

Friedel-Crafts Acylation of Ferrocene: Acetylferrocene

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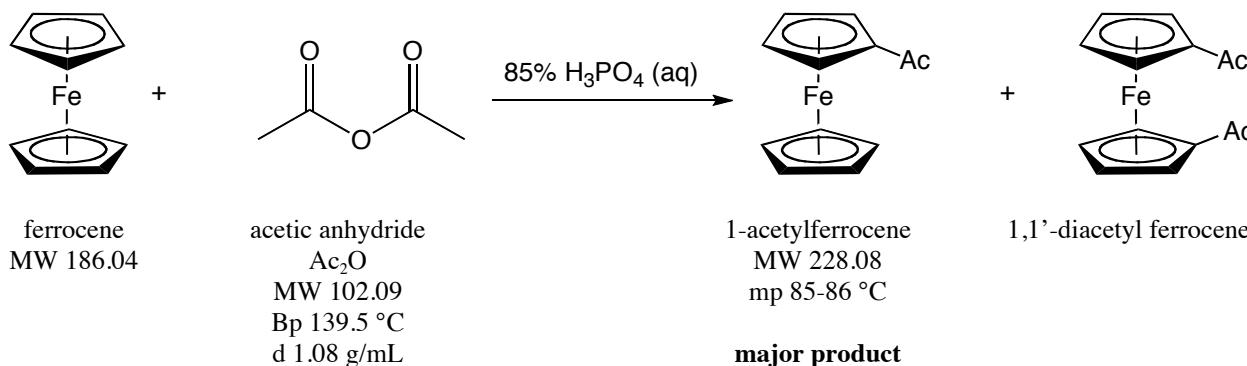
Adapted from JR Mohrig, CN Hammond, TC Morrill, and DC Neckers

Experimental Organic Chemistry (A Balanced Approach: Macroscale and Microscale) 1999, WH Freeman, NY 189-194.

Background

This experiment has two purposes. The first is to explore Friedel-Crafts acylations of aromatic molecules, and the second is to develop an understanding of column chromatography as a tool for separating organic substances.

Friedel-Crafts alkylation and acylation reactions are powerful tools for substituting larger, more complex functional groups in place of aromatic protons. In the absence of strongly π -donating activating groups, powerful Lewis acid catalysts such as aluminum chloride must be used. However, activated aromatic compounds will undergo substitution under much milder conditions. Ferrocene is highly activated, so acetylation occurs readily using a mild Brønstead-Lowry acid catalyst. In fact, ferrocene is so reactive to acetylation that a diacetyl derivative normally forms as a minor product.



We will perform this reaction under conditions that will not allow the reaction to go to completion. You should have some ferrocene remaining in your reaction mixture, as well as the 1-acetylferrocene product, and perhaps some of the 1,1'-diacetylferrocene (usually a minor product). This situation will allow us to do the column chromatography under conditions where we can readily see the materials separate as they move down the column. Column chromatography allows us to separate materials based on their relative solubility in a solvent (called the mobile phase, usually less polar than the column material) and attractions to a packed solid column (called the stationary phase, usually very polar).

Cautions

Both acetic anhydride and phosphoric acid are corrosive and will cause burns. Handle with care and immediately neutralize and wipe down any spills. Sodium hydroxide is caustic and will cause burns. Handle with care of immediately dilute and wipe down any spills.

DAY 1: Synthesis of Acetylferrocene

Begin heating a hot water bath to its boiling point using a 100 mL beaker on your stirring hotplate on your lab jack. Eventually, you will need to clamp your glassware above this water bath. Collect a 4 or 5 mL conical vial, an air-cooled condenser, and a drying tube from your microscale glassware kit. Charge the drying tube with calcium chloride, using cotton pieces on either side of it to hold it in place. Attach it to the top of the air condenser. Be sure to grease each ground glass joint and to hold them together using the screw caps!

