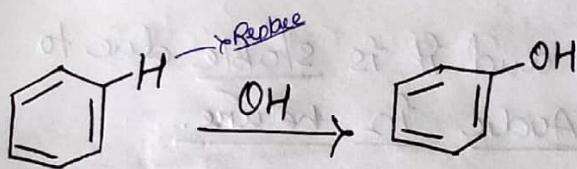


UNIT-2

Pharmaceutics

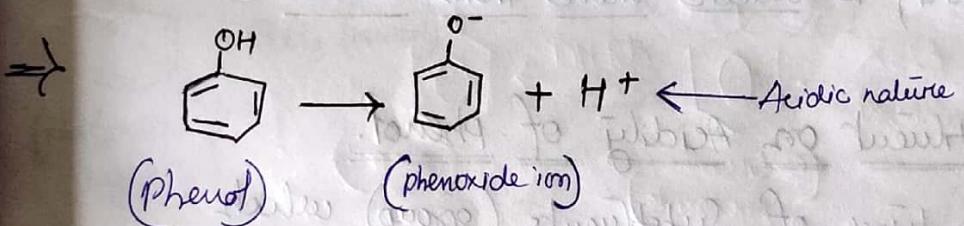
Phenols: Phenol is an aromatic organic compound in which one hydroxyl group (OH) replace one (H) atom from Benzene.



Acidity of phenol

→ When any substance dissociated into H^+ ion then it shows acidic character.

→ So, when phenol dissociated, it breaks into two, in which one is H^+ so, phenol is acidic in nature.



→ The substance or compound which release H^+ more or quickly have more acidity. (acidic)

→ The substance which is more stable after release of H^+ has more acidic.

→ So, phenol is more acidic.

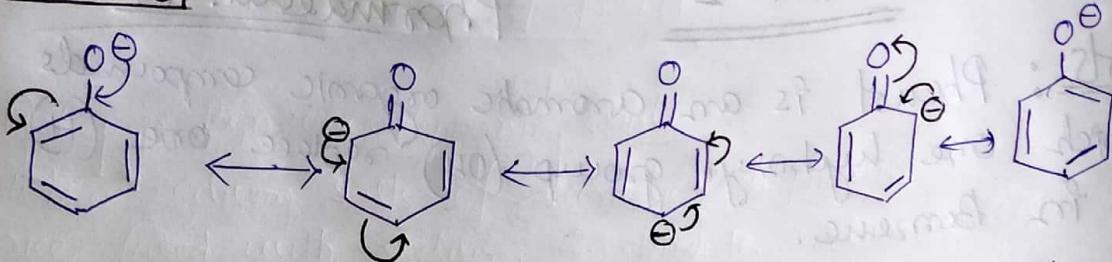
The conditions which show acidity or stability are —

i) Resonance.

ii) S character.

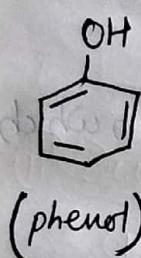
(↓) -Wibva

Resonance



So, phenol has resonance and it is stable due to resonance and it is acidic in nature.

% S character



→ Phenol has 3 sigma (-) bond, so it has sp^2 hybridisation.

In which % S character is 33.33% which is acidic more than alcohol.



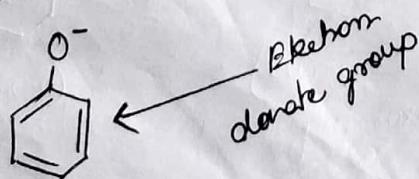
Effect of substituent on Acidity of phenol

There are two types of substituents (group) which will add or attached on phenol.

i) Electron donor group : which has ability to donate electrons. eg - CH_3 , Cl , OH , C_2H_5 etc.

ii) Electron acceptor group : which has ability to accept (gain) electrons. eg - CN , NO_2 , NH_2 etc.

• After dissociated



→ Increase electron density (\uparrow)

Unstable

Acidity (\downarrow)

Electron withdrawing group : Electron density (\downarrow)

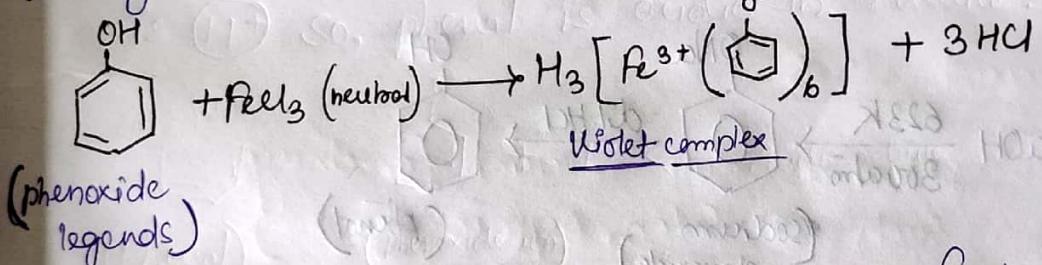
\downarrow
Stability (\uparrow)

\downarrow
Acidity (\uparrow)

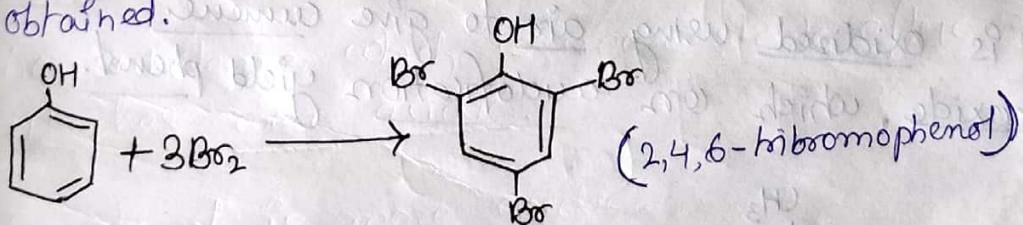
Qualitative Tests for Phenols

① Litmus Test : Phenol turns blue litmus paper pink red, this shows that phenol is acidic in nature.

