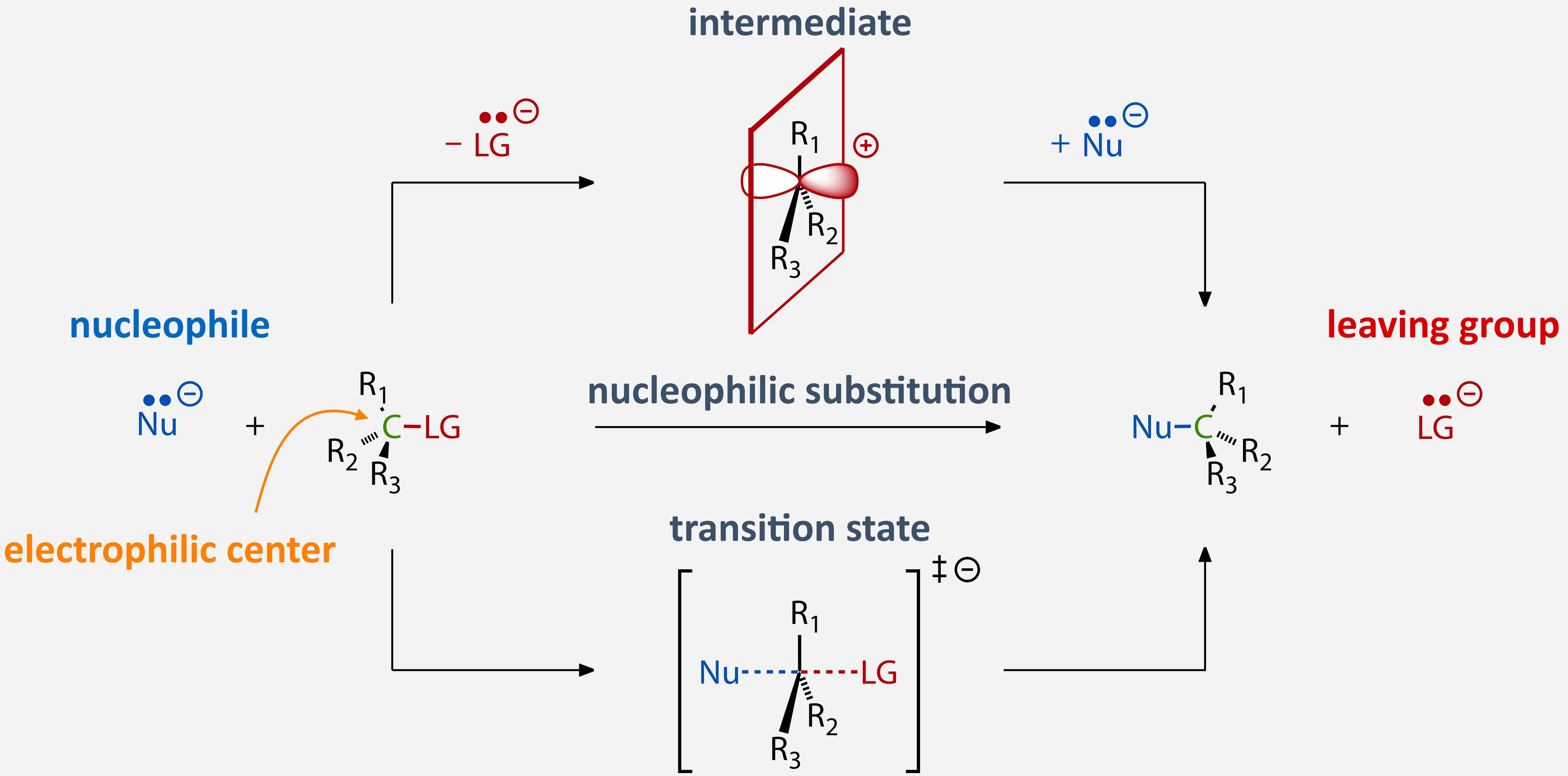
Sandmeyer Reaction

Nucleophilic Substitutions (S_N Reactions)

S_N1 Mechanism: leaving group leaves first (and allows nucleophile to come in subsequently

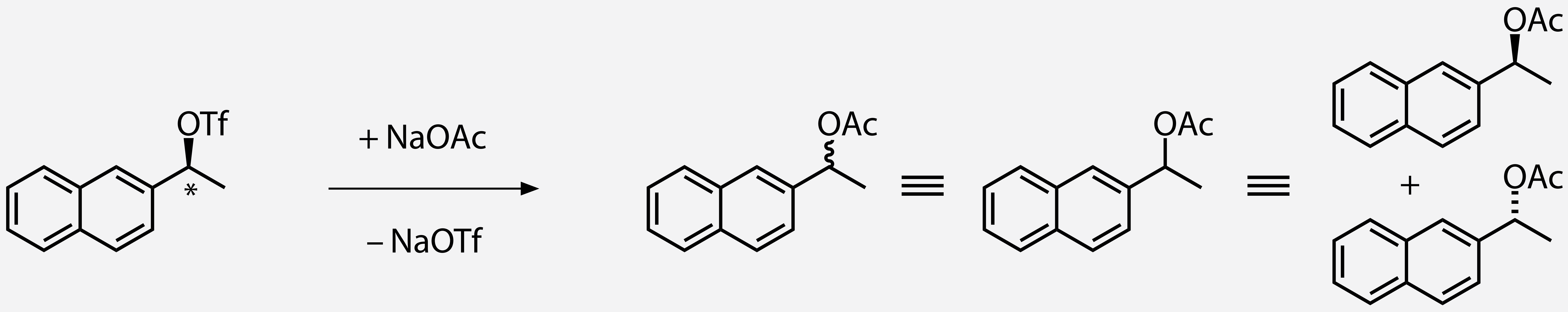


S_N2 Mechanism: nucleophile attacks (and forces leaving group to leave simultaneously)

- **nucleophile (electron pair donor)** reacts at an **electrophilic center (electron pair acceptor)**
- **nucleophile** replaces the **leaving group (which takes an electron pair with it)**

S_N1 or S_N2 Mechanism?

