert}}{\mathrm{S}^{+}}}-\ddot{\mathrm{O}}\mathrm{H}$	(sulfonic acid)	
Very strongly deactivating	$-\mathrm{CF_3}$	(trifluoromethyl)	Meta-directing
	$-\mathrm{NO_2}$	(nitro)	

Electron-Withdrawing groups behave in the same way as the trifluoromethyl group.

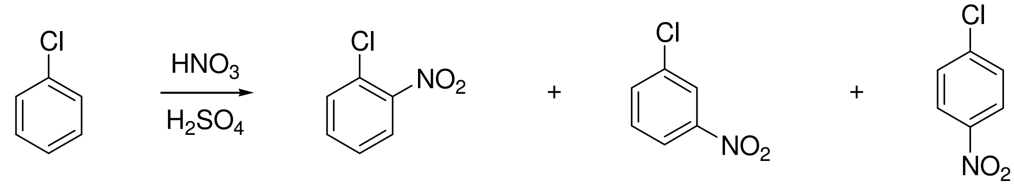
12.14 Substituent Effects in Electrophilic Aromatic Substitution: Halogens

F, Cl, Br, and I are ortho-para directing, but deactivating.

That means reaction is slower with an halogen compared to an unsbstituted benzene (deactivating), but nevertheless, the substitution reaction takes place in the *ortho* and *para* position.

For the halogens, the inductive effect outweighs the resonance effect. The weak releasing effect stabilizes the carbocations from *o*- and *p*-attack.

Example:



Chlorobenzene

o-Chloronitrobenzene (30%)

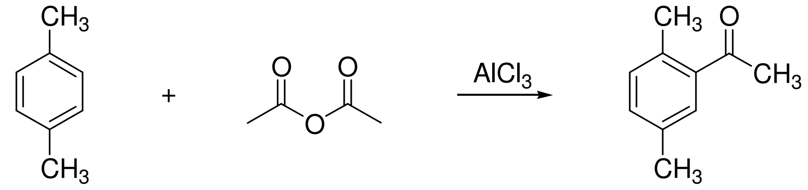
m-Chloronitrobenzene (1%)

p-chloronitrobenzene (69%)

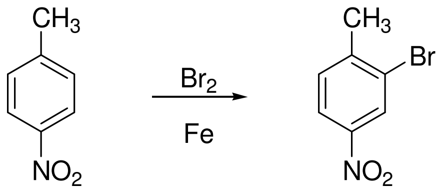
12.15 Multiple Substituent Effects

When two or more substituents are present on a ring, the regioselectivity of electrophilic aromatic substitution is generally controlled by the directing effect of the more powerful *activating* substituent.

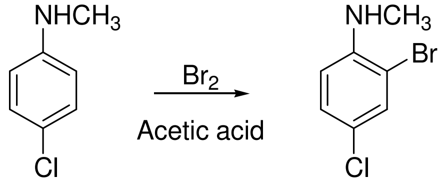
Simplest case:
All the available sites are equivalent, and substitution at any one of them gives the same product.



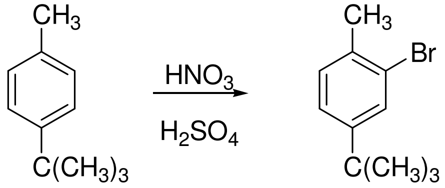
Reinforcing case:
Often directing effects of substituents reinforce each other: substitution takes place ortho to the methyl group and meta to the nitro group.

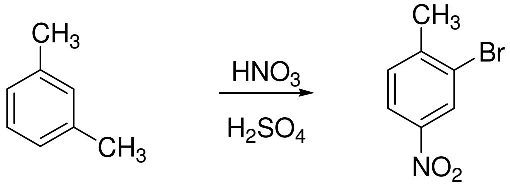


Dilemma case:
The most activating substituent controls the regioselectivity.



Steric effect cases:
When two positions are comparably activated by alkyl groups, substitution usually occurs at the less hindered site.

