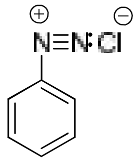
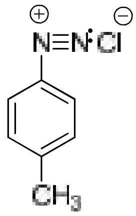
DIAZONIUM SALTS

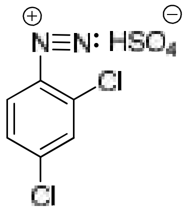
Diazonium compounds or diazonium salts are a group of organic compounds with the general molecular structure $R\text{-}N_2^+\ X^-$, where R may be any alkyl or aryl group and X may be halogens, hydrogen sulphate etc. Aryl diazonium salts have frequently been used as intermediates in organic synthesis.

Nomenclature

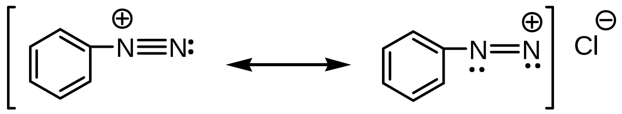
Arenediazonium compounds are ionic in nature i.e they are salts. This is well reflected in their name as they are collectively known as “Diazonium salts”(the word di refers to two, aza stands for nitrogen and the last term onium suggests the ionic nature of the compound). Thus ionic compounds containing N≡N are collectively called dizonium salts and they are named by appending the word “Diazonium” to the name of the name of the aromatic compound, followed by the name of the anion.


benzenediazonium chloride

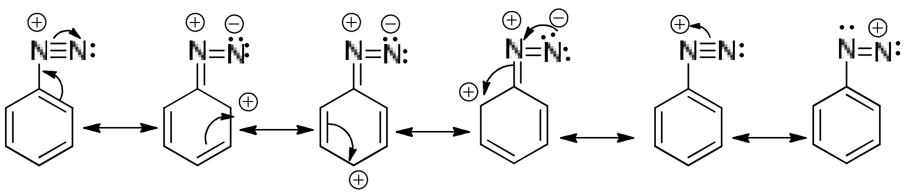

p-toluenediazonium chloride


2,4-dichlorobenzenediazonium hydrogen sulphate

Benzene diazonium chloride can thus be represented by following two electronic structures, in which the positive charged is shared by both the nitrogen atoms.



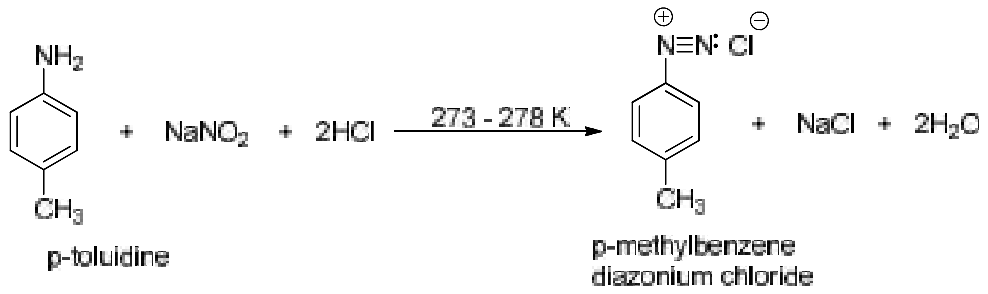
The relative stability of aromatic diazonium cation may be attributed to the delocalization of the positive charge on nitrogen on to the pi system of the ring.



Synthesis of diazonium salts

Treatment of primary amine with nitrous acid results in the formation of diazonium salt, a compound of the type Ar/R-N≡N$^+$ X$^-$, where X- is an anion like chloride, bromide, sulphate etc. But since nitrous acid is unstable, as a result it is generated in situ by treatment of sodium nitrite with strong acid such as HCl or H_2SO_4. This process of conversion of primary amine to its diazonium salt is known as **diazotization**.

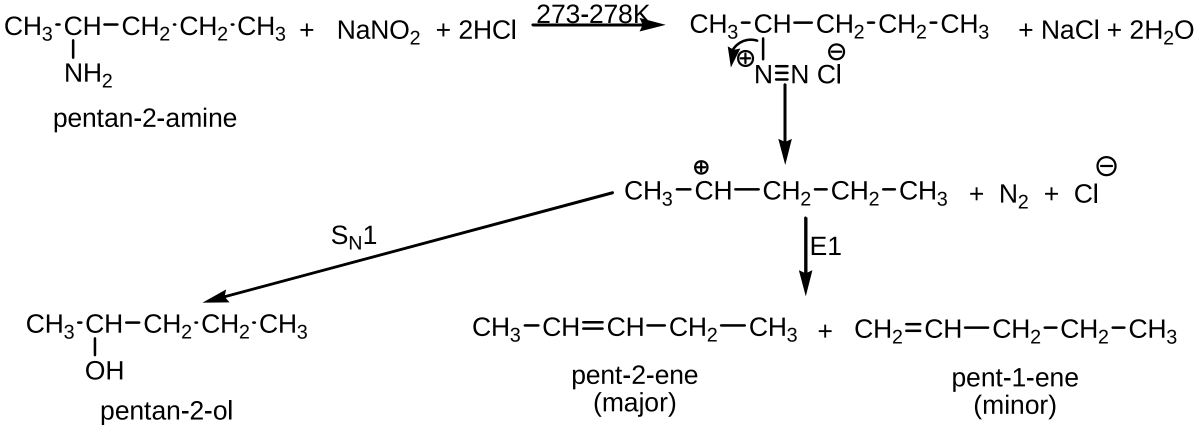
$$NaNO_2 + HCl \longrightarrow HNO_2 + NaCl$$



