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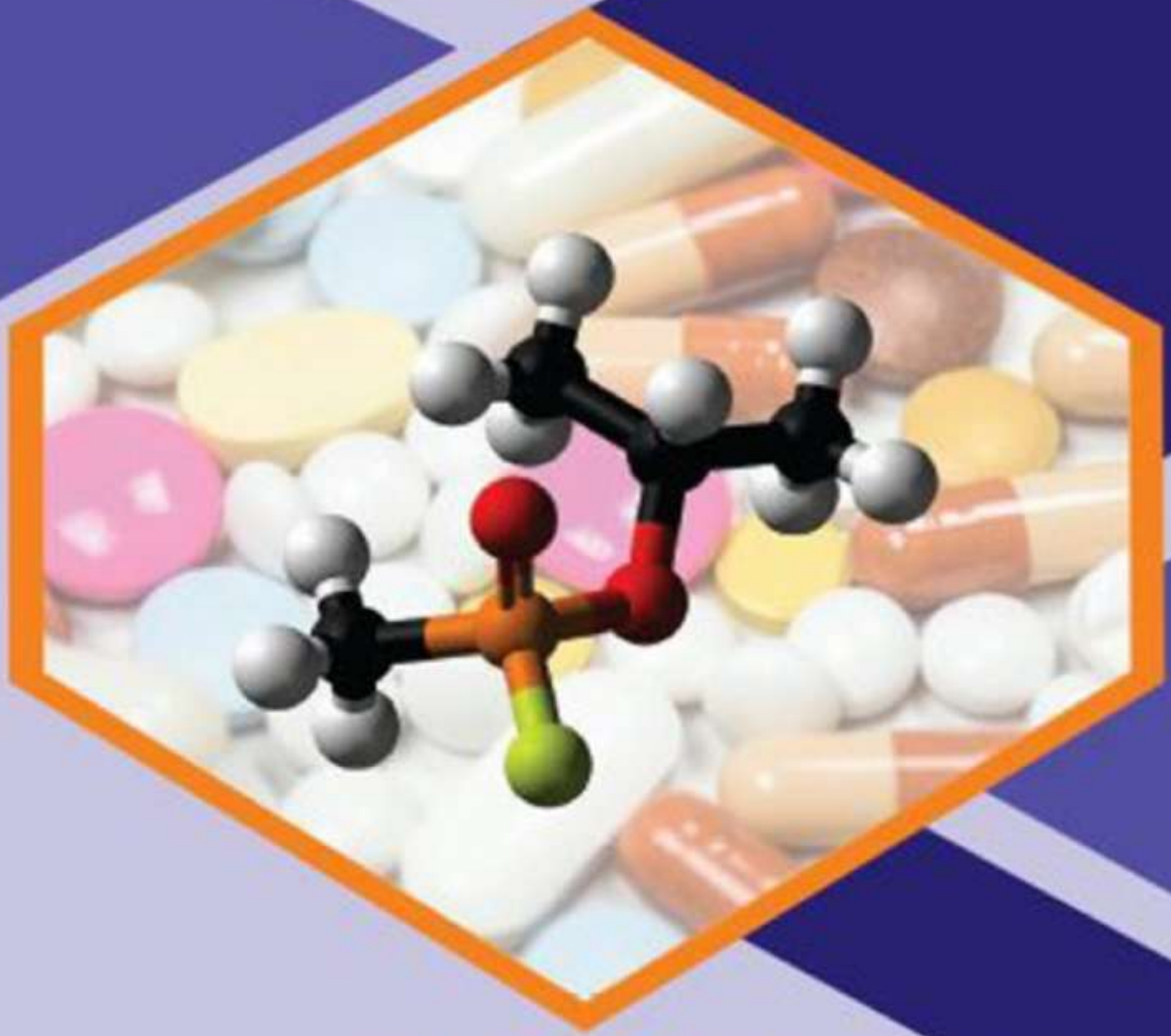
SECOND YEAR B. PHARM. | SEMESTER-III

PHARMACEUTICAL ORGANIC CHEMISTRY-II

Dr. K. G. BOTHARA



NIRALI PRAKASHAN
ADVANCEMENT OF KNOWLEDGE

A Text Book of

PHARMACEUTICAL ORGANIC CHEMISTRY-II

As per PCI Regulations

Second Year B. Pharm.

Semester – III

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Preface

Organic Chemistry deals with the name of composition of organic matter and more specifically the reasoning for the changes which it undergoes.

In the last three decades the ever growing volume and ever changing nature of our understanding about reaction mechanisms are witnessed. Author aims to describe the fundamental principles of organic chemistry with an emphasis on the characteristic reactions of various functional groups.

Special emphasis has been given to explain the basic principles and concepts underlying chemical reactions while in rest of the chapters, stress is given on structures and reactions of organic compounds. However, the wide scope of the subject has necessitated restrictions to keep the size of the book within reasonable limits.

I wish to place on record my sincere thanks to the publisher, Shri. D. K. Furia and Shri. Jignesh Furia for their kind co-operation. I am also indebted to my colleagues for giving many valuable suggestions, of which I have been glad to take advantage.

Suggestions from all corners of the profession are welcome. Author is responsible for any deficiencies or errors that remain and would be grateful if readers would call them to his attention.

Author

Pune

Syllabus

(As per PCI Regulations)

UNIT-I **10 Hours**

- **Benzene and its Derivatives**
  - A. Analytical, synthetic and other evidences in the derivation of structure of benzene, Orbital picture, resonance in benzene, aromatic characters, Huckel's rule
  - B. Reactions of benzene - nitration, sulphonation, halogenation reactivity, Friedel Crafts alkylation- reactivity, limitations, Friedel Crafts acylation.
  - C. Substituents, effect of substituents on reactivity and orientation of mono-substituted benzene compounds towards electrophilic substitution reaction
  - D. Structure and uses of DDT, Saccharin, BHC and Chloramine

UNIT-II **10 Hours**

- **Phenols**

  Phenols* - Acidity of phenols, effect of substituents on acidity, qualitative tests, Structure and uses of phenol, cresols, resorcinol, naphthols

  Aromatic Amines* - Basicity of amines, effect of substituents on basicity, and synthetic uses of aryl diazonium salts

  Aromatic Acids* - Acidity, effect of substituents on acidity and important reactions of benzoic acid.

UNIT-III **10 Hours**

- **Fats and Oils**
  - a. Fatty acids – reactions
  - b. Hydrolysis, Hydrogenation, Saponification and Rancidity of oils, Drying oils.
  - c. Analytical constants – Acid value, Saponification value, Ester value, Iodine value, Acetyl value, Reichert Meissl (RM) value – significance and principle involved in their determination.

UNIT-IV **08 Hours**

- **Polynuclear Hydrocarbons**
  - a. Synthesis, reactions
  - b. Structure and medicinal uses of Naphthalene, Phenanthrene, Anthracene, Diphenylmethane, Triphenylmethane and their derivatives

UNIT-V **07 Hours**

- **Cyclo Alkanes**

  Stabilities – Baeyer's strain theory, limitation of Baeyer's strain theory, Coulson and Moffitt's modification, Sachse Mohr's theory (Theory of strainless rings), reactions of cyclopropane and cyclobutane only.

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Unit I

FACTORS AFFECTING ELECTRON AVAILABILITY

♦ **SYNOPSIS** ♦

1.1 INTRODUCTION

The reactivity of any molecular towards a particular reaction largely depends upon its structural features. The structural features impart specific properties which influence the electron availability at a particular bond or atom. A molecule may easily be attacked by an electrophile (e.g. carbonium ion) if a region of high electron availability is present in it. Similarly nucleophiles can readily attack on the molecules containing electron-deficient positions. Such properties that govern the reactivity of a particular bond or an atom by influencing the relative availability of electrons are known as **structural effects**. The structural effects are mainly divided into

(a) Inductive effect
(b) Resonance effect
(c) Hyperconjugation
(d) Steric effects, and
(e) Tautomerism.

1.2 INDUCTIVE EFFECT

Because of the ability to attract the electrons, an electronegative atom does not allow equal sharing of the bonding electron pair, when it is bound covalently with another atom. In HCl molecule, for example, chlorine is more electronegative than hydrogen. Hence, electron pair is pulled slightly towards the chlorine atom. This results into development of partial positive charge on hydrogen and partial negative charge on chlorine.

Thus, HCl molecule is said to be polarised.

$\overset{+\delta}{H}-\overset{-\delta}{Cl}$ $(H \rightarrow Cl)$ $\quad$ $H_3C-\overset{-\delta}{Br}$ $(H_3C \rightarrow Br)$ $\quad$ $H_3C-CH_2-\overset{+\delta}{CH_2}-\overset{-\delta}{Br}$ $(H_3C \rightarrow CH_2 \rightarrow CH_2 \rightarrow Br)$

(1.1)

Table 1.1: Effect of inductive effect of halogen atom on acid strength

Acid	Structure	pKa at 25°C
(a) Acetic acid	CH_3COOH	4.76
(b) 2-chlorobutanoic acid	CH_3CH_2 CHClCOOH	2.86
(c) 4-chlorobutanoic acid	$ClCH_2CH_2COOH$	4.52
(d) Trichloroacetic acid	$Cl_3C–COOH$	0.70
(e) Trifluoroacetic acid	$F_3C–COOH$	0.23

If a large molecule possesses a polarised part, the electron-deficient carbon tries to pull electron pair from non-polarised part and induces polarisation in the adjacent carbon-carbon bonds. Thus, due to the inductive effect, polarisation is transmitted further.

An electronegative atom or a group may induce a positive charge on another atom to which it is bonded resulting in a dipolar molecule. The transmission of polarisation in the adjacent bonds due to the polarisation in one bond is called as **inductive effect**. The effect weakens steadily with increasing distance from the position of an electron negative atom. For example, 2-chlorobutanoic acid is more acidic than 4-chlorobutanoic acid. The magnitude of inductive effect is usually very small.

Depending upon the direction of the pulling of electrons, inductive effect is classified as:

(a) Positive inductive effect: This effect is exerted by the presence electron releasing functional group. For example, $–NH_2$, alkyl groups, –OH, etc.

(b) Negative inductive effect: This effect is exerted by the presence of electron withdrawing functional groups. Examples include, $–NO_2$, $–SO_3H$, $–SO_2R$, –C=O, –COOH, halogens, etc.

For example, in a molecule of methyl chloride, the chlorine atom is said to have negative inductive effect while the methyl group is said to have positive inductive effect.

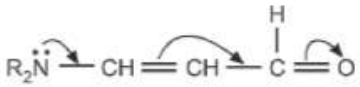
Through inductive effect, an electronegative atom tends to stabilise a nearby anion and helps to stabilise the conjugate base more than the corresponding acid. For example, iodine is less electronegative than chlorine. Hence, iodoacetic acid is less acidic than chloroacetic acid. Similarly trifluoro acetic acid is about 10^5 times more acidic than acetic acid.

Since, acidity value of any carboxylic acid depends on the ionisation of the carboxyl (–COOH) group, an electronegative atom, increases acidic nature of the carboxylic acid through inductive effect. An electronegative atom such as chlorine can withdraw electrons from a carboxyl (–COOH) group. The oxygen of the –OH group is thus made more positive and the proton is readily dissociated.

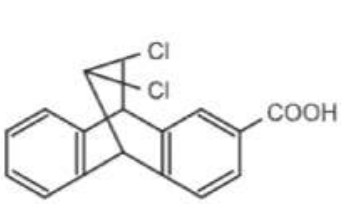
Theories of Electron Displacement:

Two mechanisms of electron displacement have been proposed. According to first mechanism, the presence of an electronegative atom induces electron dis-symmetry (i.e. unequal sharing of electrons present in the covalent bond) through electrostatic induction.

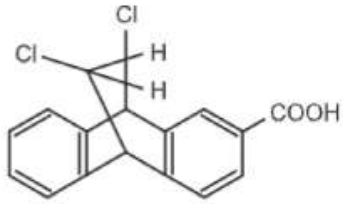
According to the second mechanism, the presence of an electronegative atom induces displacement of electron pair in the bond by an electron pair of neighbouring atom. The ejected electron pair then either remains unshared or initiates similar type of displacement further along the molecule. The displacement is usually indicated by curved arrows. For example,



Usually inductive effect operates in the ground state of the molecule through the single bonds. When it is transmitted through the solvent molecules, it is known as **Field effect**. The inductive effect depends only on the nature of the bonds while field effect depends on the geometry of the molecule. For example, inductive effect is same in compounds A and B while the field effect is different for A and B.



(A)



(B)

According to Lowry, an electron pair undergoes delocalization from bond to one of the atom of C=C bond, as an unshared pair of electrons.

(a) 

(b) 

The concept may equally be applied to conjugated double bond system.

(a) 

(b) 

The lone pair of nitrogen is transferred to a shared position between nitrogen and moves carbon; then a shared pair between C_1 and O moves to a shared position between C_2 and C_3 and finally a shared pair from C_3=O moves to place a lone pair on oxygen atom. Ingold described this process as the conjugative mechanism of electron displacement.

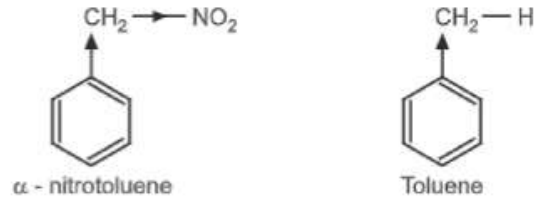
Role of Inductive Effect in a Structure

The inductive effect is quantitatively weak but is permanent and operates in the ground state of the molecule. It is responsible for the dipole moment of the molecule.

Inductive effect arises due to the tendency of an atom to attract or repel electrons of the covalent bond. The C–C bond in ethane is completely non-polar because it connects two equivalent atoms. While in a molecule like CH_3^-–Cl, the electron pair is not shared equally between carbon and chlorine due to the presence of an electronegative atom, Cl. The partial negative charge develops on chlorine. This gives rise to a partially polarised covalent bond.

Role of Inductive Effect in Reactivity

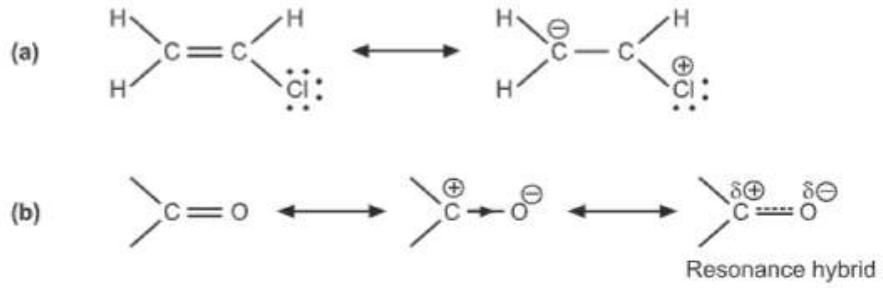
The presence of an electronegative atom is must for inductive effect to exist. Electronegativity of an atom is defined relative to hydrogen. An electronegative atom pulls electron to itself more than a hydrogen atom would if it occupied the same position in the molecule. For example, due to the presence of electron withdrawing $-NO_2$ group, the C–N and C_6H_5–C bonds in α-nitrotoluene are polarised in comparison to toluene.



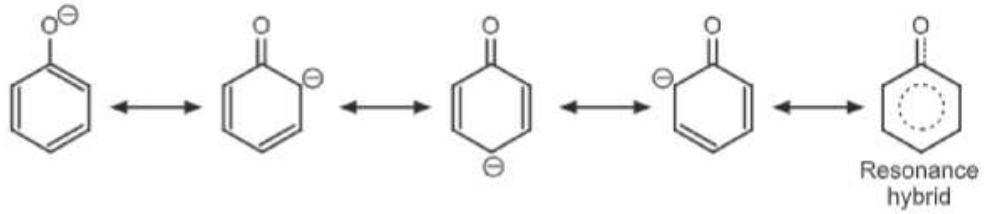
α - nitrotoluene Toluene

1.3 RESONANCE

Resonance effect may also be called as mesomeric or conjugative effect. Whenever a molecule is represented by two or more structures that have the same arrangement of atomic nuclei but different electron distribution, it is said to possess resonance effect. These readily inter-convertible structures are known as resonating, contributing or canonical structures and are shown by a double headed arrow between them. The various resonating structures differ only in electron distribution and are obtained by a slight displacement of electrons. For example,



Electron redistribution is usually possible in conjugated unsaturated system. The resulting resonance helps to increase the stability of the molecule. For example, phenoxide ion is more stable than phenol as the former shows resonance effect.



Resonance becomes important when the contributing structures are of about the same stability. The resonance hybrid is more stable than any of the resonating structures. This increase in stability is called as **Resonance energy**.

Requirements for Resonance:

(a) There can be resonance only between the structures that contain the same number of odd electrons. Resonance is not possible between a di-radical structure and a structure with all electrons paired. All atoms taking part in resonance, must lie in the same plane.

(b) Resonating structures possess approximately the same energy. All resonating structural forms do not contribute equally to the stability of the molecule. It may happen sometimes that separation of charge takes place during electron redistribution. Such charged structures possess less energy. Thus, the more stable contributing forms provide resonance energy. The most able form contributes to the greatest extent.

(c) Resonance will be observed only if the structures are equivalent with respect to the position of constituent atoms. For example, resonance does not exist between cis and trans isomers.

(d) Although resonance is seen due to electron redistribution, the resonating structures should have the same number of paired and unpaired electrons.

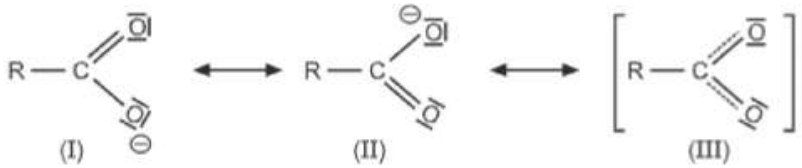
(e) Stability is decreased by an increase in charge separation. Structures that carry a negative charge on a more electronegative atom are considered to be more stable than those in which the charge is located on a less electronegative atom.

(f) More the number of equivalent resonance structures, more is the stability of the resonance hybrid.

Resonance Hybrid: Electron redistribution operating in unsaturated systems via π-bonds is known as **resonance effect**. Individual structures resulting due to such electron delocalisation are called as **resonating structures**. While the structure which represents overall electron distribution seen in all resonating structures is known as **Resonance hybrid**. The resonance hybrid is more stable than any of the resonating structures. A comparison of

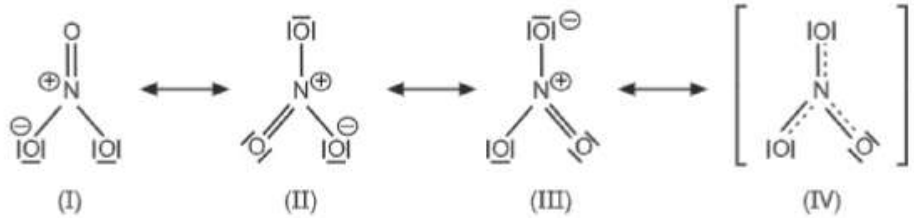
the experimental bond length value with the bond length theoretically calculated from covalent radii helps to know about the existence of a resonance hybrid. The resonance hybrid of some ions are described below.

(a) Carboxylate ion: The carboxylate ion may be represented by the following resonating structures.

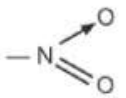


The two C–O bond lengths in carboxylic acids do not match with the bond lengths found for C=O bond in acetaldehyde and C–O bond in ether. The value (1.28 A°) lies in between the expected theoretical values for, single and double bonds. Such values are accounted for if the carboxyl group is regarded as a resonance hybrid between structures (I) and (II).

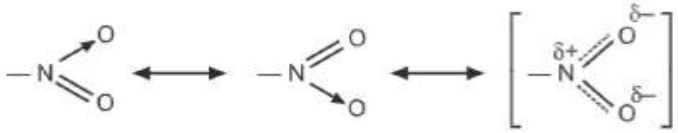
(b) Nitrate ion: It may be represented by the following resonating structures.



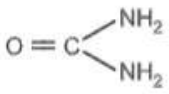
(c) Nitro group: The nitro group is usually represented as



The molecule contains one NO as a single bond and other NO as a double bond. The single bond would be expected to have a length of 1.36 A° while the double bond length would be 1.15 A°. Since, the actual value for both NO bonds in the nitro group lies (1.21 - 1.23°) between the expected theoretical values for single and double bonds, the nitro group must be regarded as a resonance hybrid of structures I and II.



(d) Urea: The molecule is usually represented as shown in the figure. The expected



bond lengths for C=O would be 1.22 A° and C–N would be 1.47 A°. The experimental values of these bonds are closely related (C=O, 1.25 A° and C–N, 1.37 A°). This means that the C=O must have single bond character and C–N bond must have double bond character. Such a situation may be justified in urea is considered as a resonance hybrid of structures (I) and (II).

(I) (II)

Types of Resonance effect:

Depending upon the electron donating or withdrawing nature, the substituents may be broadly divided into:

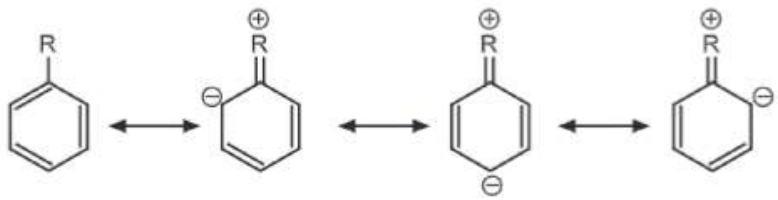
(a) Substituents having electron donating (+R) effect or positive mesomeric (+M) effect: The +R effect is observed when atom or groups donate electrons by resonance. Examples include, –OH, –SH, –O, $–COO^-$ and halogens.

(b) Substituents having electron withdrawing (–R) resonance effect or negative mesomeric (–M) effect: It is observed with the substituents that withdraw electrons by resonance. Examples include $–NO_2$, $–SO_2R$ – CN or –CO group.

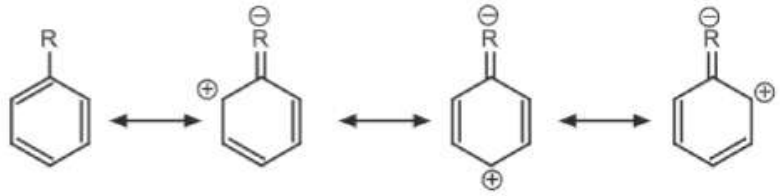
Role of Resonance in a Structure:

When resonance is possible across the aromatic rings, between substituent and functional centre, it affects the rate of conversion or equilibrium between the initial and transition states. The resonance effect will be specific for the type of substituent, functional group and reaction involved.

Resonance always results in a different distribution of electron density. For example, the orientation and ease of attack of a new functional group on benzene ring is influenced by resonance. Through +R effect, electron releasing substituent present in benzene, increases the electron density at ortho and para position, while electron withdrawing substituent creates electron deficiency at ortho and para position through –R effect.



(a) Effect of electron-donating substituent on benzene.

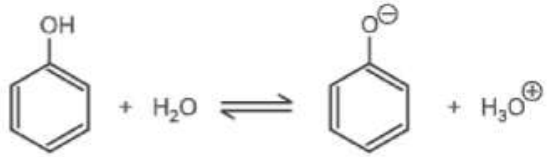


(b) Effect of electron-withdrawing substituent on benzene.

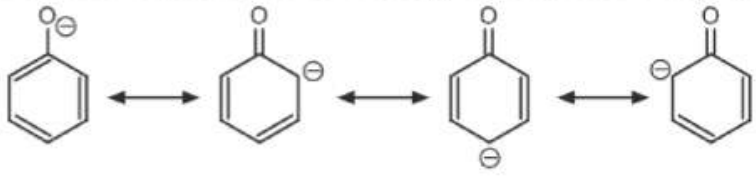
Role of Resonance on Reactivity:

(a) The effect of resonance on the transition state is considerably more or less than its effect on the unreacting molecule. For example, the electron density at $—CH_2$ in the molecule, $X—C_6H_4—CH_2—Y$ depends on the resonance effect of X. When this molecule undergoes reaction, the $—CH_2$ acquires partial carbonium ion character in transition state due to partial cleavage of $CH_2—Y$ bond. The group X, which in the unreacting molecule may have donated only slightly, may now donate electrons more in transition state.

(b) The acidity of phenol may be explained on the basis of resonance. The dissociation of phenol is a reversible reaction. As phenoxide ion is more stabilised due to resonance, the rate of forward reaction is more than the rate of backward reaction.



Similar delocalisation in phenol results in separation of charges. Since, structures showing charge separations, contribute less towards resonance hybrid, phenol is less stable than the phenoxide ion. Hence, phenol shows acidic property.



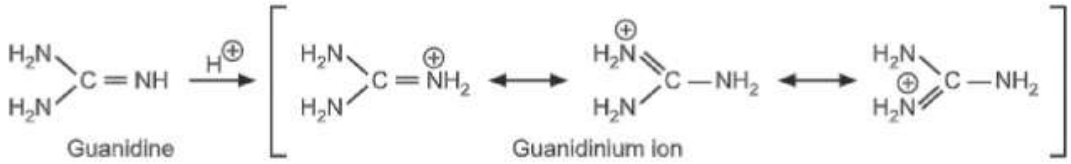
Stabilisation of phenoxide ion

(c) In comparison to π electrons, the sigma electrons are bound more tightly and so relatively unavailable for bonding to external reagents. Hence, triethylamine (pKa = 9.8) is more basic than pyridine (pKa = 5.2).

$(CH_3)_3 N$:
Trimethylamine

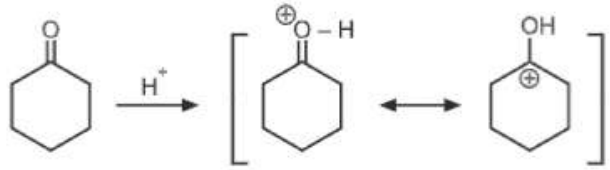
Pyridine

However due to resonance stabilisation, some double bonded heteroatoms may be strongly basic than expected. For example, guanidine undergoes almost complete ionisation to guanidinium ion due to reaonance effect.



(d) The greater basicity of 2, 6-dimethyl pyrone than cyclohexanone may also be accounted on the basis of greater resonance stabilisation.

(I)



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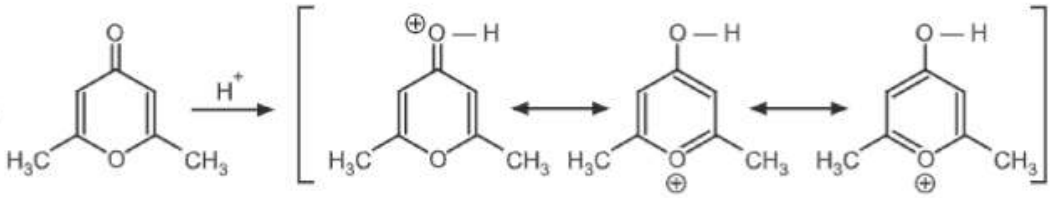
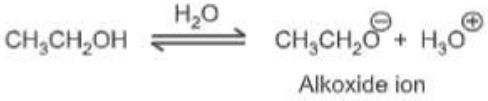
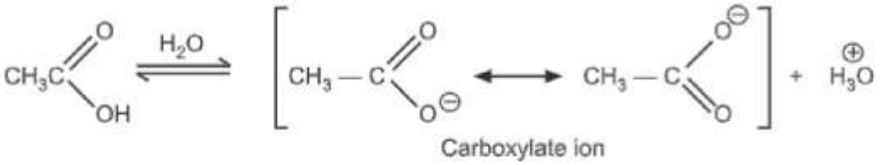


(e) Alcohols are less acidic than carboxylic acids by a factor of about 10^{11}. This increased acidity of carboxylic acids relative to alcohols can therefore be attributed to better delocalisation of electron pair of the carboxylate ion.





The conjugate base of carboxylic acid is more stabilised than an alkoxide anion. Hence, carboxylic acid undergoes faster ionisation (i.e. increased acidity) than alcohol.

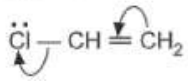
Both inductive effect and resonance effect lead to permanent polarisation of the molecule. However, resonance differs from inductive effect as mentioned in Table 1.1.

Table 1.2: Difference between inductive and resonance effect

Resonance effect	Inductive effect
1. Operaters with π bonds.	Operates with σ bonds.
2. Operates when all atoms are in the same plane.	Operates only in straight chain.
3. Operates over entire molecule.	Decreases with increasing the distance.
4. Presence of electronegative atom is not required.	Presence of electronegative atom is needed.
5. More powerful.	Less powerful.

1.4 HYPERCONJUGATION

Hyperconjugation is a modified resonance effect which involves delocalisation of σ electrons. In the molecule of vinyl chloride, an unshared pair of electrons is located on chloride, which may be delocalised as follows:

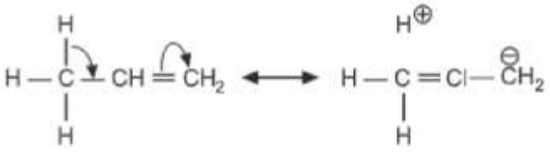


This mechanism of electron release is known as hyperconjugation. The bonding pair of C-halogen link delocalises in the direction of the halogen.

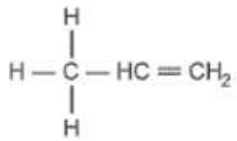
Alkyl groups are electron-donating in nature. When they are attached to a C=C bond, the C – H bonds in alkyl groups bring about hyperconjugation phenomenon as

(a)

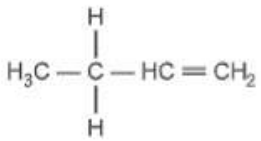
(b)



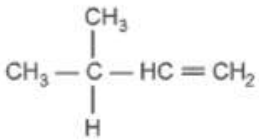
The H^+ does not become completely free. It remains in the close vicinity of the carbon to which it was attached. In methyl group, three C – H bonds could contribute to this effect, in ethyl group, two C – H bonds; in isopropyl group, one C – H bond and in tert-butyl group, there would be no C – H bond able to bring about hyperconjugation. Thus, as we go in the series methyl, ethyl, isopropyl and t-butyl, the number of α-hydrogens go on decreasing.



Methyl group



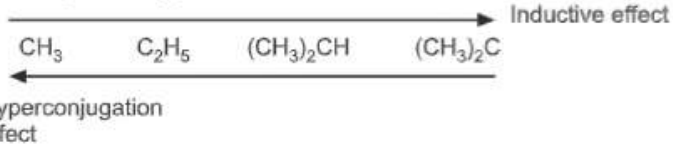
Ethyl group



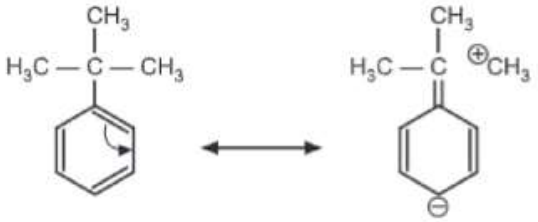
Isopropyl group

Thus, hyperconjugation can be defined as electron donating resonance effect operating through delocalisation of σ electrons of C_α – H bond.

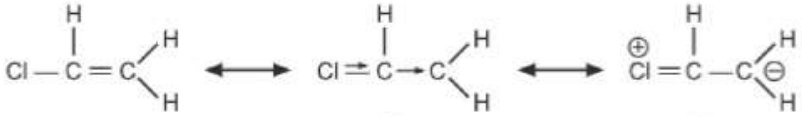
Both hyperconjugation and the inductive effect cause the release of electrons and they potentiate each other in this respect. Along a series of alkyl groups, however the magnitude of these two effects changes in opposite directions.



Besides through delocalisation of σ electrons of C_σ – H bonds, hyperconjugation is also reported to occur through delocalisation of σ electrons of C – C bond. For example, tert-butyl group can hyperconjugate with unsaturation in the benzene ring a shown below:



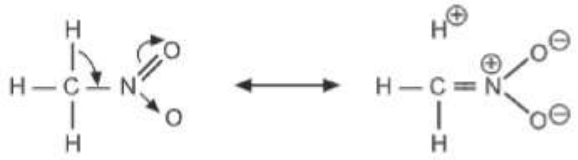
Thus, hyperconjugation is sometimes referred to as no-bond resonance. Similarly, the hyperconjugation in vinyl chloride may also be viewed in terms of resonance between structures I and II.



(I) (II)

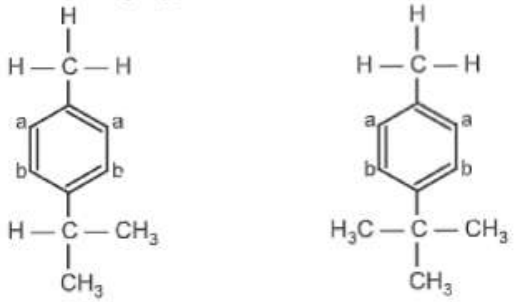
Role of Hyperconjugation in Structure:

(a) On the basis of resonance, nitromethane ethane is expected to have a dipole moment value of 2.59. However, experimental dipole moment value for nitromethane was found to be 3.15. This higher value can be accounted on the basis of hyperconjugation seen in nitromethane.



(b) The methyl group present on benzene ring has o, p-orientation effect which may be attributed to hyperconjugation as shown.

For example, in the p-substituted dialkylbenzenes, the orientating influence of two alkyl groups is controlled by hyperconjugation.



Since, a methyl group with 3 C_σ–H bond will cause much greater hyper-conjugation than either isopropyl group (with only one C_σ–H bond) or t-butyl group (with no C_σ–H bond), substitution at position 'a' will be more favoured than substitution at position 'b'.

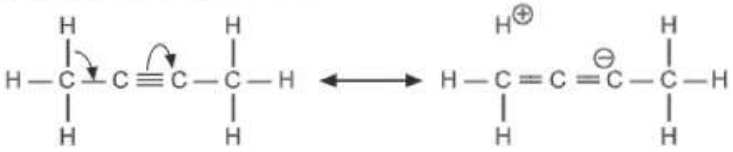
(c) 2-Methyl-1-butene is less stable than 2-methyl-2-butene. It can be accounted on the basis of hyperconjugation.

2-methyl-1-butene 2-methyl-2-butene

Since, 2-methyl-2-butene possesses nine α-hydrogen atoms compared to five α-hydrogen atoms present in 2-methyl-l-butene, the number of perconjugative structures is more for 2-methyl-2-butene. More the number of hyperconjugative structures, more is the stability.

Role of Hyperconjugation in Reactivity:

(a) Effect on bond length: Hyperconjunction decreases the bond length but this effect is not much significant. For example, the actual bond distances between the methyl and acetylenic C-atoms in dimethyl acetylene is 1.46 A° which is found to differ from the normal C–C bond distance (1.54 A°) by only 0.08 A°. This shortening occurs due to partial double bond character of the concerned bond imparted by hyperconjugation, as shown below.



Dimethyl acetylene

(b) Reverse hyperconjugation: It was observed that the C – F bond length decreases with an increase in number of fluorines on the carbon. Reverse hyperconjugation phenomenon has been suggested to account for the bond-shortening as shown below.

Because of the greater electronegativity, fluorine withdraws more 'p' than 's' electron density from the carbon, leaving the carbon in CF_4 with more 's' characters than in CHF_3. The increase in 's' character results into decrease in the bond length. For example, the C – F bond length in CF_4 was found to be 1.3 A° while that in CH_3F is 1.39 A°.

