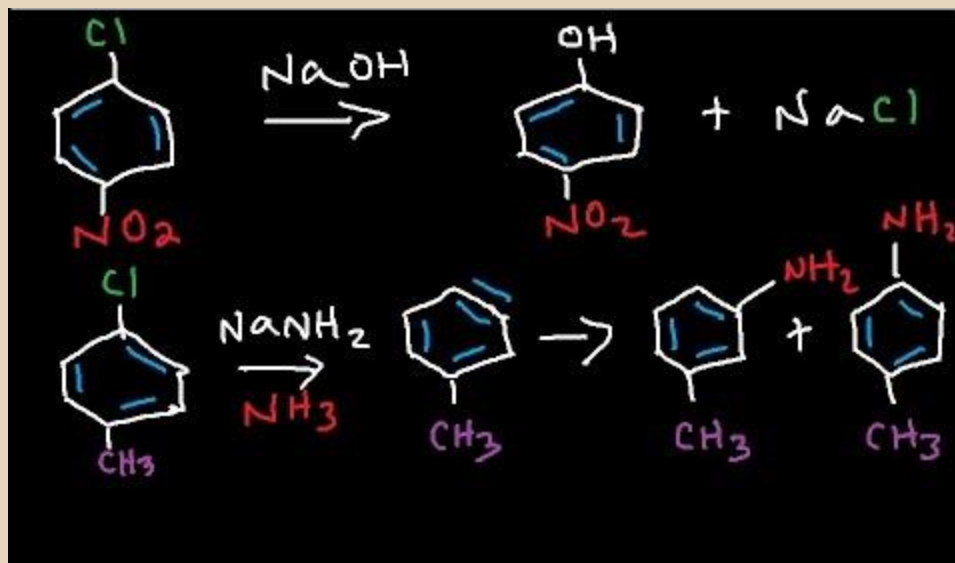


Nucleophilic Aromatic Substitution

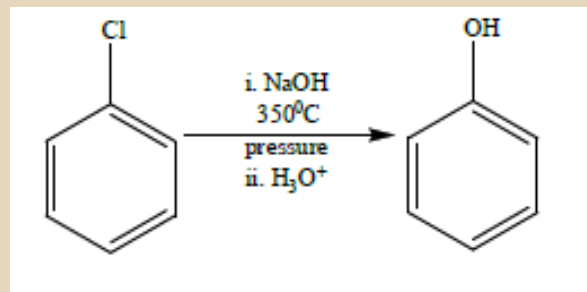


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Nucleophilic Aromatic Substitution

Normally electrophilic aromatic substitution is a reaction that is common with benzene and its derivatives. Nucleophilic substitution in an aromatic compound though not common, can be observed in many aromatic systems, which has even found industrial importance. Example is industrial synthesis of phenol from chloro benzene by Dow's process.



Since a nucleophile substitutes for the leaving group on the benzene ring, this is called ***nucleophilic aromatic substitution***.

Reaction does not go through simple SN2 or SN1 mechanism.

➤ SN2 is not possible because carbon atom is sp^2 hybridized and bromine is in same plane as that of carbon.

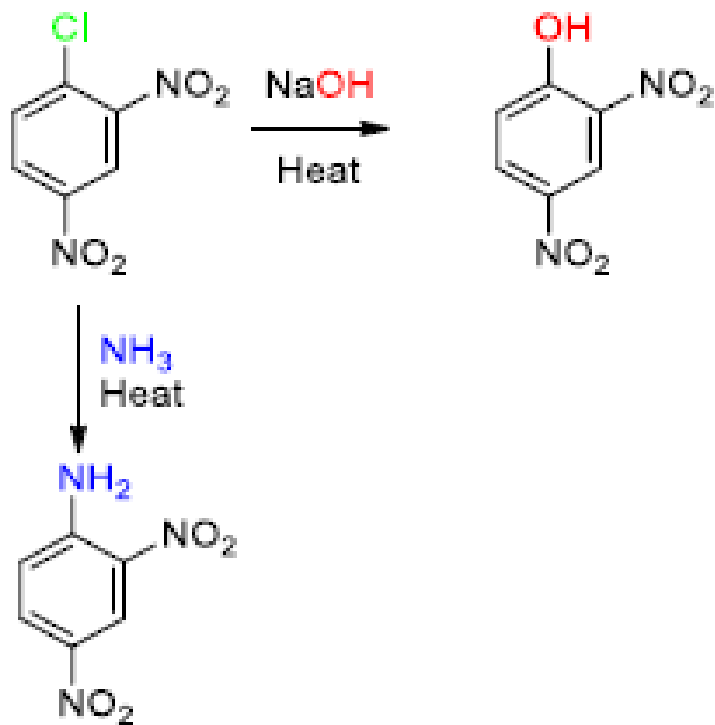
➤ Due to this hydroxyl can not attack from back side of C-Br bond as is required in SN2 reaction.