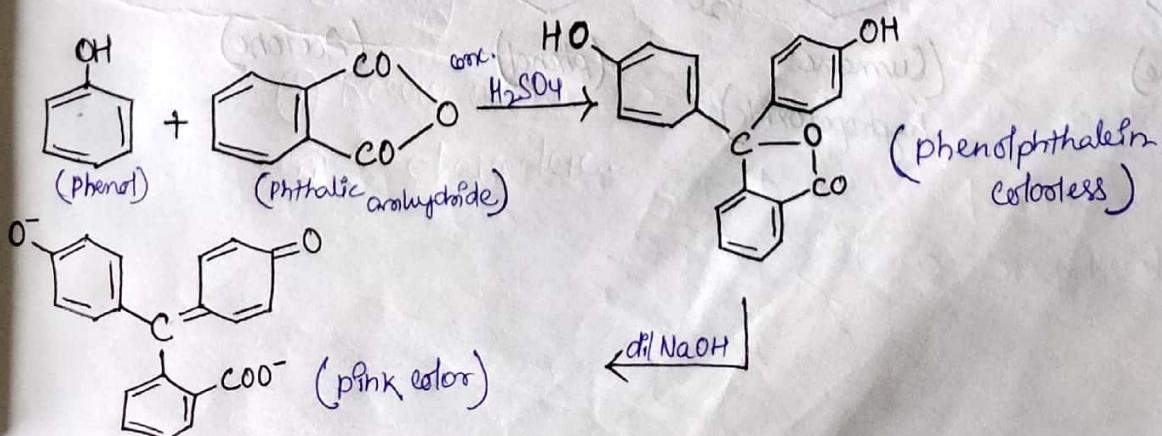
② Ferric chloride test : Aqueous solution of phenol reacts with freshly prepared ferric chloride soln gives coloured complex.
→ Mostly phenol gives dark colour.



③ Bromine water test : Take aqueous solution of phenol and add excess of bromine water. A yellowish white ppt is obtained.



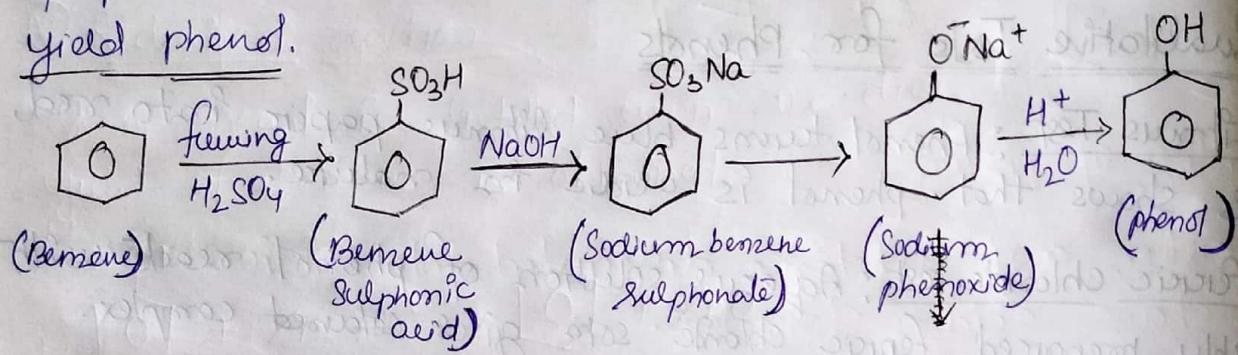
④ Phthalein Dye test : (Fluorescein test)



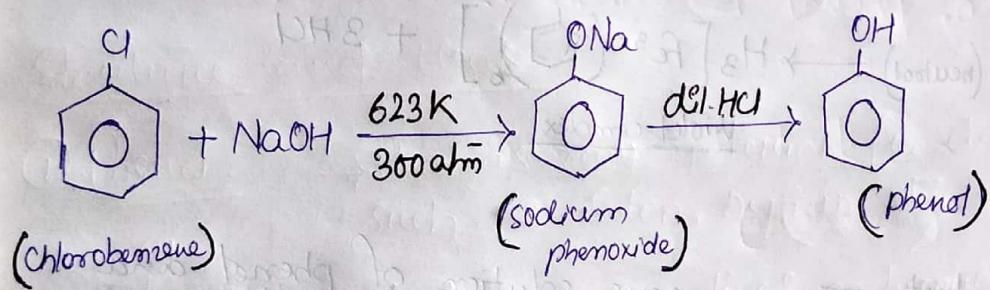
Methods of preparation of phenol

i) From Benzenesulphonic acid

When sodium salts of aromatic sulphonic acids are fused with sodium hydroxide, sodium derivatives of phenol is obtained which on acidification yield phenol.

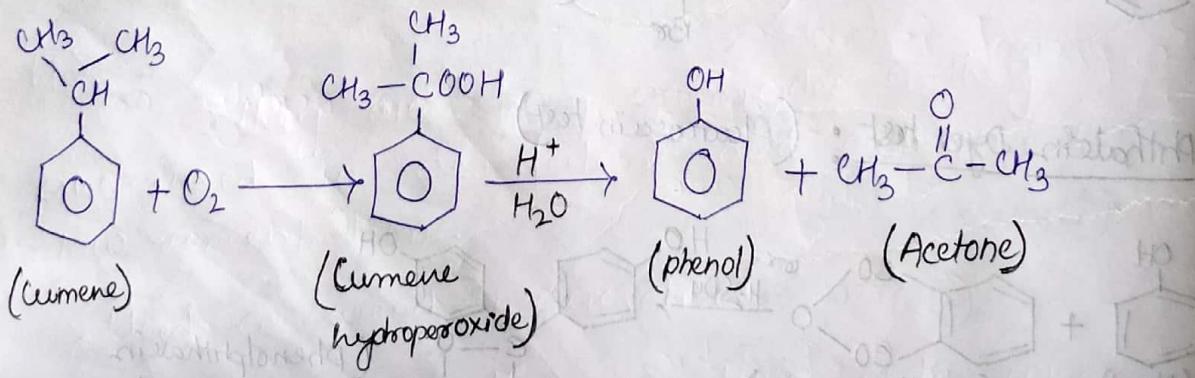


ii) Dow's process

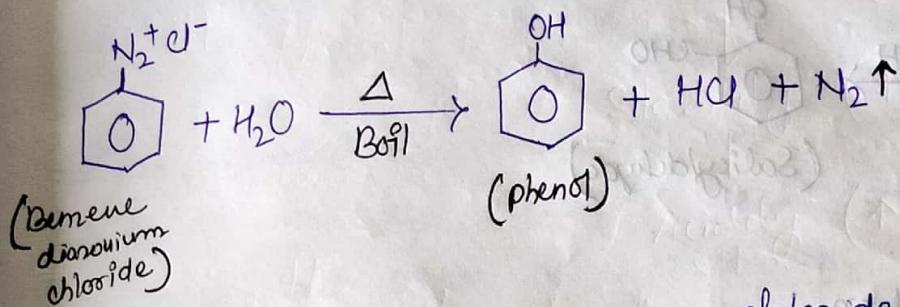


iii) From Cumene (Cumene process)

Cumene is oxidized using air to give cumene hydroperoxide, which on acidification yield phenol.