$$CH_3\text{-}\underset{NH_2}{CH}\text{-}CH_2\text{-}CH_2\text{-}CH_3 + NaNO_2 + 2HCl \xrightarrow{273\text{-}278K} CH_3\text{-}\underset{\overset{\oplus}{N}\equiv N{:}Cl^{\ominus}}{CH}\text{-}CH_2\text{-}CH_2\text{-}CH_3 + NaCl + 2H_2O$$

pentan-2-amine

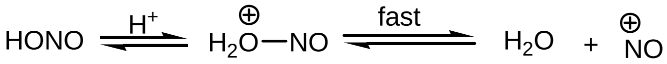
Diazonium salts of aliphatic primary amine are highly unstable even at lower temperatures, as a result as soon as they are formed they decompose, liberating nitrogen to form carbocation. The carbocation may undergo substitution and elimination reaction to give alcohol and alkene respectively. As a result diazotization of aliphatic primary amine is of little or no importance, and their reaction are also of no importance.



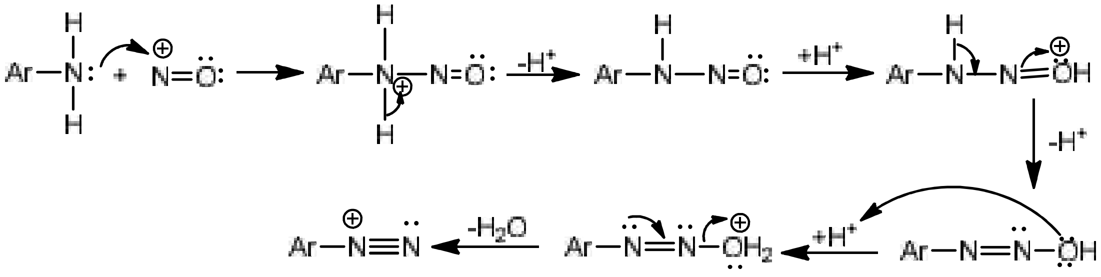
Though diazonium salts of primary aromatic amines are also unstable, but they are far more stable in comparison to diazonium salts of aliphatic primary amines and they do not decompose when the temperature of the reaction mixture is kept below 278K.

Mechanism: The reactive species in the diazotization is the nitrosonium cation, generated by the reaction of nitrous acid with acid. The electrophilic nitrosonium cation then nitrosates the nitrogen of the nucleophilic amine. After a series of protonic shifts, followed by loss of water, leads to the formation of diazonium salt.

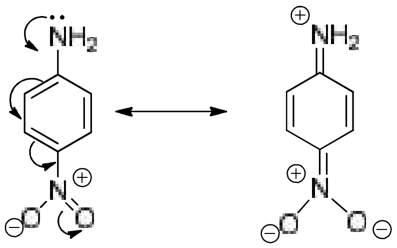
$$NaNO_2 + HCl \longrightarrow HONO + NaCl$$



$$HONO \underset{}{\overset{H^+}{\rightleftharpoons}} \overset{\oplus}{H_2O}{-}NO \overset{fast}{\rightleftharpoons} H_2O + \overset{\oplus}{NO}$$

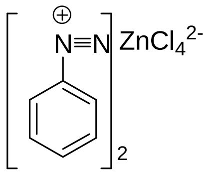


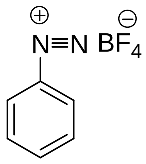
From the above mechanism it can be seen that the reaction is dependent on the nucleophilicity of the amino-nitrogen. If an electron withdrawing group is bonded to the aromatic ring, the nucleophilicity of amino nitrogen is reduced, making it difficult for the diazotization reaction to take place. For example p-nitroaniline is a weaker base in comparison to aniline because of the mesomeric (-M) and inductive (-I) effect of the nitro group. Thus diazotization of p-nitroaniline is difficult in comparison to aniline.



On the other hand electron donating groups present at ortho and para position to the amino group increases the nucleophilicity of amino nitrogen, thereby increasing the rate of diazotization process

Physical properties: Diazonium salts are generally colourless crystalline compounds, which darkens on exposure to air. Many diazonium salts of nitrates and perchlorates, when dry, they explode on being heated or being struck. As a result these salt are not isolated and soon as they are prepared in situ, they are immediately used for further synthetic preparations. However double salts made from diazonium and zinc chloride and between diazonium and tetrafluoroborates are stable at room temperature and they have been used as fast dye salts in the manufacture of naphthol-AS dyestuffs.





Chemical reactions: There are a number of synthetically useful reaction of Diazonium salts, but a distinction has been made between these reactions on the basis in which the nitrogen atoms of diazonium group are lost and those in which they are retained in the end product.

Thus the useful reaction of diazonium compounds are basically classified into two main groups.

