2016 - 2017

Phenol Synthesis

Part I

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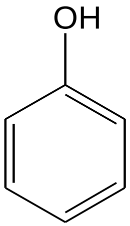
Phenols:

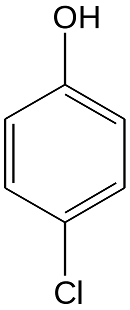
Phenols are compounds having a hydroxyl group attached directly to an aromatic ring .

Their general formula is Ar-OH, where Ar- is phenyl, substituted phenyl, or some other aryl group (e.g., naphthyl, etc.).

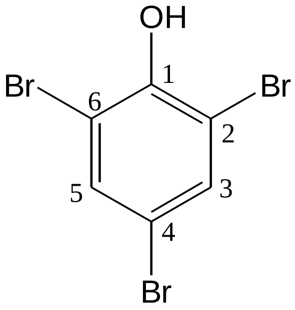
They are usually named as derivatives of the simplest member of the family, phenol.



Phenol

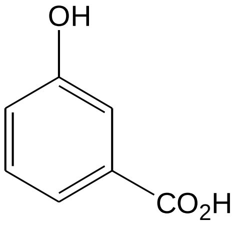


p- Chlorophenol

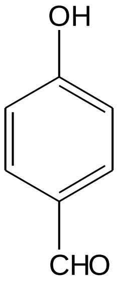


2,4,6- Tribromophenol

The -OH gr. is named as a substituent if it occurs in the same molecule with the carboxylic acid, aldehyde or ketone functionalities , which have priority in naming.

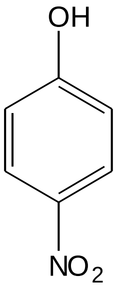


m- Hydroxy benzoic acid



p- Hydroxy benzaldehyde

but



p- Nitrophenol

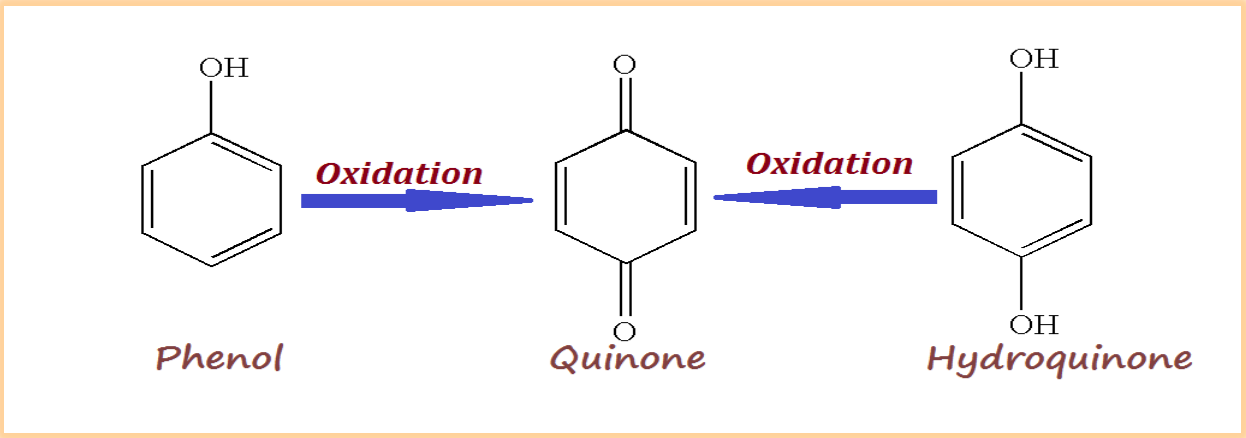
Physical properties of Phenols:

1- The simplest phenols are liquids or low-melting solids.

2- They have high boiling points.
(Because of hydrogen bonding)

3- Most phenols are essentially insoluble in water.

