Aromatic Nucleophilic Substitution Reaction

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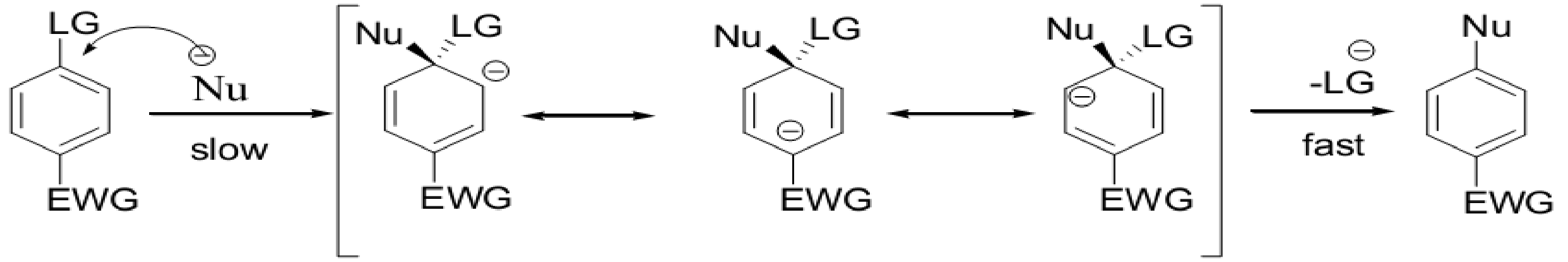
Principles

There are **four principal mechanisms** for aromatic nucleophilic substitution which are similar to that of aliphatic nucleophilic substitution. **(SN1, SN2, SNi, SET** Mechanism)

1. SNAr Mechanism- addition / elimination



CF_3, CN, CHO, COR, COOH, Br, Cl, I

Common Activating Groups for NAS

Step [1] Addition of the nucleophile (:Nu–) to form a carbanion

Addition of the nucleophile (:Nu–) forms a resonance-stabilized carbanion with a new C – Nu bond— **three resonance structures can be drawn.**

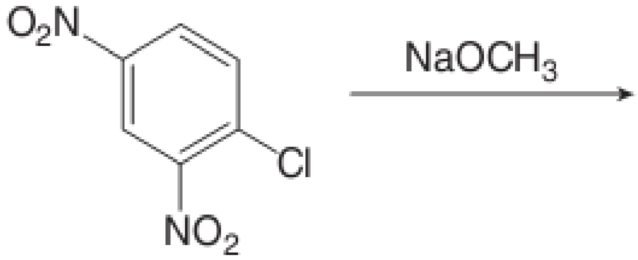
- Step is rate-determining
- Aromaticity of the benzene ring is lost

Step [2] loss of the leaving group re-forms the aromatic ring.

- This step is fast because the aromaticity of the benzene ring is restored.

Draw the products of each reaction.

a.



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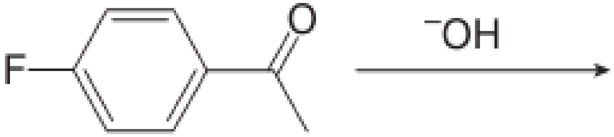

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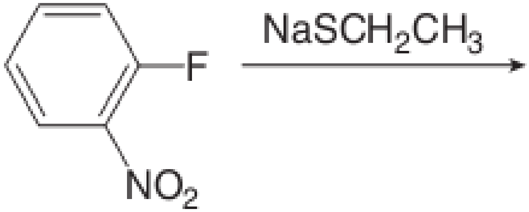
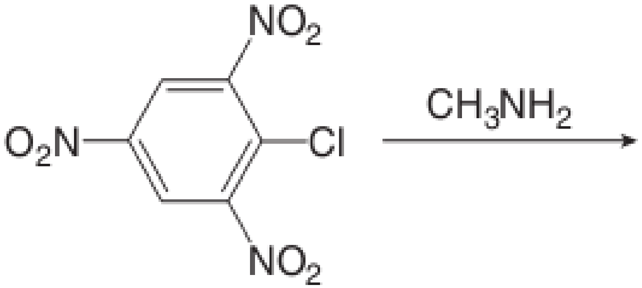


d.



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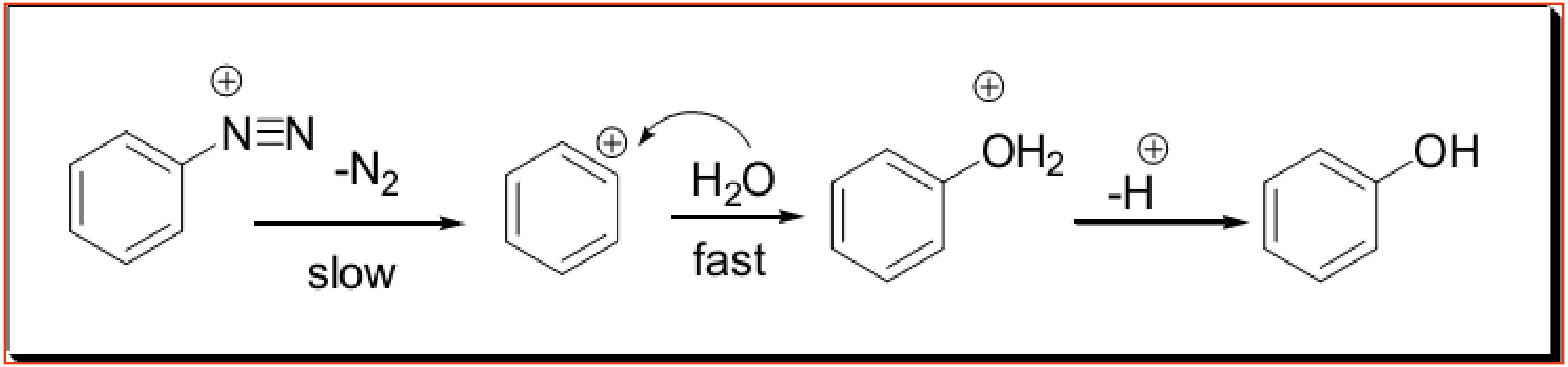
Explain why a methoxy group (CH_3O) increases the rate of electrophilic aromatic substitution, but decreases the rate of nucleophilic aromatic substitution.