Place 200 mg of dry ferrocene into the conical vial, followed by 2.0 mL of acetic anhydride. Cap the vial with the condenser/drying tube combo and swirl gently to dissolve the ferrocene in the mixture. You may want to heat it a little using the hot water bath. When it is dissolved, disconnect the apparatus between the drying tube and the condenser so that you can add 10 drops of 85% phosphoric acid; since this is a catalyst, you do not need to know the exact amount. Reattach the drying tube and warm the reaction mixture in your hot water bath for only 10 minutes. Every 2-3 minutes you should agitate the apparatus to be sure it is mixed together adequately. When it has cooked for 10 minutes, cool the vial thoroughly with an ice/water slurry.

Once cold, disconnect the drying tube and add 1.0 mL of ice water dropwise to the reaction mixture with thorough mixing. Pour the diluted reaction mixture over a ~10 g of ice in a 50 mL beaker. Neutralize this mixture by adding 10% aqueous sodium hydroxide solution in one-mL (or less) portions until the mixture tests neutral with pH paper. Most students need between 10 and 20 mL to get to neutral. Mix well after each addition of base. When it is neutral, cool the mixture to RT, and then in an ice bath before collecting the product via vacuum filtration. Wash it thoroughly with cold water in the filter apparatus, and set it aside to dry. Once dry (next lab), obtain the mass and melting point of the crude product.

Cleanup and Disposal of Day 1

The neutral reaction mixture filtrate can be flushed down the drain.

DAY 2: Column Chromatography

Assemble the column ensuring that it is clamped in a vertical position. Be sure that your column has a frit and a stopcock attached at the bottom, and a funnel at the top. Close the valve and fill the column with hexane to the bottom of the funnel. Prepare a slurry of ~4.5 g alumina (Activity III) in hexane, using ~8-10 mL of hexane. Begin to fill the column with the slurry, stirring or swirling gently to remove any air bubbles and tapping gently to **insure even packing**. As you add alumina, allow some hexane to drain from the stopcock into a flask to avoid overflowing the column but **never let the level of the solvent go below the level of the alumina!** Continue filling the column with alumina until the alumina is within approximately 3 cm of the top of the column. Make sure that the top of column is perfectly flat, and then add a small slug (~2-3 mm) of fine sand.

Drain the solvent until it is just above the surface of the sand at the top of the alumina. Again, **never let any part of the alumina go dry**. Suspend your crude acetylferrocene in 0.5 mL of dichloromethane (it will not all dissolve, but try to get most of it dissolved). Add this suspension to the top of column using a Pasteur pipet and taking care to not disturb the surface of the column. As the suspension is added, a like volume of liquid is drained from the column to maintain a constant liquid level above the surface of the alumina. Once all of the material has been transferred, several drops of pure dichloromethane are added, followed by a small amount of hexane. There should now be a thin band of material easily visible just below the surface of the alumina.

Carefully fill the column with hexane and then open the stopcock. You want to maintain a steady flow of solution through the column, which requires establishing a comfortable flow rate and constant addition of solvent to the top of the column. This process is called elution. As you elute with pure hexane, you should see unreacted ferrocene travel down the column as an orange-yellow band. Collect this material in a tared flask. Now elute with a 50:50 mixture of hexane and diethyl ether. This should bring down an orange-red band of acetylferrocene. Collect this material in a second tared flask. The diacetylferrocene will remain as a dark band at the top of the column.

The materials collected may be recovered by evaporating the solvent, then characterized by mass, melting point, and various spectroscopic techniques as specified by your instructor. In your lab write-up, be sure to comment on the amount of unreacted starting material recovered and the percent yield of crude product. The acetylferrocene may be recrystallized from hexane.

Optional Thin Layer Chromatography (TLC)

You may analyze unreacted and recovered materials as directed by your instructor. These may include unreacted ferrocene (either pure or recovered from the column), crude acetylferrocene, and recrystallized acetylferrocene. A few crystals of each sample should be dissolved in a few drops of toluene, then spotted onto silica TLC plates. The chromatogram should be developed with a 30:1 toluene:absolute ethanol solution and visualized with a UV lamp.

Cleanup and Disposal of Day 2

Any unused solvents should be placed in the organic solvents disposal container. The alumina should be dried, and then disposed of in the nonhazardous solids waste container.