1.5 STERIC EFFECTS

Functional groups are found to affect chemical properties and reactions of the molecule because of their geometric size and shape by coming in way of an attacking reagent. Structural effects which arise from spatial interaction between the groups are known as steric effects. The effect is produced by overcrowding of large bulky groups present in the vicinity of the reaction centre. Thus, steric effect arises due to hindrance where certain groups present in the molecule interferes with each other in space which is not sufficient to accommodate all of them. In steric hindrance, the sheer bulk of groups is influencing the reactivity of a site by impeding approach of a reagent to the reaction centre.

If the transition state of a reaction is not favoured by steric factors, there will be less tendency for the reaction to take place. For example, the transition state for the hydrolysis of ester requires a planar structure (hybrid sp^2 bonding at the carbonyl carbon) with bond angles of about 120°. However, due to addition of relatively large water molecule, the steric strain increases due to decrease in bond angle from 120° to 109°.

Victor Meyer has observed the following steric effects during esterification reaction:

(a) Rate of esterification is retarded when group like –F, –OH, $–CH_3$ is present ortho position.

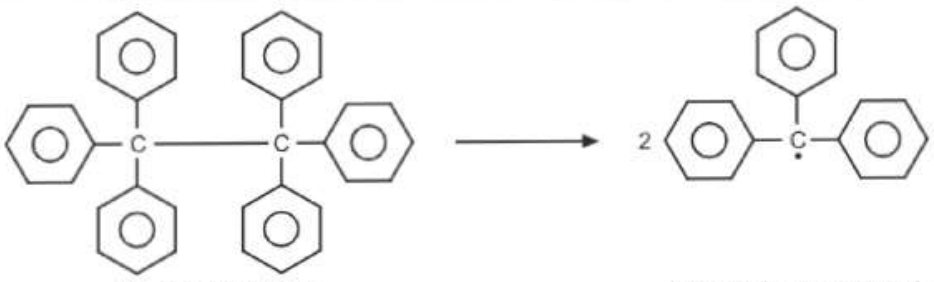
(b) If –Br, –Cl, –I, $–C_2H_5$, $–NO_2$ or — SO_3H group is present the rate of esterification is almost checked. This is because in the first group, the groups are less bulky as compared with those in second group.

As the steric effect of above groups would be negligible if they are located at m- or p-positions, Meyer named above effect as ortho effect.

Role of Steric Effect on Structure:

The steric interactions play a vital role in determining the properties of the structure. The carbon in the reagent and product is tetrahedral while carbon in the transition state is bonded to five atoms. As hydrogen atoms are replaced by the larger methyl groups, there is increased crowding around carbon. The back side of the molecule, where attack must take place, becomes increasingly inaccessible.

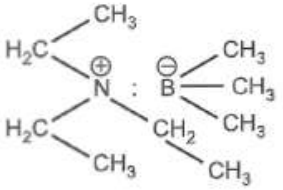
The ease of dissociation of hexaphenylethane to triphenylmethyl radicals can be partly accounted on the basis of steric effects.



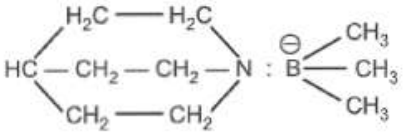
Hexaphenyl ethane Triphenyl methyl radicals

The C – C bond length in hexaphenyl ethane is slightly longer than the normal C–C bond length. This suggests that the bond is stretched by steric repulsion between two large phenyl rings. Thus, because of steric effect, the two triphenyl methyl radicals are reluctant to be link together resulting into easy dissociation of hexaphenyl ethane. It is further proved by the observation that insertion of methyl groups at ortho position into the phenyl rings of hexaphenylethane, further increases the rate of dissociation.

Similarly because of the steric hindrance between methyl groups, salt of trimethyl borane with triethylamine dissociates very readily. The same steric repulsion between methyl groups however disappears when methyl groups of triethylamine are bridged together.



Salt of trimethyl borane with triethylamine

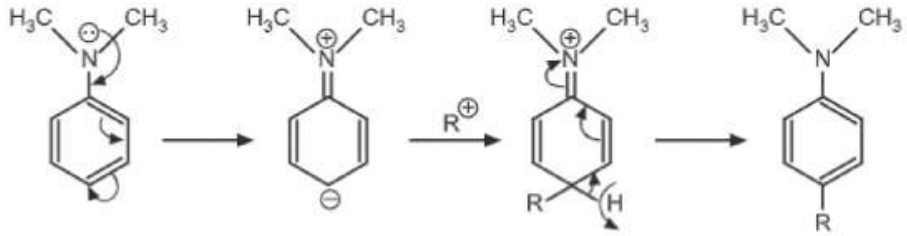


No steric repulsion due to bridging of methyl groups

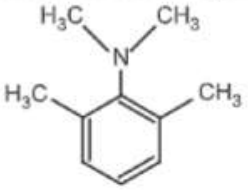
Role of Steric Effects on Reactivity:

For a reaction to occur, a particular orientation of the reactants is essential. Steric effects may disturb this optimal orientation and may significantly affect the reactivity of the molecules.

(a) N, N-dimethylaniline is much weaker base than its 2, 6-dimethyl derivative. The $-N(CH_3)_2$ group, being electron-donating activates the nucleus towards substitution at p-position through delocalisation of electrons. For this delocalisation to occur, the orbital of nitrogen which contains the electron pair is in the same plane as that of p-orbital of phenyl ring.



In 2, 6-dimethyl analogue, the two methyl groups in ortho position to $-N(CH_3)_2$ sterically interfere with the two methyl groups attached to nitrogen.

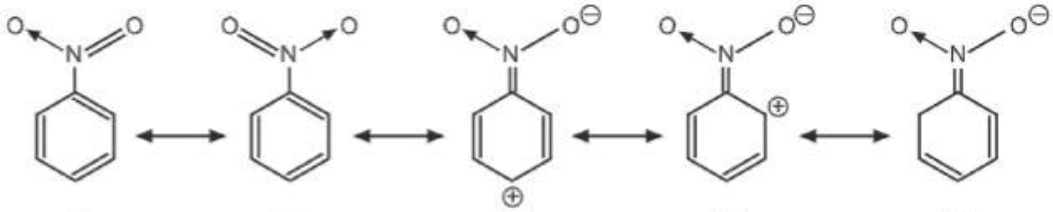


2, 6-dimethyl N, N-dimethyl aniline

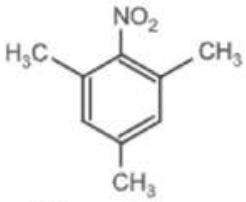
Due to this, the orbital containing electron pair on nitrogen can not remain parallel to those of benzene. Since, delocalisation of electron (i.e. resonance) can occur, electron pair remains available on the nitrogen for donation.

Therefore 2, 6-dimethyl analogue is more basic than N, N-dimethylaniline.

Another example of steric inhibition of resonance includes comparison of dipole moments of nitrobenzene and nitromesitylene.



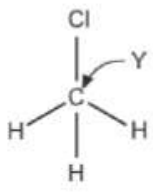
(I) (II) (III) (IV) (V)



Nitromesitylene

Nitrobenzene undergoes resonance due to delocalisation of electron pair. Such delocalisation is possible only when the nitro group remains in the same plane as that of ring. In the structure of nitromesitylene, the methyl groups do not allow the nitro group to be coplanar with the ring. The less resonance stabilisation of nitromesitylene therefore will lower down the dipole moment when compared with that of nitrobenzene.

In the above example, the large size of the nitro group also plays a role. If nitro group is replaced by smaller group, the steric effect will be eliminated. For example, in bromobenzene and bromomesitylene, there is no steric hindrance. Hence, a dipole moment of bromobenzene is 1.55 while that of bromomesitylene is 1.52.



(b) When methyl chloride undergoes SNZ hydrolysis, there is no difficulty for 'Y' to approach the carbon atom. Steric hindrance to the attack of Y will be observed if one of the hydrogen atom is replaced by other alkyl group. The formation of transition state is therefore, made very difficult.

(c) Alkyl group when present on benzene ring shows o, p-orientation effect. When nitration is carried out of toluene and t-butyl benzene, there is a decrease in the percentage of the ortho product in passing from methyl to tertbutyl benzene. The percentage of ortho product falls and that of para-product rises as the alkyl group present in the benzene ring grows in size. This is almost certainly due to steric effect.

(d) Steric hindrance to solvation is caused by the bulk of an acid or a base. It thereby lowers acidity or basicity. For example, the order of a base strength for methylamines in water is

$$(CH_3)_2\ \ddot{N} > CH_3\ddot{N}H_2 > (CH_3)_3\ddot{N}$$

Due to the presence of three electron-donating methyl groups, triethylamine should have greater basicity. However, because of the same reason, trimethyl ammonium ion is sterically more hindred and therefore gets least stabilised by solvent. Hence, triethylamine has less tendency to get converted to least stable trimethyl ammonium ion by accepting a proton. In other words, it is less basic.

1.6 TAUTOMERISM

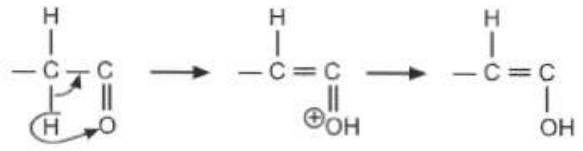
Tautomerism is the presence of interconvertible isomers which exist in equilibrium with each others. Such isomers are usually of similar energy and are called as tautomers. Tautomerism always involves the making and breaking of single σ bonds during the change of the geometry.

Let us consider an example of acetylacetone which behaves like, both as olefin-alcohol (enol) and as ketone.

Acetylacetone (Keto form) Acetylacetone (Enol form)

The word enol is derived from ene (i.e. C=C) and –OH (for the alcohol group, –OH). Both keto form and enol form are in equilibrium with each other. They differ from each other in (i) electron distribution, and (ii) position of a hydrogen atom. Such interconversion is catalysed by the presence of an acid or a base.

The requirement of enolisation is that C–H must be adjacent to a keto group. This makes the compound acidic (i.e., ionisable). The hydrogen can leave the molecule or migrate to another position in the form of a proton. The transfer of a positive charge can be illustrated by the following mechanism.

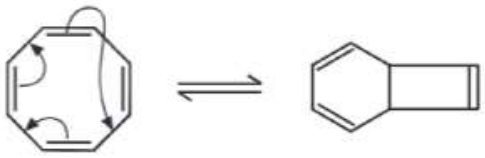


Ketone Enol

Tautomerism can further be subclassified as

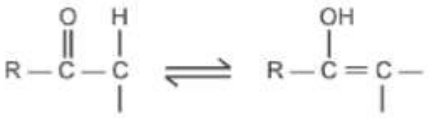
(a) Valence tautomerism, (b) Proton tautomerism.

(a) Valence tautomerism: It arises due to shift in the interatomic distances within a molecule without any loss to molecular formula. For example,



Cycloocta tetraene Bicyclic skeleton

(b) Proton tautomerism: In this type, proton is readily and rapidly shifted from one atom and binds to oxygen or nitrogen. Keto-enol tautomerism is an excellent example,

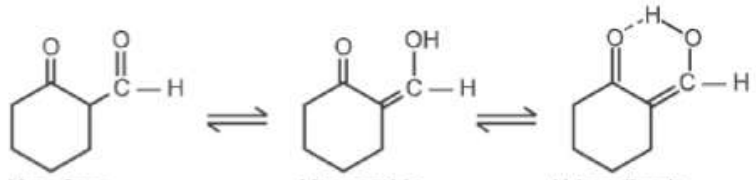


Ketone Enol

where the ketone may lose a proton which re-bond with the oxygen atom to form enol. The rate of interconversion of carbonyl and enol forms is given by tautomerisation constant. It is defined as the ratio of the acidity constant of the carbonyl and enol forms.

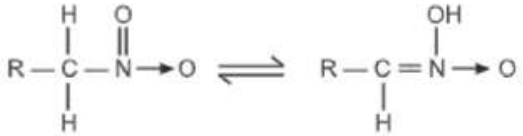
$$\text{Tautomerisation constant} = \frac{\text{Ka of carbonyl form}}{\text{Ka of enol form}}$$

Since, the carbonyl form is usually more stable than enol form, the enol forms of simple aldehydes and ketones have not been isolated in pure form. In certain cases, enol form may be isolated because of increased stability imparted due to resonance energy or hydrogen bonding. For example, both tautomeric forms of β-dicarbonyl compounds have been isolated.



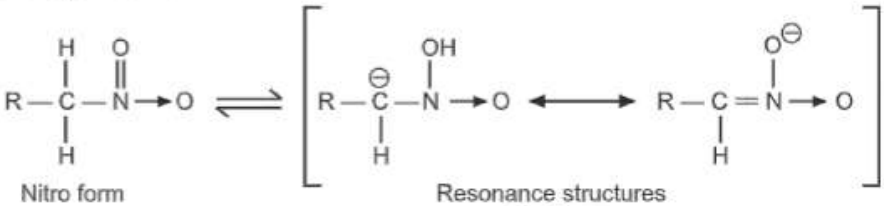
Keto form More stable enol form H-bonding in enol form

Among nitro alkanes, nitro and aci forms are possible similar to the keto and enol forms. However, the aci forms are more stables as compared to enol forms.



Nitro form Aci form

Since, the nitroalkanes containing α – H atoms are acidic due to the activating of – NO_2 on α-hydrogen atoms, an aci form is readily generated when the basic solvent removes a proton at the C_α – atom.



Nitro form

Resonance structures of aci form

Due to the resonance stabilisation of aci form, it is more stable when compared with enol form.

EXERCISE

1. What is tautomerism ? Explain with suitable examples.
2. Write notes on:
   (a) Resonance stabilization.
   (b) Hyperconjugation.
   (c) Inductive effect.
   (d) Steric effects.
   (e) Theories of electron displacement.
3. Define the term, structural effects. Explain in detail the effect of steric features on the reactivity of the substrate with suitable example.
4. Illustrate the role of inductive effect on the structure and reactivity of substrate molecules with suitable examples.
5. What do you mean by resonance hybrid ? Describe the resonance hybrid for:
   (a) Carboxylate ion
   (b) Urea
   (c) Nitro group.

❖❖❖

Unit II

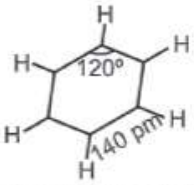
BENZENE AND ITS DERIVATIVES

♦ SYNOPSIS ♦

2.1 ANALYTICAL, SYNTHETIC & OTHER EVIDENCES IN THE DERIVATION OF STRUCTURE OF BENZENE

Thiele
(1899)

Friedrick Kekule
(1865)



Planar hexagon bond length 140 pm

X-ray diffraction shows that all six carbon-carbon bonds in benzene, are of same length, at 140 picometer (pm). The electrons for C-C bonding are distributed equally between each of the six carbon atoms. The C-C bond lengths are greater than a double bond (135 pm) but shorter than a single bond (147 pm) due to equal electron delocalization between all C-C bonds in benzene.

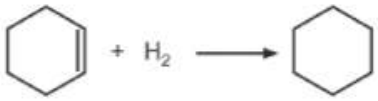
Each carbon atom in benzene has a p-orbital of completely delocalized electrons. This overlap gives rise to planar structure. From X-ray examination of benzene, electron density contour map can be obtained. In this map, a symmetrical hexagonal shape carbon-carbon bonds can be seen.

Benzene shows very similar chemical shifts for protons in 'H-MMR' spectrometry. These similar shifts again point out about same electronic surrounding (equal electron distribution) or uniform electron delocalization over all 6 carbons in benzene structure.

2.2 SYNTHETIC EVIDENCE FOR DELOCALIZATION IN BENZENE

(1) Benzene is unreactive to addition reactions. Due to presence of 03 alternate double bonds in benzene structure, the chemists of that time believe it to react easily with bromine in the dark at room temperature. But due to uniform delocalized electrons (aromaticity) between all C – C bonds, benzene regained unusual stability and does not react with bromine.

(2) The hydrogenation across double bond easily occurs.



Benzene contains 03 double bonds and should liberate three times energy that of cyclohexene. i.e., $(3x - 119) = -357$ kJ mol^{-1}. But the actual value for benzene is -208 kJ mol^{-1}. So benzene is $(357 - 119) = 152$ kJ mol^{-1} more stable than expected as it does not contain three ordinary alternate double bonds. All these three double bonds are resonating within the ring.

The benzene ring has thus delocalized electrons. Hence, all C-C bond length are same.

Summary:

(1) Benzene is a flat molecule with six carbons bonded in a planar ring. It has unusual stability.

(2) Each carbon is covalently joined to two adjoining carbons and one hydrogen. The remaining outer electron of each carbon is shared with electron of next carbon in the ring. Thus, the outer electrons of all the six carbons are delocalized above and below the plane of the ring, giving the ring the unusual stability.

(3) The six carbon atoms form a perfectly regular hexagon. There are no distinct single or double bonds within the benzene. The delocalization of the ring makes each count as one and a half bonds between the carbons. Hence, all the carbon carbon bonds have exactly the same length-somewhere between single and double bonds.

(4) Benzene resists addition reactions because these reactions would involve breaking the delocalization and losing the stability.

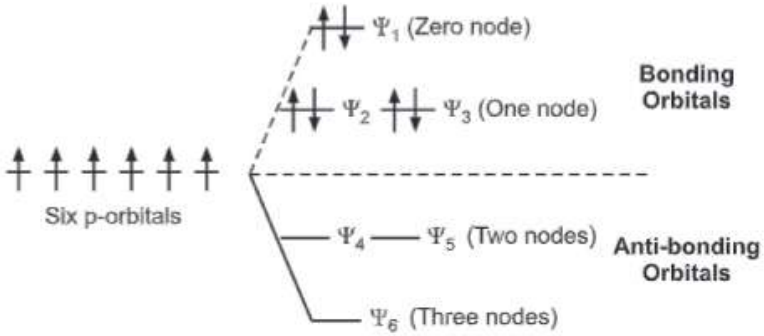
2.3 ORBITAL PICTURE OF BENZENE

The delocalization of the p-orbital carbons on the sp^2 hybridized carbons leads to aromaticity of benzene. There are a total of six p-orbital electrons that form the stabilizing electron clouds above and below the aromatic ring.

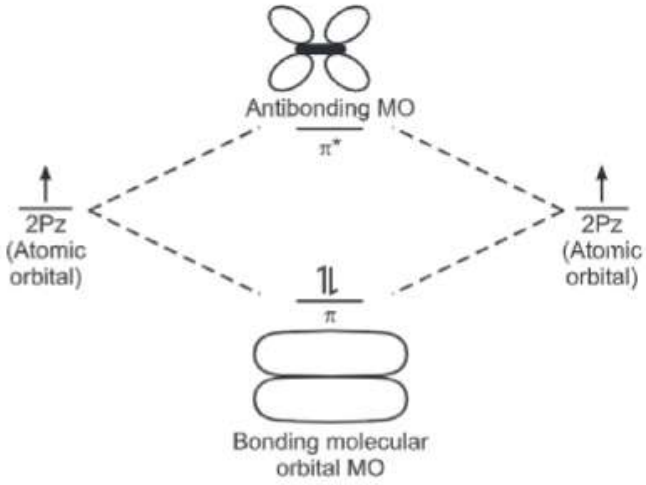
Benzene has a planar hexagonal structure in which all the carbon atoms are sp^2 hybridized and all the C-C bonds are equal in length.

Each carbon has an unhybridized p-orbital perpendicular to the plane of the ring. It makes up the conjugated π-system.

The p-orbitals (one on each carbon) linearly overlap to generate six molecular orbitals, three bonding and three antibonding. It is this completely filled set of bonding orbitals or closed shell that gives the benzene ring its thermodynamic and chemical stability.

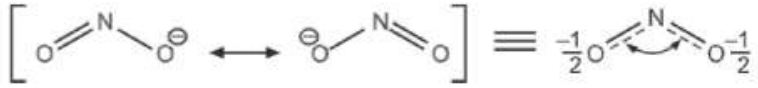


Electrons that spend most of their time between the nuclei of two atoms are placed into the boding orbitals, and electrons that spend most of their time outside the nuclei of two atoms are placed into antibonding orbitals. The bonding orbitals are at a lower energy than the antibonding orbitals. So they are the first to fill up.



2.4 RESONANCE IN BENZENE

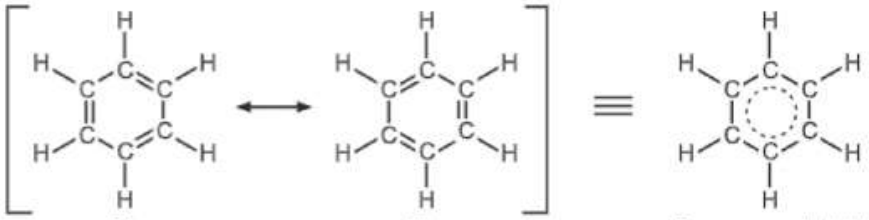
Resonance or mesomerism describes oscillations of delocalized electrons within molecule which is usually represented by several contributing structures or forms. e.g.,



Contributing structures of Nitrite anion (NO^-_2) Resonance hybrid

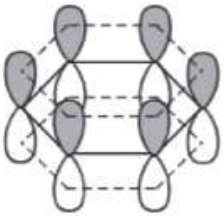
Benzene can be represented by two interconvertible structures that are equivalent in energy.

Dewar structures



Each above structure having conjugated double bonds, should easily undergo addition (e.g., hydrogenation/saturation) reactions. However, its inability to saturate suggests that the actual structure of benzene does not correspond to any one of above individual structure but rather to a combination of them (i.e., Resonance hybrid). This resonance in the benzene has been confirmed by electron diffraction, X-ray diffraction and molecular spectroscopy.

The resonance hybrid has energy below the energy of the kekule structures and is more stable. This gain in stability occurs as the six p-electrons of the carbon atoms are delocalized above and below the ring forming a continuous pi-bond instead to being localized/fixed between two carbon atoms. Hence, electron density flows uniformly around each carbon and hydrogen atom in benzene. It reflects into the strong singlet NMR signal of the six equivalent protons (Hydrogen). These six protons are equivalent because they have the same electronic environment.



π electrons delocalized around the ring, above and below the plane.

2.5 AROMATIC CHARACTERS OF BENZENE

Aromaticity refers to planar/flat ring shaped molecule with resonance bonds to impart greater stability. Thus, aromaticity describes a conjugated system made of alternating single and double bonds in a ring. Through delocalization of electrons, this conjugated system generates resonance structures or forms which are best represented by a hybrid (average) of these structures. Delocalized means instead of tied to any one specific carbon atom, each electron is shared by all six carbons in benzene ring. The term, 'aromatic' applied to all compounds that contain benzene/phenyl ring.

All aromatic compounds

(i) Have distinctive pleasant smell.

(ii) Have higher unsaturation due to alternate single and double bonds.

(iii) More chemical stability due to a delocalized conjugated π system.

(iv) Do not undergo 'addition' reactions easily.

(v) Undergo 'substitution' reactions.

(vi) Have all the C-C bonds of exactly the same length – somewhere between the single and double bonds.

(vii) The conjugated π system lowers the energy necessary for electrons to jump from the HOMO to the LUMO. This results in aromatic corresponds to absorb light in the UV spectra.

2.6 HUCKLE'S RULE

Aromaticity is used to describe a cyclic, planar molecule with a ring of resonance bonds that impart more stabiilty to the molecule. Aromaticity thus describes the extra stability of planar, cyclic conjugated molecules.

In 1931, German chemist Erich Huckel proposed a rule to define the extra stability or aromaticity or aromatic properties. To possess aromaticity, the molecule

(i) should be polyunsaturated cyclic hydrocarbon,

(ii) should be planar,

(iii) should be fully conjugated, (i.e., all atoms in the ring must be able to participate in π bonding through resonance.)

(iv) should have 4n + 2 p electrons ($n \geq 0$)

π electrons refer to electrons with π bonds or lone pair within p-orbitals.

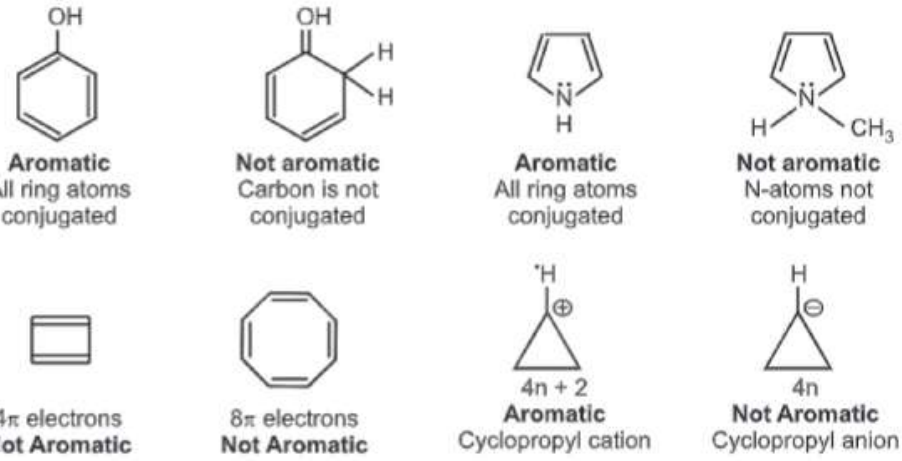
For example benzene has three double bonds. Each double bond (π bond) contains 2 π electrons. So benzene has 6 π electrons i.e., For benzene,

$$4n + 2 = 6$$
$$4n = 6 - 2 = 4$$
$$n = 1$$

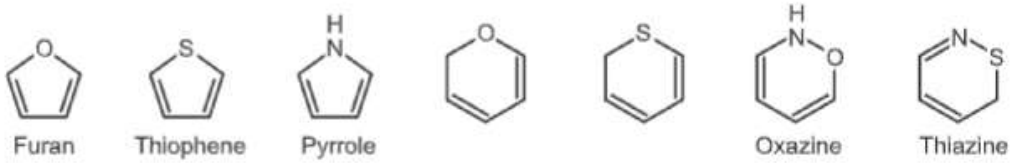
For benzene, n = 1 which is a positive value. Hence, benzene is aromatic. Huckel's rule is also applicable to anions like cyclopentadienyl anion ($C_5H_5^-$) with six π electrons. Because of its aromaticity, the anion is more stable than the neutal cyclopentadienyl radical.

The polycyclic molecules like pyrene (16 π electrons) and coronene (24 π electrons) although aromatic in nature, fail to follow Huckel's rule. Only monocyclic systems seem to follow Huckel's rule.

To become fully conjugated, an atom in the ring should not be attached to four bonds e.g., sp^3 carbon or nitrogen.



Heterocyclic compounds consists of hetero atoms like N, O and S. A large number of heterocyclic compounds follow the Huckel's rule of aromaticity e.g.,



The lone pairs of electrons present on these hetero atoms can participate in resosnance with π electrons of the ring that make these heterocyclic molecules aromatic.

2.7 AROMATIC ELECTROPHILIC SUBSTITUTION

Benzene possesses a planar structure involving sp^2 hybrid orbital of six carbon atoms. Each of these carbon atoms, projects one unhybridised 2p atomic orbital at right angle to the plane of the nucleus. The overlapping of '2p' orbitals is extended over whole system forming a cyclic π-orbital. A cloud of π electrons thus exists above and below the plane of benzene ring. This cloud protects the ring carbon atoms of benzene from the attack of nucleophilic reagents. Because of loosely held and easily available π electrons, the benzene ring serves as a base which can easily react with electron deficient species. These reactions are called as electrophilic aromatic substitutions.

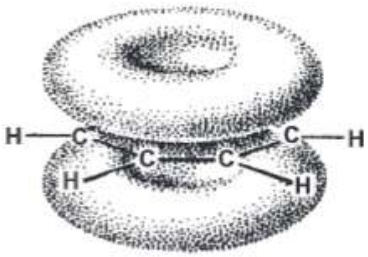


Fig. 2.1

2.8 TYPES OF ELECTROPHILIC AROMATIC SUBSTITUTION REACTIONS

This category represents a variety of reactions like nitration, sulfonation, halogenation, Friedel Craft's reactions, nitrosation and diazo coupling. Unlike other reactions, nitrosation and diazo coupling need rings of high reactivity.

(i) Nitration: $Ar - H + HONO_2 \xrightarrow{H_2SO_4} Ar - NO_2 + H_2O$

Nitro derivative

(ii) Sulphonation: $Ar - H + HOSO_3H \longrightarrow Ar - SO_3H + H_2O$

Sulphonic acid derivative

(iii) Halogenation: $Ar - H + X_2 \xrightarrow{FeX_3} Ar - X + H - X$

Aryl chloride

(iv) Friedel – Craft's alkylation:

$$Ar - H + R - X \xrightarrow{AlX_3} Ar - R + H - X$$

Alkyl benzene

(v) Friedel – Craft's acylation:

$$Ar - H + R - \overset{\overset{O}{\|}}{C} - Cl \xrightarrow{AlX_3} Ar - \overset{\overset{O}{\|}}{C} - R + H - Cl$$

Ketone

(vi) Nitrosation:

$$Ar - H + HONO \longrightarrow Ar - N = O + H_2O$$

Nitroso derivative

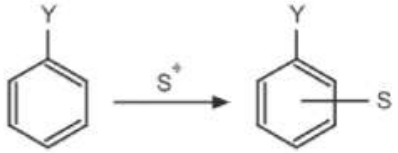
(vii) Diazo coupling:

$$Ar - H + Ar' - N_2^+ X^- \longrightarrow Ar - N = N - Ar' + H - X$$

Azo compound

2.9 CLASSIFICATION OF SUBSTITUENTS

The reactivities of benzene and a substituted benzene are compared on the basis of severity of conditions and time required for completion of reaction. When the electrophilic substitution (S^+) occurs on a benzene ring which already has a substituent, the group (Y) already present on the ring determines how readily the next substitution (reactivity) occurs and its position of attachment (orientation) in the ring.



The rate of reaction is strongly dependent upon the nature of the substituent already present in the ring. It may either be electron donating or electron withdrawing in nature. Benzene ring provides two electrons to form a new covalent bond with the electrophile, generating a carbonium ion. Hence, if 'Y' is electron donating, it increases the electron density in the ring and stabilizes the carbonium ion. Such group is called as activating group which makes the ring more reactive than benzene. If 'Y' is electron withdrawing, it pulls out the electron cloud and destabilizes the carbonium ion. Since, the attack of electrophile becomes more difficult under such circumstances, the rate of reaction of this ring is slower than that of benzene. Hence, such group is called as deactivating group.

All electron donating or activating groups direct the next substitution to ortho/para direction. Hence, they are also known as ortho/para directing groups. While all electron withdrawing or deactivating groups direct the next substitution to meta position. Hence, they are called as meta orienting substituents. Exceptionally, halogens are deactivating but cause ortho/para orientation.

Thus, on the basis of their influence on the reactivity and orientation of the ring, nearly all substituents can be categorised as follows:

(a) Activating and ortho/para directing:

e.g. $-NH_2$, $-OH$, $-OCH_3$, $-NHCOCH_3$, $-CH_3$

(b) Deactivating and meta directing:

e.g. $-NO_2$, $-COOH$, $-SO_3H$, $-CN$, $-CHO$, $-COR$, etc.

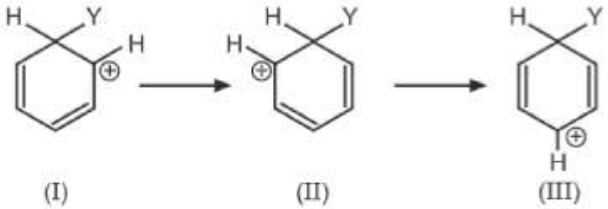
(c) Deactivating and ortho/para directing:

e.g. $-F$, $-Cl$, $-Br$, $-I$

Thus, the nitration of nitro benzene will yield chiefly the meta isomer (93%) and the rate of reaction is much slower than nitration of benzene itself. While the nitration of anisole will yield chiefly the ortho (43%) and para (56%) isomers and the rate of reaction is higher than nitration of benzene.

2.10 THEORY OF REACTIVITY

Let us consider a reaction in which an electrophile E^+ reacts with benzene ring having a substituent Y. In such a case, the positive charge is distributed around the ring, being intense at positions ortho and para to the carbon atom linked to Y. The intermediate carbonium ion will be the hybrid of the following structure.



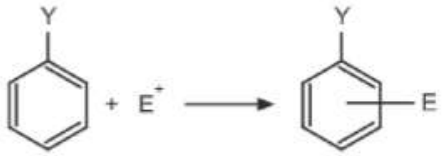
(I) (II) (III)

The stability of the carbonium ion will be governed by the nature of Y. An electron donating group will stabilize the carbonium ion by neutralizing the positive charge of the ring through electron release. The overall rate of substitution increases. While an electron withdrawing group intensifies the positive charge on the ring through electron withdrawing inductive effect. The destabilized carbonium ion thus shows a slower rate of reaction.

Thus, in electrophilic aromatic substitution, an electron donating group (Y) increases rate of reaction and an electron withdrawing group (Y) lowers the reactivity of the ring.

2.11 THEORY OF ORIENTATION

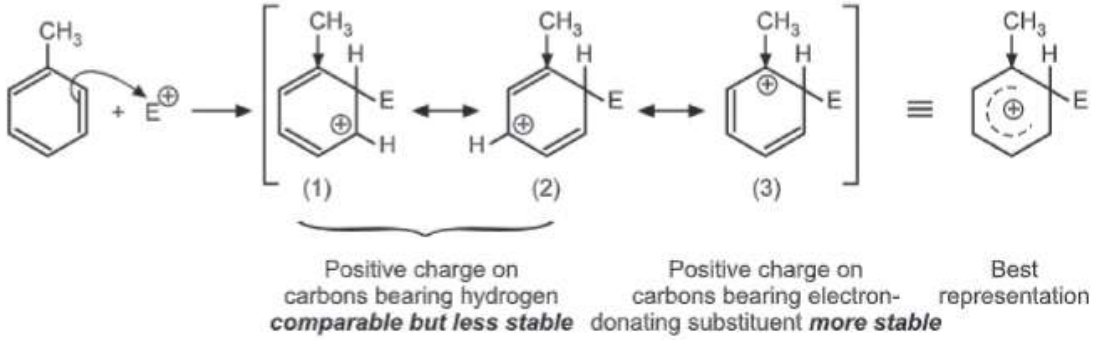
Out of two important factors that govern the reactivity of aromatic rings towards an electrophile, the first involves the electron concentration in the aromatic ring before attack. The second factor is the relative stabilities of the carbocation intermediates formed in electrophilic aromatic substitution. When an electrophile E^+ attacks the mono substituted benzene ring, the stability in terms of energy of the carbonium ion will govern the orientation of the next coming substituent.



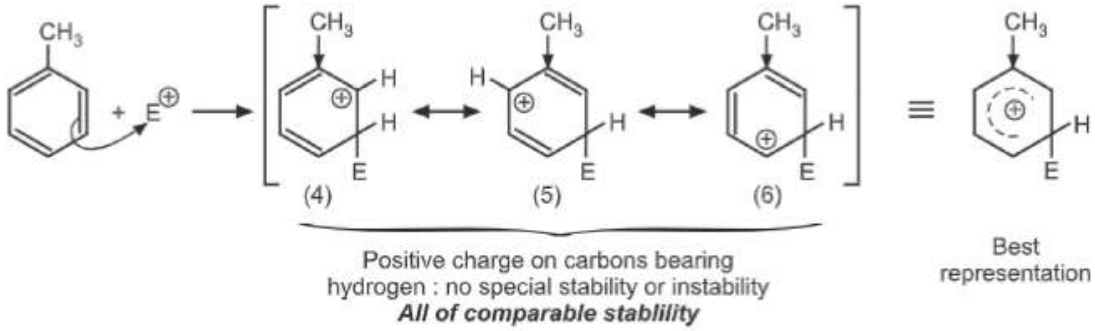
Regardless of its electron donating or electron withdrawing nature, Y exerts its influence more at ortho and para positions. Hence, ortho and para positions are more activated by an electron donating group while an electron withdrawing group deactivates ortho and para positions more than it does meta.

