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The experiments described in these materials are potentially hazardous and require a high level of safety training, special facilities and equipment, and supervision by appropriate individuals. You bear the sole responsibility, liability, and risk for the implementation of such safety procedures and measures. MIT shall have no responsibility, liability, or risk for the content or implementation of any of the material presented.

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*Experiment #4:* The Preparation of Ferrocene & Acetylferrocene

MASSACHUSETTS INSTITUTE OF TECHNOLOGY

Department of Chemistry

5.311 Introductory Chemical Experimentation

EXPERIMENT #4

THE PREPARATION OF FERROCENE &

ACETYLFERROCENES<sup>1</sup>

I. Purpose

The principal aims of this experiment are to provide background information about and experience in:

- the **synthesis and electronic structure of ferrocene (1)**,  $(\eta^5\text{-C}_5\text{H}_5)_2\text{Fe}$  [bis(pentahaptocyclopentadienyl) iron]<sup>2</sup>
- the **synthesis of an ionic liquid**, as environment for the acetylation of ferrocene
- the use of **inert atmospheres (including glove box techniques)**
- **recrystallization or sublimation**
- the use of **GC/MS** and **thin-layer chromatography** as analytical tools and **column chromatography** as a purification technique
- the concepts of **Green Chemistry** such as **Atom Economy<sup>3</sup>** and **alternative non-polluting solvents**

Ferrocene is a historically important molecule. The initial recognition of the structure of  $\text{C}_{10}\text{H}_{10}\text{Fe}$  in 1951<sup>4</sup> spawned a vast area of chemistry, *viz.*, transition metal organometallic chemistry. This field is still developing and has produced a huge number of compounds in which saturated, unsaturated, and aromatic organic fragments are bonded directly to metals. All carbon atoms in the two cyclopentadienyl rings are equally bonded to the central ion by  $\pi$  electrons in the rings. The sandwich structure proposed by Wilkinson and Fischer<sup>5,6</sup> (Nobel prize in 1973) in early

<sup>1</sup> Mircea D. Gheorghiu designed the experiment to include the acetylation of ferrocene in ionic liquid.

<sup>2</sup> The word *hapto* means in Greek *to fasten*. *Pentahapto* therefore, is to be taken as “fastened in five places.” The greek letter  $\eta$  followed by a superscript indicates how many atoms of the ligand are attached to the metal.

<sup>3</sup> Atom economy means to maximize the incorporation of all starting materials into the final product. For example, the synthesis of the ionic liquid precursor from 1-methylimidazole and iodoethane to yield 1-ethyl-3-methyl imidazolium iodide is 100% atom efficient. Visit:

<http://www.chemistry.org/portal/a/c/s/1/acdisplay.html?DOC=education%5Cgreenchem%5Cindex.html>

<sup>4</sup> Kealy, T. J.; Pauson, P. L., *Nature*, **1951**, 168, 1039.

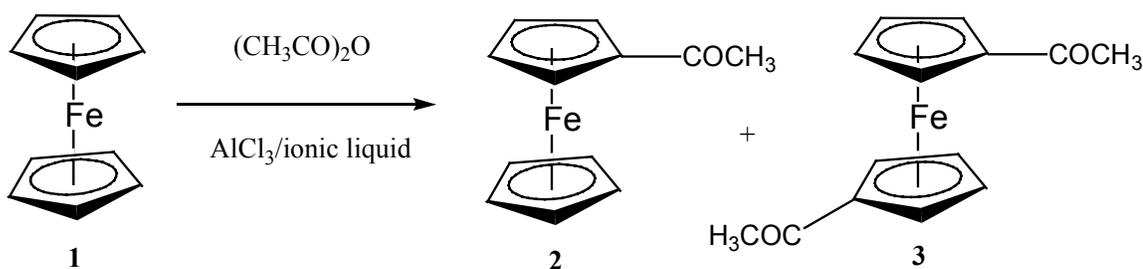
<sup>5</sup> Wilkenson, Geoffry; Rosenblum, M.; Whiting, M. C. and Woodward, R. B. “The Structure of Iron Bis-Cyclopentadienyl” *Journal of the American Chemical Society*. **1952**, 74, 2123.

<sup>6</sup> Fischer, Von E. O. and Pfab, W. “Cyclopentadien-Metallkomplexe, ein neuer typ metallorganischer Verbindungen” *Zeitschrift fur Naturforschung*. 7b **1952**, 377.

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1952 has been supported by X-ray diffraction (solid state)<sup>7</sup> and electron diffraction data (gas phase)<sup>8</sup>.

Ferrocene exhibits the properties of a typical aromatic molecule. This compound is stable to more than 500 °C. It does not react readily with acids or bases; however, it is sensitive toward oxidizing agents. Ferrocene does not undergo addition reactions typical of cyclopentadiene, but readily undergoes electrophilic aromatic substitution. Depending upon the catalyst and the reaction conditions, the major acetylation product is either the monosubstituted product **2** or the disubstituted product **3**. For a particular set of reaction conditions, the student will determine whether the major product is the orange acetylferrocene (**2**) or the red 1,1-diacetylferrocene (**3**).



## II. Safety

NOTE: The organic liquids to be used in quantity in this experiment:

- dimethylsulfoxide
- dimethoxyethane
- cyclopentadiene
- dicyclopentadiene
- 1-methylimidazole
- iodoethane

are all volatile and possess **noxious vapors**. Avoid inhalation. Carry out all designated operations in the hood.

All of the chemicals described in this section are designated with an asterisk (\*) in the text the first time they appear. This is so you will be aware of their properties.

**1. Dicyclopentadiene (C<sub>10</sub>H<sub>12</sub>):** This is a noxious liquid. It should be handled with the usual caution: do not ingest. If it is spilled on skin, rinse well with water.

<sup>7</sup> Dunitz, J. D.; Orgel, L. E.; Rich, R. A., *Acta Crystallogr.*, **1956**, *9*, 373.

<sup>8</sup> Bohn, R. K. and Haaland, A. J. *Organomet. Chem.* **1966** *5*, 470. Haaland, A. and Nilsson, J.E. *Acta Chem. Scand.* **1968** *22* 2653.

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**2. Potassium Hydroxide (KOH):** Potassium hydroxide is extremely corrosive and hygroscopic. It should be handled with caution and kept away from skin and clothing. If it spills, wash with plenty of water. Keep containers tightly closed. Powdered KOH must be handled in the hood.

**3. Iron(II) Chloride Tetrahydrate (FeCl<sub>2</sub>•4H<sub>2</sub>O):** Ferrous salts can be toxic. This chemical should be handled with the usual cautions.

