

## **I. Reactions of Amines with Nitrous Acids**

Amines are converted into diazonium ions,  $\text{N}_2^+$ , upon treatment with nitrous acid,  $\text{HNO}_2$  (often formed in-situ by reaction of  $\text{NaNO}_2$  and  $\text{HCl}$ ). Diazonium ions are excellent leaving groups, and alkyl diazonium ions are very unstable, frequently giving rise to carbocations which can undergo rearrangement and polymerization. One example of a useful reaction of alkyl diazonium compounds is the transformation of an amino acid to a hydroxy acid with retention of configuration.

*Example of an alkyl diazonium ion intermediate:*

## **II. Aryl diazonium salts**

Aryl diazonium ions are stable and can be isolated as diazonium salts. These salts undergo substitution reactions with a variety of nucleophiles. A useful reaction is the Sandmeyer reaction, which involves the use of copper salts for direct substitution of aryl diazonium ions. Acidic hydrolysis of arene diazonium ions gives phenols. Reduction of diazonium ions with hypophosphorous acid ( $\text{H}_3\text{PO}_4$ ) accomplishes a complete removal of the nitrogen atom from the ring, substituting hydrogen. Treatment of an arene diazonium salt with  $\text{KI}$  allows the formation of an aryl iodide; heat the diazonium salt with  $\text{HBF}_4$  yields an aryl fluoride. Substitution of aryl diazonium ions is a powerful method for introducing a large variety of substituents onto aromatic rings.

One may use the reactivity of an amino group to introduce substituents in the ortho and para positions of an aromatic ring and then remove the amino group altogether after diazotization or substitute yet another moiety onto the ring. Diazotization of ortho-amino acids leads to loss of  $\text{CO}_2$  and generation of benzyne, which may undergo Diels-Alder reactions with dienes.

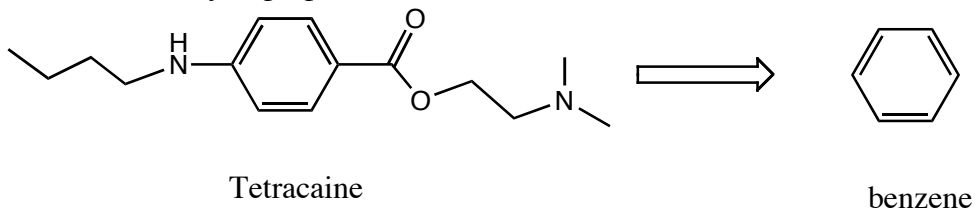
Diels-Alder Reactions of benzyne produced in situ from diazonium acids:

### III. Diazo Coupling

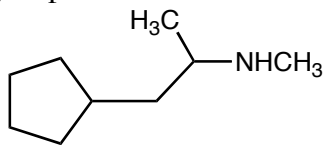
Diazo coupling reactions are used to make highly conjugated azo dyes by nucleophilic attack of electron-rich aromatics on electron-poor diazonium salts.

Additional Problems for practice:

1. How would you prepare tetracaine from benzene?

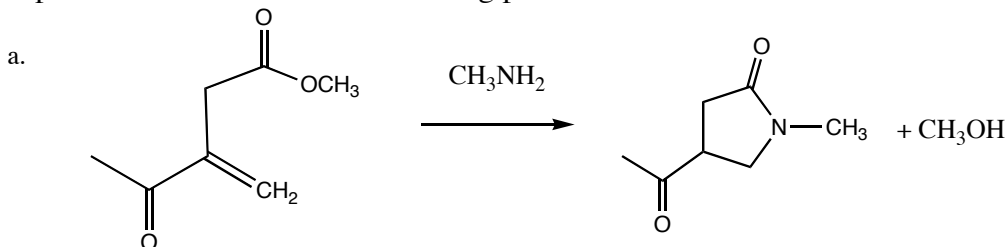


2. Propose a synthesis of cyclopentamine from materials of five carbons or less:

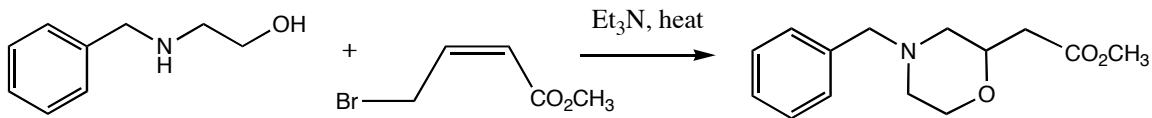


cyclopentamine

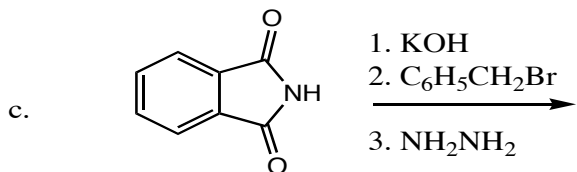
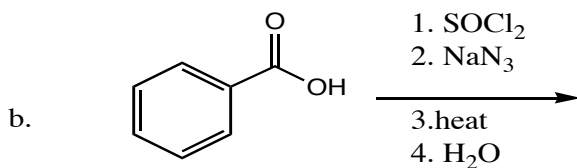
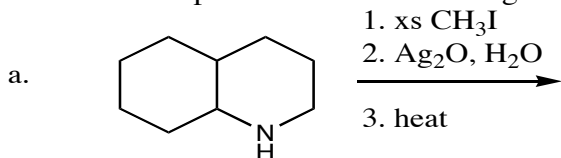
3. Propose a mechanism for the following processes:



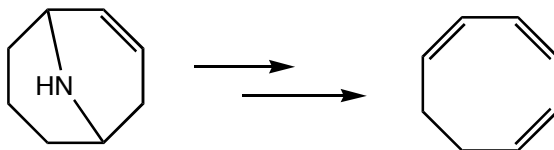
b.



4. Predict the products of the following reactions:



5. How might you use the Hoffmann elimination to accomplish the following transformation?



6. Show how Naphthalene can be made from o-nitro benzoic acid by a Diels-Alder reaction