Let us consider the electrophilic substitution of phenol. The carbocations formed from ortho, meta and para attack by an electrophile, E^+ are shown here.

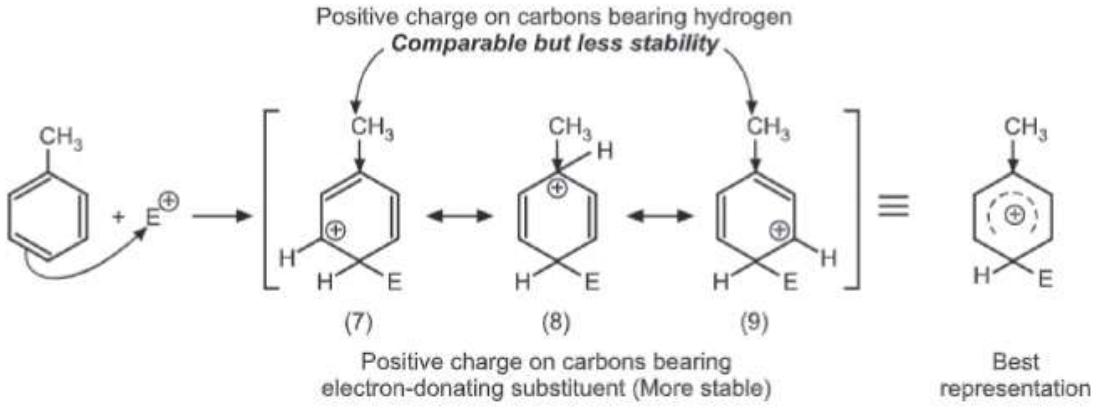
Ortho attack:



Meta attack:

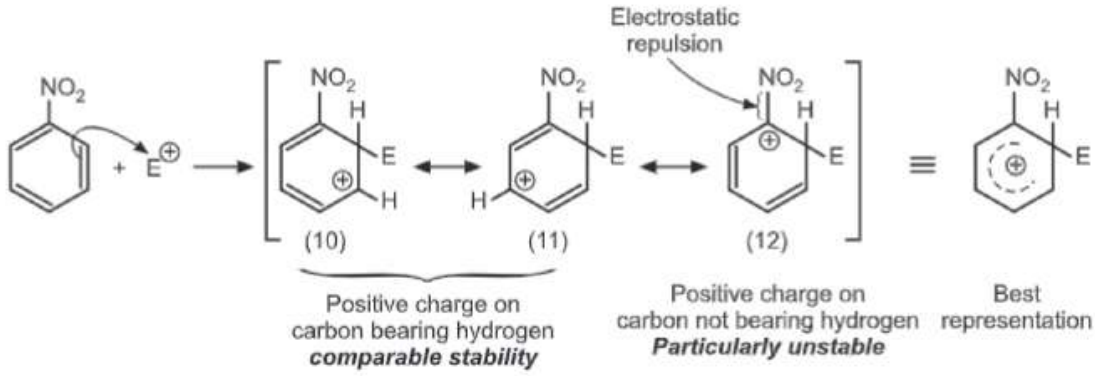


Para attack:

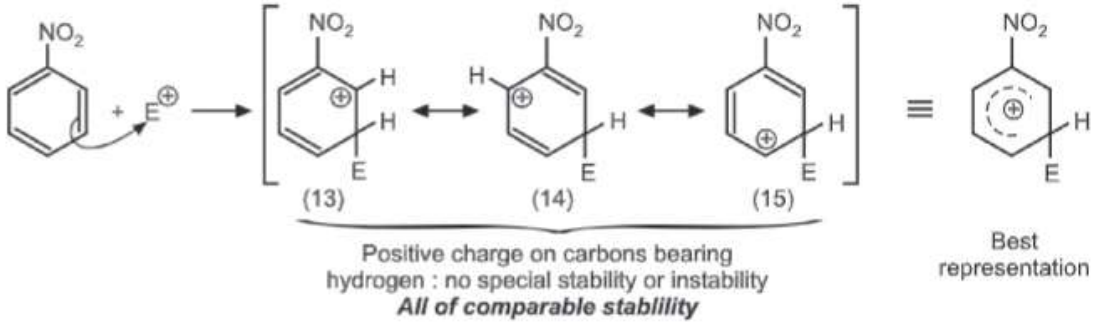


Out of nine carbocations generated, carbocations (3) and (8) are the most stable because of the electron donating hydroxyl group on the carbon bearing positive charge. Thus, we predict that ortho and para attack are favoured over meta attack in phenol. Similarly in case of nitrobenzene, because of unstable carbocations (12) and (17), meta attack is favoured. Hence, the ortho and para substitution is slower than meta substitution.

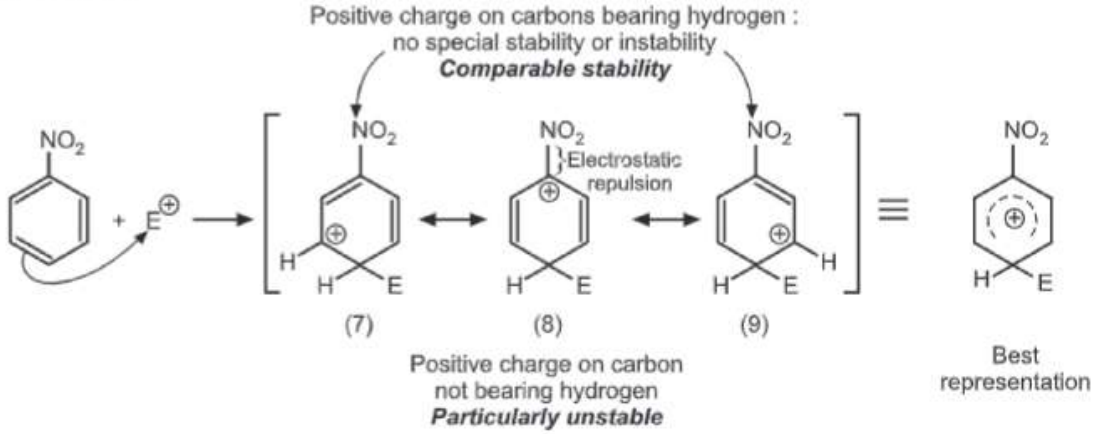
Ortho attack:



Meta attack:

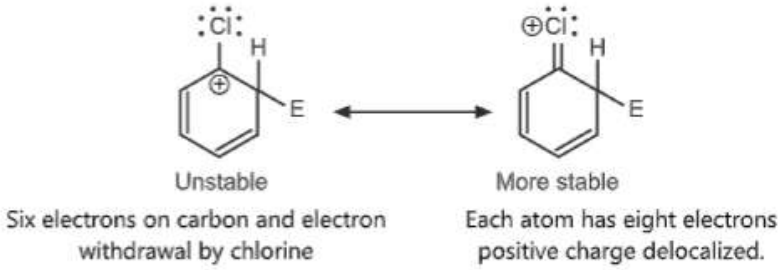


Para attack:



Halogens are unusual in their effect on electrophilic aromatic substitution. A halogen atom deactivates the ring toward further substitution compared with benzene yet it is ortho, para-directing. Because of the electron withdrawal through the inductive effect, halogen leads to a decreased affinity for electrophilic attack on the ring and decreased stability of the carbocation that results. Hence, halobenzenes are less reactive than benzene. We would predict that halogens, such as chlorine, are meta directors. Chlorine contains three unshared pairs of non-bonding electrons and unshared electron pairs adjacent to an aromatic ring can donate electrons through the resonance effect. Due to resonance effect, halogen tends to release electrons and stabilizes intermediate carbocation.

Ortho attack:



Para attack:

Unstable Much stable

Thus, the inductive effect is largely responsible for decreasing reactivity while the resonance effect is largely responsible for governing orientation. In some substituents (–NH_2, –OH), the resonance effect completely dominates the inductive effect. With the halogens, these effects are more evenly balanced. Hence they show the unusual behaviour of being deactivating but ortho, para-directing.

Table 2.1: Orientation in Aromatic Electrophilic Substitution

(A) Activating and ortho/para directing:

e.g. –NH_2, –OH, –OCH_3, –$NHCOCH_3$, –CH_3 etc.

(B) Deactivating and meta directing:

e.g. –NO_2, –COOH, –SO_3H, – CN, –CHO, –COR, etc.

(C) Deactivating and ortho/para directing:

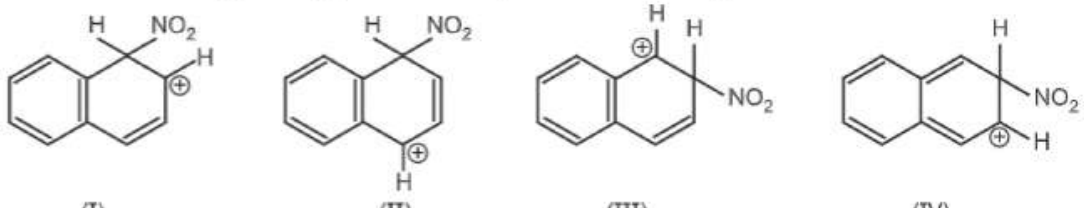
e.g. –F, –Cl, –Br, –I, etc.

The aryl group, Ar, is an ortho, para directing and a weak activating group.

2.12 ELECTROPHILIC SUBSTITUTION IN NAPHTHALENE

The aromatic compounds like naphthalene, anthracene and phenanthrene are called as polycyclic aromatic compounds because they contain two or more rings fused together containing one or more common carbon bonds. These compounds are cyclic, contain (4n + 2) π electrons and are planar. Every carbon in the ring is sp^2 hybridized. Naphthalene is aromatic (resonance energy 61 kcal/mole) and is similar to benzene in reactions.

Nitration and halogenation occur almost selectively in α-position. The transition states for both the attack (α) and (β) have four important resonating structures as follows:

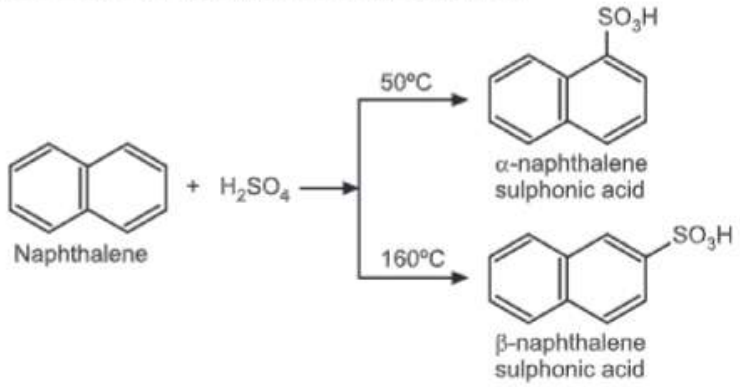


(I) (II) (III) (IV)

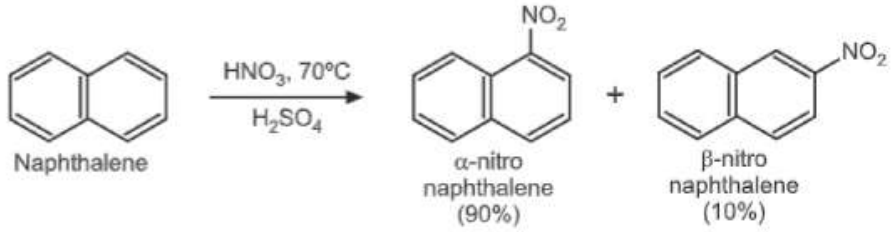
The carbocation generated by the attack of nitronium ion at α-position is a hybrid of structures (I) and (II). In both these structures, aromatic sextlet is preserved. Attack at β-position generates the carbocation that is a hybrid of (III) and (IV). Here only structure (III) has an aromatic nature. Therefore, overalll energy required to attain the transition states for α-attack is less than that of β-attack. Hence nitration would occur much more rapidly at α-position.

In case of transition state of naphthalene, atleast one ring retains its aromatic character. Since, this is not possible in benzene, the energy of the transition state for naphthalene is less than that for benzene by about 10 kcal/mole. Hence, naphthalene in general, is more reactive than benzene. For example, bromination of naphthalene occurs in absence of catalyst. Upon nitration by nitric acid in acetic acid, naphthalene gives mainly 1-nitronaphthalene while thiophen gives 2-nitrothiophen.

(a)



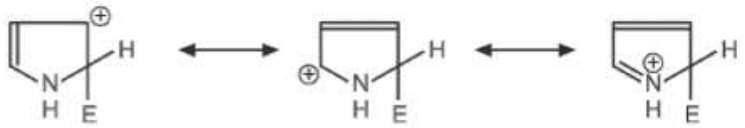
(b)



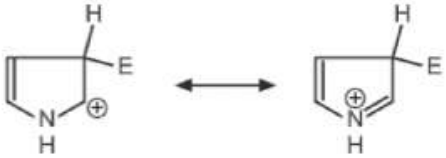
2.13 ELECTROPHILIC SUBSTITUTION IN PYRROLE

Pyridine and pyrrole are aromatic compounds and undergo electrophilic aromatic substitution reactions. Pyridine substitutes preferentially at the 3-position, whereas pyrrole substitutes at the 2-position. Pyrrole is a five membered heterocyclic compound and is more reactive than pyridine and benzene. The reason is the nitrogen atom in the ring uses its loan pair of electrons for delocalisation and stabilizes the intermediate. The positive charge resides on nitrogen, makes the ring electron rich and highly reactive for undergoing electrophilic attack. Pyrrole is so strongly activated that it undergoes Friedel-Craft's acylation even in absence of a catalyst.

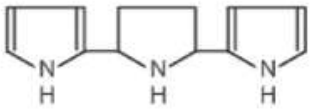
2-substitution:

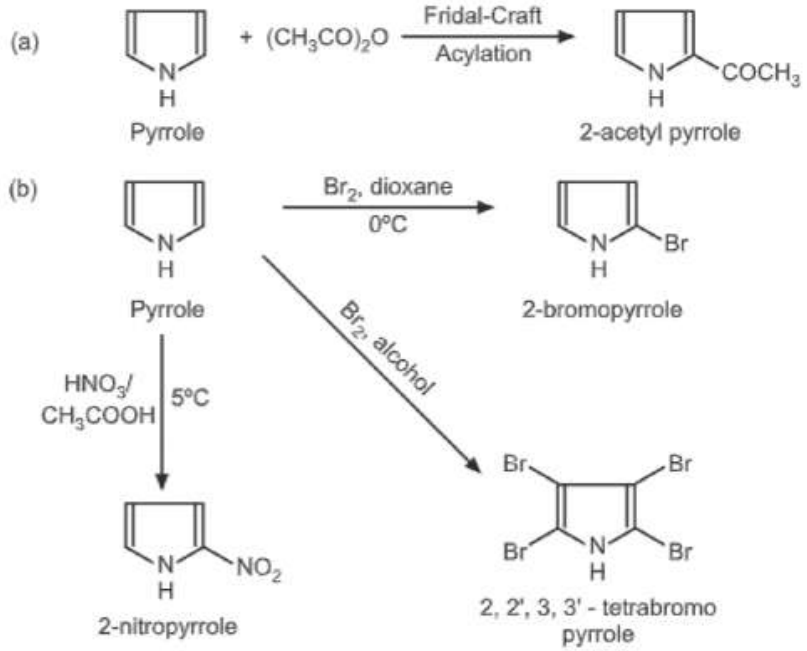


3-substitution:



The 2-substitution has three contributing structures while 3-substitution has only two. Hence, 2-substitution predominates in pyrrole and all five membered heterocycles during electrophilic substitution. However furan and thiophen are less reactive than pyrrole. Because of π excessive heterocycle, pyrrole readily undergoes polymerization in presence of acid to form trimer. This can be avoided by substituting pyrrole with electron withdrawing groups.





Pyrrole acts as a weak base as well as a weak acid. It can react with alkali bases (like KOH, NaOH) to give corresponding alkali salts.

2.14 NITRATION

The most commonly used methods of nitration based on order of their reactivity, include:

(a) a mixture of concentrated nitric acid and concentrated sulphuric acid.

(b) fuming nitric acid in acetic anhydride.

(c) concentrated nitric acid in glacial acetic acid.

(d) dilute nitric acid.

(e) nitrates of alkaline metals in the presence of sulphuric acid.

(f) nitrogen oxides.

(g) nitrates of metals in the presence of acetic anhydride and acetic acid.

(h) a mixture of nitric and sulphuric acids with glacial acetic acid or acetic anhydride.

(i) acetyl nitrate and benzoyl nitrate.

(j) nitrates.

(a) The nitration of aromatic compounds by nitric acid involves the formation of water, i.e., a decrease in the concentration of nitric acid. Dilute nitric acid is a strong oxidizing agent, resulting in the formation of by-products. To avoid this, a nitrating mixture of concentrated nitric and sulphuric acids is usually used. The best yields of nitration products are obtained when 90% sulphuric acid is employed. The nitronium ion, NO_2^+ is generated in the mixture of concentrated HNO_3 and concentrated H_2SO_4 by the following reactions,

$$H_2SO_4 + HO - NO_2 \rightleftharpoons HSO_4^- + H_2O^+ - NO_2$$

$$H_2O^+ - NO_2 \rightleftharpoons H_2O + NO_2^+$$

Nitric acid acts as a base and accepts a proton from H_2SO_4 to generate nitronium ion. Addition of water lowers the nitrating power of this method by reducing the concentration of nitronium ions. Other strong acids like $HClO_4$, HF and BF_3 are also effective in place of H_2SO_4. Many salts such as $NO_2.ClO_4$, BF_4 and $CF_3.SO_3$ can bring about nitration. Because of their explosive nature, they are not normally used for nitration.

(b) A solution of nitric acid in acetic anhydride helps to generate nitronium ion by the following equation.

$$HO - NO_2 + Ac_2O \rightleftharpoons HO - Ac + AcO - NO_2$$

$$2\ AcONO_2 \rightleftharpoons AcOAc + O_2N - O - NO_2$$

$$O_2N - O - NO_2 \rightleftharpoons NO_2^+ + NO_3^-$$

(c) Since, dilute nitric acid contains very less concentration of nitronium ion, its nitrating ability is due to the presence of small concentration of nitrous acid present in it. Nitrous acid generates nitrosonium ion, NO^+. The nitrosated ring then undergoes oxidation by nitric acid to give nitro compound. This reaction liberates nitrous acid to continue the reaction.

$$Ar - H + NO_2 \longrightarrow Ar - NO + H_2O$$

$$Ar - NO + HNO_3 \longrightarrow ArNO_2 + HNO_2$$

Hence, this system can be used for nitration of only those compounds (like phenols) which can undergo nitrosation.

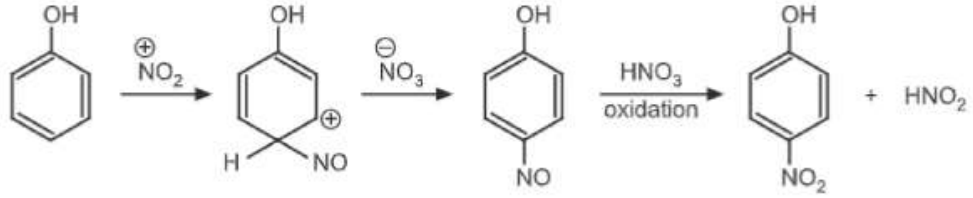


Fig. 2.2: Nitration of phenol

The general mechanisms by which nitration is found to occur are represented below:

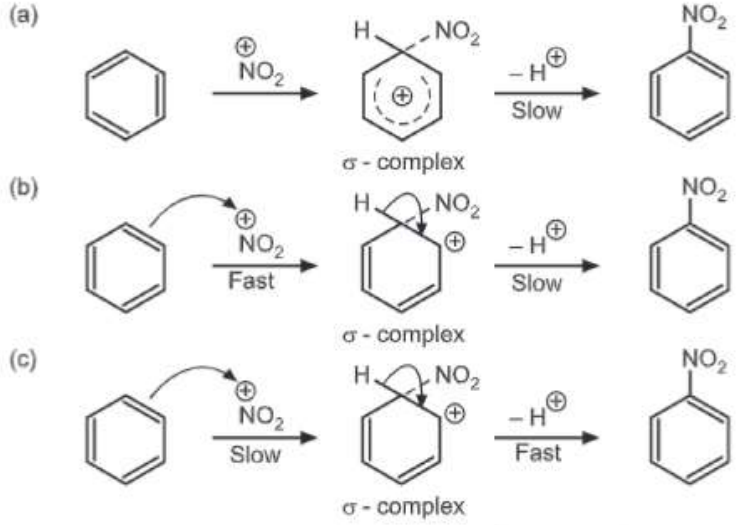


Fig. 2.3: Potential pathways for nitration

Temperature is a critical factor to govern monosubstitution. For example, benzene is converted smoothly into nitrobenzene at 50°-60°C. However, disubstitution is likely to occur if temperature exceeds 60°C.

Phenol and toluene are nitrated more readily than benzene because they contain ortho-para-directing substituents (–OH, $-CH_3$), which make it easier for a nitro group to enter the ring. The substituents $-CH_3$, $-OCH_3$, $-OC_2H_5$ and –OH accelerate nitration in an increasing order, while the substituents –COOH, $-SO_3H$ and $-NO_2$ retard it.

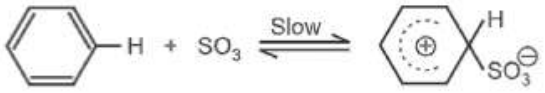
2.15 SULPHONATION

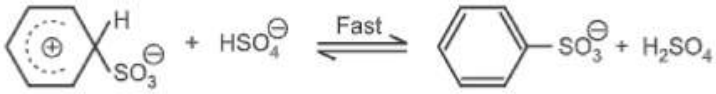
Sulphonation is the introduction of a sulpho group, $-SO_2OH$ into an organic compound. Various sulphonating agents like, concentrated H_2SO_4, oleum, sulphur trioxide, sulphur dioxide and oxygen, sulphurous acid in the form of alkali salts, sulphur dioxide and chlorine, chlorosulphonic acid, etc. may be used to carry out sulphonation.

Polycyclic aromatic hydrocarbons (like anthracene, phenanthrene) are sulphonated most easily. Naphthalene is sulphonated with difficulty and benzene, with even greater difficulty.

The sulphonation of benzene is often carried out with either concentrated H_2SO_4 or with fuming H_2SO_4 (i.e, sulphuric acid containing sulphur trioxide, SO_3). Sulphur trioxide is the effective electrophile involved in sulphonation reaction. The rate of reaction depends on the concentrations of aromatic ring and sulphur trioxide and not on sulphuric acid. It is a reversible reaction and proceeds through the following mechanism.

(a) $2H_2SO_4 \rightleftharpoons SO_3 + HSO_4^{\ominus} + H_3O^{\oplus}$

(b) 

(c) 

The water separated in the reaction reduces the concentration of sulphuric acid, which loses its sulphonating properties, and causes a reversible reaction, i.e., the hydrolysis of the sulphonic acid being formed. The reversibility of the reaction is observed when the product is treated with steam which results into replacement of $-SO_3H$ group by 'H'.

The readiness with which sulphonation takes place depends upon the nature of substituents present on the aromatic ring. Electron releasing substituents increase the ease of sulphonation reaction in the following order.

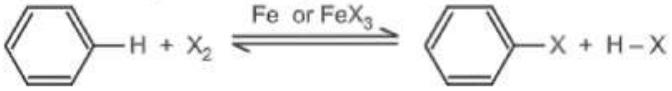
$$OH > OR > NH_2 > NHCOR > R$$

Electron withdrawing substituents and halogens hinder the introduction of the sulpho group.

Temperature condition is the critical factor in sulphonation reaction. Higher temperature not only accelerates the process, but also promotes the formation of by-products which include sulphones, polysulphonic acids and oxidation and condensation products. Temperature condition also determines the position of attack for sulpho group into the aromatic ring. For examples, at low temperatures, α-naphthalene sulphonic acid is formed several times faster than the β-isomer. In some cases, the catalyst also governs the site of attack of the sulpho group. For example, β-anthraquinone sulphonic acid is mainly formed when anthraquinone is sulphonated in absence of a catalyst while α-anthraquinone sulphonic acid is formed when it is sulphonated in presence of mercury salts.

2.16 HALOGENATION

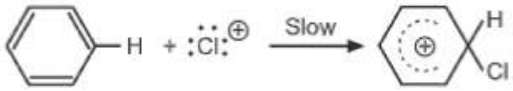
Halogenation is accomplished by treating aromatic compound with molecular halogens like Cl_2, Br_2 or I_2. Fluorination is highly exothermic and explosive. Chlorination and bromination have moderate speed and are easy to carry out. While iodination is slower reaction and is possible only with activated aromatic compounds like phenols, aniline, etc. To speed up the reaction usually iron metal, or ferric halide is added in catalytic amounts.

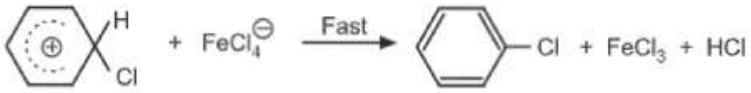


Certain Lewis acids such as $AlCl_3$ or $AlBr_3$ are also effective catalysts. The Lewis acid polarises the halogen molecule to promote an interaction between the positively charged electrophilic end of halogen molecule and π-cloud of benzene.

The general mechanism of halogenation include

(a) $FeCl_3 \rightleftharpoons FeCl_4^{\ominus} + :\ddot{\underset{\cdot\cdot}{Cl}}:^{\oplus}$

(b) 

(b) 

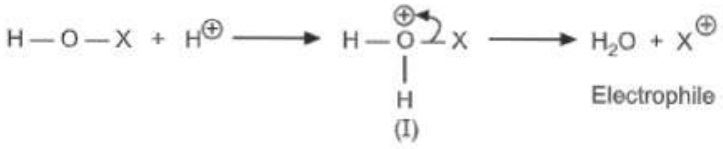
The iron atom in $FeCl_3$ is electron deficient. It may complete its octet by accepting a pair of electrons from a chlorine atom and acquires a negative charge. An electron deficient $:\ddot{\underset{\cdot\cdot}{Cl}}^{\oplus}$ ion is generated as a result, which attacks the aromatic ring.

Halogenation may also be carried out by:

(a) The use of interhalogen compounds like Br–Cl; I–Cl so that the attack of π-electron cloud will occur through the less electronegative halogen atom.

(b) Hypo-halous acid HO-X too. This reaction is slower than with molecular halogens, X_2 because OH is a poorer leaving group from $HO^{-\delta}-X^{+\delta}$ than X^- from X–X.

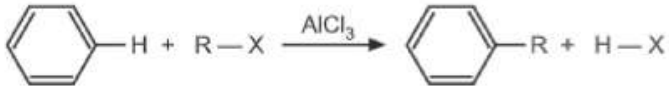
(c) In the presence of strong acid, however, H–OX becomes a very powerful halogenating agent due to the formation of a highly polarised complex as follows:



The species (I) is effective electrophile and does not get further converted into water and X^+ because H_2O is much better leaving group than Cl^-. Thus, (HOCl + acid) is more effective chlorinating agent than $Cl_2/AlCl_3$.

2.17 FRIEDEL – CRAFT'S ALKYLATION

In 1877, C. Friedel and J. Craft showed that benzene and its homologs are capable of being alkylated by alkyl halides in the presence of anhydrous $AlCl_3$. It involves the attack of either a free carbocation or a partially positive carbon atom on the electron rich π cloud of the benzene ring. In this reaction, an alkyl group is introduced in the benzene ring. When benzene is treated with an alkyl halide (R–X) in the presence of Lewis acid catalyst like anhydrous $AlCl_3$, alkyl benzene is formed.



The carbon atom of the alkyl halide is a weak electrophile. The Lewis acid polarises or ionises the C–X bond to generate an effective electrophile, R^+ to promote the substitution. Other catalysts like FeX_3, BF_3 and HF can also be used. Hydrogen fluoride helps to polarise the halogen on the alkyl halide by forming a hydrogen bond between the two molecules.

The degree of polarisation depends upon the nature of 'R' group in alkyl halide and the Lewis acid used. The Lewis acids have the following order of effectiveness.

The general mechanism of Friedel–Craft's alkylation include,

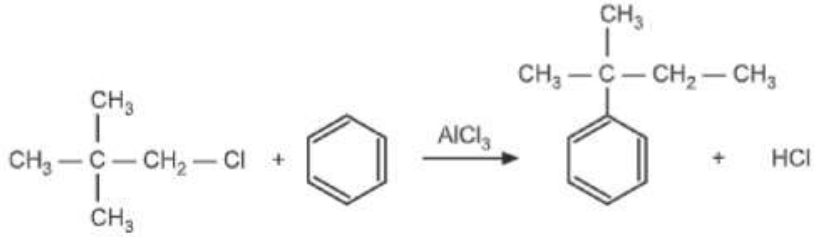
(a) $R—Cl + AlCl_3 \rightleftharpoons R^{\oplus}(AlCl_4)^{\ominus}$

(b) 

(c) 

Changing reaction conditions like solvent, temperature, concentration and catalyst often produces varying amount of rearrangement.

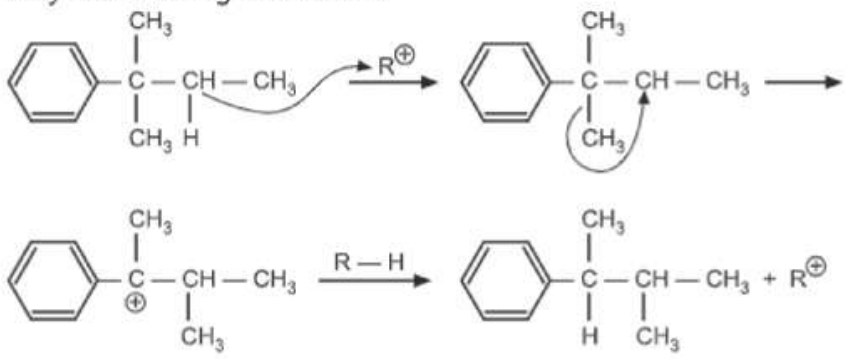
For example,



2, 2-dimethyl-1-chloropropane 2-methyl-2-phenylbutane

The less stable carbonium ions try to rearrange to more stable ones before they react with aromatic ring. Rearrangement of the side-chain may often occur after it is attached to the ring.

The 2-methyl-2-phenylbutane formed in above reaction, rearranges to 2-methyl-3-phenylbutane by the following mechanism:

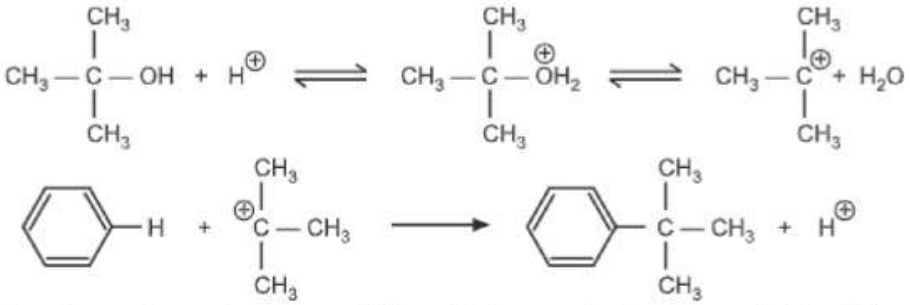


2-methyl-3-phenylbutane

The temperature has an effect on rearrangement. At low temperatures (0°C), the energy necessary for the rearrangement is not available. This yields the expected product in major amount.

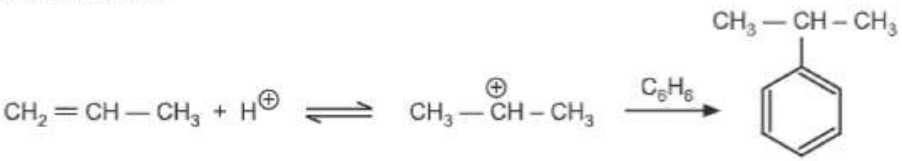
As alkenes and alcohols are capable of producing carbonium ion in acidic medium, they can also be used for alkylation. BF_3 may be used as the Lewis acid catalyst. Aromatic hydrocarbons can be alkylated by alcohol in the presence of sulphuric acid (as well as $AlCl_3$, HF, P_2O_5 and H_3PO_4). When sulphuric acid is used, it is heated to 74-80°C and, while stirring, a mixture of aromatic hydrocarbon and alcohol is slowly poured in during the course of 3-5 hours.

(a)



Alkylation depends on the nature of the substituents in the aromatic ring. The presence of halogens, nitro or sulpho group impedes the introduction of the alkyl radical. The presence of the alkyl group in the ring promotes further alkylation and mainly para substitution is favoured.

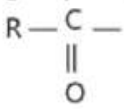
(b)



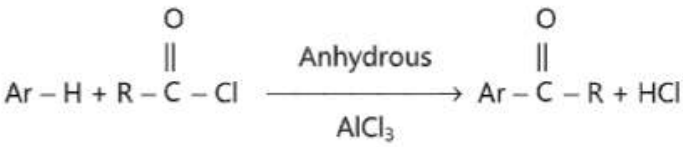
The applicability of Friedel-Craft's alkylation is limited because of formation of a mixture of mono, di and polysubstituted hydrocarbons. The desired product may also be dehydrogenated, hydrogenated, isomerized and polymerized under the influence of $AlCl_3$, thus reducing the yield and giving rise to problems in isolating the main product.

2.18 FRIEDEL-CRAFT'S ACYLATION

The acylation reaction is the replacement of the hydrogen atom of certain functional groups i.e, the hydroxyl, amino and other groups, by the residue of carboxylic acid:



Esters are obtained from acylation of alcohol and mono and disubstituted amides are obtained in amine acylation. Preparation of aromatic ketones by the interaction of aromatic hydrocarbons with acid chlorides or anhydrides in the presence of aluminium chloride is called as Friedel-Craft's acylation. This is an electrophilic substitution reaction in which the RCO–, and ArCO– moieties, referred to as acyl groups are introduced onto the rings. When an aromatic compound is treated with acid chloride and aluminium trichloride, an aromatic ketone is formed.



Aluminium trichloride acts as a Lewis acid and removes chloride from the acid chloride to produce the electrophile. The effective electrophile may be the acylium ion or a polarised complex. The reaction conditions (i.e., polarity of solvent and size of R) govern the nature of electrophile.

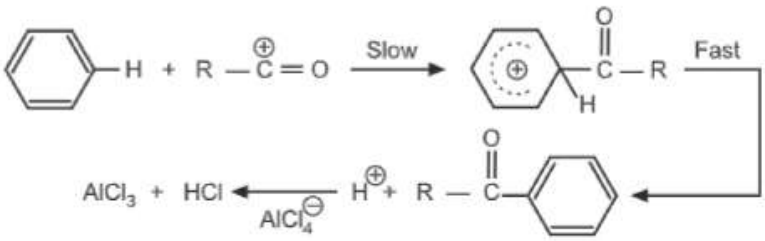
Acylium ion Polarised complex

The reaction is carried out under anhydrous conditions. More than 1 mole equivalent of $AlCl_3$ must be used for each mole of acid chloride.

