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Fundamentals of Organic Chemistry

CHEM 109

For Students of Health Colleges

Credit hrs.: (2+1)

King Saud University

College of Science, Chemistry Department

CHEM 109

CHAPTER 1. INTRODUCTION

Syllabus

Introduction

Types of chemical bonds: (*Ionic and covalent bonds*) - Atomic and molecular orbital: (*sigma and pi bond*) - Hybridization (*sp^3, sp^2, sp*) - Inductive effect, polarization, and Stability of carbocations - Classification of organic compounds and functional groups - Types of chemical reactions: (Substitution (*Free radical - electrophilic - nucleophilic*), *Elimination, Oxidation and reduction reactions*).

Lectures (2)

Aliphatic Hydrocarbons

Classes of hydrocarbons: (*saturated and unsaturated*) – Nomenclature: (*IUPAC and common names*) – Isomerism: (*Structural and Geometrical*) - Physical properties of aliphatic hydrocarbons - Preparation of saturated hydrocarbons (Alkanes): (*Hydrogenation of unsaturated hydrocarbons - Hydrolysis of alkyl Grignard reagent - Reaction of lithium dialkyl cuprates with alkyl halides*) - Reactions of saturated hydrocarbons: (*Halogenations*) - Preparation of Unsaturated hydrocarbons: (Alkenes and Alkynes): (*Elimination reactions (Dehydration, dehydrohalogenation and dehalogenation reactions) and Saytzeff rule*) - Reactions of Unsaturated hydrocarbons: (*Electrophilic addition reactions (Markovnikov's rule), hydrogenation, halogenation, hydrohalogenation, and hydration - Oxidation reactions - Acidity of alkynes*).

Lectures (4)

Syllabus

Aromatic compounds

Aromaticity: structure and bonding requirements and Hückel's rule - Nomenclature of aromatic compounds - Electrophilic aromatic substitution reactions: (*Alkylation, acylation, halogenations, nitration and sulfonation*) - Effects of substituents on electrophilic aromatic substitution reactions - Side-chain reactions: (*Oxidation of alkylbenzenes*).

Lectures (2)

Alcohols, Phenols and Ethers

Structure, classifications and nomenclature - Physical properties - Preparation of alcohols and phenols: (*Hydration of alkenes - Nucleophilic substitution reaction of alkyl halides - Reduction of aldehydes, ketones and acids - Addition of Grignard compounds to aldehydes and ketones*) - Preparation of Phenols: (*Benzene sulfonic acids*) - Preparation of ethers (*Williamson synthesis*) - Reactions of Alcohols, Phenols and Ethers: (*Salt formation of alcohols and phenols (Acidity of phenols and Reaction of Alcohols with Sodium metal) - Reactions of Alcohols and Ethers with Hydrogen halides - Conversion of Alcohols to alkyl halides - Oxidation of alcohols - Electrophilic substitution reactions of phenols*) - Alcohols with More Than One Hydroxyl Group; glycols.

Lectures (4)

1st Midterm Exam

Syllabus

Aldehydes and Ketones

Structure and Nomenclature - Physical properties - Preparation of aldehydes and ketones: (*Hydration of alkynes - Ozonolysis of alkynes - Friedel-Crafts acylation - Oxidation of alcohols*) - Reactions of aldehydes and ketones: (*Nucleophilic addition reaction (addition of hydrogen cyanide, Reduction, Grignard addition, addition of Alcohol (hemiacetal and acetal Formation), addition of ammonia and amine derivatives*).

Lectures (3)

Carbohydrates

Definitions and Classification (*monosaccharides, disaccharides and polysaccharides*) – Monosaccharides: (*Nomenclature - Structure (Optical isomerism, cyclic structure, Fischer Projection, Haworth Formulas)*) - Reactions of Monosaccharides: (*Reduction and oxidation of monosaccharides*) – Disaccharides: (Maltose, Cellobiose, Sucrose and Lactose) – Polysaccharides: (Cellulose and Starch)

Lectures (4)

Carboxylic acids and Their Derivatives

Structure and Nomenclature - Physical properties - Acidity of Carboxylic acids - Preparation: (*Hydrolysis of nitrile - Carbonation of Grignard reagents*) - Reactions of carboxylic acids: (*Salt Formation - Ester, amide, anhydride, and acid chloride formation*).

Lectures (3)

Syllabus

Amines

Structure of amines - Nomenclature of amines - Physical properties of amines - Basicity of amines - Preparation of amines: (*Reduction of nitro compounds, nitriles and amides - Alkylation of ammonia*) - Reactions of amines: (*Sulfa drugs - Diazonium salts (Formation and Replacement reactions*)

Lectures (2)

2nd Midterm Exam.

Amino Acids, Peptides ,and Proteins

- Sources, classification and Structure - The acid–base Properties of Amino Acids - Reactions of amino acids: (*The Ninhydrin Reaction, Peptides - Sanger reaction - Formation of an amide linkage (The peptide bond: Proteins)*) - Structure of proteins.

Lectures (4)

Nucleic Acids

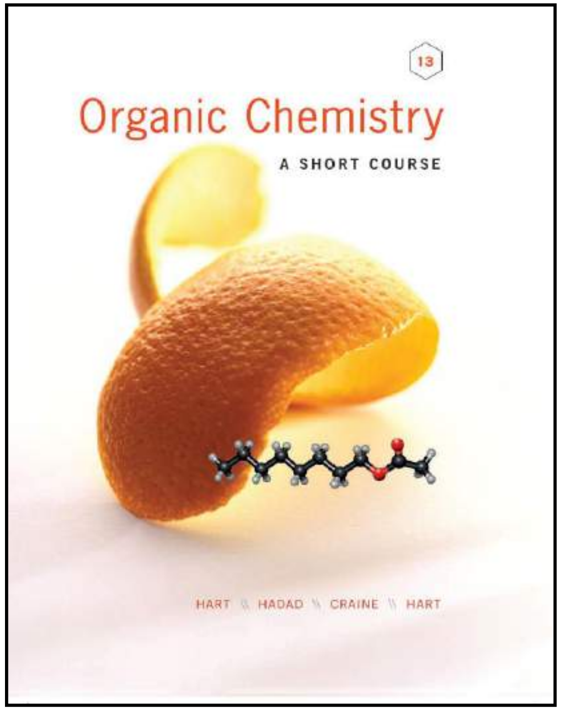
Chemical Structure: (*General structure (Nucleoside, Nucleotide and Nucleic acids) - DNA; structure - RNA; structure and types*).

Lectures (2)

Final Exam.

References

- *Organic chemistry: A short course by I Harold Hart, David J. Hart and Leslie E. Craine, Houghton Mifflin Company, USA, 2012.*
- *Elements of Organic Chemistry (second edition) is written by Isaak Zimmerman and Henry Zimmerman and published by Macmillan Publishing Co., Inc. New York in 1983.*
- أسس الكيمياء العضوية - أ.د./ سالم بن سليم الذياب - الناشر: مؤسسة نافثة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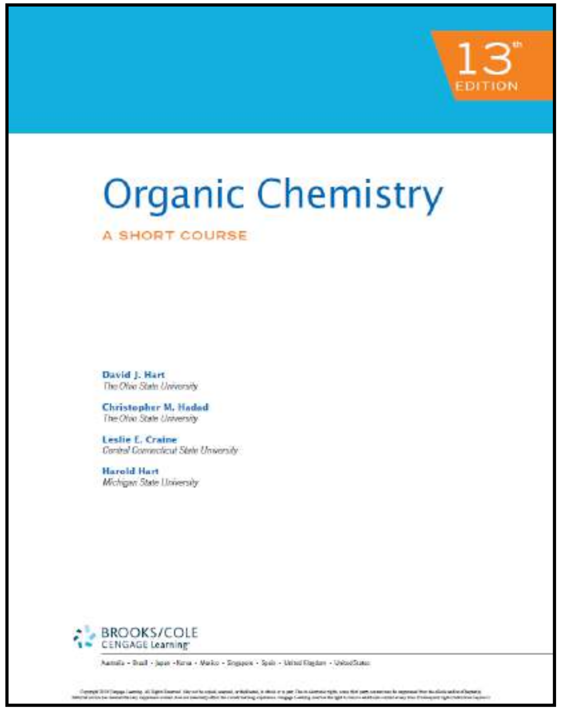
Organic Chemistry

A SHORT COURSE

HART \\ HADAD \\ CRAINE \\ HART


13th EDITION

Organic Chemistry

A SHORT COURSE

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ضوابط الاختبار البديل

شروط عقد اختبار بديل للطالب:

يمكن أن يعقد للطالب -الذي يتغيب عن الاختبار الأساسي -اختبار بديل وفقاً للشروط والضوابط التالية:

1- ألا يكون الطالب قد دخل الاختبار الأساسي للمقرر.

2- ألا يكون الطالب محروم في المقرر.

3- أن يتقد م الطالب بطلب الاختبار البديل في موعد لا يتجاوز أسبوع من عقد الاختبار الأساسي وذلك لعمادة السنة التحضيرية (فقط) وليس لمدرس المقرر .

4- أن يتقدم الطالب بعذر يقبله مجلس العمادة.

5- أن تكون الأعذار من جهات حكومية أو مصدق عليها من جهة حكومية.

6- لا يوجد اختبار بديل للاختبار البديل

Bonding, Structural Formulas, and Molecular Shapes

Organic Chemistry: Definition

- The word **Organic** can be a biological or chemical term, in biology it means anything that is living or has lived. The opposite is Non-Organic.
- **Organic Chemistry** is unique in that it deals with vast numbers of substances, both natural and synthetic.

The clothes, the petroleum products, the paper, rubber, wood, plastics, paint, cosmetics, insecticides, and drugs

- But, from the chemical makeup of organic compounds, it was recognized that one constituent common to all was ***the element carbon***.
- **Organic chemistry** is defined as *the study of carbon/hydrogen-containing compounds and their derivatives.*

The Uniqueness of Carbon

- **What is unique about the element *carbon*?**
- **Why does it form so many compounds?**
  - ***The answers lie in***
    - The structure of the *carbon* atom.
    - The position of *carbon* in the periodic table.
- **These factors enable it to form strong bonds with**
    - other carbon atoms
    - and with other elements (hydrogen, oxygen, nitrogen, halogens,…etc).
- Each **organic compound** has its own characteristic set of physical and chemical properties which depend on the *structure of the molecule*.

Atomic Structure

- **Atoms** consist of three main particles: neutrons (have no charge), protons (positively charged) and **electrons** (negatively charged).
  - Neutrons and protons are found in the nucleus.
  - Electrons are found outside the nucleus.

    Electrons are distributed around the nucleus in successive *shells* (*principal energy levels*).

- **Atom** is electrically neutral.

  i.e. Number of electrons = Number of protons

- **Atomic number** of an element is the number of protons.

Atomic Structure

- **The energy levels** are designated by capital letters (*K*, *L*, *M*, *N*, ..) or whole numbers (*n*).
- **The maximum capacity of a shell = $2n^2$ electrons.**

  n = number of the energy level.
- **For example,** the element carbon (atomic number 6)

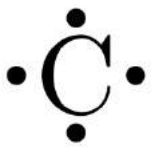
  6 electrons are distributed about the nucleus as

Shell	K	L	M	N
Number of electrons	2	4	0	0

Atomic Structure

Valance Electrons: Electron-Dot Structures

- **Valance Electrons** are those electrons located in the *outermost energy level* (*the valance shell*).
- **Electron-dot structures**
  - The symbol of the element represents the core of the atom.
  - The valance electrons are shown as dots around the symbol.



Chemical Bonding

- **In 1916 G.N. Lewis** pointed out that:

  The noble gases were stable elements and he ascribed their lack of reactivity to their having their valence shells filled with electrons.

  - 2 electrons in case of helium.
  - 8 electrons for the other noble gases.

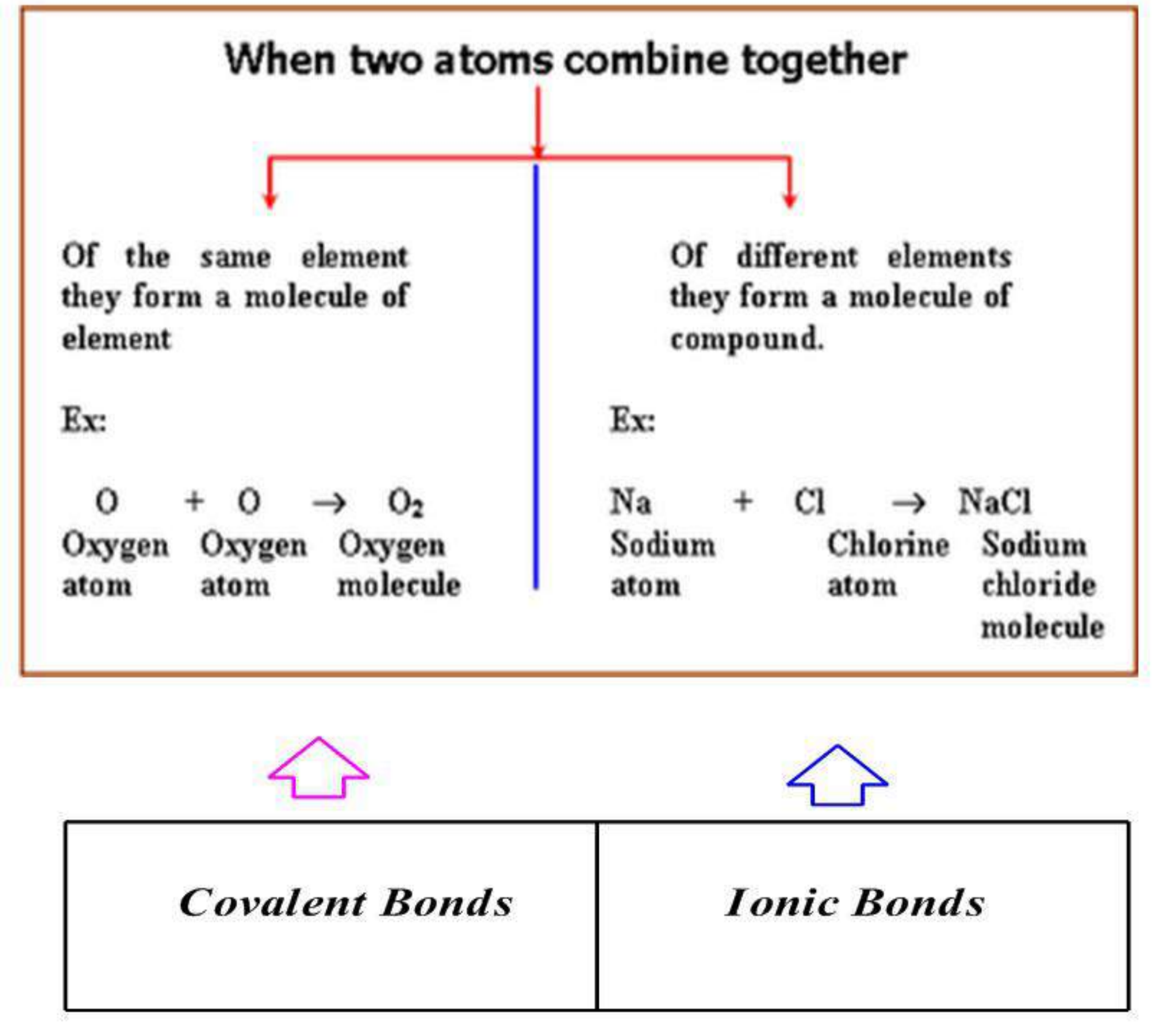
- **According to Lewis,**

  in interacting with one another atoms can achieve a greater degree of stability

  by rearrangement of the valence electrons

  to acquire the outer-shell structure of the closest noble gas in the periodic table.

Chemical Bonding



When two atoms combine together

Of the same element they form a molecule of element

Ex:

$O + O \rightarrow O_2$

Oxygen atom, Oxygen atom, Oxygen molecule

Of different elements they form a molecule of compound.

Ex:

$Na + Cl \rightarrow NaCl$

Sodium atom, Chlorine atom, Sodium chloride molecule

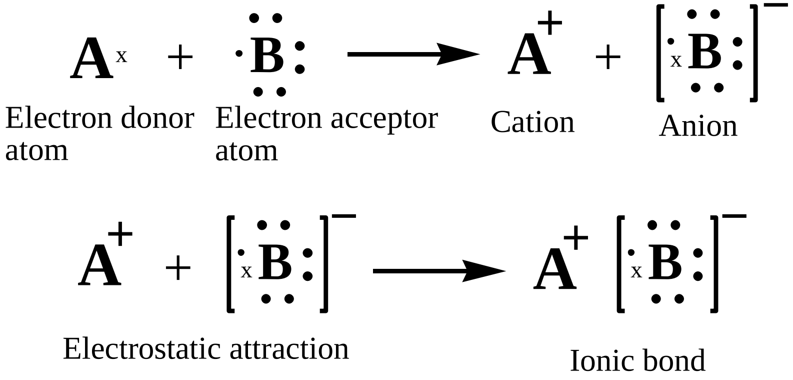
Covalent Bonds

Ionic Bonds

A) Ionic Bonds

- Elements at the left of the periodic table give up their valance electrons and become +ve *charged ions* (***cations***).
- Elements at the right of the periodic table gain the electrons and become -ve *charged ions* (***anions***).
- **Ionic bond**

  The electrostatic force of attraction between oppositely charged ions.



- The majority of ionic compounds are ***inorganic substances***.

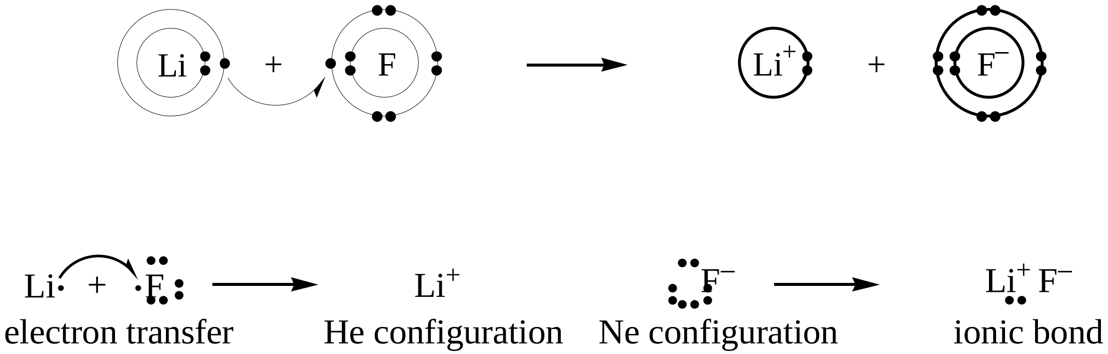
Chemical Bonding

Electronegativity Measures The Ability of An Atom To Attract Electrons

Increasing electronegativity

Decreasing electronegativity

H							
2.1							
Li	**Be**		**B**	**C**	**N**	**O**	**F**
1	1.5		2	2.5	3	3.5	4
Na	**Mg**		**Al**	**Si**	**P**	**S**	**Cl**
0.9	1.2		1.5	1.8	2.1	2.5	3
K							**Br**
0.8							2.8



B) Covalent Bonds

- Elements that are close to each other in the periodic table attain the stable noble gas configuration

  by sharing valence electrons between them.

- **Covalent bond**

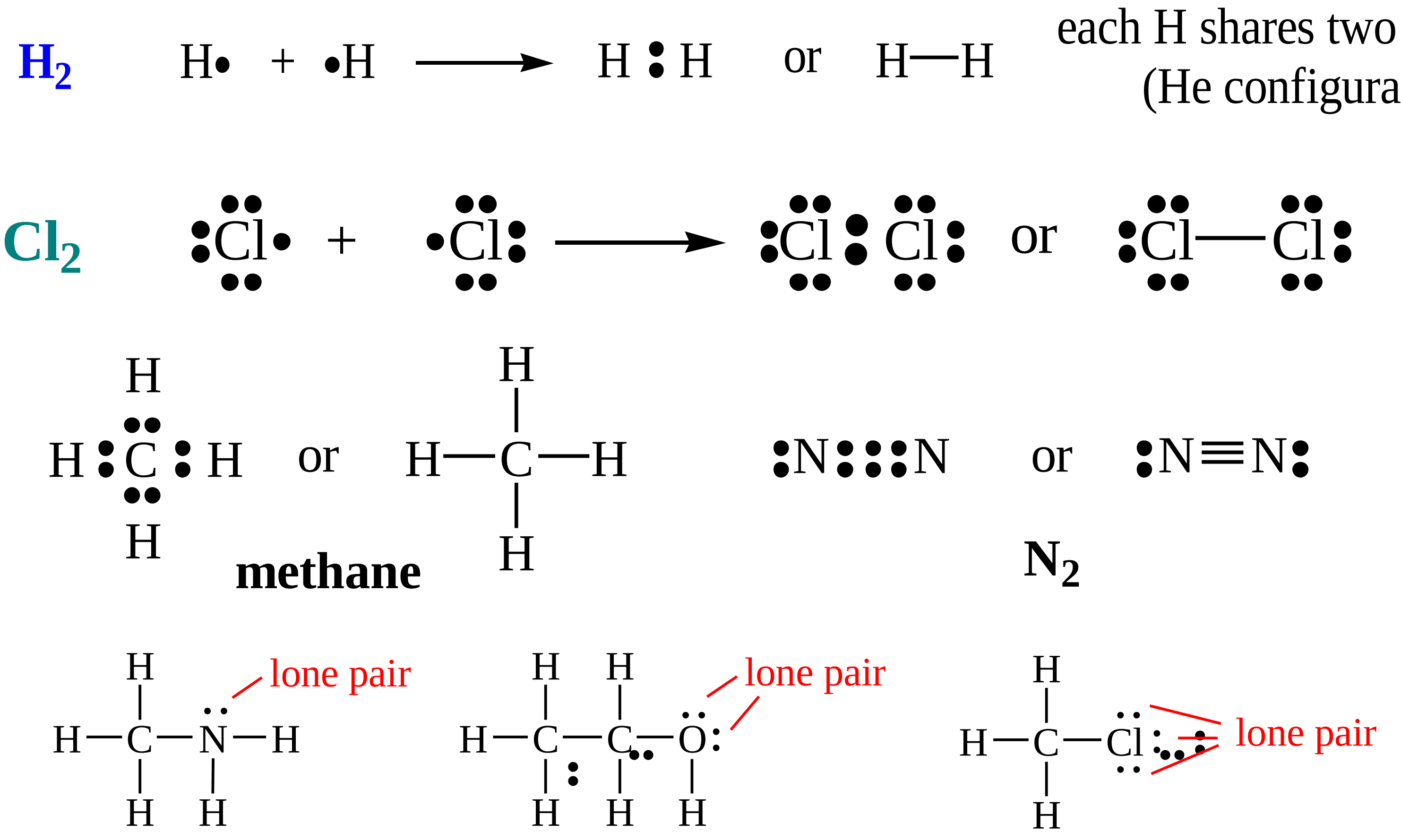
  The chemical bond formed when two atoms share one pair of electrons.

- A shared electron pair between two atoms or single covalent bond, will be represented by a dash (-).

Chemical Bonding

B) Covalent Bonds

Examples



each H shares two electrons (He configuration)

methane

methyl amime

ethanol

chloromethane

B) Covalent Bonds

- In molecules that consist of **two like atoms**;

  the bonding electrons are shared equally

  (both atoms have the same electronegativity).

- When **two unlike atoms**;

  the bonding electrons are no longer shared equally (shared unequally).

A Polar Covalent Bond

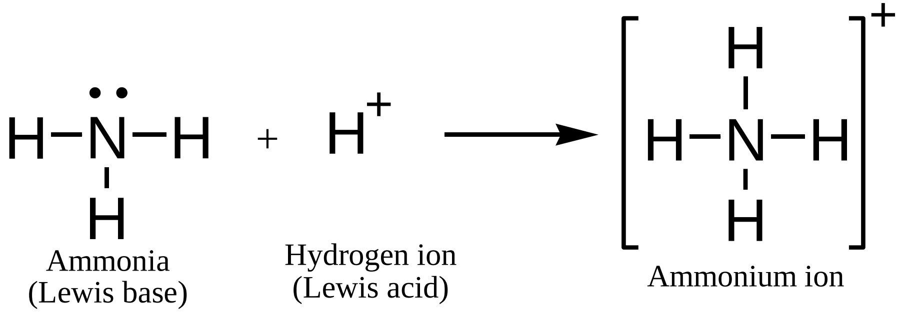
A bond, in which an electron pair is shared unequally.

➢ The more electronegative atom assumes a partial negative charge and the less electronegative atom assumes a partial positive charge.

$$\overset{+\!\!\!\longrightarrow}{\mathrm{C-O}} \quad \text{or} \quad \overset{\delta+}{\mathrm{C}}-\overset{\delta-}{\mathrm{O}}$$

B) Coordinate Covalent Bonds

- There are molecules in which one atom supplies both electrons to another atom in the formation of a covalent bond.
- **For example;**



- **Lewis base**

  The species that furnishes the electron pair to form a coordinate covalent bond.

- **Lewis acid**

  The species that accepts the electron pair to complete its valance shell.

Chemical Bonding

How Many Bonds to an Atom? Covalence Number

The number of covalent bonds that an atom can form with other atoms.

i.e. ***the covalence number*** *is equal to the number of electrons needed to fill its valance shell.*

Element	Number of valence electrons	Number of electrons in filled valence shell	Covalence number
H	1	2	1
C	**4**	**8**	**4**
N	5	8	3
O	6	8	2
F, Cl, Br, I	7	8	1

Shapes of Organic Molecules: Orbital Picture of Covalent Bonds

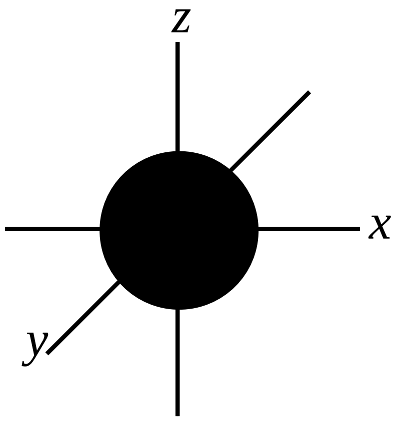
Atomic Orbitals

- **An atomic orbital** *represents a specific region in space in which an electron is most likely to be found.*
- **Atomic orbitals** are designated in the order in which they are filled by the letters *s*, *p*, *d*, and *f*.
- **Examples:**

  K shell has only one 1s orbital.

  L shell has one 2s and three 2p ($2p_x$, $2p_y$ and $2p_z$).

- **An *s* orbital** is **spherically shaped** electron cloud with the atom's nucleus and its center.

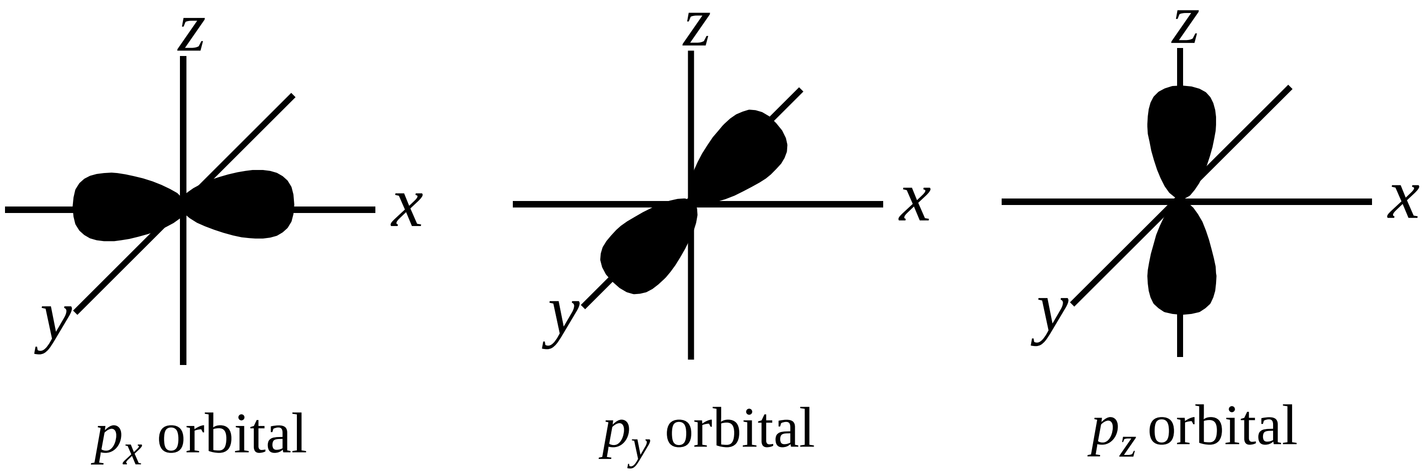


s orbital

Shapes of Organic Molecules: Orbital Picture of Covalent Bonds

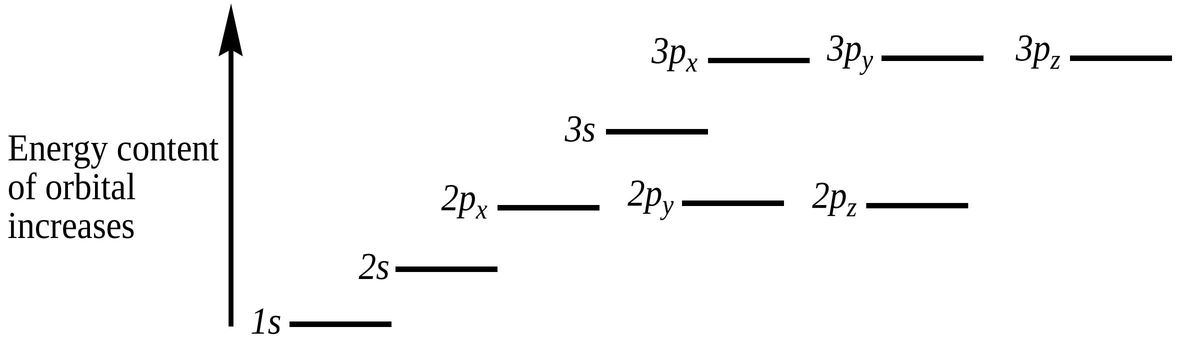
Atomic Orbitals

- A *p* orbital is a dumbbell-shaped electron cloud with the nucleus between the two lobes.
- Each *p* orbital is oriented along one of three perpendicular coordinate axes (in the *x*, *y*, or *z* direction).



Atomic Orbitals

- An energy level diagram of atomic orbitals.



- **When filling the atomic orbitals, keep in mind that**

  (1) An atomic orbital contain no more 2 electrons.

  (2) Electrons fill orbitals of lower energy first.

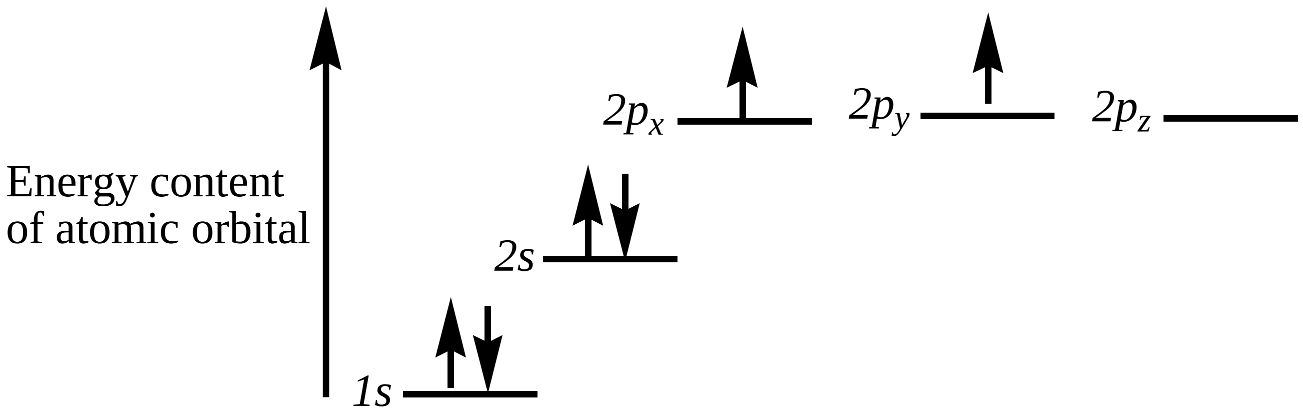
  (3) No orbital is filled by 2 electrons until all the orbitals of equal energy have at least one electron.

Shapes of Organic Molecules: Orbital Picture of Covalent Bonds

Atomic Orbitals

- The electronic configuration of carbon (atomic number 6) can be represented as

$1s^2 2s^2 sp^1{}_x 2p^1{}_y$ or $1s^2 2s^2 2p^2$



Energy level diagram for carbon.

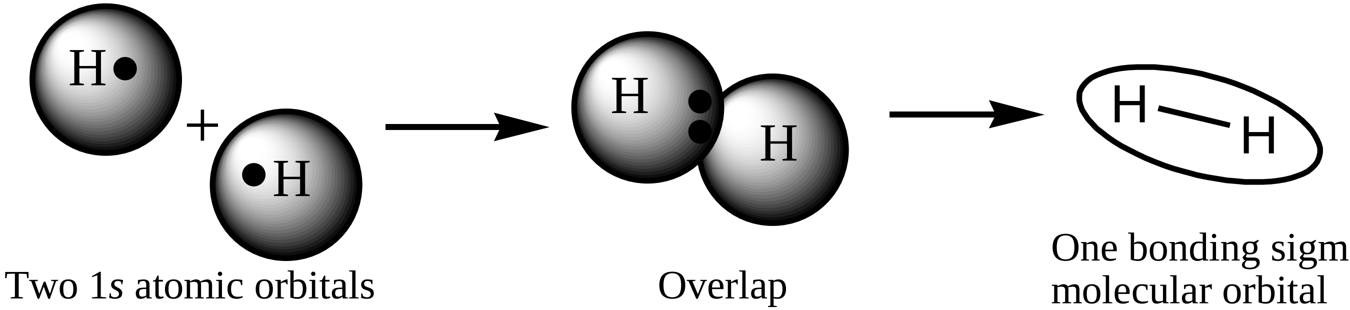
Shapes of Organic Molecules: Orbital Picture of Covalent Bonds

Molecular Orbitals

- A covalent bond consists of the overlap between two atomic orbitals to form a **molecular orbital**.

- **Example:**

Molecular orbital of H_2



Two 1*s* atomic orbitals

Overlap

One bonding sigma molecular orbital

Shapes of Organic Molecules: Orbital Picture of Covalent Bonds

Molecular Orbitals

- **Sigma bonds (σ bonds) can be formed from**
  - The overlap of two *s* atomic orbitals.
  - The end-on overlap of two *p* atomic orbitals.
  - The overlap of two an *s* atomic orbital with a *p* atomic orbital.
- **pi bonds (π bonds)** can be formed from the side-side overlap between two *p* atomic orbitals.

Bond Energy and Bond Length

- **A molecule is more stable than the isolated constituent atoms.**

  This stability is apparent in the release of energy during the formation of the molecular bond.

- **Heat of formation (bond energy)**

  The amount of energy released when a bond is formed.

- **Bond dissociation energy**

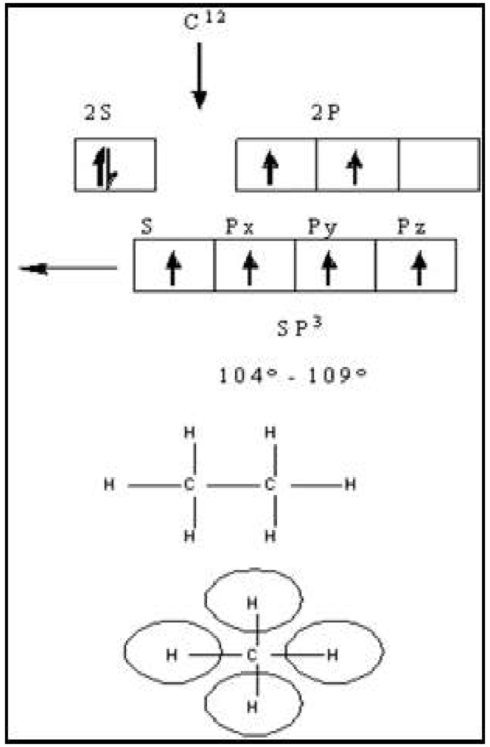
  The amount of energy that must be absorbed to break a bond.

- **Bond length**

  The distance between nuclei in the molecular structure.

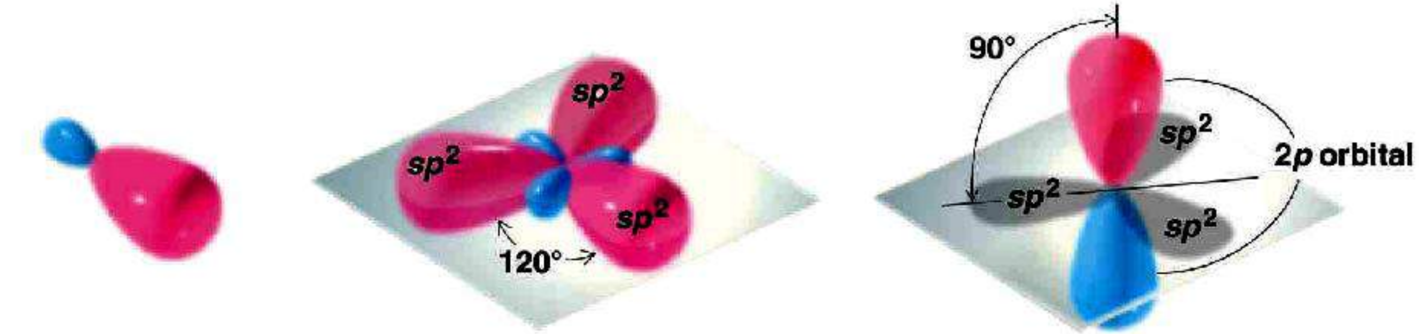
Hybridization (Alkanes sp^3)

- In the case of **alkanes sp^3**, the three *2p* orbitals of the carbon atom are combined with its *2s* orbital to form four new orbitals called "**sp^3**" hybrid orbitals.
- Four hybrid orbitals were required since there are four atoms attached to the central carbon atom.
- These new orbitals will have an energy slightly above the *2s* orbital and below the *2p* orbitals as shown in the following illustration.
- Notice that no change occurred with the *1s* orbital.
- **Regular tetrahedron** with all H-C-H **bond angles of 109.5°.**



Methane

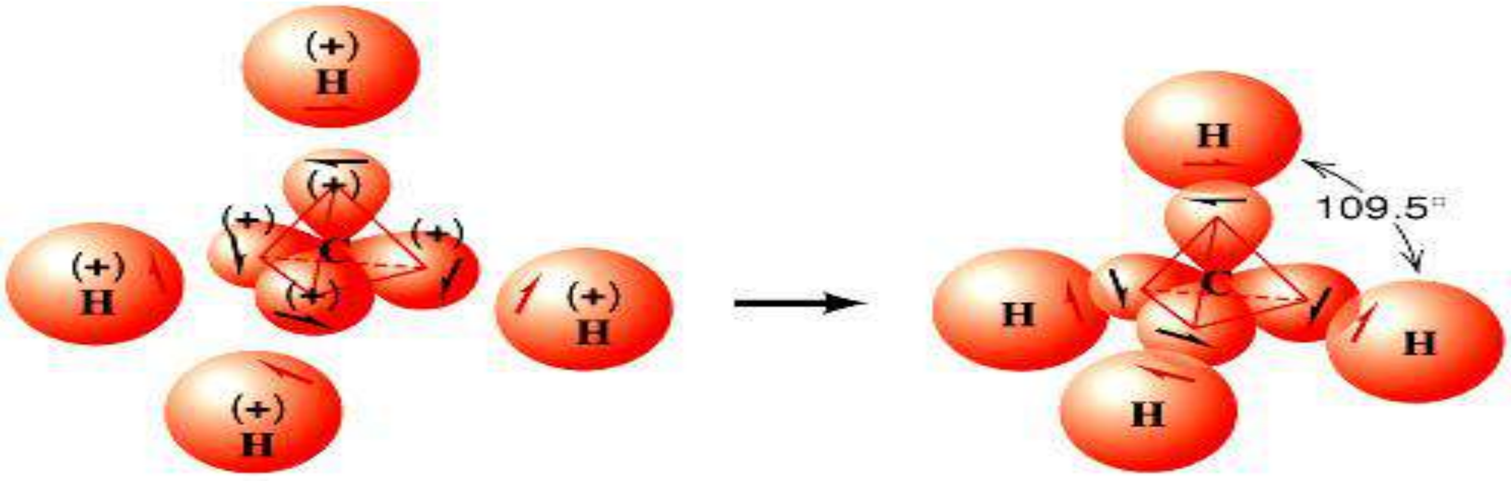
Hybridization (Alkanes sp^3)



(a) An sp^2 orbital

(b) Three sp^2 orbitals

(c) Three sp^2 orbitals and an unhybridized 2*p* orbital



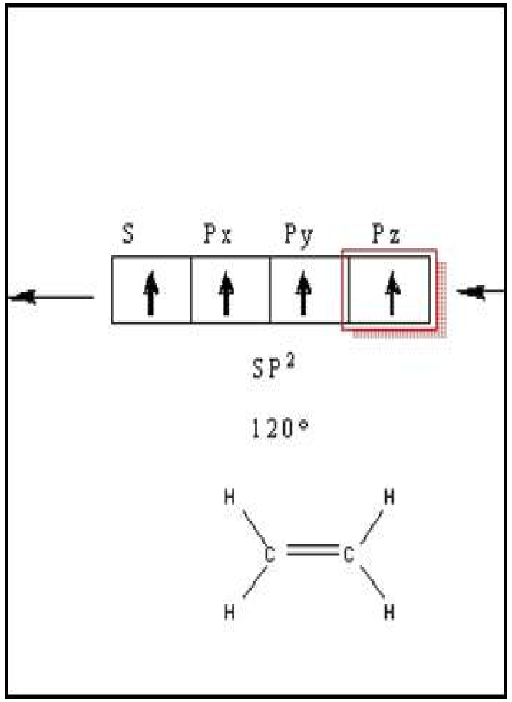
Methane, CH_4

Hybridization (Alkanes sp^2)

- In the case of **alkenes sp^2**, the $2s$ orbital is combined with only two of the $2p$ orbitals (*since we only need three hybrid orbitals for the three groups. thinking of groups as atoms and non-bonding pairs*) forming three hybrid orbitals called sp^2 hybrid orbitals.

- The other *p*-orbital remains unhybridized and is at right angles to the trigonal planar arrangement of the hybrid orbitals.

- **The trigonal planar** arrangement has **bond angles of 120°.**

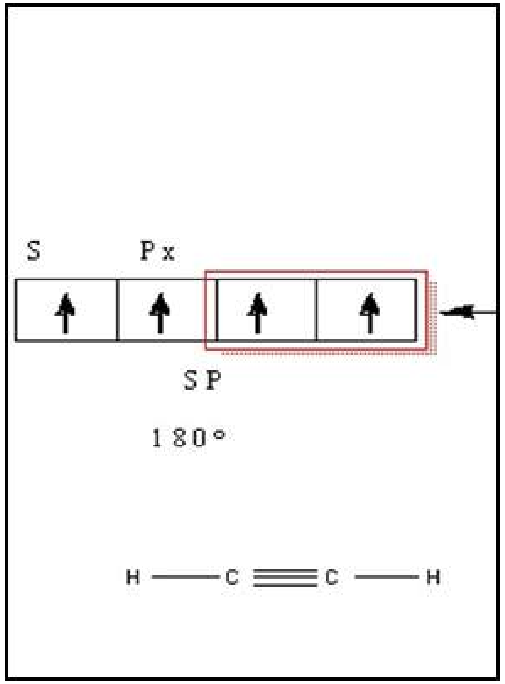


Ethene

(Ethylene)

Hybridization (Alkanes *sp*)

- In the case of **alkynes *sp***, the *2s* orbital is combined with only one of the *2p* orbitals to yield two *sp* hybrid orbitals.
- The two hybrid orbitals will be arranged as far apart as possible from each other with the result being a linear arrangement.
- The two unhybridized *p*-orbitals stay in their respective positions (at right angles to each other) and perpendicular to the **linear** molecule **(180°).**



Ethyne

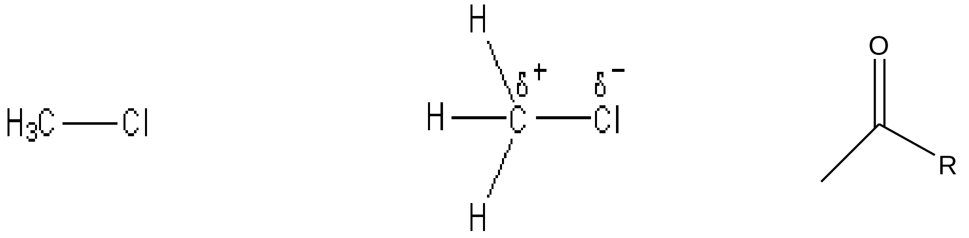
(Acetylene)

Inductive Effect

- **Inductive effect** can be defined as *the permanent displacement of electrons forming a covalent bond (sigma σ bonds) towards the more electronegative element or group*.
- The inductive effect is represented by the symbol, the arrow pointing towards the more electronegative element or group of elements.

  (+ I) effect if the substituent electron-donating

  (- I) effect if the substituent electron-withdrawing



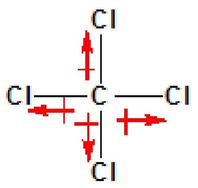
Electron-donating substituents (+I): $-CH_3$, $-C_2H_5$, $-NH_2$, OH, OCH_3, ….

Electron-withdrawing substituents (-I): $-NO_2$, -CN, $-SO_3H$, COOH, COOR,

Bond Polarity and Dipole Moment (μ)

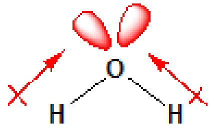
- **Dipole moment** (depends on the inductive effect).
- A bond with the electrons shared equally between two atoms is called a **nonpolar bond** like in Cl-Cl and C-C bond in ethane.
- A bond with the electrons shared unequally between two different elements is called a **polar bond**.
- The **bond polarity** is measured by its dipole moment (μ).
- **Dipole moment (μ)** defined to be the amount of charge separation (+δ and –δ) multiplied by the bond length.

CCl_4



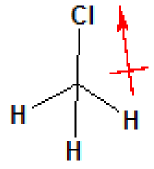
μ = zero

H_2O



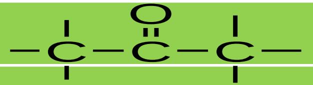
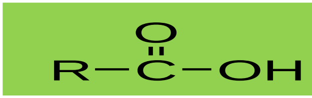
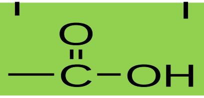
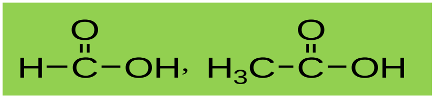
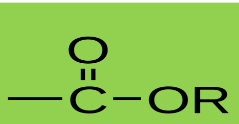
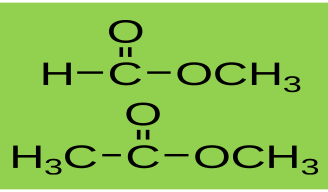
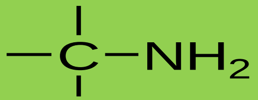
μ ≠ zero

CH_3Cl



μ ≠ zero

Functional Group is a reactive portion of an organic molecule, an atom, or a group of atoms that confers on the whole molecule its characteristic properties.

Class	General formula	Functional group	Specific
Alkane	RH	C – C (single bond)	H_3C-CH_3
Alkene	R – CH =	C = C	$H_2C=CH_2$
Alkyne	$R-C\equiv CH$	$C\equiv C$ (triple	$HC\equiv CH$
Alkyl halide	RX	-X (X = F, Cl, Br, I)	H_3C-Cl
Alcohol	R – OH	-OH	H_3C-OH
Ether	R – O –R'	- C- O – C -	$H_3C-O-CH_3$
Aldehyde	 $R-\overset{O}{\overset{\Vert}{C}}-H$	 $-\overset{O}{\overset{\Vert}{C}}-H$	 $H-\overset{O}{\overset{\Vert}{C}}-H$, $H_3C-\overset{O}{\overset{\Vert}{C}}-H$
Ketone	 $R-\overset{O}{\overset{\Vert}{C}}-R$	 $-\overset{\vert}{\underset{\vert}{C}}-\overset{O}{\overset{\Vert}{C}}-\overset{\vert}{\underset{\vert}{C}}-$	 $H_3C-\overset{O}{\overset{\Vert}{C}}-CH_3$
Carboxylic	 $R-\overset{O}{\overset{\Vert}{C}}-OH$	 $-\overset{O}{\overset{\Vert}{C}}-OH$	 $H-\overset{O}{\overset{\Vert}{C}}-OH$, $H_3C-\overset{O}{\overset{\Vert}{C}}-OH$
Ester	 $R-\overset{O}{\overset{\Vert}{C}}-OR$	 $-\overset{O}{\overset{\Vert}{C}}-OR$	 $H-\overset{O}{\overset{\Vert}{C}}-OCH_3$ $H_3C-\overset{O}{\overset{\Vert}{C}}-OCH_3$
Amine	$R-NH_2$	 $-\overset{\vert}{\underset{\vert}{C}}-NH_2$	H_3C-NH_2

Fundamentals of Organic Chemistry

CHEM 109

For Students of Health Colleges

Credit hrs.: (2+1)

King Saud University

College of Science, Chemistry Department

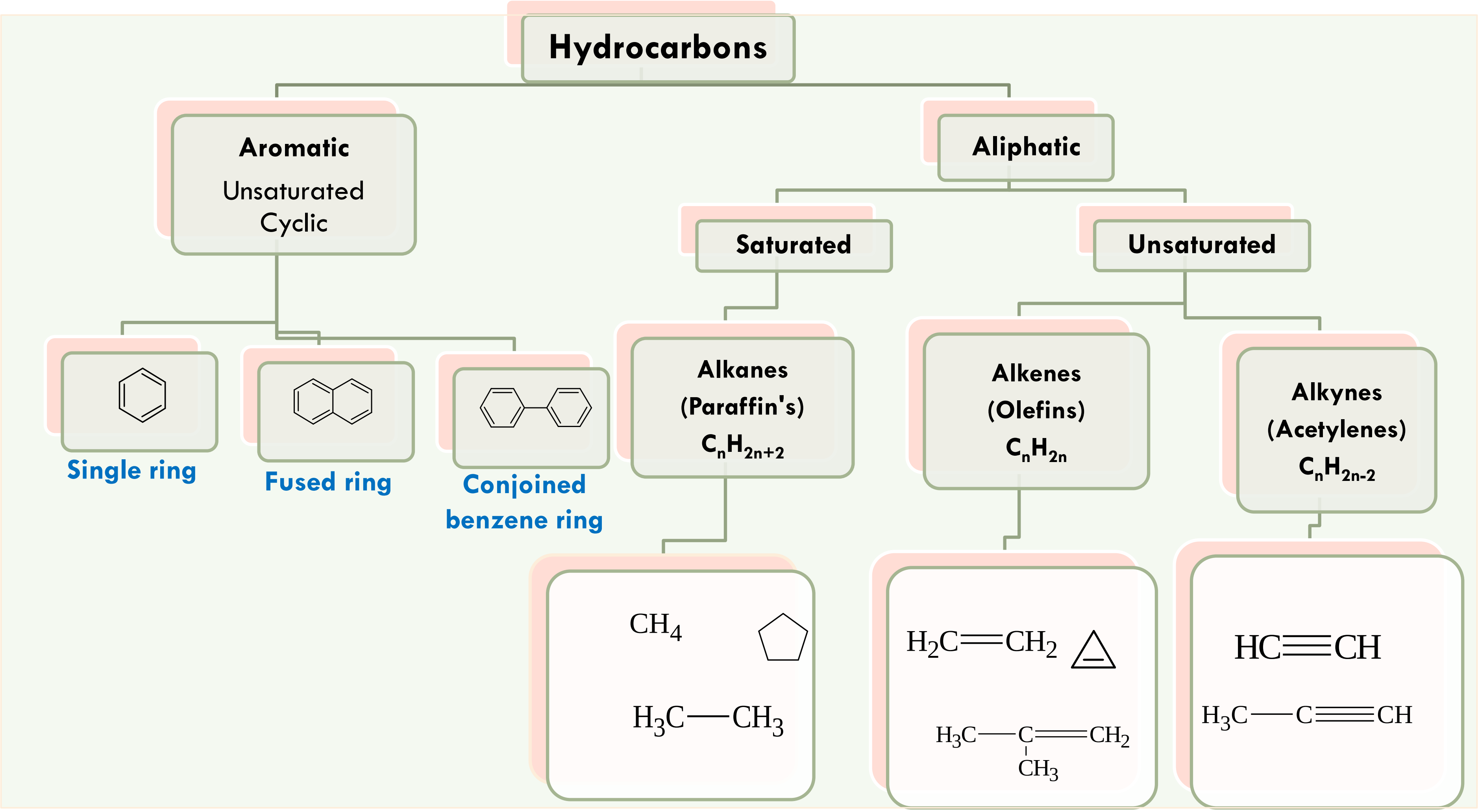
CHAPTER 2. ALIPHATIC HYDROCARBON

Hydrocarbons

- **Hydrocarbons** are Organic Compounds, which contain only the two elements **carbon** and **hydrogen**.
- **Aliphatic hydrocarbons** are subdivided into:
  - ***Saturated hydrocarbons***
    - Alkanes; C_nH_{2n+2} (*contain carbon-carbon single bond*)
    - Cycloalkanes: C_nH_{2n} (*contain carbon-carbon single bond in a single ring*)

    Alkanes and cycloalkanes are so similar that many of their properties can be considered side by side.
  - ***Unsaturated hydrocarbons***
    - Alkenes : C_nH_{2n} (contain *carbon-carbon double bond*)
    - Alkynes : $C_n H_{2n-2}$ (contain *carbon-carbon triple bond*)

Hydrocarbons



Hydrocarbons

Aromatic
Unsaturated
Cyclic

Single ring

Fused ring

Conjoined benzene ring

Aliphatic

Saturated

Alkanes (Paraffin's) C_nH_{2n+2}

CH_4

$H_3C{-}CH_3$

Unsaturated

Alkenes (Olefins) C_nH_{2n}

$H_2C{=}CH_2$

$H_3C{-}\underset{CH_3}{C}{=}CH_2$

Alkynes (Acetylenes) C_nH_{2n-2}

$HC{\equiv}CH$

$H_3C{-}C{\equiv}CH$

Saturated Hydrocarbons

1. Alkanes

- **General formula is C_nH_{2n+2}**
- In **alkanes**, the four *sp*^{3} orbitals of carbon repel each other into a TETRAHEDRAL arrangement with bond angles of 109.5° like in CH_4.
- Each *sp*^{3} orbital in carbon overlaps with the 1s orbital of a hydrogen atom to form a C-H bond.

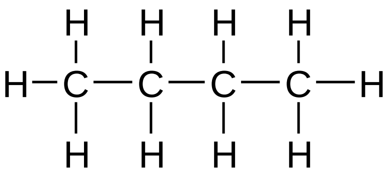
Saturated Hydrocarbons
1. Alkanes

Names, Molecular formulas and Number of Isomers of the first ten Alkanes

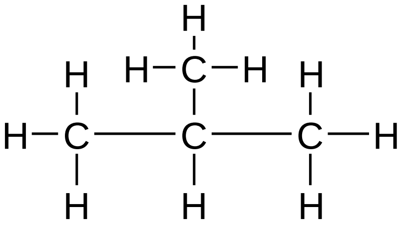
Name	Molecular Formula	Number of isomers
Methane	CH_4	1
Ethane	C_2H_6	1
Propane	C_3H_8	1
Butane	C_4H_{10}	2
Pentane	C_5H_{12}	3
Hexane	C_6H_{14}	5
Heptane	C_7H_{16}	9
Octane	C_8H_{18}	18
Nonane	C_9H_{20}	35
Decane	$C_{10}H_{22}$	75

Structural Isomerism

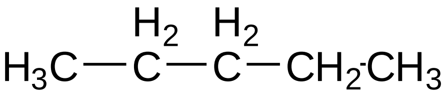
- **Isomers** are different compounds with identical molecular formulas. The phenomenon is called ***isomerism***.
- **Structural** or **constitutional isomers** are isomers which differ in the sequence of atoms bonded to each other.
- **Examples:**
  - **Butanes, C_4H_{10}.**
  - **Pentanes, C_5H_{12}.**



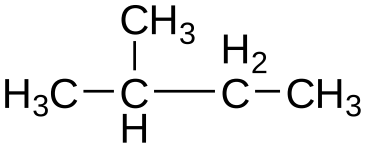
n-Butane



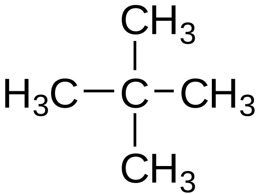
Isobutane



n-Pentane



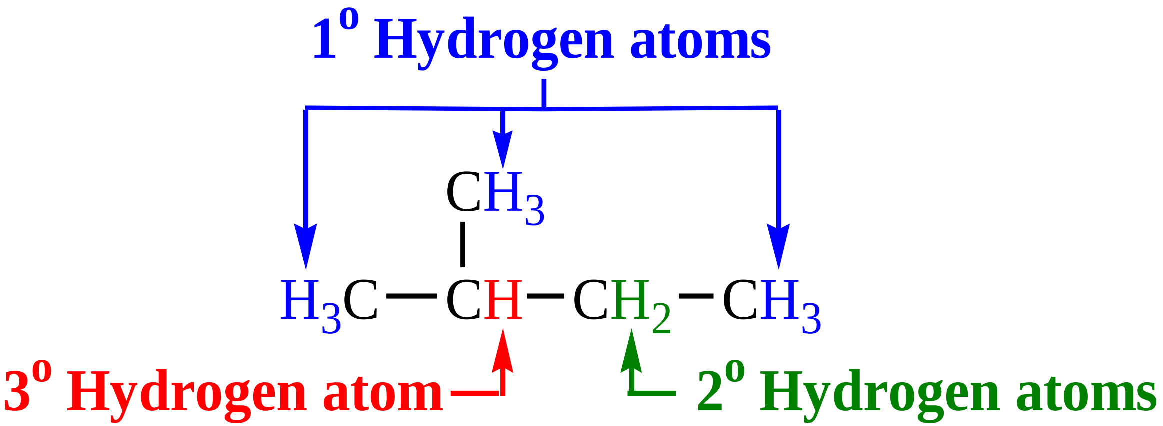
Isopentane



Neopentane

Classes of Carbons and Hydrogen

- **A primary (1°) carbon** is one that is bonded to only one other carbon.
- **A secondary (2°) carbon** is one that is bonded to two other carbons.
- **A tertiary (3°) carbon** is one that is bonded to three other carbons.



- **Hydrogens** are also referred to as 1°, 2°, or 3° according to the type of carbon they are bonded to.

Saturated Hydrocarbons

1. Alkanes

Alkyl Groups

- An **alkyl group** is an alkane from which a hydrogen has been removed.
- **General formula C_nH_{2n+1}.**
- **Alky group** is represented by **R**.
- **Nomenclature of alkyl groups by**

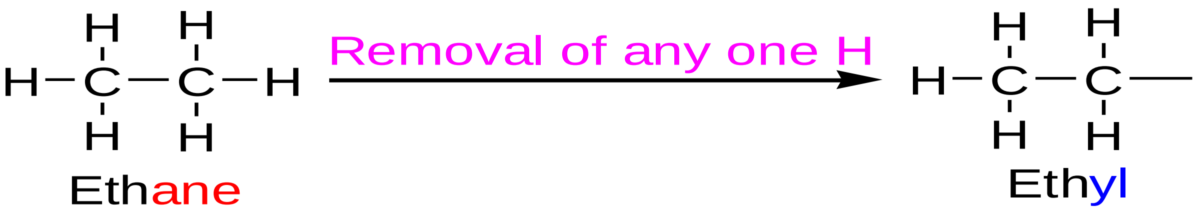
  replacing the suffix – *ane* of the parent alkane by *–yl*.

  i.e. Alkane – ane + yl = Alkyl
- **Examples:**
  - ***Methane***

CH_3- (Methane – ane + yl) = methyl

Alkyl Groups

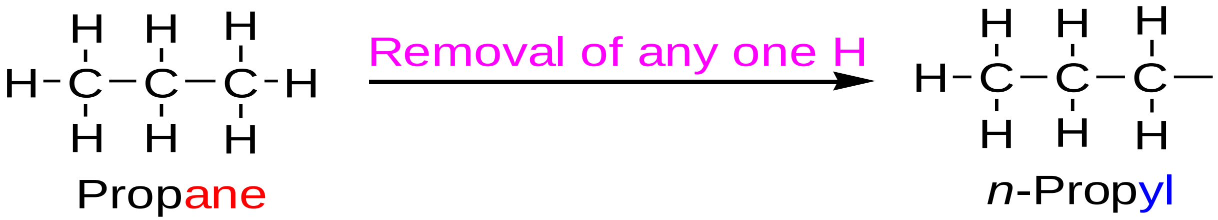
- **Ethane**



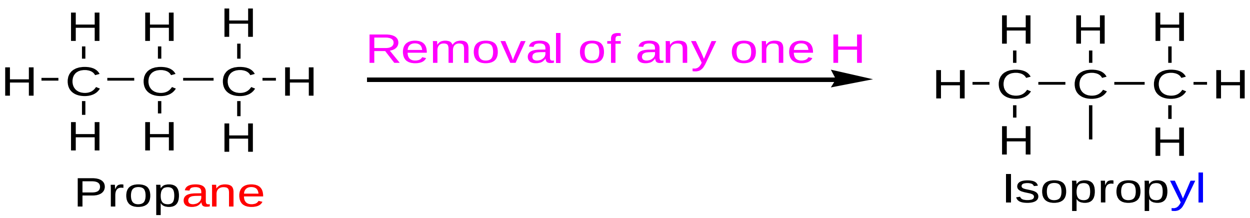
or CH_3CH_2-

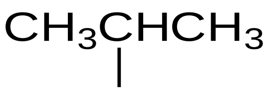
CH_3CH_2- (Ethane – ane + yl) = ethyl

- **Propane**



or $CH_3CH_2CH_2$-

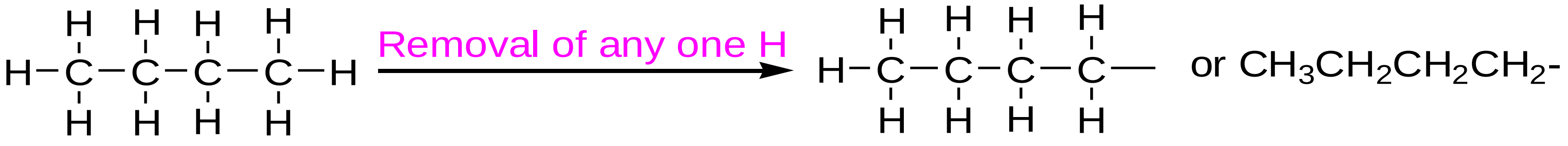


or 
$CH_3\underset{|}{C}HCH_3$

Propane – ane + yl = *n*-propyl or isopropyl

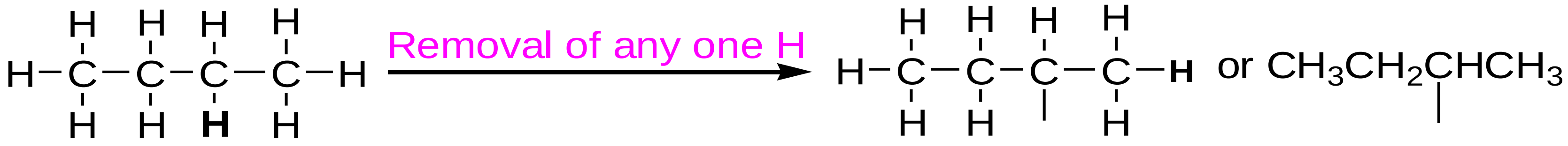
Alkyl Groups

- ***Butane***



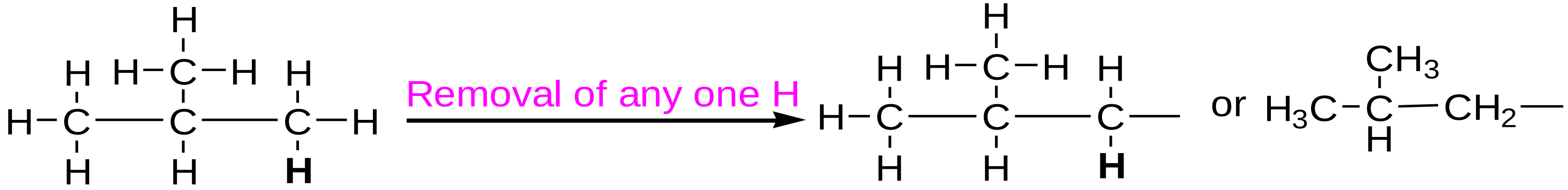
or $CH_3CH_2CH_2CH_2$-

Butane → Butyl



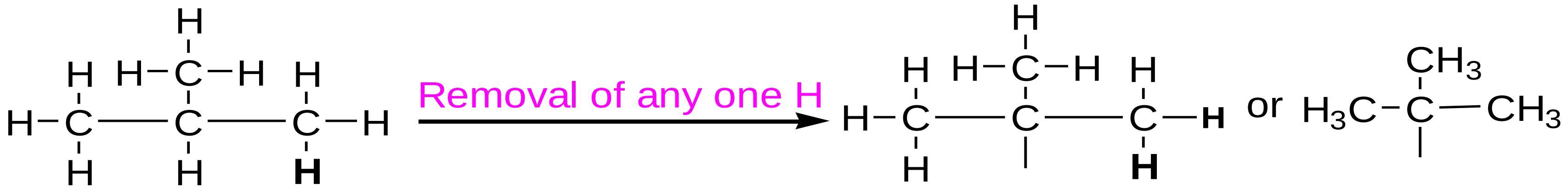
or $CH_3CH_2\underset{|}{C}HCH_3$

Butane → *sec*-Butyl



or $H_3C-\overset{CH_3}{\underset{H}{C}}-CH_2-$

Isobutane → Isobutyl



or $H_3C-\overset{CH_3}{\underset{|}{C}}-CH_3$

Isobutane → *tert*-butyl or *t*-butyl

Alkyl Groups

Alkane		Alkyl Group	Abbreviation
CH_3—H **Methane**	becomes	CH_3— **Methyl**	Me–
CH_3CH_2—H **Ethane**	becomes	CH_3CH_2— **Ethyl**	Et–
$CH_3CH_2CH_2$—H **Propane**	becomes	$CH_3CH_2CH_2$— **Propyl**	Pr–
$CH_3CH_2CH_2CH_2$—H **Butane**	becomes	$CH_3CH_2CH_2CH_2$— **Butyl**	Bu–

Nomenclature

- Most organic compounds are known by two or more names:
  - The older unsystematic names, (*Common names*).
  - The IUPAC names.

International Union of Pure & Applied Chemistry

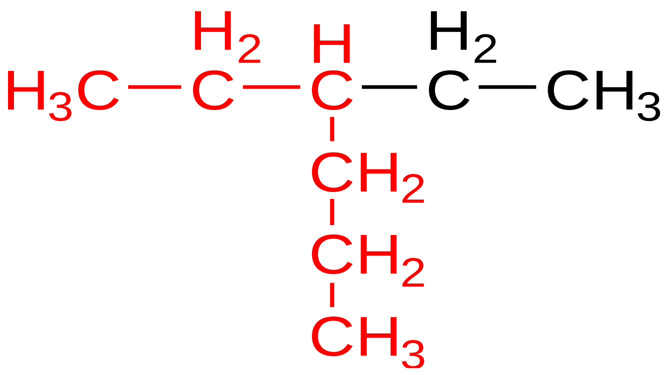
Saturated Hydrocarbons
1. Alkanes

Nomenclature

The IUPAC Rules

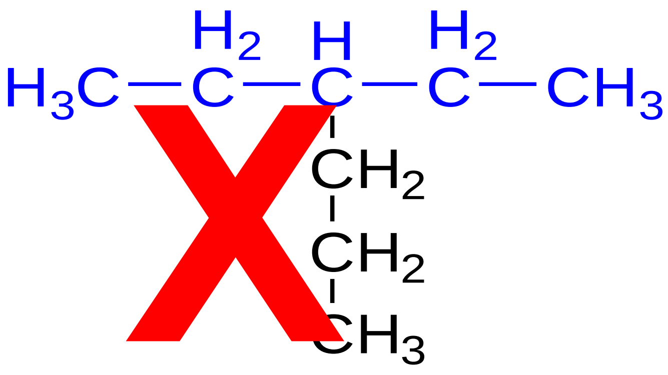
1) **Select the parent structure .**

the longest continuous chain



Ethyl hexane

not



Propyl pentane

The longest continuous chain is not necessarily straight.