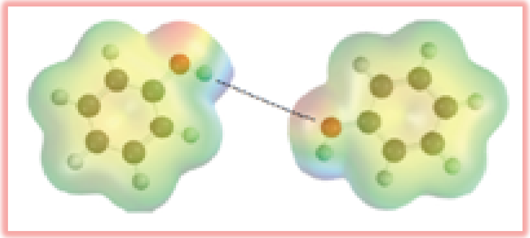
4- Phenols themselves are colorless, although they are pink to red by oxidation products.



Physical Properties of Phenol :

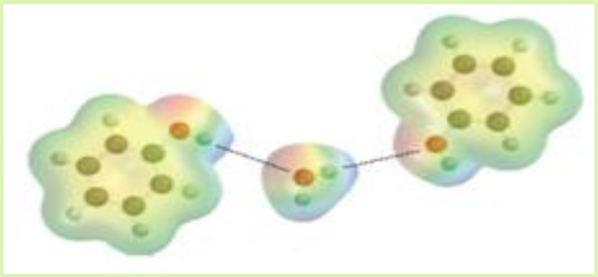
1) Colorless-pink needle-like crystals.

2) Freely soluble in organic solvents.



3) Has high B.P. (180 - 183 ^{0}C) , because of the intermolecular hydrogen bonding between phenol molecules .

4) High m.p. = 42 ^{0}C , (intermolecular H- bonding of phenol molecules) .



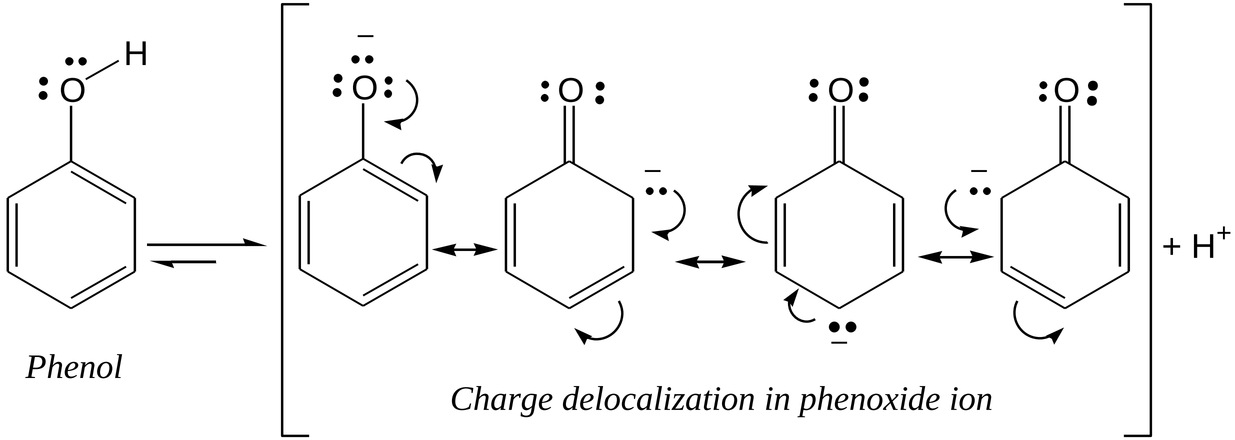
5) Slightly soluble in water (9 g / 100 ml) , because of the intermolecular H – bonding between phenol & water molecules.

6) It has a characteristic aromatic odor.

7) Phenol is a weak acid, more acidic than alcohol * & water but weaker than carboxylic acids.

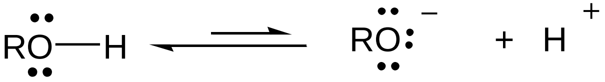
**** Because the corresponding phenoxide ions are stabilized by resonance.***