2.ArSN1 Mechanism- elimination /addition



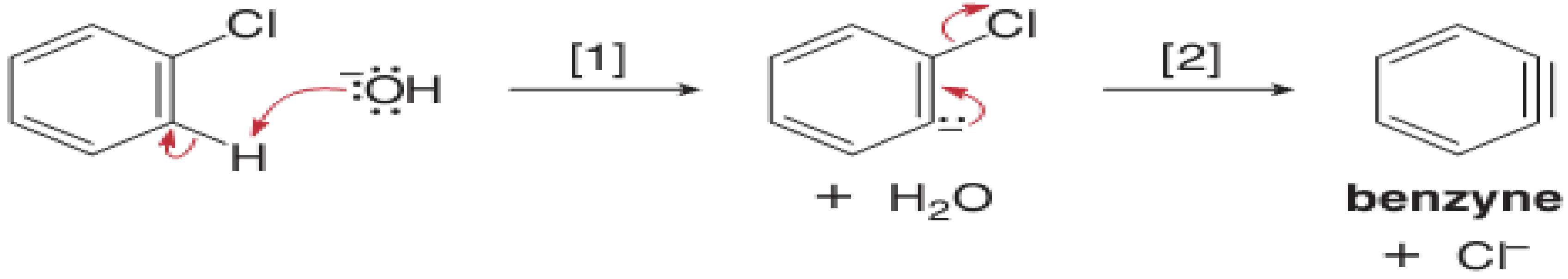
- This mechanism operates in the reaction of diazonium salts with nucleophiles.

- <u>The driving force resides in the strength of the bonding in the nitrogen molecule that makes it a particularly good leaving group.</u>

3.Benzyne Mechanism- elimination /addition

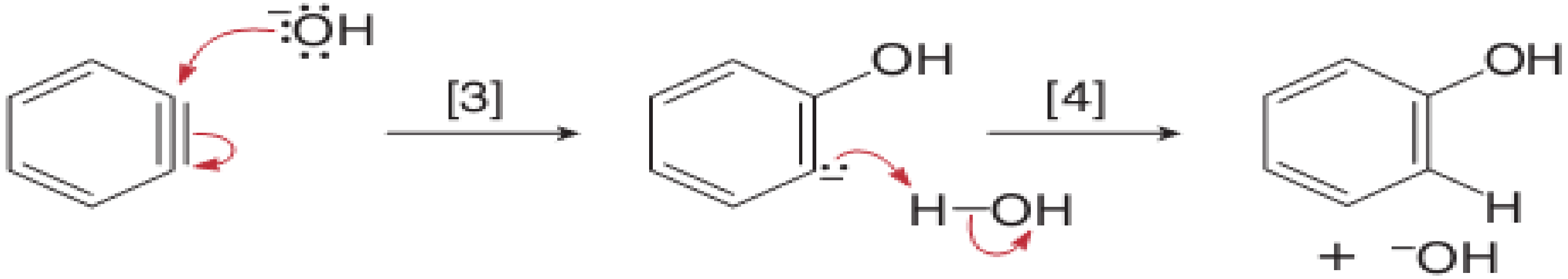
Step [1] Elimination of HX to form benzyne

Elimination of H and X from two adjacent carbons forms a reactive benzyne intermediate



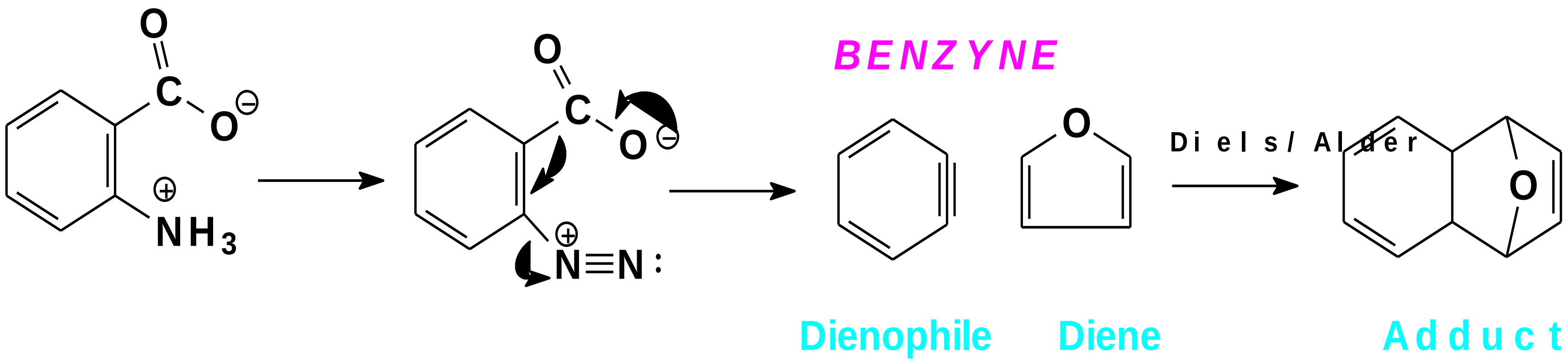
Step [2] Nucleophilic addition to form the substitution product

Addition of the nucleophile (–OH in this case) and protonation form the substitution product