The general mechanism of reaction follows as below:

(a)

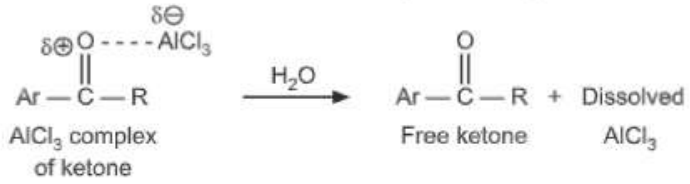
(b)



Since, the reaction is exothermic, an acid chloride or anhydride should be added dropwise to the mixture. After the acylating agent is added, the reaction mixture is heated in

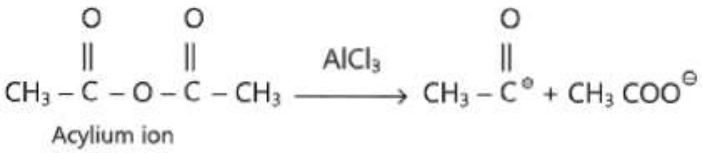
a water-bath for 1-3 hours and then poured out on ice and treated with hydrochloric acid. The ketone isolated is extracted by a solvent, the water layer is separated, and then ketone is dried and distilled.

The aluminium in $AlCl_3$ coordinates with the carbonyl oxygen of the ketone. The ketone is liberated by the addition of water which breaks up the complex.



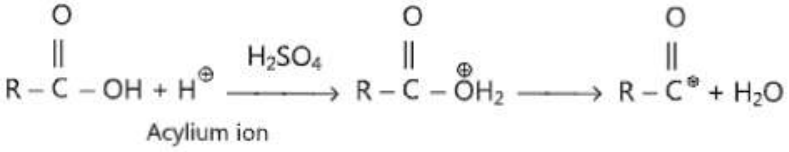
Unlike Friedel-Craft's alkylation, acylation reaction does not undergo rearrangement. It can not be carried out on deactivated (i.e, having strongly deactivating meta directors) aromatic ring. For example, benzoyl chloride can not acylate m-dinitrobenzene because of the presence of deactivating nitro groups. For the same reason, the introduction of a second acyl group onto the ring is impossible. However, the acid chloride containing one or more strongly deactivating groups may be used.

Besides acid chloride, acid anhydride may also be used to carry out acylation.

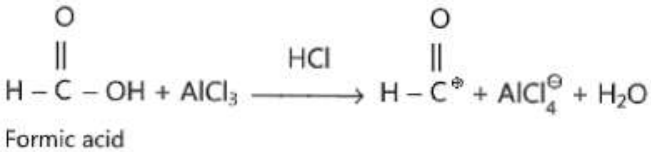


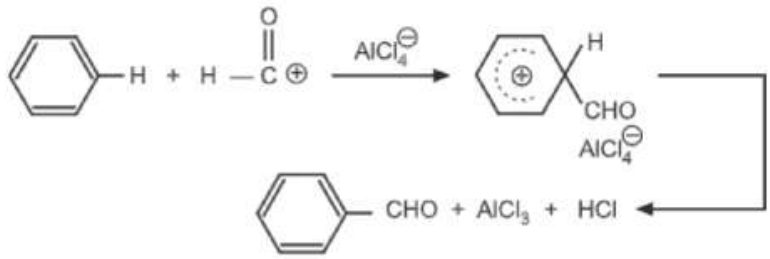
Unlike alkylation by Friedel-Craft's method, for which the presence of a small amount of aluminium chloride is enough, acylation occurs satisfactorily only when the amount of $AlCl_3$ used is far greater than that used for alkylation. In acylation by acid anhydrides, an even larger amount of $AlCl_3$ must be used (i.e., more than 2 moles of $AlCl_3$ per mole of acid anhydride) because the ketone and acetic acid, formed as a result of reaction, bind the same amount of the catalyst.

The acylium ion may also be generated from carboxylic acids by the action of conc. H_2SO_4 or HF through protonation reaction.



While to carry out formylation, Gattermankoch reaction is suggested in which HCOOH, HCl and $AlCl_3$ are used.



(b) 

Since, many organic solvents react with $AlCl_3$, selection of a proper solvent for Friedel-Craft's reaction is problematic. Usually carbon disulphide, nitrobenzene, petroleum ether or excess of aromatic hydrocarbon is used.

2.19 NITROSATION

Nitrosation is an electrophilic aromatic substitution reaction in which the nitrosonium ion, NO^+ is an effective electrophile. The nitrous acid (HNO_2) is generated in both diazotization and nitrosation reaction. It is converted to nitrosonium ion through the following steps.

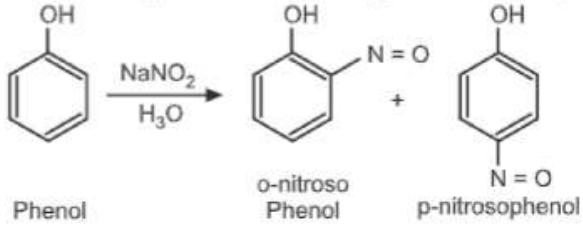
(a) $2NHO_2 \rightleftharpoons H_2O + N_2O_3 \equiv O = N - O - N = O$

Nitrous acid anhydride

(b) $O = N - O - N - O \longrightarrow NO_2^{\ominus} + NO^{\oplus}$

Nitrous acid anhydride Nitrosonium ion

In fact, in many diazotization reactions of primary amines, nitrosonium ion may be acting as a reactive species. For nitrosation to occur on an aromatic ring, the ring should be activated by the presence of strong electron-releasing substituents (i.e., phenols).



Phenol o-nitroso Phenol p-nitrosophenol

Nitrosonium hexafluorophosphate $NO^+PF_6^-$ may also be used as an effective nitrosating agent.

2.20 DIAZO COUPLING

The diazotization reaction, discovered by Griess in 1858, consists in the formation of diazonium salts when primary aromatic amines interact with nitrous acid in an acidic medium.

Diazo coupling comprises of diazotization of primary amine and coupling of diazotized salt with phenols. Since, diazonium cation is a weak electrophile, it can only attack highly activated aromatic rings like phenols or amines that results in the formation of the azo compounds Ar – N = N – Ar.

The diazocoupling occurs easily with phenols and with somewhat greater difficulty with amines. The azo compounds are very stable and are usually brightly coloured. Their colour is due to the presence of a chromophore (–N = N–) in the molecule. The diazo coupling reactions are routinely used in the manufacture of azo dyes. Primary amines react with sodium nitrite and dilute HCl to form diazanium cation. The reaction is carried out at low temperature usually around 0°C, because of the relative instability of these salts.

$$R-NH_2 + O=N-OH \xrightarrow[0^\circ C]{HCl} R-N=N-OH + H_2O$$

The aliphatic diazonium cations are less stable than aromatic diazonium cations where a stabilizing effect is provided by the π-orbital system of the nucleus.

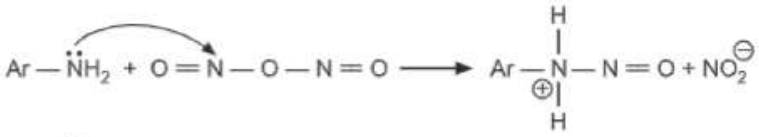
The general mechanism of diazotization include

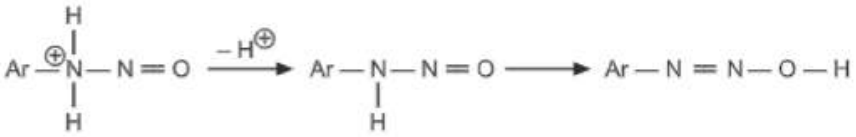
(a) $NaNO_2 + HCl \longrightarrow HNO_2 + NaCl$

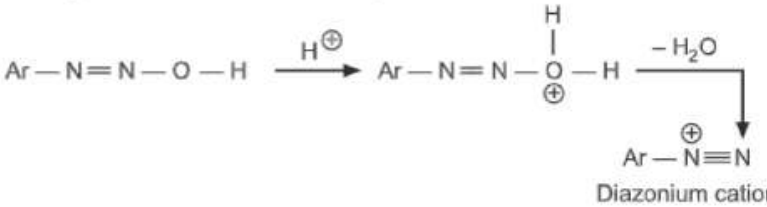
Nitrous acid

(b) $2HNO_2 \rightleftharpoons H_2O + O=N-O-N=O$

Nitrous acid anhydride

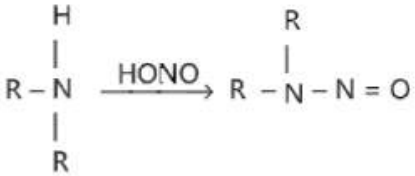
(c) 

(d) 

(e) 

Diazonium cation

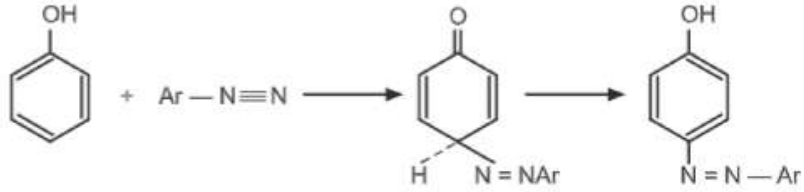
Secondary amines react with nitrous acid to give N-nitroso amines while tertiary amines do not react with nitrous acid. Nitrosation of the ring may often result if an aromatic tertiary amine is used.



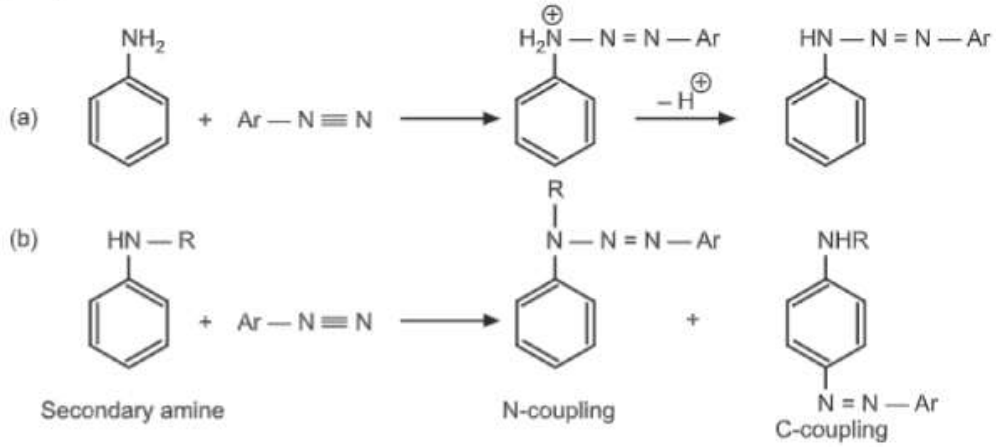
Secondary amine **N-nitrosoamine**

In a strongly acidic medium, neither aromatic amine nor phenol is capable of undergoing coupling reaction due to the very low concentrations of free amine (owing to the formation of diazonium salts) and the phenolate ion (phenol dissociation is strongly suppressed). In a strongly alkaline medium, a free base known as diazohydroxide (Ar–N = N–OH) separates from a diazonium salt which then forms a salt (Ar–N = N–ONa) which is not capable to undergo azo coupling.

Since, diazonium cations exist in acidic or slightly basic solution, the coupling reactions are carried out under these pH conditions. For example, coupling of diazotized cation with phenoxide ion takes place in basic medium.



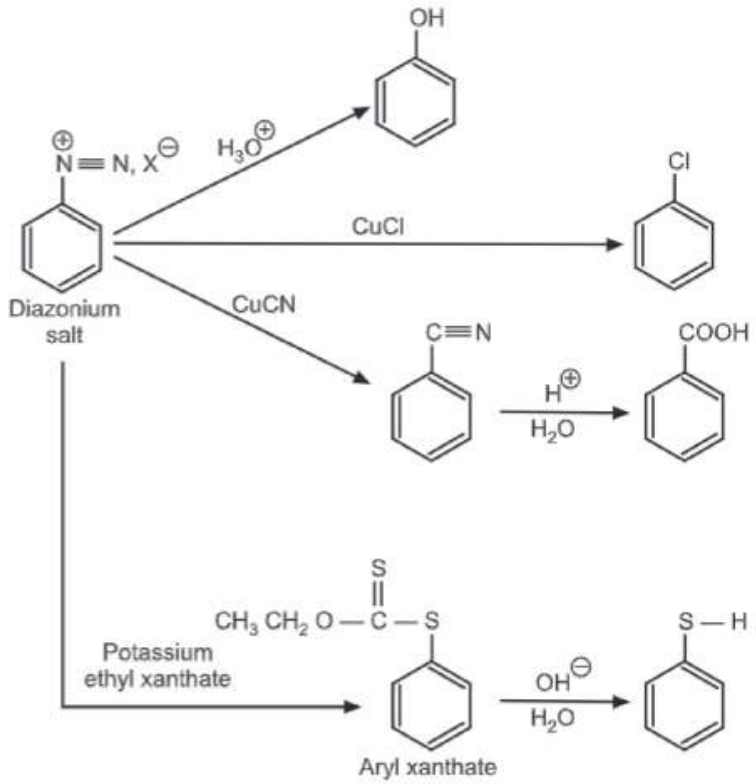
Because of the bulkiness of attacking electrophile, ArN_2^+, coupling normally takes place at the para position. Primary and secondary arylamines in slightly acidic condition, undergo coupling with diazonium cation.



The primary amines undergo coupling reaction at nitrogen. With secondary amine, some coupling may also occur at carbon atom of the ring. With tertiary amine, coupling takes place only on carbon atom of the ring.

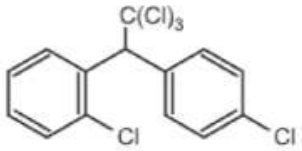
Amines which form diazonium salts are called **diazo components** of a dye, while phenols and amines which enter azo coupling are called as **azo components**. The activity of diazo components is enhanced by halogens and electron withdrawing groups. These substituents reduce the activity of azo components.

Upon warming in acidic solution, the diazonium compound may be transferred to phenols, aromatic amines or other suitable functional group added to the solution. Diazonium salts from primary aromatic amines are versatile synthetic tools to get a wide variety of organic compounds.



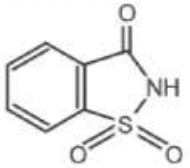
2.21 STRUCTURE AND USES

(1) DDT (Dichloro diphenyl trichloroethane): It is a colourless, tasteless and odourless crystalline compound. Commercially, it is a mixture of several isomers with highest components (77%) of the p, p' isomer.



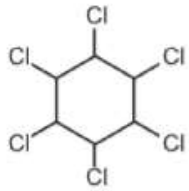
It was earlier used as an agricultural insecticide. Presently, it is mainly used for the control of malaria and visceral leishmaniasis.

(2) Saccharin (Benzoic sulfimide): It is an artificial sweetener having a bitter or metalic after taste. It is chemically inert and heat stable.



It is used as an artificial sweetener alone or in combination with other sweeteners in the carbonated soft drinks and by diabetic people.

(3) Benzene hexachloride (BHC): It is a white to yellowish crystalline, water soluble poisonous solid used mainly as an insecticide. The insecticidal properties were identified more with the γ (gamma) – isomer, also known as lindane. In 2009, agricultural use of lindane was banned while its use as a second-line pharmaceutical treatment for lice and scabies is still permitted.



(4) Chloramine (Monochloroamine): The term chloramine refers to monochloramine (H_2N–Cl), dichloramine (HN–Cl_2) and nitrogen trichloride (N–Cl_3). Monochloramine is an unstable colourless liquid. It is used in the form of dilute aqueous solution as a drinking water disinfectant. It is an oxidizing agent. Chloramine provides longer lasting water disinfection.

EXERCISE

1. What do you mean by resonance hybrid ? Describe the resonance hybrid for:
   (a) Carboxylate ion (b) Urea (c) Nitro group.
2. Give the reasons:
   (a) Phenol is considered as an acidic compound.
   (b) Alcohols are less acidic than carboxylic acids.
   (c) The methyl group present on the benzene ring shows o, p-orientation effect.
   (d) N, N – dimethylaniline is much weaker base than its 2, 6 – dimethyl analogue.
3. List four Friedel-Craft's catalysts in the increasing order of their reactivity. Name three types of aliphatic compounds which may take part in a Friedel-Craft's reaction.
4. What is the principal disadvantage in the use of the Friedel-Craft's reaction in the synthesis of alkyl substituted aromatic hydrocarbons ?
5. Explain the chemical reactivity of benzene ring with reference to resonance effect.
6. Whether addition or substitution is the most important type of reaction of the benzene ring ?
7. (a) List four ortho-para directing groups in the increasing order of their strength.
   (b) List five meta directing groups in the increasing order of their strength.
8. Explain theory of orientation and reactivity in electrophilic substitution of benzene.
9. Nitration of Nitro benzene yields only m-dinitro benzene. Explain why?
10. Write a note on nitration of benzene.
11. Explain Huckle Rule for aromaticity with example.
12. Explain in short 'Rules of Aromaticity'.
13. Write reaction mechanism of aromatic electrophilic sulphonation.
14. Discuss the effect of substituents on orientation and reactivity in monosubstituted benzene.

❖❖❖

Unit III

PHENOLS, AROMATIC AMINES AND AROMATIC ACIDS

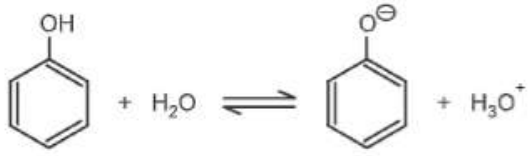
♦ **SYNOPSIS** ♦

3.1 INTRODUCTION

Phenols are organic compounds containing benzene ring bonded to a hydroxyl group.

Acidity of phenols: Phenols are more acidic than alcohols but less acidic than carboxylic acids. The acidity of phenol is due to its ability to lose hydrogen ion to form phenoxide ion.

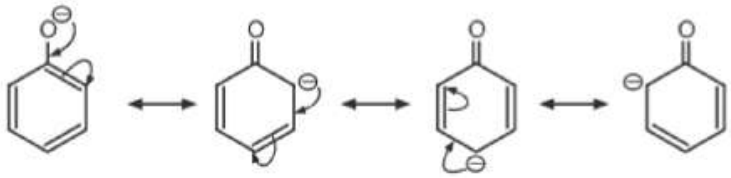
Phenol is a weak acid. For example,



Phenol Phenoxide ion

The negative charge on the oxygen atom is delocalized around the ring. As a result, the negative charge is no longer entirely localized on the oxygen but is spread out around the whole ion.

The negative charge of phenolate ion is stabilized by resonance. This makes the phenoxide ion more stable.



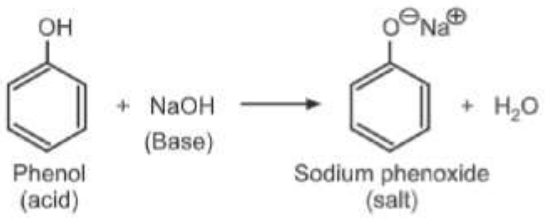
Resonance structures of phenoxide ion

(3.1)

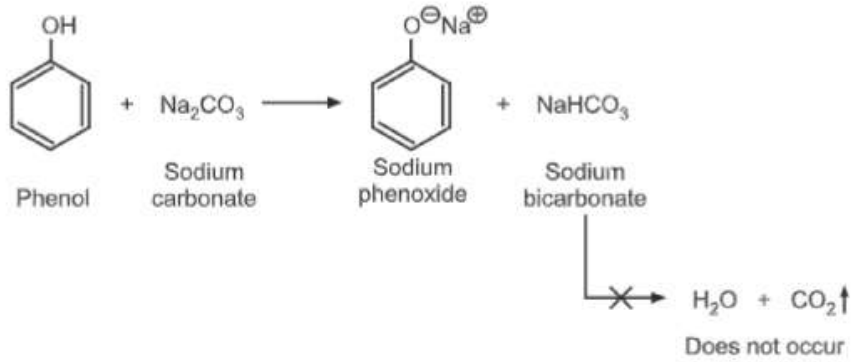
Acidic characteristics of phenol:

(i) pH of dilute solution of phenol in water ranges between 5 – 6.

(ii) Phenol reacts with sodium hydroxide solution to give colourless solution containing sodium phenoxide.

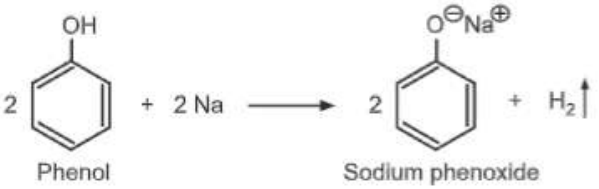


(iii) Due to weak acidic nature, phenol partially reacts with sodium carbonate to give sodium phenoxide and sodium bicarbonate.



Unlike other carboxylic acids, phenol is not acidic enough to react with sodium bicarbonate to produce carbon dioxide and water.

(iv) Like other acids, phenol reacts with metallic sodium/potassium to give hydrogen gas. Phenol being a weak acid it is a slow reaction.



Effects of Substituents on Acidity:

The resonance structures of phenoxide ion explain the delocalization of negative charge at ortho and para positions of the benzene ring.

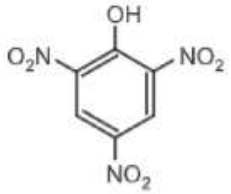
Substituents, particularly those located ortho or para to the –OH group, can dramatically influence the acidity of the phenol due to resonance and/or inductive effects.

Electron withdrawing groups like $–NO_2$, –COOH increase the stability of phenoxide ion.

Table 3.1: Effect of Substitutents on acidity of phenol

Electron releasing substituents			Electron withdrawing substituents		
Sr. No.	**Compound**	**pKa**	**Sr. No.**	**Compound**	**pKa**
1.	Phenol	10.0	1.	o-Nitrophenol	7.2
2.	o-Methylphenol	10.3	2.	p-Nitrophenol	7.2
3.	p-Methylphenol	10.3	3.	m-Nitrophenol	8.4
4.	o-Methoxyphenol	10.0	4.	o-Chlorophenol	8.6
5.	p-Methoxyphenol	10.2	5.	p-Chlorophenol	9.4
6.	p-Aminophenol	10.5	6.	p-Bromophenol	9.3

Hence, these groups increase the acidity of phenols, if attached at ortho or/and para positions to the hydroxyl group. For example, the influence of a nitro substituent is over ten times stronger in the para-location than at meta. Additional nitro groups have an additive effect if they are positioned at ortho and para positions. For example, 2,4,6-trinitrophenol (picric acid) is a very strong acid.



Picric acid

While electron donating groups like – CH_3, – OH, $-NH_2$ decrease the acidity of phenols as they prohibit the formation of phenoxide ion.

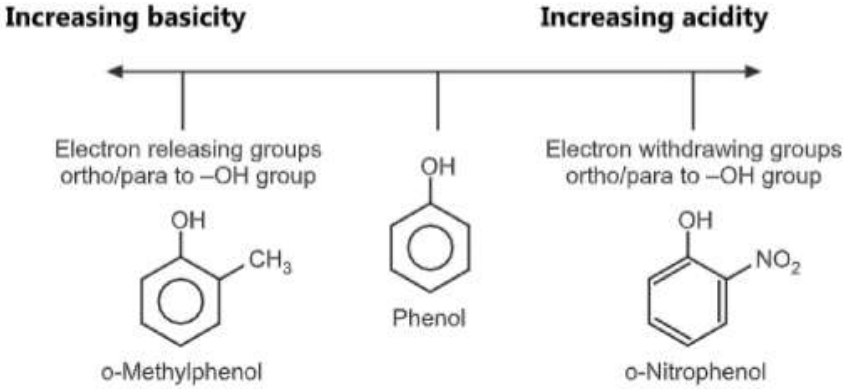
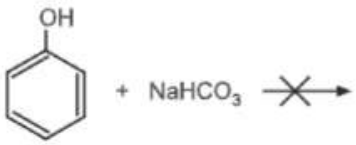
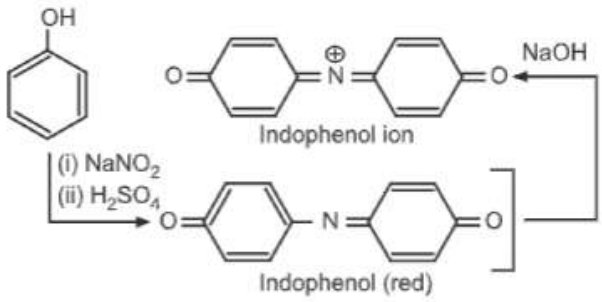
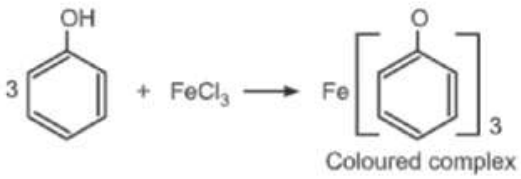
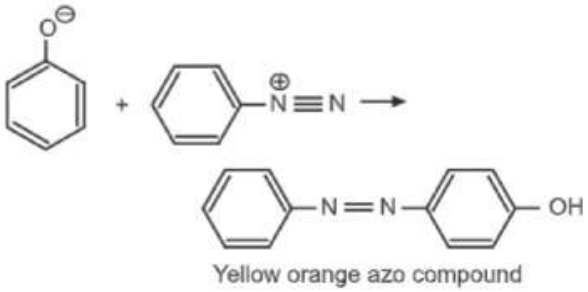


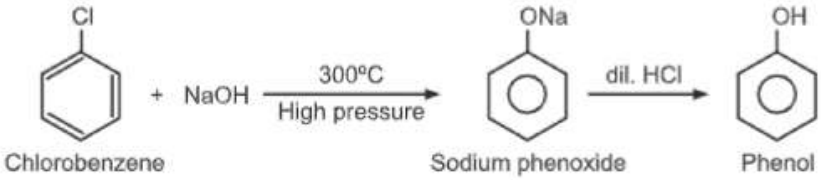
Table 3.2: Qualitative tests for Phenol

Sr. No.	Name of test	Particulars
1.	Reaction with NaOH and $NaHCO_3$ 	Soluble in NaOH solution. Insoluble in and no release of CO_2 gas from $NaHCO_3$ (except strongly acidic phenols, like 2, 4-dinitrophenol, picric acid, etc.)
2.	Lieberman nitroso Test 	A pinch of $NaNO_2$ added to 0.2 ml of phenol solution. Heated gently till the $NaNO_2$ melts. Add conc. H_2SO_4 dropwise followed by excess of NaOH. The nitrosamine gave rise to a red colour in acid solution which changes to blue and then green when the solution was made alkaline.
3.	Ferric chloride Test 	1-2 drops of 1% aqueous ferric chloride solution added to aqueous solution of phenol gives a red, blue, green or purple colour precipitate.
4.	Azo-Dye Test 	Aqueous $NaNO_2$ solution is added to solution of aniline in dil. HCl with cooling, immediately add phenol solution. A bright orange saffron colour precipitate is observed.

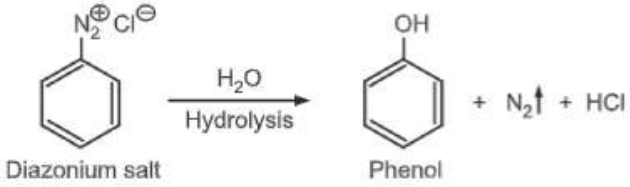
3.2 GENERAL METHODS OF PREPARATION OF PHENOLS

Phenol was initially obtained by fractional distillation of coal tar.

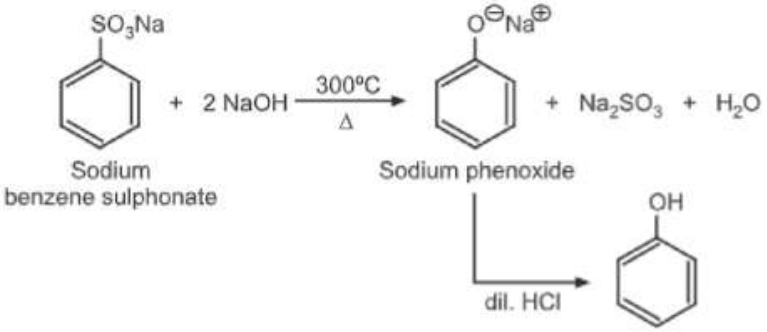
(a) Dows process: When chlorobenzene is heated with caustic soda at 300°C at 300 atm. pressure, sodium phenoxide is formed. It, upon acidification, gets converted to phenol.



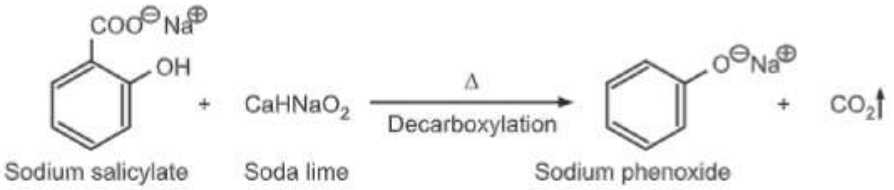
(b) From diazonium salt: A diazonium salt when warmed in presence of water, produces phenol.



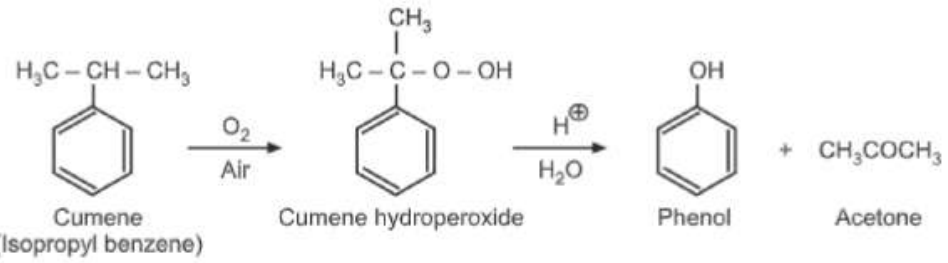
(c) From benzene sulphonate: When benzene sulphonate is heated with caustic soda at 300°C, sodium phenoxide is formed which upon acidification gives phenol.



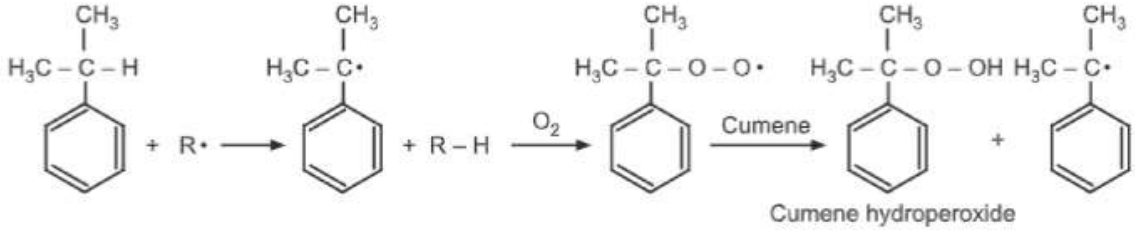
(d) From salicylic acid: Sodium salicylate when heated with sodalime undergoes decarboxylation to give sodium phenoxide which on acidification gives phenol.



(e) Acidic oxidation of cumene: Cumene is oxidized in presence of air to give cumene hydroperoxide. The formation of cumene hydroperoxide proceeds by a free radical chain reaction.

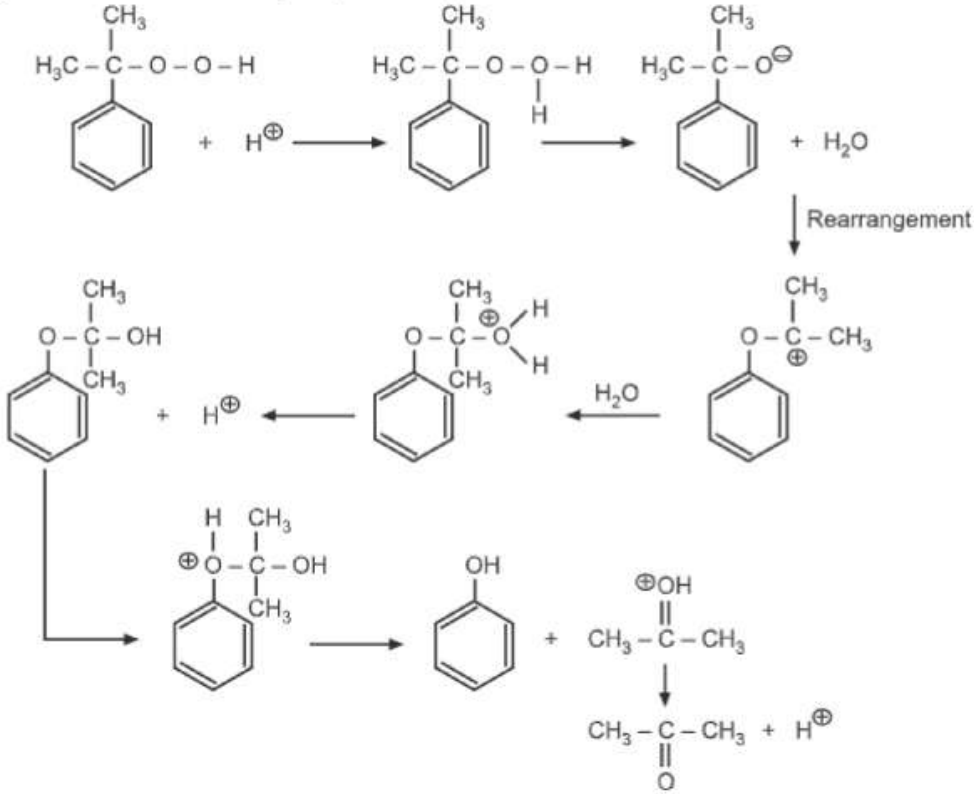


The creation of the tertiary free radical is the initial step in the reaction.

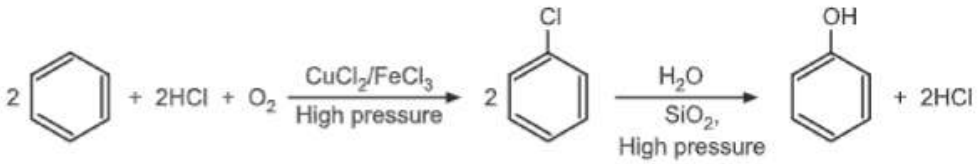


In the next step, the free radical is attached to O_2 molecule. Finally, the hydroproxide free radical abstracts a hydrogen free radical from a second molecule of cumene to form cumene hydroperoxide and a new tertiary free radical.

The degradation of cumene hydroperoxide proceeds via a carbocation mechanism.

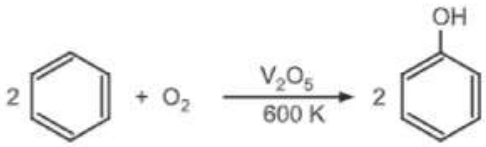


(f) From benzene (Rachig's method):



This method involves heating of benzene, HCl and air over a catalyst (mixture of $CuCl_2$ and $FeCl_3$) at high pressure of 500 K to give chlorobenzene which is then heated with super heated steam at high pressure at 750 K to give phenol.

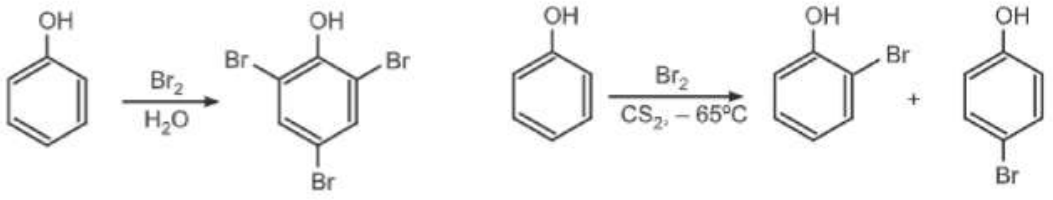
In yet another method, benzene and air is passed over V_2O_5 at 600 K. Benzene is thus oxidised to give phenol.



