Name of Unit	Phenols, Aromatic Amines and Aromatic Acids.
Subject /Course Name	Pharmaceutical Organic Chemistry-II
Subject/Course ID	BP301T
Class: B.Pharm. Semester	3rd
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Learning Outcome of Module 02

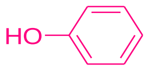
LO	**Particular**	**Course Outcome Code**
LO1	To understand the Phenols, Aromatic amines and Aromatic acids	BP301.5
LO2	To gain knowledge about different methods to prepare Phenols, Aromatic amines and Aromatic acids	BP301.5
LO3	To understand acidity and basicity	BP301.5
LO4	To gain the knowledge of uses of some compounds.	BP301.5

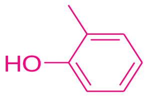
Module Content Table

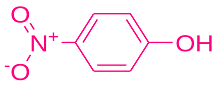
Topic
• Introduction • Physical properties of Phenol • Acidity of Phenol and effect of substituent on acidity • Method of preparation of Phenol • Structure and uses of Cresol, resorcinol, napthols • Method of preparation of Aromatic amines • Basicity of amines, effect of substituent on basicity • Synthetic uses of aryl diazonium salt • Method of preparation of aromatic acids • Reactions of Aromatic acids • Acidity of aromatic acids and effect of substituent on acidity

INTRODUCTION OF PHENOL

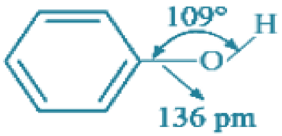
Phenol (also called carbolic acid) is **an aromatic organic compound with the molecular formula C_6H_5OH**. It is a white crystalline solid that is volatile. The molecule consists of a phenyl group ($-C_6H_5$) bonded to a hydroxy group (−OH).


Phenol


2-methylphenol


4-Nitrophenol

In phenol, hydroxy functional group is directly attached to the **sp^2 hybridized** carbon atom of the benzene ring. The interaction of six unhybridized **2pz orbitals** of carbon atoms of the benzene ring leads to the formation of delocalized pi-electron clouds. The **C-O-H bond angle** in phenol is **109^0**. The carbon-oxygen bond length (**136pm**).



Phenol

PHYSICAL PROPERTIES

1.Pure phenol is a white crystalline solid, smelling of disinfectant. It has to be handled with great care because it causes immediate white blistering to the skin. The crystals are often rather wet and discolored.

2. **Melting and Boiling Points: -**It is useful to compare phenol's melting and boiling points with those of methylbenzene (toluene). Both molecules contain the same number of electrons and are a very similar shape. That means that the intermolecular attractions due to van der Waals dispersion forces are going to be very similar.

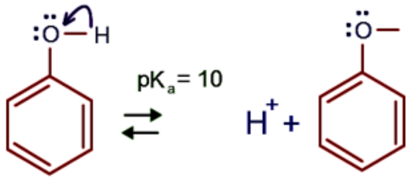
Compound	MELTING POINT (^OC)	BOILING POINT(^OC)
Phenol	40-43	182
Methylbenzene	-95.0	111

The reason for the higher values for phenol is in part due to permanent dipole-dipole attractions due to the electronegativity of the oxygen - but is mainly due to hydrogen bonding. Hydrogen bonds can form between a lone pair on an oxygen on one molecule and the hydrogen on the -OH group of one of its neighbors

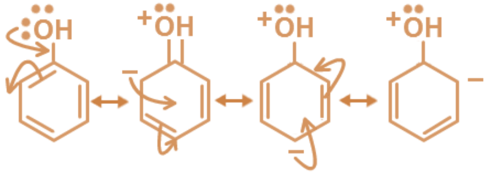
3. **Solubility in Water:** -Phenol is moderately soluble in water - about 8 g of phenol will dissolve in 100 g of water. If you try to dissolve more than this, you get two layers of liquid. The top layer is a solution of phenol in water, and the bottom one a solution of water in phenol. Phenol is somewhat soluble in water because of its ability to form hydrogen bonds with the water.

ACIDITY OF PHENOL

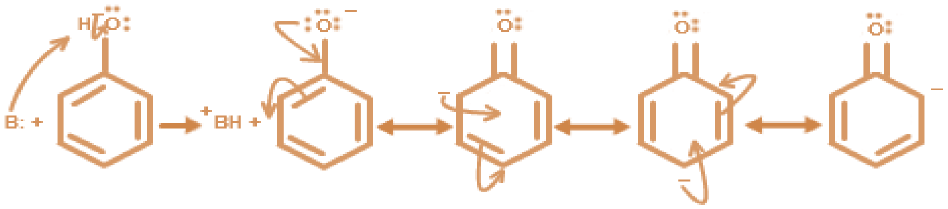
Compare to alcohols, phenols are stronger acid as the pKa value for phenol is 10 while for alcohols it’s close to. Because of acidic nature, phenols can turn blue litmus red and react with aqueous alkali to form phenate. Both reactions are not shown by alcohols. Compare to carboxylic acids, phenols are weaker acid.



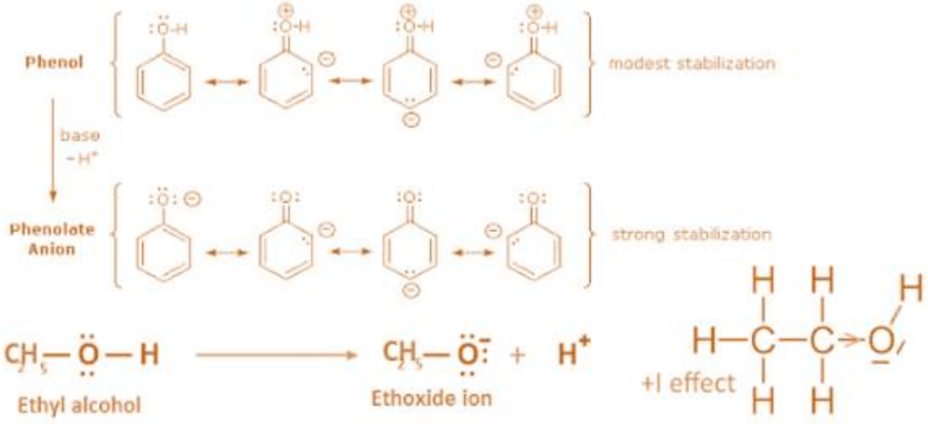
Hence hydroxy group bonded to benzene ring is much more acidic than hydroxy group to alcohol. This is because of the resonance in phenol. Because of the resonance in phenol, the oxygen atom acquires a positive charge which weakens the oxygen-hydrogen bond and facilitates the release of a proton.



The deprotonation of phenol forms phenoxide ion or phenate which also exists as a resonance.



Hence both phenol and phenoxide ion are stabilized by resonance. Compare to phenol, phenoxide ion is more stable as the negative charge gets delocalized over benzene ring. But the resonating structure of phenol involves the separation of negative and positive charges. Therefore phenol has greater tendency to form phenate by releasing the proton. The deprotonation of alcohol forms alkoxide ion which is not stable due to negative inductive effect of alkyl group and alcohols become less acidic than phenol.



In **Ethoxide**, the resonance is not possible and The **+ I effect** of the hydrocarbon chain increases the electron density between **O** and **H** and decreases the chances of **H^+** to leave the alcohol. The more the chain is long and branched the greater the effect, the less will the alcohol be acid.

Effect of Substituent on Acidity of Phenol

As the acidic nature of phenol is due to the resonance stabilization of phenate compare to phenol. Therefore the presence of any substituent on aromatic ring which can stabilized the phenoxide ion will tend to increases the acidity of phenol. While any substituent which destabilized the phenate ion by increasing the negative charge will decrease the acidic nature of phenol.

In other words; the presence of **Electron Withdrawing Group** on benzene ring in phenol **increase the acidity** of phenol and **electron releasing group** will **decrease the acidity**. For example; if there is a **nitro group** substituted on phenol, it will increase the acidic nature of phenol. Hence **nitrophenol** will be more acidic than **phenol** as **nitro group** imparts **negative mesomeric effect** and **negative inductive effect**, hence acts as **electron withdrawing group**.

The position of **nitro group** on **phenol** will affect the acidity of **phenol**. A nitro group at **-ortho** and **para**-position withdraws electrons from **hydroxy group** of **phenol** by stronger **–M effect** while nitro group at -meta position withdraws electrons by **weaker –I** effect only, as **meta** position cannot involve in resonance with **hydroxy group**. Hence **o-** and **p-nitrophenols** are more acidic than **m-nitrophenol**. Similarly as the number of nitro groups increases on phenol, the acidic nature of phenol increases. The decreasing order of acidity of **nitrophenols** is as given below.

