33. Arene Diazonium Ion Reactions

A. Introduction

In the previous laboratory experiment, you explored the functionalization of benzene via electrophilic aromatic substitution reactions. In these reactions, a hydrogen on the aromatic ring is substituted with some electrophile. In this experiment, you will expand upon the functionalization of benzene by substitution of a diazonium ion ($-N_2^{\oplus}$) with a variety of different species.

First, the diazonium ion must be generated. A diazonium ion is generated by reacting an amine with nitrous acid generated by mixing sodium nitrite ($NaNO_2$) and a strong acid such as H_2SO_4 or HCl. When the amine is on an aromatic ring, an aryldiazonium ion is formed. Generation of the aryl amine is relatively simple. First, benzene or a benzene derivative is subjected to electrophilic nitration conditions to provide nitrobenzene. The nitro group is then reduced to the amino group. One commonly employed reduction is Sn/HCl. Alternatively, H_2, Pd/C can be used to reduce a nitro group to an amine. (Figure 1)

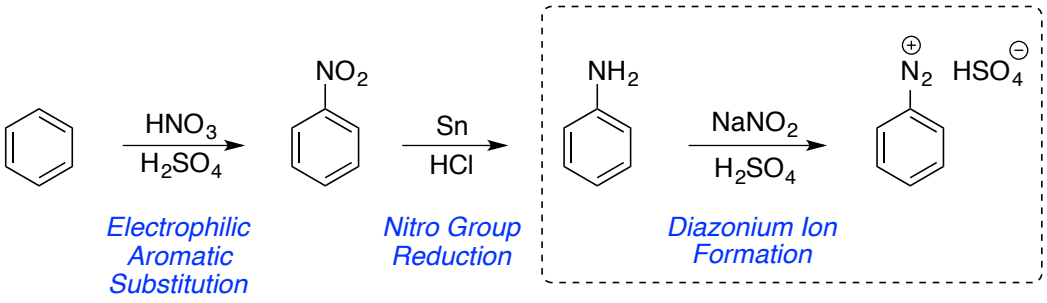
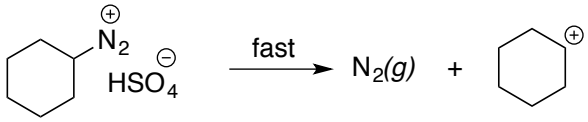


Figure 1. Generation of the Arene Diazonium Ion

Diazonium ion formation begins by mixing sodium nitrite ($NaNO_2$) with a strong acid such as sulfuric acid (H_2SO_4). This results in the *in situ* generation of nitrous acid, HNO_2 (Step 1, Figure 2). Next, as shown in figure 2, step 2, the nitrous acid is protonated followed by the loss of water to form the nitrosonium ion, which is a very powerful electrophile. The nitrosonium then adds to the amine as shown in figure 2, step 3. After several steps, water is lost and the aryldiazonium ion is formed.

The aryldiazonium ion is relatively stable and can exist for an extended period of time when maintained at a low temperature. Due to their enhanced stability the aryldiazonium ions are much more useful than their alkyl diazonium ion counterparts. Alkyl diazonium ions rapidly lose nitrogen gas to form a carbocation that decomposes via a variety of reaction pathways.



