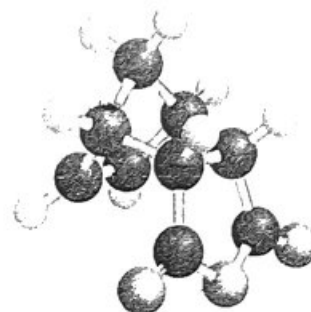
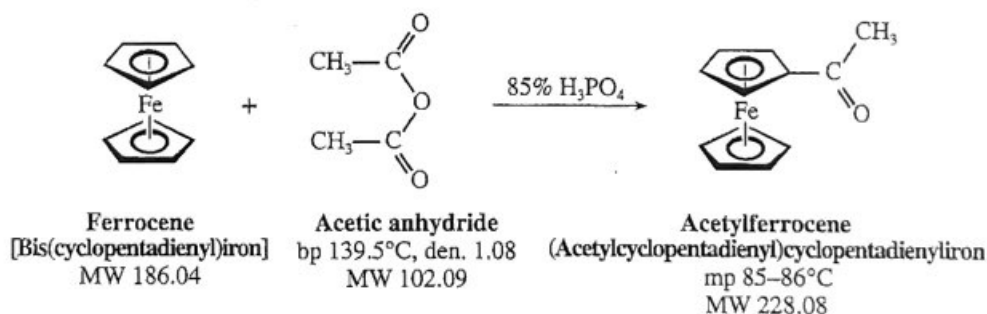


Friedel–Crafts Acylation of Ferrocene: Acetylferrocene



PRELAB EXERCISE: How many possible isomers could exist for diacetylferrocene? Explain. Calculate the volume of 3 M aqueous sodium hydroxide needed to neutralize the acetic and phosphoric acids in the synthesis of acetylferrocene.



The Friedel–Crafts acylation of benzene requires aluminum chloride as the catalyst. However, ferrocene, with a very high π -electron density that has been referred to as a superaromatic compound, can be acylated under much milder conditions with phosphoric acid as a catalyst. Because the acetyl group is a deactivating substituent, the addition of a second acetyl group, which requires more vigorous conditions, will occur in the nonacetylated cyclopentadienyl ring to give 1,1'-diacetylferrocene. Because ferrocene gives just one monoacetyl derivative and just one diacetyl derivative, it was assigned an unusual sandwich structure.

Acetylferrocene and ferrocene (both highly colored) are easily separated by column chromatography (see Chapter 9).



Macroscopic Procedure

IN THIS EXPERIMENT, ferrocene reacts with acetic anhydride in an acid-catalyzed Friedel-Crafts reaction to give acetylferrocene. Excess acetic anhydride is removed by reaction with water to give acetic acid, and then base is added to react with the acetic acid. The crude product is isolated by filtration and then purified by crystallization from hexane. There is obvious separation of these components by chromatography because the unreacted ferrocene is yellow, and the acetyl product is red-orange.



Both acetic anhydride and phosphoric acid are corrosive to tissue. Handle both with care and wipe up any spills immediately.



Hexanes are extremely flammable. No flames!



Video: *Macroscale Crystallization*



See Web Links

In a 25-mL round-bottomed flask, place 3.0 g of ferrocene, 10.0 mL of acetic anhydride, and 2.0 mL of 85% phosphoric acid. Equip the flask with a reflux condenser and a calcium chloride drying tube. Warm the flask gently on a hot water or steam bath while swirling to dissolve the ferrocene; then heat strongly for an additional 10 minutes. Pour the reaction mixture onto 50 g of crushed ice in a 400 mL beaker and rinse the flask with 10 mL of ice water. Stir the mixture for a few minutes with a glass rod, add 75 mL of 3 M sodium hydroxide solution (the solution should still be acidic), and then add solid sodium bicarbonate (be careful of foaming) until the remaining acid has been neutralized. Stir and crush all lumps, allow the mixture to stand for 20 minutes, and then collect the product by suction filtration. Press the crude material as dry as possible between sheets of filter paper, save a few crystals for TLC analysis, transfer the remainder to an Erlenmeyer flask, and add 40 mL of hexanes to the flask. Boil the solvent on a hot water or steam bath for a few minutes and then decant the dark-orange solution into another Erlenmeyer flask, leaving a gummy residue of polymeric material. ~~Treat the solution with decolorizing charcoal and filter it through a fluted filter paper placed in a warm stemless funnel that is seated into an appropriately-sized Erlenmeyer flask.~~ Evaporate the solvent (use an aspirator tube; see Fig. 8.11 on page 174) until the volume is about 20 mL. Set the flask aside to cool slowly to room temperature. Beautiful rosettes of dark orange-red needles of acetylferrocene will form. After the product has been cooled in ice, collect it on a Büchner funnel and wash the crystals with a small quantity of cold solvent.