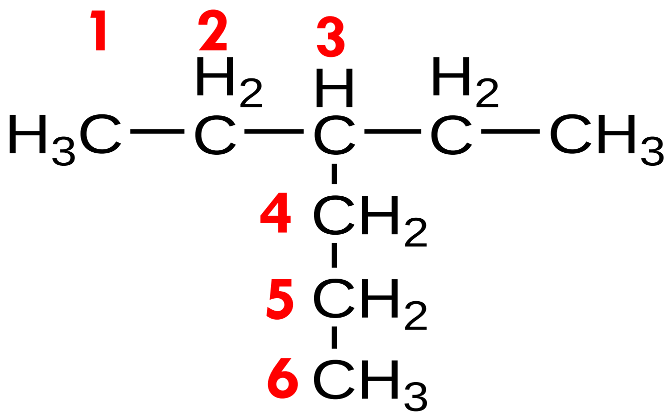
Saturated Hydrocarbons
1. Alkanes

Nomenclature

The IUPAC Rules

2) Number the carbons in the parent chain

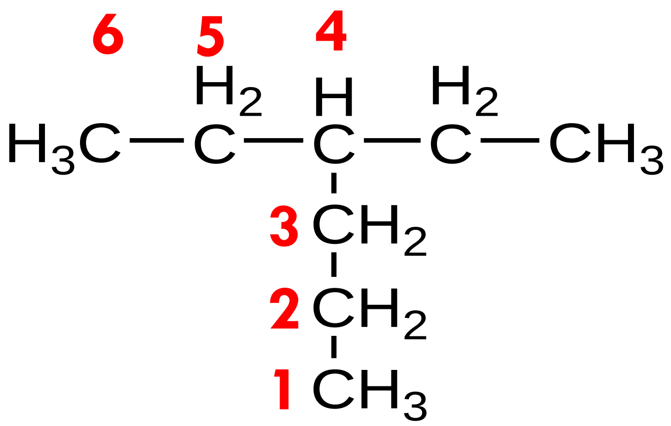
starting from the end which gives the lowest number for the substituent



$H_3C-\overset{H_2}{C}-\overset{H}{\underset{CH_2CH_2CH_3}{C}}-\overset{H_2}{C}-CH_3$

3-Ethyl hexane

not



$H_3C-\overset{H_2}{C}-\overset{H}{\underset{CH_2CH_2CH_3}{C}}-\overset{H_2}{C}-CH_3$

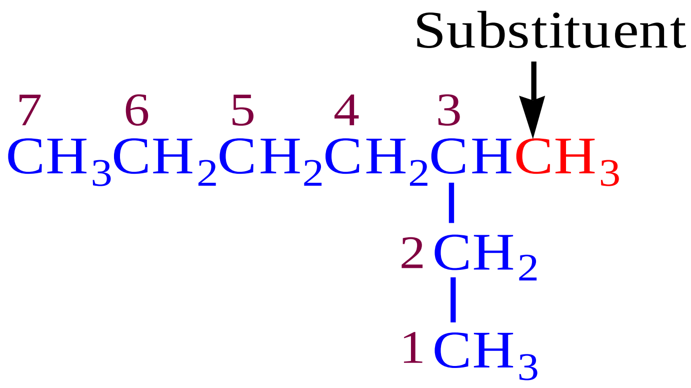
~~**4-Ethyl hexane**~~

Saturated Hydrocarbons
1. Alkanes

Nomenclature

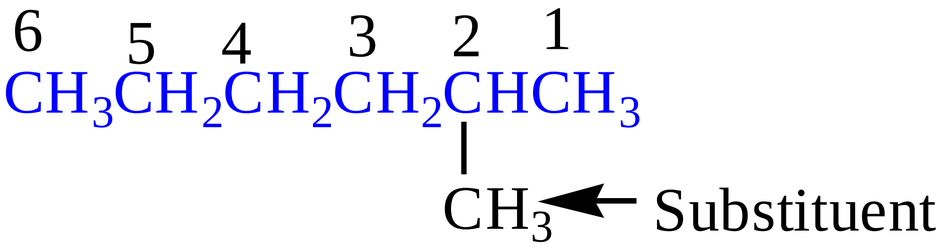
The IUPAC Rules

2) Number the carbons in the parent chain



$$\overset{7}{\mathrm{CH_3}}\overset{6}{\mathrm{CH_2}}\overset{5}{\mathrm{CH_2}}\overset{4}{\mathrm{CH_2}}\underset{\substack{|\\ 2\,\mathrm{CH_2}\\ |\\ 1\,\mathrm{CH_3}}}{\overset{3}{\mathrm{CH}}}\mathrm{CH_3}$$

3-Methylheptane



$$\overset{6}{\mathrm{CH_3}}\overset{5}{\mathrm{CH_2}}\overset{4}{\mathrm{CH_2}}\overset{3}{\mathrm{CH_2}}\underset{\substack{|\\ \mathrm{CH_3}}}{\overset{2}{\mathrm{CH}}}\overset{1}{\mathrm{CH_3}}$$

2-Methylpentane

Nomenclature

The IUPAC Rules

To name the compound;

1) The position of the substituent on the parent carbon chain by a number.
2) The number is followed by a hyphen (-).
3) The combined name of the substituent (ethyl).
4) The parent carbon chain (hexane)

3 - Ethyl hexane

Saturated Hydrocarbons
1. Alkanes

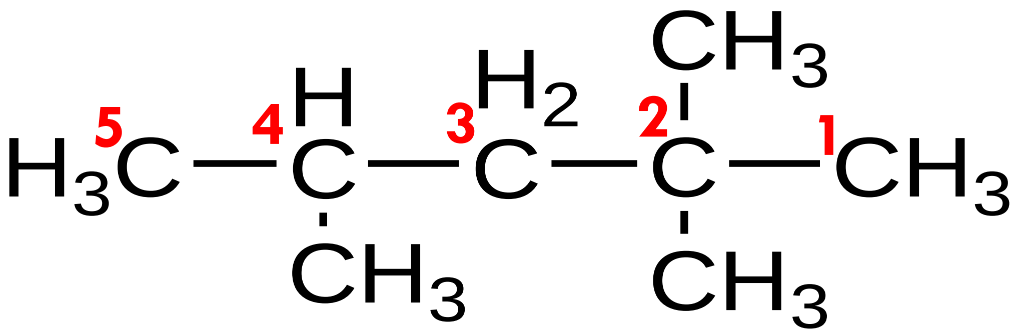
Nomenclature

The IUPAC Rules

3) If the **same alkyl substituent** occurs more than once on the parent carbon chain,

the prefixes di-, tri-, tetra-, penta-, and so on

are used to indicate two, three, four, five, and so on.



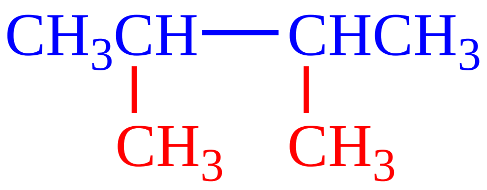
$$H_3C-\underset{CH_3}{\overset{H}{C}}-\overset{H_2}{C}-\underset{CH_3}{\overset{CH_3}{C}}-CH_3$$

2,2,4- Tri methyl pentane

Saturated Hydrocarbons
1. Alkanes

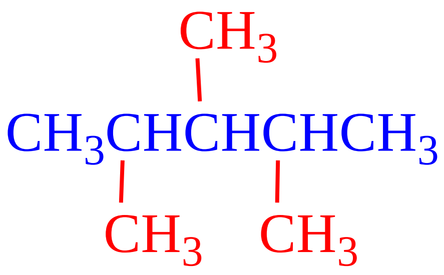
Nomenclature

The IUPAC Rules



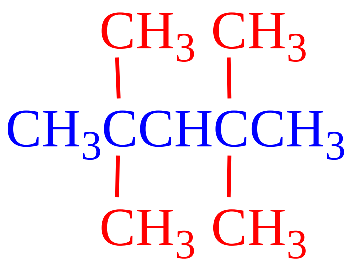
$$CH_3\underset{\underset{CH_3}{|}}{CH}-\underset{\underset{CH_3}{|}}{CH}CH_3$$

2,3-Dimethylbutane



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

2,3,4-Trimethylpentane



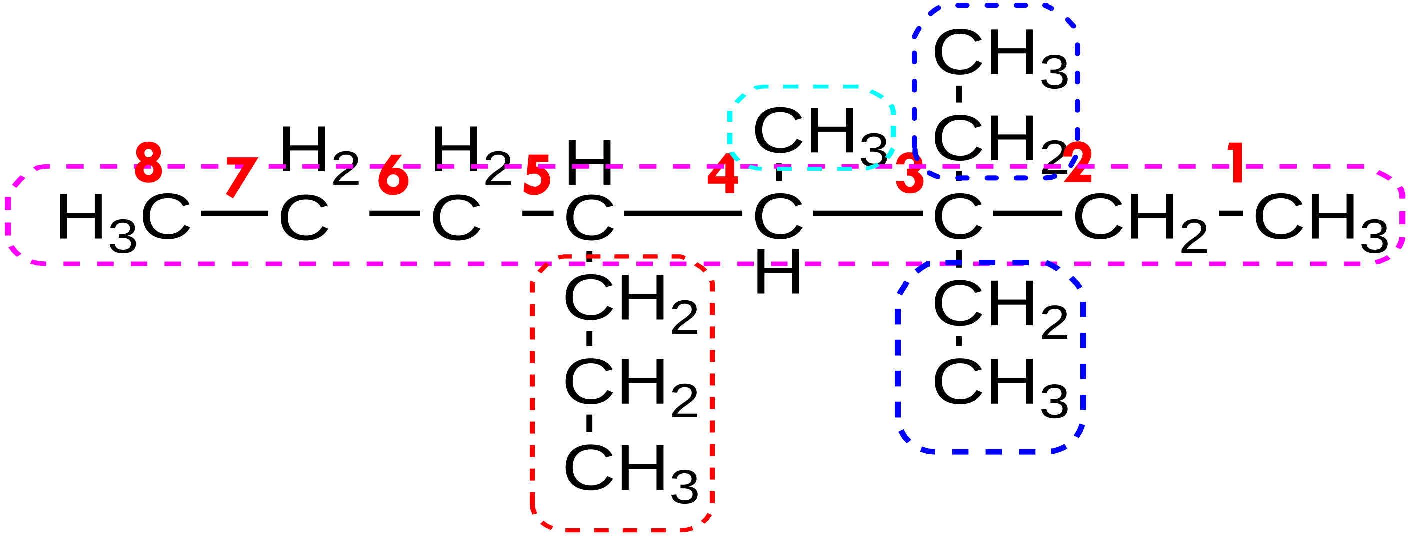
$$CH_3\overset{\overset{CH_3}{|}}{\underset{\underset{CH_3}{|}}{C}}CH\overset{\overset{CH_3}{|}}{\underset{\underset{CH_3}{|}}{C}}CH_3$$

2,2,4,4-Tetramethylpentane

The IUPAC Rules

4) If **different alkyl substituents** are attached on the parent carbon chain,

they are named in order of alphabetical order.



3,3- di ethyl
4- methyl
5- propyl

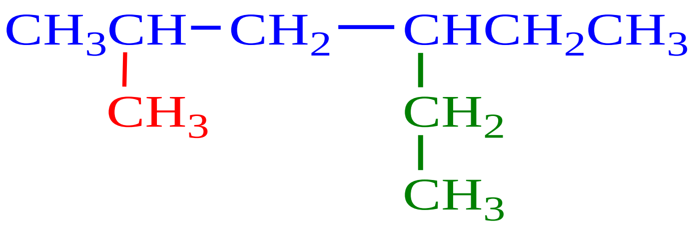
3,3-Diethyl -4-methyl - 5-propyl octane

Saturated Hydrocarbons
1. Alkanes

Nomenclature

The IUPAC Rules

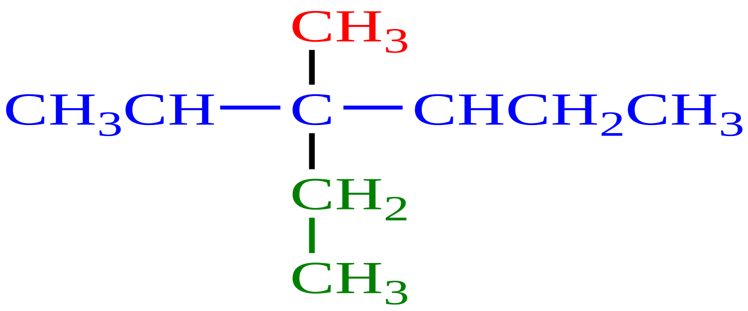
Note that each substituent is given a number corresponding to its location on the longest chain. The substituent groups are listed alphabetically.



$$\underset{CH_3}{CH_3CH}-CH_2-\underset{\underset{CH_3}{CH_2}}{CHCH_2CH_3}$$

4-Ethyl-2-methylhexane

5) When two substituent are present on the same carbon, use the number twice.



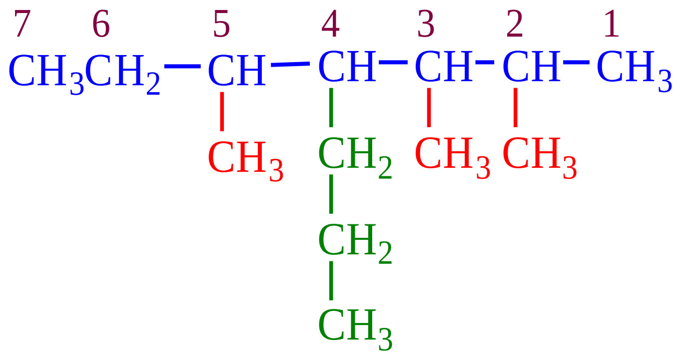
$$CH_3CH-\overset{CH_3}{\underset{\underset{CH_3}{CH_2}}{C}}-CHCH_2CH_3$$

3-Ethyl-3-methylhexane

Nomenclature

The IUPAC Rules

6) When two chains of equal length compete for selection as the parent chain, choose the chain with the greater number of substituents.



$$\underset{7}{CH_3}\underset{6}{CH_2}-\underset{CH_3}{\underset{|}{\overset{5}{CH}}}-\underset{CH_2CH_2CH_3}{\underset{|}{\overset{4}{CH}}}-\underset{CH_3}{\underset{|}{\overset{3}{CH}}}-\underset{CH_3}{\underset{|}{\overset{2}{CH}}}-\overset{1}{CH_3}$$

2,3,5-Trimethyl-4-*n*-propylheptane

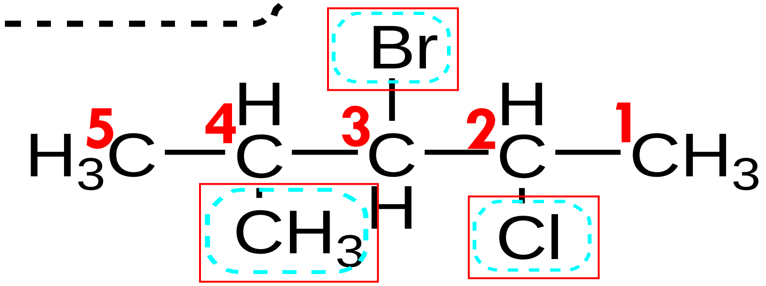
Saturated Hydrocarbons
1. Alkanes

Nomenclature

The IUPAC Rules

7) If **substituents other than alky groups** are also presents on the parent carbon chain; all substituents are named alphabetically.

-F	fluoro
-Cl	chloro
-Br	bromo
-I	iodo
$-NO_2$	nitro
$-NH_2$	amino
-CN	cyano


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

2-chloro
3-bromo
4- methyl

3-bromo -2-chloro -4-methyl pentane

Saturated Hydrocarbons
1. Alkanes

Sources of Alkanes

○ The two principal sources of alkanes are petroleum and natural gas.

Petroleum and natural gas constitute the chief sources of

- Alkanes up to 40 Carbons
- Aromatic
- Alicyclic (Cyclic aliphtic hydrocarbons)
- Heterocyclic

Saturated Hydrocarbons
1. Alkanes

Sources of Alkanes

Petroleum Refining

Some components of refined petroleum

Fraction	Boiling range (°C)	Caron content
Gas	Below 20	C1 – C4
Petroleum ether	20 – 60	C5 – C6
Naphtha	60 – 100	C6 – C7
Gasoline	40 – 200	C5 – C10
Kerosine	175 – 325	C11 – C18
Gas oil	300 – 500	C15 – C40
Lubricating oil, asphalt,	Above 400	C15 – C40

Physical Properties of Alkanes, Alkenes and Alkynes

Those properties that can be observed without the compound undergoing a chemical reaction.

A. Physical States

C1 (C2) to C4 are gases,
C5 to C17 are liquids,
C18 and larger alkanes are wax –like solids.

B. Solubility

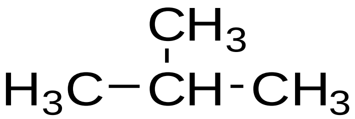
- Alkanes, Alkenes and Alkynes are nonpolar compounds.
- Their solubility " Like dissolve like"
- Alkanes, Alkenes and Alkynes are soluble in the nonpolar solvents;
  carbon tetrachloride, CCl_4 and benzene,
- Alkanes, Alkenes and Alkynes are insoluble in polar solvents like water.

C. Boiling Points

$CH_3CH_2CH_2CH_3$

n-Butane

b.p.=0°C



$H_3C-\overset{CH_3}{\overset{|}{C}}H-CH_3$

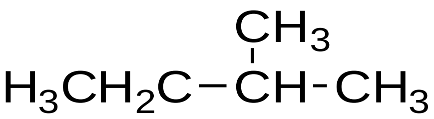
Isobutane

b.p.=-12°C

$CH_3CH_2CH_2CH_2CH_3$

n-Pentane

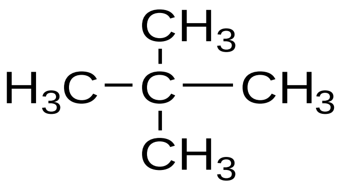
b.p.=36°C



$H_3CH_2C-\overset{CH_3}{\overset{|}{C}}H-CH_3$

Isopentane

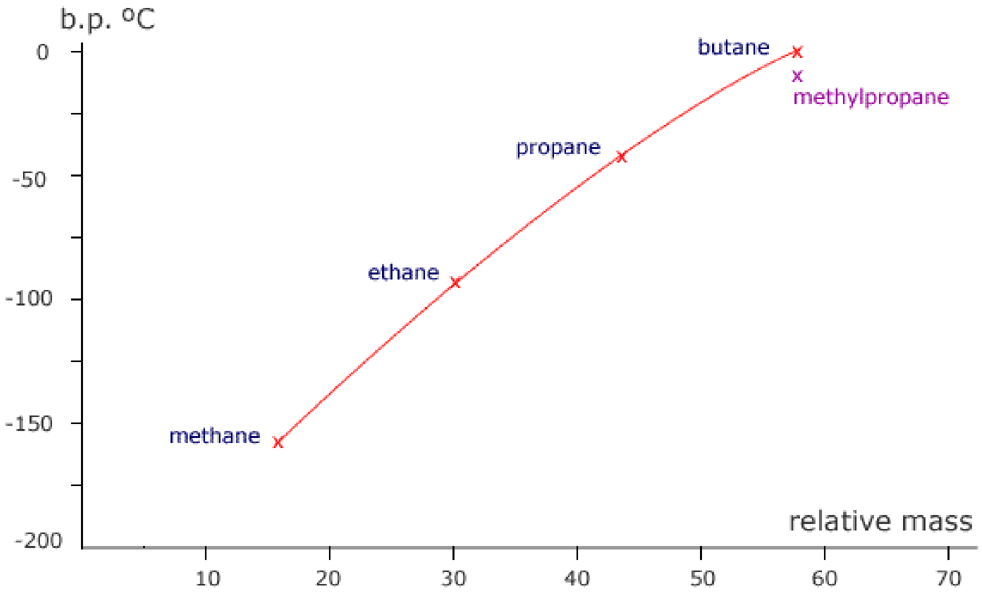
b.p.=28°C



$H_3C-\underset{CH_3}{\underset{|}{\overset{CH_3}{\overset{|}{C}}}}-CH_3$

Neopentane

b.p.=9.5°C



Graph showing boiling point of the alkanes against relative mass

- ○ Boiling point decreases with increasing branches
- ○ Boiling point increases with increasing molecular weight.

Preparation of Alkanes

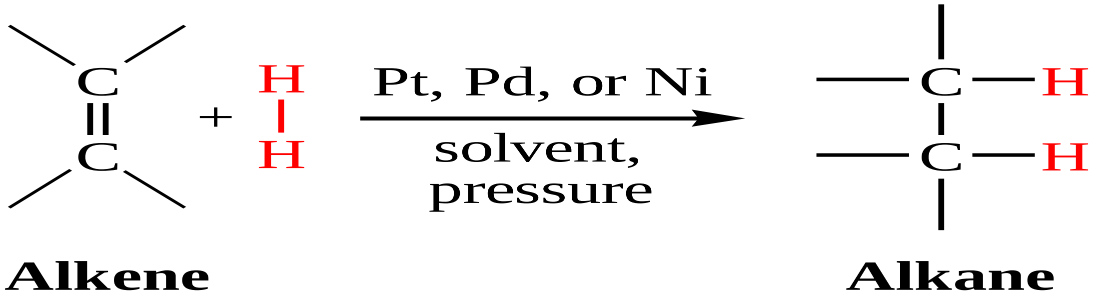
1) Hydrogenation of Alkenes and Alkynes

A great number of alkanes can be obtained by fractional distillation of crude petroleum and subsequent reactions as follows:

1. **Catalytic hydrogenation:**

   Alkenes and alkynes react with hydrogen in the presence of metal catalysts such as nickel, palladium, and platinum to produce alkanes.

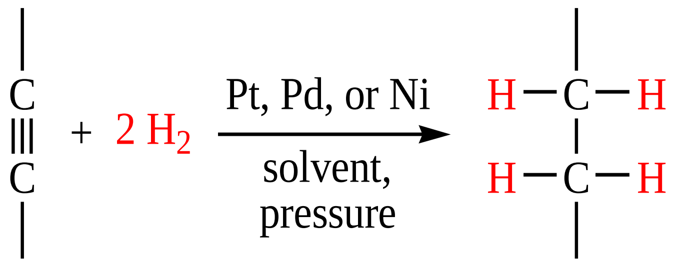
General Reaction



Saturated Hydrocarbons
1. Alkanes

Preparation of Alkanes

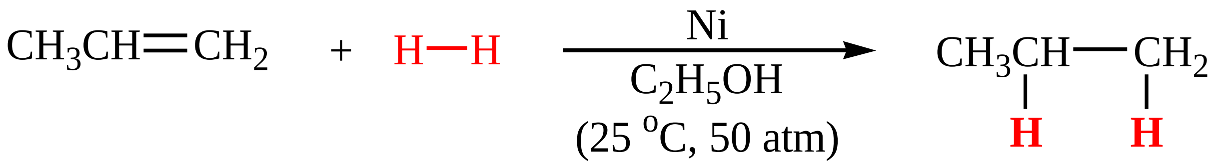
1) Hydrogenation of Alkenes and Alkynes



$$\mathrm{-C{\equiv}C-} + 2\,H_2 \xrightarrow[\text{solvent, pressure}]{\text{Pt, Pd, or Ni}} \mathrm{-\overset{\displaystyle H}{\underset{\displaystyle H}{C}}-\overset{\displaystyle H}{\underset{\displaystyle H}{C}}-}$$

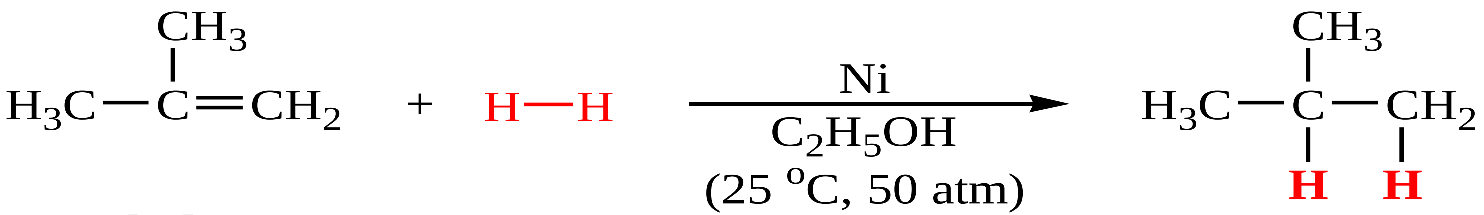
Alkyne **Alkane**

- *Specific Examples*



$$CH_3CH{=}CH_2 + H{-}H \xrightarrow[\substack{C_2H_5OH \\ (25\ ^oC,\ 50\ atm)}]{Ni} \underset{\displaystyle H}{CH_3CH}{-}\underset{\displaystyle H}{CH_2}$$

propene **propane**



$$H_3C{-}\overset{\displaystyle CH_3}{C}{=}CH_2 + H{-}H \xrightarrow[\substack{C_2H_5OH \\ (25\ ^oC,\ 50\ atm)}]{Ni} H_3C{-}\overset{\displaystyle CH_3}{\underset{\displaystyle H}{C}}{-}\underset{\displaystyle H}{CH_2}$$

2-Methylpropene **Isobutane**

2) Hydrolysis of Grignard Reagent

$$R{-}MgX + HOH \longrightarrow RH + MgX(OH)$$

Alkyl magnesium halide
(Grignard reagent)

- *Grignard reagents* **react readily with any source of protons to give hydrocarbons.**

$$CH_3CH_2Br + Mg \xrightarrow{\text{Dry Ether}} CH_3CH_2MgBr$$

Ethyl bromide → Ethyl magnesium bromide (Grignard reagent)

$$CH_3CH_2MgBr + HOH \longrightarrow CH_3CH_3 + MgBr(OH)$$

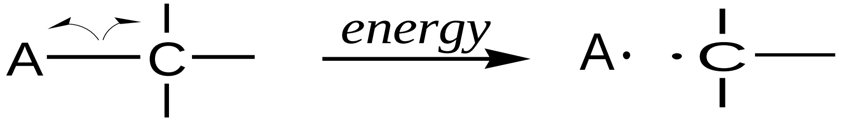
Ethane

3) By coupling of alkyl halides with dialkyl cuprate (all kinds of alkanes)

$$(CH_3CH_2)_2CuLi \xrightarrow{CH_3Br} CH_3CH_2CH_3$$

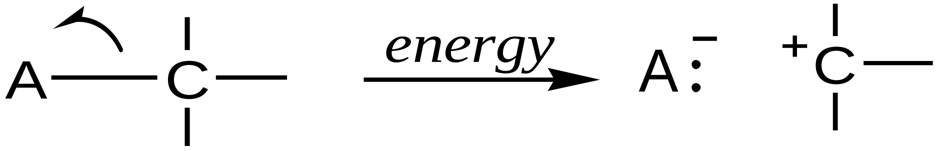
Notations for bond breaking and bond making

- **A covalent bond can be broken in either two ways,**
  - **Homolytic cleavage.**

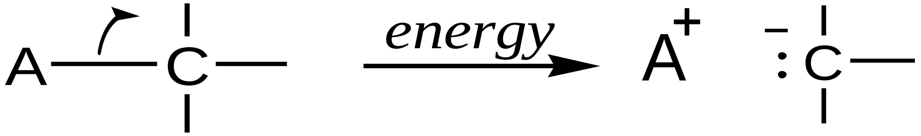


Free radicals

  - **Heterolytic cleavage.**



Carbocation



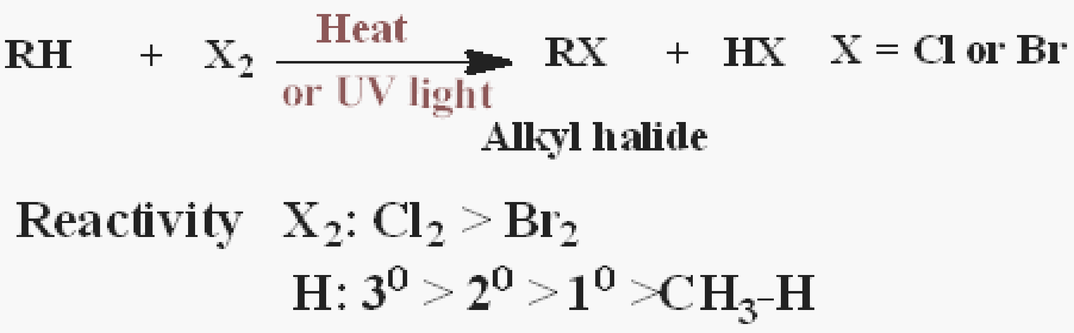
Carboanion

Reactions of Alkanes

Saturated hydrocarbons undergo very few reactions, so they are called Paraffinic hydrocarbons. (Latin *parum*, little; *affinis*, affinity)

Halogenation

The halogenation of an alkane appears to be a simple free radical substitution in which a C-H bond is broken and a new C-X bond is formed

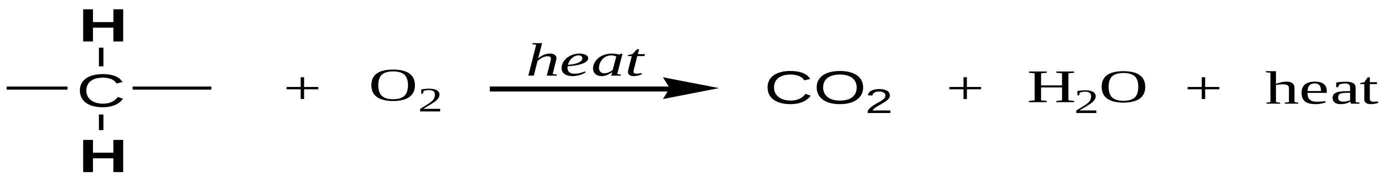


$$RH + X_2 \xrightarrow[\text{or UV light}]{\text{Heat}} \underset{\text{Alkyl halide}}{RX} + HX \quad X = Cl \text{ or } Br$$

Reactivity $X_2: Cl_2 > Br_2$

$H: 3^0 > 2^0 > 1^0 > CH_3\text{-}H$

Combustion



$$-\overset{H}{\underset{H}{C}}- + O_2 \xrightarrow{heat} CO_2 + H_2O + \text{heat}$$

An alkane

Reactions of Alkanes

A. Halogenation

- **Substitution reaction of alkanes,**

  i.e. replacement of hydrogen by halogen,
  usually chlorine or bromine, giving alkyl chloride or alkyl bromide.

- **Flourine reacts explosively with alkanes**

  It is unsuitable reagent for the preparation of the alkyl flourides.

- **Iodine is too unreactive**

  It is not used in the halogentaion of alkanes.

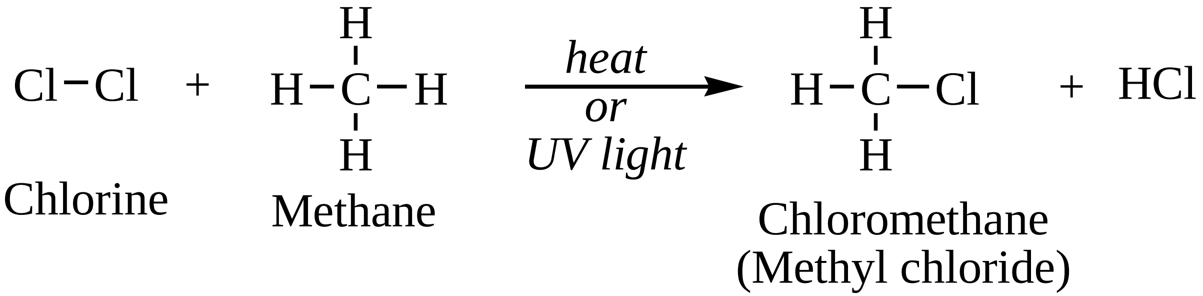
- **Halogenation of alkanes take place at**

  high temperatures or under the influence of ultraviolet light

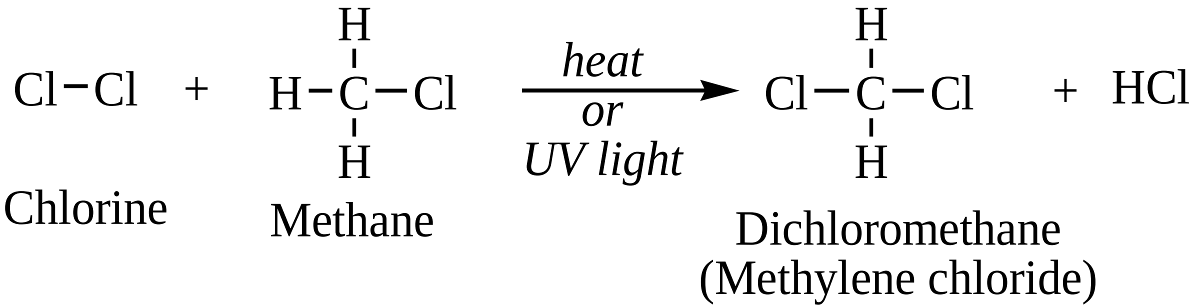
Reactions of Alkanes

A. Halogenation

- Chlorination of an alkane usually gives a mixture of products



$$Cl-Cl + CH_4 \xrightarrow[\text{or UV light}]{\text{heat}} CH_3Cl + HCl$$



$$Cl-Cl + CH_3Cl \xrightarrow[\text{or UV light}]{\text{heat}} CH_2Cl_2 + HCl$$

2. ALKENES

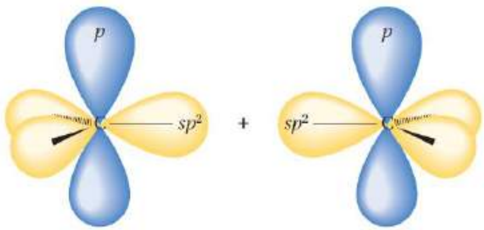
The Structure of Alkenes

- **Alkenes** are ydrocarbons that contain a ***carbon–carbon double bond***.
- **Alkenes are also *Olefins*.**
- **General formula is C_nH_{2n}**
- The simplest members of the **Alkenes** series are **C_2 & C_3**

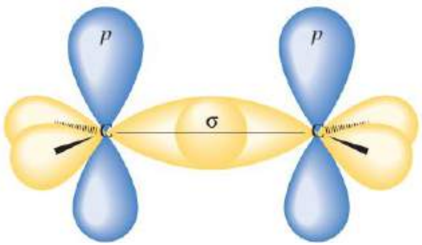
	$CH_2=CH_2$	$H_3C-CH=CH_2$
Common name:	Ethylene	Propylene
IUPAC name:	Ethene	Propene

The Structure of Alkenes

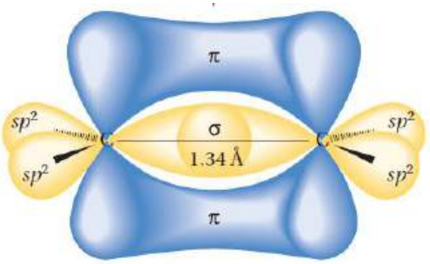
- Hybridization; ***sp*^{2}-hybridized orbitals**
- The angle between them is 120° and bond length C=C (1.34 Å).
- A **trigonal planar.**



two *sp*^{2}-hybridized carbons with *p* orbitals parallel



the σ bond is formed by two electrons in overlapping *sp*^{2} orbitals



the π bond is formed by two electrons in overlapping parallel *p* orbitals

Nomenclature of Alkenes

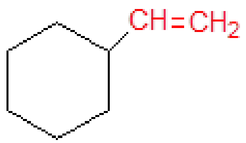
Common Names

- The simplest members of the alkene and alkyne series are frequently referred to by their older common names, ethylene, acetylene, and propylene.

$CH_2{=}CH_2$	$HC{\equiv}CH$	$CH_3CH{=}CH_2$
ethylene	acetylene	propylene
(ethene)	(ethyne)	(propene)

- Two important groups also have common names; They are the **vinyl** and **allyl** groups.
- These groups are used in common names.

$CH_2{=}CH{-}$	$CH_2{=}CHCl$
vinyl	vinyl chloride
(ethenyl)	(chloroethene)
$CH_2{=}CH{-}CH_2{-}$	$CH_2{=}CH{-}CH_2Cl$
allyl	allyl chloride
(2-propenyl)	(3-chloropropene)



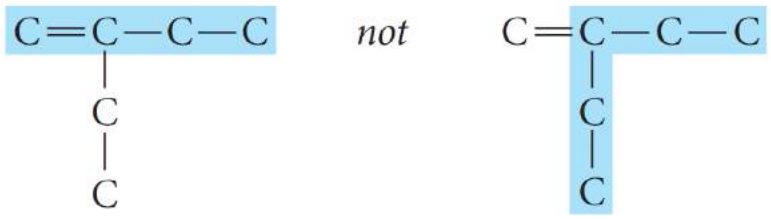
Common name: Vinyl cyclohexane
IUPAC name: Cyclohexylethene

Nomenclature of Alkenes

The IUPAC Rules

The IUPAC rules for naming alkenes are similar to those for alkanes, but a few rules must be added for naming and locating the multiple bonds.

1. The ending ***-ene*** is used to designate a carbon–carbon double bond.
2. Select the **longest chain that includes *both <u>carbons of the double bond</u>***.

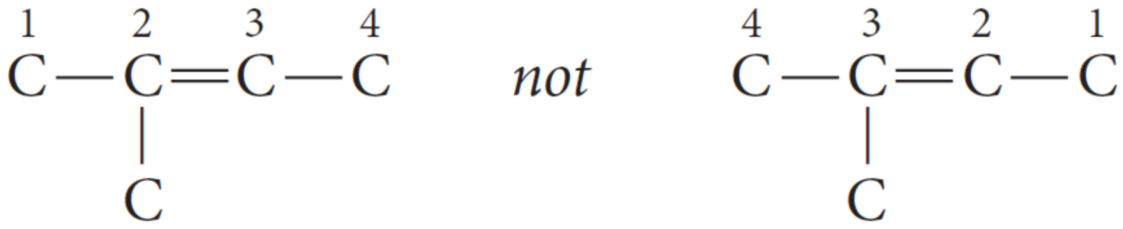


3. **Number the chain from the end nearest the double bond** so that the carbon atoms in that bond have the lowest possible numbers.


$$\overset{1}{C}-\overset{2}{C}=\overset{3}{C}-\overset{4}{C}-\overset{5}{C} \quad \textit{not} \quad \overset{5}{C}-\overset{4}{C}=\overset{3}{C}-\overset{2}{C}-\overset{1}{C}$$

Nomenclature of Alkenes

If the multiple bond is equidistant from both ends of the chain, number the chain from the end nearest the first branch point.



4. Indicate the **position of the multiple bond using the *lower numbered carbon atom*** of that bond.

$\overset{1}{\mathrm{CH_2}}{=}\overset{2}{\mathrm{C}}\mathrm{H}\overset{3}{\mathrm{C}}\mathrm{H_2}\overset{4}{\mathrm{C}}\mathrm{H_3}$ 1-butene, *not* 2-butene

Nomenclature of Alkenes

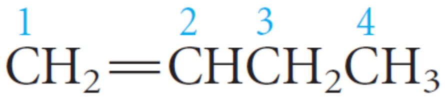
NOTES

The root of the name (*eth-* or *prop-*) tells us the number of carbons, and the ending (*-ane*, -*ene*, or -*yne*) tells us whether the bonds are single, double, or triple.

No number is necessary in these cases, because in each instance, only one structure is possible.

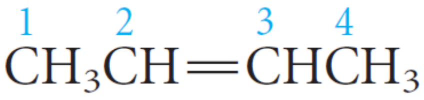
CH_3CH_3 ethane	$CH_2{=}CH_2$ ethene	$HC{\equiv}CH$ ethyne
$CH_3CH_2CH_3$ propane	$CH_2{=}CHCH_3$ propene	$HC{\equiv}CCH_3$ propyne

With four carbons, a number is necessary to locate the double bond.



$$\overset{1}{C}H_2{=}\overset{2}{C}H\overset{3}{C}H_2\overset{4}{C}H_3$$

1-butene

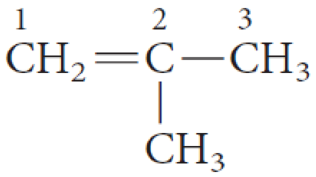


$$\overset{1}{C}H_3\overset{2}{C}H{=}\overset{3}{C}H\overset{4}{C}H_3$$

2-butene

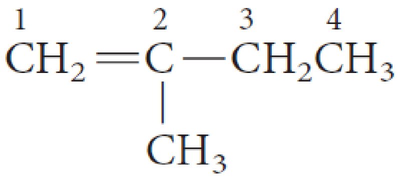
Nomenclature of Alkenes

- Branches are named in the usual way.



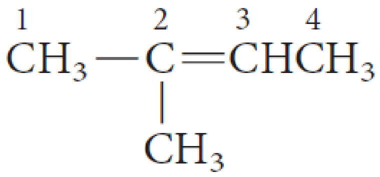
$\overset{1}{\mathrm{CH_2}}{=}\underset{\substack{|\\ \mathrm{CH_3}}}{\overset{2}{\mathrm{C}}}{-}\overset{3}{\mathrm{CH_3}}$

methylpropene
(isobutylene)



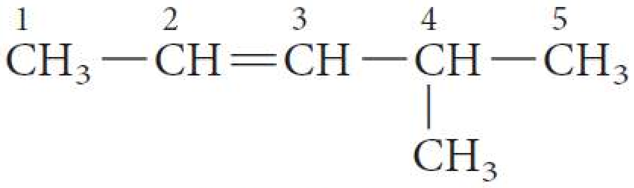
$\overset{1}{\mathrm{CH_2}}{=}\underset{\substack{|\\ \mathrm{CH_3}}}{\overset{2}{\mathrm{C}}}{-}\overset{3}{\mathrm{CH_2}}\overset{4}{\mathrm{CH_3}}$

2-methyl-1-butene



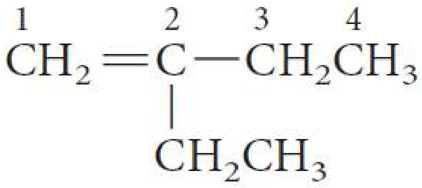
$\overset{1}{\mathrm{CH_3}}{-}\underset{\substack{|\\ \mathrm{CH_3}}}{\overset{2}{\mathrm{C}}}{=}\overset{3}{\mathrm{CH}}\overset{4}{\mathrm{CH_3}}$

2-methyl-2-butene



$\overset{1}{\mathrm{CH_3}}{-}\overset{2}{\mathrm{CH}}{=}\overset{3}{\mathrm{CH}}{-}\underset{\substack{|\\ \mathrm{CH_3}}}{\overset{4}{\mathrm{CH}}}{-}\overset{5}{\mathrm{CH_3}}$

4-methyl-2-pentene
(*Not* 2-methyl-3-pentene; the chain is numbered so that the double bond gets the lower number.)

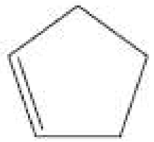


$\overset{1}{\mathrm{CH_2}}{=}\underset{\substack{|\\ \mathrm{CH_2CH_3}}}{\overset{2}{\mathrm{C}}}{-}\overset{3}{\mathrm{CH_2}}\overset{4}{\mathrm{CH_3}}$

2-ethyl-1-butene
(Named this way, even though there is a five-carbon chain present, because that chain does not include both carbons of the double bond.)

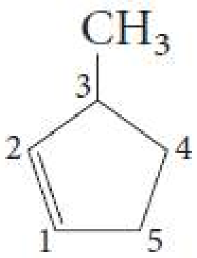
Nomenclature of Alkenes

- With **cyclic hydrocarbons**, we start numbering the ring with the carbons of the double bond.



cyclopentene

(No number is necessary, because there is only one possible structure.)



3-methylcyclopentene

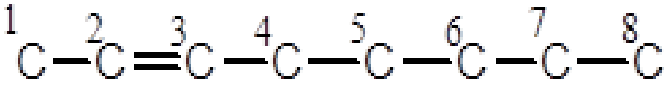
(Start numbering at, and number through the double bond; 5-methylcyclopentene and 1-methyl-2-cyclopentene are incorrect names.)

Nomenclature of Alkenes

Example: **Write the structural formula of 4-Isopropyl-3,5-dimethyl-2-octene.**

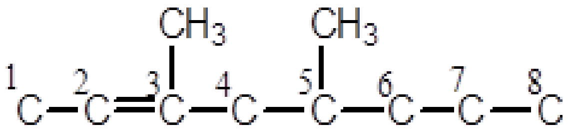
1) The parent carbon chain is an **Octene.**

The double bond is located between the 2nd and 3rd carbons.



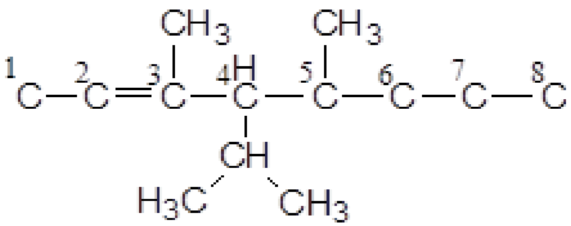
$\overset{1}{C}-\overset{2}{C}=\overset{3}{C}-\overset{4}{C}-\overset{5}{C}-\overset{6}{C}-\overset{7}{C}-\overset{8}{C}$

2) Two **methyl groups** are attached on the parent carbon chain, one on carbon 3 and the other on **carbon 5.**

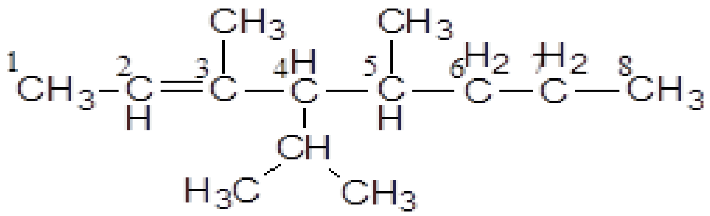


$\overset{1}{C}-\overset{2}{C}=\overset{CH_3}{\overset{|}{\overset{3}{C}}}-\overset{4}{C}-\overset{CH_3}{\overset{|}{\overset{5}{C}}}-\overset{6}{C}-\overset{7}{C}-\overset{8}{C}$

3) An **isopropyl group** is attached on **carbon 4.**



4) Put the missing hydrogens to get the correct structure.

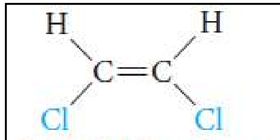


Geometric Isomerism in Alkenes

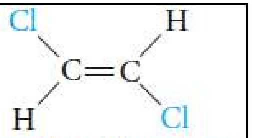
- In **alkenes**, geometric isomerism is due to restricted rotation about the carbon - carbon double bond.

Geometric isomers

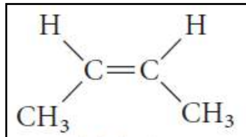
A) when W differs from X and Y from Z, Alkenes exist as geometric isomers



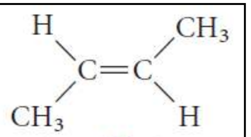
cis-1,2-dichloroethene
bp 60°C, mp −80°C



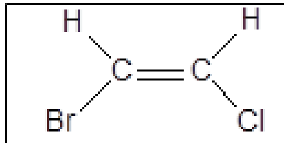
trans-1,2-dichloroethene
bp 47°C, mp −50°C



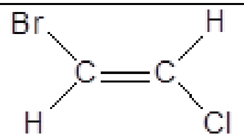
cis-2-butene
bp 3.7°C, mp −139°C



trans-2-butene
bp 0.3°C, mp −106°C



cis-1-Bromo-2-chloroethene

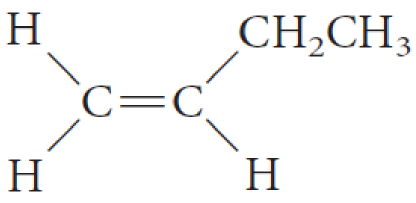


trans-1-Bromo-2-chloroethene

- ***cis* isomer;** when two similar groups are on the **same side** of the double bond.
- ***trans* isomer;** when two similar groups are on the **opposite sides** of the double bond.
- They have **different physical properties** and can be separated by fractional crystallization or distillation.

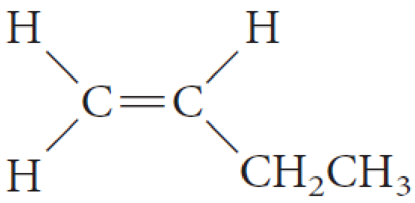
Geometric Isomerism in Alkenes

B) If (W = X or Y = Z), geometric isomerism is not possible.

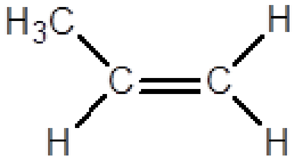


1-butene

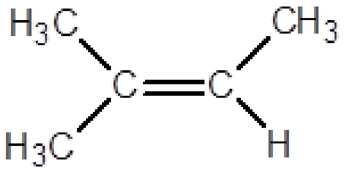
is identical to



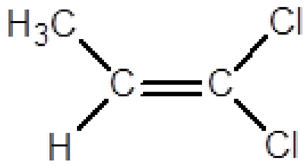
1-butene



Propene



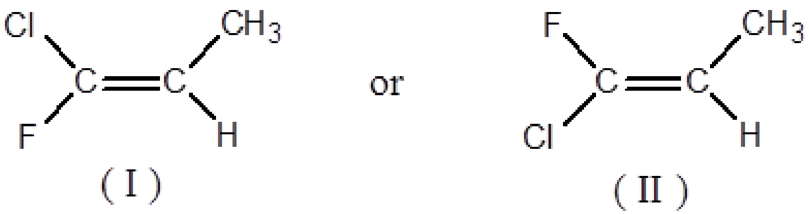
2-Methyl-2-butene



1,1-Dichloropropene

Geometric Isomerism in Alkenes

- For alkenes with four different substituent such as



Another system, the *E, Z* system,

- **Basically, the E,Z system works as follows;**

  Arrange the groups on each carbon of the C=C bond in order of priority

- **The priority depends on atomic number:**

  The higher the atomic number of the atom directly attached to the double-bonded carbon, the higher the priority.

Thus, in structure (I),

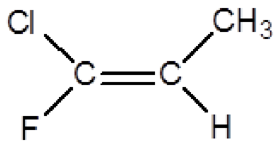
Cl > F, and CH_3 > H.

Geometric Isomerism in Alkenes

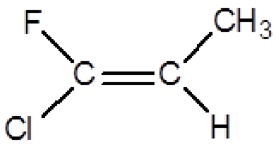
- If the two groups of **higher priority** are on the **same side** of the C=C plane,
  The isomer is labeled *Z;* (from the German *zusammen*, together).

- **If the two groups of higher priority are on opposite sides of the C=C plane,**
  The isomer is labeled E; (from the German entgegen, opposite).

Priority: Cl > F, CH_3 > H

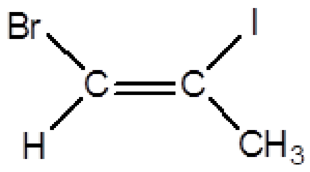


Z-1-Chloro-1-fluoropropene
(Cl and CH_3 on same side)



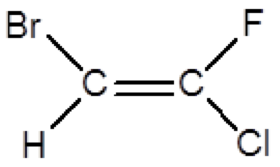
E-1-Chloro-1-fluoropropene
(Cl and CH_3 on opposite side)

Priority: Br > H, I > CH_3



Z-1-Bromo-2-iodopropene

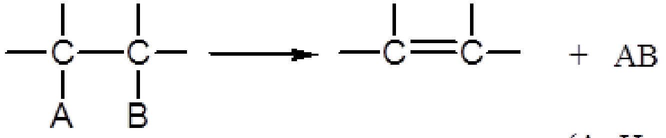
Priority: Br > H, Cl > F



E-1-Brfomo-2-chloro-2-fluoroethene

Preparation of Alkenes

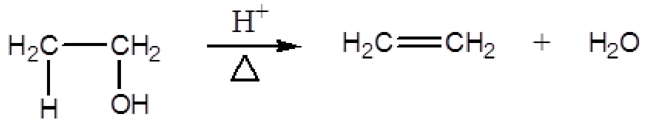
- **Alkenes** are prepared by *Elimination* of an atom or group of atoms from adjacent carbons to form *carbon-carbon double bond.*



(A=H or halogen;
B=OH or halogen)

1) Dehydration of Alcohols

- *When an alcohol is heated in the presence of a mineral acid catalyst, It readily loses a molecule of water to give an* ***alkene.***



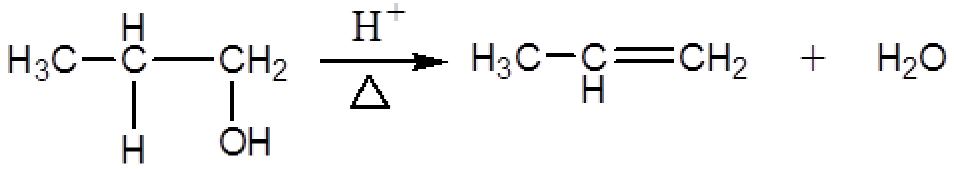
IUPAC name:	Ethanol	Ethene
Common name:	Ethyl alcohol	Ethylene

- The acid *catalysts* most commonly used are sulfuric acid, H_2SO_4, and phosphoric acid, H_3PO_4.

Preparation of Alkenes

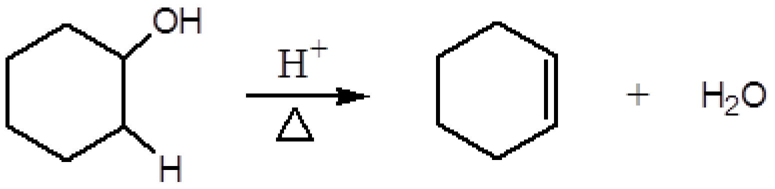
1) Dehydration of Alcohols

Removal of OH group and a proton from two adjacent carbon atoms using mineral acids such as H_2SO4 or H_3PO_4



$$H_3C-\overset{H}{\underset{H}{C}}-\underset{OH}{CH_2} \xrightarrow[\Delta]{H^+} H_3C-\underset{H}{C}=CH_2 + H_2O$$

IUPAC name:	1-Propanol	Propene
Common name:	*n*-Propyl alcohol	Propylene



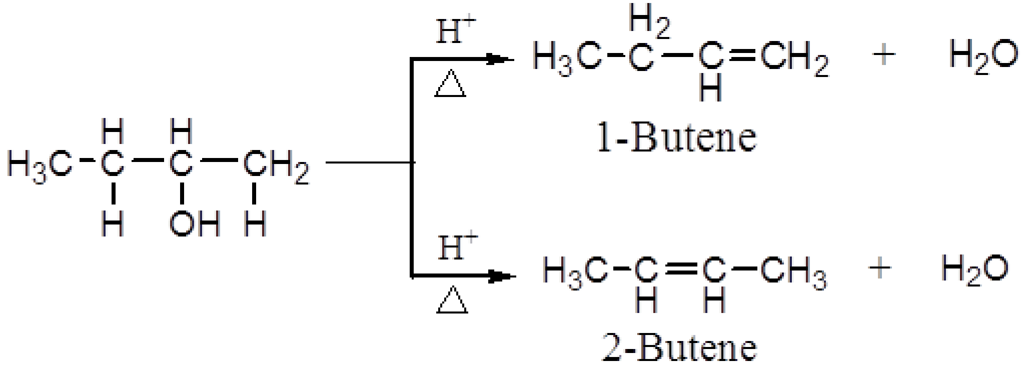
IUPAC name:	Cyclohexanol	Cyclohexene
Common name:	Cyclohexyl alcohol	

1) Dehydration of Alcohols

Which Alkene Predominates?; Saytzeff's Rule

The loss of water from adjacent carbon atoms, can give rise to more than one alkene.

Example: *the dehydration of 2-butanol.*



2-butene is the major (with two alkyl substituents attached to C=C)

Saytzeff's Rule applies

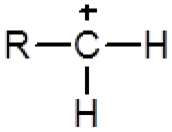
In every instance in which more than one Alkene can be formed

The major product is always the alkene with the most alkyl substituents attached on the double-bonded carbons.

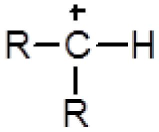
Preparation of Alkenes

1) Dehydration of Alcohols

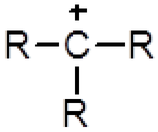
- **Classes of Carbocations**



1° carbocation



2° carbocation



3° carbocation

according to the number of carbon atoms attached to the positively charged carbon.

The ease of formation and the stabilities of carbocations follow the order

3° > 2° > 1°

←

Ease of formation and stabilities of carbocations

- **Generally**

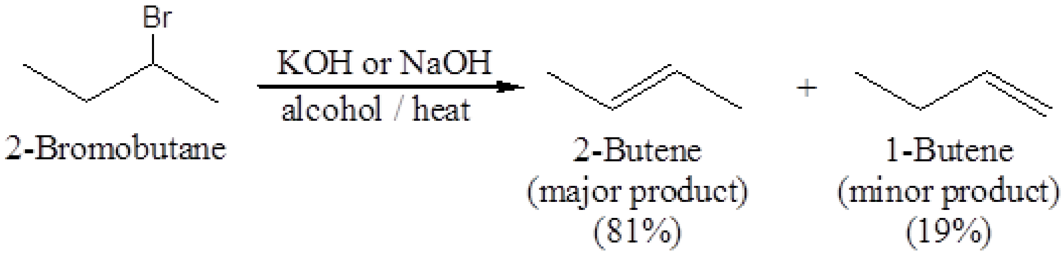
1. The dehydration of alcohols requires an acid catalyst.
2. The predominant alkene formed follows Saytzeffs rule.
3. The reaction proceeds *via* a carbocation intermediate.
4. The stabilities of carbocations and the ease of dehydration of alcohols follows the order 3° > 2° > 1°.

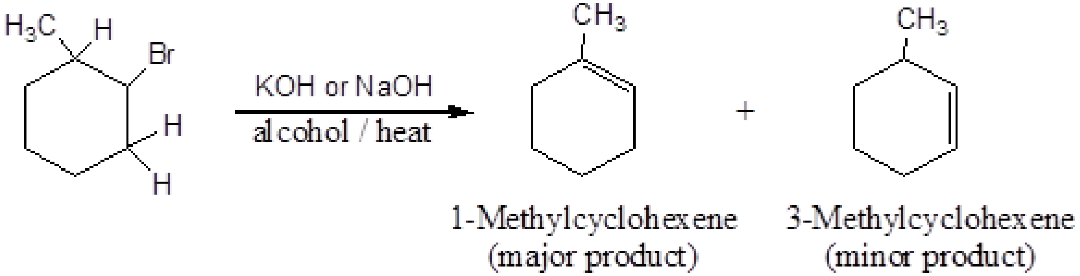
Preparation of Alkenes

2) Dehydrohalogenation of Alkyl Halides

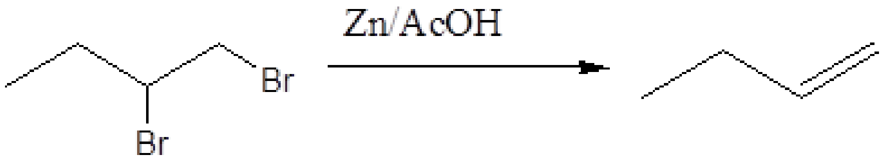
- Alkenes can also be prepared under alkaline conditions.

heating an alkyl halide with a solution of KOH or NaOH in alcohol, yields an alkene.





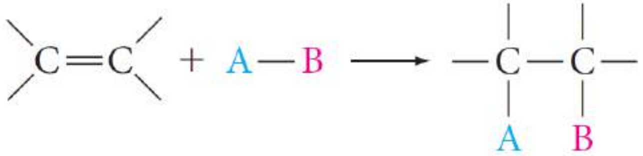
3) Dehalogenation of Vicinal Dibromides



Reactions of Alkenes

- The chemistry of alkenes can be divided into two general types of reactions:

(1) Electrophilic Addition Reactions



Addition of Symmetric and Unsymmetric Reagents to symmetric Alkenes.

1. Addition of Hydrogen: Catalytic Hydrogenation
2. Addition of Halogens: Halogenation

Addition of Unsymmetric Reagents to Unsymmetric Alkenes; Markovnikov's Rule.

1. Addition of Hydrogen Halides
2. Addition of Sulfuric Acid
3. Addition of Water: Hydration
4. Addition of HOX: Halohydrin Formation

Reactions of Alkenes

(2) Substitution Reactions

$$R—H + A—B \longrightarrow R—A + H—B$$

(3) Oxidation Reactions

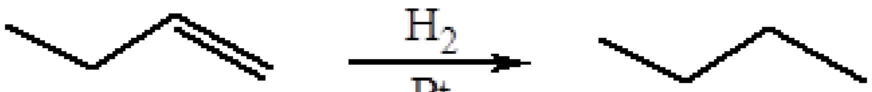
1. Ozonolysis
2. Oxidation Using $KMnO_4$

Reactions of Alkenes

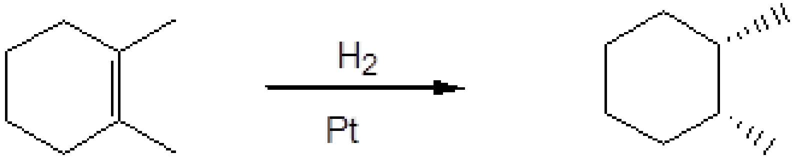
Electrophilic Addition Reactions

1. Addition of Hydrogen: Hydrogenation

Addition of a mole of hydrogen to carbon-carbon double bond of Alkenes in the presence of suitable catalysts to give an Alkane.



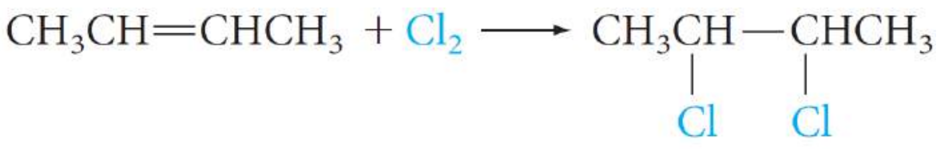
1-Butene Butane



1,2-Dimethylcyclohexene *cis*-1,2-Dimethylcyclohexane

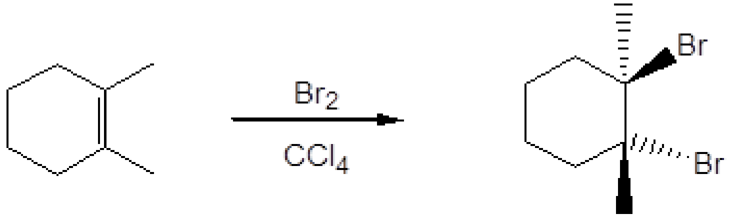
2. Addition of Halogen: Halogenation

*When an **alkene** is treated at room temperature with a solution of bromine or chlorine in carbon tetrachloride to give the corresponding vicinal dihalide (two halogens attached to adjacent carbons)*



$$CH_3CH=CHCH_3 + Cl_2 \longrightarrow CH_3\underset{\displaystyle Cl}{\underset{|}{CH}}-\underset{\displaystyle Cl}{\underset{|}{CH}}CH_3$$

2-butene 2,3-dichlorobutane



1,2-Dimethylcyclohexene *trans*-1,2-Dibromocyclohexane

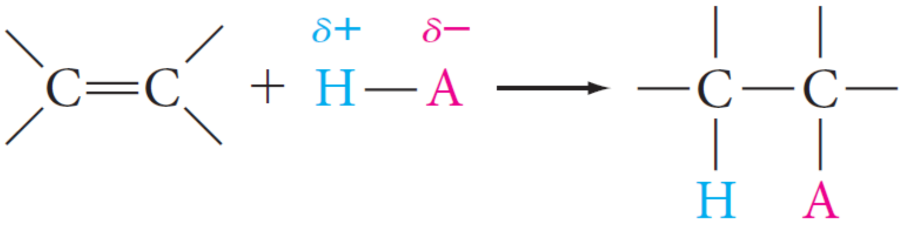
- **Iodine** is too unreactive and will not add to the double bond.
- **Fluorine** is too reactive and reacts explosively with an alkene.

Electrophilic Addition Reactions

3. Addition of Acids

- **A variety of acids add to the double bond of alkenes.**

  The hydrogen ion (or proton) adds to one carbon of the double bond, and the remainder of the acid becomes connected to the other carbon.



- Acids that add in this way are the **hydrogen halides** (H-F, H-Cl, H-Br, H-I), and **water** (H-OH).

Note that

- Any electron-deficient species is called an electrophile.
- Any electron-rich species is called a nucleophile.

Reactions of Alkenes

Electrophilic Addition Reactions

Examples of Electrophile:

- i) Positive reagents: protons (H^+), alkyl group R^+ , nitronium ion (NO_2^+), etc.…
- ii) Neutral reagents having positively polarized centers: HCl, bromine (because it can be polarized so that one end is positive).
- iii) Lewis acids: molecules or ions that can accept an electron pair ⇒ BF_3 and $AlCl_3$.
- iv) Metal ions that contain vacant orbitals: the silver ion (Ag^+), the mercuric ion (Hg^{2+}), and the platinum ion (Pt^{2+}).

Examples of Nucleophile:

a)Negative ions

e.g. $\mathrm{H\underset{\cdot\cdot}{\ddot{O}}\colon^{-}}$ Hydroxide ion, $\mathrm{H\underset{\cdot\cdot}{\ddot{S}}\colon^{-}}$ Hydrosulphide ion, $\mathrm{R\underset{\cdot\cdot}{\ddot{O}}\colon^{-}}$ Alkoxide ions,

$\mathrm{\colon N{\equiv}C\colon^{-}}$ Cyanide ion, $\mathrm{\colon\underset{\cdot\cdot}{\ddot{X}}\colon^{-}}$ Halide ions, ...etc.

b) Neutral molecules

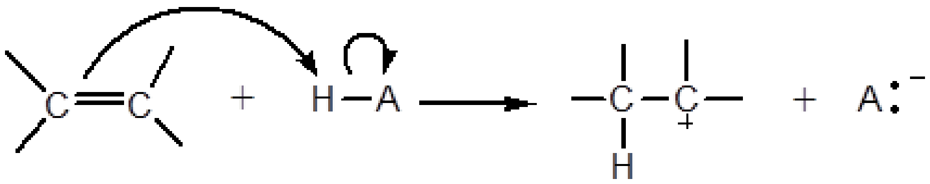
e.g. $\mathrm{H_2\underset{\cdot\cdot}{\ddot{O}}}$, $\mathrm{R{-}\underset{\cdot\cdot}{\ddot{O}}{-}H}$, $\mathrm{R{-}\underset{\cdot\cdot}{\ddot{O}}{-}R}$, $\mathrm{H_3\ddot{N}}$, $\mathrm{R_3\ddot{N}}$, ...etc.

Electrophilic Addition Reactions

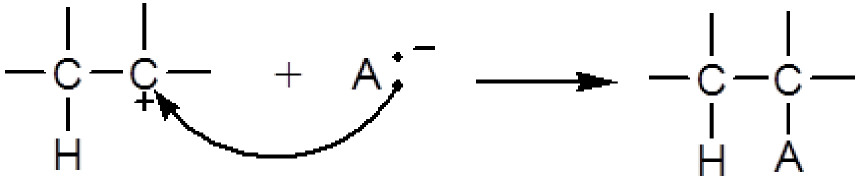
3. Addition of Acids

- **The addition of H—A to an alkene is believed to be a two-step process.**

Step 1. The hydrogen ion (the electrophile) attacks the ∏-electrons of the alkene, forming a C—H bond and a carbocation.



Step 2. The negatively charged species A: - (a nucleophile) attacks the carbocation and forms a new C—A bond.



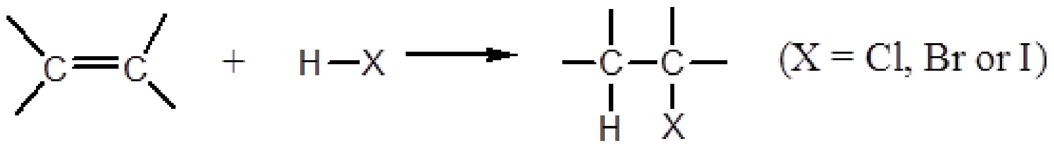
- The attack by an electrophilic reagent on the ∏-electrons, falls in a general category called **electrophilic addition reactions.**

Electrophilic Addition Reactions

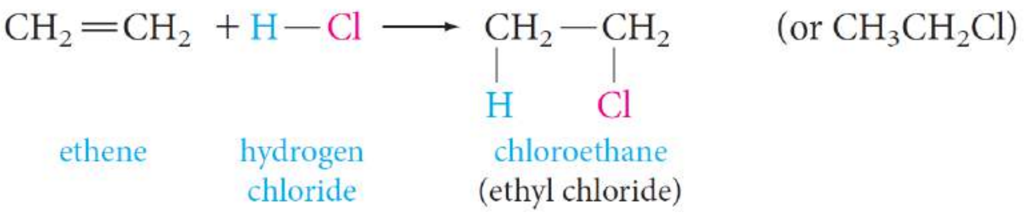
3.1. Addition of Hydrogen Halide

Alkenes react with hydrogen chloride, HC1, hydrogen bromide, HBr and hydrogen iodide, HI, to form alkyl halides, RX.

