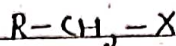
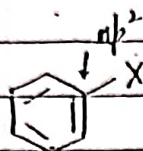


Nucleophilic Aromatic Substitution Reactions

Haloarenes are relatively unreactive towards NSR as compared to haloalkanes.



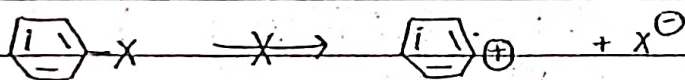
⇒ C-X bond is much stronger and stronger formed by sp^2-p overlap ⇒ sp^3-p overlap

⇒ delocalisation ∴ partial double bond character

∴ Substitution reactions take place only under drastic condⁿ of temp, pressure and reagent concⁿ.

Haloarenes don't follow usual S_N1 and S_N2 mechanisms:
because

- ⇒ C-X bond requires high energy for its cleavage
- ⇒ S_N1 is not followed because phenyl cation so formed is highly unstable.



(it is possible only in the case of world's best leaving group: $-\overset{\oplus}{\text{N}}=\text{N}$)

- ⇒ In S_N2 , the steric hindrance due to aromatic ring shields the back side attack of nucleophile.

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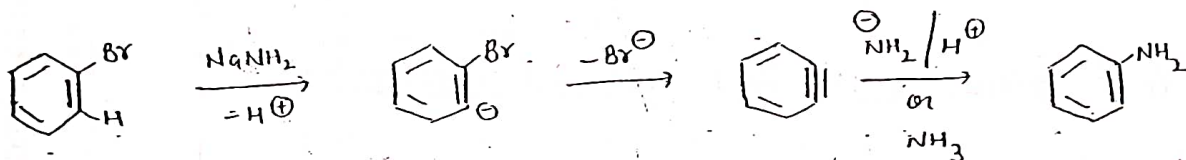
However, appropriately substituted compounds do undergo nucleophilic substitution reactions successfully.

- i) By introducing \ominus withdrawing substituents at o- and p- positions to the leaving group of an aromatic ring.
- ii) By using strong bases
- iii) By replacing N_2 gas from diazonium salts with the help of nucleophile.

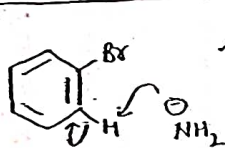
* Elimination-Addition Mechanism *

(Benzyne Mechanism)

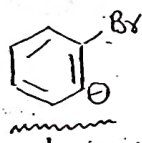
When simple aryl halides react with strong bases like $NaNH_2$, base (NH_2^-) abstracts a proton adjacent to the C-X unit. The resulting carbanion displaces the halide ion to generate benzyne which is ultimately attacked by NH_2^- or its protonated derivative ammonia (NH_3) to form aromatic amines.



Elimination Step:



all nucleophiles that are very basic can carry out this reaction.

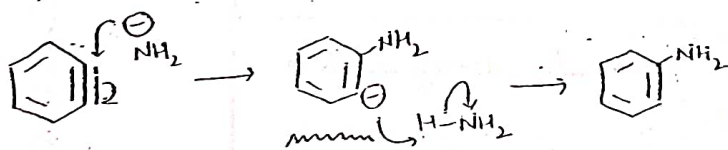


stabilisation of carbanion by the electronegativity of Br is weak \therefore only strong bases can do the reaction.



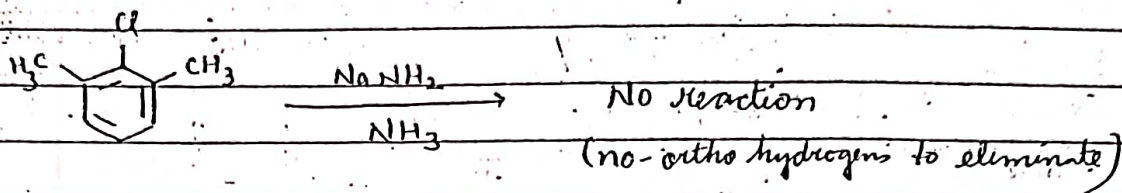
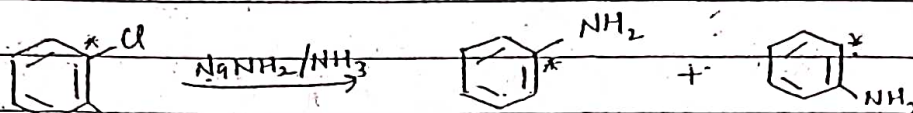
(benzyne is electrophilic as the weak third bond can be attacked by nucleophiles.)

Addition Step:

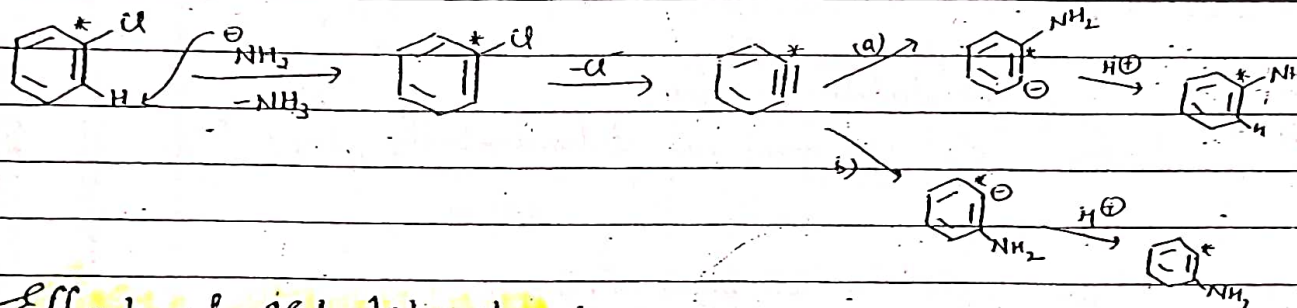


Symmetry in the mechanism:

Benzene is formed from an ortho carbanion and it gives an ortho carbanion when it reacts with nucleophiles.

