PHA284

Organic Chemistry II

Ankara University
Faculty of Pharmacy
Department of Pharmaceutical Chemistry

Aryl Halides and Nucleophilic Aromatic Substitution

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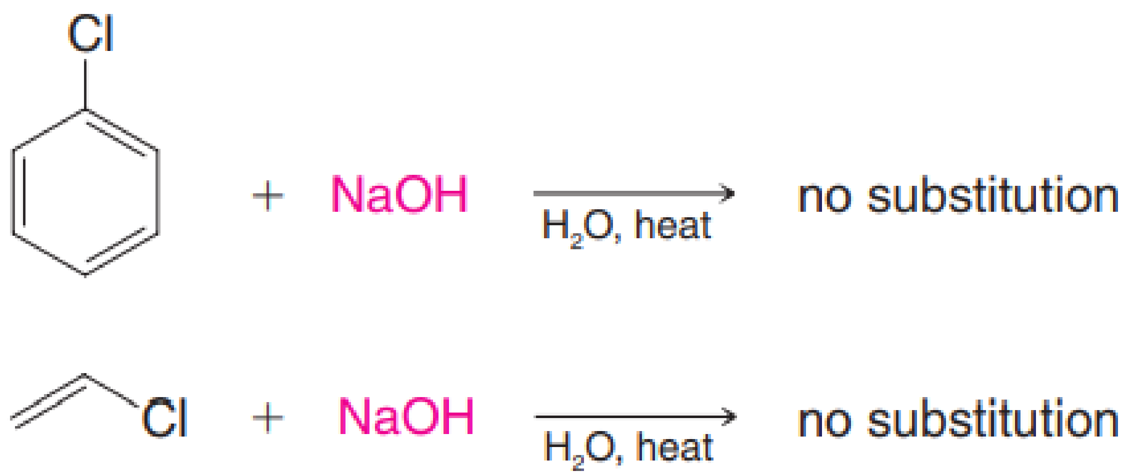


Aryl halides can be remarkably reactive toward nucleophiles if they bear certain substituents or when we allow them to react under the proper conditions.

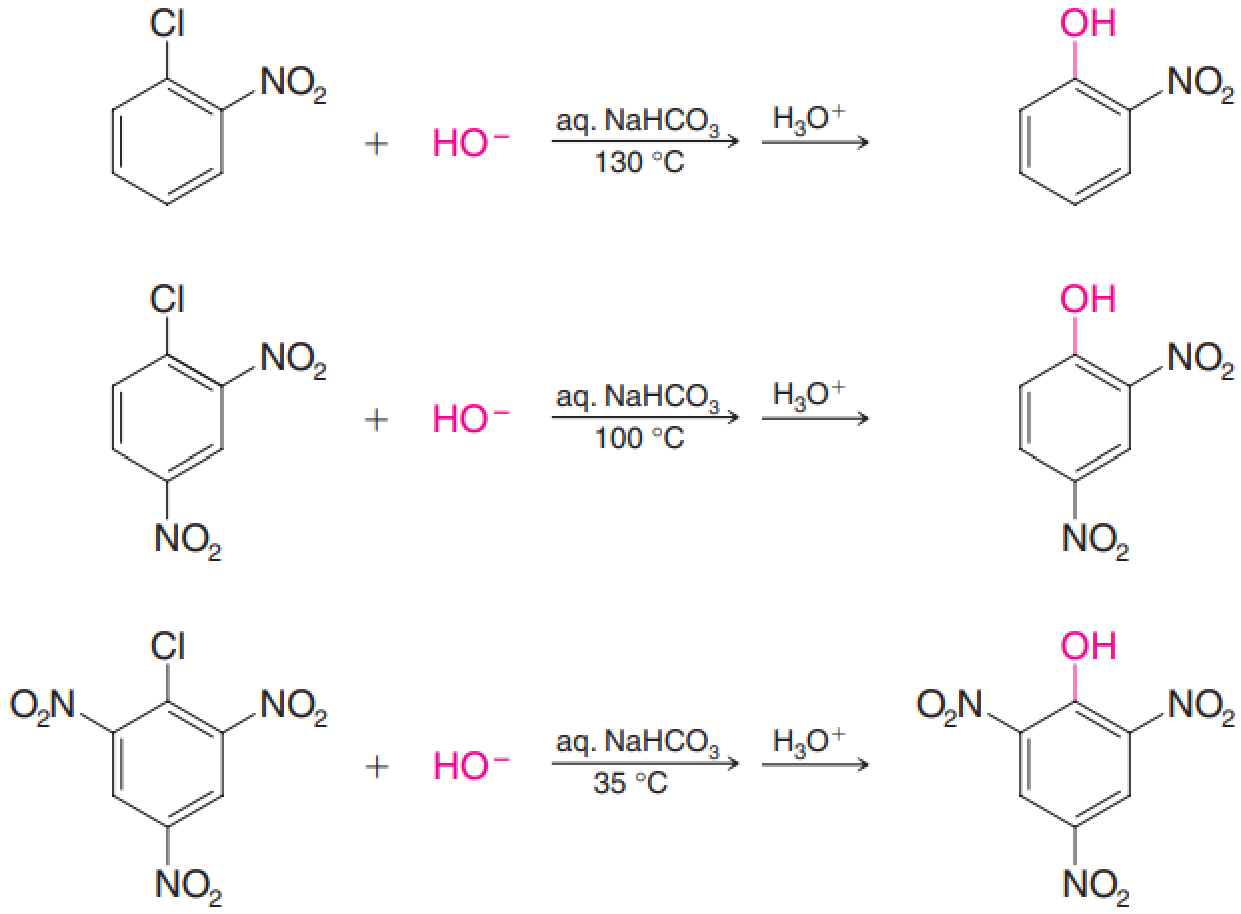
- **A- Nucleophilic Aromatic Substitution by Addition–Elimination: The S_NAr Mechanism:**