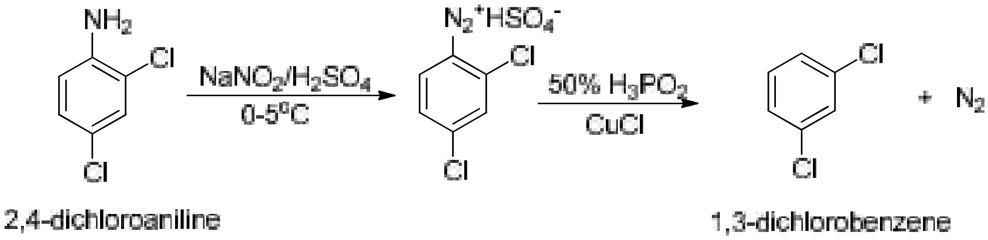
(i) Reactions in which the diazo group has been substituted by other functional group.
(ii) Reactions in which the diazo group is retained

Reactions involving replacement of diazo group by other functional groups

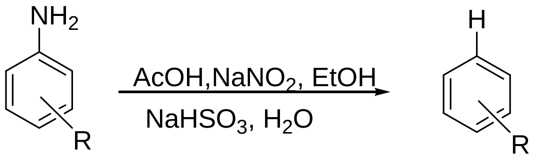
(i) **Replacement by H- Deamination reaction:** Replacement of diazonium group by hydrogen, thereby effecting the overall removal of amino group is known as **deamination**. The diazo group can be reduced by a variety of reagents like phosphinic acid or hypophosphorous acid (H_3PO_2) in the presence of copper (I) salts, ethanol (C_2H_5OH), triphenylphosphine, formaldehyde (HCHO), and by metals such as zinc (Zn), tin and hydrochloric acid (Sn/HCl) etc. But hypophosphorous acid remains the most selective reducing agent for deamination, since it exhibits a high degree of selectivity for the protonolysis of diazo group in comparison to other groups that may be present on the arene ring.

$$ArN_2^+Cl^- + CH_3CH_2OH \xrightarrow{\Delta} ArH + N_2 + HCl + CH_3CHO$$

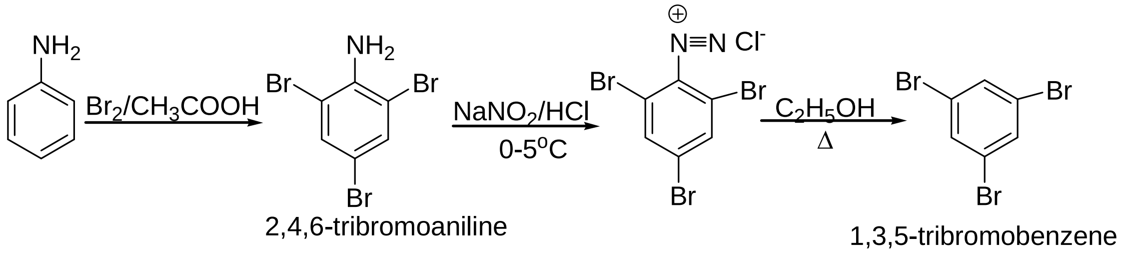
$$ArN_2^+Cl^- + H_3PO_2 + H_2O \xrightarrow{Cu^+} ArH + N_2 + HCl + H_3PO_3$$



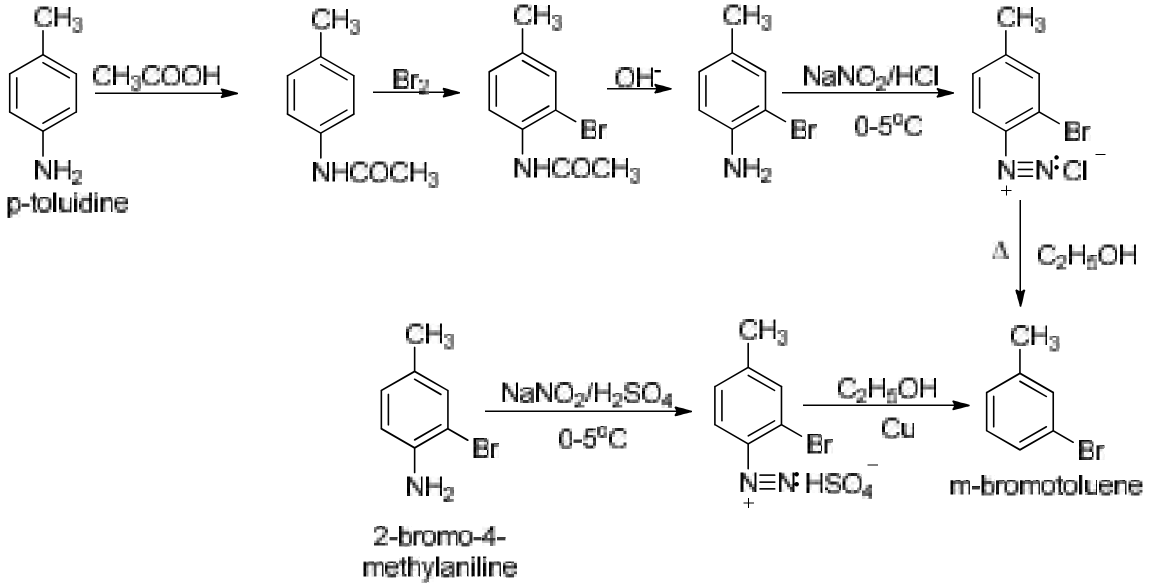
A free radical mechanism has been proposed for this reduction reaction with hypophosphoros acid, in which copper (I) ion acts as a one electron reducing agent. The overall reaction is basically a two step process involving diazotization followed by reduction. However now this two step process has been replaced by 'one-pot reaction' in which the diazotization-dediazotization takes place in one step