2,4,6-trinitrophenol > 2,4-dinitrophenol > 4-Nitrophenol > 2-Nitrophenol > Phenol

Electron Donating Groups like amino (-NH_2), alkyl (-R) decreases the acidity of phenol. For example, cresol or methyl phenols are less acidic compare to phenol due to positive inductive effect as well as hyperconjugation of methyl group. As both of these effects increases the electron density on hydroxy group and results in low acidity of phenols. Hyperconjugation can operate only at ortho and para position while inductive effect operates at all the three positions. Therefore o-cresol is least acidic. The decreasing order of acidity is as follow.

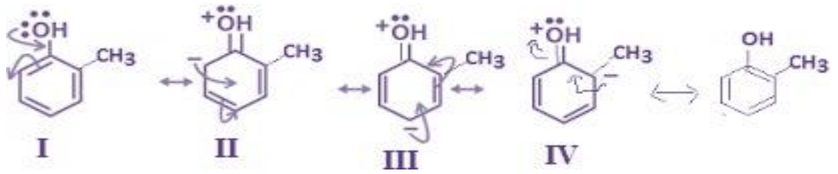
Phenol > m-cresol > p-Cresol > o-cresol

Some of the substituted phenols with their pKa values are as follow.

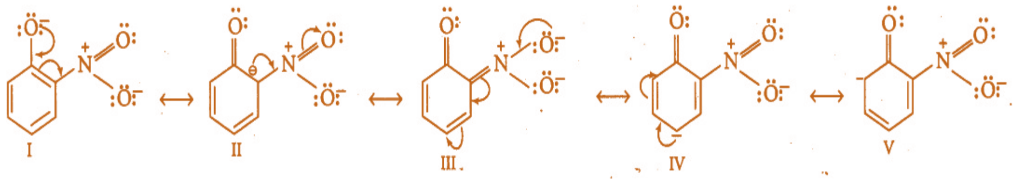
Compound	**pKa**	**Substituent**	**Effect of substituent**
Phenol	10.0	-	-
o-Methoxyphenol	10.0	-OCH_3	+M and -I

o-Methyl phenol	10.3	$-CH_3$	+I and hyperconjugation
o-Chlorophenol	8.6	-Cl	-I and +M
o-Nitrophenol	7.2	$-NO_2$	-M and -I
m-nitrophenol	8.4	$-NO_2$	-M and -I
p-Methoxyphenol	10.2	$-OCH_3$	+M and -I
p-Methyl phenol	10.3	$-CH_3$	+I and hyperconjugation
p-Chlorophenol	9.4	-Cl	-I and +M
p-Nitrophenol	7.2	$-NO_2$	-M and -I

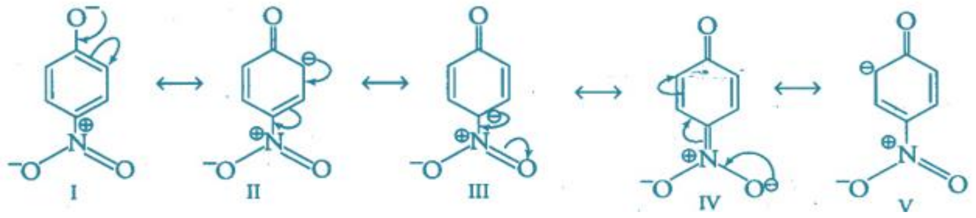
Resonating structure of ortho cresol



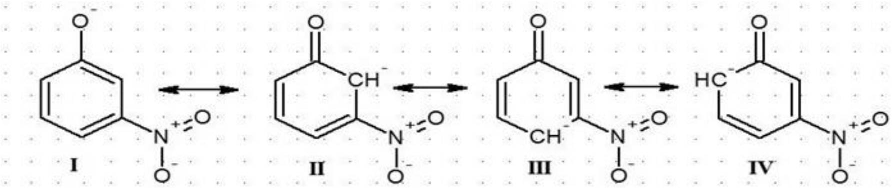
Resonating structures of o-nitro phenoxide ions (o-nitro phenol)



Resonating structures of p-nitrophenoide ion (p-nitrophenol)



Resonance forms of m-nitrophenol



Why is meta -nitrophenol less acidic than para-nitrophenol

The acidity of nitrophenols (or any acid for that matter) is determined by the stability of the conjugate base. In the case of m-nitrophenol and p-nitrophenol, the relative stability can be determined by looking at the resonance structures.

Whereas p-nitrophenol has an additional resonance structure where the negative charge is delocalized onto the oxygen of the nitro group, which is highly electronegative and therefore stabilize the charge effectively. This stabilization is not possible in the case of m-nitrophenol because there is no opportunity via resonance fordelocalization onto the nitro group.

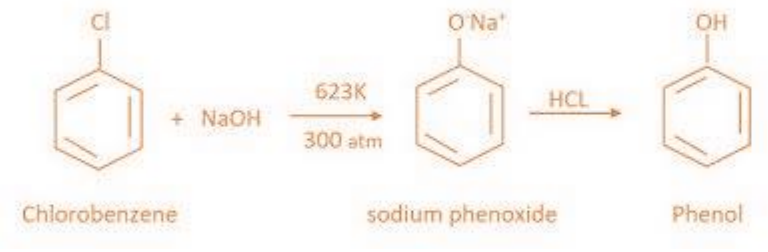
Why is picric acid more acidic than benzoic acid?

Picric acid is more acidic than benzoic acid because picric acid contains three NO2 groups which is electron withdrawing group. Presence of electron withdrawing group on ring increases acidic character on the other hand presence of electron donating group on ring decreases the acidic character.

METHODS OF PREPARATION OF PHENOL: -

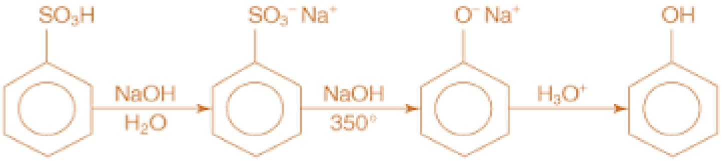
1. **Preparation of Phenols from Haloarenes: -**

   Chlorobenzene is an example of haloarenes which is made by mono replacement of the benzene ring. When chlorobenzene is reacted with sodium hydroxide at 623K and 320atm sodium phenoxide is formed. Finally, sodium phenoxide on acidification makes phenols.



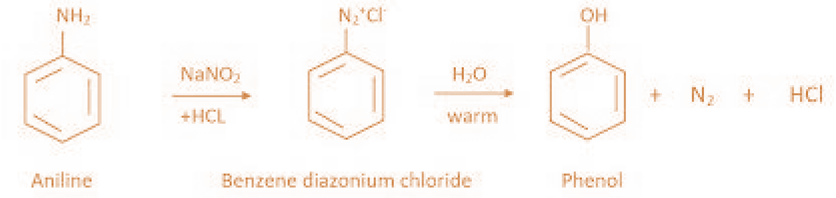
2. **Preparation of Phenols from Benzene Sulphonic Acid: -**

   Benzene sulphonic acid can be acquired from benzene by reacting it with oleum. Benzene sulphonic acid, hence formed, is fused with molten sodium hydroxide at a very high temperature which leads to the development of sodium phenoxide. Lastly, sodium phenoxide on acidification gives phenols.



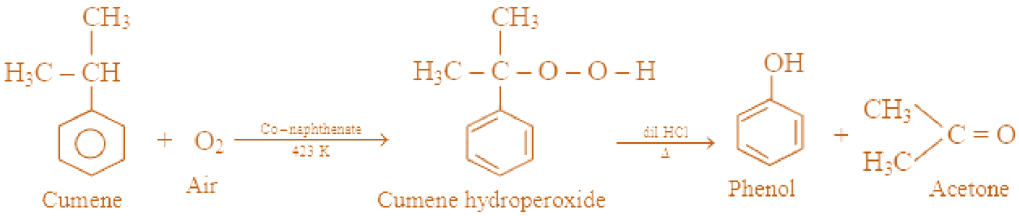
3. Preparation of Phenols from Diazonium Salts: -

When an aromatic primary amine is fused with nitrous in the presence of HCl ($NaNO_2$ + HCl) acid at 273 – 278 K, diazonium salts are gained. These diazonium salts are extremely reactive in nature. Upon warming with water, these diazonium salts, to end hydrolyze to phenols. Phenols can also be acquired from diazonium salts by treating it with dilute acids.