3.3 REACTIONS OF PHENOLS

Phenol undergoes electrophic aromatic substitution reactions. Due to electron donating nature of the –OH group, the next substitution takes place preferrably at ortho and/or para positions to –OH group.

(a) Bromination: An aqueous bromine solution brominates all ortho and para positions on the ring to give a white precipitate of 2, 4, 6-tribromophenol.



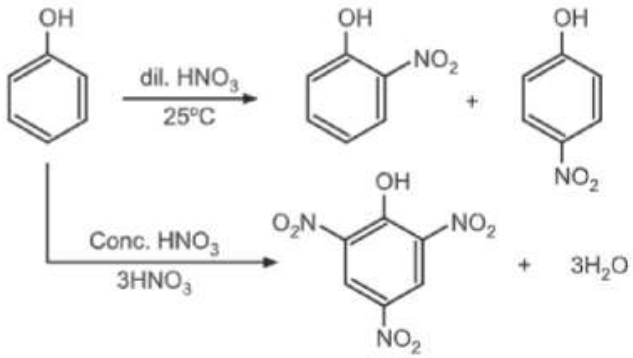
2, 4, 6-tribromophenol

Orthobromo product

p-bromo

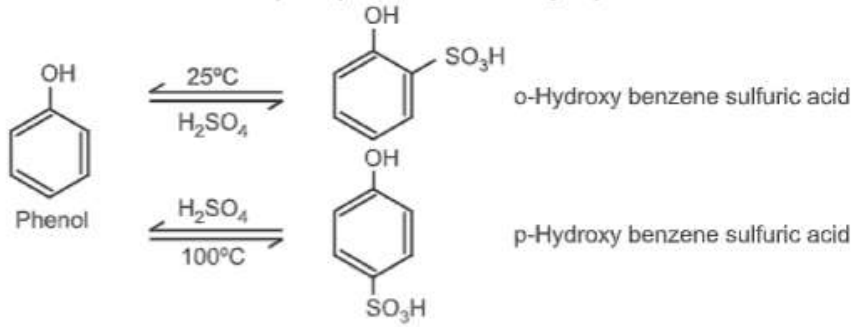
Monobromination is done by running the reaction at extremely low temperature in carbon disulfide solvent.

(b) Nitration: Phenol, when treated with dil. HNO_3 at room temperature gives mono-nitrated derivatives. While 2, 4, 6-trinitrophenol is obtained when phenol is treated with conc. HNO_3.

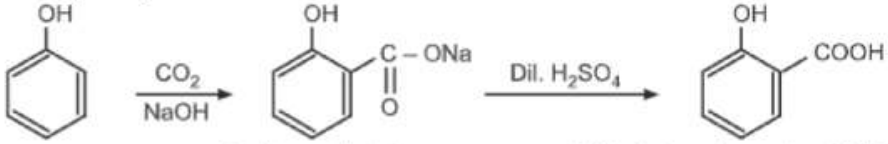


2, 4, 6-trinitrophenol (Picric acid)

(c) Sulfonation: Phenol reacts with conc. H_2SO_4. At 25°C, the ortho product predominates while at 100°C, the para product is the major product.

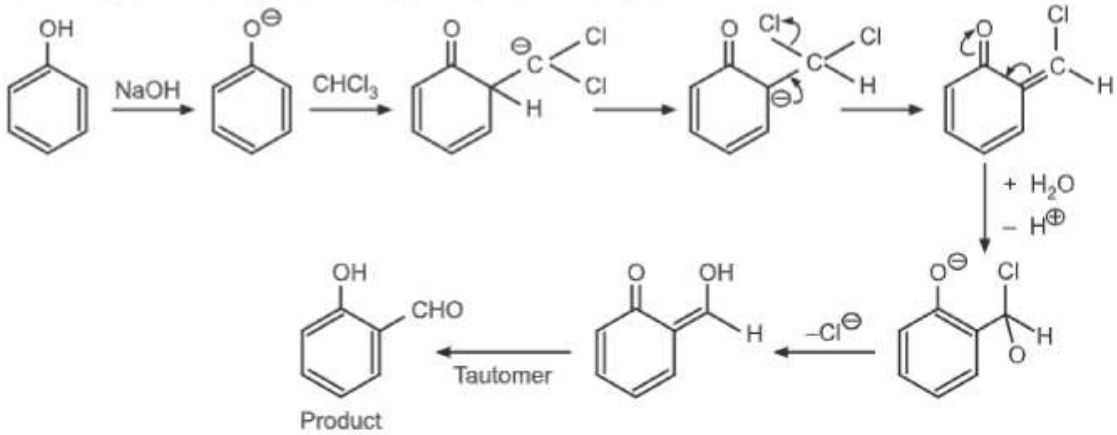


(d) Kolbe's reaction: Phenol reacts with a weak electrophile i.e., CO_2 in basic conditions to give o-hydroxybenzoic acid.



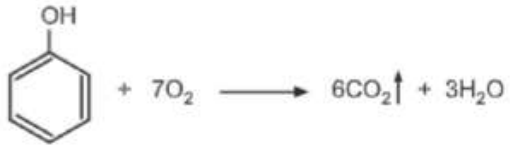
Sodium salicylate Ortho hydroxybenzoic acid (Salicylic acid)

(e) Reimer-Tiemann reaction: Phenol reacts with chloroform in the presence of sodium hydroxide to give ortho hydroxy benzaldehyde.



Product

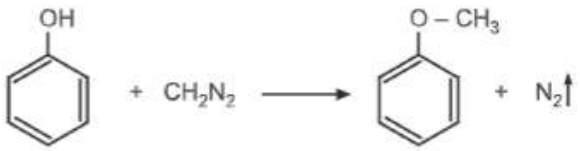
(f) Combustion of phenol: Phenol burns in presence of oxygen to give carbon dioxide and water. Phenol tends to burn in air with an extremely smoky flame due to the high proportion of carbon in phenol.



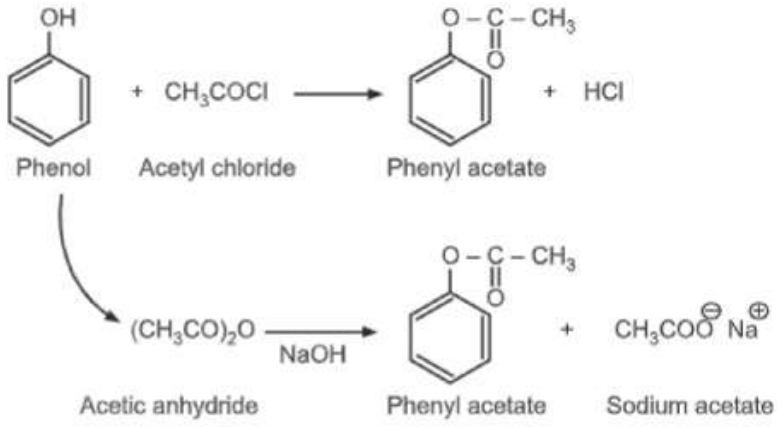
(g) Reduction of phenol: Phenol is reduced to benzene when it is distilled with zinc dust or when phenol vapour is passed over granules of zinc at 400°C.

$$C_6H_5OH + Zn \longrightarrow C_6H_6 + ZnO$$

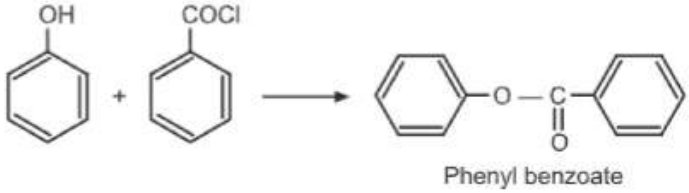
(h) Phenol reacts with diazomethane in the presence of boron trifluoride (BF_3) to give anisole.



(i) Esterification of phenol: Unlike alcohols, phenol reacts with carboxylic acid at very slow rate. Hence, highly reactive forms of carboxylic acids like acid chlorides/acid anhydrides are used instead of carboxylic acids. For example,

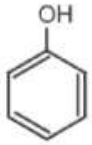


When a mixture of phenol and benzoyl chloride are shaken in the presence of dil. NaOH solution, phenyl benzoate is formed. This is an example of Schotten-Baumann reaction.



3.4 STRUCTURE AND USES

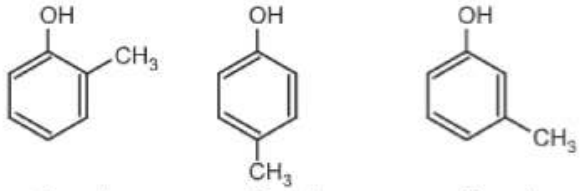
(1) Phenol: It is used as antiseptic and disinfectant. It is also used as a starting material to make plastics, explosives (e.g. picric acid) and drugs (e.g. aspirin). Substituted phenols are used in dye industries to make azo dyes.



Phenol

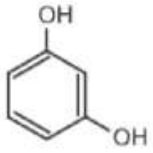
Phenolic resins are extensively used in electric switches and automobiles due to their property of withstanding extreme conditions of heat and resistance to electricity. Phenol is also used in cosmetic industry in manufacturing of sunscreen and hair colouring solution.

(2) Cresol (Methyl phenols): There are three forms of cresol. The mixture of all three forms is known as tricresol. Cresols are precursors used in plastics, dyes and pharmaceutical industries. p-Cresol is mainly used in production of antioxidants like butylated hydroxytoluene (BHT).



o-Cresol p-Cresol m-Cresol

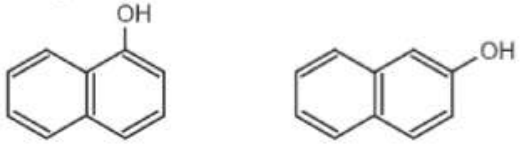
(3) Resorcinol (m-dihydroxybenzene): It is a colourless needle shaped compound easily soluble in water, alcohol and ether. Externally, it is used as an antiseptic and disinfectant.



Benzenediol

It is also used in 1-2% concentration topically in acne treatment. It can be used as anti-dandruff agent in shampoo or in sunscreen lotions. It is used internally in the doses of 125-250 mg in the treatment of gastric ulcers.

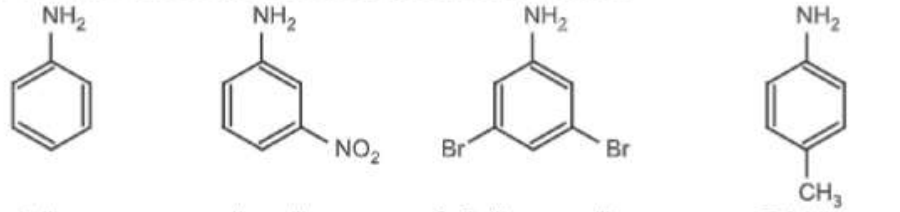
(4) Naphthols: Naphthols are fluorescent white/colourless compounds. α-naphthol is a precursor to a variety of insecticides and pharmaceuticals. Besides naphthol undergoes azo coupling to give various azo dyes.



1-naphthol (α-naphthol) 2-naphthol (β-naphthol)

3.5 AROMATIC AMINES

Aromatic amines are named as the derivatives of aniline.



Aniline | m-nitroaniline | 3, 5-dibromoaniline | Toluidine (p-methylaniline)

In the salts of amines, the positive charge is present on the nitrogen. This cation is called as **ammonium** (or **anilinium** in aromatic amines). The salt is named by prefixing ammonium to the name of the anion. For example,

NH_4Cl	$(NH_4)_2SO_4$	NH_4NO_3
Ammonium chloride	Ammonium sulphate	Ammonium nitrate

Because of the polar nature, amines can form intermolecular hydrogen bonds. Hence, they have higher boiling points than non-polar compounds having the same molecular weight. Amines are basic in nature. If exposed to air, aromatic amines ($Ar - NH_2$) are readily oxidised to $Ar - NO_2$.

3.6 PREPARATION OF AMINES

Reduction, replacement or rearrangement reactions may be used to get aliphatic amines.

(A) Aliphatic amines are prepared by the reaction between either an alcohol or an alkyl halide and ammonia.

(a) $CH_3OH + NH_3 \xrightarrow[430^\circ C]{Al_2O_3} \underset{(50\%)}{CH_3NH_2} + \underset{(20\%)}{(CH_3)_2NH} + \underset{(30\%)}{(CH_3)_3N}$

Copper chromite or alumina (Al_2O_3) may be used as a catalyst. Using a large excess of ammonia, the yield of primary amine may be increased.

(b) $CH_3(CH_2)_3CH_2Cl + NH_3 \xrightarrow{170^\circ C} \underset{(60\%)}{CH_3 - (CH_2)_3CH_2NH_3Cl} + \underset{(40\%)}{[CH_3(CH_2)_3CH_2]_2NH.HCl}$

Butyl chloride

The order of reactivity of alkyl halide is

alkyl iodide > alkyl bromide > alkyl chloride

(B) Similarly by the reduction of a nitroalkane, an amine is obtained. Metal and acid or catalytic reduction may be used for this purpose.

$$CH_3CH_2-NO_2 + 3H_2 \longrightarrow CH_3CH_2-NH_2 + 2H_2O$$

It is a commonly used method for the preparation of primary amines. One of the commonly used rearrangement reactions to get amine is Hofmann degradation or Hafmann rearrangement.

(C) Hofmann degradation may be represented by the following reaction.

$$R-\overset{\overset{O}{\|}}{C}-NH_2 + Br_2 \longrightarrow R-\overset{\overset{O}{\|}}{C}-NHBr \xrightarrow[\text{Rearrangement}]{-HBr} \begin{matrix} R-N=C=O \\ \downarrow H_2O \\ R-NH_2 + CO_2 \end{matrix}$$

(D) Primary, secondary or tertiary amides may be reduced to corresponding amines by refluxing with diborane in tetrahydrofuran.

$$\underset{2^\circ \text{ amide}}{R-\overset{\overset{O}{\|}}{C}-NHR'} \xrightarrow{B_2H_6} \underset{2^\circ \text{ amine}}{RCH_2-NH-R'}$$

(E) Aldehyde or ketone may be converted to corresponding amine by treatment with excess of ammonia and hydrogen under pressure over Raney nickel at 60° - 150°C.

$$R-\overset{\overset{O}{\|}}{C}-R' + NH_3 \xrightarrow{H_2/Ni} R-\overset{\overset{R'}{|}}{CH}-NH_2 + H_2O$$

Alternatively excess ammonium chloride and H_2 over platinum catalyst may be used. Such type of reaction is known as **reductive alkylation**.

(F) Primary amines may be obtained by reduction of alkyl cyanides or oximes.

(a) $R-C\equiv N \xrightarrow{Na/C_2H_5OH} R-CH_2-NH_2$

(b) $\underset{\text{Oxime}}{R-CH=N-OH} \xrightarrow{Na/C_2H_5OH} R-CH_2-NH_2 + H_2O$

(G) Miscellaneous methods of preparation of amines :

(i) Curtius reactions :

$$RCON_3 \xrightarrow{CH_3OH} RNCO \xrightarrow{CH_3OH} RNHCO_2CH_3 \xrightarrow{NaOH} RNH_2$$

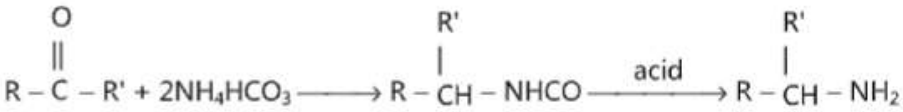
(ii) Lossen rearrangement :

$$RCONHOH \xrightarrow{acid} H_2O + RNCO \xrightarrow{acid} RNH_2$$

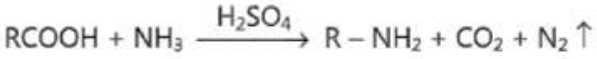
(iii) Wurtz reaction :

$$RN=CO + 2KOH \longrightarrow RNH_2 + K_2CO_3$$

(iv) Leuckart reaction :

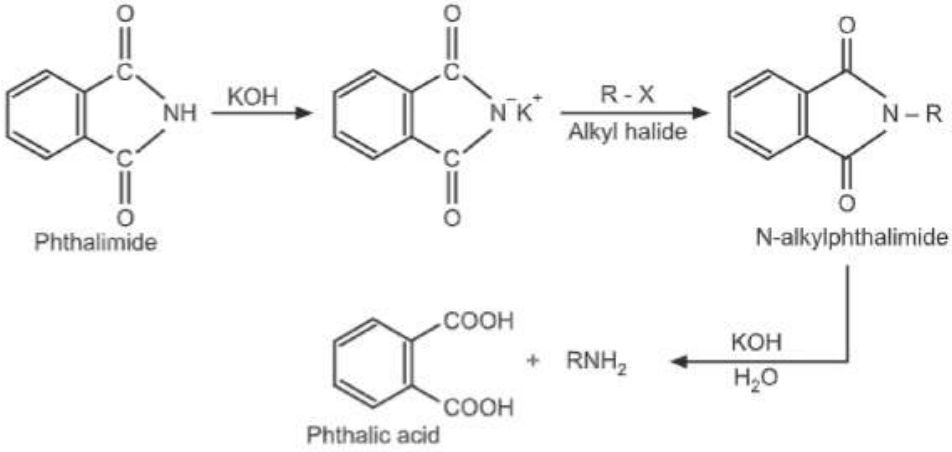


(v) Schmidt reaction :

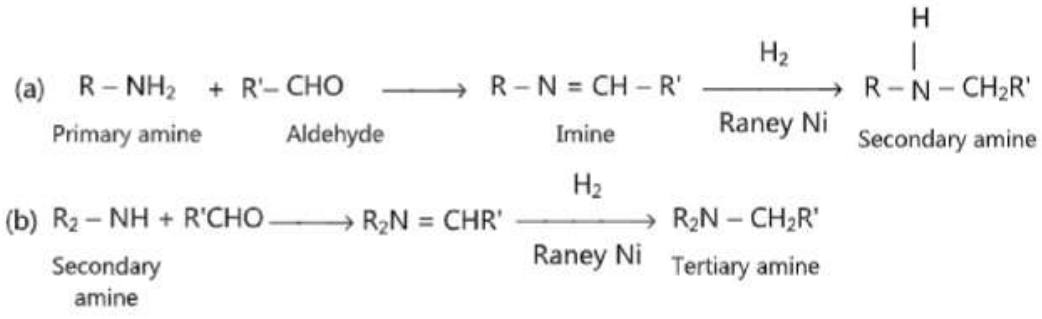


(vi) Grignard reaction :

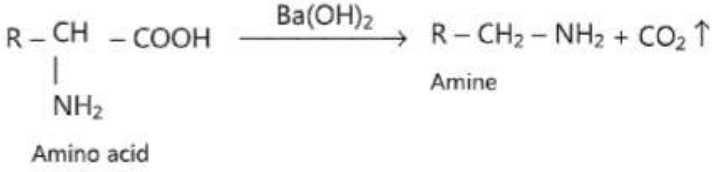
(vii) Gabriel's phthalimide synthesis :



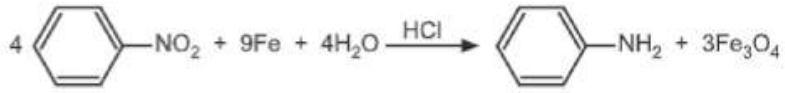
(viii) Henze reaction (for secondary and tertiary amine) :



(ix) Decarboxylation of amino acids :

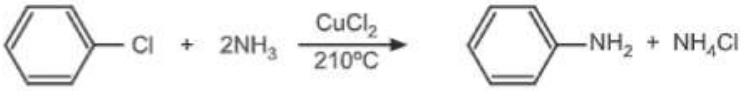


The preparation of aromatic amines does not differ principally from the methods used for aliphatic amines. For example, reduction of a nitro compound may be carried out either by catalytic hydrogenation or by the reagents like iron and a dilute HCl.



Nitrobenzene Aniline

Similarly a chloro compound or phenol may be treated with ammonia (i.e. ammonolysis) at high temperature and high pressure in the presence of a catalyst to get aromatic amine.



Chlorobenzene Aniline

Hofmann rearrangement and many other rearrangement reactions specified in the preparation of aliphatic amines are equally applicable in the preparation of aromatic amines.

3.7 SEPARATION OF AMINE MIXTURE

The mixture containing the three amine salts and the quaternary salt, is distilled with potassium hydroxide solution to get three amines to be separated through distillation. The quaternary salt remains unchanged in KOH solution in the distillation flask.

The distillate containing three amines is treated with p-toluene sulphonyl chloride. The reaction mixture is then made alkaline with potassium hydroxide. Primary amine gives N-alkyl sulphonamide which remains soluble in alkaline medium due to formation of a potassium salt.

(a) $R - NH_2 + CH_3 - C_6H_4 - SO_2Cl \longrightarrow [CH_3 \cdot C_6H_4 \cdot SO_2\bar{N} - R]\, K^+$

Primary amine — p-toluene sulphonyl chloride — Soluble potassium salt

(b) Secondary amine forms N, N-dialkyl sulphonamide. Since, it can not form potassium salt, it remains insoluble in alkaline medium.

$$R - NH - R' + CH_3 - C_6H_4 - SO_2Cl \longrightarrow CH_3 \cdot C_6H_4 \cdot SO_2 - \underset{\displaystyle R}{\overset{|}{N}} - R'$$

Secondary amine — p-toluene sulphonyl chloride — Insoluble sulphonamide

(c) While tertiary amine does not react with p-toluene sulphonyl chloride, hence it can be readily separated by distillation.

$R_3 - N + CH_3 - C_6H_4 - SO_2Cl \longrightarrow$ No reaction

Tertiary amine

The insoluble N, N-dialkyl sulphonamide is separated from the reaction mixture by filtration. It upon refluxation with 70% H_2SO_4 or 30% HCl, gives secondary amine.

The original reaction mixture now contains only soluble primary amine sulphonamide which on acidification generates N-alkyl sulphonamide. After filtration, the solid is refluxed with 70% H_2SO_4 or 30% HCl to give primary amine.

3.8 REACTIONS OF AMINES

The principle reactions of amines are related to the replacement of –H from the nitrogen atom; thus they are limited to primary and secondary amines.

All the amines are basic due to the presence of a lone pair of electron on the nitrogen atom which may be used for protonation. For example,

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

Amine — Amine hydrochloride

(b) $R\ddot{N}H_2 + HOH \rightleftharpoons RNH_3OH \rightleftharpoons R\overset{+}{N}H_3 + OH^-$

(c) When heated at high temperature, an amine salt decomposes to give a molecule of alkyl halide.

$$R_3N \cdot HCl \xrightarrow{\Delta} RCl + R_2NH \xrightarrow[\Delta]{HCl} RCl + RNH_2 \xrightarrow[\Delta]{HCl} RCl + NH_4Cl$$

Amine salt

(A) Reactions shown by primary amines :

(1) When heated with ethanolic potassium hydroxide and chloroform, primary amine yields isocyanide.

$$R{\cdot}NH_2 + 3KOH + CHCl_3 \longrightarrow RNC + 3KCl + H_2O$$

Isocyanide

(2) Hofmann mustard oil reaction: When warmed with carbon disulphide, primary amine forms a dithiocarbamic acid. The latter gives alkyl isothiocyanate upon decomposition by mercuric chloride.

$$R - NH_2 + CS_2 \rightarrow S = C\begin{matrix}NHR\\SH\end{matrix} \xrightarrow{HgCl_2} RN = C = S + HgS + 2HCl$$

Dithiocarbamic acid — Alkyl isothiocyanate

(3) Schiff base is formed when primary amine reacts with an aldehyde.

$$R{-}NH_2 + C_6H_5CHO \longrightarrow C_6H_5CH = N - R + H_2O$$

Amine — Benzaldehyde — Schiff base

(4) An alcohol is obtained when primary amine reacts with nitrous acid.

$$C_2H_5NH_2 + HONO \longrightarrow C_2H_5OH + H_2O + N_2\uparrow$$

(5) Upon oxidation by potassium permanganate, primary amine may give an aldehyde or a ketone.

(i) $\underset{\text{Amine}}{RCH_2 - NH_2} \xrightarrow{(O)} \underset{\text{Imine}}{RC = NH} \xrightarrow{(O)} \underset{\text{An aldehyde}}{RCHO} + NH_3$

(ii) $\underset{\text{Amine}}{R_2CH - NH_2} \xrightarrow{(O)} \underset{\text{Imine}}{R_2C = NH} \xrightarrow{(O)} \underset{\text{Ketone}}{R_2C = O} + NH_3$

(B) Reactions shown by secondary amines :

(1) A dithiocarbamic acid formed due to reaction of secondary amine with carbon disulphide, does not undergo decomposition by mercuric chloride.

$$R_2 - NH_2 + CS_2 \longrightarrow S = C\begin{matrix}NHR_2\\SH\end{matrix} \xrightarrow{HgCl_2} \text{No decomposition}$$

(2) Schiff base is formed when secondary amine reacts with an aldehyde containing α-hydrogen.

$$R_2 - NH + CH_3 - CHO \longrightarrow R_2 - N = CH - CH_3 + H_2O$$

(3) A diamine is obtained upon oxidation of secondary amine by potassium permanganate.

$$R_2NH \xrightarrow{KMnO_2} R_2N - NR_2$$

(4) Secondary amine reacts with nitrous acid to form insoluble oily nitrosamine. Nitrogen gas is not evolved.

$$R - \underset{|}{\overset{H}{N}} - R' + HONO \longrightarrow \underset{\text{Dialkylnitrosamine}}{R - \underset{|}{\overset{N = O}{N}} - R'} + H_2O$$

This reaction is the basis of Libermann's nitroso reaction.

(C) Reactions shown by tertiary amines :

(1) Potassium permanganate does not cause oxidation of tertiary amine. However, hydrogen peroxide oxidises latter to give amine oxide.

$$\underset{\text{Tertiary amine}}{R_3N} + [O] \longrightarrow \underset{\text{Amine oxide}}{R_3N - O}$$

(2) A nitrite salt is obtained when tertiary amine is treated with nitrous acid.

$$(CH_3CH_2)_3N + HONO \longrightarrow [(CH_3CH_2)_3\,NH]^+\,NO_2^-$$

(3) When tertiary amine is treated with cyanogen bromide, a dialkyl cyanamide is obtained. The latter upon hydrolysis with acid or alkali gives a secondary amine.

(i) $R_3N + Br - CN \longrightarrow R_2NCH + R - Br$

(ii) $R_2NCN \xrightarrow{H_2O} R_2NCOOH \longrightarrow R_2NH + CO_2 \uparrow$

(D) Reactions shown by primary and secondary amines :

(1) Amines react with acid chlorides or anhydrides to give N-acyl amide. For example,

(a) $R - NH_2 + CH_3COCl \longrightarrow CH_3CO - NHR + HCl$

(b) $R_2NH + (CH_3CO)_2O \longrightarrow CH_3CONR_2 + CH_3COOH$

(2) Mono or dihalide derivatives are obtained when amines are treated with halogen in the presence of alkali.

(a) $R - NH_2 + X_2 \xrightarrow{NaOH} R - NH - X + HX$

$R - NH - X \xrightarrow[X_2]{} R - \underset{\displaystyle X}{\underset{|}{N}} - X + HX$

(b) $R_2 - NH + X_2 \xrightarrow{NaOH} R_2 - N - X + HX$

(3) Upon treatment with nitrosyl chloride, primary amine gives alkyl chloride while secondary amine gives nitrosamine.

(a) $R - NH_2 + NOCl \longrightarrow RCl + H_2O + N_2\uparrow$

(b) $R_2 - NH + NOCl \longrightarrow R_2N \cdot NO + HCl$

(4) Primary amine reacts with Grignard reagent as follows :

(a) $R - NH_2 + CH_3Mg\,X \xrightarrow{25^\circ C} CH_4 + R - NH - MgX$

(b) $RNHMgX + CH_3MgX \xrightarrow{\Delta} CH_4 + RN\,(MgX)_2$

While secondary amine reacts with only one molecule of a Grignard reagent.

(c) $R_2NH + CH_3MgX \longrightarrow CH_4 + R_2N\,(MgX)$

(5) Substituted ureas are formed when amines are treated with phenyl isocyanate.

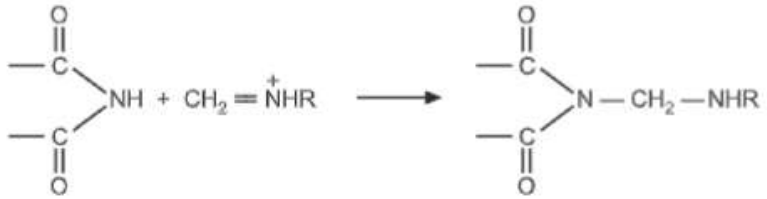
(a) $R - NH_2 + C_6H_5NCO \longrightarrow R - NHCONHC_6H_5$

(b) $R - NH - R + C_6H_5NCO \longrightarrow R - \underset{\displaystyle R}{\underset{|}{N}}CONHC_6H_5$

(6) Mannich reaction is reported to occur when compound containing acidic hydrogen is treated with amine and formaldehyde.

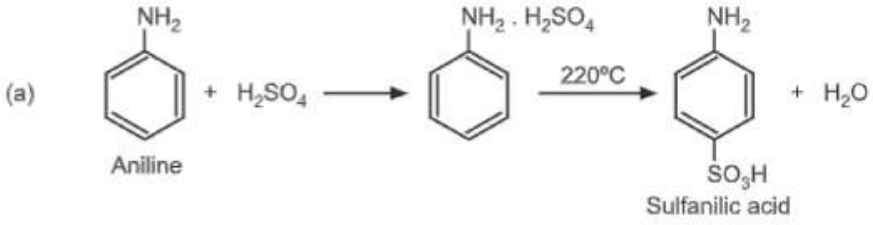
(a) $R - NH_2 + HCHO \longrightarrow CH_2 = \overset{+}{N}HR$

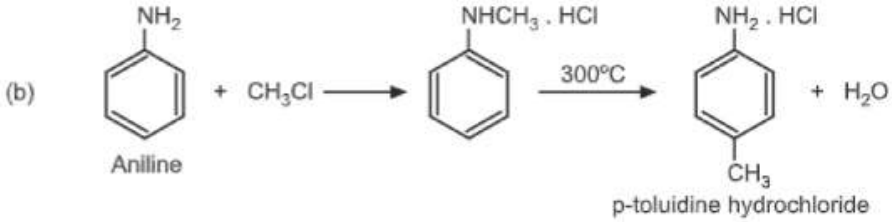
(b)



Compound having acidic hydrogen Mannich base

The reactions of aromatic amines are centered around the amino group, with the amino group generally being the point of the initial attack. The product obtained, may then rearrange usually at high temperature to give a compound with a ring substitution releasing the free amino group.





3.9 BASICITY OF AMINES

Ammonia is the strong base. Amines are considered to be the alkyl or aryl derivative of ammonia.

(i) Electron releasing nature of alkyl groups: The lone pair of electrons on the nitrogen atom of amines makes these compounds basic. The greater the availability of the lone pair electrons on nitrogen, the greater will be basicity. It means basicity increases with increasing negative charge on nitrogen.

Because alkyl groups donate electrons to the more electronegative nitrogen, the inductive effect makes the electron density on the alkyl amine's nitrogen greater than nitrogen of ammonia. Hence, we expect the tertiary alkyl amines are most basic in series.

But this is not so. In reality, the order of basicity is

2° amine > 1° amine - 3° amine > ammonia

This is because of

(ii) Steric hindrance: The size of an alkyl group creates steric hindrance for attack of a proton (H^+) to the lone pair of electrons present on the nitrogen. So, the more the number of alkyl groups attached, lesser will be the basicity.

(iii) Solvation of amines: The basic strength of an amine in water is also governed by the extent to which the cation formed by uptake of a proton, can undergo solvation and so become stabilized. Tertiary amine cation has less solvation and so the stability. Hence, the introduction of third alkyl group to form tertiary amine actually decreases the basic strength.

The number of hydrogen bonds possible when 1° amines are dissolved in water is the greatest, implying that they are most stable amine, the least being 3° amines.

The combined effect of (i) electron releasing nature of alkyl groups, (ii) steric hindrance and (iii) the solvation of amines causes the basicity order in the amines to be

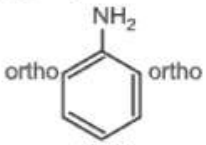
2° amine > 1° amine - 3° amine > ammonia

In aromatic amines, aniline is very weak base. The base weakening effect is more pronounced with the attachment of further phenyl group to the nitrogen atom.

Aniline > Diphenyl amine > Triphenyl amine

Effect of Substituents on Basicity:

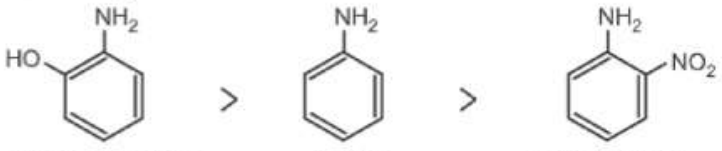
Aniline is the simplest aromatic amine. The effect of substituent on the basicity of aniline depends on the electron withdrawing or donating nature of the substituent present at ortho position to $-NH_2$ group in aniline. Usually electron donating groups make the aniline more basic while electron withdrawing groups make aniline less basic.



Aniline

Ortho substituted anilines are less basic than the same substituent in the para position. This is due to the steric hinderance created by ortho substituent, physically getting in the way of the lone pair.

(i) Effect of ortho substituent: For example, electron withdrawing group $-NO_2$ in ortho nitro aniline, withdraws electron density from the benzene ring which results in decrease in electron density on N-atom. Hence, ortho nitro aniline has less basicity than aniline. The order of basicity is



o-Hydroxy aniline > Aniline > o-Nitro aniline

(ii) Stearic hindrance of substituents: Bulky substituents at ortho position in aniline may cause the loss of planarity of $-NH_2$ group. It inhibits delocalization of lone pair of electron from nitrogen to the benzene ring. It thus increases electron density on N-atom and hence basicity of amine.

(iii) H-bonding: The lone pair on N-atom may get involved in H-bonding with hydrogen atom attached to electronegative atom of the –ortho substituent present in the ring. It thus decreases electron density on N-atom and hence basicity of amine.

The number of hydrogen bonds possible when 1° amines are dissolved in water is the greatest, implying that they are most stable amine, the least being 3° amines.

The combined effect of (i) electron releasing nature of alkyl groups, (ii) steric hindrance and (iii) the solvation of amines causes the basicity order in the amines to be

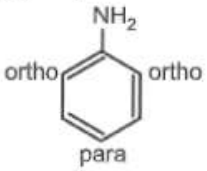
2° amine > 1° amine - 3° amine > ammonia

In aromatic amines, aniline is very weak base. The base weakening effect is more pronounced with the attachment of further phenyl group to the nitrogen atom.

Aniline > Diphenyl amine > Triphenyl amine

Effect of Substituents on Basicity:

Aniline is the simplest aromatic amine. The effect of substituent on the basicity of aniline depends on the electron withdrawing or donating nature of the substituent present at ortho position to $-NH_2$ group in aniline. Usually electron donating groups make the aniline more basic while electron withdrawing groups make aniline less basic.



Aniline

Ortho substituted anilines are less basic than the same substituent in the para position. This is due to the steric hinderance created by ortho substituent, physically getting in the way of the lone pair.

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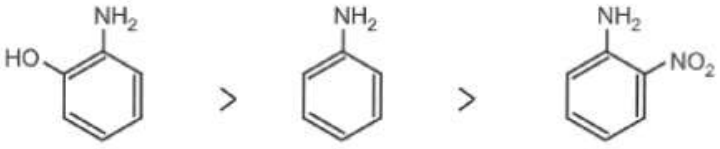


o-Hydroxy aniline Aniline o-Nitro aniline

(ii) Stearic hindrance of substituents: Bulky substituents at ortho position in aniline may cause the loss of planarity of $-NH_2$ group. It inhibits delocalization of lone pair of electron from nitrogen to the benzene ring. It thus increases electron density on N-atom and hence basicity of amine.