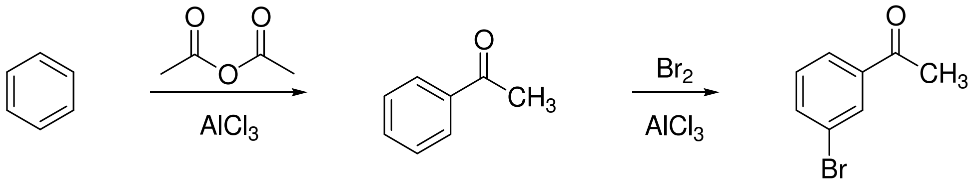




12.16 Regioselective Synthesis of Disubstituted Aromatic Compounds

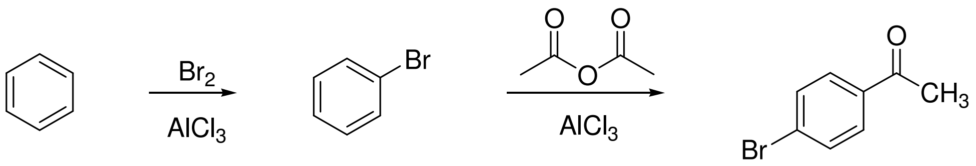
Factors to Consider
The order of introduction of substituents to ensure correct orientation in the final product.

When the meta-directing acetyl group is introduced first, the final product is ***m***-bromoacetophenone.



m-Bromoacetophenone

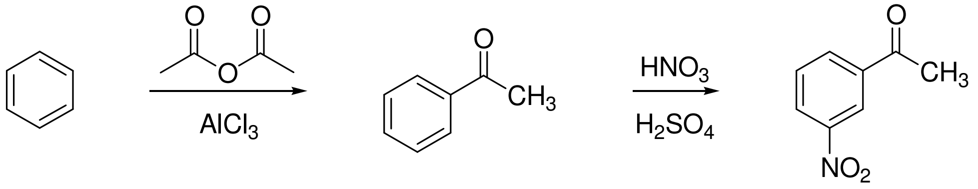
When the ortho, para-directing bromine is introduced first, the major product is ***p***-bromoacetophenone.



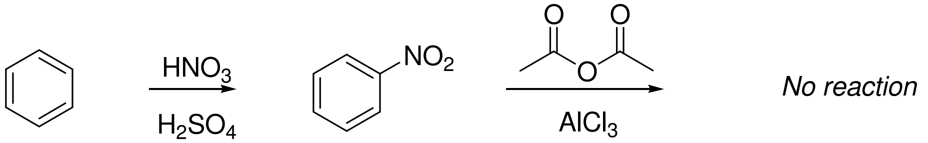
p-Bromoacetophenone

Friedel-Crafts alkylation reactions cannot be carried out on strongly deactivated aromatics.

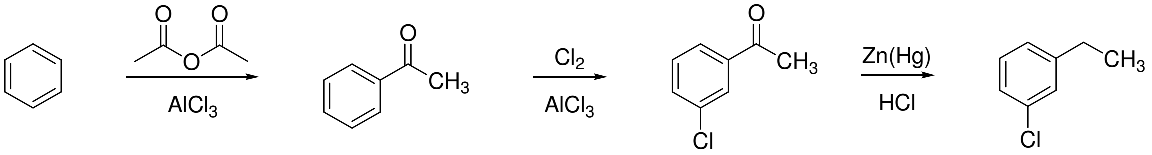
Nitrobenzene is so unreactive that the next Friedel-Crafts reaction will not take place.



m-Nitroacetophenone

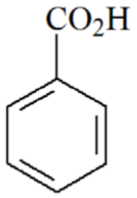


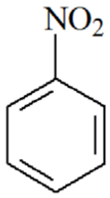
Sometimes electrophilic aromatic substitution must be combined with a functional group transformation

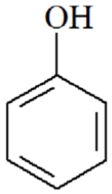


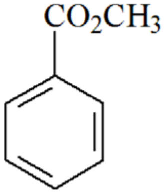
Extra Problems :

1. Which of the following aromatic compounds reacts faster than benzene in electrophilic aromatic bromination?

A) 

B) 

C) 

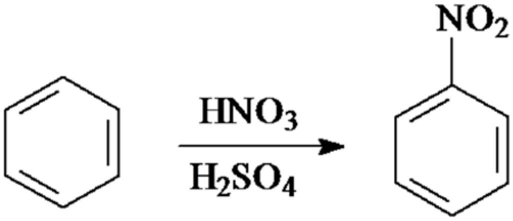
D) 

A) A B) B C) C D) D

2. Nitration of benzoic acid has a reaction rate which is __________ than the nitration rate of benzene and gives primarily the _____________ product(s).

