Amines
3 – Reactions

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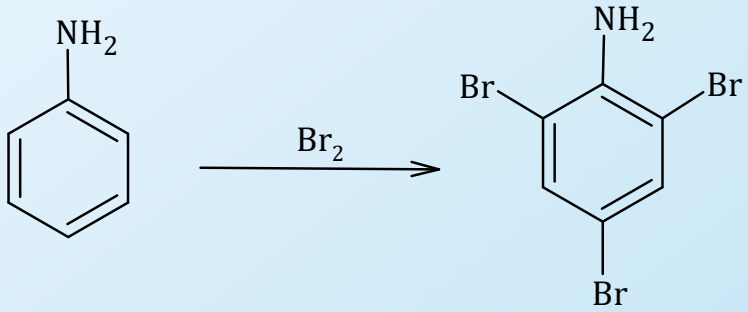
Reaction of Amines – Electrophilic Substitution

Amines can undergo a number of reactions, many of which we have covered:

- Substitution reactions with alkyl halides
- Reaction with carbonyls to form imines and enamines
- Reactions with carboxylic acids to form amides.

Some reactions specific to amines are covered here.

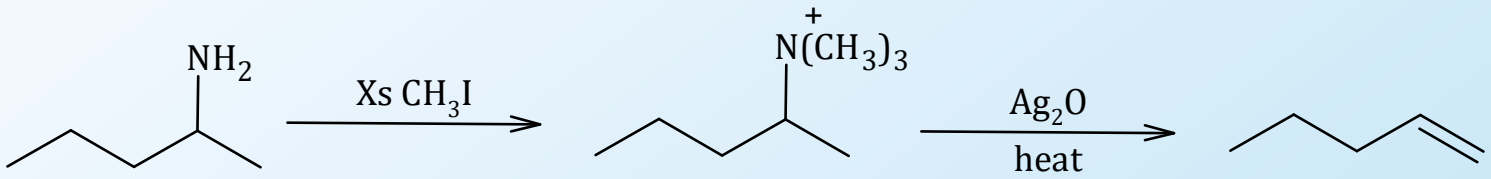
1) <u>Electrophilic reaction of aniline</u>: Aniline is a highly activated benzene ring and can undergo electrophilic substitution like bromination without any catalyst.



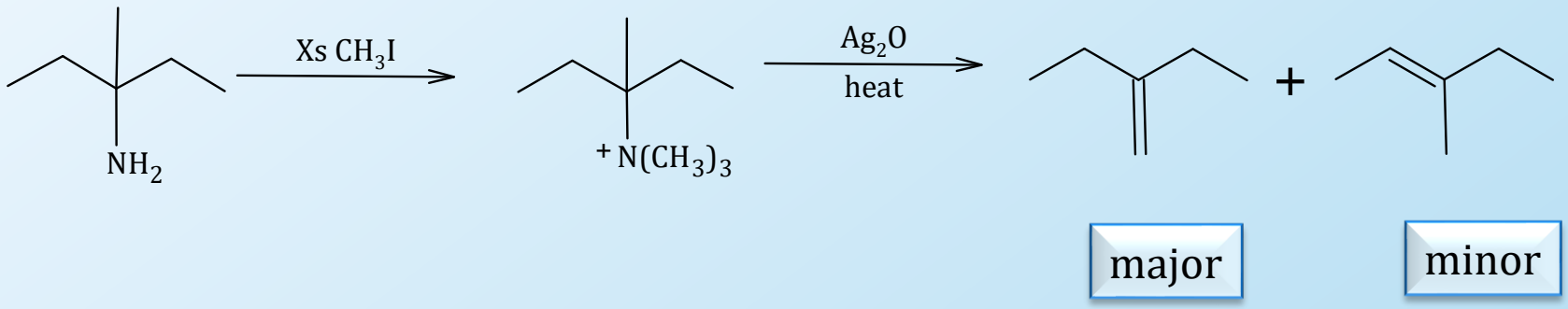
Reaction of Amines – Hoffman Elimination

2) <u>Hoffman Elimination</u>: Amines groups can be eliminated to give alkenes on treatment with excess of alkyl halide and silver oxide with heat. NH_2^- is a poor leaving group, but when it converts to a quarternary alkylammonium ion, it becomes a good leaving group. Because of its bulkiness, the product is usually the Hoffman product (less stable alkene).