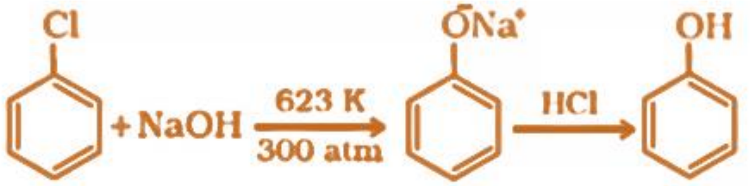
4. Preparation of Phenols from Cumene: -

Cumene is an organic compound acquired by Friedel-Crafts alkylation of benzene with propylene. On oxidation of cumene (isopropyl benzene) in the presence of air, cumene hydroperoxide is found. Upon further action of cumene hydroperoxide with dilute acid, phenols are produced. Acetone is also made as one of the by-products of this reaction in large quantities. Therefore, phenols prepared by these techniques need purifications.



5. Dow Process: -

In this process, chlorobenzene is reacted with dilute sodium hydroxide at a temperature of about 300°C and 3000 psi pressure. The following figure exemplifies the Dow process.

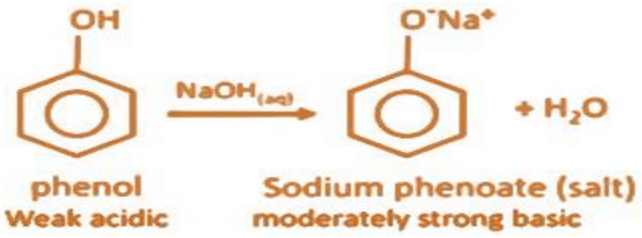


CHEMICAL REACTIONS OF PHENOL: -

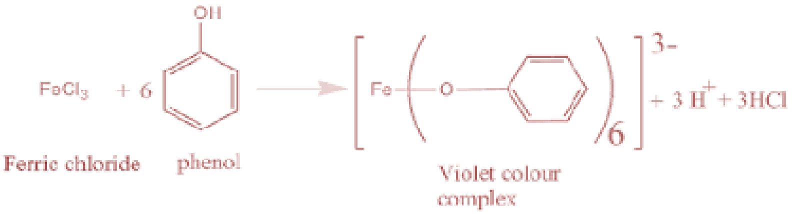
The reactions of phenol are the reactions of the -OH group and the benzene ring.

1. Reactions of -OH group: -

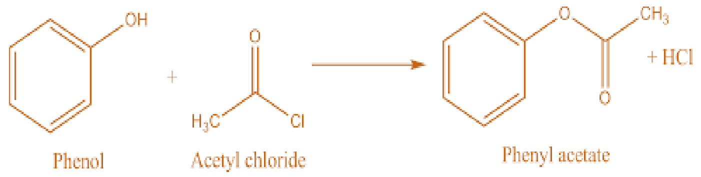
i) **Formation of Salts:** - Phenol is acidic. It reacts with sodium hydroxide or sodium metal to form salts.



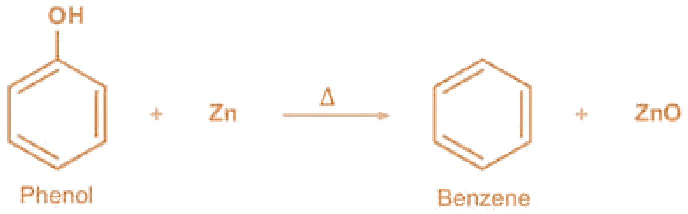
ii) **Reaction with $FeCl_3$: -** Phenol reacts with neutral FeCl3 solution to give violet color complex which is soluble in water.



iii) **Formation of Esters: -**Phenol reacts with acid chlorides in aqueous alkali solution to give phenyl esters.



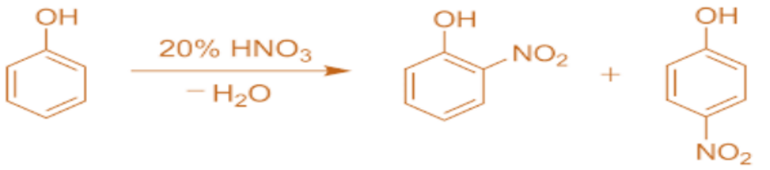
iv) **Reaction with Zinc Dust: -** When phenol is distilled with zinc dust, low yield of benzene is obtained.

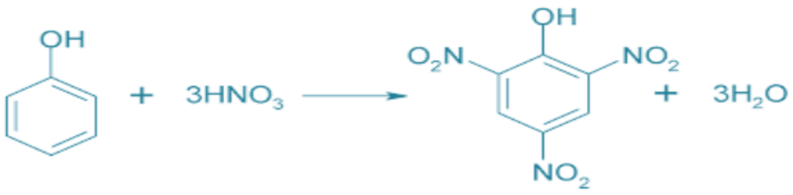


2) **Reactions of Benzene Ring: -**The hydroxy group in a phenol molecule exhibits a strong activating effect on the benzene ring because it provides a ready source of electron density for the ring. This directing influence is so strong that you can often accomplish substitutions on phenols without the use of a catalyst.

i) **Nitration of Phenols-** Phenols upon treatment with dilute nitric acid undergo nitration at low temperature (298 K) to give a mixture of ortho and para nitrophenols. The mixture formed is further separated into ortho and para nitrophenols by steam distillation on the basis of their volatility.

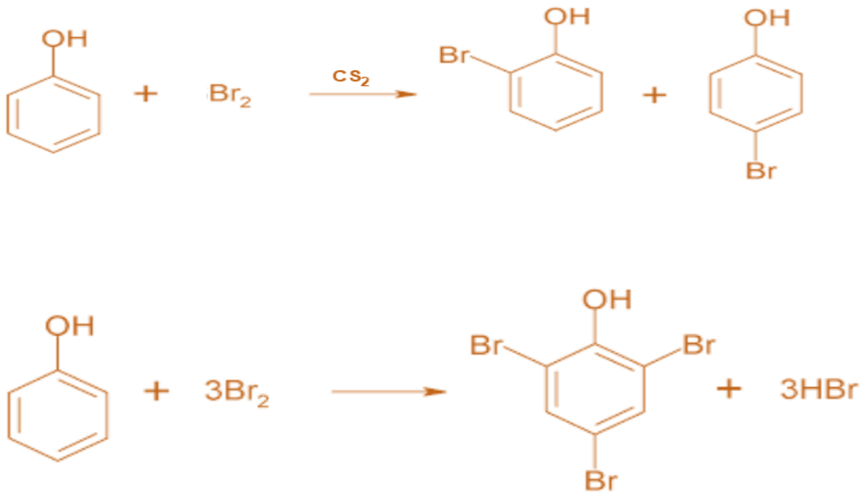
When phenol is treated with concentrated nitric acid, the nitration results in the formation of 2, 4, 6-trinitrophenol (commonly called picric acid).



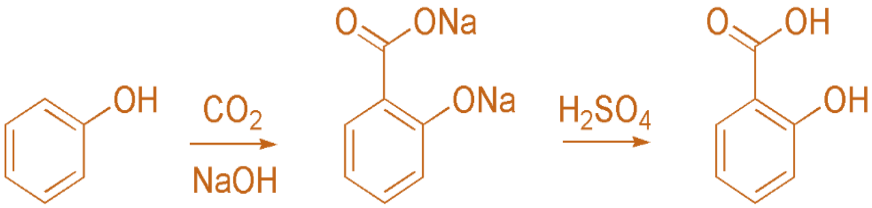


ii) **Halogenation of Phenols: -** Due to a highly activating effect of the hydroxyl group in phenols, they undergo halogenation even in the absence of Lewis acids. When phenols are treated with bromine in the presence of a solvent of low polarity like $CHCl_3$ at low temperatures, Mono bromophenols are formed.

