Exp't 30

The Sandmeyer Reaction: 2-Iodobenzoic Acid

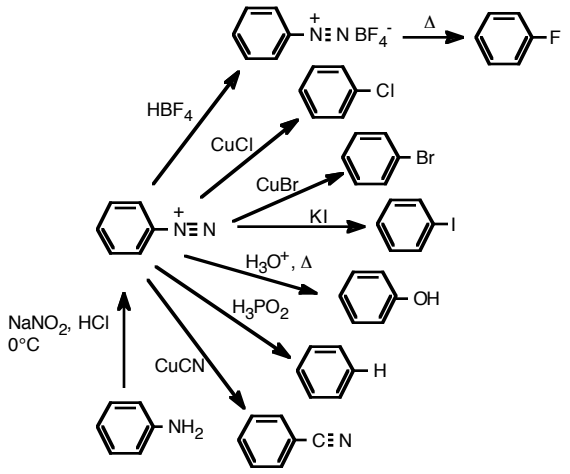
from K. L. Williamson, *Macroscale and Microscale Organic Experiments,* 2nd Ed. 1994, Houghton Mifflin, Boston *p 558, Revised 10/31/98*

Prelab Exercise

Outline the steps necessary to prepare 4-bromotoluene, 4-iodotoluene, and 4-fluorotoluene from benzene.

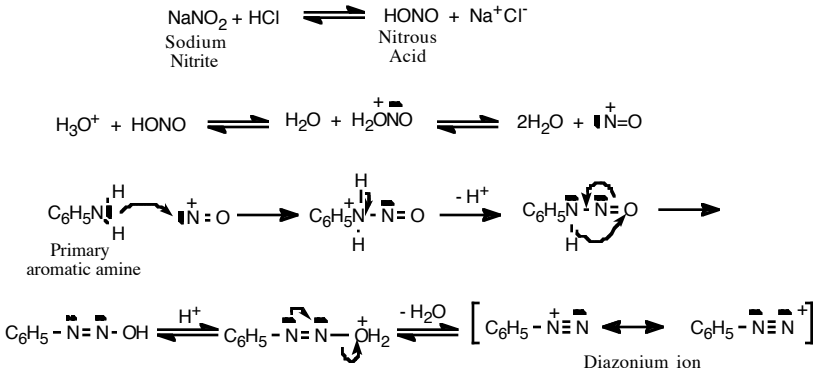
Introduction

The Sandmeyer reaction is a versatile means of replacing the amine group of a primary aromatic amine with a number of different substituents:

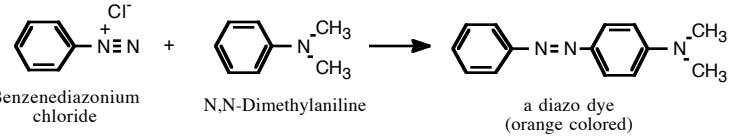


Scheme I

The diazonium salt is formed by the reaction of nitrous acid with the amine in acid solution. Nitrous acid is not stable and must be prepared *in situ*; in strong acid it dissociates to form nitroso ions, ^+NO, which attack the nitrogen of the amine. The intermediate so formed loses a proton, rearranges, and finally loses water to form the resonance-stabilized diazonium ion.



The diazonium ion is reasonably stable in aqueous solution at 0°C; on warming up it will form the phenol, as seen in Scheme I. A versatile functional group, it will undergo all the reactions depicted there as well as couple to aromatic rings activated with substituents such as amino and hydroxyl groups to form the huge class of azo dyes (see Exp't 31).

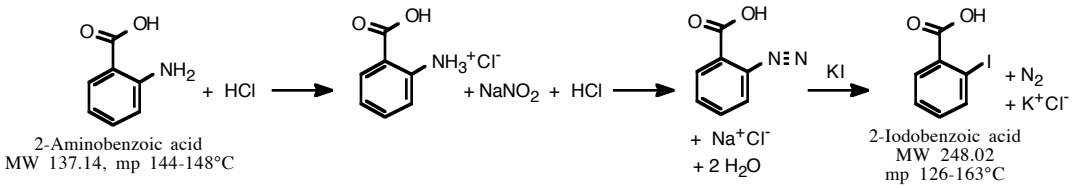


Diazonium salts are not ordinarily isolated because the dry solid is explosive.

TLC

You are required to run a TLC to monitor the progress of the reaction. Plates should have three spots (or lanes) on the origin: one for the main organic starting material that is being transformed, one for a cospot (starting material and the reaction mixture), and one for the reaction mixture.

Synthesis of 2-Iodobenzoic Acid



2-Aminobenzoic acid
MW 137.14, mp 144-148°C

2-Iodobenzoic acid
MW 248.02
mp 126-163°C

A 250-mL round-bottomed flask containing 6.9 g of anthranilic acid, 50 mL of water, and 12 mL of concentrated hydrochloric acid is heated until the solid is dissolved. The mixture is then cooled in ice. When the temperature reaches 0 to 5°C, a solution of 3.6 g of sodium nitrite ($NaNO_2$) in 25 mL of water is added slowly. After 5 min, a solution of 8.5 g of potassium iodide in 12 mL of water is added, (whereupon, a brown complex partially separates). The mixture is let stand without cooling for 5 min and then carefully warmed on a bowl of lukewarm water maintained at ~ 45 °C on a hot plate with occasional swirling. When the reaction reaches about 40°C, a vigorous reaction ensues, characterized by gas evolution and separation of a tan solid. After reacting for 10 min, the mixture is heated to ~90°C for 10 min on the hot plate and then cooled in ice.

Isolation and Purification

A pinch of sodium bisulfite is added to destroy any iodine present, and the granular dark tan to brown product is collected and washed with water. The still-moist product is dissolved in 35 mL of 95% ethanol, and the brown solution is decolorized with Norit pellets and then diluted with 15 mL of hot water. The solution is brought to the boiling point, filtered hot, diluted with 15 to 20 mL of cold water, and allowed to stand. 2-Iodobenzoic acid separates in large, slightly yellow needles (mp 164°C); even if fairly brown crystals are obtained, it is still possible to get a good mp; yield is approximately 8.3g (71%). Take a TLC of starting material and isolated product.

Analysis

In addition to TLC analysis, you may be instructed to analyze your final product by IR, NMR or MS. Analyze your sample according to your Assignment sheet and the instructions on Sample Preparation in Lab Guide.

Cleaning Up

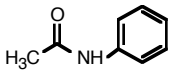
The reaction mixture filtrate and mother liquor from the crystallization are combined, neutralized with solid sodium carbonate, and flushed down the drain with a large excess of water. Norit is placed in the solid waste bin.

Questions

1. Nitric acid is generated by the action of sulfuric acid on sodium nitrate. Nitrous acid is prepared by the action of hydrochloric acid on sodium nitrite. Why is nitrous acid prepared *in situ*, rather than obtained from the reagent shelf? Hint: What is the brown gas evolved during the acidification of sodium nitrite? Refer to a freshman text like Brown and Lemay for information on nitrous acid.

2. What by-product would be obtained in high yield if the diazotization of *p*-toluidine were carried out at 30°C instead of 0 to 5°C?

3. How would 4-bromoaniline be prepared from acetanilide?



acetanilide