
Chemistry 211: Organic Chemistry 1

Syllabus

Kinetics and Energetics of Reactions; Hydrocarbons, Multiple Bonds; Aromatic Compounds; Chemistry of C-Halogens Bond; Chemistry of Hydroxyl group; Ethers, Thiols and Thioethers .

Chapter 1: Kinetics and Energetics of Reactions

1.1 Reaction

A chemical reaction takes place when a molecule (starting material or a reactant) is transformed into another molecule (product) under a specified condition such as temperature, pressure, concentration, state of the reacting species etc. When a reaction takes place, bonds are broken and new ones formed which indicates that there is a need for energy input or output for a reaction to occur.

A reaction may be a one-step (no intermediate step) or a multi-step process (involves formation of intermediates) and is affected by factors such as: physical state of participating species, steric hindrance, reaction conditions, type of reactants (electron rich or deficient) etc. The step involved in chemical reactions is called the **reaction mechanism** for that process. The reaction mechanism describes how a chemical change occurs and is described as a theoretical construct or model for a chemical change. The mechanism can then be proven experimentally to establish the mechanism. Each step of a reaction mechanism is called an **elementary step**

The **elementary step** is a process whereby the reactant is converted to the product by passing through one transition stage with no intermediate stage. The step always occurs by simple nuclear motions that occurs simultaneously with no intermediate stage and is characterized by forward and reverse microscopic rate constants.

1.2 Types of Reaction

There are four major types of reactions:

(1) **Displacement**: Involves removal of an atom or group of atoms from the central atom (usually carbon). The displacement could be electrophilic (E): $Ph + NO_2^+ \rightarrow Ph\text{-}NO_2 + H^+$,
Nucleophilic (N) e.g. $NC^- + R\text{-}Cl \rightarrow NC\text{-}R + Cl^-$ or
Radical mechanism (R) (halogenations of alkanes)
Usually the displaced atom is hydrogen, group of atoms or any other atom

(2) **Addition:** Adding an atom, molecule or ion to another molecule. It could be initiated by electrophilic, nucleophilic or radical mechanism. The attack is usually on C-C multiple bonds (E, R) e.g. $\mathbf{H_2C{=}CH_2 + HF} \rightarrow H_3C\text{-}CH_2\text{-}F$
or by nucleophilic attack on C-O bonds

(3) **Elimination:** Opposite reaction of addition reaction. Involves loss of hydrogen and a loss of another atom or group of atoms to from an unsaturated bond

$CH_3CH_2F \rightarrow CH_2{=}CH_2 + HF$

(4) **Rearrangement:** this involves rearrangement of the skeleton of a compound (carbon compounds). It may sometimes involve rearrangement through an intermediate in a chemical reaction. The rearrangement process may involve a cation, anion, radicals, carbonium ions or other electron deficient species. Rearrangement is often accompanied by addition or elimination reaction.

$$\mathbf{Me_2C(OH)\text{-}C(Me_2)OH \xrightarrow{H^+} Me_3C\text{-}C{=}O(Me)}$$

1.3. Factors that Affects a chemical Reaction

- There are many factors that affect a chemical reaction: type of bonds (single, multiple, conjugated, polarized etc)

- Others include availability of electrons (electron density), resonance, steric effect, reagent type (electron donating or withdrawing, nucleophilic, electrophilic, carbonium etc)

Chapter 2 Energetics, Kinetics and Mechanism of a Chemical Reaction

2.1 Chemical Reaction and Energy Change

- A chemical reaction involves converting a starting material (reactants) to a product: A↔ B
- There is always an equilibrium between the reactant and the product
- The direction of a reaction depends on the stability of the reactant versus the product at equilibrium
- Whichever of the two is the more stable determines the direction of the reaction
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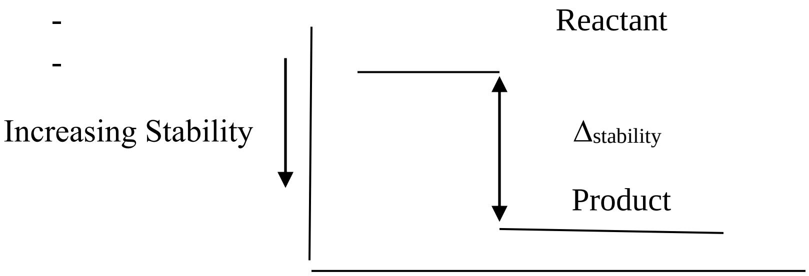


- Conversion of reactants to products is always accompanied by an energy change which can be measured simply as the heat of reaction, ΔH (enthalpy, difference between bond energies of the product and the reactants)
- However, ΔH is not a sufficient measure of the difference in stability of the reactant vs. product
- Other factors like the entropy ΔS contributes to the measure of stability of the reactant vs. product (second law of thermodynamics i.e. every ordered system always wants to be disordered)
- The most stable condition tends to have the minimum energy or enthalpy and maximum entropy
- Hence change in energy in going from a reactant to a product is expressed by the equation:

$$\Delta G\ \Delta H = \Delta H - T\Delta S \text{ (T= absolute temperature)}$$

- ΔG is also related to the equilibrium constant (K) by the equation :

$$-\Delta G = 2.303RT\log K$$

- As the value of $-\Delta G$ becomes larger, value of K also becomes larger and the formation of the product is more favored.

2.2 Entropy of a Chemical Reaction

- Consider and equilibrium reaction: $\mathbf{A \leftrightarrow B + C}$, the entropy of this reaction can be explained in terms of (i) the number of molecules or new substances formed (ii) the total # of ways in which its total energy can be distributed among all possible molecules or substances arising because of the reaction and (iii) the number of ways in which each molecules quantum energy will be shared between its translational, rotational, vibrational energies. Oftentimes, it is the translational energy that will take the largest share of each molecule's quantum energy.

- For example, when calcium carbonate is heated, it decomposes to carbon dioxide and water

$$CaCO_{3s} \rightarrow CO_{2g} + H_2O_g$$

- There is an increase in the number of molecules (2 on product side vs. one on reactant side), which indicates an increase in translational degrees of freedom: results into increase in entropy.
- The term $-T\Delta S$ in the equation $\Delta G\ \Delta H = \Delta H - T\Delta S$ becomes larger,
- If $-T\Delta S > \Delta H_{\text{endothermic or exothermic}}$, then ΔG will be largely negative which favors formation of the products
- The converse is also very true: if the reaction is reversed, there will be a decrease in the number of molecules form (decrease in degrees of translational energy, e.g. cyclisation reactions),
- hence, decrease in the value of entropy and the term $-T\Delta S < \Delta H$ may be sufficiently small such that

- ΔG may be largely positive, which then favors formation of the reactants
- However, if ΔH is sufficiently negative (exothermic), the reaction may favor formation of the product.

2.3 Kinetics of a Chemical Reaction

- The value of ΔG only tells us how far a reaction can go (in the direction of the product or reactant)

- it will not tell us how fast a reaction can go in forming a product

- For example, cellulose can be oxidized thus: $(C_6H_{10}O_5)_n + 6nO_2 \leftrightarrow 6nCO_2 + 5nH_2O$

- ΔG is largely negative, hence the reaction is totally converted to carbon dioxide and water

- Paper is also cellulose but it can stay in room full of oxygen for a very long time before it starts to be oxidized

- the first reaction is fast while the second reaction (paper oxidation) is very slow even thou both has a very large negative value of ΔG

- In any reaction, there is an energy barrier that needs to be surmounted in converting a reactant to a product as shown in the energy profile below. This energy barrier is called the activation energy

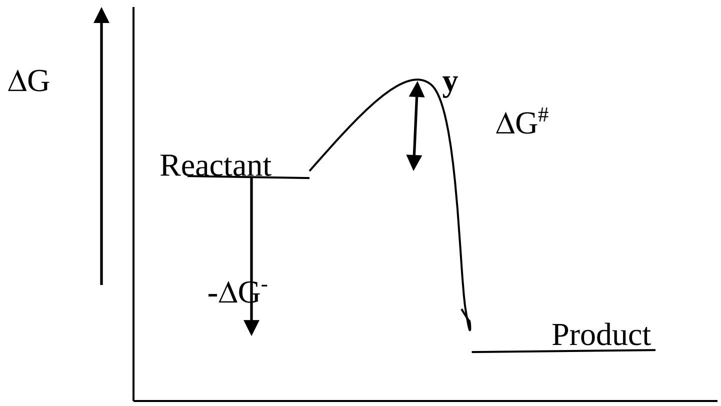


Figure 2.1 Energy Profile

2.4 Reaction Rate and free Energy of Activation

- The position **y** in the energy profile shown above is the least stable position in the process of forming the product

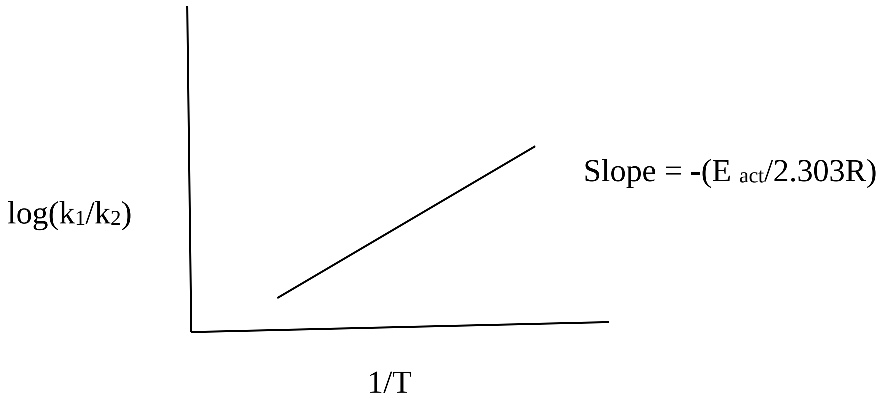
- This position is called the **activated complex** or **activated transitional state (AC)**

- The AC is not a stable state, hence it cannot be isolated or detected but it is a state through which a reactant has to pass through (transient) to form a product

- For example, in the hydrolysis of bromomethane, new C-OH bond is formed simultaneously when the existing C-Br is broken in the transitional state (AC state).

$$HO^- + CH_3\text{-}Br \rightarrow [\, HO \ldots . C(H_3) \ldots .. Br]^{\#} \rightarrow HO\text{-}CH_3 + Br^-$$

- The height of the barrier **y** in figure 2.1 is called the activation energy $\Delta E^{\#}$ (E_{act})
- The higher the value of $\Delta G^{\#}$ the slower the reaction will be
- $\Delta G^{\#} = \Delta H^{\#} - T\Delta S^{\#}$ where $\Delta H^{\#}$ is the enthalpy of activation (energy needed to stretch and break a bond in the transition state) and $\Delta S^{\#}$ the entropy of activation
- The rate of reaction (formation of product), $k = Ae^{-E_{act}/RT}$ (Arrhenius equation)
- $\text{Log}_{10}\, k = (-E_{act}/2.303RT) + \log_{10}A$
- R is the gas constant = 8.32 J/mol degree and A is a reaction constant (depends on the number of successive collisions or related to the entropy $\Delta S^{\#}$)
- Plot log k vs. 1/T, the slope will be $-E_{act}/R$ and the intercept will be log A
- We may also calculate E_{act} by performing the reaction at two different temperatures and obtain their rates of reaction, hence: $\mathbf{\log(k_1/k_2) = -(E_{act}/2.303R)[1/T_1 - 1/T_2]}$



2.5 Kinetics and the Rate Limiting Step

- Rate of a reaction is determined by measuring how fast reactants disappear or a product appear at a particular temperature and time and relate it to the concentration of one, or all of the reactants or products. This can be done by calculation or by using graphs

- There are various methods that can be used to do this measurement. The method could be by **direct determination**: drawing aliquots at specific times and do titrimetric determinations or by **indirect determinations**: observing specific changes using conductimetric, coulometric, colorimetric, spectrometric, spectroscopy etc. The data obtained by these methods can then be matched with different concentrations either by calculation or graphically until a reasonable fit is found (suggest the rate law or equation).

- For example, in the reaction: **$CH_3Br + {}^{-}OH \rightarrow CH_3OH + Br^{-}$** (1)

- The rate equation is found to be: **Rate = $-\frac{d[CH_3Br]}{dt} = k[CH_3Br][{}^{-}OH]$** (2)
-
- The rate equation can also be expressed as: **$[CH_3Br] = [CH_3Br]_0 e^{-kt}$ (Arrhenius)** (3)

  $$\mathrm{In}\frac{[CH_3Br]}{[CH_3Br]_0} = -kt \quad (4)$$

  Where $[CH_3Br]_0$ is the initial concentration and $[CH_3Br]$ the final concentration after time t(sec). A plot of the Arrhenius expression (eqn. 4) vs. time gives a straight line and the **slope** is **-k**

- **Kinetic order of a reaction (KO):** the overall kinetic order of a reaction, n, is the sum of all the exponent of all concentrations appearing on the right side (product side) of a rate equation. In the rate equation shown above, the overall KO is second order
- KO may be evaluated in respect to the concentration of any of the term on the right side of a rate equation: in the equation shown above, rate is first order wrt $[CH_3Br]$ or $[{}^{-}OH]$
- There are more complex reactions with higher kinetic orders: such as second, third etc
- **Assignment**

  The following data were obtained for the reaction: $I^{-}_{aq} + OCI^{-}_{aq} \rightarrow IO^{-} + CI^{-}_{aq}$

	$[I^-]$ mol/dm^3	$[OCI^-]$ mol/dm^3	Initial Rate mol/dm^2/s
I	1.8×10^{-3}	2.1×10^{-3}	5.4×10^{-5}
II	3.6×10^{-3}	2.1×10^{-3}	10.8×10^{-5}
III	1.8×10^{-3}	6.3×10^{-3}	4.9×10^{-4}

(i)What is the order of the reaction with respect to $[I^-]$ and $[OCI^-]$

(ii) Calculate the rate constant using the results of experiment

(iii) What is the rate law or rate equation for this reaction?

Answer: (a) reaction rate is the velocity with which reactants are used up (disappearance) to form products or the velocity at which products are formed while reaction mechanism is the pathway by which reactants are converted into products

(bi) Rate = $k[I^-][OCI^-]$ Using experiments I and II

$$5.4 \times 10^{-5} = k[1.8 \times 10^{-3}]^x[2.1\times10^{-3}]^y \quad (1)$$

$$10.8 \times 10^{-5} = k[3.1 \times 10^{-3}]^x[2.1\times10^{-3}]^y \quad \text{(2) Divide equation (2) by (1)}$$

$$10.8 \times 10^{-5}/(5.4\times10^{-5}) = k/k\,(3.1\times10^{-3}/1.8 \times 10^{-3})^x(2.1\times10^{-3}/2.1\times10^{-3})^y$$

$2 = 2^x$ hence x = 1 and therefore, the order wrt. I^- is 1

Using equation I and III

$5.4 \times 10^{-5} = k[1.8 \times 10^{-3}]^x[2.1\text{x}10^{-3}]^y$ (1)

$4.9 \times 10^{-4} = k[1.8 \times 10^{-3}]^x[6.3\text{x}10^{-2}]^y$ (2). Divide equation 2 by 1

$4.9 \times 10^{-4}/5.4 \times 10^{-5}5.4 \times 10^{-5} = k(1.8 \text{ x}10^{-3}/1.8\text{x}10^{3})^x(6.3 \times 10^{-2}/2.1 \times 10^{-3})^y$

$3^2 = 3^y$ and y = 2, therefore, the order wrt. $[OCI^-]$ is 2

b (ii) $k = Rate/[I^-]\,[OCI^-] = 10.8 \text{ x}10^{-5}/\,[1.8 \times 10^{-3}]^1[2.1\text{x}10^{-3}]^2 = 68.03\ dm^6/mol^2s$

b(iii) $Rate = 68.03[I^-]\,[OCI^-]^2$

- **Rate Limiting step:** In general, organic reactions are multi-steps and each step occur at different rates. The slowest step in converting the reactant to the product determines the rate of the reaction and is called the **rate limiting step.**

2.6 Kinetic and Thermodynamic Control

- Sometimes a reaction may produce 2 or more products which imply that there are alternative routes available for the reactants to react. For example, nitration of benzaldehyde may produce either ortho, meta or para nitrobenzaldehydes. The proportion of each product in the mixture depends on its rate of formation. The fastest rate produces the largest product: this called **kinetic control.**

- Not all reactions are controlled by Kinetic process. Sometimes, some reactions are reversible or products are interconvertible. In this case, the product mixture may be dictated by stabilities of each product and not by how fast the alternative reactions occur. This reaction is said to be **equilibrium or thermodynamic** controlled. For example, Friedel-Crafts alkylation of methyl-benzene with benzyl chloride ($GaBr_3$ as catalyst) gave a higher yield of m-Toluene (46%) at longer time of reaction than at shorter time of reaction compared to the o- and p- isomers. This may be due to the fact that the isomers can isomerizes or are interconvertible. The proportions of the product in the final product mixture is thermodynamically controlled rather than been kinetically controlled.

Chapter 3 Hydrocarbons

3.1 Hydrocarbons

- Compounds that contain only carbon and hydrogen are called hydrocarbons

- There are two major groups of hydrocarbons: Acyclic (straight chains) and Cyclic (ring structures

- There are different types of acyclic or cyclic hydrocarbons: alkanes, cycloalkane, alkenes, cycloalkene, alkyne, and arenes (aromatics)

- Each one of hydrocarbons forms a homologous series. A homologous series is a group of compounds with similar chemicals structures and graded physical and chemical properties which differ from each other by a constant amount of atoms in their structural backbone (skeleton) e.g the alkane, alkenes, alcohols etc.

3.2 Nomenclature

International Union of Pure and Applied Chemistry (UPAC) Nomenclature

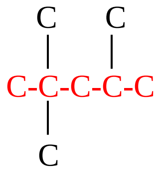
IUPAC rules is the system that is used in naming organic compounds. Naming system is called **Nomenclature** which gives a systematic way of giving names to all compounds. There are basic rules that are applicable to all classes of organic compounds and are supported by specific rules that are peculiar to each class of compounds.

Basic Rules

1. Some organic compounds only have generic names and no systematic names: methane, ethane, propane butane

2. A continuous chain is a chain where all carbon atoms are connected to no more than 2 other carbon atoms: C-C-C-C (Fig.1a)

3. A branched chain is a chain where 1 or more carbons atoms are connected to 2 or more other carbon atoms:



$$\begin{array}{ccccccccc} & & C & & & & C & & \\ & & | & & & & | & & \\ C & - & C & - & C & - & C & - & C \\ & & | & & & & & & \\ & & C & & & & & & \end{array}$$

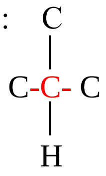
(Fig.1b)

4. Choose the longest continuous straight chain as the skeleton of the compound to be named: In Fig. 1b, there are 5 straight chains but the longest continuous chain is the one containing 5 carbon atoms

5. Use Latin word for the number of carbon skeleton to prefix the skeleton: pent (5C), hex(6C), hept(7) etc

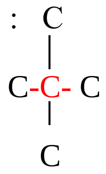
6. If the skeleton is unbranched the compound is called 'normal' (n-): C-C-C-C-C is called n-pentane

7. Organic compounds with 2 methyl groups (secondary carbon) at the end of an otherwise straight chain is prefixed 'iso': :



$$\begin{array}{c} C \\ | \\ C\text{-}C\text{-}C \\ | \\ H \end{array}$$

8. Organic compounds with 3 methyl groups (tertiary carbon) at the end of an otherwise straight chain is prefixed 'neo': :



$$\begin{array}{c} C \\ | \\ C\text{-}C\text{-}C \\ | \\ C \end{array}$$

9. Alkyl groups is one that contains only carbon and hydrogen atoms and is attached to the main skeleton of an organic compound

10. If the carbon of the alkyl group at the point of attachment is bonded to one carbon, that carbon is called a primary (1^0) carbon (alkyl group). If is bonded to 2 C atoms; it is called a secondary carbon or alkyl group (2^0) and if it is bonded to 3 C atoms, it is called a tertiary carbon or alkyl group

11. Common Alkyl groups: methyl, ethyl, propyl, butyl, etc.

3.3 Hybridized Orbital

Carbon atoms mix up its s- and p- orbital's to form sp, sp^2, sp^3, sp^3d, sp^3d^2 hybridized orbital's which it uses in all its reactions.

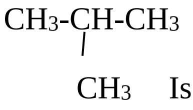
3.4 Isomerism

Isomers are compounds with the same molecular formula (MF) but different molecular structures. There are 3 types of isomers of carbon.