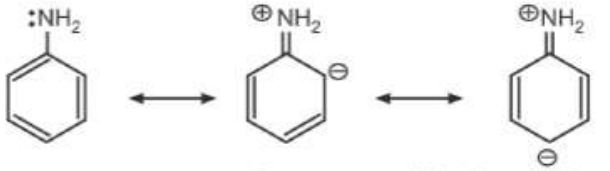
(iii) H-bonding: The lone pair on N-atom may get involved in H-bonding with hydrogen atom attached to electronegative atom of the –ortho substituent present in the ring. It thus decreases electron density on N-atom and hence basicity of amine.

In methoxy anilines, the order of basicity is

p-methoxy aniline > m-methoxy aniline > o-methoxy aniline

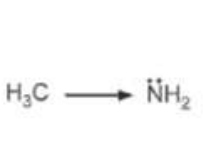
p-Methoxy group is increasing electron density on the ring by (+) resonance and keep the nitrogen lone pair more localized on nitrogen. The m-methoxy group removes electron density from N-atom by (–) inductive effect, making it less basic than aniline. While the basicity of o-methoxy aniline is influenced by both resonance and inductive effects operating in opposite directions. In addition, H-bonding further decreases its basicity.

Aromatic amines are considerably weaker bases than aliphatic amines. Aniline is less basic than methylamine. In aniline, the lone pair of electrons on the nitrogen is partly engaged with aromatic ring through resonance.

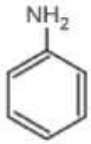


Resonance stabilization of aniline

Hence, the electron density on nitrogen is reduced resulting into less basic nature. While in methylamine, electron density on N-atom increases due to electron donating methyl group (i.e., (+) inductive effect).



Methyl amine
More basic due to
(+) Inductive effect



Aniline
Less basic due to
(–) Resonance effect

In general the order of basicity in amines is as follows:

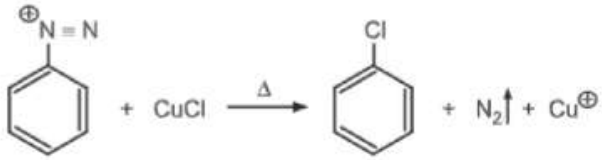
Aliphatic amines > Heterocyclic Aliphatic amines > Heterocyclic aromatic amines > Aromatic amines

3.10 SYNTHETIC USES OF ARYL DIAZONIUM SALTS

Diazonium salts are prepared by treatment of aromatic amines with the nitrous acid generated in-situ from sodium nitrite and excess mineral acid. Diazonium compounds are not isolated and once prepared, they are used immediately in further reactions. Aryl diazonium salts have wide range of synthetic applications.

For example, Diazonium salts are unstable but highly active intermediates used in the synthesis of large variety of aromatic compounds.

(a) Sandmeyer reaction (Aryl halides): Benzene diazonium salt heated with cuprous chloride or cuprous bromide respectively dissolved in HCl or HBr gives chlorobenzene or bromobenzene respectively.



(b) Gatterman reaction (Aryl halides): Benzene diazonium salt is warmed with copper powder and HCl or HBr to produce chlorobenzene or bromobenzene respectively.

(c) Craig method: 2-Aminopyridine reacts with sodium nitrite, hydrobromic acid and excess bromine to give 2-bromopyridine.

2-Aminopyridine 2-Bromopyridine

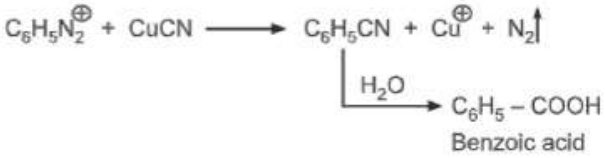
(d) Balz-Schiemann reaction: Fluorobenzene is produced by thermal decomposition of benzene diazonium fluoroborate.

(e) Replacement by nitro group: Benzene diazonium salt is treated with sodium nitrite in presence of copper to give nitrobenzene.

(f) Replacement by a hydroxyl group: Aqueous solution of aryl diazonium salt when heated to 100°C, gives phenols.

(g) Replacement by hydrogen: Aryldiazonium salts are reduced by hypophosphorous acid or sodium stannite to give benzene.

(h) Replacement by cyano group: When heated with cuprous cyanide, the diazonium salts are converted into respective aryl nitriles.



Benzoic acid

(i) Replacement by a thio group: Aryl diazonium salt is treated with potassium ethyl xanthate followed by hydrolysis gives thiophenol.

$$C_6H_5N_2^{\oplus} + C_2H_5OCS_2^{\ominus} \longrightarrow \underset{\text{Intermediate}}{C_6H_5SCSOC_2H_5} \longrightarrow C_6H_5SH + HOCSOC_2H_5$$

(j) Replacement by phenyl: Benzene diazonium salt is treated with benzene in the presence of sodium hydroxide gives diphenyl.

$$C_6H_5N_2^{\oplus}Cl^{\ominus} + C_6H_6 \longrightarrow C_6H_5 - C_6H_5 + N_2\uparrow + HCl$$

(k) Replacement by a carboxyl group: Aryl diazonium fluoroborate reacts with an aliphatic carboxylic acid gives corresponding aromatic carboxylic acid.

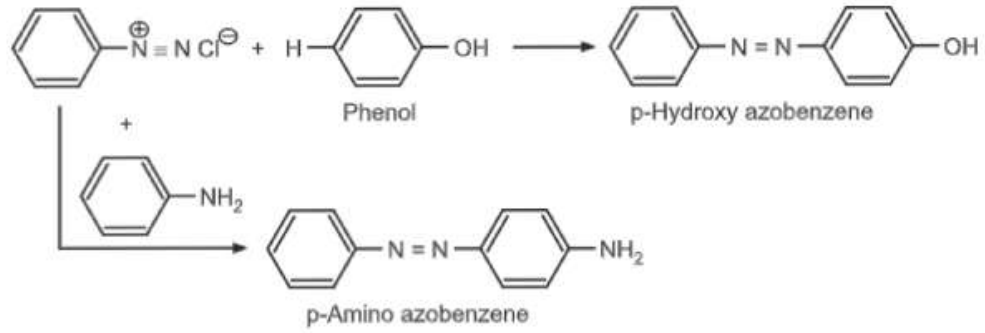
$$\left[Ar - N_2^{\oplus}\right] BF_4^- + R - COOH \longrightarrow Ar - CO_2H + BF_3 + N_2 + R - F$$

(l) Meerwein arylation: Aryl diazonium salt reacts with compounds containing activated double bonds to give phenylated compounds.

$$Ar - N_2^{\oplus}Cl^{\ominus} + Ar'CH = CHCO_2H \longrightarrow ArC = C - C_6H_5 + N_2\uparrow + CO_2\uparrow + HCl$$

(m) Coupling reactions: Coupling reactions are electrophilic substitution reactions, where arydiazonium salts are reacted with another aromatic compound to give azodyes.

e.g.,



3.11 AROMATIC ACIDS

These compounds are represented by the general formula, R – COOH, where R may be H, alkyl or aryl group. Their molecular structure is characterised by the presence of atleast one carboxyl (–COOH) group $C_nH_{2n+1}COOH$.

According to the IUPAC system of nomenclature, the aliphatic acids are named by replacing the ending 'e' in the name of the corresponding hydrocarbon by - oic acid.

By considering the carboxyl group at number 1, the substituents or the position of the side-chain may then be indicated in the name.

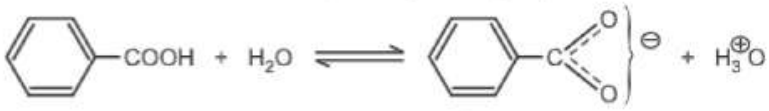
For example,

HCOOH	$CH_3CH(CH_3)-COOH$	$CH_2(CH_2-COOH)_2$
Methanoic acid	2-methylpropanoic acid	Butan-1, 4-dioic acid

Because of the polar nature, the molecules of carboxylic acids can form hydrogen bonds with each other and are soluble in alcohol, benzene and ether.

Acidic Strength of Aromatic Carboxylic Acids:

Aromatic carboxylic acids are more acidic than other categories of organic compounds but are weaker than mineral acids like HCl, HNO_3 and H_2SO_4.



Carboxylate ion

The aromatic carboxylate ion exists in variety of resonance structures due to attached benzene ring. This enhances the stability of carboxylate ion to much more extent. Hence, aromatic carboxylic acid always tries to exist in more stable carboxylate ion form by donating a proton. Due to the resonance effect, phenyl group increases the acidity of carboxylic acid.

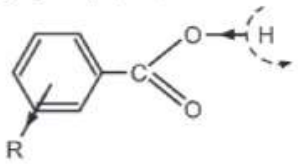
Effects of Substituents on Acidity:

The electronic effects of the substituents may be divided into:

(a) Resonance effects: These effects arise due to transmission (delocalization) of electron density through the π bonds, and

(b) Inductive effects: These involve pulling or releasing the electrons through σ bonds or through solvents. When a substituent does not have lone pairs of electrons or charge that can be delocalized in the aromatic nucleus, then only, the inductive effects are responsible to explain degree of acidity in aromatic carboxylic acids.

Since, the inductive effect operates through σ bonds, it diminishes rapidly with increasing distance from the carboxyl group (i.e., number of σ bonds in between).



(Electron withdrawing)

The nature and position of substituents account for relative strengths of substituted benzoic acids. Electron withdrawing group present on the benzene at meta (3 and 5) positions causes the electrons of the –O–H linkage to be brought more under the control of the oxyben thus facilitating the removal of the carboxylic proton.

The electron withdrawing power of some of the common substituents is

$$COOH > NO_2 > Halogens > C_6H_5.$$

The position of substituent on phenyl ring is also important. For example, 2-halobenzoic acids are more acidic than 3-halobenzoic acids which are more acidic than the 4-halobenzoic acids.

In ortho substituted benzoic acids, a bulky substituent located close to the – COOH, prevent the nearly coplanar alignment of the phenyl and carboxylic groups thought to be essential for the stability of molecule. This steric hindrance of bulky substitutent placed ortho to – COOH, leads to substantial increase in the acidity value.

Finally, H-bonding appears to affect the strength of certain ortho substituted benzoic acids.

3.12 GENERAL METHODS OF PREPARATION

Aliphatic carboxylic acids are usually prepared by:

(a) The oxidation of primary alcohols and aldehydes
(b) Hydrolysis of acid derivatives like amides
(c) Hydrolysis of cyanides
(d) Reaction of Grignard reagent with carbon dioxide
(e) Reaction of sodium alkoxide with carbon monoxide under pressure

(a) Acid dichromate oxidises alcohols, aldehydes or ketones to give carboxylic acids.

(i) $R_2CH - OH \xrightarrow{[O]} R_2C = O \xrightarrow{[O]} RCO_2H$

(ii) $CH_3CHO + O_2\ (AIR) \xrightarrow{Catalyst} CH_3COOH$

Beside $KMnO_4$, sometimes HNO_3 may be used as an oxidising agent.

(b) In general, any acid derivative may be hydrolysed under suitable conditions to the corresponding acid.

Example, $CH_3COCl + H_2O \longrightarrow CH_3COOH + HCl$

Acetyl chloride — Acetic acid

$CH_3CONH_2 + H_2O \longrightarrow CH_3COONH_4 \xrightarrow{H^+} CH_3COOH + \overset{\oplus}{N}H_4$

Acetamide

(c) Grignard reagent adds to a carbonyl group of carbon dioxide to give carboxylic acid.

$$R - CH_2MgX + \underset{\|}{\overset{O}{C}} = O \longrightarrow R - CH_2 - \underset{\|}{\overset{O}{C}} - OMgX \xrightarrow{H_2O} R - CH_2COOH + Mg(OH)X$$

Grignard reagent

(d) Cyanides may also be hydrolysed with acid or alkali to give carboxylic acids.

$$\underset{\text{Cyanide}}{RC \equiv N} \xrightarrow{H_2O} R - \underset{OH}{\overset{|}{C}} = NH \longrightarrow \underset{\text{Amide}}{R - CONH_2} \xrightarrow{H_2O} \underset{\text{Acid}}{RCOOH} + NH_3$$

(e) When a sodium alkoxide is heated with carbon monoxide under pressure, the sodium salt of the corresponding acid is obtained.

$$RONa + CO \longrightarrow RCOONa$$

3.13 GENERAL REACTIONS OF THE CARBOXYLIC ACIDS

The reactivity of both, aliphatic and aromatic carboxylic acids is due to the presence of a carboxyl (–COOH) group. The carboxyl group contains both, a carbonyl (–C=O) and an alcoholic (–OH) functions. The reactions due to carbonyl group lead to the formation of acid derivatives while reactions involving remainder of the molecules result in the substituted acids.

(a) Neutralisation: Because of the acidic properties, carboxylic acids form salts upon neutralisation by alkalies.

$$\underset{\text{Acetic acid}}{CH_3COOH} + NaOH \longrightarrow \underset{\text{Sodium acetate}}{CH_3COONa^+} + H_2O$$

(b) Reactions due to the carbonyl (C=O) group: Upon catalytic hydro-genation or with lithium aluminium hydride, carboxylic acids may be converted to corresponding alcohols by the replacement of carbonyl oxygen with hydrogen atoms.

$$CH_3\overset{\overset{O}{\|}}{C} - OH + 2H_2 \xrightarrow{\text{Catalyst}} CH_3CH_2OH + H_2O$$

Catalytic hydrogenation at high temperature and under high pressure may lead to the formation of alkane from carboxylic acid.

$$CH_3COOH + 3H_2 \xrightarrow[\Delta]{Ni} CH_3CH_3 + 2H_2O$$

Similarly alkane is obtained when the anhydrous sodium salt of a carboxylic acid is heated with soda-lime.

$$RCO_2Na + NaOH\ (CaO) \longrightarrow R - H + Na_2CO_3$$

(c) Reactions due to the –OH group : The hydroxyl group of the carboxyl moiety may be replaced by alkoxy, halogen or amine group to give ester, acid chloride and amide respectively.

For example,

(i) $\underset{\text{Acid}}{R-COOH} + \underset{\text{Alcohol}}{R'-OH} \longrightarrow \underset{\text{Ester}}{R-COOR'} + H_2O$

(ii) $3\underset{\text{Acid}}{R-\overset{\overset{O}{\|}}{C}-OH} + PCl_3 \longrightarrow 3\underset{\text{Acid chloride}}{R-\overset{\overset{O}{\|}}{C}-Cl} + H_3PO_3$

(iii) $\underset{\text{Acid}}{R-\overset{\overset{O}{\|}}{C}-OH} + NH_4OH \longrightarrow R-\overset{\overset{O}{\|}}{C}-O-NH_4 + H_2O$

$$R-\overset{\overset{O}{\|}}{C}-O-NH_4 \longrightarrow \underset{\text{Amide}}{R-\overset{\overset{O}{\|}}{C}-NH_2} + H_2O$$

(d) Miscellaneous reactions:

(i) With the exception of formic acid, carboxylic acids are extremely resistant to oxidation. However, upon prolonged heating with oxidising agent, carboxylic acid produces carbon dioxide and water as the end products.

(ii) α-Halogen acids are obtained when carboxylic acid is heated with chlorine or bromine in the presence of a small amount of phosphorus.

$$R-CH_2COOH + Br_2 \xrightarrow{\text{Phosphorus}} R-\underset{\underset{Br}{|}}{CH}-COOH$$

$$R-\underset{\underset{Br}{|}}{CH}-COOH + Br_2 \xrightarrow{\text{Phosphorus}} R-\underset{\underset{Br}{|}}{\overset{\overset{Br}{|}}{C}}-COOH$$

(iii) In the presence of sulphuric acid, carboxylic acid is converted to a primary amine.

$$\underset{\text{Acid}}{R-COOH} + NH_3 \xrightarrow{H_2SO_4} \underset{\text{Primary amine}}{RNH_2} + CO_2 + N_2\uparrow$$

3.14 DERIVATIVES OF CARBOXYLIC ACIDS

These compounds are derived from acid by the replacement of –H, –OH or = O of the carboxyl group (–COOH) present in the molecule.

Replacement of hydrogen from – COOH gives rise to salt (e.g. RCOONa) while replacement of –OH from COOH gives ester, anhydride, acid chloride or amide. Although quite dissimilar in most of their physical and chemical properties, acid derivatives have one property in common i.e. their ability to readily hydrolysed back to original carboxylic acid. Let us consider the methods of preparation and reactions of each of these acid derivatives.

Esters:

Esters are prepared by the reaction of an acid with an alcohol. It is a reversible reaction.

$$\underset{\text{Acid}}{CH_3COOH} + \underset{\text{Alcohol}}{CH_3OH} \rightleftharpoons \underset{\text{Ester}}{CH_3COOCH_3}$$

While naming an ester, the name of the alkyl group of the alcohol is followed by the name of the acid with the ending -ic changed to -ate. For example,

$$\underset{\text{Ethyl acetate}}{CH_3 - COOC_2H_5} \qquad \underset{\text{Isopropyl propionate}}{C_2H_5 - COOCH(CH_3)_2}$$

General Methods of Preparation of Esters:

The reaction between carboxylic acid and an alcohol in presence of 3 to 5% concentrated sulphuric acid or dry HCl to give an ester is known as esterification. It is reversible reaction.

$$\underset{\text{Acetic acid}}{CH_3COOH} + CH_3OH \rightleftharpoons \underset{\text{Methyl acetate}}{CH_3COOCH_3} + H_2O$$

The equilibrium may be shifted to promote forward reaction by the use of dehydrating agents to remove the water (by-product) or by distillation to remove the ester during the reaction.

Esters are also prepared by the treatment of an acid anhydride, acid chloride or ketene with an alcohol.

(a) $\underset{\text{Acetyl chloride}}{CH_3 - COCl} + CH_3OH \longrightarrow \underset{\text{Methyl acetate}}{CH_3COOCH_3} + HCl$

(b) $\underset{\text{Ketene}}{CH_2 = C = O} + CH_3CH_2OH \longrightarrow \underset{\text{Ethyl acetate}}{CH_3COOC_2H_5}$

(c) $\begin{matrix} CH_3CO \\ \diagdown \\ \quad O \\ \diagup \\ CH_3CO \end{matrix} + C_2H_5OH \longrightarrow \underset{\text{Ethyl acetate}}{CH_3COOC_2H_5} + CH_3COOH$

Other commonly used methods for the preparation of esters include:

(d) $CH_3COOAg + C_2H_5I \longrightarrow CH_3COOC_2H_5 + AgI$
Silver acetate — Ethyl acetate

(e) $CH_3COOH + CH_3CH = CH_2 \xrightarrow{H^+} CH_3COOCH(CH_3)_2$
Acetic acid — Isopropyl acetate

(f) $CH_3COOH + HC \equiv CH \xrightarrow[Hg^{++}]{H^+} CH_3COOCH = CH_2$
Acetic acid — Acetylene — Vinyl acetate

(g) $CH_3COOH + H_2C-CH_2 \longrightarrow CH_3COOCH_2CH_2OH$ (O bridge)

$RCOOK + (CH_3)_2SO_4 \longrightarrow RCOOCH_3 + CH_3KSO_4$
Potassium salt of the acid — Dimethyl sulphate — Methyl ester

General Reactions of Esters :

Although esters are comparatively unreactive, their reactivity may be represented by following reaction.

$$R-\overset{\overset{O}{\|}}{C}-O-R' + H-A \rightleftharpoons R-\overset{\overset{O}{\|}}{C}-A + R'-OH$$

where A may be $-OH$, $-NH_2$ or OR.

For example:

(1) Hydrolysis (where, A is – OH): It is just reverse reaction to esterification. It is catalysed by presence of either alkali or mineral acid.

$$R-COOR' + H-OH \rightleftharpoons RCOOH + R'-OH$$
Ester — Acid — Alcohol

$$CH_3COOC_2H_5 + H_2O \rightleftharpoons CH_3COOH + C_2H_5OH$$

(2) Ammonolysis (where, A is $-NH_2$): Esters react with ammonia to form amides.

$$CH_3COOC_2H_5 + NH_3 \rightleftharpoons CH_3CONH_2 + C_2H_5OH$$
Ethyl acetate — Acetamide

(3) Alcoholysis (where, A is $-NH_2$): An alcohol part of an ester may be replaced by another alcohol moiety if the ester is refluxed with excess of another alcohol. The reaction is catalysed by presence of an acid or sodium alkoxide. The process is also known as trans-esterification.

$$CH_3COOC_2H_5 + CH_3OH \xrightleftharpoons{CH_3ONa} CH_3COOCH_3 + C_2H_5OH$$
Ethyl acetate — Methyl acetate

Similar to this is acidolysis where the acid part of the ester is replaced by another acid moiety. For example,

$$R'COOR + R_1CO_2H \rightleftharpoons R_1COOR + R'COOH$$

(4) Reduction: Esters may be reduced to alcohols by sodium and alcohol, lithium aluminium hydride or by hydrogen using a copper chromite catalyst.

$$RCOOR' \xrightarrow{H_2} RCH_2OH + R'OH$$

(5) When treated with sodamide in liquid ammonia, esters get converted to the acid amide and the condensation product. For example,

(a) $CH_3COOC_2H_5 + NaNH_2 \longrightarrow CH_3CONH_2 + C_2H_5ONa$

(b) $CH_3COOC_2H_5 + NaNH_2 \longrightarrow \overset{+}{N}H_3\,[CH_2COOC_2H_5]^-\,Na^+$

$\overset{\oplus}{N}H_3\,[CH_2COOC_2H_5]^-\,Na^+ + CH_3COOC_2H_5 \longrightarrow CH_3COCH_2COOC_2H_5 + C_2H_5OH$

Anhydrides: When two molecules of same carboxylic acid condensed with the release of water, acid anhydride is formed.

$$2\,RCOOH \longrightarrow R-\overset{O}{\overset{\|}{C}}-O-\overset{O}{\overset{\|}{C}}-R + H_2O$$

The general methods used for the preparation of an acid anhydride include:

(a) Acid anhydride is generated when the acid vapour is passed over a mixture of sodium ammonium hydrogen phosphate and boron phosphate at 630°C.

$$\underset{\text{Acetic acid}}{2CH_3COOH} \xrightarrow{-H_2O} \underset{\text{Acetic anhydride}}{(CH_3CO)_2O}$$

(b) In the presence of a catalyst, an aldehyde may be oxidised to get acid anhydride.

(i) $\underset{\text{Acetaldehyde}}{CH_3CHO} + O_2 \xrightarrow[\text{Catalyst}]{60^\circ C} \underset{\text{Peracetic acid}}{CH_3-\overset{O}{\overset{\|}{C}}-OOH}$

(ii) $CH_3\overset{O}{\overset{\|}{C}}-OOH + CH_3CHO \longrightarrow \underset{\text{Acetic anhydride}}{CH_3-\overset{O}{\overset{\|}{C}}-O-\overset{O}{\overset{\|}{C}}-CH_3} + H_2O$

(c) In the presence of a mercuric ions as a catalyst, acetylene reacts with glacial acetic acid to give acetic anhydride and acetaldehyde.

(i) $HC\equiv CH + 2CH_3COOH \xrightarrow{Hg^{++}} \underset{\text{Ethylidene diacetate}}{CH_3CH(OCOCH_3)_2}$

(ii) $CH_3CH\,(OCOCH_3)_2 \longrightarrow \underset{\text{Acetic anhydride}}{CH_3-\overset{O}{\overset{\|}{C}}-O-\overset{O}{\overset{\|}{C}}-CH_3} + CH_3CHO$

(d) Similarly when ketene reacts with glacial acetic acid, acetic anhydride is formed.

$$\underset{\text{Ketene}}{CH_2 = C = O} + CH_3COOH \longrightarrow (CH_3CO)_2O$$

The ketene is obtained by the pyrolysis of acetone or by the dehydration of acetic acid.

(e) When chlorine is passed into a mixture of sodium acetate and sulphur dichloride, acetic anhydride is formed.

$$8CH_3COONa + SCl_2 + 2Cl_2 \longrightarrow 4(CH_3CO)_2O + 6NaCl + Na_2SO_4$$

(f) When acid chloride is allowed to react with anhydrous sodium acetate, acetic anhydride is formed.

$$CH_3COONa + CH_3COCl \longrightarrow (CH_3CO)_2O + NaCl$$

Reactions of Acetic Anhydride:

(a) Hydrolysis: Acetic anhydride is slowly hydrolysed in water to give back two molecules of original acid. The rate of hydrolysis is increased by the presence of alkali.

$$(CH_3CO)_2O + H_2O \longrightarrow 2CH_3COOH$$

(b) Acid anhydride forms an acid derivative (i.e. ester, amide) by reaction with alcohols and amines.

(i)
$$\underset{\text{Anhydride}}{CH_3-\overset{O}{\overset{\|}{C}}-O-\overset{O}{\overset{\|}{C}}-CH_3} + C_2H_5OH \longrightarrow \underset{\text{Ester}}{CH_3COOC_2H_5} + CH_3COOH$$

(ii)
$$\underset{\text{Anhydride}}{CH_3-\overset{O}{\overset{\|}{C}}-O-\overset{O}{\overset{\|}{C}}-CH_3} + NH_3 \longrightarrow \underset{\text{Amide}}{CH_3CONH_2} + CH_3COOH$$

(c) When treated with dry hydrogen chloride, acetic anhydride gives acetyl chloride.

$$\underset{\text{Acetic anhydride}}{(CH_3CO)_2O} + HCl \longrightarrow \underset{\text{Acetyl chloride}}{CH_3COCl} + CH_3COOH$$

(d) When treated with aldehyde, acetic anhydride form alkylidene acetate.

$$\underset{\text{Acetic anhydride}}{(CH_3CO)_2O} + CH_3CHO \longrightarrow \underset{\text{Ethylidene acetate}}{CH_3CH(OCOCH_3)_2}$$

(e) A powerful oxidizing agent, acetyl peroxide is prepared by the action of barium peroxide on acetic anhydride.

$$\underset{\text{Acetic anhydride}}{(CH_3CO)_2O} + \underset{\text{Barium peroxide}}{BaO_2} \longrightarrow \underset{\text{Acetyl peroxide}}{CH_3CO - O - OCOCH_3}$$

Acid Chlorides:

Acid chlorides are the most reactive of the acid derivatives. They are obtained by replacing the – OH of carboxyl group with chlorine. They are named by replacing the -ic of the name of the acid by -yl and replacing the word acid by halide. For example,

$$\underset{\text{Acetic acid}}{CH_3 - \overset{\overset{O}{\|}}{C} - OH} \qquad \underset{\text{Acetyl chloride}}{CH_3 - \overset{\overset{O}{\|}}{C} - Cl}$$

General methods of preparation of acid chlorides:

(a) Acid chlorides are usually prepared by treatment of the corresponding acid with the halide of a phosphorous (i.e. PCl_3 or PCl_5) or sulphur acid (i.e. thionyl chloride, $SOCl_2$). For example,

(i) $3CH_3COOH + PCl_3 \longrightarrow 3CH_3COCl + H_3PO_3$

(ii) $CH_3COOH + PCl_5 \longrightarrow CH_3COCl + POCl_3 + HCl$

(iii) $CH_3COOH + SOCl_2 \longrightarrow CH_3COCl + HCl + SO_2\uparrow$

(iv) $\underset{\text{Sodium acetate}}{2CH_3COONa} + \underset{\text{Sulphuryl chloride}}{SO_2Cl_2} \longrightarrow \underset{\text{Acetyl chloride}}{2CH_3COCl} + Na_2SO_4$

(b) Acid bromides may be prepared by treating acid chloride with excess of dry hydrogen bromide.

(i) $RCOCl + HBr \longrightarrow RC(=O) - Br + HCl$

(ii) $2CH_3COOH + PBr_3 \longrightarrow 3CH_3COBr + H_3PO_3$

General reactions of acid chlorides:

(1) Acid chlorides are easily hydrolysed back to the original acid.

$$RCOCl + H_2O \longrightarrow RCOOH + HCl$$

(2) Aldehydes or alcohols may be obtained upon reduction of acid chlorides.

$$RCOCl \xrightarrow[Pd]{H_2} RCHO \xrightarrow[Pd]{H_2} RCH_2OH$$

(3) Acylation (i.e. attachment of CH_3CO - group) occurs when acid chloride reacts with amines, Grignard reagent or sodium salt of the fatty acid.

(i) $CH_3COCl + R-NH_2 \longrightarrow R-NH-COCH_3 + HCl$

Acetyl chloride — Amine — Amide

(ii) $CH_3COCl + C_2H_5OH \longrightarrow CH_3CO-OC_2H_5 + HCl$

Acetyl chloride — Alcohol — Ester

(iii) $CH_3COCl + RMgX \longrightarrow CH_3COR + MgXCl$

Acetyl chloride — Grignard reagent — Ketone

(iv) $CH_3COCl + CH_3COONa \longrightarrow CH_3CO-O-COCH_3 + NaCl$

Acetyl chloride — Sodium acetate — Acetic anhydride

(4) An aromatic ketone is formed when benzene is allowed to undergo Friedel-Craft's reaction with acetyl chloride.

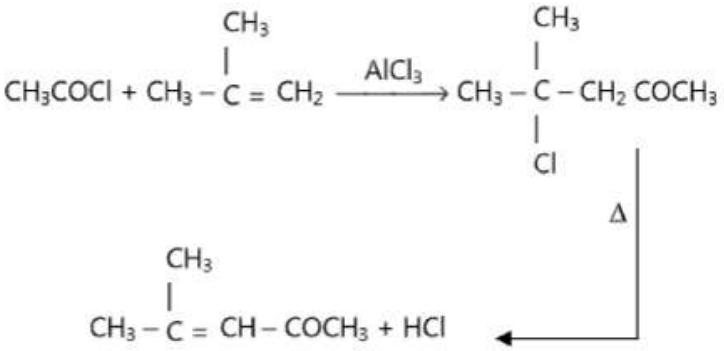
$$C_6H_6 + CH_3COCl \longrightarrow C_6H_5COCH_3 + HCl$$

(5) Ester is obtained when acid chloride is heated with an ether in the presence of anhydrous zinc chloride as a catalyst.

$$RCOCl + R'-O-R' \xrightarrow{ZnCl_2} RCOOR' + R'Cl$$

Acid chloride — Ether — Ester

(6) Similarly in the presence of zinc chloride or aluminium chloride, acid chloride reacts with an olefin to give unsaturated ketone.



Amides: These are the compounds characterised by the presence of an amide (–$CONH_2$) functional group. When the hydroxyl group of the carboxylic acid is replaced by the –NH_2 group, an amide is formed. Depending upon the number of hydrogen atoms replaced from –NH_2 by an acyl (RCO–) group, amides are further sub-classified as primary amide ($RCONH_2$), secondary amide $(RCO)_2NH$ and tertiary amide $(RCO)_3N$. They are named by using the suffix - amide in place of -ic acid in carboxylic acid. e.g.,

CH_3CONH_2	$CH_3CONHCH_3$	$CH_3CONHBr$
Acetamide	N-methylacetamide	N-bromoacetamide

If there is a substitutent on the nitrogen atom, it is indicated by N proceeding the name of the group or atom.

General methods of preparation of amides:

(a) Ammonolysis: When the concentrated ammonia solution is treated with an acid chloride, ester or acid anhydride, an amide is formed. e.g.,

(i) $RCOCl + 2NH_3 \longrightarrow RCONH_2 + NH_4Cl$

(ii) $RCOOR' + NH_3 \longrightarrow RCONH_2 + R'OH$

(iii) $(RCO)_2O + 2NH_3 \longrightarrow RCONH_2 + RCOONH_4$

If instead of ammonia, primary or secondary amine is used, N-substituted amide is obtained.

(iv) $RCOCl + R'NH_2 \longrightarrow RCONHR' + HCl$

(b) Dehydration: The heating of an ammonium salt gives an amide by dehydration.

$$CH_3-\overset{\overset{O}{\|}}{C}-ONH_4 \xrightarrow{\Delta} CH_3CONH_2 + H_2O$$

(c) When carboxylic acid is heated with urea, amide is formed. For example,

$$CH_3COOH + CO(NH_2)_2 \longrightarrow CH_3CONH_2 + CO_2\uparrow + NH_3\uparrow$$

(d) Hydrolysis of alkyl cyanides with polyphosphoric acid gives amide.

$$RC\equiv N + H_2O \xrightarrow{H^+} RCONH_2$$

General Reactions of Amides:

(a) Graded hydrolysis of an amide by water occurs to give first, the ammonium salt and then, the parent acid. The presence of acids or bases speeds up the rate of hydrolysis.

$$CH_3-\overset{\overset{O}{\|}}{C}-NH_2 + H_2O \longrightarrow CH_3-\overset{\overset{O}{\|}}{C}-ONH_4 \xrightarrow{H^+} CH_3COOH + \overset{+}{N}H_4$$

(b) Primary amine with one carbon atom less, is obtained when an amide is heated with bromine (or chlorine) and alkali.

$$CH_3-\overset{\overset{O}{\|}}{C}-NH_2 + Br_2 + 4KOH \longrightarrow CH_3NH_2 + 2KBr + K_2CO_3 + 2H_2O$$

Thus, method of preparation of a primary amine from an amide is known as Hofmann degradation. Primary amine is also obtained when an amide is reduced by sodium and ethanol, diborane, lithium, aluminium hydride or by catalytic hydrogenation.

$$CH_3CONH_2 \xrightarrow{LiAlH_4} CH_3CH_2NH_2$$

(c) Amides have both, acidic and basic properties. Because of the acidic features, mercury compounds are formed when amides are treated with mercuric oxide.

$$2CH_3CONH_2 + HgO \longrightarrow (CH_3CONH)_2Hg + H_2O$$

Because of the basic nature, unstable salts are formed when amides are treated with mineral acids.

$$CH_3CONH_2 + HCl \longrightarrow CH_3CONH_2 \cdot HCl$$

(d) When an amide is treated with nitrous acid, an acid is obtained with the liberation of nitrogen gas

$$CH_3CONH_2 + HONO \longrightarrow RCOOH + H_2O + N_2\uparrow$$

(e) Alkyl cyanides are obtained due to dehydration of amide by phosphorus pentoxide.

$$CH_3CONH_2 \xrightarrow[\Delta]{P_2O_5} CH_3C\equiv N + H_2O$$

Hydrazides:

Hydrazides are obtained when hydrazine (NH_2NH_2) is treated with the esters or acid chlorides.

$$RCOOC_2H_5 + H_2N-NH_2 \longrightarrow RCONHNH_2 + C_2H_5OH$$

$$RCOCl + H_2N-NH_2 \longrightarrow RCONHNH_2 + HCl$$

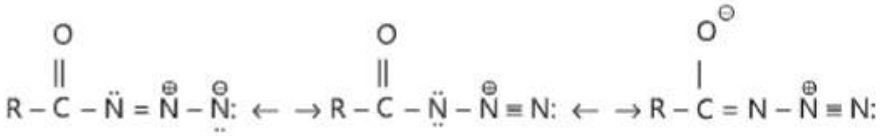
Hydrazides may be hydrolysed to get the original acid. The rate of hydrolysis of hydrazides is less than the rate of hydrolysis of amide.

$$CH_3CONHNH_2 + H_2O \longrightarrow CH_3COOH + H_2N - NH_2$$

Acid hydrazides form acid azides when treated with nitrous acid.

$$\underset{\text{Hadrazide}}{CH_3CONHNH_2} + HONO \longrightarrow \underset{\text{Azide}}{CH_2CON_3} + 2H_2O$$

The structure of an acid azion is represented by the following formulae :



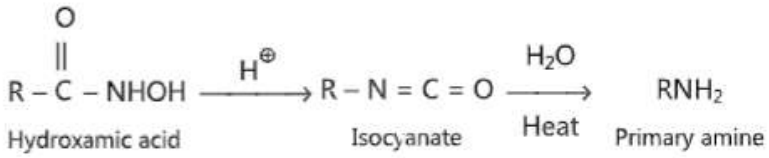
Hydroxamic Acids:

When hydroxylamine is treated with an ester or an acid chloride, hydroxamic acid is obtained.