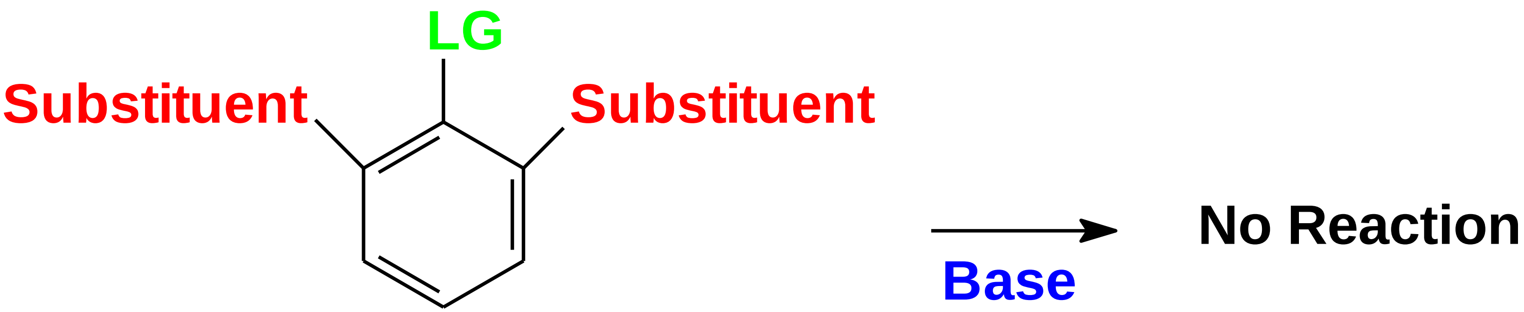


Evidence for the Benzyne Mechanism

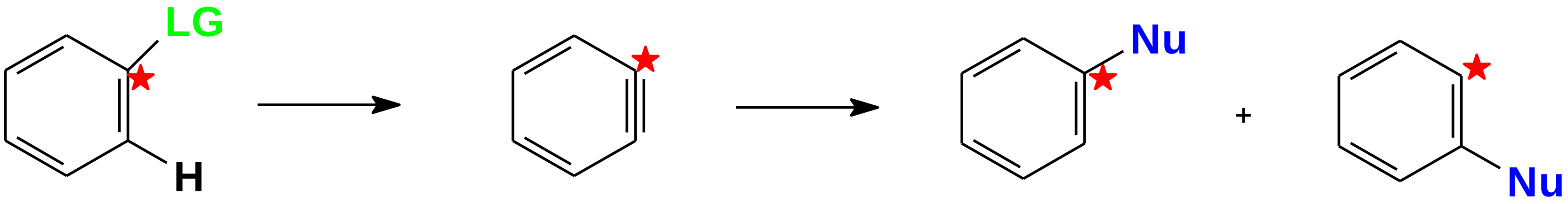
Trapping in Diels/Alder Reaction

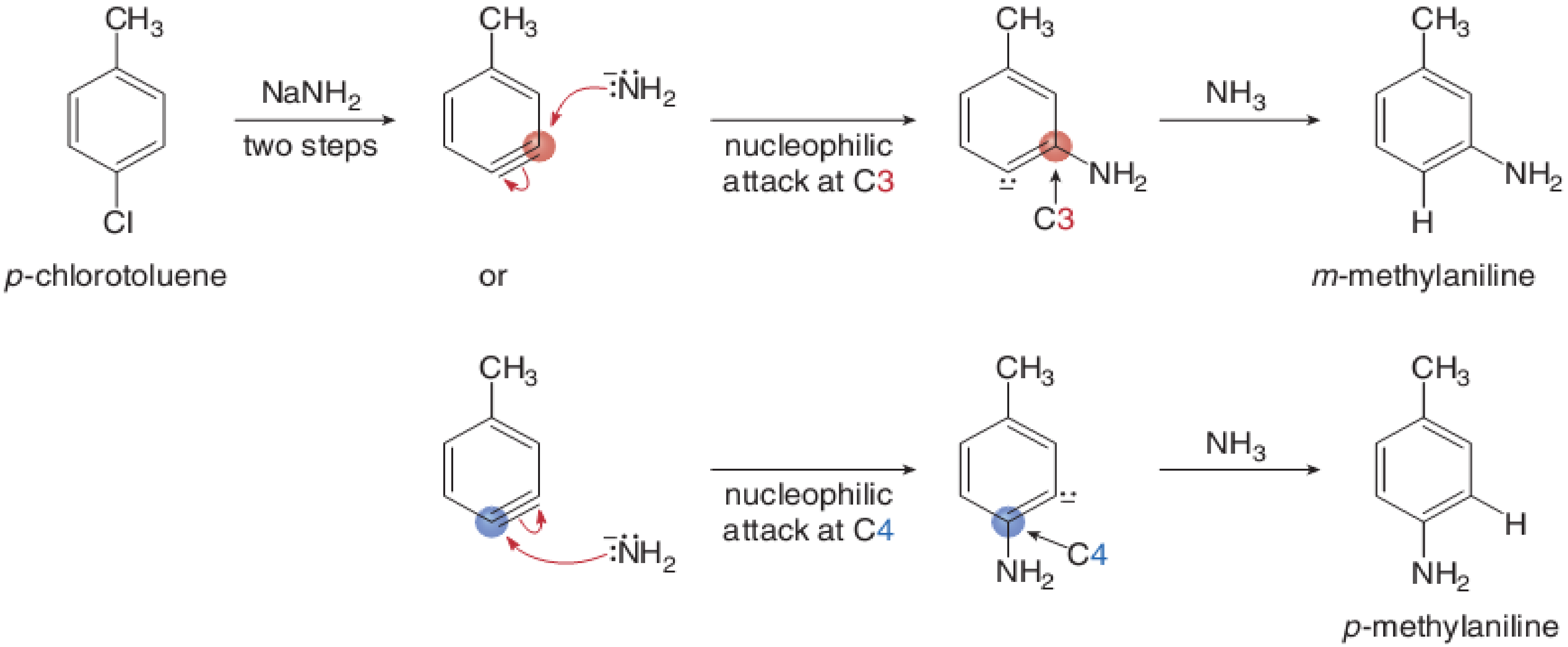


Substrate Modification – absence of a hydrogens



Isotopic Labeling



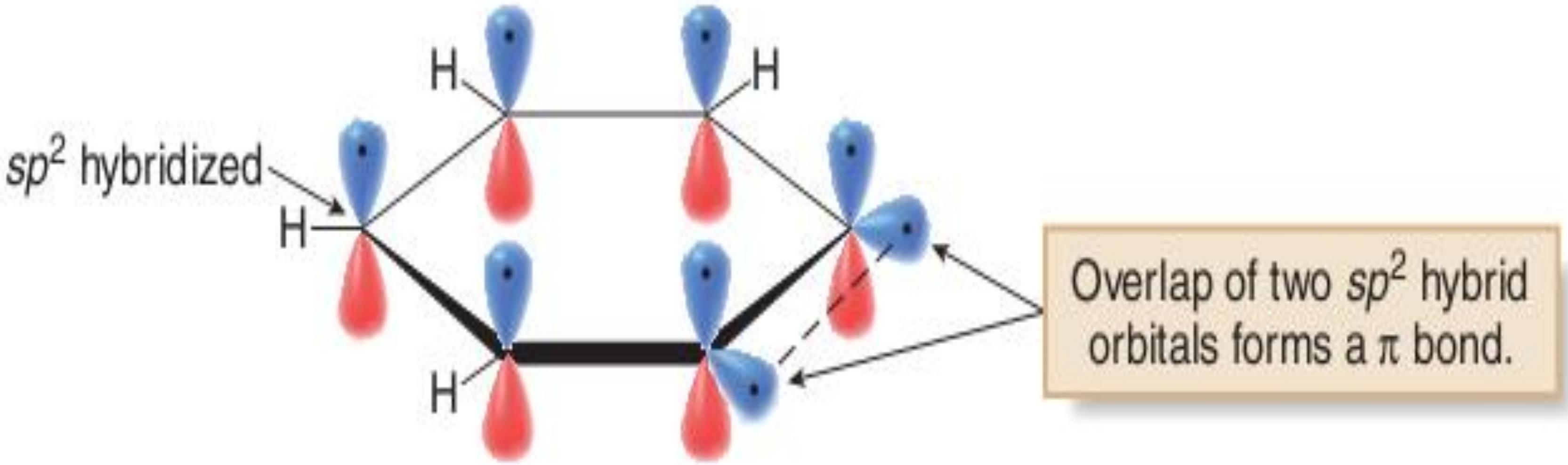


Structure of Benzyne

- **The σ bond is formed by overlap of two sp2 hybrid orbitals.**

- **One π bond is formed by overlap of two p orbitals perpendicular to the plane of the molecule**

- **Second π bond formed by the side-by-side overlap of sp2 hybrid orbitals, not p orbitals.** This π bond, located in the plane of the molecule, is extremely weak