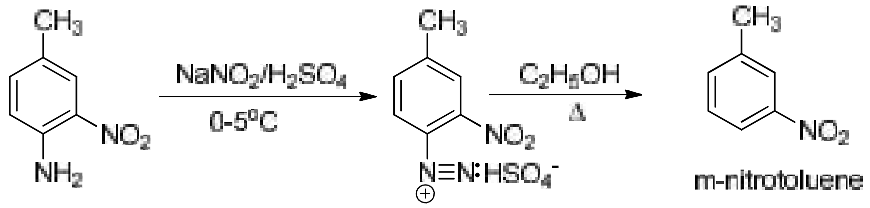
Application: This deamination of amines offers a useful method for the synthesis of trihalogen arenes which otherwise cannot be synthesized by direct halogenations of arenes. Direct halogenations of benzene would give the monohalogenated product, however halogenations of aniline which has an activating amino group directs halogenations to its ortho and para position. Removal of the amino group gives the desired product.



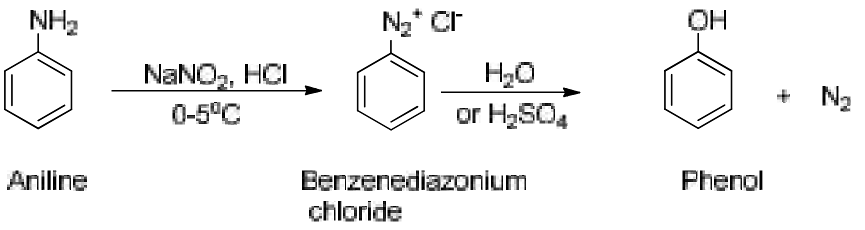
Similarly it is not possible to synthesize meta derivative of arenes having ortho/para directing group for example it is not possible to obtain meta halogen derivative of toluene, because methyl being ortho/para directing group, it will always give mixture of o-halo toluene and p-halo toluene. However m-bromotoluene can be synthesized from p- toluidine or directly from 2-bromo-4-methylaniline in the following manner.

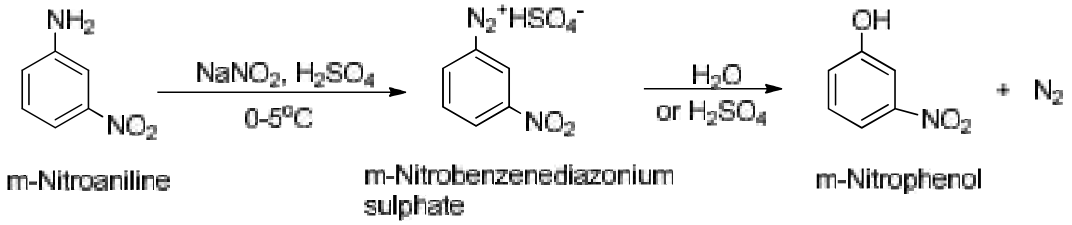


Similarly m-nitrotoluene can be synthesized from 4-methyl 2-nitroaniline



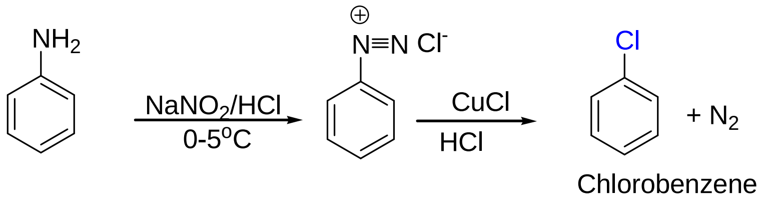
(ii) **Replacement by hydroxyl group**-Hydrolysis of arenediazonium salts: This is a more versatile method for the synthesis of phenols, as the conditions required for carrying out the reaction are very mild. Aniline or its substituted derivatives on reaction with sodium nitrite and hydrochloric acid/sulphuric acid at lower temperatures are converted to diazonium chloride/sulphate, which on hydrolysis with water or acid or heat yields phenols.