(a) $R-C(=O)-OC_2H_5 + NH_2OH \longrightarrow R-C(=O)-NHOH + C_2H_5OH$

(b) $R-C(=O)-Cl + NH_2OH \longrightarrow R-C(=O)-NHOH + HCl$

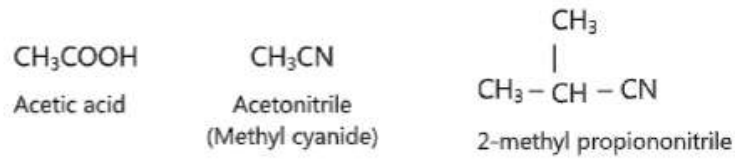
Primary amine is obtained when hydroxamic acid is treated with strong inorganic acid. This reaction is known as Lossen rearrangement. For example,



$$\underset{\text{Hydroxamic acid}}{R-C(=O)-NHOH} \xrightarrow{H^{\oplus}} \underset{\text{Isocyanate}}{R-N=C=O} \xrightarrow[\text{Heat}]{H_2O} \underset{\text{Primary amine}}{RNH_2}$$

Nitriles:

Upon hydrolysis, nitriles get converted to acids. Hence, they are considered to be derivatives of acids. Nitriles are named by replacing the -ic ending of the corresponding acid by -onitrile and delating the word acid. For example,



CH_3COOH — Acetic acid

CH_3CN — Acetonitrile (Methyl cyanide)

$CH_3-CH(CH_3)-CN$ — 2-methyl propiononitrile

Nitriles are usually prepared:

(a) by treating alkyl halide with a sodium cyanide.

$$CH_3CH_2Cl + NaCN \longrightarrow CH_3CH_2CN + NaCl$$

(b) or by dehydration of an amide.

$$CH_3CONH_2 + P_2O_5 \xrightarrow{-H_2O} CH_3CN + 2HPO_3$$

Because of the unsaturation (– C ≡ N) present in the nitrile group, most of its reactions involve addition.

(a) $$\underset{\text{Acetonitrile}}{CH_3CN} + 2H_2 \xrightarrow[\text{Catalyst}]{Ni} \underset{\text{Primary amine}}{CH_3CH_2NH_2}$$

(b) $$CH_3CN + H_2O \longrightarrow CH_3CONH_2 \xrightarrow[H_2O]{H^+} CH_3COOH + \overset{\oplus}{N}H_4$$

EXERCISE

1. Give the common name and IUPAC name of each of following acids:
   (a) HCOOH
   (b) $CH_3CHOHCOOH$
   (c) $HOOCCH_2CH_2COOH$
   (d) CH_2ClCH_2COOH
   (e) $CH_3CH_2CH_2CH_2COOH$
2. What is the basic difference between a carboxyl group and a carbonyl group?
3. Match the following :

(a) Critic acid	(1) Vitamin activity
(b) Lactic acid	(2) Lemons
(c) Tartaric acid	(3) Sediment from wine vats
(d) Acetyl salicylic acid	(4) Sour apples
(e) p-aminobenzoic acid	(5) Sour milk
(f) Formic acid	(6) Vinegar
(g) Acetic acid	(7) Food preservatives
(h) Sodium benzoate	(8) Goat acid
(i) Caproic acid	(9) Rancid butter
(j) Malic acid	(10)Sting in ant bites
(k) Butyric acid	(11)Aspirin

4. Arrange the following acids in the increasing order of acidity:
   (a) formic acid (b) acetic acid
   (c) sulphuric acid (d) trichloroacetic acid.
5. Write equation illustrating two general methods used for the preparation of organic acids.
6. How can one distinguish among α, β and γ hydroxy acids ?
7. What reaction do all acid derivatives have in common ? Illustrate this reaction with reference to different types of acid derivatives.
8. Write equations representing two general methods used to prepare esters.
9. Write equations to show the use of ethyl acetoacetate in the preparation of
   (a) an acid and (b) a ketone.
10. Describe two general methods of preparation of an acid chloride.
11. "Acid chlorides are the most reactive of the acid derivatives". Illustrate above statement with suitable examples.
12. Describe the general methods of preparation of acid anhydrides with the help of suitable examples.
13. With reference to acid derivatives, write reaction equations illustrating each of the following :
   (a) Hydrolysis (b) Ammonolysis
   (c) Hofmann degradation (d) Alcoholysis
   (e) Acylation.
14. Write down important reactions of carboxylic acids.
15. Discuss in detail methods of preparation of carboxylic acids.
16. Discuss different methods of synthesis of acid chlorides.
17. What are carboxylic acid derivatives? Give brief account on effect of substituents on acidity of carboxylic acid and different methods of their preparation.
18. Write note on 'Acidity of aromatic acids'.
19. What is effect of substituent on acidity of aromatic acids?
20. Draw the resonating structures of benzoic acid.
21. Write about Hell-Volhard-Zelinsky reaction.
22. Which are the different derivatives of carboxylic acids? Enlist them and write short note on any two of them.

23. Explain any four methods of preparation of phenols.
24. Explain why phenols are much more acidic than alcohol but less than carboxylic acids.
25. Explain various reactions of phenol.
26. Explain effect of substituents on acidity of phenol.
27. What are the qualitative tests of phenols?
28. Draw the structure of phenol, cresol, resorcinol and naphthols with their uses.
29. What are phenols? Write about their physical properties and nomenclature.
30. Write about coupling with diazonium salt reaction in phenols.
31. Explain following reactions:
    (a) Kolbe reaction
    (b) Reimer - Tieman reaction
    (c) Mannic reaction
32. Write in detail the methods of preparation of phenol from cumene hydroperoxide.
33. Write resonating structures of phenol?
34. Explain ammonolysis of ester along with examples.
35. Explain various reactions of amine.
36. Explain various methods of preparation of amine.
37. Explain chemical test for distinction between primary, secondary and tertiary amine.
38. Write method of separation of amine mixture.
39. Classify amines giving structure of each class?
40. What is effect of substituent on basicity of amines?
41. What are the different synthetic uses of aryl diazonium salts?
42. Explain Sandmeyer reaction involved in aromatic amines.
43. Draw resonating structures of aniline.
44. Write note on 'Hoffmann Degradation of amides'.
45. What is Gabriel synthesis?

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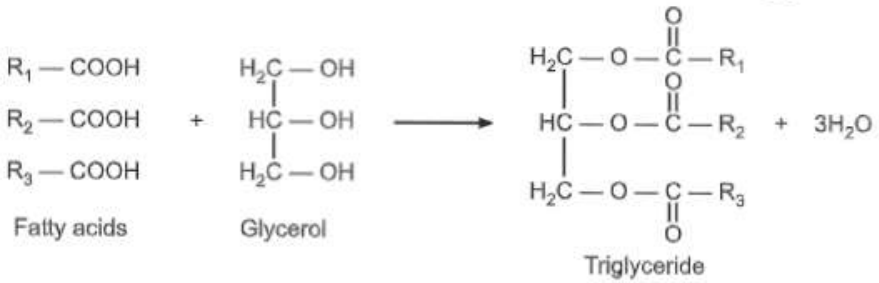
Unit IV

FATS AND OILS

♦ **SYNOPSIS** ♦

4.1 INTRODUCTION

Triglycerides are the esters of three fatty acid chains and the alcohol, glycerol.



If the glycerol is esterifies at all –OH sites by same fatty acid (i.e., $R_1 = R_2 = R_3$), the resulting ester is called as a **simple triglyceride**. While if glycerol is esterified by two or three different fatty acids, the resulting ester is called as a mixed triglyceride. A triglyceride existing in solid state at 25°C is called as fat while that exists in liquid state at 25°C is called as an oil.

Naturally occurring fats and oils are complex mixture of mixed triglyceride. Fats contain triglycerides with a long and saturated fatty acid chains and usually obtained from animal sources. Oils contain triglycerides with a short and unsaturated fatty acids chain and usually obtained from plant origin.

Table 4.1: Comparison between Fat and Oil

Sr. No.	Fat	Oil
1.	Colourless, odourless and tasteless.	Colourless, odourless and tasteless.
2.	Solid at room temperature.	Liquid at room temperature.
3.	Animal origin.	Plant and fish origin.
4.	Long and saturated fatty acid chain.	Short and unsaturated fatty acid chain.

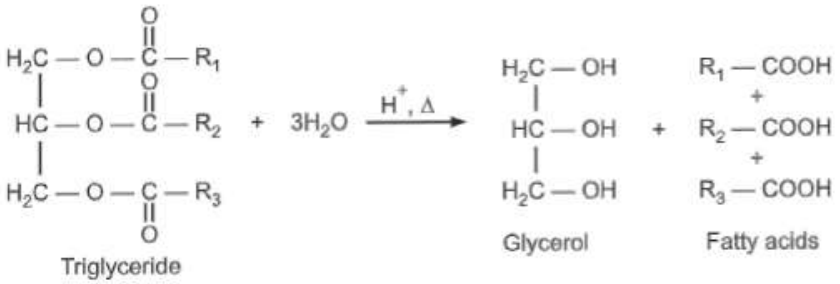
The fatty acids present in triglycerides can be classified as:

Table 4.2: Types of Fatty acids

Sr. No.	Criteria	Classification	Example
1.	Length of carbon chain	Long chain (>12 carbons)	Stearic acid
		Medium chain (6 – 12 carbons)	Lauric acid
		Short chain (< 6 carbons)	Butyric acid
2.	Degree of unsaturation	Saturated	Stearic acid
		Unsaturated	Oleic acid
3.	Location of double bonds	Omega-3-fatty acid	Alfa linolenic acid
		Omega-6-fatty acid	Arachidonic acid

4.2 CHEMICAL REACTIONS

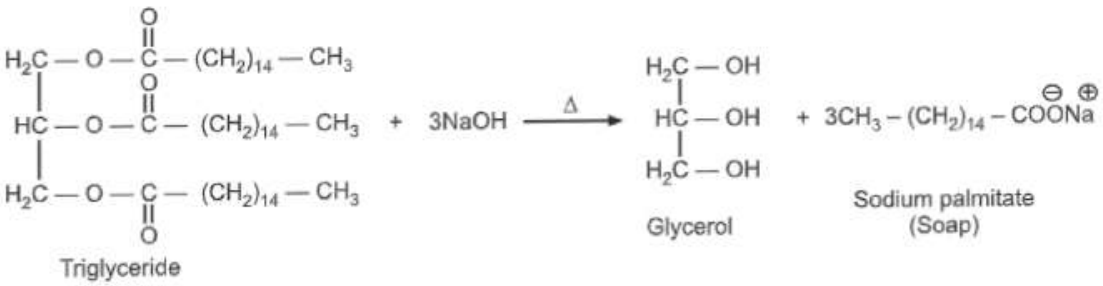
(a) Hydrolysis: Triglycerides undergo hydrolysis under the condition of acid digestion or saponification.



The triglyceride will be transformed to glycerol and fatty acid with step by step hydrolysis of each of three ester linkages. It can be carried out in the presence of acid and heat or with suitable lipase enzyme under biological conditions.

When these fatty acids are neutralized with base, they produce carboxylate ions which are used as soaps. The hydrolysis and neutralization can be carried out simultaneously using base like, NaOH. It produces soap in a one step reaction called **saponification**.

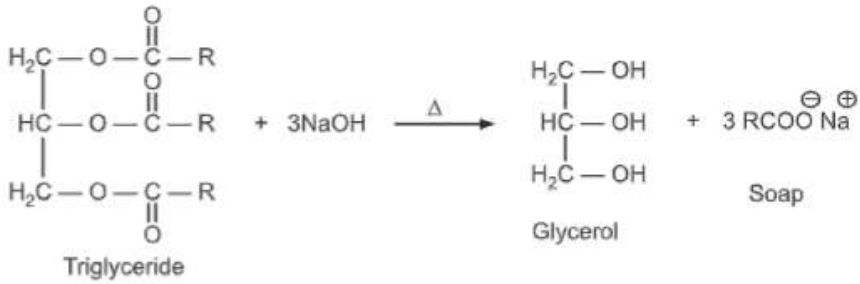
For example,



(b) Hydrogenation (Reduction): It converts unsaturated compounds (oils) into saturation derivatives (fats) in presence of a catalyst such as nickel, palladium or platinum. Hydrogenation is typically carried out by bubbling H_2 gas through the heated oil, in the presence of a metal catalyst. Oils are usually only partially hydrogenated, so that the product is not completely saturated, giving a semisolid fat.

In absence of a catalyst, very high temperature is usually required to carry out hydrogenation. Hydrogenation is carried out at different temperatures and pressures depending upon degree of unsaturation in substrate and the activity of the catalyst. Natural unsaturated fatty acids have cis double bonds. The catalysts and reaction conditions used for hydrogenation reactions can also lead to isomerization at site of unsaturation (i.e., from cis to trans) across double bond.

(c) Saponification: When a triglyceride is hydrolyzed with a strong base like NaOH, Soap (fatty acid sodium salts) is formed. Saturated fats upon NaOH hydrolysis produce hard soaps while KOH is used with oils (unsaturated fats) to produce soft/liquid soaps.



(d) Rancidity: When triglycerides containing short chain fatty acids (like butyric acid, pentanoic acid), are hydrolyzed, the carboxylic acid products are foul smelling and foul tasting (i.e. rancid). Air oxidation of fatty acids may sometimes cleave the double bonds to form short chain carboxylic acids. These oxidation products are foul tasting and smell horrible. Rancidity may also develop due to bacterial hydrolysis of triglycerides.

(e) Drying of oils: It is used to determine moisture content of the oil. Moisture content of oils and fats is the loss in mass of the sample on heating at 105 – 110°C in hot air oven for 1 hr. under specified conditions. After heating the sample, it is cooled and weighed. The process is repeated until change in the weight between two successive observations does not exceed 1 mg.

$$\text{Moisture and volatile matter (w/w\%)} = \frac{W_1 \times 100}{W}$$

where, W_1 = Loss in gm of the material on drying.

W = Weight in gm of the material taken for test.

4.3 ANALYTICAL CONSTANTS

(i) Acid Value: It is defined as the number of milligrams of KOH required to neutralize the free fatty acids present in one gram of fat. Sodium hydroxide may also be used. Phenolphthalein is used as an indicator. It is a relative measure of rancidity as free fatty acids are normally formed during decomposition of glycerides during storage. Other decomposition products include peroxides, low molecular weight aldehydes and low molecular weight ketones. This results in foul smell and odour (rancidity) and affect the quality of fats. This value is calculated only for animal and vegetable oils and fats. It is not applicable to waxes.

The acid value is calculated using the following equation

$$\text{Acid value} = \frac{V_{NaOH} \times 5.61}{W}$$

where, V_{NaOH} = Volume of sodium hydroxide titrant (ml) used.

W = Weight of the fatty oil (g) being examined.

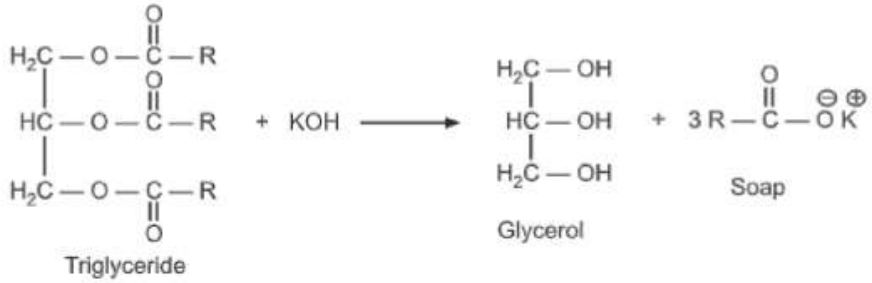
The acid value in given sample of fat/oil should not be more than the value specified in the individual monograph.

In case of colourless sample, phenolphthalein is an indicator of choice. In case of strong coloured samples (e.g., palm oil sometimes has a strong orange colour), it is difficult to identify end point of titration using phenolphthalein. In such a case, bromothymol blue may be used to give colour change from orange or yellow (in acidic solution) to a darker greenish colour (in neutral condition). It slowly turns into blue at alkaline condition.

(ii) Saponification Value: Saponification literally means "Soap making". This is done by warming a known amount of the fat with a strong acqueous caustic soda solution, which converts the free fatty acid present in the fat into a soap (which is a salt). This soap is then removed and the amount of fat remaining is then determined.

It is a measure of the total free and combined acids espectially in a fat, wax or resin expressed as the number of mg of KOH required for the complete saponification (to form soap) of one gram of sample.

The long chain fatty acids have a relatively fewer number of carboxylic functional groups per unit mass of the fat as compared to short chain fatty acids. Hence long chain have a low saponification value.



Procedure: The sample is first saponified by adding 0.5 mol/L ethanolic potassium hydroxide solution and then the excessive KOH is neutralized with 0.5 mol/L HCl.

(i) $RCOOH + KOH \longrightarrow RCOOK + H_2O$

Free fatty acid (Soap)

(ii) $KOH + HCl \longrightarrow KCl + H_2O$

Formula:

$$\text{Saponification value (mg/g)} = (B - T) \times TF \times Cl \times KI/\text{size},$$

where,

i) B = Blank level (25.029 ml)

ii) T = Titration volume (ml)

iii) TF = Reagent factor HCl (1.006)

iv) Cl = Concentration conversion coefficient for KOH in equivalence (56.11 × 0.5 = 28.05 mg/ml)

v) KI = Unit conversion coefficient (1)

vi) Size; sample size.

Significance of saponification value:

(a) It indicates the length of the carbon chain of the acid present in the sample. Higher the value, greater is the percentage of short chain acids.

(b) It gives an idea about the average molecular weight of the fat or oil. Higher the value, the lower will be the molecular weight of the fat.

(iii) Ester value: The ester value is the number of mg of potassium hydroxide required to saponify the esters in 1.0 g of the sample.

Initially, the sample is saponified. It is then hydrolysed to alcohol and free fatty acids using excess of standard KOH solution. The excess of alkali is back titrated. The ester value is calculated by

$$\text{Ester value} = \frac{(B_{HCl} - A_{HCl}) \times 28.05}{W}$$

where,

B_{HCl} = Volume (ml) of HCl consumed by the blank

A_{HCl} = Volume (ml) of HCl consumed by the actual test, and

W = Weight (g) of the sample taken.

The ester value is calculated by substracting the acid value of an oil from the saponification value of the same oil. It is more oftenly used to categorize waxes.

(iv) Iodine value (IV): The iodine value is an important analytical characteristic of oils and fats. It measures the degree of unsaturation of an oil, fat or wax. The greater the iodine value, the more will be unsaturation and the higher is the susceptibility to oxidative rancidity.

Higher the unsaturation, the greater the possibility of the oils to go rancid.

The quantity of thiosulfate required for blank minus the quantity required for sample gives thiosulphite equivalent of iodide absorbed by the fat or oil sample.

The bracked figures in following sequence are Iodine value of respective oil, arranged as per increasing order of saturation.

Coconut oil	>	Butter	>	Palm oil	>	Peanut oil	>	Cotton seed oil
(7.5 – 10.5)		(25-42)		(44-54)		(82 – 107)		(99 – 113)

Iodine value is defined as the amount of iodine in grams that is taken up by 100 g of the oil, fat or wax. The determination is carried out by dissolving a weighed sample in a non-polar solvent such as cyclohexane, then adding glacial acetic acid. The double bonds react with an excess of a solution of iodine monobromide in glacial acetic acid. (Hanus method) Mercuric ions are added to speed up the reaction. At the end, the excess of iodine monobromide is decomposed to iodine by the addition of aqueous potassium iodide solution, which is then titrated with standard sodium thiosulphate solution.

Calculation: Iodine value (IV) is calculated by using the following formula.

$$\text{Iodine Value (IV)} = \frac{(B - S) \times IF \times 100}{\text{Sampel mass (g)}}$$

$$\text{Iodine Factor (IF)} = \frac{0.01269 \times N\ Na_2S_2O_3}{0.1}$$

N = Normality of thiosulphate solution

B = ml thiosulphate for blank

S = ml thiosulphate for sample

(v) Acetyl Value: The acetyl value is the amount of potassium hydroxide (mg) required to neutralize the acetic acid liberated by the hydrolysis of 1 g of the acetylated substance. It thus measures the free hydroxyl groups in the given sample of fat or oil. For example, acetyl value of castor oil (Recin oil) = 150 because it is rich in recinoleic acid. While the oils containing no hydroxyl fatty acids have acetyl value in the range of 5 – 15.

The acetyl value is calculated by

$$\text{Acetyl value} = \frac{1335\ (b - a)}{1335 - a}$$

where,

a = Saponification value of the sample; and

b = Saponification value of the acetylated sample.

(vi) Reichert Meissl (RM) Value: During storage, the oils and the fats undergo physical and chemical changes with the accumulation of primary and secondary oxidation products. The Reichert Meissl value indicates the amount of soluble volatile fatty acids presents in a given sample. It is the number of ml of 0.1 N aqueous alkali solution necessary for the neutralization of the water soluble volatile fatty acids distilled and filtered from 5 g of a given saponified fat.

Procedure: Pour 100 ml of the filtrate containing the soluble volatile acids into a titration flask. Add 0.1 ml of phenolphthalein indicator and titrate with the 0.1 N NaOH solution until the liquid becomes pink. The RM value can be calculated by

$$\text{Reichert Meissl Value} = 1.10\ (T_1 - T_2)$$

where,

T_1 = Volume in ml of 0.1 N NaOH solution used for sample.

T_2 = Volume in ml of 0.1 N NaOH solution used for blank.

RM value is substantially a measure of lowest fatty acids of ghee namely butyric and caproic acids. The RM value is no longer sufficient to trace the adulteration of butter.

EXERCISE

1. Elaborate the difference between fats and oils.
2. Discuss in detail the hydrolysis, hydrogenation and saponification reactions with reference to fats and oils.
3. Highlight the significance and principle involved in determination of following analytical parameters of fats and oils.
   (i) Acid value (ii) Saponification value
   (ii) Ester value (iv) Acetyl value
   (v) Iodine value
4. What is the significance and principle involved in determination of Reichert Meissl (RM) value?

❖❖❖

Unit V

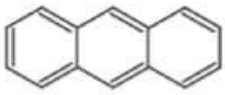
POLYNUCLEAR HYDROCARBONS

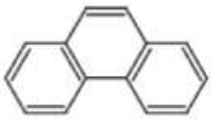
♦ **SYNOPSIS** ♦

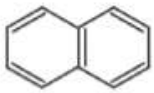
5.1 INTRODUCTION

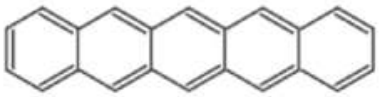
These are uncharged, lipophilic molecules made up of fused multiple aromatic rings. They contain carbon and hydrogen atoms only. The 2, 3 and 4 rings containing polycyclic aromatic hydrocarbons (PNH) are volatile and exist in the gas phase while larger size molecules exist as colourless, pale yellow, pale green or white coloured solids.

Examples include


Anthracene


Phenanthrene


Naphthalene

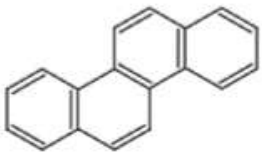

Tetracene

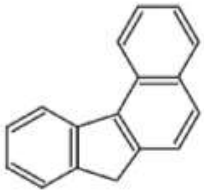

Pyrene


Coronene

These compounds are primary found in natural sources like coal and petroleum products. They are generated by burning garbage, wood, incomplete combustion of fossil fuels and also present in cigarette smoke.


Triphenylene

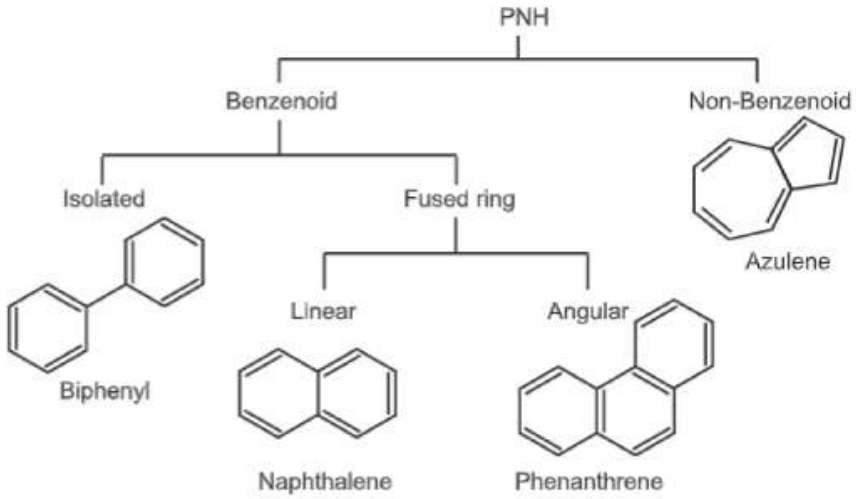

Chrysene


Benzo[c]fluorene

They are typically found as complex mixtures. Combustion at lower temperature (e.g., cigarette smoke) generates low molecular weight PNHs whereas high temperature industrial process typically generates high molecular weight PNHs.

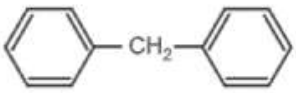
5.2 CLASSIFICATION OF POLYNUCLEAR HYDROCARBONS

They are classified as:



5.3 DIPHENYLMETHANE

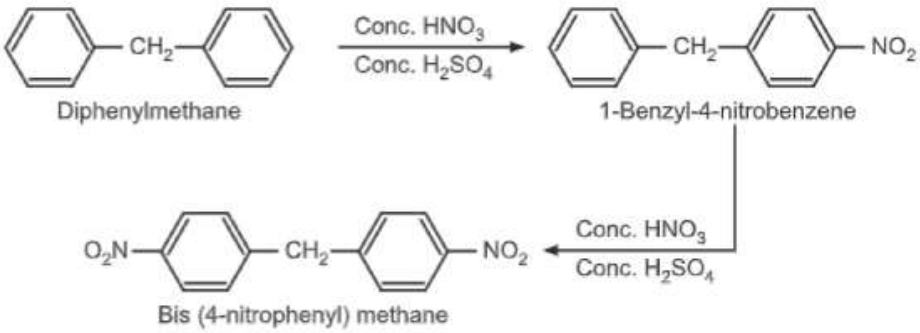
It is a colourless to pale yellow low melting solid. Commercial diphenylmethane should be at least 97% pure. It must be free of halogens and have minimum melting point of 24°C. It is used as a fragrance in perfumes, soaps and shampoo.



Diphenylmethane

Chemical reactions:

(i) Nitration: It undergoes nitration when heated with conc. HNO_3/conc. H_2SO_4 mixture.

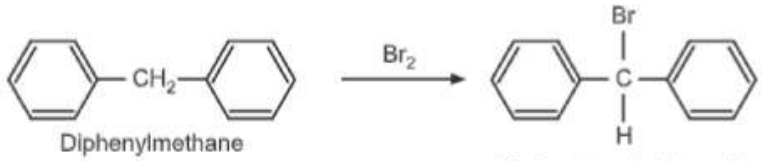


Diphenylmethane

1-Benzyl-4-nitrobenzene

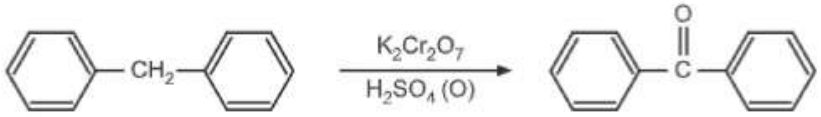
Bis (4-nitrophenyl) methane

(ii) Halogenation: When treated with liquid bromine, it undergoes bromination at methane carbon.



Diphenylmethane — Diphenyl methyl bromide

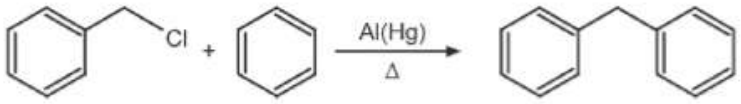
(iii) Oxidation: Upon oxidation, diphenylmethane gives benzophenone.



Diphenylmethane — Benzophenone

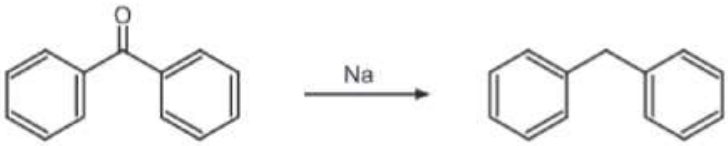
Synthesis:

(1) Diphenylmethane can be synthesized by Friedel Crafts' alkylation of benzyl chloride with benzene in presence of amalgamated aluminium turnings.



Benzyl chloride — Diphenylmethane

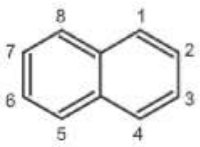
(2) Diphenylmethane can be synthesized by reduction of benzophenone using metallic sodium.



Benzophenone — Diphenyl methane

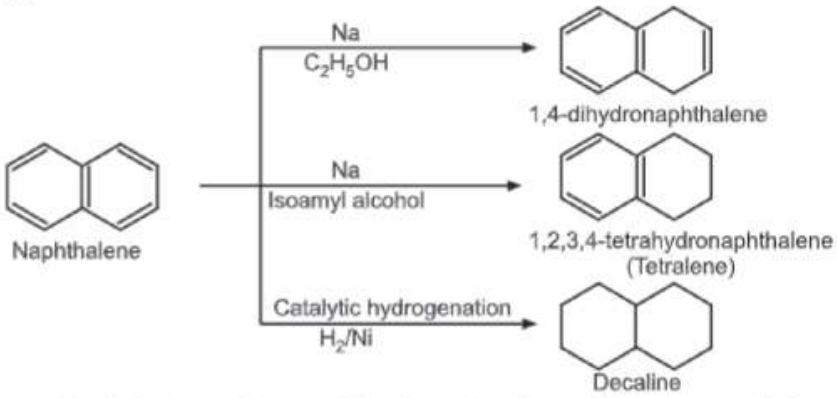
5.4 NAPHTHALENE

It is the simplest PNH. It occurs as a white crystalline solid with a characteristic strong odour. It is obtained from either coal tar or petroleum distillation. It is used as dyes, plastics, lubricants and explosives. When high levels of naphthalene vapours are inhaled, it could cause nausea, vomitting and headache.

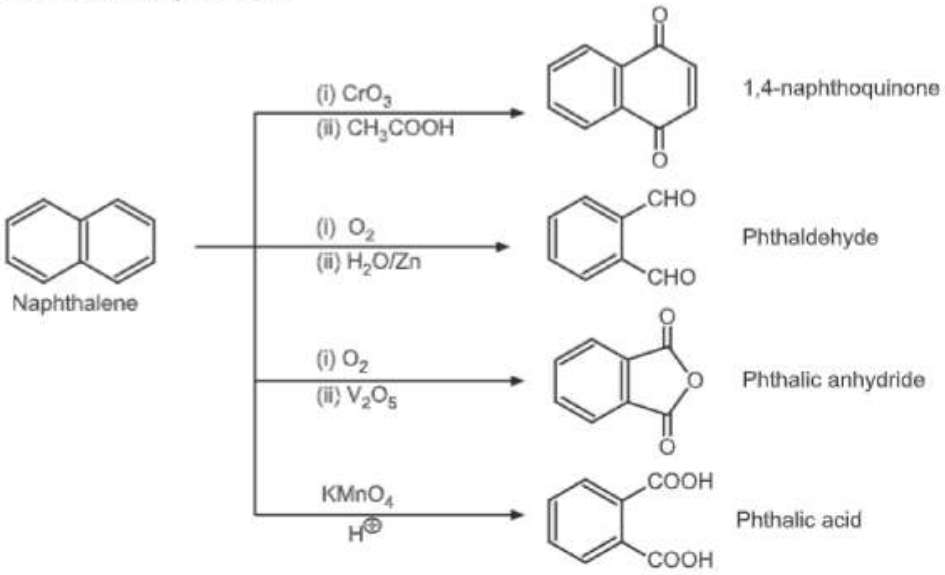


Chemical reactions:

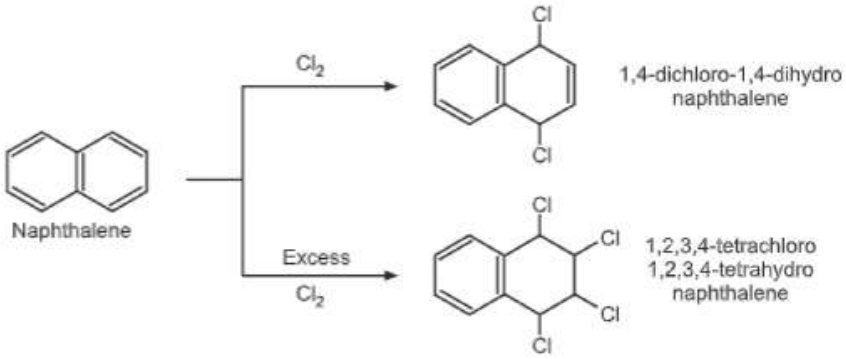
(i) Reduction: Naphthalene can be partially or fully reduced under different reagent conditions.



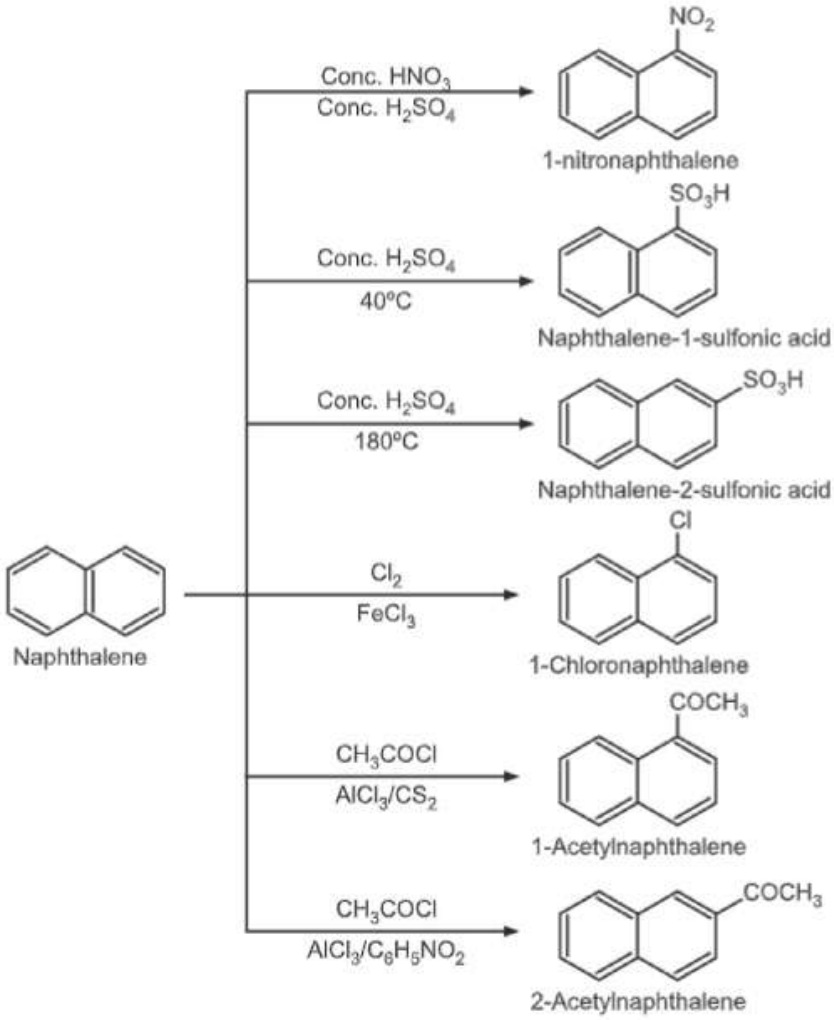
(ii) Oxidation: Naphthalene when oxidized under four different conditions, gives four different oxidized products.