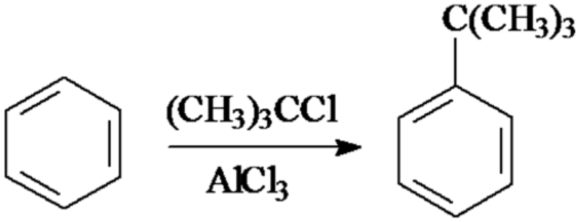
A)	slower, *meta*	C)	faster, *ortho,para*
B)	slower, *ortho,para*	D)	faster, *meta*

3. Which one of the following is the electrophile in the reaction shown below?



A) benzene B) NO_3^- C) NO_2^+ D) H_2SO_4

4. What is the electrophile in the Friedel-Crafts alkylation reaction below?



A) $AlCl_3$ B) Cl^- C) benzene D) $(CH_3)_3C^+$

5. Which one of the following reactions does <u>not</u> give *tert*-butylbenzene?

A)	benzene + $(CH_3)_3CCl/AlCl_3$	C)	benzene + $(CH_3)_3CH/AlCl_3$
B)	benzene + $(CH_3)_2C{=}CH_2/H_2SO_4$	D)	benzene + $(CH_3)_3COH/H_2SO_4$

6. What is(are) the product(s) of the following reaction?

$$C_6H_6 \quad + \quad CH_3CH_2CH_2Cl \xrightarrow{AlCl_3}$$

A) C6H5CH2CH2CH3
B) C6H5CH(CH3)2
C) C6H5CH2CH2CH2C1
D) a mixture of C6H5CH2CH2CH3 and C6H5CH(CH3)2

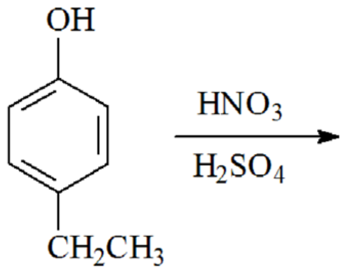
7. Rank the following compounds in order of decreasing reactivity to aromatic electrophilic bromination.

I. benzene II. toluene III. benzoic acid IV. phenol

A)	IV > II > I > III	C)	II > I > IV > III
B)	IV > III > II > I	D)	II > III > IV > I

8. Which of the following groups are ortho/para directors?
I. $–NO_2$ II. $–OCH_3$ III. $–CO_2CH_3$ IV. $–CH_3$
A) I and III B) II and III C) II and IV D) III and IV

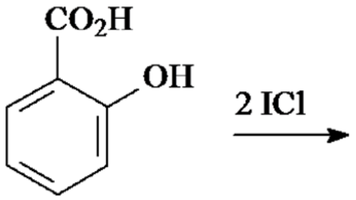
9. What is the major product of the following reaction?

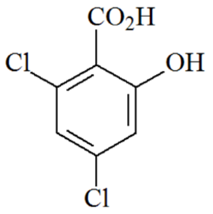


A) 4-ethyl-2-nitrophenol
B) 4-ethyl-3-nitrophneol
C) 1-ethyl-4-nitrobenzene
D) 4-nitrophenol

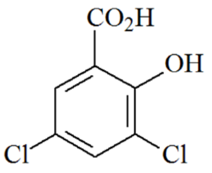
10. Which isomer of dichlorobenzene gives a single mononitration product?
A) ortho B) meta C) para D) none of them

11. Salicylic acid reacts with two equivalents of ICl to give one of the products below. Which one is it? (Hint: Cl is more electronegative than I.)

