Names: _____ *Sec.* _____
Chem 227/ Dr. Rusay

Postlab : Chiral Compounds and Green Chemistry: Reduction of a ketone by sodium borohydride and baker's yeast

PART IV:
A) Edit the procedures for each Method below on the handout to suggest how they might be improved.

METHOD 1: Reduction of Ethyl Acetoacetate with Sodium Borohydride

Add sodium borohydride (1.5 g, 40 mmol, MW 37.83) to ethanol (25 mL) in a 100-mL round-bottomed flask, and cool the resulting mixture to 0 °C. To this mixture add a solution of the ethyl acetoacetate (5.0 g, 38 mmol, MW 130.14) in ethanol (15 mL), and stir the resulting solution at 0 °C for 15 minutes, then at room temperature for 15 minutes.

Evaporate the solvents on a rotary evaporator, and suspend the resulting white solid in dichloromethane (30 mL). Add 1 M hydrochloric acid (30 mL) drop-wise to quench the reaction. (**CAUTION:** The addition of HCl will cause frothing and will release hydrogen gas.) Add the hydrochloric acid slowly and while the flask is on ice. Separate the organic layer. Extract the aqueous layer two times with dichloromethane (20 mL). Combine the organic layers and dry using magnesium sulfate. Filter off the magnesium sulfate and evaporate the solvent using a rotary evaporator with a water bath temperature no higher than 30 °C.

METHOD 2: Chiral Reduction of Ethyl Acetoacetate with Baker's Yeast

Fermentation Apparatus. Equip a 500-mL Erlenmeyer flask with a magnetic stirring bar and a one-hole rubber stopper with a glass tube leading to a beaker or a test tube containing a solution of barium hydroxide. Protect the barium hydroxide from air by adding some mineral oil or xylene to form a layer above the barium hydroxide. A precipitate of barium carbonate will form, indicating that carbon dioxide is being evolved during the course of the reaction. Oxygen from the atmosphere is excluded through the use of the trap.

Add 100 mL of tap water, 30 g of sucrose, and about 3.5 g (one package) of dry baker's yeast to the flask. Add these materials, while stirring, in the order indicated. Attach the trap to the fermentation flask. Stir this mixture for about 1 hour, preferably in a warm location. Add 4.0 grams of ethyl acetoacetate and allow the fermenting mixture to stand at room temperature until the next laboratory period, stirring vigorously. If your laboratory is equipped with a shaker, place your flask in the shaker until the next laboratory period.

After this time, prepare a second warm (about 40°C) solution of 30 g sucrose in 100-mL tap water. Add this solution, along with 3.5 g (one package) of dry baker's yeast to the fermenting mixture and allow it to stir for 48 hours (with the trap attached) at room temperature.

Place about 8 g of Filter Aid in a beaker with about 20 mL of water. Stir the mixture vigorously and then pour the contents into a small Büchner funnel (with filter paper) while applying a gentle vacuum, as in a vacuum filtration. Be careful not to let the Filter Aid dry completely. This procedure will cause a thin layer of Filter Aid to be deposited on the filter paper. Discard the water that passes through this filter. Decant as much of the clear supernatant fluid as possible and pass

it through this filter, using very gentle suction. Filter the residue through the same filter. The extremely tiny yeast particles are trapped in the pores of the Filter Aid.

Wash the residue with ~20 mL of water, allowing the water to pass into the flask containing the filtered reaction mixture. Add ~30 g of sodium chloride and stir the mixture vigorously for 5 minutes. Extract the aqueous solution with three separate 30-mL portions of diethyl ether using a 250-mL separatory funnel. Be careful not to shake the separatory funnel too vigorously to prevent the formation of emulsions. If an emulsion should develop, drain the aqueous solution from the separatory funnel up to the level of the emulsion. Add 2-3 mL of water to the separatory funnel and swirl the mixture to break up the emulsion. Drain the remaining water from the separatory funnel.