- **B- Nucleophilic Aromatic Substitution through an Elimination–Addition Mechanism: Benzyne**

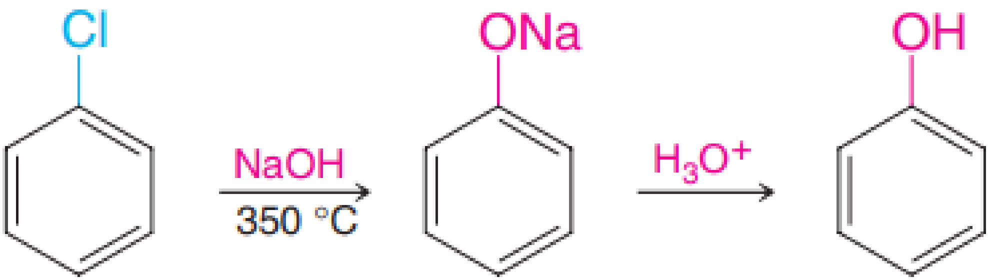
- **C- Phenylation**

Nucleophilic substitution reactions of aryl halides *do* occur readily when an electronic factor makes the aryl carbon bonded to the halogen susceptible to nucleophilic attack.

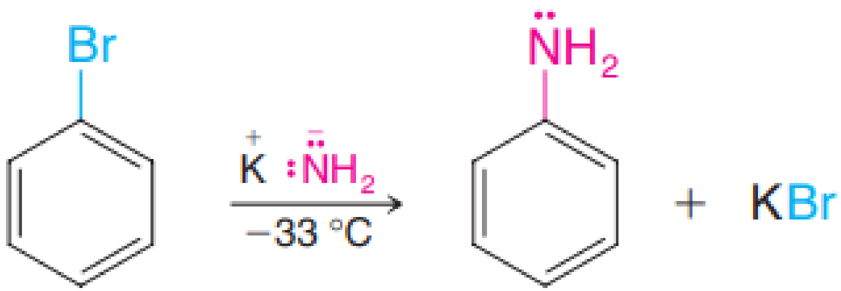
A- Nucleophilic Aromatic Substitution by Addition–Elimination: The S_NAr Mechanism:



- **B-Nucleophilic Aromatic Substitution through an Elimination–Addition Mechanism: Benzyne**