<u>Example:</u>



<u>Example:</u>



Reaction of Amines – Nitrous Acid

Nitrous acid, a weak acid, is prepared by treating sodium nitrite, $NaNO_2$,with H_2SO_4 or HCl at 0-5 ^oC. It is not a stable acid and has to be generated "in situ" which means created and used immediately.

$$HCl_{(aq)} + NaNO_{2\,(aq)} \xrightarrow{0\text{-}5\ ^oC} HONO_{(aq)} + NaCl_{(aq)}$$

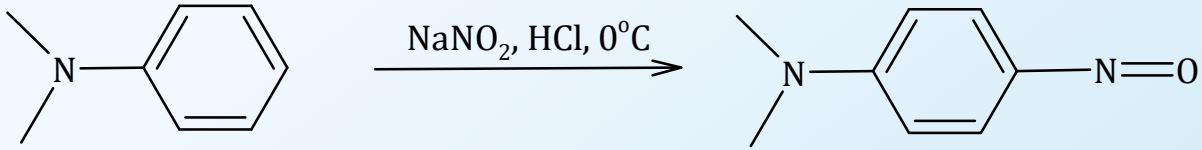
$$H_2SO_{4\,(aq)} + 2NaNO_{2\,(aq)} \xrightarrow{0\text{-}5\ ^oC} 2\ HONO_{(aq)} + Na_2SO_{4\,(aq)}$$

In its reactions with amines, nitrous acid:

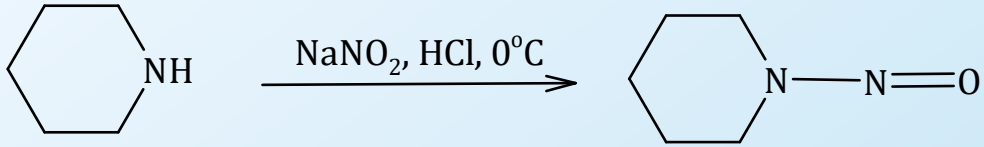
- participates in proton-transfer reactions.
- Is a source of the nitrosyl cation, NO^+, a weak electrophile.

Reactions of Amines – Nitrous Acid with 3º and 2º Amines

Reaction with 3° amines: These do not react with nitrous acids.



Reaction with 2° Amines: These react with NO^+ to give N-nitrosamines.

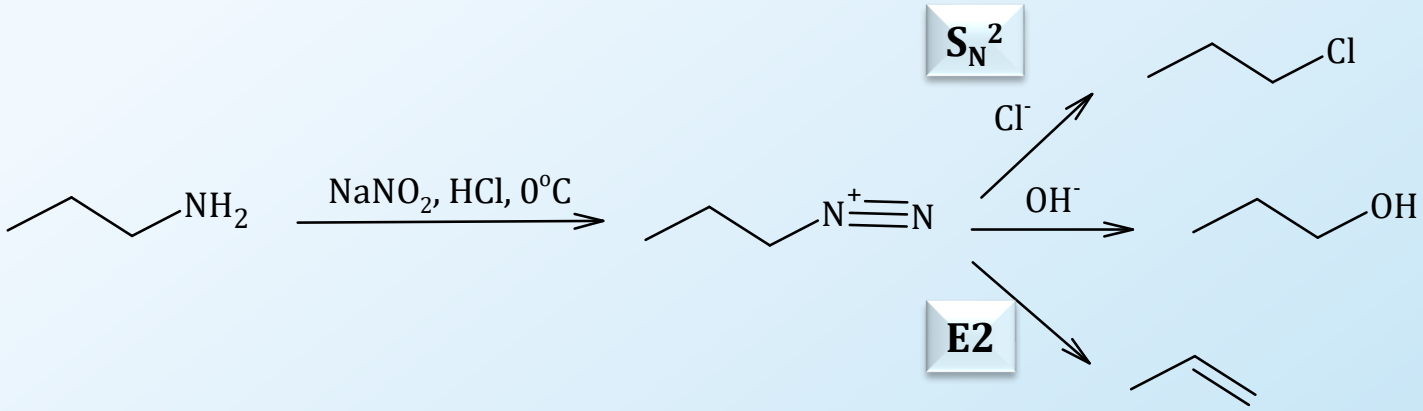


N – Nitroso amines are studied more for their toxicity.