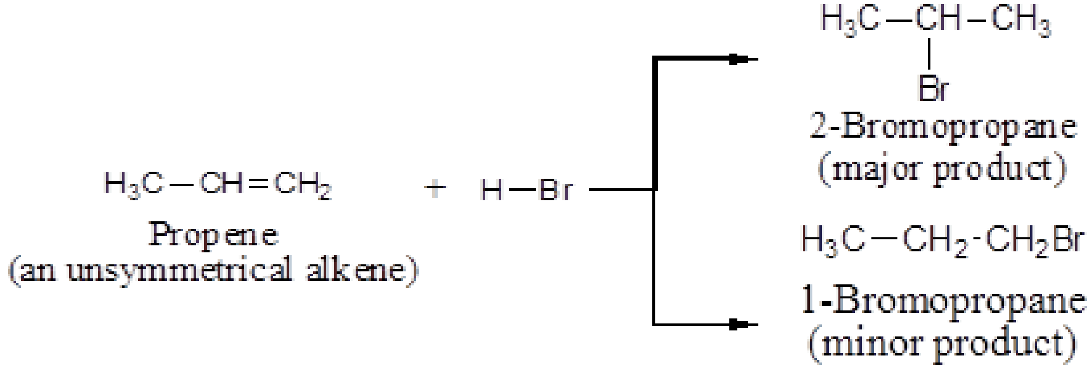
General equation



Examples;



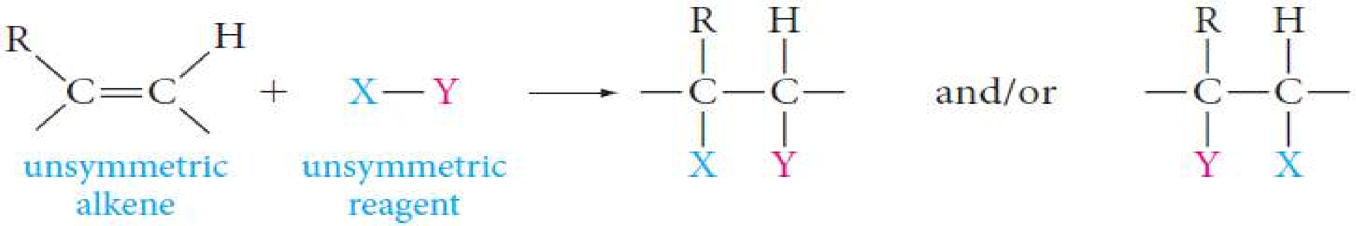
$$CH_2{=}CH_2 + H{-}Cl \longrightarrow \underset{H}{CH_2}{-}\underset{Cl}{CH_2} \quad (\text{or } CH_3CH_2Cl)$$



Reactions of Alkenes

Electrophilic Addition Reactions

- **Reagents and alkenes can be classified as either symmetric or unsymmetric** with respect to addition reactions.
  - If a reagent and/or an alkene is symmetric, only one addition product is possible.
  - But if *both* the reagent *and* the alkene are *unsymmetric,* two products are, in principle, possible.



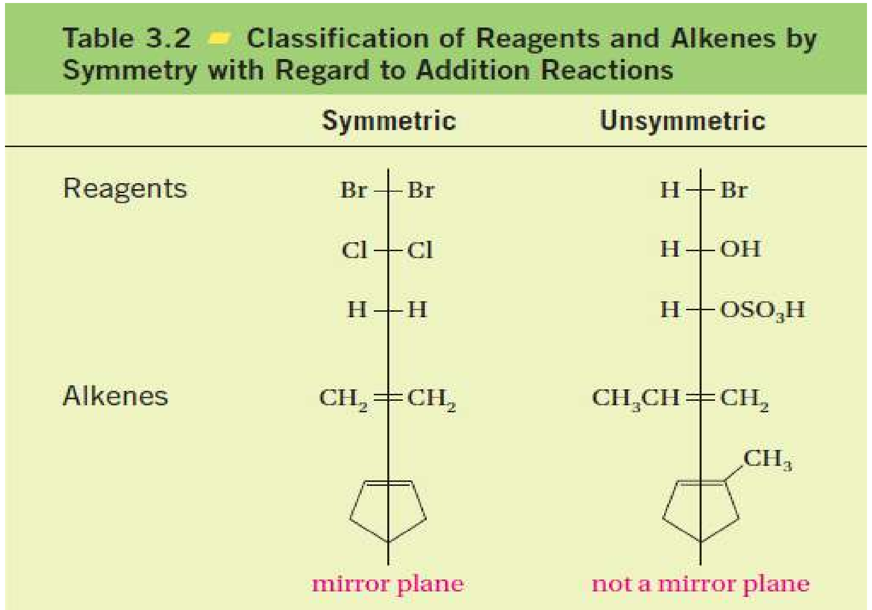


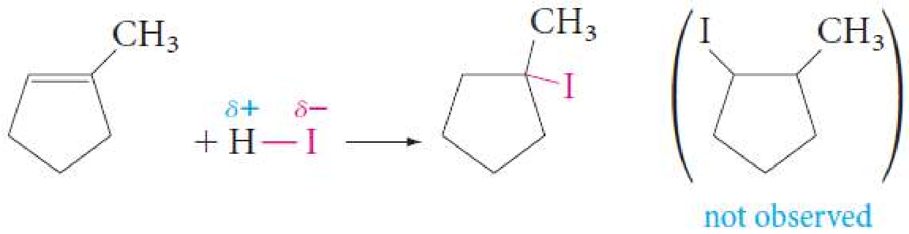
Table 3.2 ▰ Classification of Reagents and Alkenes by Symmetry with Regard to Addition Reactions

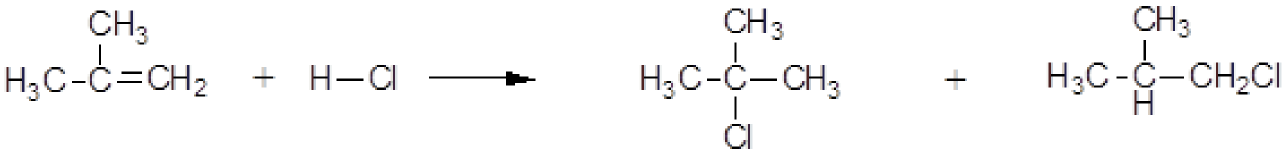
	Symmetric	Unsymmetric
Reagents	Br—Br	H—Br
	Cl—Cl	H—OH
	H—H	$H—OSO_3H$
Alkenes	$CH_2=CH_2$	$CH_3CH=CH_2$
		CH_3
	mirror plane	not a mirror plane

Electrophilic Addition Reactions

Markovnikov’s Rule

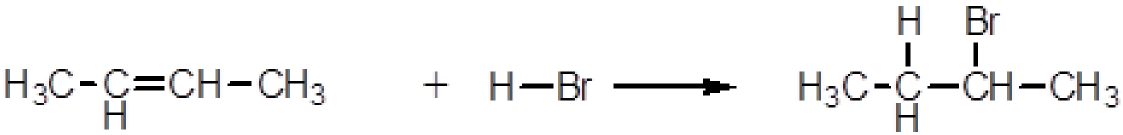
In electrophilic addition of H—X *to* ***Unsymmetrical Alkenes*** *the hydrogen of the hydrogen halide adds to the double-bonded carbon that bears the greater number of hydrogen atoms and the negative halide ion adds to the other double-bonded carbon.*





$$H_3C-\overset{\overset{\large CH_3}{|}}{C}=CH_2 \;+\; H-Cl \longrightarrow H_3C-\underset{\underset{\large Cl}{|}}{\overset{\overset{\large CH_3}{|}}{C}}-CH_3 \;+\; H_3C-\underset{H}{\overset{\overset{\large CH_3}{|}}{C}}-CH_2Cl$$

2-Chloro-2-methylpropane (major product) 1-Chloro-2-methylpropane (minor product)



$$H_3C-\underset{H}{C}=CH-CH_3 \;+\; H-Br \longrightarrow H_3C-\underset{H}{\overset{\overset{\large H}{|}}{C}}-\overset{\overset{\large Br}{|}}{CH}-CH_3$$

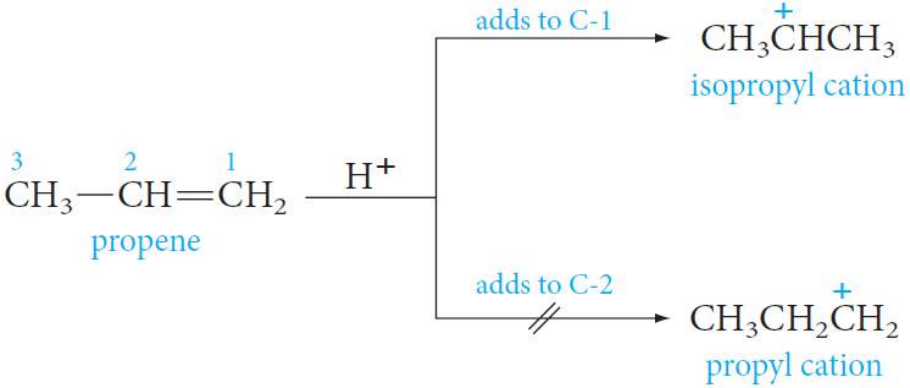
2-Butene
(a symmetrical alkene)

2-Bromobutane
(only one product possible)

Electrophilic Addition Reactions

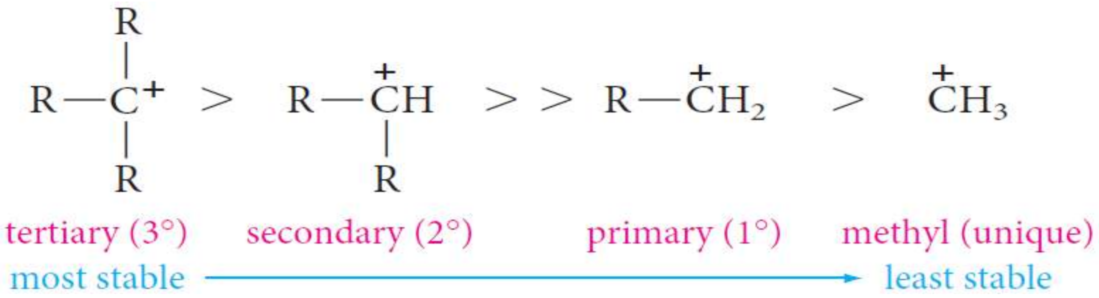
Explanation for Markovnikov's Rule

Example; *Addition of HBr to propene*



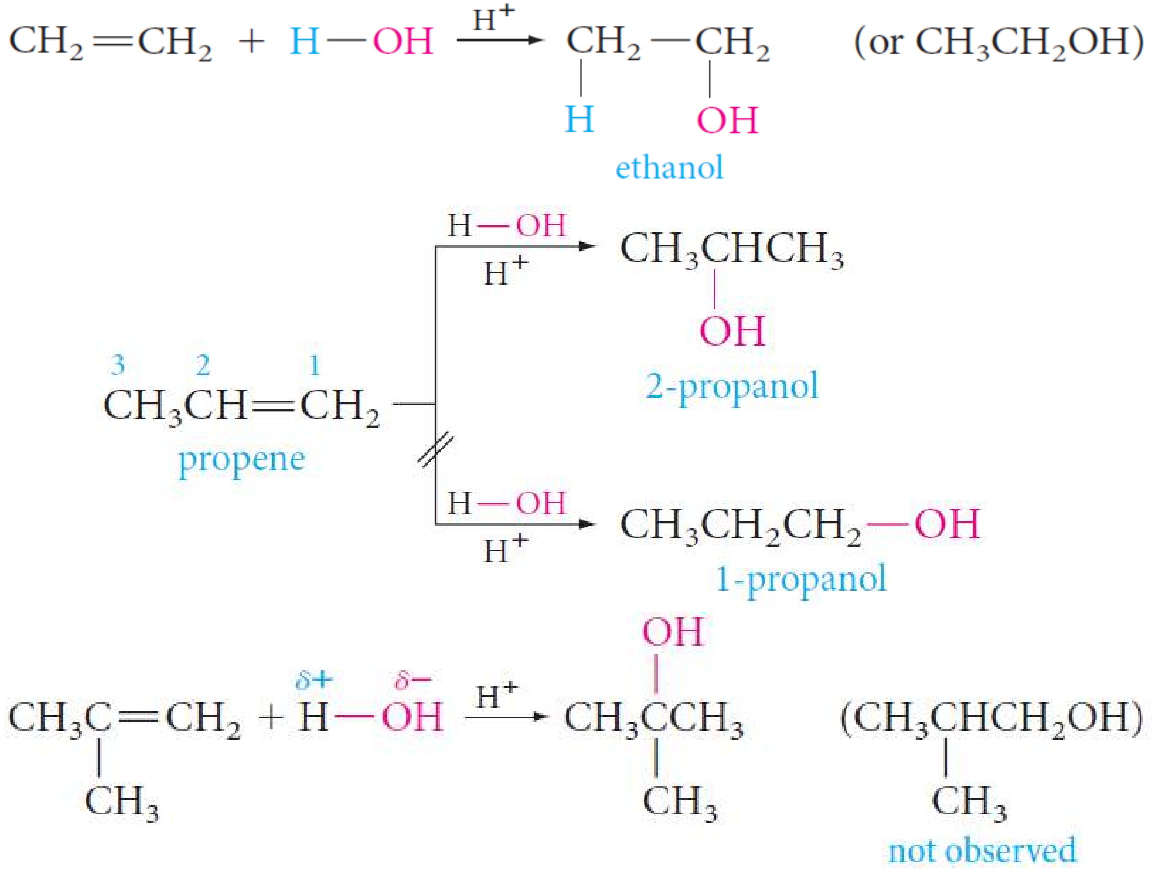
- **In modern terms Markovnikov's rule can be restated:**

  The addition of an unsymmetrical reagent HX *to an unsymmetrical alkene proceeds in such a direction as to produce the more stable carbocation.*



3.2. Addition of Water: Hydration

If an acid catalyst is present, water (as H-OH) adds to alkenes and the product is alcohol.



$$CH_2{=}CH_2 + H{-}OH \xrightarrow{H^+} \underset{H}{CH_2}{-}\underset{OH}{CH_2} \quad (\text{or } CH_3CH_2OH)$$

ethanol

$$\overset{3}{C}H_3\overset{2}{C}H{=}\overset{1}{C}H_2 \xrightarrow[H^+]{H{-}OH} CH_3\underset{OH}{CH}CH_3$$

propene → 2-propanol

$$CH_3CH{=}CH_2 \overset{H{-}OH}{\underset{H^+}{\not\longrightarrow}} CH_3CH_2CH_2{-}OH$$

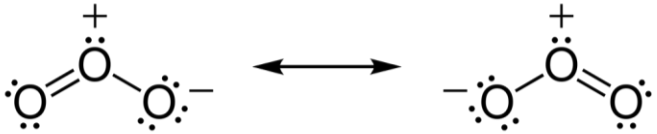
1-propanol

$$CH_3\underset{CH_3}{C}{=}CH_2 + \overset{\delta+}{H}{-}\overset{\delta-}{OH} \xrightarrow{H^+} CH_3\overset{OH}{\underset{CH_3}{C}}CH_3 \quad (CH_3\underset{CH_3}{CH}CH_2OH)$$

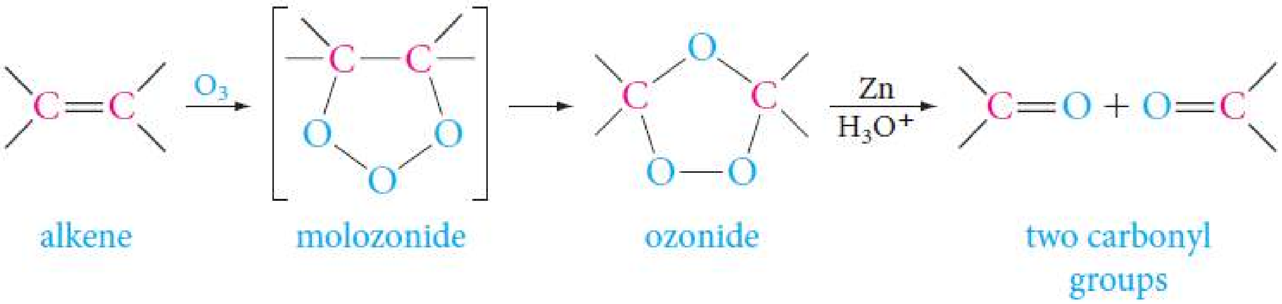
not observed

Oxidation Reactions

1. Ozonolysis



- The first product, a molozonide, is formed by cycloaddition of the oxygen at each end of the ozone molecule to the carbon–carbon double bond.
- This product then rearranges rapidly to an ozonide (explosive if isolated).
- They are usually treated directly with a reducing agent, commonly zinc and aqueous acid, to give carbonyl compounds as the isolated products.



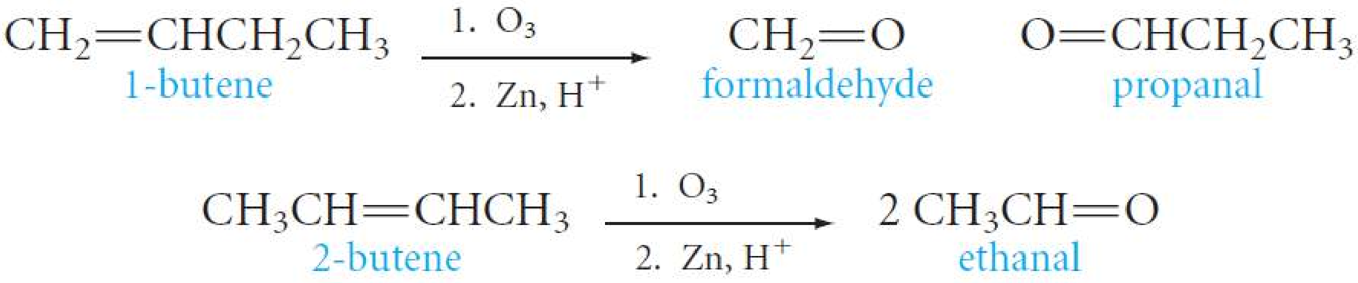
Reactions of Alkenes

Oxidation Reactions

1. Ozonolysis

- Ozonolysis can be used to locate the position of a double bond.
- **Example;**

Ozonolysis of 1-butene gives two different aldehydes, whereas 2-butene gives a single aldehyde.

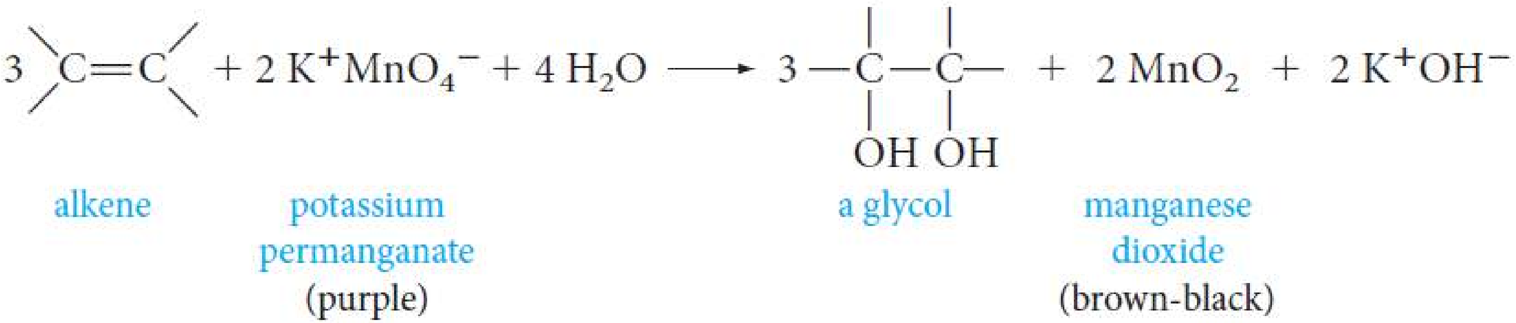


$$\underset{\text{1-butene}}{CH_2{=}CHCH_2CH_3} \xrightarrow[\text{2. Zn, H}^+]{\text{1. O}_3} \underset{\text{formaldehyde}}{CH_2{=}O} \quad \underset{\text{propanal}}{O{=}CHCH_2CH_3}$$

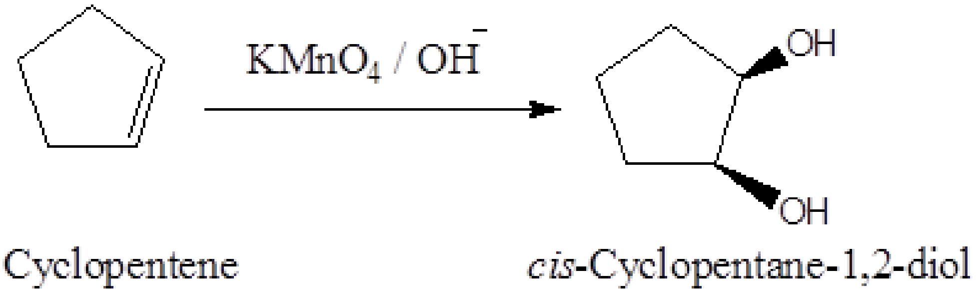
$$\underset{\text{2-butene}}{CH_3CH{=}CHCH_3} \xrightarrow[\text{2. Zn, H}^+]{\text{1. O}_3} \underset{\text{ethanal}}{2\ CH_3CH{=}O}$$

2. Oxidation Using $KMnO_4$

Alkenes react with alkaline potassium permanganate to form glycols (compounds with two adjacent hydroxyl groups).



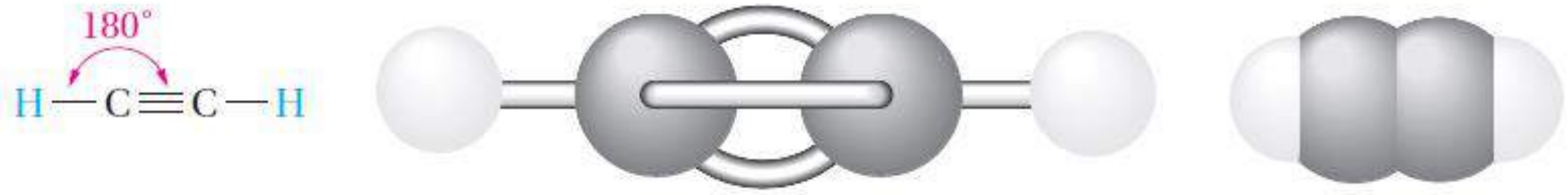
Hexane does not react with purple $KMnO_4$ (left); cyclohexene (right) reacts, producing a brown-black precipitate of MnO_2.



3. ALKYNES

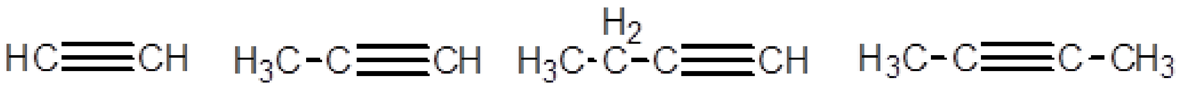
The Structure of Alkynes

- **Alkynes** are hydrocarbons that contain a ***carbon–carbon triple bond***.
- **Alkynes** are also known as *Acetylenes*.
- General formula is C_nH_{2n-2}
- Hybridization; ***sp*-hybridized orbitals**
- The angle between them is **180°** and the bond length **1.20 A°**
- **Linear.**



Nomenclature of Alkynes

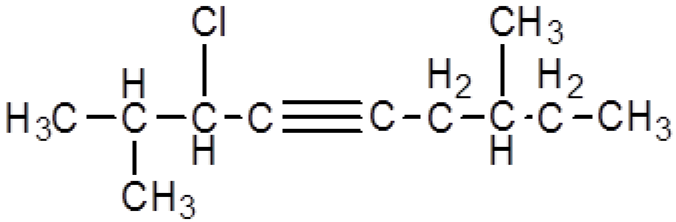
- The simplest members of the Alkenes series are C_2 & C_3
- Named are derived from the corresponding alkanes by replacing the –ane ending by –yne.
- IUPAC rules as discussed for Alkenes .



$HC\equiv CH \quad H_3C{-}C\equiv CH \quad H_3C{-}\overset{H_2}{C}{-}C\equiv CH \quad H_3C{-}C\equiv C{-}CH_3$

IUPAC name:	Ethyne	Propyne	1-Butyne	2-Butyne
Common name:	Acetylene			

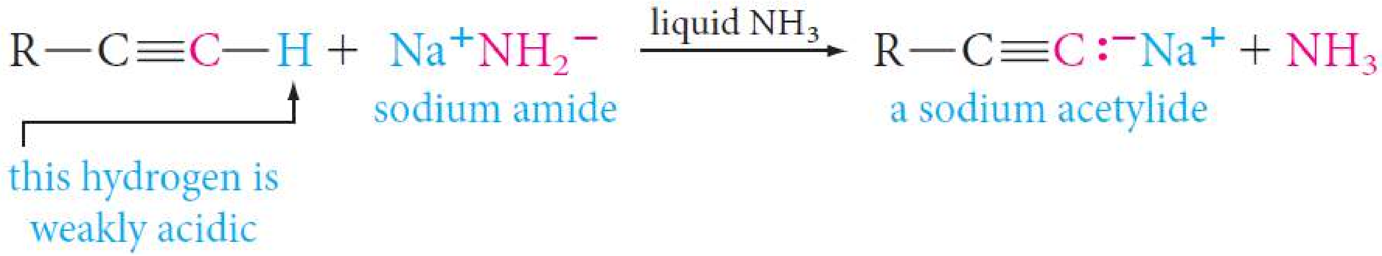
- **Example:**



3-Chloro-2,7-dimethyl-4-nonyne

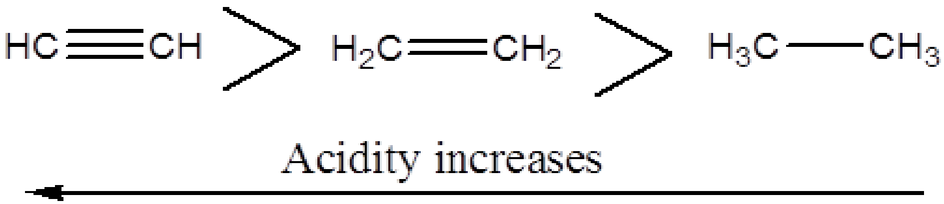
Acidity of Alkynes

- A hydrogen atom on a triply bonded carbon (**Terminal Alkyne**) is weakly acidic and can be removed by a very strong base (as Sodium amide).



$$R-C\equiv C-H + Na^{+}NH_2^{-} \xrightarrow{\text{liquid } NH_3} R-C\equiv C:^{-}Na^{+} + NH_3$$

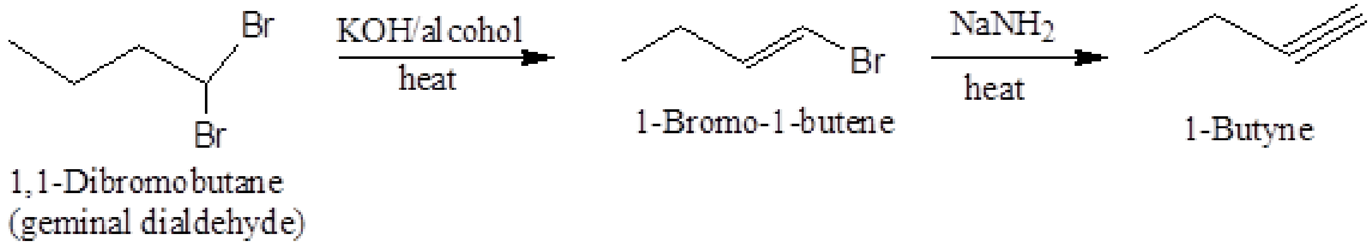
- Internal alkynes (**Non-Terminal Alkyne**) have no exceptionally acidic hydrogens.
  - Relative Acidity of the Hydrocarbon.
    Terminal alkynes, are more acidic than other hydrocarbons

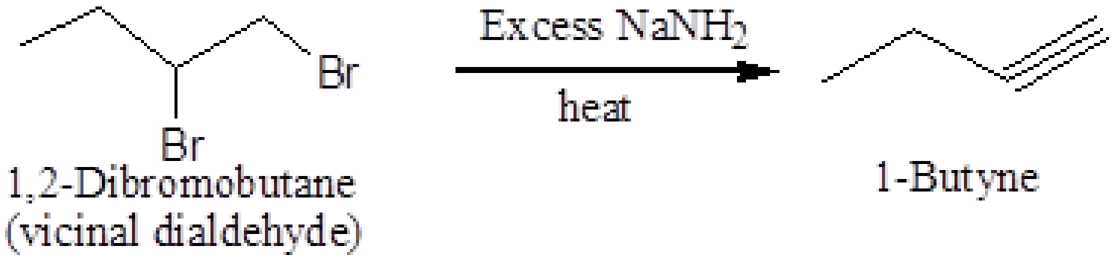


$$HC\equiv CH > H_2C=CH_2 > H_3C-CH_3$$

Preparation of Alkynes

1) Dehydrohalogenation of Alkyl dihalides

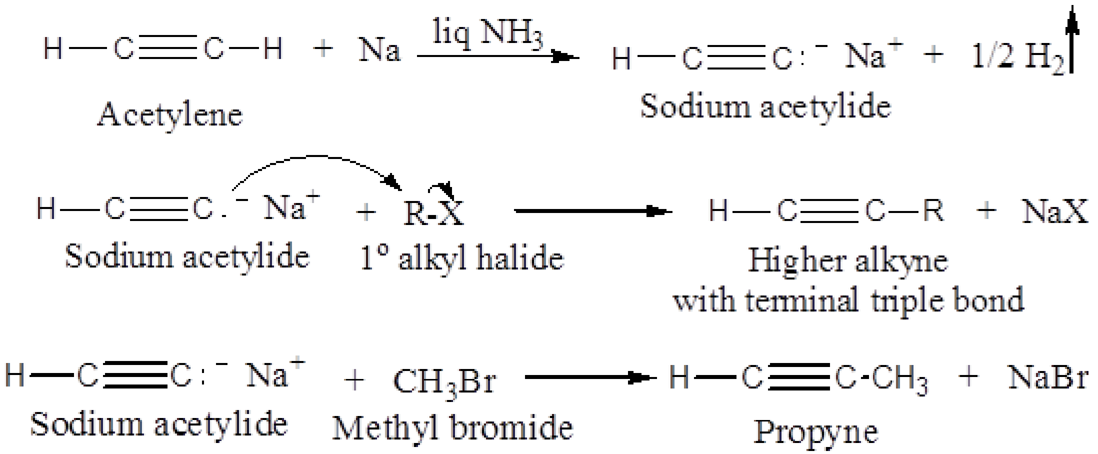




Preparation of Alkynes

2) Reaction of Sodium Acetylide with Primary Alkyl Halides

- **Acetylene**

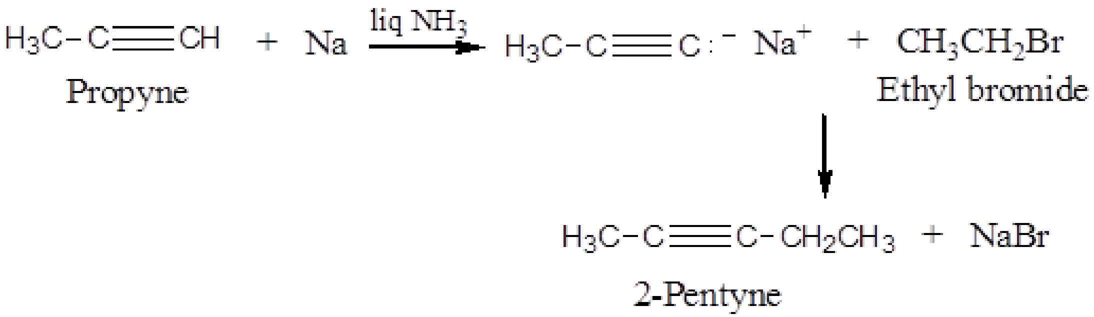


$$\underset{\text{Acetylene}}{H-C\equiv C-H} + Na \xrightarrow{\text{liq } NH_3} \underset{\text{Sodium acetylide}}{H-C\equiv C:^- \; Na^+} + 1/2\ H_2\uparrow$$

$$\underset{\text{Sodium acetylide}}{H-C\equiv C:^- \; Na^+} + \underset{1^\circ \text{ alkyl halide}}{R\text{-}X} \longrightarrow \underset{\text{Higher alkyne with terminal triple bond}}{H-C\equiv C-R} + NaX$$

$$\underset{\text{Sodium acetylide}}{H-C\equiv C:^- \; Na^+} + \underset{\text{Methyl bromide}}{CH_3Br} \longrightarrow \underset{\text{Propyne}}{H-C\equiv C\text{-}CH_3} + NaBr$$

- **Monosubstituted Acetylenes**



$$\underset{\text{Propyne}}{H_3C-C\equiv CH} + Na \xrightarrow{\text{liq } NH_3} H_3C-C\equiv C:^- \; Na^+ + \underset{\text{Ethyl bromide}}{CH_3CH_2Br}$$

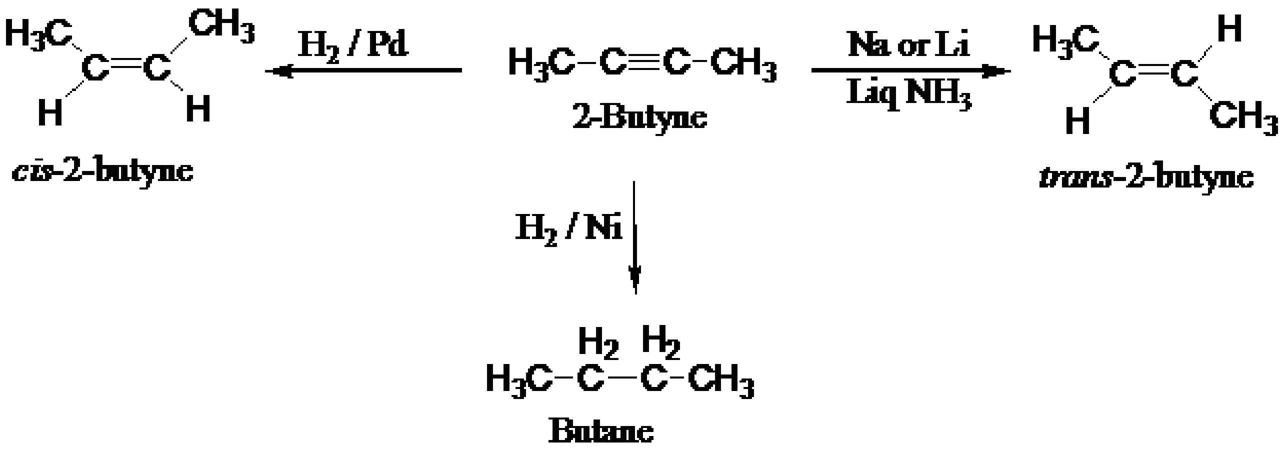
$$\downarrow$$

$$\underset{\text{2-Pentyne}}{H_3C-C\equiv C-CH_2CH_3} + NaBr$$

Electrophilic Addition Reactions

1. Addition of Hydrogen: Hydrogenation

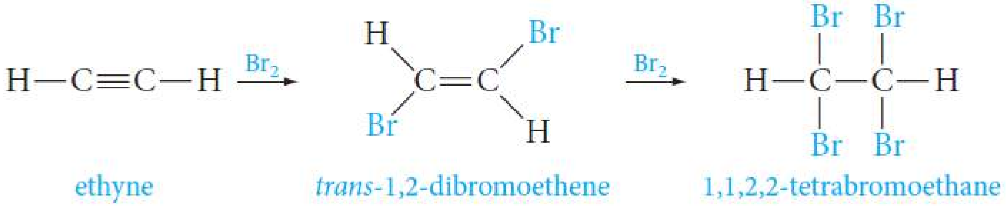
- With an ordinary nickel or platinum catalyst, alkynes are hydrogenated all the way to alkanes.
- However, a special palladium catalyst (called Lindlar's catalyst) can control hydrogen addition so that only one mole of hydrogen adds. In this case, the product is a *cis* alkene.



Electrophilic Addition Reactions

2. Addition of Halogen: Halogenation

Bromine adds as follows; In the first step, the addition occurs mainly *trans*.



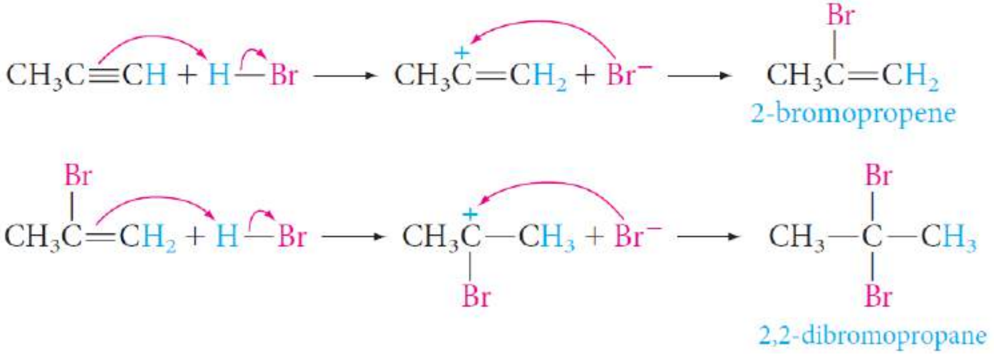
ethyne

trans-1,2-dibromoethene

1,1,2,2-tetrabromoethane

3. Addition of Hydrogen Halide

With unsymmetric triple bonds and unsymmetric reagents, Markovnikov’s Rule is followed in each step, as shown in the following example:



$$CH_3C{\equiv}CH + H{-}Br \longrightarrow CH_3\overset{+}{C}{=}CH_2 + Br^- \longrightarrow CH_3\overset{\overset{\large Br}{|}}{C}{=}CH_2$$

2-bromopropene

$$CH_3\overset{\overset{\large Br}{|}}{C}{=}CH_2 + H{-}Br \longrightarrow CH_3\underset{\underset{\large Br}{|}}{\overset{+}{C}}{-}CH_3 + Br^- \longrightarrow CH_3{-}\underset{\underset{\large Br}{|}}{\overset{\overset{\large Br}{|}}{C}}{-}CH_3$$

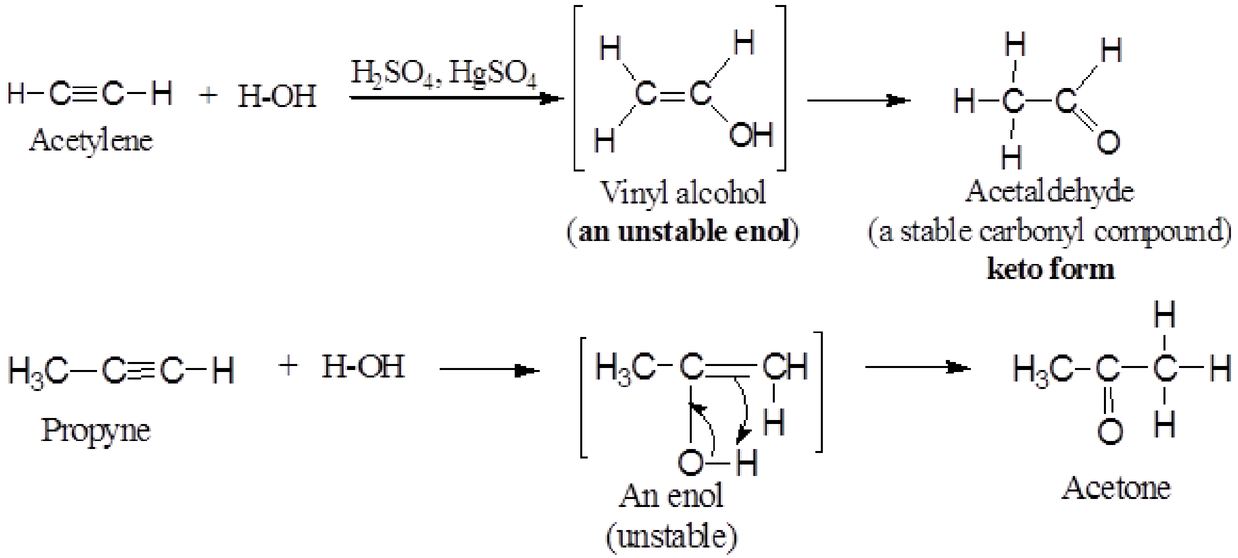
2,2-dibromopropane

Preparation of Alkenes

Electrophilic Addition Reactions

4. Addition of Water: Hydration

- **Addition of water to alkynes** requires not only an acid catalyst but mercuric ion as well.
- Although the reaction is similar to that of alkenes, the initial product - a vinyl alcohol or enol - rearranges to a carbonyl compound (keto form).
- The keto form of aldehydes and ketones are in equilibrium with the enol form.
- The keto from predominates at equilibrium for most simple aldehydes and ketones.
- The inter conversion is called **keto-enol tautomerization.**



Fundamentals of Organic Chemistry

CHEM 109

For Students of Health Colleges

Credit hrs.: (2+1)

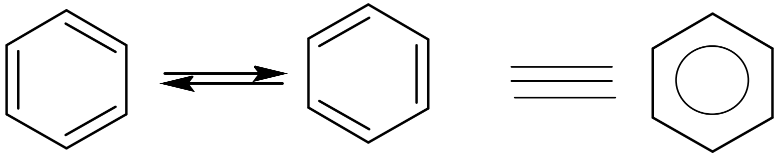
King Saud University

College of Science, Chemistry Department

CHAPTER 3. AROMATIC HYDROCARBONS

Aromatic Hydrocarbons

- Originally called **aromatic** due to fragrant odors, although this definition seems inaccurate as many products posses distinctly non-fragrant smells!
- Currently a compound is said to be aromatic if it has ***benzene-like in its properties***.



- Their properties differ markedly from those of aliphatic hydrocarbons.

  Aromatic hydrocarbons undergo electrophilic substitution whereas **aliphatic hydrocarbons** undergo ionic addition to double and triple bonds and free radical substitution.

The Structure of Benzene Ring

- **Benzene** is the ***parent hydrocarbon of aromatic compounds***, because of their special chemical properties.
- Today a compound is said to be **aromatic** if it is ***benzene-like in its properties***.

Structure of Benzene

- Molecular formula = C_6H_6

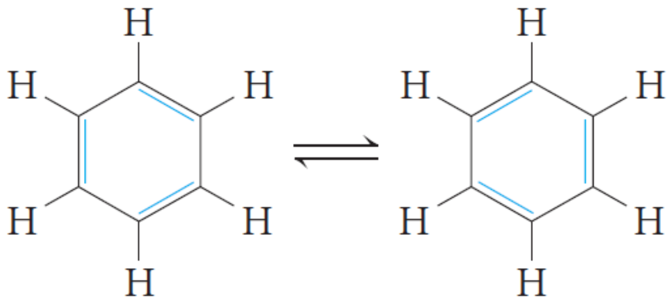
  The carbon-to-hydrogen ratio in benzene, suggests a ***highly unsaturated structure.***

- *Benzene reacts mainly by* ***substitution***.

  It does not undergo the typical addition reactions of alkenes or alkynes.

The Structure of Benzene Ring

- **Kekulé structure for benzene.**
  - *He suggested that six carbon atoms are located at the corners of* ***a regular hexagon****, with one hydrogen atom attached to each carbon atom.*
  - *He suggested that* ***single and double bonds alternate*** *around the ring (conjugated system of double bonds).*
  - *Kekulé suggested that the single and double bonds exchange positions around the ring so rapidly that the typical reactions of alkenes cannot take place.*



the Kekulé structures for benzene

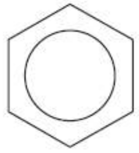
The Structure of Benzene Ring

- ***Resonance Model for Benzene.***

(I) (II)
Contributing structures

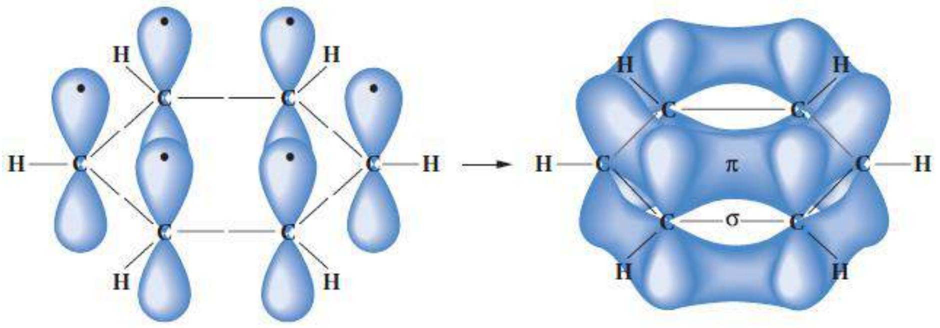
(III)
Resonance hybrid

Kekulé



delocalized pi cloud

- *Benzene is planar.*
- *All of the carbon–carbon bond lengths are identical*: 1.39 A°, intermediate between typical *single (1.54A°)* and *double (1.34 A°)* carbon–carbon bond lengths.
- Each carbon is therefore sp2-hybridized.
- Bond angles of 120°.



Aromatic Character (Aromaticity)

To be classified as aromatic, a compound must have:

❶ Cyclic structure

❷ Cyclic structure contains what looks like a continuous system of alternating double and single bonds

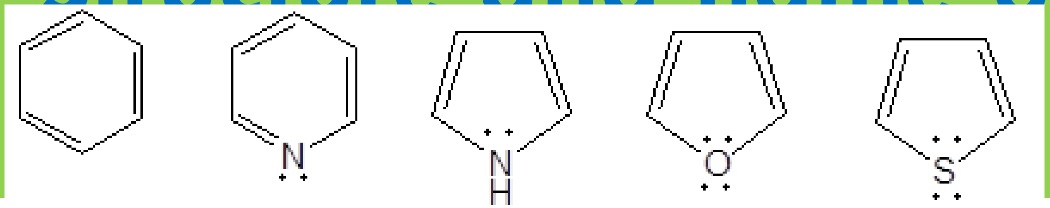
❸ Aromatic compounds must be planar

❹ Fulfill Huckel rule

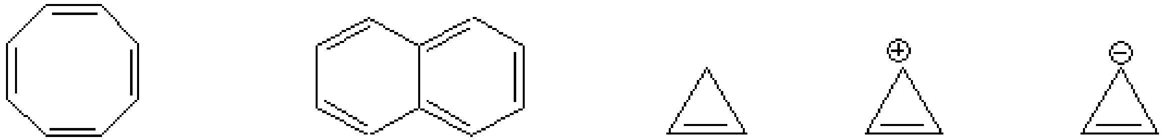
The number of $\prod$ *electrons in the compound* $= (4n + 2)$

Where ($n = 0, 1, 2, 3$, and so on).

Aromatic Character (Aromaticity)

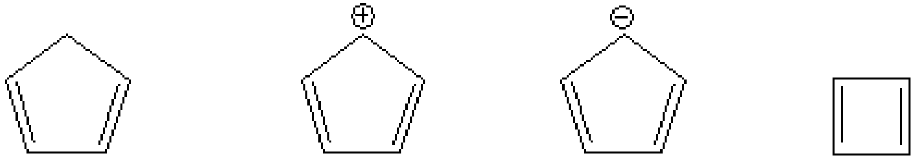
n	4n + 2	Structure and name of
1	6	 Benzene Pyridine Pyrrole Furan Thiophene

Examples



4n+2 = 8 10 2 2 4

n= 1.5 2 0 0 0.5

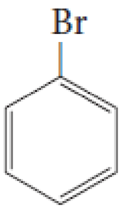


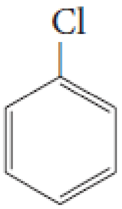
4n+2 = 4 4 6 4

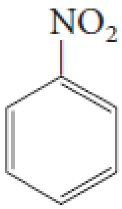
n= 0.5 0.5 1 0.5

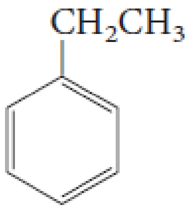
Nomenclature of Aromatic Compounds

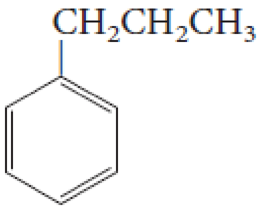
- **Monosubstituted benzenes** that do not have common names accepted by IUPAC are named as derivatives of benzene.


bromobenzene

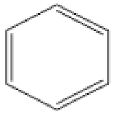

chlorobenzene

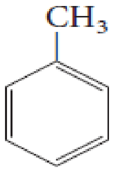

nitrobenzene

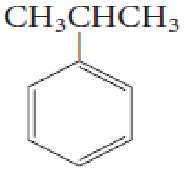

ethylbenzene

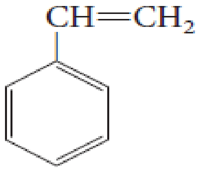

propylbenzene

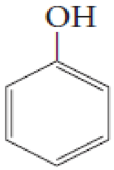
Common names are accepted by IUPAC (parent compounds).

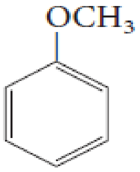

benzene

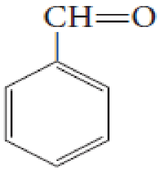

toluene

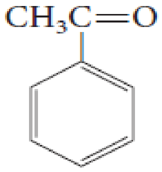

cumene

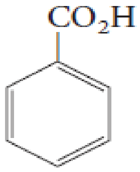

styrene

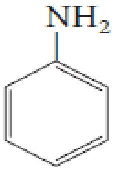

phenol


anisole


benzaldehyde

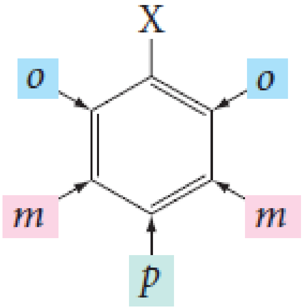

acetophenone


benzoic acid

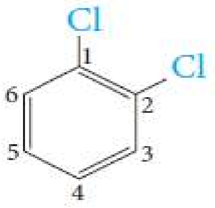

aniline

Nomenclature of Aromatic Compounds

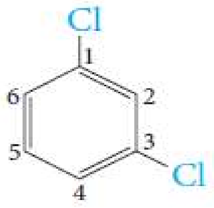
- When **two substituents** are present, *three isomeric structures are possible.*
  - They are designated by the prefixes; *ortho- (o-), meta- (m-)* and *para- (p-).*
  - If substituent X is attached to carbon 1; o- groups are on carbons 2 and 6, *m-* groups are on carbons 3 and 5, and *p-* groups are on carbon 4.



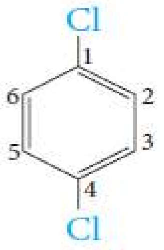
- **Examples;**



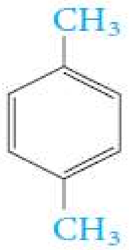
ortho-dichlorobenzene



meta-dichlorobenzene



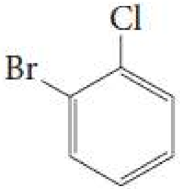
para-dichlorobenzene



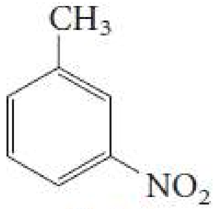
para-xylene*

Nomenclature of Aromatic Compounds

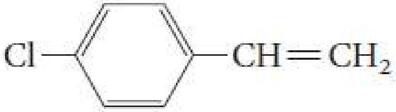
- The prefixes; *ortho-* (o-), *meta-* (*m-*) and *para-* (*p-*) are used when the two substituents are not identical.



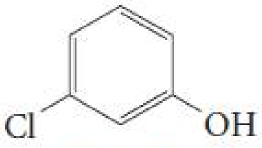
o-bromochlorobenzene
(note alphabetical order)



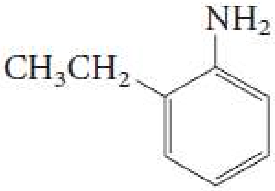
m-nitrotoluene



p-chlorostyrene

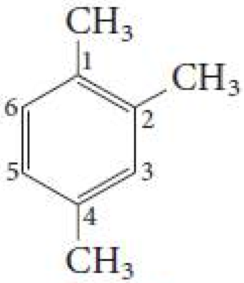


m-chlorophenol

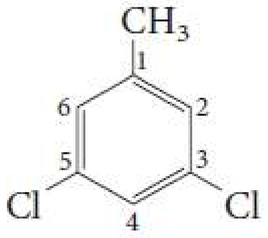


o-ethylaniline

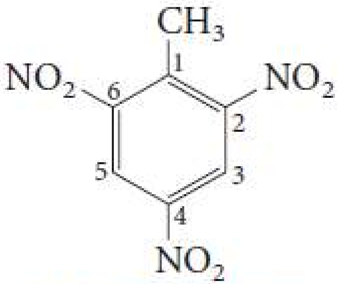
- When **more than two substituents** are present, their positions are designated by numbering the ring.



1,2,4-tri-
methylbenzene



3,5-dichlorotoluene

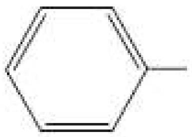


2,4,6-trinitrotoluene
(TNT)

Nomenclature of Aromatic Compounds

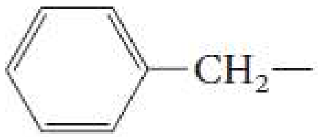
- Two groups with special names occur frequently in aromatic compounds; the **phenyl group** and the **benzyl group**.

C_6H_5- or



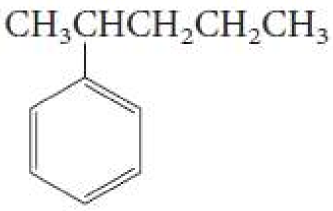
phenyl group

$C_6H_5CH_2-$ or

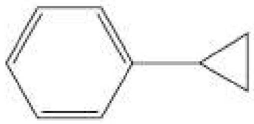


benzyl group

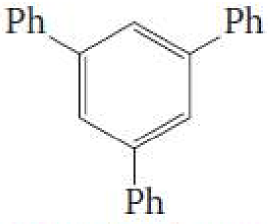
- **Examples;**



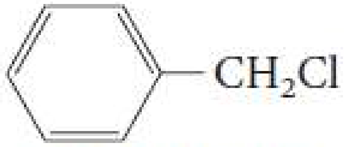
2-phenylpentane
(or 2-pentylbenzene)



phenylcyclopropane
(or cyclopropylbenzene)



1,3,5-triphenylbenzene

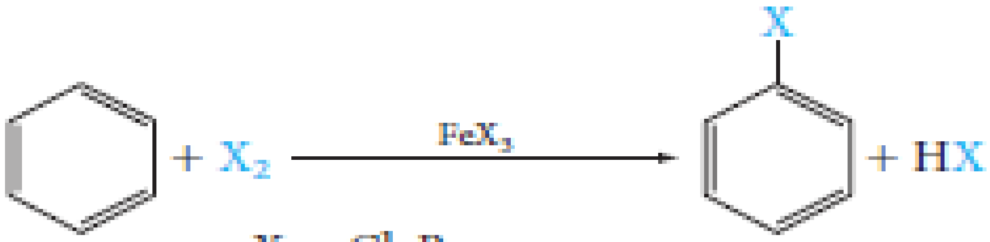


benzyl chloride

Reactions of Benzene

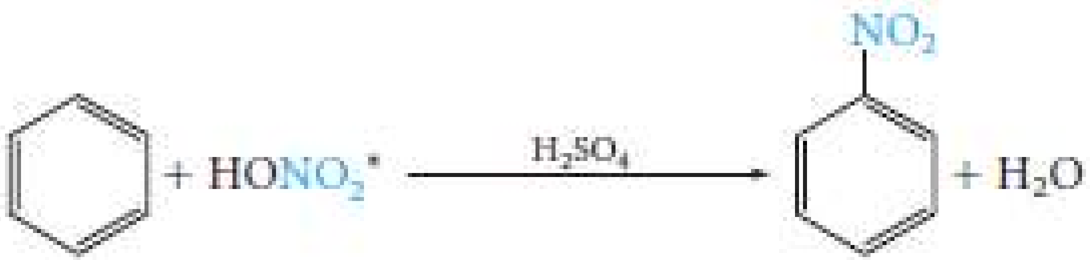
Electrophilic Aromatic Substitution Reactions

1) Halogenation

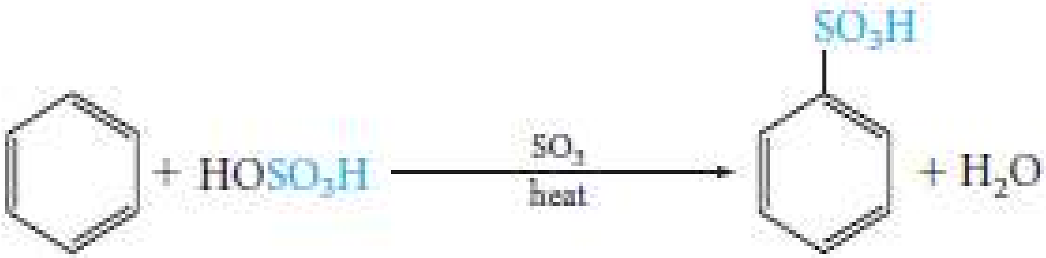


X = Cl, Br

2) Nitration



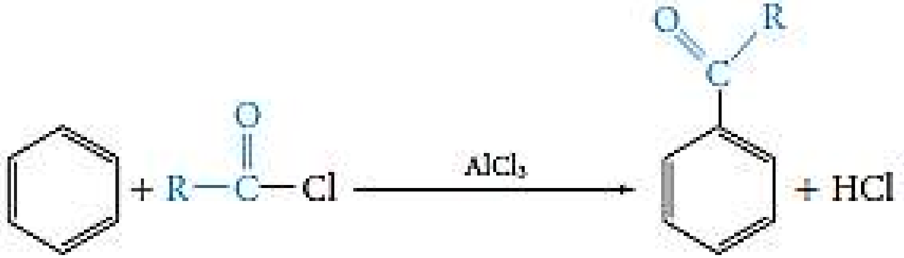
3) Sulfonation



Electrophilic Aromatic Substitution Reactions

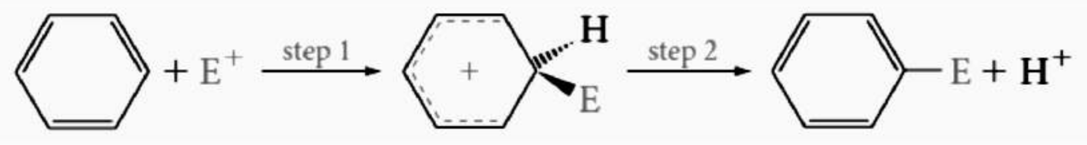
4) Alkylation (Friedel-Crafts)

5) Acylation (Friedel-Crafts)



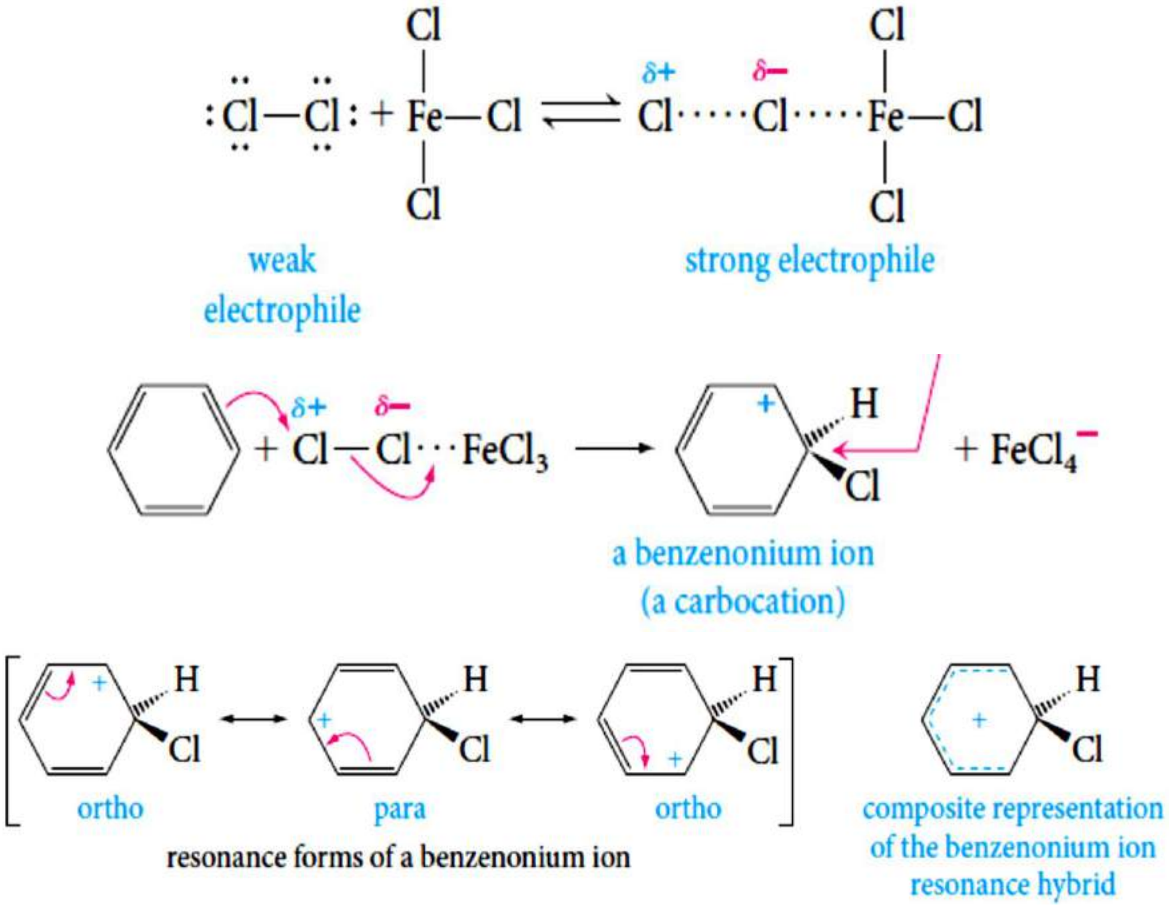
The Mechanism of Electrophilic Aromatic Substitution

We can generalize this two-step mechanism for all the electrophilic aromatic substitutions.



The Mechanism of Electrophilic Aromatic Substitution

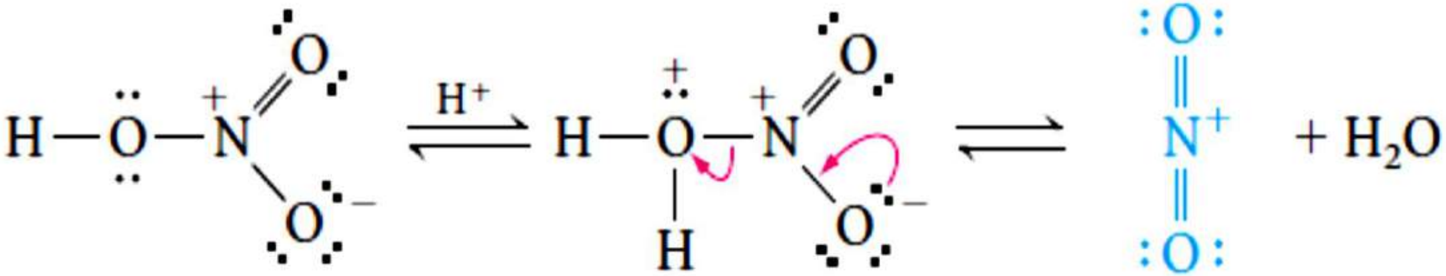
- **Halogenation**



The Mechanism of Electrophilic Aromatic Substitution

Nitration

In aromatic nitration reactions, the sulfuric acid catalyst protonates the nitric acid, which then loses water to generate the nitronium ion (NO_2^+), which contains a positively charged nitrogen atom.



nitric acid

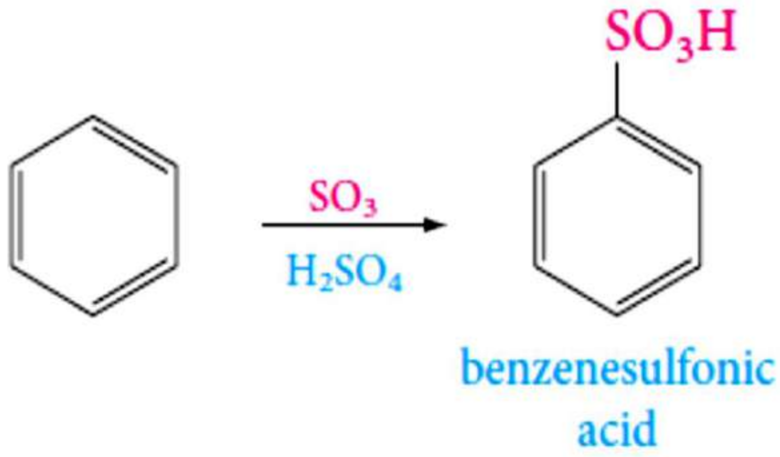
protonated nitric acid

nitronium ion

The Mechanism of Electrophilic Aromatic Substitution

➢ Sulfonation

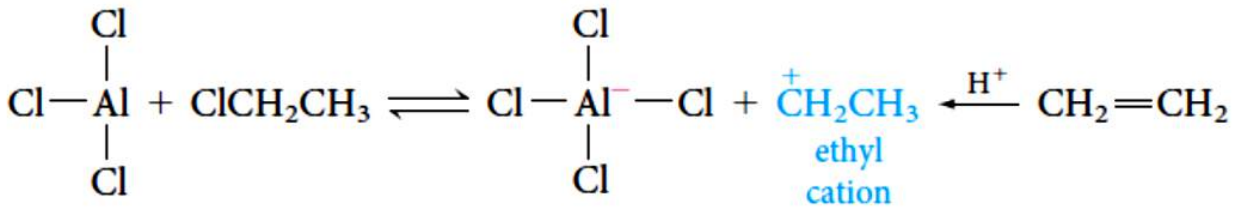
We use either concentrated or fuming sulfuric acid, and the electrophile may be sulfur trioxide, SO_3*, or protonated sulfur trioxide,* $^{+}SO_3H$.



The Mechanism of Electrophilic Aromatic Substitution

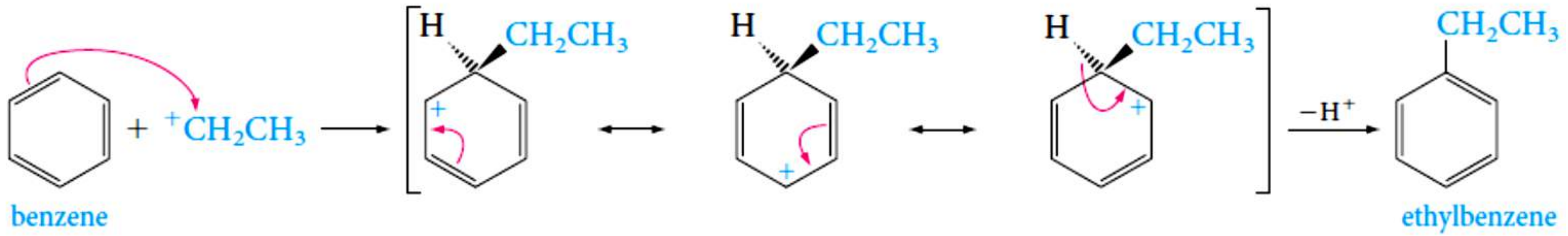
➢ Friedel–Crafts Alkylation

The electrophile is a carbocation, which can be formed either by removing a halide ion from an alkyl halide with a Lewis acid catalyst (for example, $AlCl_3$) .



$$\mathrm{Cl{-}}\underset{\mathrm{Cl}}{\overset{\mathrm{Cl}}{\mathrm{Al}}} + \mathrm{ClCH_2CH_3} \rightleftharpoons \mathrm{Cl{-}}\underset{\mathrm{Cl}}{\overset{\mathrm{Cl}}{\mathrm{Al}^-}}\mathrm{{-}Cl} + \underset{\text{ethyl cation}}{\overset{+}{\mathrm{C}}\mathrm{H_2CH_3}} \xleftarrow{H^+} \mathrm{CH_2{=}CH_2} \qquad (4.20)$$

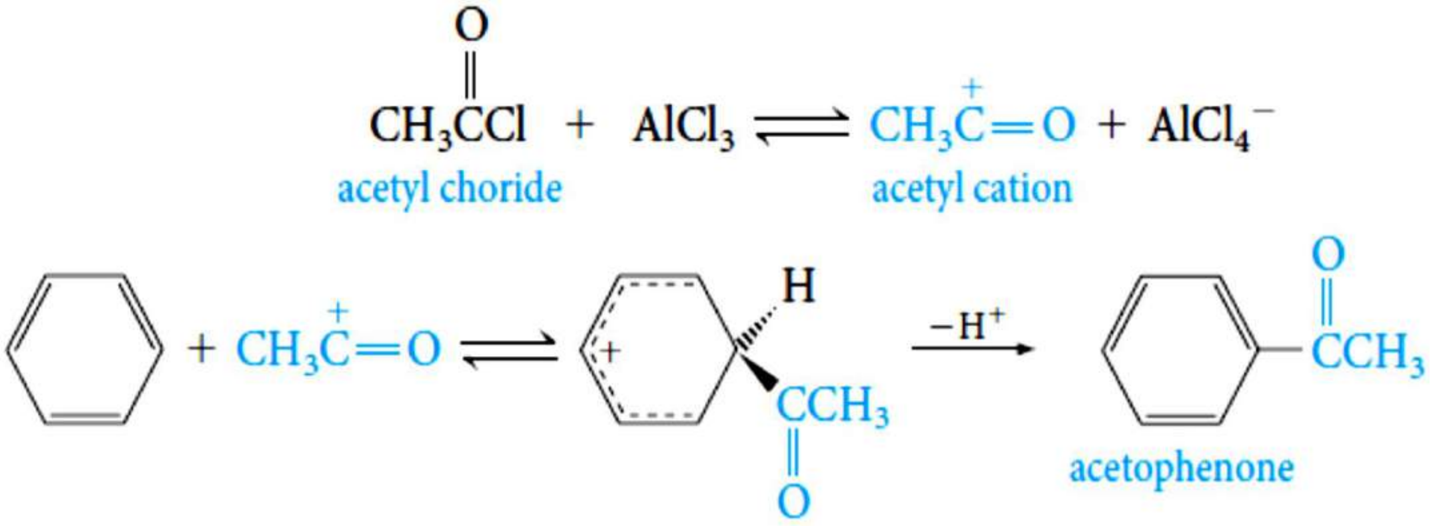
(4.20)



The Mechanism of Electrophilic Aromatic Substitution

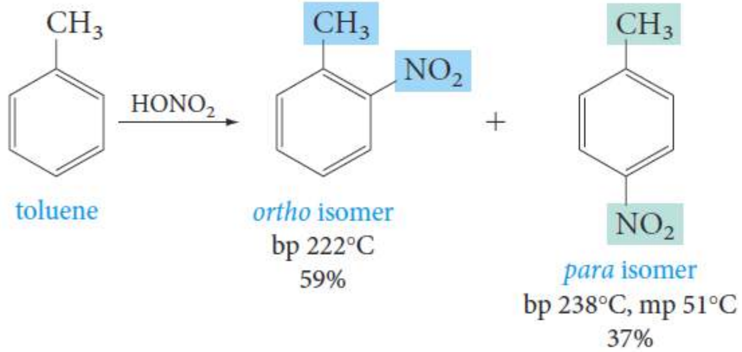
➢ Friedel–Crafts Acylation

The electrophile is an acyl cation generated from an acid derivative, usually an acyl halide. The reaction provides a useful general route to aromatic ketones.