➤ SN1 is possible in some cases but is unfavorable because the aryl cation formed will be planar but will not contain empty p orbital. Instead it will have filled p orbital as it is part of the aromatic system.

➤ Also, C-X bonds of aryl halides are shorter and stronger than those of aliphatic halides because of the hybridized state and the resonance, hence, ionization to form a cation is a high energy process.

Such a mechanism is observed only with leaving group such as gaseous nitrogen.

For example 2,4-dinitrochlorobenzene will undergo reactions with nucleophiles such as ammonia and hydroxide, where the chlorine becomes displaced

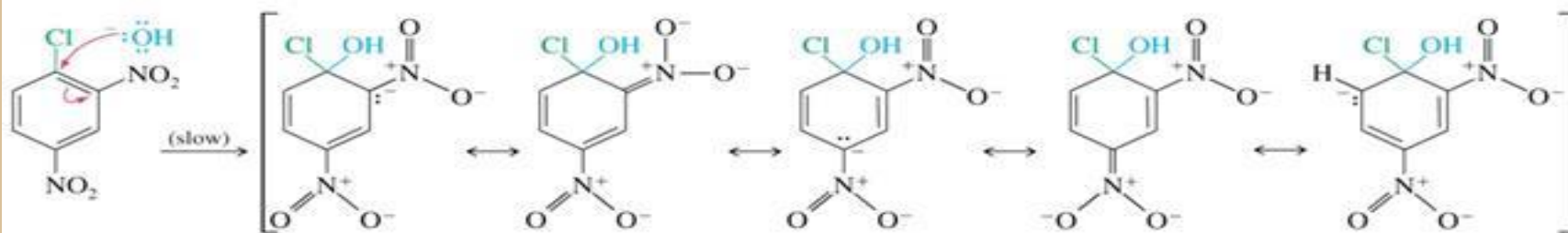


However, *it is also possible for nucleophiles to displace halide ions (i.e. good leaving groups) from aryl halides if there are strong electron withdrawing groups bound to the ring (and especially if they are located ortho and para to the halide).*

The Addition Elimination Mechanism

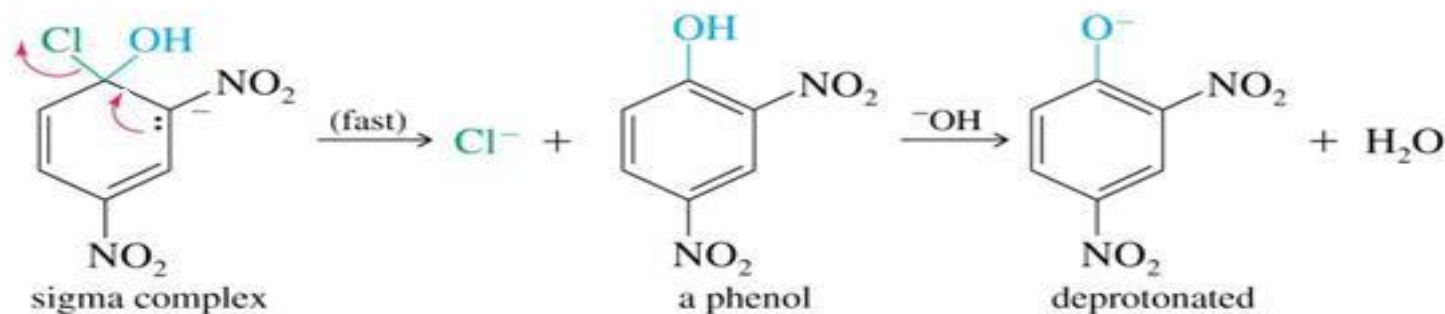
In the reaction of OH^- with 2,4-dinitrochloro benzene, the OH^- attacks the carbon bearing the Cl, a δ^- complex is formed. The δ^- charge is delocalized over the ortho and para positions, and further delocalized into the electron withdrawing groups (conveniently located at these positions). Loss of Cl^- from the sigma complex gives 2,4-dinitrophenol

Step 1: Attack by hydroxide gives a resonance-stabilized sigma complex.