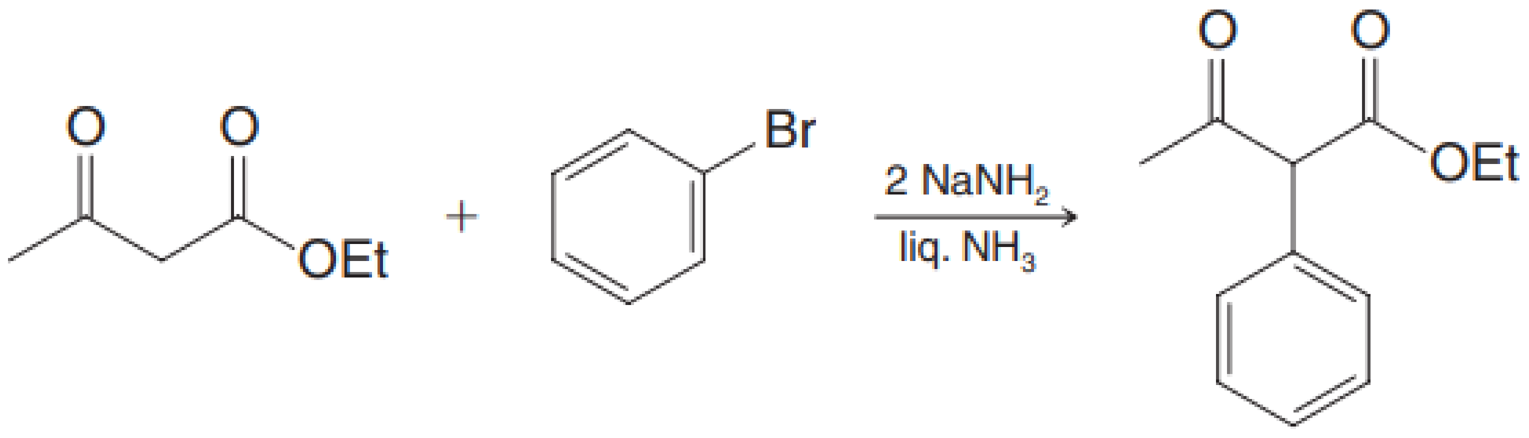
Phenol



Aniline

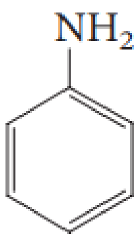
C- Phenylation

- Reactions involving benzyne can be useful for formation of a carbon–carbon bond to a phenyl group (a process called phenylation).

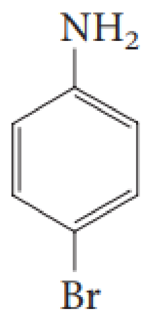


Aromatic amines

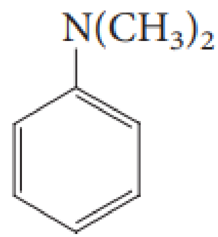
Aromatic amines



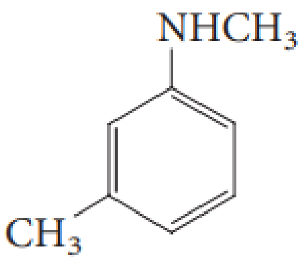
aniline
(benzenamine)



p-bromoaniline
(4-bromobenzenamine)

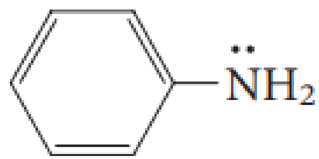


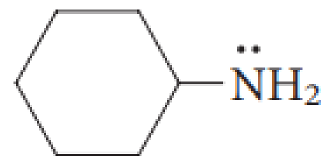
N,*N*-dimethylaniline
(*N*,*N*-dimethylbenzenamine)



m-methyl-*N*-methylaniline, or
N-methyl-*m*-toluidine
(*N*-methyl-3-methylbenzenamine)