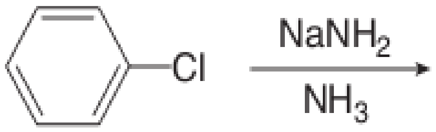


Overlap of two sp^2 hybrid orbitals forms a π bond.

Problems

Draw the products of each reaction.

a.



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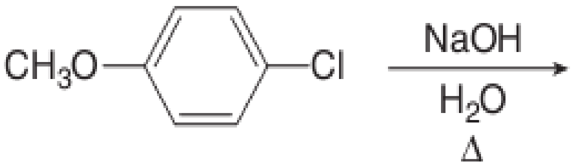

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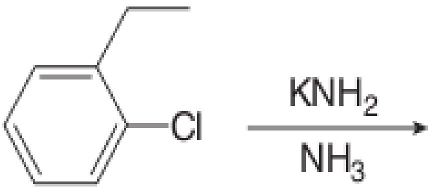

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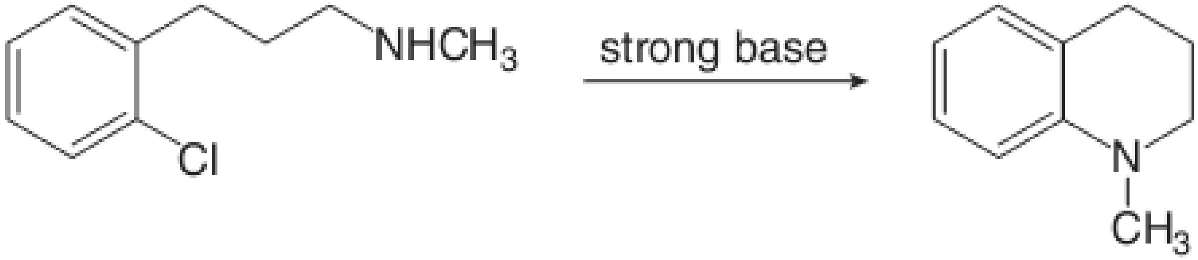
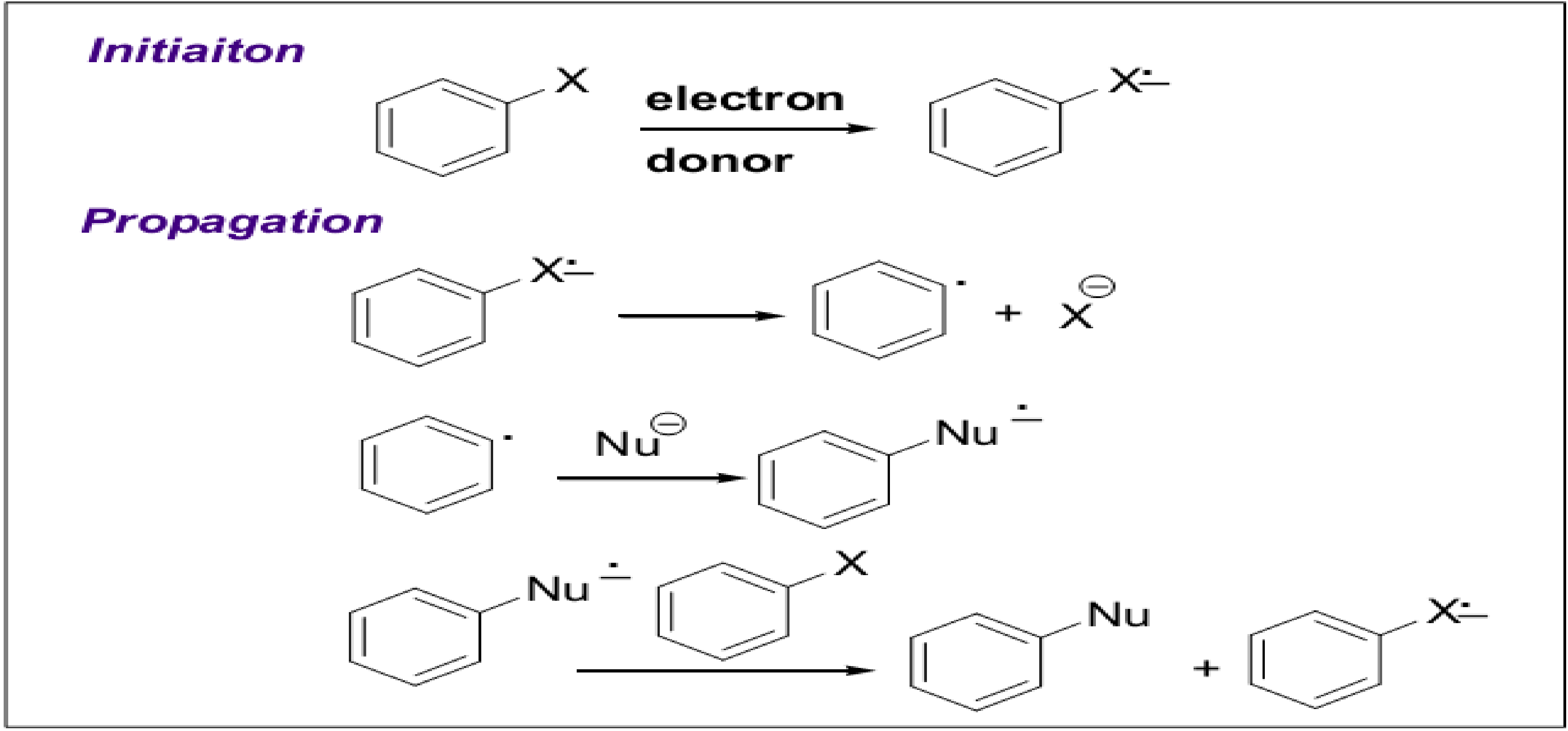
Draw all products formed when m-chlorotoluene is treated with KNH_2 in NH_3

Draw a stepwise mechanism for the following reaction.