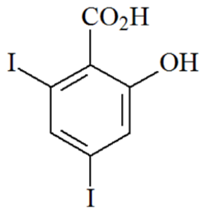




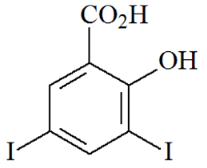
A)



B)



C)



D)

A) A B) B C) C D) D

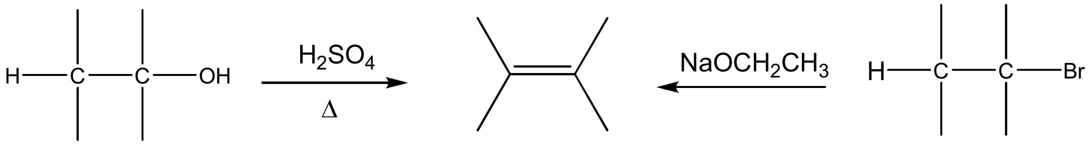
12. Nitration of chlorobenzene has a reaction rate which is __________ than the nitration rate of benzene and gives primarily the _____________ product(s).
A) faster, ortho/para B) faster, meta C) slower, ortho/para D) slower, meta

13. Which one of the following substituents is deactivating and ortho-para directing in electrophilic aromatic substitution reactions?
A) –Cl B) –N(CH3)2 C) –CO2H D) –CH=CH2

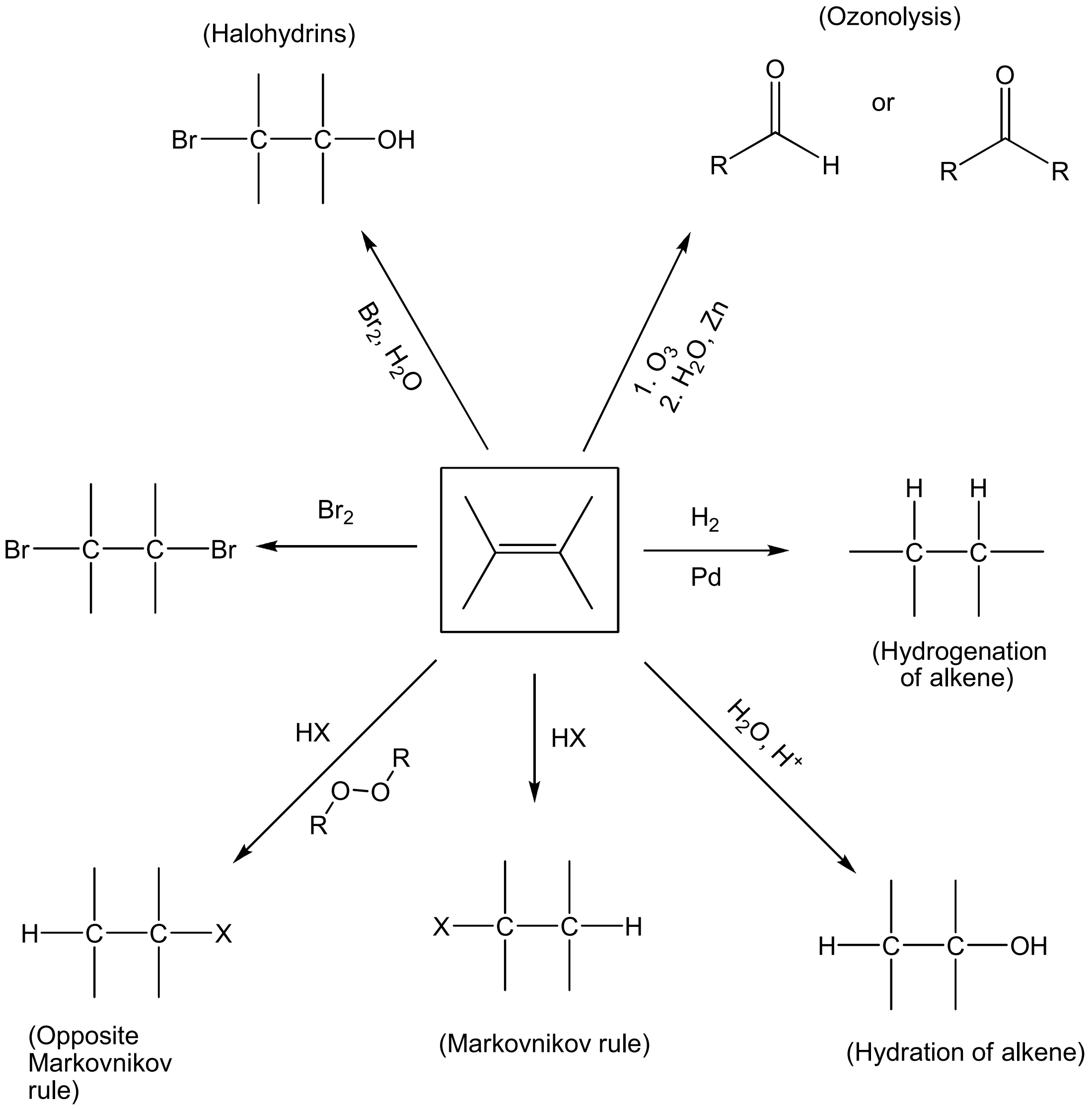
Answers: 1)C 2)A 3)C 4)D 5)C 6)D 7)A 8)C 9)A 10)C 11)D 12)C 13)A