**4. Dimethyl Sulfoxide (DMSO):** DMSO has the ability to render the skin permeable to many chemical compounds. Substances ordinarily regarded as harmless on the skin become dangerous toxic substances when the nonpermeability of the skin has been altered by the application of dimethylsulfoxide. Consequently, keep dimethylsulfoxide off the hands; if it is accidentally spilled on the skin, the area should be washed promptly with a strong soap or detergent and plenty of water.

**5. Hydrochloric Acid (HCl):** Conc. HCl (12 N) is a strong acid. Contact with the skin will cause burns. If any gets on you or your clothing, rinse immediately with water. Dilute HCl (3N or less) is less hazardous but will still burn the skin and produce holes in clothing.

**6. Acetone (CH<sub>3</sub>COCH<sub>3</sub>):** Acetone is an organic solvent and should be treated with normal caution: keep away from flames, dispose in the organic waste. It also has the ability to increase the permeability of skin and should therefore not be spilled over hands, etc.

**7. Aluminum Chloride (AlCl<sub>3</sub>):** Anhydrous aluminum chloride releases HCl when it comes in contact with water. It should therefore be treated with the same precautions as for HCl.

**8. Acetic anhydride (CH<sub>3</sub>CO)<sub>2</sub>O:** Acetic anhydride causes severe burns. It is harmful if inhaled or swallowed, has an irritating vapor and is combustible. Do not get liquid or vapors in eyes, or skin or on clothing. Wash thoroughly after handling. Keep in a tightly closed container.

**9. Hexane (C<sub>6</sub>H<sub>14</sub>), ethyl acetate (CH<sub>3</sub>COOC<sub>2</sub>H<sub>5</sub>), and methanol (CH<sub>3</sub>OH):** These are common organic solvents and should be handled accordingly; keep away from flames, do not inhale, dispose of in the organic waste container.

**10. Silica gel (SiO<sub>2</sub>):** Silica gel is a common chromatographic support. It may be irritating to skin, eyes and mucous membrane. Prolonged or repeated inhalation may cause damage to the respiratory system. Do not breathe dust. Do not get into eyes. Avoid prolonged or repeated contact with skin.

**11. Iodoethane (C<sub>2</sub>H<sub>5</sub>I)** Vesicant! Toxic! Target organs are nerves, liver, and kidneys. It is light and moisture sensitive. It is stabilized with copper.

**12. 1-Methylimidazole (C<sub>4</sub>N<sub>2</sub>H<sub>6</sub>):** It is corrosive(will cause burns), combustible and hygroscopic. Keep away from heat and open flame. Handle and store under nitrogen.

### III. A. General References

The following references are relevant to the preparation and properties of ferrocene and related metallocenes.

1. Wilkinson, G. *J. Organomet. Chem.* **1975**, *100*, 273
2. Birmingham, J. "Synthesis of Cyclopentadiene Metal Compounds," *Adv. Organometallic Chem.*, **1965**, *2*, 365.
3. Coates, G. E.; Greene, M.L.H.; Wade, K. "*Organometallic Compounds*," Vol. 2, Methuen and Co., London, 1968, pp 90-115.
4. Jolly, W. L. *Inorg. Chem.*, **1967**, *6*, 1435.
5. Cotton, F. A.; Wilkinson, G. "*Advanced Inorganic Chemistry*," 5th Edition, Wiley, New York, 1988, pp 78, 80-82, 716, 1176.
6. Rosenblum, M. "*Chemistry of the Iron Group Metallocenes*" Part one, Wiley, New York
7. King, R.B. "*Transition Metal Organometallic Chemistry: An Introduction*," Academic Press, New York, 1965.
8. Seddon, K.R. "Ionic Liquids: Neoteric Solvents for Research and Industrial Applications", Proc. 2<sup>nd</sup> International Workshop on Green Chemistry in China (Chengdu, May 1999).
9. Freemantle, M. "Eyes on Ionic Liquids", *Chem. and Eng. News* p. 37 – 50, May 15, 2000.
10. Stark, A., MacLean, B.L., and Singer, R.D. "1-ethyl-3-methylimidazolium halogenoaluminate ionic liquids as solvents for Friedel-Crafts acylation reactions of ferrocene", *J. Chem. Soc. Dalton Trans.*, **1999**, 63 – 66.

### III. B. Lab Manual References

1. Mohrig, J. R., Noring C, Schatz, P. and Morrill, T. Techniques in Organic Chemistry, W. H. Freeman 2003 (ISBN 0-7167-6638-8) (**Shorthanded as Mohrig**)
2. Skoog, D.A. West, D.M., and Holler, F.J., *Fundamentals of Analytical Chemistry*, 7<sup>th</sup> Ed., Saunders College Publishing: Fort Worth, 1996. (**Shorthanded as Skoog**)
3. Leonard, J.; Lygo, B.; Procter, G. "*Advanced Practical Organic Chemistry*," 2<sup>nd</sup> Ed., Blackie Academic & Profesional, London, 1995. (**Shorthanded as LLP**; it is available in Room 4-449)
4. Zubrick, J., W., "*The Organic Chem Lab Survival Manual*," 5<sup>th</sup> Ed., Willey, New York, 2001. (**Shorthanded as Z**; it is available in Room 4-449).

### IV. Experimental Procedure

#### Students work in teams of two on the preparation of ferrocene and acetylation

In the directions below, adhere closely to the quantity of materials used in each step. The yields given for each preparation, although not necessarily optimal, correspond to a competent execution of each step. Yields substantially lower indicate poor technique, and may necessitate repetition of the step.

It is important that partners carefully study the experiment before beginning to maximize efficient use of laboratory time. It is important to prepare the apparatus and chemicals for the synthesis of ferrocene while the distillation of the cyclopentadiene monomer is in progress. Because of the instability of the cyclopentadiene monomer, it must be used immediately after cracking. The total operation requires about four hours.