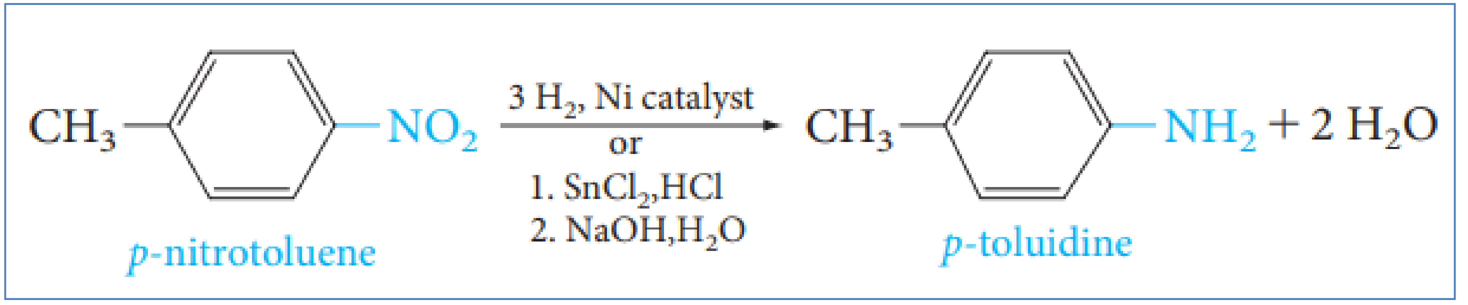
Basicity of Aromatic amines



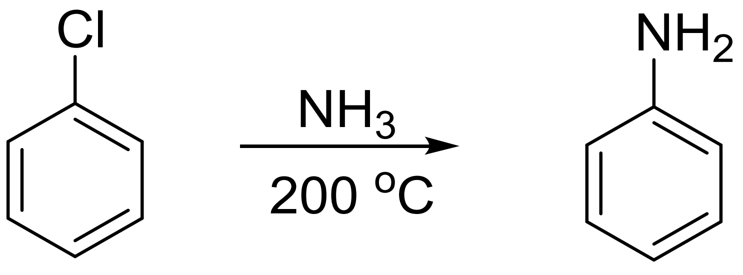


	aniline	cyclohexylamine
pK_a of ammonium ion	4.62	9.8

Preparation of Aromatic amines

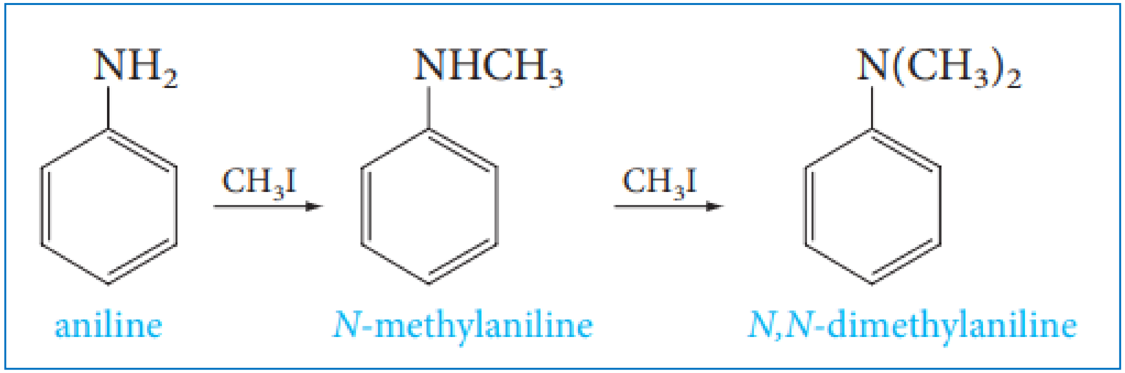


Preparation of Aromatic amines



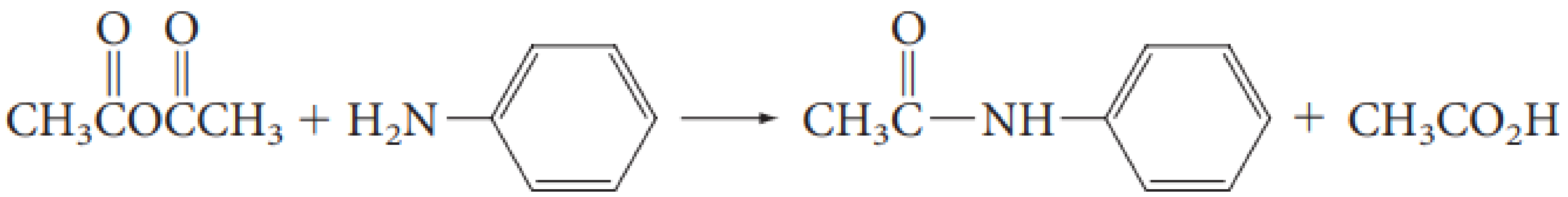