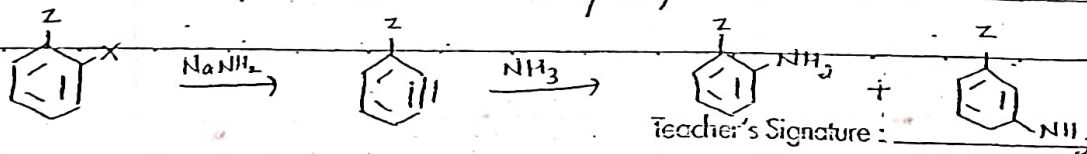
Proof for elimination-addition reacⁿProof for benzyne intermediate

These two products are possible only if reacⁿ proceeds through benzyne intermediate.

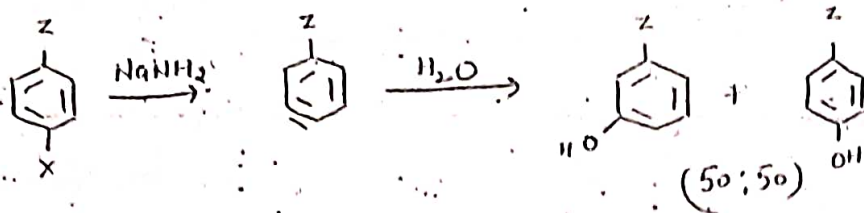
Effect of Substituents

The only thing that is to remember is the stability of carbanion so formed.

Substituent at the o- and p- position to the leaving group.

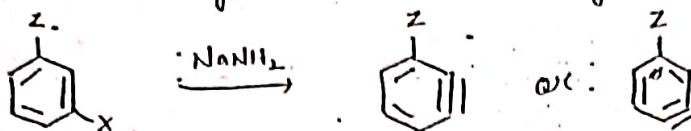


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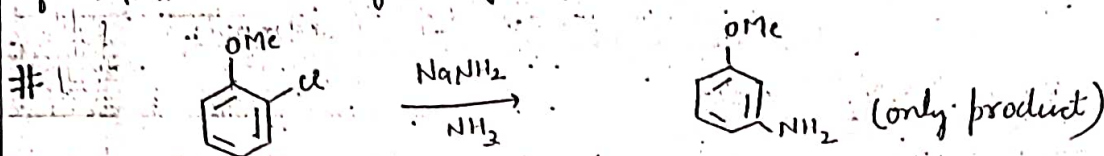


In case of meta:

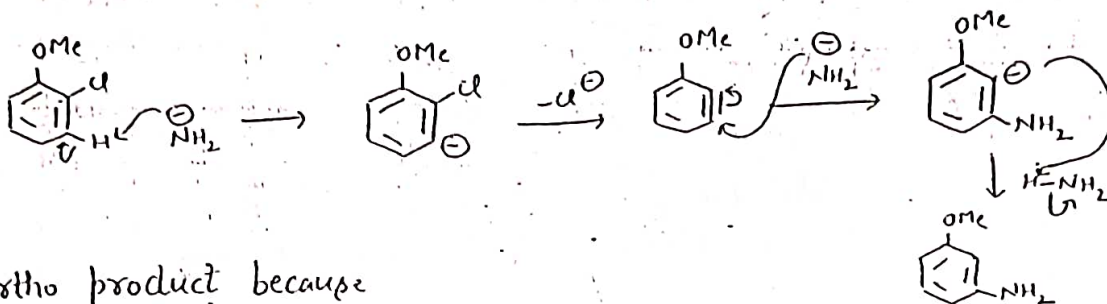
anyne can be generated in two ways:



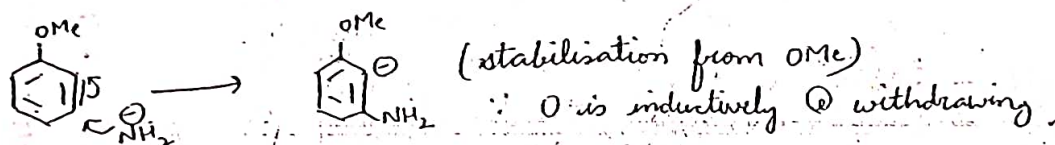
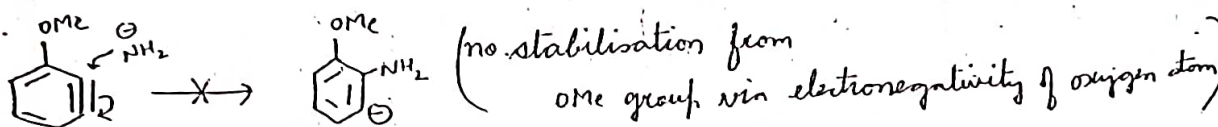
acidity of H depends upon nature of Z; if Z is EWG \rightarrow removal of O-H
 if EDG \rightarrow removal of β -Hydrogen



Mech:



No ortho product because

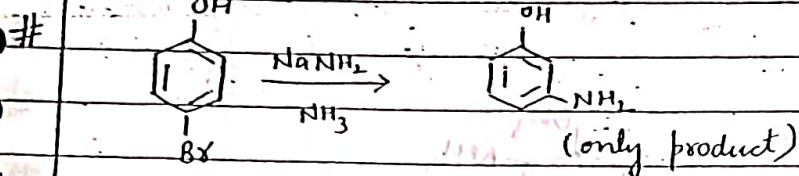
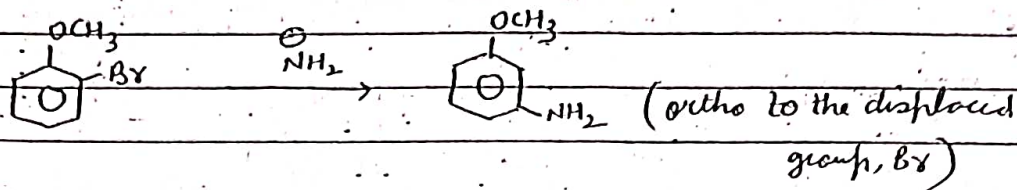


Sterically, it is better for the amide ion to attack away from the OMe group rather than come in alongside it. Nucleophilic attack on benzene has to occur in the plane of benzene ring because that is where the orbitals are.