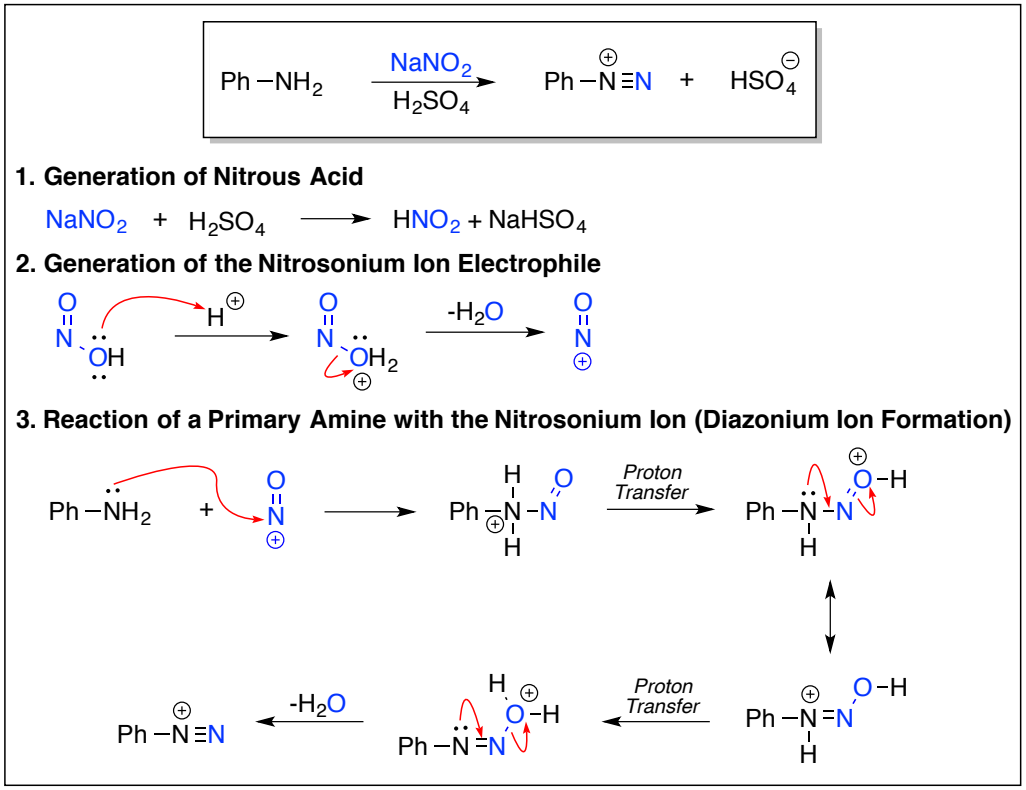


Figure 2. Mechanism for Diazonium Ion Formation

Reaction of the aryldiazonium ion with a variety of nucleophilic reagents allows for the preparation of an array of different aromatic molecules. Many of these reactions are shown in figure 3. The preparation of aryl chlorides and bromides via reaction of the aryldiazonium ion with CuCl and CuBr, respectively, is known as the Sandmeyer reaction. Similarly, reaction with CuCN produces an aryl nitrile and reaction with $CuNO_2$ replaces the diazonium ion with a nitro group. When copper conditions are employed, the reaction is thought to proceed via a radical pathway. Other conditions include reacting the aryl diazonium ion with water to provide phenol, potassium iodide to provide an aryl iodide, and tetrafluoroboric acid to provide an aryl fluoride.