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



Phenol

Charge delocalization in phenoxide ion



Charge localized on the oxygen atom in alkoxide ions

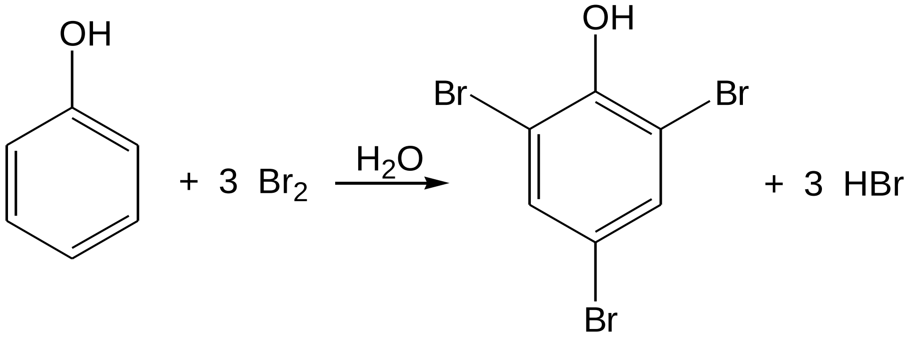
Aqueous hydroxides convert phenols into their salts ; aqueous mineral acids convert the salts back into the free phenols.

$$\text{Ar-OH} \underset{H^{+}}{\overset{OH^{-}}{\rightleftharpoons}} \text{Ar-O}^{-}$$

Phenol
(weak acid)
Insoluble in water

Phenoxide ion
(salt)
Soluble in water

8) Phenol reacts with bromine water to give 2,4,6 – Tribromophenol, (white precipitate), which is the Principle of phenol assay.



2,4,6- Tribromophenol

Uses of Phenol:

Phenol is one of the oldest antiseptics . It has bactericidal and bacterostatic properties besides it's caustic & slight anesthetic activities.

It denatures proteins while in high concentrations it precipitates them.

It is used in 0.1 – 1 % in lotions & ointments.

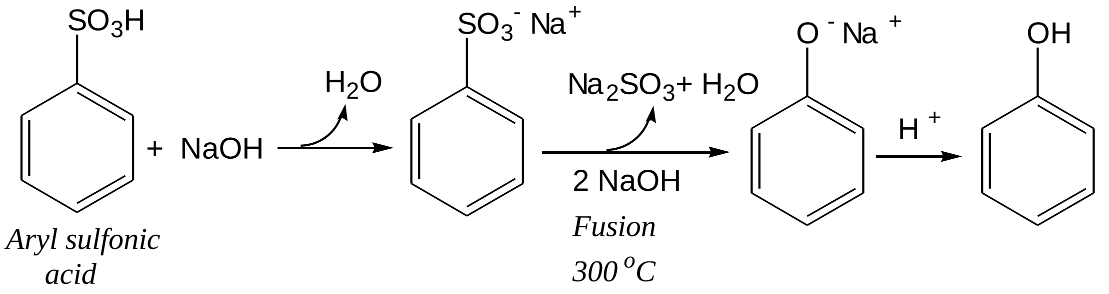
Preparation of Phenol:

In the early of 19th century, phenol was obtained from coal tar in low yield by extraction with alkali, Now phenol is commercially produced synthetically.

In the laboratory, Phenol is generally prepared by one of the three methods.

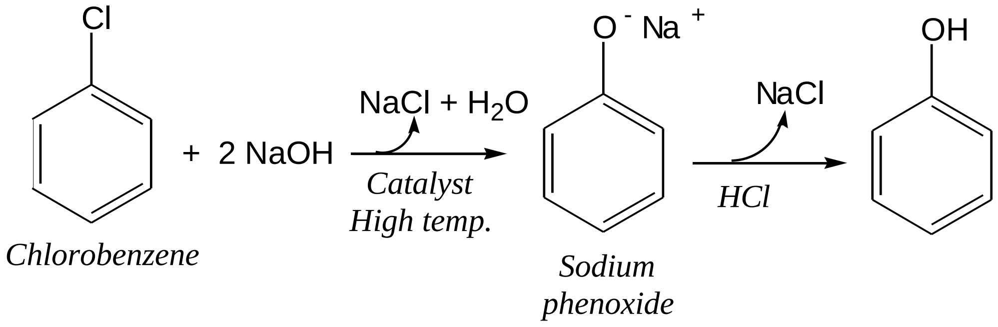
1- From aryl sulfonic acids :

An aryl sulfonic acid yields the corresponding phenol on heating it with molten NaOH (fusion).

