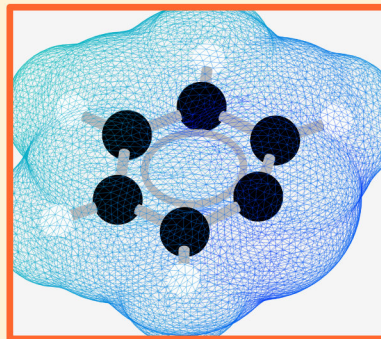


HIGHLIGHTS

- Nucleophilic aromatic substitution of a suitably functionalized arene ring (addition-elimination).
- Substitution via an aryne intermediate (elimination-addition).
- Substitution of a diazonium salt (nitrogen gas as leaving group) by an ionic mechanism.
- Substitution of a diazonium salt (nitrogen gas as leaving group) by a radical mechanism.



Substituted benzene rings are normally considered electron rich. The π cloud of delocalized electrons is ready to attack a suitably activated electrophile, and the classic reactions of aromatic rings are electrophilic aromatic substitution. But, in certain situations, it is possible to reverse this reactivity, and attack a benzene ring with a nucleophile. This can be an effective method to functionalize an arene ring. There are four reactions that are routinely described as nucleophilic aromatic substitution, and are summarized here. The first is S_NAr or nucleophilic aromatic substitution, and it requires that the arene is activated by powerful electron withdrawing groups correctly positioned relative to a leaving group. The second requires a strong base to form an aryne intermediate. The last two substitute the phenomenal leaving group, nitrogen by either an ionic or radical mechanism. Full details are in other handouts - this is just the summary.

CHEMISTRY CLASSICS

NUCLEOPHILIC AROMATIC SUBSTITUTION

SUMMARY

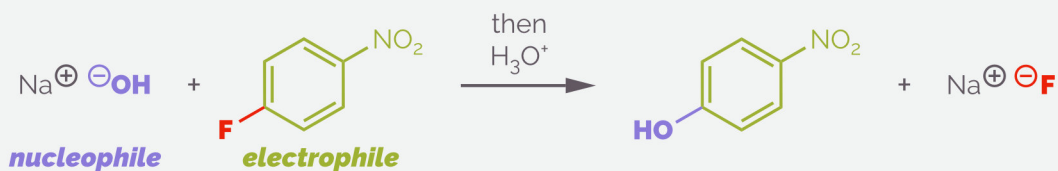


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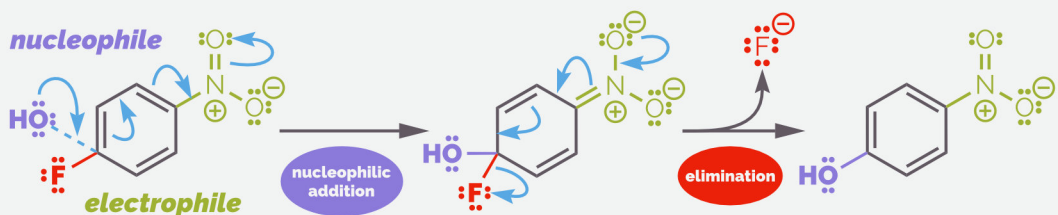


Nucleophilic Aromatic Substitution Summary

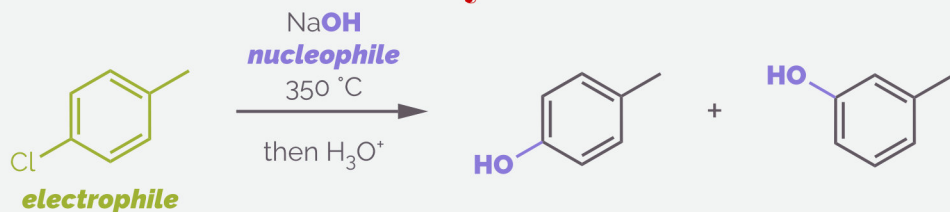
1. Nucleophilic aromatic substitution



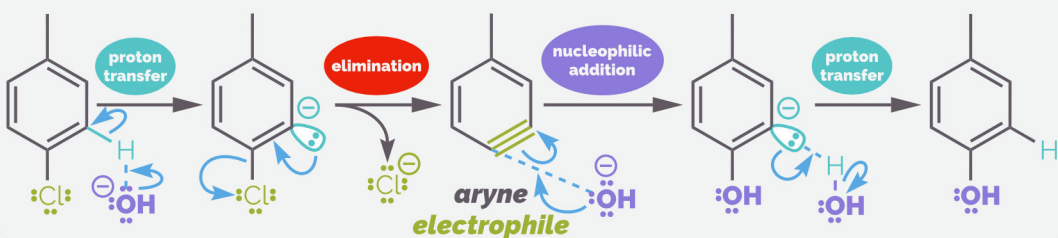
Requirements: Electron poor aromatic ring with EWG *ortho* or *para* to leaving group
Nucleophiles: R_2NH , N_3^- , RO^- , RS^- , NC^-
Notes: addition-elimination mechanism, stabilization of anionic intermediate vital



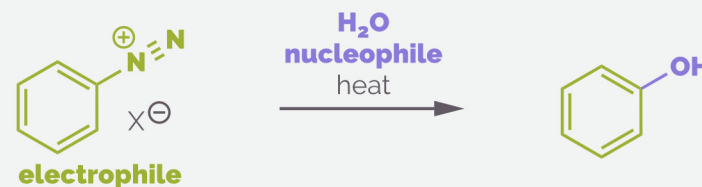
2. Substitution via an aryne intermediate



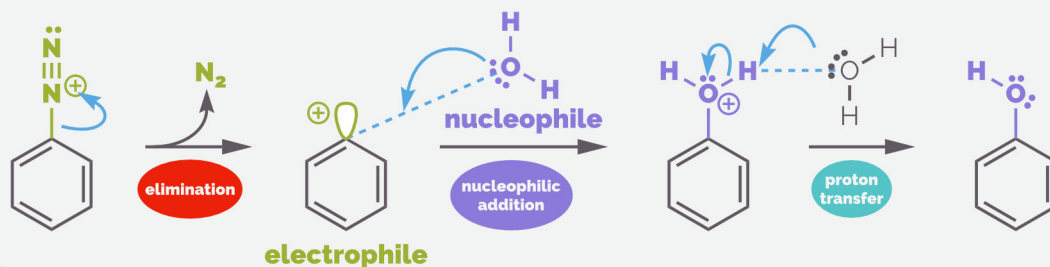
Requirements: Nucleophile is a strong base
Nucleophiles: R_2N^- , RO^-
Notes: aryne intermediate leads to mixture of regioisomers



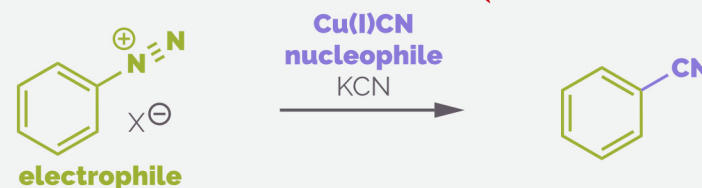
3. Diazonium salt substitution (ionic reaction)



Requirements: Diazonium salt (normally made from aryl amine)
Nucleophiles: N, O, H and halides
Notes: Diazonium salt moderately stable, diazotization of anilines allows formation



4. Diazonium salt substitution (radical reaction)



Requirements: Diazonium salt and a copper(I) reagent (or other reductant)
Nucleophiles: halides and nitrile
Notes: Aryl radicals can be problematic