- consider leaving group quality, stabilization of the carbocation, and nucleophile

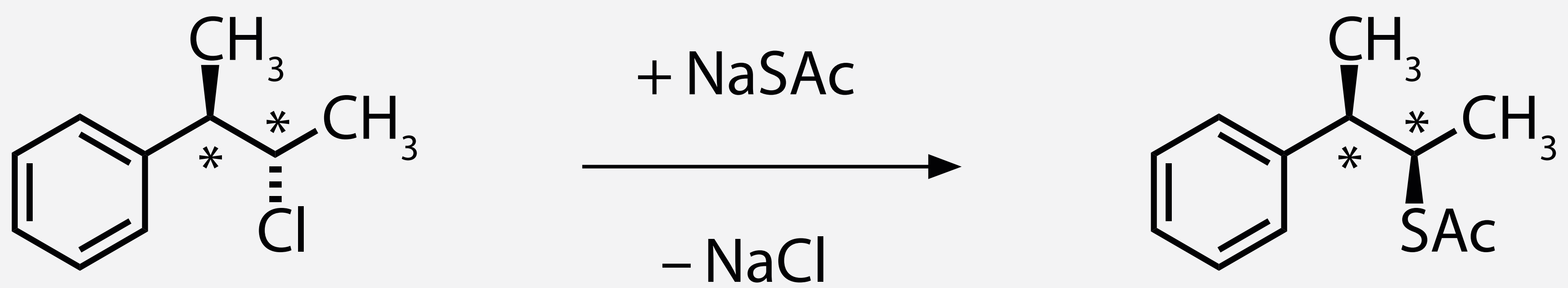


excellent leaving group
well-stabilized carbocation

S_N1

loss of stereochemical information

racemic mixture



non-stabilized carbocation
good nucleophile

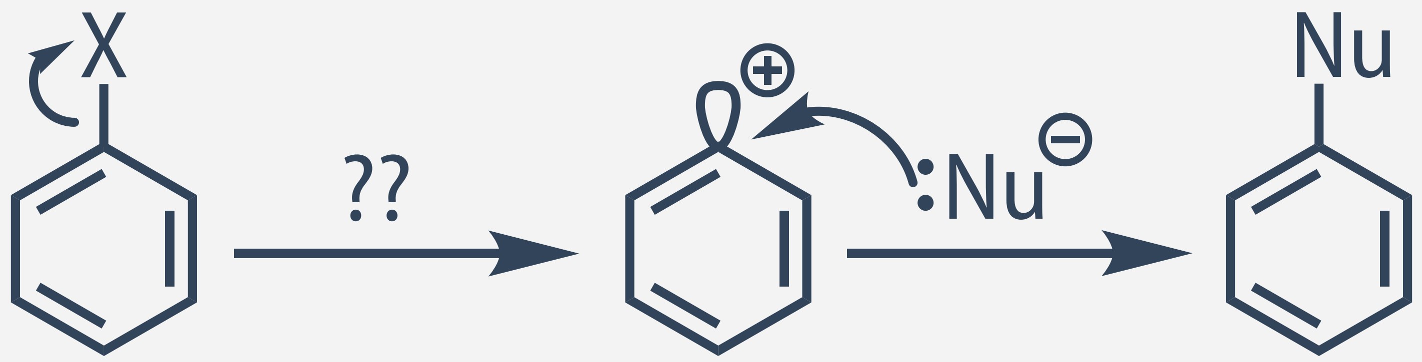
S_N2

inversion of stereoconfiguration

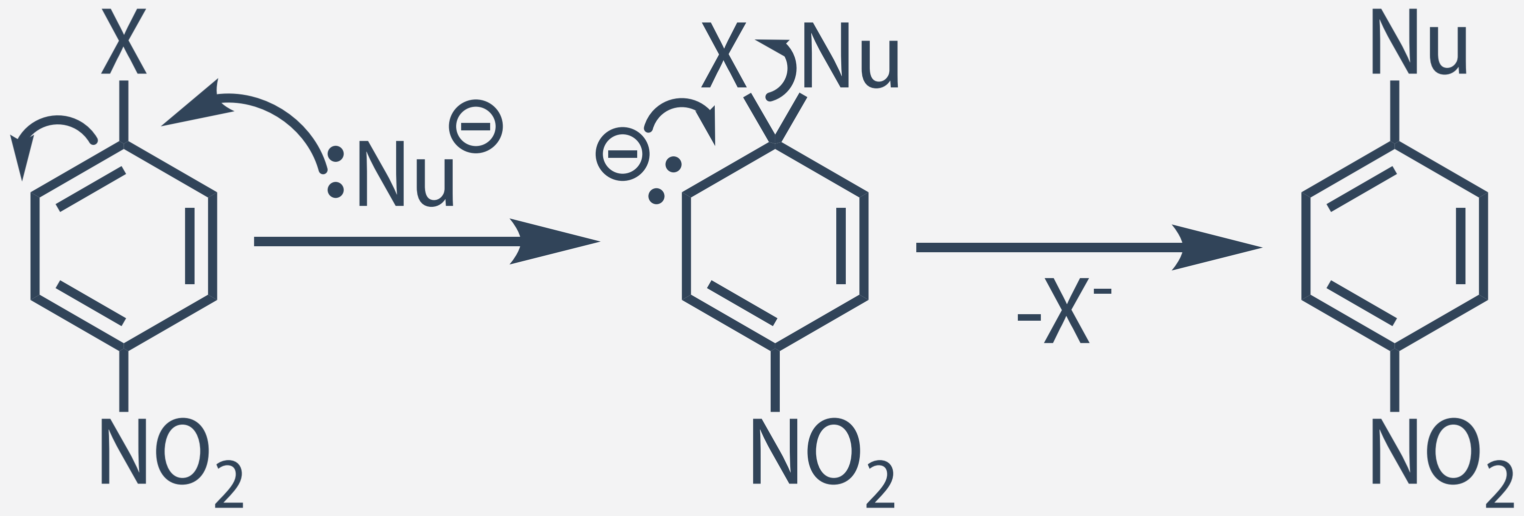
- **consider explicitly the stereochemical consequences (also in nomenclature of the products)**