Collect the ether extracts in a 125-mL Erlenmeyer flask, add ~1 gram of anhydrous magnesium sulfate, stopper the flask, and allow the solution to dry for at least 5 minutes. Decant the liquid into a beaker, add a boiling stone, and evaporate the ether using a warm water bath in the hood and a stream of air or nitrogen to recover the liquid ester. You should recover about 2-3 mL of liquid.

Prepare a small chromatography column in the following manner. Place a small plug of cotton in a 5-inch Pasteur pipet. Tamp the cotton to form a loose plug. Add alumina on top of the cotton plug to form a column 1 cm high. Tap the pipet with your finger to pack the alumina. Using a second Pasteur pipet, add the crude hydroxyester to the column. Rinse the remaining crude product onto the column using 1-2 mL of methylene chloride. Collect the eluted product in a 10-mL Erlenmeyer flask.

Use a dropper bulb to force the liquid material through the chromatography column. Dry the organic layer over anhydrous magnesium sulfate for about 10 minutes. Decant the dried solution into a pre-weighed 10-mL beaker. Evaporate the solvent in a warm water bath (at about 60°C) using a gentle stream of air or nitrogen. Weigh the beaker again in order to determine the weight of the pure hydroxyester obtained.

METHOD 3: Chiral Reduction of Ethyl Acetoacetate by Sodium Borohydride and (L)-Tartaric Acid

Place a magnetic stir bar in a 50-mL round-bottomed flask and add approximately 15 mL of tetrahydrofuran (THF). Add sodium borohydride (0.50 g, 13 mmol, MW 37.83) to the flask and begin stirring. To the suspension, add (L)-tartaric acid (2.0 g, 13 mmol, MW 150.09) and stir for 15 minutes. Cool the flask on an ice bath and add ethyl acetoacetate (0.44 g, 3.4 mmol, MW 130.14). Remove the flask from the ice bath and stir for 1 hour.

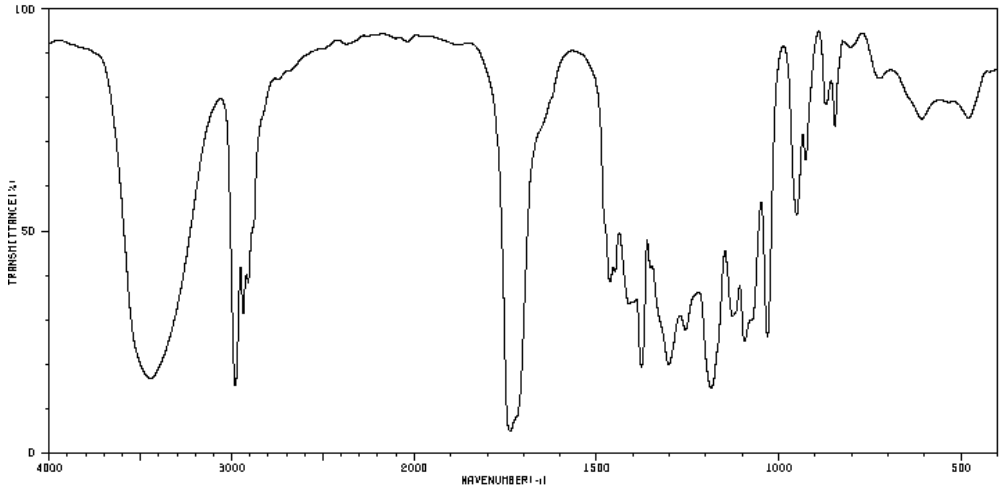
Quench the reaction with 15 mL of 1 M hydrochloric acid. Recall that addition of the acid will cause violent frothing and the formation of hydrogen gas. The acid should be added drop-wise while the flask is on an ice bath and the reaction is stirring. After adding the HCl, remove the flask from the ice bath and stir the solution for 10 minutes.