Step 2: Loss of chloride gives the product.

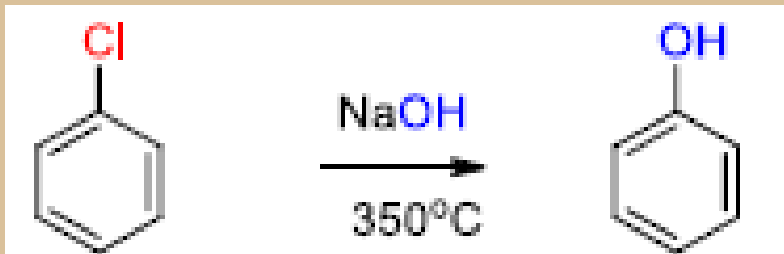
Step 3: Excess base deprotonates the product.



The Benzyne Mechanism

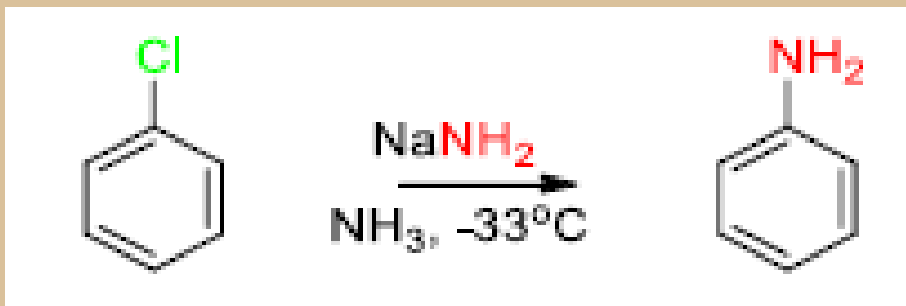
(*Elimination Addition Mechanism*).

The previous addition elimination reaction mechanism required powerfully electron withdrawing groups on the benzene ring. However, under forcing conditions, unactivated halobenzenes can react with strong bases.

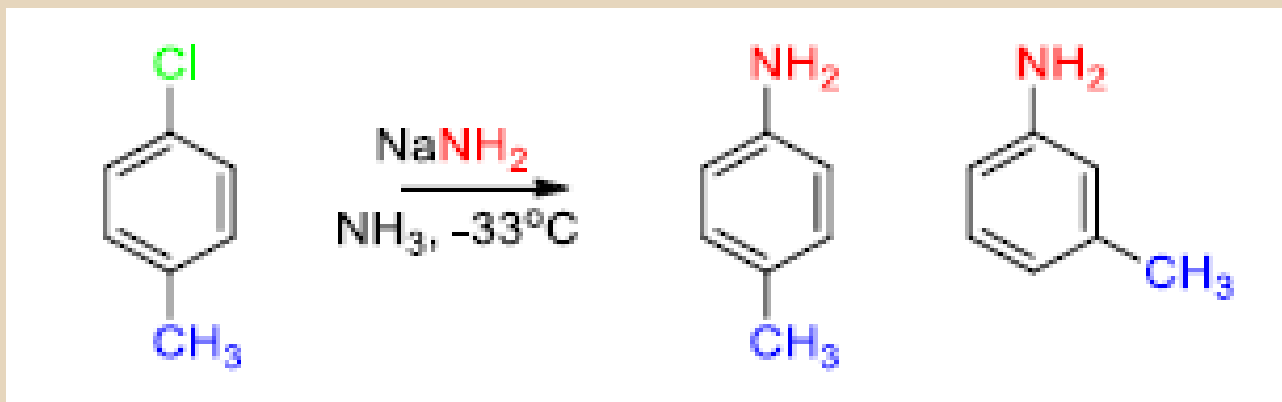


For example, phenol is produced commercially via the reaction of sodium hydroxide with chlorobenzene.

Analogously, aniline is produced via reaction of chlorobenzene with sodium amide.