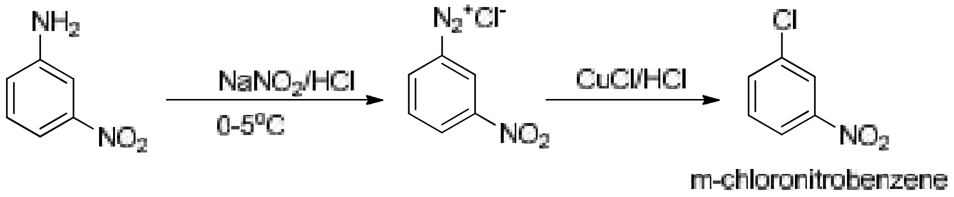


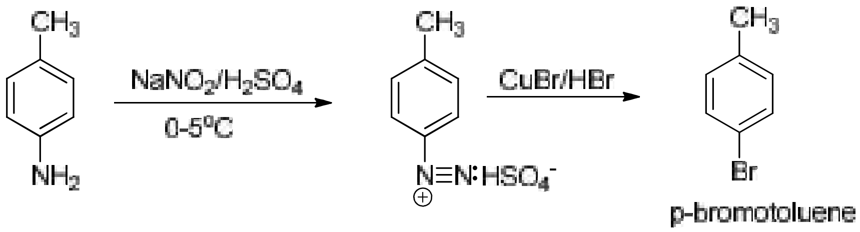


(iii) Replacement by halogens

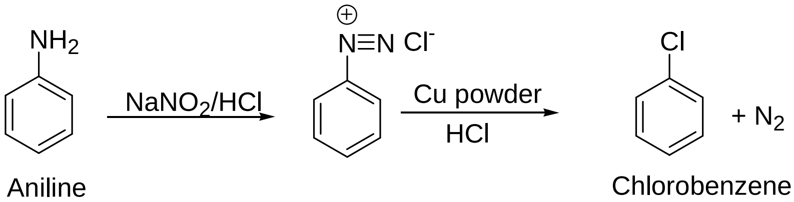
(a) Replacement by Cl, Br - Sandmeyer's Reaction: Diazotization of primary aryl amines with nitrous acid, followed by treatment of the aryl diazonium ion with cuprous chloride, cuprous bromide yields the corresponding aryl chloride, aryl bromide respectively.

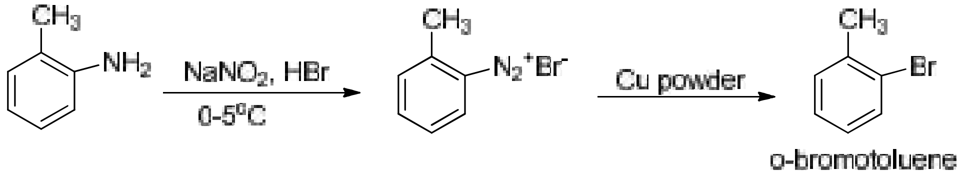




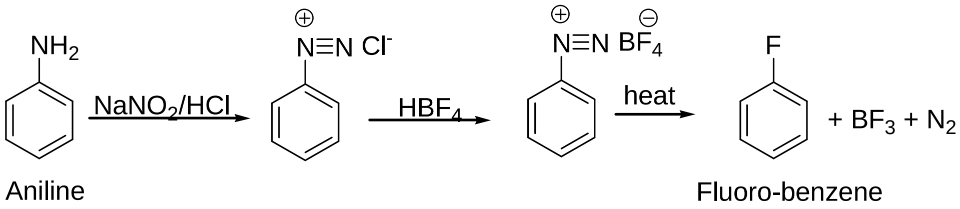


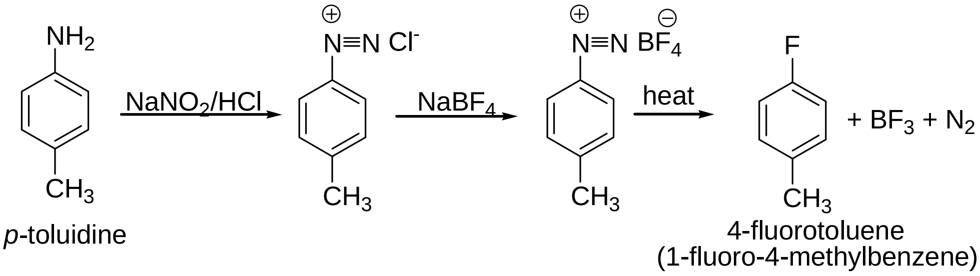
Gattermann reaction: This reaction named after German chemist Ludwig Gatterman is originally used for the synthesis of aromatic aldeydes, but synthesis of aryl halides from diazonium salt are also included into this reaction. The reaction is a modification of Sandmeyer's reaction and instead of cuprous salts, finely divided copper or copper bronze is used for the decomposition of diazonium salt solution.





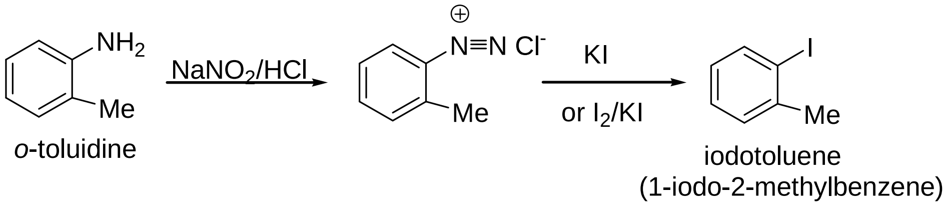
(b) Replacement by fluorine- Balz-Schiemann reaction: Diazotization of primary arylamine with nitrous acid followed by treatment of the synthesized diazonium salt with fluoroboric acid yields aryl diazonium fluoroborate salt.