(1) Structural Isomers: these have same MF but different arrangement of its carbon atoms. For example, butane can be:

$CH_3\text{-}CH_2\text{-}CH_2\text{-}CH_3$ or

Butane

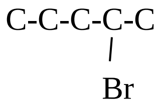


$$CH_3\text{-}\underset{\displaystyle CH_3}{\underset{|}{CH}}\text{-}CH_3$$

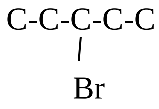
Isobutane

(2) Positional Isomers: these have the same substituent(s) on different carbon atoms. For example: 3-bromopentane can be represented in three different ways

C-C-C-C-C-Br



$\mathrm{C{-}C{-}C{-}\underset{\underset{\displaystyle Br}{|}}{C}{-}C}$



$\mathrm{C{-}C{-}\underset{\underset{\displaystyle Br}{|}}{C}{-}C{-}C}$

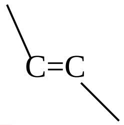
1-bromopentane 2-bromopentane 3-bromopentane

(iii) Geometrical Isomers: this involves unsaturated hydrocarbons with the unsaturation at different positions in the basic skeleton of the organic compound. For example butene can be written as:

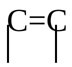
C-C-C=C or C-C=C-C

1-butene 2-butene

The multiple bonds confer specific shapes and configuration to the molecule. When substituent's are on opposite side of the multiple bonds, the configuration is called trans-configuration and it they are on the same side, the configuration is called trans-configuration



Trans configuration



Cis-configuration

Assignment: 1. Write structural isomers for hexane?

2. Write structural and condensed formulas for the following compounds (i) 4-t-butyl,2—methyl,3-ethyl heptane (ii) 2,6-dimethyl,3—ethyl heptane

3.5 Polymerization: Saturated or unsaturated organic molecules like ethylene can open up its double bond by radical chain or condensation mechanism to form giant molecules called polymers. This process is called polymerization.

Initiation: $\mathrm{RO{:}OR} \rightarrow \mathbf{2RO^{\cdot}}$ **(1)**

Propagation: $\mathrm{RO^{\cdot} + CH_2{=}CH_2 \rightarrow RO{-}CH_2CH_2^{\cdot}}$ (2)

$\mathrm{RO{-}CH_2CH_2^{\cdot} + CH_2{=}CH_2 \rightarrow ROCH_2CH_2CH_2CH_2^{\cdot} \rightarrow -\!\!\rightarrow}$

Termination: $\mathrm{RO^{\cdot} + RO(CH_2)_nCH_2^{\cdot} \rightarrow ROCH_2(CH_2)_nRO}$

$\mathrm{2\ RO(CH_2)_nCH_2^{\cdot} \rightarrow RO(CH_2)_nCH_2\ CH_2(CH_2)_nCH_2RO}$

3.6 Alkanes

- Alkanes are organic compounds that contain only carbon and hydrogen. They have saturated bonds and hence are called paraffin hydrocarbons

- It forms a homologous series with the formula C_nH_{2n+2} (n= 1- ∞)

- Methane is the simplest member and the next three members are ethane, propane and butane

- Higher members use prefixes (Latin words) that describes the number of carbon atoms in their skeletons: pentane, hexane, heptanes etc

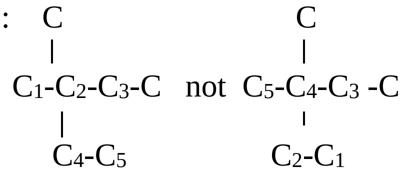
3.6.1 Nomenclature

1. All alkanes names ends with the suffix –‘ane’

2. Choose the longest continuous straight chain as the skeleton of the compound and use the Latin word for the # of carbon atoms in the skeleton to prefix its name: C-C-C-C-C – pentane

3. Number the parent hydrocarbon starting from the end of the chain

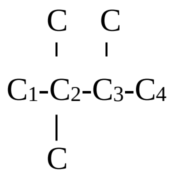
4. Assign numbers to the substituent’s (side chain). The direction of numbering is chosen to give the least numbers to the side chains:



$$\begin{array}{lll} & C & \\ & | & \\ C_1- & C_2 & -C_3-C \\ & | & \\ & C_4-C_5 & \end{array} \quad \text{not} \quad \begin{array}{lll} & C & \\ & | & \\ C_5- & C_4 & -C_3\ -C \\ & | & \\ C_2-C_1 & & \end{array}$$

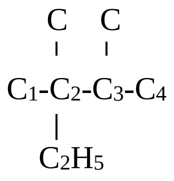
2, 3-dimethyl pentane   not 3,4- dimethyl pentane

5. if there are 2 identical substituent’s on the same carbon, numbers are supplied for each substituent: 2,2,3-trimethylbutane



$$\begin{array}{cccc} & C & C & \\ & | & | & \\ C_1- & C_2- & C_3- & C_4 \\ & | & & \\ & C & & \end{array}$$

6. When there ≥ 2 substituent’s on a carbon chain, the substituent’s are arranged (1) alphabetically or (2) in increasing order of complexity

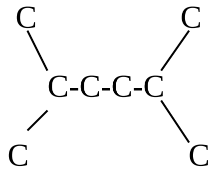


$$\begin{array}{cccc} & C & C & \\ & | & | & \\ C_1- & C_2- & C_3- & C_4 \\ & | & & \\ & C_2H_5 & & \end{array}$$

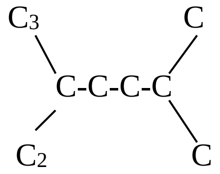
2-ethyl, 2,3-dimethylbutane

Assignment

1. Name each of the following hydrocarbons by IUPAC rule



2.



3.7 Physical Properties of Alkanes

- Each member of this homologous series increases by a CH_2- unit. This adds a fairly constant increment to the density, boiling and melting point of the member of this series. For example, the boiling point of hexane and heptanes are 69^0C and 98^0C respectively

- Branched alkanes do not show a gradation in physical properties like the n-alkanes. However, for a set of its isomers, volatility increases with branching

3.7.1 Spectroscopy Properties

- **Infra Red:** Shows C-H stretching frequency at 2850-3000 cm^{-1}. C-C frequencies are weak. CH_2 and CH_3 shows C-H bending vibrations at 1400- 1470 cm^{-1} and a weak band for CH_3 at 1380 cm^{-1}

- **Ultra Violet (UV):** No UV absorption above 200 cm^{-1}, hence they are good solvents for the determination of other substances

- **Nuclear Magnetic Resonance (NMR):** Reasonably characteristics but difficult to interpret because the changes in chemical shifts between the different types of protons are small. Easy to distinguish between normal or branched alkanes by inspecting integral ratio of the resonances of the CH_3 centered at 0.9ppm and CH_2 centered at 1.25 ppm.

- **Mass Spectrometry:** Very useful and applicable to all alkanes

- Lower members of the homologues are liquids and higher members are oils or wax.

3.8 Chemical Reactions

- In general alkanes are unreactive; hence they are called saturated hydrocarbons or paraffin's. At normal temperatures, strong mineral acids (HCL, H_2SO_4) or oxidizing agens (Br), oxygen, potassium permanganate do not react with alkanes

- Combustion: At high temperatures, alkanes burn in excess oxygen to give carbon dioxide and water: $CH_4 + 3/2O_2 \rightarrow CO_2 + H_2O$. Alkanes are used as fuel to produce energy and heat. Cracking of alkane produces different fractions such as: gas fraction (C_1-C_5), gasoline ((C_6-C_{10}), Kerosene (C_{11}-C_{12}), Light gas oil (C_{13}-C_{17}), Heavy gas oil, lubricating oil (C_{18}-C_{25}), Lubricants and waxes (C_{26}-C_{38})

- **Radical Chain Mechanism Reactions (RCM).**

RCM: consist of 3 stages: (i) **Activation stage:** Occur when sample is exposed to light and heat radiation to form radicals.

$$\mathbf{CH_4} \xrightarrow{\boxed{\text{hϷ}/\Delta}} \mathbf{CH_3^{\cdot}} + H^{\cdot}$$

(ii) **Propagation:** Radicals multiplies itself and form other types

$$H^{\cdot} + CH_4 \rightarrow CH_3^{\cdot} + H_2$$

$$CH_3^{\cdot} + \mathbf{CH_4} \rightarrow \mathbf{CH_3^{\cdot}} + CH_4$$

(iii) Termination: Radicals react with each other to form neutral molecules which end the reaction process

$$\mathbf{CH_3^{\cdot}} + CH_3^{\cdot} \rightarrow CH_3CH_3$$

$$H^{\cdot} + CH_3^{\cdot} \rightarrow CH_4$$

RCM occurs with oil which turns it **rancid**

- **Halogenation:** Only chlorine and bromine halogenations of alkanes work very well at high temperatures (≥300^0C) and in the gas phase. Halogenation with chlorine works in the dark by thermal dissociation of the chlorine atoms: $RC\text{-}H + X_2 \rightarrow RCX + H\text{-}X$ (X= halogens)
- **Nitration**: Also occurs at very high temperatures (425^0C) and in vapor phase with nitric acid or nitrogen tetroxide: $RC\text{-}H + HNO_3 \rightarrow RNO_2 + H_2O$

3.9 Cycloalkane

3.9.1 Cycloalkanes are alkanes with their carbon atoms linked together by single bonds to form a ring. The unsubstituted ones forms a homologous series with the formula C_nH_{2n}. The changes in their chemical properties are more significant when compared to their acyclic analogs because of angle strain and steric hindrance present in their structures. Stereoisomerism plays an important in the shape and conformations of the cycloalkanes.

3.9.2. Nomenclature

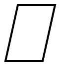
- Cycloalkanes are named by adding the prefix **cyclo-** to the name of the corresponding acyclic analog e.g. cyclobutane, cyclopentane etc

- Substituent's are give numbers according to their position such that the sum of the numbers is kept to the barest minimum

- Substituent's are arranged in alphabetic order

- Cycloalkyl groups are cycloalkanes group that has lost one hydrogen atom e.g. cyclobutyl, cyclopentyl etc

- We can use structures that contain the same number of vertices to represent the structures of cycloalkanes e.g.



Cyclobutane

3.9.3 Physical Properties

Except cyclopropane, the MP and BP of cycloalkanes are slightly higher than that of the acyclic analog.

IR: the IR signals are similar to those of acyclic alkanes. However, the CH**2** frequency show between 1440-1470 cm^{-1}. The size of the ring affects the actual position of this frequency.

UV Shows no absorption above 2000 cm^{-1} and hence are good solvents for UV analysis of other substances

NMR: Shows only one sharp line at room temperature. Substitution on the ring only show small shifts with closely space lines that cannot be easily resolved

3.9.4 Conformations of Cycloalkanes

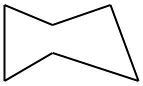
- We shall use cyclohexane as an example.

- Arrangement of carbons of atoms and the orientation of the attached hydrogen atoms determines which form of cyclohexene is stable and contributes to the structure of cyclohexene

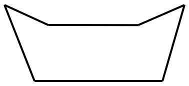
- Cyclohexane has 6 carbon atoms that are expected to be arranged as a regular hexagon with C-C bond angles of 120^0. Normal valence bond angle of carbon is 109.5^0 (tetrahedral, valence of 4).

- The hexagonal planar structure shows an **angle strain** of 10.5^0 ($120-109.5^0$). at each carbon atom. This strain makes the planar hexagonal shape unstable relative to a normal cyclohexane with a normal bond angle. Also this structure will have the hydrogen's occupy eclipsed (lying directly in close and opposite positions) position which will increase repulsion. The energy to increase the bond angle to 120 at each carbon is approximately 11.4 kcal which is high. Hence, this conformation is not stable and favorable.

- If we try to hold the C-C bond angle to 109.5^0, the two possible arrangements will lead to the formation of a boat and chair shape (conformation)

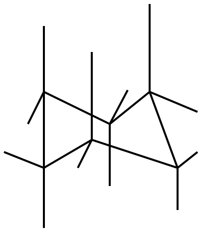


Chair



Boat

- The boat conformation is less stable compared to the chair conformation because of the repulsive interactions (**steric hindrance**) of its hydrogen atoms
- The chair conformation is the more stable with its hydrogen atoms staggered around the C ring, hence less steric hindrance.



- The chair conformation has 6 equivalent adjacent H atoms lying in the plane of the ring (**equatorial**) and 6 equivalent H atoms lying above and below (3up, 3 down, **axial**) the ring at distances that causes less repulsive interaction (steric hindrance) between them
- The equilibrium mixture of cyclohexane contains 99% of the chair conformation which is true for all cycloalkane molecules
- Evidence has shown that the two conformers rapidly converts into one another (e.g. in methylcyclohexane, the rate of exchange is estimated to be 10^6 times/sec) This process of rapid conformer inversion is called **ring inversion** (**Walden**) and the rate of conversion is called **inversion frequency**

3.10 Chemical Properties

- The ring strain of cycloalkanes makes them to be very reactive. Their reactivity is comparable to those of unsaturated hydrocarbons

- Chemical reactivity opens up the ring to form acyclic compounds with the relief of the strain as the driving force.

- They undergo substitution reactions such as halogenations and nitration with less isomeric products been formed.

3.11 Cis and Trans Isomerism

Cycloalkanes experience what is called **stereoisomerism (compounds with the same structural formulas but different spatial arrangements of its various groups)**

- Example is the chair and both conformers of hexane
- In substituted cyclohexanes, the ring inversion may not readily occur and they form what is called geometrical isomers or **cis and trans isomers**
- The substituent may lie above the plane of the ring (cis conformer) or one above and one below (trans conformer)

3.12 Alkenes

Acyclic alkenes form the homologous series with a formula of C_nH_{2n}. Its structure contains one double bond called an "**olefinic linkage",** hence, they are also called **olefins (oil formers).**

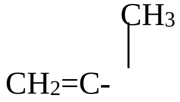
3.12.1 Nomenclature

- The nomenclature follows the same rule like that of alkanes

- The longest straight chain (skeleton) containing the double bond is given the name of the corresponding alkane but its name is ended with the word **"ene**" e.g. ethylene, propylene, butane etc

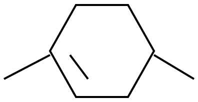
- The chain is numbered such that the **first carbon of the double bound** gets the lowest number.

- The alkyl group or radical formed by alkenes has its name ending with the suffix **"enyl"** and are called **"alkenyl"**. For example,

$CH_2=CH-$	$CH2=CHCH_2-$	 $CH_2=\overset{\overset{CH_3}{\vert}}{C}-$
Ethenyl (vinyl)	2-propenyl	isopropenyl (1methylethenyl)

- Hydrogen directly attached to the unsaturated carbon is called the **vinyl** hydrogen

- Cycloalkenes are name like the acyclic analog with the numbering starting at one of the unsaturated carbons such that the sum of the numbers is kept at the minimum and the name prefixed with ‘cyclo’
-



1,4-dimetylcyclohexene

- Alkenes with more than one double bond are called alkadienes (2 double bonds), alkatrienes (3 double bonds) etc
- Alkenes with consecutive double bonds are called **cumulated alkenes** and the ones with alternating double bonds are called **conjugated** alkenes

3.12.2 Physical Properties

IR: Alkenes has a characteristic stretching vibrations of the double bond (C=C) at 1650 cm^{-1}, vinyl C-H absorption bands at 1420, 1000 and 915 cm^{-1}, and C-H of CH_2CH_2 group at 3100 cm^{-1}

UV: Unconjugated alkenes absorbs energy of 2000 – 1000 A just like other materials like air, quartz sample cell and other solvents, hence its spectra cannot be easily distinguished. For conjugated double bonds, then the wavelength of absorption shifts to > 2000A and can be used to distinguish alkenes

NMR: Vinyl hydrogen’s shows chemical shift around 4.6 -5.3 ppm which are 2.5-4.5 ppm downfield compared to those of corresponding acyclic or cyclic alkanes

3.12.3 Structure of Alkenes

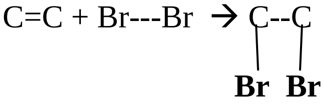
- the double bond present in the structure of alkenes introduces restriction of rotation of the atoms attached to the carbons of the double bond

- This restriction introduces geometric isomerism to alkenes (formation of cis and trans isomers)

3.12.4 Chemical Reactions of Alkenes

- Alkenes undergo electrophilic and nucleophilic additions across the C=C double bonds

- In these reactions, one of the double bond is broken and two new groups are added across the double bond to give a saturated hydrocarbon:



$$\mathrm{C{=}C + Br{-}{-}{-}Br \rightarrow \underset{\mathbf{Br}}{\underset{|}{C}}{-}{-}\underset{\mathbf{Br}}{\underset{|}{C}}}$$

- The electrons in a double bond are further removed from the bond axis than those of single bonds hence they are much available for reaction with electrophiles (electron loving agents)
- Electrophiles (electron loving) are good agents that can initiate reactions with an alkene. They accept electrons from an electron donating agent (nucleophiles)
- Nucleophiles (nucleus loving agent) are electron donating agents and are hence poor reaction initiators with alkenes

Assignment: Classify the following molecule as either an electrophilic or nucleophilic agent: H_2SO_4, Br_2, $NaNH_2$, NH_3, HBF_4

3.12.5 Hydrogenation of Alkenes

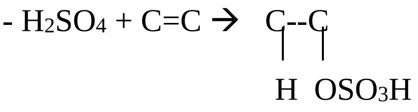
- Addition of a hydrogen molecule to an alkene is a very exothermic process that proceeds by radical chain mechanism.

- A mixture of Hydrogen and ethene at $\leq 200^0$C is stable but unstable to thermal, photochemical processes, and some metal catalysts (nickel, platinum and palladium)

$$H_2 + C{=}C \rightarrow CH_3CH_3 \quad \Delta H = -32.8\ \text{kcal}$$

3.12.6 Electrophilic Addition to C=C Bonds

- Halogens (Cl_2, Br_2, I_2), Halides (HCl, HBr etc) hypohalous (HOCl, HOBr etc), water, sulfuric acid easily adds to C=C bonds



$$-\ H_2SO_4 + C{=}C \rightarrow \underset{H}{C}{-}{-}\underset{OSO_3H}{C}$$

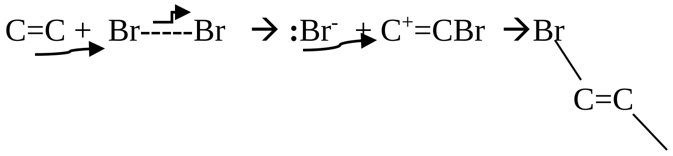
- **Hydration with Water:** $C{=}C + H_2O \xrightarrow{H^+} CH_3CH_2OH$

3.12.7 Halogenation

- Halogenation with bromine occurs in the dark by **polar addition mechanism**

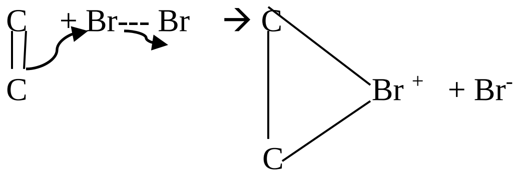
- the reaction occurs by ionic or polar mechanism instead of radical chain mechanism

- the bromine molecule undergo heterolytic fission to form ions which adds across the double bond to form a carbonium intermediate that form the trans alkyl halides



Br

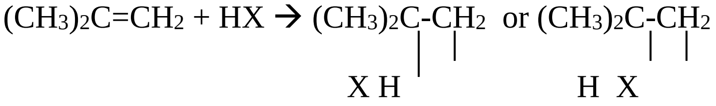
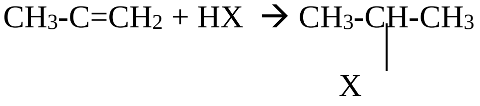
- If there are other nucleophiles present in solution, it will compete for reaction with the intermediate carbonium ion, hence resulting into multiple products
- Addition of bromine is sterospecific to form a trans product. The suggestion is that the step to form the carbonium ion involves the formation of a bridge intermediate called a bromonium bridge (both C atoms of the C=C bond is bonded to the added bromine ion



- Attack by the bromide ion occurs with the carbon opposite the bridge, hence a trans product is formed

3.12.8 Orientation in Addition To Alkenes

Markownikoff's Rule:

- Involves the addition of unsymmetrical substance like HX to unsymmetrical alkene
- The reaction can theoretically give two products
- 
  $(CH_3)_2C{=}CH_2 + HX \rightarrow (CH_3)_2\underset{X}{C}\text{-}\underset{H}{C}H_2$ or $(CH_3)_2\underset{H}{C}\text{-}\underset{X}{C}H_2$
- **Markownikoff's Rule: In addition of HX to an unsymmetrical C=C, the hydrogen of the HX substance goes to that carbon of the double bond that carries the greater number of hydrogen's.**
- 
  $CH_3\text{-}C{=}CH_2 + HX \rightarrow CH_3\text{-}\underset{X}{C}H\text{-}CH_3$
- The rule is universal when applied to **polar additions** to compounds with one double bond
- The reaction is a slow reaction under polar conditions

Anti-Markownikoff's Addition: Addition of Unsymmetrical Reagents

- In the presence of light, peroxides and free radical initiators, and the hydrogen of HX (except HF, HI) adds to an unsymmetrical C=C at the carbon that carries the least number of hydrogen's.