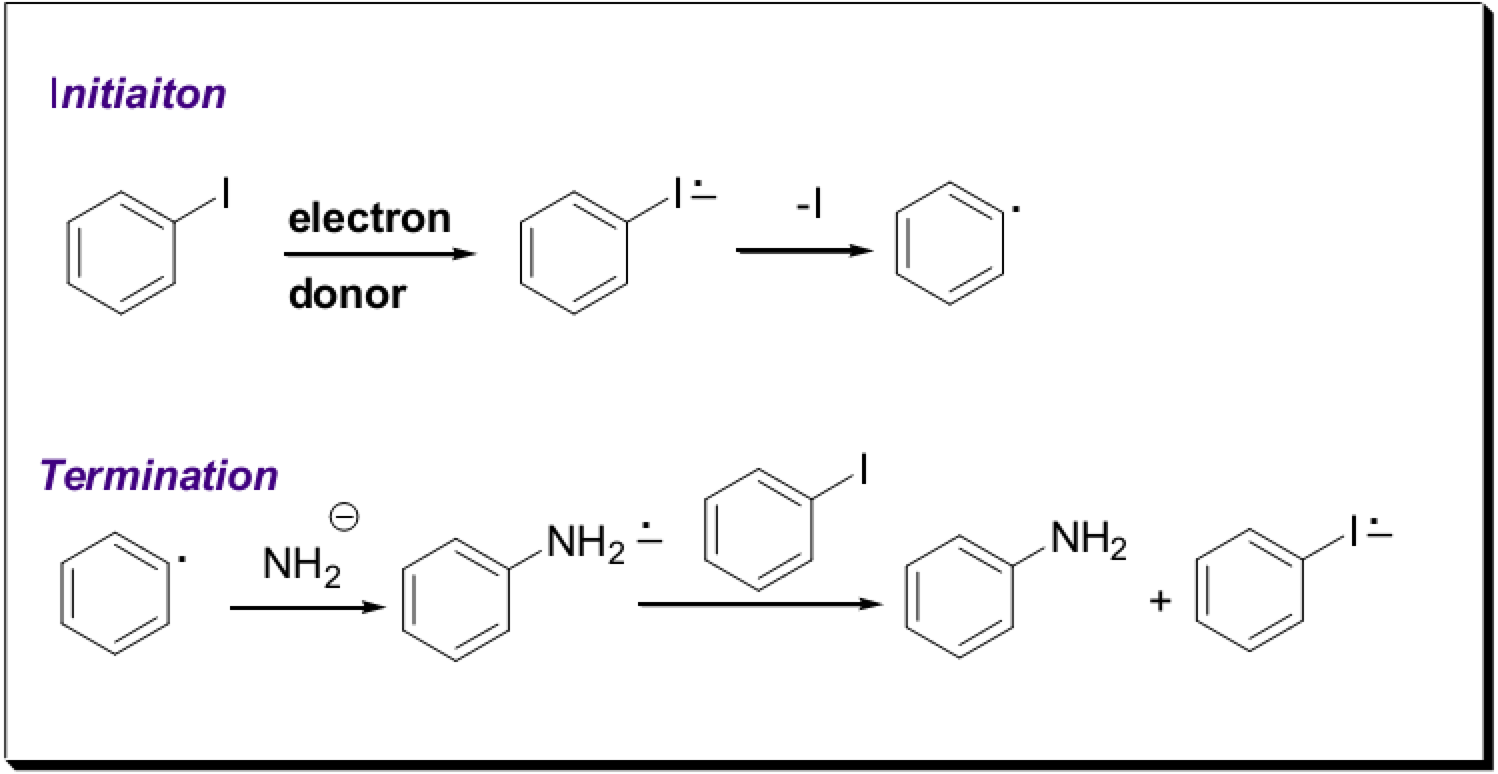


4. $ArS_{RN}1$ Mechanism

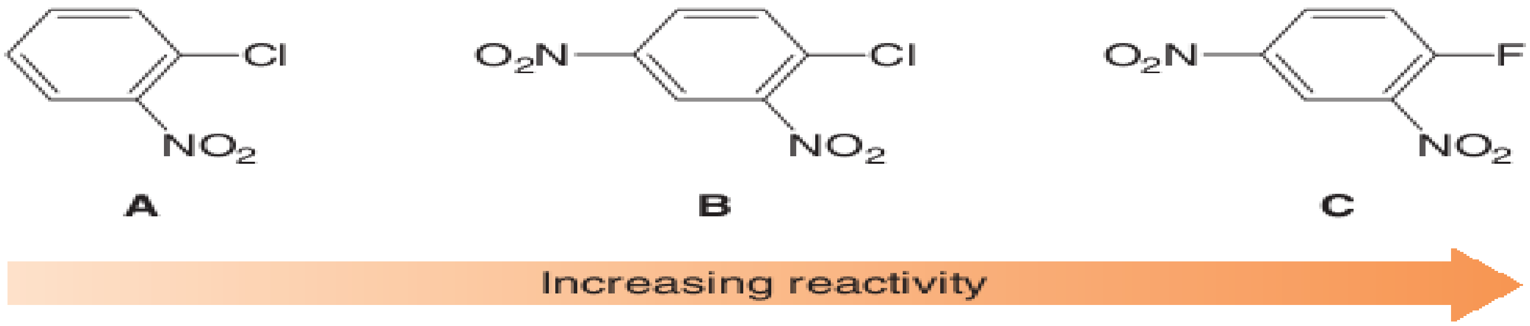
Unactivated aryl halides proceed nucleophilic substitution with typically enolates, amide ion and thiol anion via a chain reaction involving anion radicals in that the initiation step is an electron transfer.