**Readings:** Before starting the experiment, please read about the techniques that you will use:

FRACTIONAL DISTILLATION:	<b>Mohrig:</b> Chapter 11.1-11.4
HEATING MANTLES AND POWERSTATS (Variacs)	<b>Mohrig:</b> Chapter 6.2, <b>Z:</b> pages 171-175;
REACTIONS UNDER INERT ATMOSPHERE:	<b>LLP:</b> Chapter 9.2.2.
MAGNETIC STIRRING:	<b>LLP:</b> Chapter 9.6.1
CLAMPING AND SUPPORT OF REACTION APPARATUS:	<b>Mohrig:</b> Chapter 7, <b>Z:</b> Chapter 19
SUBLIMATION:	<b>Mohrig:</b> Chapter 12, <b>LLP:</b> Chapter 11.4;
SYRINGES AND NEEDLES:	<b>Z:</b> Chapter 8.
MELTING POINTS:	<b>Mohrig:</b> Chapter 10
Recrystallization:	<b>Mohrig:</b> Chapter 9

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Drying Agents:	<b>Mohrig</b> Chapter 8.7-8.9, <b>LLP</b> Chapter V.
Thin-Layer Chromatography:	<b>Mohrig</b> Chapter 15, <b>LLP</b> pages 145-152.
Procedure for Extraction:	<b>Mohrig</b> Chapter 8.1-8.4, <b>Z</b> , Chap. 15.
TLC and column chromatography:	<b>Mohrig</b> Chapter 17.1-17.7
Gas-Liquid chromatography	<b>Mohrig</b> Chapter 16, <b>Skoog</b> Chapter 31
Mass Spectrometry	<b>Mohrig</b> Chapter 20.1-20.2

**Videos: MIT Digital Laboratory Techniques Manual**

View the following videos (links to the videos are on the course 5.311 website) prior to using these techniques in the laboratory:

- #3 TLC Basics
- #5 Reaction Work-up I: Extracting, Washing and Drying
- #6 Reaction Work-up II: Using the Rotovap
- #7 Filtration
- #8 Sublimation
- #9 Recrystallization
- #10 Column Chromatography
- #11 Use of Balances

**A. Preparation of Ferrocene**

**1. Cracking of Cyclopentadiene Dimer**

Cyclopentadiene monomer is not stable. It undergoes spontaneous Diels-Alder addition to itself to produce the dimer and higher polymers. Commercial dicyclopentadiene must be thermally degraded to the monomer, which is used in the preparation of ferrocene.

The TA will crack the dicyclopentadiene using the apparatus shown in Figure 1. The 250 mL three neck round bottom flask contains approximately 100 mL of the commercially available dicyclopentadiene\*. The TA will connect the heating mantle to a Variac, and turn on the water flow to the condenser. After checking that all joints are well sealed and that the apparatus is stable, they will insert a vent needle and the needle connected to a nitrogen source in the rubber stopper of the receiver flask and flush the system for a few minutes with nitrogen.

The TA will begin the cracking process by heating the distillation flask until it is hot to the touch (Variac setting 80-90) and as necessary adjust the heating (i.e., the Variac setting) to avoid "flooding" of the Vigreux column. During this time the liquid in the flask will begin to froth and the plates in the Vigreux column will become wet with condensate, indicating that the cracking process is taking place. The temperature at the top of the column should rise to 39-41 °C (the monomer collection temperature) and droplets from vapor condensation should appear in the condenser. With careful temperature control, the rate of distillation into the receiver flask should not exceed 2-3 drops of monomer per second. If the rate of cracking decreases, a periodic increase

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in the Variac setting may be required. The TA will provide each pair of students with 1.0 mL of cyclopentadiene monomer. The monomer must be used immediately (ideally within an hour or two) or the cracking and distillation procedure will have to be repeated. To slow the rate of dimerization keep the monomer in an ice bath until it is used in Part A2.<sup>9</sup>

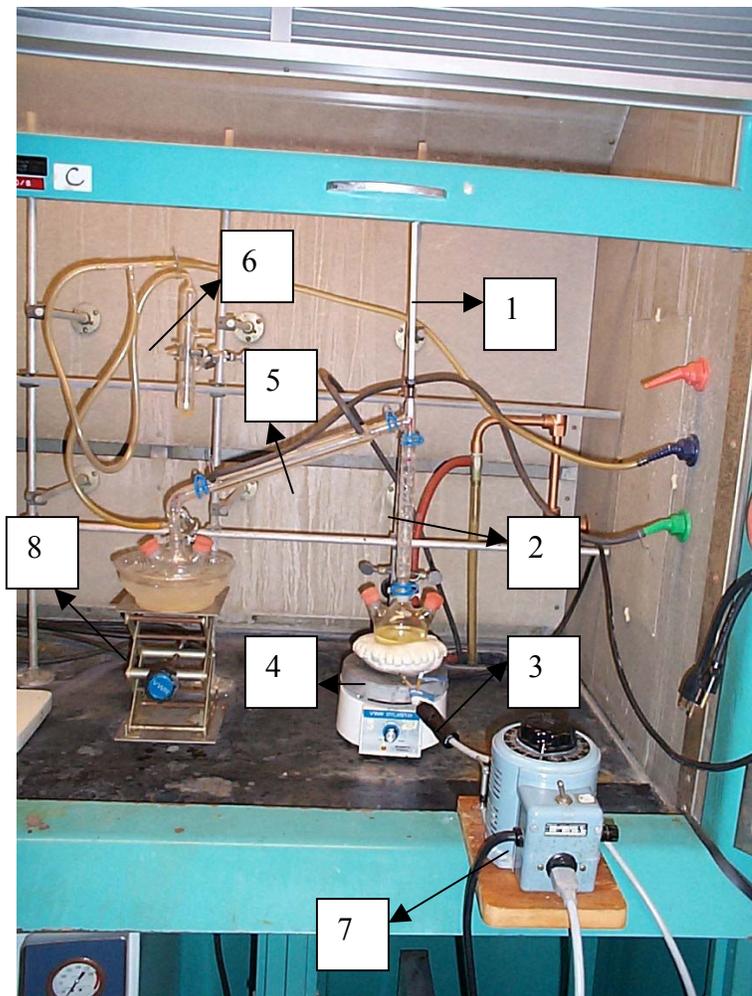
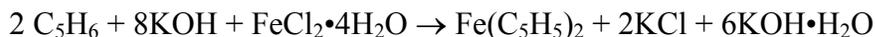


Fig. 1. Cracking of dicyclopentadiene

- |                               |                     |
|-------------------------------|---------------------|
| 1. Thermometer                | 5. Condenser        |
| 2. Vigreux column             | 6. Nitrogen bubbler |
| 3. Heating mantle             | 7. Variac           |
| 4. 3 Necks round bottom flask | 8. Ice-water        |

<sup>9</sup> If the distillation is delayed and the actual preparation of ferrocene is not started by 3 pm, there will not be enough time to complete the operation within the laboratory period