- the reaction is fast and **occur by free radical mechanism** (RCM)

$$CH_3CH{=}CH_2 + HBr \xrightarrow{ROOR} CH_3CH_2CH_2Br$$

RCM: **Initiation:** $ROOR \longrightarrow 2RO^{\cdot}$

$$RO^{\cdot} + HBr \longrightarrow ROH + Br^{\cdot}$$

$$RO^{\cdot} + HBr \longrightarrow ROBr + H^{\cdot}$$

Chain Propagation: $CH_3CH{=}CH_2 + Br^{\cdot} \longrightarrow CH_3CH^{\cdot}\text{-}CH_2Br$

O $CH_3CH^{\cdot}\text{-}CH_2Br + HBr \longrightarrow CH_3CH_2CH_2Br + Br^{\cdot}$

Chain Termination: $R^{\cdot} + R^{\cdot} \longrightarrow$ R-R (R= alkyl or other radical)

3.12.9 Other Reactions

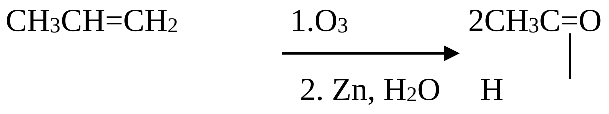
I. Addition of Boron Hydrides (Hydroboration): Adds BH_3. Addition is in 3 steps

$$6CH_2{=}CH_2 + B_2H_6 \xrightarrow{0^0} 2(CH3CH2)_3B + 6H_2O_2 \xrightarrow{(OH^-,\ 25\text{-}30^0)} 6CH_3CH_2OH + 2B(OH)_3$$

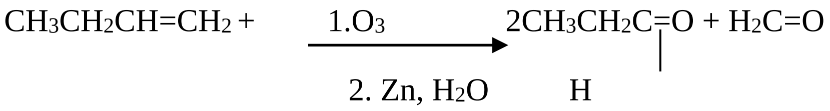
(tripropylborane)

$$\xrightarrow{^+H} 3CH_3CH_2CH_3 + B(OH)_3$$

II. Oxidation Using Ozone:



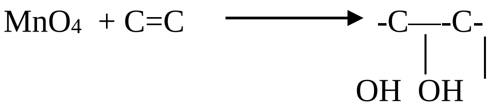
$$CH_3CH{=}CH_2 \xrightarrow[2.\ Zn,\ H_2O]{1.O_3} 2CH_3\underset{H}{\underset{|}{C}}{=}O$$



$$CH_3CH_2CH{=}CH_2 + \xrightarrow[2.\ Zn,\ H_2O]{1.O_3} 2CH_3CH_2\underset{H}{\underset{|}{C}}{=}O + H_2C{=}O$$

- This reaction can be used to locate the position of the double bond in an alkene

- Hydroxylation with Oxidizing Agents (MnO_4, OsO_4)



$$MnO_4 + C{=}C \longrightarrow \text{-}\underset{OH}{\underset{|}{C}}\text{—-}\underset{OH}{\underset{|}{C}}\text{-}$$

- cis diol is formed. The overall reaction is the addition of hydrogen peroxide

III. Polymerization

- A polymer is a long chain molecule with a reoccurring structural units e.g. $R(CH_2CH_2)_nR$
- Generation of polymers is by chain reaction (mechanism)
- The chain mechanism could be generated by:
-
- **Anion**: $Y^- + (CH_2{=}CH_2)_n \rightarrow Y{:}CH_2(CH_2\text{-}CH_2)_nCH_2CH_2^- \xrightarrow{H^+} Y{:}CH_2(CH_2\text{-}CH_2)_nCH_2CH_3$
- An intermediate carbanion is formed which propagates the polymer. The reaction can be terminated by adding a proton. This reaction does not readily occur. It only occurs with ethylene with electron withdrawing substitutes
-
- **Cation**: reaction is started by addition of a polar reagent such as HX. This generates an intermediate carbonium ion that propagates the reaction. The reaction can be terminated by the loss of a proton. Ethylene does not undergo this type of reaction because it does not have enough electron donating groups to stabilized the intermediate
-
- $HY + (CH_2{=}CH_2)_n \rightarrow Y{:}CH_2(CH_2\text{-}CH_2)_nCH_2CH_2^+ \xrightarrow{-H^+} Y{:}CH_2(CH_2\text{-}CH_2)_nCH_2CH_3$
-
- **Free radical mechanism:** This reaction occurs with hydrogen peroxide at high temperatures and pressure. Typical pressure is 1000 atms and temp > 100^0

3.13. Alkynes

- Alkynes are also called acetylenes and they are compounds with carbon-carbon triple bonds

- They form a homologous series with a general formula of C_nH_{2n-2} where n = 2 -∞

- the simplest member of the group is acetylene with a formula of C_2H_2. It is a linear molecule with a C≡C bond distance of 1.2A ,2 C-H bond distance of 1.6A and bond angle of 180^0

- the triple bond consist of one σ bond and 2π bonds.

3.13.1 Nomenclature

- The name of the longest straight chain ends with the word **'yne'**

- The first carbon with the triple bond gets the lowest n umber

- Other system of naming for alkanes and alkenes suffices

- Compounds with more than on triple bonds are called alkadiynes, alkatrieynes etc depending on the number of triple bonds present in the compounD

- There are compounds with mixed bonds (double and triple). They are called **alkenynes**. The number of double or triple bonds is reflected in the name. e.g alkadienynes etc

- In numbering such compounds, the double bond takes preference over the triple bond e.g.

$HC{\equiv}C\text{-}CH{=}CH\text{-}CH{=}.CH_2$ is called 1,3-hexadiene-5-yne

- The alkyl ion formed from alkynes are called **alkynyl**

3.13.2 Physical Properties

- The BP, MP, densities, and the heat of combustion of alkynes are higher than those of the corresponding alkanes and alkenes

- The physical properties increase with increasing chain length

3.13.3 Spectroscopic Properties

- IR: C-H stretching of the carbon triple bond at 3300 cm^{-1}, the $HC{\equiv}C$ stretching at 2100 cm^{-1}For highly substituted alkynes, these bonds are absent or of very low intensities that are not discernible

UV: absorbs UV below 2000A @ 1500 and 1700 cm^{-1}. Absorb at > 2000 A when conjugated (2100-2275 cm^{-1})

NMR: the proton attached to the triple carbon shows up at around 185 cps (~3 ppm) which is similar to that of alkyl protons

3.13.4 Acetylene

- Formula is C_2H_2

- Preparation: Hydrolysis of calcium carbide- $CaC_2 + 2H_2O \rightarrow HC{\equiv}CH + Ca(OH)_2$

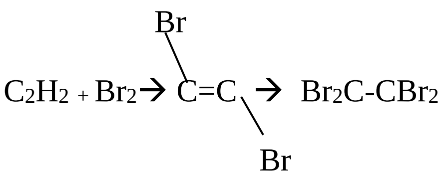
- Much less stable compared to its constituting elements: $C_2H_2 \leftrightarrow 2C + H_2$ $\Delta H = -54.2$ kcal

- Used by welders as acetylene dissolved in acetone @> 200psi

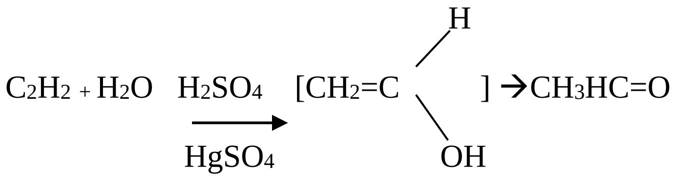
- Combustion: $C_2H_2 + O_2 \rightarrow CO_2 + H_2O$ $\Delta H = -311.0$ kcal and gives flame temperature of 2800^0

3.13.5 Addition Reaction of Alkynes

- Halogenation: is a two step process. The first process produces trans-alkene and the second step produces the tetra- halo product



$$C_2H_2 + Br_2 \rightarrow \overset{Br}{C}{=}\underset{Br}{C} \rightarrow Br_2C\text{-}CBr_2$$

- Hydrolysis: 
$C_2H_2 + H_2O \xrightarrow[HgSO_4]{H_2SO_4} [CH_2=C\overset{H}{\underset{OH}{}}] \rightarrow CH_3HC=O$

- Dimerization: can dimerize to give butenyne (vinyl acetylene)

- $2C_2H_2 \xrightarrow{Cu(NH_3)_2^+Cl^-} CH_2=CH-C\equiv CH$

- Cu, Hg, and Ni are often used as catalyst in the reactions of alkynes. They form complexes with alkynes which probably increases their solubility in water

- Reacts with boron hydrides to form anti-Markownikoff's product (vinyl boranes). The product in the presence of acetic acids forms alkenes

$$CH_3CH_2C\equiv C-H + BR_2-H \rightarrow CH_3CH_2CH=CHBR_2$$

- Acetylene and 1-alkynes form salts in the presence of a strong base. In this case it acts as an acid

$$R-C\equiv C-H + K^+ {}^-NH_2 \xrightarrow{NH_3} R-C\equiv C^-K^+ + NH_3$$

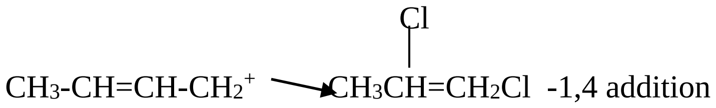
3.13.6 Bifunctional Compounds: Alkadienes

- Organic compounds can be classified according to their functional group: hydrocarbon (alkane, alkene, alkyne, aromatic), halides, alcohols, carboxylic acid etc or by the type of reactions common to a homologous series.

- Some organic compounds have more than one functional group in its structure and hence are called polyfunctional compounds: alkadienes, acetamide, carboxylic acids, vinyl chloride etc. These functional groups modify the properties of each other. Sometimes, the functional groups are separated (isolated) from each other (C=C-C-C-C=C) and it reacts like alkenes, conjugated (C=C-C=C-C=C, alkadienes) or cumulative (C=C=C=C)

3.13.6.1. 1,3 or Conjugated Dienes: The double bonds in these compounds are separated by a CH_2 group and hence are classified as conjugated dienes. Their reaction is like those of normal alkenes (free radical, polar addition, catalytic hydrogenation) but does so more readily.

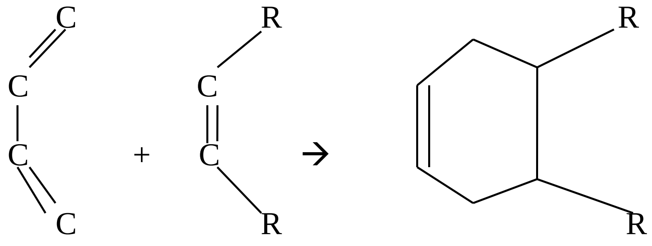
- the common reaction is either the 1,2 or 1,4- addition reaction with an intermediate carbonium ion at carbon 1 or 3



$$CH_3\text{-}CH{=}CH\text{-}CH_2^+ \rightarrow CH_3\overset{Cl}{C}H{=}CH_2Cl$$ -1,4 addition

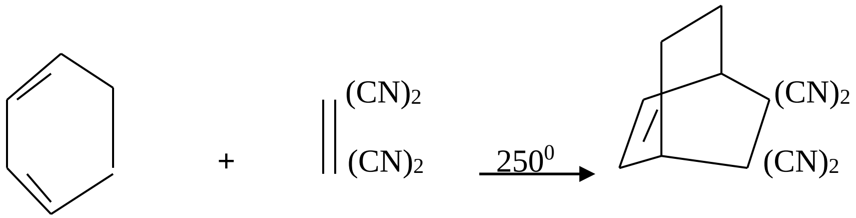
3.13.6.2 1, 4 Cycloaddition: Diels-Alder Reaction

- Diels- Alder reaction involves 1, 4 addition of a diene and a dienophile (alkene) to form a cyclic unsaturated compound



R = H, CN, CO_2H, -COR etc

- The reaction is stereo specific because its diene react as the cis conformer to form a ring with a cis configuration. It also serves as intermediates in the synthesis of natural products



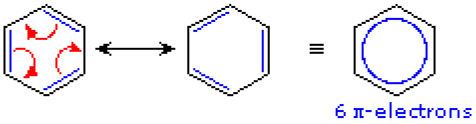
- A polymer made of the same unit is called a **homopolymer**. If the units are not identical, then it will be called a **copolymer**. If a monomer polymerizes nonstereospecifically (forms cis and trans, 1, 2 addition etc), the polymer is still called a **copolymer**.
- Raw polymers are tacky and of little direct use except as adhesives or cement. It can however be transformed by **vulcanization** by adding sulphur and catalysts (**accelerators**) to it to form cross linked polymers (rubbers, cross linked with C-S bonds)
- Vulcanized rubber are very elastic, flexible, abrasive resistance, and resistant to chemicals and can be used as casing for batteries
- Common dienes use in making synthetic rubbers include: 1,3-butadiene, 2-chloro-1,3-butadiene (chloroprene) and 2-methyl-1,3-butadiene (isoprene)

Chapter 4 Aromatic Compounds

4.1 Introduction

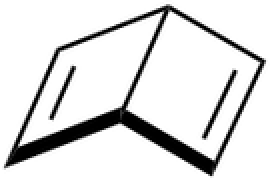
Aromatic compounds are compounds based on the molecule called *benzene* which has a formula C_6H_6. The presently accepted structure of a regular-hexagonal, planar ring of carbons was suggested by Kekule and then adopted as the structure of benzene molecule. The exceptional thermodynamic and chemical stability of this system was attributed to resonance stabilization of a conjugated cyclic triene.

Benzene:



Here, two structurally and energetically equivalent electronic structures for a stable compound are written, but no single structure provides an accurate or even an adequate representation of the true molecule. The six-membered ring in benzene is a perfect hexagon (all carbon-carbon bonds have an identical length of 1.40 Å). The cyclohexatriene contributors would be expected to show alternating bond lengths, the double bonds being shorter (1.34 Å) than the single bonds (1.54 Å). An alternative representation for benzene (circle within a hexagon) emphasizes the pi-electron delocalization in this molecule, and has the advantage of being a single diagram. In cases such as these, the electron delocalization described by resonance enhances the stability of the molecules, and compounds composed of such molecules often show exceptional stability and related properties.

Other structures were suggested by other scientists. For example Dewar suggested a bicyclic isomer named bicyclo[2.2.0]hexa-2,5-diene shown in the figure below:



4.2 Other aromatics

Benzene rings may be joined together (fused) to give larger polycyclic aromatic compounds. A few examples are drawn below, together with the approved numbering scheme for substituted derivatives. The peripheral carbon atoms (numbered in all but the last three examples) are all bonded to hydrogen atoms. Unlike benzene, all the C-C bond lengths in these fused ring aromatics are not the same, and there is some localization of the pi-electrons such as shown in Figure 4.1 below.

As the number of benzene increases, the aromatic compounds changes from been a planar molecule to molecules with helical structures with increasing curvatures that finally closes up to form a structure that looks like a football . For example, the six benzene rings in *coronene* are fused in a planar ring; whereas the six rings in *hexahelicene* are not joined in a larger ring, but assume a helical turn, due to the crowding together of the terminal ring atoms. This helical configuration renders the *hexahelicene* molecule chiral, and it has been resolved into stable enantiomers having specific rotations of 3700º. The archetypical compound of curvature close-up is C_{60} which has been named **buckminsterfullerene**

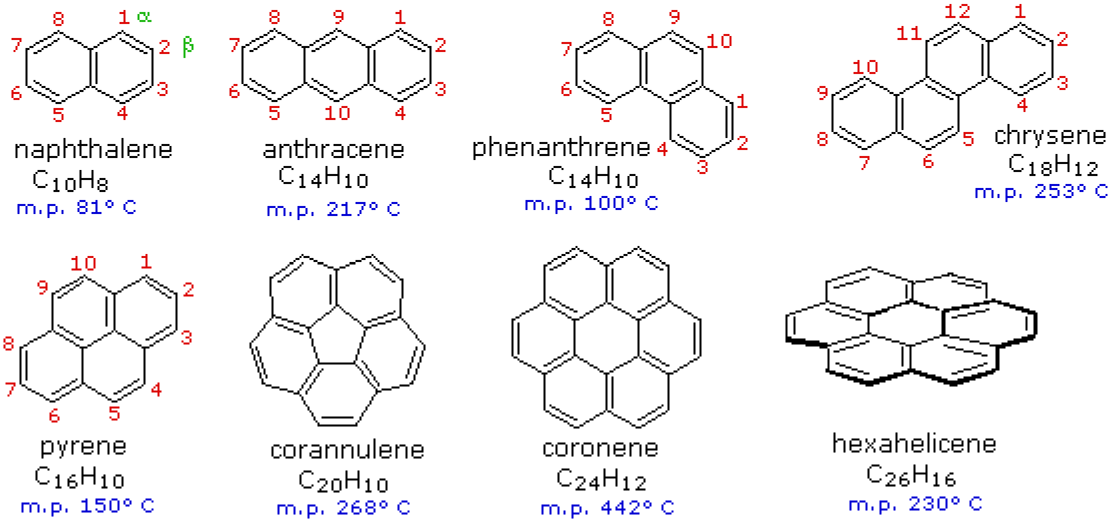


Figure 4.1 Structures of some few Aromatic Compounds

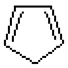
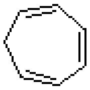
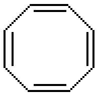
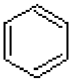
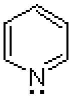
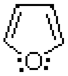
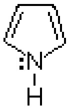
As these extended aromatic compounds become larger, the ratio of hydrogen to carbon decreases. For example, the symmetrical hexacyclic compound coronene has a H/C ratio =1/2, compared with 1 for benzene. If we were to imagine fused ring systems of this kind to be further extended in space, the H/C ratio would approach zero, and the resulting compound would be a form of carbon (allotropes). Such a carbon allotrope exists and is called **graphite**. Another well-characterized carbon allotrope is **diamond**. The structures for these two forms of carbon are very different. Diamond is an extended array of sp^3 hybridized carbon atoms; whereas, graphite consists of overlapping sheets of sp^2 hybridized carbon atoms arranged in a hexagonal pattern.

Many unsaturated cyclic compounds have exceptional properties that we now consider characteristic of "aromatic" systems. The following compounds in Table 4.1 are illustrative:

The first three compounds (cyclic polyenes) have properties associated with alkenes in general. Each reacts readily with bromine to give addition products, as do most alkenes. The thermodynamic change on introducing double bonds into the carbon atom ring is also typical of alkenes (a destabilization of ca.26 kcal/mol for each double bond). Conjugation offsets this increase in energy by a small amount (4-6 kcal/mol).

The remaining four compounds exhibit very different properties, and are considered aromatic. Benzene and pyridine are relatively unreactive with bromine, requiring heat and/or catalysts to force reaction, the result of which is substitution rather than addition. Furan and pyrrole react more rapidly with bromine, but they also give substitution products. This tendency to favor substitution rather than addition suggests that the parent unsaturated ring system has exceptional stability. Thermodynamic measurements support this conclusion. The enhanced stability, often referred to as **aromatic stabilization**, ranges (in the above cases) from a low of 16 kcal/mol for furan to 36 kcal/mol for benzene.

Table 4.1

Compound	**Structural Formula**	**Reaction with Br$_2$**	**Thermodynamic Stabilization**
1,3-Cyclopentadiene		Addition (0 ºC)	Slight
1,3,5-Cycloheptatriene		Addition (0 ºC)	Slight
1,3,5,7-Cyclooctatetraene		Addition (0 ºC)	Slight
Benzene		Substitution	Large
Pyridine		Substitution	Large
Furan		Substitution (0 ºC)	Moderate
Pyrrole		Substitution	Moderate

When one of the six equivalent H atoms is removed, the result is the group called the **phenyl group,** C$_6$H$_5^-$

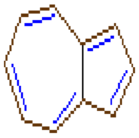
Aromatic compounds are named by assigning numbers to the carbon atoms on the aromatic ring with the carbon that has a substituent's been given the least number. For example, with toluene, the carbon with the methyl group is given the number 1.

4.3 Factors Required for Aromaticity

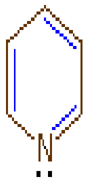
- A planar (or near planar) cycle of sp^2 hybridized atoms, the p-orbitals of which are oriented parallel to each other. These overlapping p-orbitals generate an array of π-molecular orbitals.
- These π-orbitals are occupied by 4n+2 electrons (where n is an integer or zero). This requirement is known as **The Hückel Rule**. All the aromatic compounds discussed above have 6 π-electrons (n=1).

1,3-Cyclopentadiene and 1,3,5-cycloheptatriene both fail to meet the first requirement, since one carbon atom of each ring is sp^3 hybridized and has no p-orbital. Cyclooctatetraene fails both requirements, although it has a ring of sp^2 hybridized atoms. This molecule is not planar (a geometry that would have 135° bond angles). Angle strain is relieved by adopting a tub-shaped conformation; consequently, the p-orbitals can only overlap as isolated pairs, not over the entire ring. Furthermore, cyclooctatetraene has 8 π-electrons, a number not consistent with the Hückel Rule.