Reactions Summary from *202-BZF-05 Organic Chemistry I*

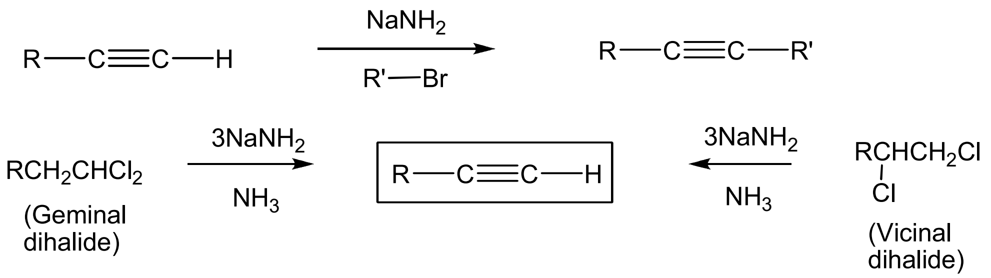
Preparation of Alkenes: Chapter 5.



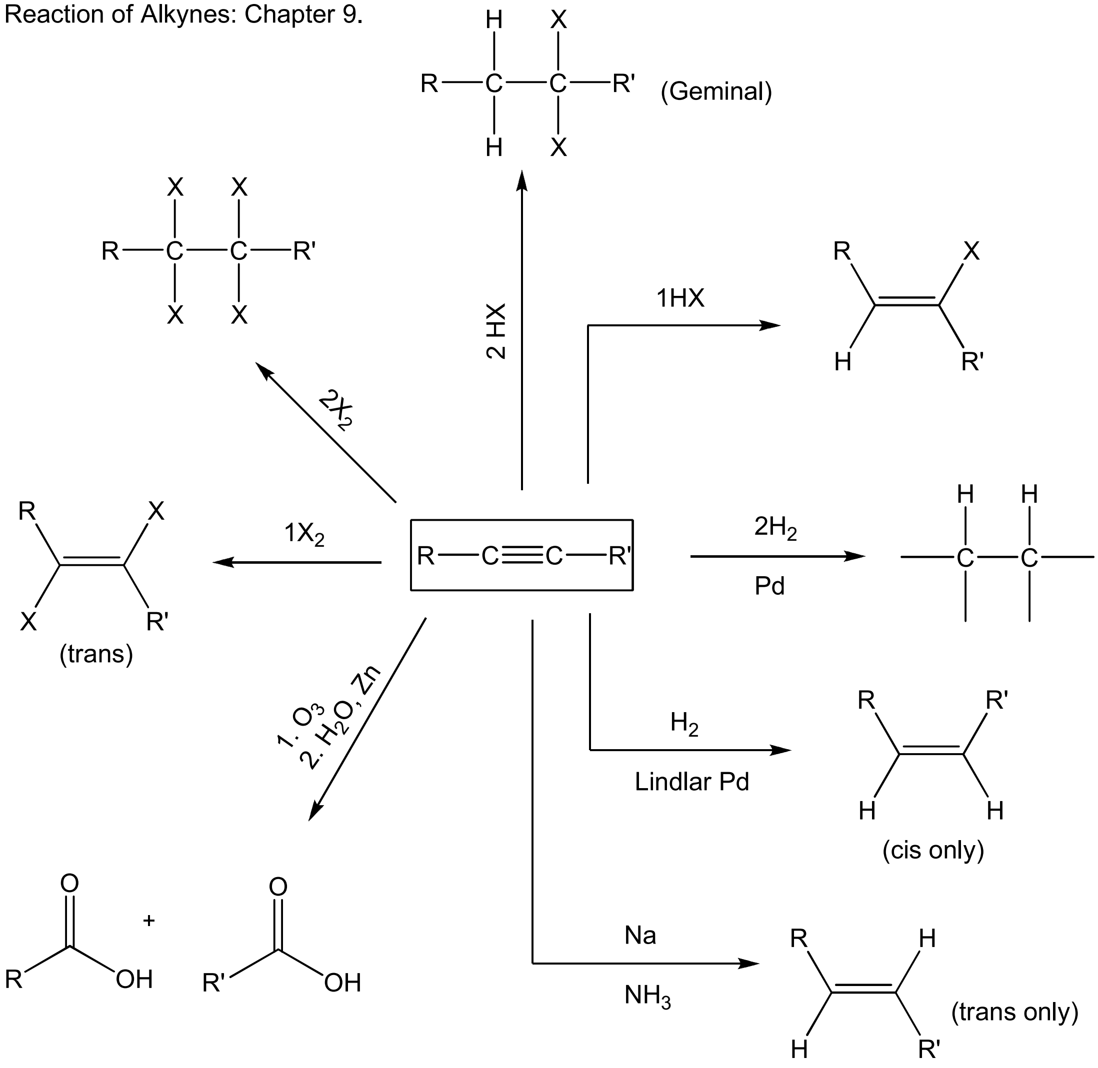
Reactions of Alkenes: Chapter 6.