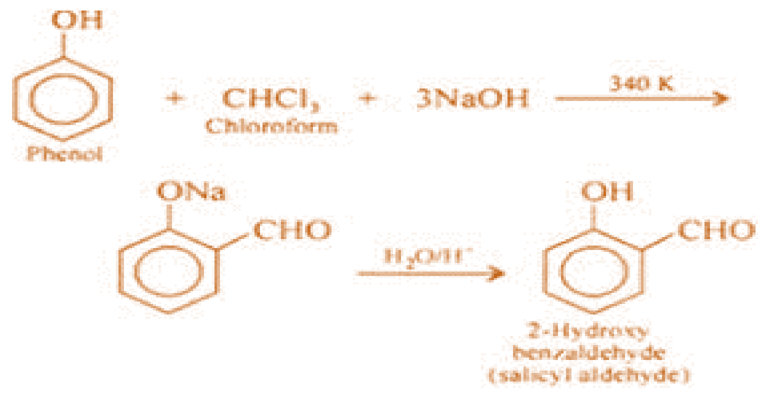
When phenol is treated with bromine water, a white precipitate of 2, 4, 6-tribromophenol is formed.



iii) **Kolbe's Reaction-**When phenol is treated with sodium hydroxide, phenoxide ion is formed. This phenoxide ion formed is highly reactive towards electrophilic substitution reactions. Upon treatment with a weak electrophile (carbon dioxide), it undergoes electrophilic substitution reaction to form Ortho-hydroxybenzoic acid. This reaction is popularly known as Kolbe's reaction.



iv) **Reimer-Tieman Reaction -**When phenol is treated with chloroform in the presence of sodium hydroxide, an aldehyde group is formed at the ortho position of the benzene ring. This reaction is popularly known as the Reimer-Tieman reaction.



QUALITATIVE TESTS FOR PHENOL: -

Identification of Phenols-Ferric Chloride

Compounds with a phenol group will form a blue, violet, purple, green, or red-brown color upon addition of aqueous ferric chloride. This reaction can be used as a test for phenol groups.

1) Iron (III) Chloride Test for Water-Soluble Phenols

$$3\ ArOH + FeCl_3 \xrightarrow[\text{pyridine}]{} \underset{\text{colored complex}}{Fe(OAr)_3}$$

Procedure: The iron (III) chloride test for phenols is not completely reliable for acidic phenols, but can be administered by dissolving 15 mg of the unknown compound in 0.5 mL of water or water-alcohol mixture and add 1 to 2 drops of 1% aqueous iron (III) chloride solution.

Observation: A red, blue, green, or purple color observed.

2) Iron (III) Chloride - Pyridine Test for Water-Insoluble Phenols

Procedure (for water-insoluble phenols or less reactive phenols)**:** A more sensitive test for phenols consists of dissolving or suspending 15 mg of the unknown in 0.5 mL of methylene chloride and adding 3-5 drops of a 1% solution ferric chloride in methylene chloride. Add a drop of pyridine and stir.

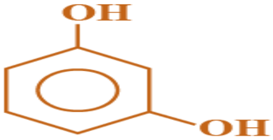
Observation: Addition of pyridine and stirring will produce a color if phenols or enols are present.

USES OF PHENOL: -

- Approximately two-third of the total phenol produced worldwide is used to prepare reagents used in plastic manufacturing industries.
- The polymerization reaction of phenol with formaldehyde is used to commercially prepare phenolic resins.
- Phenol is also used in the study and extraction of bio-molecules. Molecular biology finds application of phenol in the extraction of nucleic acids from tissue samples for further investigations.
- Phenol is also used in cosmetic industry in the manufacturing of sunscreens, skin lightening creams and haircoloring solutions.
- Phenol is also a versatile precursor to a large collection of drugs, most notably aspirin but also many herbicides andpharmaceutical drugs.

Cresols

Cresols (also hydroxytoluene) are organic compounds which are methylphenols. They are a widely occurring natural and manufactured group of aromatic organic compounds, which are categorized as phenols (sometimes called phenolics). Cresols have a disinfectant and corrosive effect due to the degradation of proteins.



o-cresol

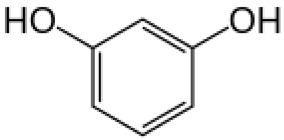
USES OF CRESOLS: -

- Mixed cresols are used as disinfectants, preservatives, and wood preservatives.
- o-Cresol is used as a solvent, disinfectant, and chemical intermediate.
- m-Cresol is used to produce certain herbicides, as a precursor to the pyrethroid insecticides, to produce antioxidants and to manufacture the explosive, 2,4,6-nitro-m-cresol.
- p-Cresol is used largely in the formulation of antioxidants and in the fragrance and dye

industries.

Resorcinol

Resorcinol (or resorcin) is a benzenediol (*m*-dihydroxy benzene).

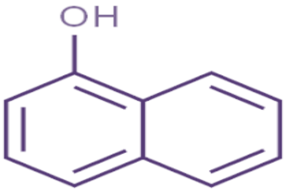


Uses of Resorcinol

- It is an antiseptic and disinfectant, and is used 5 to 10% in ointments in the treatment of chronic skin diseases such as psoriasis, hidradenitis suppurativa, and eczema.
- It has also been employed in the treatment of gastric ulcers in doses of 125 to 250 mg in pills, and is said to beanalgesic and hemostatic (stops bleeding) in its action.
- A 2% solution used to treat external vaginal itching and irritation.
- **Resorcinol** is a skin protectant and topical analgesic.

Naphthol

Naphthol is a fluorescent colorless (or occasionally yellow) crystalline solid with the formula $C_{10}H_7OH$. It has two isomers of 1-naphthol and 2-naphthol, differing by the location of the hydroxyl group on the naphthalene ring. The naphthol's are naphthalene homologues of phenol, but more reactive.



Uses of Naphthol: -

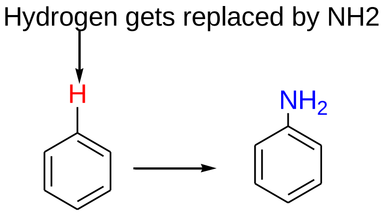
- Naphthol (both 1 and 2 isomers) are used as biomarkers for livestock and humans exposed to polycyclic aromatic hydrocarbons.
- 1-Naphthol is a precursor to a variety of insecticides including carbaryl and

pharmaceuticals including nadolol. It undergoes azo coupling to give various azo dyes, but these are generally less useful than those derived from 2-naphthol.

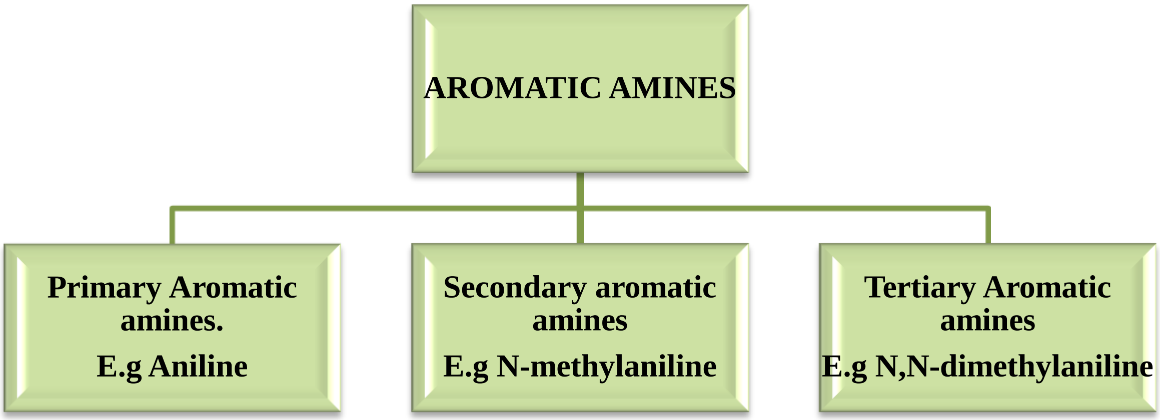
- In **Molisch's test**, 1-naphthol dissolved in ethanol, known as Molisch's reagent, is used as reagent for detecting the presence of carbohydrates.
- The **Sakaguchi test** uses 1-naphthol with sodium hypobromite to detect the presence of arginine in proteins.
- The **Voges–Proskauer Test** uses 1-naphthol in potassium hydroxide (KOH) solution to detect the breakdown of glucose into acetoin which is used by bacteria for external energy storage. A positive test will be indicated by the appearance of a red color of the original yellow solution.

AROMATIC AMINES

These are the organic compounds in which NH_2 group replace one hydrogen of the benzene ring and formed aromatic amines.