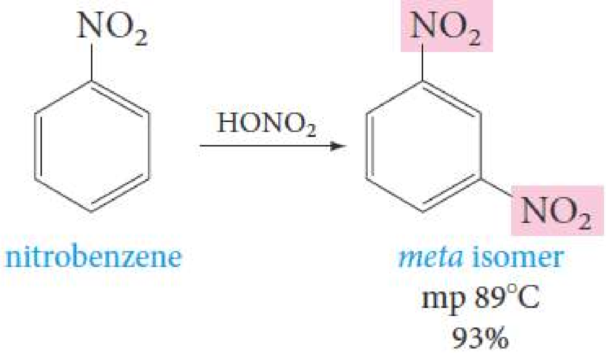


Disubstituted Benzenes: Orientation

- Substituents already present on an aromatic ring determine the position taken by a new substituent.
- **Example;** nitration of toluene gives mainly a mixture of o- and *p*-nitrotoluene.



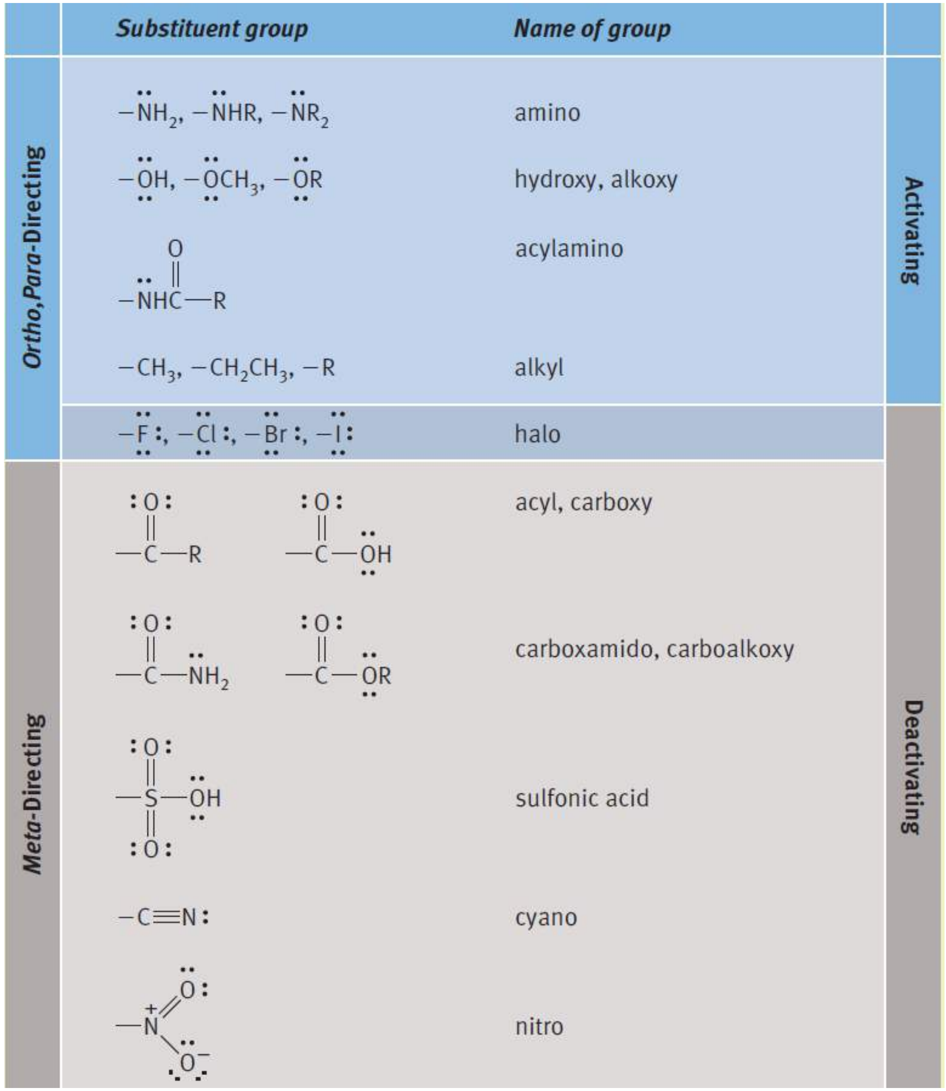
- On the other hand, nitration of nitrobenzene under similar conditions gives mainly the *meta* isomer.



Disubstituted Benzenes: Orientation& Reactivity

Directing and Activating Effects of Common Functional Groups

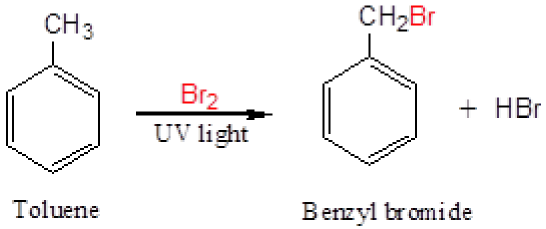
- *Substituents that* *release electrons* *to the ring will* *activate the ring* *toward electrophilic substitution.*
- *Substituents that* *withdraw electrons* *from the ring will* *deactivate the ring* *toward electrophilic substitution.*

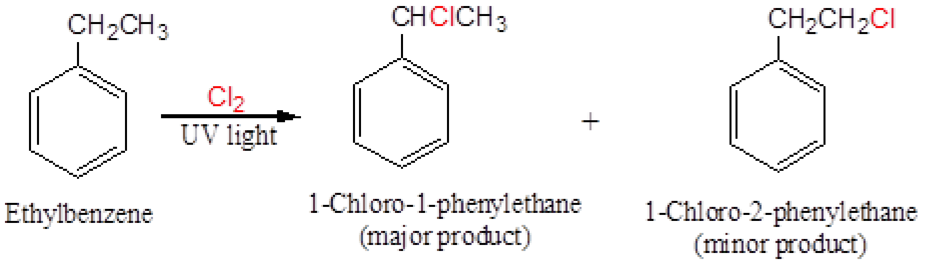


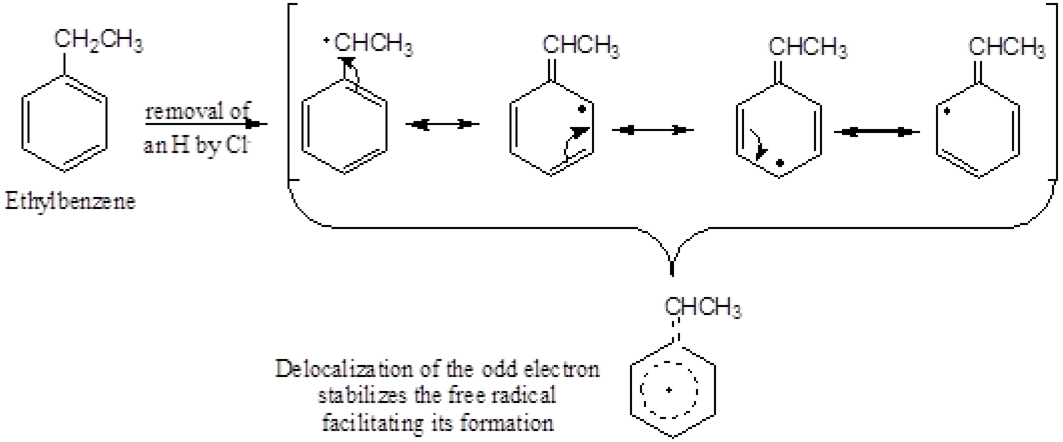
	Substituent group	*Name of group*	
Ortho, Para-Directing	$-\ddot{N}H_2$, $-\ddot{N}HR$, $-\ddot{N}R_2$	amino	Activating
	$-\ddot{O}H$, $-\ddot{O}CH_3$, $-\ddot{O}R$	hydroxy, alkoxy	
	$-\ddot{N}HC(=O)-R$	acylamino	
	$-CH_3$, $-CH_2CH_3$, $-R$	alkyl	
	$-F$, $-Cl$, $-Br$, $-I$	halo	Deactivating
Meta-Directing	$-C(=O)-R$, $-C(=O)-OH$	acyl, carboxy	
	$-C(=O)-NH_2$, $-C(=O)-OR$	carboxamido, carboalkoxy	
	$-S(=O)_2-OH$	sulfonic acid	
	$-C\equiv N:$	cyano	
	$-\overset{+}{N}(=O)-O^-$	nitro	

Side-Chain Reactions of Benzene-Derivatives

1. Halogenation of an Alkyl Side Chain



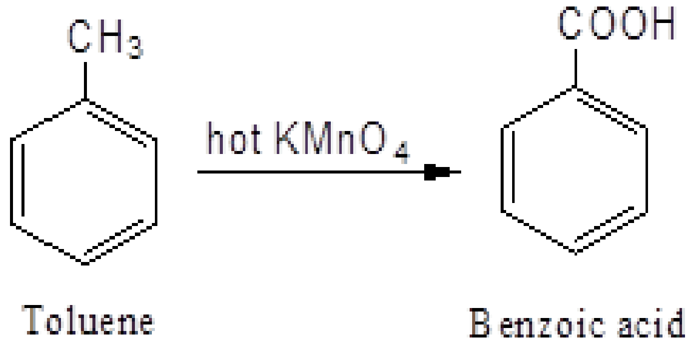


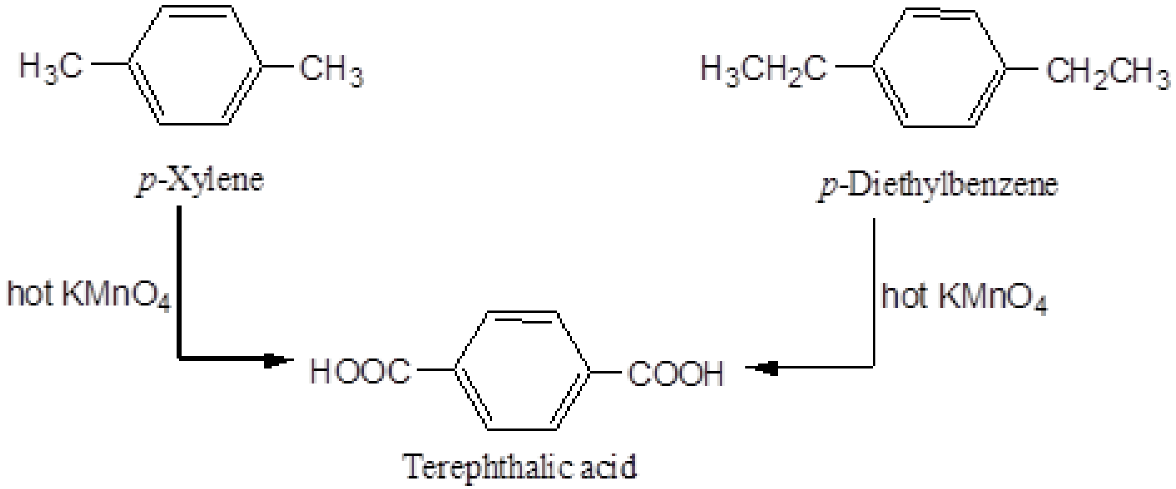


Side-Chain Reactions of Benzene-Derivatives

2. Oxidation of an Alkyl Side Chain

- Conversion into a carboxyl group, -COOH, by treatment with hot potassium permanganate.
- Regardless the length of the alkyl chain, the product is always the same.





(a raw material used in synthesizing Dacron and other polyesters)

Fundamentals of Organic Chemistry

CHEM 109

For Students of Health Colleges

Credit hrs.: (2+1)

King Saud University

College of Science, Chemistry Department

CHAPTER 4. ALCOHOLS, PHENOLS AND ETHERS

Alcohols, Phenols and Ethers

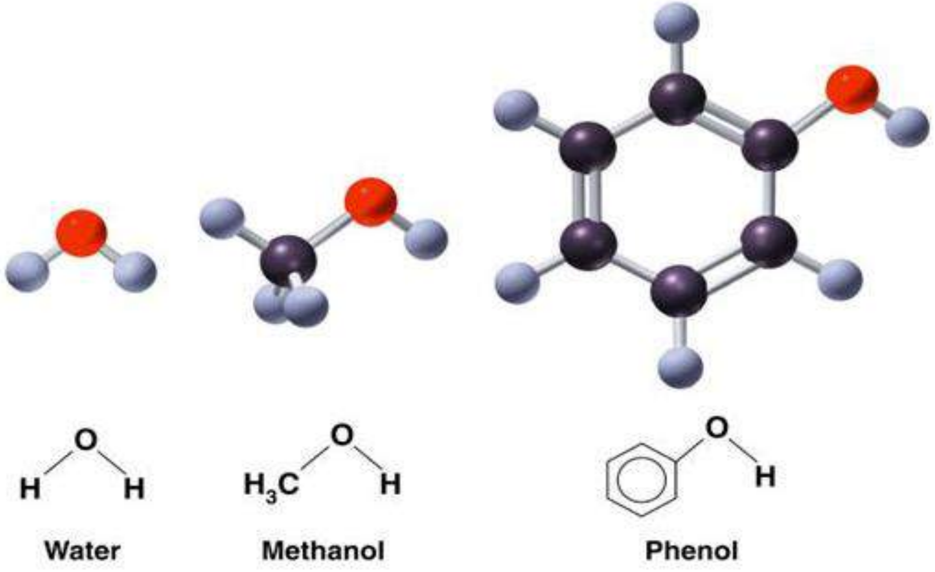
- **Alcohols, ethers and phenols have a common functional group, the hydroxyl group, -OH.**

H-O-H	R-OH	R-O-R	Ph-O-H
Water	**Alcohol**	**Ethers**	**Phenol**

- **Alcohols** are compounds whose molecules have a hydroxyl group attached to a *saturated* carbon atom.
- **Phenols** are compounds that have a hydroxyl group attached directly to a ***benzene ring .***
- **Ethers** are compounds whose molecules have an oxygen atom bonded to two carbon atom.

Alcohols and Phenols

- **Alcohols and phenols** may be viewed as organic *derivatives of water*.



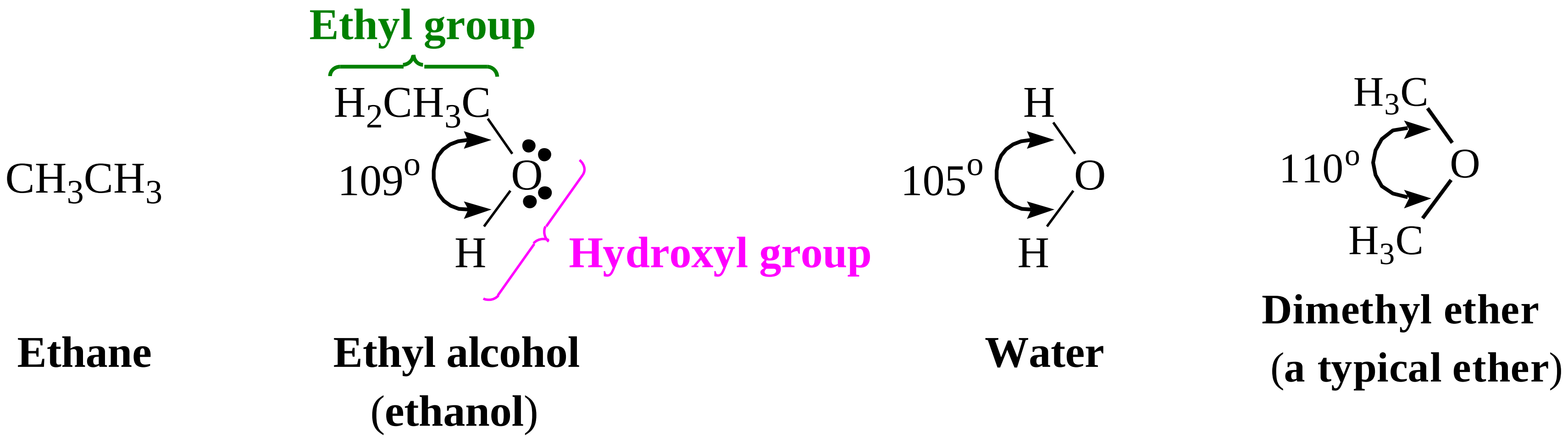
- **Alcohols** have the general formula R-OH, and structurally similar to water, but with one of the hydrogens replaced by an alkyl group.
- **Phenols** have a hydroxyl group attached directly to an aromatic ring.

Alcohols

- Alcohols can be viewed in two ways structurally:

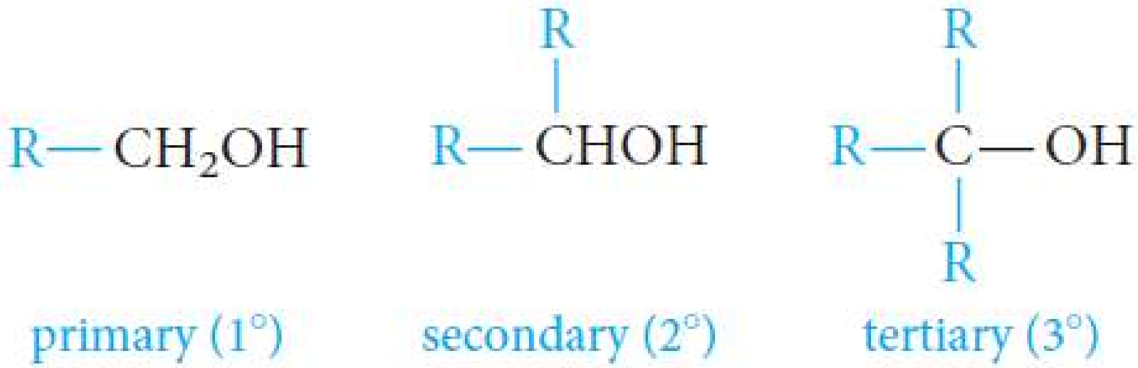
  (1) as **hydroxyl derivatives** of alkanes

  and (2) as **alkyl derivatives** of water.



Classification of Alcohols

- **Alcohols** are classified as primary (1°), secondary (2°), or tertiary (3°), depending on whether one, two, or three organic groups are connected to the hydroxyl-bearing carbon atom.



$$R{-}CH_2OH \qquad R{-}\overset{\overset{\displaystyle R}{|}}{C}HOH \qquad R{-}\underset{\underset{\displaystyle R}{|}}{\overset{\overset{\displaystyle R}{|}}{C}}{-}OH$$

- **Methyl alcohol**, which is not strictly covered by this classification, is usually grouped with the primary alcohols.

Nomenclature of Alcohols

- The **common names** for the simplest alcohols consist of alkyl group attached to the hydroxyl function followed by the word alcohol: Alkyl *alcohol* .
- In the **IUPAC system**, alcohols are named according to the following rules.

1. Select the longest continuous carbon chain that *contains the* -OH *group*.

   Drop the –e ending of the parent alkane and replace it by the suffix *-ol*: *Alkanol*

2. When isomers are possible, the chain is numbered so as to give the functional group (-OH) the *lowest possible number*.

CH_3OH

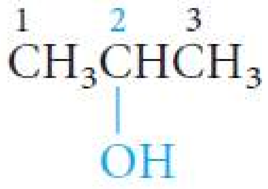
methanol
(methyl alcohol)

CH_3CH_2OH

ethanol
(ethyl alcohol)

$\overset{3}{C}H_3\overset{2}{C}H_2\overset{1}{C}H_2OH$

1-propanol
(*n*-propyl alcohol)



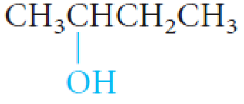
$\overset{1}{C}H_3\underset{OH}{\overset{2}{C}H}\overset{3}{C}H_3$

2-propanol
(isopropyl alcohol)

Nomenclature of Alcohols

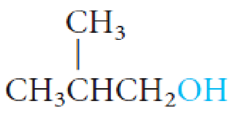
$CH_3CH_2CH_2CH_2OH$

1-butanol
(*n*-butyl alcohol)



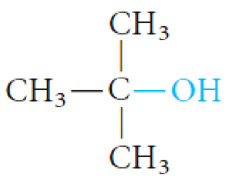
$CH_3\underset{\underset{OH}{|}}{C}HCH_2CH_3$

2-butanol
(*sec*-butyl alcohol)



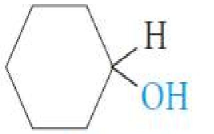
$CH_3\overset{\overset{CH_3}{|}}{C}HCH_2OH$

2-methyl-1-propanol
(isobutyl alcohol)

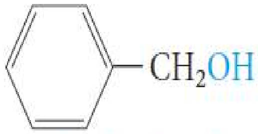


$CH_3-\overset{\overset{CH_3}{|}}{\underset{\underset{CH_3}{|}}{C}}-OH$

2-methyl-2-propanol
(*tert*-butyl alcohol)



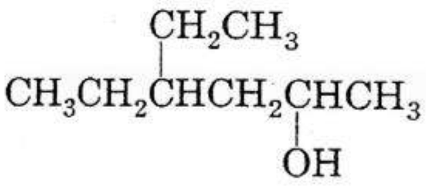
cyclohexanol
(cyclohexyl alcohol)



phenylmethanol
(benzyl alcohol)

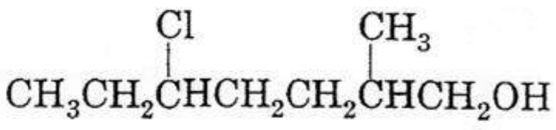
3. When alkyl side chains or other groups are present, they are named alphabetically and their positions are indicated by a number.

The position of the functional group (-OH) is always given the lowest possible number at the end of the name.



$CH_3CH_2\overset{\overset{CH_2CH_3}{|}}{C}HCH_2\underset{\underset{OH}{|}}{C}HCH_3$

4-Ethyl-2-hexanol
(*not* 3-Ethyl-5-hexanol)

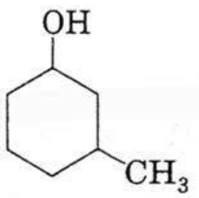


$CH_3CH_2\overset{\overset{Cl}{|}}{C}HCH_2CH_2\overset{\overset{CH_3}{|}}{C}HCH_2OH$

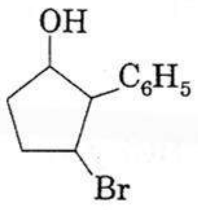
5-Chloro-2-methyl-1-heptanol
(*not* 3-Chloro-6-methyl-7-heptanol)

Nomenclature of Alcohols

For cyclic alcohols, numbering always starts from the carbon bearing the -OH group.



3-Methylcyclohexanol
(*not* 1-Methyl-3-cyclohexanol)



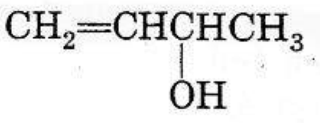
3-Bromo-2-phenylcyclopentanol
(*not* 1-Bromo-2-phenyl-3-cyclopentanol)

4. With Unsaturated Alcohols; If a molecule contains both an -OH group and a C=C or C-C triple bond, the -OH group takes preference before the double or triple bonds in getting the lower number.

The name should include (if possible) both the hydroxyl and the unsaturated groups, even if this does not make the longest chain the parent hydrocarbon.

$CH_2{=}CHCH_2OH$

2-propen-1-ol
(allyl alcohol)

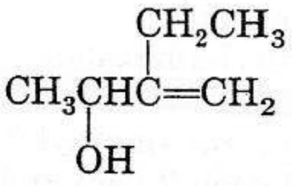


$CH_2{=}CH\underset{OH}{C}HCH_3$

3-Buten-2-ol
(*not* 1-Buten-3-ol)

$HC{\equiv}CCH_2CH_2OH$

3-Butyn-1-ol
(*not* 1-Butyn-4-ol)



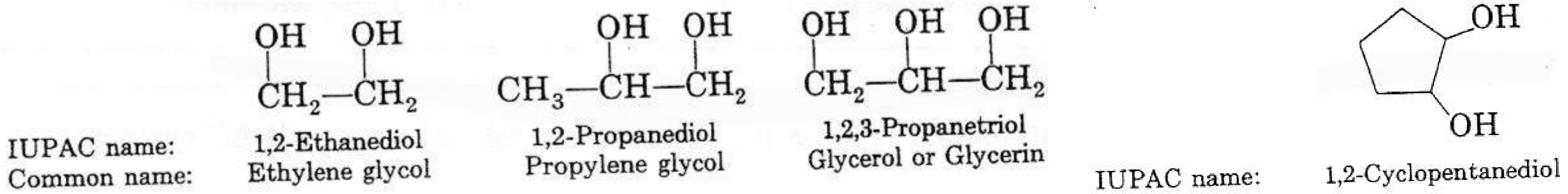
$CH_3\underset{OH}{C}H\overset{CH_2CH_3}{C}{=}CH_2$

3-Ethyl-3-buten-2-ol
(longest chain including C=C)

Nomenclature of Alcohols

Alcohols with More Than One Hydroxyl Group

- Compounds with two adjacent alcohol groups are called *glycols*.
  The most important example is ethylene glycol.
- Compounds with more than two hydroxyl groups are also known, and several, such as glycerol and sorbitol, are important commercial chemicals.



$\overset{OH}{CH_2}-\overset{OH}{CH_2}$ $CH_3-\overset{OH}{CH}-\overset{OH}{CH_2}$ $\overset{OH}{CH_2}-\overset{OH}{CH}-\overset{OH}{CH_2}$

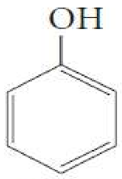
IUPAC name:	1,2-Ethanediol	1,2-Propanediol	1,2,3-Propanetriol
Common name:	Ethylene glycol	Propylene glycol	Glycerol or Glycerin

IUPAC name: 1,2-Cyclopentanediol

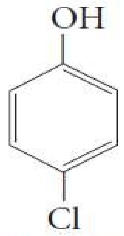
- *Ethylene glycol is used as the "permanent" antifreeze in automobile radiators and as a raw material in the manufacture of Dacron.*
- *Ethylene glycol is completely miscible with water.*
- *Glycerol is a syrupy, colorless, water-soluble, high-boiling liquid with a distinctly sweet taste. Its soothing qualities make it useful in shaving and toilet soaps and in cough drops and syrups.*

Nomenclature of Phenols

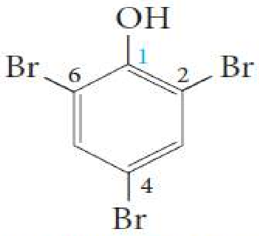
- **Phenols** are usually named as derivatives of the parent compounds.



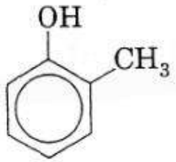
phenol



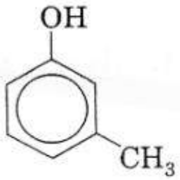
p-chlorophenol



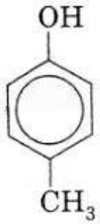
2,4,6-tribromophenol



o-Cresol

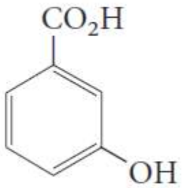


m-Cresol



p-Cresol

- The hydroxyl group is named as a substituent when it occurs in the same molecule with carboxylic acid, aldehyde, or ketone functionalities, which have **priority in naming**.



m-hydroxy
benzoic acid

p-hydroxybenzaldehyde

but

p-nitrophenol
(*not p*-hydroxynitrobenzene)

Physical Properties of Alcohols

Physical State

- *The simplest alcohol, methanol, is a liquid at room temperature.*
  In contrast, alkanes from methane to butane are gases.

Solubility

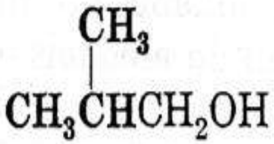
- *The lower alcohols are completely miscible with water.*
- *As the number of carbons in the alcohol increases, the solubility in water decreases.*

Boiling Points

- *Series of normal alcohols; The boiling points increase with increase in molecular weights.*
- *A comparison of boiling points among isomeric alcohols; The boiling points decrease as the number of alkyl branches from the carbinol group increases.*

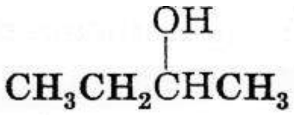
$CH_3CH_2CH_2CH_2OH$

1-Butanol
(mol wt = 74; bp = 118°C)



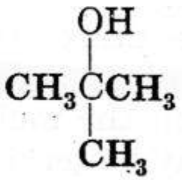
$CH_3\overset{CH_3}{\overset{|}{C}}HCH_2OH$

2-Methyl-1-propanol
(mol wt = 74; bp = 108°C)



$CH_3CH_2\overset{OH}{\overset{|}{C}}HCH_3$

2-Butanol
(mol wt = 74; bp = 99.5°C)



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

2-Methyl-2-propanol
(mol wt = 74; bp = 83°C)

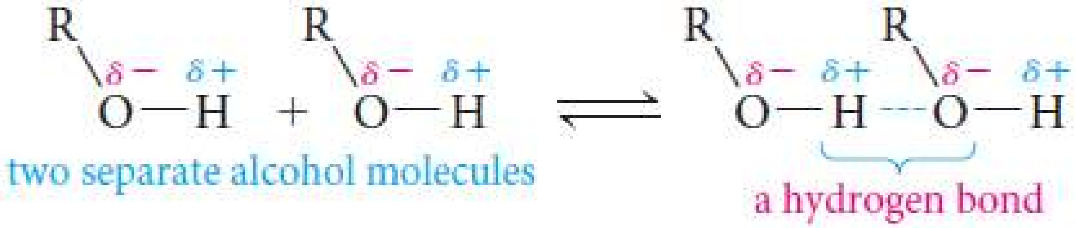
Hydrogen Bonding in Alcohols

- The **boiling points** (bp’s) of alcohols are much higher than those of ethers or hydrocarbons with similar molecular weights.

	CH_3CH_2OH	CH_3OCH_3	$CH_3CH_2CH_3$
mol wt	46	46	44
bp	+78.5°C	−24°C	−42°C

Why? Because alcohols form *hydrogen bonds* with one another.

The O-H bond is polarized by the high electronegativity of the oxygen atom and places a partial positive charge on the hydrogen atom and a partial negative charge on the oxygen atom.



Two or more alcohol molecules thus become loosely bonded to one another through hydrogen bonds.

Hydrogen Bonding in Alcohols

- Consequently, alcohols have relatively high boiling points because they must supply enough heat to break the hydrogen bonds before each molecule.
- Hydrogen bonds are weaker than ordinary covalent bonds.
- Water, of course, is also a hydrogen-bonded liquid.
- The lower molecular-weight alcohols can readily replace water molecules in the hydrogen bonded network.
- This accounts for the complete miscibility of the lower alcohols with water.
- However, as the organic chain lengthens and the alcohol becomes relatively more hydrocarbon like, its water solubility decreases.

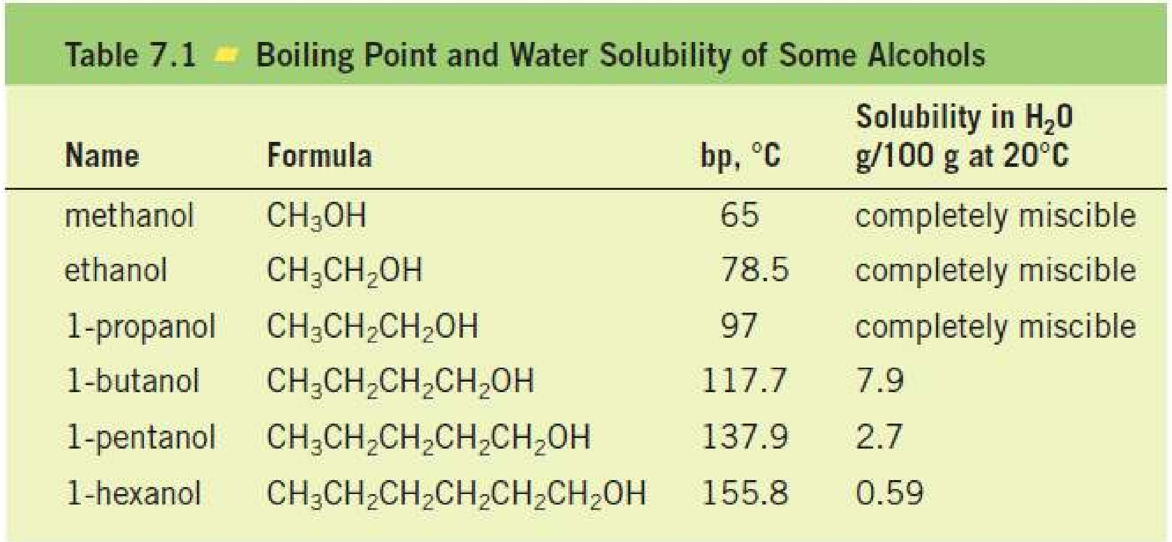


Table 7.1 Boiling Point and Water Solubility of Some Alcohols

Name	Formula	bp, °C	Solubility in H_2O g/100 g at 20°C
methanol	CH_3OH	65	completely miscible
ethanol	CH_3CH_2OH	78.5	completely miscible
1-propanol	$CH_3CH_2CH_2OH$	97	completely miscible
1-butanol	$CH_3CH_2CH_2CH_2OH$	117.7	7.9
1-pentanol	$CH_3CH_2CH_2CH_2CH_2OH$	137.9	2.7
1-hexanol	$CH_3CH_2CH_2CH_2CH_2CH_2OH$	155.8	0.59

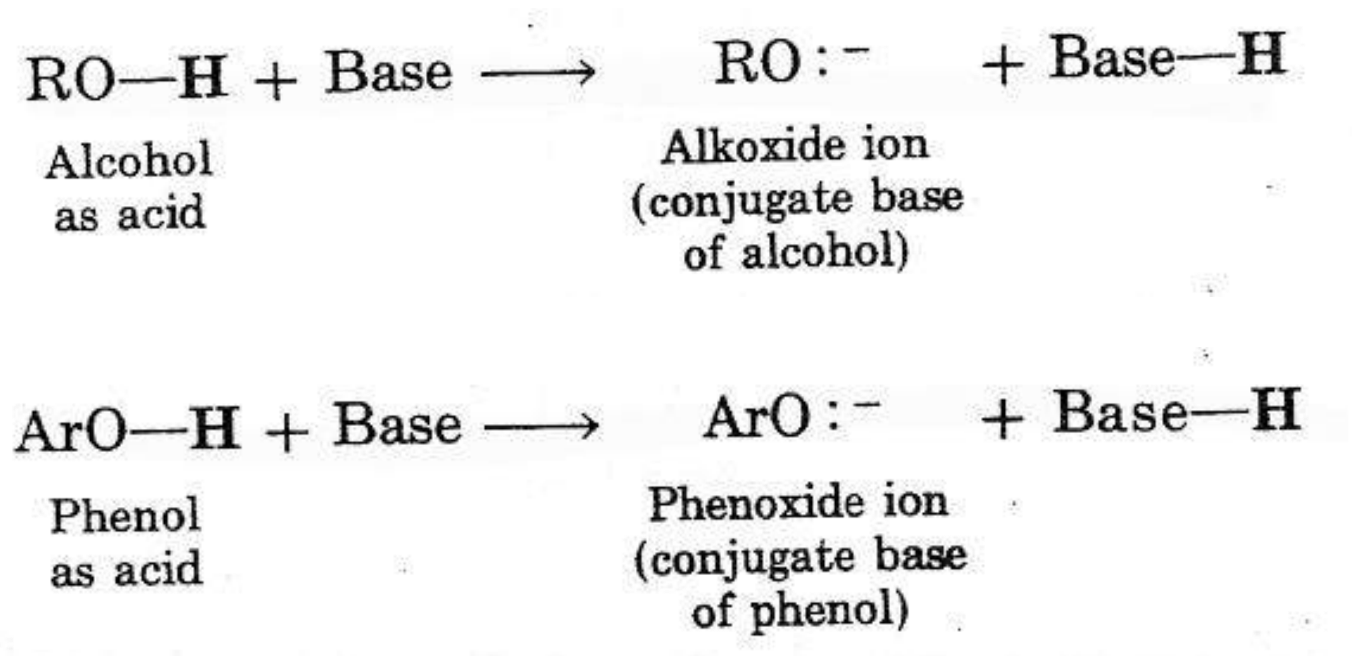
Physical Properties of Phenols

- **Phenol** is a colorless, crystalline, low-melting solid, with a high boiling point, that is moderately soluble in water.
- Most other phenols also are solids, with slight solubility in water and high boiling points.
- The most significant physical property that distinguishes alcohols from phenols is the acidity of phenols.

The Acidity of Alcohols and Phenols

- **Like water, alcohols and phenols are weak acids.**

The hydroxyl group can act as a proton donor, and dissociation occurs in a manner similar to that for water



$$\mathrm{RO{-}H} + \mathrm{Base} \longrightarrow \mathrm{RO{:}^-} + \mathrm{Base{-}H}$$

Alcohol
as acid

Alkoxide ion
(conjugate base
of alcohol)

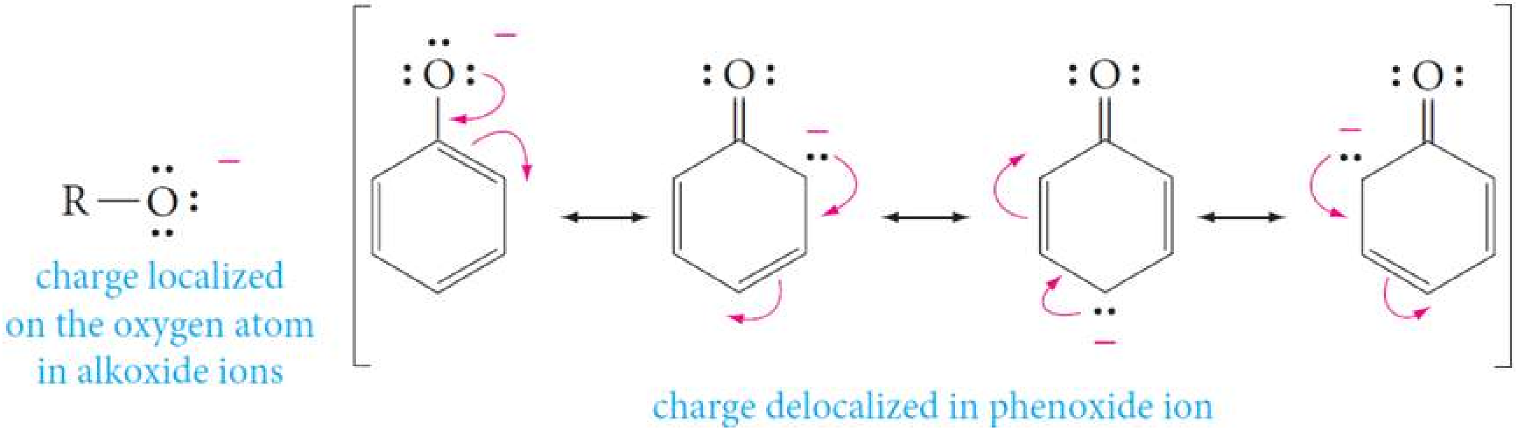
$$\mathrm{ArO{-}H} + \mathrm{Base} \longrightarrow \mathrm{ArO{:}^-} + \mathrm{Base{-}H}$$

Phenol
as acid

Phenoxide ion
(conjugate base
of phenol)

The Acidity of Alcohols and Phenols

- **Phenols are stronger acids than alcohols** mainly because the corresponding phenoxide ions are stabilized by resonance.

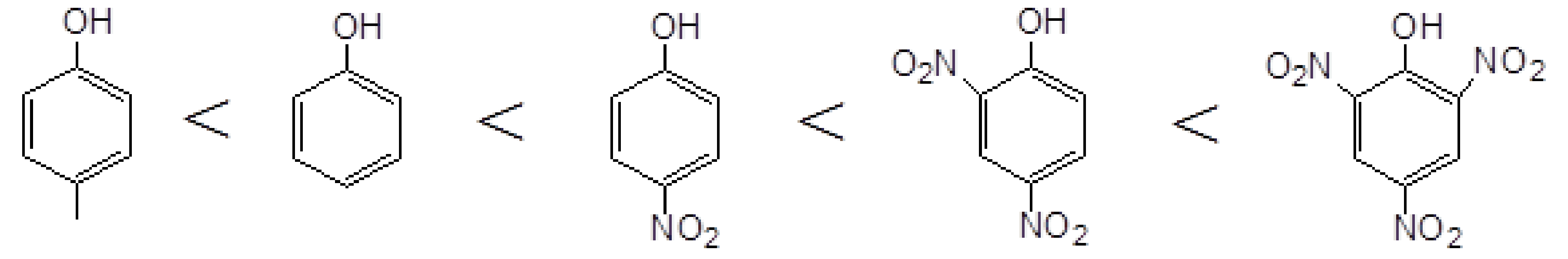


The negative charge of an alkoxide ion is concentrated on the oxygen atom, but the negative charge on a phenoxide ion can be delocalized to the ortho and para ring positions through resonance.

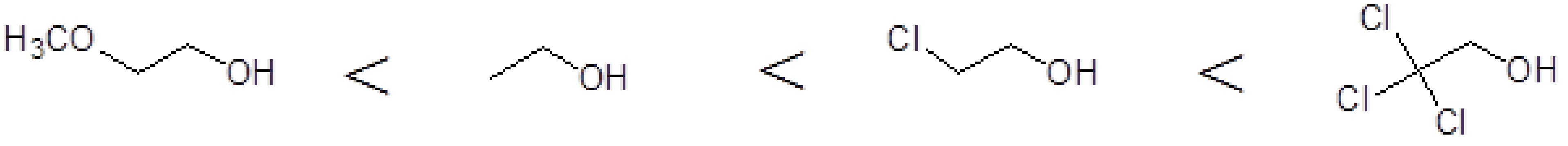
Because phenoxide ions are stabilized in this way, the equilibrium for their formation is more favorable than that for alkoxide ions

The Acidity of Alcohols and Phenols

- All **electron-withdrawing groups increase acidity** by stabilizing the conjugate base. **Electron-donating groups decrease acidity** because they destabilize the conjugate base.



4-Methylphenol (*p*-Cresol) < Phenol < 4-Nitrophenol < 2,4-Dinitrophenol < 2,4,6-Trinitrophenol (Picric acid)



Methoxyethanol < Ethanol < Chloroethanol < Trichloroethanol

The Acidity of Alcohols and Phenols

- **Alkoxides**, the conjugate bases of alcohols, can be prepared by the reaction of an alcohol with sodium or potassium metal.

$$2\,\mathrm{R}\ddot{\underset{\cdot\cdot}{\mathrm{O}}}\!-\!\mathrm{H} + 2\,\mathrm{K} \longrightarrow 2\,\mathrm{R}\ddot{\underset{\cdot\cdot}{\mathrm{O}}}{:}^{-}\ \mathrm{K}^{+} + \mathrm{H}_2$$

alcohol

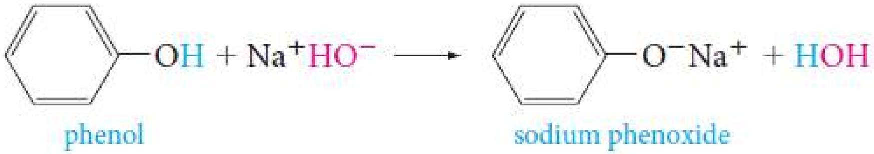
potassium alkoxide

- Treatment of alcohols with sodium hydroxide <u>does not convert</u> them to their alkoxides.

  This is because alkoxides are stronger bases than hydroxide ion, so the reaction goes in the reverse direction.
  Since alcohols are weaker acids than water, it is not possible to form the salt of an alcohol in aqueous alkaline solutions.

- Treatment of phenols with sodium hydroxide <u>converts</u> them to phenoxide ions.

$$\mathrm{ROH} + \mathrm{Na}^{+}\mathrm{HO}^{-} \not\rightleftharpoons \mathrm{RO}^{-}\mathrm{Na}^{+} + \mathrm{H_2O}$$

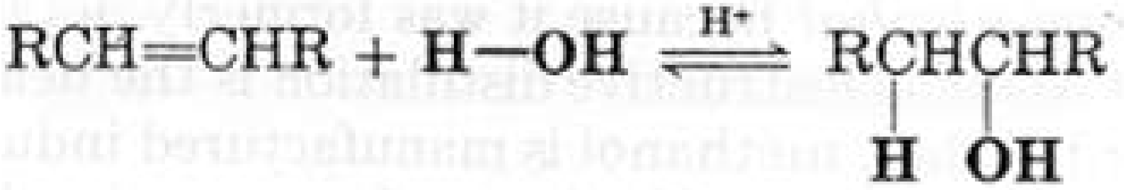


Preparation of Alcohols

○ ***From Alkenes***

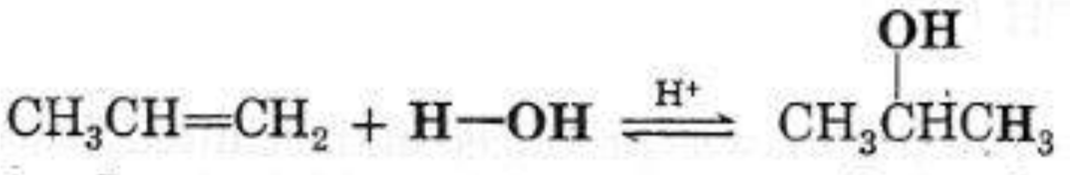
A. Hydration of Alkenes

1. Addition of water to a double bond in the presence of an *acid catalyst, H^+*.



$$\mathrm{RCH{=}CHR} + \mathrm{H{-}OH} \overset{H^+}{\rightleftharpoons} \mathrm{R}\underset{\mathrm{H}}{\underset{|}{\mathrm{CH}}}\underset{\mathrm{OH}}{\underset{|}{\mathrm{CH}}}\mathrm{R}$$

2. The addition *follows Markovnikov's rule*.



$$\mathrm{CH_3CH{=}CH_2} + \mathrm{H{-}OH} \overset{H^+}{\rightleftharpoons} \mathrm{CH_3}\overset{\mathrm{OH}}{\overset{|}{\mathrm{C}}}\mathrm{HCH_3}$$

Propene

2-Propanol (major product)

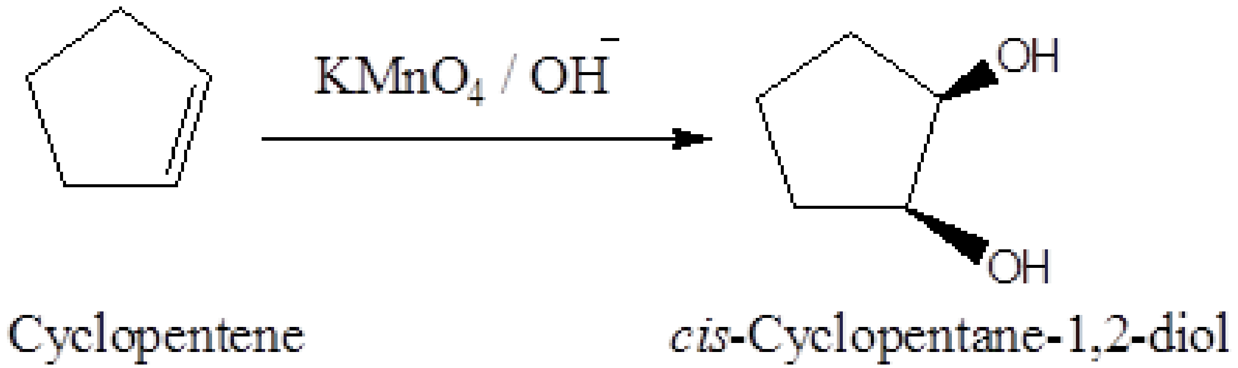
3. *It is not possible to prepare primary alcohols* except Ethanol.

Preparation of Alcohols

From Alkenes

B. Oxidation of Cycloalkenes

Alkenes react with alkaline potassium permanganate to form glycols (compounds with two adjacent hydroxyl groups).

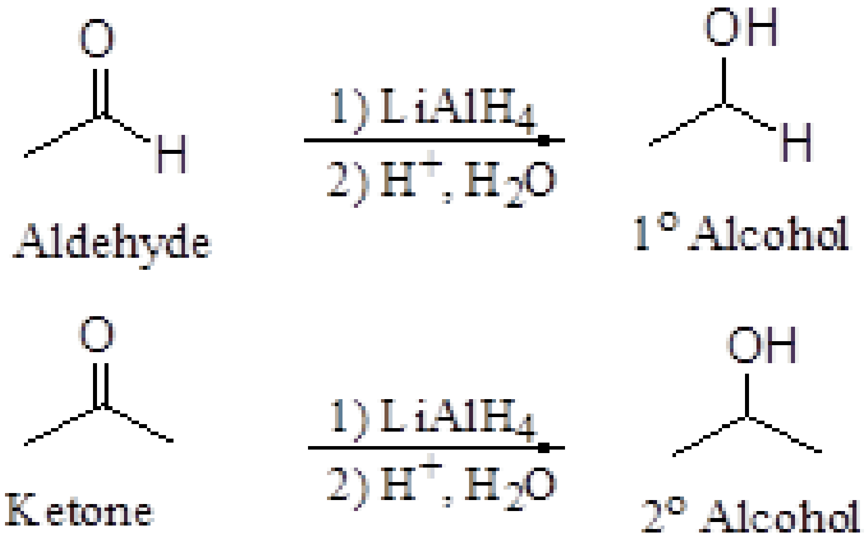


Preparation of Alcohols

- ## *Nucleophilic Substitution of Alkyl Halide*

- ## *Reduction of Ketones, and Aldehydes*

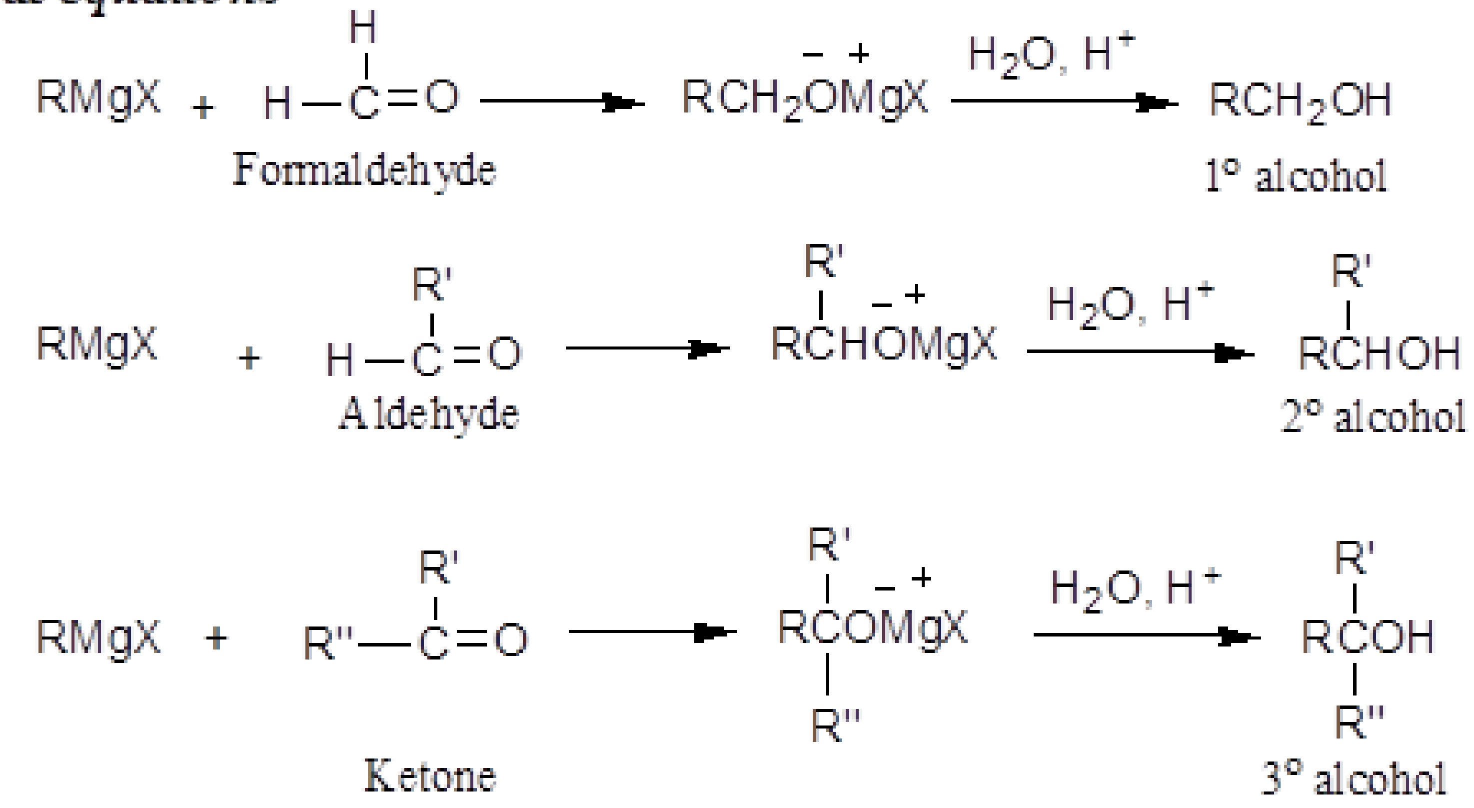
Aldehydes and ketones are easily reduced to primary and secondary alcohols, respectively.



Preparation of Alcohols

- ## *Addition of Grignard's Reagent to Aldehydes and Ketones*

General equations



$$RMgX + H-\overset{H}{\overset{|}{C}}=O \longrightarrow RCH_2\overset{-}{O}\overset{+}{Mg}X \xrightarrow{H_2O,\ H^+} RCH_2OH$$

$$RMgX + H-\overset{R'}{\overset{|}{C}}=O \longrightarrow R\overset{R'}{\overset{|}{C}}H\overset{-}{O}\overset{+}{Mg}X \xrightarrow{H_2O,\ H^+} R\overset{R'}{\overset{|}{C}}HOH$$

$$RMgX + R''-\overset{R'}{\overset{|}{C}}=O \longrightarrow R\underset{R''}{\underset{|}{\overset{R'}{\overset{|}{C}}}}\overset{-}{O}\overset{+}{Mg}X \xrightarrow{H_2O,\ H^+} R\underset{R''}{\underset{|}{\overset{R'}{\overset{|}{C}}}}OH$$

Reactions of Alcohols and Phenols

- **Alcohols** undergo two kinds of reactions:
  - **Those that involve the breaking of the oxygen-hydrogen bond (CO-H).**
  - **Those that involve the rupture of the carbon-oxygen bond (C-OH).**
- **Phenols** do not participate in reactions where the C-OH bond is broken.

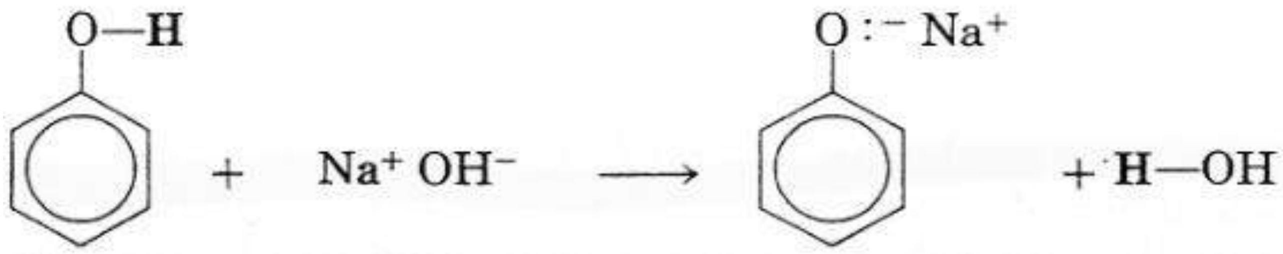
Reactions of Alcohols

A) Those that involve the breaking of the oxygen-hydrogen bond (CO-H).

1) Reactions of Alcohols and Phenols as Acids: Salt Formation.

$$R{-}OH + Na^+\,OH^- \longrightarrow \text{No reaction}$$

$$\underset{\text{Methanol}}{2\,CH_3O{-}\mathbf{H}} + 2\,Na \longrightarrow \underset{\text{Sodium methoxide}}{2\,CH_3O{:}^-\,Na^+} + \mathbf{H_2}\uparrow$$



Phenol (as an acid)

Sodium hydroxide (a base)

Sodium phenoxide (a salt)

Reactions of Alcohols

B) Those that involve the rupture of the carbon-oxygen bond (C-OH).

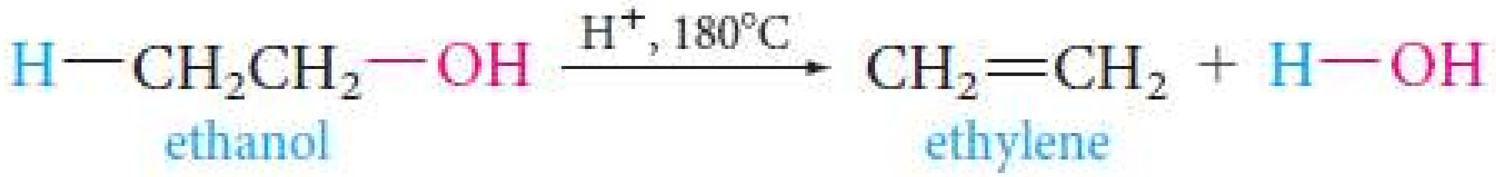
1) The Reaction of Alcohols with Hydrogen Halides: Alkyl Halides

Alcohols react with hydrogen halides (HCl, HBr and HI) to give alkyl halides.

$$\underset{\text{alcohol}}{R{-}OH} + H{-}X \longrightarrow \underset{\text{alkyl halide}}{R{-}X} + H{-}OH$$

2) Dehydration of Alcohols: Formation of Alkenes

Alcohols can be dehydrated by heating them with strong acid.

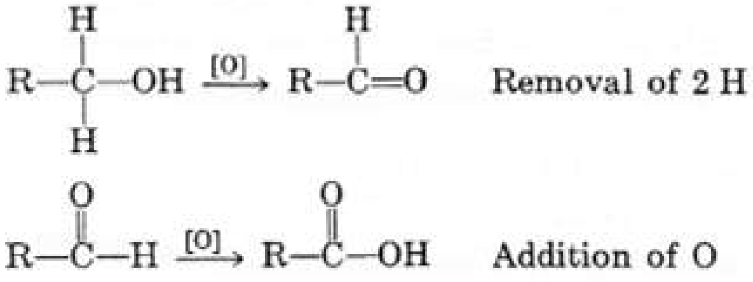


$$\underset{\text{ethanol}}{H{-}CH_2CH_2{-}OH} \xrightarrow{H^+,\ 180°C} \underset{\text{ethylene}}{CH_2{=}CH_2} + H{-}OH$$

Reactions of Alcohols

C) Oxidation Reactions

- **Oxidation** is the removal of H from a compound and/or the addition of O to a compound.



$$R-\underset{H}{\overset{H}{C}}-OH \xrightarrow{[O]} R-\overset{H}{C}=O$$

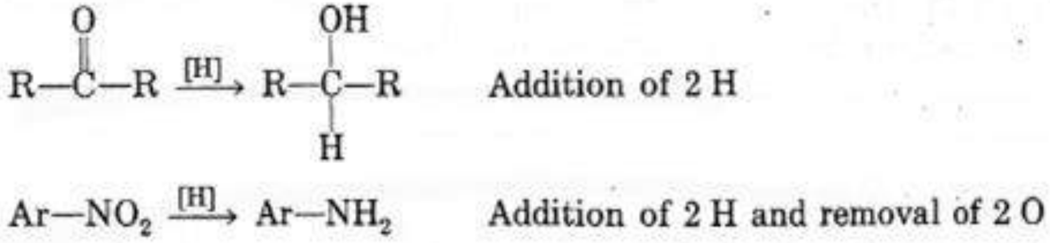
Removal of 2 H

$$R-\overset{O}{\overset{\|}{C}}-H \xrightarrow{[O]} R-\overset{O}{\overset{\|}{C}}-OH$$

Addition of O

An oxidizing agent is the chemical reagent that does the oxidation.

- **Reduction** is the addition of H to a compound and/or the removal of O from a compound.



$$R-\overset{O}{\overset{\|}{C}}-R \xrightarrow{[H]} R-\underset{H}{\overset{OH}{C}}-R$$

Addition of 2 H

$$Ar-NO_2 \xrightarrow{[H]} Ar-NH_2$$

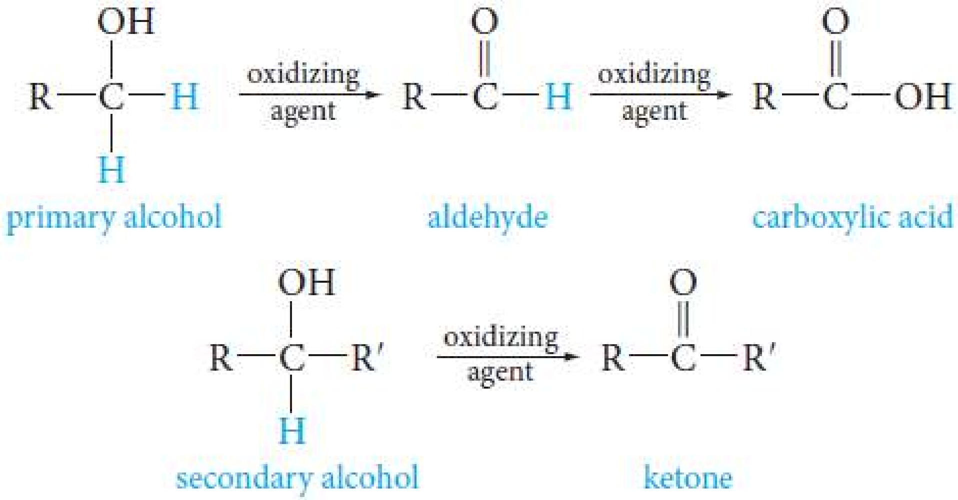
Addition of 2 H and removal of 2 O

A reducing agent is a substance that does the reduction.

Reactions of Alcohols

C) Oxidation Reactions

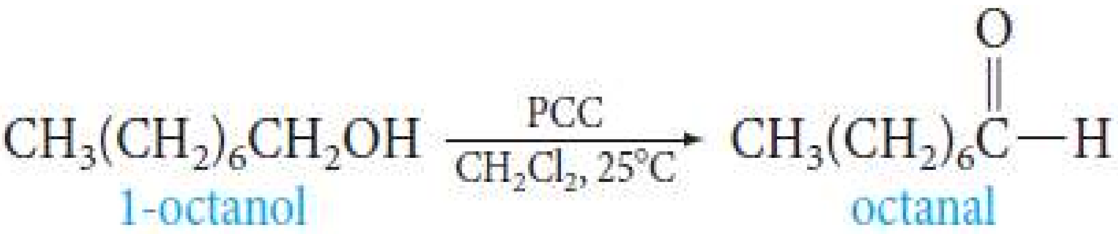
- **Alcohols with at least one hydrogen attached to the hydroxyl-bearing carbon can be oxidized to carbonyl compounds.**
  - **Primary alcohols** give aldehydes, which may be further oxidized to carboxylic acids.
  - **Secondary alcohols** give ketones.
  - **Tertiary alcohols**, having no hydrogen atom on hydroxyl-bearing carbon, *do not undergo oxidation*.



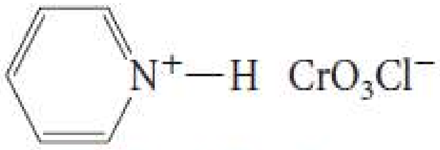
Reactions of Alcohols

C) Oxidation Reactions

- **Primary alcohols**, oxidation can be stopped at aldehyde stage by special reagents, such as “pyridinium chlorochromate (PCC)”.



$$CH_3(CH_2)_6CH_2OH \xrightarrow[CH_2Cl_2,\ 25°C]{PCC} CH_3(CH_2)_6\overset{\overset{\displaystyle O}{\|}}{C}-H$$

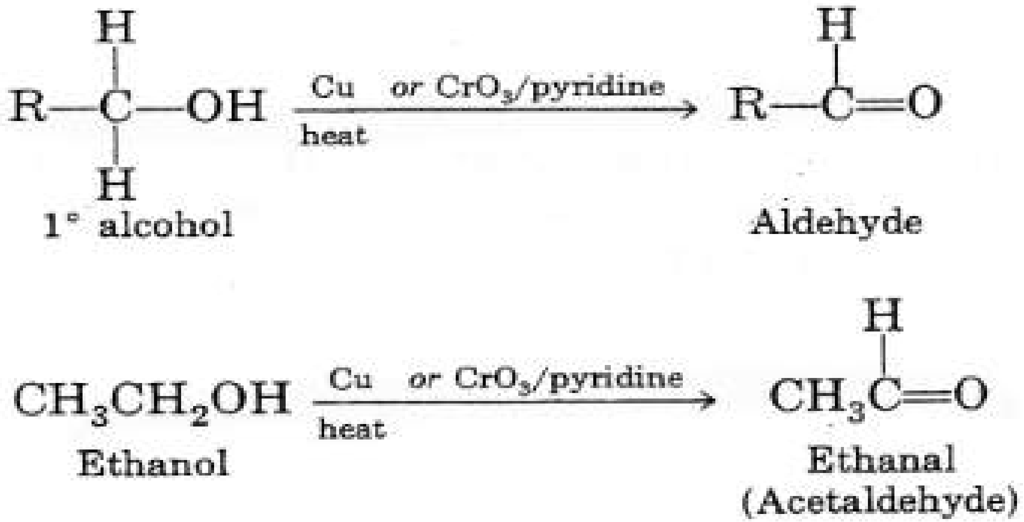


pyridinium chlorochromate
(PCC)

Reactions of Alcohols

C) Oxidation Reactions

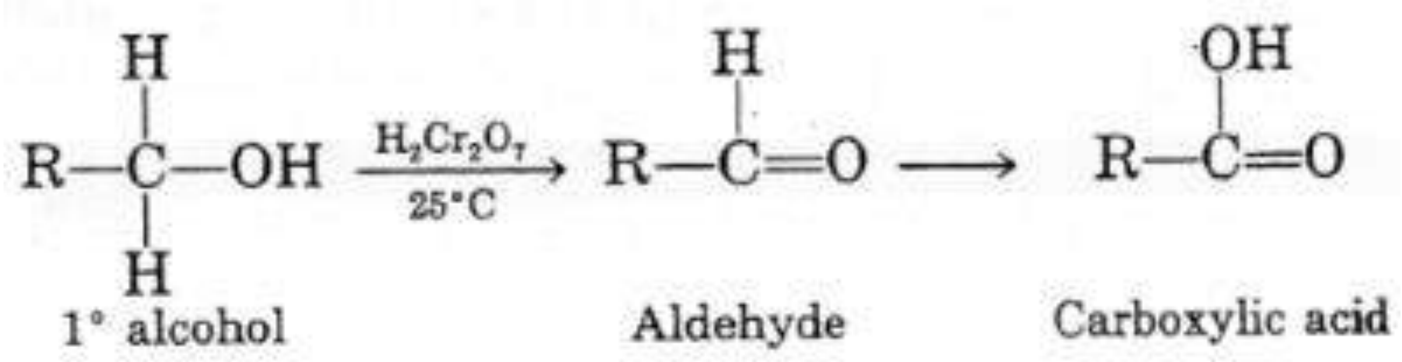
- **Primary alcohols** yield aldehydes when treated with *mild* oxidizing agents such as hot metallic copper or CrO_3 in pyridine.