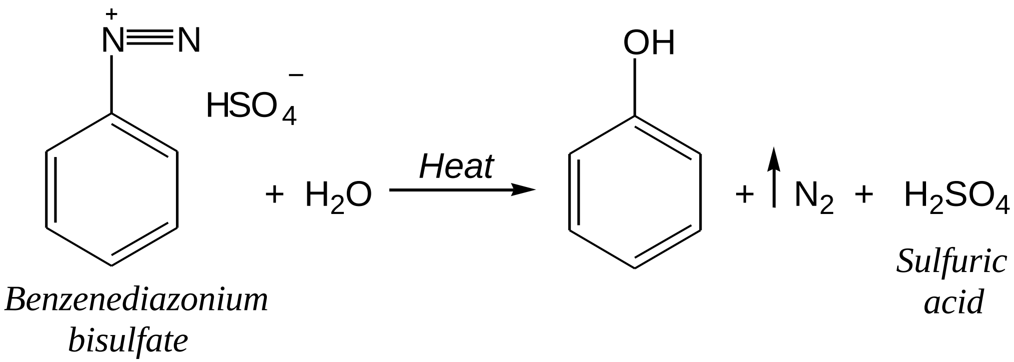


2- From haloarenes (Aryl halides) :

An aryl halide is hydrolyzed by treating it with 10% NaOH sol. at high temp. in the presence of a catalyst.



3- From hydrolysis of diazonium salts :

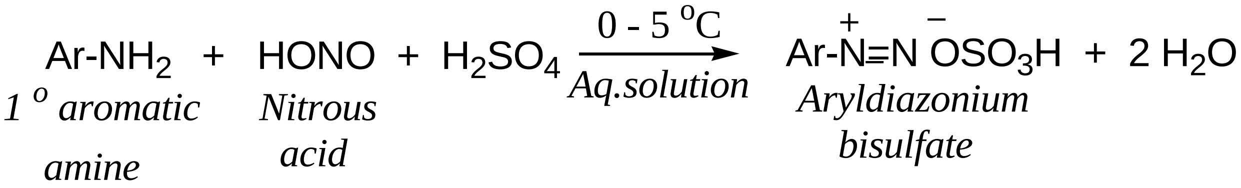


In our laboratory today , for synthesis of phenol we shall use the last procedure , namely that of the diazotization of aniline & subsequent hydrolysis both because of it's simplicity and because of it typifies a close reaction.

Both phenol (99% purity) & liquefied phenol (phenol 800 g and sufficient water to make 1000 g) are official in the pharmacopia .

Diazonium salts :

They can be formed by treating an aromatic 1°- amine with nitrous acid, HNO_2 ,(Obtained from a mixture of $NaNO_2$ & H_2SO_4) at 0°C .



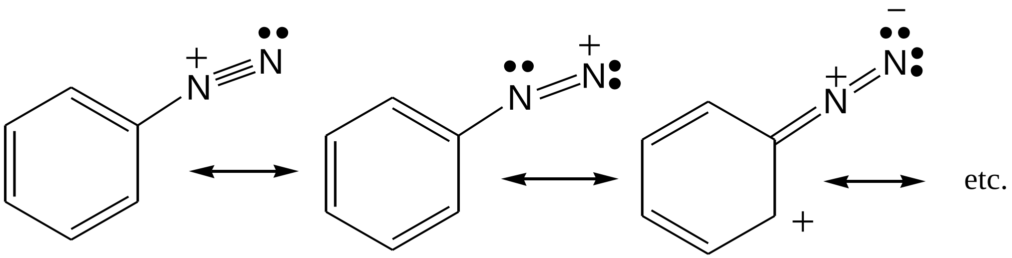
$$\text{Ar-NH}_2 + \text{HONO} + \text{H}_2\text{SO}_4 \xrightarrow[\text{Aq.solution}]{0 - 5\ ^{o}\text{C}} \text{Ar-}\overset{+}{\text{N}}\equiv\text{N}\ \overset{-}{\text{O}}\text{SO}_3\text{H} + 2\ \text{H}_2\text{O}$$

Properties of Diazonium Salts:

1-In acid solution, aromatic diazonium cpd.s show all properties of salts as they are solids, soluble in water , insoluble in organic solvent.