The initiation of the reaction is generally either by solvated electron (sodium in liquid ammonia) or with photochemical excitation in that the nucleophile is the electron donar.



- **Reactivity effect of substrate structure**
- **Reactivity effect of leaving group**
- **Reactivity effect of attacking nucleophile**

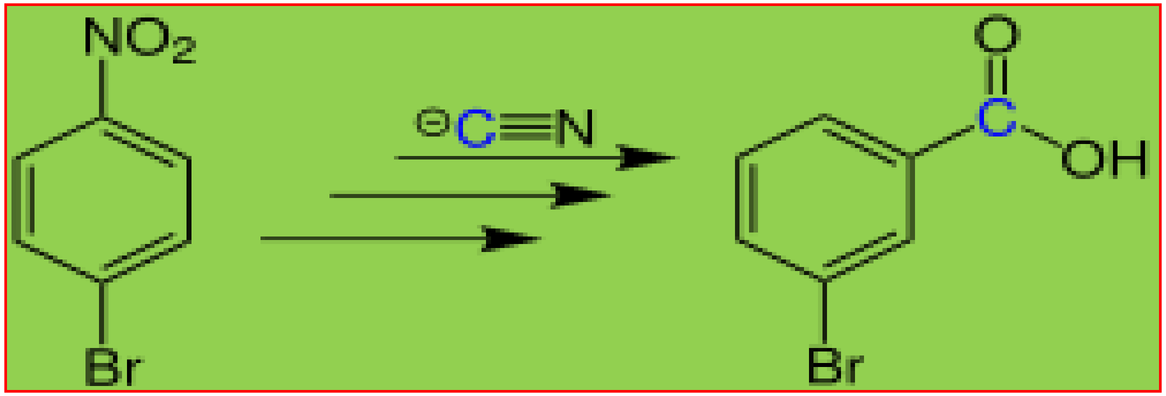


Increasing the electronegativity of the halogen increases the reactivity of the aryl halide. A more electronegative halogen stabilizes the intermediate carbanion by an inductive effect, making aryl fluorides (ArF) much more reactive than other aryl halides, which contain less electronegative halogens.

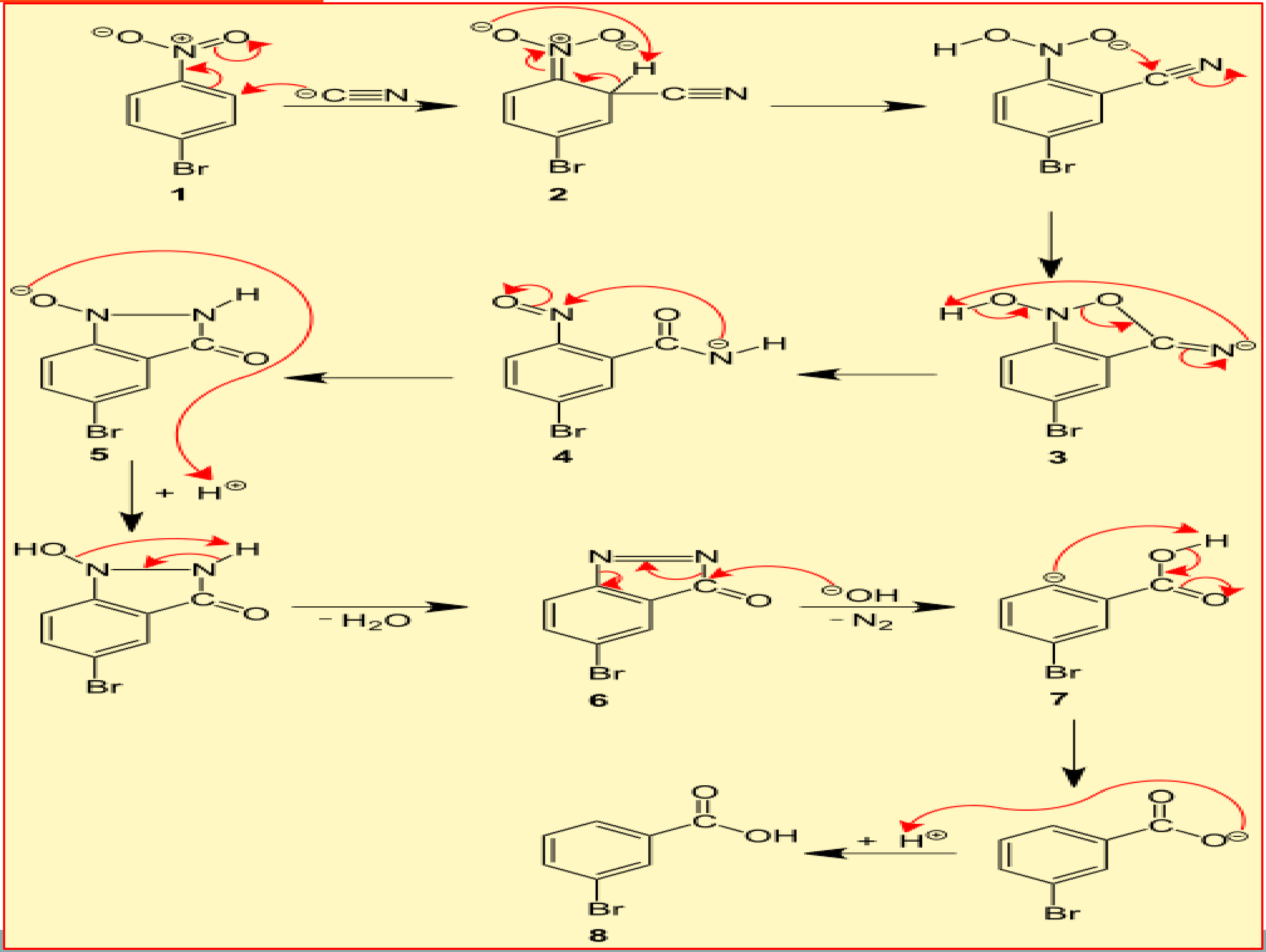
Increasing the number of electron-withdrawing groups increases the reactivity of the aryl halide. Electron-withdrawing groups stabilize the intermediate carbanion, and by the Hammond postulate, lower the energy of the transition state that forms it.

