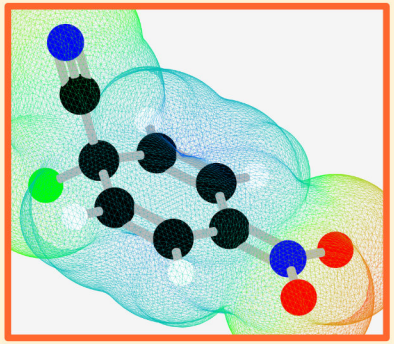
HIGHLIGHTS

- Addition-Elimination mechanism for nucleophilic aromatic substitution (S_NAr).
- Substrate must meet three criteria that:
  - Electron withdrawing group that allows electrons to flow out of the ring acts as an activating group.
  - An electron withdrawing group that can act as a leaving group.
  - The leaving group and the activating group must be either *ortho* or *para* to each other.
- Nucleophiles are normally nitrogen or oxygen-based although the cyanide anion can also be used.



Normally, aromatic rings are considered electron rich and are good nucleophiles in the classic electrophilic aromatic substitution (S_EAr) reaction. There are three common ways of reversing this normal reactivity, and permitting the ring to be attacked by a nucleophile. Each of these methods has a different mechanism. The first version of nucleophilic aromatic substitution (S_NAr) involves an addition-elimination mechanism. Before it is possible, the benzene derivative must meet certain criteria. First, the benzene ring must be loaded with electron withdrawing groups. Ideally, at least one of these should allow electrons to flow out of the ring. Secondly, there must be an electron withdrawing group that can act as a leaving group. Thirdly, this leaving group must be either *ortho* or *para* to the activating group. This requirement leads to a stable anionic intermediate with the electrons outside the ring.

CHEMISTRY CLASSICS

NUCLEOPHILIC AROMATIC SUBSTITUTION

ADDITION-ELIMINATION

Nucleophilic Aromatic Substitution 1

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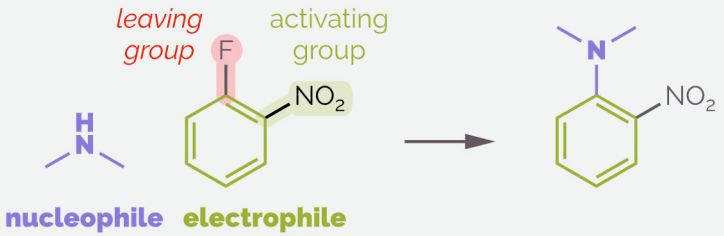
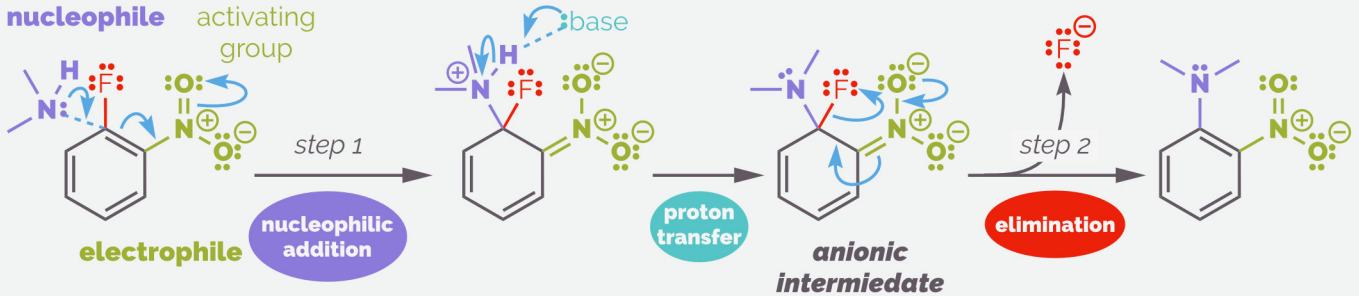
1. Introduction