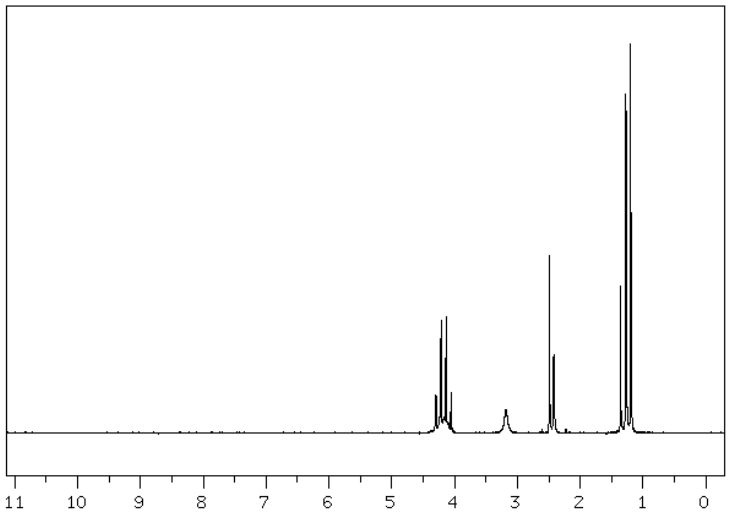
Extract the solution two times with ethyl acetate (30 mL). If your separatory funnel is not large enough to allow sufficient mixing of the aqueous wash with your organic layer, you may need to separate the extracts into two portions. Wash the extracts with saturated aqueous sodium bicarbonate solution (40 mL) and separate the layers. Wash the organic layer with saturated aqueous sodium chloride solution (40 mL) and again separate the layers. Aqueous layers should be kept until you are certain the product is in the organic layer. Dry the organic layer with magnesium sulfate. Filter off the magnesium sulfate.

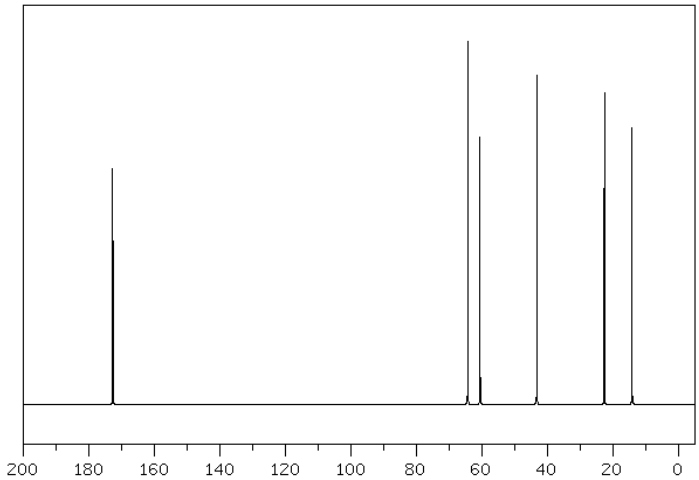
Use a rotary evaporator to remove the solvent. Using a 5.75" Pasteur pipette, prepare a microscale column with neutral alumina as the absorbent and dichloromethane as the eluent. (See pages 160-165 of your laboratory guide for background.) Place a small piece of cotton in the pipette and carefully push it to the bottom. The cotton should allow liquid to freely move through the column. Fill the pipette with approximately 1.5" of alumina. Add dichloromethane (2 mL) to the column allowing it to drain through the alumina until the solvent surface is just above the alumina surface. This fraction of dichloromethane can be properly discarded. Prepare a 25-mL round-bottomed flask to collect the product. Transfer the product from the 250-mL round-bottomed flask to the wet column. Rinse the round-bottomed flask with dichloromethane (1-2 mL) to dissolve any remaining product and add this to the column. Allow the mixture to flow through the column until the solvent level just reaches the alumina. Add dichloromethane (2 mL) to the column and again allow the mixture to pass through the column as before. Repeat with another portion of the solvent (2 mL) to elute the product from the column. Use a rotary evaporator to remove the solvent.

B) Submit a short final report which is to be typed with molecular structures drawn using a template or electronically with ISIS Draw, Marvin or similar structural drawing software program for each reaction. The report must follow the general format of the publication that you were provided in the previous handout. Use the spectroscopy data for each Method's product which follows. Lab Notebook pages for each method are to be attached to the typed report.

