Exp’t 63

The Friedel-Crafts Reaction:
2-(4-methylbenzoyl)benzoic acid


revised 10/13/98

Prelab Exercise:
Draw the mechanism for the cyclization of 2-benzoylbenzoic acid to anthraquinone (shown below) using concentrated sulfuric acid.

Introduction:
The Friedel-Crafts reaction of phthalic anhydride with excess toluene as solvent and two equivalents of aluminum chloride proceeds rapidly and gives a complex salt of 2-(4-methylbenzoyl)benzoic acid in which one mole of aluminum chloride has reacted with the acid function to form the salt RCO₂⁺AlCl₂⁻ (shown below) and a second mole is bound to the carbonyl group.

On addition of ice and hydrochloric acid, the complex is decomposed and basic aluminum salts are brought into solution.

Anthracene is synthesized using a very similar protocol.

Precautions:
Aluminum chloride is very hygroscopic and releases hydrogen chloride upon reaction with water, including moisture in the air. It should be stored in a dessicator jar. The aluminum chloride should be weighed in a small, dry, stoppered vial or reaction tube on the balance in the hood at desk number 3. The quality of the aluminum chloride determines the success of the experiment.
**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.

**Procedure: 2-(4-Methylbenzoyl)benzoic acid**
Into a dry 10 x 100 mm reaction tube place 150 mg of phthalic anhydride and 0.75 mL of anhydrous toluene. Cool the mixture in an ice bath, and then add 300 mg of anhydrous aluminum chloride.\(^1\) (Note: Aluminum chloride is very moisture sensitive and should be weighed quickly. Cap the bottle immediately after use). Cap the tube with a septum connected to Teflon tubing leading to another reaction tube, which contains a piece of damp cotton to act as a trap for the hydrogen chloride liberated in the reaction. To thread a Teflon tube through a septum, make a hole through the septum with a needle, and then push a toothpick through the hole. Push the Teflon tube firmly onto the toothpick, and then pull and push on the toothpick. The tube will slide through the septum. Finally, pull the tube from the toothpick.

Mix the contents of the tube thoroughly by flicking the tube. Warm the tube by the heat of the hand. If the reaction does not start, warm the tube very gently in a beaker of warm water or hold it over the sand bath for a few seconds. At the first sign of vigorous boiling or evolution of hydrogen chloride (as evidenced by testing the gas coming out of the end of the teflon tube on a wet piece of pH test paper), hold the tube over the ice bath in readiness to cool it if the reaction becomes too vigorous. Continue this gentle, cautious heating until the reaction proceeds smoothly enough to reflux it on the hot sand bath. This will take about 5 min.

Heat the reaction mixture on the sand bath until evolution of hydrogen chloride almost ceases, then cool it in ice, and add around 1 g of ice in small pieces. Allow each little piece to react before adding the next. Mix the reaction mixture well during this hydrolysis using a glass rod. After the reaction subsides, add 0.1 mL of concentrated hydrochloric acid and 1mL of water.

Mix the contents of the tube thoroughly, and make sure the mixture is at room temperature. Add 0.5 mL more water, mix the solution well, ascertain that it is at room temperature, and then add 1.5 mL of ether (use the wet ether found in a supply bottle in each hood) and break up any lumps in the tube with a stirring rod. Stopper the tube and shake it vigorously to complete the
hydrolysis and extraction. Allow the layers to separate, and then remove the aqueous layer with a Pasteur pipette. Add 0.1 mL of concentrated hydrochloric acid and 0.15 mL of water. Shake the mixture vigorously again, and remove the aqueous layers.

Transfer the organic layers to a small test tube containing calcium chloride pellets. Allow the solution to dry for 5 min., and then transfer it back to the clean dry reaction tube, rinsing the drying agent with a small quantity of ether. Add a boiling chip, and boil off the solvents until the volume in the tube is 0.5 mL, then add hexanes until the solution is slightly turbid, indicating that the product is beginning to crystallize. Allow the product to crystallize at room temperature and then at 0°C. Collect the crystals on a Hirsch funnel by vacuum filtration. Pure 2-(4-methylbenzoyl)benzoic acid melts at 138 to 139 °C, the yield should be about 0.2 g.

*Note: Celite may speed up the filtration.*

**Analyses:**
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 the Lab Guide.

**Cleaning Up:**
Combine all aqueous layers, neutralize with sodium carbonate, remove the aluminum hydroxide by filtration, and flush the filtrate down the drain. The aluminum hydroxide and calcium chloride pellets, after being freed of organic solvent, can be placed in the nonhazardous solid waste container. Benzene, ether, and hexanes go in the organic solvents waste container.

**Post Lab Questions:**
1. Calculate the number of moles of hydrogen chloride liberated in the microscale synthesis of 2-benzoylbenzoic acid. If this gaseous acid were dissolved in water, hydrochloric acid would be formed.
   How many milliliters of concentrated hydrochloric acid would be formed in this reaction? The concentrated acid is 12 M in HCl.
2. Write a mechanism for the formation of 2-(4-methylbenzoyl)benzoic acid from toluene and phthalic anhydride using an aluminum chloride catalyst.