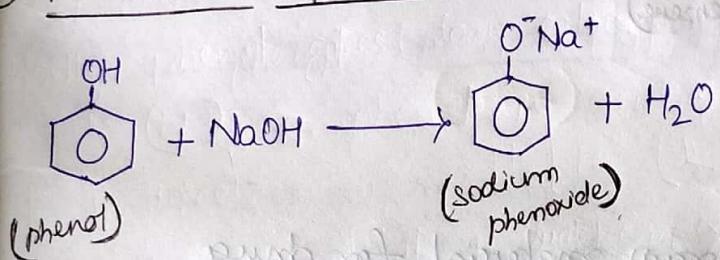
(iv) From Benzene diazonium salts



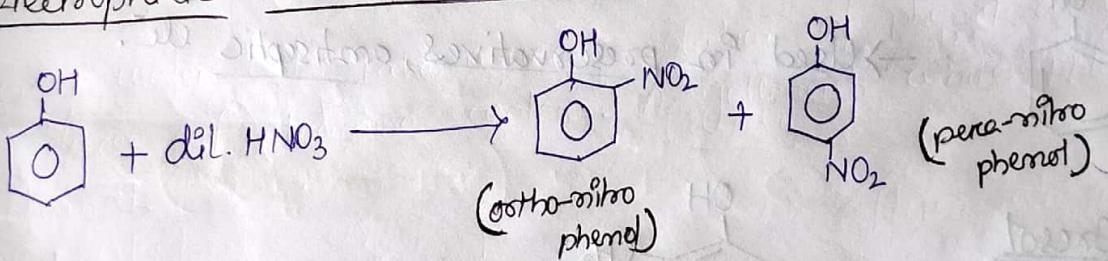
When Benzenediazonium chloride salt is heated (boil) with water it produce phenol with liberation of N_2 gas.

Chemical Reactions

① Formation of Soils

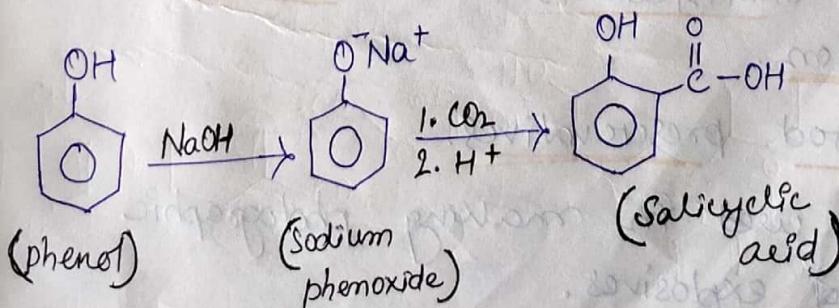


(ii) Electrophilic Substitution rxn (Nitration)

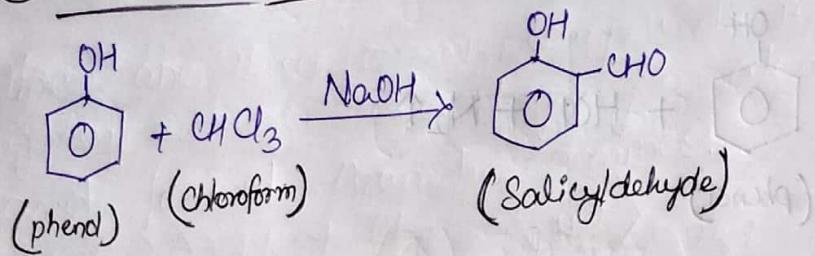


(ii) Kolbe's reaction

i) Kolbe's reaction
Phenol reacts with sodium hydroxide to form sodium phenoxide, which reacts with CO₂ to form salicylic acid.

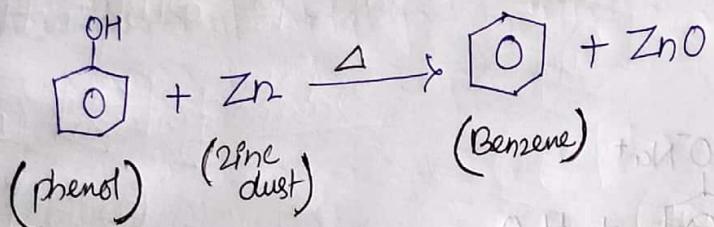


PV Reimer-Tiemann Reaction



① Reduction reaction

When phenol is distilled with zinc dust, low yield of benzene is obtained.



Structure and Uses

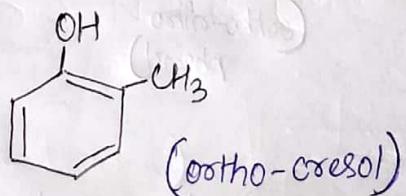
① Phenol



→ Used as raw material for drug such as Salon, Aspirin etc.

→ Used for preservatives, antiseptic etc.

② Cresol

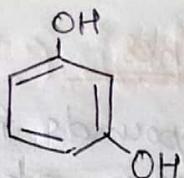


Uses: → They are strong germicides, so they are used in disinfectants and antiseptics in low concentration.

→ Used as wood preservatives.

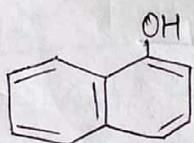
→ m-cresol is used for making photographic developer and explosives.

(ii) Resorcinol



- Used for manufacturing of resins.
- It is topically used to treat acne, eczema, psoriasis and other skin disorders.
- Also used as a disinfectant or an antiseptic for pharmaceutical products.