CLASSIFICATION



AROMATIC AMINES

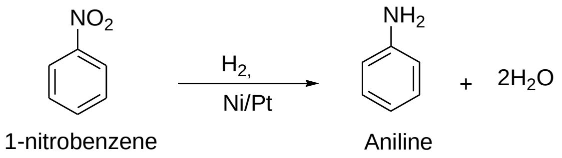
Primary Aromatic amines.
E.g Aniline

Secondary aromatic amines
E.g N-methylaniline

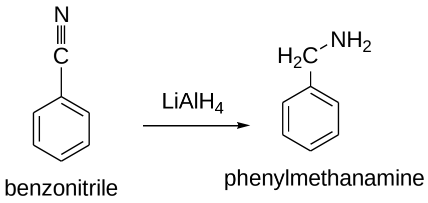
Tertiary Aromatic amines
E.g N,N-dimethylaniline

METHOD OF PREPARATION OF AROMATIC AMINES

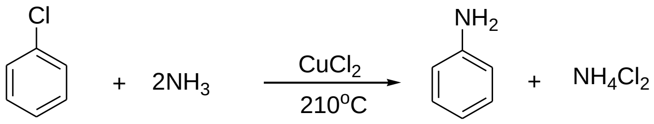
1. **By Reduction of Nitro compounds-** When nitrobenzene is reacted with H_2 gas in the presence of catalyst Ni/Pt it gives aniline.



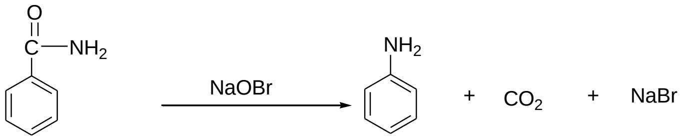
2. **By Reduction of Nitriles-** When aromatic nitriles undergo a reduction reaction with lithium aluminium hydride it gives aromatic amines.



3. **By ammonolysis of chlorobenzene-** When chlorobenzene undergoes ammonolysis in the presence of copper dichloride at high temperature it gives aromatic amines.



4. **Hoffman Rearrangement reaction-** When acetamide is treated with sodium hypobromide, ammonia group in acetamide is rearrange their position and shift towards ring and produce aniline.



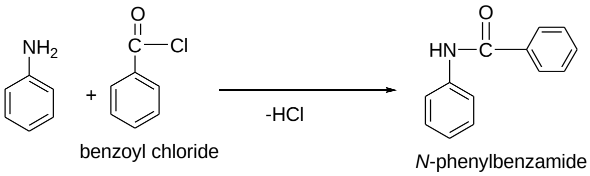
PHYSICAL PROPERTIES OF AROMATIC AMINES

1. They are colourless liquid or solid, but in the presence of light they undergoes oxidation and turn brown in colour.

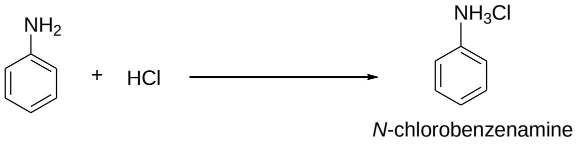
2. They are polar compound and can form intermolecular hydrogen bonding.
3. They are highly toxic substance and some are carcinogenic.
4. They are not readily water soluble due to the presence of bulkier phenyl group.

CHEMICAL REACTIONS

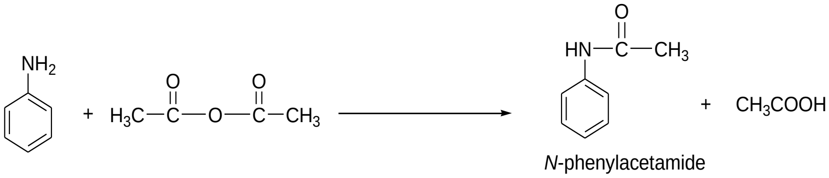
1. **Formation of amides-** When aromatic amines react with acyl chloride it produce Benzylamide with the formation of amide linkage.



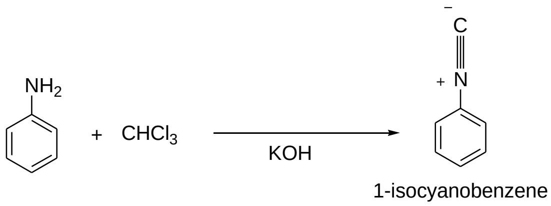
2. **Formation of salt-** When aromatic amine treated with HCl it produce benzeneaminum chloride.



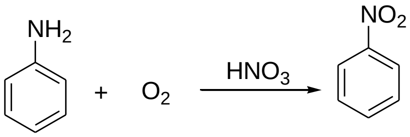
3. **Acetylation –** When aromatic amine is treated with acetic anhydride it forms acetanilide.



4. **Carbylamine reaction-** When aniline react with chloroform or potassium hydroxide it produce carbylamines.

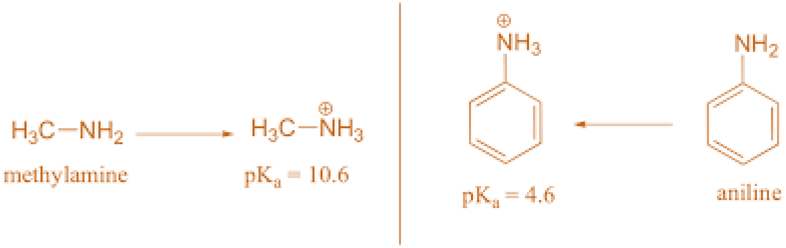


5. **Oxidation-** When aromatic amines undergoes oxidation in the presence of nitric acid it gives nitrobenzene.

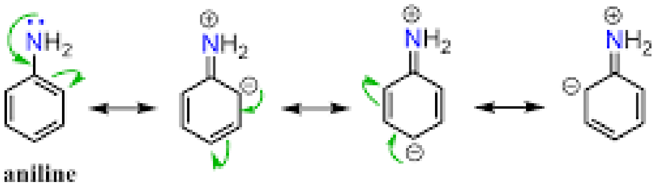


BASICITY OF AROMATIC AMINES

The basicity of a compound is a measure of a compounds ability to accept a proton. Aniline accept a proton as follows.



In aliphatic amines, non-bonding electron pair of N is localized and is fully available for coordination with a proton. On the other hand, in aromatic amines, the non-bonding electron pair is delocalized into benzene ring by resonance.



The Non-bonding electron pair in the hybrid being dispersed over the benzene ring as also the N atom, is less available for protonation . hence, aromatic amines are less basic than aliphatic amines which shows no resonance.

EFFECTS OF SUBSTITUENTS ON BASICITY

The basicity of aromatic amines is greatly influenced by the position as well as nature of the substituent present on the benzene ring. The ortho and para position not meta position of the group determine its net effect on the electron density on nitrogen The nature of the group determine its inductive effect (Whether +I and -I) or resonance effect (-R or +R) which operatesvat the position on Aromatic ring.

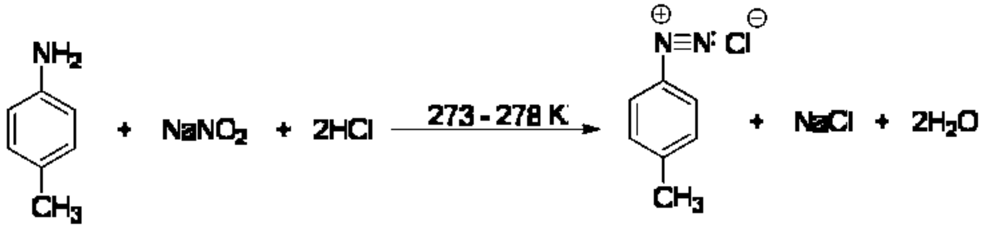
It has been found that

1. **Electron releasing group-** such as $-CH_3$, $-OCH_3$, -OH, $-NH_2$ increase the basicity of amines.
   This is due to the fact, that electron releasing groups tend to increase the electron density on the amino group and thus the lone pair of electron on nitrogen becomes more available for sharing with an acid. At the same time substituent also stabilize the substituted anilinium ion by the dispersal of positive charge on nitrogen and thus increase its stability relative to parent amine. It is therefore quite natural that electron releasing substituent increase the basicity of aromatic amines.
2. **Electron withdrawing group-** such as $-NO_2$, -CN, -X, on the other hand, decrease the basic strength by decreasing the electron density on the amino group and thus the lone pair of electron becomes less available for sharing with an acid. Moreover, these substituents also do not satisfy the positive charge on substituted anilinium ion and decrease the stability relative to parent amine.

SYNTHETIC APPLICATIONS OF ARYL DIAZONIUM SALT

Aryl diazonium salt are prepared by the action of an aromatic primary amine with nitrous acid at about 0-5^{o}C.