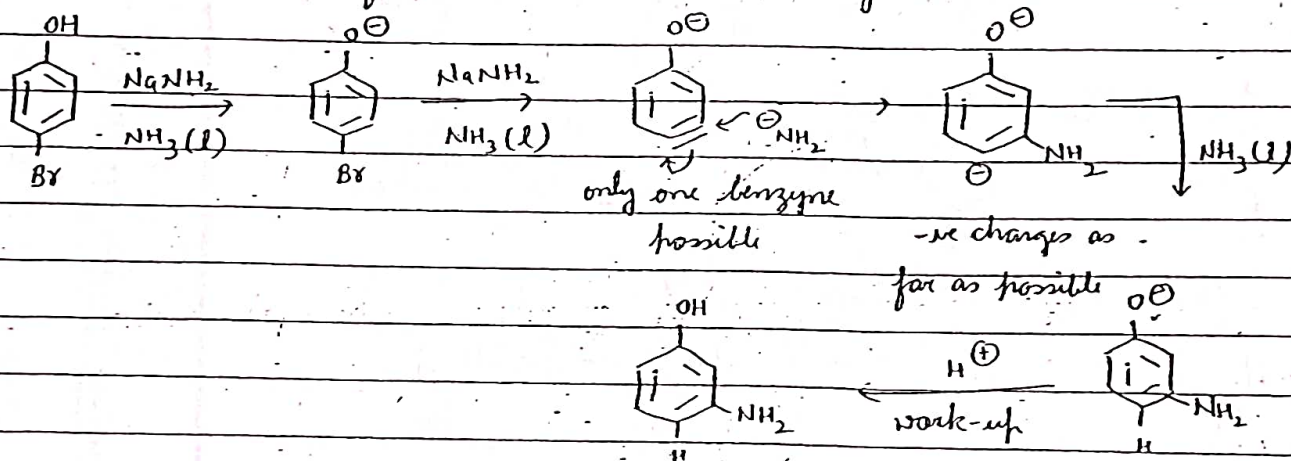
Cine-Substitution

When the aromatic nucleophilic substitution occasionally occurs at different positions and incoming group enters ortho to the displaced group, then it is known as cine substitution.

Example



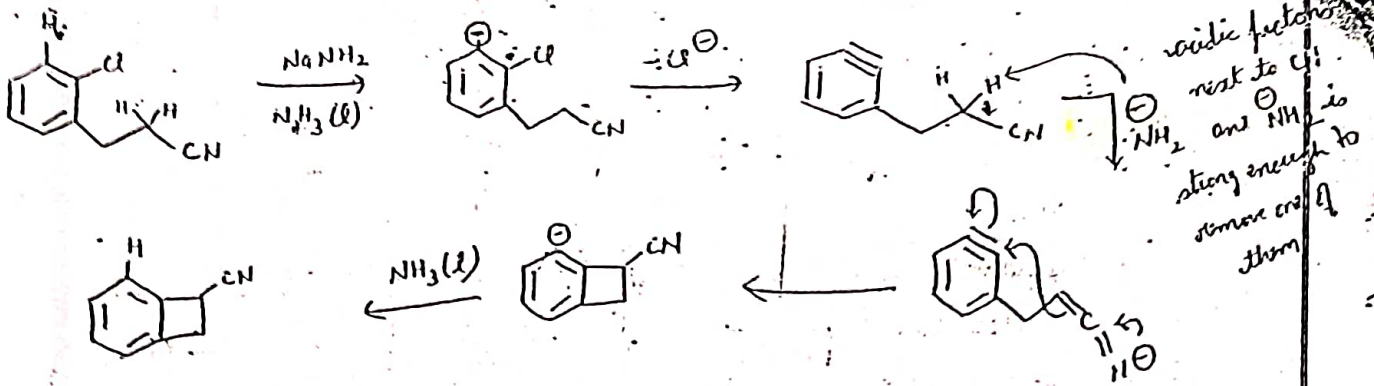
If the substituent is an \ominus repelling anion, m-product is formed exclusively because this puts the product anion as far as possible from the anion already there.