(iv) Naphthols

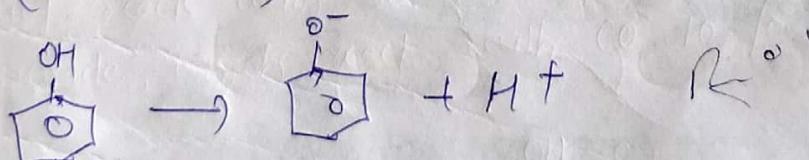
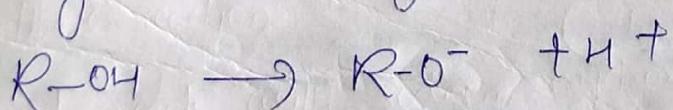
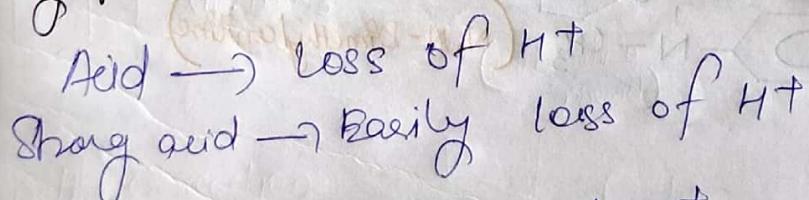


α -Naphthols

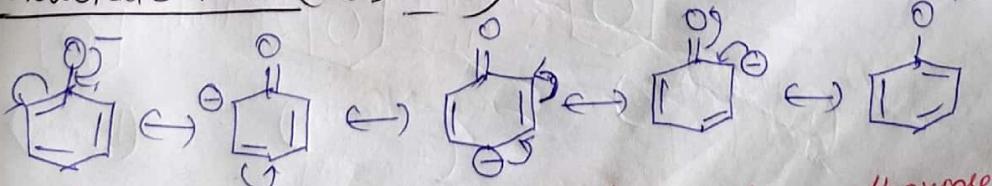
The monohydroxy derivatives of naphthalene are called naphthols.

- Used as insecticides and also making for dyes.
- Sometimes it is also used for perfumery.

Q: Why phenols are more acidic than alcohol?



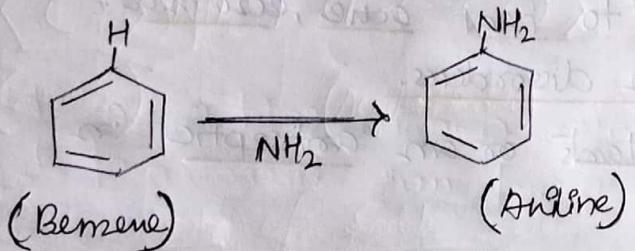
Phenoxyde ions (Resonance)



(Phenoxyde ions are more stable than alkoxole ions)
⇒ So phenols are more acidic than alcohols.

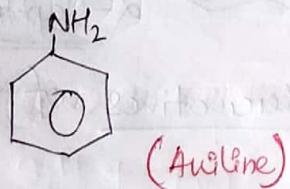
Aromatic Amines

These are those organic compounds for which $(-\text{NH}_2)$ group replace one hydrogen atom on benzene and formed Aromatic amines.

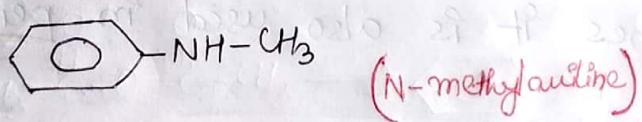


It is also of three types : —

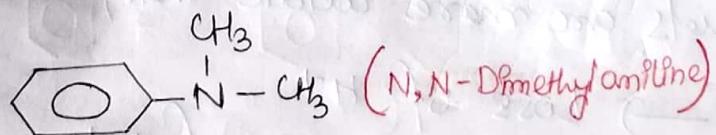
i) Primary amines



ii) Secondary amines



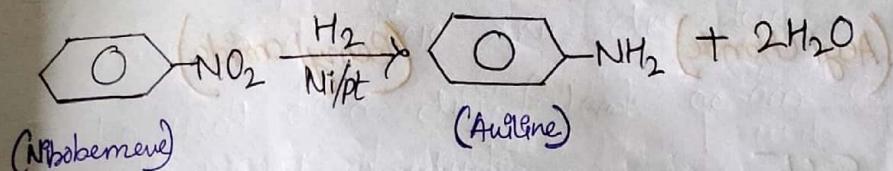
iii) Tertiary amines



Methods of preparation (Amines)

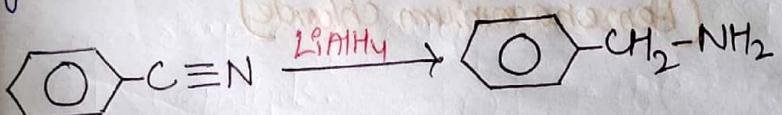
i) By Reduction of Nitrocompound

When nitrobenzene is react with H_2 gas pass in the presence of catalyst Ni/pt, it gives Aniline. (ar. amines)



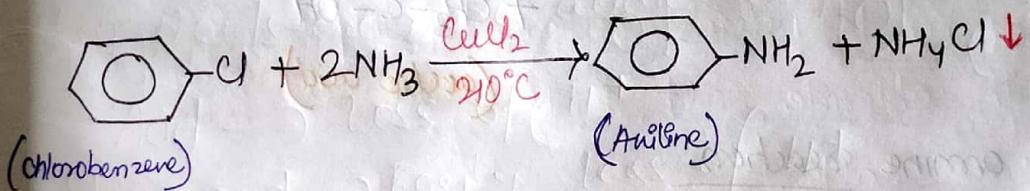
ii) By Reduction of nitriles

When aromatic nitriles undergoes reduction with reducing agent like LiAlH₄, it produce aromatic amines.



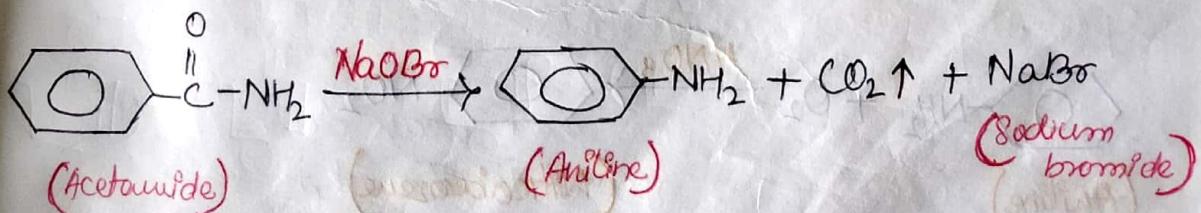
iii) By ammonolysis of chlorobenzene

When chlorobenzene undergoes ammonolysis (react with ammonia) in the presence of copper dichloride at high temp, produces aromatic amines.