Reactions of Amines – Nitrous Acid with 1° Aliphatic Amines

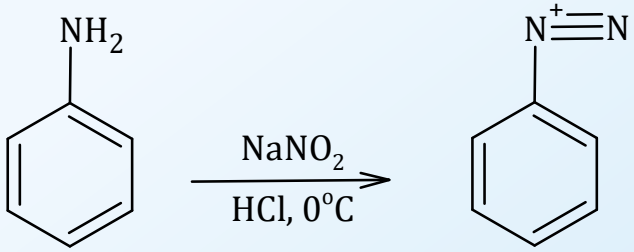
Primary amines form diazonium salts on treatment with nitrous acids. These diazonium ions are unstable and lose N_2 to give a carbocation which can then:

1. React with a nucleophile to give a substitution product.
2. Lose a proton to give an alkene.

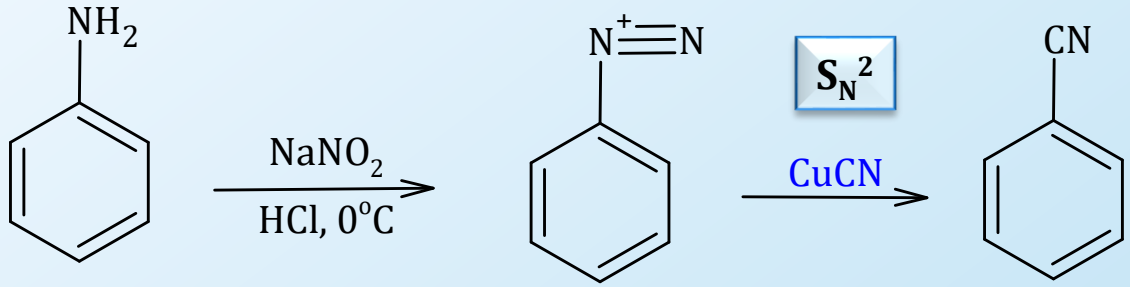


Reactions of Amines – Nitrous Acid with 1° Aromatic Amines

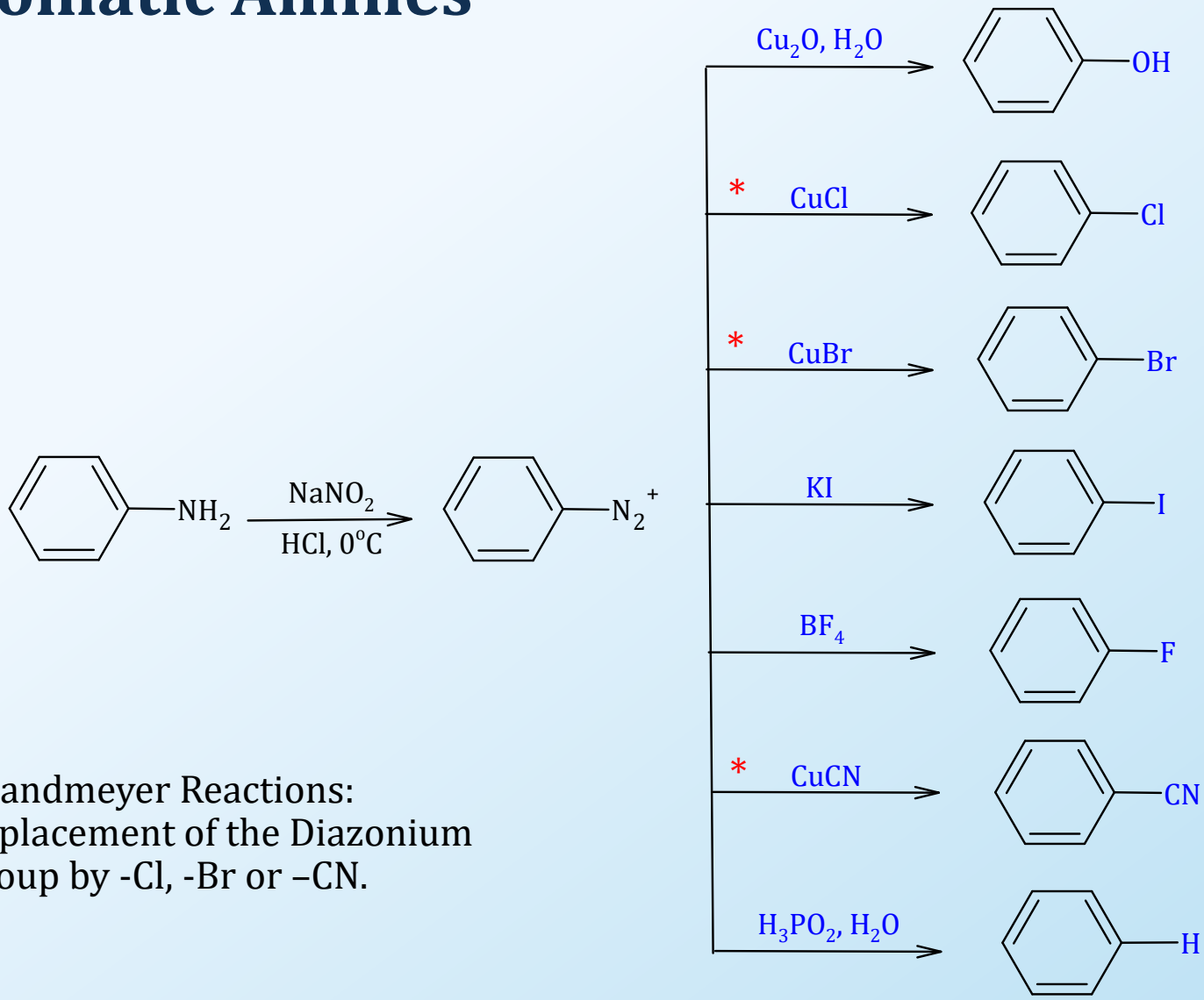
Primary aromatic amines react with HNO_2, yielding stable arenediazonium salts.