Reactions of Alcohols

C) Oxidation Reactions

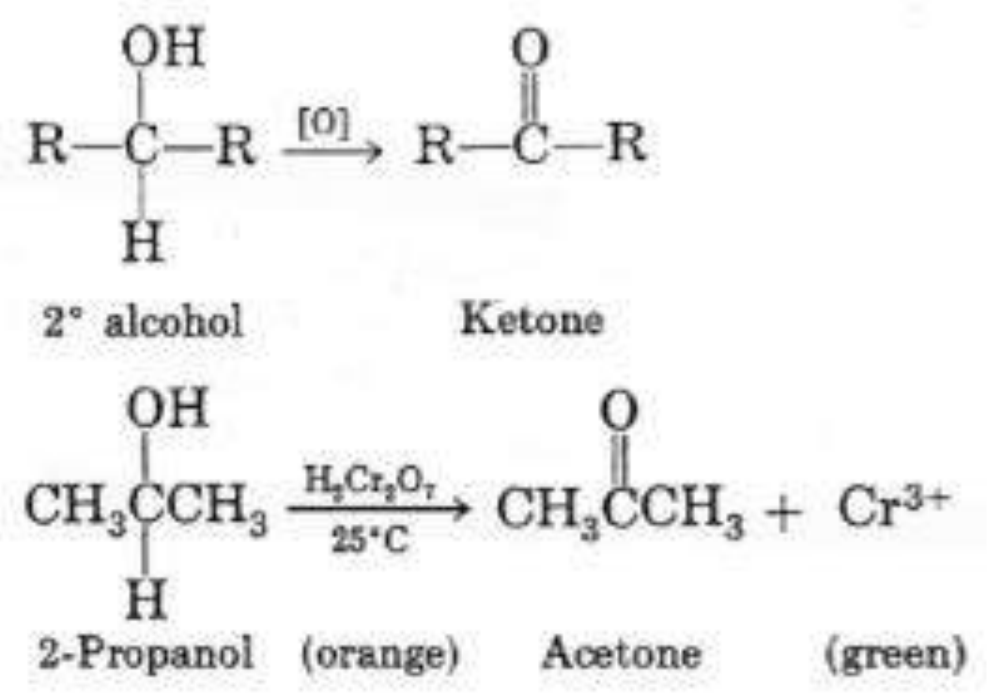
- **Primary alcohols** yield aldehydes when treated with *stronger oxidizing agents*, such as chromic acid, $H_2Cr_2O_7$, or neutral potassium permanganate, $KMnO_4$, the intermediate aldehydes formed initially are oxidized further to carboxylic acids.



Reactions of Alcohols

C) Oxidation Reactions

- **Secondary alcohols**, when treated with *any of the oxidizing agents* mentioned previously, yield ketones.



Preparation of Phenols

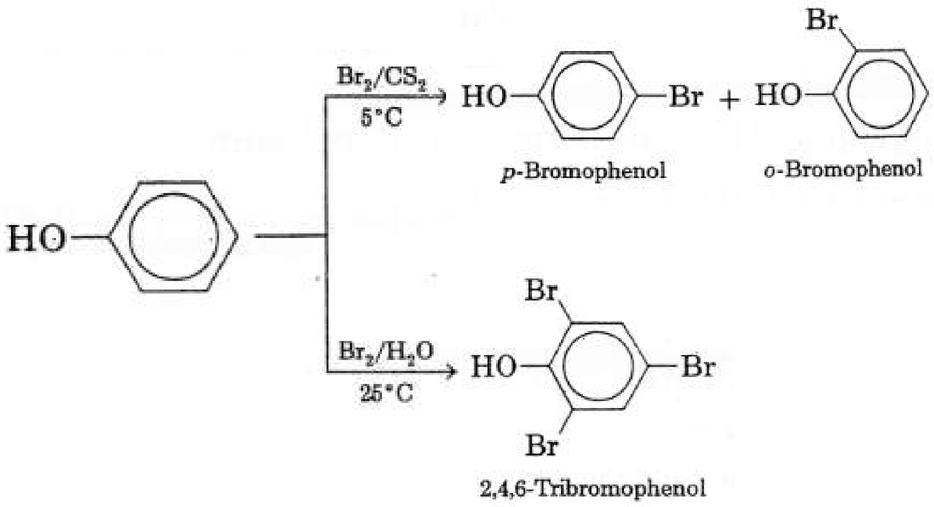
○ ***The Alkali Fusion of Sulfonates***

The alkali fusion of sulfonates involves the following steps;

1. **Sulfonation** of an aromatic ring.
2. **Melting** (**fusion**) of the aromatic sulfonic acid with sodium hydroxide to give a phenoxide salt.
3. **Acidification** of the phenoxide with HCl to produce the phenol.

Reactions of Phenols

- **Halogenation takes place *without catalyst*.**



- **The products depend on the solvent used.**
  - In *aprotic solvents* (solvents that do not release protons) (CCl_4, CS_2)-bromination gives a mixture of o- and *p*-bromophenol.
  - In *protic solvents (solvents that can release protons)* (H_2O)-halogenation gives a trisubstituted phenol is produced.

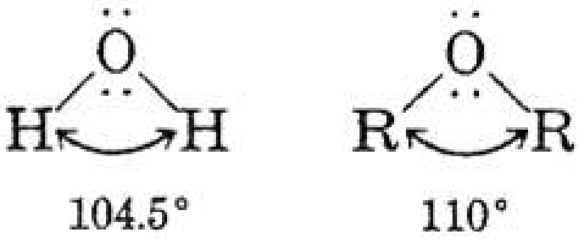
Ethers

Structure of Ethers

- All **ethers** are compounds in which two organic groups are connected to a single oxygen atom.
- The **general formula for an ether** is R-O-R’, where R and R’ may be identical or different, and they may be alkyl or aryl groups

R—O—R, Ar—O—R, or Ar—O—Ar

- The geometry of simple ethers is similar to that of water.



Structure of Ethers

- **The ether is classified as**
  - **Symmetrical ethers;**

    When the organic groups attached to the oxygen are identical.

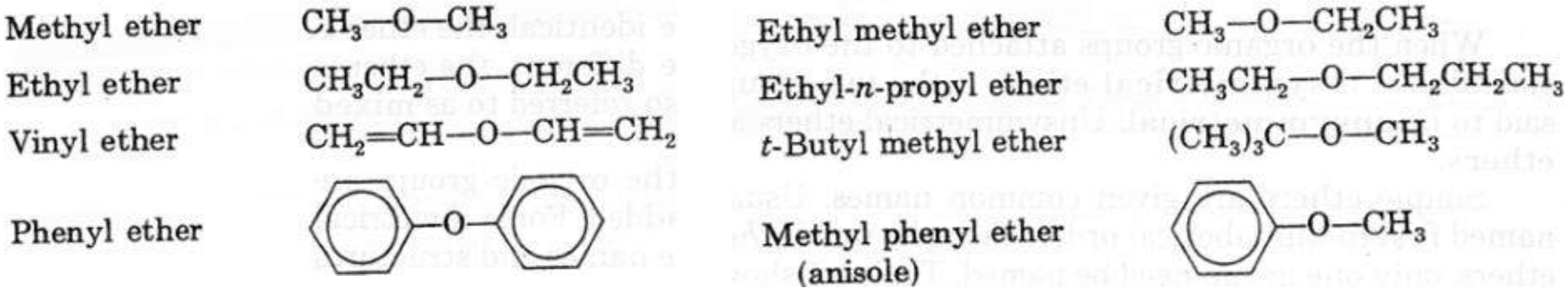
  - **Unsymmetrical ethers (mixed ethers);**

    When the organic groups attached to the oxygen are different.

Nomenclature of Ethers

Common Names

Ethers are usually named by giving the name of each alkyl or aryl group, in alphabetical order, followed by the word *ether.*

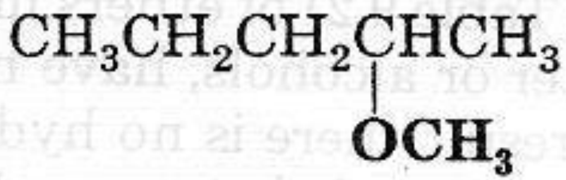


Methyl ether	$CH_3{-}O{-}CH_3$	Ethyl methyl ether	$CH_3{-}O{-}CH_2CH_3$
Ethyl ether	$CH_3CH_2{-}O{-}CH_2CH_3$	Ethyl-*n*-propyl ether	$CH_3CH_2{-}O{-}CH_2CH_2CH_3$
Vinyl ether	$CH_2{=}CH{-}O{-}CH{=}CH_2$	*t*-Butyl methyl ether	$(CH_3)_3C{-}O{-}CH_3$
Phenyl ether		Methyl phenyl ether (anisole)	

Nomenclature of Ethers

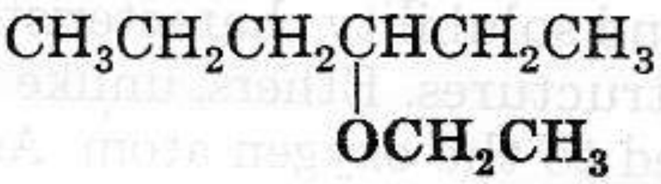
IUPAC System

For ethers with more complex structures, it may be necessary to name the -OR group as an alkoxy group. In the IUPAC system, the smaller alkoxy group is named as a substituent.



$$CH_3CH_2CH_2\underset{\displaystyle OCH_3}{\underset{|}{C}}HCH_3$$

2-Methoxypentane



$$CH_3CH_2CH_2\underset{\displaystyle OCH_2CH_3}{\underset{|}{C}}HCH_2CH_3$$

3-Ethoxyhexane

$H_3CO{-}CH_2CH_2OH$

2-Methoxyethanol

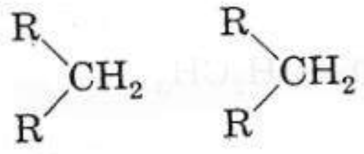
Physical Properties of Ethers

Physical State

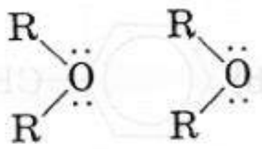
Ethers are colorless compounds with characteristic, relatively pleasant odors.

Boiling Points

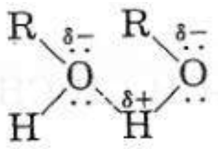
- *They have lower boiling points (bp,s) than alcohols with an equal number of carbon atoms.*
- In fact, an ether has nearly the same bp as the corresponding hydrocarbon in which a -CH_2- group replaces the ether's oxygen.
- *Because of their structures (no O-H bonds), ether molecules cannot form hydrogen bonds with one another.*



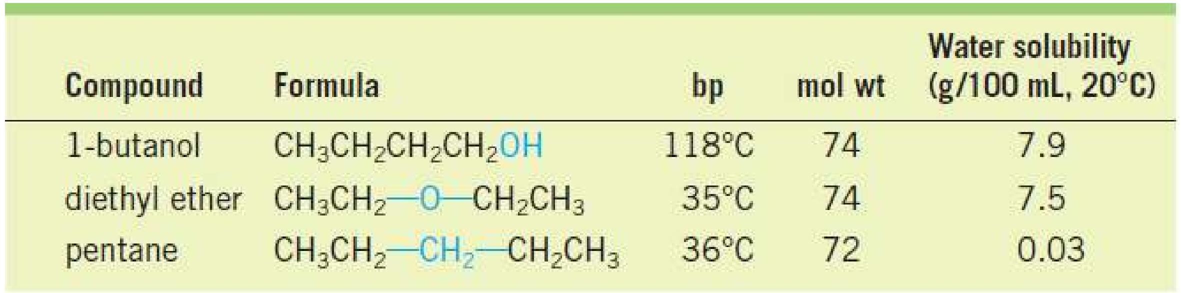
Alkanes: No hydrogen bonding between molecules; low boiling points



Ethers: No hydrogen bonding between molecules; low boiling points



Alcohols: Hydrogen bonding between molecules; high boiling points

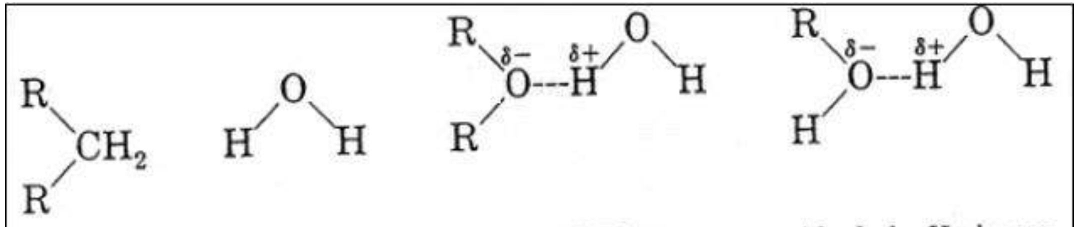


Compound	Formula	bp	mol wt	Water solubility (g/100 mL, 20°C)
1-butanol	$CH_3CH_2CH_2CH_2OH$	118°C	74	7.9
diethyl ether	$CH_3CH_2—O—CH_2CH_3$	35°C	74	7.5
pentane	$CH_3CH_2—CH_2—CH_2CH_3$	36°C	72	0.03

Physical Properties of Ethers

Solubility

- Low-molecular-weight ethers, such as dimethyl ether, are quite soluble in water.
- *Ether molecules can form hydrogen bonds to water.*



Alkanes: No hydrogen bonding with water; insoluble

Ethers: Hydrogen bonding with water; soluble

Alcohols: Hydrogen bonding with water; soluble

Structure	Name	Mol.wt.	Bp (°C)	Solubility in H_2O At 20 °C
$CH_3CH_2CH_3$	propane	44	−42	insoluble
CH_3OCH_3	methyl ether	46	−24	soluble
CH_3CH_2OH	ethanol	46	78	soluble
$CH_3CH_2CH_2CH_3$	*n*-butane	58	−0.5	insoluble
$CH_3CH_2OCH_3$	ethyl methyl ether	60	8	soluble
$CH_3CH_2CH_2OH$	1-propanol	60	97	soluble
$CH_3(CH_2)_3CH_3$	*n*-pentane	72	35	insoluble
$CH_3CH_2OCH_2CH_3$	ethyl ether	74	36	7.5 g/100 g
$CH_3(CH_2)_2CH_2OH$	1-butanol	74	118	7.9 g/100 g
$CH_3(CH_2)_5CH_3$	*n*-heptane	100	98	insoluble
$CH_3(CH_2)_2O(CH_2)_2CH_3$	*n*-propyl ether	102	91	0.2 g/100 g
$CH_3(CH_2)_4CH_2OH$	1-hexanol	102	157	0.6 g/100 g

Preparation of Ethers

- **There are *two general methods* for synthesizing ethers.**

1) Dehydration of alcohols

It is used commercially and in the laboratory to make certain symmetrical ethers.

2) Williamson synthesis

General laboratory method used to prepare all kinds of ethers, symmetrical and unsymmetrical.

Preparation of Ethers

1) Dehydration of Alcohols

It takes place in the presence of acid catalysts (H_2SO_4, H_3PO_4) (intermolecular reaction)

$$\text{R—OH} + \text{H—OR} \xrightarrow[\text{heat}]{H^+} \text{R—O—R} + H_2O$$

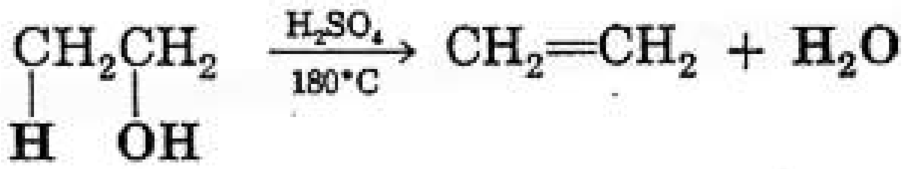
Example;

The most important commercial ether is diethyl ether. It is prepared from ethanol and sulfuric acid.

$$\underset{\text{ethanol}}{CH_3CH_2OH + HOCH_2CH_3} \xrightarrow[140°C]{H_2SO_4} \underset{\text{diethyl ether}}{CH_3CH_2OCH_2CH_3} + H_2O$$

Scope and Limitations

- When ethyl alcohol is dehydrated by sulfuric acid at 180° C, the dominant product is ethylene.



$$\underset{H\quad\;\; OH}{CH_2CH_2} \xrightarrow[180^\circ C]{H_2SO_4} CH_2{=}CH_2 + H_2O$$

Ethyl alcohol Ethylene

- **To prepare ethyl ether**
  - Dissolve ethyl alcohol in sulfuric acid at ambient temperature.
  - Heat the solution to 140°C while adding more alcohol.

$$2\ CH_3CH_2OH \xrightarrow[140^\circ C]{H_2SO_4} CH_3CH_2{-}O{-}CH_2CH_3 + H_2O$$

Ethyl alcohol Ethyl ether

Preparation of Ethers

2) Williamson Synthesis

- This method has two steps;
  1) An alcohol is converted to its alkoxide by treatment with a reactive metal (sodium or potassium).

$$2\,ROH + 2\,Na \longrightarrow 2\,RO^{-}Na^{+} + H_2$$

  2) Displacement is carried out between the alkoxide and an alkyl halide.

$$RO^{-}Na^{+} + R'{-}X \longrightarrow ROR' + Na^{+}X^{-}$$

  - To obtain the best yields of mixed dialkyl ethers, we select a 1° rather than a 2°or 3°alkyl halide and react it with a sodium alkoxide
  - To prepare an alkyl aryl ether, we must be careful not to pick a combination in which one of the reagents has a halogen directly attached to an aromatic ring.

2) Williamson Synthesis

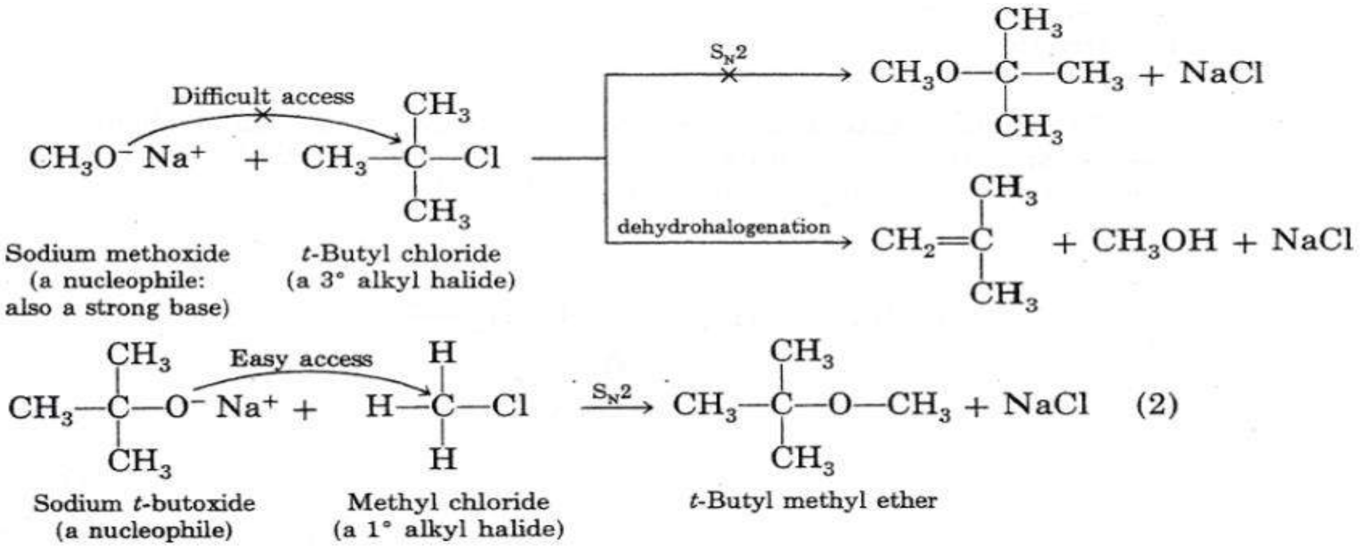
- **Example 1; Preparation of *t*-butyl methyl ether, $(CH_3)_3C\text{-}O\text{-}CH_3$.**
  - **In theory, this could be done by either of two reactions.**

1. You could react sodium methoxide, $CH_3O^-Na^+$, with *t*-butyl chloride, $(CH_3)_3C\text{-}Cl$.

   This combination leads to dehydrohalogenation to an alkene, an elimination reaction.

2. You could react sodium *t*-butoxide, $(CH_3)_3C\text{-}O^-Na^+$, with methyl chloride, CH_3Cl.

   This route gives the desired ether by substitution.

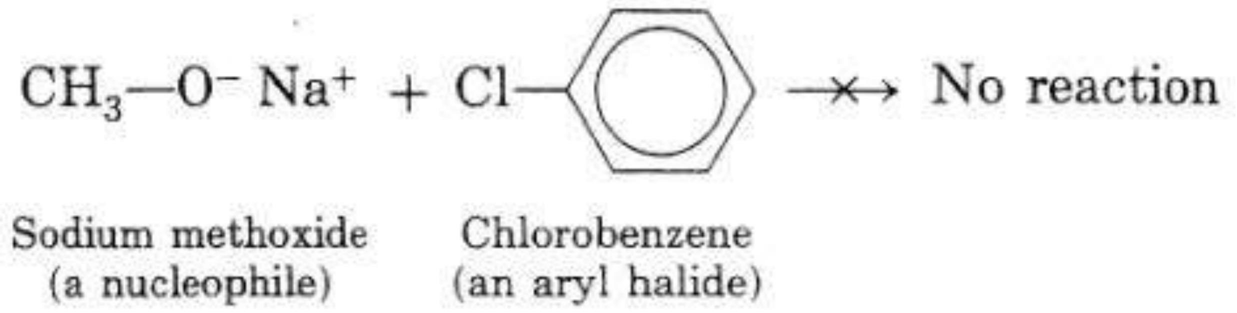


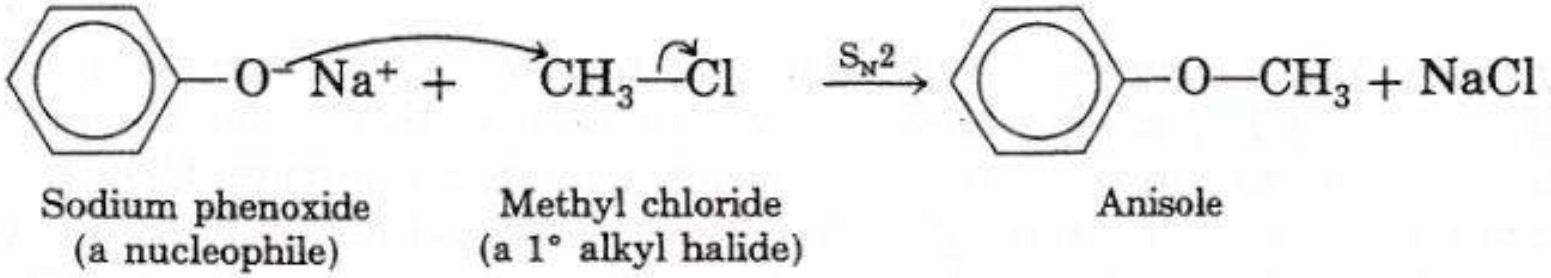
Preparation of Ethers

2) Williamson Synthesis

Example 2; **Assume you need to synthesize methyl phenyl ether (anisole), CH_3-O-C_6H_5, by the Williamson method.**

- *In theory, you could obtain anisole in either of two ways.*





Reactions of Ethers

- **Ethers** are quite stable compounds.
- The **ether** linkage does not react with bases, reducing agents, oxidizing agents, or active metals.
- ***Ethers*** *react only under strongly acidic conditions.*

Preparation of Ethers

Cleavage of Ethers by Hot Concentrated Acids

- When **ethers** are heated in concentrated acid solutions, the ether linkage is broken.

$$CH_3CH_2-\ddot{\underset{\cdot\cdot}{O}}-CH_2CH_3 + \underset{\text{(conc)}}{HI} \xrightarrow[\text{heat}]{} CH_3CH_2OH + CH_3CH_2I$$

- The acids most often used in this reaction are HI, HBr, and HCl.
- If an *excess of acid* is present, the alcohol initially produced is converted into an alkyl halide by the reaction.

$$R-OH + HX \longrightarrow RX + H_2O$$

For example,

$$CH_3CH_2-O-CH_2CH_3 + \underset{\text{(conc)}}{2\,HBr} \xrightarrow[\text{heat}]{} 2\,CH_3CH_2Br + H_2O$$

Fundamentals of Organic Chemistry

CHEM 109

For Students of Health Colleges

Credit hrs.: (2+1)

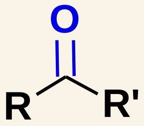
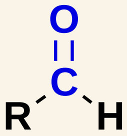
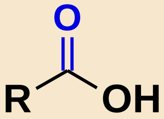
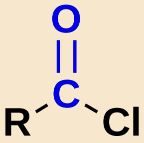
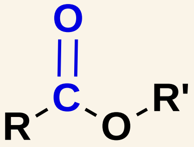
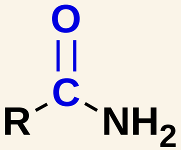
King Saud University

College of Science, Chemistry Department

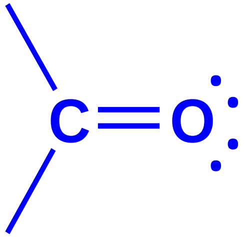
CHAPTER 5. ALDEHYDES & KETONES

Aldehydes & Ketones

Common Classes of Carbonyl Compounds

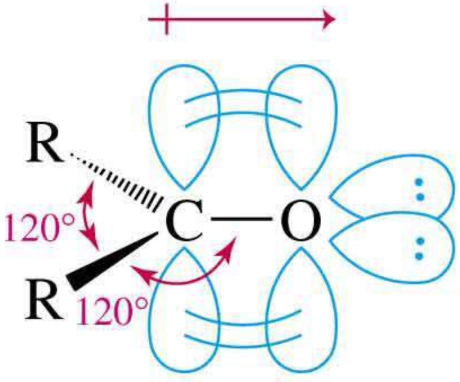
Class	General Formula	Class	General Formula
Ketones		Aldehydes	
Carboxylic acids		Acid Chlorides	
Esters		Amides	

Aldehydes & Ketones



The carbonyl group

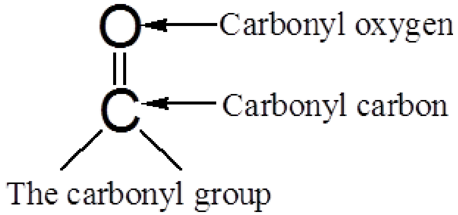
- Carbon is ***sp*²** **hybridized**.
- **C=O bond** is shorter, stronger, and more polar than C=C bond in alkenes.



	length	*energy*
ketone C=O bond	1.23 Å	178 kcal/mol (745 kJ/mol)
alkene C=C bond	1.34 Å	146 kcal/mol (611 kJ/mol)

Structure of Aldehydes and Ketones

- **Aldehydes and ketones** are characterized by the presence of the carbonyl group.

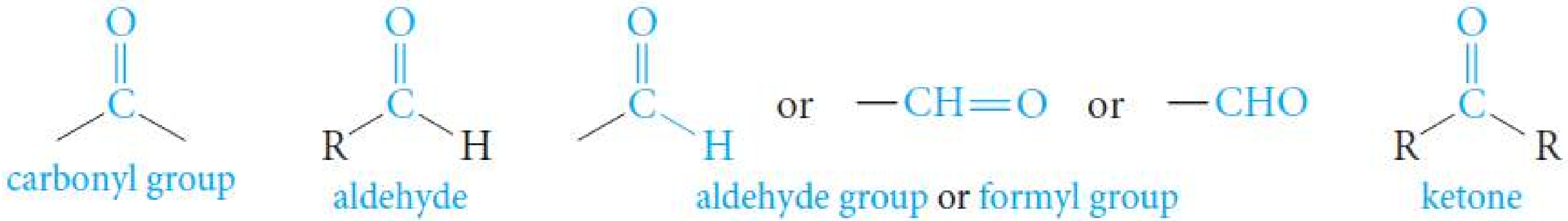


- **Aldehydes** have at least one hydrogen atom attached to the carbonyl carbon atom.

  The remaining group may be another hydrogen atom or any aliphatic or aromatic organic group.

  The -CH=O group characteristic of aldehydes is often called a formyl group.

- In **ketones,** the carbonyl carbon atom is connected to two other carbon atoms.

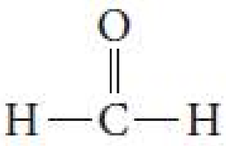


Nomenclature of Aldehydes

IUPAC System

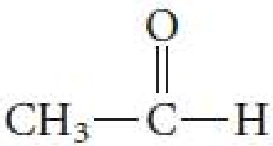
- *Aliphatic aldehydes* ***are named by dropping the suffix -e from the name of the hydrocarbon that has the same carbon skeleton as the aldehyde and replacing it with the suffix -al.***

Alkane - e+ *al = Alkanal*



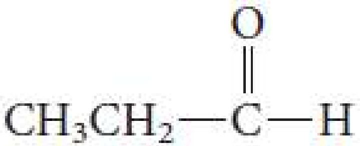
$H-\overset{O}{\overset{\|}{C}}-H$

methanal
(formaldehyde)



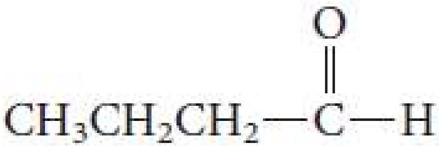
$CH_3-\overset{O}{\overset{\|}{C}}-H$

ethanal
(acetaldehyde)



$CH_3CH_2-\overset{O}{\overset{\|}{C}}-H$

propanal
(propionaldehyde)



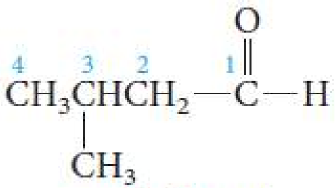
$CH_3CH_2CH_2-\overset{O}{\overset{\|}{C}}-H$

butanal
(*n*-butyraldehyde)

Nomenclature of Aldehydes

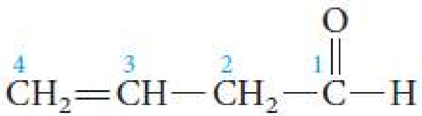
IUPAC System

- ***Substituted aldehydes,*** *we number the chain starting with the aldehyde carbon.*
  - *-CH=O group is assigned the number 1 position.*
  - *Aldehyde group has priority over a double bond or hydroxyl group.*



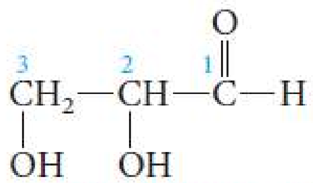
$\overset{4}{C}H_3\overset{3}{C}H(CH_3)\overset{2}{C}H_2-\overset{\overset{O}{\|}}{\overset{1}{C}}-H$

3-methylbutanal



$\overset{4}{C}H_2=\overset{3}{C}H-\overset{2}{C}H_2-\overset{\overset{O}{\|}}{\overset{1}{C}}-H$

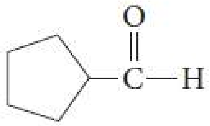
3-butenal



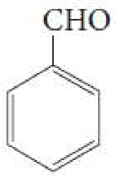
$\underset{OH}{\overset{3}{C}H_2}-\underset{OH}{\overset{2}{C}H}-\overset{\overset{O}{\|}}{\overset{1}{C}}-H$

2,3-dihydroxypropanal
(glyceraldehyde)

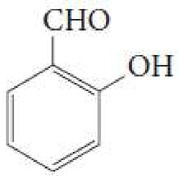
- ***Cyclic aldehydes,*** *the suffix –carbaldehyde is used.*



cyclopentanecarbaldehyde
(formylcyclopentane)



benzaldehyde
(benzenecarbaldehyde)

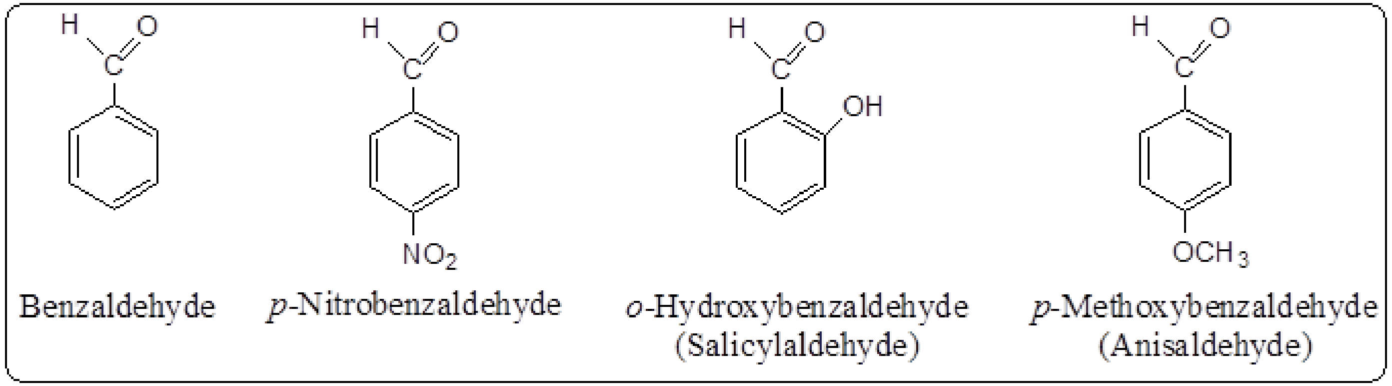


salicylaldehyde
(2-hydroxybenzenecarbaldehyde)

Nomenclature of Aldehydes

IUPAC System

- ***Aromatic aldehydes*** *are usually designated as derivatives of the simplest aromatic aldehyde, benzaldehyde*.



Benzaldehyde

p-Nitrobenzaldehyde

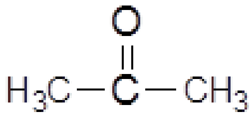
o-Hydroxybenzaldehyde (Salicylaldehyde)

p-Methoxybenzaldehyde (Anisaldehyde)

Nomenclature of Aldehydes

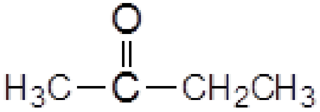
Common Names

- Common names of ketones are formed by adding the word *ketone* to the names of the alkyl or aryl groups attached to the carbonyl carbon. Alkyl ketone.
- In still other cases, traditional names are used.



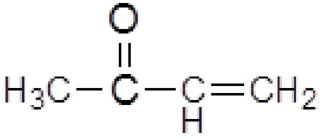
$H_3C-\overset{O}{\overset{\|}{C}}-CH_3$

Acetone
(Dimethyl ketone)



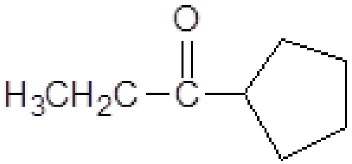
$H_3C-\overset{O}{\overset{\|}{C}}-CH_2CH_3$

Methyl ethyl ketone

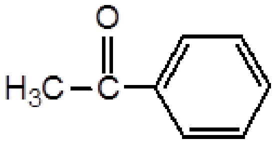


$H_3C-\overset{O}{\overset{\|}{C}}-\underset{H}{C}=CH_2$

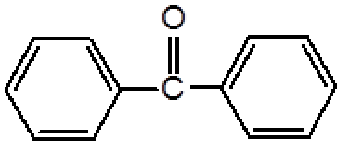
Methyl vinyl ketone



Ethyl cyclopentyl ketone



Methyl phenyl ketone
(Acetophenone)

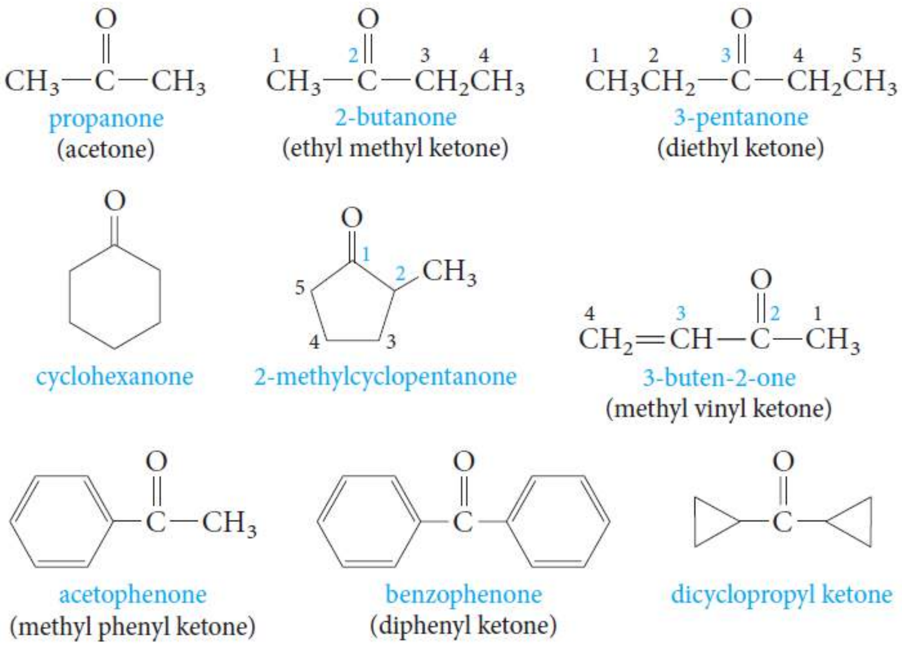


Diphenyl ketone
(Benzophenone)

Nomenclature of Ketones

IUPAC System

- In the IUPAC system, the ending for ketones is -one.
- The chain is numbered so that the carbonyl carbon has the lowest possible number.
- For cyclic ketones, numbering always starts from the C=O group.
- The prefix "oxo" is used when the ketone is not the principal functional group.



propanone
(acetone)

2-butanone
(ethyl methyl ketone)

3-pentanone
(diethyl ketone)

cyclohexanone

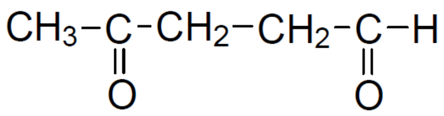
2-methylcyclopentanone

3-buten-2-one
(methyl vinyl ketone)

acetophenone
(methyl phenyl ketone)

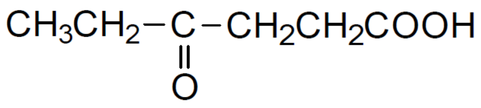
benzophenone
(diphenyl ketone)

dicyclopropyl ketone



$CH_3-\underset{\underset{O}{\|}}{C}-CH_2-CH_2-\underset{\underset{O}{\|}}{C}-H$

4-oxopentanal



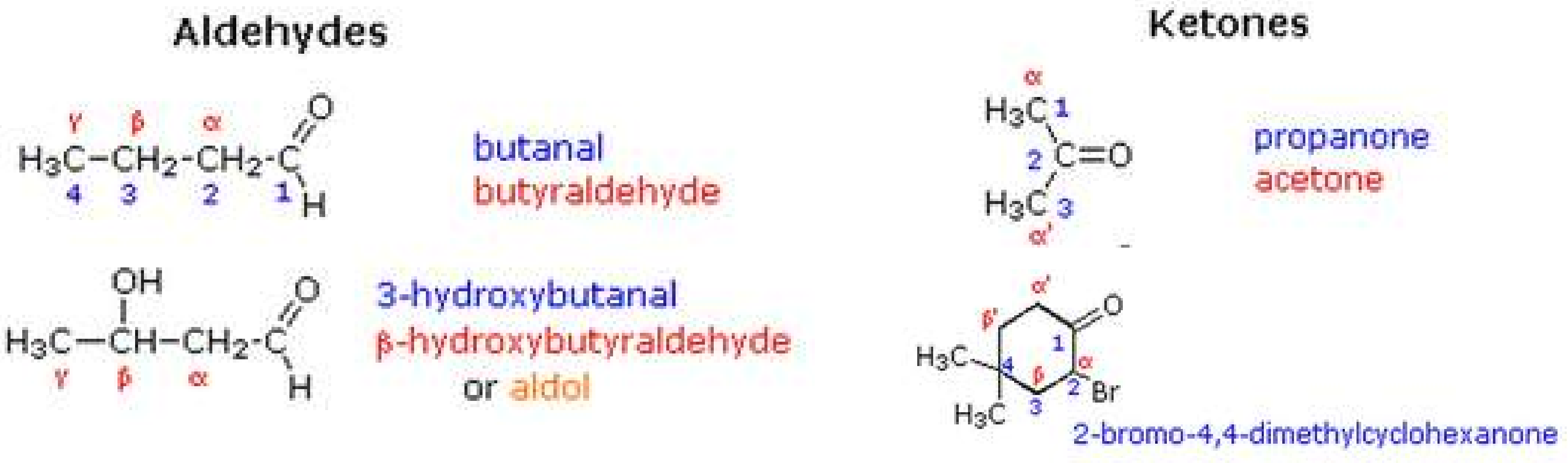
$CH_3CH_2-\underset{\underset{O}{\|}}{C}-CH_2CH_2COOH$

4-oxohexanoic acid

Nomenclature of Aldehydes Ketones

NOTES

- **In common names** carbon atoms near the carbonyl group are often designated by Greek letters.
- The atom adjacent to the function is *alpha* (α), the next removed is *beta* (β) and so on. Since ketones have two sets of neighboring atoms, one set is labeled α, β etc., and the other α', β' etc.



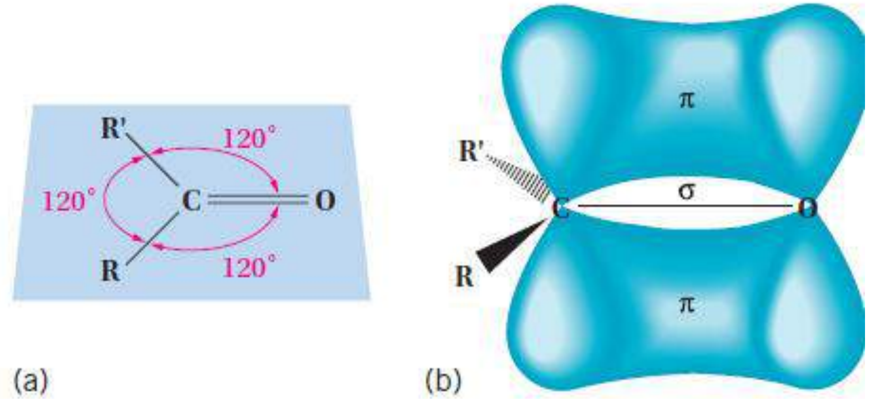
- **The functional group priority order in nomenclature system** is as following:

  Acid and derivatives >aldehyde> ketone> alcoho > amine > alkene > alkyne > ether

The Carbonyl Group

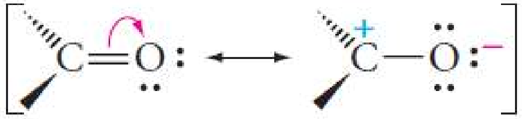
The structure and properties of the carbonyl group.

- The carbon–oxygen double bond consists of a sigma bond and a pi bond.
- The carbon atom is sp^2-hybridized. The three atoms attached to the carbonyl carbon lie in a plane with bond angles of 120°.
- The pi bond is formed by overlap of a *p* orbital on carbon with an oxygen *p* orbital.
- There are also two unshared electron pairs on the oxygen atom.
- The C=O bond distance is 1.24A, shorter than the C-O distance in alcohols and ethers (1.43A) .



The Carbonyl Group

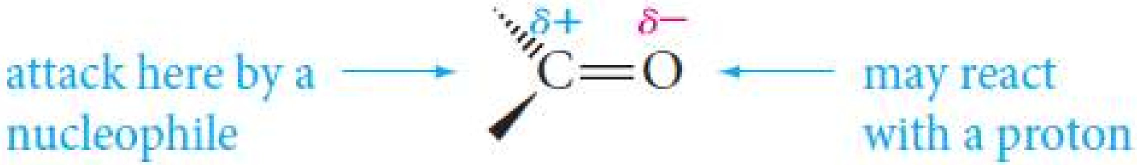
- Oxygen is much more electronegative than carbon. Therefore, the electrons in the C=O bond are attracted to the oxygen, producing a highly polarized bond.



resonance contributors to the carbonyl group

polarization of the carbonyl group

- As a consequence of this polarization, *most carbonyl reactions involve* nucleophilic attack *at the carbonyl carbon,* often accompanied by addition of a proton to the oxygen (electron rich).



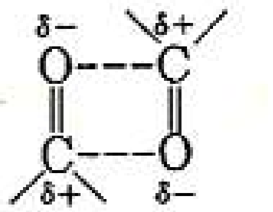
Physical Properties of Aldehydes and Ketones

Boiling Points

- Carbonyl compounds boil at higher temperatures than hydrocarbons, but at lower temperatures than alcohols of comparable molecular weight.

$CH_3(CH_2)_4CH_3$ hexane (bp 69°C) $CH_3(CH_2)_3CH{=}O$ pentanal (bp 102°C) $CH_3(CH_2)_3CH_2OH$ pentanol (bp 118°C)

- This is due to the intermolecular forces of attraction, called dipole-dipole interactions, which is stronger than van der Waals attractions but not as strong as hydrogen bonds.

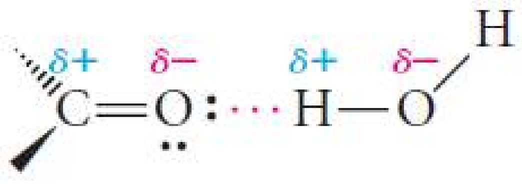


Dipole-dipole attractions among carbonyl compounds

Physical Properties of Aldehydes and Ketones

Solubility

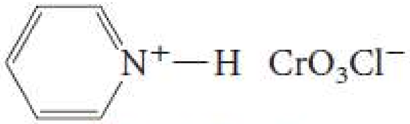
- Carbonyl compounds as aldehydes and ketones have a C=O bond, but no O-H bond, cannot form hydrogen bonds with themselves.
- The polarity of the carbonyl group also affects the solubility properties of aldehydes and ketones.
- Carbonyl compounds with low molecular weights are soluble in water as they can form hydrogen bonds with O-H or N-H compounds.



Preparation of Aldehydes and Ketones

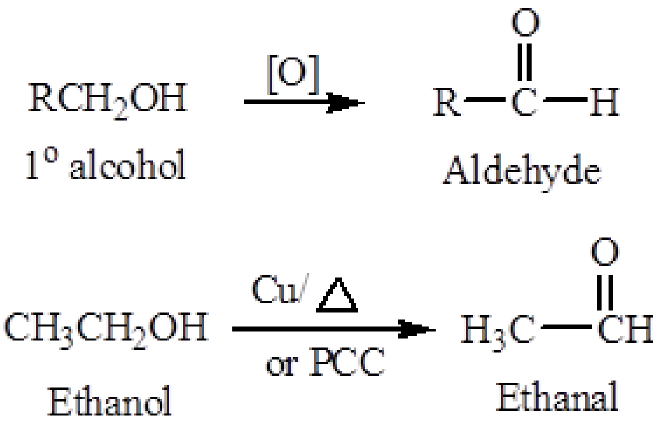
1) Oxidation of Primary and Secondary Alcohols

- Chromium reagents, such as pyridinium chlorochromate (PCC), are commonly used in the laboratory.



pyridinium chlorochromate
(PCC)

- Oxidation of **primary alcohols**, under controlled conditions, yields aldehydes.



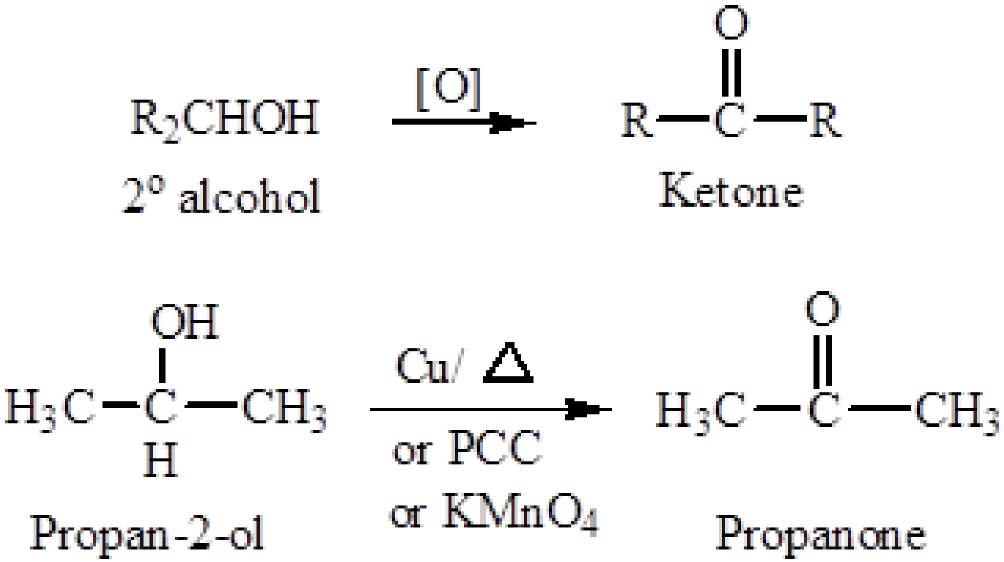
$$\underset{\text{1° alcohol}}{RCH_2OH} \xrightarrow{[O]} \underset{\text{Aldehyde}}{R-\overset{\overset{\displaystyle O}{\|}}{C}-H}$$

$$\underset{\text{Ethanol}}{CH_3CH_2OH} \xrightarrow[\text{or PCC}]{Cu/\Delta} \underset{\text{Ethanal}}{H_3C-\overset{\overset{\displaystyle O}{\|}}{C}H}$$

Preparation of Aldehydes and Ketones

1) Oxidation of Primary and Secondary Alcohols

- Oxidation of **secondary alcohols** yields ketones.

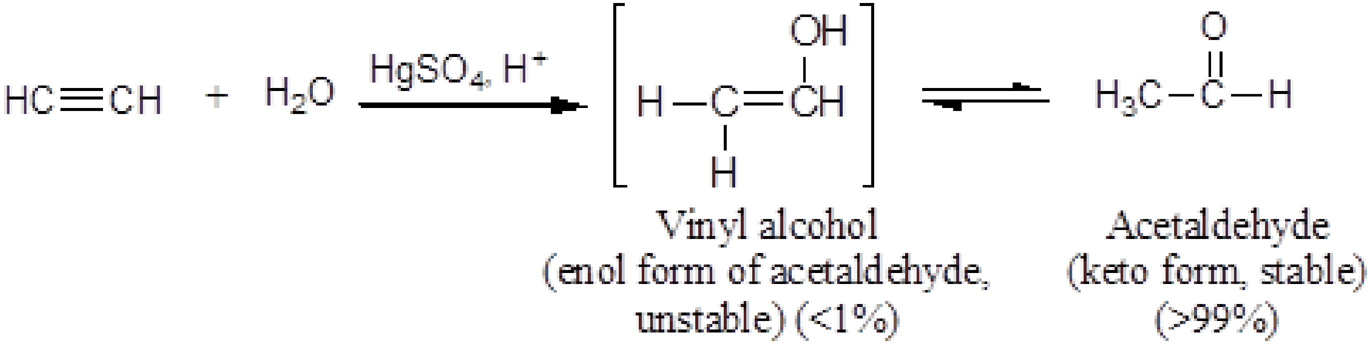


$$R_2CHOH \xrightarrow{[O]} R-\overset{\overset{\large O}{\|}}{C}-R$$

$$H_3C-\overset{\overset{OH}{|}}{\underset{H}{C}}-CH_3 \xrightarrow[\text{or PCC} \\ \text{or } KMnO_4]{Cu/\ \Delta} H_3C-\overset{\overset{\large O}{\|}}{C}-CH_3$$

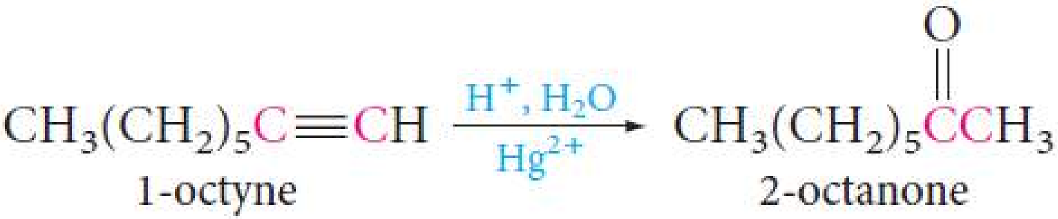
2) Hydration of Alkynes

- Hydration of acetylene yields acetaldehyde (catalyzed by acid and mercuric).



2) Hydration of Alkynes

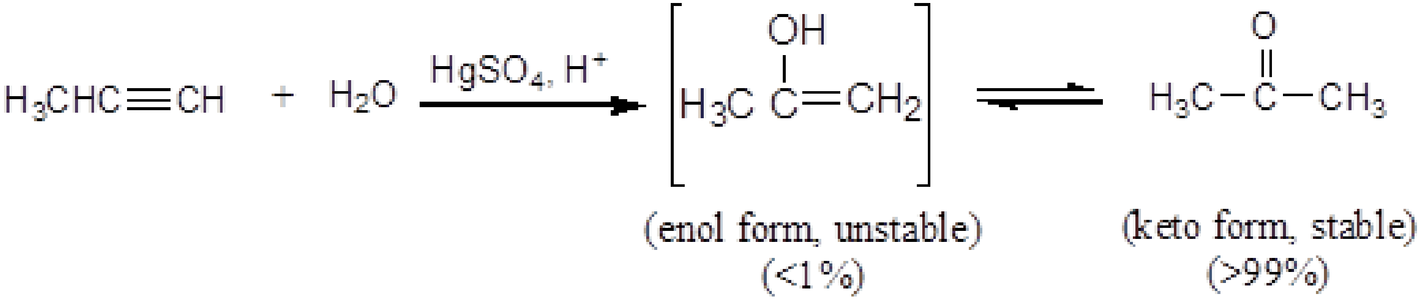
- Hydration of terminal alkynes EXCEPT acetylene yields ketones (catalyzed by acid and mercuric).



$$CH_3(CH_2)_5C{\equiv}CH \xrightarrow[Hg^{2+}]{H^+,\ H_2O} CH_3(CH_2)_5\overset{\displaystyle O}{\overset{\|}{C}}CH_3$$

1-octyne

2-octanone



$$H_3CHC{\equiv}CH + H_2O \xrightarrow{HgSO_4,\ H^+} \left[H_3C\overset{\displaystyle OH}{\overset{|}{C}}{=}CH_2 \right] \rightleftharpoons H_3C-\overset{\displaystyle O}{\overset{\|}{C}}-CH_3$$

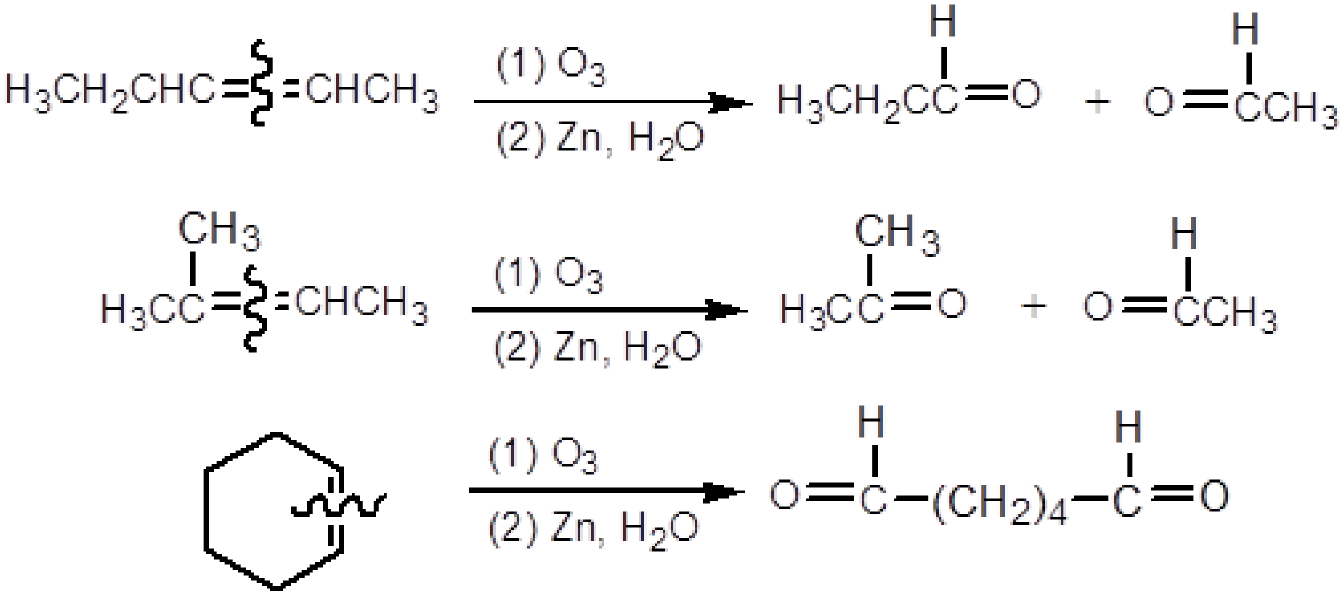
(enol form, unstable)
(<1%)

(keto form, stable)
(>99%)

Preparation of Aldehydes and Ketones

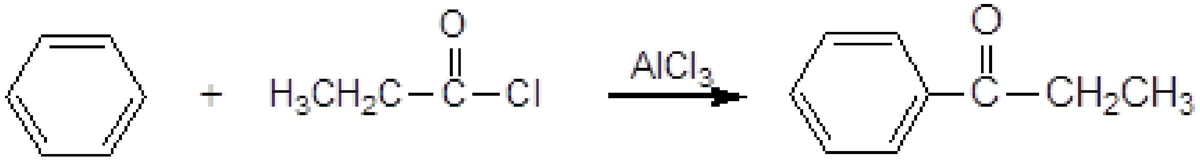
3) Ozonolysis of Alkenes

Product (aldehyde or ketone) depends on the structure of alkene.



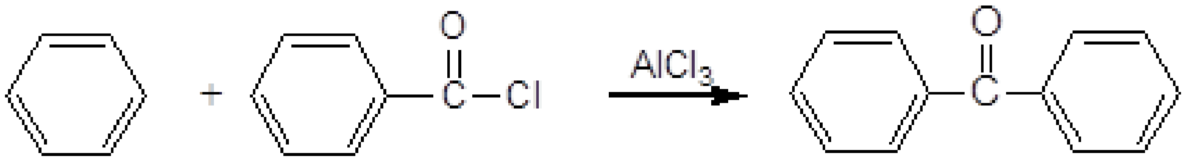
4) Friedel-Crafts Acylation

Preparing ketones that contain an aromatic ring.



Propionyl chloride

Ethyl phenyl ketone
(Prpiophenone)

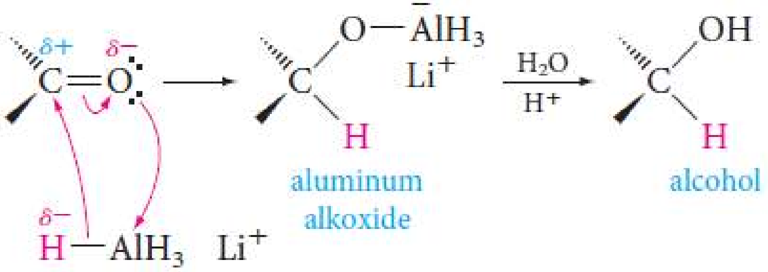


Benzoyl chloride

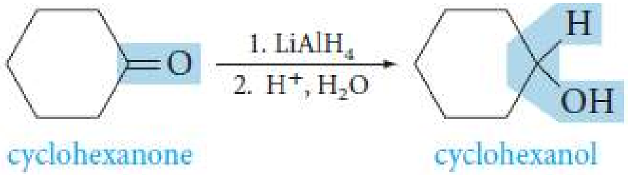
Diphenyl ketone
(Benzophenone)

A) Reduction of Carbonyl Compounds

- Aldehydes and ketones are easily reduced to primary and secondary alcohols, respectively.
- The most common metal hydrides used to reduce carbonyl compounds are lithium aluminum hydride ($LiAlH_4$) and sodium borohydride ($NaBH_4$).

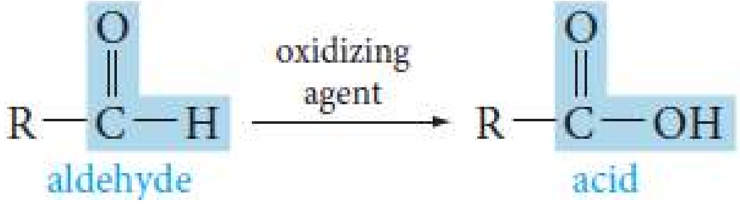


- **Example:**



B) Oxidation of Carbonyl Compounds

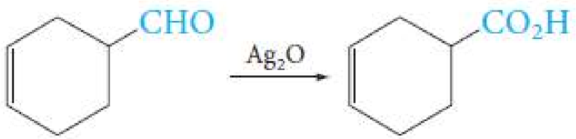
- Oxidation of aldehydes gives a carboxylic acid with the same number of carbon atoms.
- Because the reaction occurs easily, many oxidizing agents, such as $KMnO_4$, CrO_3, Ag_2O and peracids will work.



$$R-\overset{\overset{\displaystyle O}{\|}}{C}-H \xrightarrow{\text{oxidizing agent}} R-\overset{\overset{\displaystyle O}{\|}}{C}-OH$$

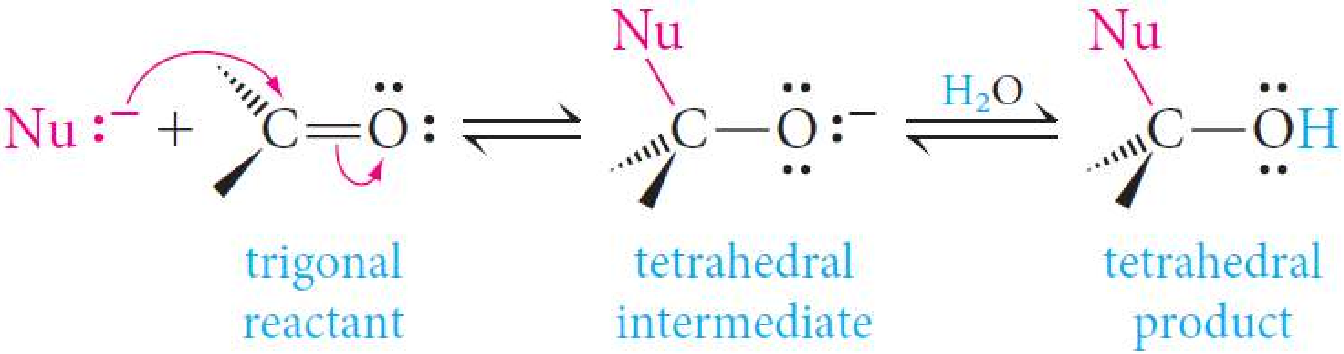
- **Example:**

$$CH_3(CH_2)_5CH{=}O \xrightarrow[\text{(Jones' reagent)}]{CrO_3,\ H^+} CH_3(CH_2)_5CO_2H$$



C) Nucleophilic Addition Reactions

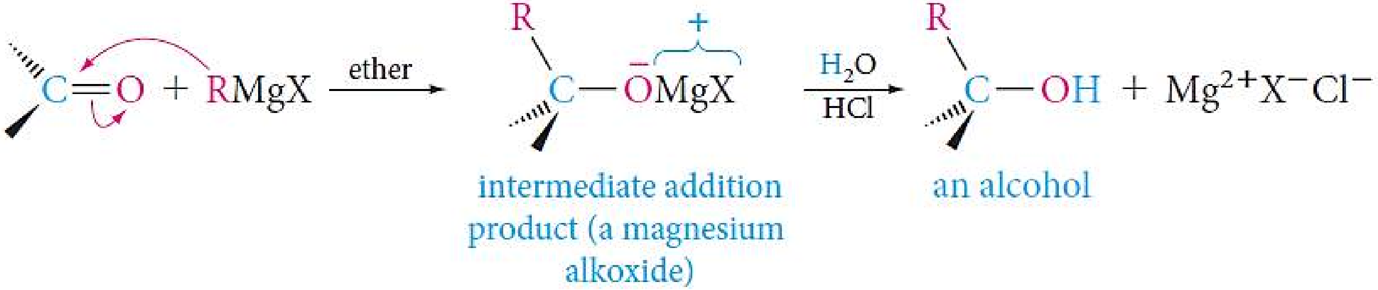
- Nucleophiles attack the carbon atom of a carbon-oxygen double bond because that carbon has a partial positive charge.
- The overall reaction involves addition of a nucleophile and a proton across the pi bond of the carbonyl group (when carried out in alcohol or water).

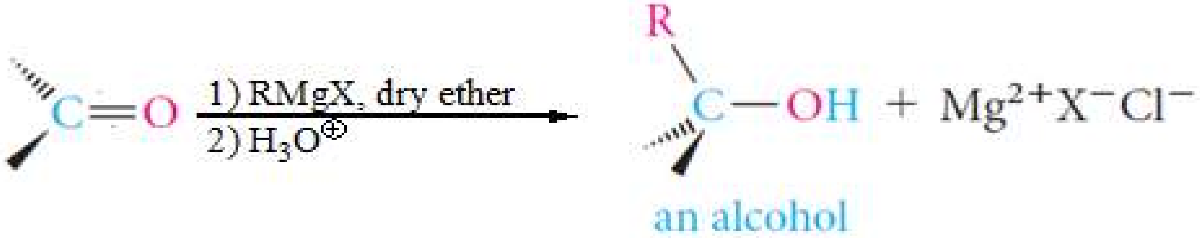


C) Nucleophilic Addition Reactions

1) Addition of Grignard Reagents: Formation of Alcohols

- *Grignard reagents act as carbon nucleophiles toward carbonyl compounds.*
- The reaction of a Grignard reagent with a carbonyl compound provides a useful route to alcohols.



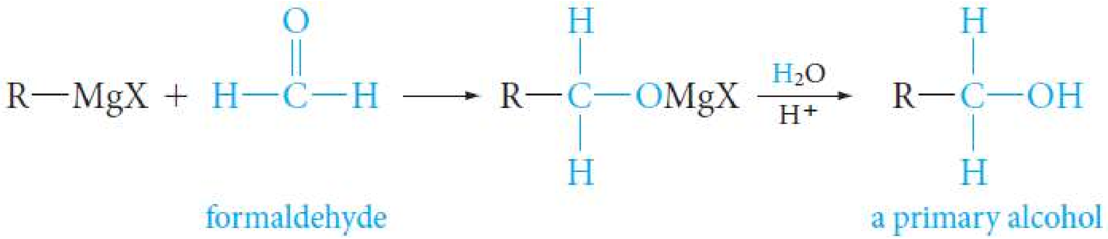


- The type of carbonyl compound chosen determines the class of alcohol produced.

