

A Multi-step Synthesis. Benzaldehyde to Benzoin. Benzoin to Hydrobenzoin and Benzil. Benzil to Tetraphenylcyclopentadienone.

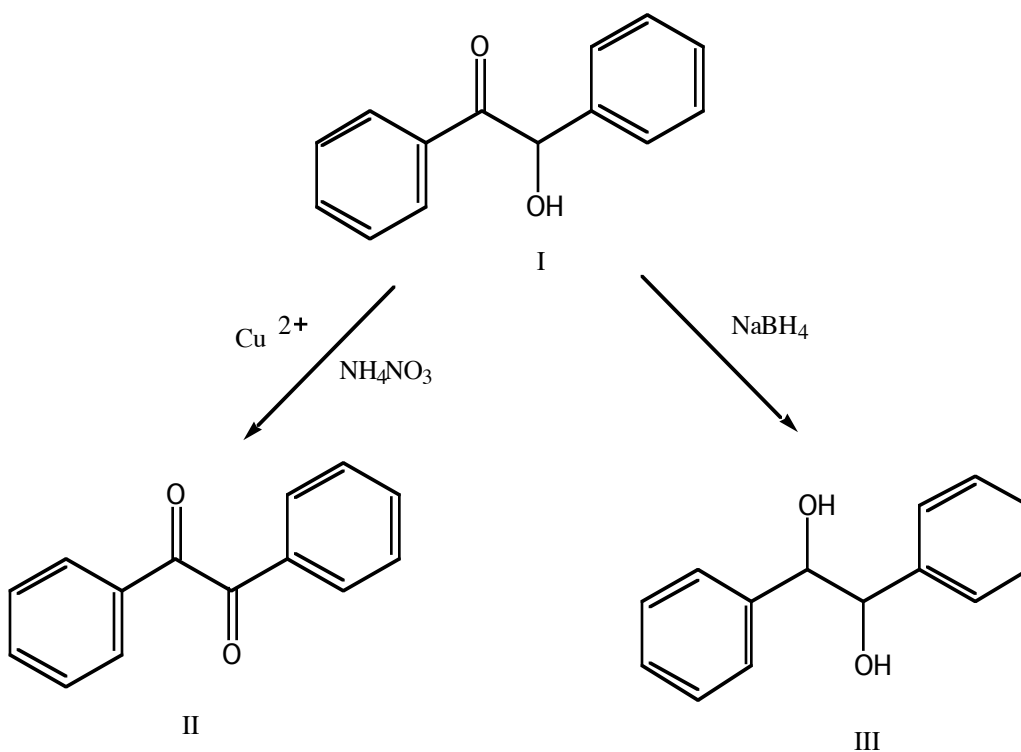
This experiment will be carried out over two lab periods. One report will be written for both weeks. Include an "Experimental" section as in the Grignard write-up. Good planning and execution will be essential for completion of the experiment. IR's, TLC's, and MP's, and final recrystallizations should be done during lulls in the action. Much of this can be done during Week 2.

Pre-Week 1. The Benzoin Condensation. Benzaldehyde to Benzoin.

Benzaldehyde is allowed to react in the presence of sodium hydroxide and thiamine for one week, according to the procedure in Williamson, p. 616, 617. Work-up of the reaction is done at the beginning of the following lab period to yield benzoin which will be used in subsequent reactions. A sample should be kept for recrystallization and analysis by mp, ir and tlc. The reflux in the following oxidation must be started as soon as possible.

Week 1. The Oxidation and Reduction of Benzoin

Benzoin (I), having both a secondary alcohol and a ketone functional group can be oxidized to a diketone, benzil (II), or reduced to a diol, hydrobenzoin (III). In this experiment, the commonly used reducing agent, sodium borohydride, is used for the reduction. The oxidation can be accomplished with any of several oxidizing agents, including nitric acid. Nitric acid oxidation however produces toxic nitrogen dioxide gas. In the experiment described herein, a catalytic amount of copper (II) is used as the oxidizing agent, with ammonium nitrate used to regenerate the catalyst.