The N_2 then can be substituted by any nucleophile. This is unusual since benzene ring does not undergo S_N2 reactions.



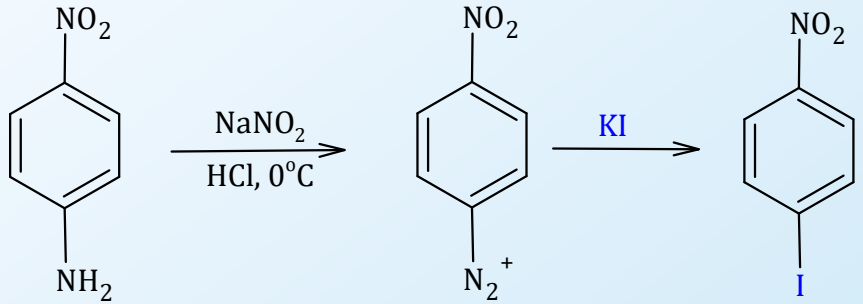
Reactions of Amines – Nitrous Acid with 1° Aromatic Amines



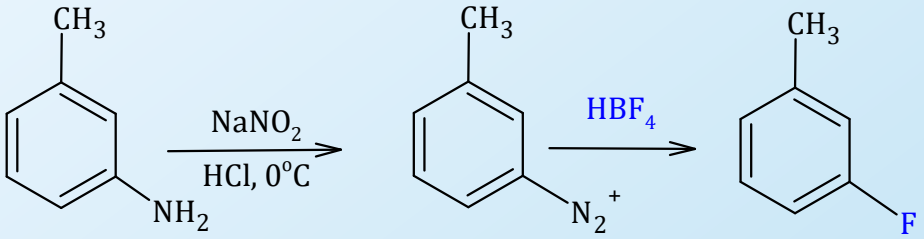
* Sandmeyer Reactions: Replacement of the Diazonium Group by -Cl, -Br or –CN.