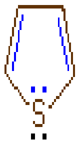
Benzene is the archetypical aromatic compound. It is planar, bond angles=120°, all carbon atoms in the ring are sp^2 hybridized, and the pi-orbitals are occupied by 6 electrons. The aromatic heterocycle pyridine is similar to benzene, and is often used as a weak base for scavenging protons. Furan and pyrole have heterocyclic five-membered rings, in which the heteroatom has at least one pair of non-bonding valence shell electrons. By hybridizing this heteroatom to a sp^2 state, a p-orbital occupied by a pair of electrons and oriented parallel to the carbon p-orbitals is created. The resulting planar ring meets the first requirement for aromaticity, and the π-system is occupied by 6 electrons, 4 from the two double bonds and 2 from the heteroatom, thus satisfying the Hückel Rule.



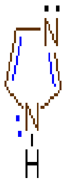
azulene



pyridine



thiophene

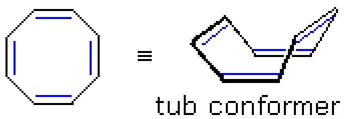


imidazole

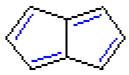
Four illustrative examples of aromatic compounds are shown above. The sp^2 hybridized ring atoms are connected by brown bonds, the π-electron pairs and bonds that constitute the aromatic ring are colored blue. Electron pairs that are not part of the aromatic π-electron system are black. The first example is azulene, a blue-colored 10 π-electron aromatic hydrocarbon isomeric with naphthalene. The second and third compounds are heterocycles having aromatic properties. Pyridine has a benzene-like six-membered ring incorporating one nitrogen atom. The non-bonding electron pair on the nitrogen is not part of the aromatic π-electron sextet, and may bond to a proton or other electrophile without disrupting the aromatic system. In the case of thiophene, a sulfur analog of furan, one of the sulfur electron pairs (colored blue) participates in the aromatic ring π-electron conjugation. The last compound is imidazole, a heterocycle having two nitrogen atoms. Note that only one of the nitrogen non-bonding electron pairs is used for the aromatic π-electron sextet. The other electron pair (colored black) behaves similarly to the electron pair in pyridine.

4.4 Antiaromaticity

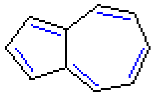
Conjugated ring systems having 4n π-electrons (e.g. 4, 8, 12 etc. electrons) not only fail to show any aromatic properties, but appear to be less stable and more reactive than expected. As noted above, 1,3,5,7-cyclooctatetraene is non-planar and adopts a tub-shaped conformation. The compound is readily prepared, and undergoes addition reactions typical of alkenes. Catalytic hydrogenation of this tetraene produces cyclooctane. Planar bridged annulenes having 4n π-electrons have proven to be relatively unstable. Examples of 8 and 12-π-electron systems are shown below, together with a similar 10 π-electron aromatic compound.



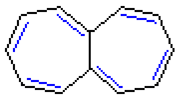
tub conformer
(non-planar)
cyclooctatetraene stable b.p. 142 °C
gives alkene-like reactions
8 π-electrons



pentalene (planar)
very unstable
8 π-electrons



azulene (planar)
aromatic stability
10 π-electrons



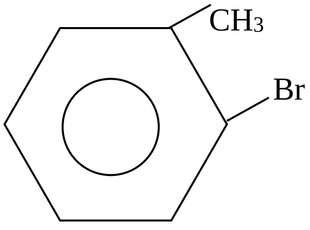
heptalene (planar)
very unstable
12 π-electrons

The simple C_8H_6 hydrocarbon pentalene does not exist as a stable compound, and its hexaphenyl derivative is air sensitive. The 12-π-electron analog heptalene has been prepared, but is also extremely reactive (more so than cyclooctatetraene). On the other hand, azulene is a stable 10-π-electron hydrocarbon that incorporates structural features of both pentalene and heptalene. Azulene is a stable blue crystalline solid that undergoes a number of typical aromatic substitution reactions. The unexpected instability of 4n π-electron annulenes has been termed "**antiaromaticity**".

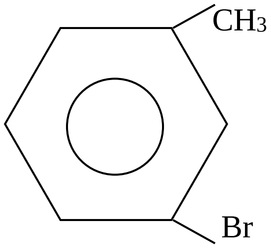
4.5 Nomenclature

Benzene and its derivatives are similar to hydrocarbon in that they are insoluble in water but soluble in organic solvents. They also have higher boiling points than alkanes with the same number of carbon atoms. This so because of its delocalization of its electrons which increases the attractive forces within the ring.

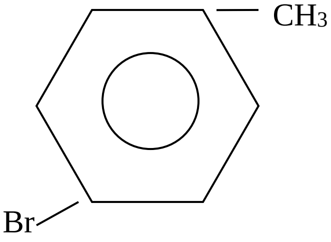
When there are 2 or more substituent’s or the ring , the adjacent carbon to the substituted carbon is called ortho- (o-) carbon, the one adjacent to the o-carbon is called meta- (m-) and the one adjacent to the m- carbon is called para- (p-) carbon.



o-toluene



m-bromotouluene



p-bromotoulene

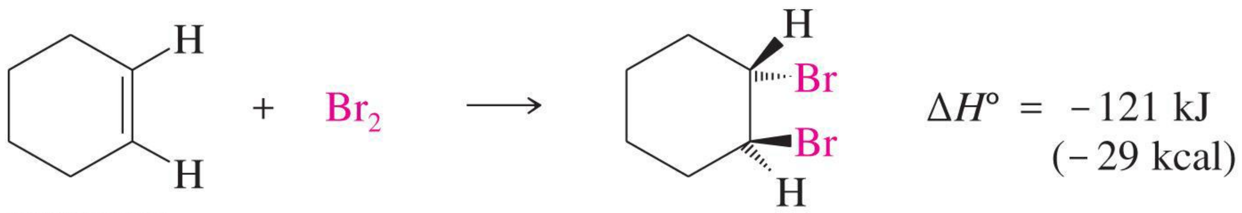
The presence of one substituent on the ring determines where on the ring another substitution is going to occur. The following rule applies to the position where the incoming carbon will be attached:

Electron donating species: NH_2 -, -OR, -OH, -OCOR, -R, -X (R- alkyl, X= halogens) are o- and p- directors (from strongest to weakest

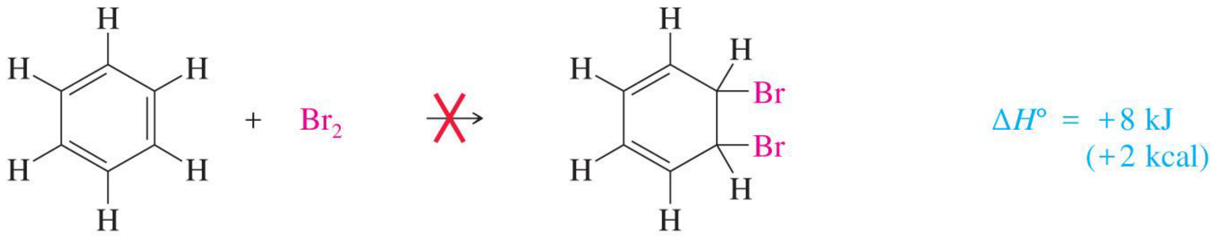
Electron Withdrawing species: Meta (m-directors): NO_2-, -CN, -SO_3H, -CHO, -COR, -COOH, -COOR (from strongest to weakest)

4.6 Reactions of Aromatic Compounds

A Comparison with Alkenes
Alkenes react spontaneously with bromine to give addition products e.g

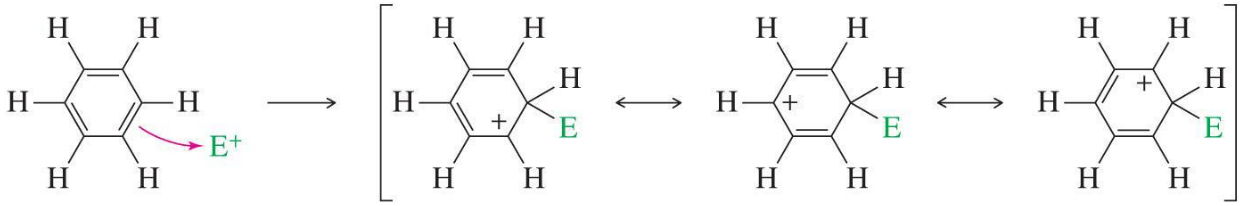


This reaction is exothermic by 29kcal/mol.
An analogous addition reaction between benzene and bromine would be endothermic by 2kcal.



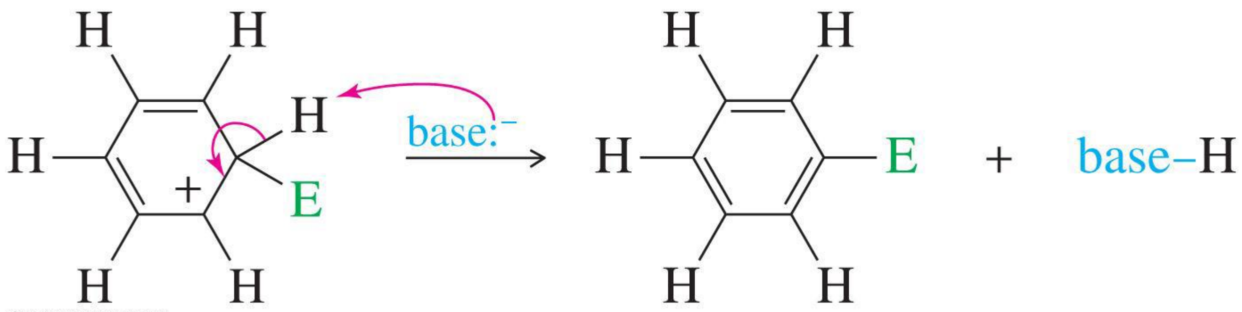
The destruction of the **aromatic** sextet causes this endothermicity. This reaction is not observed under normal reaction conditions. The substitution of bromine for hydrogen is an overall exothermic process, but requires a catalyst to convert the bromine molecule into a more reactive electrophile

B Just like an alkene, benzene has clouds of π electrons above and below its sigma bond framework. Although the π electrons are in a stable aromatic system, they are still available for reaction with **strong** electrophiles.
This generates a carbocation which is resonance stabilized (but not aromatic).



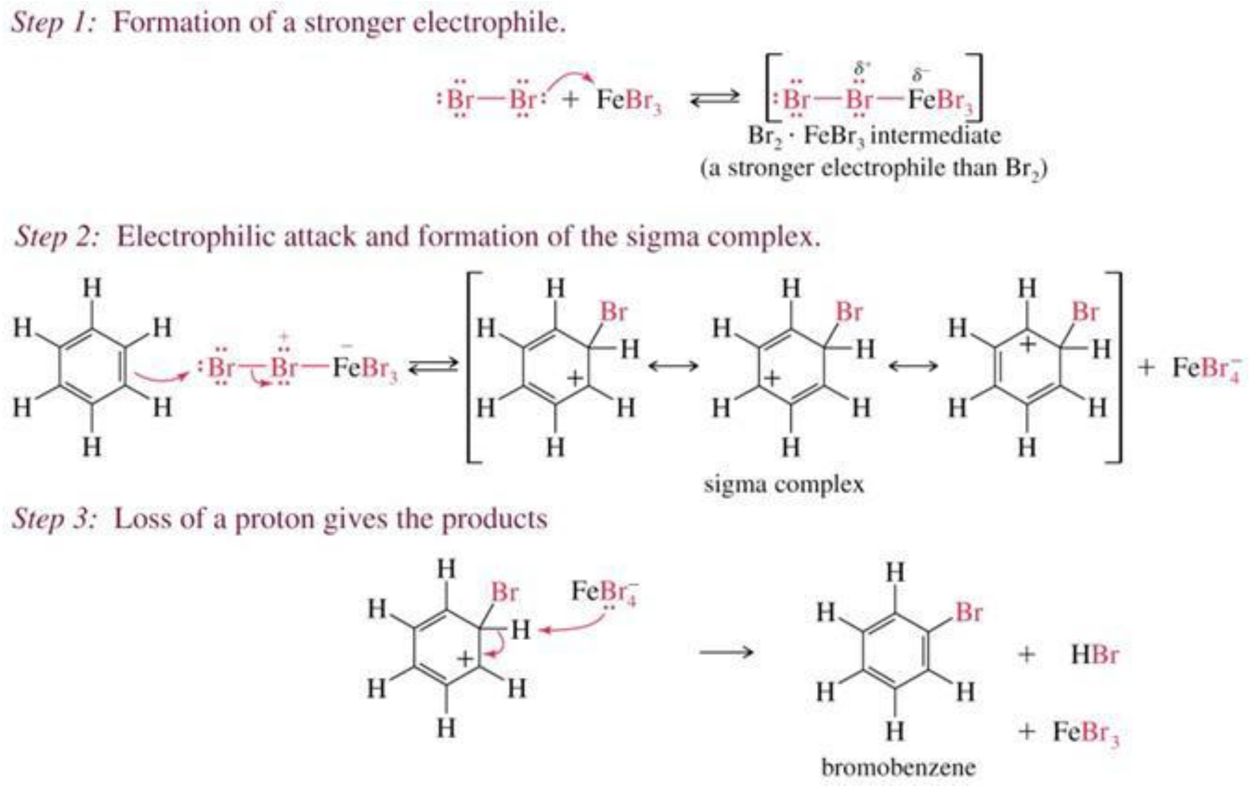
sigma complex (arenium ion)

This cation is called a **sigma complex** because the electrophile is joined to the benzene ring through a new sigma bond. The sigma complex (also called an arenium ion) is **not** aromatic since it contains an sp3 carbon (which disrupts the required loop of p orbitals).
The loss of aromaticity required to form the sigma complex explains the highly endothermic nature of the first step. (That is why we require strong electrophiles for reaction).
The sigma complex wishes to regain its aromaticity, and it may do so by either by a reversal of the first step (i.e. regenerate the starting material) or by loss of the proton on the sp3 carbon (leading to a **substitution** product).



When a reaction proceeds this way, it is **electrophilic aromatic substitution**.
There are a wide variety of electrophiles that can be introduced into a benzene ring in this way, and so electrophilic aromatic substitution is a very important method for the synthesis of substituted aromatic compounds.

Bromination of Benzene
Bromination follows the same general mechanism for the electrophilic aromatic substitution (EAS).
Bromine itself is **not** electrophilic enough to react with benzene.
But the addition of a strong **Lewis acid** (electron pair acceptor), such as FeBr3, catalyses the reaction, and leads to the **substitution** product.
The bromine molecule reacts with FeBr3 by donating a pair of its electrons to the Lewis acid, which creates a more polar Br-Br bond, and thus a more **reactive** electrophile.
Benzene will now attack this electrophile to generate the sigma complex.


Step 1: Formation of a stronger electrophile.

Step 2: Electrophilic attack and formation of the sigma complex.

Step 3: Loss of a proton gives the products

4.7 Other Electrophilic Aromatic Substitution Reactions

1. Chlorination: $C_6H_6 + Cl_2 \xrightarrow{AlCl_3} C_6H_5Cl + HCl$

2. Iodination: $2C_6H_6 + I_2 \xrightarrow{2HNO_3} 2C_6H_5I + 2H_2O + 2NO_2$

The nitric acid is a strong **oxidizer** (i.e. removes electrons, converts iodine into I+), this makes the iodine a much stronger electrophile.

$2H+ + 2HNO_3 + I_2 \longrightarrow 2I^+ + 2NO_2 + 2H_2O$

The nitric acid is consumed in the reaction, it is therefore a **reagent**, not a catalyst.

3. Nitration: $C_6H_6 + HNO_3 \xrightarrow{H_2SO_4} C_6H_5NO_2 + H_2O$

4. Sulfonation: $C_6H_6 + SO_3 \xrightarrow{H_2SO_4} C_6H_5SO_3H$

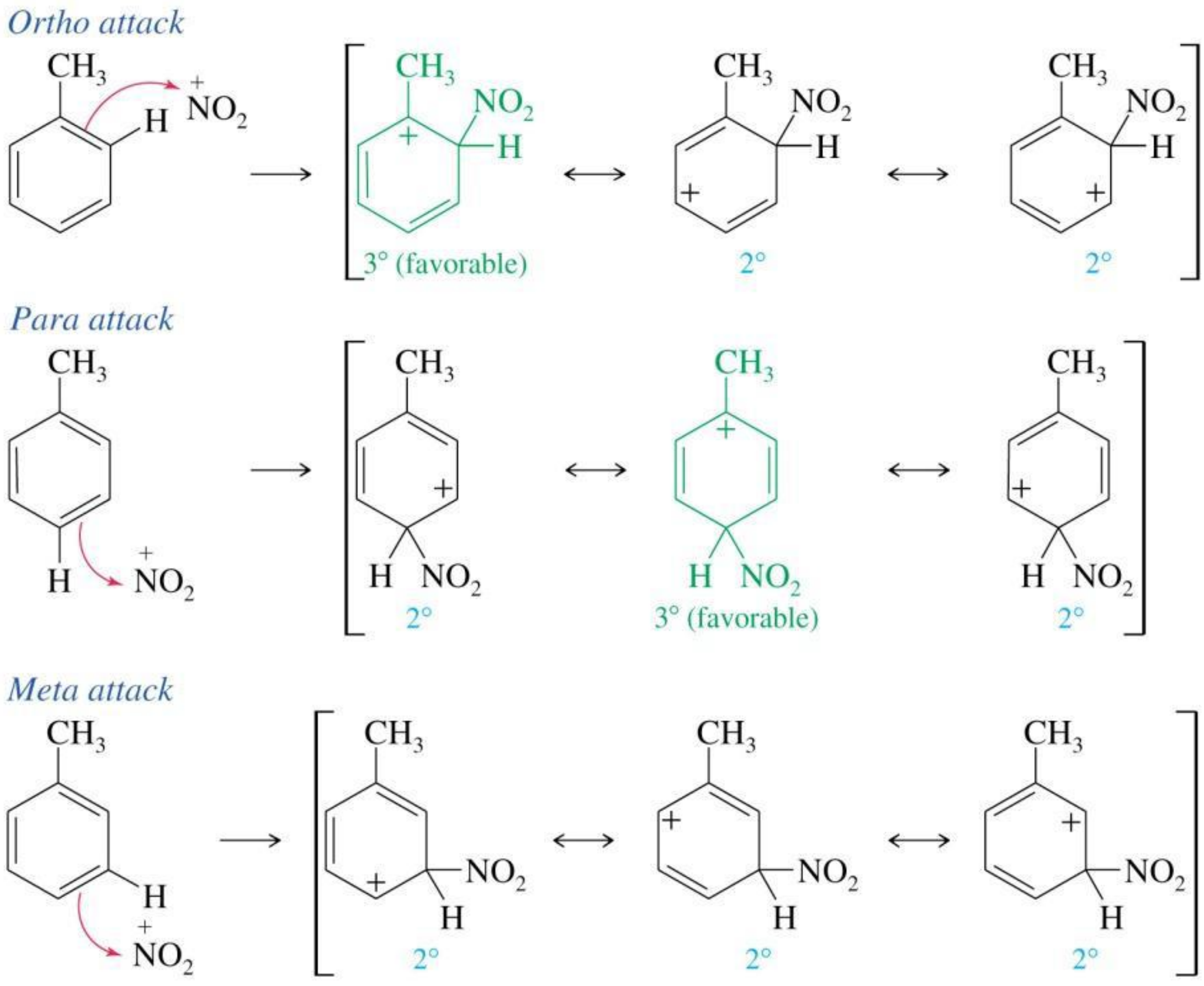
5. Desulfonation: $C_6H_5SO_3H + H_2O \xrightarrow{heat} C_6H_6 + H_2SO_4$

6. Hydrogen-Deuterium Exchange: $C_6H_6 + D_3O^+ \xrightarrow{H_2SO_4} C_6H_5D + D_2OH$

4.8 Reactions of Substituted Aromatic Compounds

The rate of substitution for an alkyl substituted benzene is faster than that of benzene itself because the alkyl group inductively stabilizes the intermediate sigma complex that is formed.

If we consider the electrophilic substitution reaction (EAS) of adding a nitro group to toluene, the reaction process which produces the sigma intermediate complex is shown below:

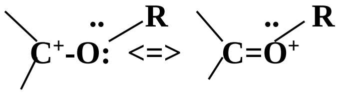


In the case of toluene, ortho (and para) attack result in the positive charge being spread over two secondary carbons and one tertiary carbon atom (the one bearing the CH3 group).
Since the sigma complexes for ortho (and para) attack have resonance forms with tertiary carbons, they are more **stable** that the corresponding resonance forms for benzene's reaction with nitronium ion. Thus toluene reacts **faster** than benzene at the ortho and para positions.