Nucleophilic Substitution on Aromatic Systems

- typical S_N1 nucleophilic substitution - formation of carbocation intermediate

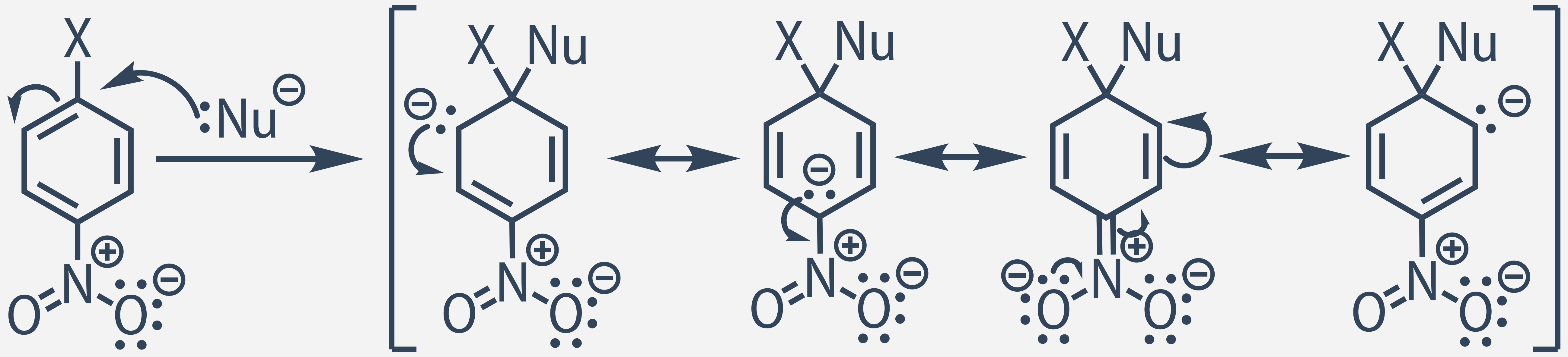


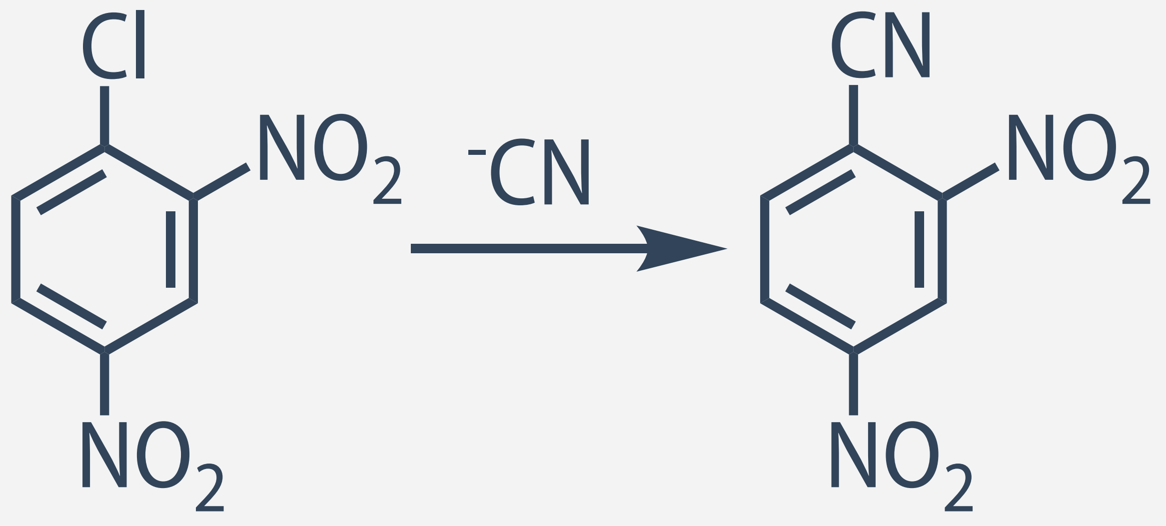
- S_{NAr} - addition-elimination mechanism

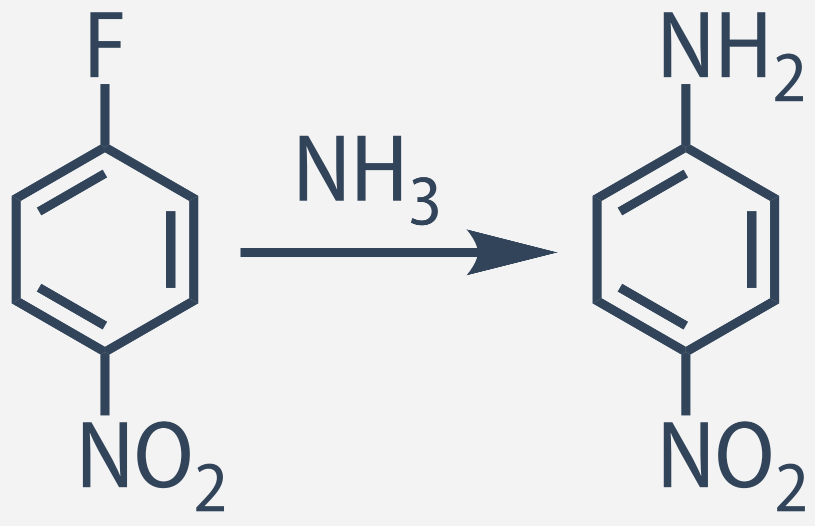


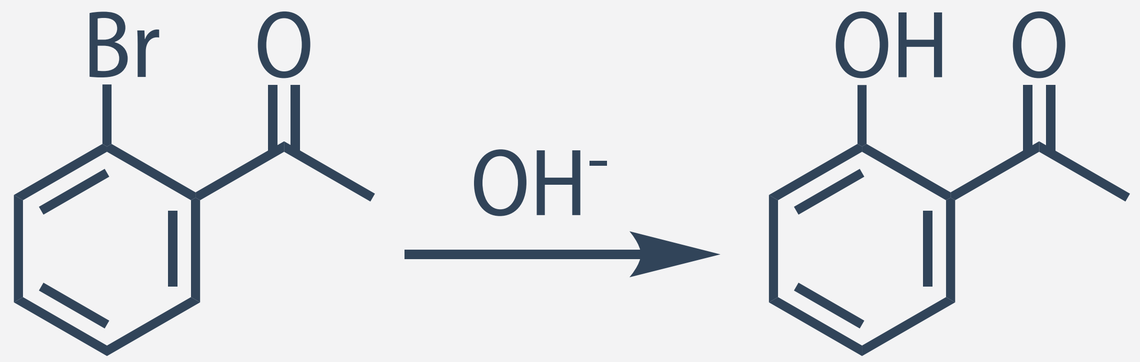
Addition-Elimination Mechanism - S_{NAr}