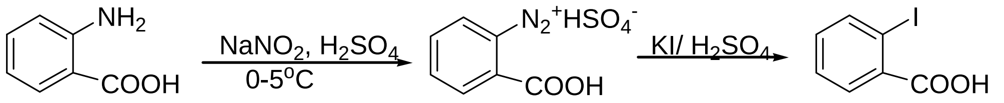




The mechanism of the reaction is believed to proceed with the decomposition of aryl diazonium fluoroborate (1)to aryl cation intermediate, which immediately forms aryl fluoride and boron trifluoride by reaction of the aryl cation with tetrafluoroborate.

(c) Replacement by iodine: Replacement of diazo group by iodo does not takes place with the aid of copper (I) iodide as catalyst, as it is not soluble in water. The iodo group is however introduced by warming the diazonium salt solution with potassium iodide or a solution of iodine in potassium iodide.

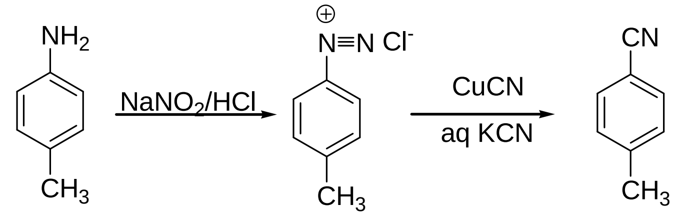




2-aminobenzoic acid
(anthranilic acid)

2-iodobenzoic acid

(iv) Replacement by cyano group: The replacement of diazo group by cyano group is special case of Sandmeyers reaction often referred to as **modified Sandmeyers reaction**. The reaction involves treatment of diazonium salt solution with a solution of copper (I) cyanide in aqueous potassium cyanide.

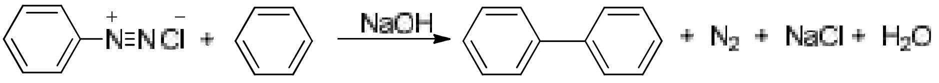


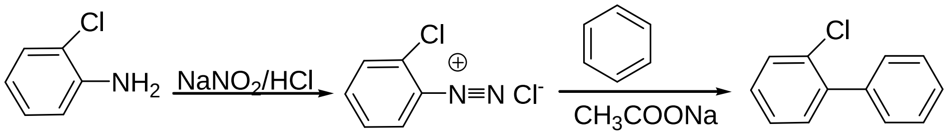
p-toluidine

4-tolunitrile
(4-methylbenzonitrile)

(v) Replacement by aryl group: A number of methods are available in which the diazo group is replaced by an aryl group.

(a) **Gomberg-Bachmann reaction**: The reaction involves treatment of diazonium salt with an arene in the presence of dilute sodium hydroxide. The product of the reaction are biaryl derivatives.

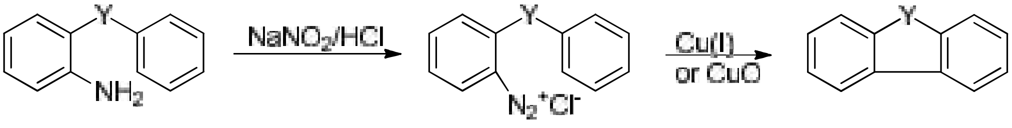




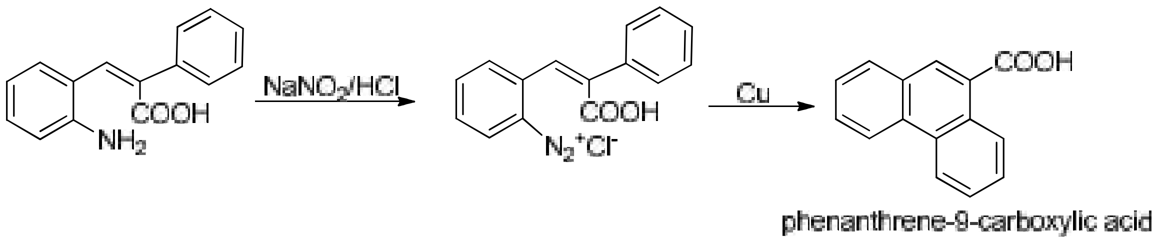
2-chloroaniline
(2-chlorobenzenamine)

2-chlorobiphenyl

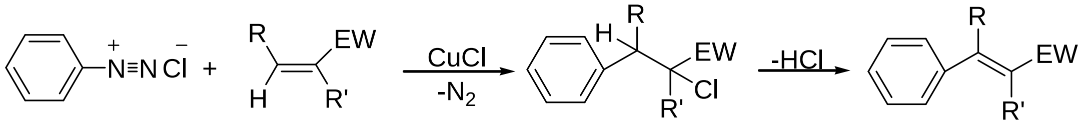
(b) **Pschorr reaction**: The reaction chiefly accounts for the synthesis of phenanthrene or its derivatives via diazotization followed by intramolecular ring closure process using copper



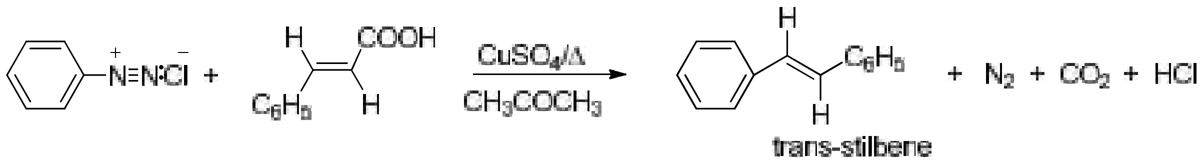
Y= CH=CH, O,S, NH, CH_2 etc



(c) **Meerwein arylation**: In this reaction addition of aryldiazonium salt to an alkene, which is bonded to an electron withdrawing group like COOH, COOR, NO_2 etc in the presence of copper (I) salt take place.