When reaction of toluene occurs at the meta- position, then the resonance forms of the sigma complex put positive charge over 3 secondary carbons - the same as for benzene.
Therefore meta- substitution of toluene does not show any (significant) enhancement of rate relative to benzene. The methyl group is electron donating, and so stabilizes the intermediate sigma complex, and therefore the TS leading to it.
This effect is pronounced in ortho and para attack since these give rise to resonance structures which contain tertiary carbons, and are therefore more stable.
Meta substitution does not show these huge stabilizations, and is only slightly more stable then the unsubstituted benzene case.

4.8.1 Effect of Substituent’s with Nonbonding electrons on EAS

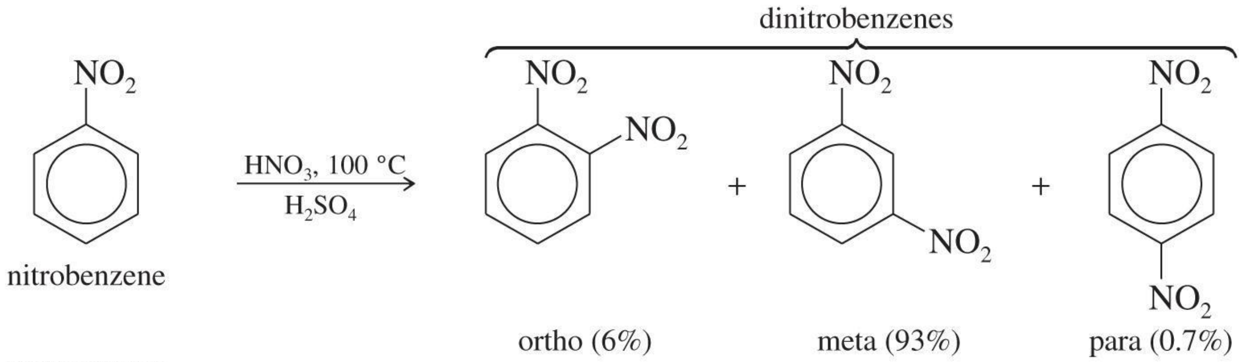
Substituent’s with non bonding electron like a methoxy group (CH_3O^-) in anisole for example, undergoes nitration around 10,000 times faster than benzene, and about 400 times faster than toluene. Since oxygen is more electronegative than carbon, it may seem strange that methoxy is a better activating group than methyl for EAS. However, the difference is that the methoxy group has **lone pairs** which can be used to stabilize adjacent positive charges through resonance.



This type of stabilization is called **resonance stabilization**.
The oxygen atom is said to be resonance donating, or pi donating since it is donating electron density through a π bond in one of the resonance structures. Therefore any substituent with a lone pair of electrons on the **atom directly bonded** to the benzene ring can provide this resonance stabilization of the sigma complex for ortho and para attack.

4.8.2 Deactivating Meta-Directing Substituent’s

In the same way that electron donating groups activate the ortho and para positions, an electron withdrawing group deactivates the ortho and para positions. This selective deactivation leaves the meta- position as the most reactive site for attack. Meta directors deactivate the meta-position much less than they deactivate the ortho and para positions. For example, Nitrobenzene is about 100,000 times **less** reactive than benzene towards EAS.
Nitration of nitrobenzene requires concentrated nitric and sulfuric acids at temperatures above 100°C. This proceeds slowly, and the dinitrobenzene product produces three isomers, with the meta- isomer being the major one.



4.8.3 Exceptions to the Rule

Halogen substituent's are the exception to these rules. Halogen substituents are deactivating, yet are ortho and para directors. They are unusual (special/interesting) since they show an interesting dichotomy of features:
1) The halogens are very electronegative. They can powerfully withdraw electron density from the ring inductively through the sigma bond (therefore **deactivating**).

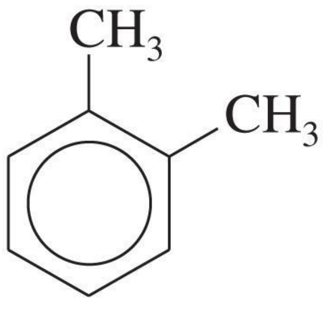
2) The halogens have lone pairs of electrons that can donate electron density (resonance donation) through σ bonding (therefore ortho and para directors).

These effects oppose one another and make the halogens the exceptions to the previous generalizations. Attack at the ortho (or para) position generates a sigma complex that can put the positive charge adjacent to a halogen substituent. The halogen uses its lone pair to stabilize this charge, generating a halonium ion structure. Reaction at the meta- position does not allow for the positive charge to be placed adjacent to the halogen, and therefore does not result in any stabilization.
Halogens are **deactivating** because of the inductive withdrawal of electron density from the ring, yet are ortho para directors since they can use resonance donation to stabilize adjacent carbocations.

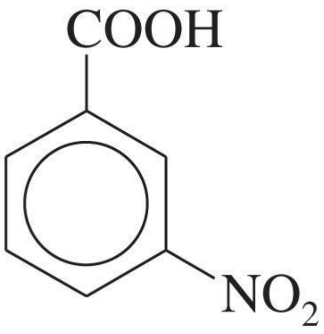
4.8.3 Effects of More than One Substituent's

Two or more substituents produce a combined effect on the reactivity of an aromatic ring. For example we can predict that xylenes (dimethyl benzenes) will be activated to EAS, and that a nitrobenzoic acid will be deactivated to EAS (relative to benzene). However, the relative reactivity (and directing effect) of Toluic acid is less obvious.

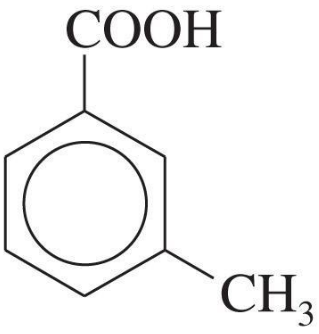
In some cases the orientation of addition is easy to predict (directing effects are complementary). For meta- xylene, there are two sites which are ortho to one methyl group and para to the other (double reinforcement). In some cases the orientation of addition is easy to predict (directing effects are complementary). For meta- xylene, there are two sites which are ortho to one methyl group and para to the other (double reinforcement).



o-xylene
activated

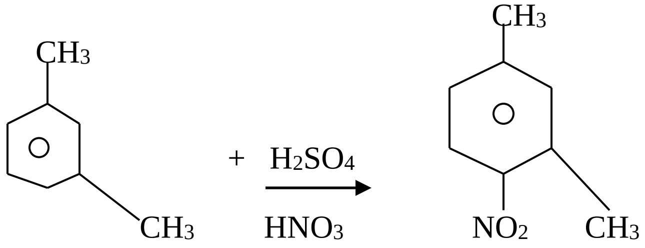


m-nitrobenzoic acid
deactivated

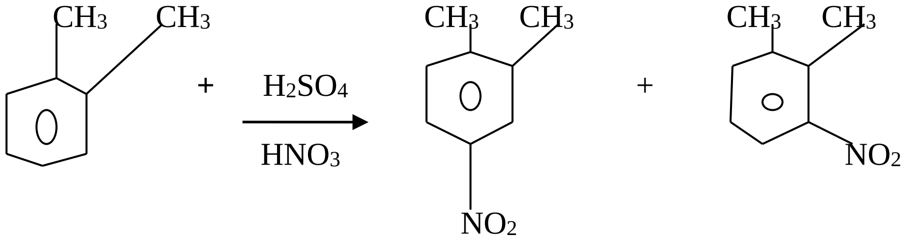


m-toluic acid
not obvious

Therefore, EAS would be directed preferentially to those sites. Another site is doubly reinforced, yet since it is between the two methyl groups, it is sterically hindered, and is therefore of reduced reactivity.



It is more complicated if the directing effects conflict with each other. Often in these cases, mixtures of products are produced. E.g. o-xylene is activated at all positions, and so mixtures of nitrated products are observed.



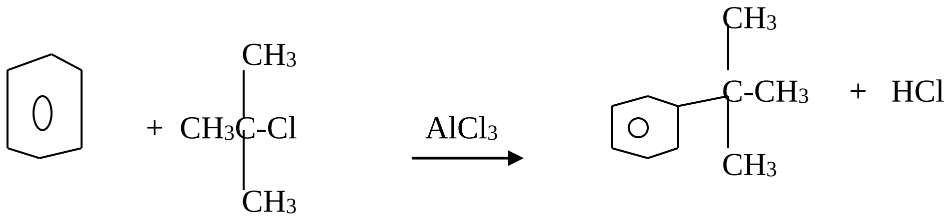
When there is a conflict between an activating group and a deactivating group, usually the activating group dominates the orientation of substitution.
Generally, activating groups are stronger directors than deactivating groups.
Substituent’s can be divided into three groups, differing in the strength of their directing abilities.

1) Powerful o/p directing groups with lone pairs (resonance stabilizers)
2) Moderate o/p directors such as alkyl groups and halogens
3) Meta directors (from strongest to weakest).

If two substituents are in conflict of directing abilities, the stronger one will win.
If they are in the same class, then mixtures will be produced.

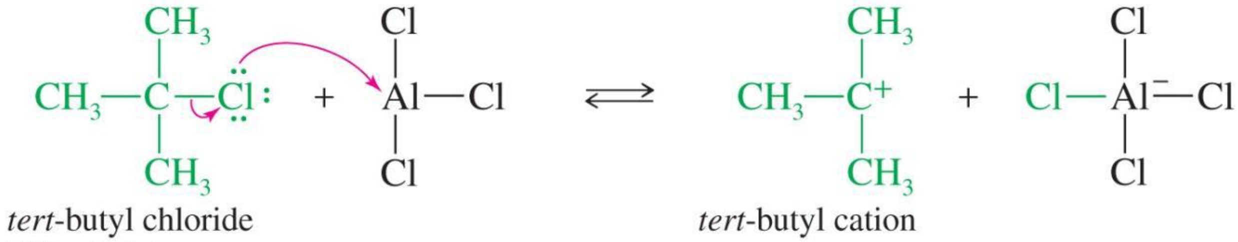
4.9 Friedel-Crafts Alkylation

Carbocations are electrophiles, and can therefore be useful reagents for forming new C-C bonds in EAS processes. Friedel and Craft demonstrated that benzene would react with alkyl halides in the presence of a Lewis acid (e.g. AlCl3) to produce alkyl benzenes. This reaction became known as **Friedel-Crafts alkylation**.

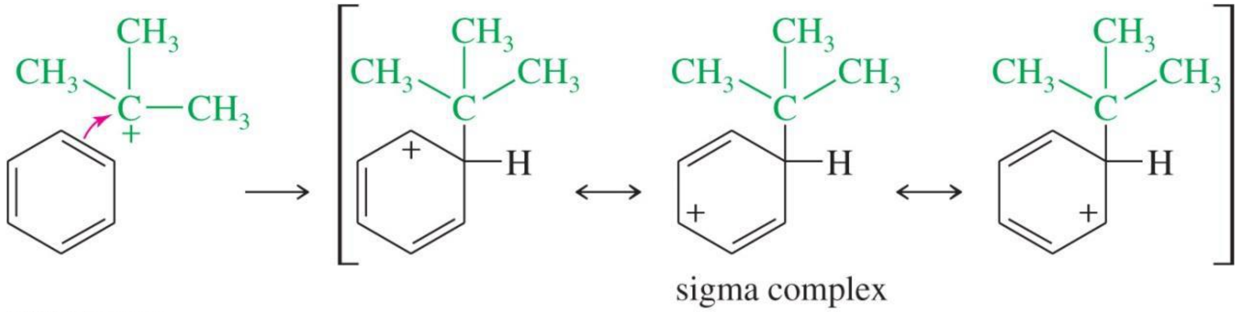


This alkylation is a typical EAS type reaction.

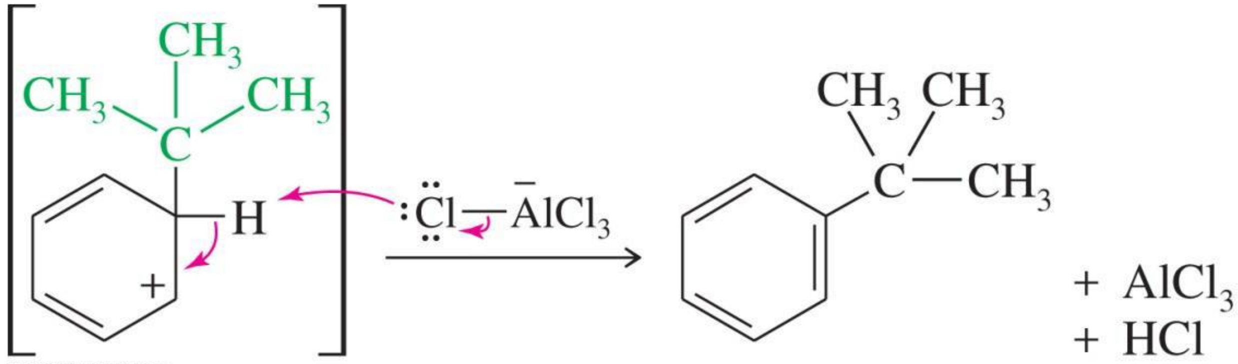
The t-butylchloride reacts with the Lewis acid to generate the t-butyl carbocation



The t-butyl carbocation acts as the electrophile, and forms a sigma complex.



This is followed by loss of a proton, giving t-butyl benzene as the product and The Lewis acid catalyst is regenerated in the last step.



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4.9.1 Limitations of the Friedel-Crafts Reaction

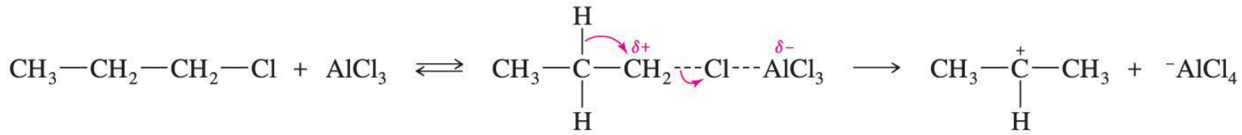
There are (unfortunately) three drawbacks or limitations to these Friedel-crafts reactions:

1) They only work with activated benzenes, benzene itself and halobenzenes. Strongly deactivated aromatics cannot be used in these reactions.

Systems such as nitrobenzene, benzenesulfonic acids and phenyl ketones all fail to react.
2) Since these reactions involve carbocations (or carbocation like) species, there is the possibility of carbocation rearrangements.

Certain alkyl groups can be introduced without rearrangement (t-butyl-, isopropyl-, ethyl-) but consider what happens when we try to introduce an n-propyl group.

Ionization with rearrangement gives isopropyl cation



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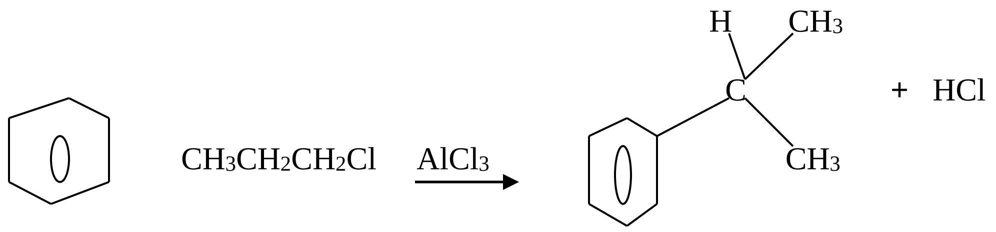
The carbocation-like intermediate can **rearrange** into a more stable carbocation.
In trying to introduce an n-propyl group, we end up introducing an isopropyl group.



3) Alkyl groups are activating for EAS processes. Therefore, the product of a Friedel-Craft reaction is more reactive than the starting material. This means that multiple alkylations are difficult to avoid.

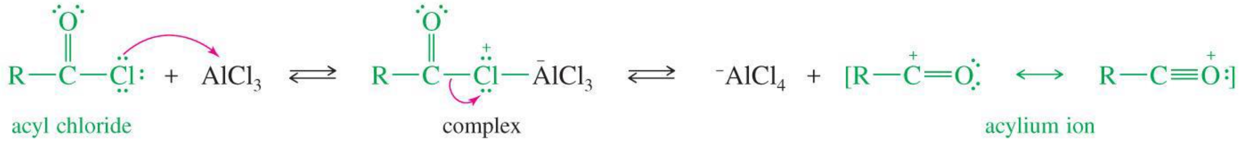
Even if only 1 equivalent of alkylating agent is added, a mixture of polysubstituted products is recovered along with unreacted benzene.

4.10 The Friedel-Crafts Acylation

An acyl group is a substituent which contains an alkyl group bound to a carbonyl group (R-$\overset{|}{\text{C}}$=O)
An acyl chloride is the same as an acid chloride.
In the presence of a Lewis acid, an acyl chloride reacts with benzene to produce a phenyl ketone (or acylbenzene). This Friedel-Crafts **acylation** is the same as the alkylation except that an acyl chloride is used instead of an alkyl chloride, and that an acyl group is incorporated instead of an alkyl group

4.10.1Mechanism of Acylation

The mechanism is very similar to before except the carbonyl group helps to stabilize the cationic intermediate. The acyl halide reacts with the Lewis acid, and loss of AlCl4- generates a resonance stabilized acylium ion.



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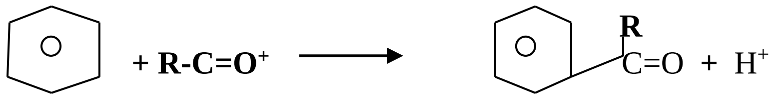
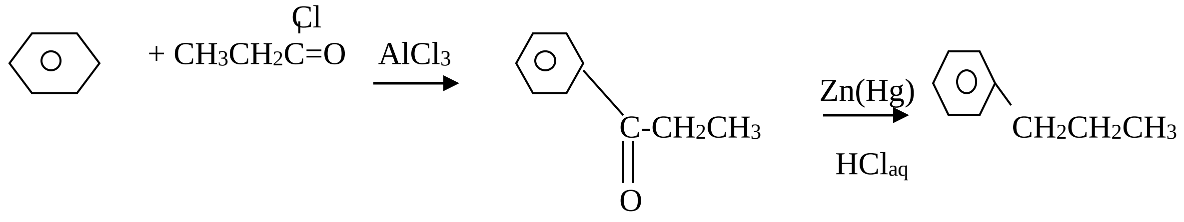
The acylium ion is a strong electrophile, and reacts with benzene generating an acylbenzene.



The product is a ketone, and since this is a deactivating group, poly-substitution does not occur. (Advantage over alkylation) The Friedel-Crafts acylation however also still does not work with strongly deactivated systems.

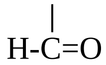
4.11 The Clemmensen Reduction Reaction

The Friedel Craft acylation reaction can be used to prepare alkyl benzenes that cannot be prepared directly by alkylation. All that is needed to do is to reduce the acyl group to an alkyl (CH_2) group after acylating the benzene ring. This is achieved by Clemmensen Reduction.
The reagents used are a zinc/mercury amalgam and aqueous hydrochloric acid.
Therefore to synthesize n-propyl benzene (which we could not do via direct FC alkylation), we can acylate using propanoyl chloride, and then reduce the phenyl ketone product which gives our final product



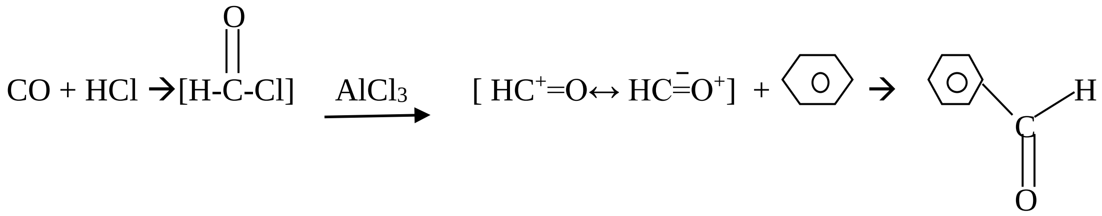
4.12 Synthesis of Benzenealdehydes (Gatterman-Koch Formylation)

The addition of a formyl group to benzene cannot be achieved by FC acylation since the required formyl chloride is not stable. The formyl group is represented by:



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

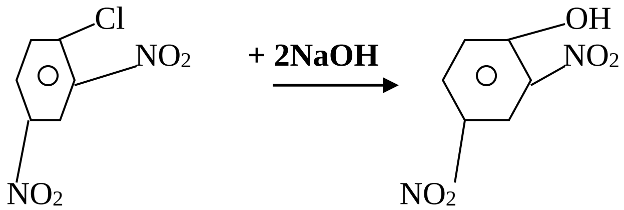
An alternative which overcomes this problem is the Gatterman-Koch reaction. A high pressure mixture of carbon monoxide and HCl together with a catalyst can generate a formyl cation, which can then react with benzene to produce formyl benzene (more often called benzaldehyde).



