5. Acylation of Ferrocene

M. Jones: Ferrocene, 12.7, structure on page 572.

J.R. Mohrig, C.N. Hammond, and P.F. Schatz: Technique 15, 15.1 – 15.8, pgs 177 – 189
Technique 17, 17.1 – 17.7, pgs 190 – 226

This procedure has been adapted from the microscale procedure described in the third edition of *Macroscale and Microscale Organic Experiments* by Kenneth L. Williamson (Houghton Mifflin, Boston, 1999).

Background

Ferrocene. In this laboratory, you will acylate ferrocene (Figure 1). Ferrocene is an organometallic compound, which behaves like an aromatic compound. As one would suppose, an organometallic compound contains both a hydrocarbon and a metal. Sometimes this molecule is referred to as a "sandwich" complex because the iron is "sandwiched" between two rings.

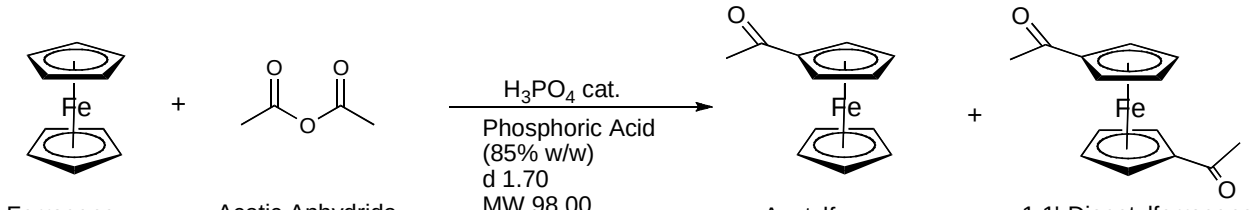

Figure 1. The overall reaction for the acylation of ferrocene.

One way to look at this molecule is to think of it as containing two cyclopentadienyl anions (formal -1 charge per each ring) and an iron atom with a +2 charge. Cyclopentadienyl anion is an aromatic compound, and its π electrons bond to the iron to yield an overall neutral complex.

The reactivity of ferrocene is similar to other aromatic compounds. Therefore, it can undergo electrophilic aromatic substitution in a very similar mechanism to that of benzene.

In this experiment, ferrocene is acylated using acetic anhydride with a catalytic amount of phosphoric acid. There are two possible products, acetylferrocene and 1,1'-diacetylferrocene, which will be identified at the end of this reaction.

Cautions:
-Take extra care when handling the acetic anhydride and phosphoric acid.
-Make sure to use a clean spatula and reaction tube. The reaction tubes should be cleaned with soap, water and a brush first, rinsed thoroughly, and dried (if needed rinse with acetone).
-Make sure to return the top to the bottles.

Experiment

Preparing a TLC Plate. Obtain a TLC plate from your TA. Handle the plate carefully so that you do not disturb the adsorbent coating or get it dirty. As in Figure 2 at the end of this document, use a ruler and pencil to measure 0.5 inches from the bottom of the plate, and gently draw a line across the plate. This is the origin line where you will spot your samples on the plate. On the origin line, starting 0.5 cm from the end of the plate, make a small tick mark every 1 cm. You will be spotting a different sample on each tick mark: 1) pure ferrocene, 2) your product before running the column, 3) the yellow fraction, 4) the orange fraction, and 5) the red fraction (if you collect one). Mix a small amount of pure ferrocene with a minimal amount of hexanes. Using a microcapillary, spot the pure ferrocene on the first tick mark of the TLC plate. The remaining spots will be added later.

Reaction Workup. Add 200 mg of ferrocene, 1.0 mL of acetic anhydride, and 0.3 mL of phosphoric acid to a large reaction tube and stir. Heat the tube to a gentle reflux using a water bath with constant stirring for 10 minutes. Note the color during the reaction. Cool the reaction tube to room temperature. Add dropwise 1.5 mL of ice water, followed by 3M NaOH solution until the resulting product mixture tests neutral (pH paper). Collect the solid via vacuum filtration. You will be purifying your product using column chromatography with alumina as your stationary phase.