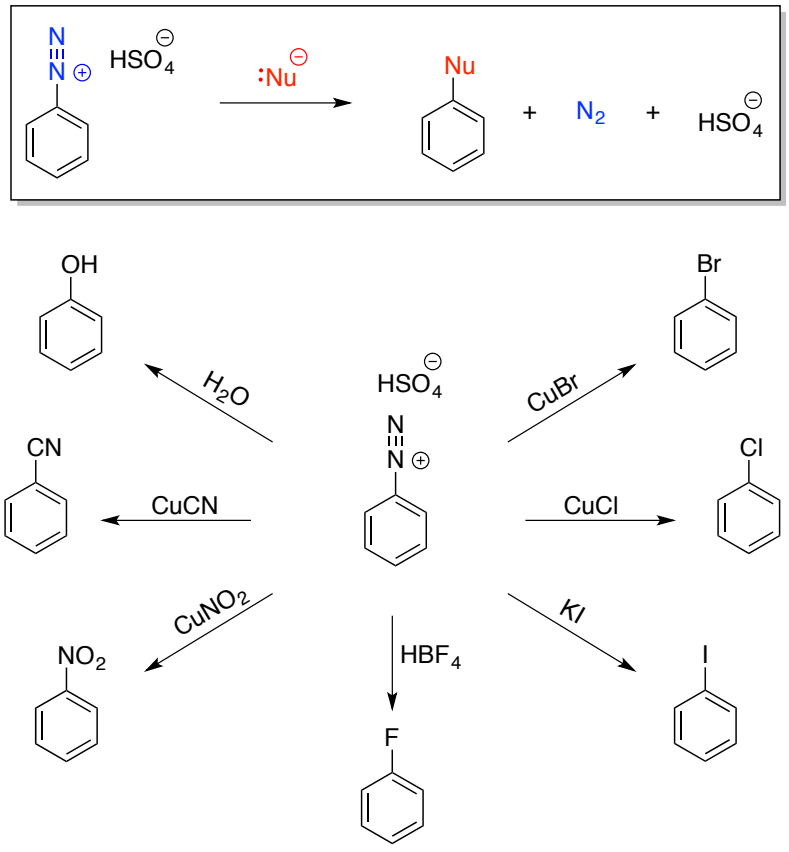


Figure 3. Typical Diazonium Ion Displacement Reactions

In the laboratory experiment, you will start with anthranilic acid (*ortho*-aminobenzoic acid). The amino group will be first be converted into a diazonium ion. This diazonium ion will be divided into two equal portions. One portion will be hydrolyzed with water to provide salicylic acid. The second portion will be reacted with potassium iodide to provide *o*-iodobenzoic acid. (Figure 4)

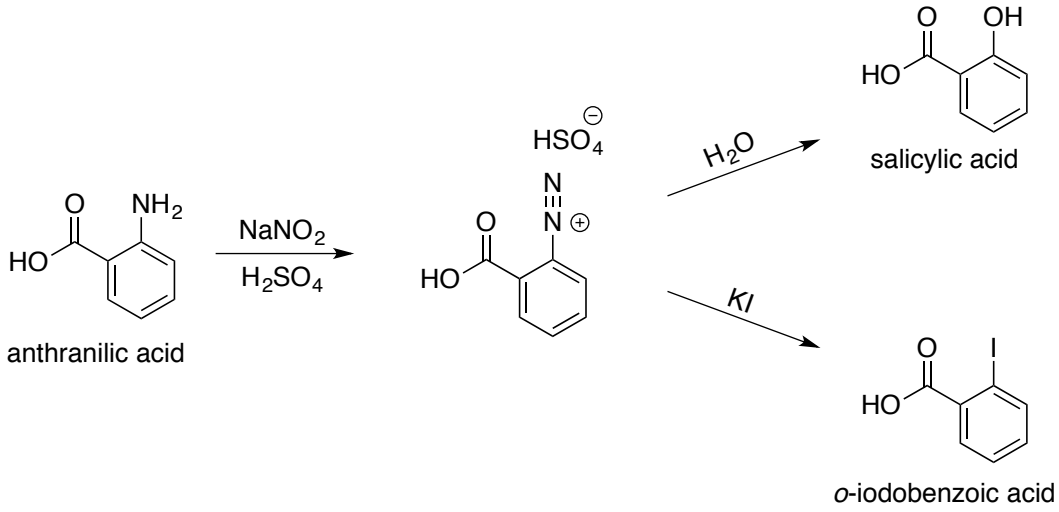


Figure 4. Conversion of Anthranilic Acid to the Diazonium Ion and Subsequent Displacement Reactions

B. Experimental Procedure

1. Preparation of the Aryldiazonium Ion

Add 300 mg of anthranilic acid to a small Erlenmeyer flask. Dissolve the solid in 3.5 mL of water and add 1.2 mL of 1.0 M H_2SO_4. Carefully warm the solution until all anthranilic acid has dissolved at which time you should cease heating and cool the solution in an ice bath for 5 min. You may see the formation of precipitate during the cooling stage.

In a small test tube supported in an ice bath prepared using a small beaker, Dissolve 188 mg of sodium nitrite in 2.3 mL of water. Allow this solution to cool in the ice bath for 5 min.

At this point, both solutions should be thoroughly cooled. Using a pipet, slowly add the sodium nitrite solution to the anthranilic acid solution. You should swirl the flask during addition to aid in mixing. Following addition, a clear solution should result.

The reaction can be monitored by testing for a slight excess of sodium nitrite. The presence of sodium nitrite can be determined using starch iodide paper. Dip a glass rod into the solution and then touch the rod onto the starch iodide paper. A dark blue color indicates the presence of excess sodium nitrite. If a positive test is not obtained, add additional sodium nitrite to the solution until excess is present.

At this stage, you should have approximately 7 mL of solution containing the diazonium ion of anthranilic acid. Divide this solution equally into two 6-inch test tubes cooled in an ice bath. You will carry out one reaction with the first portion and your lab partner will carry out the second reaction with the second portion of solution.

Approximately how many mmol of aryldiazonium is present in each portion? _____

2. Synthesis of Salicylic Acid

Take the first portion of aryldiazonium ion, and heat this solution in a boiling water bath for 10 min then cool the solution in an ice bath. Record any observations as to how the solution changes during these two steps. Collect the solid by Hirsch filtration. Wash the solid thoroughly with ice-cold water.