- the first step is addition of the nucleophile - intermediate stabilized by resonance
- the presence of electron-withdrawing group in *ortho* or *para* position is necessary to stabilize the formed carbanion



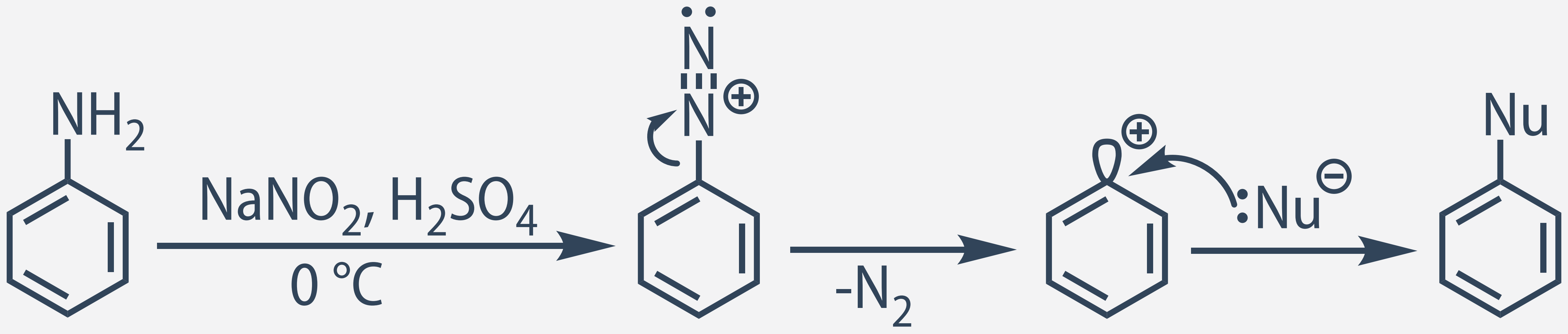


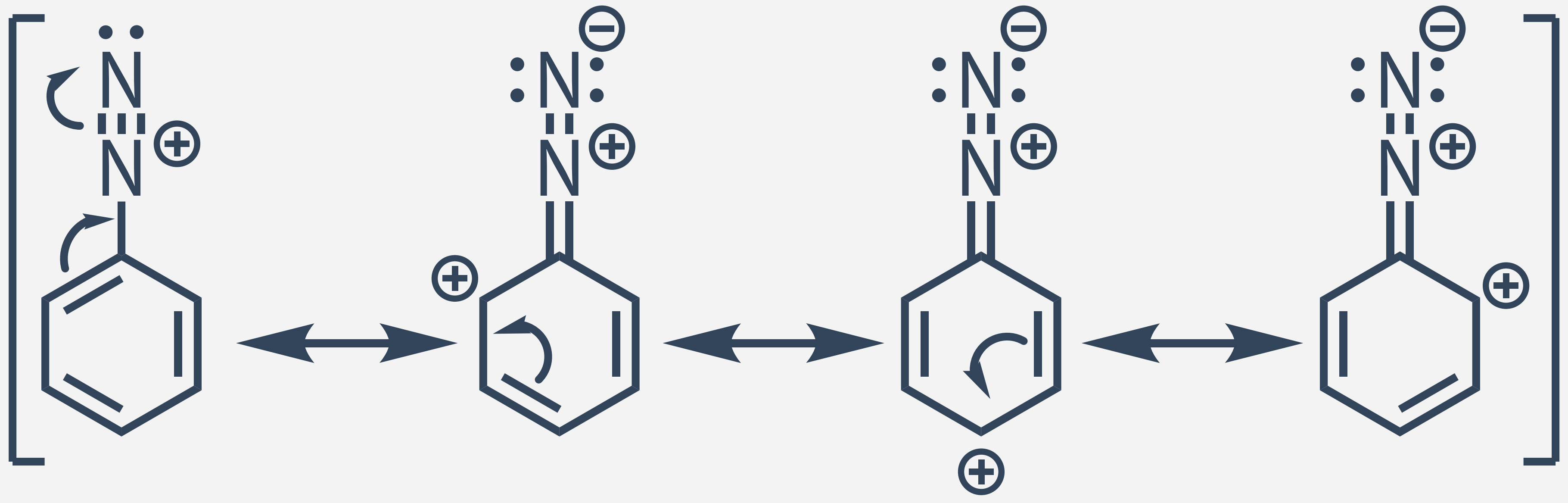




Monomolecular Nucleophilic Substitution on Aromatic Systems - S_N1

- the **best** possible leaving group - nitrogen gas
- conversion of amines to diazonium salts