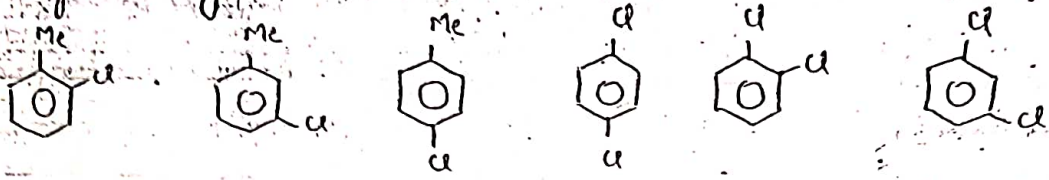
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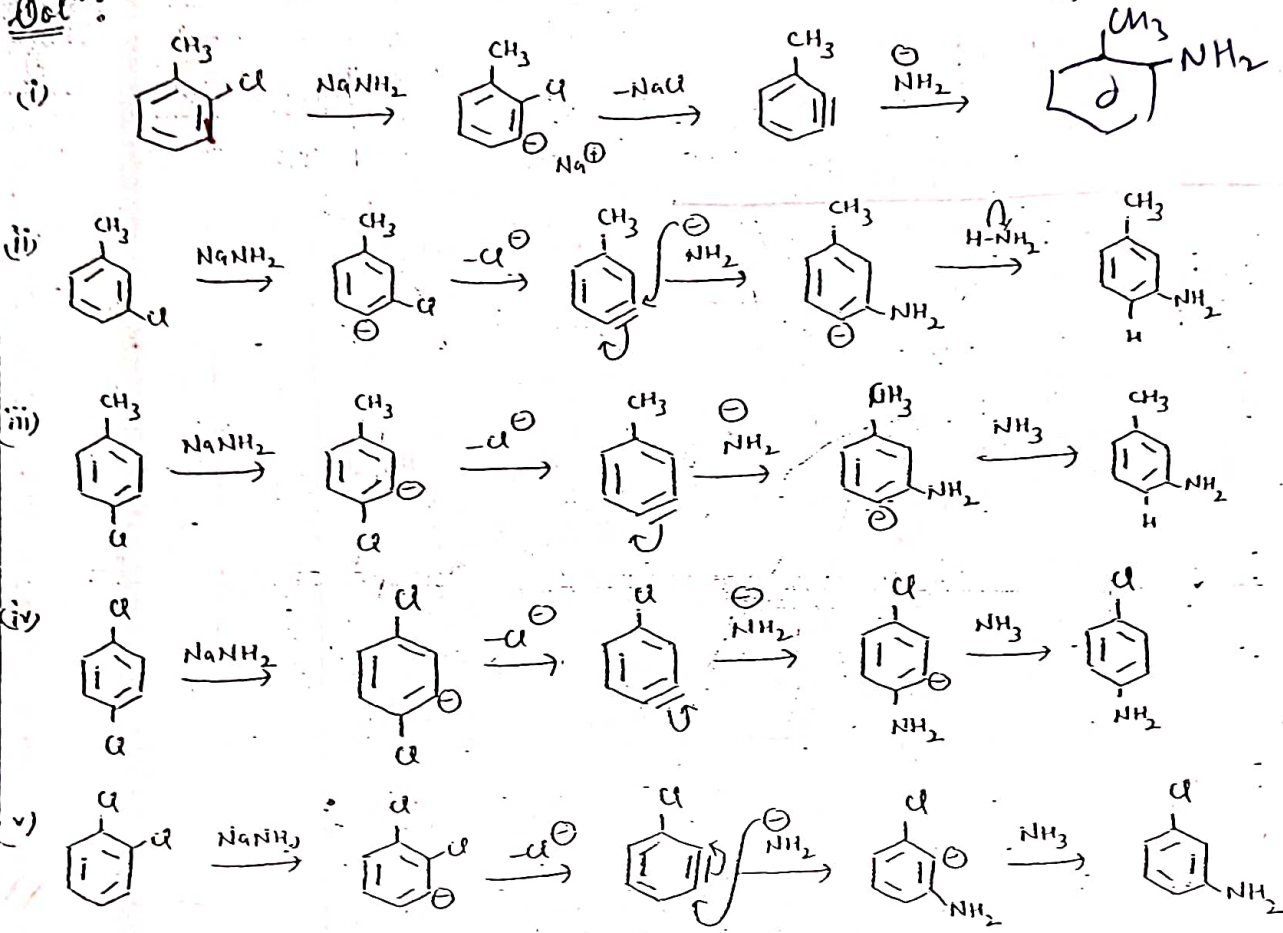
11. One case where selectivity of attack is no problem is in reaction with intramolecular nucleophiles.

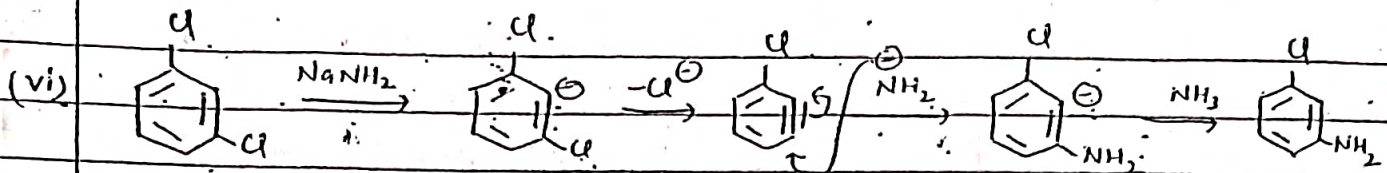


Ques: Write the products formed on reacⁿ with NaNH₂ in each of the following substrates:



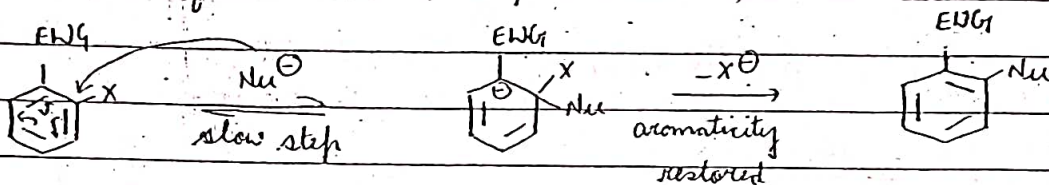
Solⁿ:





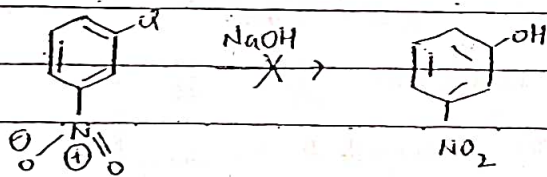
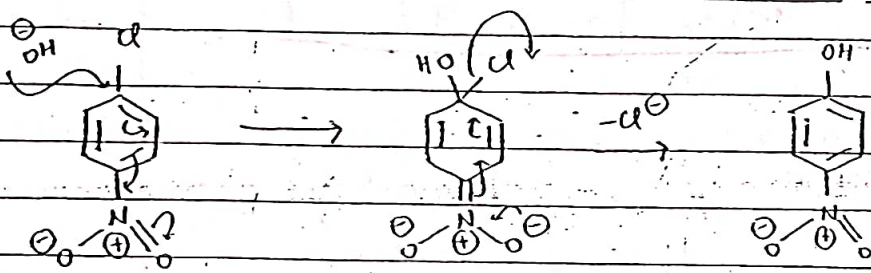
* Addition-Elimination Mechanism * (S_NAr Mechanism)

The first step of reacⁿ is the initial attack of nucleophile at the carbon (where the leaving group is attached) which disrupts the π cloud and forms a carbanion which is stabilised by resonance. This is a slow step i.e. r.d.s. In the second step, aromaticity is restored through elimination of an ionic species.



A typical nucleophilic aromatic substitution has:

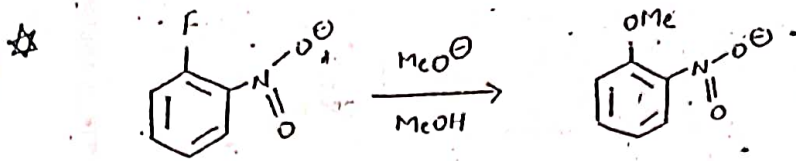
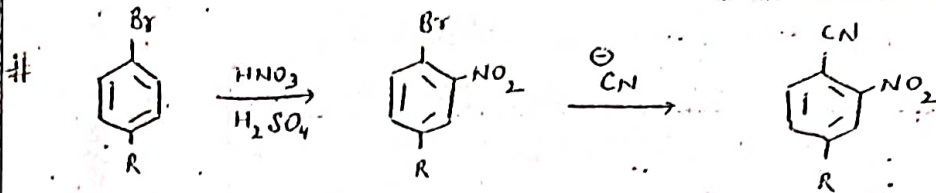
- i) an oxygen, nitrogen or cyanide nucleophile.
- ii) a halide as a leaving group
- iii) a carbonyl, $-NO_2$ or $-CN$ group o- or p- to the leaving group



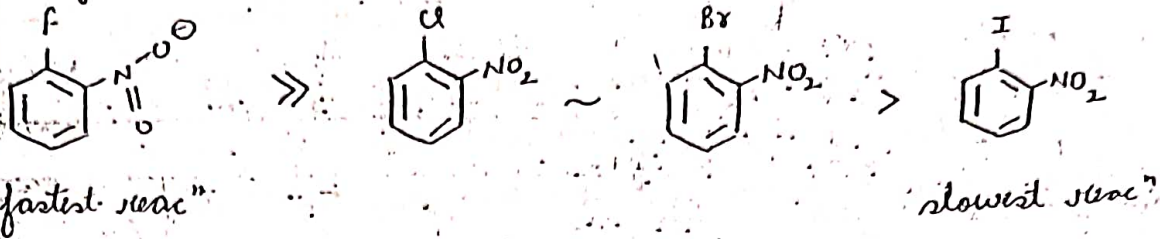
($-NO_2$ can't stabilise the -ve charge generated through resonance)

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Reactivity of *o*-halo-1-nitrobenzene in nucleophilic aromatic subⁿ



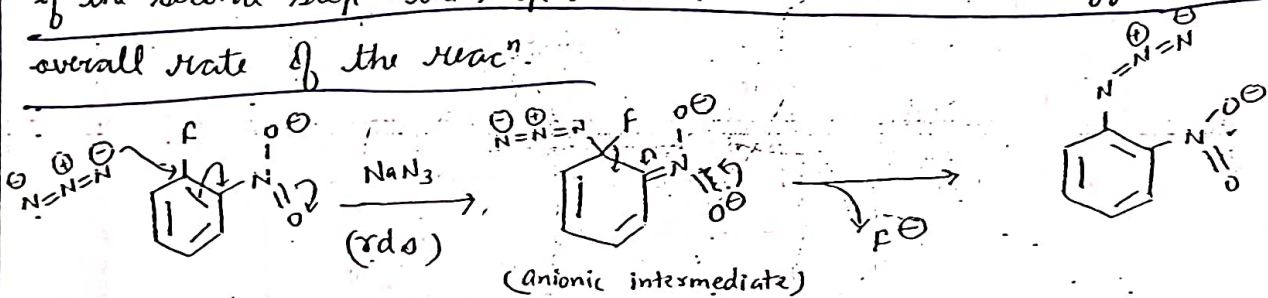
Should not be so because:

- ⇒ C-F is the strongest bond of all C-X bonds ∴ difficult to break
- ⇒ F is not a good leaving group (the order is I > Br > Cl > F)

Explanation for the above order:

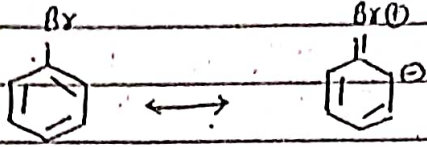
In the two-step mechⁿ of addition-elimination mechⁿ; the first step is slow and hence rate determining (because it disturbs aromaticity) and the second step is not important to the rate.

∴ How good a leaving group is, does not matter because the rate of the second step - the step where F⁻ leaves - has no effect on the overall rate of the reacⁿ.