• The Von Richter Rearrangement

- When aromatic nitro compound are treated with cyanide ion, then nitro group is displaced & carboxylic group entereds always ortho to displaced group.
- This reaction is cin substitution
- Best results are obtained when EWG is present at o/p
- Reaction gives a small yeild. (-20%)

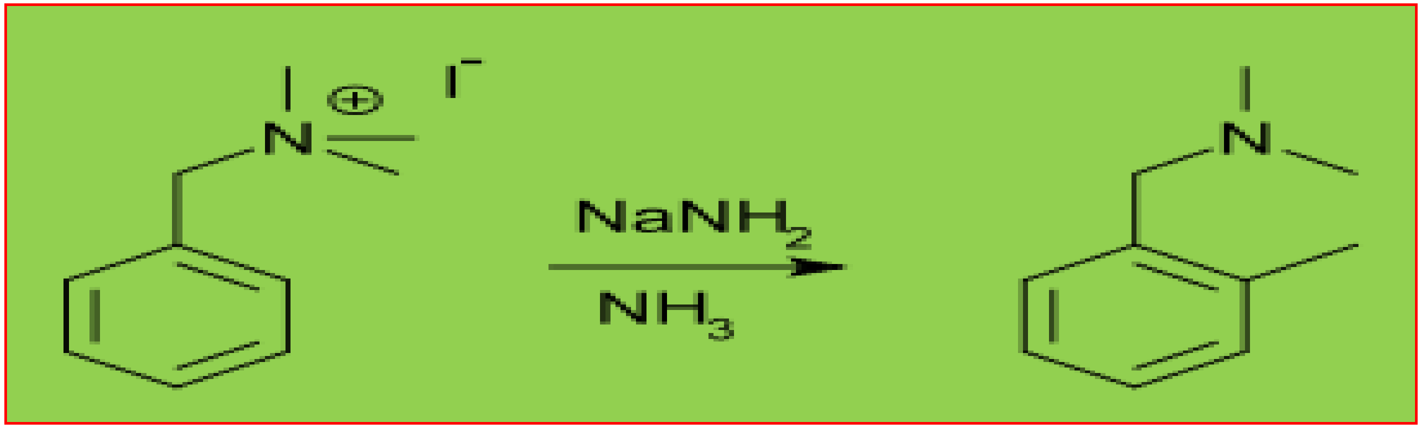


Mechanism

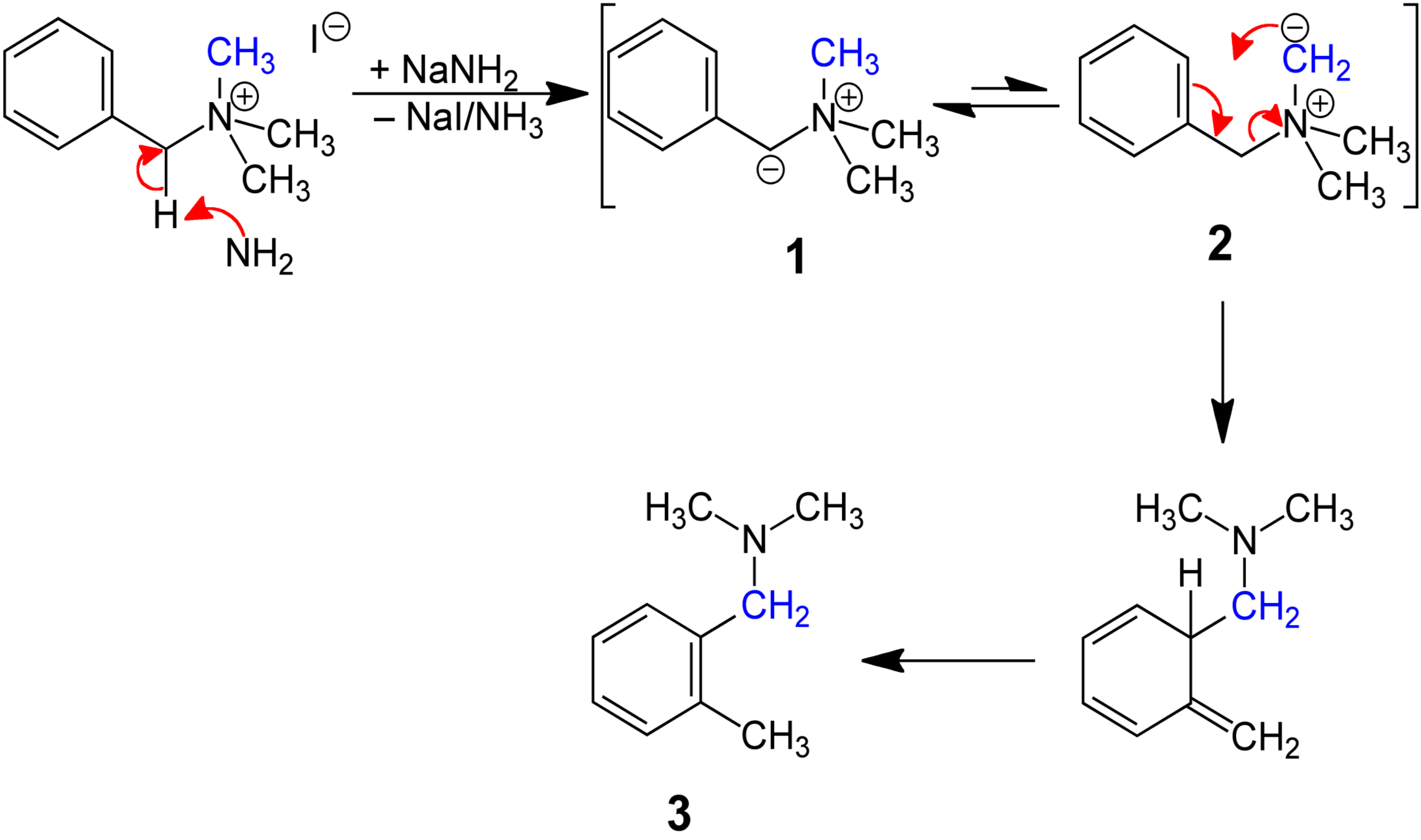


• Sommlet-Hauser Rearrangement

- When benzylic quaternary salt are treated with alkali metal amide then it gives ortho substituted benzylic tertiary amide
- Process is contined untill all ortho position of ring blocked.
- Mechanism is [2,3] sigmatropic rearrangement.
- Benzyllic proton is acedic