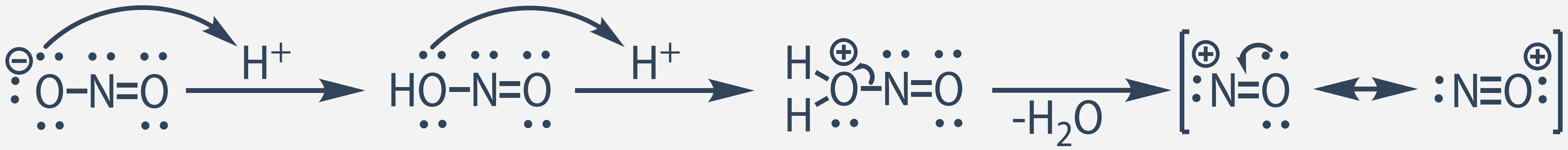




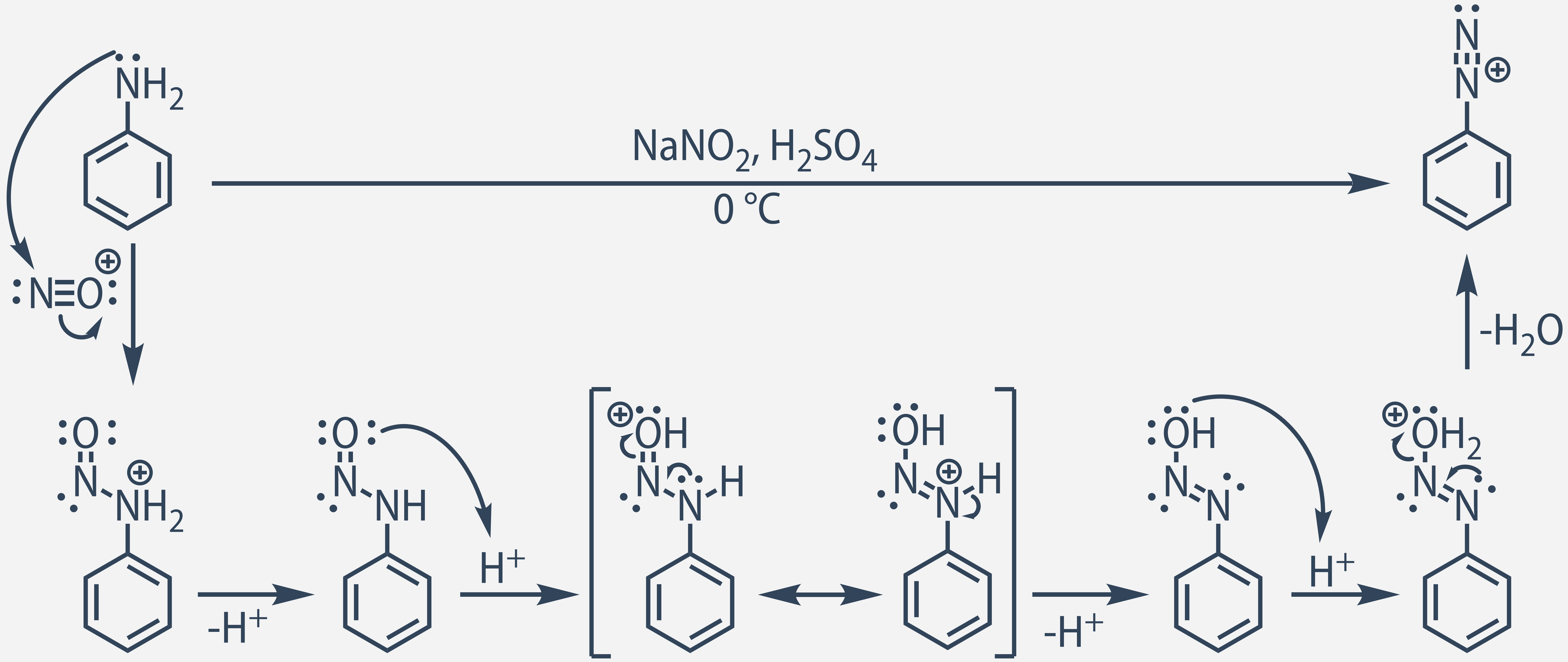
- **aromatic diazonium salts are particularly stable due to resonance**