2- Solutions of aromatic diazonium salts, *(arenedia -zonium ions)*, are moderately stable & can be kept at 0°C for several hours*, while , diazonium salts derived from aliphatic 1°-amines decompose readily even at 0 °C to yield the corresponding alcohol.

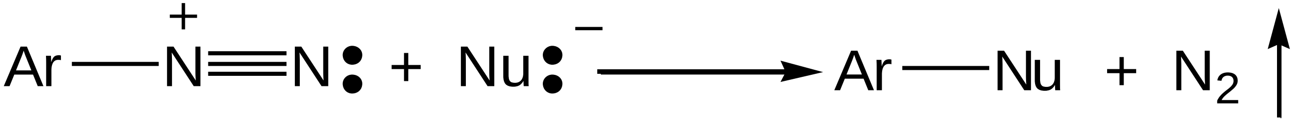
** Aromatic diazonium salts are more stable, because of the resonance interaction between the diazonio group & the aromatic ring.*



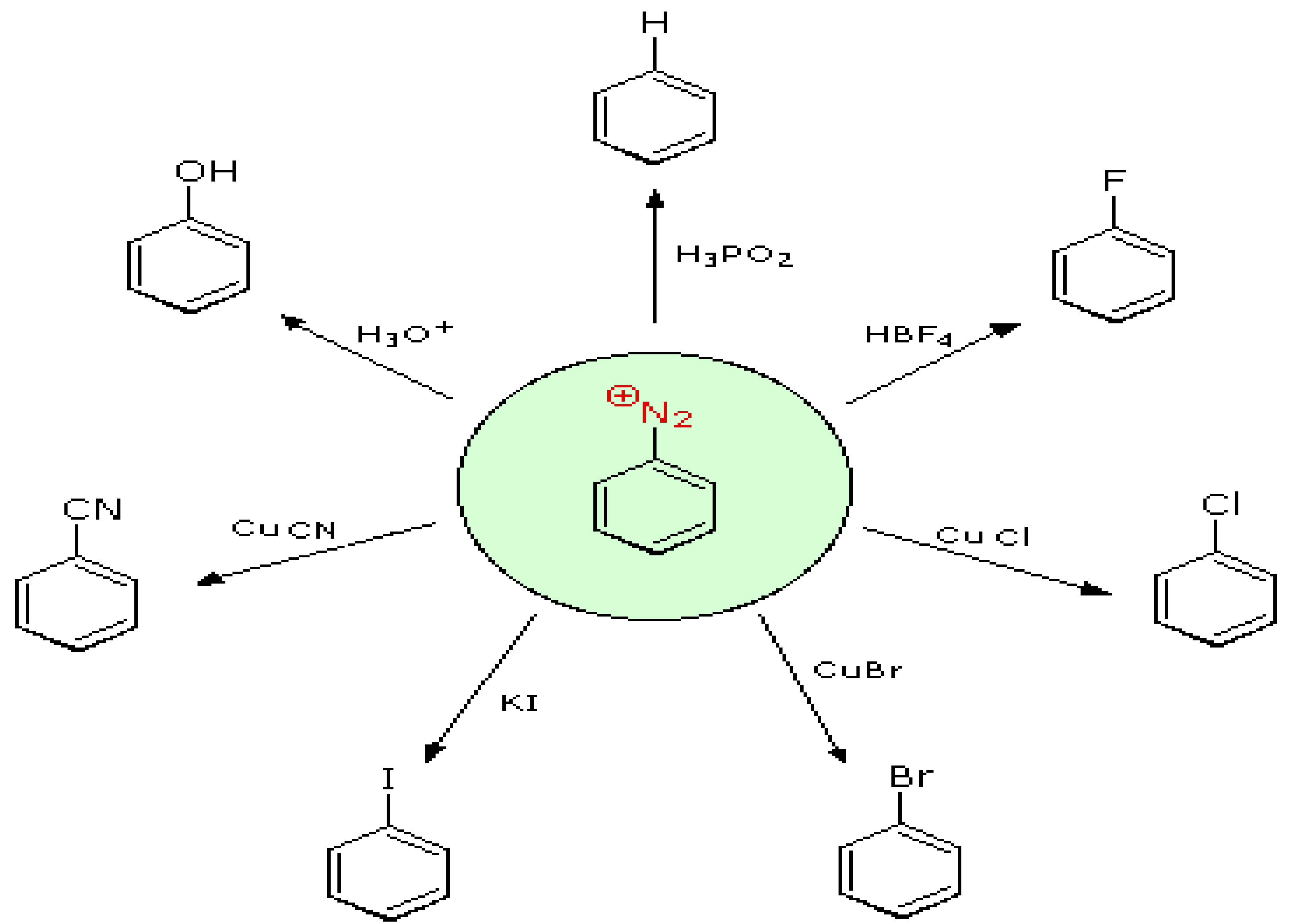
3- **Solid diazonium salts are very sensitive to shock when perfectly dry, and detonate violently upon gentle heating; they are therefore, of little value for preparative work. Happily, most of the useful reactions of diazonium cpd.s can be carried out with the readily - accessible aqueous solutions, so that the solid (explosive) diazonium salts are rarely required.**

