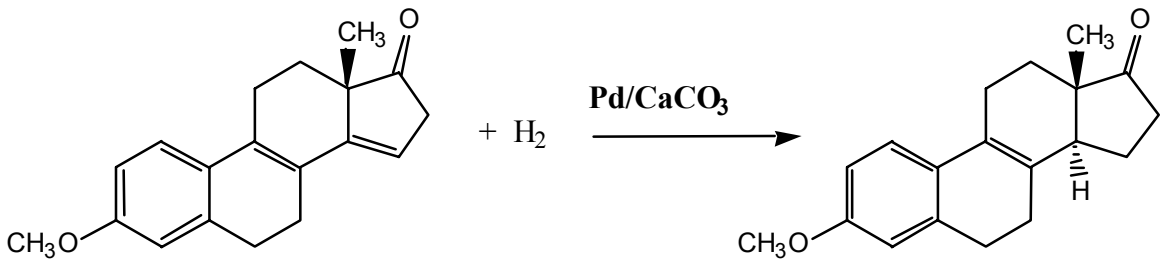
STEP 3:

3-METHOXY-1,3,5(10),8(9)-ESTRATETRAENE-17-ONE



1. Procedure

Dissolve the starting material, 3-methoxy-1,3,5(10),8(9),14(15)-estrapentaene-17-one in toluene (~ 0.05 M) in a 500-mL, three-necked, round-bottomed flask equipped with a magnetic stirbar and two rubber septa on the side necks. **NOTE: Be sure to calculate how much material you can use in the reaction. The water buret has a maximum capacity of 250 mL of hydrogen gas and you need to fill with 1.2 eq. of hydrogen.** Add the catalyst, (5% palladium on calcium carbonate, 30 wt% relative to estrapentaeneone). Connect the center neck of the reaction flask to the atmospheric pressure hydrogenation apparatus shown in Figure 3. Do not start stirring yet. Make sure you perform the next few steps under the ***direct supervision*** of a teaching assistant.

Before attaching the hydrogen tank hose, open stopcock 2 and the burette stopcock to the atmosphere. Raise the leveling bulb so that the gas burette is filled with water up to the level of stopcock. Close the burette stopcock. Attach the vacuum hose and the hydrogen tank hose to stopcock 2 as shown. With stopcock 2 closed and the Firestone Valve open, open the hydrogen tank and adjust the regulator to give a slight positive gas pressure (note 1). Open the system to vacuum by turning stopcock 2. Evacuate the flask until the solvent just bubbles. After bubbling calms down, stir rapidly to thoroughly degas the solution. The flask should get cold as xylenes are pulled off.

Stop stirring and then turn stopcock 2 to fill the system with hydrogen (note 2). Repeat at least three times. (Note: The more thoroughly the system is degassed and saturated with hydrogen, the faster the subsequent hydrogenation proceeds. A little extra time here can can save a lot of time later on). Detach the leveling bulb from the ring stand and lower it below the level of the water in the buret. Now open the burette stopcock and continue to lower the leveling bulb to fill the hydrogen burette with the appropriate amount of gas (at least 1.2 equivalents). Record the initial water level in the buret. Turn stopcock 2 to a neutral, closed position. Leave the burette stopcock open, and begin stirring. Reattach the leveling bulb at an elevated position on the ring stand. Close and disconnect the hydrogen tank for the next user.

To accelerate the reaction, use a crystallizing dish with warm tap water to warm the reaction flask to room temperature. The reaction flask should turn dark black over the course of a few minutes and the water level in the buret should begin to visibly rise as the reaction speeds up. If neither of these should occur after a few minutes, consult a teaching assistant for troubleshooting. Monitor the amount of hydrogen consumed by reading the burette volume every few minutes. To read the gas burette, raise or lower the leveling bulb until the water level is the same in both the bulb and burette.

The reaction is complete when at least one equivalent of gas has been consumed (typically less than one hour). When the reaction is complete, remove the hydrogen from solution by three pump-backfill cycles using nitrogen in an opposite fashion to which the solution was saturated with hydrogen. Remove the catalyst by suction filtration through a Celite pad (note 4). Evaporate the solvent (note 5) on the rotary evaporator or under vacuum. (Use a dry ice- or liquid nitrogen-cooled solvent trap between the vacuum line and the product solution.) The resulting oil may solidify upon concentration from ether. Examine the final reaction product by TLC and NMR spectroscopy. Purify your product by a suitable technique (either column chromatography with using an appropriate eluent or recrystallization from 1:1 ether/pentane or pure methanol).

2. Notes

1. Hydrogen is a flammable, potentially explosive gas. Check for open flames or spark sources before opening the tank.

2. The glass float in the Firestone valve allows excess pressure to vent but prevents entry of air when the system is under vacuum.