Diazonium Salt Formation - Mechanism

- formation of nitrosyl (nitrosonium) ion as reactive intermediate

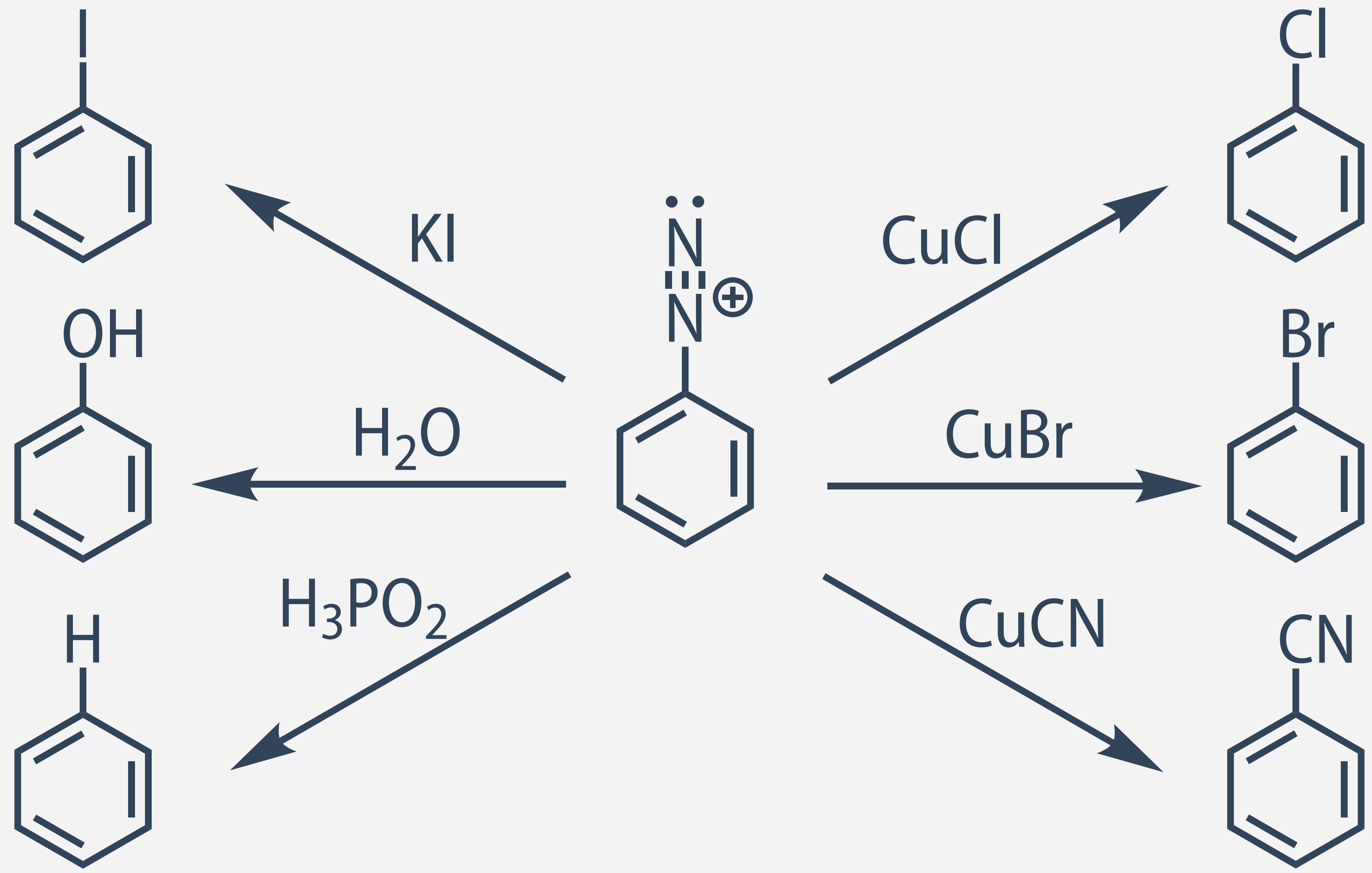


- conversion of amine group to diazonium salt



Monomolecular Nucleophilic Substitution on Aromatic Systems - S_N1

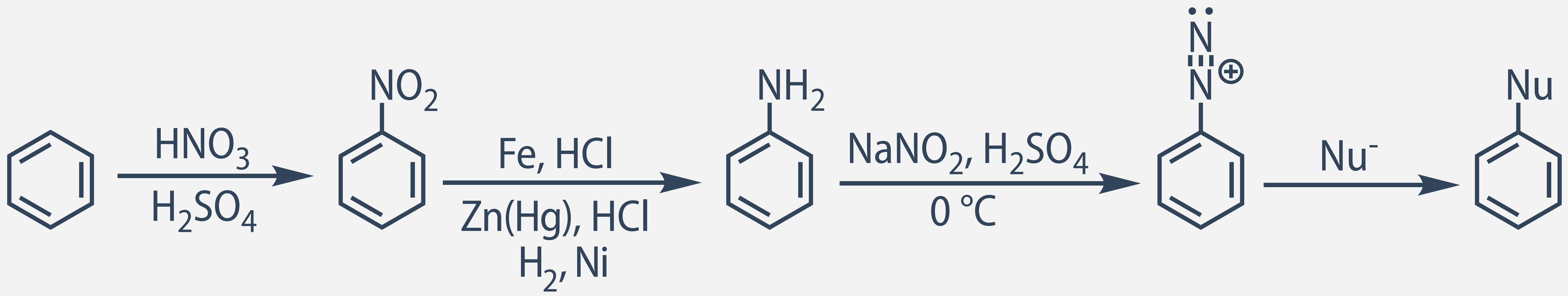
- careful nucleophile choice required for different desired substituents
- Sandmeyer - application of copper(I) salts as catalysts



- **versatility of possible nucleophiles leads to many possible functions in the product**
- **one of the few ways to synthesize phenols**

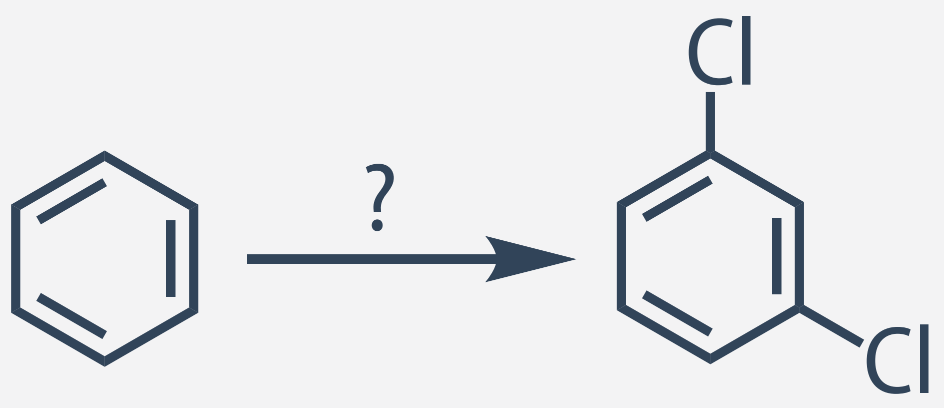
Sandmeyer Reaction in Synthetic Routes

1. easy introduction of nitro group to aromatic systems
2. simple reduction of nitro group to amino group
3. conversion of amino group to diazonium salt
4. substitution with the desired nucleophile

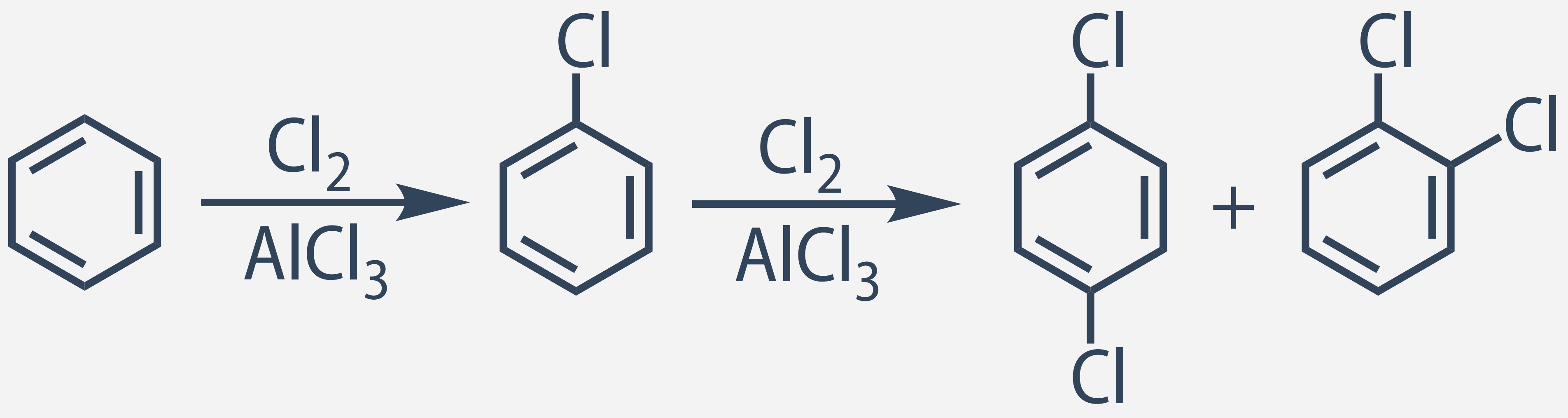


- **nitro group is *meta* directing and amino group is *ortho* and *para* directing**
- **products with different regiochemistry can be obtained if the modification is done at different stages of the sequence above**