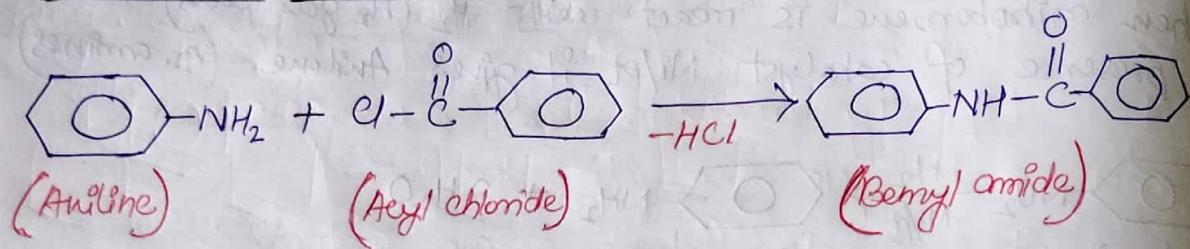
IV Hoffmann rearrangement reaction

When acetamide is treated with Sodium hypobromide (NaOBr) Ammonia group in acetamide is rearrange their position and shift toward ring and produce aniline. (ar. amines)

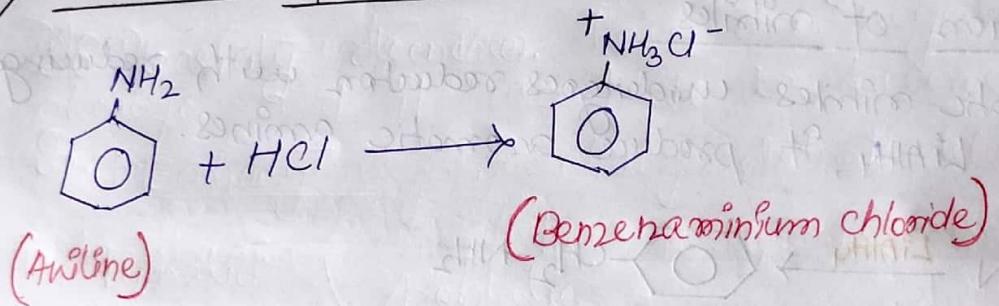


Chemical Reactions (Amines)

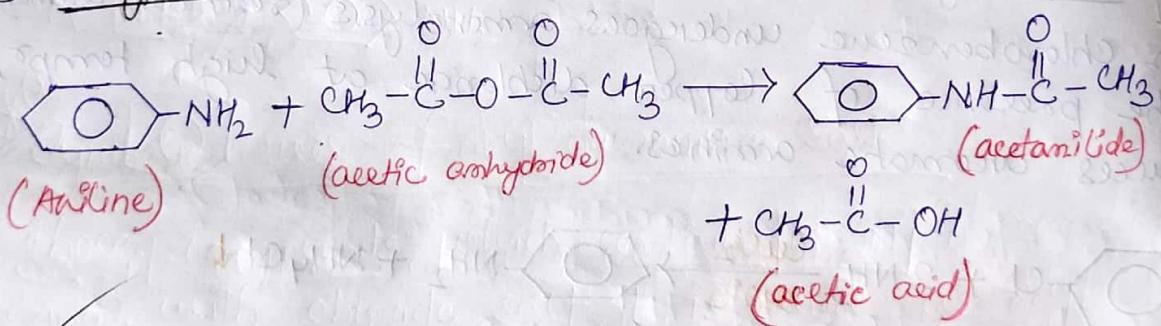
① Formation of Amides



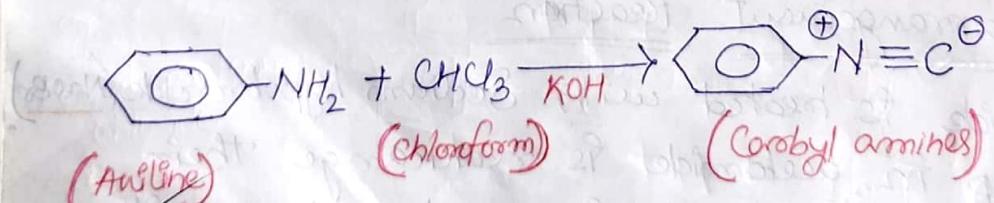
Formation of Soils



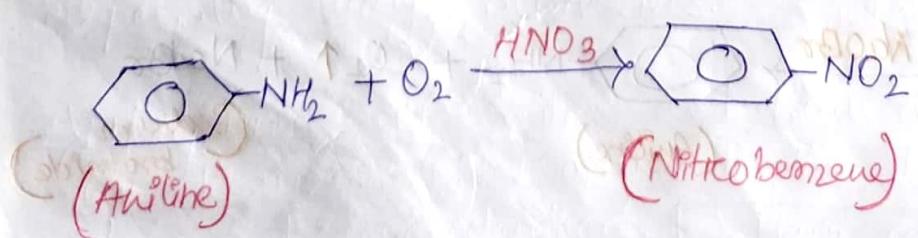
(iii) Acetylation



Carbonyl amine reaction

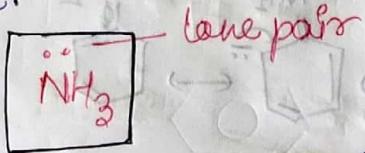


Oxidation



Basicity of Amines

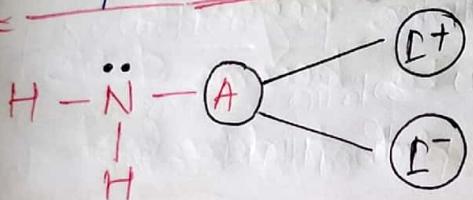
Lewis concept: Those element which accept lone pair are called acid and those which donate lone pair are called base.



(Due to presence of lone pair in ammonia)

So, Ammonia contain lone pair, so it is basic in nature.

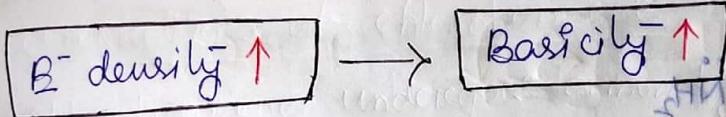
So, All of their derivatives are also basic in nature.



Electron Density

The more electron/lone pair, the more e⁻ density.

L^+ → Electron Releasing group (donating group)



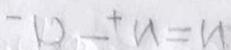
e.g.: Alkyl compound, CH_3 , CH_2 etc.