When the double bond is present adjacent to the carboxylic group, then sometime the arylation as well as decarboxylation reaction takes place simultaneously.



(vi) **Replacement by arsenic group-Bart reaction**: The reaction named after H.Bart [German Patent-250264, 1910] is a reaction of diazonium compound with alkali arsenite such as sodium arsenate in presence of cupric salt or powdered silver or copper powder, resulting in the formation of aryl arsonic acid.

$$C_6H_5{-}N_2^+Cl^- + Na_3AsO_3 \longrightarrow C_6H_5AsO_3Na_2 + NaCl + N_2$$

$$C_6H_5AsO_3Na_2 + 2HCl \longrightarrow C_6H_5AsO_3H_2 + 2NaCl$$

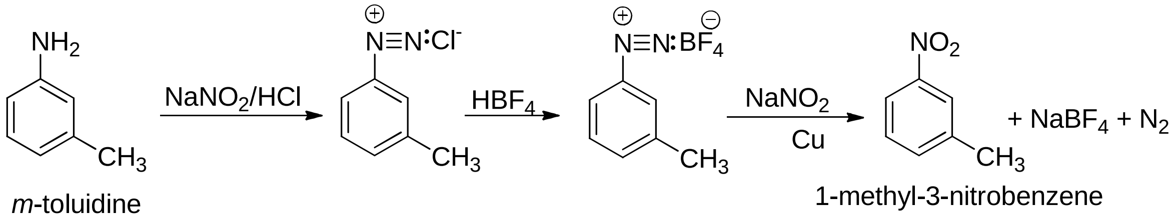
E.Scheller (British Patent 268172, 1912) however improved the Bart reaction and carried out diazotization of primary amines in presence of arsenic chloride with traces of cuprous chloride.

$$C_6H_5{-}NH_2 + HNO_2 + AlCl_3 + H_2O \longrightarrow C_6H_5AsO_3H_2 + N_2 + 3HCl$$

(vii) Replacement by thiol group (SH): Thiol group is introduced by treating the diazonium salt with potassium ethyl xanthate followed by hydrolysis.

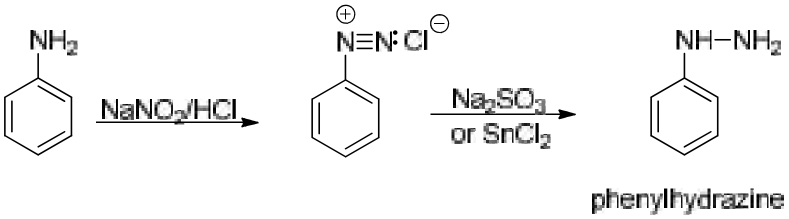
$$C_6H_5{-}N_2^+Cl^- + C_2H_5OCS_2^-K^+ \longrightarrow C_6H_5S_2OC_2H_5 \xrightarrow{H^+} C_6H_5SH$$

(viii) Replacement by nitro group: Nitro group is introduced by treating arenediazonium fluoroborate with an aqueous solution of sodium nitrite in the presence of copper powder



Reactions in which Nitrogen of diazo group is retained

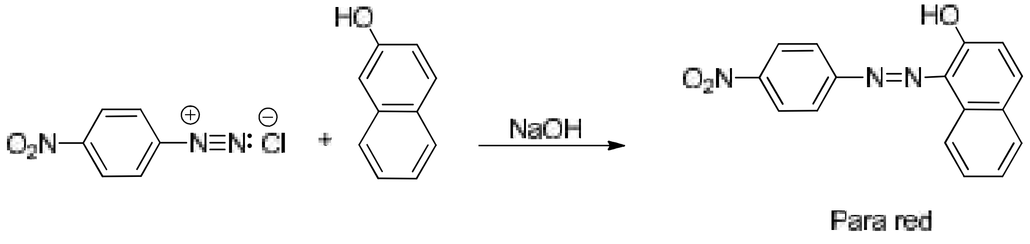
(i) Reduction to arylhydrazines: Arylhydrazines are synthesized by reducing diazonium salts with sodium sulphite or stannous chloride followed by acidification with hydrochloric acid. The hydrochloride derivative crystallizes out on cooling, which on treatment with sodium hydroxide liberates the free hydrazine derivative.

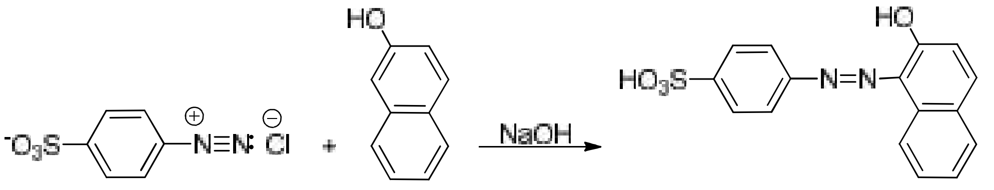


(ii) **Coupling reactions**: Coupling reactions are those in which diazonium salts are linked or coupled with another molecule. The amine that is to be diazotized is referred to as diazonium component and the compound with which it is linked is called the coupling component. The whole reactions is commonly called **azo coupling**.