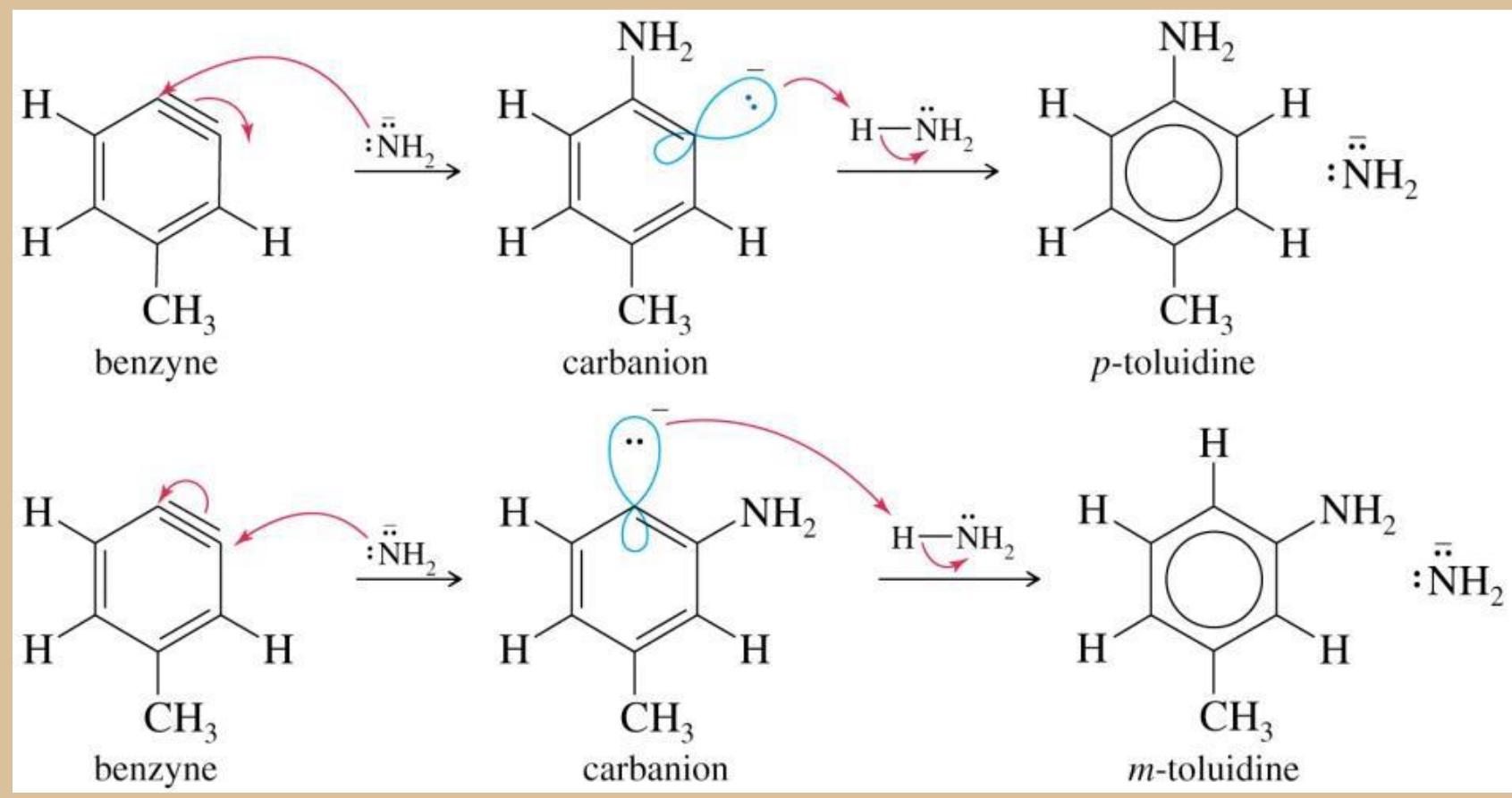
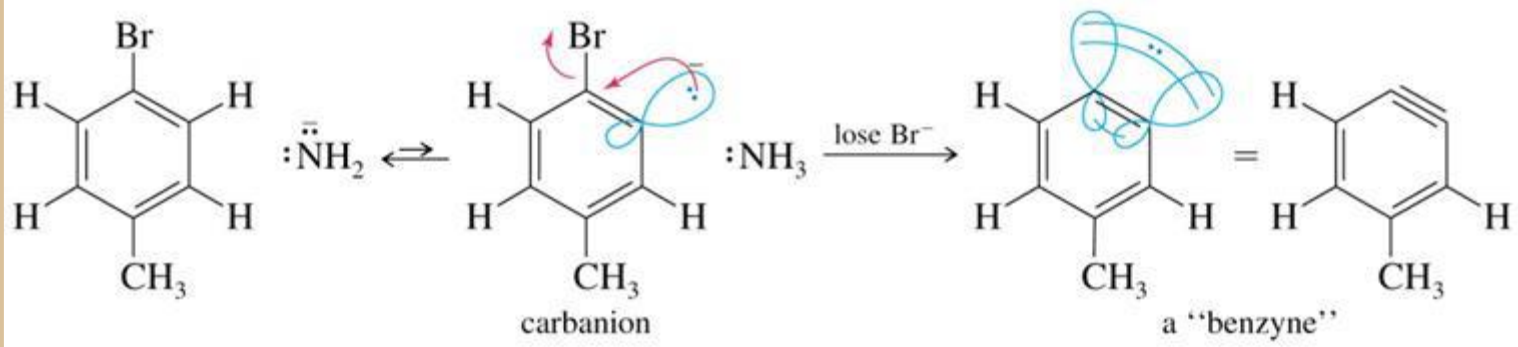