L^- → Electron withdrawing group (accept electron)

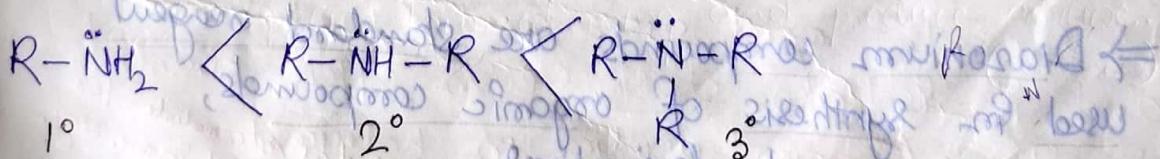


e.g. - X (halogen group)

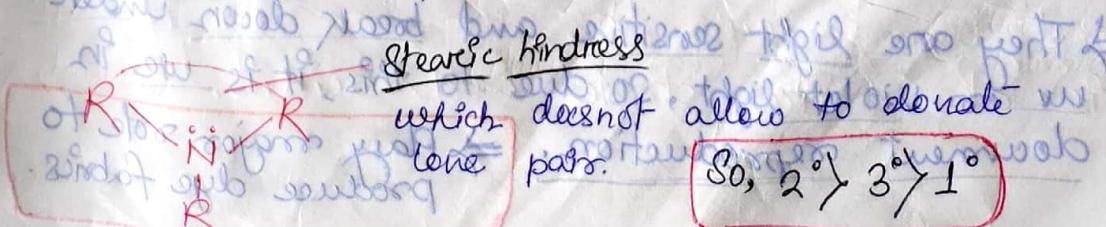
[less nuclearity]



Take our e.g. —

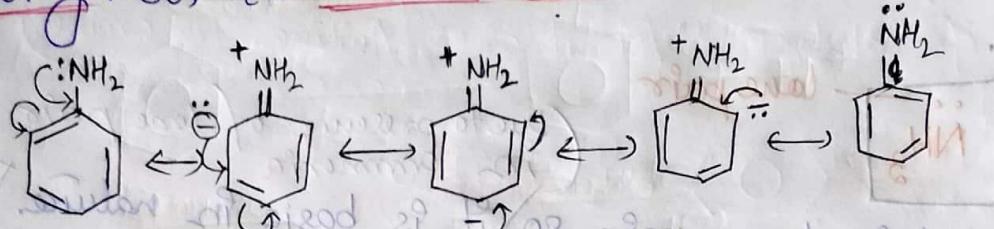


But, there are some exceptions for 3° amines —



→ But for Aromatic Amines? —

Lone pair of ammonia is delocalised in benzene ring. So, it can not donate lone pair.

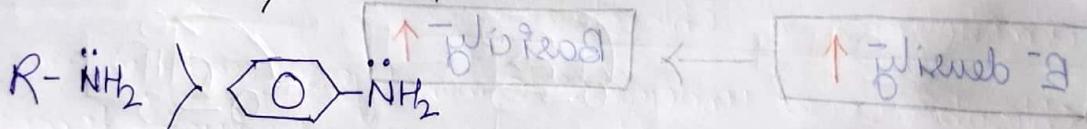


So, due to resonance, electron density is decreased.
So, basicity decreases.

So, Basicity

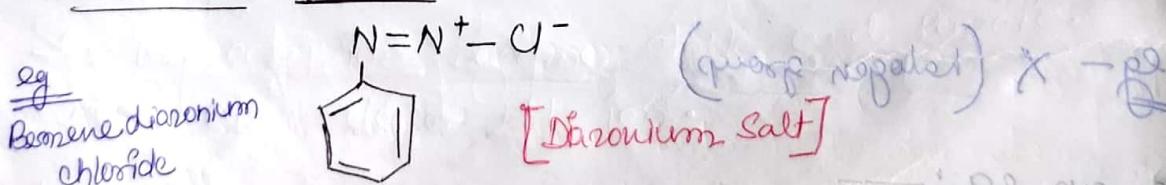


Aliphatic amines > Aromatic amines



Synthetic uses of Aryl diazonium Salts

Those compounds which contain $N=N$ in aromatic ring with chloride salt, it is called as Aryl diazonium salts.



⇒ Diazonium compounds are standard reagent used for synthesis of organic compounds, especially aryl derivatives.

⇒ They are light sensitive and break down under UV or violet light, so due to this, it is used in document reproduction.

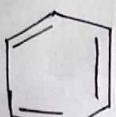
⇒ Play major role to produce dye fabrics.

Aromatic Acids

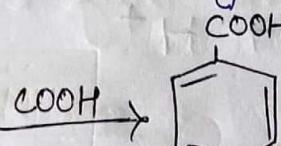
⑩

Aromatic Acids: When carboxylic acid replaced one hydrogen atom from benzene ring, then it forms Aromatic acids.

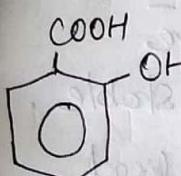
e.g.:



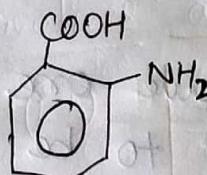
Benzene



Benzene acid

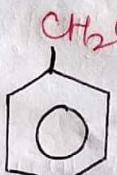


Salicylic acid



Anthraconic acid

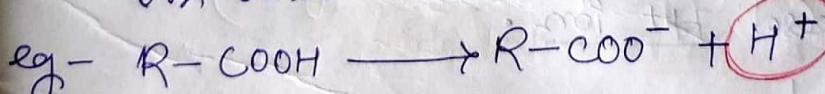
NOTE Phenylacetic acid and other similar compounds for which the carboxylic acid group is not directly attached to the aromatic ring called side chain aromatic acid.



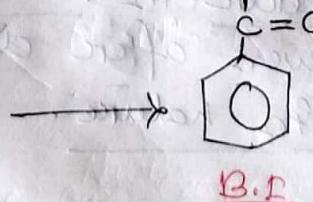
(Phenylacetic acid)

Acidity of Aromatic Acid

Acid: Those substance which release H^+ ion on dissociation.



So, in aromatic acid,

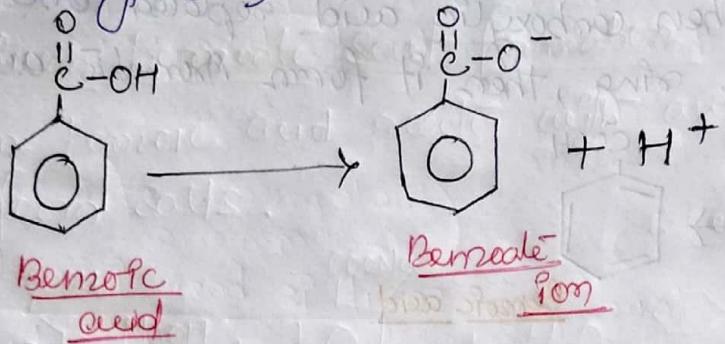


B.O.A

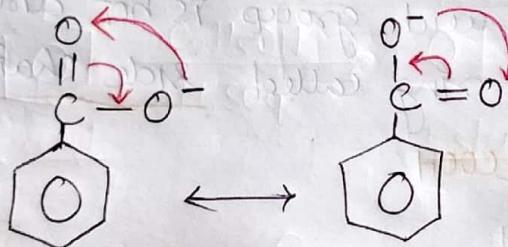
Stability & Acidity

\Rightarrow As we know that, the compound which has more resonance is more stable which means more acidic.