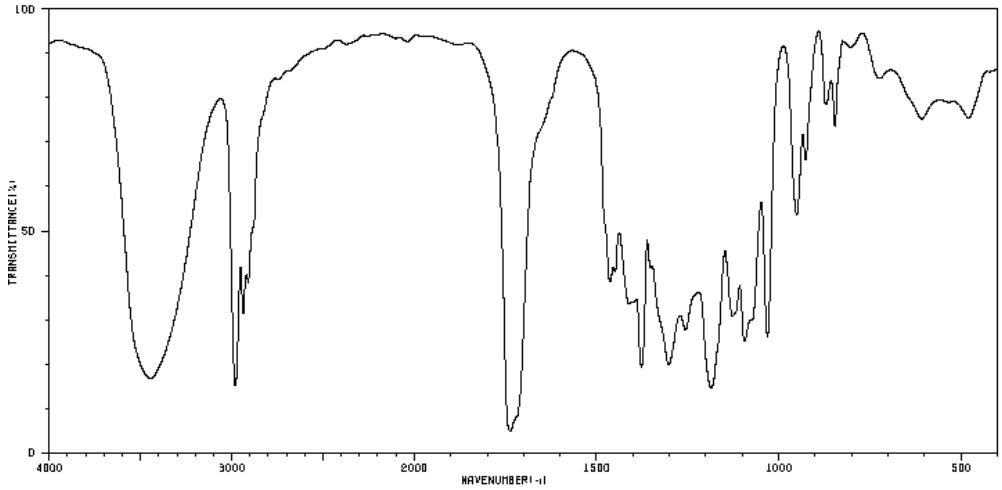
Spectroscopy Data: ***Method 1***

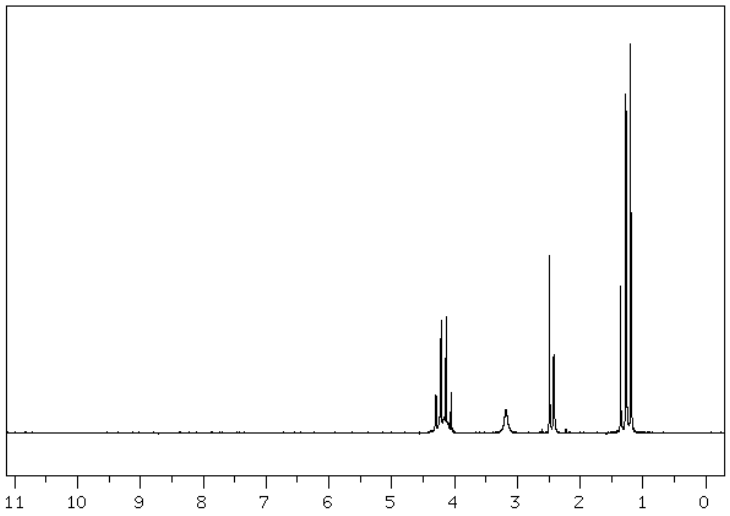


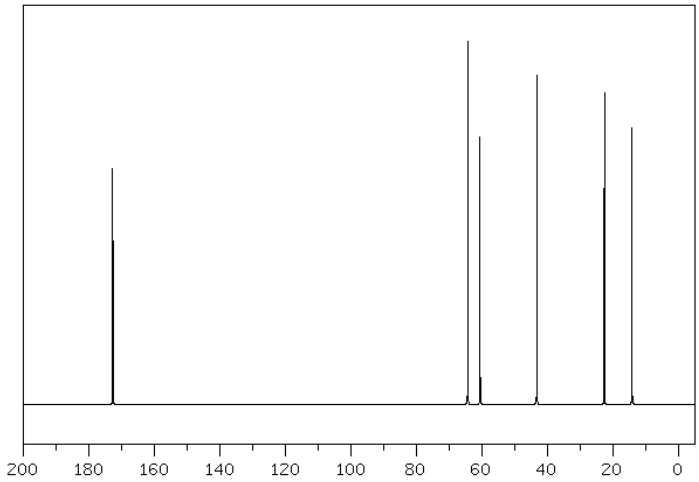




Spectroscopy Data: ***Method 2***







Spectroscopy Data: ***Method 3***