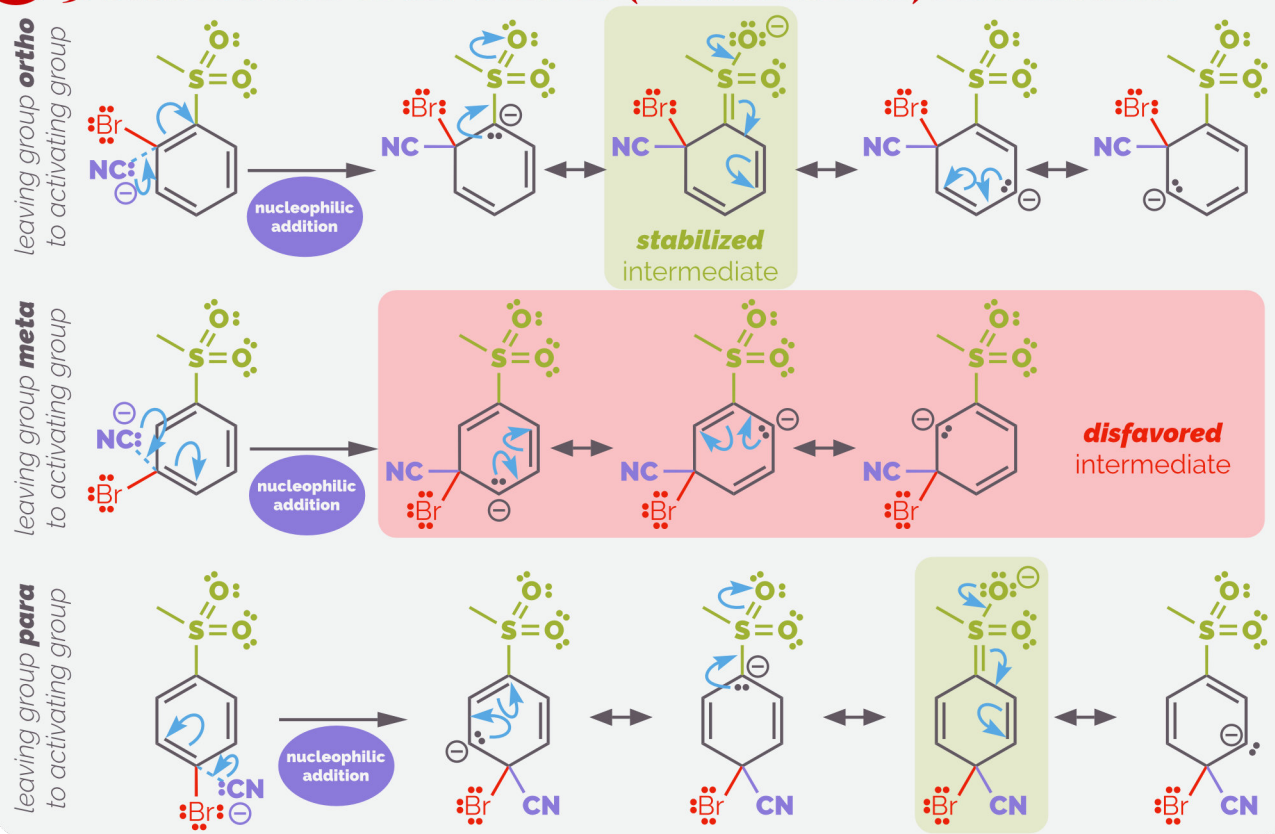


Must be electron withdrawing activating group EWG
Must be leaving group LG
Must have correct placement of EWG & LG

2. General mechanism - Addition-elimination version of S_NAr

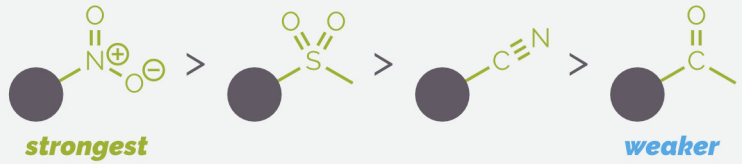


3. Stabilization of the anionic (Meisenheimer) intermediate

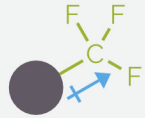


4. Criteria

1. activating group
normally allows electrons delocalized outside of aromatic ring



strong inductive effect also works



2. leaving group
normally a halide - fluoride best as it activates aromatic ring
sulfonate esters also work

3. position of leaving group & activating group
must be ortho or para (see box 3)

4. nucleophiles
oxygen, nitrogen, sulfur or cyanide are the most common