Before running the Column. In preparation to run your column, add 30 mL of hexanes to a large reaction tube and cap. Add 10 mL of 50:50 hexanes:*tert*-butyl methyl ether mixture to small reaction tube and cap. Both of these solutions should be ready to go before you start running your column.

Making the Column. Obtain a micro-column that is fitted with a fritted disc (frit), column tip, and small funnel. Clean the column with a small amount of acetone. If your column does not have a frit, you may pack it with a small cotton plug at the tip. Assemble the column, tip and funnel.

Wet-loading the Column. Add 3 g of alumina and 10 mL of hexanes to a 50 mL Erlenmeyer flask. Swirl the contents for a few seconds then hold the flask at an angle so the alumina settles in a corner. Use a pipette to transfer the alumina/hexanes mixture into the micro-column. Continue to add additional hexanes as necessary until most of the alumina has been transferred into the column. Keep hexanes running through the column until you are ready to add your product.

Prepping the Reaction Product for Wet-loading. After vacuum filtering your reaction product, add 5 mL of refluxing hexanes to your product. Heat on a hotplate to dissolve the solid. Allow the solution to cool to room temperature. If solid reforms, try crushing the solid with a glass rod; if necessary, add additional hexanes **dropwise** until all the solid dissolves.

Wet-loading the Reaction Mixture. With a clean pipette, slowly add hexanes from the large reaction tube to the column until the liquid level covers the solid alumina. Do not let the column go dry! Once the level of hexanes is just above the alumina, slowly (so as to not disturb the alumina) pipette the solution containing your reaction product into the column. Be sure to discard the initial amount of hexanes before the first fraction elutes off. Once the solution mixture is right above the alumina, add ½ pipette of clean hexanes and allow the liquid level to come down right above the alumina once more. Repeat this process until the first fraction (yellow) is separated from the second fraction (orange); you should be able to see white alumina between the two layers. Once this occurs, you can fill and refill the column with hexanes as necessary until the first fraction is completely eluted off. Make sure to collect the first fraction into a clean, preweighed 50 mL Erlenmeyer flask.

Once the first fraction is eluted off, allow the liquid level to come down just above the alumina level and begin adding 50:50 hexanes/*tert*-butyl methyl ether until the second fraction elutes off. Make sure to collect the second fraction into a clean, preweighed 50 mL Erlenmeyer flask. Collect the third fraction (red, you may not have this one) into a clean, preweighed 50 mL Erlenmeyer flask.

Using different microcapillaries, spot your yellow, orange and red (if you collected it) fractions onto the third, fourth, and fifth tick marks, respectively, on the TLC plate. Add a boiling stick to each vial and evaporate off the solvent. Reweigh each vial. Take a melting point of each product.

Developing a TLC Plate: You will now perform a TLC of your products against your starting material using the silica plates as your stationary phase and

95:5 hexanes:ethyl acetate as your mobile phase. Start by adding 10 mL of 95:5 hexanes:ethyl acetate to a 50 mL beaker. Place the prepared TLC plate into the developing beaker, cover with an inverted 400 mL beaker, and leave it undisturbed on your bench top. Make sure the solvent does not cover the origin line! The solvent will gradually rise up the TLC plate by capillary action. Allow the plate to develop until the solvent is about a 0.5 cm below the top of the plate. Remove the plate from the beaker and immediately mark the solvent front with a pencil. Allow the plate to dry. If there are any colored spots, circle them lightly with a pencil. Most samples are not colored and need to be visualized with a UV lamp. Hold a UV lamp over the plate and circle any spots you see. Keep your TLC plate and turn it in stapled to the front of your post lab.

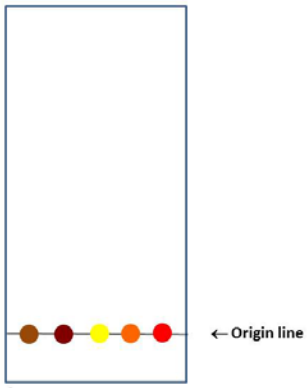

Figure 2: TLC Plate.