Diazonium salts being weak electrophiles, as a consequence they react with those aromatic systems which are activated by strong electron donating groups. It is for this reason diazonium salts usually undergo coupling reactions with phenols and aromatic amines in alkaline, neutral or mild acidic medium to yield highly coloured azo compounds. This type of coupling is often referred to as **C-coupling**.

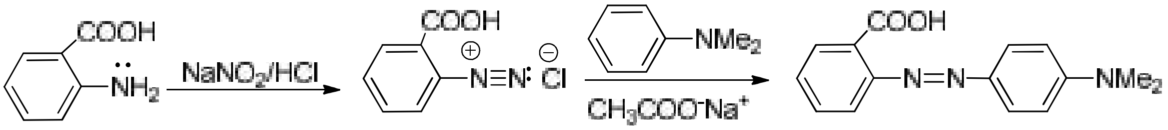
Coupling with phenols:Coupling of diazonium salts with phenols is usually carried out in the pH range of 8-11, and in this pH range the phenols are usually present as phenoxide ion.





Orange II (acidic dye)

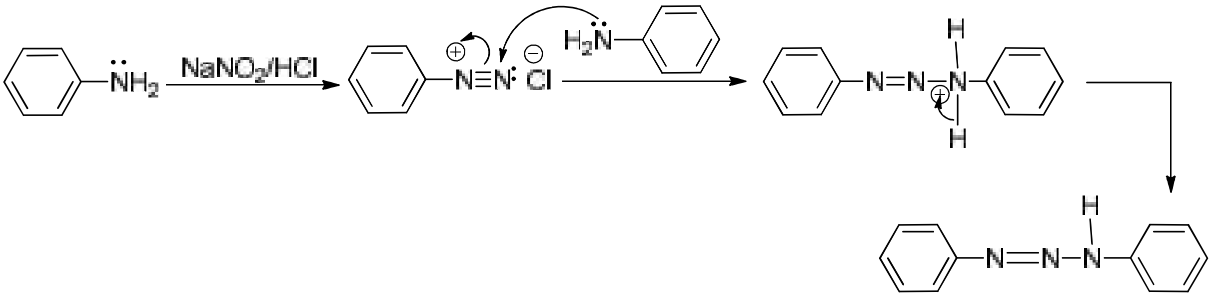
Coupling with amines: Tertiary amines react with diazonium salts in a similar manner as phenols, except that the coupling reaction is carried out in slight acidic medium.



Anthranilic acid

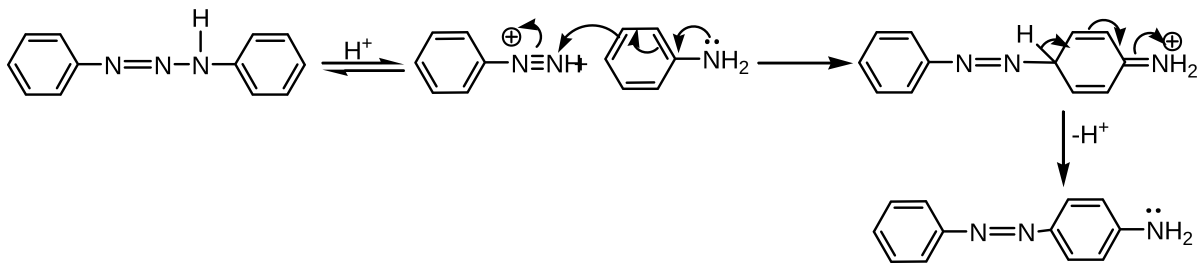
Methyl red

Coupling of diazonium salts with primary amines, readily takes place at the nitrogen of the diazonium ion in weakly acidic medium, leading to the formation of diazoamino compounds. This type of coupling is referred to as N-coupling.



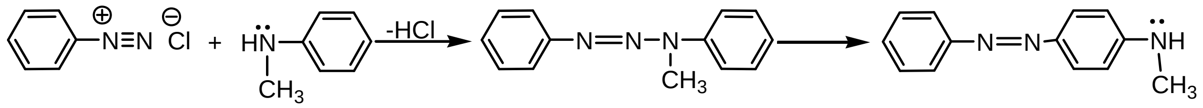
Diaminoazobenzene

When the formation of diaminoazobenzene takes place under acidic conditions, then it undergoes rearrangement to p-aminoazobenzne. Alternatively rearrangement can also take place by heating (below 50^{o}C) diaminazobenzene in aniline with aniline hydrochloride . When the p-position is blocked, then the rearrangement takes place at o-position.



p-aminoazobenzene

Like primary amines, Coupling of diazonium salts with secondary amines, also takes place at the nitrogen of the diazonium ion. The diazoamino compounds, as soon as it is formed immediately rearranges to azo compound.



p-methyldiazoaminobenzene p-methylaminoazobenzene