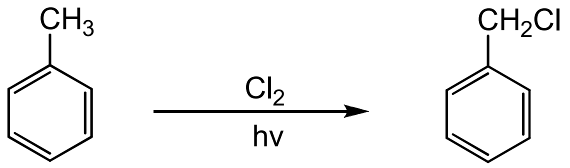
Preparation of Alkynes: Chapter 9.

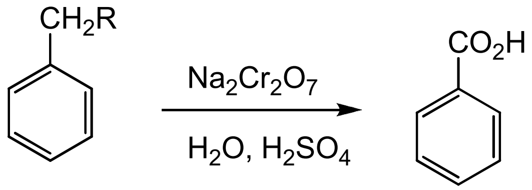


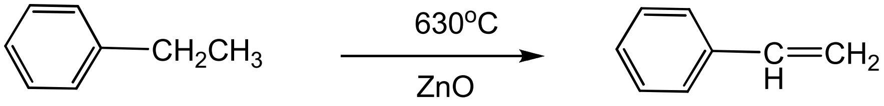
Reaction of Alkynes: Chapter 9.

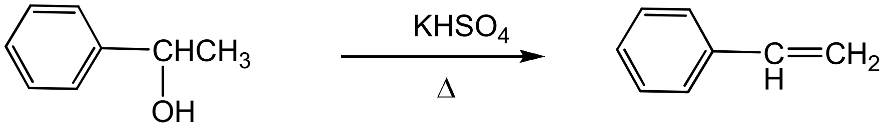


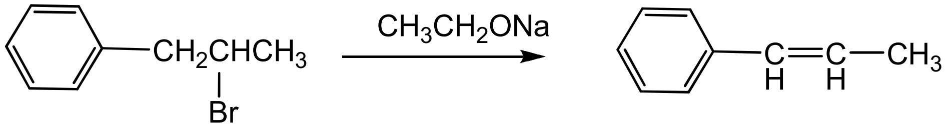
Reaction of Arenes: Chapter 11.