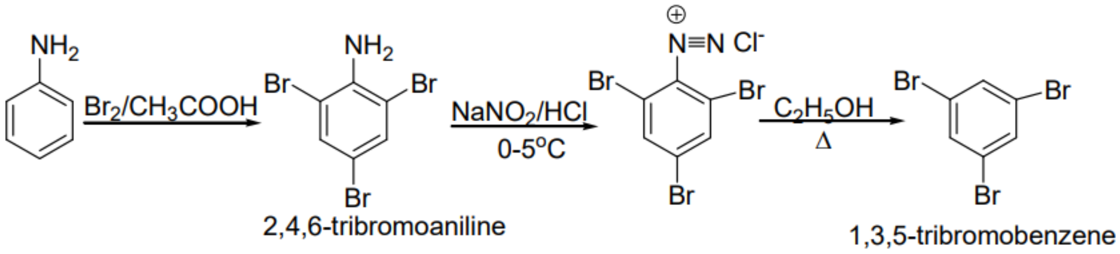
$$NaNO_2 + HCl \longrightarrow HNO_2 + NaCl$$



Diazonium salts are very useful intermediate in the synthesis of a number of aromatic compounds. Some of them are as follows.

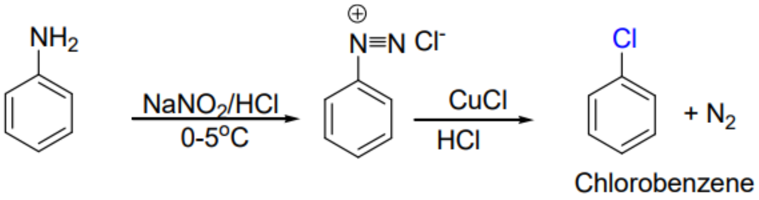
1. **Replacement of Hydrogen-**

   Synthesis of 1,3,5,-tribromobenzene



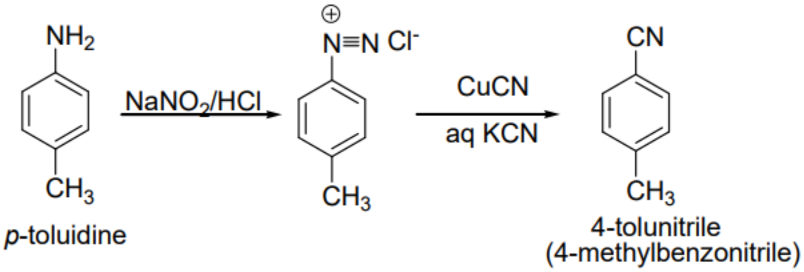
2. **Replacement by halogen atom**

   Synthesis of chlorobenzene



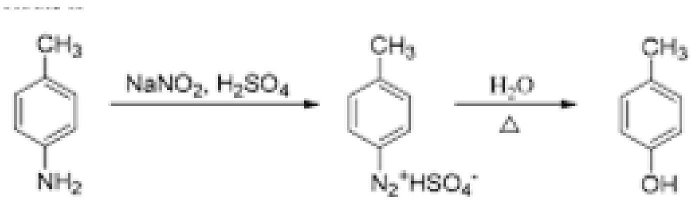
3. **Replacement by Cyano group**

   Synthesis of p-toluinitrile



4. Replacement by hyroxy group

Synthesis of o-cresol

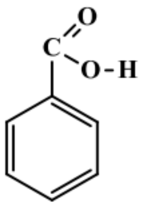


AROMATIC ACIDS

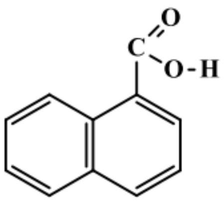
Aromatic acids are compounds in which one or more carboxyl groups (-COOH) attached directly to the aromatic ring. They are named by the common system as derivatives of parent benzoic acid.

Aromatic carboxylic acids are of two types.

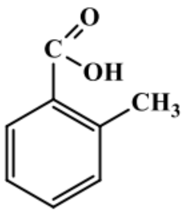
i. Those in which the carboxyl group is attached directly to aromatic nucleus.



Benzoic acid

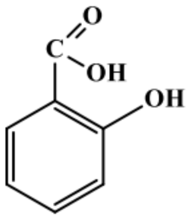


∝ - Naphthoic acid



***o*-Methylbenzoic acid**

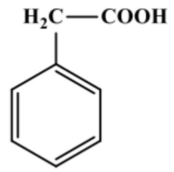
(o-Toluic acid)



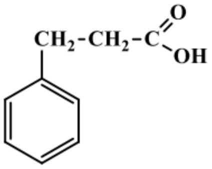
***o*-Hydroxybenzoic acid**

(Salicylic acid)

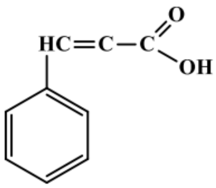
ii. Those in which the carboxyl group is attached to the side chain.



Phenyl ethanoic acid
(Phenylacetic acid)



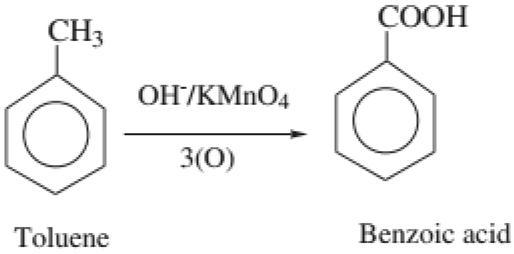
3-Phenylpropanoic acid



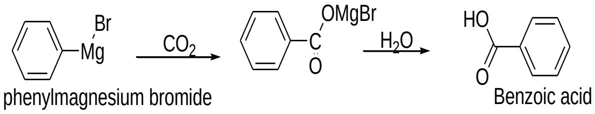
3-Phenylpropenoic acid
(Cinnamic acid)

METHOD OF PREPARATION

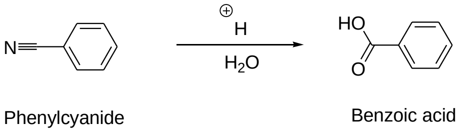
1. By oxidation of alkylbenzene with acidic potassium permanganate or sodium dichromate.



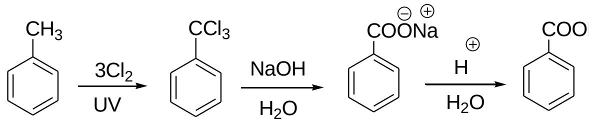
2. By reaction of phenylmagnesium bromide with carbon dioxide followed by acid hydrolysis of the addition product.



3. By acid hydrolysis of Phenyl cyanide



4. By basic hydrolysis of benzotrichloride. Benzotrichloride is obtained by chlorination of toluene.

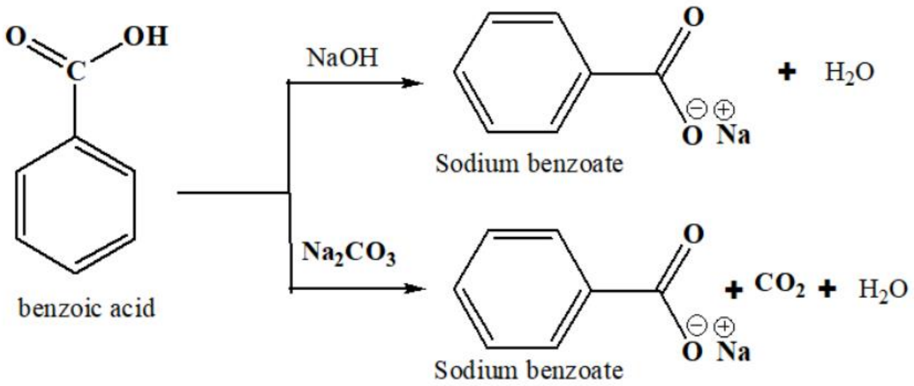


PHYSICAL PROPERTIES

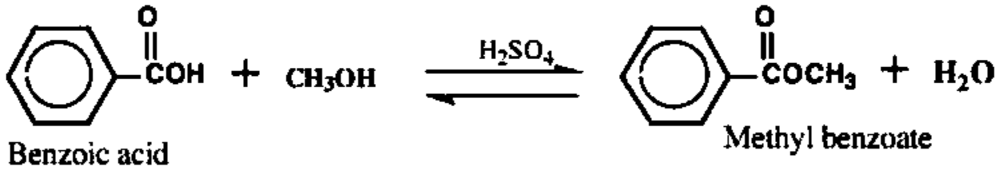
1. Benzoic acid is a colourless solid.
2. It has melting point of 122°C.
3. It is soluble in hot water diethyl ether, ethanol and benzene.
4. Benzoic acid is a slightly stronger acid than acetic acid.