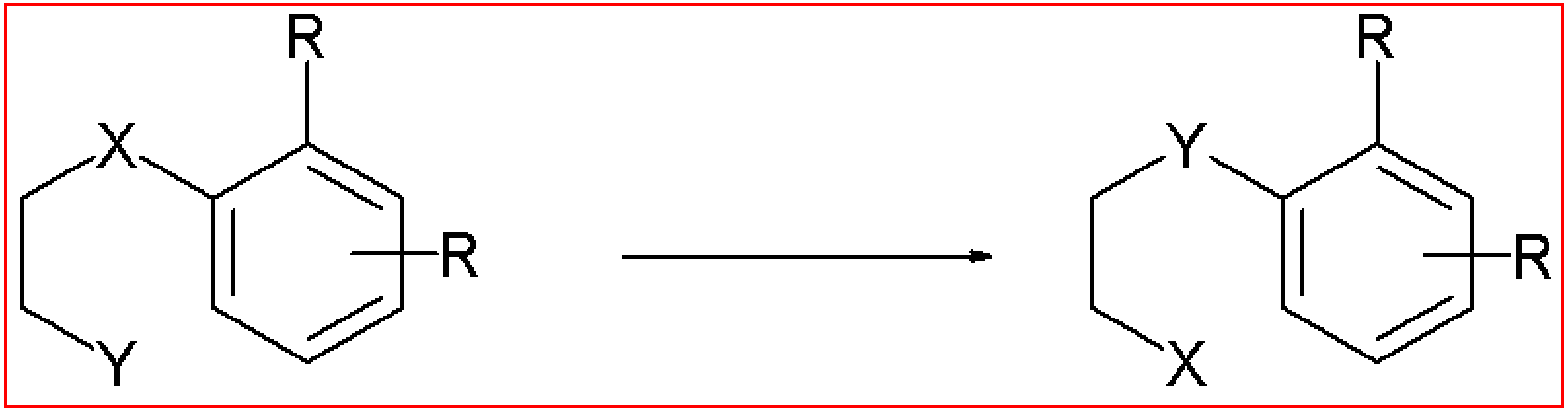


Mechanism

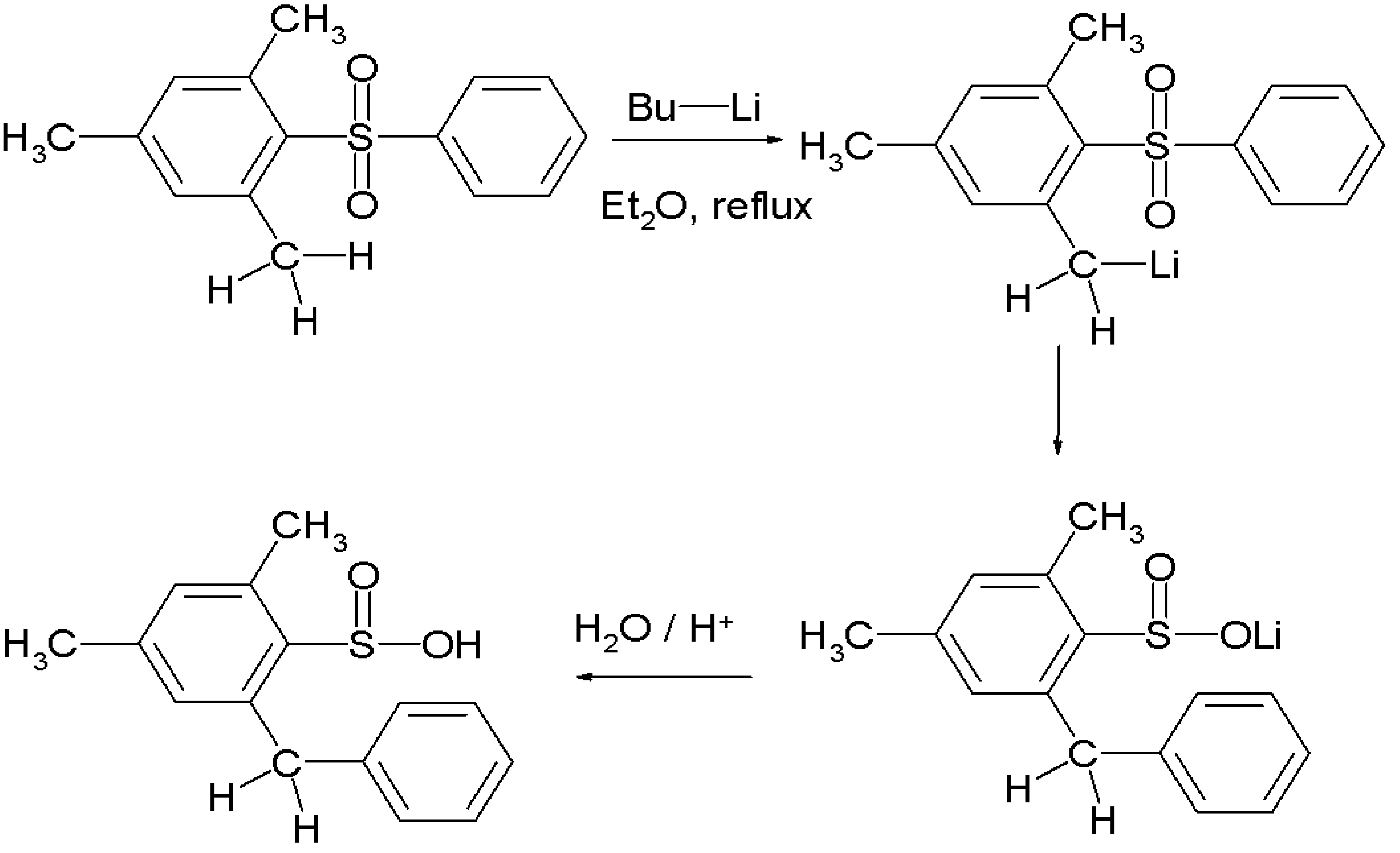


• Smiles Rearrangement

- It is a intramolecular nucleophilic substitution
- EWG o/p to LG favors
- EDG o/p to incoming nucleophile favors



Mechanism



THANK U…. Friends!!

……for your co-operation..