4.13Nucleophilic Aromatic Substitution Reactions (NAS)

Normally, **electrophilic** aromatic substitution is the type of reaction mechanism we associate most commonly with benzene derivatives. However, it is also possible for nucleophiles to displace halides ions (i.e. good leaving groups) from aryl halides if there are strong electron withdrawing electron groups bound to the ring (and especially if they are located ortho and para to the halide).

Since a nucleophile substitutes for the leaving group on the benzene ring, this is called ***nucleophilic aromatic substitution***. For example 2,4-dinitrochlorobenzene will undergo reaction with nucleophiles such as ammonia and hydroxide, where the chlorine becomes displaced.



The mechanism of this nucleophilic substitution is interesting since it **cannot** proceed by the SN2 mechanism because the aryl halide cannot provide a suitable geometry for back side attack of the nucleophile (aryl ring blocks the attack of the nucleophile).

Yet the SN1 mechanism also cannot operate since the reaction is not found to be unimolecular, and strong nucleophiles are required. (Also we would not expect ionization of the aryl halogen bond to give an aryl cation to proceed easily).

There are two different possible reaction mechanisms for NAS.

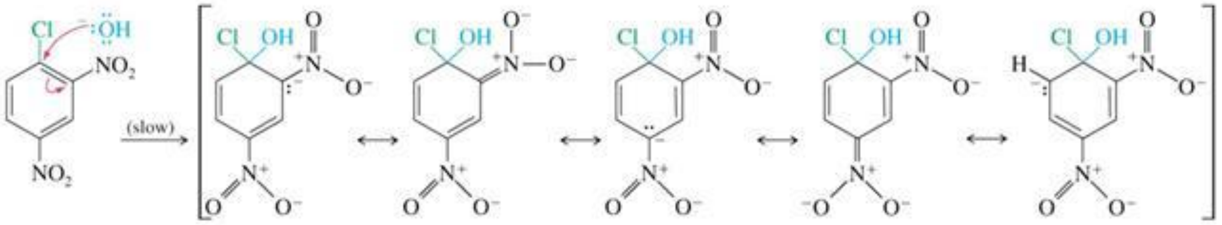
1) Addition Elimination Mechanism

2) Elimination Addition Mechanism (The Benzyne mechanism)

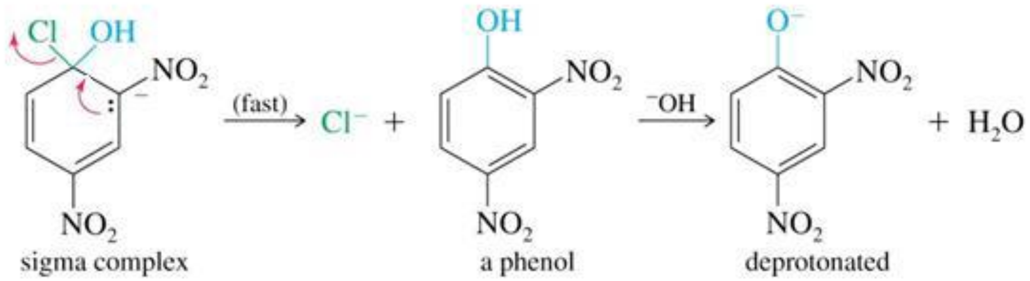
(a) The Addition Elimination Mechanism

Consider the reaction of hydroxide ion with 2,4-dinitrochlorobenzene.

Step 1: Attack by hydroxide gives a resonance-stabilized sigma complex.



Step 2: Loss of chloride gives the product. *Step 3:* Excess base deprotonates the product.



When the nucleophile attacks the carbon bearing the chlorine, a negatively charged sigma complex is generated.

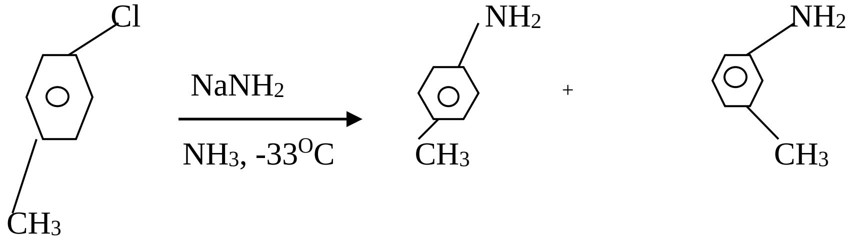
The negative charge is delocalized over the ortho and para positions, and further delocalized into the electron withdrawing groups (conveniently located at these positions).

Loss of chloride from the sigma complex generates 2,4-dinitrophenol.

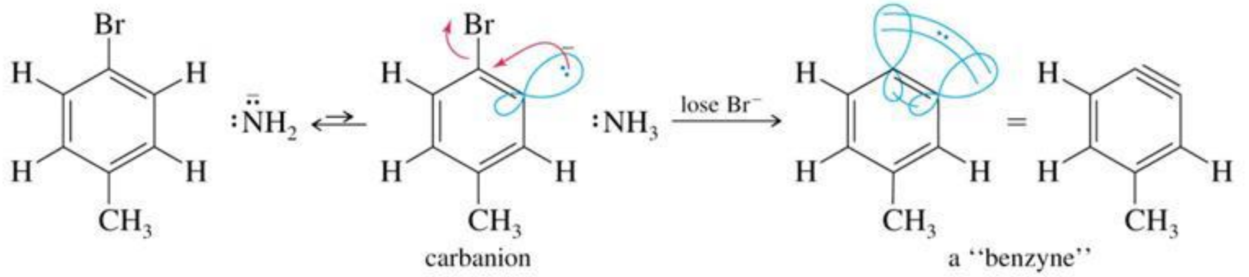
(This is like the mechanism for EAS, but with the benzene reacting with a **nucleophile** instead of an electrophile).

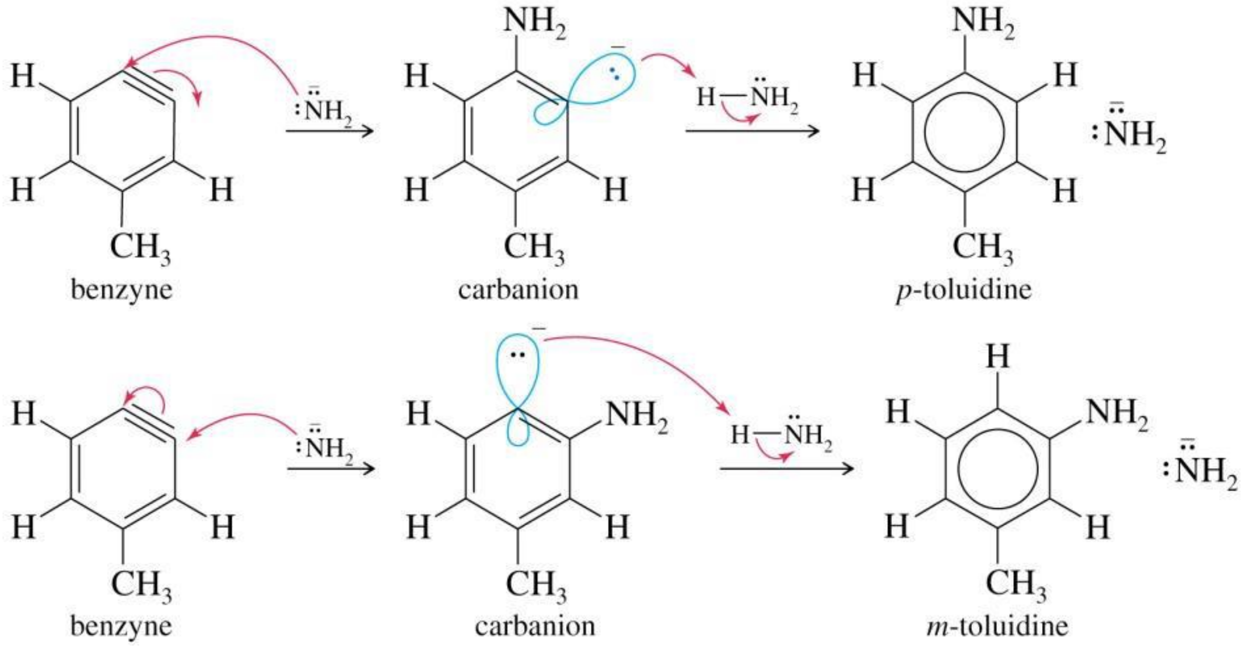
(B) The Benzyne Mechanism (Elimination Addition Mechanism)

The previous addition elimination reaction mechanism required powerfully electron withdrawing groups on the benzene ring. However, under forcing conditions, unactivated halobenzenes can react with strong bases. A clue to the mechanism of this type of reaction was provided by the reaction below:



The products were found to be a 50:50 mixture of meta- and para substituted compounds. These two isomers can be explained as coming from the same intermediate, a **Benzyne**





The reagent used acts as a strong base, and abstracts the proton adjacent to the leaving group. The anion can expel the leaving group, thus generating a neutral species and another π bond (making a triple bond). This is called a benzyne (benzene + alkyne) which is a very reactive intermediate. The triple bond is reactive since it is very strained (should be linear). The amide nucleophile attacks the triple bond, generating a carbanion, which then gets protonated to give the product. The attack on the triple bond may occur with equal probability (and energy) at either end, or thus the 50:50 mixture results.

4.14 Addition Reaction of Benzene

Although **substitution** is by far the most common reaction type of benzene and it derivatives, addition reactions can occur if forcing conditions are employed.

4.14.1Chlorination

For example, if benzene is treated with an excess of chlorine under conditions of heat and pressure, then 6 chlorine atoms will add, generating 1,2,3,4,5,6-hexachlorocyclohexane. This is a

$$C_6H_6 + 3Cl_2 \xrightarrow{h\nu} C_6H_6Cl_6$$

free radical mechanism

4.14.2 Catalytic Hydrogenation

The addition of hydrogen to benzene occurs at elevated temperatures and pressures, and requires a catalyst

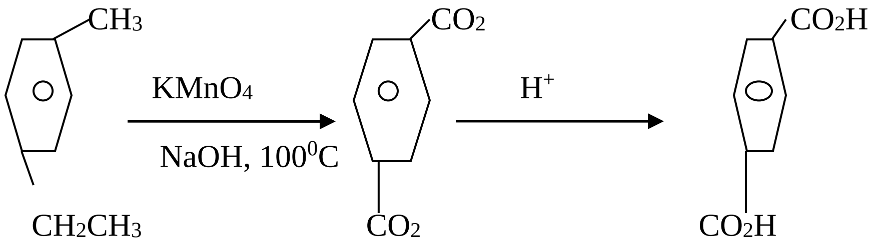
$$C_6H_6 + 3H_2 \longrightarrow C_6H_{12}$$

Catalyst/pressure

4.15 Reactions of the Side Chains in Benzene Derivatives

4.15.1 Permanganate Oxidation

An aromatic ring imparts extra stability to the carbon atoms **directly** bonded to it.
Therefore when an alkyl benzene is oxidized with permanganate, the product is the carboxylate salt of di-benzoic acid.

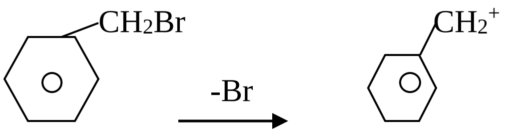


4.15.2 Nucleophilic Substitution at the Benzylic Position

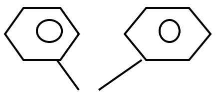
In the same way that allylic halides are more reactive than normal alkyl halides in both SN1 and SN2 reaction, benzylic halides are even more reactive.

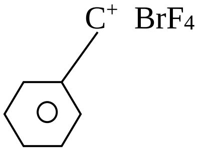
4.15.2.1First Order Reactions

First order nucleophilic substitutions require ionization of the substrate to generate the carbocation, and benzylic cations are resonance stabilized.



Therefore benzylic halides undergo SN1 reactions very easily. If a benzylic cation has more than one phenyl group as a substituent then the stabilizing effects are additive, and these are very stable systems. For example, the triphenylmethyl tetrafluoroborate salt is a **stable** ionic solid.

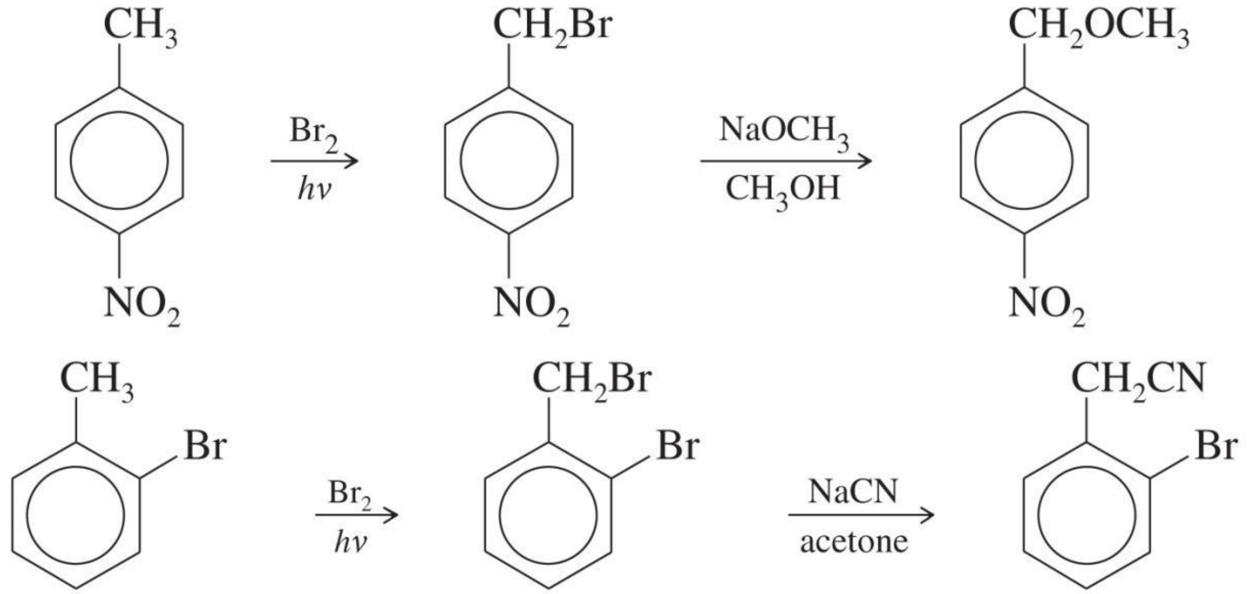




4.15.3 Second Order Reactions

Just like allylic halides, benzylic halides are around 100 times more reactive than primary alkyl halides in SN2 reactions.

During the displacement, the p orbital that partially bonds to the nucleophile and leaving group also overlaps with the π electrons of the aromatic ring. This conjugation lowers the energy of the TS and so enhances reaction rate. SN2 reactions of benzyl halides are good methods for converting aromatic methyl groups into different functional groups, via halogenation, followed by SN2 substitution.



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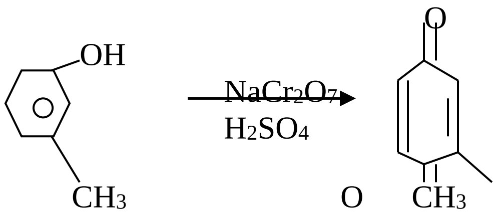
4.15. 3 Reactions of Phenols

Phenols behave very similarly to aliphatic alcohols, with the exceptions that (a) they form more stable phenoxide ions (vs. alkoxide ions), and (b) they do not undergo either acid catalyzed reactions or back side attack (e.g. no reaction with HBr). The aromatic ring in phenol also gives rise to some unique phenol reactions.

4.15.3.1 Oxidation of Phenols to Quinones

Oxidation of normal alcohols gives either carbonyl products (aldehydes/ketones) or carboxylic acids. However, oxidation of phenols gives conjugated 1,4-diketone products, which are called quinones

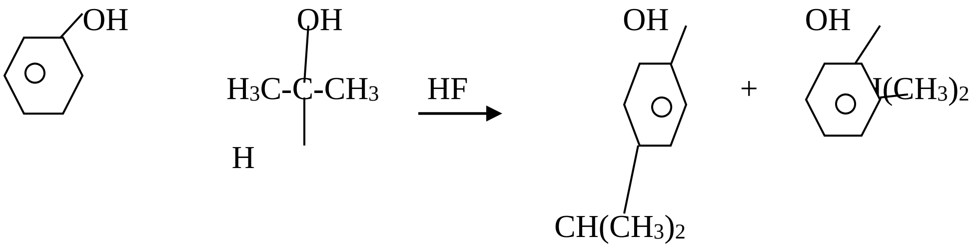
.



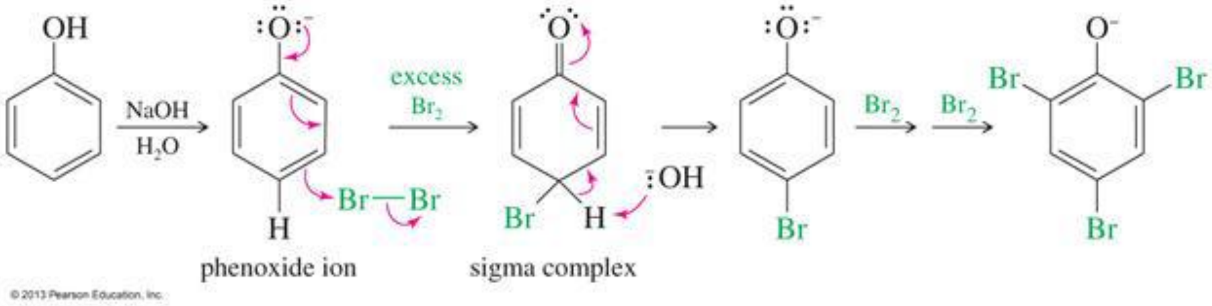
Most commonly this is achieved with chromic acid, although some phenols will auto-oxidize in the presence of air (oxygen).

4.15.3.2 Electrophilic Aromatic Substitution

Phenol is a very reactive substrate for EAS since the non-bonding electrons stabilize the sigma complex from attack at the ortho and para positions. The high reactivity of phenol allows the use of **weak** Lewis acid catalysts (e.g. HF) in alkyl-or acylations which helps prevent the possibility of overreaction.



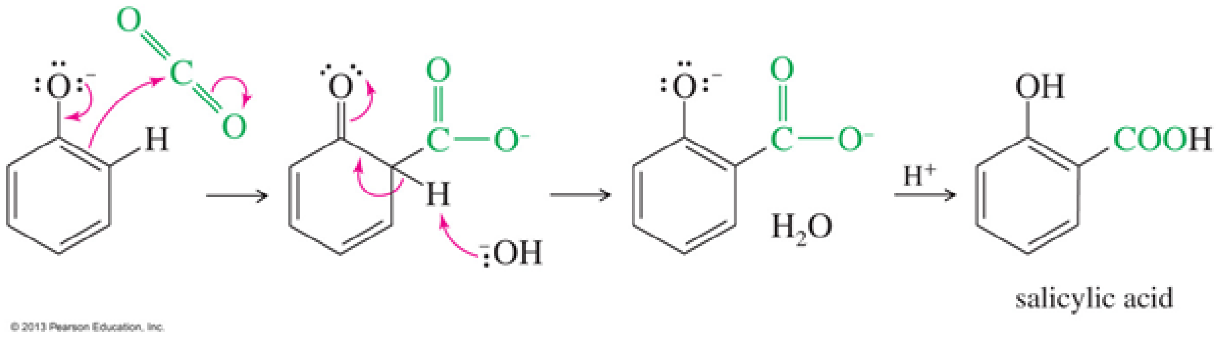
Phenoxide anions are even more reactive towards EAS, and the neutral sigma complexes that are formed resemble quinone type structures.



phenoxide ion

sigma complex

Phenoxide anions are so strongly activated that they even undergo EAS with carbon dioxide (a weak electrophile) e.g.



This is a useful and common industrial process (aspirin synthesis).

Chapter 5 Chemistry of C-Halogens Bond

5.1 Introduction

Organic **halogen** compounds are a large class of natural and synthetic chemicals that contain one or more halogens (fluorine, chlorine, bromine, or iodine) combined with carbon and other elements. The simplest organochlorine compound is chloromethane, also called methyl chloride (CH_3Cl). Other simple organohalogens include bromomethane (CH_3Br), chloroform ($CHCl_3$), and carbon **tetrachloride** (CCl_4). Some texts refer to this class of compounds as halogenoalkanes or alkyl halides.

5.2 Preparation

Organohalogens can be made in various ways

- (a) Preparation from Alcohols (nucleophilic substitution)

  $C_2H_5OH + HCl \longrightarrow C_2H_5Cl + H_2O$

- Preparation from Alkanes (radical substitution)

  $C_2H_6 + Cl_2 \xrightarrow{hv} C_2H_5Cl + HCl$

- Preparation from Alkenes (electrophilic addition)

  $CH_2{=}CH_2 + Cl_2 \longrightarrow ClCH_2CH_2Cl$

- Preparation by halogen exchange.*It is generally used for preparing iodoalkanes.