Reactions of Amines – Nitrous Acid with Aromatic Amines

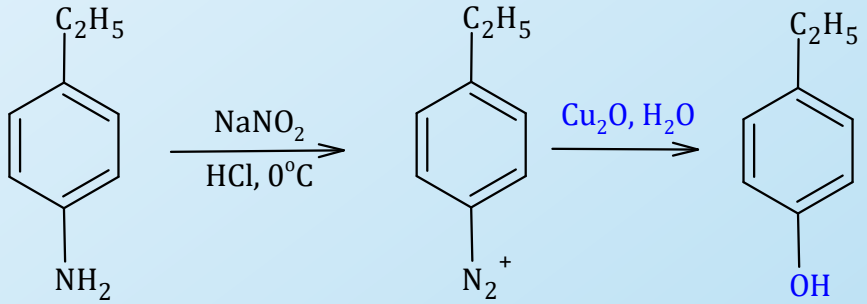
- Replacement with Iodine



- Replacement with Fluorine

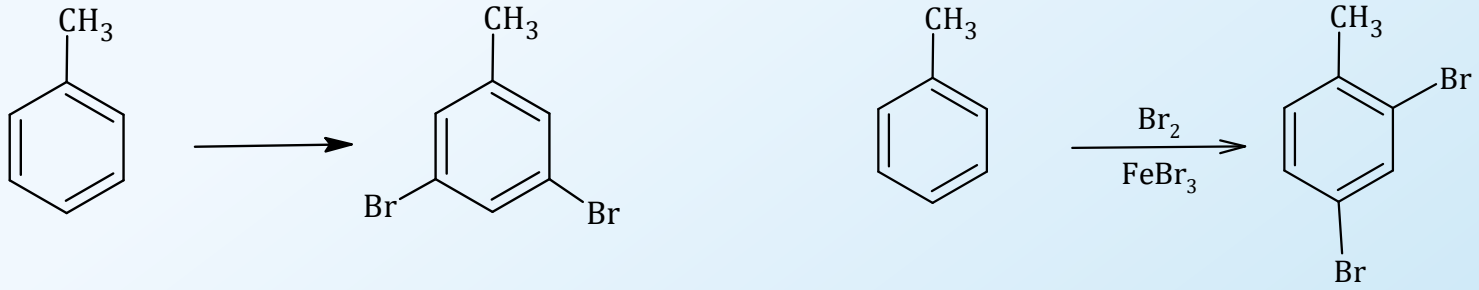


- Replacement with Hydroxide

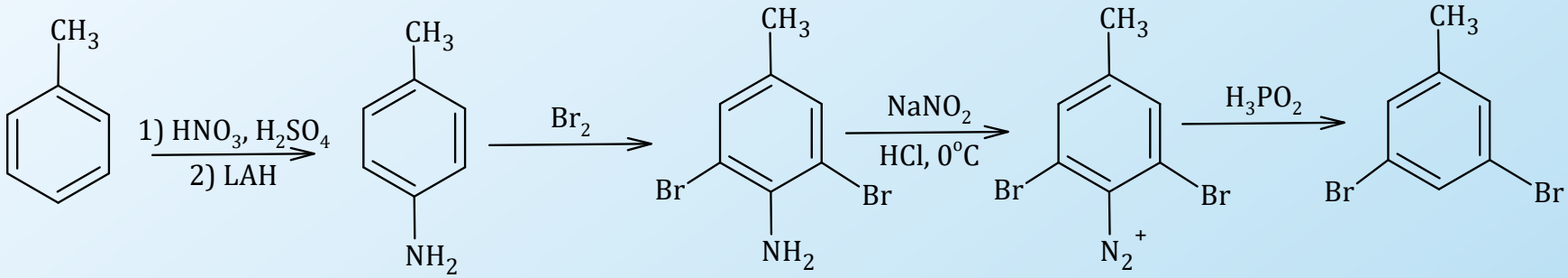


Reactions of Amines – Nitrous Acid with Aromatic Amines – Synthetic Applications

3, 5-dibromotoluene cannot be made directly from either toluene or bromobenzene. Bromination of toluene will give o, p – substitution.



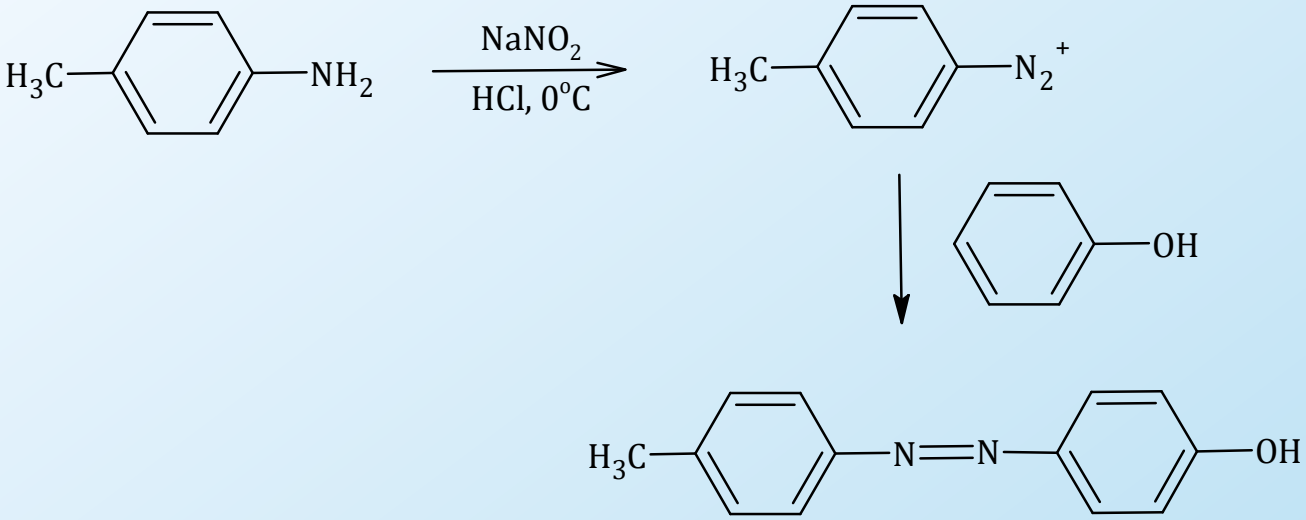
However, making p-methylaniline followed by bromination and then removing the amino group can do this reaction successfully.