4- Diazonium salts are useful synthetic intermediates since they undergo a large number of reactions, which can be divided in to two classes :

a- Replacement reactions **;** **in which the diazonio group (-N_2^+) is replaced by a variety of other nucleophiles, (e.g., -OH , -I , -Br , -Cl , -F, -CN, -NO_2 , -SO_2H , -Ar & -H) which become attached directly to the aromatic ring & the other product is N_2 gas.**

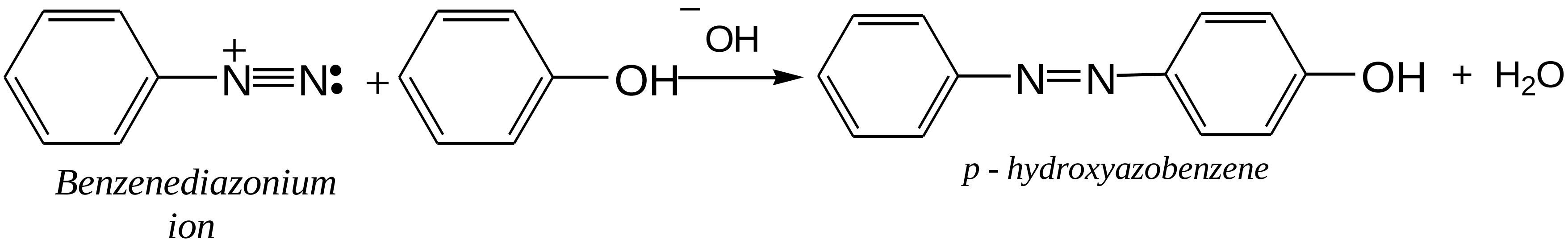


$$Ar-\overset{+}{N}\equiv N: + Nu:^{-} \longrightarrow Ar-Nu + N_2\uparrow$$


H
H_3PO_2
OH
H_3O^+
F
HBF_4
$N_2^{\oplus}$
CN
CuCN
Cl
Cu Cl
I
KI
Br
CuBr

b- Coupling reactions: in which the nitrogen is retained in the product.

Aryl diazonium ions react with strongly activated rings (phenols & aromatic amines) to give azo compounds, contain azo group, -N=N- .