Reactions of Aromatic amines

- **Alkylation:**



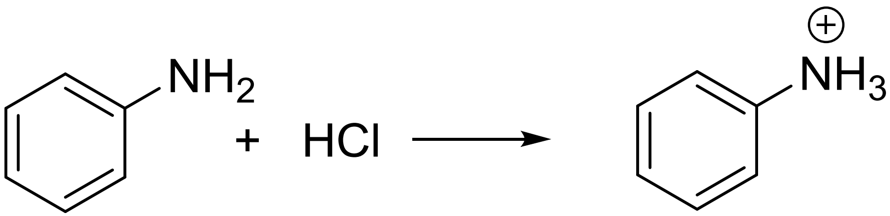
Reactions of Aromatic amines

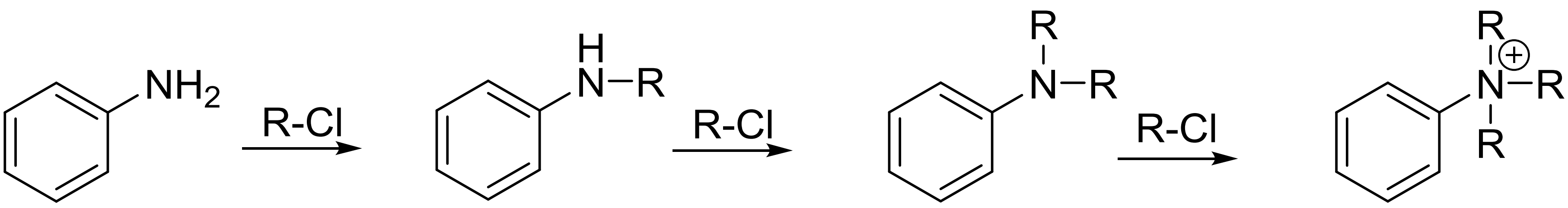
- **Amidification:**

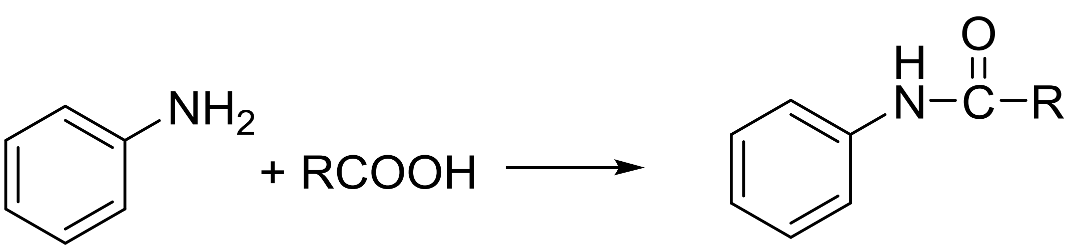


acetic anhydride aniline acetanilide

Reactions of Aromatic amines