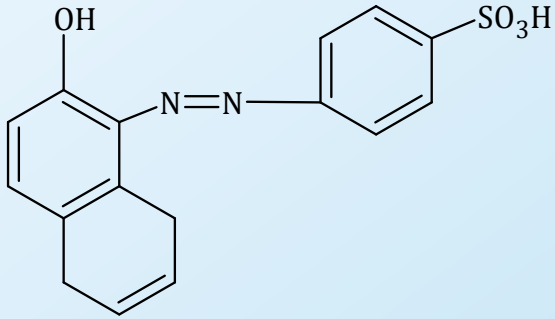
Reactions of Amines – Nitrous Acid with Aromatic Amines – Diazonium Coupling Reaction

Aromatic diazonium salts react as electrophiles with highly reactive aromatic compounds such as phenol and aromatic tertiary amines. This reaction is called a diazo coupling reaction.

Phenol and aniline derivatives undergo coupling almost exclusively at the para position unless this position is blocked.



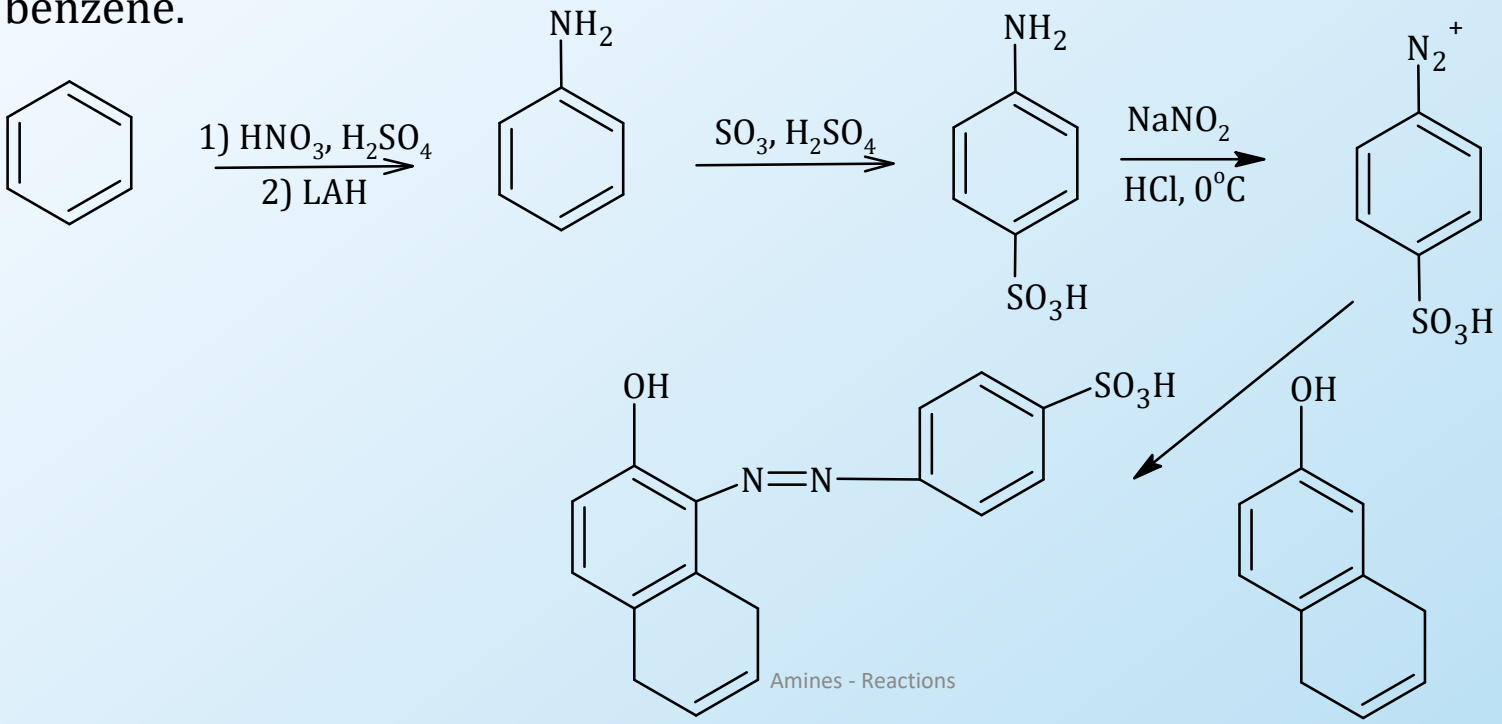
Coupling Reaction