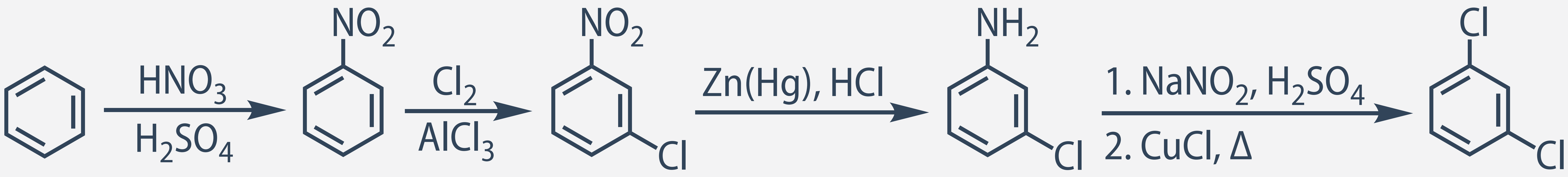
1,3-dichlorobenzene from benzene



- two halogenations via electrophilic aromatic substitution

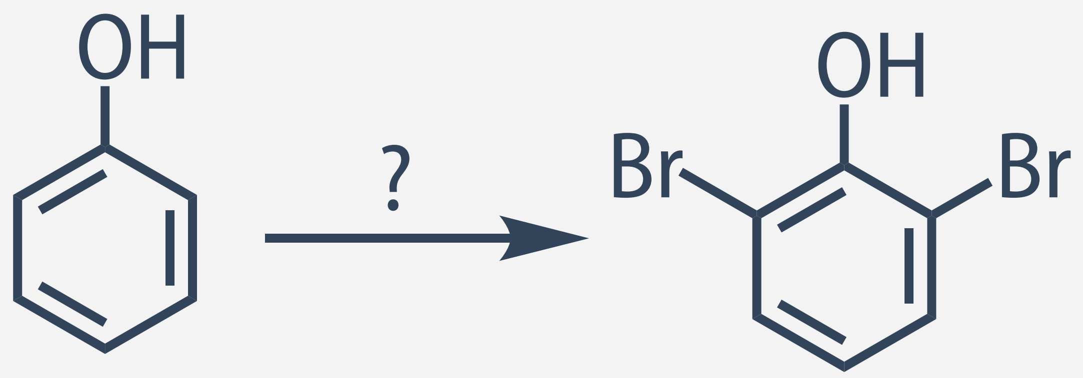


- route via Sandmeyer reaction

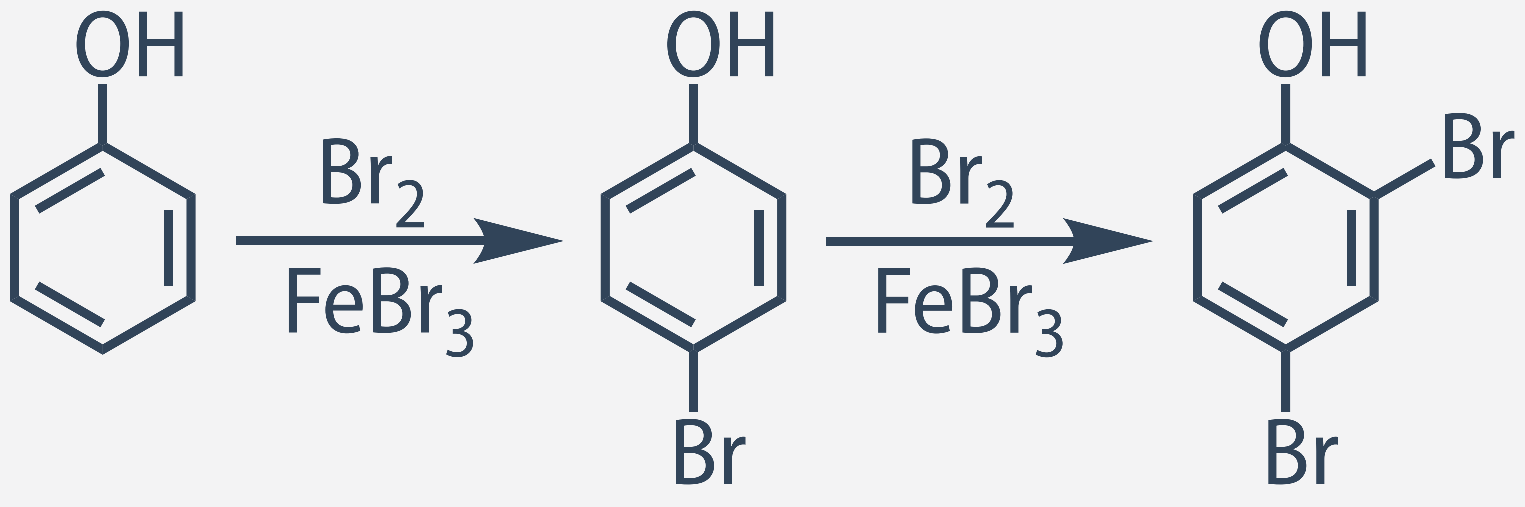


- ***meta* product is selectively obtained via the second sequence**

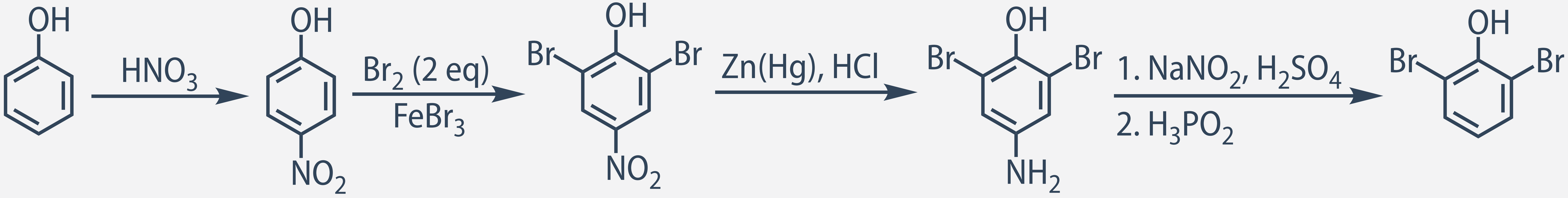
2,6-dibromophenol from phenol



- two halogenations via electrophilic aromatic substitution

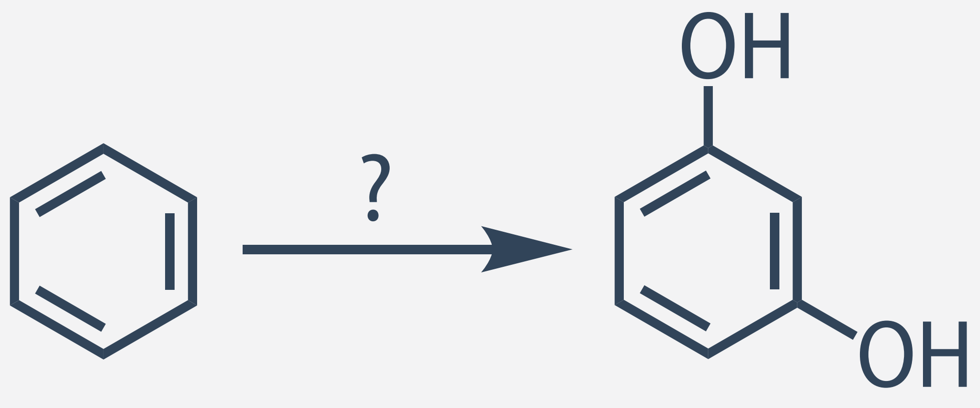


- route via Sandmeyer reaction

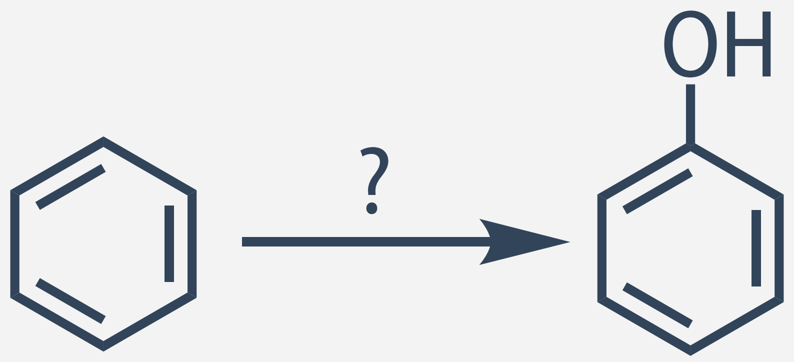


- **di-*ortho* product is selectively obtained via the second sequence**