C) Nucleophilic Addition Reactions

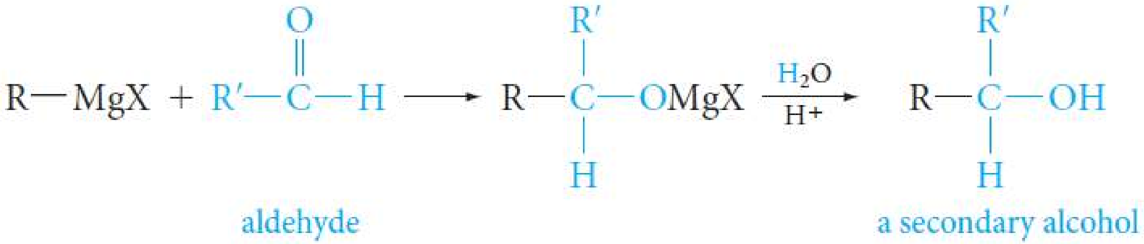
1) Addition of Grignard Reagents: Formation of Alcohols

- *Formaldehyde gives primary alcohols.*



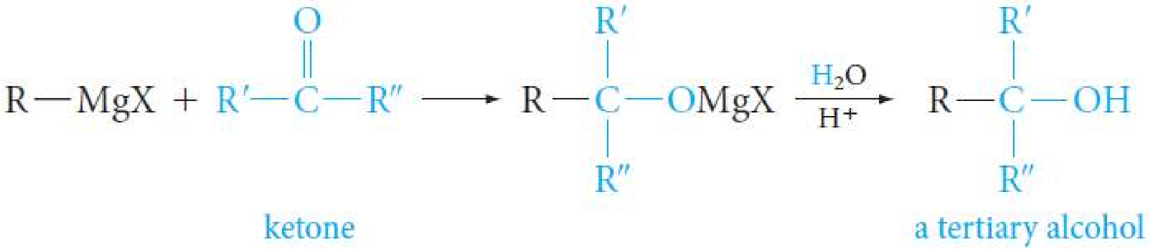
$$R{-}MgX + H{-}\overset{\overset{O}{\|}}{C}{-}H \longrightarrow R{-}\underset{H}{\overset{H}{C}}{-}OMgX \xrightarrow[H^+]{H_2O} R{-}\underset{H}{\overset{H}{C}}{-}OH$$

- *Other aldehydes give secondary alcohols*



$$R{-}MgX + R'{-}\overset{\overset{O}{\|}}{C}{-}H \longrightarrow R{-}\underset{H}{\overset{R'}{C}}{-}OMgX \xrightarrow[H^+]{H_2O} R{-}\underset{H}{\overset{R'}{C}}{-}OH$$

- *Ketones give tertiary alcohols.*



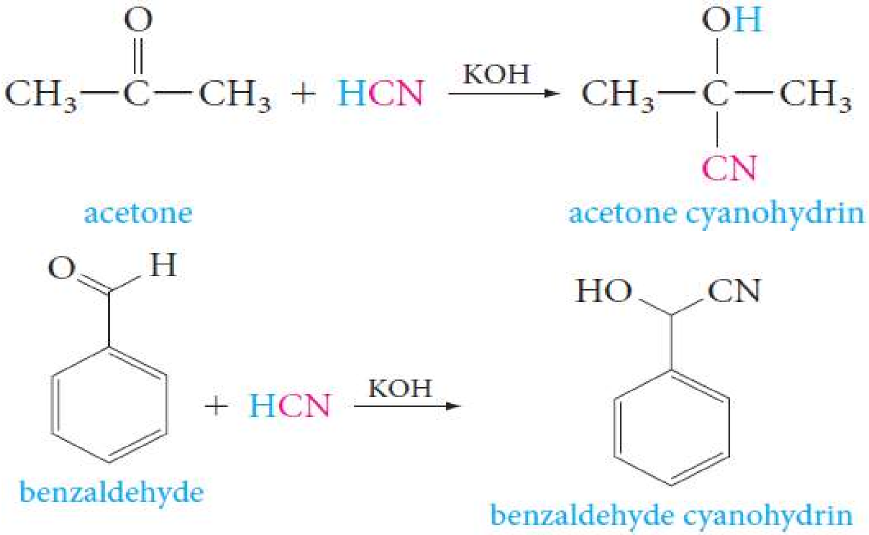
$$R{-}MgX + R'{-}\overset{\overset{O}{\|}}{C}{-}R'' \longrightarrow R{-}\underset{R''}{\overset{R'}{C}}{-}OMgX \xrightarrow[H^+]{H_2O} R{-}\underset{R''}{\overset{R'}{C}}{-}OH$$

2) Addition of Hydrogen Cyanide: Formation of Cyanohydrins

- Hydrogen cyanide adds to the carbonyl group of aldehydes and ketones to form cyanohydrins, compounds with a hydroxyl and a cyano group attached to the same carbon.

a cyanohydrin

- **Example**



acetone

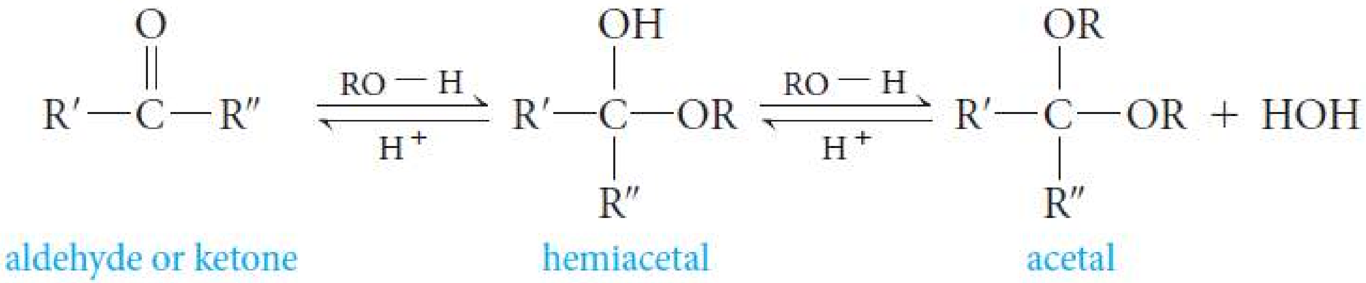
acetone cyanohydrin

benzaldehyde

benzaldehyde cyanohydrin

3) Addition of Alcohols: Formation of Hemiacetals and Acetals

- *Alcohols add to the C=O bond, the OR group becoming attached to the carbon and the proton becoming attached to the oxygen.*
- Aldehydes and ketones react with alcohols to form, first, hemiacetals and then, if excess alcohol is present, acetals.

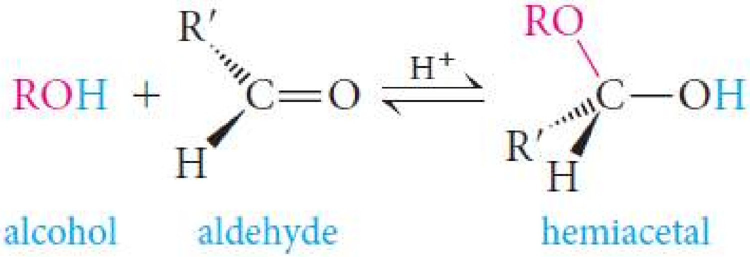


$$R'-\overset{\overset{\large O}{\|}}{C}-R'' \underset{H^+}{\overset{RO-H}{\rightleftharpoons}} R'-\underset{\underset{\large R''}{|}}{\overset{\overset{\large OH}{|}}{C}}-OR \underset{H^+}{\overset{RO-H}{\rightleftharpoons}} R'-\underset{\underset{\large R''}{|}}{\overset{\overset{\large OR}{|}}{C}}-OR + HOH$$

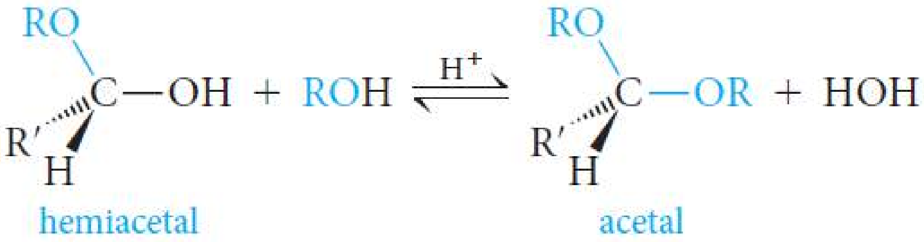
C) Nucleophilic Addition Reactions

3) Addition of Alcohols: Formation of Hemiacetals and Acetals

- **Hemiacetals;** it contains both alcohol and ether functional groups on the same carbon atom.

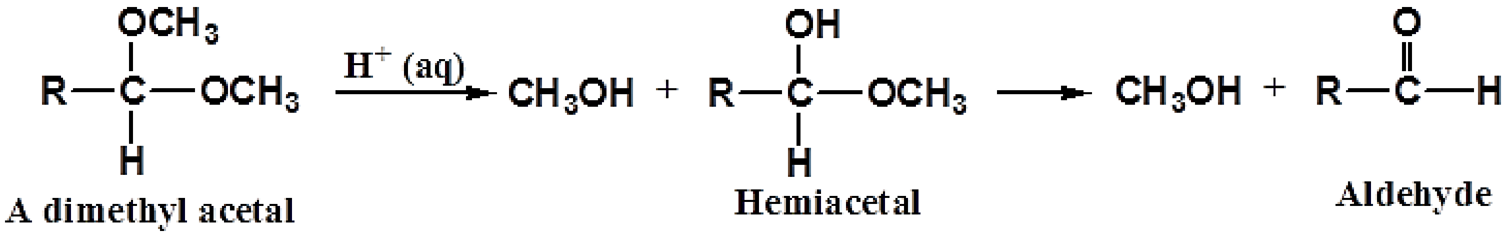


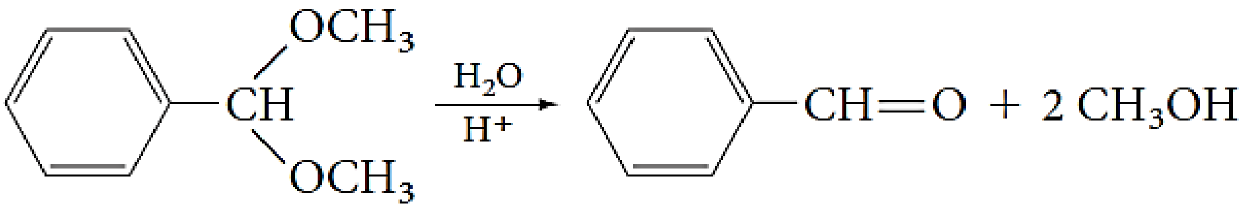
- **Acetals** have two ether functions at the same carbon atom.



3) Addition of Alcohols: Formation of Hemiacetals and Acetals

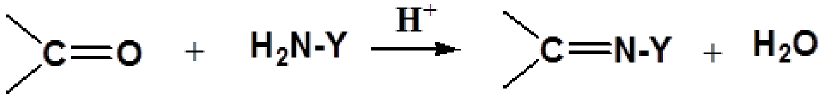
- The reverse of acetal formation, called acetal hydrolysis.
- Acetal can be hydrolyzed to its aldehyde or ketone and alcohol components by treatment with excess water in the presence of an acid catalyst.

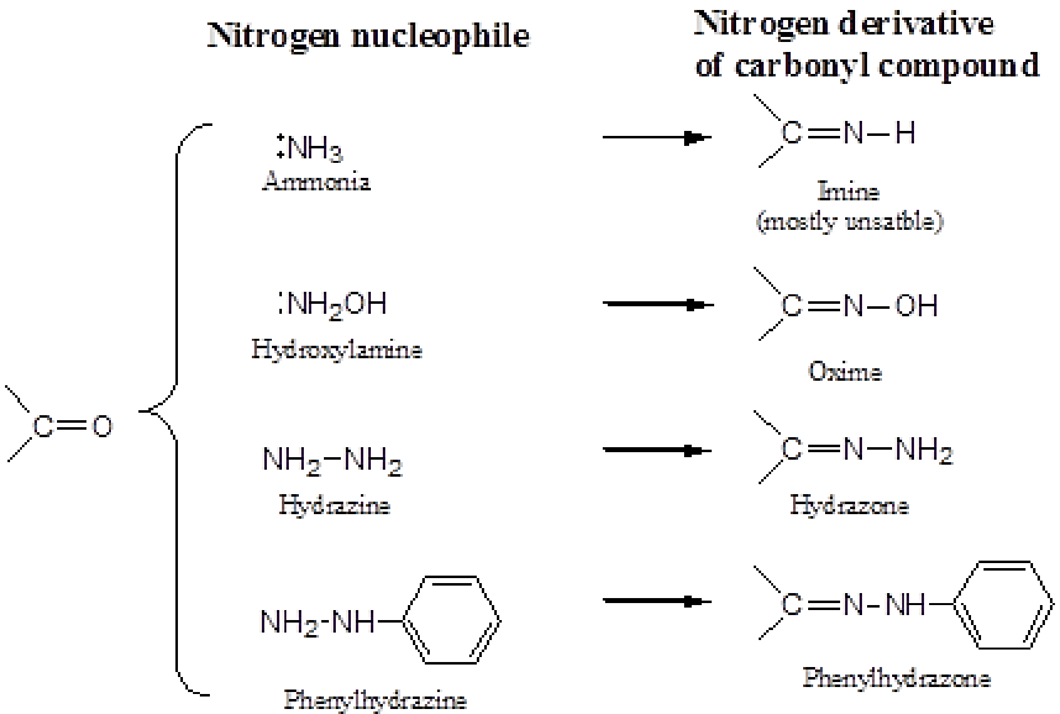




4) Addition of Ammonia and Ammonia Derivatives

The addition of nitrogen nucleophile, such as ammonia(NH_3) and substituted ammonia (NH_2-Y).





Fundamentals of Organic Chemistry

CHEM 109

For Students of Health Colleges

Credit hrs.: (2+1)

King Saud University

College of Science, Chemistry Department

CHAPTER 6. CARBOHYDRATES

Carbohydrates

- **The word *carbohydrate* can be expressed as *hydrates of carbon* because molecular formulas of these compounds.**

Example;

Glucose has the molecular formula $C_6H_{12}O_6$, which might be written as $C_6(H_2O)_6$.

- ***Carbohydrates* are polyhydroxyaldehydes, polyhydroxyketones, or substances that give such compounds on hydrolysis.**

- **The chemistry of *carbohydrates* is mainly the combined chemistry of two functional groups: the hydroxyl group and the carbonyl group.**

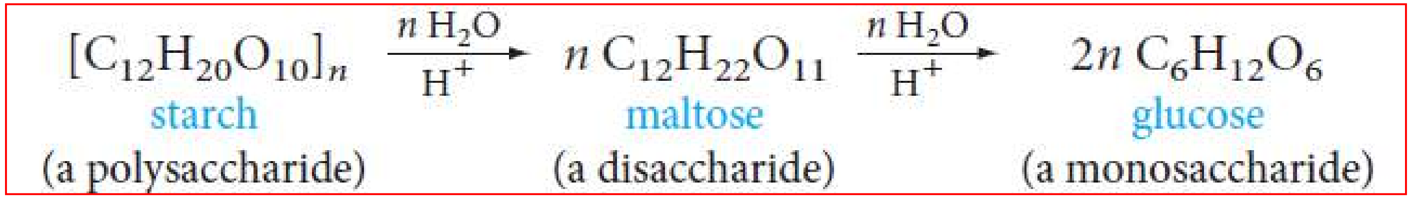
Carbohydrates

- *Carbohydrates* are usually classified according to their structure as monosaccharides, oligosaccharides, or polysaccharides.

  The term *saccharide* comes from Latin (*saccharum*, sugar) and refers to the sweet taste of some simple carbohydrates.

- **The three classes of carbohydrates are related to each other through hydrolysis.**

$$\text{polysaccharide} \xrightarrow[H^+]{H_2O} \text{oligosaccharides} \xrightarrow[H^+]{H_2O} \text{monosaccharides}$$



$$\underset{\substack{\text{starch}\\ \text{(a polysaccharide)}}}{[C_{12}H_{20}O_{10}]_n} \xrightarrow[H^+]{n\,H_2O} \underset{\substack{\text{maltose}\\ \text{(a disaccharide)}}}{n\,C_{12}H_{22}O_{11}} \xrightarrow[H^+]{n\,H_2O} \underset{\substack{\text{glucose}\\ \text{(a monosaccharide)}}}{2n\,C_6H_{12}O_6}$$

Carbohydrates

- ***Monosaccharides*** **(or simple sugars)** are carbohydrates that cannot be hydrolyzed to simpler compounds.

- ***Oligosaccharides*** **(from the Greek *oligos*, few)** contain at least two and generally no more than a few linked monosaccharide units.

They may be called disaccharides, trisaccharides, and so on, depending on the number of units, which may be the same or different.

Example; Maltose is a disaccharide made of two glucose units.

Sucrose is made of two different monosaccharide units: glucose and fructose.

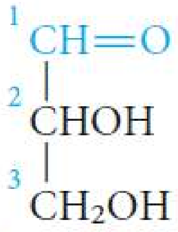
- ***Polysaccharides*** contain many monosaccharide units - sometimes hundreds or even thousands. Usually, but not always, the units are identical.

Example;

Starch and cellulose, contain linked units of the same monosaccharide, glucose.

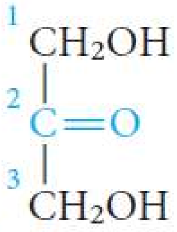
Monosaccharides

- **Monosaccharides** are classified according to:
  - The number of carbon atoms present (triose, tetrose, pentose, hexose, and so on).
  - Whether the carbonyl group is present as an aldehyde (aldose) or as a ketone (ketose).
- There are only two trioses: glyceraldehyde and dihydroxyacetone.
- Glyceraldehyde is the simplest aldose, and dihydroxyacetone is the simplest ketose.
- Each is related to glycerol in that each has a carbonyl group in place of one of the hydroxyl groups.



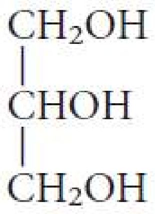
$$\begin{array}{l} {}^{1}\,CH{=}O \\ \quad | \\ {}^{2}\,CHOH \\ \quad | \\ {}^{3}\,CH_2OH \end{array}$$

glyceraldehyde
(an aldose)



$$\begin{array}{l} {}^{1}\,CH_2OH \\ \quad | \\ {}^{2}\,C{=}O \\ \quad | \\ {}^{3}\,CH_2OH \end{array}$$

dihydroxyacetone
(a ketose)

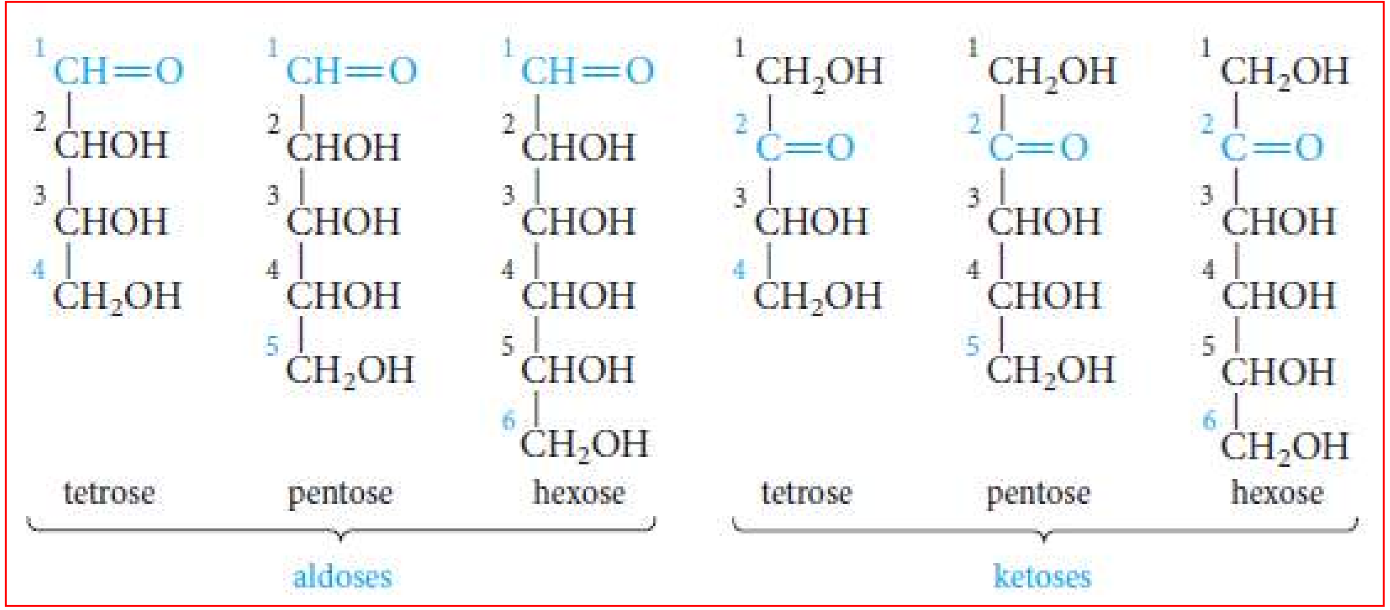


$$\begin{array}{l} CH_2OH \\ \;| \\ CHOH \\ \;| \\ CH_2OH \end{array}$$

glycerol

Monosaccharides

- Other **aldoses or ketoses** can be derived from glyceraldehyde or dihydroxyacetone by adding carbon atoms, each with a hydroxyl group.
- In **aldoses**, the chain is numbered from the aldehyde carbon.
- In most **ketoses**, the carbonyl group is located at C-2.



Monosaccharides

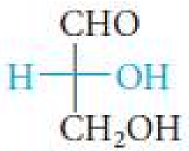
Chirality in Monosaccharides; Fischer Projection Formulas and D,L-Sugars

R-(+)-glyceraldehyde

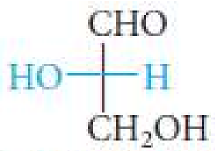
Fischer projection formula for R-(+)-glyceraldehyde

- He used a small capital d to represent the configuration of (+)-glyceraldehyde, with the hydroxyl group on the *right*; its enantiomer, with the hydroxyl group on the *left*, was designated L-(2)-glyceraldehyde.

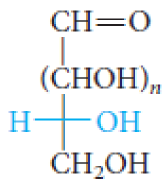
The most oxidized carbon (CHO) was placed at the top.



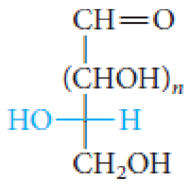
D-(+)-glyceraldehyde



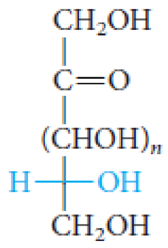
L-(−)-glyceraldehyde



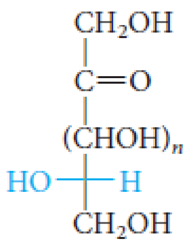
a D-aldose



an L-aldose

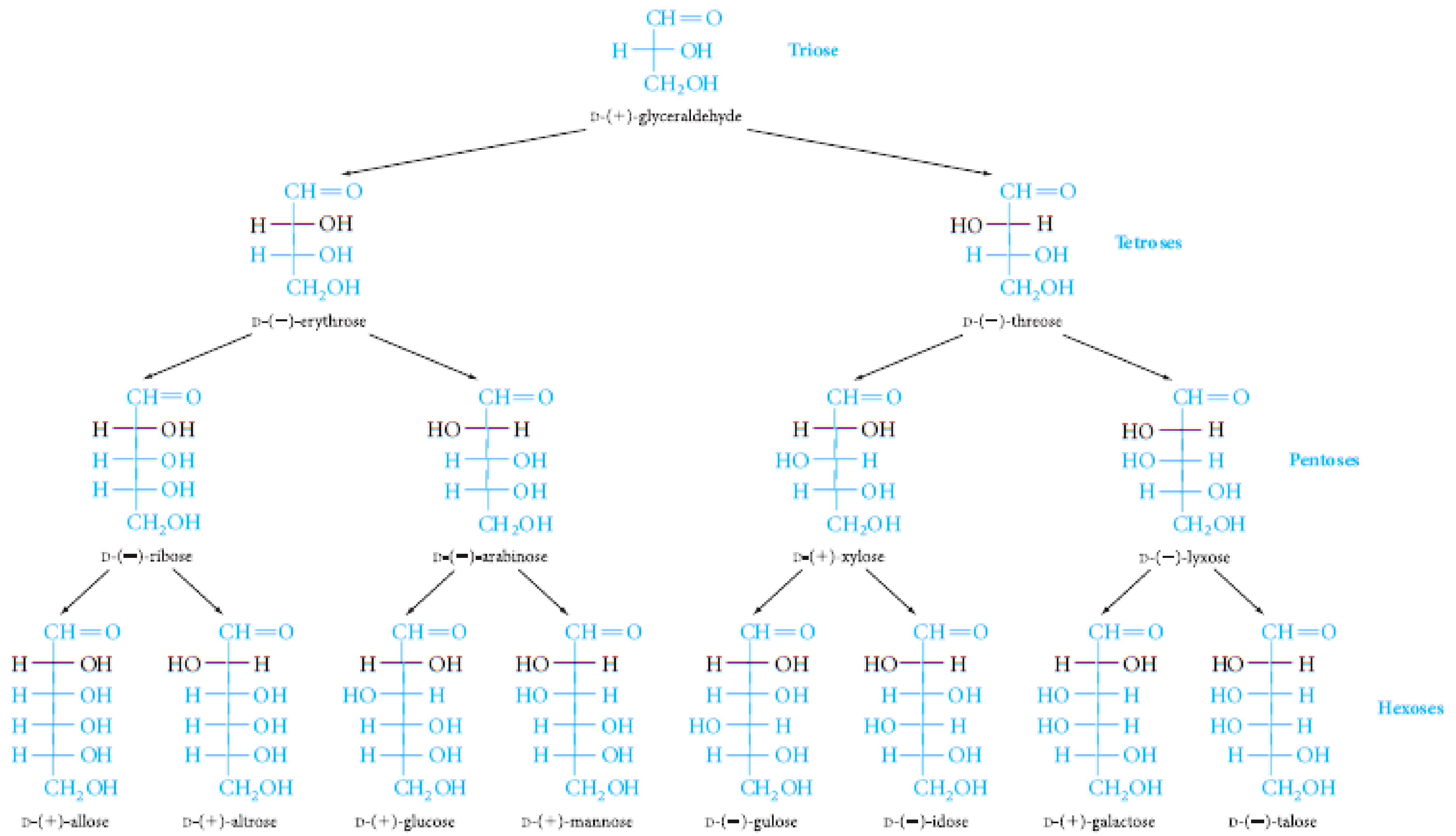


a D-ketose



an L-ketose

Monosaccharides



Monosaccharides

- **Diastereomers;** when two or more stereoisomers of a compound have different configurations at one or more (but not all) of the equivalent (related) stereocenters and are not mirror images of each other.

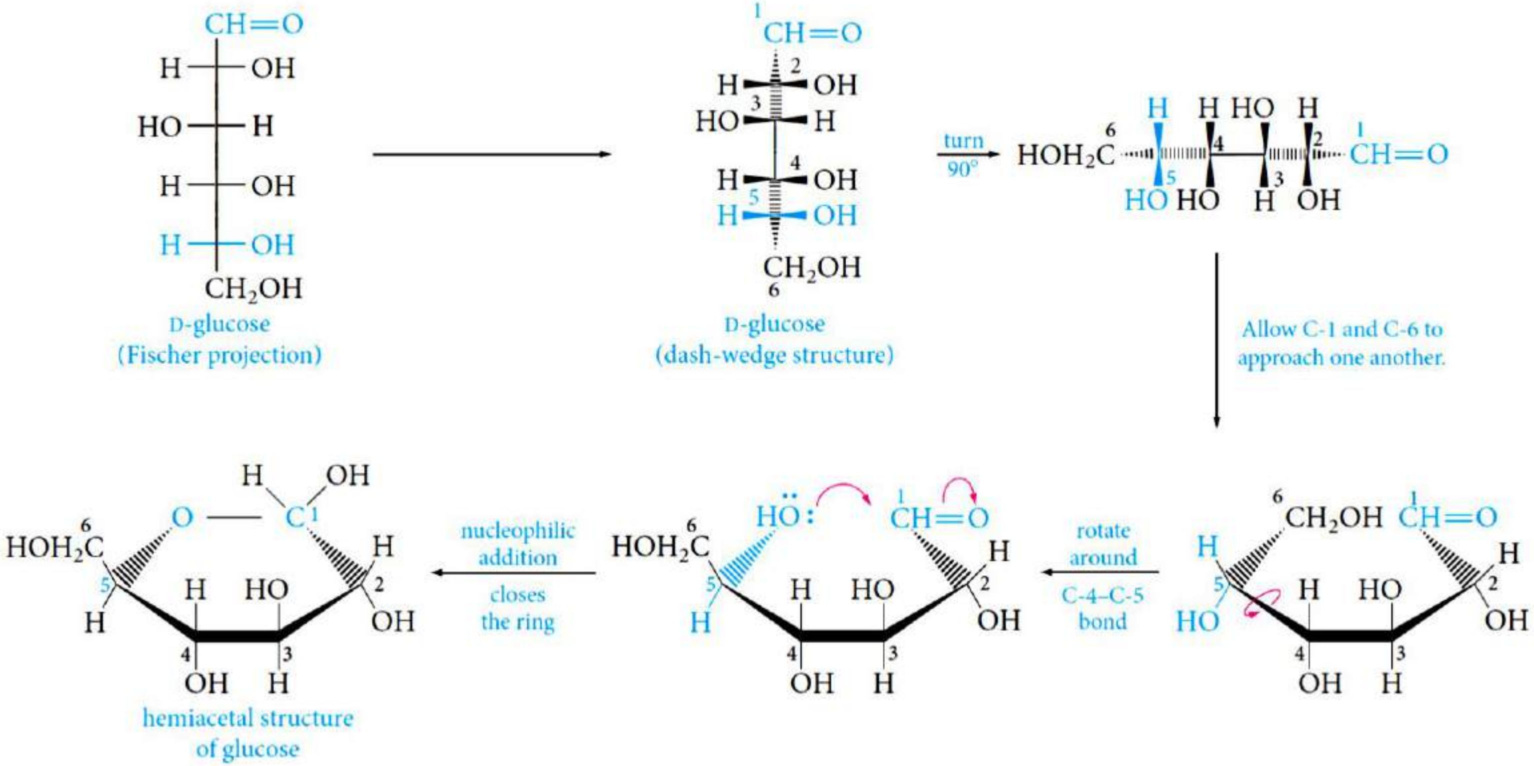
- ***Epimers***; A special name is given to diastereomers that differ in configuration *at only one stereogenic center*.
- Each pair has the same configurations at all **stereogenic centers** except one.

- ***Examples;***
  - D-(-)-Erythrose and D-(-)-threose are not only diastereomers, they are epimers.
  - D-glucose and D-mannose are epimers (at C-2).
  - D-glucose and D-galactose are epimers (at C-4).

- **Dextrorotation (+)** and **levorotation** (-) are terms describing circular direction of rotating plane-polarized light.
  - **Dextrorotatory (+);** If the light rotates clockwise, (rotation to the right).
  - **Levorotatory (-);** if it rotates counterclockwise, (rotation to the left).

The Cyclic Hemiacetal Structures of Monosaccharides

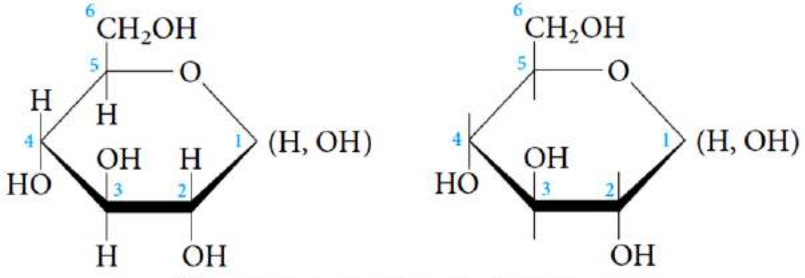
- ***Monosaccharides*** *exist mainly in cyclic, hemiacetal forms* and not in the acyclic aldo- or keto-forms.



Manipulation of the Fischer projection formula of D-glucose to bring the C-5 hydroxyl group in position for cyclization to the hemiacetal form.

Haworth Projection

- The carbons are arranged clockwise numerically, with C-1 at the right.
- Substituents attached to the ring lie above or below the plane.

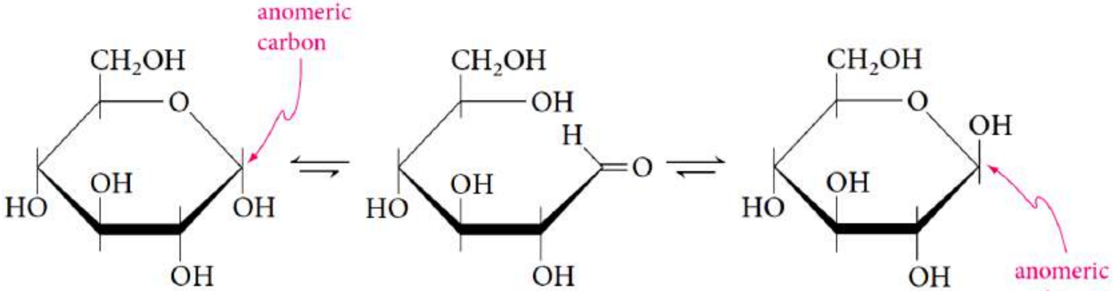


Haworth projection formulas for D-glucose

- **Carbons 1 through 5** are part of the ring structure, but carbon 6 (the -CH_2OH group) is a substituent on the ring.
- **C-1 is special**.
  C-1 is the hemiacetal carbon (it carries a hydroxyl group, and it is also connected to C-5 by an ether linkage).
- **C-2**, **C-3**, and **C-4** are secondary alcohol carbons.
- **C-6** is a primary alcohol carbon.
- **Hydroxyl groups on the *right*** in the Fischer projection are *down* in the Haworth projection (and conversely.
- **hydroxyl groups on the *left*** in the Fischer projection are *up* in the Haworth projection).
- For **D-sugars**, the terminal -CH_2OH group is *up* in the Haworth projection; for **L-sugars**, it is down.

Anomeric Carbons; Mutarotation

- **Anomeric carbon;** The hemiacetal carbon, the carbon that forms the new stereogenic center.
- **Anomers;** Two monosaccharides that differ only in configuration at the anomeric center are (a special kind of epimers).
- **Anomers** are called α or β, depending on the position of the hydroxyl group.
- **For monosaccharides** in the D-series, the hydroxyl group is "down" in the α anomer and "up" in the β anomer.



α-D-glucose (36%)
(mp 146°C)
[α]+112°

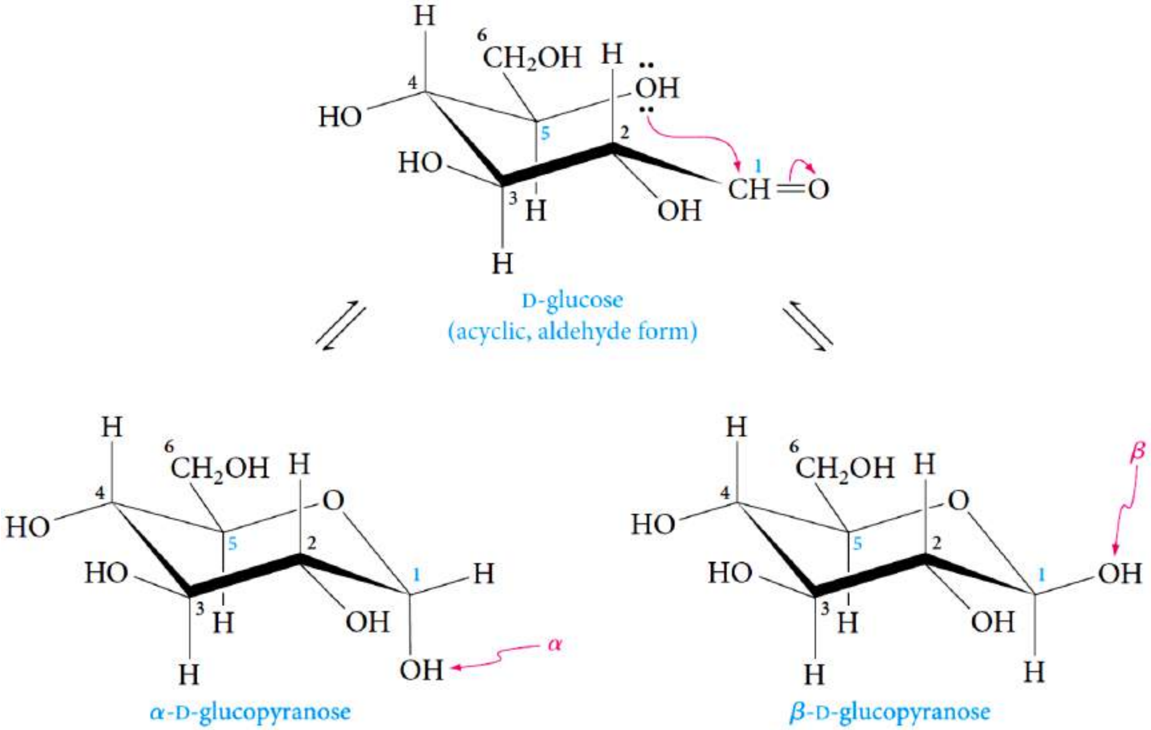
D-glucose
(acyclic, aldehyde form)

β-D-glucose (64%)
(mp 150°C)
[α]+19°

- If D-glucose is crystallized from methanol, the pure α form is obtained.
- Crystallization from acetic acid gives the β form.
- The α and β forms of D-glucose are *diastereomers.*

Conformations of Pyranoses; Chair Conformation

- **At the anomeric carbon (C-1)**, where the hydroxyl group may be axial (in the α anomer) or equatorial (in the β anomer).



D-glucose (acyclic, aldehyde form)

α-D-glucopyranose

β-D-glucopyranose

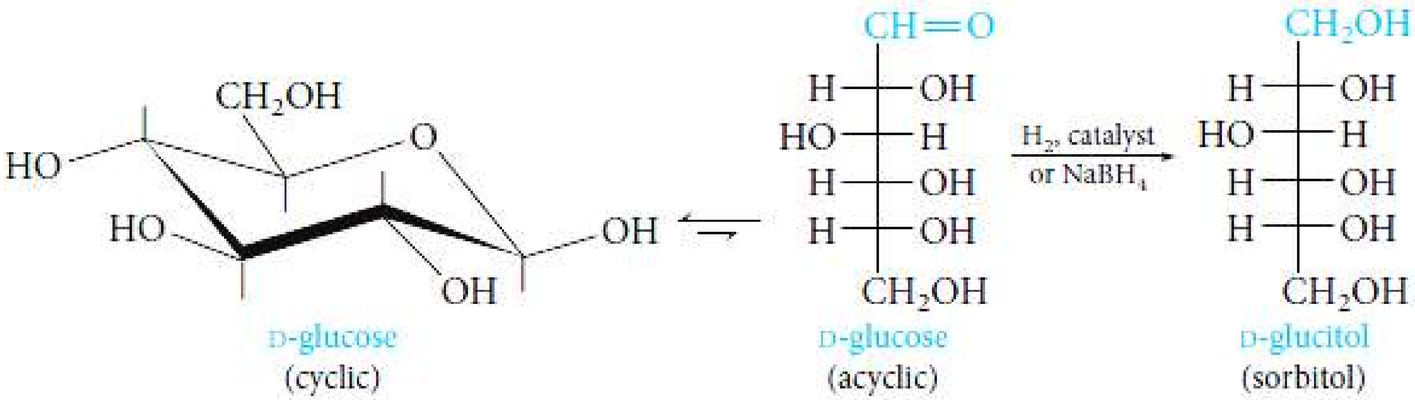
Reactions of Monosaccharides

1) Reduction of Monosaccharides

- The **carbonyl group of aldoses and ketoses** can be reduced by various reagents to give polyols, called alditols.
- **Example;**

Catalytic hydrogenation or reduction with sodium borohydride ($NaBH_4$) converts D-glucose to D-glucitol (sorbitol).

- **Sorbitol** is used commercially as a sweetener and sugar substitute.



2) Oxidation of Monosaccharides

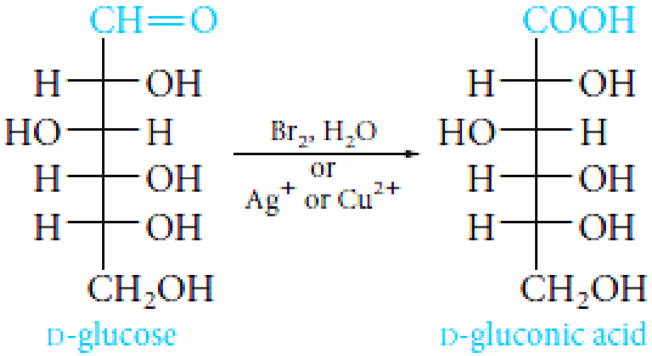
2.1. With Mild Oxidizing Agents

- The oxidation of aldoses is so easy that they react with such mild oxidizing agents as
  - Tollens' reagent (Ag^+ in aqueous ammonia),
  - Fehling's reagent (Cu^{2+} complexed with tartrate ion),
  - Benedict's reagent (Cu^{2+} complexed with citrate ion).
- These aldehyde groups can be easily oxidized to acids which are called aldonic acids.
- A carbohydrate that reacts with Ag^+ or Cu^{2+} is called a reducing sugar

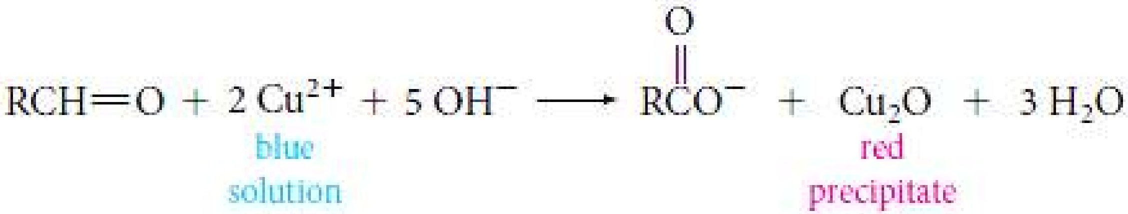
2) Oxidation of Monosaccharides

2.1. With Mild Oxidizing Agents

- **Example;** D-glucose is easily oxidized to D-gluconic acid.



- With the copper reagents, the blue solution gives a red precipitate of cuprous oxide, Cu_2O.



$$\underset{}{RCH{=}O} + \underset{\substack{\text{blue}\\\text{solution}}}{2\,Cu^{2+}} + 5\,OH^- \longrightarrow R\overset{\overset{O}{\|}}{C}O^- + \underset{\substack{\text{red}\\\text{precipitate}}}{Cu_2O} + 3\,H_2O$$

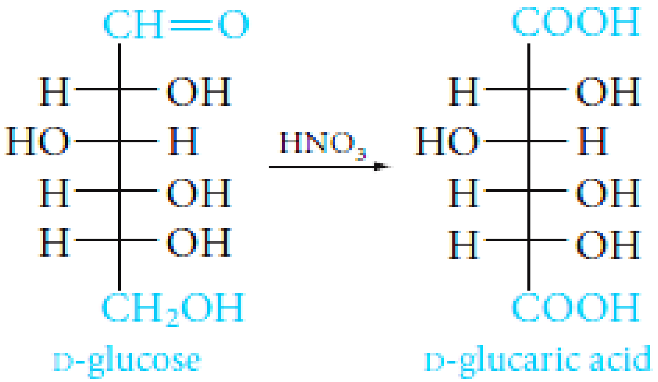
Reactions of Monosaccharides

2) Oxidation of Monosaccharides

2.2. With Strong Oxidizing Agents

- Stronger oxidizing agents, such as aqueous nitric acid.
- The aldehyde group and the primary alcohol group can be oxidized, producing dicarboxylic acids called aldaric acids.
- **Example;**

D-glucose gives D-glucaric acid.

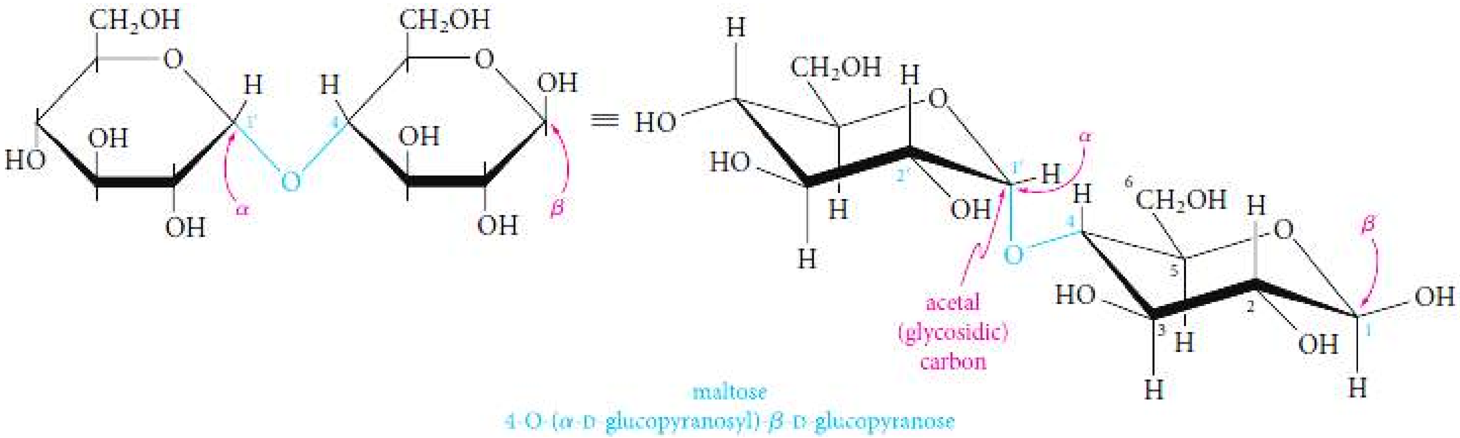


Disaccharides

- **The most common oligosaccharides are disaccharides.**
- **In a disaccharide,**

  two monosaccharides are linked by a glycosidic bond between the anomeric carbon of one monosaccharide unit and a hydroxyl group on the other unit.

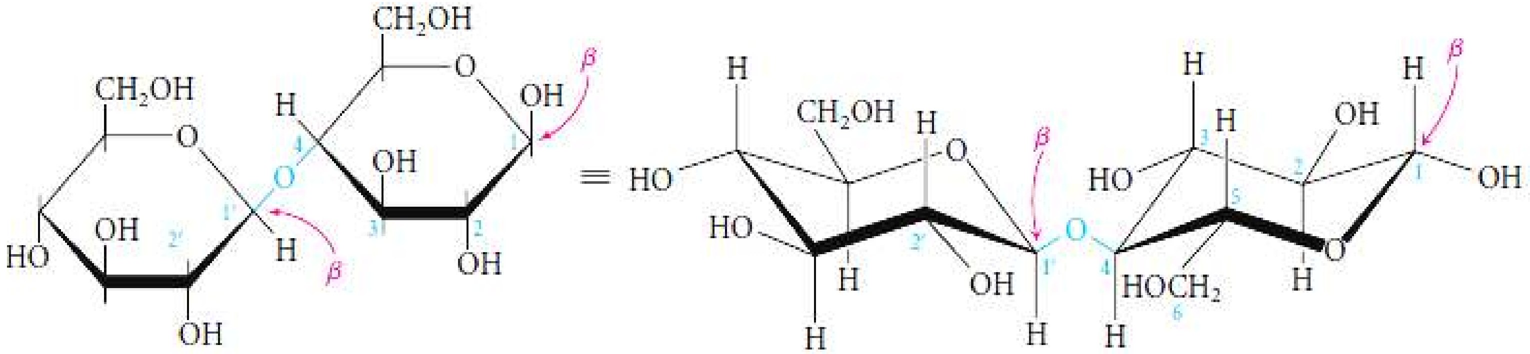
Maltose



maltose
4-O-(α-D-glucopyranosyl)-β-D-glucopyranose

- **Maltose** is the disaccharide obtained by the partial hydrolysis of starch.
- Further hydrolysis of maltose gives only **D-glucose**.
- **Maltose** must, therefore, consist of two linked glucose units.
- It turns out that the anomeric carbon of the left unit is linked to the C-4 hydroxyl group of the unit at the right as an acetal (glycoside).
- The configuration at the anomeric carbon of the left unit is α.

Cellibiose



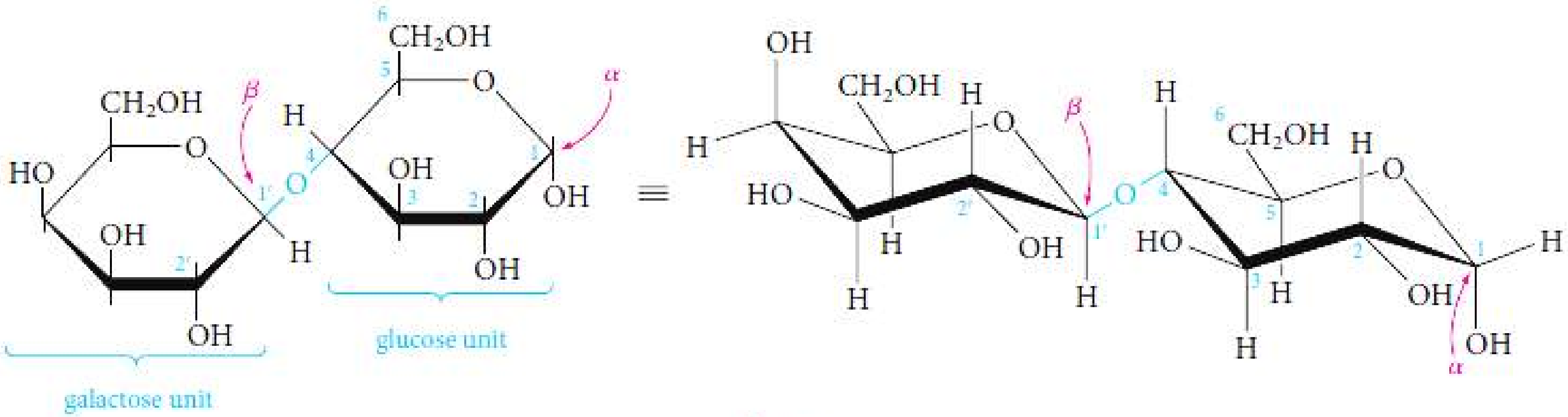
cellobiose

4-O-(β-D-glucopyranosyl)-β-D-glucopyranose

- **Cellobiose** is the disaccharide obtained by the partial hydrolysis of cellulose.
- Further hydrolysis of cellobiose gives only **D-glucose.**
- **Cellobiose** must therefore be an isomer of maltose.
- In fact, **cellobiose** *differs from maltose* only *in having the* β *configuration at C-1 of the left glucose unit.*

Disaccharides

Lactose

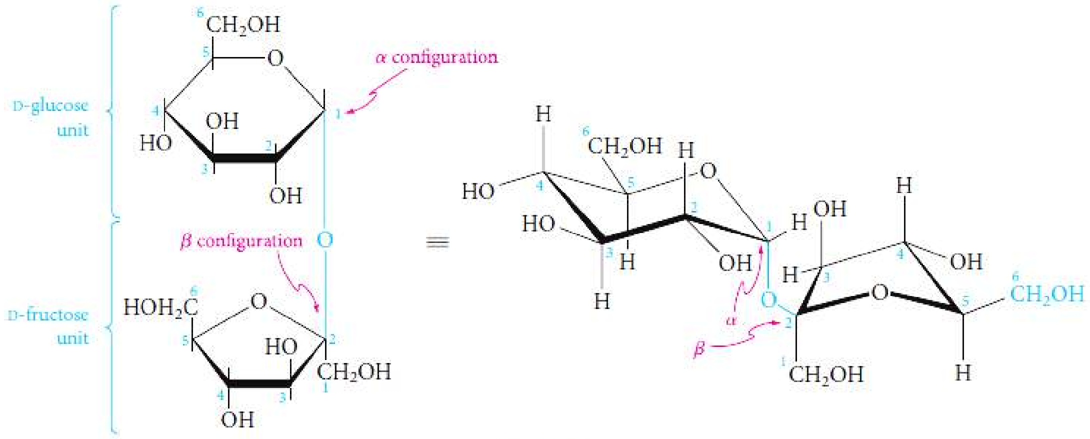


lactose
4-O-(β-D-galactopyranosyl)-α-D-glucopyranose

- **Lactose** is the major sugar in human and cow's milk (4% to 8% lactose).
- Hydrolysis of lactose gives equimolar amounts of **D-galactose and D-glucose**.
- The anomeric carbon of the galactose unit has the β configuration at C-1 and is linked to the hydroxyl group at C-4 of the glucose unit.

Disaccharides

Sucrose



sucrose
α-D-glucopyranosyl-β-D-fructofuranoside
(or β-D-fructofuranosyl-α-D-glucopyranoside)

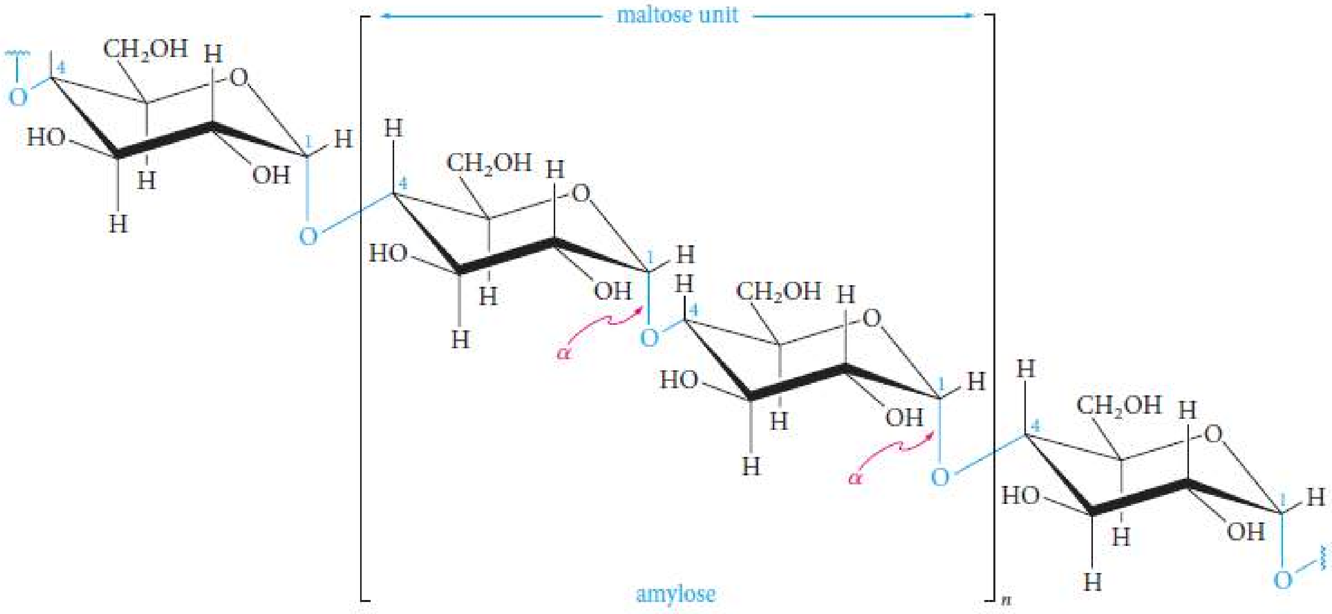
- **The most important commercial disaccharide is sucrose, ordinary table sugar.**
- **Sucrose** occurs in all photosynthetic plants, where it functions as an energy source.
- It is obtained commercially from sugar cane and sugar beets, in which it constitutes 14% to 20% of the plant juices.
- **Sucrose** is very water soluble (2 grams per milliliter at room temperature) because it is polar due to the presence of eight hydroxyl groups on its surface.
- Hydrolysis of sucrose gives equimolar amounts of **D-glucose and the ketose D-fructose**.

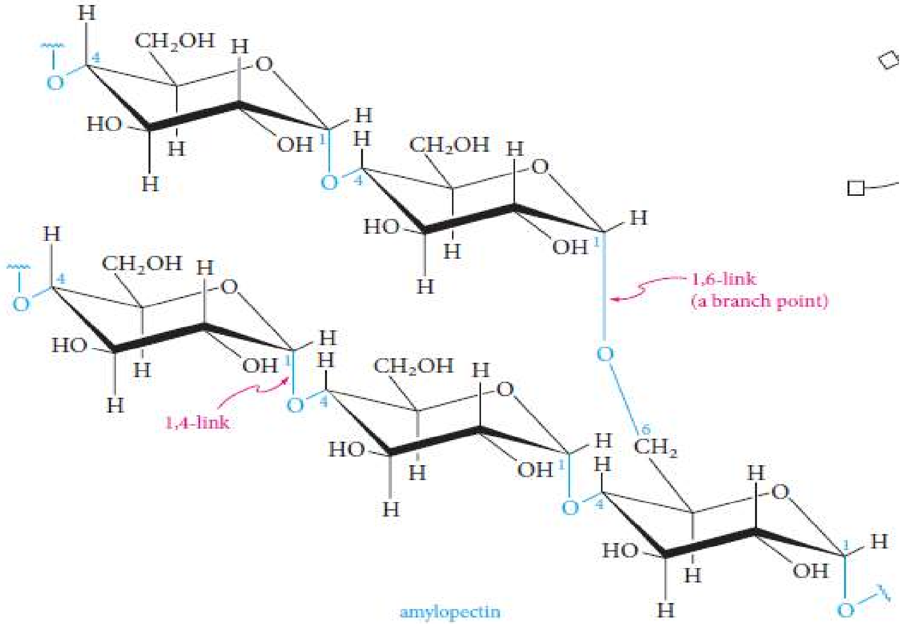
Polysaccharides

- **Polysaccharides** contain many linked monosaccharides and vary in chain length and molecular weight.
- Most **polysaccharides** give a single monosaccharide on complete hydrolysis.
- The monosaccharide units may be linked linearly, or the chains may be branched.

Starch

Polysaccharides





Polysaccharides

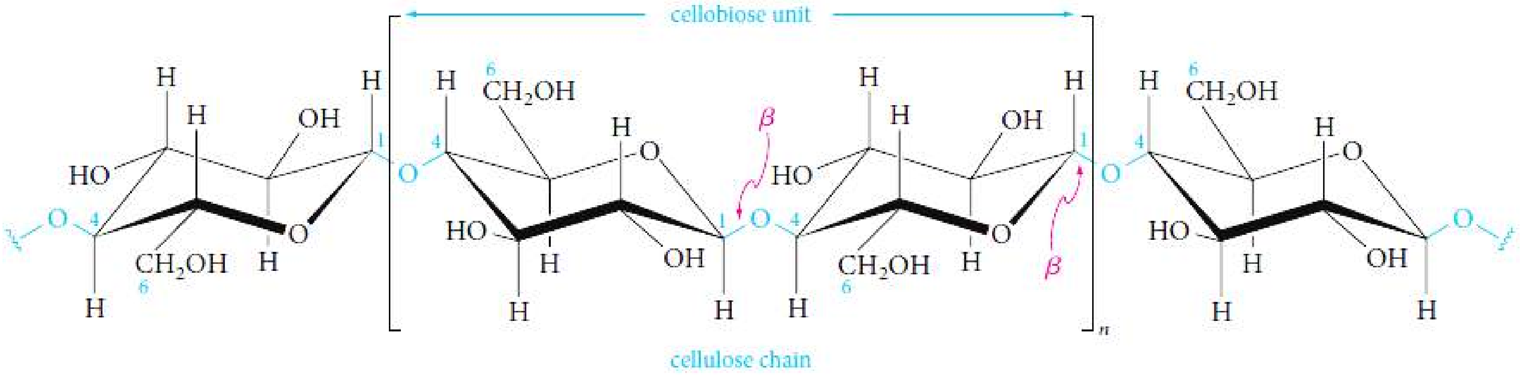
Starch

- **Starch** is the energy-storing carbohydrate of plants.
- It is a major component of cereals, potatoes, corn, and rice.
- **Starch** is made up of glucose units joined mainly by 1,4-α-glycosidic bonds, although the chains may have a number of branches attached through 1,6- α -glycosidic bonds.
- **Partial hydrolysis of starch gives maltose, and complete hydrolysis gives only D-glucose.**
- **Starch** can be separated by various techniques into two fractions: amylose and amylopectin.
- **In amylose**, which constitutes about 20% of starch, the glucose units (50 to 300) are in a continuous chain, with 1,4 linkages.
- **Amylopectin** is highly branched. Although each molecule may contain 300 to 5000 glucose units, chains with consecutive 1,4 links average only 25 to 30 units in length.
- These chains are connected at branch points by **1,6 linkages.**

Glycogen

- **Glycogen** is the energy-storing carbohydrate of animals.
- Like starch, it is made of 1,4- and 1,6-linked glucose units.
- **Glycogen** has a higher molecular weight than starch (perhaps 100,000 glucose units), and its structure is even more branched than that of amylopectin, with a branch every 8 to 12 glucose units.
- **Glycogen** is produced from glucose that is absorbed from the intestines into the blood; transported to the liver, muscles, and elsewhere; and then polymerized enzymatically.
- **Glycogen** helps maintain the glucose balance in the body by removing and storing excess glucose from ingested food and later supplying it to the blood when various cells need it for energy.

Cellulose



- **Cellulose** is an *unbranched* polymer of glucose joined by 1,4-β-glycosidic bonds.
- It consists of linear chains of **cellobiose units.**
- These linear molecules, containing an average of 5000 glucose units, aggregate to give fibrils bound together by hydrogen bonds between hydroxyls on adjacent chains.
- **Cellulose fibers** having considerable physical strength are built up from these fibrils, wound spirally in opposite directions around a central axis.
- Wood, cotton, hemp, linen, straw, and corncobs are mainly **cellulose.**

Fundamentals of Organic Chemistry

CHEM 109

For Students of Health Colleges

Credit hrs.: (2+1)

King Saud University

College of Science, Chemistry Department

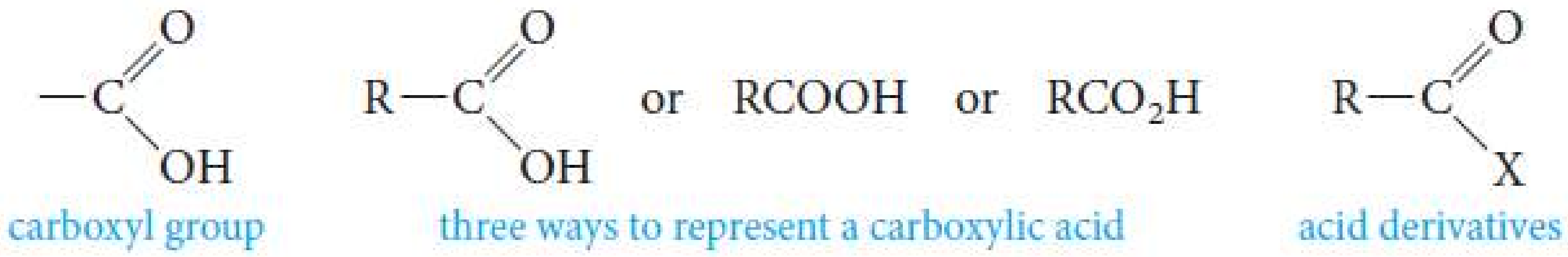
CHAPTER 7. CARBOXYLIC ACIDS AND THEIR DERIVATIVES

Structure of Carboxylic Acids

- The functional group common to all carboxylic acids is the carboxyl group.

  The name is a contraction of the parts: the carbonyl and hydroxyl groups.

- The general formula for a carboxylic acid can be written in expanded or abbreviated forms.



Structure of Carboxylic Acids

- **Depending on whether an R or an Ar.** residue is attached to the carboxyl group; Carboxylic acids are classified as aliphatic or aromatic.

  - **Aliphatic Carboxylic Acids.**

$R-COOH$ (R = H or alkyl) CH_3-COOH

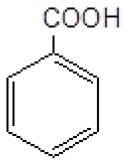
Aliphatic acid

Acetic acid

  - **Aromatic Carboxylic Acids.**

$Ar-COOH$ $(R = C_6H_5\text{-})$

Aromatic acid



Benzoic acid

- **Fatty acids.**

  Long straight-chain carboxylic acids with even numbers of carbons, which were first isolated from fats and waxes.

Nomenclature of Acids

Common Names

- The **common names** of carboxylic acids all end in *-ic acid*.
- These names usually come from some Latin or Greek word that indicates the original source of the acid.
- **Common name**, substituents are located with Greek letters, beginning with the α– carbon atom.

IUPAC System

- We replace the final e in the name of the corresponding alkane with the suffix *-oic* and add the word *acid*.

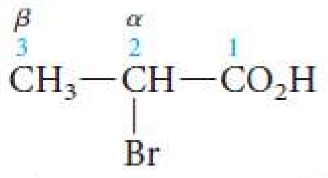
Alkane- e + *oic acid* = *Alkanoic acid*

- **IUPAC system**, the chain is numbered beginning with the carboxyl carbon atom, and substituents are located in the usual way.

Nomenclature of Acids

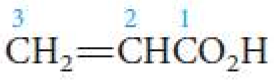
Carbon atoms	Formula	Source	Common name	IUPAC name
1	HCOOH	ants (Latin, *formica*)	formic acid	methanoic acid
2	CH_3COOH	vinegar (Latin, *acetum*)	acetic acid	ethanoic acid
3	CH_3CH_2COOH	milk (Greek, *protos pion*, first fat)	propionic acid	propanoic acid
4	$CH_3(CH_2)_2COOH$	butter (Latin, *butyrum*)	butyric acid	butanoic acid
5	$CH_3(CH_2)_3COOH$	valerian root (Latin, *valere*, to be strong)	valeric acid	pentanoic acid
6	$CH_3(CH_2)_4COOH$	goats (Latin, *caper*)	caproic acid	hexanoic acid
7	$CH_3(CH_2)_5COOH$	vine blossom (Greek, *oenanthe*)	enanthic acid	heptanoic acid
8	$CH_3(CH_2)_6COOH$	goats (Latin, *caper*)	caprylic acid	octanoic acid
9	$CH_3(CH_2)_7COOH$	pelargonium (an herb with stork-shaped seed capsules; Greek, *pelargos*, stork)	pelargonic acid	nonanoic acid
10	$CH_3(CH_2)_8COOH$	goats (Latin, *caper*)	capric acid	decanoic acid

Nomenclature of Acids



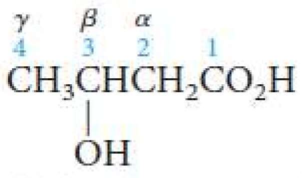
$$\overset{\beta}{\underset{3}{}}CH_3-\underset{Br}{\underset{|}{\overset{\alpha}{CH}}}-CO_2H$$

2-bromopropanoic acid
(α-bromopropionic acid)



$$CH_2=CHCO_2H$$

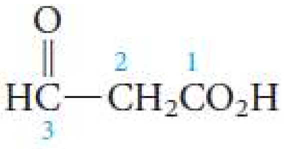
propenoic acid
(acrylic acid)



$$CH_3\underset{OH}{\underset{|}{CH}}CH_2CO_2H$$

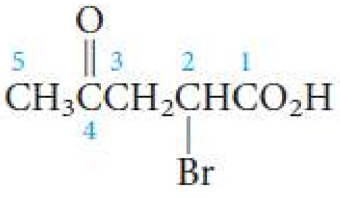
3-hydroxybutanoic acid
(β-hydroxybutyric acid)

- **The carboxyl group has priority over alcohol, aldehyde, or ketone** functionality in naming.
- The prefix **oxo-** is used to locate the carbonyl group of the aldehyde or ketone.



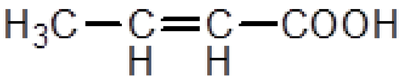
$$H\overset{O}{\overset{\|}{C}}-CH_2CO_2H$$

3-oxopropanoic acid



$$CH_3\overset{O}{\overset{\|}{C}}CH_2\underset{Br}{\underset{|}{CH}}CO_2H$$

2-bromo-4-oxopentanoic acid



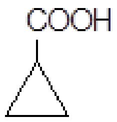
$$H_3C-\underset{H}{C}=\underset{H}{C}-COOH$$

But-2-enoic acid
(2-Butenoic acid)

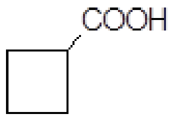
Nomenclature of Acids

- **Cycloalkane carboxylic acid**

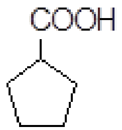
When the carboxyl group is attached to a ring, the ending ***-carboxylic acid*** *is added to the name of the parent* ***cycloalkane****.* ***(i.e. Cycloalkanecarboxylic acid)***



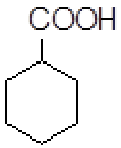
Cyclopropanecarboxylic acid



Cyclobutanecarboxylic acid

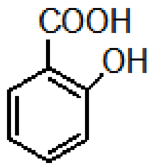


Cyclopentanecarboxylic acid



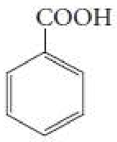
Cyclohexanecarboxylic acid

- **Aromatic acids** are named by attaching the suffix *-oic acid* or *-ic acid* to an appropriate prefix derived from the aromatic hydrocarbon.

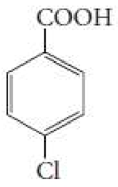


Common name: Salicylic acid

IUPAC name : 2-Hydroxybenzenecarboxylic acid



benzoic acid
(benzenecarboxylic acid)



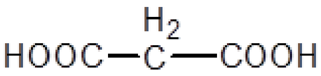
p-chlorobenzoic acid
(4-chlorobenzenecarboxylic acid)

Nomenclature of Acids

- **Dicarboxylic acids** (*acids that contain two carboxyl groups*) are known almost exclusively by their common names.

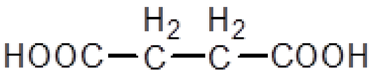
HOOC—COOH

Oxalic acid



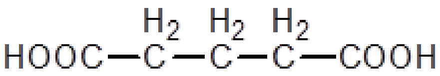
$HOOC-\overset{H_2}{C}-COOH$

Malonic acid



$HOOC-\overset{H_2}{C}-\overset{H_2}{C}-COOH$

Succinic acid



$HOOC-\overset{H_2}{C}-\overset{H_2}{C}-\overset{H_2}{C}-COOH$

Glutaric acid

- **Aliphatic dicarboxylic acids** are given the suffix *-dioic acid* in the IUPAC system.

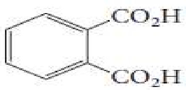
$HO_2\overset{1}{C}-\overset{2}{C}H_2\overset{3}{C}H_2-\overset{4}{C}O_2H$

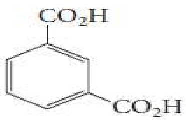
butanedioic acid

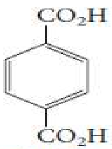
$HO_2C-C\equiv C-CO_2H$

butynedioic acid

- The three **benzenedicarboxylic acids** are generally known by their common names.