Both the oxidation and reduction will be carried out on the same day. The oxidation requires a 1.5 hr reflux period so that reaction should be set up first. While the oxidation is proceeding, the reduction will be carried out. It is important to plan well so that everything can be done in one lab period.

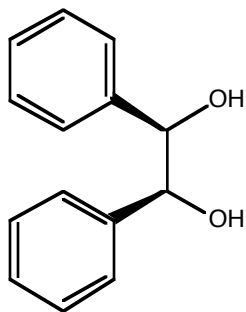
Oxidation of Benzoin. Because the procedure for the oxidation will be taken from an article in the library it is essential that you find the article and prepare the prelab outline well in advance of the lab. Find the journal article, "The Catalytic Oxidation of Benzoin to Benzil", J. Am. Chem. Soc. **1948**, *70*, 3666 and, using the procedure in that reference (small run), plan a synthesis of benzil starting with 0.0025 mol of benzoin, scaling down the quantities of all other reagents by the same factor. Note that reaction time remains the same. Heat carefully on the heating mantle, with swirling (not shaking) until the vigorous evolution of nitrogen subsides then adjust the heat for a gentle reflux. (On the small scale used here, nitrogen evolution may not be vigorous and in fact may not be noticed. Once the reactants are dissolved, assume nitrogen evolution is complete and proceed with the reflux.) **While the 1.5 hour reflux is taking place, carry out the next reaction, "Reduction of Benzoin".**

After the 1.5 hr reflux, modify the procedure for the work-up as follows: cool the reaction mixture until the flask is just warm to the touch then add it to about 2.5 mL of ice-water, with stirring. Cool the mixture in an ice bath for 5 - 10 min and collect the product by suction filtration. Temporarily break the vacuum by lifting the filter slightly off of the filter flask, cover the crystals with 2 mL of ice-cold rinse water, and immediately reattach the vacuum to remove most of the water. Allow the product to dry at least overnight, weigh it, calculate a % yield, obtain an ir spectrum (mull) and determine the mp. Save the product for a subsequent reaction.

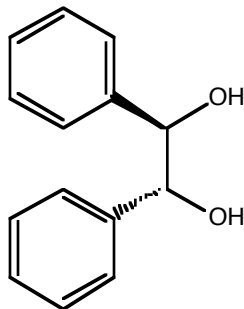
Reduction of Benzoin. In a 50 mL Erlenmeyer flask, dissolve 1.0 g of benzoin in 10 mL of ethanol (all of the benzoin may not dissolve - this is ok). Carefully add, in small portions, over 5 minutes, 0.20 g of sodium borohydride, with swirling. This reaction is exothermic and care must be taken to not add the borohydride too rapidly. After addition is complete, allow the reaction to proceed at room temperature for 20 min, with frequent swirling. While cooling in an ice bath, add 15 mL water, then 0.5 mL 6M HCl. Add another 5 mL of water and allow the mixture to stand for 20 min with frequent swirling. Collect the product by suction filtration and rinse with 50 mL of water. Recrystallize about 50 mg of the solid by dissolving it in 0.5 mL warm ethanol, adding 1 mL of warm water and allowing it to cool to rt then in an ice bath for at least 45 minutes, an hour if time allows. While this is crystallizing, work up the oxidation reaction, which should be finished refluxing at this point. Once the crystallization of hydrobenzoin is complete, separate the crystals from the solvent, rinse, and allow them to dry at least overnight. A mp and ir spectrum (mull) will be determined and a tlc run.

On the stereochemistry of the reduction. Reduction of benzoin can lead to different stereoisomers - a *meso* compound and a pair of enantiomers. Using the mp of the product, decide which, if any, isomer predominates in the reduction reaction. In the

discussion, explain why one isomer might predominate. (Hint: the hydroxyl group in benzoin can coordinate with the borohydride, thus causing a hydride to add to the carbonyl from the side on which the hydroxyl group is situated. Using models and considering the stability of the benzoin conformers, try to predict on which side of the carbonyl the hydride will be delivered.)



meso - isomer



one isomer of an
enantiomeric pair

(pws, 4 apr 03)