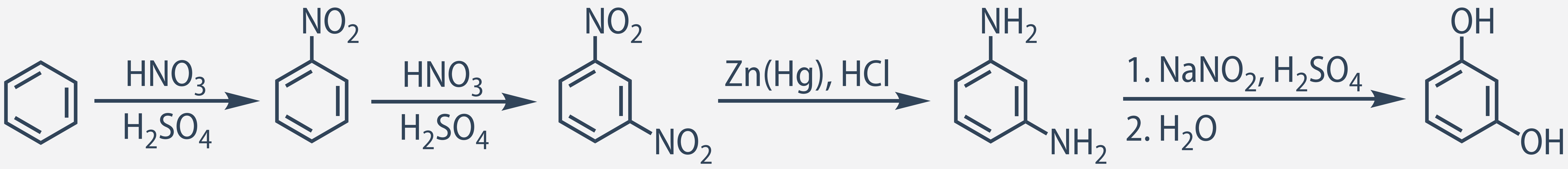
resorcinol (1,3-dihydroxybenzene) from benzene



- phenol synthesis via electrophilic aromatic substitution?

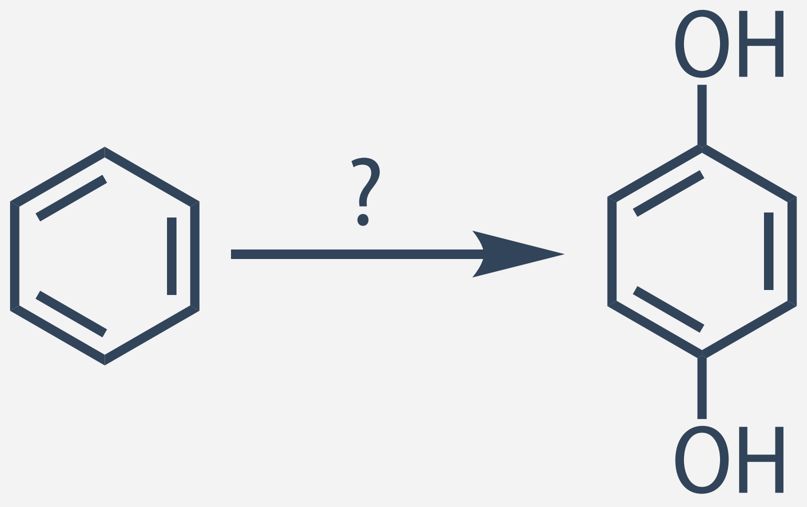


- route via Sandmeyer reaction

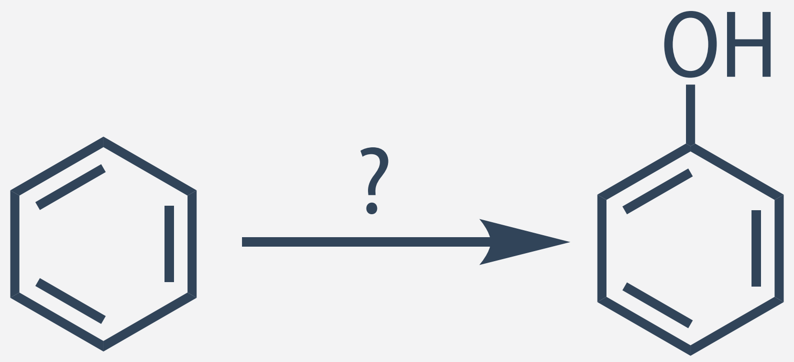


- ***meta* product is selectively obtained via the second sequence**

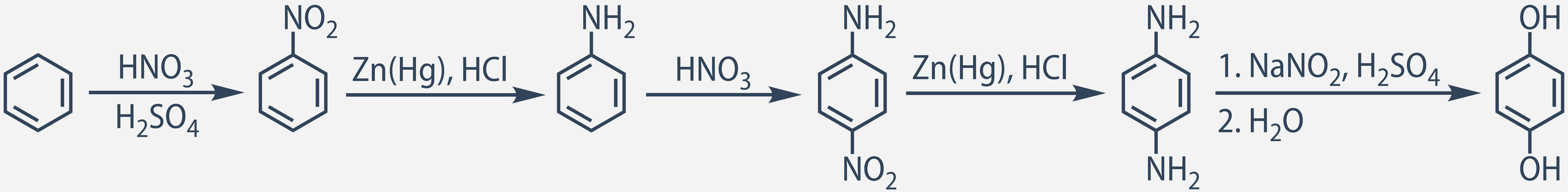
hydroquinone (1,4-dihydroxybenzene) from benzene



- phenol synthesis via electrophilic aromatic substitution?



- route via Sandmeyer reaction



- ***para* product is selectively obtained via the second sequence**