## 2. Synthesis of Ferrocene<sup>10</sup>



### Reagents required:

Cyclopentadiene	1.0 mL (0.88 g; FW=66.10; 13.31 mmole)
Potassium hydroxide	4.0 g (FW=56.11; 71.30 mmole)
Iron(II) chloride tetrahydrate (FeCl <sub>2</sub> •4H <sub>2</sub> O)	1.3 g (FW=198.81; 6.54 mmole)
Dimethoxyethane (CH <sub>3</sub> OCH <sub>2</sub> CH <sub>2</sub> OCH <sub>3</sub> )	12 mL
Dimethylsulfoxide (CH <sub>3</sub> SOCH <sub>3</sub> )	6 mL
Hydrochloric acid 12N	9 mL
Ice	20 g

Insert and secure two rubber septa in the side necks of a 100-mL three neck (14/20) round bottom flask(RB). Add a 1" magnetic stir bar. In the hood (see figure 2), add 4.0 g of finely powdered KOH<sup>11</sup> through a powder funnel placed in the middle neck of the RB. Because KOH is extremely hygroscopic, work rapidly. From the graduated buret (located in the hood) add 12 mL of 1,2-dimethoxyethane to a beaker. Pour the 1,2-dimethoxyethane from the beaker through the powder funnel into the RB washing in all the residual KOH from the funnel. Start the stirring.

Replace the powder funnel with a dropping funnel (DF) with pressure-equalization arm. Connect the adaptor on the top of the DF to one of the arms of a T connector on the nitrogen line. Attach the remaining arms of the T connector to the nitrogen line inlet and to a bubbler, respectively. Insert a vent syringe needle through one rubber septum and start flushing with N<sub>2</sub>. After 3-5 minutes, remove the needle. Use a syringe to add the cyclopentadiene monomer (1.0 mL) through the septum while stirring. Allow the mixture to stir for 10 minutes.

The mixture of cyclopentadiene monomer and potassium hydroxide slurry (it will not completely dissolve) should appear pink, but may turn either dark green or black. This coloration is due to oxidation of small amounts of the cyclopentadiene anion and is not detrimental to this particular procedure. Pure cyclopentadiene solutions are colorless. In other organometallic preparations more scrupulous efforts to eliminate oxygen must be followed.

Pulverize 1.3 g of FeCl<sub>2</sub>•4H<sub>2</sub>O\* and dissolve it in 6 mL dimethylsulfoxide\* (in a flask to facilitate dissolving the iron chloride, and transfer to the dropping funnel, rinsing with a small quantity of DMSO to insure complete transfer). Ferrous chloride tetrahydrate is sparingly soluble in dimethylsulfoxide; however, the prescribed weight will dissolve in 6 mL DMSO in the funnel. While stirring, add the iron solution at a rate of about 20 drops per minute. Continue stirring the

<sup>10</sup> Adapted from Jolly, W.L. *"The Synthesis and Characterization of Inorganic Compounds"*, Prentice-Hall Inc., Englewood Cliffs, N.J., 1970, pp 484-88 and Jolly, W.L. *Inorg. Syn.*, **1968**, *11*, 120.

<sup>11</sup> The finely powdered KOH results by grounding pellets in the food blender that is located in the hood near the cracking apparatus.

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reaction mixture for an additional 30 minutes. Monitor the nitrogen flow during the reaction as pressure has a tendency to change.

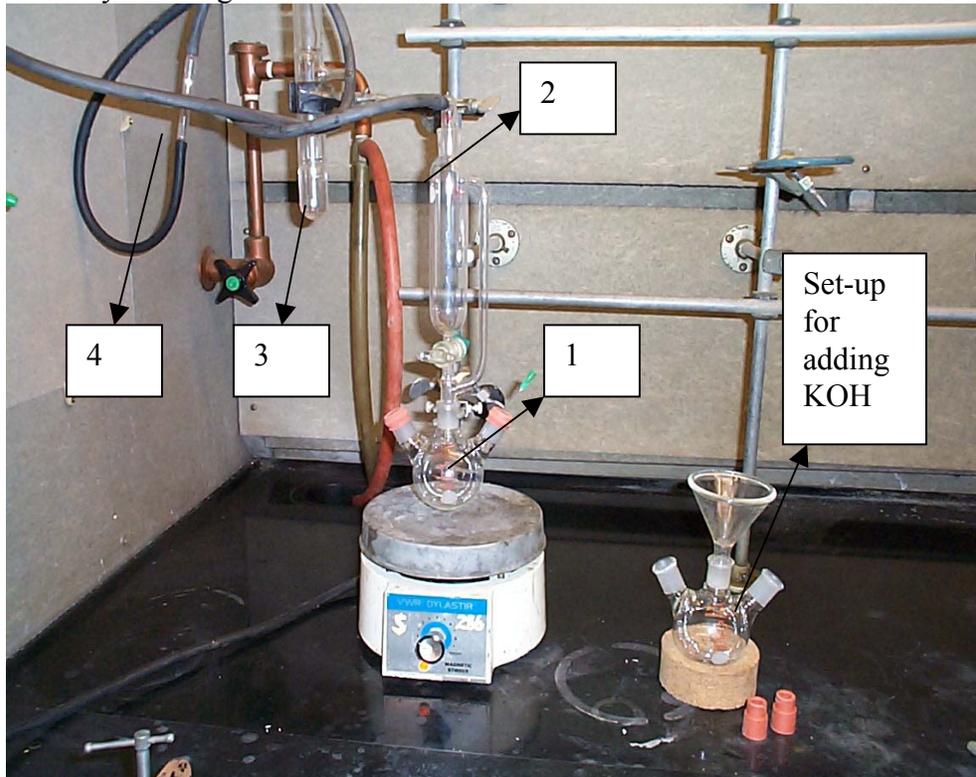


Fig. 2. Apparatus for the preparation of ferrocene.

1. 100-mL 3 necks round bottom flask.
2. Dropping funnel with pressure-equalization arm.
3. Nitrogen bubbler.
4. T connection.

Prepare a mixture of 9 mL of 12N HCl\* and approximately 20 g of ice by slowly adding acid to the ice in a 250-mL beaker. Stop the nitrogen flow and add the contents of the reaction flask to the ice slurry. Prepare and rinse the reaction flask with an additional 10 mL portion of HCl/ice<sup>14</sup> and stir the resulting mixture for about 15 minutes. It is important that this mixture remain cold ( $\sim 0$  °C) during the addition and subsequent stirring. If the temperature rises, slow down the rate of addition and/or add more ice. Collect the resulting precipitate (ferrocene) on a Büchner funnel. Wash the ferrocene with four 15 mL portions of water. A typical yield of ferrocene is 1.0 g. Spread the solid ferrocene out on a watch glass and let it dry further overnight.