To purify the product, dissolve the solid in ~1 mL of methanol in a small test tube. Filter this solution through a pipet filtration assembly prepared from a small cotton plug, 1 cm of sand, 1 cm of activated charcoal, and a second 1 cm of sand. Collect the solution in a pre-weighed vial. Flush the filter with 0.5 mL of methanol and collect this filtrate along with the first portion. Add 1.5 mL of water and scratch the wall of the vial to initiate crystallization. Cool the solution in an ice bath for 10-15 min and collect the resulting solid via Hirsch filtration. Record the yield, melting point, and IR spectrum of the product.

Chemical Test to Detect the Presence of a Phenol

The product of the reaction, salicylic acid, contains a phenol group. The $FeCl_3$ chemical test can be used to test for the presence of phenols. Dissolve a few milligrams of your product in methanol and add a few drops of $FeCl_3$ solution. Record the results of this chemical test in your notebook.

3. Synthesis of *ortho*-Iodobenzoic Acid

Remove the second portion of diazonium ion solution from the ice bath. Add 193 mg (1.16 mmol) of potassium iodide dissolved in 1 mL of water. Heat this solution in a boiling water bath for 10 min. Allow the solution to cool to room temperature and add several drops of and aqueous solution $NaHSO_3$ to reduce excess iodine. Cool the solution in an ice bath then collect the crystals via Hirsch filtration. Wash the solid product with ice-cold water.

To purify the product, dissolve the solid in ~1 mL of methanol in a small test tube. Filter this solution through a pipet filtration assembly prepared from a small cotton plug, 1 cm of sand, 1 cm of activated charcoal, and a second 1 cm of sand. Collect the solution in a pre-weighed vial. Flush the filter with 0.5 mL of methanol and collect this filtrate along with the first portion. To this solution, add water (~1.5 mL) dropwise via pipet until the solution becomes cloudy. Heat this solution to dissolve the precipitate then allow it to cool slowly at room temperature at which time crystals should form. Cool the mixture containing the crystals in an ice bath for 10 min. Collec the crystals via Hirsch filtration washing with ice-cold water. Record the yield, melting point, and IR spectrum of the product.

Just as in part 2, dissolve a few milligrams of product in methanol and add $FeCl_3$ solution to test for the presence of phenol. Record the results in your notebook and compare these with the results in part 2.

C. Pre-Lab Questions

1. Explain why aryldiazonium ions are more stable than alkyldiazonium ions?

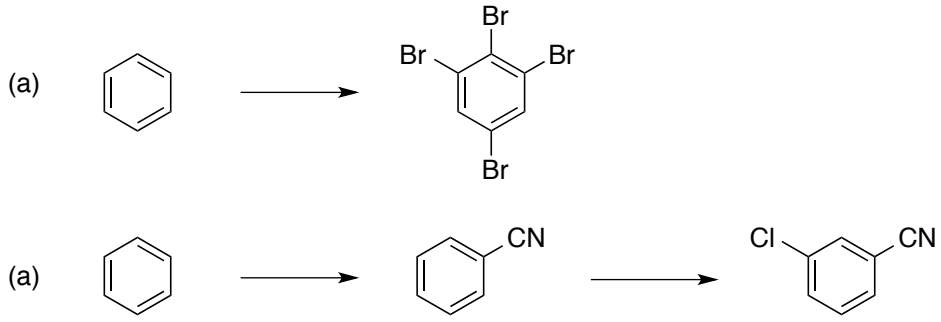
2. You will prepare *ortho*-iodobenzoic acid and salicylic acid in the laboratory experiment. Which of these products do you expect to give a positive $FeCl_3$ text? Explain.

3. Secondary amines cannot be converted to diazonium ions. Using the mechanism shown in figure 2 as a guide, show the reaction of dimethylamine with the nitrosonium ion. Where in the mechanism does the reaction stop? Show this product and the mechanistic steps leading up to it.

D. Post-Lab Questions

1. Describe the results of the $FeCl_3$ test in parts 2 and 3 of the experiment. Which product gave a positive chemical test?

2. Starting with benzene, show how the molecules shown below can be prepared using reactions discussed in the past two experiments.



3. What absorptions in the IR spectrum of each of your products can be used to help you confirm their structures?