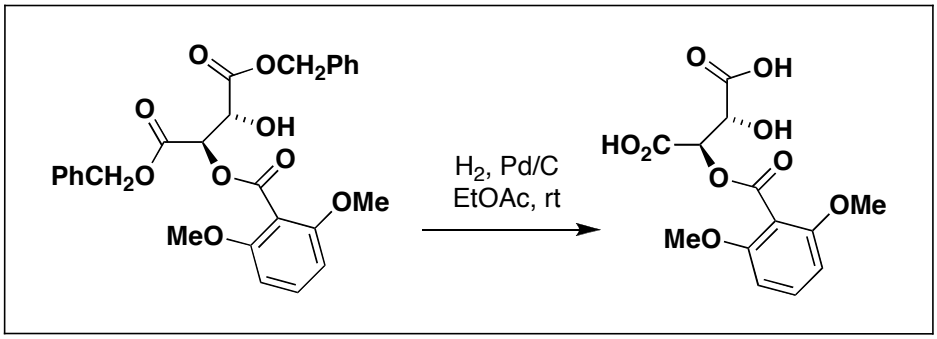
5.37 Introduction to Organic Synthesis Laboratory

Spring 2009

Days 5-6 Deprotection of Benzyl Esters by Hydrogenolysis



Day 5: Setting Up the Hydrogenation Reaction

Equipment: Disposable glass pipettes and pipette bulbs, balloons, 250-mL three-necked round-bottomed flask, reflux condenser, three-way stopcock with inlet adapter, magnetic stirbar, oil bubbler, 2 glass stoppers, 100-mL graduated cylinder, ethyl acetate, palladium on carbon.

Equip a 250-mL, three-necked, round-bottomed flask with a magnetic stirbar, two glass stoppers in the side necks, and a reflux condenser in the center neck. The condenser simply functions as a "spacer" and is not connected to a water line. The top of the condenser is fitted with an inlet adapter connected to a three-way stopcock. One branch of the stopcock is connected by tygon tubing to the nitrogen line, and the other branch to an oil bubbler to allow for the monitoring of the nitrogen flow rate. Flush the reaction flask with nitrogen for 5 min by closing the bubbler off at the three-way stopcock and opening one of the side necks of the flask as an outlet for the nitrogen. After 5 min, charge the flask with 10% palladium on carbon (10% by weight to the amount of dibenzyl ester that you will be using). Next, add 90 mL of ethyl acetate carefully, washing any palladium on carbon off the walls of the inside of the flask so that all of the catalyst is under the surface of the solvent. Finally, add the dibenzyl ester via dispo pipette, using 10 mL of ethyl acetate to rinse the flask and pipette used for the transfer. Continue flushing the flask with nitrogen for 3-4 min and then seal the side neck with a glass stopper.

Prepare two "hydrogen balloons" by connecting each balloon to a 5-cm length of tygon tubing and securing the balloon to the tubing using copper wire. Wrap the connection with electrical tape to further ensure a tight seal. Turn the stopcock on your flask so that it is open to the nitrogen line and flask, and closed off from the oil bubbler. Detach from the stopcock the tygon tubing leading to the bubbler, and replace it on the stopcock with a balloon filled with hydrogen. Turn the stopcock so as to close off the nitrogen line and to open the flask to the hydrogen balloon, simultaneously loosening a glass stopper on a side neck so as to allow the flask to be flushed with hydrogen. Next, turn the stopcock to close off the balloon, remove and refill the balloon with hydrogen, and flush the flask with hydrogen a second time. Close the side neck tightly with the glass stopper, remove and refill the balloon with hydrogen as described above, and replace the freshly filled balloon on the stopcock. Attach a a second balloon filled with hydrogen to the other branch of the stopcock in place of the nitrogen line. The stopcock should then be turned so that both balloons are open to the flask and the reaction mixture is stirring under an atmosphere of hydrogen. A photograph of a typical reaction

setup is shown in Figure 2 below. After 24 h, it will be necessary to refill the balloons with hydrogen which may be lost by diffusion. The hydrogenolysis reaction will be allowed to run until your next laboratory period.