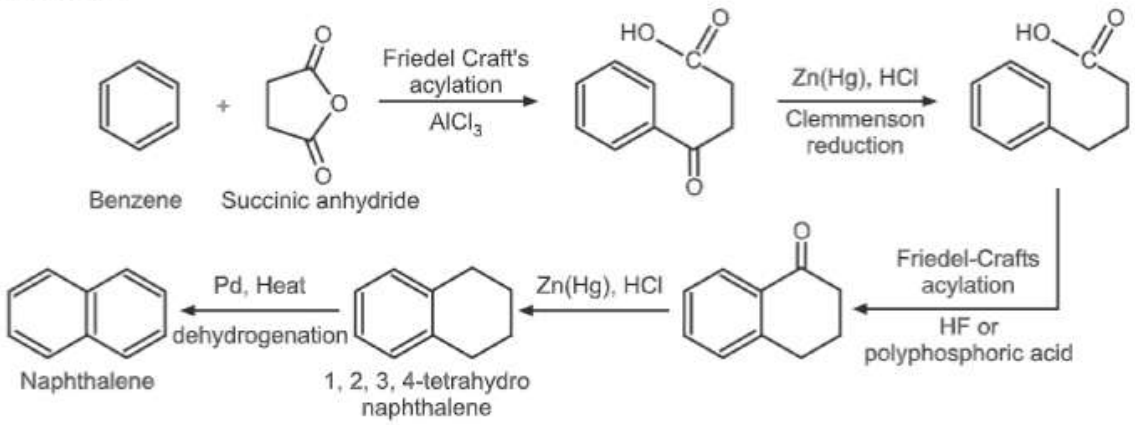
(iii) Chlorination:



(iv) Electrophilic substitution reactions

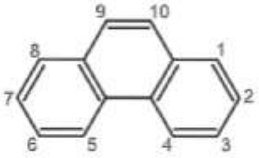


Synthesis:



5.5 PHENANTHRENE

It appears as colourless monoclinic crystals with a faint aromatic odour. Its solution exhibits blue fluorescence. It is composed of phenyl and anthracene, hence the name is phenanthrene. Anthracene is the linear isomer of phenanthrene.

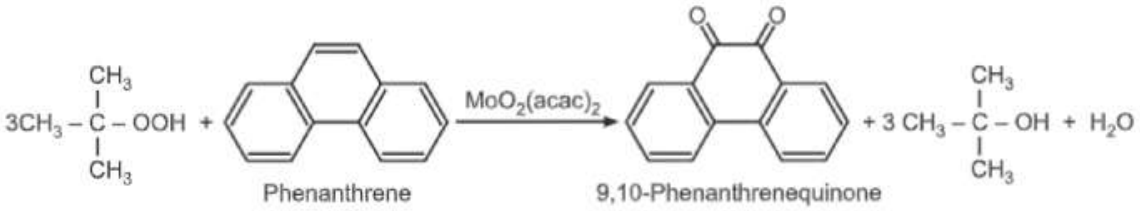


Phenanthrene

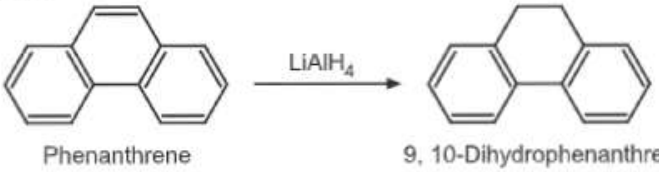
It is used as an adhesive and sealant. Exposure to this compound may cause irritation to the skin and respiratory tract.

Phenanthrene undergoes addition reactions on the double bond between 9 and 10 which showed a strong olefinic character. The 9, 10-bond in phenanthrene closely resembles an alkene double bond in both its length and chemical reactivity. Hence, all chemical reactions of phenanthrene occur across 9, 10-bond.

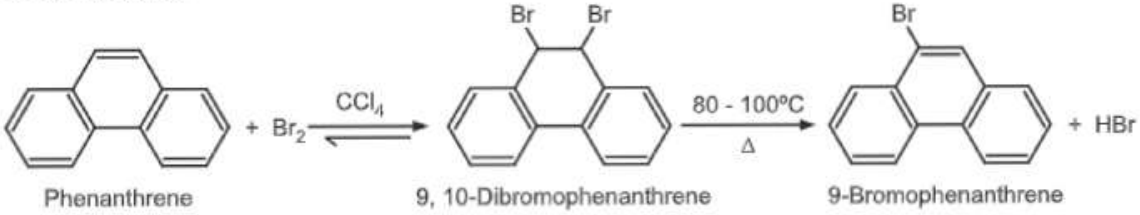
(1) Oxidation: Using, tert-butyl hydroperoxide and molybdenum acetylacetonate [MoO_2 (acac)$_2$] it can be oxidized to phenanthrenequinone.



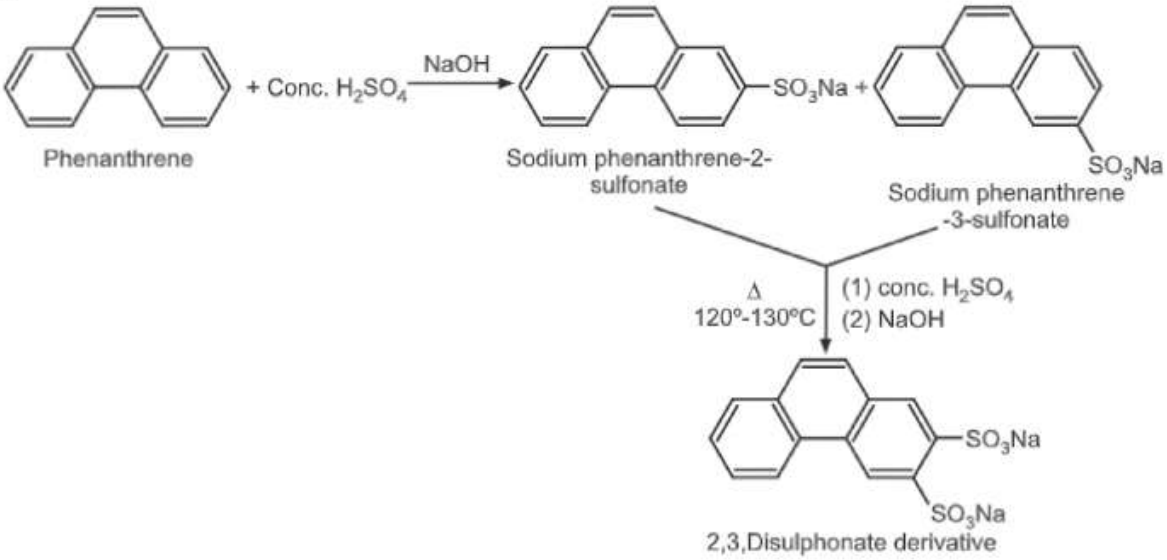
(2) Reduction: When the solid lithium aluminium hydride is vigorously shaken with molten phenanthrene at high temperature, phenanthrene is reduced to 9, 10-dihydrophenanthrene.



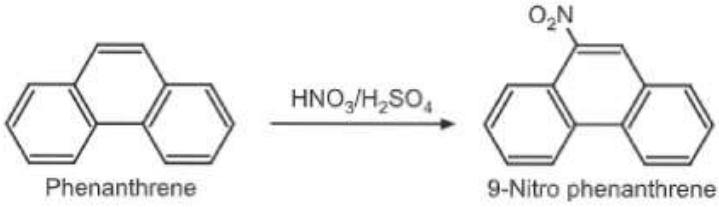
(3) Halogenation: Phenanthrene forms a crystalline dibromide which is sufficiently stable to be isolated. The dibromide can be converted further to mono bromo product by gentle heating.



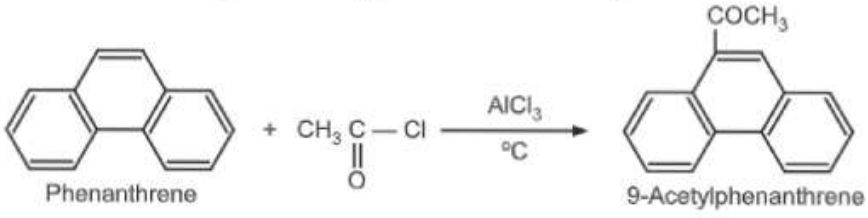
(4) Sulfonation: When phenanthrene is treated with conc. H_2SO_4, following two products are obtained after neutralization with NaOH.



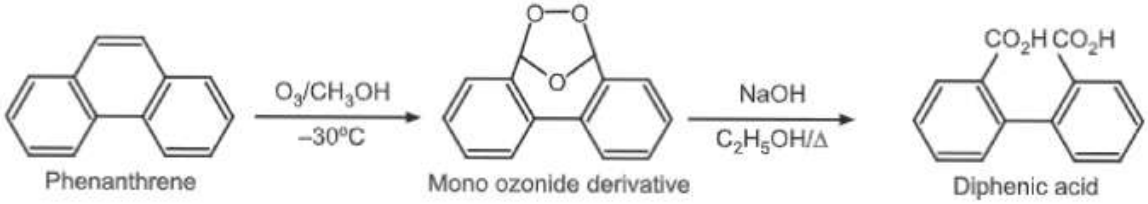
(5) Nitration: Upon treatment with nitrating mixture, phenanthrene gives 9-nitro derivative.



(6) Acylation: Phenanthrene undergoes acylation with acetyl chloride in the presence of aluminium chloride at 0°C to give 9-acetylphenanthrene acetyl.

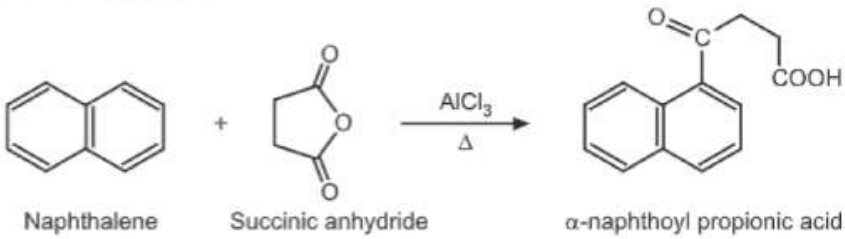


(7) Ozonolysis: Phenanthrene reacts quickly with one mole of ozone at the 9, 10-double bond to give mono ozonide derivative which upon further thermal decomposition, gives 2'-formyl-2-biphenyl carboxylic acid.



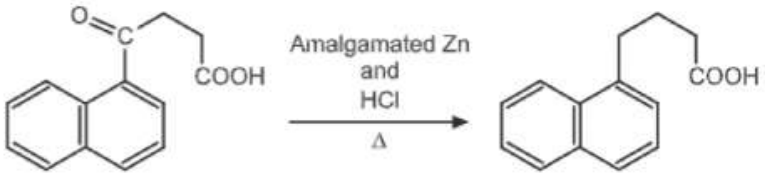
Synthesis:

(i) Friedel Craft's acylation:



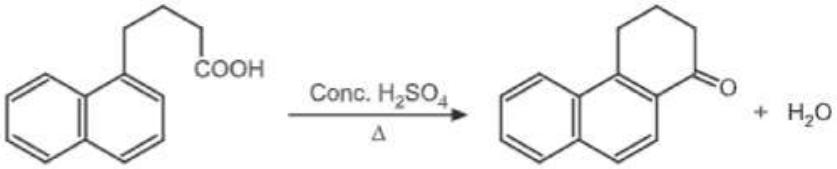
Naphthalene + Succinic anhydride → α-naphthoyl propionic acid

(ii) Clemmensen reduction

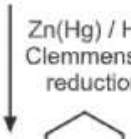


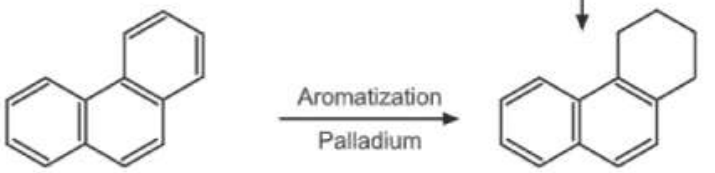
α-naphthoyl propionic acid → γ-naphthoyl butyric acid

(iii) Ring closure



α-naphthoyl butyric acid → 1-keto-1,2,3,4 tetrahydro phenanthrene

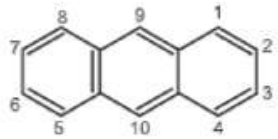




Phenanthrene → 1,2,3,4 tetrahydro phenanthrene

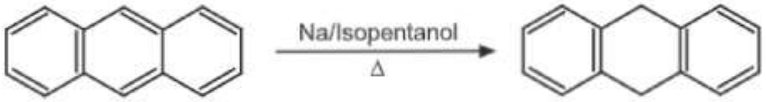
5.6 ANTHRACENE

It is present in anthracene oil and green oil fraction of coal tar. It is a colourless solid. In the solution form, it exhibits a blue fluorescence.



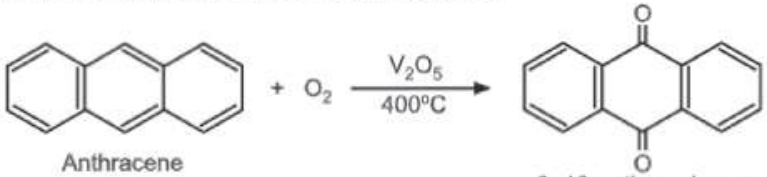
Chemical Reactions: Electrophilic substitution reactions occur at 9, 10 positions.

(i) Reduction: When treated with sodium and isopentanol, anthracene gives 9, 10-dihydroanthracene.



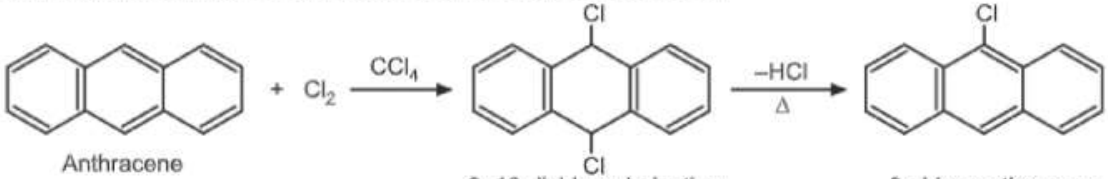
Anthracene 9, 10-Dihydroanthracene

(ii) Oxidation: It is oxidised to 9, 10-anthraquinone



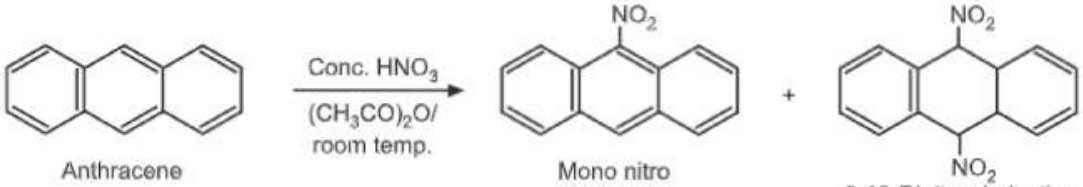
Anthracene 9, 10-anthraquinone

(iii) Halogenation: Anthracene readily reacts with halogen to form anthracene dihalide which upon heating, decomposes to give 9-haloanthracene.



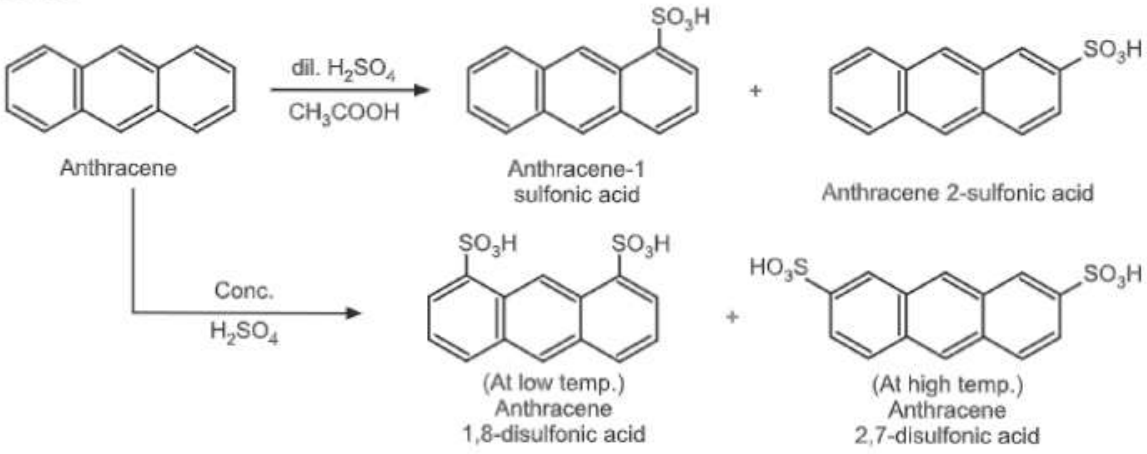
Anthracene 9, 10-dichloro derivative 9-chloroanthracene

(iv) Nitration:



Anthracene Mono nitro derivative 9,10-Dinitro derivative

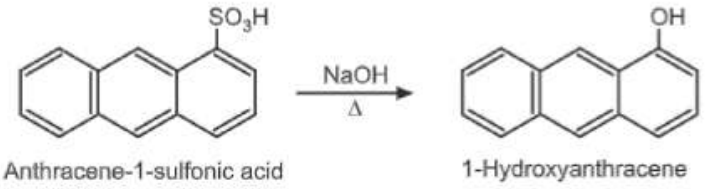
(v) Sulfonation: Anthracene is readily sulfonated to give a mixture of 1- and 2-sulfonic acids.



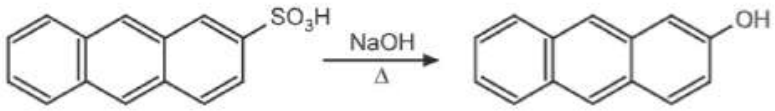
Anthracene Anthracene-1 sulfonic acid Anthracene 2-sulfonic acid

(At low temp.) Anthracene 1,8-disulfonic acid (At high temp.) Anthracene 2,7-disulfonic acid

(vi) Hydroxy anthracenes (Anthrols):

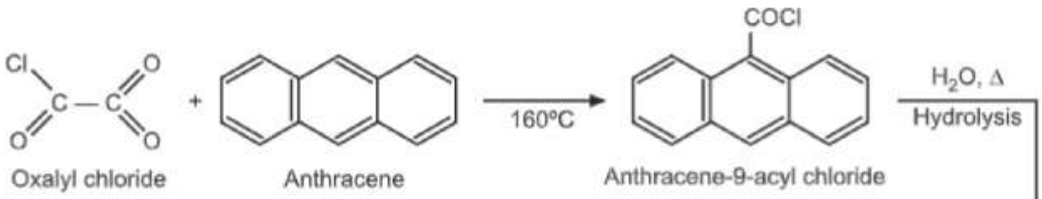


Anthracene-1-sulfonic acid — 1-Hydroxyanthracene



Anthracene-2-sulfonic acid — 2-Hydroxyanthracene

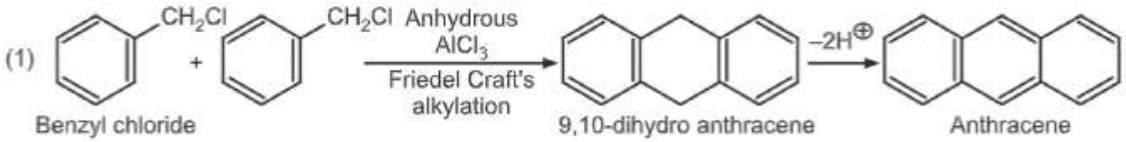
(vii) Anthracene carboxylic acids:



Oxalyl chloride — Anthracene — Anthracene-9-acyl chloride — 9-Anthroic acid

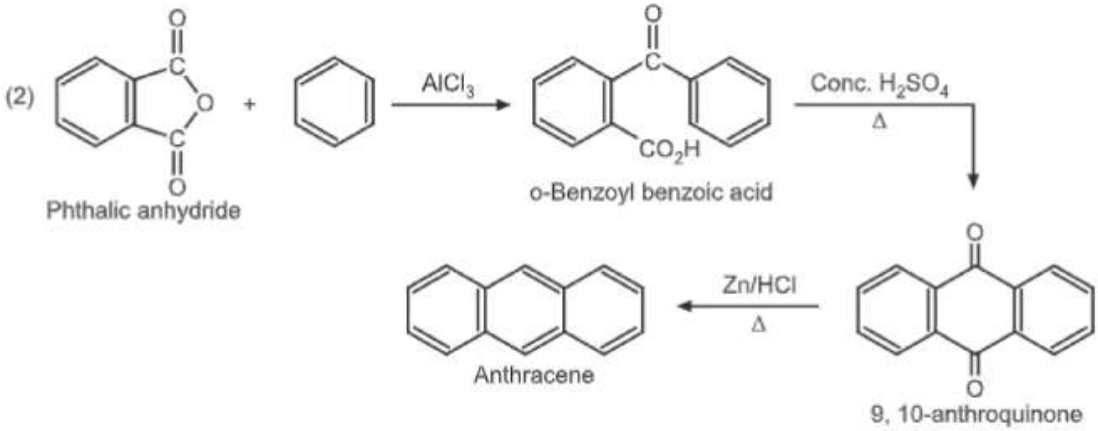
Synthesis:

(1)



Benzyl chloride — 9,10-dihydro anthracene — Anthracene

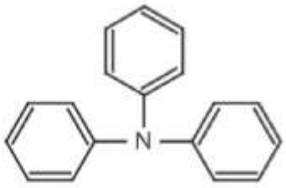
(2)



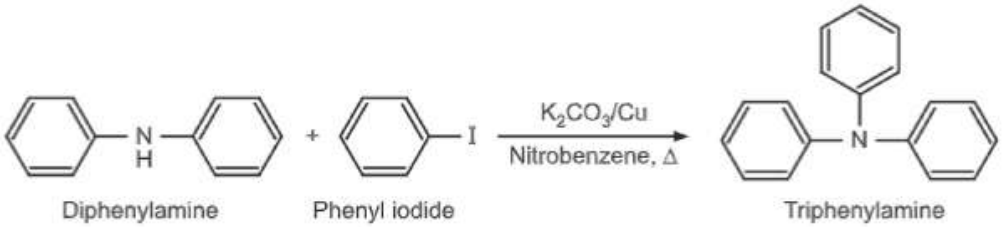
Phthalic anhydride — o-Benzoyl benzoic acid — 9, 10-anthroquinone — Anthracene

5.7 TRIPHENYLMETHANE

It is a off-white lumpy solid having a characteristic odour. It decomposes upon burning and produces toxic fumes including nitrogen oxide. The compound is not basic but its aqueous solution is a weak base.



It can be synthesized by treating diphenylamne with phenyl iodide.



Diphenylamine Phenyl iodide Triphenylamine

EXERCISE

1. Discuss the synthesis and reactions of –
   (a) Diphenylmethane,
   (b) Naphthalene and
   (c) Phenanthrene.
2. Draw the structure and medicinal uses of –
   (a) Naphthalene
   (b) Anthracene
   (c) Triphenylmethane.
3. Sketch out the synthesis and reactions of –
   (a) Anthracene, and
   (b) Triphenylmethane
4. Give the classification of polynuclear hydrocarbons with suitable example from each class.

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Unit VI

CYCLOALKANES

♦ **SYNOPSIS** ♦

6.1 INTRODUCTION

Cycloalkanes contain rings of minimum three carbon atoms linked together by single bonds. Cycloalkanes are saturated since all the carbon atoms that make up the ring are single bonded to other atoms. These compounds are represented by general formula $(CH_2)_n$. Examples consists of

Cyclopropane (60°) | Cyclobutane (90°) | Cyclopentane (108°) | Cyclohexane (120°) | Cycloheptane (129°) | Cyclooctane (135°)

The bond angle in each cycloalkane is given by the formula

$$\text{Bond angle} = \frac{180\,(n-2)}{n};$$

where, n = No. of sides of cycloalkane

The natural angle for tetrahedral carbon is 109°. Hence, rings of 5 and 6 carbon atoms (i.e., bond angle of 108° and 120°) have bond angle close to that of 109°. Such rings do not have angle strain and are therefore more stable than the other rings which deviate from 109° by greater amount. Cycloalkanes are relatively unreactive compounds except 3 to 4 membered strained rings which are as reactive as alkenes.

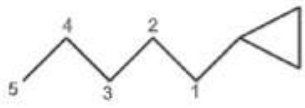
6.2 NOMENCLATURE

Cycloalkanes are named by adding the prefix "cyclo" to the alkane name having same number of carbon atoms as those in the ring. The IUPAC nomenclature rules are as follows:

(i) The parent ring is the largest ring in the molecule.

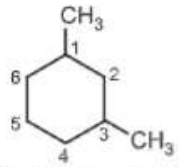
(ii) If an alkyl chain attached to cycloalkane, has a greater number of carbons then the alkyl chain is considered as a parent and the cycloalkane as a cycloalkyl substituent,

For example,



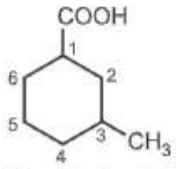
Cyclopropyl-n-pentane

(iii) While numbering the carbons of a cycloalkane, the numbering should start from substituted carbon e.g.

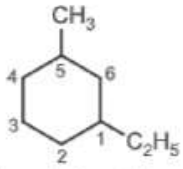


1, 3-Dimethyl cyclohexane

(iv) With two different substituents, assign the lower number to the substituents alphabetically while numbering the ring, e.g.,



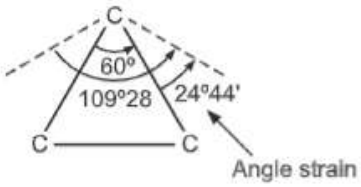
1-carboxy-3-methyl cyclohexane



1-ethyl-3-methyl cyclohexane

6.3 BAEYER'S STRAIN THEORY

Since carbon atom is tetrahydral in nature, the angle between any two bonds should be 109°28'. Thus any deviation from this value would result into an internal strain in the molecule. When an open chain organic compound is converted into a cyclic compound, a definite distortion of this normal angle of 109° takes place leading to a lot of strain in the molecule.

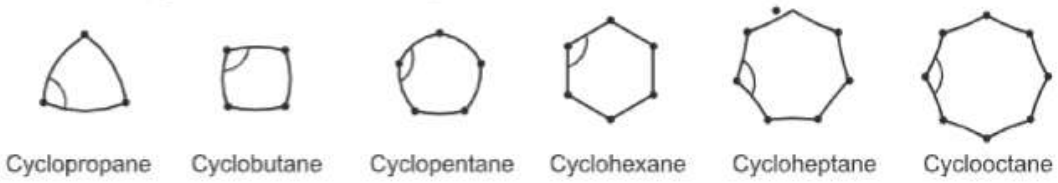


Small rings, such as three and four membered rings have their bond angle (60° and 90° respectively) deviating much from the ideal angle 109° of a tetrahydral carbon. Thus, these rings possess a significant amount of ring strain. A ring with 5 to 7 carbons is considered to have minimal to zero angle strain. Examples include cyclopentane, cyclohexane and cycloheptane. However, a ring with 8 to 12 carbons possesses a moderate strain.

Table 6.1: Strain Energies of Cycloalkanes

Sr. No.	Name	Strain Energy (kcal/mole)	Sr. No.	Name	Strain Energy (kcal/moles)
1.	Cyclopropane	27.6	6.	Cyclooctane	9.6
2.	Cyclobutane	26.4	7.	Cyclononane	12.6
3.	Cyclopentane	6.5	8.	Cyclodecane	12.0
4.	Cyclohexane	0	9.	Cyclododecane	2.4
5.	Cycloheptane	6.3			

Ring strain (Banana Bond): In case of greater ring strain, the bonds are curved. In case of strain free rings, the bonds are straight.



Cyclopropane Cyclobutane Cyclopentane Cyclohexane Cycloheptane Cyclooctane

The molecular strain is the summation of

(a) Torsional distortion (Pitzer strain): It originates from closeness of bulky substituents in a particular conformation

(b) Bond angle distortion (Baeyer strain): It originates from deviation of bond angle from 109°28', and

(c) Linear bond stretching or compression (Van der Waals strain)

In 1885, German chemist, Adolf Von Baeyer proposed that the stability of cycloalkane depends on the amount by which the angles between the chemical bonds deviate from the ideal angle 109°28' of a tetrahydral carbon. The amount of deviation is the measure of the strain of the ring. Greater the strain, the less stable is the ring. Cyclopentane (bond angle is 108°) is the least strained and most stable ring. He assumed that all cycloalkane rings are planar. Hence, strain increases with the size of the ring.

Limitations of Baeyer's Strain Theory:

Baeyer postulated that the ring strain increases with the size of the ring. He assumed that all cycloalkane rings are planar. However another German chemist, H. Sachse is 1890 suggested that the ring strain in bigger sized rings can be relieved if we place them in chair and boat conformations rather in planner conformation. It is found to be practically correct.

He proposed that large rings need not be strained, because the carbons need not be coplanner. In 1918, 25 years after Sachse theory of strainless rings, Ernst Mohr proved its correctness on the basis of the X-ray structure of diamond using X-ray diffraction.

For example, the ring strain and ring stability of higher rings were no way differ much from that of cyclopentane.

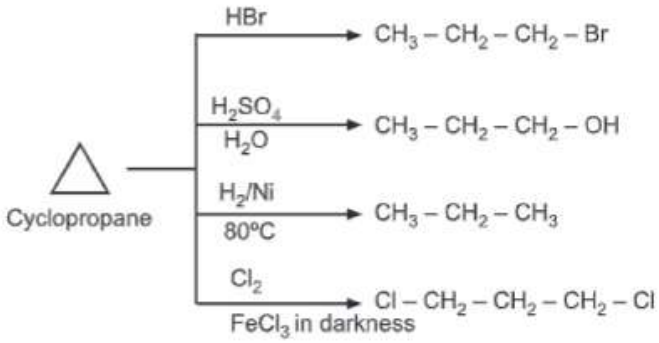
Coulson and Moffitt's Modification:

Due to a triangular planar structure of cyclopropane, the bond angles between carbon-carbon bonds are expected to be 60°. It is very less than the ideal stable angle of 109° as per the sp^3 hybridization of the carbon atoms. This leads to a considerable amount of ring strain in the molecule. Coulson and Moffitt suggested that rehybridization occurs in cyclopropane wherein the carbon-carbon bonds are bent outwards so that the bond angle becomes 104° which consequently reduces the level of ring strain. These bonds are called as 'bent bonds' or 'banana bonds'.

Thus, the C–C bonds have more p-character while the C–H bonds have more s-character. Hence, cyclopropane is much more reactive than alkanes or other higher ring system.

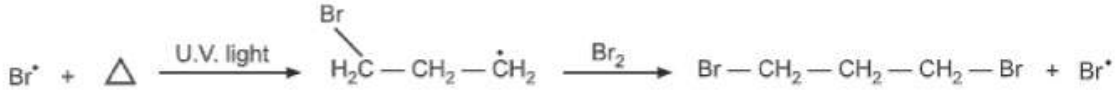
6.4 REACTIONS OF CYCLOPROPANE

(a) Addition reactions: These reactions lead to opening of the ring to relieve the ring strain. In these reactions, the reagent attaches at two terminals of the resulting propane chain.



The electrophilic addition in substituted cyclopropanes generally follows Markovnikov's rule wherein hydrogen adds carbon which already contains more hydrogens. Nucleophilic addition to cyclopropane is possible only when an electron – withdrawing group is present on the ring.

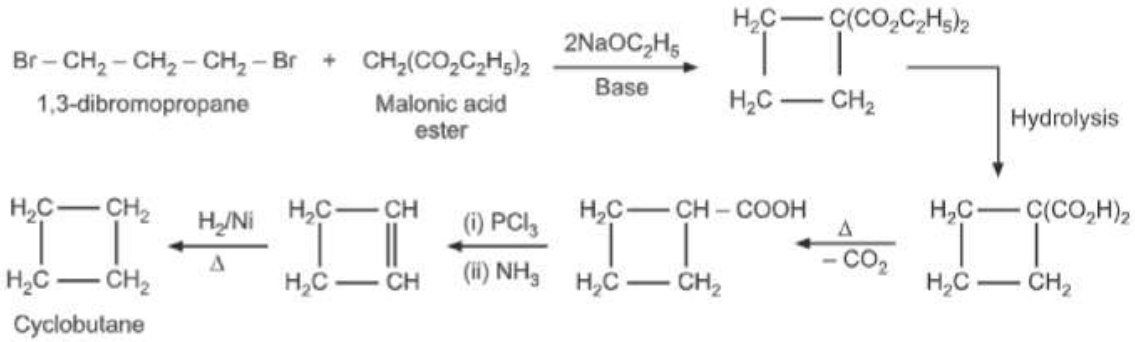
Addition of free radicals to cyclopropane is also reported. Thus bromine adds to a cyclopropane ring in presence of UV light via a free radical mechanism.



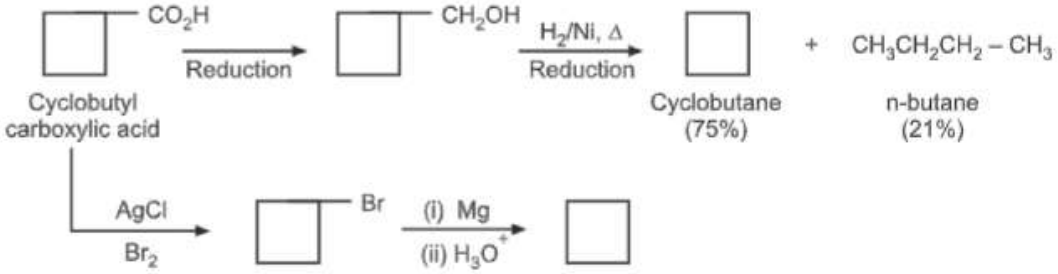
6.5 REACTIONS OF CYCLOBUTANE

Cyclopropane and cyclobutane are present in gaseous state at room temperature while remaining cycloalkanes exist in liquid state. Due to angle strain, the C–C bonds in cyclopropane and cyclobutane are weak. Because of these weak bonds, cyclobutane undergoes reactions similar to that of cyclopropane.

Cyclobutane (b.p. –15°): It was first prepared by Willstatter (1907), using the Hofmann exhaustive methylation reaction.



The yield of cyclobutane obtained by ring closure of 1,4-dihalogen alkanes. In yet another method, cyclobutane carboxylic acid may be covereted to cyclobutane by following routes.



EXERCISE

1. Discuss the synthesis and reactions of cyclopropane.
2. Discuss the synthesis and reactions of cyclobutane.
3. What is ring strain? Illustrate Baeyer's strain theory. What are its limitations?
4. What is Coulson and Moffitt's modification?
5. Elaborate Sache Mohr's theory of strainless rings?

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