3. Avoid the temptation to add more catalyst if the reaction is proceeding too slowly. **Never** add catalyst to a reaction vessel under a hydrogen atmosphere. The exothermicity of hydrogen chemisorption will ignite the atmosphere.

4. Do not allow the catalyst-containing filtrate to become dry. It now contains chemisorbed hydrogen which may ignite upon exposure to oxygen. Dispose of the filtrate in the appropriate waste container, not the trash can.

5. Toluene is both toxic and flammable. Avoid breathing the fumes. Dispose of the waste solvent in the solvent waste container. Never pour organic waste in the sink.

3. Characterization and Report

Determine the yield of product, both crude and purified.

Characterize the purified material by IR, ^{1}H and ^{13}C NMR, and melting point.

Assess the purity of the final material based on the spectral data.

Tabulate and assign the spectral data

List the TLC conditions used and the R_f values of starting material and product.

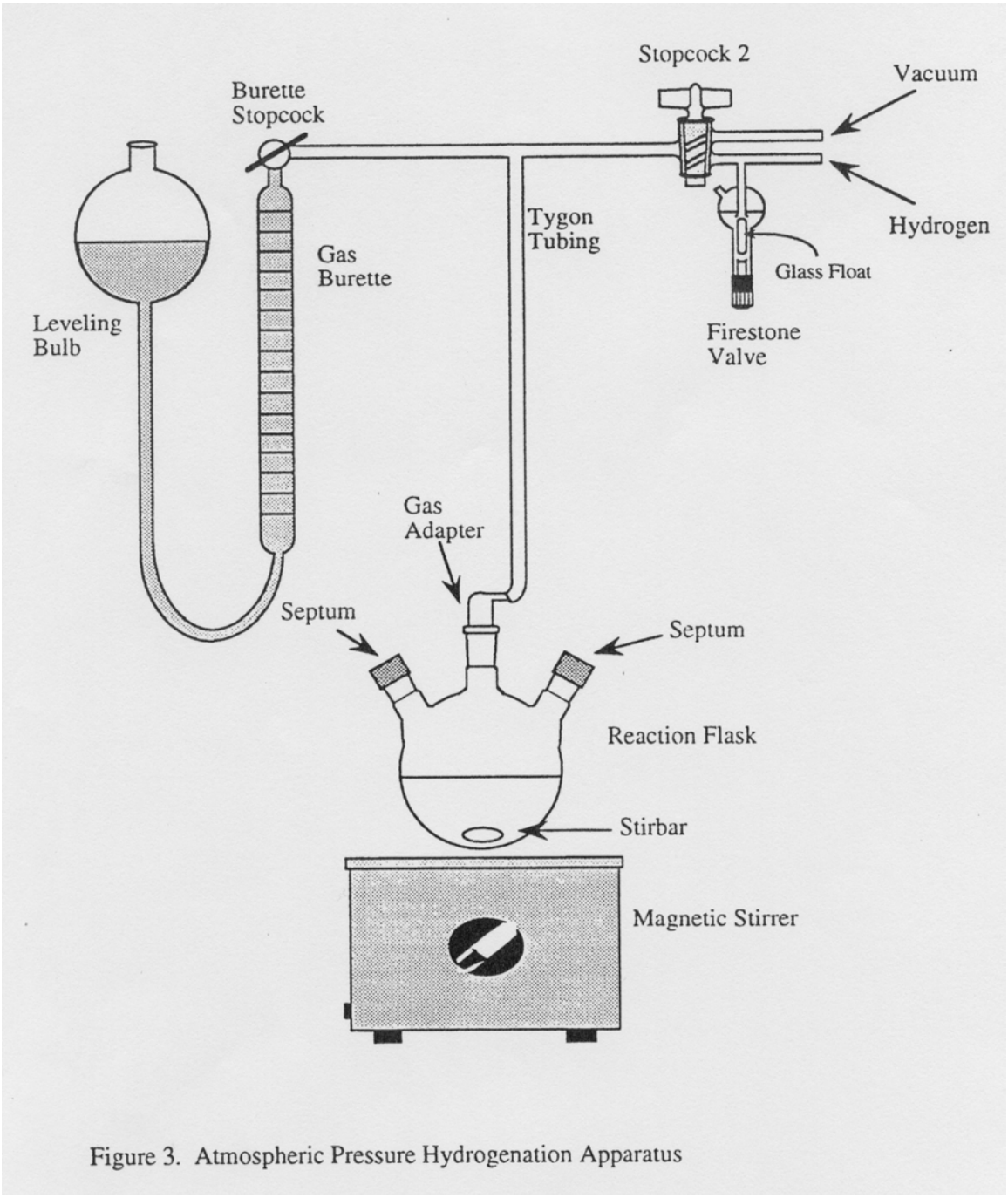


Figure 3. Atmospheric Pressure Hydrogenation Apparatus