  $C_2H_5Cl + HI \longrightarrow C_2H_5I + HCl$

- Preparation from silver salts of acids

$$C_2H_5Cl + AgI \longrightarrow C_2H_5I + AgCl$$

- Aromatic organohalogens such as chlorobenzene are synthesized by treatment of benzene with halogen and a Lewis acid **catalyst** such as aluminum chloride

$$Ph + Cl_2 \xrightarrow{AlCl_3} PhCl + HCl$$

5.3 Naming Haloalkanes

Haloalkanes are named by adding a prefix to the name of the alkane from which they are derived. The prefix denotes the particular halogen used.

F = *Fluoro-*
Cl = *Chloro-*
Br = *Bromo-*
I = *Iodo-*

If other substituents need to be named, all prefixes are still put in alphabetical order. When necessary, numbers identify substituent locations.

Example names of haloalkane

	IUPAC name	**Common name**
CH_3—F	Fluoromethane	Methyl fluoride
CH_3—Cl	Chloromethane	Methyl chloride
CH_3—Br	Bromomethane	Methyl bromide
CH_3—I	Iodomethane	Methyliodide
F—CH_2—F	Difluoromethane	Methylene fluoride
Cl—CH_2—Cl	Dichloromethane	Methylene chloride
F—CH_2—Cl	Chlorofluoromethane	
CHBrClF	Bromochlorofluoromethane	
$HCCl_3$	Trichloromethane	Chloroform
CHX_3	Haloforms (X=halogen)	
CCl_4	Tetrachloromethane	Carbon tetrachloride
CH_3CHCl_2	1,1-Dichloroethane	
	(Dibromomethyl)cyclohexane	

5.4 Physical Properties

R-X bond polarity: C—F > C—Cl > C—Br > C—I

atom	**electronegativity**	**difference from C** (= 2.5)
F	4.0	1.5
Cl	3.0	0.5
Br	2.8	0.3
I	2.5	0.0

The difference in electronegativity of the carbon-halogen bonds range from 1.5 in C-F to almost 0 in C-I. This means that the C-F bond is extremely polar, though not ionic, and the C-I bond is almost nonpolar.

Physical appearance: Haloalkanes are colourless when pure. However bromo and iodo alkanes develop colour when exposed to light. Many volatile halogen compounds have sweet smell.

Boiling point: Haloalkanes are generally liquids at room temperature. Haloalkanes generally have a boiling point that is higher than the alkane they are derived from. This is due to the increased molecular weight due to the large halogen atoms and the increased intermolecular forces due to the polar bonds, and the increasing polarizabilty of the halogen.

For the same alkyl group, the boiling point of haloalkanes decreases in the order RI > RBr > RCl > RF.This is due to the increase in van der Waals forces when the size and mass of the halogen atom increases.

For isomeric haloalkanes, the boiling point decrease with increase in branching. But boiling points of dihalobenzenes are nearly same; however the para-isomers have higher melting points as it fits into the crystal lattice better when compared to ortho- and meta-isomers.

Density: Haloalkanes are generally more dense than the alkane they are derived from and usually more dense than water. Density increases with the number of carbon and halogen atom. It also increases with the increase in mass of halogen atom.

Solubility: The haloalkanes are only very slightly soluble in water, but dissolves in organic solvents. This is because for dissolving haloalkanes in water the strong hydrogen bonds present in the latter has to be broken. When dissolved in organic (non polar) solvents, the intermolecular attractions are almost same as that being broken.

Bond Length: C—F < C—Cl < C—Br < C—I

bond length (pm)	
C-F	138
C-Cl	177
C-Br	193
C-I	214

Larger atoms means larger bond lengths, as the orbitals on the halogen is larger the heavier the halogen is. In F, the orbitals used to make the bonds is 2s and 2p, in Cl, it's 3s and 3p, in Br, 4s and 4p, and in I, 5s and 5p. The larger the principal quantum number, the bigger the orbital. This is somewhat offset by the larger effective nuclear charge, but not enough to reverse the order.

5.4.1 Structure and properties

- Alkyl halide compounds are mostly dense liquids and solids that are insoluble in water.
- The halogens are all more electronegative than carbon and this makes the carbon-halogen bond a polar bond with a slight positive charge ($\delta +$) residing on the carbon end of the bond and a slight negative charge ($\delta -$) on the halogen end.
- The carbon-halogen bond strength decreases in the order C-F > C-Cl > C-Br > C-I
- Alkyl fluorides tend to be less reactive than other alkyl halides, mainly due to the higher strength of the C-F bond.

5.5 Chemical Reactivity

The reactivity of organo halogens varies enormously. The war gases phosgene (ClCOCl) and mustard ($ClCH_2CH_2SCH_2CH_2Cl$) are very reactive and highly toxic, whereas most other organo halogen compounds are relatively **inert** . Nevertheless, organo halogens undergo many chemical transformations. One common reaction is elimination, induced by the action of a strong base

Bond strength: C—F > C—Cl > C—Br > C—I

bond strength (kJ mol^{-1})	
C-F	484
C-Cl	338

C-Br	276
C-I	238

The orbitals C uses to make bonds are 2s and 2p. The overlap integral is larger the closer the principal quantum number of the orbitals is, so the overlap is larger in the bonds to lighter halogens, making the bond formation energetically favorable.

Bond reactivity: C—F < C—Cl < C—Br < C—I

Stronger bonds are more difficult to break, making them less reactive. In addition, the reactivity can also be determined by the stability of the corresponding anion formed in solution. One of the many trends on the periodic table states that the largest atoms are located on the bottom right corner, implying that iodine is the largest and fluorine being the smallest. When fluorine leaves as fluoride (if it does) in the reaction, it is not so stable compared to iodide. Because there are no resonance forms and inductive stabilizing effects on these individual atoms, the atoms must utilize their own inherent abilities to stabilize themselves. Iodide has the greatest surface area out of these four elements, which gives it the ability to better distribute its negative charge that it has obtained. Fluorine, having the least surface area, is much more difficult to stabilize. This is the reason why iodine is the best leaving group out of the four halogens discussed.

5.6 Test For Haloalkanes

Determination of Haloalkanes: A famous test used to determine if a compound is a haloalkane is the Beilstein test, in which the compound tested is burned in a loop of copper wire. The compound will burn green if it is a haloalkane. The numbers of fluorine, chlorine, bromine and iodine atoms present in each molecule can be determined using the sodium fusion reaction, in which the compound is subjected to the action of liquid sodium, an exceptionally strong reducing agent, which causes the formation of sodium halide salts. Qualitative analysis can be used to discover which halogens were present in the original compound; quantitative analysis is used to find the quantities.

5. 7 Substitution reactions of haloalkanes

R-X bonds are very commonly used throughout organic chemistry because their polar bonds make them reasonably reactive. In a **substitution reaction**, the halogen (X) is replaced by another substituent (Y). The alkyl group (R) is not changed.

The ":" in a chemical equation represents a pair of unbound electrons

A general substitution reaction

Y: + R—X → R—Y + X:

Substitutions involving haloalkanes involve a type of substition called **Nucleophilic substitution**, in which the substituent Y is a **nucleophile**. A nucleophile is an electron pair donor. The nucleophile replaces the halogen, an *electrophile*, which becomes a **leaving group**. The leaving group is an electron pair acceptor. Nuclephilic substition reactions are abbreviated as S_N reactions.

"Nu" represents a generic nucleophile.

General nucleophilic substitution reactions

Nu:$^-$ + R—X → R—Nu + X:$^-$
Nu: + R—X → R—Nu$^+$ + X:$^-$

Common Nucleophiles

Reagent	**Nucleophile**	**Name**	Product	Product name
NaOH/KOH	:O$^-$H	Hydroxide	R—OH	Alcohol
NaOR'	:O$^-$R'	Alkoxide	R—O—R'	Ether
	:S$^-$H	Hydrosulfide	R—SH	Thiol
NH_3	:NH_3	Ammonia	R—NH_3^+	Alkylammonium ion
KCN	:C$^-$N	Cyanide	R—CN	Nitrile
AgCN	Ag-CN:	Silver cyanide	R-NC	isonitrile
	:C$^-$≡C—H	Acetylide	R-C≡C—H	Alkyne
NaI	:I$^-$	Iodide	R—I	Alkyl Iodide
R'$^-$M$^+$	:R'$^-$	Carbanion	R-R'	Alkane
KNO_2	O=N—O	Nitrite	R–O—N=O	Alkyl nitrite
$AgNO_2$	Ag—Ö—N=O	Silver nitrite	R—NO_2	Nitroalkane

$LiAlH_4$	H	Hydrogen	RH	alkane
R'COOAg	$R'COO^-$	Alkanoate	R'COOR	Ester

Example: Suggest a reaction to produce the following molecule.

1-ethoxy-3-methylbutane

Answer:

1-bromo-3-methyl Butane + Ethanolate

OR

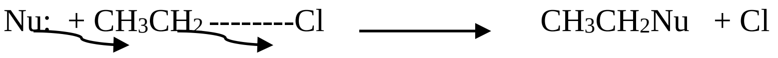
3-methylbutan-1-olate + Bromoethane

Any halogen could be used instead of Br

5.7.2 Reaction mechanisms

Nucleophilic substitution can occur in two different ways. S_N2 involves a **backside attack**. S_N1 involves a **carbocation intermediate**.

S_N2 mechanism



$$Nu{:} + CH_3CH_2\text{--------}Cl \longrightarrow CH_3CH_2Nu + Cl$$

Illustration of the Sn2 mechanism.

First, the electrons in the nucleophile attack the central carbon atom from the side opposite the leaving group (in this case, a halogen). The electrons forming the bond between the central carbon atom and the halogen move to the halogen, causing the halogen to leave the molecule.

S_N1 mechanism

$$CH_3CH_2\text{--------}Cl \longrightarrow CH_3CH_2^+ + Nu{:} \longrightarrow CH_3CH_2Nu + Cl^-$$

Illustration of the Sn1 mechanism.

First, in the presence of a polar solvent, the C-X bond breaks, forming the carbocation. This carbocation intermediate is highly reactive. In this case, it reacts with water. Note that the water may attack from either side.

5.7.2.1 Comparison of S_N1 and S_N2 mechanism

Stereochemistry:
S_N2 - Configuration is inverted (i.e. R to S and vice-versa).
S_N1 - Product is a mixture of inversion and retention of orientation because the carbocation can be attacked from either side. In theory the products formed are usually racemic due to the 50% change of attack from the planar conformation. Interestingly, the amount of the inverted product is often up to 20% greater than the amount of product with the original orientation. Saul Winstein has proposed that this discrepancy occurs through the leaving group forming an ion pair with the substrate, which temporarily shields the carbocation from attack on the side with the leaving group.

5.7.3Rate of reaction:

S_N2 - Rate depends on concentrations of both the haloalkane and the nucleophile. S_N2 reactions are fast.
S_N1 - Rate depends only on the concentration of the haloalkane. The carbocation forms much slower than it reacts with other molecules. This makes S_N1 reactions slow.

5.7.3.1 Role of solvent:

S_N2 - Polar aprotic solvents favored. Examples: Acetone, THF (an ether), dimethyl sulfoxide, n,n-dimethylformamide, hexamethylphosphoramide (HMPA).
Nonpolar solvents will also work, such as carbon tetrachloride (CCl_4)
Protic solvents are the worst type for S_N2 reactions because they "cage," or solvate, the nucleophile, making it much less reactive.
S_N1 - Polar protic solvents favored. Examples: H_2O, Formic acid, methanol.
Aprotic solvents will work also, but protic solvents are better because they will stabilize the leaving group, which is usually negatively charged, by solvating it. Nonpolar solvents are the worst solvent for S_N1 reactions because they do nothing to stabilize the carbocation intermediate.

5.7.3.2 Role of nucleophile:

S_N2 - Good nucleophiles favored
S_N1 - Any nucleophile will work (since it has no effect on reaction rate)

Carbocation stability:
3° carbon - most stable = S_N1 favored
2° carbon - less stable = either could be favored
1° carbon - seldom forms = S_N2 favored
CH_3^+ - never forms = S_N2 favored
The reason why the tertiary carbocation is most favored is due to the inductive effect. In the carbocation intermediate, there is a resulting formal charge of +1 on the carbon that possessed

the haloalkane. The positive charge will attract the electrons available. Because this is tertiary, meaning that adjacent carbon atoms and substituents are available, it will provide the most electron-density to stabilize this charge.

Example

5.7.3.4 Grignard reagents

Grignard reagents are created by reacting magnesium metal with a haloalkane. The magnesium atom gets between the alkyl group and the halogen atom with the general reaction:

R-Br + Mg → R-Mg-Br

Gringard reagents are very reactive and thus provide a means of organic synthesis from haloalkanes. For example, adding water gives the alcohol R-OH. Basic: R-X + Mg → R-Mg-X For example (X=Cl and R=CH3): CH3-Cl + Mg → CH3MgCl (methylmagnesiumchloride)

5.7.3.5 Elimination reactions

With alcoholic potassium hydroxide, haloalkanes lose H-X and form the corresponding alkene. Very strong bases such as KNH_2/NH_3 convert vic-dihalides (haloalkanes with two halogen atoms on adjacent carbons) into alkynes.

5.8 Toxicity

As with all chemicals, "the dose makes the poison." The chlorine-containing insecticide dichlorodiphenyltrichloroethane (DDT) is highly effective in killing disease-ridden mosquitoes, ticks, and fleas, but it is virtually nontoxic to mammals. The fluorine-containing pesticide "1080," or fluoroacetic acid (FCH_2CO_2H), is highly toxic and often lethal to all mammals. The industrial and **combustion** by-product dioxin is highly toxic to some animals but not to others; in humans, dioxin causes the skin disease chloracne.

5.9 Use

Organohalogens are widely used in industry and society. Chloromethane is used as a solvent in rubber polymerization. Bromomethane is an important fumigant; the related halons ($CBrClF_2$ and $CBrF_3$) are better fire extinguishants than carbon dioxide.

Eighty-five percent of all pharmaceutical agents and **vitamins** involve chlorine chemistry; many drugs require chlorine, fluorine, or bromine to be effective. Ceclor and Lorabid are used to treat ear infections, Toremifene is a breast-cancer drug, and the natural antibiotic vancomycin is used to fight penicillin-resistant infections. Benzyl chloride is used to synthesize the drugs phenobarbital, benzedrine, and demerol. Inhalation anesthetics include the organofluorines desflurane, sevoflurane, and enflurane ($CHClFCF_2OCHF_2$). Perfluorocarbons, such as perfluorotributylamine ($[CF_3CF_2CF_2CF_2]_3N$), are used as blood substitutes or blood extenders ("artificial blood") and are used for coronary angioplasty. The insecticide DDD (mitotane), related to DDT, is used to treat inoperable adrenal cancer. Vinyl chloride ($CH_2=CHCl$), a carcinogenic gas, is polymerized to polyvinyl chloride (PVC), a plastic of great versatility and safety. PVC is an invaluable component of building materials, consumer goods, medical equipment, and many other everyday products. More than 2.2 billion kilograms (5 billion pounds) of PVC are used annually for wire, cable, and other electrical applications. The chlorine in PVC makes this plastic flame retardant and ideal for construction and furnishing applications. Polytetrafluoroethylene (Teflon) is the polymer of tetrafluoroethylene ($CF_2=CF_2$). Because of its chemical stability (very strong carbon-fluorine bonds), it has many diverse applications in our society; best known perhaps are the coatings used to make "nonstick" cookware. Trichloroethylene ($CHCl=CCl_2$) and tetrachloroethylene ($CCl_2=CCl_2$, "Perc") are widely used solvents in the dry cleaning industry.

Organohalogens are essential for crop production and protection as herbicides and insecticides. Ninety percent of grain farms utilize these chemicals in food production. Polychlorinated biphenyls (PCBs) were introduced in 1929 as insulators in capacitors and transformers in the electric power industry, as lubricants and coolants in vacuum pumps, as paint additives, and in food packaging. The manufacture and use of PCBs were discontinued in 1977 because of their adverse effects on the environment. Their effect on humans is still unknown.

Chlorofluorocarbons (CFCs or freons) are strongly implicated in causing the ozone hole, and are being phased out of use as refrigerants, dry cleaning solvents, propellants, fire extinguishants, and foam-blowing agents. These chemicals include CFC-11 (CCl_3F), CFC-13 ($CClF_3$), and CFC-112 (CCl_2FCCl_2F). Replacements for CFCs are the hydrochlorofluorocarbons (HCFCs) and the hydrofluorocarbons (HFCs), both of which have no impact on stratospheric ozone and have low global warming potential. Examples include HCFC-21 ($CHCl_2F$) and HFC-152 (FCH_2CH_2F).

5.10 Natural Occurrence

Many are the same as synthetic chemicals. They are biosynthesized by marine organisms, bacteria, fungi, plants, insects, and some mammals, including humans. Algae, wood-rotting fungi, mushrooms, several trees, phytoplankton, and even potatoes produce chloromethane. Termites are a major producer of chloroform, and several vegetables produce bromomethane. One hundred organohalogens have been found in the favorite edible seaweed of native Hawaiians.

Chloride and bromide salts are normally present in plants, wood, soil, and minerals; as a result, forest fires and volcanoes produce organohalogens. Meteorites contain organochlorines. Global emissions of chloromethane from the **biomass** are 5 million tons per year, whereas synthetic emissions are only 26,000 tons per year. Volcanoes also emit hydrogen chloride (3 million tons/year) and hydrogen fluoride (11 million tons/year), both of which can react with organic compounds to produce organohalogens. Chlorofluorocarbons have been detected in volcanic emissions in Guatemala and Siberia, but a study of volcanoes in Italy and Japan indicates that they may not be a major source of environmental CFCs.

Seaweeds contain hundreds of organohalogens (see Figure 4). Telfairine, like the synthetic insecticide lindane, is a powerful insecticide. These organohalogens are used by marine life in chemical defense (natural pesticides). The "smell" of the ocean is likely due to the myriad **volatile** organohalogens produced by seaweeds.

Organohalogens also serve as hormones. Vegetables such as lentils, beans, and peas synthesize the growth hormone 4-chloro-3-indoleacetic acid. A cockroach produces two chlorine-containing steroids as aggregation pheromones. Female ticks use 2,6-dichlorophenol as a sex attractant. Thyroid hormones (see Figure 1) contain iodine, and an organobromine is involved in the mammalian sleep phenomenon.

Just as iodine is used to treat cuts and chlorine (bleach) to disinfect bathrooms, our white blood cells generate chlorine and bromine to kill germs and fight infection. The sponge **metabolite** spongistatin and the blue-green alga cryptophycin, both of which contain a chlorine atom essential for biological activity, are powerful anticancer drugs. Ambigol, found in terrestrial blue-green alga, is active against human immunodeficiency virus (HIV). An Ecuadorian frog produces an organochlorine that is 500 times more potent than morphine; a synthetic analog is under development as a new anesthetic.

Although some synthetic organohalogens are toxic contaminants that need to be removed from the environment, the vast majority of organohalogens have little or no toxicity. Organic halogen compounds continue to play an essential role in human health and well being as chemists pursue the study of these fascinating chemicals

Chapter 6 Chemistry of Hydroxyl Group

6.1 What are Alcohols?

Alcohols are organic compounds with and hydroxyl group attached to its skeleton (R-OH). It has a general formula $C_nH_{2n+1}OH$ where n =1 – infinity

The smallest member (n=1) is methanol (CH_3OH). Alcohols with long hydrocarbon chains are called fatty alcohols

6.2 Physical Properties of Alcohols

Hydrogen bonding

Physical properties of alcohols of comparable molecular weight with hydrocarbons are markedly different from each other especially for the lower members. They are less volatile, have higher melting and boiling points, and greater solubility in water. The differences diminish as the molecular weight increases. The difference is because of the OH group attached to the hydrocarbon skeleton confers some polarity on the molecule which allow attraction between molecules. This will lead to association of alcohol molecules especially in liquid and solids. The hydrogen of one molecule is attracted to the oxygen of a neighboring molecule. This bonding is called Hydrogen bonding. The bond strength of an H-bond is about 5-10 kcal which is much less than a regular chemical bond but contributes to the bond strength of alcohol and why alcohol boils at a higher boiling point that its corresponding hydrocarbons of similar weight (CH_3CH_2OH-78.5 ^0C/ CH_3CH_3-30^0C). The lower member of alcohols is very miscible with water because of the hydrogen bonding. The physical properties of the higher molecular weight alcohols are similar to that of the corresponding hydrocarbon.

6.3 Spectroscopic Properties

Infrared- gas – sharp peal at 3700 cm^{-1} liquid (hydrogen bonding effect) broad and faint peak at 3600-3350 cm^{-1}. The frequency of absorption is a reflection of the strength of the H-bond. The lower the frequency the stronger the bond

NMR- ~ 3 ppm. H- bonding also affect the chemical shift of the OH group. The chemical shift depends on the nature of solvent, concentration and temperature of operation. OH resonates at a lower field relative to TMS as the strength of the H- bond increases.

