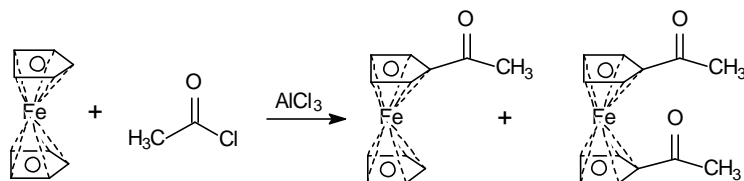


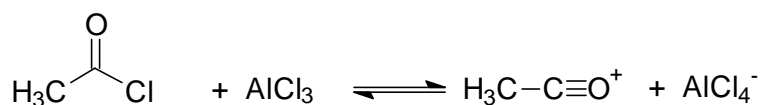


Chromatography of Ferrocene Derivatives¹



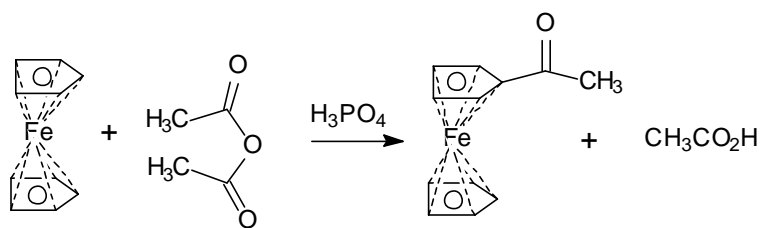
Since the initial preparations of ferrocene, $\text{Fe}(\text{C}_5\text{H}_5)_2$, in 1951, numerous investigators have examined the reactions of this compound to determine whether the cyclopentadienyl rings are similar to benzene in their chemical reactivity. In fact, many substitution reactions on the cyclopentadienyl rings do occur, and ferrocene usually undergoes these reactions more readily than does benzene. These observations have been interpreted to indicate that the cyclopentadienyl rings in ferrocene are "more aromatic" than benzene. Regardless of how one defines aromaticity, it is at least clear that ferrocene readily undergoes electrophilic substitution. One such substitution reaction is that of acetylation in the presence of a Friedel-Crafts catalyst.

The role of the Lewis acid AlCl_3 is presumably to participate in the generation of the electrophile, $\text{CH}_3\text{C}\equiv\text{O}^\oplus$.

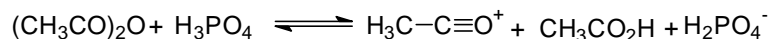


Whether the mono- or diacetyl product is obtained is determined by the amounts of reactants and the conditions of the reaction.

In this experiment, the acetylation of ferrocene will be carried out under milder conditions to yield primarily the monoacetyl product.



The electrophile, $\text{CH}_3\text{C}\equiv\text{O}^\oplus$, is probably produced by the reaction,



Since H_3PO_4 produces a relatively small concentration of $\text{CH}_3\text{C}\equiv\text{O}^\oplus$ compared to that generated in the reaction of CH_3COCl with AlCl_3 , only small amounts of the monoacetyl derivative are converted to the disubstituted compound.

¹Derived from Angelici, R. J., *Synthesis and Technique in Inorganic Chemistry*, 2nd Edition, W. B. Saunders Company, Philadelphia, PA, 1977.

Thin Layer Chromatography

While the chemistry of ferrocene is novel and extensive, it is left to the reader to pursue this topic in further depth through the references given at the end of this experiment. One of the primary purposes of this experiment is to illustrate standard chromatographic techniques that are used in the separation of pure compounds from complex reaction mixtures. In the acetylation reaction of ferrocene, a solid mixture of primarily $\text{Fe}(\text{C}_5\text{H}_5)_2$ and $\text{Fe}(\text{C}_5\text{H}_5)(\text{C}_5\text{H}_4\text{COCH}_3)$ is obtained. The remainder of this experiment is concerned with chromatographic methods of separating these two complexes. Thin layer chromatography (TLC) will be used to explore what chromatographic conditions are necessary to separate the compounds; employing these conditions, column chromatography will be utilized to separate the pure ferrocenes on a larger scale.

Separations effected by both TLC and column chromatography are based on the tendency of molecules to adsorb to certain adsorbents. The adsorbents most frequently used in TLC and column chromatography are silica gel and alumina. In TLC, a thin layer (0.1 to 2 mm thick) of the adsorbent is fixed to the surface of a flat plate. While there are many variations of this technique, microscope slides (2.5 x 7.5 cm) are commonly employed and will be used in this experiment as the plate. Two microscope slides are placed back to back and dipped into a stirred chloroform or chloroform-methanol slurry of the adsorbent (silica gel in this experiment).