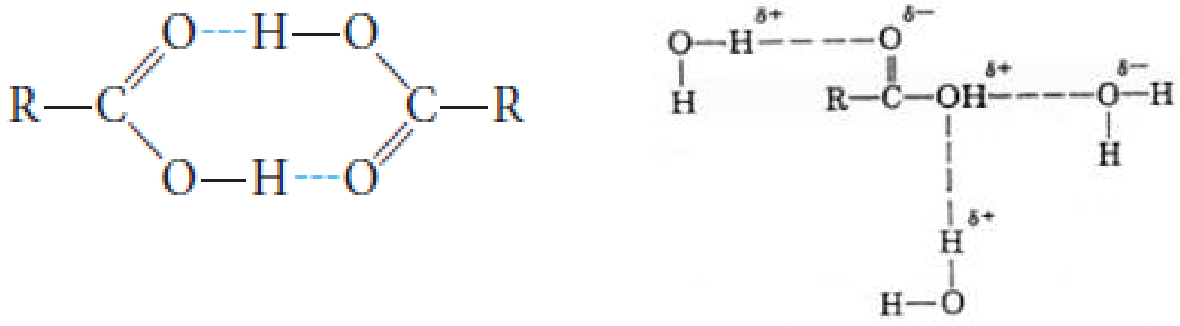




Common name:	phthalic acid	isophthalic acid	terephthalic acid
IUPAC name:	Benzene-1,2-dicarboxylic acid	Benzene-1,3-dicarboxylic acid	Benzene-1,4-dicarboxylic acid

Physical Properties of Acids

- **Carboxylic acids** are polar and they form hydrogen bonds with themselves or with other molecules.
- **Carboxylic acids form dimer**, with the individual units held together by two hydrogen bonds between the electron-rich oxygens and the electron-poor hydrogens.



Boiling Points

Therefore, they have high boiling points for their molecular weights-higher even those of comparable alcohols.

Physical Properties of Acids

Solubility in water

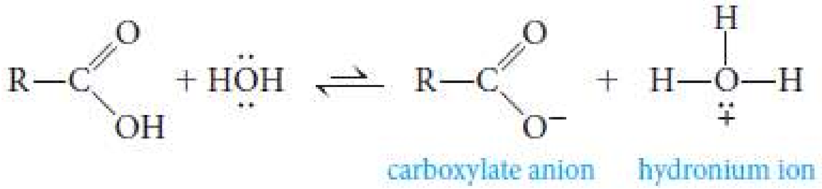
Hydrogen bonding also explains the water solubility of the lower molecular weight carboxylic acids.

- The first four aliphatic acids (formic through butyric) are completely miscible in water.
- Aromatic acids are insoluble in water.

Structure	Name	Mol. Wt.	b.p. °C	Solubility in H_2O at 25°C
$HCOOH$	Formic acid	46	100	Very soluble
CH_3CH_2OH	Ethyl alcohol	46	78	Very soluble
CH_3COOH	Acetic acid	60	118	Very soluble
$CH_3CH_2CH_2OH$	*n*-Propyl alcohol	60	97	Very soluble
$CH_3(CH_2)_3COOH$	Valeric acid	102	187	4.0 g/100 g H_2O
$CH_3(CH_2)_4CH2OH$	*n*-Hexyl alcohol	102	156	0.6 g/100 g H_2O
Ph-COOH	Benzoic acid	122	250	Insoluble
Ph-CH_2CH_2OH	3-Phenylethanol	122	250	Insoluble

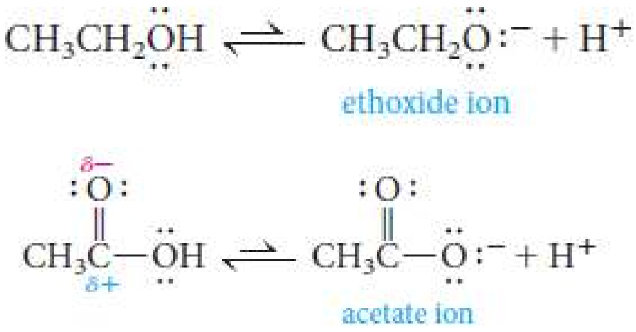
Acid Strength and Structure

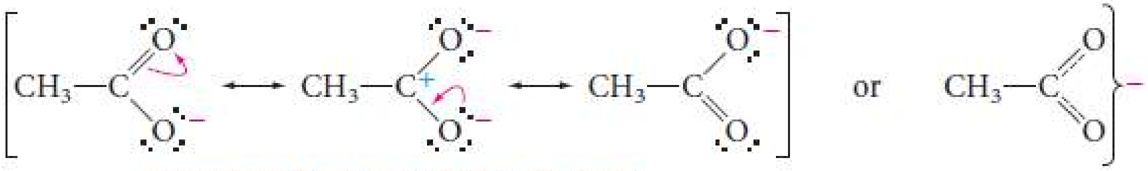
- **Carboxylic acids** (RCOOH) dissociate in water, yielding a carboxylate anion ($RCOO^-$) and hydronium ion.



Why carboxylic acids are more acidic than alcohols?

- In ethoxide ion, the negative charge is localized on a single oxygen atom.
- In acetate ion, on the other hand, the negative charge can be delocalized through resonance.





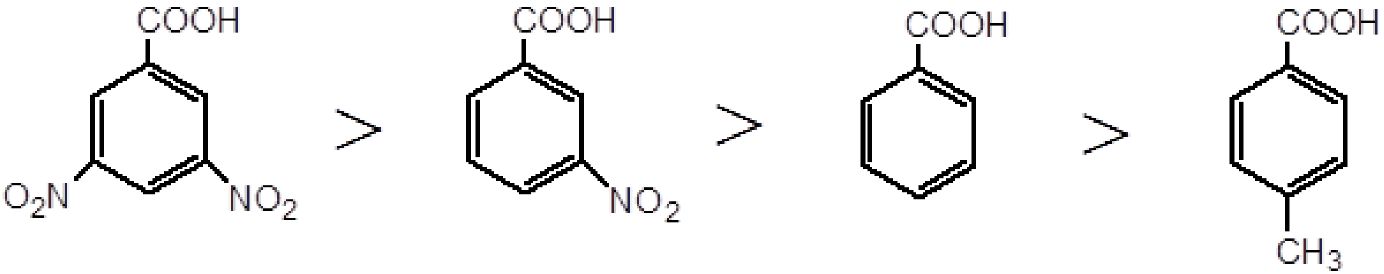
resonance in a carboxylate ion (acetate ion)

Acid Strength and Structure

Effect of Structure on Acidity; the Inductive Effect

- Acidities can vary depending on what other groups are attached to the molecule.
- Recall that *electron-withdrawing groups (-I) enhance acidity*, *and* *electron-releasing groups (+I) reduce acidity*.

  This effect relays charge through bonds, by displacing bonding electrons toward electronegative atoms, or away from electropositive atoms.



Acid Strength and Structure

Effect of Structure on Acidity; the Inductive Effect

- **Formic acid is a substantially stronger acid than acetic acid.**

  This suggests that the methyl group is more electron-releasing (hence anion-destabilizing and acidity-reducing) than hydrogen.

$$HCOOH > CH_3COOH > CH_3CH_2COOH > CH_3CH_2CH_2COOH$$

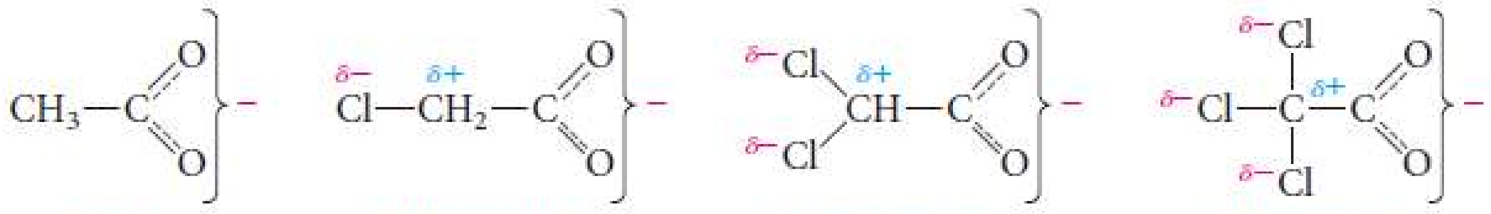
- **Example:** acetic acid with those of mono-, di-, and trichloroacetic acids.

  Comparison of acid strengths of acetic Acid and chlorinated acetic acids

$$Cl_3CCOOH > Cl_2CHCOOH > ClCH_2COOH > CH_3COOH$$

Acid Strength and Structure

Effect of Structure on Acidity; the Inductive Effect



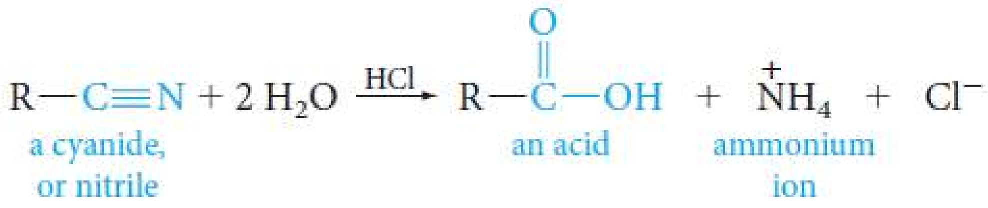
The more chlorines, the greater the effect and the greater the strength of the acid.

- **Comparison of acid strengths** of butyric acid and the monochlorinated acids.

Preparation of Acids

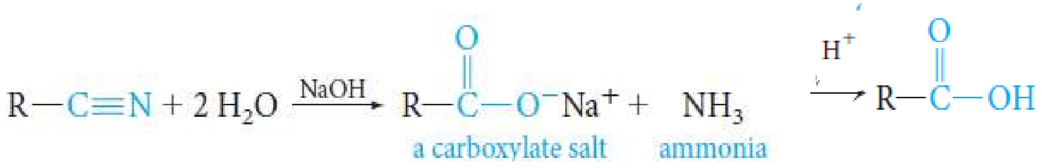
1) Hydrolysis of Cyanides (Nitriles)

- **The reaction requires either acid or base.**
- **In acid**, the nitrogen atom of the cyanide is converted to an ammonium ion.



$$\underset{\text{a cyanide, or nitrile}}{\mathrm{R{-}C{\equiv}N}} + 2\,\mathrm{H_2O} \xrightarrow{\mathrm{HCl}} \underset{\text{an acid}}{\mathrm{R{-}\overset{\overset{O}{\|}}{C}{-}OH}} + \underset{\text{ammonium ion}}{\overset{+}{\mathrm{N}}\mathrm{H_4}} + \mathrm{Cl^-}$$

- **In base**, the nitrogen atom is converted to ammonia and the organic product is the carboxylate salt, which must be neutralized in a separate step to give the acid.



$$\mathrm{R{-}C{\equiv}N} + 2\,\mathrm{H_2O} \xrightarrow{\mathrm{NaOH}} \underset{\text{a carboxylate salt}}{\mathrm{R{-}\overset{\overset{O}{\|}}{C}{-}O^-Na^+}} + \underset{\text{ammonia}}{\mathrm{NH_3}} \qquad \xrightarrow{\mathrm{H^+}} \mathrm{R{-}\overset{\overset{O}{\|}}{C}{-}OH}$$

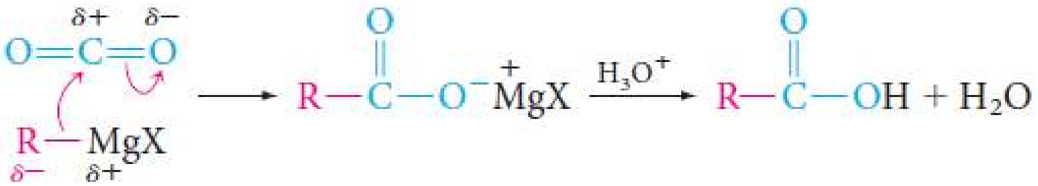
- **Alkyl cyanides** are generally made from the corresponding alkyl halide.

$$\underset{\substack{\text{propyl bromide}\\ \text{(1-bromopropane)}}}{\mathrm{CH_3CH_2CH_2Br}} \xrightarrow{\mathrm{NaCN}} \underset{\substack{\text{butyronitrile}\\ \text{(butanenitrile)}}}{\mathrm{CH_3CH_2CH_2CN}} \xrightarrow[\mathrm{H^+}]{\mathrm{H_2O}} \underset{\substack{\text{butyric acid}\\ \text{(butanoic acid)}}}{\mathrm{CH_3CH_2CH_2CO_2H}} + \mathrm{NH_4^+}$$

2) Reaction of Grignard Reagents with Carbon Dioxide (Carbonation of Grignard Reagent)

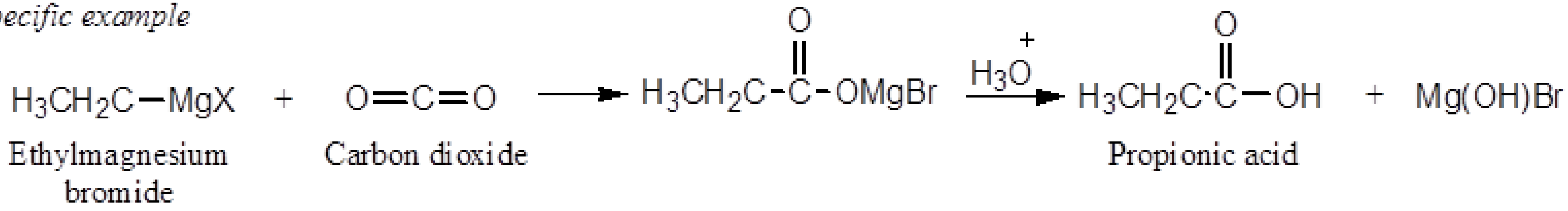
Preparation of Acids

- **Grignard reagents** add to the carbonyl group of carbon dioxide to give acids, after protonation of the intermediate carboxylate salt with a mineral acid like aqueous HCl.
- **The acid obtained has one more carbon atom** (*the reaction provides a way to increase the length of a carbon chain*).



$$\overset{\delta-}{R}-\overset{\delta+}{MgX} + \overset{\delta-}{O}=\overset{\delta+}{C}=O \longrightarrow R-\overset{\overset{O}{\|}}{C}-O^{-}\overset{+}{Mg}X \xrightarrow{H_3O^+} R-\overset{\overset{O}{\|}}{C}-OH + H_2O$$

Specific example

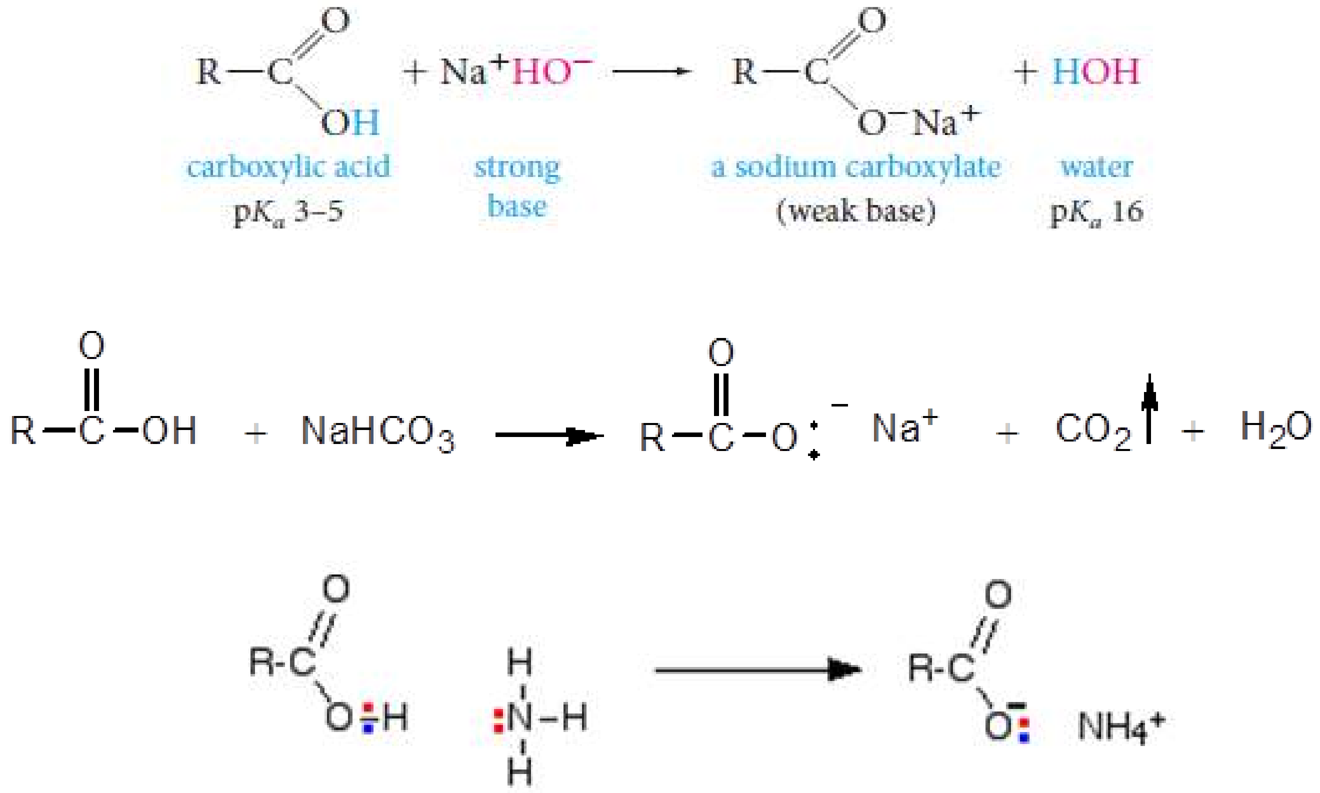


$$H_3CH_2C-MgX + O=C=O \longrightarrow H_3CH_2C-\overset{\overset{O}{\|}}{C}-OMgBr \xrightarrow{H_3\overset{+}{O}} H_3CH_2C-\overset{\overset{O}{\|}}{C}-OH + Mg(OH)Br$$

Reactions of Acids

1) Reactions with Bases: Salt Formation

- **Carboxylic acids, when treated with a strong base, form carboxylate salts.**

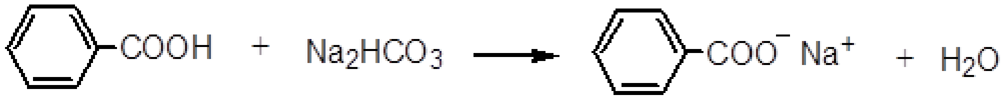


Reactions of Acids

1) Reactions with Bases: Salt Formation

- Examples.

Phenol

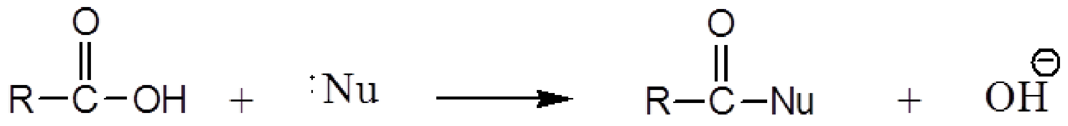


Benzoic acid

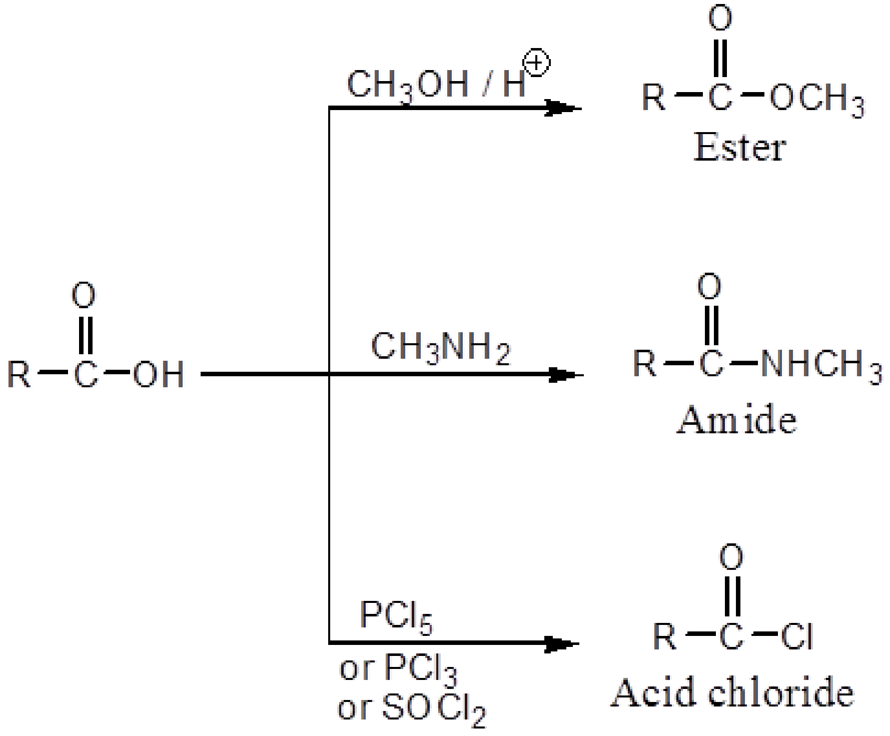
Sodium benzoate

Reactions of Acids

2) Nucleophilic Substitution Reactions

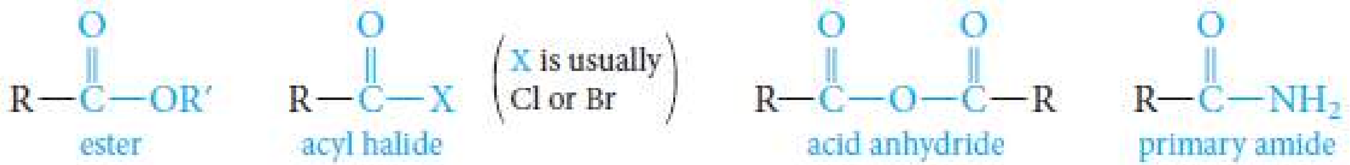


$$R-\overset{O}{\overset{\|}{C}}-OH + :Nu \longrightarrow R-\overset{O}{\overset{\|}{C}}-Nu + OH^{\ominus}$$



Carboxylic Acid Derivatives

- **Carboxylic acid derivatives** are compounds in which the hydroxyl part of the carboxyl group is replaced by various other groups.



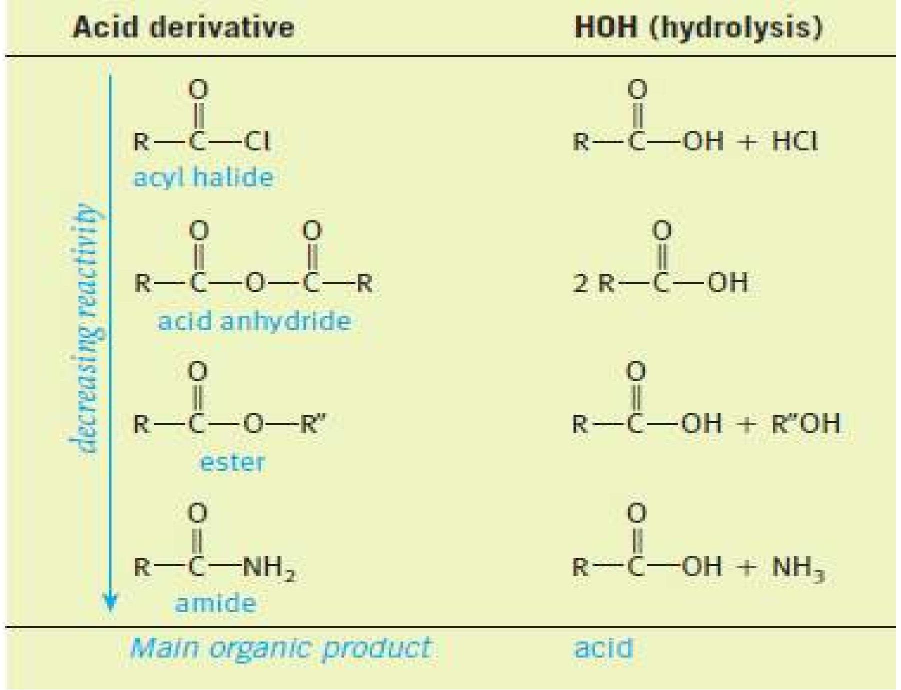
$R-\overset{O}{\overset{\|}{C}}-OR'$ ester

$R-\overset{O}{\overset{\|}{C}}-X$ acyl halide (X is usually Cl or Br)

$R-\overset{O}{\overset{\|}{C}}-O-\overset{O}{\overset{\|}{C}}-R$ acid anhydride

$R-\overset{O}{\overset{\|}{C}}-NH_2$ primary amide

- All acid derivatives can be hydrolyzed to the corresponding carboxylic acid.



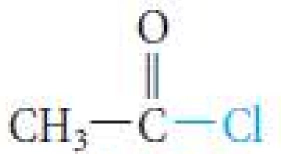
Acid derivative	HOH (hydrolysis)
$R-\overset{O}{\overset{\|}{C}}-Cl$ acyl halide	$R-\overset{O}{\overset{\|}{C}}-OH + HCl$
$R-\overset{O}{\overset{\|}{C}}-O-\overset{O}{\overset{\|}{C}}-R$ acid anhydride	$2\ R-\overset{O}{\overset{\|}{C}}-OH$
$R-\overset{O}{\overset{\|}{C}}-O-R''$ ester	$R-\overset{O}{\overset{\|}{C}}-OH + R''OH$
$R-\overset{O}{\overset{\|}{C}}-NH_2$ amide	$R-\overset{O}{\overset{\|}{C}}-OH + NH_3$
Main organic product	acid

Carboxylic Acid Derivatives

Acid Chloride

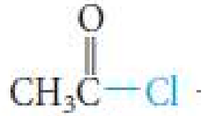
- **Acyl chlorides** have the general formula RCOCl.
- **Acyl chlorides** are more common and less expensive than bromides or iodides.
- **Nomenclature:**

  Acyl chlorides, or acid chlorides, are named by replacing the *-ic acid* ending of the parent acid by *-yl chloride*.



$CH_3-\overset{\overset{O}{\|}}{C}-Cl$

acetyl chloride



$CH_3\overset{\overset{O}{\|}}{C}-Cl$

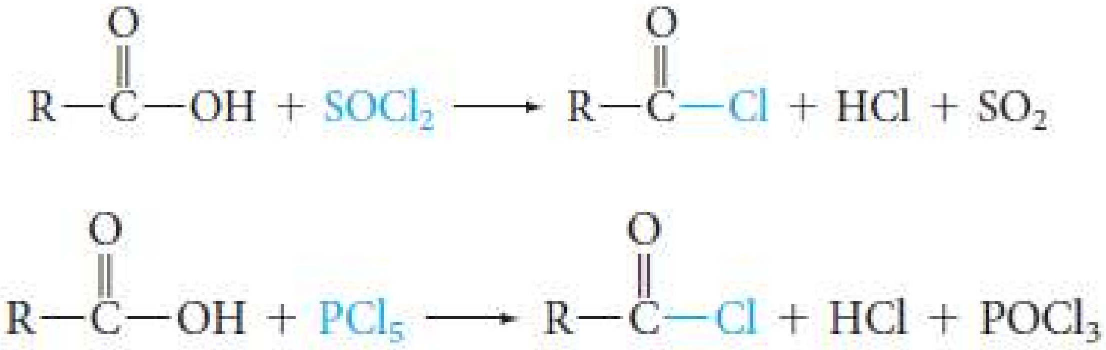
acetyl chloride

Carboxylic Acid Derivatives

Acid Chloride

- **Preparation:**

  They can be prepared from acids by reaction with thionyl chloride or phosphorous pentachloride.



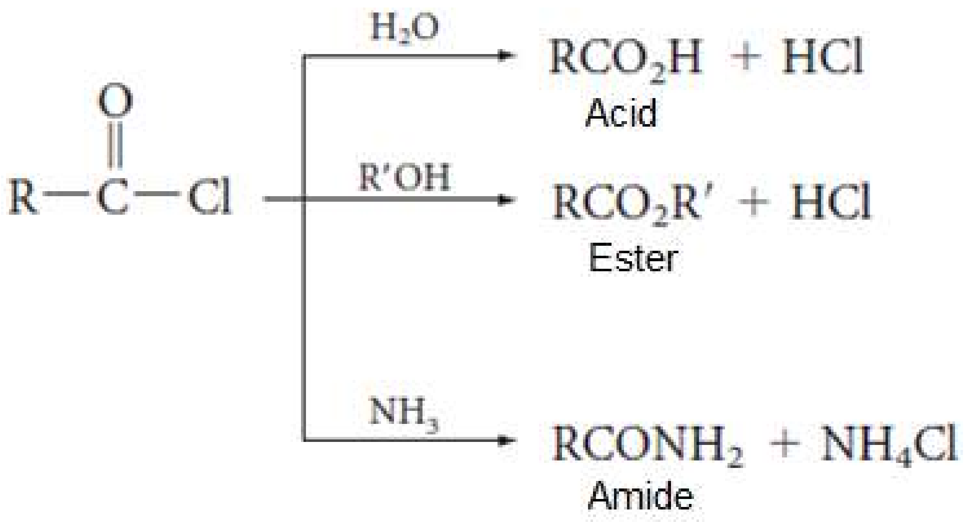
$$R-\overset{O}{\overset{\|}{C}}-OH + SOCl_2 \longrightarrow R-\overset{O}{\overset{\|}{C}}-Cl + HCl + SO_2$$

$$R-\overset{O}{\overset{\|}{C}}-OH + PCl_5 \longrightarrow R-\overset{O}{\overset{\|}{C}}-Cl + HCl + POCl_3$$

Carboxylic Acid Derivatives

Acid Chloride

- **Reactions:** *They can react rapidly with most nucleophile.*



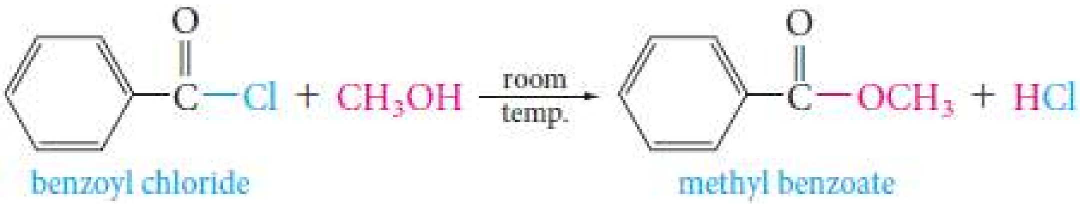
Carboxylic Acid Derivatives

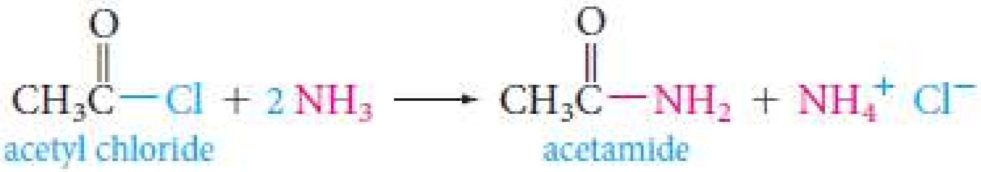
Acid Chloride

- **Examples:**

$$CH_3-\overset{O}{\overset{\|}{C}}-Cl + HOH \xrightarrow{\text{rapid}} CH_3-\overset{O}{\overset{\|}{C}}-OH + HCl$$

acetyl chloride · acetic acid · (fumes)





$$CH_3\overset{O}{\overset{\|}{C}}-Cl + 2\,NH_3 \longrightarrow CH_3\overset{O}{\overset{\|}{C}}-NH_2 + NH_4^+\ Cl^-$$

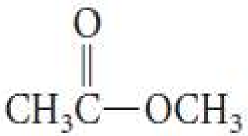
acetyl chloride · acetamide

Carboxylic Acid Derivatives

Esters

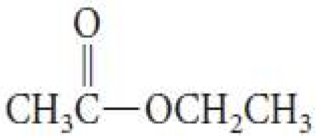
- **Esters** are derived from acids by replacing the –OH group by an –OR group and have the general formula $R^{/}COOR$.

- **Nomenclature:**
  - They are named in a manner analogous to carboxylic acid salts.
  - The R part of the –OR group is name first, followed by the name of the acid, with the *–ic acid* ending changed to *–ate*.



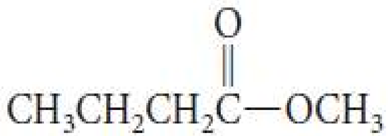
$CH_3\overset{\overset{O}{\|}}{C}-OCH_3$

methyl acetate
(methyl ethanoate)



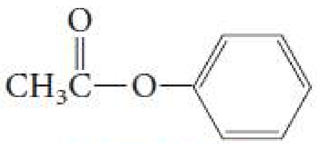
$CH_3\overset{\overset{O}{\|}}{C}-OCH_2CH_3$

ethyl acetate
(ethyl ethanoate)

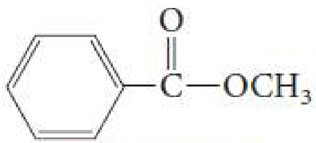


$CH_3CH_2CH_2\overset{\overset{O}{\|}}{C}-OCH_3$

methyl butanoate
bp 102.3°C



phenyl acetate

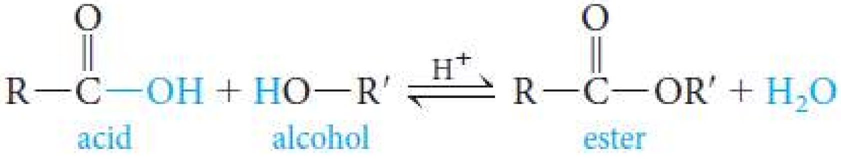


methyl benzoate

Carboxylic Acid Derivatives

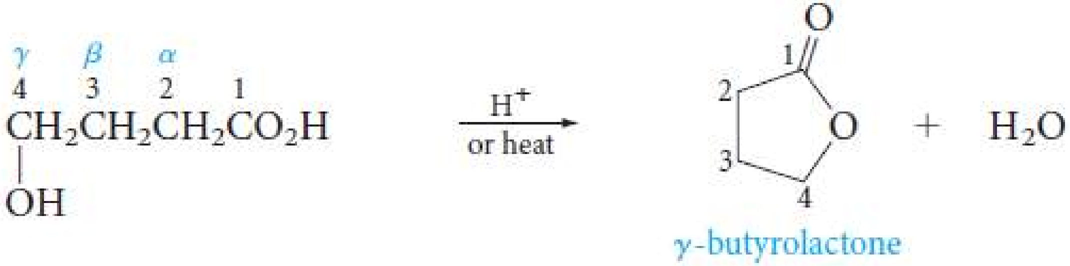
Esters

- **Preparation:**
  When a carboxylic acid and an alcohol are heated in the presence of an acid catalyst (HCl or H_2SO_4), an equilibrium is established with the ester and water.



$$\underset{\text{acid}}{R-\overset{\overset{\displaystyle O}{\|}}{C}-OH} + \underset{\text{alcohol}}{HO-R'} \overset{H^+}{\rightleftharpoons} \underset{\text{ester}}{R-\overset{\overset{\displaystyle O}{\|}}{C}-OR'} + H_2O$$

- **Cyclic esters (lactones)** can be prepared from hydroxy acids if these groups can come in contact through bending of the chain.

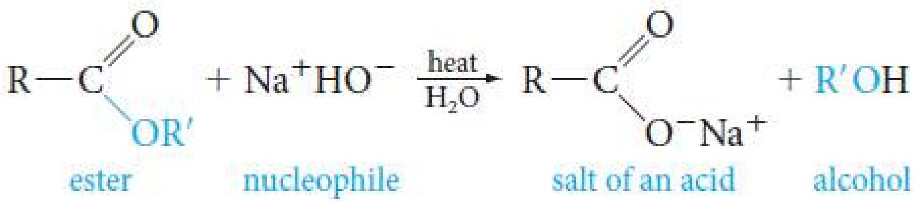


Carboxylic Acid Derivatives

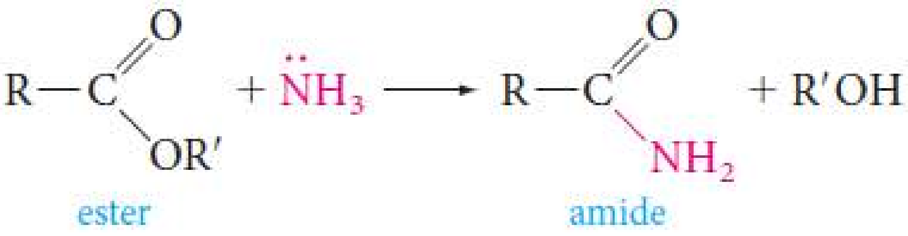
Esters

➢ Reactions

- **Saponification;** esters are commonly hydrolyzed with base.



- Ammonia converts esters to **amides**.

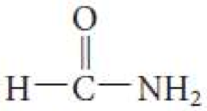


Carboxylic Acid Derivatives

Amides

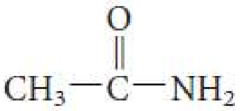
- **Amides** are the least reactive of the common carboxylic acid derivatives.
- Primary amides have general formula **$RCONH_2$**.
- **Nomenclature:**

  Amides are named by replacing the *–ic or –oic acid* ending of the acid name, either the common or the IUPAC name, with the *–amide* ending.



$H-\overset{\overset{O}{\|}}{C}-NH_2$

formamide
(methanamide)

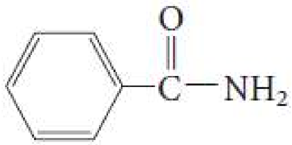


$CH_3-\overset{\overset{O}{\|}}{C}-NH_2$

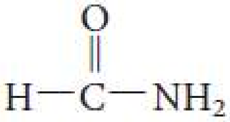
acetamide
(ethanamide)

$CH_3CH_2CH_2\overset{\overset{O}{\|}}{C}-NH_2$

butanamide

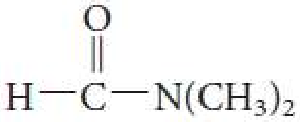


benzamide
(benzenecarboxamide)



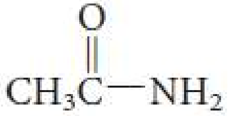
$H-\overset{\overset{O}{\|}}{C}-NH_2$

formamide



$H-\overset{\overset{O}{\|}}{C}-N(CH_3)_2$

N,N-dimethylformamide



$CH_3\overset{\overset{O}{\|}}{C}-NH_2$

acetamide

$CH_3\overset{\overset{O}{\|}}{C}-N(CH_3)_2$

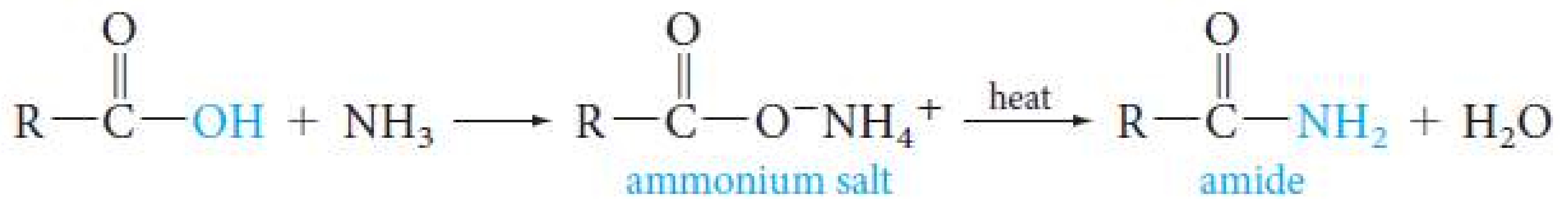
N,N-dimethylacetamide

Carboxylic Acid Derivatives

Amides

➢ **Preparation:**

- They can be prepared by the reaction of ammonia with esters, with acyl halides, or with acid anhydrides.
- Amides can also prepared by heating the ammonium salts of acids.



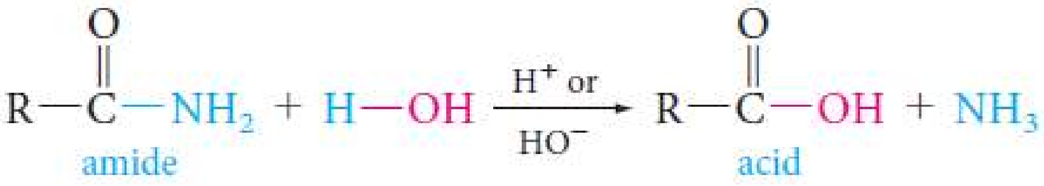
$$R-\overset{O}{\overset{\|}{C}}-OH + NH_3 \longrightarrow R-\overset{O}{\overset{\|}{C}}-O^{-}NH_4^{+} \xrightarrow{\text{heat}} R-\overset{O}{\overset{\|}{C}}-NH_2 + H_2O$$

Carboxylic Acid Derivatives

Amides

➢ Reactions

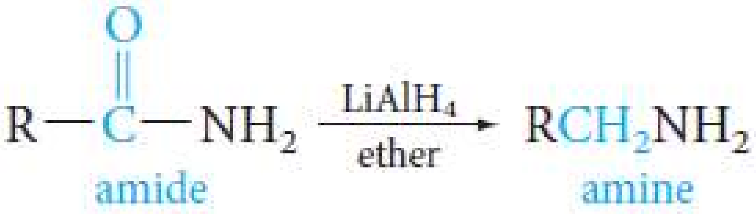
- **Amides** react with nucleophiles and they can be hydrolyzed by water.



$$R-\overset{O}{\overset{\|}{C}}-NH_2 + H-OH \xrightarrow[HO^-]{H^+ \text{ or}} R-\overset{O}{\overset{\|}{C}}-OH + NH_3$$

amide acid

- **Amides** can be reduced by lithium aluminums hydride to give amines.



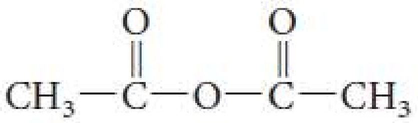
$$R-\overset{O}{\overset{\|}{C}}-NH_2 \xrightarrow[\text{ether}]{LiAlH_4} RCH_2NH_2$$

amide amine

Carboxylic Acid Derivatives

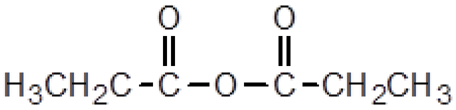
Acid Anhydrides

- **Acid anhydrides** have general formula RCOOCOR.
- **Nomenclature:**
  The name of an anhydrides is obtained by naming the acid from which is derived and replacing the word acid with anhydride.



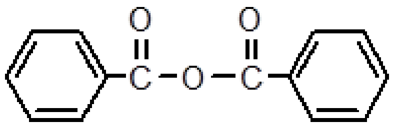
$CH_3-\overset{O}{\overset{\|}{C}}-O-\overset{O}{\overset{\|}{C}}-CH_3$

ethanoic anhydride or acetic anhydride

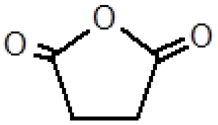


$H_3CH_2C-\overset{O}{\overset{\|}{C}}-O-\overset{O}{\overset{\|}{C}}-CH_2CH_3$

IUPAC name: Propanoic anhydride
Common name: Propionic anhydride



Benzoic anhydride



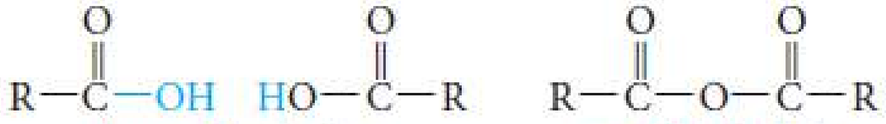
Succinic anhydride

Carboxylic Acid Derivatives

Acid Anhydrides

Preparation

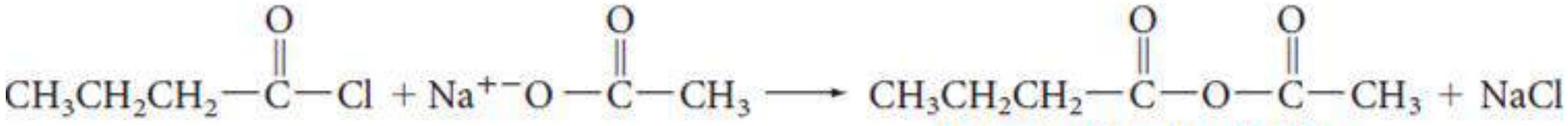
- **Acid anhydrides** are derived from acids by removing water from two carboxyl groups and connecting the fragments.



$$R-\overset{O}{\overset{\|}{C}}-OH \quad HO-\overset{O}{\overset{\|}{C}}-R \qquad R-\overset{O}{\overset{\|}{C}}-O-\overset{O}{\overset{\|}{C}}-R$$

two acid molecules an acid anhydride

- **Anhydrides** can also be prepared from acid chlorides and carboxylate salts. *This method is used for preparing anhydrides derived from two different carboxylic acids (mixed anhydrides).*



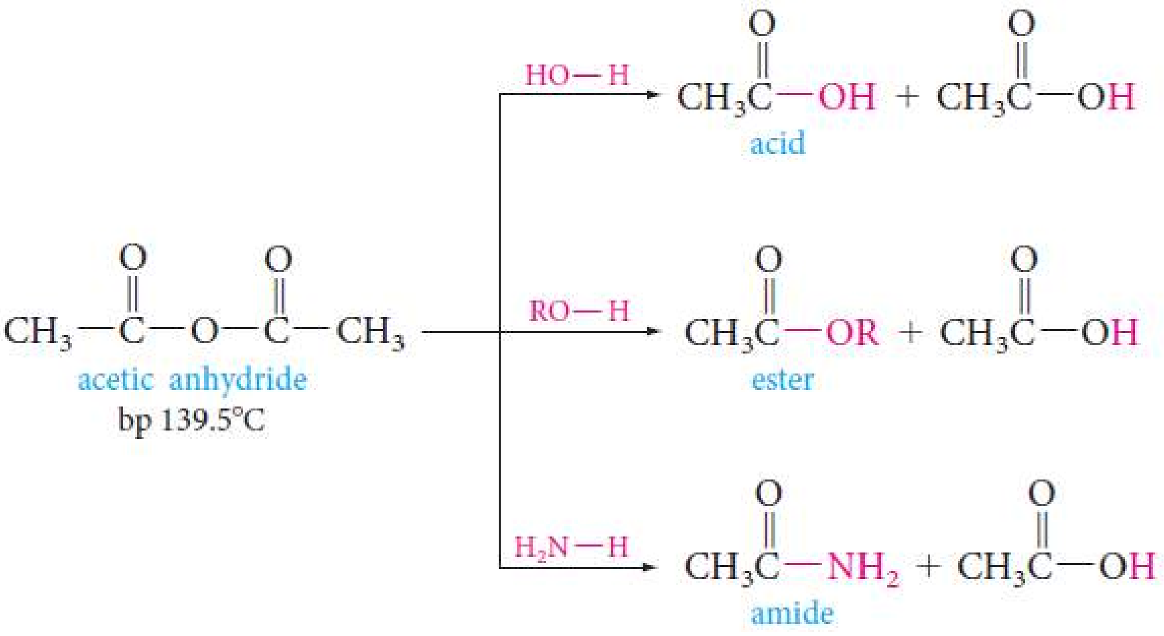
$$CH_3CH_2CH_2-\overset{O}{\overset{\|}{C}}-Cl + Na^{+}\,{}^{-}O-\overset{O}{\overset{\|}{C}}-CH_3 \longrightarrow CH_3CH_2CH_2-\overset{O}{\overset{\|}{C}}-O-\overset{O}{\overset{\|}{C}}-CH_3 + NaCl$$

butanoic ethanoic anhydride

Carboxylic Acid Derivatives

Acid Anhydrides

- **Reactions**
  - **Anhydrides** undergo nucleophilic acyl substitution reactions (*They are more reactive than esters, but less reactive than acyl halides*).



Fundamentals of Organic Chemistry

CHEM 109

For Students of Health Colleges

Credit hrs.: (2+1)

King Saud University

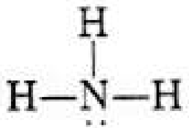
College of Science, Chemistry Department

CHEM 109

CHAPTER 8. AMINES

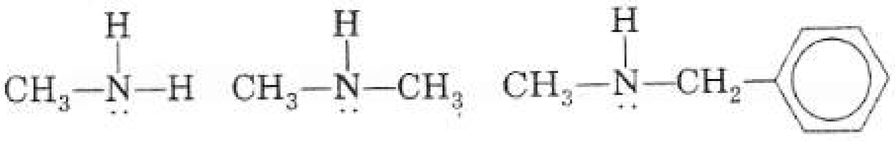
Structure and Classification of Amines

- **Amines** are compounds that derived from ammonia by replacement of one, two, or three hydrogens by alkyl or aryl groups.



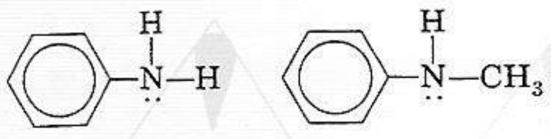
Ammonia

- **Aliphatic amines** contain *only alkyl* groups bonded directly to the nitrogen atom.



Aliphatic amines

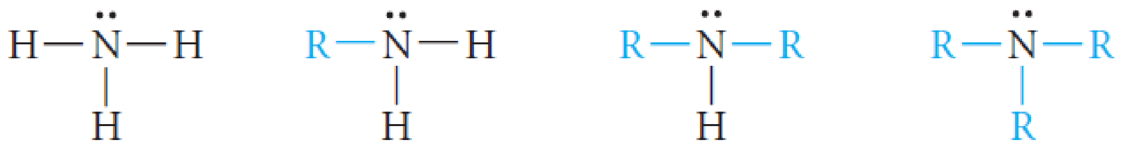
- **Aromatic amines** are those in which one or more aryl groups are bonded directly to nitrogen.



Aromatic amines

Classification and Structure of Amines

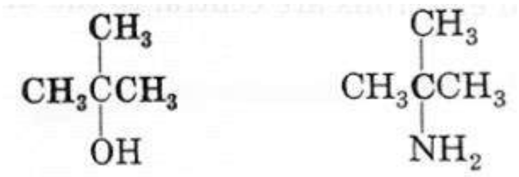
- The relation between **ammonia and amines** is illustrated by the following structures:



ammonia primary amine secondary amine tertiary amine

- **Amines** are classified as **primary**, **secondary**, **or** **tertiary**, *depending on whether one, two, or three organic groups are attached to the nitrogen*.

- **NOTE:**



t-Butyl alcohol (3° alcohol) *t*-Butylamine (1° amine)

  - *t*-butyl alcohol is a tertiary alcohol (because three carbons are attached to the carbinol carbon).
  - *t*-butyl amine is a primary amine (because only one carbon is attached directly to the nitrogen atom).

Nomenclature of Amines

Common Names

- **Amines** are named by specifying the alkyl groups attached to the nitrogen and adding the suffix –*amine* (*Alkylamine*).

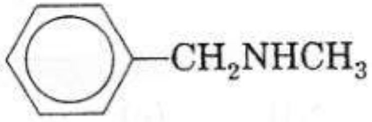
$CH_3CH_2NH_2$
ethylamine
(primary)

$(CH_3CH_2)_2NH$
diethylamine
(secondary)

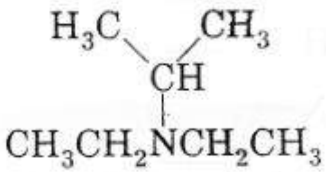
$(CH_3CH_2)_3N$
triethylamine
(tertiary)

CH_3NH_2
Methylamine

$CH_3NHCH_2CH_3$
Ethylmethylamine


Benzylmethylamine

CH_3NHCH_3
Dimethylamine



$$CH_3CH_2\overset{\overset{\displaystyle H_3C\ \ \ CH_3}{\displaystyle CH}\,|}{N}CH_2CH_3$$

Diethylisopropylamine

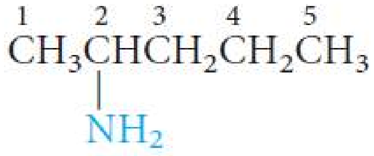
Nomenclature of Amines

IUPAC System

- The amino group, $-NH_2$, is named **as a substituent**.

$CH_3CH_2NH_2$

aminoethane



$$\overset{1}{C}H_3\overset{2}{C}H(NH_2)\overset{3}{C}H_2\overset{4}{C}H_2\overset{5}{C}H_3$$

2-aminopentane

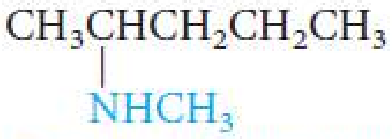
- Amines can be named as **alkanamines**.

$CH_3CH_2CH_2NH_2$

propanamine

$$CH_3CH(NH_2)CH_3$$

2-propanamine



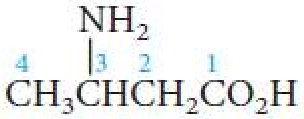
$$CH_3CH(NHCH_3)CH_2CH_2CH_3$$

N-methyl-2-pentanamine

Nomenclature of Amines

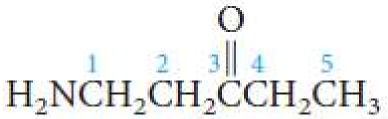
IUPAC System

- When **other functional groups** are present, the amino group, -NH_2, is named as a substituent.



$CH_3\overset{NH_2}{\overset{|}{C}}HCH_2CO_2H$

3-aminobutanoic acid



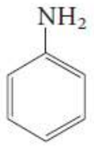
$H_2NCH_2CH_2\overset{O}{\overset{\|}{C}}CH_2CH_3$

1-amino-3-pentanone

$CH_3NHCH_2CH_2OH$

2-methylaminoethanol

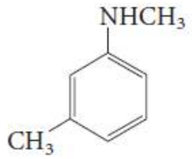
- **Aromatic amines** are named as derivatives of aniline.
- In the CA system, aniline is called benzenamine.



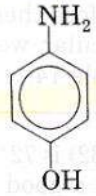
aniline
(benzenamine)

p-bromoaniline
(4-bromobenzenamine)

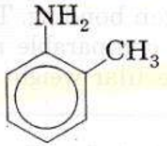
N,*N*-dimethylaniline
(*N*,*N*-dimethylbenzenamine)



m-methyl-*N*-methylaniline, or
N-methyl-*m*-toluidine
(*N*-methyl-3-methylbenzenamine)



p-Hydroxyaniline
(*p*-Aminophenol)



o-Toluidine

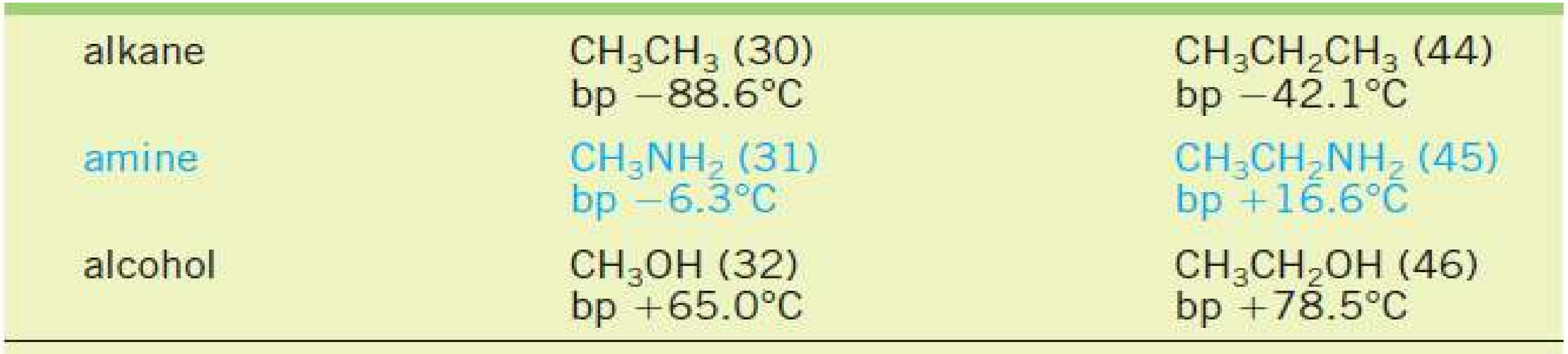
p-Toluidine

Physical Properties of Amines

Boiling Point

- **Methylamine and ethylamine are gases**, but primary amines with three or more carbons are liquids.
- **Primary amines** boil well above alkanes with comparable molecular weights, but below comparable alcohols.

Intermolecular N-H· · ·N hydrogen bonds are important and raise the boiling points of primary and secondary amines but are not as strong as the O-H· · ·O bonds of alcohols. The reason for this is that nitrogen is not as electronegative as oxygen.



alkane	CH_3CH_3 (30) bp −88.6°C	$CH_3CH_2CH_3$ (44) bp −42.1°C
amine	CH_3NH_2 (31) bp −6.3°C	$CH_3CH_2NH_2$ (45) bp +16.6°C
alcohol	CH_3OH (32) bp +65.0°C	CH_3CH_2OH (46) bp +78.5°C

Physical Properties of Amines

Boiling Point

- **Tertiary amines** are also polar compounds, but because hydrogen is not bonded to nitrogen, these amines are incapable of intermolecular hydrogen bonding.

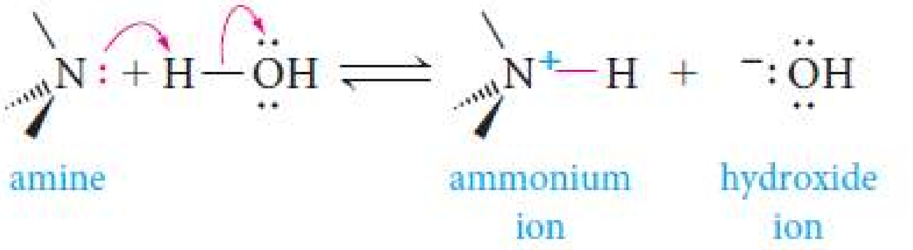
Their boiling points are Lower than primary and secondary amines of identical molecular weights and Higher than those of alkanes of similar molecular weight.

Solubility in Water

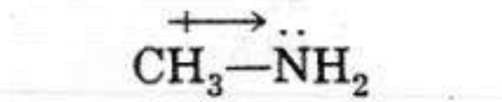
- **All three classes of amines** can form hydrogen bonds with the -OH group of water (that is, O-H· · ·N).
- **Primary and secondary amines** can also form hydrogen bonds with the oxygen atom in water: N-H· · ·O.
- **Amines** with up to six carbons show appreciable solubility in water.

The Basicity of Amines

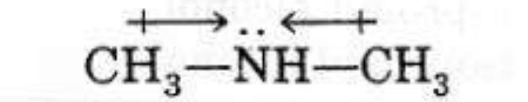
- **The unshared pair of electrons** on the nitrogen atom dominates the chemistry of amines.
- Because of this electron pair, **amines are both basic and nucleophilic**.
- Aqueous solutions of amines are basic because of the following equilibrium:



  - Electron-donating groups increase the basicity of amines.
  - Electron-withdrawing groups decrease their basicity.


$CH_3-\ddot{N}H_2$

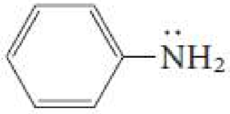
One electron-donating group


$CH_3-\ddot{N}H-CH_3$

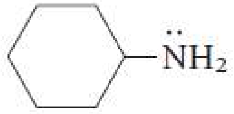
Two electron-donating groups

The Basicity of Amines

- **Aromatic amines are much weaker than aliphatic amines or ammonia.**
  - **Example:** aniline is less basic than cyclohexylamine.

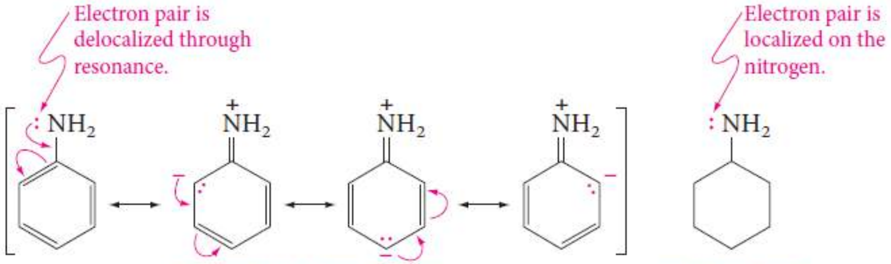


aniline



cyclohexylamine

The reason is the resonance delocalization of the unshared electron pair that is possible in aniline, but not in cyclohexylamine:

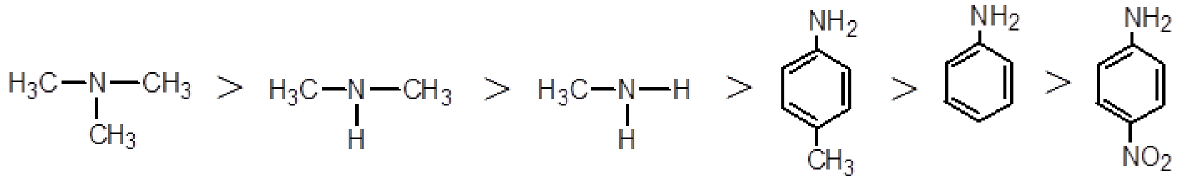


Electron pair is delocalized through resonance.

Electron pair is localized on the nitrogen.

resonance structures of aniline

cyclohexylamine

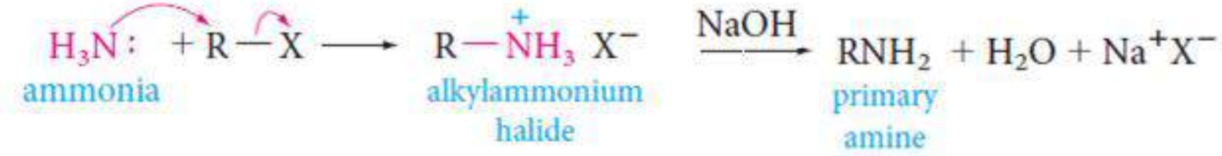


Preparation of Amines

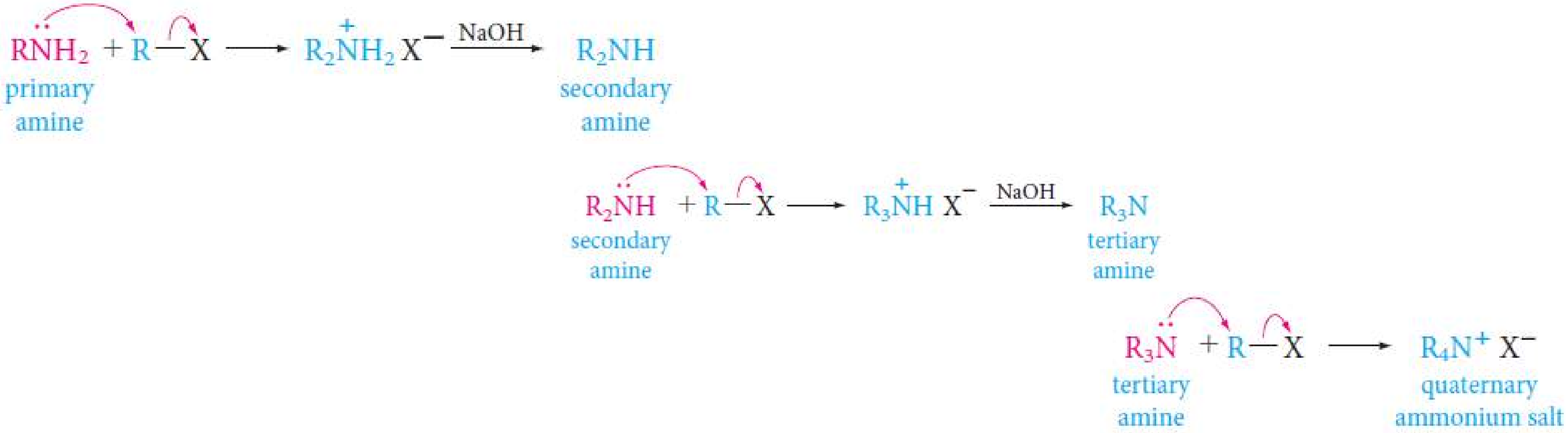
1) Alkylation of Ammonia

- **Ammonia** reacts with alkyl halides to give amines via a two-step process.

  The first step is a nucleophilic substitution reaction. The free amine ***can then be obtained from its salt by treatment with a strong base***



- **Primary, secondary, and tertiary amines** can be similarly alkylated.

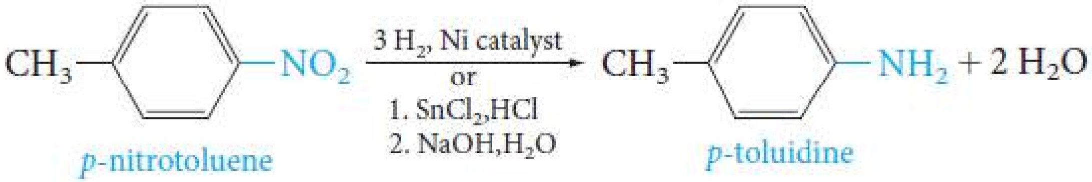


Preparation of Amines

2) Reduction of Nitro Groups

- The best route to **aromatic primary amines** is by reduction of the corresponding nitro compounds.

The nitro group is easily reduced, either catalytically with hydrogen or by chemical reducing agents.



Preparation of Amines

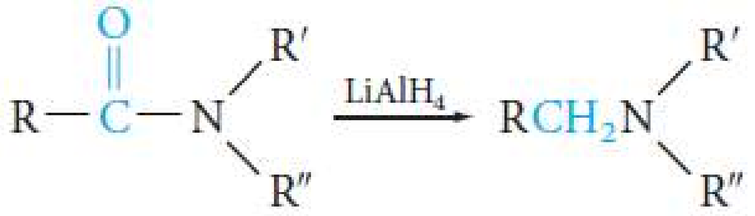
3) Reduction of Nitriles

- **Reduction of nitriles** (cyanides) gives primary amines.

$$R{-}C{\equiv}N \xrightarrow[\text{or } H_2,\ Ni]{LiAlH_4} RCH_2NH_2$$

4) Reduction of Amides

- **Amides** can be reduced to amines with lithium aluminum hydride.



(R′ and R″ may be H or organic groups.)

Reactions of Amines

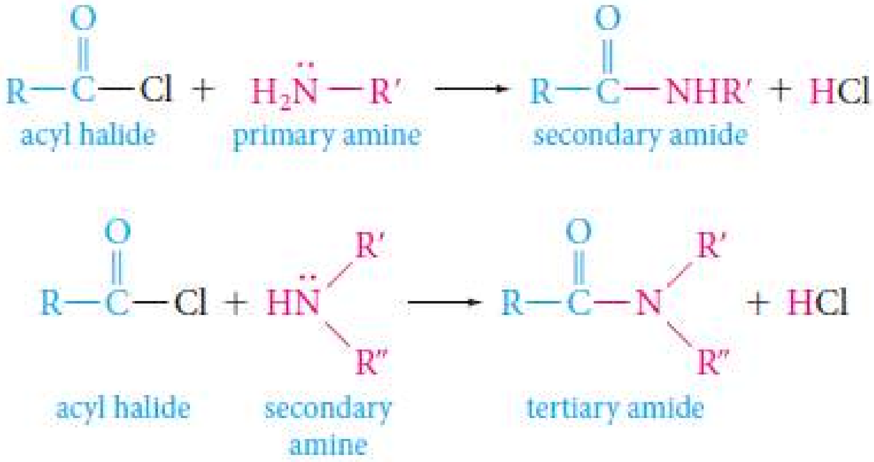
1) Reactions with Acids: Salt Formation

Amines react with strong acids to form alkylammonium salts.


$$R-\ddot{N}H_2 + HCl \longrightarrow R\overset{+}{N}H_3\ Cl^-$$

2) Acylation of Amines: Amides Formation

Primary and secondary amines react with acyl halides to form amides.


$$R-\overset{O}{\overset{\|}{C}}-Cl + H_2\ddot{N}-R' \longrightarrow R-\overset{O}{\overset{\|}{C}}-NHR' + HCl$$
$$R-\overset{O}{\overset{\|}{C}}-Cl + H\ddot{N}R'R'' \longrightarrow R-\overset{O}{\overset{\|}{C}}-NR'R'' + HCl$$

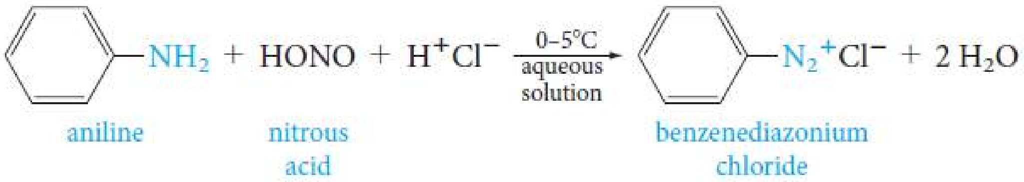
Reactions of Amines

3) Imines Formation

Primary amines, R-NH_2 or ArNH_2, undergo nucleophilic addition with aldehydes or ketones in an acidic buffer to give substituted imines.

4) Aromatic Diazonium Salts

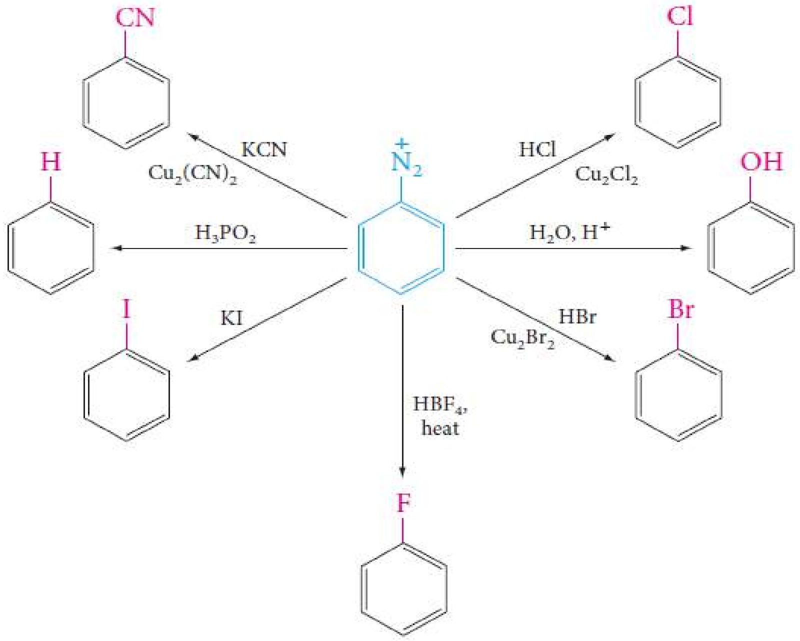
- Primary aromatic amices react with nitrous acid at 0°C to yield aryldiazonium ions. *The process is called **diazotization**.*



Reactions of Amines

4) Aromatic Diazonium Salts

- They are useful in synthesis because the diazonio groum ($-N_2^+$) can be replaced by nucleophiles; the other product is nitrogen gas.