F⁻ in fact slows down the second step (relative to, say, Cl⁻), but it accelerates the first step simply by its enormous inductive effect. It is most electronegative of all and stabilises the anionic intermediate, assisting the acceptance of \ominus by benzene ring.

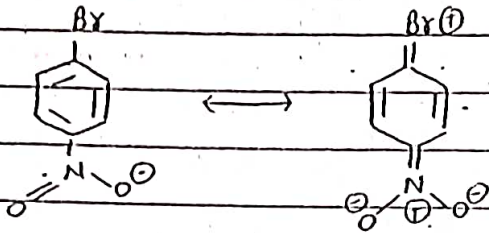
Some textbooks tell you that nucleophilic aromatic subⁿ doesn't happen with ordinary aryl halides because of the conjugation between the lp of X[⊖] and the aromatic system.



This is supposed to stop the reacⁿ by making C-Br bond stronger. THIS IS NONSENSE.

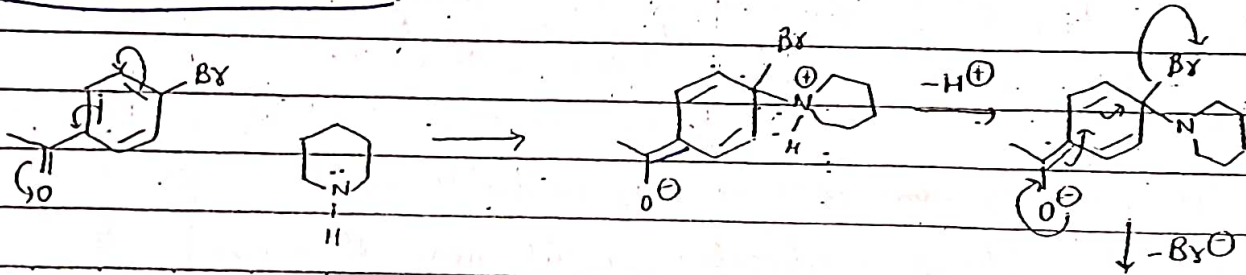
The reacⁿ doesn't happen on simple aryl halides because there is no available mechanism.

But the above textbooks reason can be proved wrong. The conjugation in this nitro compound is much better than in bromobenzene, so it should be even less reactive.



But is ~~so~~ very reactive.

⇒ The strength of the bond to the leaving group doesn't effect the efficiency of nucleophilic aromatic subⁿ because the bond is not broken in rds step.

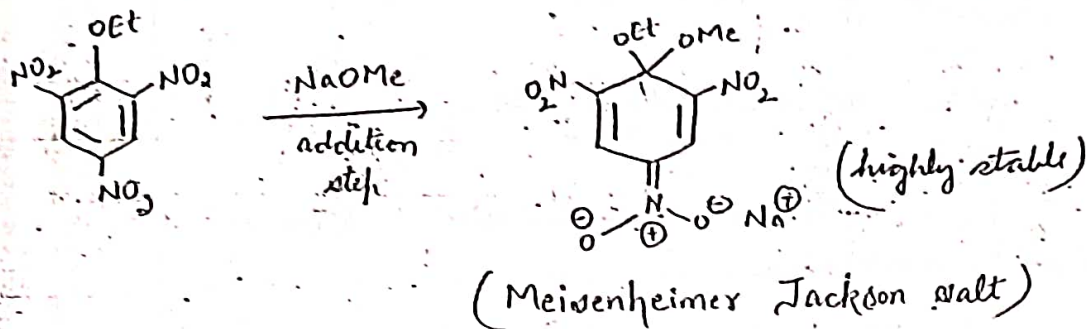


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Evidence for mechanism

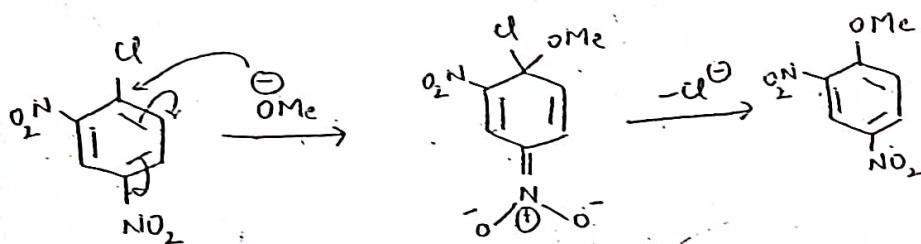
It includes the isolation of intermediate species and their structural characterisation by NMR and X-ray crystallography. These intermediate species are referred to as "Meisenheimer" or "Meisenheimer Jackson" salts. These salts were coloured and isolated by Meisenheimer in 1902 from the reacⁿ of 2-ethoxy-1,3,5-trinitrobenzene with NaOMe.



Ipso effect

attack of the nucleophile (Nu^-) on the carbon of the aromatic system bearing the leaving group followed by elimination