The azo coupling results in compounds which are highly conjugated and which often absorb light in the visible region and so are commonly used as dyes.

The - $SO_3^-Na^+$ group is added to the molecule to add water solubility and to link the dye to the polar fibers of wool, cotton etc.

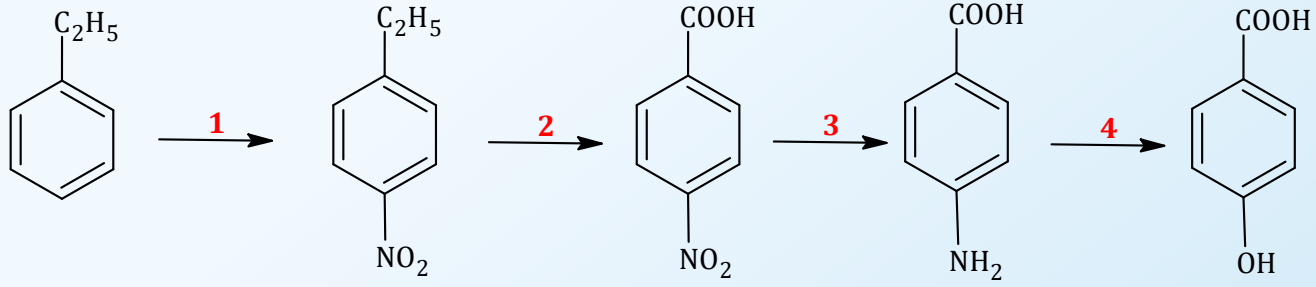
Below is the synthesis of the dye on the right starting from benzene.



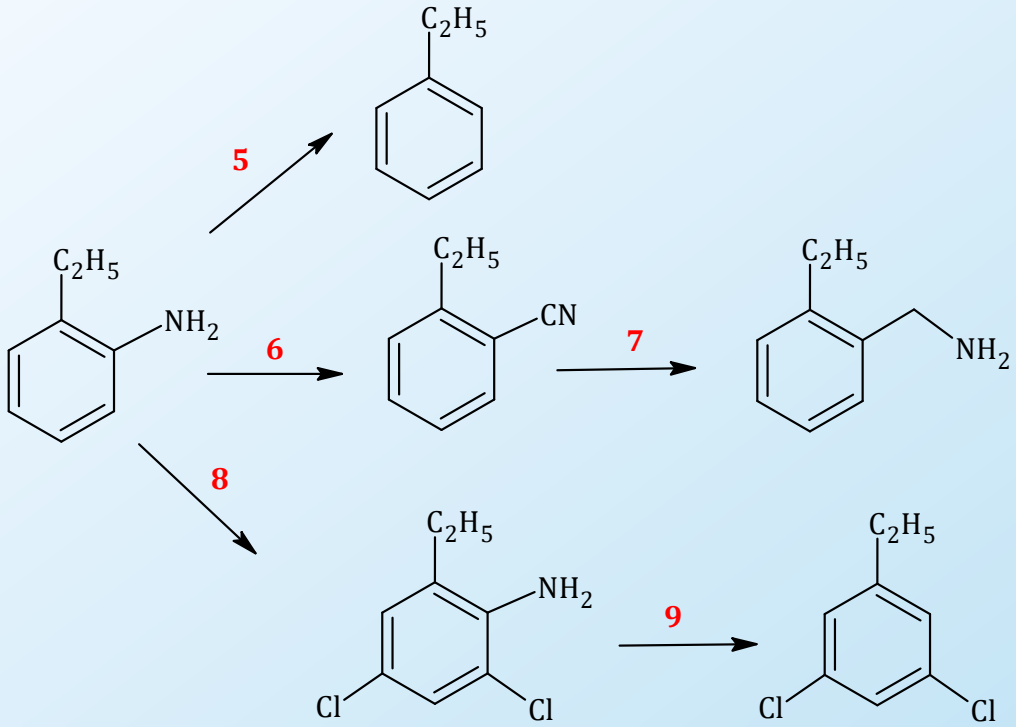
Problems

What reagents do you need to carry out the following reactions.