Perform a TLC analysis on your product. Dissolve very small samples of pure ferrocene, the crude reaction mixture, and recrystallized acetylferrocene, each in a few drops of toluene. Spot the three solutions with microcapillaries on silica gel plates, and develop the chromatogram with 3:1 toluene and an absolute ethanol mixture. Visualize the spots under a UV lamp, if the silica gel has a fluorescent indicator, or by adsorption of iodine vapor. Do you detect unreacted ferrocene in the reaction mixture and/or a spot that might be attributed to diacetylferrocene?

Cleaning Up. The reaction mixture filtrate can be flushed down the drain. Unused recrystallization and TLC solvents should be placed in the organic solvents waste container. The decolorizing charcoal, once free of solvent, can be placed in the non-hazardous solid waste container. If local regulations do not allow for the evaporation of solvents, dispose of the wet alumina in the waste container provided.

Erlenmeyer flask. Evaporate the solvent (use an aspirator tube) until the volume is about 20 mL. Set the flask aside to cool slowly to room temperature. Beautiful rosettes of dark orange-red needles of acetylferrocene will form. After the product has been cooled in ice, collect it on a Büchner funnel and wash the crystals with a small quantity of cold solvent.

Analyze your product by thin-layer chromatography. Dissolve very small samples of pure ferrocene, the crude reaction mixture, and recrystallized acetylferrocene, each in a few drops of toluene; spot the three solutions with microcapillaries on silica gel plates; and develop the chromatogram with 3:1 toluene-absolute ethanol. Visualize the spots under a UV lamp, if the silica gel has a fluorescent indicator, or by adsorption of iodine vapor. Do you detect unreacted ferrocene in the reaction mixture and/or a spot that might be attributed to diacetylferrocene?

← stop

Cleaning Up The reaction mixture filtrate can be flushed down the drain. Unused recrystallization and thin-layer chromatography solvents should be placed in the organic solvents container. The decolorizing charcoal, once free of solvent, can be placed in the nonhazardous solid waste container.

Questions

1. What is the structure of the intermediate species that attacks ferrocene to form acetylferrocene? What other organic molecule is formed?
2. Why does the second acetyl group enter the unoccupied ring to form diacetylferrocene?

EXPERIMENT

ACETYLFERROCENE



Microscale Procedure

IN THIS EXPERIMENT, ferrocene reacts with acetic anhydride in an acid-catalyzed Friedel-Crafts reaction to give acetylferrocene. Excess acetic anhydride is removed by reaction with water to give acetic acid, and then base is added to react with the acetic acid. The crude product is isolated by filtration and then chromatographed on alumina. There is obvious separation of these components on a chromatography column because the unreacted ferrocene is yellow, and the acetyl product is red-orange.



Handle acetic anhydride and phosphoric acid with care. Wipe up spills immediately.



Photo: Capping a Reaction Tube with a Septum; Video: Microscale Filtration on the Hirsch Funnel

To 93 mg of dry sublimed ferrocene (see Chapter 49) in a 10 × 100 mm reaction tube, add 0.35 mL (0.38 g) of acetic anhydride followed by 0.1 mL (170 mg) of 85% phosphoric acid. Cap the tube with a septum bearing an empty syringe needle, and warm it on a steam bath or in a beaker of boiling water while agitating the mixture to dissolve the ferrocene. Heat the mixture for an additional 10 minutes, and then cool the tube thoroughly in ice. Carefully add to the solution 0.5 mL of ice-water dropwise with thorough mixing, followed by the dropwise addition of a 3 M aqueous sodium hydroxide solution until the mixture is neutral (test with indicator paper and avoid an excess of base). Collect the product on a Hirsch funnel, wash it thoroughly with water, and press it as dry as possible between sheets of filter paper. Save a sample of this material for melting-point and thin-layer chromatographic (TLC) analyses, and purify the remainder by column chromatography.

Column Chromatography



Photo: Column Chromatography; Video: Column Chromatography

Follow the procedure as given in Chapter 9 for packing a microscale chromatography column and adding the sample (about 90 mg of a ferrocene/acetylferrocene mixture). Use Brockman activity III alumina as the adsorbent.

Add 1-2 mL (pipette-full) of product mixture in hexane. Use bulb to force through ("load" sample onto silica gel)

Carefully add hexanes to the column and begin to elute the product from the column. Unreacted ferrocene will move down the column as a yellow band. Collect this in a 10-mL flask. Wash any crystalline material that collects on the tip of the valve into the flask with a few drops of ether. Then elute the column with a 50:50 mixture of hexanes and ether. This will move the acetylferrocene down as an orange-red band. Collect this in a separate 10-mL Erlenmeyer flask. Ferrocene is highly symmetrical and nonpolar, while the acetyl compound is the opposite. These properties govern the order of elution from the chromatography column. Spot a TLC plate with these two solutions as well as the crude acetylferrocene and the ferrocene starting material, and analyze as described in the next section. Any diacetylferrocene will be seen as a dark band at the top of the column. Evaporate the solvents under reduced pressure and determine the weights of the residues (Fig. 32.1).