Fundamentals of Organic Chemistry

CHEM 109

For Students of Health Colleges

Credit hrs.: (2+1)

King Saud University

College of Science, Chemistry Department

CHEM 109

CHAPTER 9. AMINO ACIDS, PEPTIDES AND PROTEINS

Sources, Classification and Structure of Amino Acids

- **Proteins** are naturally occurring polymers composed of amino acid units joined one to another by amide (or peptide) bonds.

  Example, animal hair and muscle, egg whites, and hemoglobin are all proteins.

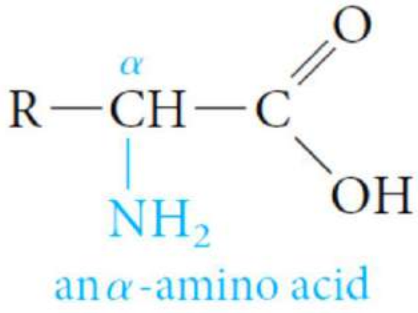
- **Peptides** are oligomers of amino acids that play important roles in many biological processes.

  Example, the peptide hormone insulin controls our blood sugar levels.

- **Proteins, peptides, and amino acids** are essential to the structure, function, and reproduction of living matter.

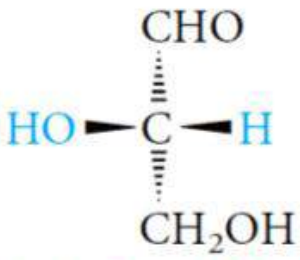
Sources, Classification and Structure of Amino Acids

- **The** **amino acids** obtained from protein hydrolysis are α-amino acids.
- **The** **amino group** is on the **α -carbon atom**, the one adjacent to the carboxyl group.

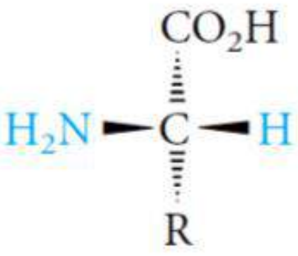


- With the exception of glycine, where R = H, a-amino acids have a **stereogenic center at the α -carbon**.
- All except glycine are therefore **optically active**.
- They have the **L-configuration** relative to glyceraldehyde .
- **Note that the** **Fischer convention**, used with carbohydrates, is also applied to amino acids.

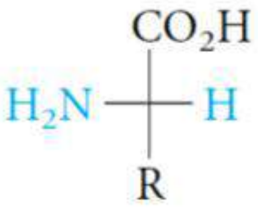
Sources, Classification and Structure of Amino Acids



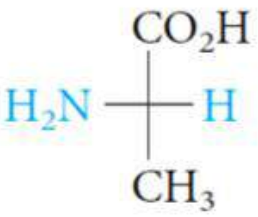
L-(−)-glyceraldehyde



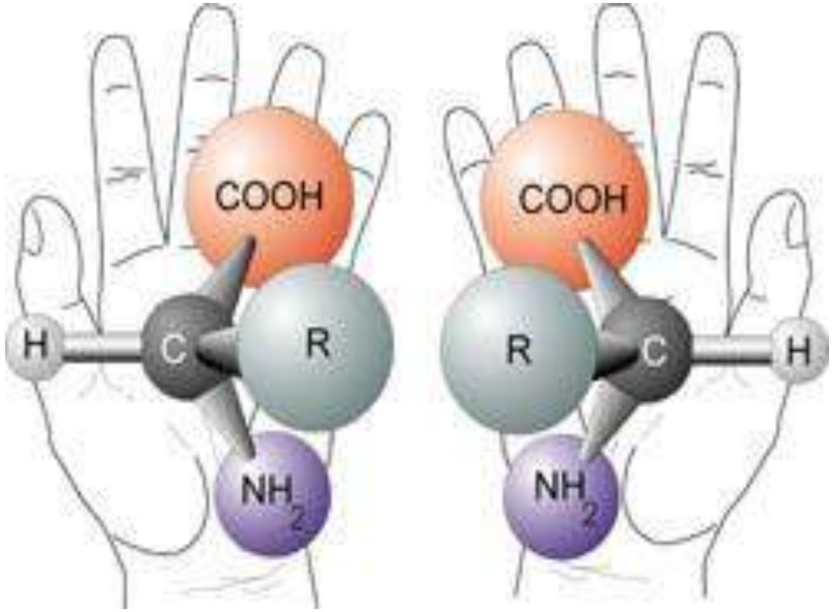
a naturally occurring L-amino acid



Fischer projection formula of an L-amino acid



L-(+)-alanine



Sources, Classification and Structure of Amino Acids

List of the 20 α-amino acids commonly found in proteins.

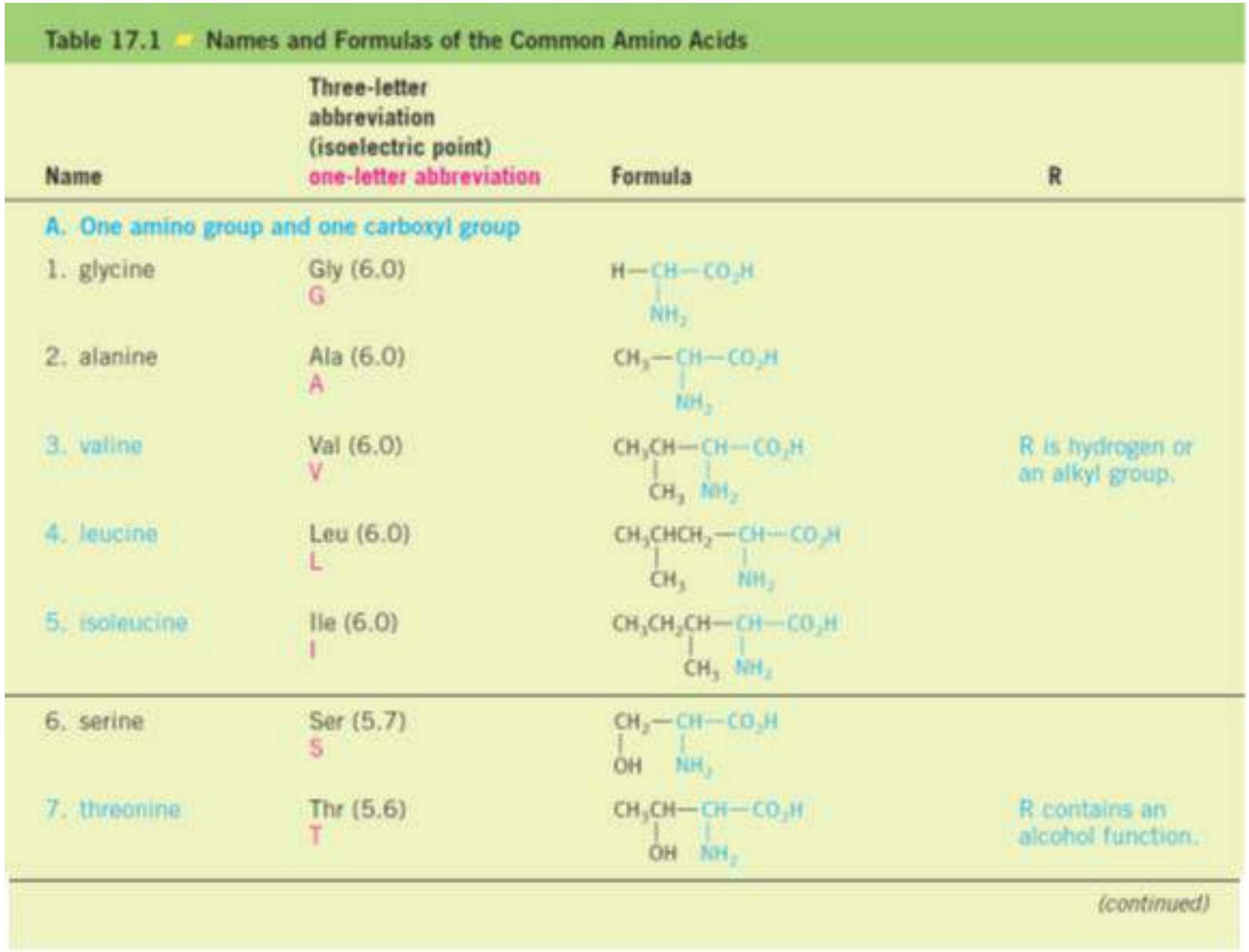


Table 17.1 Names and Formulas of the Common Amino Acids

Name	Three-letter abbreviation (isoelectric point) one-letter abbreviation	Formula	R
A. One amino group and one carboxyl group			
1. glycine	Gly (6.0) G	$H-\underset{NH_2}{\underset{\vert}{CH}}-CO_2H$	R is hydrogen or an alkyl group.
2. alanine	Ala (6.0) A	$CH_3-\underset{NH_2}{\underset{\vert}{CH}}-CO_2H$	
3. valine	Val (6.0) V	$CH_3\underset{CH_3}{\underset{\vert}{CH}}-\underset{NH_2}{\underset{\vert}{CH}}-CO_2H$	
4. leucine	Leu (6.0) L	$CH_3\underset{CH_3}{\underset{\vert}{CH}}CH_2-\underset{NH_2}{\underset{\vert}{CH}}-CO_2H$	
5. isoleucine	Ile (6.0) I	$CH_3CH_2\underset{CH_3}{\underset{\vert}{CH}}-\underset{NH_2}{\underset{\vert}{CH}}-CO_2H$	
6. serine	Ser (5.7) S	$\underset{OH}{\underset{\vert}{CH_2}}-\underset{NH_2}{\underset{\vert}{CH}}-CO_2H$	R contains an alcohol function.
7. threonine	Thr (5.6) T	$CH_3\underset{OH}{\underset{\vert}{CH}}-\underset{NH_2}{\underset{\vert}{CH}}-CO_2H$	

(continued)

Sources, Classification and Structure of Amino Acids

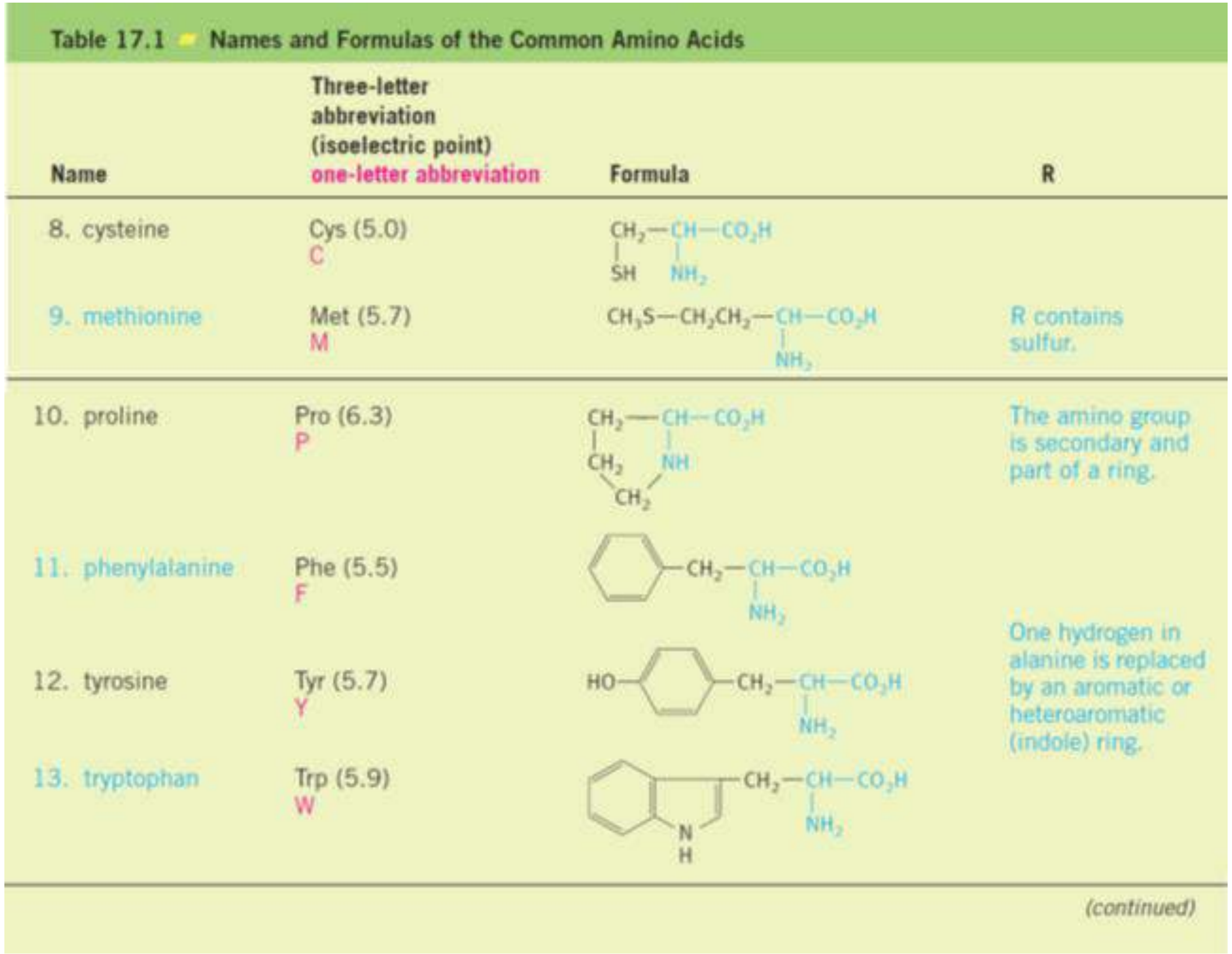


Table 17.1 Names and Formulas of the Common Amino Acids

Name	Three-letter abbreviation (isoelectric point) one-letter abbreviation	Formula	R
8. cysteine	Cys (5.0) C	$\underset{\mathrm{SH}}{\mathrm{CH_2}}-\underset{\mathrm{NH_2}}{\mathrm{CH}}-\mathrm{CO_2H}$	R contains sulfur.
9. methionine	Met (5.7) M	$\mathrm{CH_3S-CH_2CH_2}-\underset{\mathrm{NH_2}}{\mathrm{CH}}-\mathrm{CO_2H}$	
10. proline	Pro (6.3) P	$\mathrm{CH_2-CH-CO_2H}$, $\mathrm{CH_2}$, NH, $\mathrm{CH_2}$	The amino group is secondary and part of a ring.
11. phenylalanine	Phe (5.5) F	$-\mathrm{CH_2}-\underset{\mathrm{NH_2}}{\mathrm{CH}}-\mathrm{CO_2H}$	One hydrogen in alanine is replaced by an aromatic or heteroaromatic (indole) ring.
12. tyrosine	Tyr (5.7) Y	$\mathrm{HO}-$ $-\mathrm{CH_2}-\underset{\mathrm{NH_2}}{\mathrm{CH}}-\mathrm{CO_2H}$	
13. tryptophan	Trp (5.9) W	$-\mathrm{CH_2}-\underset{\mathrm{NH_2}}{\mathrm{CH}}-\mathrm{CO_2H}$, N, H	

(continued)

Sources, Classification and Structure of Amino Acids

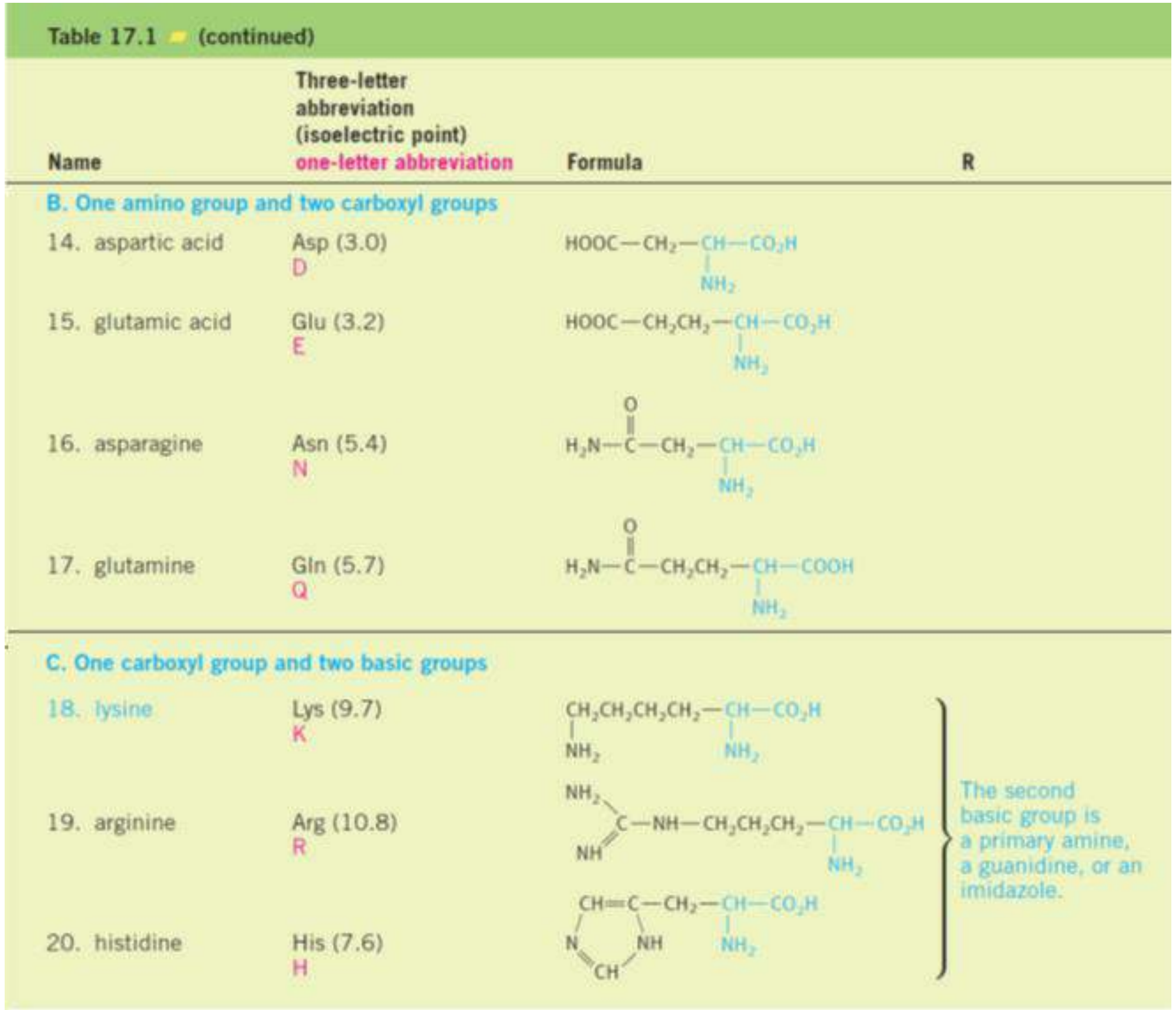


Table 17.1 (continued)

Name	Three-letter abbreviation (isoelectric point) one-letter abbreviation	Formula	R
B. One amino group and two carboxyl groups			
14. aspartic acid	Asp (3.0) D	$HOOC-CH_2-\underset{NH_2}{CH}-CO_2H$	
15. glutamic acid	Glu (3.2) E	$HOOC-CH_2CH_2-\underset{NH_2}{CH}-CO_2H$	
16. asparagine	Asn (5.4) N	$H_2N-\overset{O}{\overset{\Vert}{C}}-CH_2-\underset{NH_2}{CH}-CO_2H$	
17. glutamine	Gln (5.7) Q	$H_2N-\overset{O}{\overset{\Vert}{C}}-CH_2CH_2-\underset{NH_2}{CH}-COOH$	
C. One carboxyl group and two basic groups			
18. lysine	Lys (9.7) K	$\underset{NH_2}{CH_2}CH_2CH_2CH_2-\underset{NH_2}{CH}-CO_2H$	The second basic group is a primary amine, a guanidine, or an imidazole.
19. arginine	Arg (10.8) R	$\overset{NH_2}{\underset{NH}{C}}-NH-CH_2CH_2CH_2-\underset{NH_2}{CH}-CO_2H$	
20. histidine	His (7.6) H	$\underset{\underset{CH}{N \quad NH}}{CH{=}C}-CH_2-\underset{NH_2}{CH}-CO_2H$	

Sources, Classification and Structure of Amino Acids

- **The** **amino acids** are known by common names.
- Each also has a **three-letter abbreviation** based on this name, which is used when writing the formulas of peptides, and a one-letter abbreviation used to describe the amino acid sequence in a protein.

Sources, Classification and Structure of Amino Acids

- **The amino acids are classified into:**
  - **Essential amino acids**

    Eight amino cannot be synthesized by adult humans and therefore must be included in the diet in the form of proteins.

    e.g. Valine, Leucine, Isoleucine, Threonine, Methionine, Phenylalanine, Tryptophan, and Lysine.

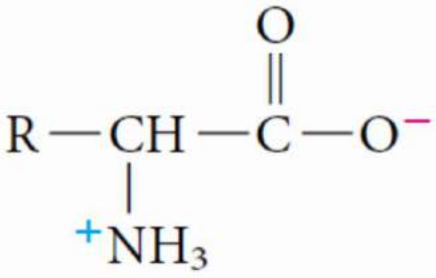
  - **Non-essential amino acids**

    Twelve amino acids can be synthesized in the body from other foods.

    e.g. Glycine, Alanine, Serine, Cysteine, Proline, Tyrosine, Aspartic acid, Glutamic acid, Asparagine, Glutamine, Arginine, and Histidine.

The Acid–Base Properties of Amino Acids

- The **carboxylic acid and amine functional groups** are *simultaneously* present in amino acids, and we might ask whether they are mutually compatible since one group is acidic and the other is basic.
- **Amino acids** with one amino group and one carboxyl group are better represented by a dipolar ion structure.



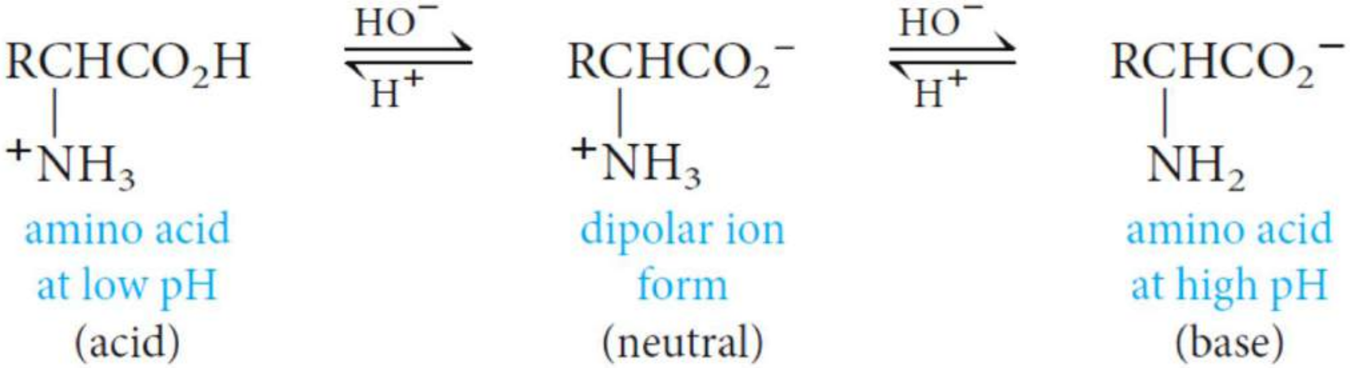
$$\mathrm{R{-}\underset{\underset{{}^{+}NH_3}{|}}{CH}{-}\overset{\overset{O}{\|}}{C}{-}O^{-}}$$

dipolar structure of an α-amino acid

The Acid–Base Properties of Amino Acids

- The **amino group** is protonated and present as an ammonium ion, whereas the carboxyl group has lost its proton and is present as a carboxylate anion.
- This **dipolar structure** is consistent with the salt-like properties of amino acids, which have rather high melting points and relatively low solubility in organic solvents.
- **Amino acids are *amphoteric*.**

  They can behave as acids and donate a proton to a strong base, or they can behave as bases and accept a proton from a strong acid.

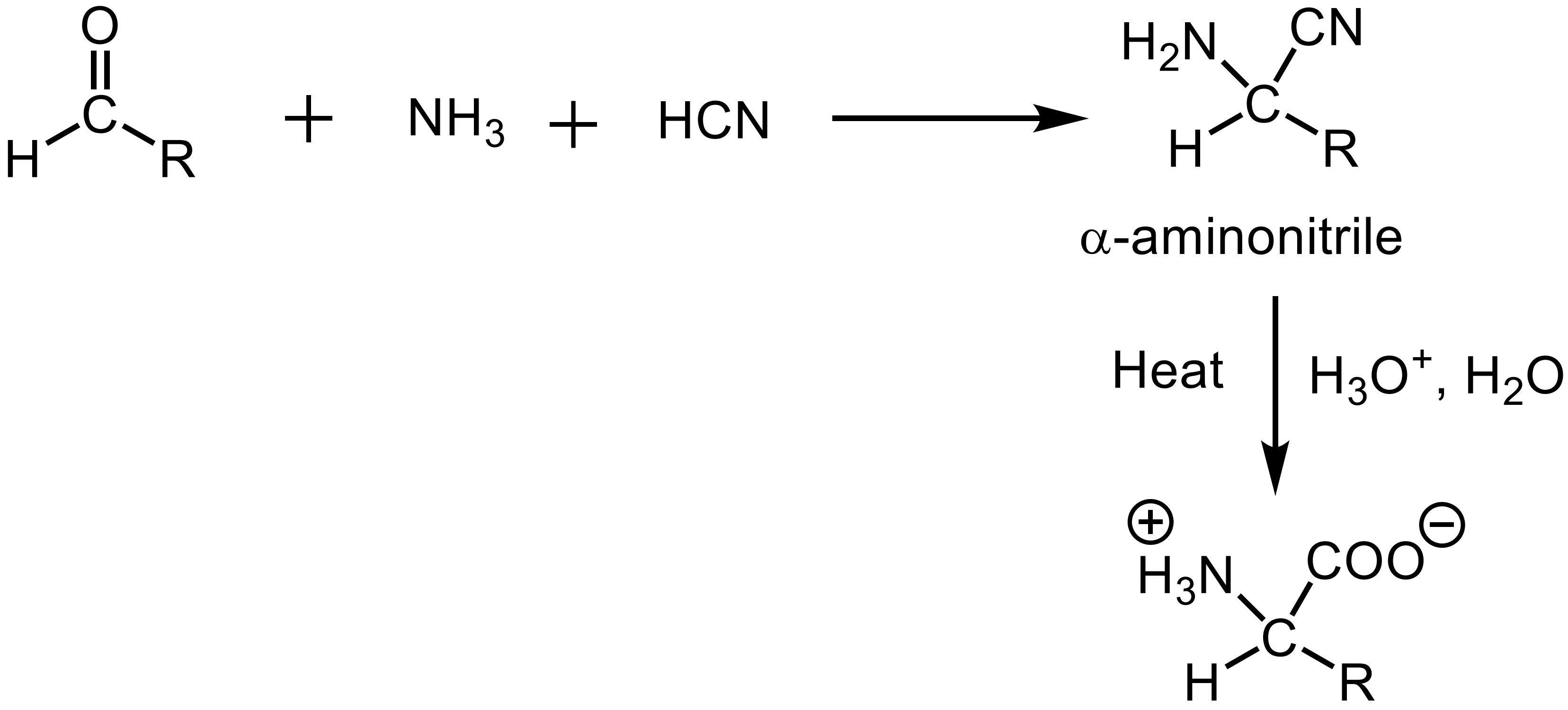


$$\underset{^{+}NH_3}{RCHCO_2H} \underset{H^+}{\overset{HO^-}{\rightleftharpoons}} \underset{^{+}NH_3}{RCHCO_2^-} \underset{H^+}{\overset{HO^-}{\rightleftharpoons}} \underset{NH_2}{RCHCO_2^-}$$

- The **isoelectric point (pl)**, the amino acid will be dipolar and have a net charge of zero.

Synthesis of Amino Acids

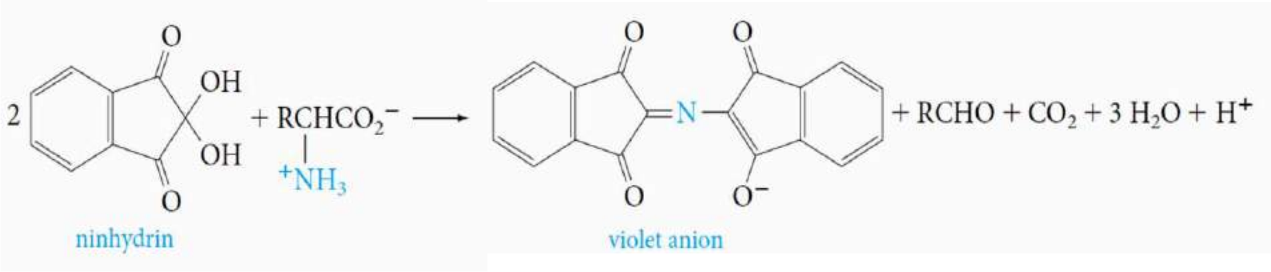
Strecker Synthesis: **Recall reductive amination and Cyanohydrin formation.**



Reactions of Amino Acids

1) The Ninhydrin Reaction

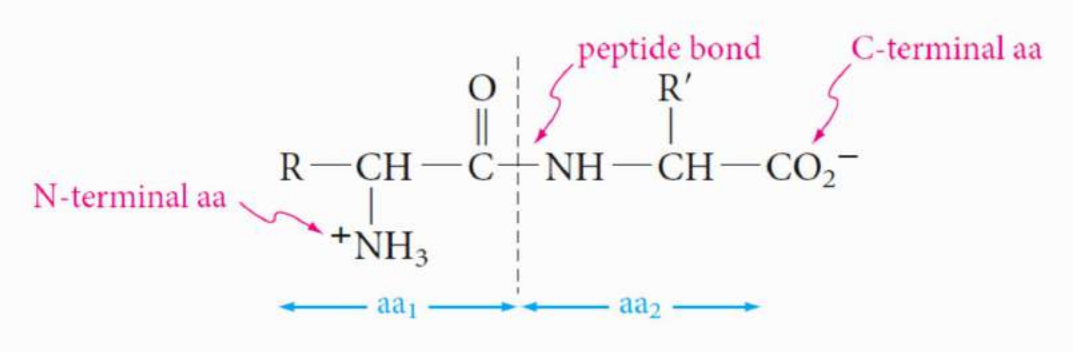
- **Ninhydrin** is a useful reagent for detecting amino acids and determining the concentrations of their solutions.
  - *Ninhydrin is the hydrate of a cyclic triketone, and when it reacts with an amino acid, a violet dye is produced.*



- Only the **nitrogen atom of the violet dye** comes from the amino acid (primary amino group); the rest of the amino acid is converted to an aldehyde and carbon dioxide.
- **Only proline**, which has a secondary amino group, reacts differently to give a **yellow dye**, but this, too, can be used for analysis.

2) Formation of an amide linkage
(The peptide bond: Proteins)

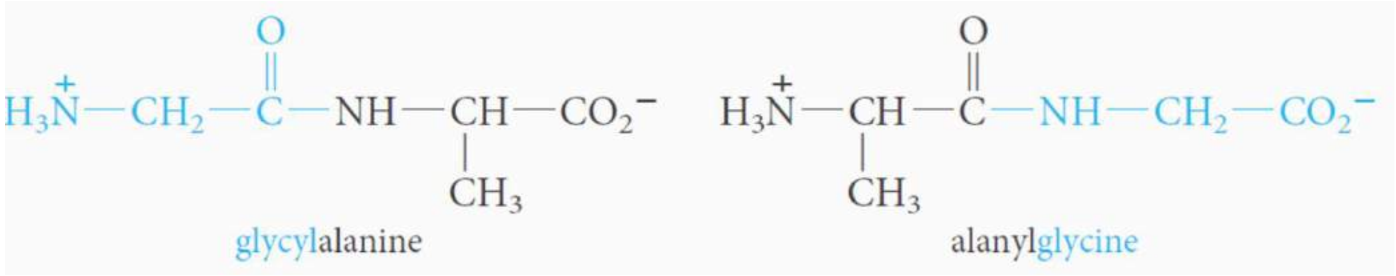
- **Amino acids** are linked in **peptides and proteins** by an amide bond (***peptide bond***) between the carboxyl group of one amino acid and the α-amino group of another amino acid.
- A molecule containing only *two* amino acids (the shorthand aa is used for amino acid) joined in this way is a **dipeptide**:



- By convention, the **peptide bond** is written with the amino acid having a free $^{+}NH_3$ group at the left and the amino acid with a free CO_2^- group at the right.
- These amino acids are called, respectively, the **N-terminal amino** acid and the **C-terminal** amino acid.

2) Formation of an amide linkage
(The peptide bond: Proteins)

- We often write the formulas for peptides in a kind of shorthand by simply linking the **three-letter abbreviations for each amino acid**, *starting with the N-terminal one at the left.*
- **For example;** glycylalanine is Gly—Ala, and alanylglycine is Ala—Gly.



$$H_3\overset{+}{N}-CH_2-\overset{\overset{O}{\|}}{C}-NH-\underset{\underset{CH_3}{|}}{CH}-CO_2^- \qquad H_3\overset{+}{N}-\underset{\underset{CH_3}{|}}{CH}-\overset{\overset{O}{\|}}{C}-NH-CH_2-CO_2^-$$

glycylalanine

alanylglycine

Structure of Proteins

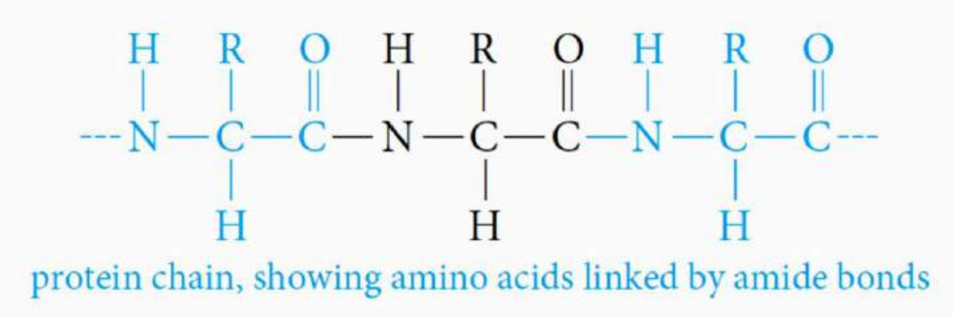
- **Proteins** are biopolymers composed of many amino acids connected to one another through amide (peptide) bonds.
- Some **proteins** are major components of structural tissue (muscle, skin, nails, and hair).
- Others transport molecules from one part of a living system to another.
- **The main features of peptide and protein structure.**
  - ***Primary structure;***

    How many amino acids are present and what their sequence is in the peptide or protein chain.
  - ***Secondary, tertiary, and quaternary structures;***

    Three-dimensional aspects of peptide and protein structure, usually referred to as their.

The Primary Structure of Proteins

- The **backbone of proteins** is a repeating sequence of one nitrogen and two carbon atoms.



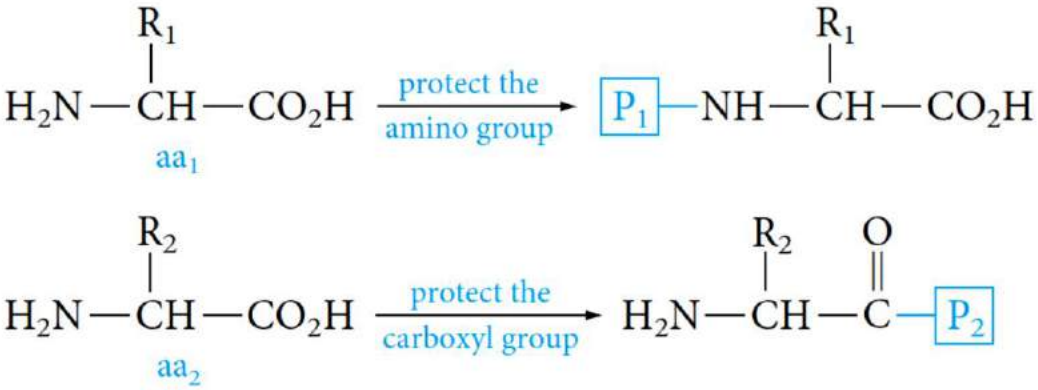
protein chain, showing amino acids linked by amide bonds

- **Peptides and proteins** can be hydrolyzed to their amino acid components by heating with 6 M HCl.
- An instrument called an **amino acid analyzer** is used to determine the amino acids mixture.

Peptide Synthesis

- Many methods have been developed to link amino acids in a controlled manner.

  To link the carboxyl group of one amino acid to the amino group of a second amino acid, we must first prepare each compound by protecting the amino group of the first and the carboxyl group of the second.

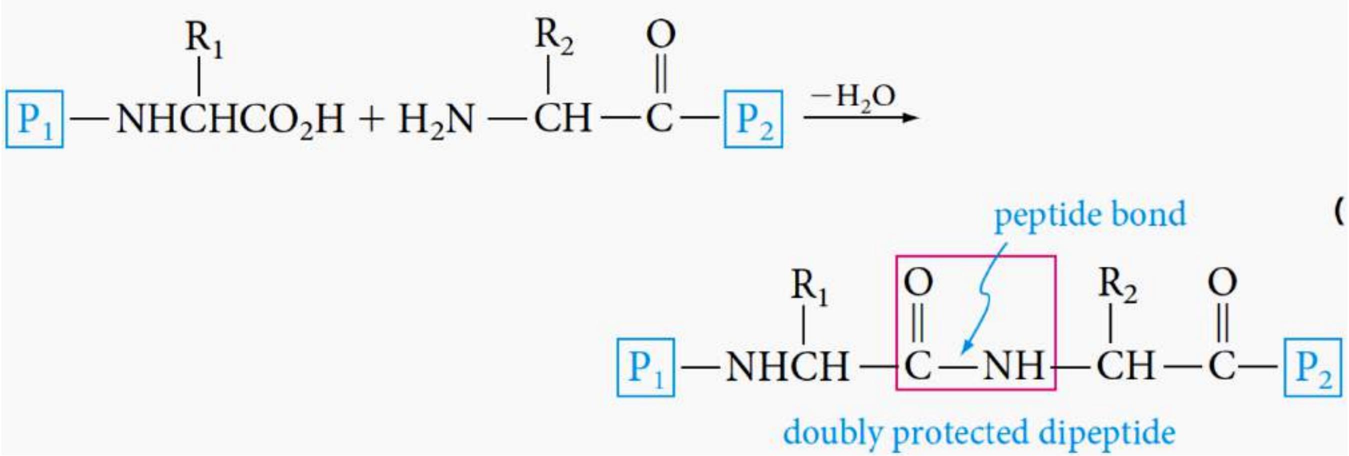


$$H_2N-CH(R_1)-CO_2H \xrightarrow[\text{amino group}]{\text{protect the}} \boxed{P_1}-NH-CH(R_1)-CO_2H$$

$$H_2N-CH(R_2)-CO_2H \xrightarrow[\text{carboxyl group}]{\text{protect the}} H_2N-CH(R_2)-C(=O)-\boxed{P_2}$$

Peptide Synthesis

- In this way, we can control the linking of the two amino acids so that the carboxyl group of aa_1 combines with the amino group of aa_2.



Fundamentals of Organic Chemistry

CHEM 109

For Students of Health Colleges

Credit hrs.: (2+1)

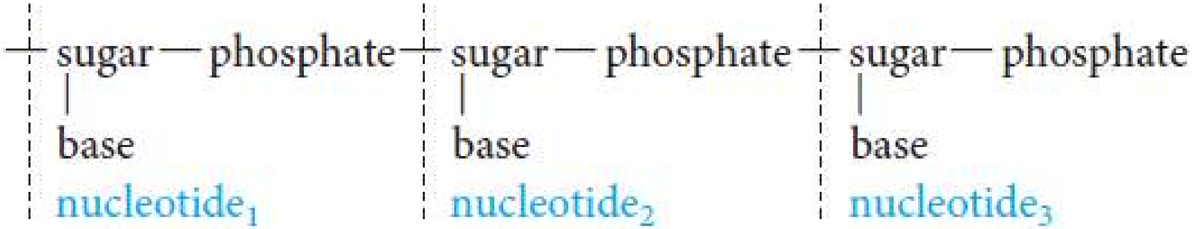
King Saud University

College of Science, Chemistry Department

CHAPTER 10. NUCLEIC ACID

The General Structure of Nucleic Acids

- The overall structure of the **nucleic acid** itself is a macromolecule with a backbone of sugar molecules connected by phosphate links and with a base attached to each sugar unit.



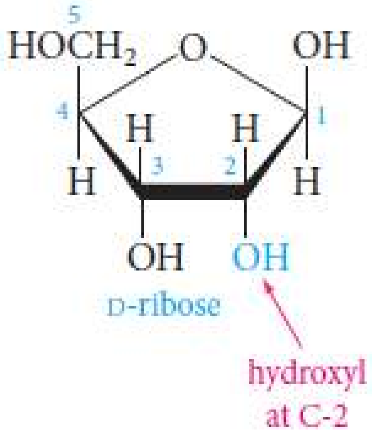
schematic structure of a nucleic acid

- **Nucleic acids** are high polymers consisting of a ***pentose sugar containing a heterocyclic base and a phosphate moiety***.

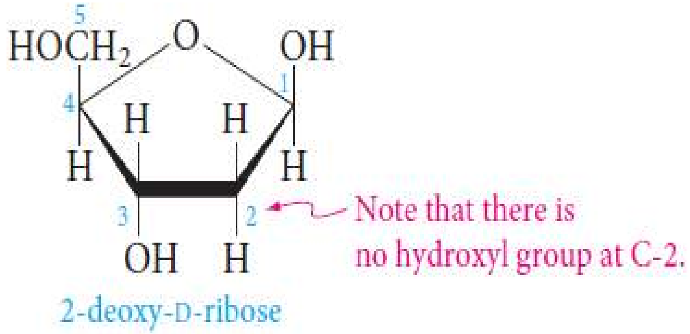
The General Structure of Nucleic Acids

Pentose Sugar

- **Ribonucleic acid (RNA)** contains the pentose **ribose**.
- **Deoxyribonucleic acid (DNA)** contains the pentose **deoxyribose**.



D-ribose

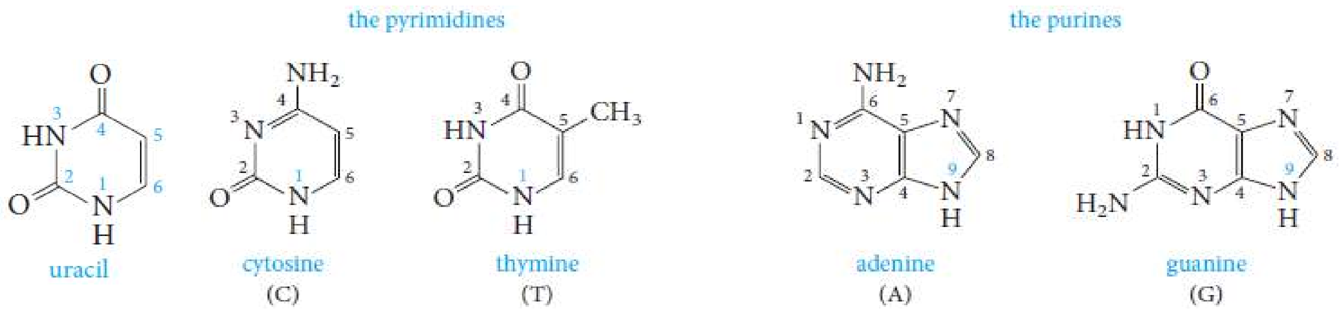


2-deoxy-D-ribose

The General Structure of Nucleic Acids

Heterocyclic Base

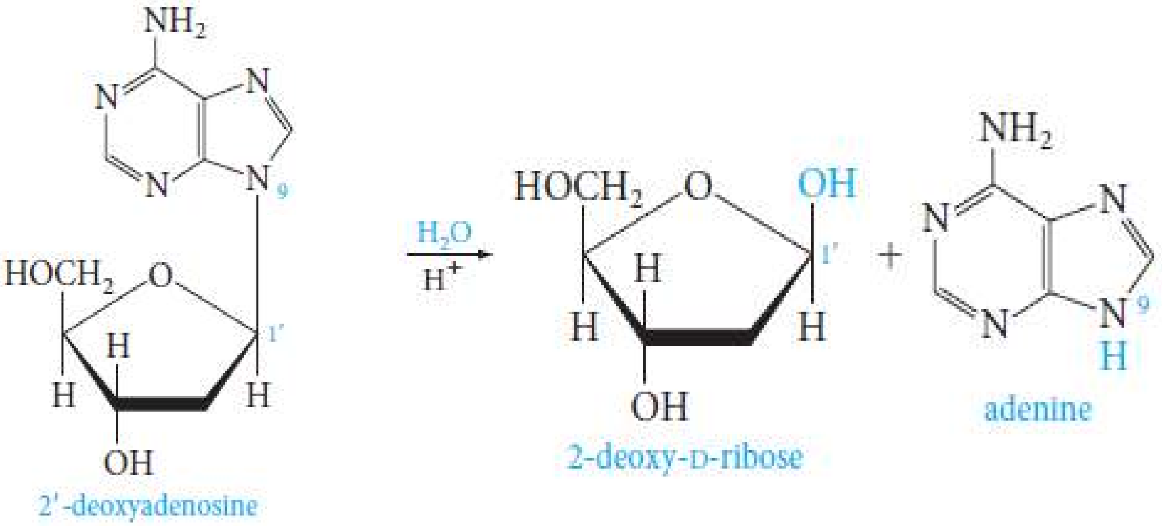
- The sugars also contain a **pyrimidine or purine base** present on the 1-carbon replacing the hydroxyl group with a base.



- Both DNA and RNA contain **adenine and guanine.**
- **Uracil** is found only in RNA.
- **Thymine or methyluracil** is found only in DNA.

The General Structure of Nucleic Acids

- The **combination of the pentose sugar and** a purine or pyrimidine **base** is called a **nucleoside**.



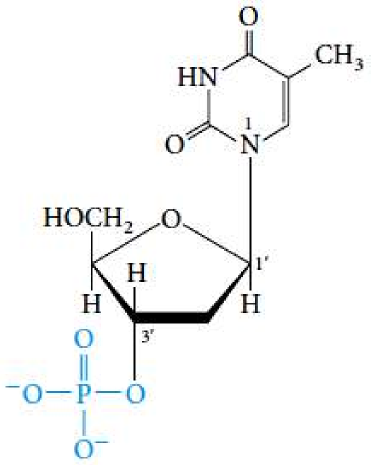
The General Structure of Nucleic Acids

- **Nucleotides** are **phosphate esters of nucleosides**.

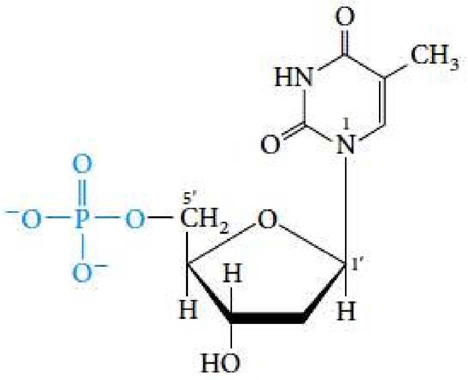
  A hydroxyl group in the sugar part of a nucleoside is esterified with phosphoric acid.

  In DNA nucleotides, either the 5’ or the 3’ hydroxyl group of 2-deoxy-d-ribose is esterified.

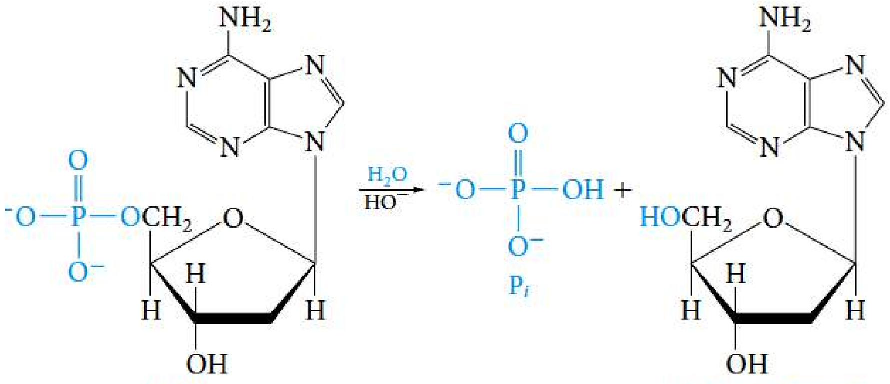
- **Nucleotides** can be **hydrolyzed** by aqueous base (or by enzymes) to **nucleosides and phosphoric acid**.



2′-deoxythymidine
3′-monophosphate



2′-deoxythymidine
5′-monophosphate



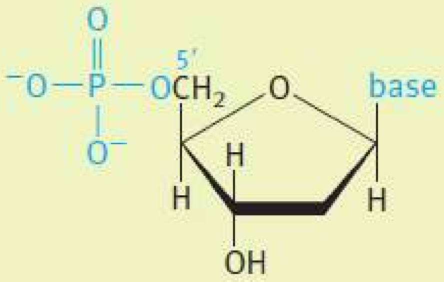
dAMP
(nucleotide)

2′-deoxyadenosine
(nucleoside)

The General Structure of Nucleic Acids

- **Nucleotides** are named as the 3’- or 5’-monophosphate esters of a nucleoside.
- In these abbreviations, letter d stands for 2-deoxy-d-ribose, the next letter refers to the heterocyclic base, and MP stands for monophosphate.

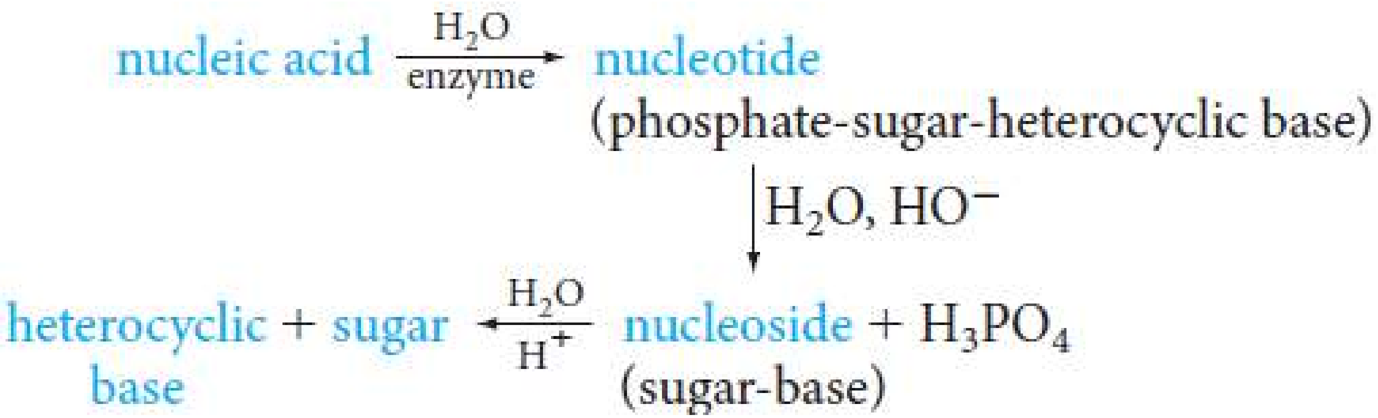
Table 18.1 The Common 2-Deoxyribonucleotides



Base	Monophosphate name	Abbreviation
cytosine (C)	2′-deoxycytidine 5′-monophosphate	dCMP
thymine (T)	2′-deoxythymidine 5′-monophosphate	dTMP
adenine (A)	2′-deoxyadenosine 5′-monophosphate	dAMP
guanine (G)	2′-deoxyguanosine 5′-monophosphate	dGMP

The General Structure of Nucleic Acids

- Hydrolysis of nucleic acids gives **nucleotides**, which are the building blocks of nucleic acids, just as amino acids are the building blocks of proteins.



- **Nucleic acids** are polynucleotides attached by the phosphate moieties through the 3′ and 5′ sites on the pentose.
- The **name nucleic acid** is derived from the fact that they are acidic, containing a phosphoric acid moiety, and are found in the nuclei of cells.

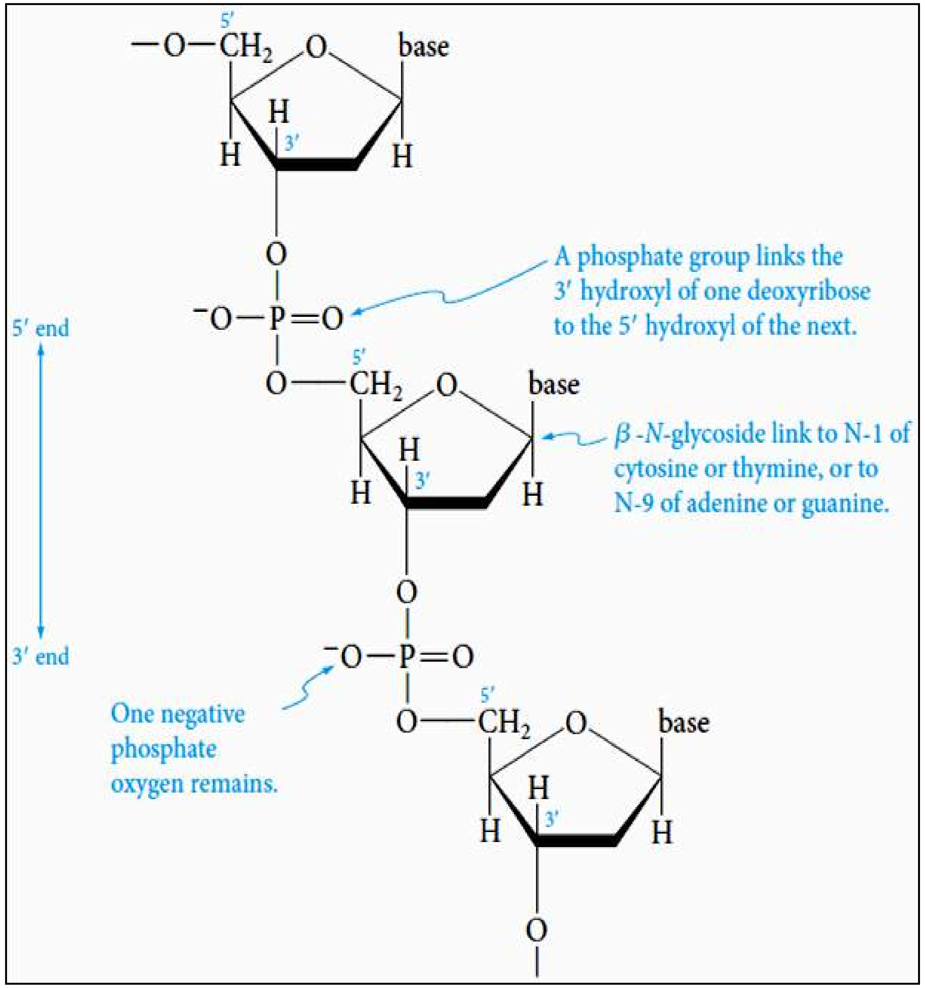
The General Structure of Nucleic Acids

- **Nucleoproteins**, which are conjugated proteins, may be separated into nucleic acids and proteins in aqueous sodium chloride.
- The name "**nuclein**" which was coined by Miescher in 1869 to describe products isolated from nuclei in pus, was later changed to nucleic acid.
- **Pure nucleic acid** was isolated by Levene in the early 1900s.
- He showed that either D-ribose or D-deoxyribose was present in what are now known as **ribonucleic acid (RNA) and deoxyribonucleic acid (DNA).**
- **There are two major types of nucleic acids:**
  - **Deoxyribonucleic acid (DNA) and**
  - **Ribonucleic acid (RNA).**

Deoxyribonucleic Acid (DNA)

The Primary Structure of Deoxyribonucleic Acid (DNA)

p-5′-A-3′-p-5′-A-3′-p-5′-A-3′



A phosphate group links the 3′ hydroxyl of one deoxyribose to the 5′ hydroxyl of the next.

β-N-glycoside link to N-1 of cytosine or thymine, or to N-9 of adenine or guanine.

One negative phosphate oxygen remains.

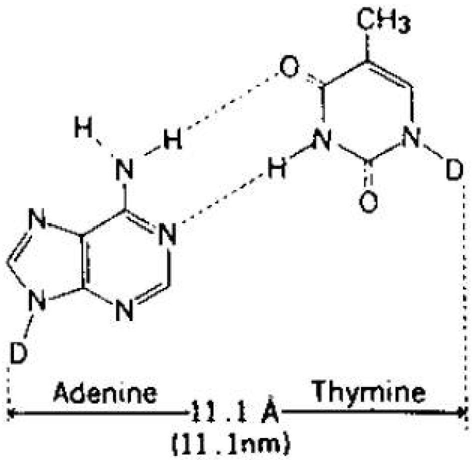
A segment of a DNA chain

Deoxyribonucleic Acid (DNA)

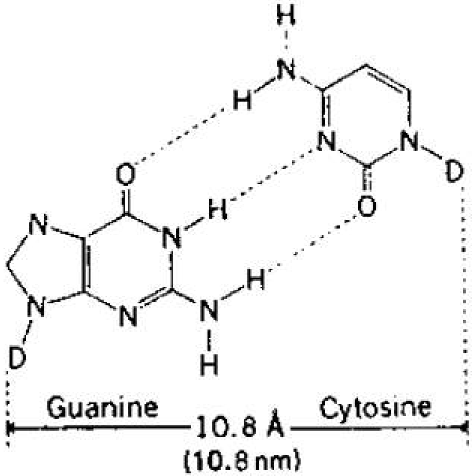
- In deoxyribonucleic acid (DNA), **2-deoxy-d-ribose** and **phosphate units** alternate in the backbone.
- The 3’ hydroxyl of one ribose unit is linked to the 5’ hydroxyl of the next ribose unit by a **phosphodiester bond**.
- The **heterocyclic base** is connected to the anomeric carbon of each deoxyribose unit by a β-*N*-glycosidic bond.
- In DNA, there are **no remaining hydroxyl groups** on any deoxyribose unit.
- Each phosphate, however, still has one acidic proton that is usually ionized **at pH 7**, leaving a negatively charged oxygen.
- If this proton were present, the substance would be an acid; hence the name **nucleic acid**.
- A complete description of any particular DNA molecule, which may contain thousands or even millions of nucleotide units, would have to include the exact sequence of heterocyclic bases (**A, C, G, and T**) along the chain.

Deoxyribonucleic Acid (DNA)

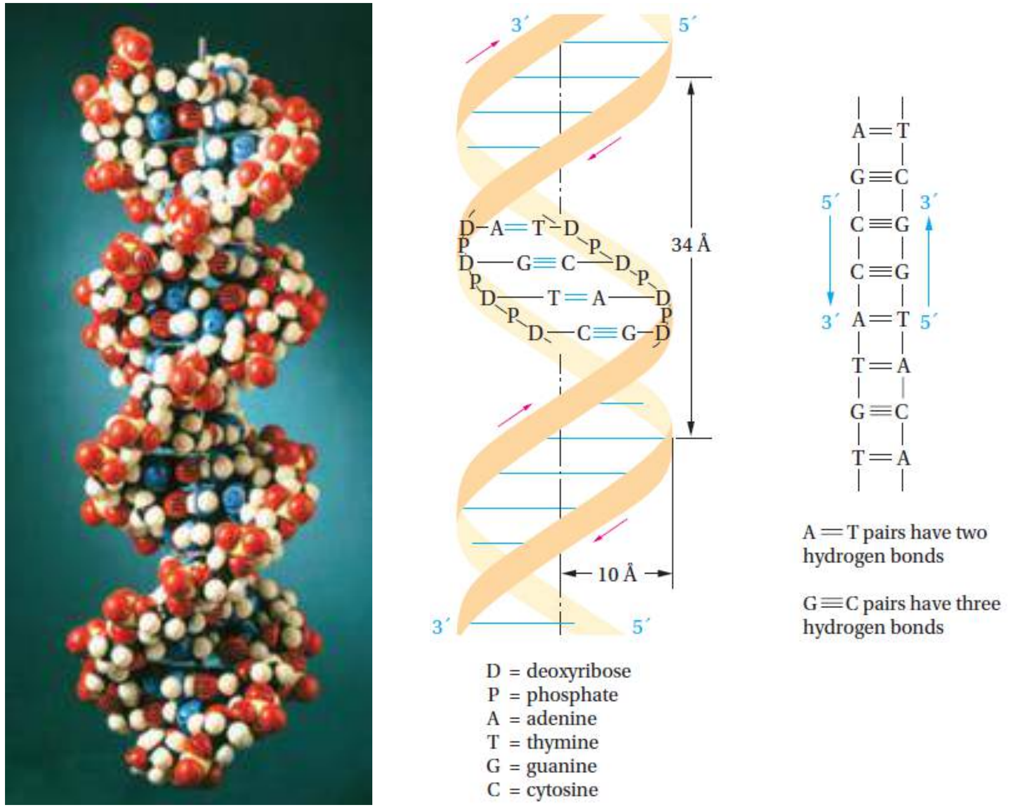
Secondary DNA Structure; the Double Helix



Two hydrogen bonds



Three hydrogen bonds



Model and schematic representations of the DNA double helix.

The space-filling model at the left shows the base pairs in the helix interior, in planes perpendicular to the main helical axis. The center drawing shows the structure more schematically, including the dimensions of the double helix. At the far right is a schematic method for showing base pairing in the two strands.

Deoxyribonucleic Acid (DNA)

- In **1953**, when **Watson and Crick**, working together in Cambridge, England, proposed the **double helix model for DNA**.
- They received simultaneous supporting x-ray data for their proposal from Rosalind Franklin and Maurice Wilkins in London.

- **The important features of their model follow:**

1. DNA consists of **two helical polynucleotide chains coiled** around a common axis.
2. The **helices are right-handed**, and the two strands run in opposite directions with regard to their 3' and 5' ends.
3. The **purine and pyrimidine bases lie *inside* the helix**, in planes perpendicular to the helical axis; the **deoxyribose and phosphate groups form the outside** of the helix.

Deoxyribonucleic Acid (DNA)

4. The two chains are held together **by;**

- *Purine–pyrimidine base pairs* connected by hydrogen bonds.
- *Adenine is always paired with thymine, and*
- *Guanine is always paired with cytosine.*

5. The **diameter of the helix** is 20 A.

Adjacent base pairs are separated by 3.4 A and oriented through a helical rotation of 36°.

There are therefore 10 base pairs for every turn of the helix (360°), and the structure repeats every 34 A.

6. There is no restriction on the sequence of bases along a polynucleotide chain. The exact sequence carries the genetic information.

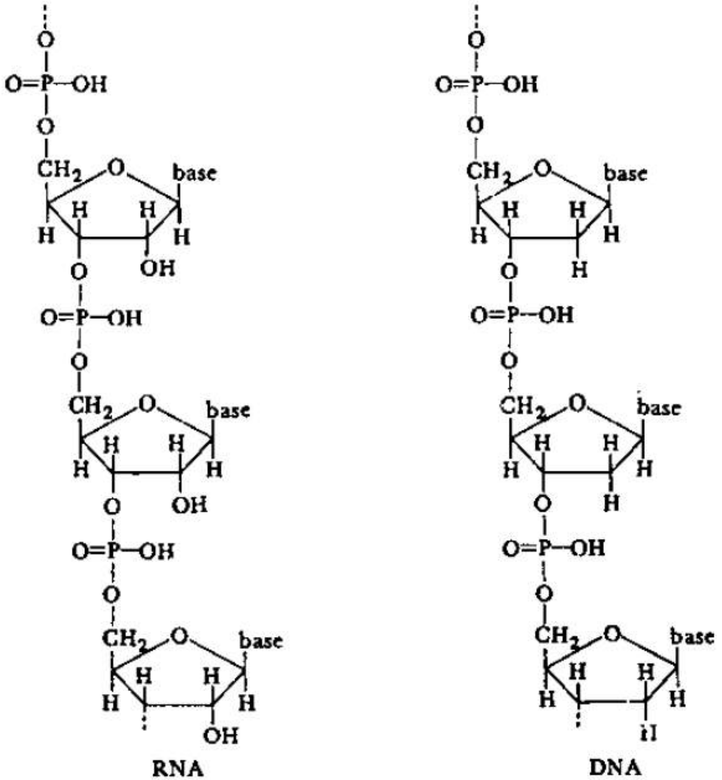
Ribonucleic Acid (RNA)

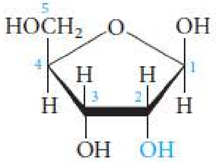
- **Ribonucleic acids (RNA) differ from DNA in three important ways:**

  (1) The sugar is D-ribose;

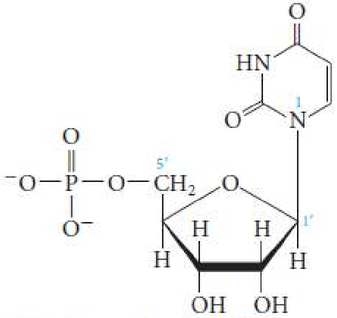
  (2) Uracil replaces thymine as one of the four heterocyclic bases; and

  (3) Most RNA molecules are single stranded, although helical regions may be present by looping of the chain back on itself.




D-ribose


uracil


uridine-5′-monophosphate (UMP)

Ribonucleic Acid (RNA)

- The **transcription product of DNA is always single-stranded RNA**.
- The **single strand** generally assumes a right-handed helical conformation mainly caused by base-stacking interactions also present in the DNA.
- The **order of interaction** is purine-purine >> purine-pyrimidine > pyrimidine-pyrimidine.
- The **purine–purine interaction** is so strong that a pyrimidine separating two purines is often displaced from the stacking order to allow the interaction between the two purines to occur.
- **Base paring** is similar to that of the DNA except that uracil generally replaces thymine.

Ribonucleic Acid (RNA)

- For coupled RNA the two strands are antiparallel as in DNA.
- Where complementary sequences are present, the predominant double-stranded structure is an A form right-handed double helix.
- Many RNAs are **combinations of complementary two-stranded helices**, single-stranded segments, as well as other complex structures.

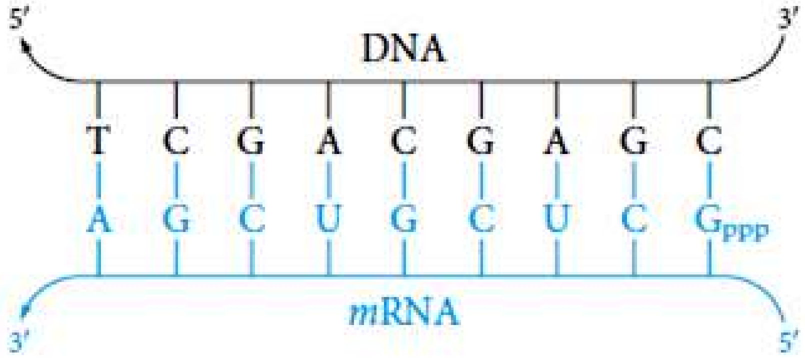
Ribonucleic Acid (RNA)

Cells contain three major types of RNA.

1) Messenger RNA (mRNA)

- **mRNA** varies greatly in size from about 75 units to over 3000 nucleotide units giving a molecular weight of 25,000 to one million.
- It is present at a percentage of about 5% of the total RNA in a cell.
- **mRNA** is involved in transcription of the genetic code and is the template for protein synthesis.

- There is a specific **mRNA** for every protein synthesized by the cell.
- The **base sequence** of mRNA is complementary to the base sequence in a single strand of DNA, with U replacing T as the complement of A.



Ribonucleic Acid (RNA)

2) Transfer RNA (tRNA)

- **tRNA** has about 73–94 nucleotides with a corresponding molecular weight range of 23,000–30,000.
- It is present in the cell at a level of about 15%.
- **tRNA** carries amino acids in an activated form to the ribosome for peptide bond formation, in a sequence determined by the mRNA template.
- Each **tRNA** has a three-base sequence, C-C-A, at the 3’ hydroxyl end, where the amino acid is attached as an ester.

Ribonucleic Acid (RNA)

3) Ribosomal RNA (rRNA)

- It comprises about 80% of the total cellular RNA (tRNA = 15%, mRNA = 5%) and is the main component of the ribosomes.
- Its molecular weight is large, and each molecule may contain several thousand nucleotide units.
- **rRNA** is a part of the protein synthesizing machinery of cells, ribosomes.