Benzenediazonium ion

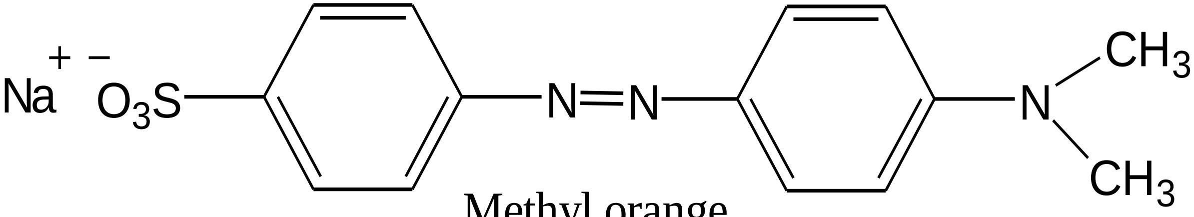
p - hydroxyazobenzene

This electrophilic aromatic substitution reaction is called diazo coupling **, because in the product , two aromatic rings are coupled by the azo group.**

Para coupling is preferred , if the para position is blocked by another substituent , ortho coupling can occur.

All azo compounds are colored and many are used commercially as dyes for cloth & in color photography.

e.g., **Methyl orange is an azo compound used in acid base titration as indicator .**



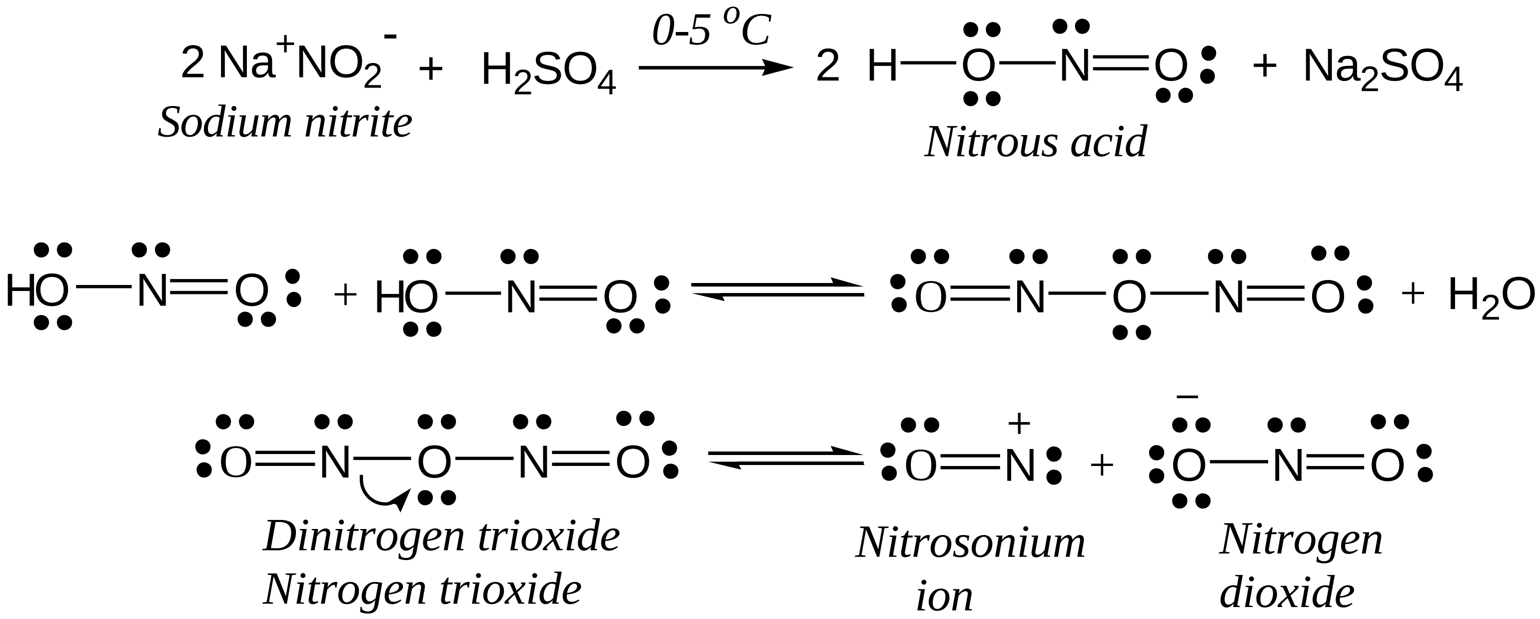
Methyl orange

red in acid, yellow in base

Mechanism of Diazotization:

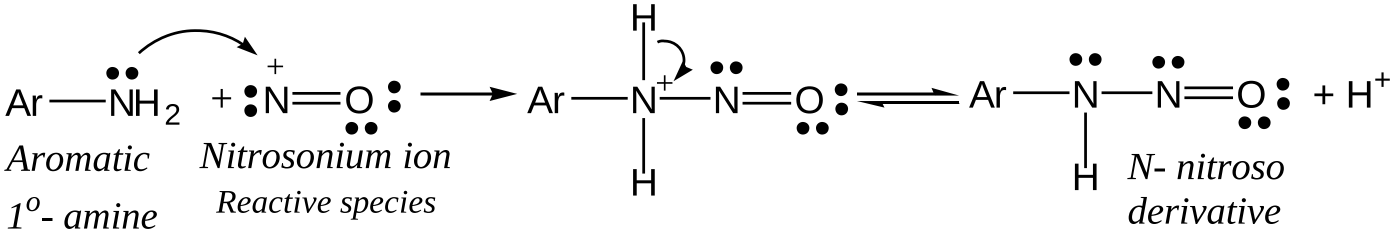
1- **Generation of** *Nitrous Acid* that acts as a source of *Nitrosonium* ion.

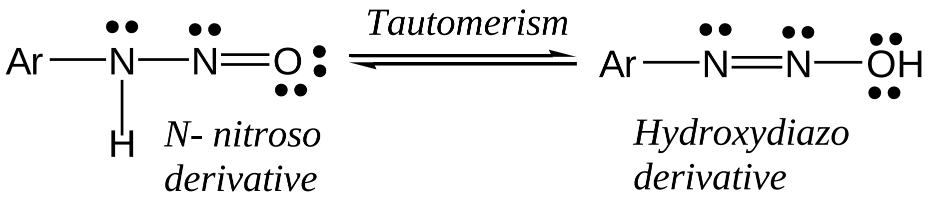
Nitrous acid **is generated by treating an aqueous solution of $NaNO_2$, sodium nitrite , with a strong acid at ice temperature*.**



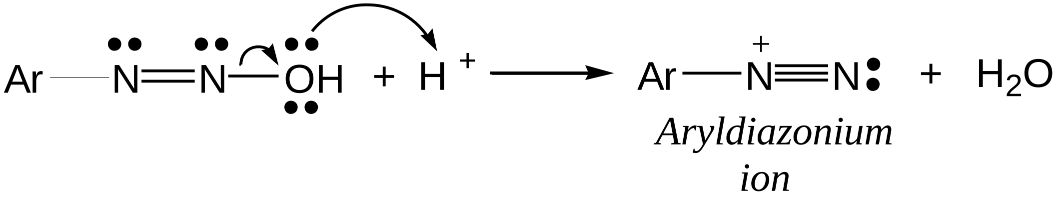
**** Nitrous acid decomposes rapidly at room temperature , so it's prepared as needed at ice temperature where it's reasonably stable.***

2- Nucleophilic attack of the 1°- amine on the nitrosonium ion , followed by proton loss.





Hydroxydiazo derivative in acidic conditions yields aromatic diazonium ion.**



***** In the final product, Diazonium salt, there are <u>no</u> N-H bonds ; both hydrogens of the amino group are lost, so only 1°- amines can be diazotized, (2° & 3°- amines do react with HNO_2, but their reactions are different & less important in synthesis).***