Purify some of the ferrocene by sublimation and the remainder by recrystallization from hexane unless otherwise directed by the TA. Ferrocene is a crystalline, diamagnetic material which

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<sup>14</sup> Be careful! The flask may grow very hot if insufficient ice is used!

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is extremely stable to air, moisture or light. It is moderately to extremely soluble in practically all nonpolar or weakly polar solvents.

Purification by Sublimation

Sublimation may be conducted in a 100 x 15 mm culture dish as shown in figure 3. Transfer a weighed portion of ferrocene to the "bottom" of the culture dish sufficient to cover the center of the dish to a thickness of about 5 mm (about 200 mg). Cover with the larger half of the culture dish and place the apparatus on a variable temperature hot plate. Slowly raise the temperature until the ferrocene sublimates to the upper half of the dish. The sublimation will proceed slowly. Cool the top culture dish by placing a beaker filled with ice water on top of it to facilitate the sublimation. Turn off the heat or remove the dish from the heat<sup>15</sup>, allow it to cool and recover the sublimed ferrocene. This procedure may be repeated several times until all the ferrocene is purified.<sup>16</sup> Do not heat over 100 °C (a small beaker with 0.5-1 cm of water placed on the hotplate next to the sublimation apparatus is a useful 100°C indicator).

Determine the melting point of each sublimation batch. [NOTE: **All melting points must be taken in melting point tubes closed off with parafilm.**]

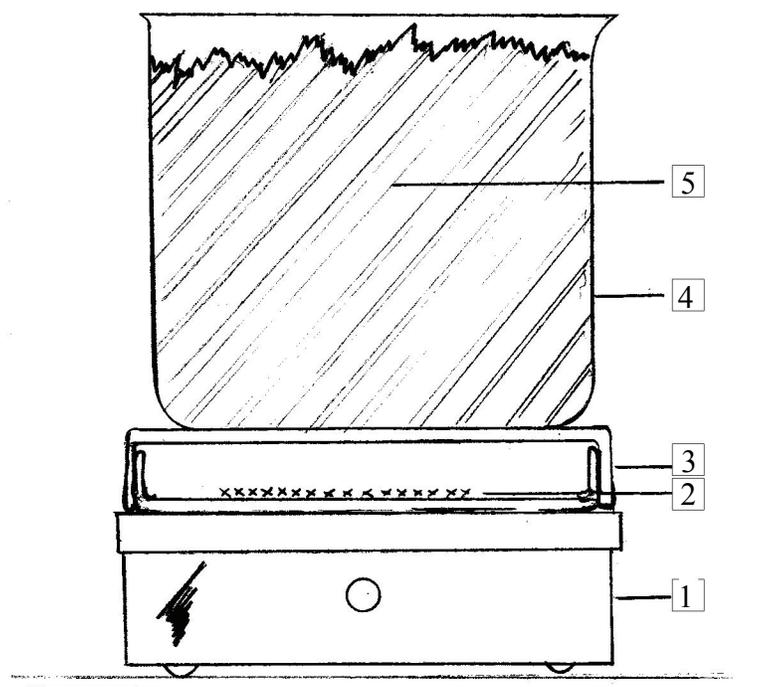


Fig3: Apparatus for the sublimation of ferrocene

1. Hot plate 2. Ferrocene 3. Petri dish 4. Beaker 400-mL 5. Water-ice

<sup>15</sup> The needles of ferrocene will readily fall back to the lower dish if bumped.

<sup>16</sup> Acetone may be used to clean the glassware used in this synthesis. A concentrated solution of KOH in water may be used to clean the petri dishes after the sublimation step.

### Purification by Recrystallization

The solubility of ferrocene in hexane is 5 g/75 mL. If the crude ferrocene does not dissolve in a quantity of hot hexane proportional to this solubility, the ferrocene is contaminated with iron salts. Filter the mixture before proceeding with the recrystallization. Additional crops of ferrocene may be recovered by concentration of the mother liquor. Determine the melting point of each successive crop in a tube sealed with parafilm.

### After purification

Place the final product in a tared vial. Determine the yield and report the mass along with the melting point. If the melting point is less than 171 °C, the product does not have an acceptable state of purity. Recrystallize or sublime the product until its melting point equals or exceeds 171 °C (lit. 173-174 °C).

### **The Electronic Structure of Ferrocene: Semiempirical PM3 Calculations with PC Spartan Pro**

To gain an understanding of the electronic structure of ferrocene carry out the computations outlined in Appendices 1 and 2. Answer the questions below in your written or oral report.

#### **Questions:**

- A. The relative energies of the frontier MOs of ferrocene are controversial.<sup>17</sup> UV photoelectron spectroscopy data indicates the HOMO has largely  $d_{z^2}$  character. To the contrary, quantum chemistry computations at every level of sophistication suggest the HOMO does not have  $d_{z^2}$  character. What Fe atomic orbitals participate in the ferrocene HOMO according to your PM3 calculation?
- B. Examine the PM3 output file and the graphical representations (see Appendix 1). Which is the first MO with significant  $d_{z^2}$  character?
- C. Use the PM3 output file to fill in the table below for the occupied MOs of ferrocene (in descending order). Include the energy level (eV, two decimals), symmetries and the sign and magnitude of the iron atomic orbital coefficient (ignore orbitals with coefficients less than 0.01) which participates in the molecular orbitals. Append Table 1 to your Written or Oral Report.

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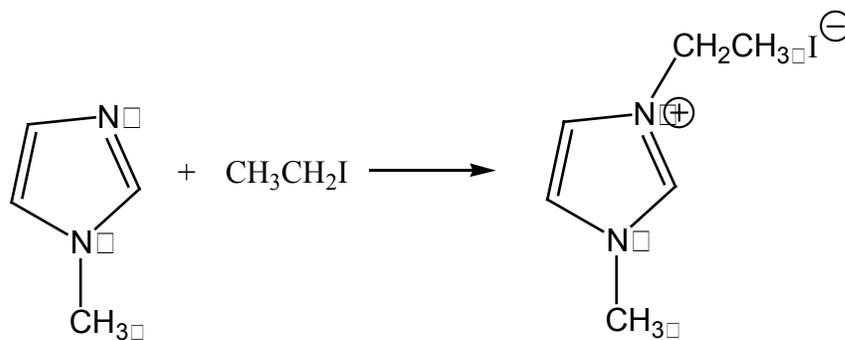
<sup>17</sup> Cotton, F. A.; Wilkinson, G. *Advanced Inorganic Chemistry*, 5<sup>th</sup> Edition, Wiley: New York; 1988, page 80, Fig. 2-15; Miessler, G. L.; Tarr, D. A. *Inorganic Chemistry*, 2<sup>nd</sup> Edition, Prentice Hall: Upper Saddle River, NJ; 1998, page 454. Both books are available for consultation upon request from Dr. Mircea Gheorghiu. Also see: Douglas, B.; McDaniel, D.; Alexander, J. *Concepts and Models of Inorganic Chemistry*, 2<sup>nd</sup> Edition, Wiley, New York; 1983, page 588.