In Aromatic acids, After dissociation it release H^+ charge (ion) and it become acidic.



Now, Benzolate ion have one negative charge and it want to be become stable. But this negative charge didnot delocalised into benzene ring, because O⁻ is attached to carbon (c) atom.



So, it delocalised (-) charge into both Oxide ion through shering.

So, Benzolate ion become stable and Benzolic acid also release H^+ ion.

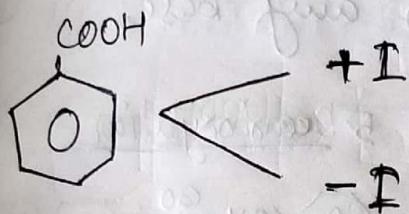
So, It proof that,

Aromatic acid are acidic for nature and it is also stable even after dissociation. So it is strong acidic for nature.

And, Benzene ring has resonance so it is also more stable and acidic.

Effect of Substituent on Acidity

Substitute: which replace any hydrogen in benzene



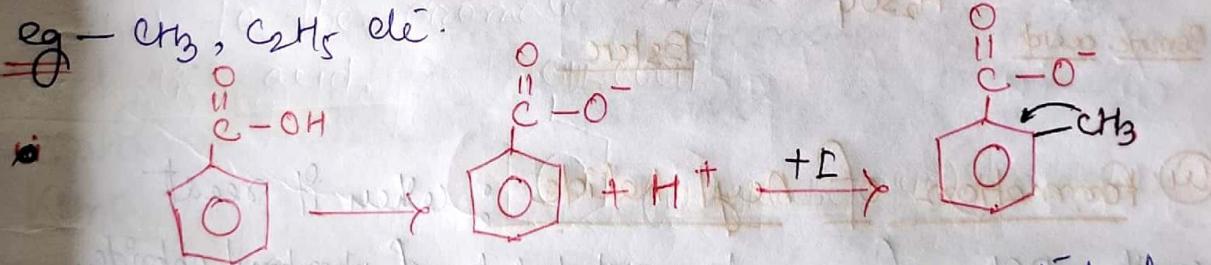
There are probably to join two types of group:-

① +I (Electron Donating group)

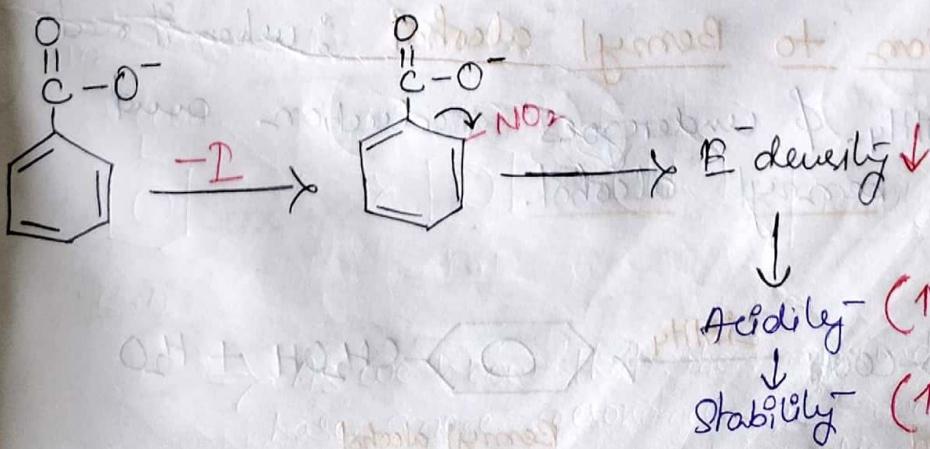
② -I (Electron withdrawing group)

① Electron donating group: when it attached, it increase electron density and the more electron, the compound more unstable.

e.g. -CH₃, C₂H₅ etc.



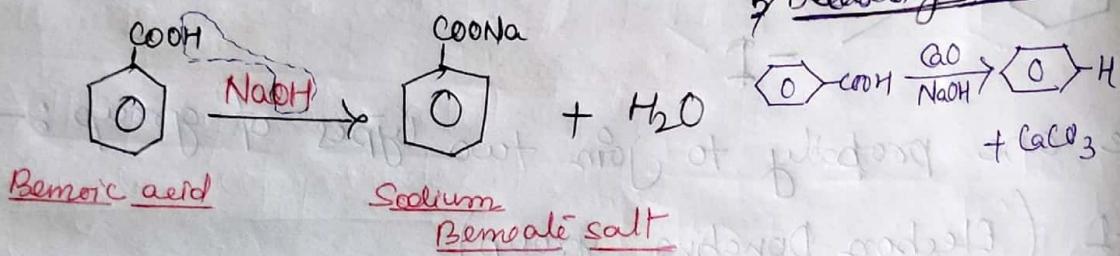
② Electron withdrawing group: when it attached, it receive electron from aromatic acid and decrease electron density, so compound is stable. (More acidic) e.g. -NO₂, Cl etc. (F, Cl, Br, I)



Important reactions of Benzoic acid

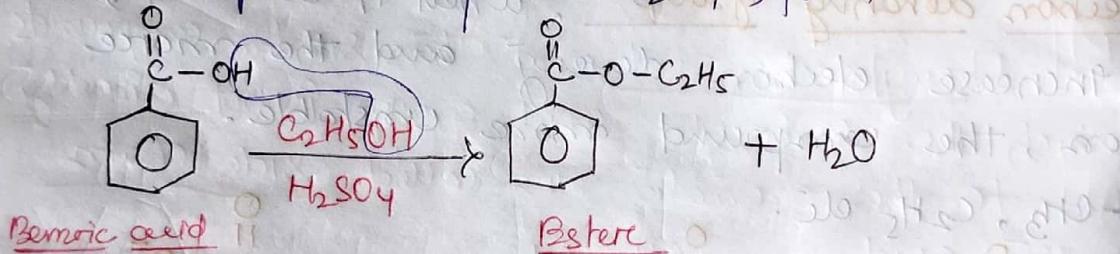
① Sodium benzoate salt formation

When benzoic acid reacts with any base, it forms salts.