a)



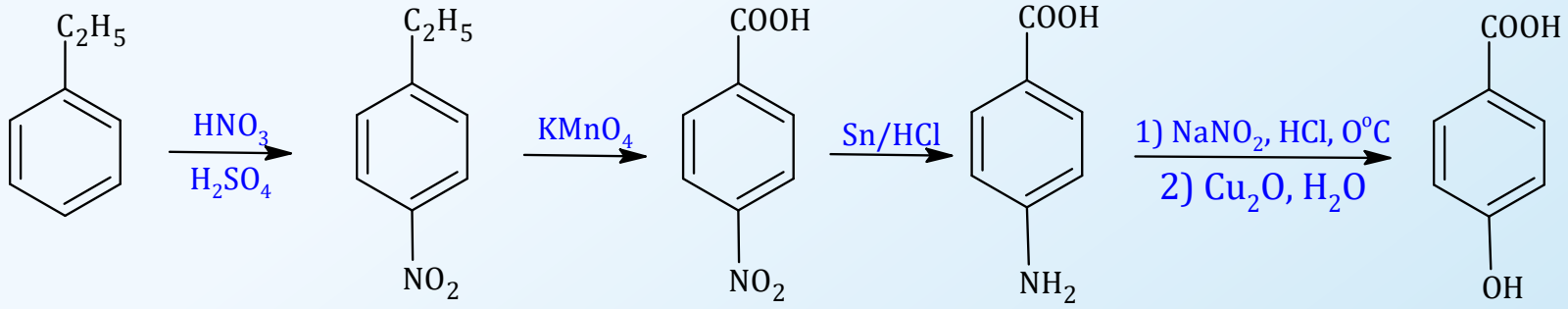
b)



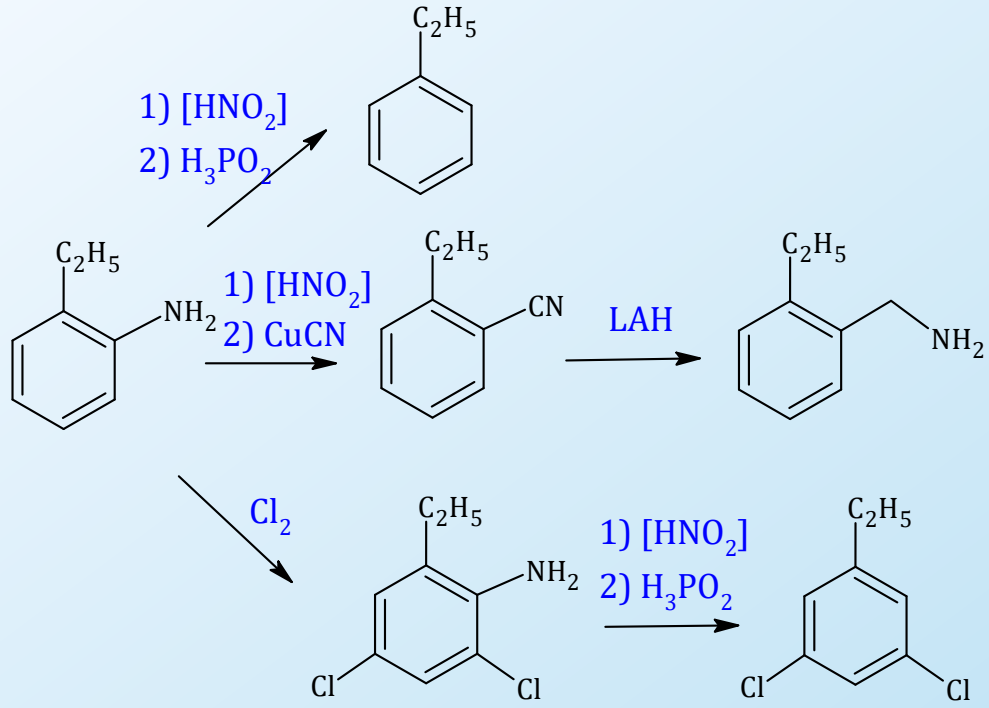
Problems - Answers

What reagents do you need to carry out the following reactions.

a)



b)



Key Concepts

- Hoffman Elimination
- Diazonium salts
- Coupling reaction
- Aromatic synthesis