## B. Acetylation of Ferrocene in an ionic liquid.

In 1996, it was reported that Friedel-Crafts<sup>18</sup> acetylation of ferrocene<sup>19</sup> can be conducted in ionic liquids. The ionic liquids act both as solvent and as Lewis<sup>20</sup> acid catalysts. Although information on ionic liquids started to appear in 1976, only in the early 1990's did it become increasingly evident that ionic liquids provide much milder reaction conditions at lower temperatures, and, equally important, offer the possibility of replacing polluting volatile organic solvents such as chlorinated hydrocarbons. It suffices to note that ionic liquids possess virtually zero vapor pressure over an average temperature range of 300 °C. On the contrary, many solvents now used in synthetic chemistry have high vapor pressure and toxic properties. For example, in the previous version of this experiment the acetylation of ferrocene was carried out in dichloromethane, a volatile compound (b.p. 45 °C). Even though dichloromethane has anaesthetic and narcotic effects and is a potential carcinogen, 29,000 metric tons of the substance were released by U.S. industry in 1994 (down from 46,000 tons in 1990). Room temperature ionic liquids may be viewed as promising “green” solvent systems.

In this experiment you will synthesize and work with the ionic liquid<sup>21</sup> derived from 1-ethyl-3-methylimidazolium iodide ([emim]I) admixed with various amounts of aluminum chloride (AlCl<sub>3</sub>). The ionic liquid is shorthand as [emim]I•(AlCl<sub>3</sub>)<sub>x</sub>. When  $x < 1.0$  equivalents of AlCl<sub>3</sub>, the **ionic liquid is a Lewis base** because it contains AlCl<sub>4</sub><sup>-</sup> and Cl<sup>-</sup>. If  $x=1.0$ , **the ionic liquid is Lewis neutral**. When  $x>1.0$ , then Al<sub>2</sub>Cl<sub>7</sub><sup>-</sup> becomes increasingly dominant (see the equilibrium below), and the **ionic liquid is a Lewis acid**. The TAs will assign each pair of students a set of the acetylation conditions from those given in Table 1.



<sup>18</sup> **Prof. James Mason Crafts** (1839-1917, born in Boston, Massachusetts) **served as President of MIT from 1897 to 1900**. Charles Friedel (1832-1899; French chemist) and James Crafts reported in 1877 the alkylation of benzene ring with alkyl chlorides in the presence of aluminum chloride as catalyst. Publication of this paper marks the an increased role of the US in chemical research .

<sup>19</sup> (a) Surette, J.K.D; Green, L.; Singer, R. D. *Chem. Commun.*, **1996**, 2753; (b) Stark, A.; MacLean, B. L.; Singer, R. D. *J.Chem.Soc.,Dalton Trans.*, **1999**, 63.

<sup>20</sup> **Gilbert Newton Lewis** (1875-1946, born in Weymouth, Massachusetts), **Professor of Chemistry at MIT from 1905 through 1912**.

<sup>21</sup> See General References 8 – 10, Section III.

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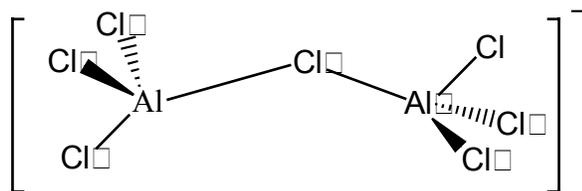


Table 1. Acetylation Conditions. Please fill in the table with your sections results, and include this table with your written or oral report.

Exp.	[emim]I	AlCl <sub>3</sub> (equivalents)	mono- acetylated ferrocene (mole %)	bis- acetylated ferrocene (mole %)	Who conducted the experiment.
1	1 (5 g)	1.2 (3.36 g)			
2	1 (5 g)	1.4 (3.92 g)			
3	1 (5 g)	1.6 (4.48 g)			
4	1 (5 g)	1.8 (5.04g)			
5	1 (5 g)	2.0 (5.6 g)			

The number of products in the reaction mixture will be determined by thin-layer chromatography and GC/MS (gas-chromatography/mass spectroscopy). The products are isolated by column chromatography.

### **1. Synthesis of [emim]I.**

This straight forward synthesis will be carried out by your TA in advance of the experiment due to both time and waste considerations. You are responsible for knowing how the reaction was carried out and the chemistry behind it. They will scale up the procedure given below (which on a larger scale requires an ice bath due to the reaction's exothermicity):

- Clamp above a stir plate a 50-mL RB flask (**19/20**) containing a 0.5" magnetic stir bar.
- Add 3.2 mL (40 mmol) of methylimidazole.
- Seal the flask with a septum.
- Insert the syringe needle of the nitrogen line and an additional needle for vent into the septum. Flush for 2-3 minutes with nitrogen.
- Remove the nitrogen and vent needles.
- Via a syringe, in small portions, add 3.8 mL (48 mmol) of iodoethane. Iodoethane comes in a sureseal bottle and is stored under nitrogen. Proper transfer techniques are required to avoid contamination of the iodoethane and maintain its nitrogen environment.

**Experiment #4:** The Preparation of Ferrocene & Acetylferrocene

- Because [emim]I is light sensitive, wrap the flask with aluminum foil and continue the stirring until the next lab day. The white solid, [emim]I is formed in almost quantitative yield.

NOTE: The septum must be wired on for transfer into the glove box. Bend the sharp ends of the wire such that there is no chance of poking the gloves when removing the wire.