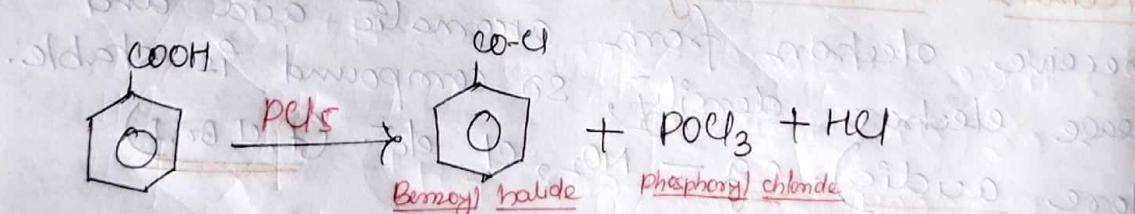
② Ester formation

It reacts with alcohols. In the presence of conc. H₂SO₄, form ester.



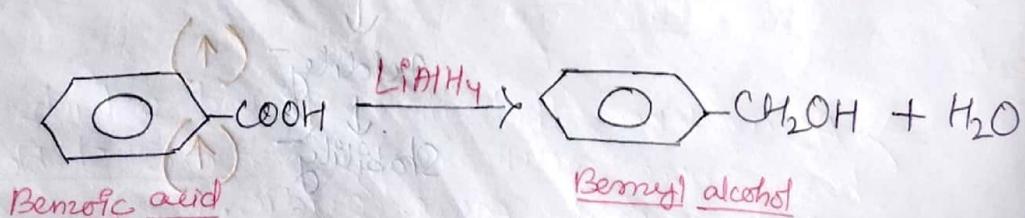
③ Formation of Acetyl halide

When it reacts with PCl₅, forms benzylic halide & phosphoryl chloride.

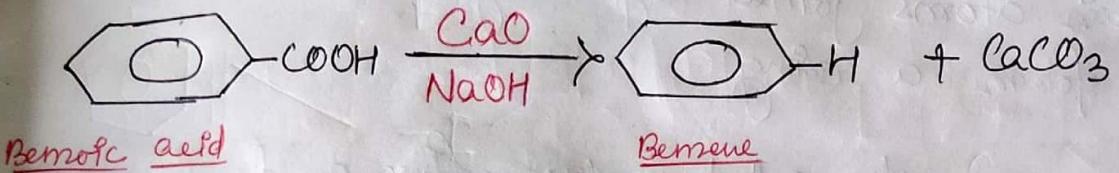


④ Reduction to Benzyl alcohol

When it reacts with LiAlH₄ & undergoes reduction and it gives benzyl alcohol.



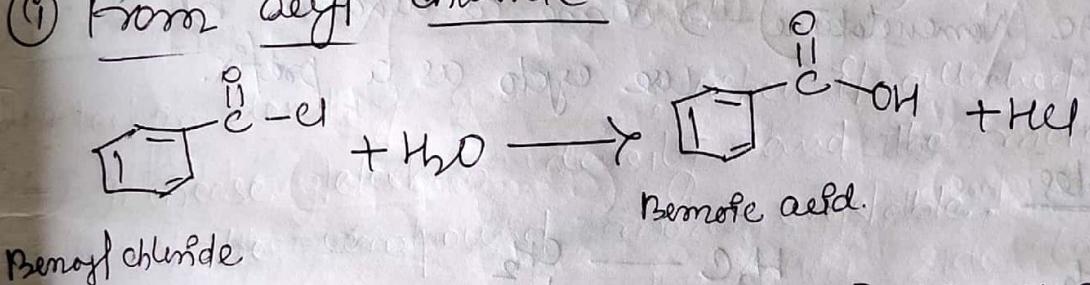
① Dearboxylation: when it reacts with CaO in the presence of NaOH then after dearboxylation it gives benzene and release CaCO_3 .



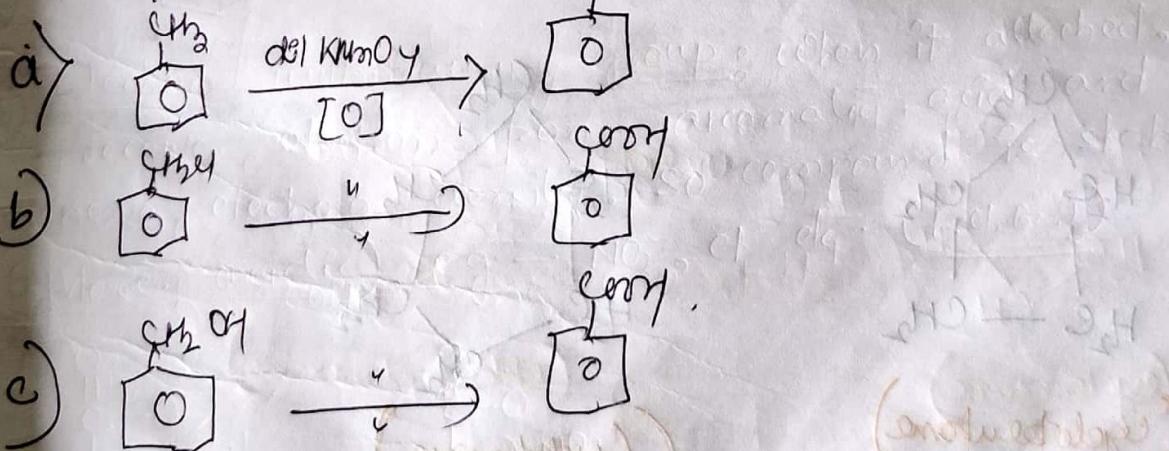
Preparations

(Benzene Acid)

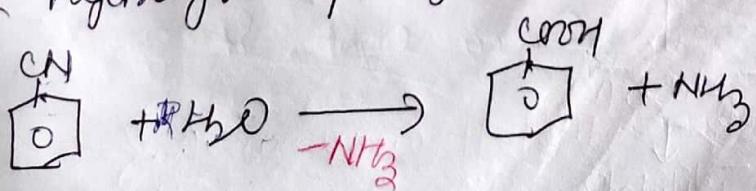
① From benzyl chloride



② By the oxidation of aromatic compound containing aliphatic side chain to presence of $\text{KMnO}_4 / \text{K}_2\text{CrO}_4$.



③ By hydrolysis of cyanobenzene



Properties of B. Acid

See \rightarrow Last page

Properties of Benzoic Acid

- Colourless solid
- Slightly soluble H_2O but completely soluble in benzene, ether etc.
- M.P. = $122^\circ C$
- B.P. = $250^\circ C$
- Acid in nature

Benzoic acid

Acetic acid.