e.g.:-

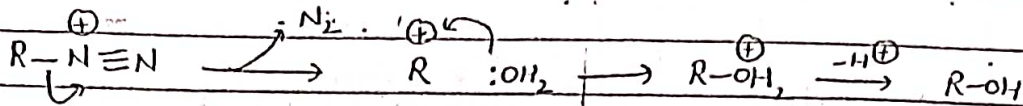


* S_N1 Mechanism *

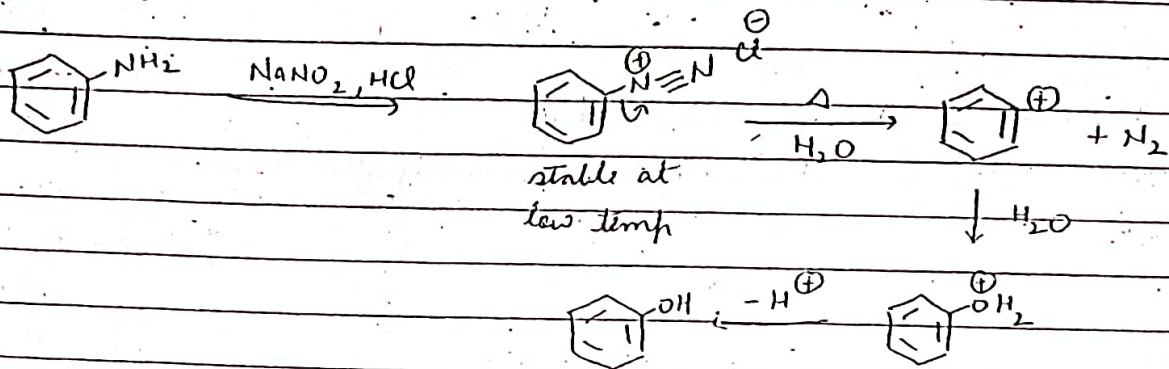
\Rightarrow is unimolecular and very rare for aryl halides. Generally, these kind of mechanisms have been proposed for the reaction of diazonium salts ($\text{R}-\text{N}^{\oplus} \equiv \text{N}$).

If R is an alkyl group, diazonium salt is very unstable and loses $\text{N}_2(\uparrow)$ immediately to give a planar carbocation which normally reacts

with a nucleophile in S_N1 process or loses a proton in an E_1 process.



If R is an aryl group, carbocation is less stable because and that makes the loss of N_2 slower. If diazotisation is done at low temp, diazonium salt is stable and can be reacted with various nucleophiles.

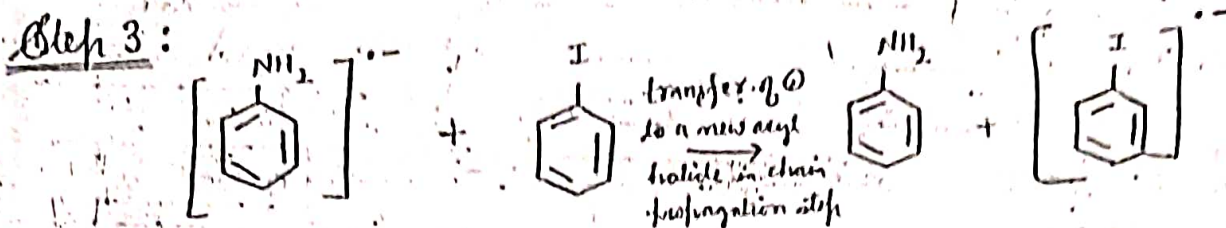
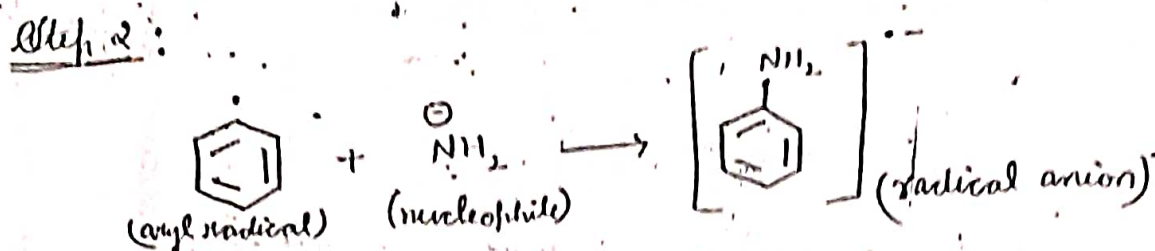
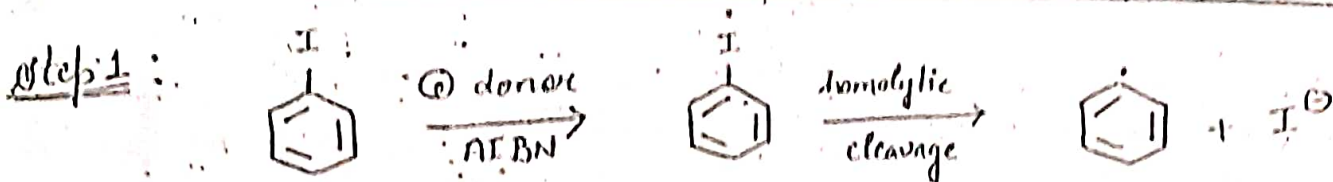


Rate is independent of nucleophile

* $S_{RN}1$ Mechanism *

Besides the benzoyne mechanism, "free radical mech" is also been observed in various aryl systems in which \ominus donor is required to initiate the reaction. In the last step, the aryl halide radical halide is formed. \therefore the "rest" follows the "chain mech".