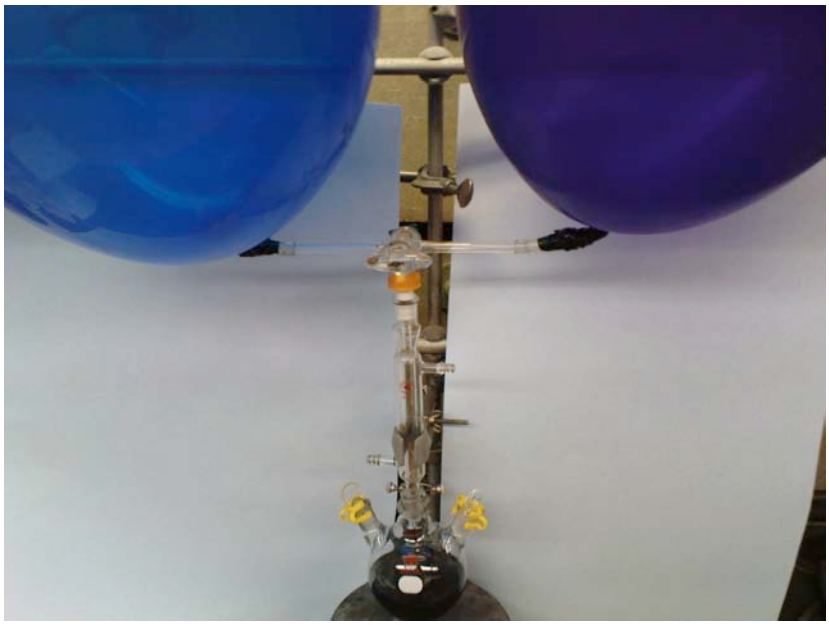


Figure 2. Hydrogenolysis reaction setup.

Day 6: Workup of the Hydrogenation Reaction

Equipment: Glass-backed silica TLC plates, glass capillary TLC spotters, TLC chambers with filter paper, TLC developing stock solutions (ceric ammonium molybdenate, phosphomolybdic acid, and p-anisaldehyde), small vials, disposable glass pipettes and pipette bulbs, sand bath, 100-mL graduated cylinder, Buchner funnel, 500-mL Erlenmeyer filter flask, round-bottomed flasks (100 and 250 mL), inlet adapter, Celite.

Confirm that the hydrogenolysis is complete by TLC analysis of a sample of the reaction mixture withdrawn via a side neck with your TLC spotter (close off the balloons before opening the neck!). Use 3:1:5 hexane-ether-dichloromethane as eluant for the TLC analysis. Suction filter the reaction mixture through a 1.5-cm pad of Celite in a Buchner funnel into a 250-mL Erlenmeyer filter flask. Before filtering your mixture, run some ethyl acetate through the Celite and then pack it down in the funnel using a stopper or the bottom of a small vial. Be sure to wash the solid thoroughly with three 20-mL portions of ethyl acetate. Do not allow the solid to become dry as it may ignite! Leave the solid damp after the third wash and transfer the material immediately to the special palladium waste container as described in Section VI.

Transfer the filtrate to a tared, 250-mL, round-bottomed flask (using a small amount of dichloromethane to rinse the Erlenmeyer) and concentrate the filtrate by rotary evaporation. Transfer the resulting material to a 100-mL round-bottomed flask using methanol. Concentrate this

solution and record the weight of your crude product. Equip the flask with an inlet adapter and attach it by rubber tubing to a vacuum pump. Dry the crude product for 24-48 h under vacuum (less than 1 Torr) at 80 °C in a sand bath. It is important to thoroughly dry the product as residual organic solvent will result in diminished enantioselectivity in the asymmetric Diels-Alder reaction. Record the weight of the dried product; you should obtain 3.0-3.5 g of the diacid. This can be performed on the "off day"for your group between Day 6 and Day 7 of the experiment, or can be postponed until the beginning of Day 7.