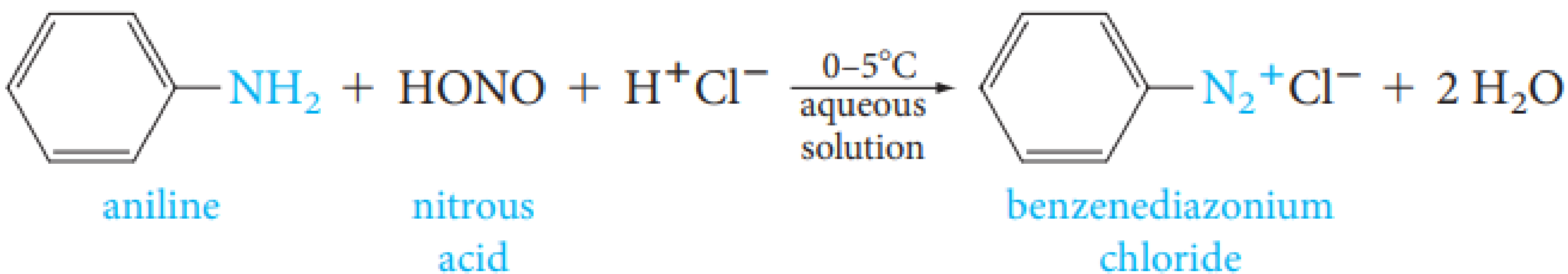




$Ar\text{-}NH_2 + RCOCl \longrightarrow Ar\text{-}N\text{-}CO\text{-}R$

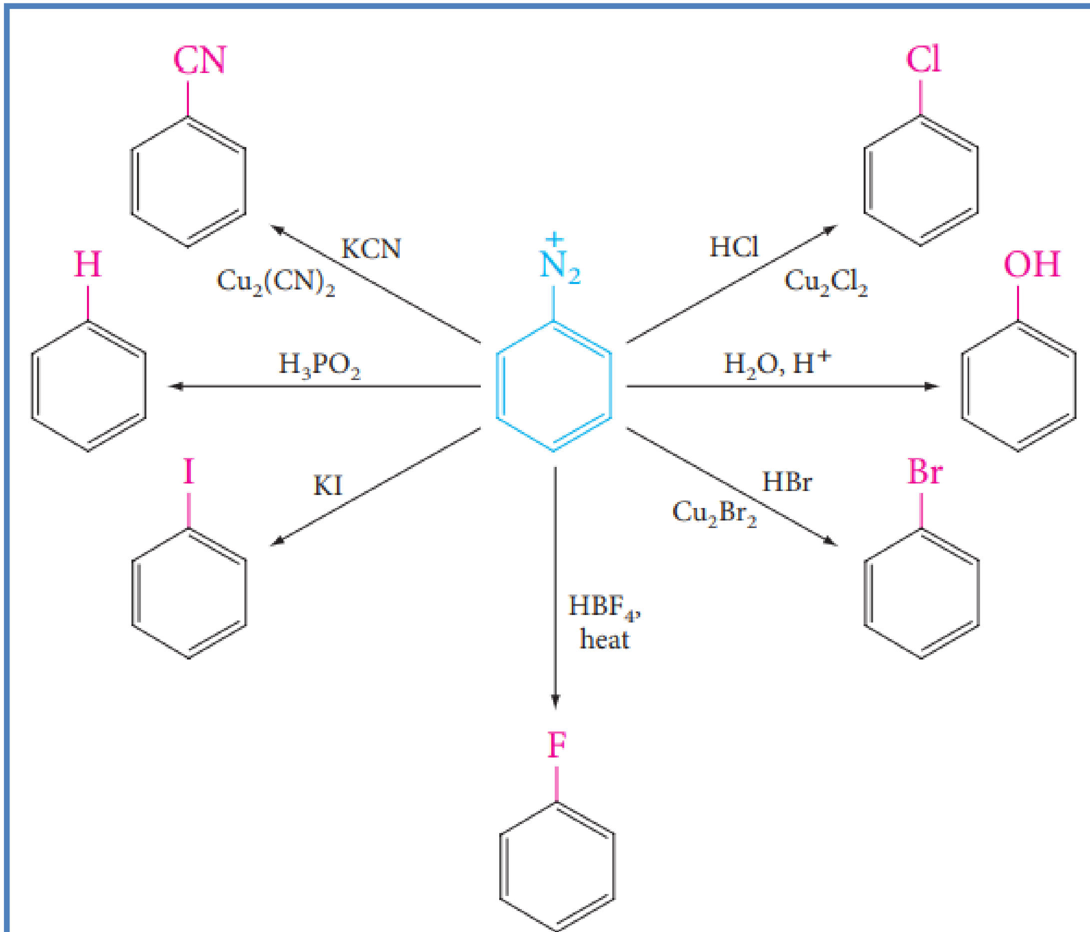
Aromatic amines

Aromatic Diazonium Compounds

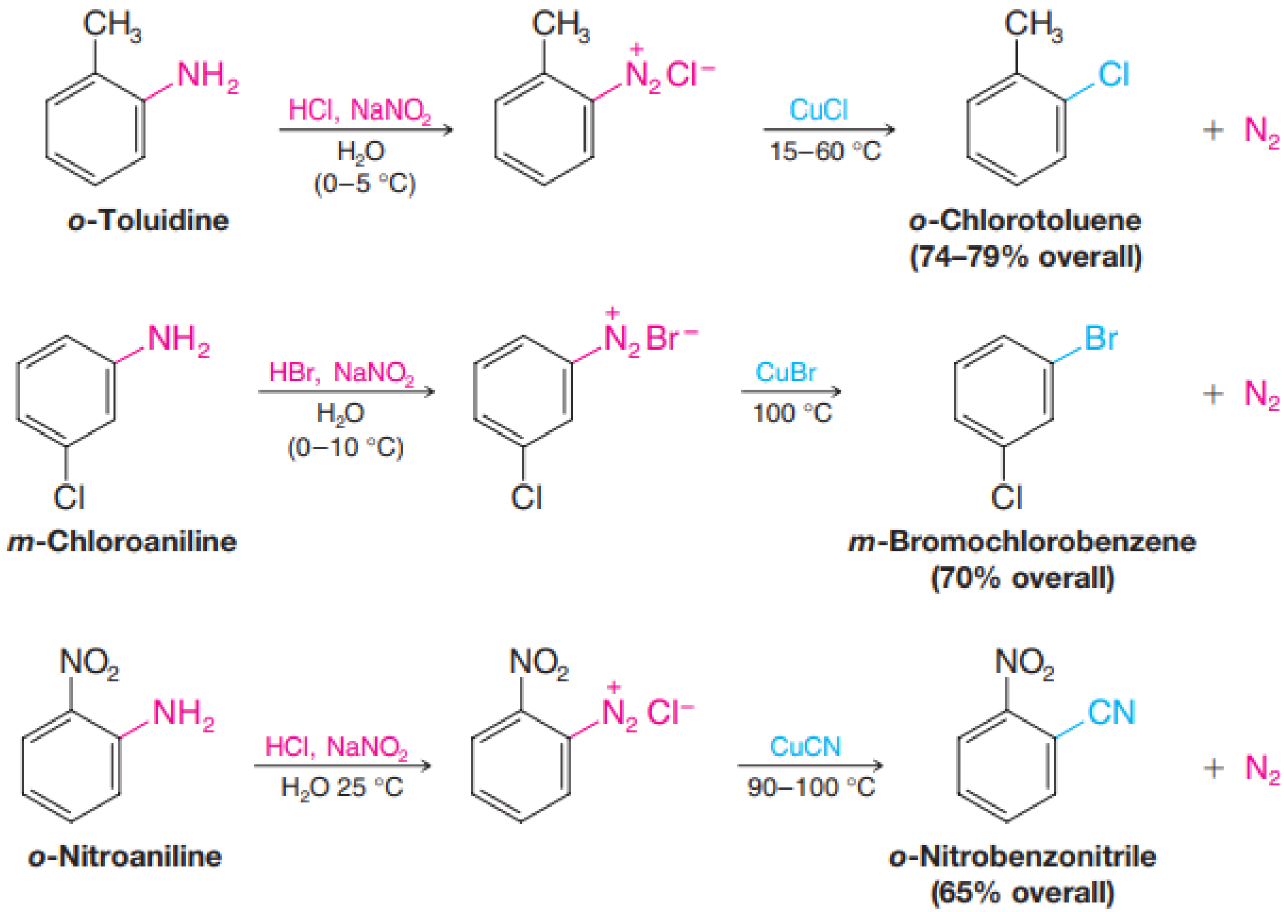


Aromatic Diazonium Compounds

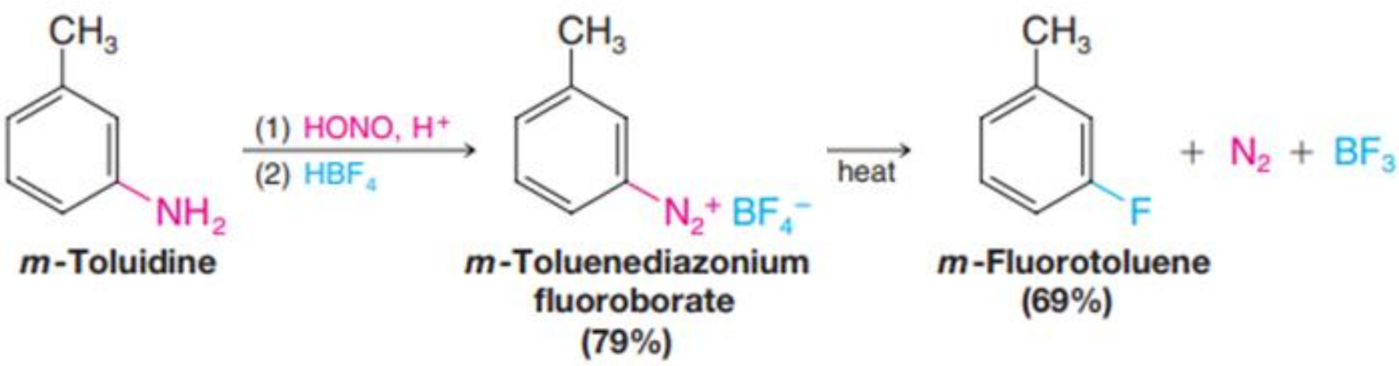