**2. Preparation of 1-ethyl-3-methylimidazolium halogenoaluminate ([emim]I.(AlCl<sub>3</sub>)<sub>x</sub>) ionic liquid.**

**Please handle AlCl<sub>3</sub> carefully to avoid spills in the glove box!**

**You are responsible for cleaning all spills inside the glove box before leaving for the day!!!**

- Read this section carefully and think through what you will need inside the glove box. Place all items in a large evaporating dish for transfer into the glove box. Every item you bring into the glove box must be removed from the glove box at completion of work inside the box.
- Transfer while still warm, an oven dried 50-mL RB flask(**19/20**) containing a half inch magnetic stir bar, into the prechamber and then into the glove box (along with all other required items).
- Weigh in a plastic boat 5g (21 mmol) [emim]I. Add it to the RB flask through the powder funnel. Begin stirring.
- Weigh in a plastic boat the amount of AlCl<sub>3</sub> assigned by your TA. AlCl<sub>3</sub> must be added, with stirring, in small portions through the powder funnel. You will notice the content of the flask gradually becomes liquid (it should be colorless, but if it is red it is still OK). You have synthesized the ionic liquid of Lewis acidity corresponding to the amount of added AlCl<sub>3</sub>. Stir for 10 more minutes, then proceed to step 3.

**3. Acetylation of ferrocene with acetic anhydride in ionic liquid.**

- Still in the glove box, add in small portions a total of 0.25 g (1.35 mmol) ferrocene (weighed in a plastic boat in the glove box or weighed previously on the bench top and placed in a vial) through the powder funnel to the ionic liquid you have just synthesized. The solution should become greenish-brown.
- Stir for an additional 10 minutes. Meanwhile, in the hood set up a stir plate (see the figure 4), with an ice-water bath and a clamp.

**Experiment #4:** The Preparation of Ferrocene & Acetylferrocene

- Return to the glove box and cap the flask with a septum. To avoid spilling wait until it is out of the glove box to fold over and secure the septum.
- Transfer the flask to the glove box antechamber along with all items you initially brought into the glove box.
- Secure the septum after the RB is removed from the antechamber, connect it to the nitrogen line (add a syringe needle for venting) and immerse the RB flask into the ice-water bath as shown in figure 4. Wait about 2-4 minutes for the content of the RB flask to reach 0-5 °C.
- Add, with a syringe, small portions of the 0.25 mL (2.70 mmol) acetic anhydride. The solution should become purple. Stir the solution for 2 hours at 0-5 °C.
- Remove the septum cap and with efficient stirring, add very small portions of the product in the RB flask to an 80-mL beaker containing 25 mL 2M HCl and approximately 50 g of ice.
- Extract with 4x25 mL of CH<sub>2</sub>Cl<sub>2</sub> (dichloromethane).
- Dry the dichloromethane over anhydrous Na<sub>2</sub>SO<sub>4</sub>. Remove the drying agent by filtration and rotavap the solvent from the acetylation product. Obtain the crude weight.

**Experiment #4:** The Preparation of Ferrocene & Acetylferrocene

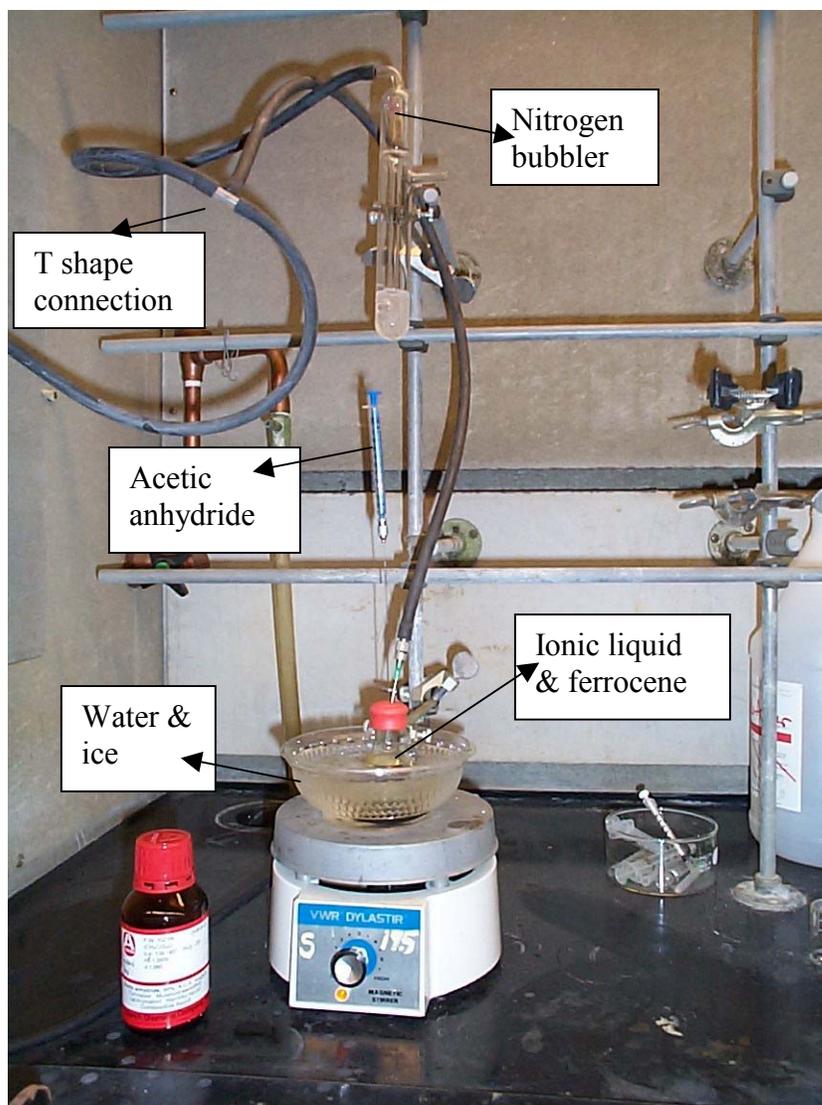


Figure 4. Ferrocene acetylation apparatus.

**3A. Characterization by GC-MS**

The combination of gas chromatography and mass spectrometry (GC/MS) is a powerful analytical tool. Your Teaching Assistant will show you how to run a GC/MS in order to assess the relative molar content of ferrocene (FW = 186), monoacetylferrocene (FW = 228) and diacetylferrocene (FW=270) in your product mixture.

**3B. Thin-Layer Chromatography of Acetylation Product**

To determine the product distribution of the reaction mixture, an aliquot will be analyzed by thin-layer chromatography. TLC silica gel plates are available from the stockroom. A tiny spot

**Experiment #4:** The Preparation of Ferrocene & Acetylferrocene

of the dichloromethane solution of the acetylation product is applied to the TLC plate using a micro-capillary tube. Development is conveniently conducted in plastic snap-top jars (Fig. 5). A 5-1/2 cm size filter paper placed in the jar is used to saturate the chamber with solvent vapor. Be certain the solvent level is below the point where the plate was initially spotted.