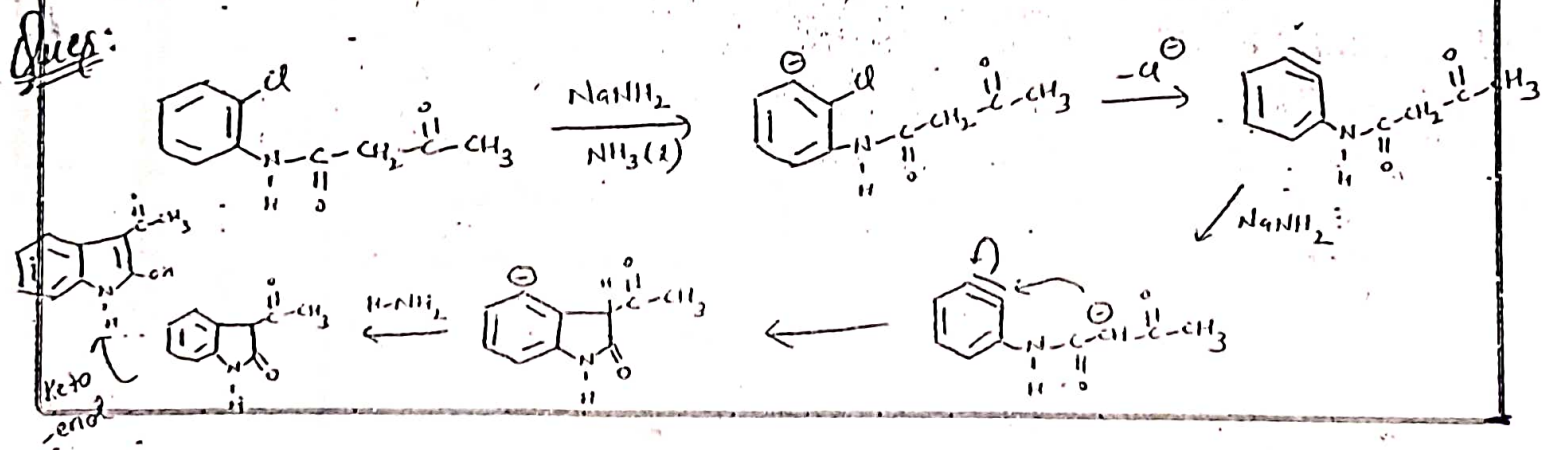
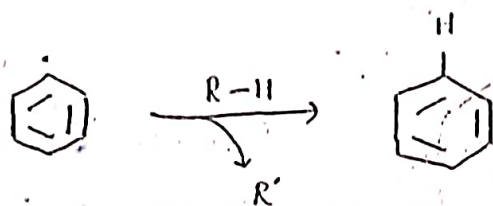
This type of mech" can be proposed for the substrates like aryl iodides.



Radical-Nucleophilic Aromatic Substitution or $S_{RN}1$ is a type of subⁿ reactⁿ in which a certain substituent on an aromatic compound is replaced by a nucleophile through an intermediary free radical species.

Termination Step:

The phenyl radical can abstract any loose proton from R-H forming anene



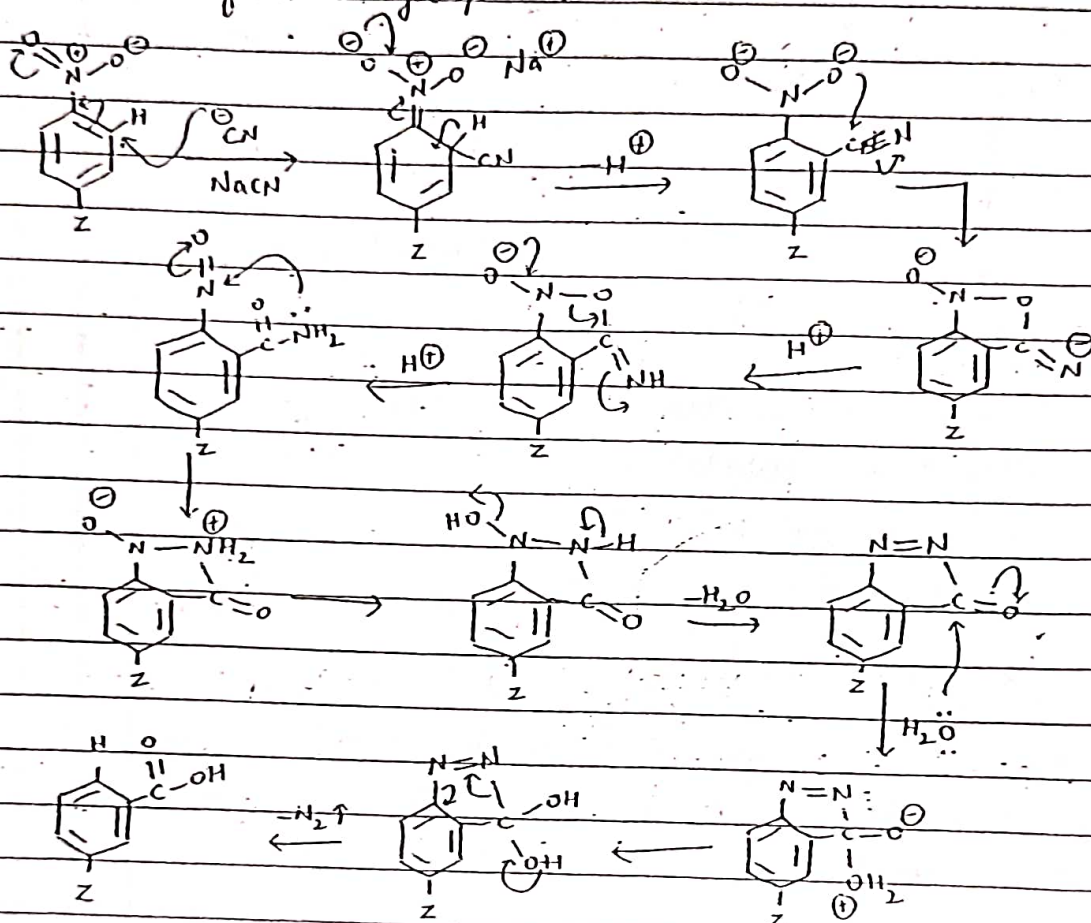
Non Richter Rearrangement

OR

Hydro-de-nitro-cine-substitution

The treatment of aromatic compounds with cyanide ion to afford aromatic carboxylic acid is known as Von Richter Rearrangement.

In this reacⁿ, carboxylic group enters with substitution with the removal of nitro group.



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