The nucleophile always takes the position on the benzene ring that was occupied by the diazonio group.



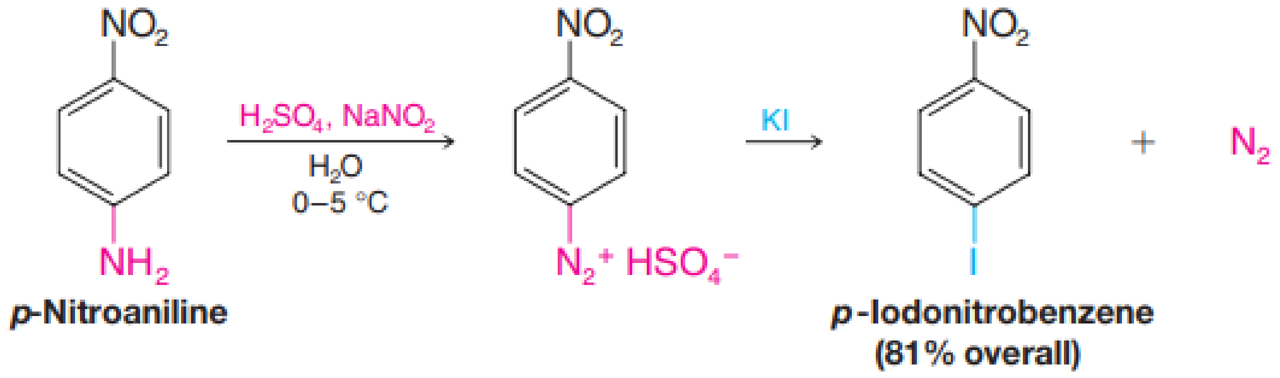
Replacement of the Diazonium Group by -Cl, -Br, or –CN:



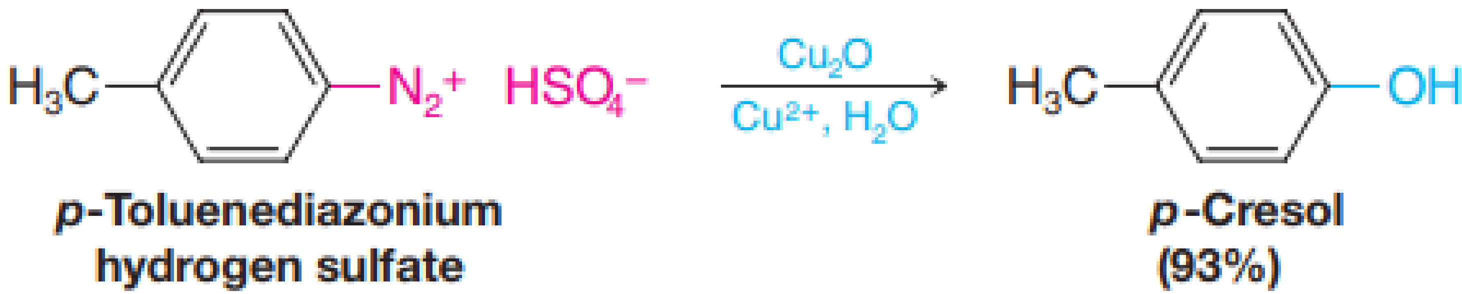
Replacement of the Diazonium Group by –F:



Replacement of the Diazonium Group by –I :

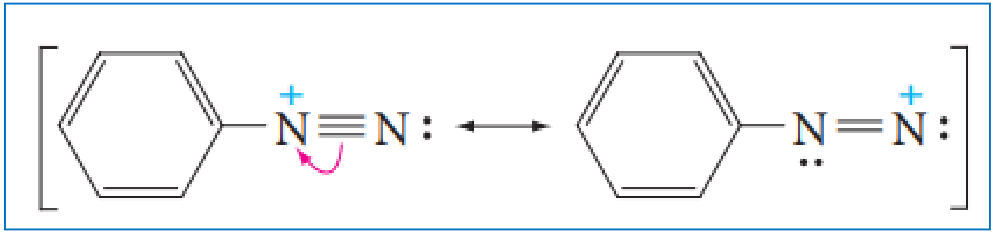


Replacement by –OH :



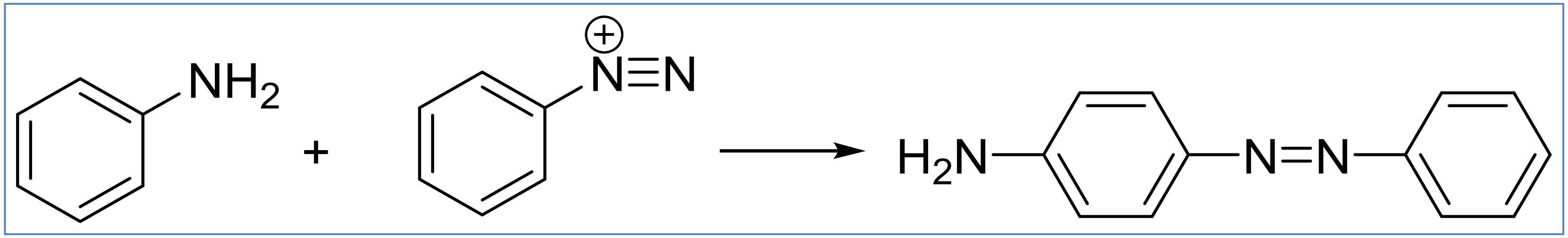
Aromatic Diazonium Compounds

Diazo coupling



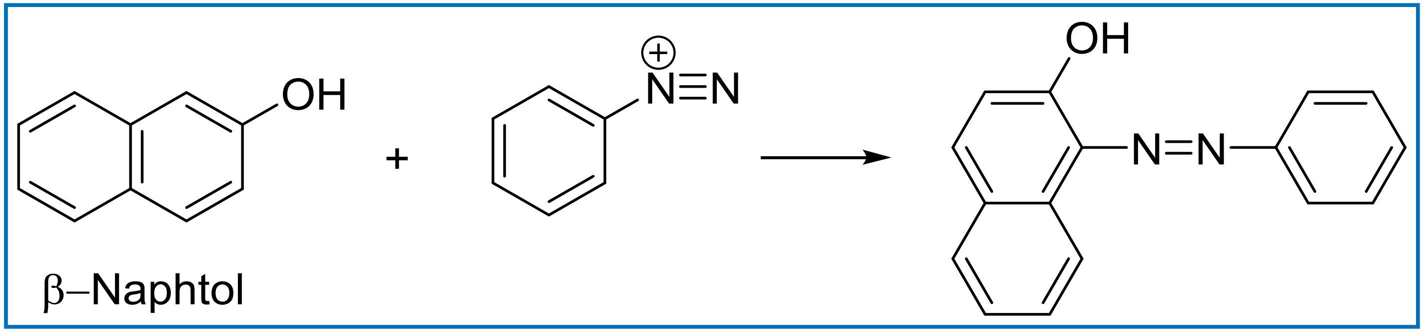
Aromatic Diazonium Compounds

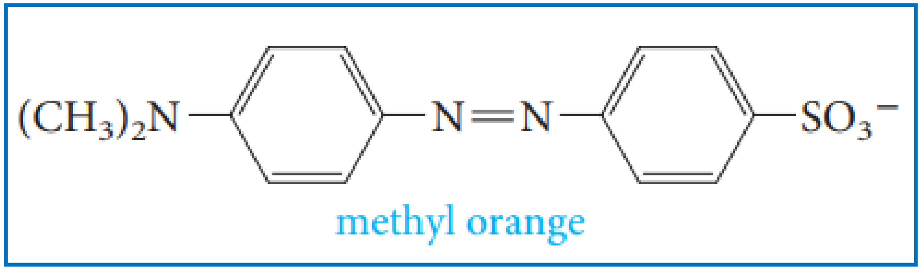
Diazo coupling



4-(phenyldiazenyl)aniline
p-Aminoazobenzene
4-phenylazoaniline

- ***Diazo coupling***





References

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