Hexanes are extremely flammable. No flames!

Solvents (cont'd)

hexanes; followed by hexanes containing 1%, 2%, 5%, 10%, 25%, and 50% ether; pure ether; ether and dichloromethane mixtures; followed by dichloromethane and methanol mixtures. Either diethyl ether or *t*-butyl methyl ether can be used, but *t*-butyl methyl ether is recommended. Solvents such as methanol and water are normally not used because they can destroy the integrity of the stationary phase by dissolving some of the silica gel. Some typical solvent combinations are hexanes-dichloromethane, hexanes-ethyl acetate, and hexanes-toluene. An experimentally determined ratio of these solvents can sufficiently separate most compounds.

Petroleum ether: mostly isometric pentanes.

TABLE 9.3 Elution Order for Solutes

Alkanes (first)
Alkenes
Dienes
Aromatic hydrocarbons
Ethers
Esters
Ketones
Aldehydes
Amines
Alcohols
Phenols
Acids (last)

Compound Mobility

The ease with which different classes of compounds elute from a column is indicated in Table 9.3. Molecules with nonpolar functional groups are least adsorbed and elute first, while more polar or hydrogen-bonding molecules are more strongly adsorbed and elute later. The order is similar to that of the eluting solvents—another application of “like dissolves like.”

Sample and Column Size

Chromatography columns can be as thin as a pencil for milligram quantities to as big as a barrel for the industrial-scale separation of kilogram quantities. A microscale column for the chromatography of about 50 mg of material is shown in Figure 9.1; columns with larger diameters, as shown in Figures 9.2 and 9.3, are used for macroscale procedures. The amount of alumina or silica gel used should generally weigh at least 30 times as much as the sample, and the column, when packed, should have a height at least 10 times the diameter. The density of silica gel is 0.4 g/mL, and the density of alumina is 0.9 g/mL, so the optimum size for any column can be calculated.

Packing the Column



Microscale Procedure

Before you pack the column, tare several Erlenmeyer flasks, small beakers, or 20-mL vials to use as receivers. Weigh each one carefully and mark it with a number on the etched circle.

Uniform packing of the chromatography column is critical to the success of this technique. Two acceptable methods for packing a column are dry packing and slurry packing, which normally achieve the best results. Assemble the column as depicted in Figure 9.1. To measure the amount of adsorbent, fill the column one-half to two-thirds full; then pour the powder out into a small beaker or flask. Clamp the column in a vertical position and close the valve. Always grasp the valve with one hand while turning it with the other. Fill the column with a non-polar solvent such as hexanes almost to the top.

Dry Packing Method. This is the simplest method for preparing a microscale column. Slowly add the powdered alumina or silica gel through the funnel while gently tapping the side of the column with a pencil. The solid should “float” to the bottom of the column. Try to pack the column as evenly as possible; cracks, air bubbles, and channels in the powder will lead to a poor separation.

Slurry Packing Method. To slurry pack a column, add about 8 mL of hexanes to the adsorbent in a flask or beaker, stir the mixture to eliminate air bubbles, and



Photo: Column Chromatography, Video: Column Chromatography

FIG. 9.1
A microscale chromatographic column.



FIG. 9.2
A macroscale chromatographic column.

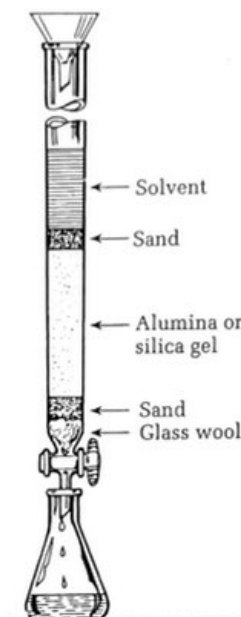


FIG. 9.3
A chromatographic tube on a ring stand.



then (this is the hard part) swirl the mixture to get the adsorbent suspended in the solvent and immediately pour the entire slurry into the funnel. Open the valve, drain some solvent into the flask that had the adsorbent in it and finish transferring the slurry to the column. Place an empty flask under the column and allow the solvent to drain to about 5 mm above the top surface of the adsorbent. Tap the column with a pencil until the packing settles to a minimum height. Try to pack the column as evenly as possible; cracks, air bubbles, and channels in the packed column will lead to a poor separation.

The slurry method normally gives the best column packing, but it is also the more difficult technique to master. Whether the dry packing or slurry packing method is chosen, the most important aspect of packing the column is creating an evenly distributed and packed stationary phase. The slurry method is often used for macroscale separations.

Once the column is loaded with solvent and adsorbent, place a flask under it, open the stopcock (use two hands for the microscale column), and allow the solvent level to drop to the top of the packing. Avoid allowing the solvent level to go below the stationary phase (known as letting the column "run dry") because this allows air bubbles and channel formation to occur, which leads to a poor separation.