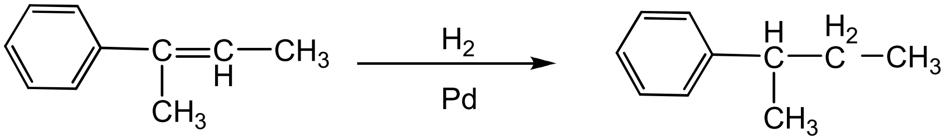


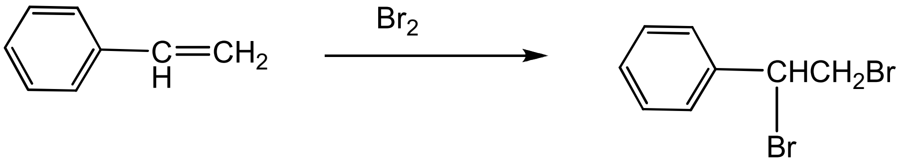


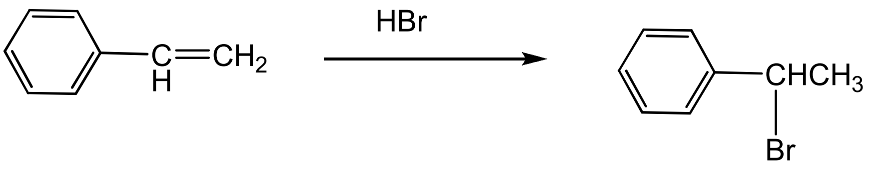


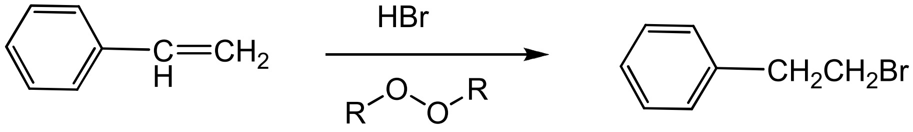




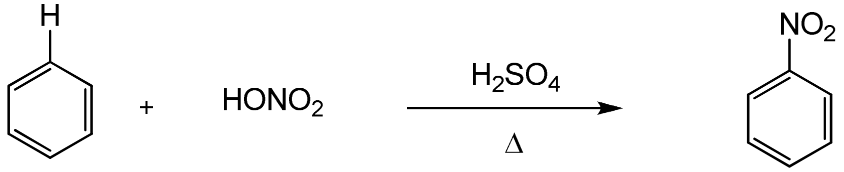


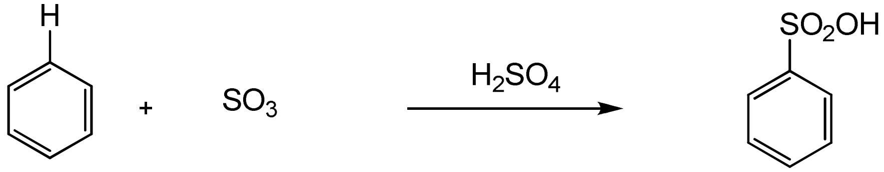


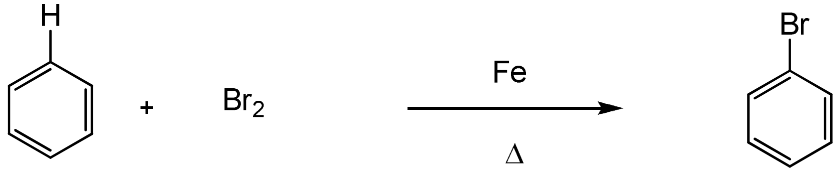




Reaction of Arenes: Chapter 12.







See also the substituents effects in electrophilic aromatic substitution : activating and deactivating substituents.