REACTIONS OF CARBOXYLIC ACID

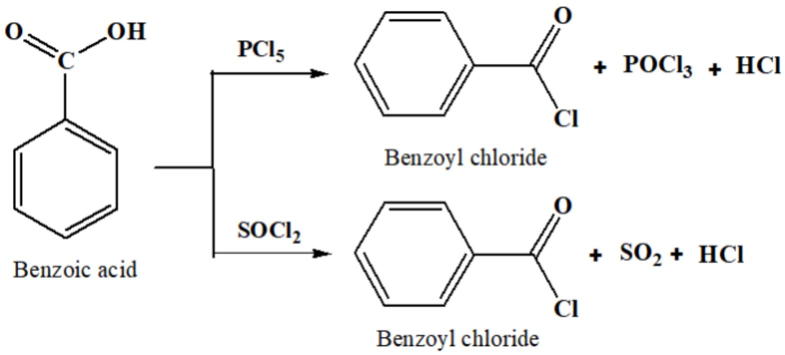
1. **Salt formation:** Benzoic acid reacts with sodium hydroxide or sodium carbonate to form sodium benzoate.



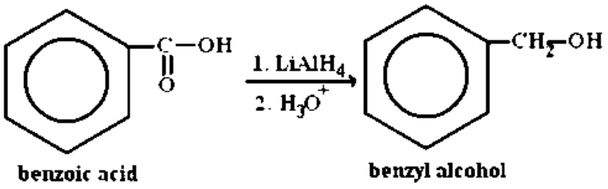
2. **Esterification of benzoic acid: -** The acid-catalyzed reaction between a carboxylic acid and an alcohol to give an ester and water.
   The alcohol is usually used as the solvent, and therefore present in excess.
   The acid must be strong; sulfuric acid, phosphoric acid, or p-toluenesulfonic acid are often used for this purpose.



3. **Acyl halide formation:** Benzoic acid reacts with phosphorus pentachloride or thionyl chloride to form benzoyl chloride.



4. **Reduction of Benzoic acid to Benzoyl alcohol:** Benzoic acid undergoes reduction with lithium aluminium hydride to give benzyl alcohol.



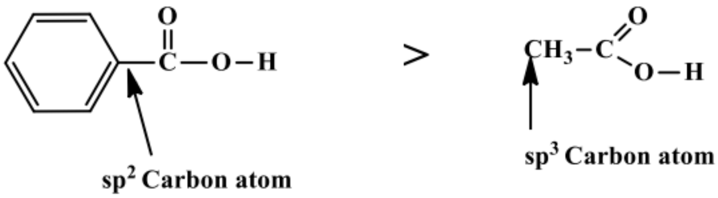
ACIDITY OF AROMATIC ACIDS AND EFFECT OF SUBSTITUENT ON ACIDITY

Aromatic carboxylic acids are stronger acids than aliphatic carboxylic acids (eg. benzoic acid, has pKa of 4.2 and is slightly stronger acid than acetic acid, pKa= 4.8).

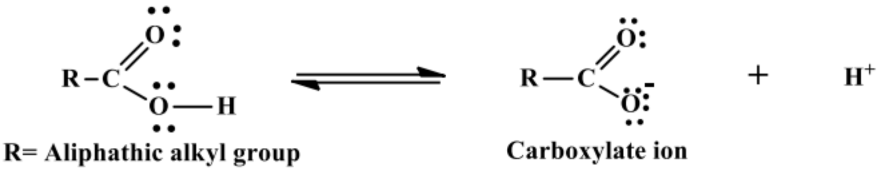
$K_a \propto 1/pK_a$, $K_a \propto$ Acidity

$pK_a \propto$ 1/Acidity

In benzoic acid, carboxylic group is bonded an sp^2 hybridised carbon atom, which is more electronegative than sp3 hybridised carbon atom of acetic acid.



The greater electronegativity of sp2 hybridised carbon atom is used to explain the resultant or apparent electron withdrawing inductive effect that the phenyl group demonstrates in stabilising the carboxylate anion.

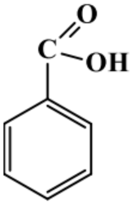


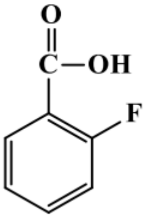
R= Aliphathic alkyl group

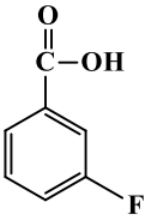
Carboxylate ion
(destabilised by +I effect of R)

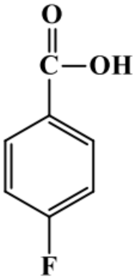
Carboxylate ion
(stabilised by -I effect of
C_6H_5 or phenyl group)

Acidity of substituted benzoic acids depends on the nature and position of the substituents. All the fluoro benzoic acids are more acidic than benzoic acid.

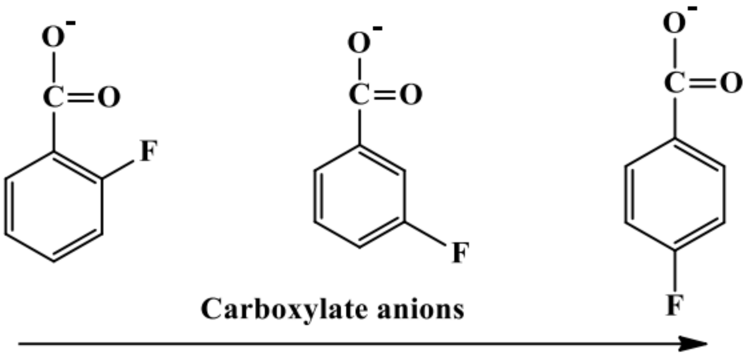






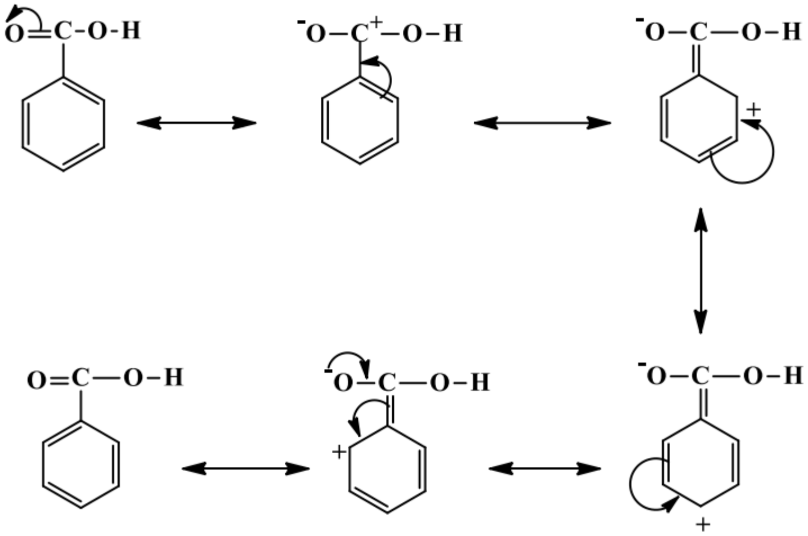


o-fluorobenzoic acid, in which the F-atom is nearest to the carboxylic acid, is the strongest acid of the four, p-fluorobenzoic acid, in which the the F-atom is farthest from carboxylic acid, is only slightly more acidic than benzoic acid. The electronegative F-atom exerts/maintains its effect through the bonds and through space, withdrawing e- density from the viscinity of the carboxylic group and hence, stabilizes the carboxylate anion.

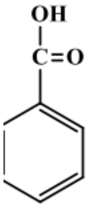


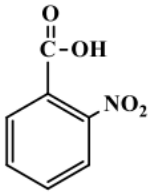
Carboxylate anions

1. increase in the distance between COOHand F
2. decrease in –I effect of F
3. decrease in stability
4. decrease in acidity of conjugate acid

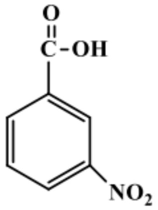


Hence, the acidity of these four acids can only be explained by the consideration of inductive powers (-I) of group. For some substituents, the inductive effect is not sufficient to explain the experimental observations. p-Nitrobenzoic acid is stronger than m- nitrobenzoic acid. This observation contrast with the observed acidity for fluorobenzoic acid for which acid strength decreases as electron withdrawing group is moved further away from carboxylic acid.