Prepare two solutions for thin-layer application; one of ferrocene and another of the acetylation product by dissolving 20 mg of material in 2 mL of ether (if the dichloromethane has already been rotovapped off the product). Spot several (see below) silica plates with a spot of pure ferrocene and a spot of acetylation product.

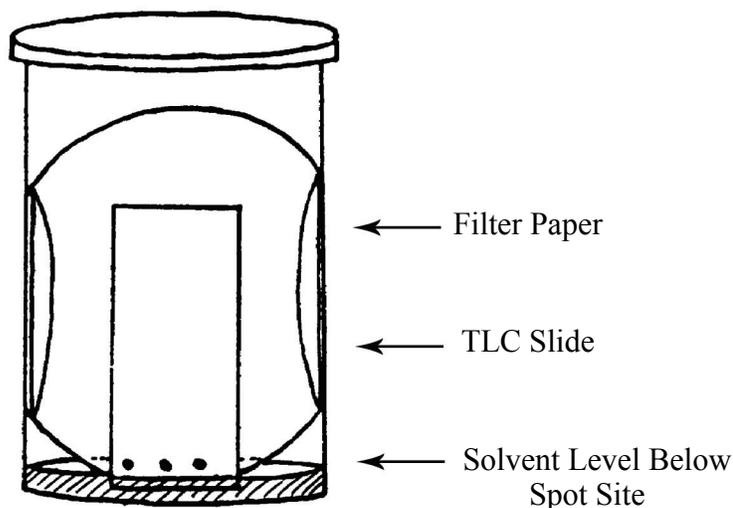


Fig. 5. Thin-layer chromatography developing chamber from glass vial with plastic snap-cap.

Develop the chromatograms in each of the following solvent mixtures to determine which combination provides optimal resolution. Start with hexane-ethyl acetate 10:1 and then gradually increase the polarity (for example: 7:1; 5:1; 3:1; 2:1) to hexane-ethyl acetate 1:1.

When the solvent has traveled to within a centimeter of the top of the plate, remove it from the development tank and mark the solvent front on the plate with a pencil. Allow the plate to dry in the air. Record in your notebook a trace of each chromatogram. Determine the  $R_f$  of each component for the solvent system which best separates the species. Rationalize why this solvent provides the best resolution. Positive identification of the ferrocene spot can be made at this time. Reserve the spotting solutions (and/or a few drops of the unrotovapped solution) for comparison by thin layer chromatography with the purified acetylferrocene and/or diacetylferrocene you obtain after column chromatography.

### 3C. Column Chromatography

#### Check-out from the Stockroom the “ferrocene” chromatography column.

To separate the acetylferrocene from ferrocene and 1,1-diacetylferrocene, prepare a column using silica gel.\* **Use your experience with TLC to guide your solvent choice for column chromatography – in making your choice you may wish to consider the different goals of TLC and column chromatography.** Discuss you plan with your TA prior to preparing the column.

To obtain a well packed column, fill with the initial solvent or solvent mixture chosen (hereafter referred to as “solvent”) to about 70% of the desired column height. Weigh out about 1.5 g of silica gel in a 25 mL beaker, and prepare a slurry of the silica gel by adding a small amount of the chosen solvent and swirling. Add the slurry through a funnel to the solvent in the column until a column of 9 cm is obtained. In the course of adding the slurry it may be necessary to drain some solvent from the column by opening the stopcock and to add more solvent to the silica gel in the beaker. **Do not allow the solvent level in the column to fall below the level of the silica gel.** Wash down any silica gel adhering to the sides of the column with additional portions of solvent. Apply a 0.5 cm layer of sand to the top of the column to protect the surface of the adsorbent. Drain the column to a point midway through the top sand layer.

To apply the sample, dissolve the dry crude product<sup>22</sup> **in as small a volume** of ether as possible (less than 1-2 mL). Apply it to the walls of the column with a disposable pipet. Wash down any solution adhering to the sides of the column with a small (<1 mL) aliquot of the chosen solvent system delivered from a disposable pipet. By alternately draining a small amount of solvent from the column and adding more to the top, the sample may be washed from the layer of sand onto the top of the adsorbent. Open the stopcock and add solvent cautiously to avoid disturbing the top layer of sand and adsorbent.

Colored bands should appear as one species is eluted down the column more readily than the other(s). Collect the eluant containing the first colored species in a tared 25 mL round bottom flask. If necessary, add more solvent to complete the elution. Once the first band has been eluted, you may wish to adjust the solvent system to favor the elution of subsequent bands. Collect each colored eluant in a separate tared round bottom. You should have the same number of colored fractions as spots on the original TLC plates.

Check the colored fractions by thin-layer chromatography to verify that each contains a single component. Evaporate the solvent from each colored fraction with a rotary evaporator. Determine the weight of each component and verify its identity by melting point. If the component is not of satisfactory purity, it should be recrystallized. Acetyl ferrocene may be recrystallized from hexane, diacetylferrocene from chloroform\*-hexane.

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<sup>22</sup> Do not attempt to separate more than 0.5 gram of material on the 15 cm column. Overloading the column will result in severe streaking, poor resolution, and crystallization on the tip.

**Experiment #4:** The Preparation of Ferrocene & Acetylferrocene

Table II. Melting Points of Acetylferrocene Compounds

<u>Compound</u>	<u>mp</u>
Acetylferrocene	84.0 - 84.5 °C <sup>23</sup>
Diacetylferrocene	127.5 - 128.5 °C <sup>24</sup> , 130 - 131 °C <sup>25</sup>

Calculate the percent yield of each isolated component of the acetylation product. Correlate the product distribution with that predicted for the particular reaction conditions. Submit all samples of ferrocene, acetylferrocene, and diacetylferrocene and all other product in appropriately labeled vials to your teaching assistant.

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<sup>23</sup> Graham, P.J.; Lindsey, R.V.; Parshell, G.W.; Peterson, M.L.;G.M. Whitman, G, M. *J. Amer. Chem. Soc.*, **1957**, 79, 3416.

<sup>24</sup> Rosenblum, M.; Woodward, R.B. *J. Amer. Chem. Soc.*, **1958**, 80, 5443.

<sup>25</sup> Woodward, R.B.; Rosenblum, M.; Whiting, M.C. *J. Amer. Chem. Soc.*, **1952**, 74, 3458.