PERIODIC TABLE OF THE ELEMENTS

atomic number
atomic mass
Symbol
English name
French name*

*all are masculine

1 1.0079 **H** hydrogen hydrogène																	2 4.003 **He** helium hélium
3 6.941 **Li** lithium lithium	4 9.012 **Be** beryllium béryllium											5 10.811 **B** boron bore	6 12.011 **C** carbon carbone	7 14.007 **N** nitrogen azote	8 15.9994 **O** oxygen oxygène	9 18.998 **F** fluorine fluor	10 20.18 **Ne** neon néon
11 22.99 **Na** sodium sodium	12 24.31 **Mg** magnesium magnésium											13 26.98 **Al** aluminum aluminium	14 28.086 **Si** silicon silicium	15 30.974 **P** phosphorus phosphore	16 32.07 **S** sulfur soufre	17 35.453 **Cl** chlorine chlore	18 39.95 **Ar** argon argon
19 39.098 **K** potassium potassium	20 40.08 **Ca** calcium calcium	21 44.96 **Sc** scandium scandium	22 47.87 **Ti** titanium titane	23 50.94 **V** vanadium vanadium	24 51.996 **Cr** chromium chrome	25 54.94 **Mn** manganese manganèse	26 55.85 **Fe** iron fer	27 58.93 **Co** cobalt cobalt	28 58.69 **Ni** nickel nickel	29 63.546 **Cu** copper cuivre	30 65.39 **Zn** zinc zinc	31 69.72 **Ga** gallium gallium	32 72.61 **Ge** germanium germanium	33 74.922 **As** arsenic arsenic	34 78.96 **Se** selenium sélénium	35 79.904 **Br** bromine brome	36 83.80 **Kr** krypton krypton
37 85.468 **Rb** rubidium rubidium	38 87.62 **Sr** strontium strontium	39 88.91 **Y** yttrium yttrium	40 91.22 **Zr** zirconium zirconium	41 92.91 **Nb** niobium niobium	42 95.94 **Mo** molybdenum molybdène	43 98 **Tc** technetium technétium	44 101.07 **Ru** ruthenium ruthénium	45 102.91 **Rh** rhodium rhodium	46 106.42 **Pd** palladium palladium	47 107.87 **Ag** silver argent	48 112.411 **Cd** cadmium cadmium	49 114.82 **In** indium indium	50 118.71 **Sn** tin étain	51 121.76 **Sb** antimony antimoine	52 127.60 **Te** tellurium tellure	53 126.904 **I** iodine iode	54 131.29 **Xe** xenon xénon
55 132.91 **Cs** cesium césium	56 137.33 **Ba** barium baryum	57 138.91 **La** lanthanum lanthane	72 178.49 **Hf** hafnium hafnium	73 180.95 **Ta** tantalum tantale	74 183.84 **W** tungsten tungstène	75 186.21 **Re** rhenium rhénium	76 190.21 **Os** osmium osmium	77 192.22 **Ir** iridium iridium	78 195.08 **Pt** platinum platine	79 196.97 **Au** gold or	80 200.59 **Hg** mercury mercure	81 204.38 **Tl** thallium thallium	82 207.2 **Pb** lead plomb	83 208.98 **Bi** bismuth bismuth	84 209 **Po** polonium polonium	85 210 **At** astatine astate	86 222 **Rn** radon radon
87 223 **Fr** francium francium	88 226.03 **Ra** radium radium	89 227.03 **Ac** actinium actinium	104 261 **Rf** rutherfordium rutherfordium	105 262 **Unp** unnilpentium unnilpentium	106 266 **Unh** unnilhexium unnilhexium	107 264 **Uns** unnilseptium unnilseptium	108 269 **Uno** unnilloctium unnilennium	109 268 **Une** unnilennium unnilennium	110 269 **Uun** ununnilium ununnilium	111 272 **Uuu** unununium unununium	112 277 **Uub** ununbium ununbium						

58 140.12 **Ce** cerium cérium	59 140.91 **Pr** praseodymium praséodyme	60 144.24 **Nd** neodymium néodyme	61 145 **Pm** promethium prométhium	62 150.36 **Sm** samarium samarium	63 151.96 **Eu** europium europium	64 157.25 **Gd** gadolinium gadolinium	65 158.93 **Tb** terbium terbium	66 162.50 **Dy** dysprosium dysprosium	67 164.93 **Ho** holmium holmium	68 167.26 **Er** erbium erbium	69 168.93 **Tm** thulium thulium	70 173.04 **Yb** ytterbium ytterbium	71 174.97 **Lu** lutetium lutécium
90 232.038 **Th** thorium thorium	91 231.036 **Pa** protactinium protactinium	92 238.029 **U** uranium uranium	93 237.048 **Np** neptunium neptunium	94 244 **Pu** plutonium plutonium	95 243 **Am** americium américium	96 247 **Cm** curium curium	97 247 **Bk** berkelium berkélium	98 251 **Cf** californium californium	99 252 **Es** einsteinium einsteinium	100 257 **Fm** fermium fermium	101 258 **Md** mendelevium mendélévium	102 259 **No** nobelium nobélium	103 262 **Lr** lawrencium lawrencium