6.4 Preparation of Alcohols

1. Hydration of Alkenes- $CH_2{=}CH_2 \xrightarrow{H_2O,\ 10\%\ H_2SO_4,\ 240^0} CH_3CH_2OH$

2. Hydroboration of alkyl boranes wit Hydrogen Peroxide-

$$(CH_2)_3B + 3H_2O_2 \longrightarrow (CH_2)_3OH + B(OH)_3$$

3. Addition of Hypohalous acids to alkenes and alkadienes
   $CH_2{=}CH_2 + HOCl \longrightarrow ClCH_2CH_2OH$
   $CH_2{=}CHCH_2CH{=}CH_2 + HOCl \longrightarrow CH_2{=}CHCH_2CHClCH_2OH$
4. Hydrolysis of Alkyl and Alkenyl halides
   $CH_3Cl + H_2O \longrightarrow CH_3OH + HCl$
   $CH_2{=}CHCH_3 + \xrightarrow{Cl_2,\ H_2O} CH_2{=}CHCH_2OH + HCl$
5. Addition of Grignard Reagent to Carbonyl compounds
   $CH_3MgI + HC{=}O \longrightarrow CH_3CH_2OH + MgIOH$

6. Reduction of Carbonyl Compounds
   $(CH_2)_3C{=}O \; + \xrightarrow{LiAlH_4,\ H_2O,\ H^+} (CH_2)_3COH$

7. Fermentation of Carbohydrates
   $C_6H_{12}O_6 \xrightarrow{\text{fermentation}} C_5H_{11}OH + CO_2$

6.5 Chemical Reactions of Alcohols

6.5.1. Reactions Involving the O-H Bond

(a) **Acids and Bases**

Many reactions involve the O-H bond leaving the C-O bond intact. Examples include salt formation with acids and bases

Alcohols is similar to water in nature because they are amphoteric. They act as acids or bases in many cases. The dissociation constant, K of ethanol is 1.0 x 10^{-18} shich is close to that of water $(10^{-14})^{.}$

$CH_3CH_2OH + NaNH_2 \longrightarrow CH_3CH_2ONa + NH_3$ – acid behavior

The order of the acid behavior of alcohols is $1^0 > 2^0 > 3^0$. The anion of alcohols (RO^-) are called alkoxides

Alcohols are weak base relative to water and are converted to stable salts with strong acids

$CH_3CH_2OH + HBr \longrightarrow CH_3CH_2OH_2^+ + Br^-$

(b) Ether Formation- Williamson Synthesis

Alcohols forms an alkoxide which is a strong base that reacts with alkyl halides or sulfates to form ethers. This reaction is called **Williamson Synthesis** (SN_2 Reaction)

$CH_3I + CH_3CH_2OH \longrightarrow CH_3CH_2OCH_3 + HI$

Complications in this reaction may occur because the reaction is also accompanied by strong E_2 reactions. E_2 reactions depend on the structure of the halide and the alkoxide and temperature. Primary halide with a secondary alkoxide gives an SN_2 product

$CH_3I + CH_3CH_2OH \longrightarrow CH_3CH_2OCH_3 + HI$

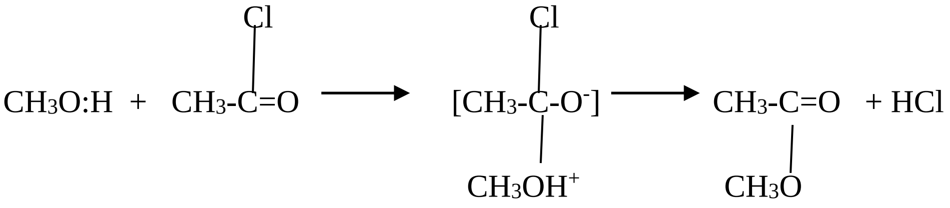
while a primary alkoxide and a secondary halide give an elimination product

$CH_3O^- + (CH_3)_2CHI \longrightarrow CH_3CH{=}CH_2 + CH_3OH$

(c) **Ester Formation**

The lone pair of electron on the oxygen of the alcohol makes alcohol a good Lewis base in a reaction with a Lewis acid. Examples of Lewis acids (electron acceptor) include Boron trifluoride, acyl halides carboxylic anhydrides and carboxylic acids. Acyl halides have a very electrophilic carbonyl carbon-hydrogen bond that can react with powerful

Lewis bases like alcohol to form an ester. The reaction is an addition-elimination reaction process. Little amount of strong mineral acids catalyzes formation of esters from alcohols. Esterification is a reversible reaction. Steric hindrance in the alcohol or acid affects the rate of formation an ester. It slows down the reaction. The ease of formation of an ester is $1^0 > 2^0 > 3^0$ CH_3O



$$CH_3O{:}H + CH_3\text{-}\overset{Cl}{C}{=}O \longrightarrow [CH_3\text{-}\underset{CH_3OH^+}{\overset{Cl}{C}}\text{-}O^-] \longrightarrow CH_3\text{-}\underset{CH_3O}{C}{=}O + HCl$$

6.5.2 Reactions Involving the C-O bond of Alcohols

(a) Halide formation

Reactions of alcohols with a strong acid like HBr breaks the C-O bond of the alcohol to form an alkyl halide

$R\text{-}OH + HBr \longrightarrow RBr + H_2O$

The reaction is reversible and favored by the presence of strong acid such as sulfuric acid and the concentration of water in the reaction. The reaction proceeds first by protonating the alcohol (alkyloxonium ion) and then followed by nucleophilic displacement of water molecule by the halide ion.

Thionyl chloride ($SOCl_2$) is a good reagent that can be used to prepare alkyl halides form alcohol

$ROH + SOCl_2 \longrightarrow RCl + HCl + SO_2$

(b) Esters of sulfuric acid- Dehydration of Alcohols

$H_2SO_4 + ROH \longrightarrow ROSO_3H + H_2O$

Most alcohols can also dehydrate to give ethers or alkenes

$ROH + H^+ \longrightarrow R{=}CH_2 + H_2O$

$ROH + H^+ \xrightarrow{ROH} ROR + H_2O$

(C) Oxidation of Alcohols

Alcohols can be oxidized to ketones and carboxylic acids

$RCH_2OH \xrightarrow{[O]} RCOH \xrightarrow{[O]} RCOOH$

$R_2CHOH \xrightarrow{[O]} R_2C{=}O$

1^0 Alcohols gives aldehyde before been oxidized to a carboxylic acid while 2^0 and 3^0 alcohols gives ketones.

6.6 Polyhydric Alcohols

Polyhydric alcohols are alcohols with more than one OH group. The simplest polyhydric alcohol is methylene glycol (diol). Polyhydric alcohols with OH group on different carbons are relatively stable, highly soluble in water and insoluble in non-polar solvents and with high boiling point because of hydrogen bonding. 1,2- diols are prepared by oxidation of alkenes with oxidizing agent like osmium tetroxide and potassium permanganate. Ethylene glycol has a lot of commercial usage such as antifreeze and detergents. Trihydric alcohols (glycerol) also has great commercial use such as synthesizing fatty acids esters (soap) and humectants.

6.7. Unsaturated Alcohols

The simplest unsaturated alcohol is vinyl alcohol which is unstable ($CH_2=CHOH$) Its ester has great commercial use. Unsaturated alcohols behave more like alkenes in their reaction because of the unsaturation in them

Exercise

1. What type of infrared absorption bands due to hydroxyl groups would you expect for trans-cyclobutane-1,2 diol (a) in very dilute solution (b) in moderately concentrated solution and (c) as pure solution
2. Predict the major product of the following reactions?
   (a) $(CH_3)_2CCH_2I + C_2H_5O^-$
   (b) $(CH_3)_3CBr + CH_3O^-$
   (c) $C_6H_{12}\text{-}Cl + (CH_3)_3CBO^-$
   (d) $PhCH_2Br + (CH_3)_2CHCH_2O^-$
   (e) $(CH_3)_2CHCH_2Br + C_6H_5CH_2O^-$
3. In the esterification of an acid with an alcohol, how could you distinguish between C-O and O-H cleavage of the alcohol using heavy oxygen (^{18}O) as a tracer?

$$CH_3O\text{-}|\text{-}H + RCO\text{-}|\text{-}OH \xrightarrow{H^+} RCOOCH_3 + H_2O$$

$$CH_3\text{-}|\text{---}OH + RCOO\text{--}|\text{-}H \xrightarrow{H^+} RCOOCH_3 + H_2O$$

4. What type of alcohols might conceivably react by C-O cleavage, and what side reactions would you anticipate for such alcohols
5. The reaction of methyl acetate with sater to give methanol anc acetic acid is catalyzed by strong mineral acids such as sulfuric acid, Furthermore, when the hydrolysis is carried

out in ^{18}O water, the following exchange takes place faster than the formation of methanol.

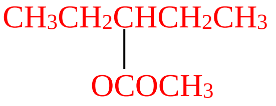
$$CH_3COOCH_3 + H_2O^{18} \xrightarrow{H^+} CH_3CO^{18}OCH_3 + H_2O$$

No methanol $CH_3{}^{18}OH$ is formed in the hydrolysis under this conditions

(a) Write a stepwise mechanism which is harmony with the acid hydrolysis catalysis ans with the result obtained in ^{18}O water. Mark the steps of the reaction that indicated to be fast or slow

6. Show how you would synthesize each of the following substances from the given organix starting materials and other necessary organic or inorganic reagents. Specify reagents and conditions?

(a) $CH_3CH_2CH_2C(CH_3)_2Cl$ from $CH_3CH_2CH_2COH$

(b) 
$CH_3CH_2\underset{OCOCH_3}{\underset{|}{C}}HCH_2CH_3$ from CH_3CH_2OH

(c) $(CH_3)_2CHCH_2Br$ from $(CH_3)_3COH$

(d) $(CH_3)_3CCH_2CH_3$ from $(CH_3)_3COH$

Chapter 7 Ethers

7.1 Introduction

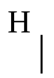
When the Hydrogen of the hydroxyl group of alcohols is replaced by a hydrocarbon group an ether is formed. An ether can be represented as ROR, where R are alkyl groups which may be the same or different. Ethers could be acyclic, cyclic aromatic, saturated or unsaturated. Ethers are not very reactive except in the presence of an acid because its C-O bond is not easy to break. Because of this, ethers are often used as solvents in other reactions. Typical ethers used as solvents are diethyl, diisopropyl, tetrahydrofuran and 1,4 dioxane ethers. Common names for some ethers are: Cellosolve (Monoalkyl ethers of diethylene glycol), carbitols (Monoalkyl ethers of triethylene glycol), polyglymes (Monoalkyl ethers of di ethylene glycol), triglyme (Monoalkyl ethers of triethylene glycol)

7.2 Reactions of Ethers

(i) **Bases**: Ethers do not react with bases. However, certain strong bases like alkali metal alkyls react destructively with ethers

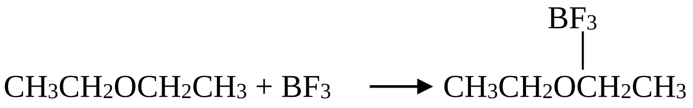
$$CH_3ONa + CH_3CH_2OCH_2CH_3 \longrightarrow CH_4 + CH_2{=}CH_2 + CH_3CH_2ONa$$

(2) **Acids:** Ethers are weak acids and will react with strong acids (HBr, H_2SO_4, $HClO_4$) to form unstable oxonium salts



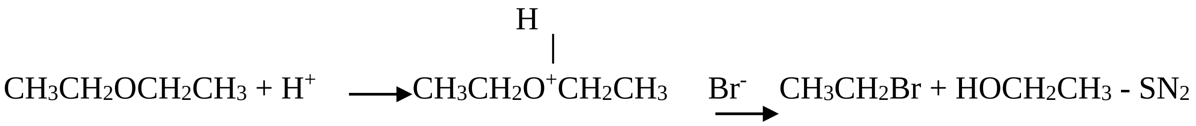
$CH_3CH_2OCH_2CH_3 + HBr \longrightarrow CH_3CH_2O^+CH_2CH_3 + Br^-$

and stable coordination complexes with Lewis acids such as BF_3

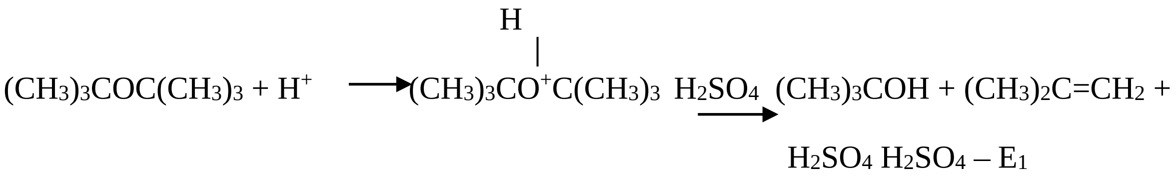


$$CH_3CH_2OCH_2CH_3 + BF_3 \longrightarrow CH_3CH_2\overset{BF_3}{\overset{|}{O}}CH_2CH_3$$

Acid activated ethers (oxonium ions) are more reactive than neutral ethers and are susceptible to nucleophilic substitution and elimination reactions



$$CH_3CH_2OCH_2CH_3 + H^+ \longrightarrow CH_3CH_2\overset{H}{\overset{|}{O^+}}CH_2CH_3 \xrightarrow{Br^-} CH_3CH_2Br + HOCH_2CH_3 - S_N2$$



$$(CH_3)_3COC(CH_3)_3 + H^+ \longrightarrow (CH_3)_3C\overset{H}{\overset{|}{O^+}}C(CH_3)_3 \xrightarrow{H_2SO_4} (CH_3)_3COH + (CH_3)_2C{=}CH_2 + H_2SO_4\ H_2SO_4 - E_1$$

(3) Radicals

Ethers react with radicals and cannot be used in free radical reactions. In the presence of oxygen, ethers undergo autoxidation to form peroxides which are unstable are explosive. Common ether solvents like diethyl, diisopropyl, tetrahydrofuran and 1,4-dioxane ethers are easily contaminate with peroxides after a long time of storage

Cyclic Ethers

The simplest ether is ethylene oxide (CH_2CH_2O) and its reaction is an exception to the generalization that ethers are resistant to cleavage because of the strain in the ring which readily opens under mild conditions to form other products such as ethylene glycol, diethylene glycol, cellosolves and carbitols. Trimethylene oxide is lesser known but it also readily open up for reaction, Tetrahydrofuran ($(CH_2)_4O$)) is very stable and is miscible with water. It is often used instead of diethyl ether in Grignard reactions and reduction with Lithium aluminum hydride.

Exercise

Predict the products likely to be formed on cleavage of the following ethers with hydrobromic acid

(a) $CH_2{=}CHCH_2OCH_3$
(b) $CH_3CH_2OCH{=}CH_2$
(c) $(CH_3)_3CCH_2OCH_3$
(d) $(CH_2)_4O$

(e) Ph-O-CH_3

Chapter 8 Thiols and Thioethers

8.1 Introduction

Sulfur is below oxygen in group VI of the periodic table. Its chemistry is different to its oxygen analog because sulfur is not electron attracting as oxygen. In this regard, sulfur electron attracting ability lies between that of carbon and nitrogen and is very reluctant to forming double bonds. Hence, thiocarbonyl compounds (-C=S-) are not common and unstable with respect to polymerization due to low effectiveness of π-type overlap involving 3p orbitals. Also the element S_2 unlike O_2 is unstable and only stable in elemental form as cyclic S_8. The inability of S to form double bond with Carbon is also exhibited by Si and phosphorus and no stable compound of C=S and C=P is known. Despite of lack of π- bonding by S, many chemistry of sulfur compounds are influenced by π- type bonding through the overlap of empty d-orbitals in sulfur. Π-d bonding is possible when sulfur is bonded to atoms like oxygen: here both σ bonds with oxygen and π bonding may form through sharing of lone pairs of electron on oxygen with the empty d- orbital of sulfur (p_x-d_x overlap). The p_x-d_x double bond is differences from the normal p- p_x-d_x double bond because it occurs because sulfur expanded its octet shell to hold more than eight electrons. It is evident that a double bond character exist is compounds such as dimethyl sulfoxide ($((CH_3)_2SO_2$ from its IR signal, high polarity of S-O bond and the bond distances of the –O bond.

8.2 Nomenclature

Sulfur compounds are classified as whether sulfur is bivalent or more than bivalent. Bivalent sulfur compounds are structural analog of the oxygen counterparts. Sulfur derivatives are names with the prefix *thiol* with the name of the corresponding oxygen analog e.g.

CH_3CH_2OH	CH_3CH_2SH	Ph-OH	Ph-SH	$(CH_2)_4$	$(CH_2)_3S$
Ethanol	ethanethiol	Phenol	Thiophenol	Cyclobutane	thiacyclobutane

8.3 Thiols

Thiols (Mercaptans) are derivatives of H_2S just as alcohols are derivatives of H_2O. Acyclic and aromatic thiols are volatile and have rotten egg smell just like hydrogen sulfide (H_2S). Thiols and other sulfur compounds exist in crude petroleum and makes its refining difficult because they poison metal catalyst that are used in refining the petroleum. Thiols have both animal and plant origin. For example, butanethiol is present in skunk secretion, propanethiol is release when onion is cut and cysteine has thiol group are important in protein and enzymes chemistry

8.4. Preparation of Thiols

(1) Using alkyl halides, sulfates or sulfonates : $CH_3CH_2Br + NaSH \longrightarrow CH_3CH_2SH + NaBr$

(2) Grignard Reagents with Sulfur: Ph –MgBr $\xrightarrow{S, H^+, H_2O}$ Ph-SH + MgBrOH

Thiols do not form strong hydrogen bonding hence low molecular weight thiols have low boiling point than their corresponding alcohols (ethanol, 78^0C, and ethane thiol, 35^oC). However this differences in boiling point decrease as the chain length increases.

8.4.1 Spectroscopy

Lack of extensive hydrogen bonding results into weak IR signal at 2600-2550 cm^{-1}(S-H stretching). Change of concentration, state or solvents does not affect the IR signals of S-H stretching frequency because of lack of extensive hydrogen bonding.

Sulfur is less electronegative than oxygen hence they are stronger acids than the corresponding alcohols. Thiols readily form insoluble salts with heavy metals especially mercury, hence the origin of the name Mercaptans for thiols. Salts of thiols are called Mercaptides.

8.5 Chemical Reactions of Thiols

1. Thioethers: $CH_3CH_2Br + NaSH \rightarrow CH_3CH_2SH + NaBr$

$CH_3CH_2SH + NaSH \rightarrow CH_3CH_2SNa + H_2S \xrightarrow{CH_3CH_2Br} (CH_3CH_2)_2S + NaBr$

2. **ThioEsters**: $CH_3CH_2SH + CH_3COCH_3 \rightarrow CH_3COSCH_2CH_3 + HCl$

3. **Oxidation**: $RSH + [O] \rightarrow RS^{\cdot} + H[O] \quad 2RS^{\cdot} \rightarrow$ RS-S-R (disulfide)

$RSH \xrightarrow{[O]} RS\text{-}S\text{-}R \xrightarrow{HNO_3, [KMnO_4], [H_2O_2]} ROSOR \rightarrow RSO_2\text{-}SO_2\text{-}R \rightarrow RSO_3H$

disulfide thiosulfonate ester disulfone sulfonic acid

$RSH \xrightarrow{[O]} RS\text{-}OH \xrightarrow{HNO_3, [KMnO_4], [H_2O_2]} ROSOH \rightarrow RSO_3H$

Sulfenic acid sulfinic acid sulfonic acid

8.6 Organic Sulfides (Thioethers)

Preparation

1. $CH_3CH_2Br + NaSH \rightarrow CH_3CH_2SH + NaBr \xrightarrow{CH_3CH_2Br} (CH_3CH_2)_2S + NaBr$
2. $CH_3CH_2SH + CH_2{=}CH_2 \longrightarrow CH_3CH_2SCH_2CH_3$

8.6.2 Chemical Reactions

Thioethers undergo two important reactions involving the electron pairs on sulfur. They act as nucleophiles towards compounds that undergo nucleophilic displacement readily to give sulfonium salts which are rather oxidized to sulfoxides and sulfones

1. $(CH_3)_2S + CH_3I \leftrightarrow (CH_3)_3SI^-$

   trimethylsulfonium iodide

2. $(CH_3)_2S \xrightarrow[H_2O_2,\ CH_3CO_2H]{[O]} (CH_3)_2S{=}O \xrightarrow[H_2O_2,\ CH_3CO_2H]{[O]} (CH_3)_2SO_2$

   Dimethyl sulfoxide dimethyl sulfone

Sulfonium salts when substituted with three different groups can be separated into optical isomers