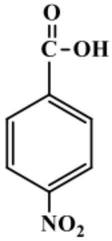




Strong inductive effect and resonance effect



Only inductive effect

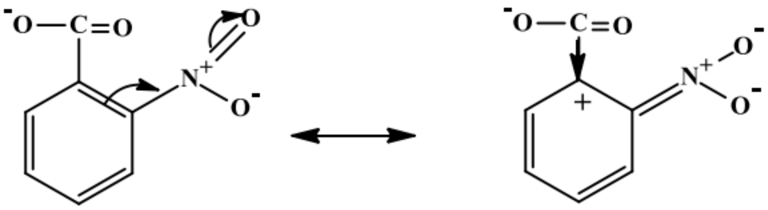


Weak inductive effect and strong resonance effect

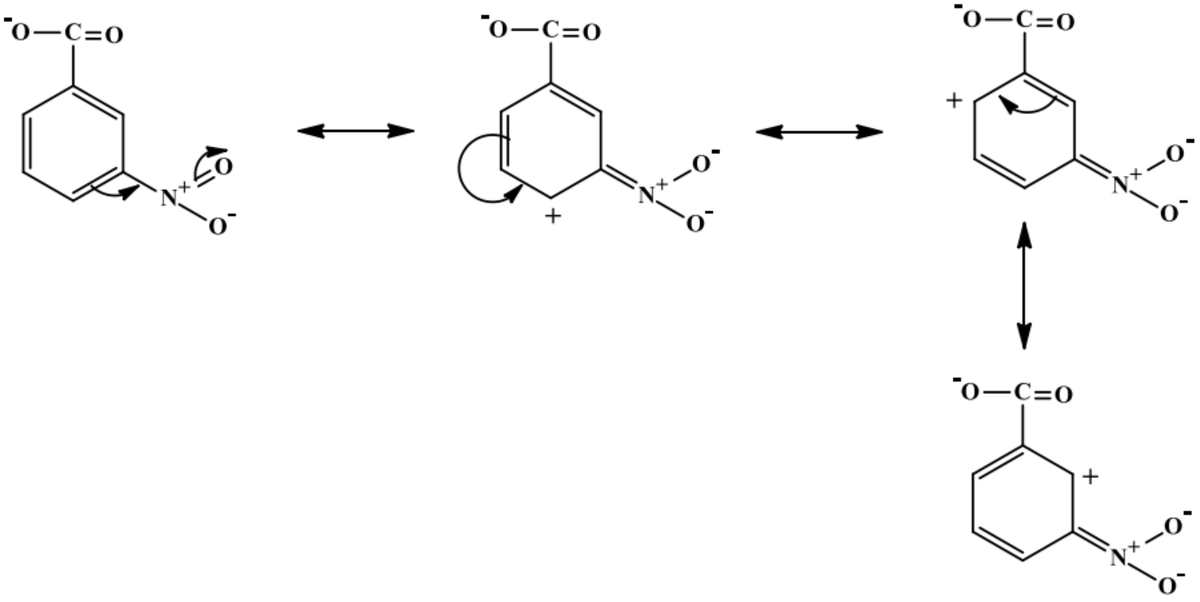
Resonance contributors having positive charge at carbon atom containing the carboxylate anion can be written for ortho and para isomers of nitrobenzoic acid, whereas the nitro group in meta position exert/maintain mainly an inductive effect.

The carboxylate anion in each case is stabilised by combination of withdrawing effect. All the nitrobenzoic acids are stronger than benzoic acid. In o-nitrobenzoic acid, the strongest acid of three isomers, the inductive effect is stronger and a resonance effect is also present. In p-nitrobenzoic acid, a resonance effect is observed but inductive effect is weak.

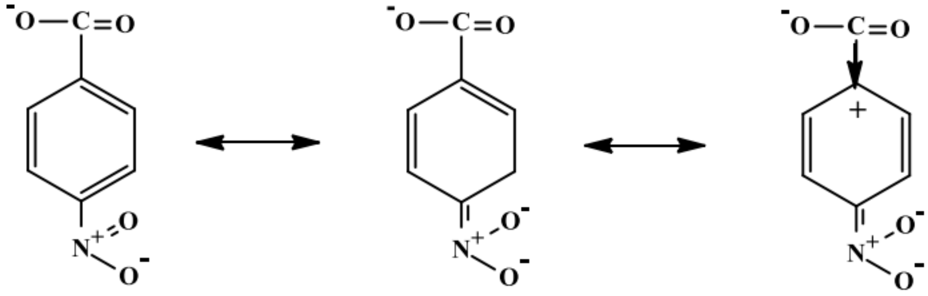
Ortho:



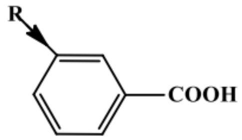
Meta:

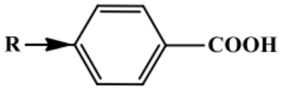


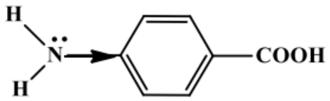
Para:



m-Nitrobenzoic acid is weaker than p-nitrobenzoic acid, reconfirm that when the resonance effect operates, it is more important than inductive effect.







An electron releasing substituent i.e. meta or para to the carboxylic group decreases the acid strength of a carboxylic acid derivatives. By releasing electron, the substituent stabilises the unionised acid and destabilises the anion. Therfore, substituents (-NH2, -OH) that activate the aromatic ring towards electrophilic aromatic substitution, decreases acidity because they donate electron through inductive effect. Substituents (-NO2) that deactivate the aromatic ring towards electrophilic substitution, increases acidity because they withdraw electron from usually through the inductive effect.

ERG (decreases acidity)

EWG (increases acidity)

The ortho substituted benzoic acids (electron releasing or electron withdrawing) are considerable stronger than meta and para. This effect is known as ortho effect. The reasons for this are not entirely known although there may be stearic effect from having two substituents ortho to one another

2 MARKS QUESTION

1) What are phenols? Give any three methods of preparation of phenol. Write a note on acidity of phenol.
2) What are phenols? Explain the reactions of phenol. Discuss the effect of substituent’s on acidity of phenol.
3) What are phenols? Give physical properties of it.
4) Give structure and uses of Resorcinol.
5) What are the uses of triphenylmethane?
6) Why phenol is acidic?
7) Give structure and uses of diphenylmethane.
8) Structure and use of Cresol and Resorcinol.
9) Write any two Qualitative tests for Phenol.
10) Why direct nitration of aromatic amines is not recommended.
11) Why sulphoantion of aromatic amine is done under drastic condition.
12) Give synthetic applications of aryl diazonium salt.
13) Give mechanism of Carbylamine reaction.
14) Define aromatic aminee give its classification.
15) What is librmann nitroso reaction.
16) What happens when aromatic amines react with nitrous acid
17) How aromatic amines are prepred by chemical reduction.
18) Write 2 methods of preprtion of aromatic amines.
19) Discuss ammonolysis of alkyl halide
20) What is ortho effect?
21) Give any two methods for preparation of benzoic acid.
22) Comment on acidic nature of aromatic acid.
23) Why electrophilic substitution reaction of aromatic acid takes place at m-position only?
24) Describe general method of preparation of aromatic acid.
25) What happens when benzoic acid is treated with concentrated nitric acid in the presence of concentrated sulphuric acid?

5 or 10 MARKS QUESTION

1) Why phenols are acidic in nature? Explain effect of substituents on acidity of phenols.
2) Give structure, synthesis and importance of diphenylmethane.
3) Explain the methods of preparations and chemical reactions of Phenol.
4) Give structure, preparation and properties of phenol.
5) Explain the preparation and effect of substituents on the acidic character of phenols.
6) What happens if Phenol reacts with Dilute and Conc. Nitric acid?
7) Write a note on the structure, properties, and uses of phenol
8) Discuss the various methods of preparation of aromatic amines.
9) Enamurate the chemical properties of aromatic amines.
10) What are aromatic amines. Discuss its physical and chemical properties with mechanism.
11) Discuss the ring substitution reactions of aromatic amines.
12) Give mechanism of hoffman degradation reaction and reduction of aldehyde and ketones.
13) What is ortho effect. How does it influence the basicity of aromatic amines.
14) Write a note on basicity of aromatic amines.
15) Give the method of preparation of Aromatic acids.
16) Explain in detail the acidity of aromatic acids.
17) Write a note on chemical reactions of aromatic carboxylic acid.
18) Discuss in detail the effect of substituent on acidity.