A clue to the mechanism of this type of reaction was provided by the below reaction:



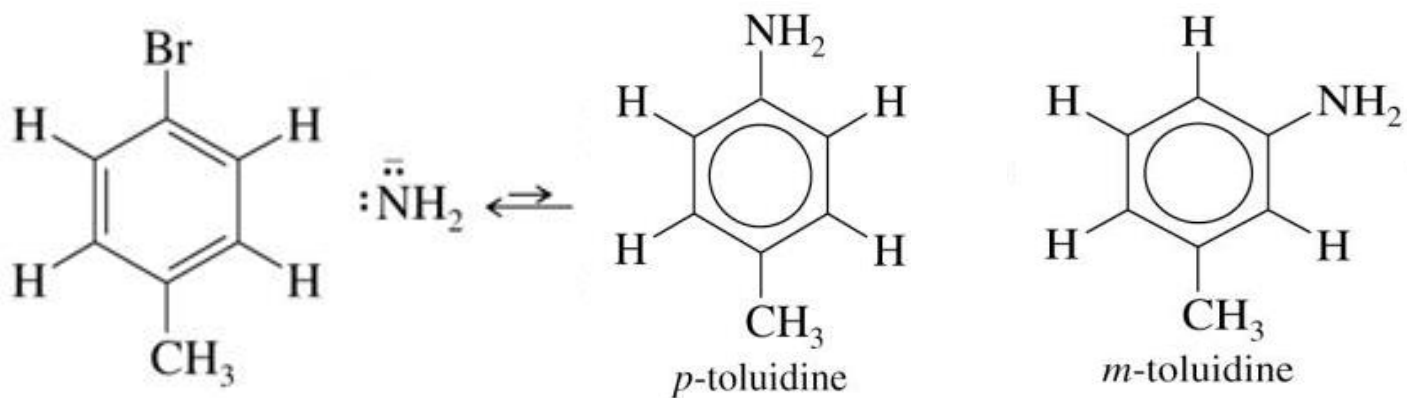
The products were found to be a 50:50 mixture of meta and para substituted compounds.

These two isomers can be explained as coming from the same intermediate, a **Benzyne**.



Through nucleophilic substitution reaction bromo toluene upon reaction with a strong base like NaNH_2 in liquid NH_3 give toluene .

- Reaction goes through different mechanism than stated earlier.
- It involves formation of a benzyne intermediate hence name benzyne mechanism.
- It is reverse of normal addition-elimination mechanism.
- Sometimes it is called elimination-addition mechanism.



- The reagent used acts as a strong base, and abstracts the proton adjacent to the leaving group.
- The anion can expel the leaving group, thus generating a neutral species and another π bond (making a triple bond). This is called a benzyne (benzene + alkyne). The benzyne is a reactive intermediate.
- The triple bond is reactive since it is very strained (should be linear). The amide nucleophile attacks the triple bond, generating a carbanion, which then gets protonated to give the product.
- The attack on the triple bond may occur with equal probability (and energy) at either end, and thus the 50:50 mixture results.

- Due to the presence of electronegative bromine, ortho proton is relatively more acidic, resulting in its removal by the base.
- Benzyne intermediate is formed from this carbanion by syn-periplanar elimination of the bromide ion.
- Benzyne intermediate appears like an alkyne in its representation with triple bond in the benzene ring. However, this triple bond is not like an usual triple bond as it is formed by the lateral overlap between two sp^2 hybridized orbitals outside the ring.