The slides are separated and allowed to dry in air for several minutes. A small amount of the sample to be separated is dissolved in a small volume of a suitable solvent. With a capillary, a spot (3 to 5 mm in diameter) of the solution is placed on the silica gel 8 to 10 mm from the end of the slide. Allow it to dry and then add more of the solution to the same spot. The spot should be kept small for maximum separation of the components. This slide is then placed in a weighing bottle that contains a little solvent (~4 mm deep). The solvent level should be lower than the spot on the slide. Close the bottle and allow the solvent to rise up the silica gel, and if the proper solvent was chosen the mixture will begin to separate and move up the plate behind the solvent front. If different compounds move up the silica gel at different rates they, will be separated.

When the solvent has moved about three-fourths of the way up the silica gel, the plate should be removed. If the compounds in the mixture are colored, it will be obvious if a separation occurs. If one or more of the compounds are colorless, their locations on the slide can usually be established by placing the air-dried slide in a weighing bottle containing a few crystals of iodine. The iodine sublimes and adsorbs in the areas where the compounds are located. Thus, dark brown spots on the plate indicate the locations of the components of the original sample. If the solvent that was chosen for the separation does not separate the components of the mixture, another more or less polar solvent should be tried until a solvent that gives a separation is found. The solvent that does give a separation will then be used in the larger scale isolation of the compounds by column chromatography.

The separation of mixtures into their components by TLC is governed by the nature of the adsorbent and the solvent. The forces that attract a compound to the silica gel on a TLC plate are assumed to be largely polar. The separation of a mixture of compounds therefore depends to a large extent on the differences in adsorption tendencies of the components. The nature of this adsorption is very complex and poorly understood. Silica gel, for example, is largely SiO_2 or hydrated forms of SiO_2 , sometimes written as $\text{Si}(\text{OH})_4$ or $\text{SiO}_2 \cdot x\text{H}_2\text{O}$. It does however, contain significant amounts of other inorganic salts whose amounts vary from one silica gel preparation to another.

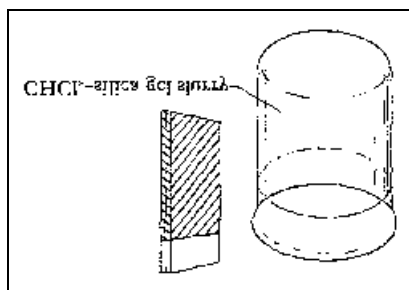


Fig. 1

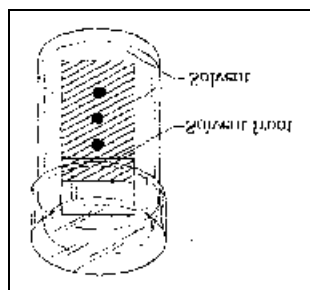


Fig. 2

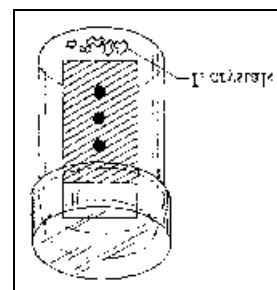


Fig. 3

When silica gel is heated in strongly acid or basic solutions, it acquires acidic or basic properties and even can act to some extent like cation or anion exchange column. Acid-treated silica gel strongly adsorb (or binds) basic compounds such as amines, whereas base-treated silica gel adsorbs acidic compounds. For silica gels that are neutral (i.e., when it is washed with water, the wash is approximately neutral) there are even differences in adsorption depending upon the water content of the silica gel. The most active form is obtained by heating under vacuum a 160°C for 4 hours. Most of the water is driven off the silica gel leaving sites where other polar molecules might adsorb. Less strongly adsorbing silica gel can be prepared by adding 10, 15, or 20 per cent H_2O to occupy some of the adsorption sites. By altering the water content, it is therefore possible to alter the degree of adsorption of a compound on a TLC plate.

The extent of adsorption is also determined by the compound's solubility in the solvent and the affinity of the solvent for the adsorption sites. Polar solutes will adsorb strongly to the silica gel when a relatively nonpolar solvent is used. If a solvent of higher polarity is used, the solute will be more soluble in it, and the solvent will have a greater tendency to adsorb to the silica gel by displacing some of the solute molecules. Both of these factors favor less adsorption and faster migration up the TLC slide as the polarity of the solvent is increased.

The choice of solvent is not easy, but generally a solvent that dissolves the desired compound moderately well will allow the compound to move up the plate but not as fast as the solvent. It can only be hoped that the impurities do not move at the same rate as does the compound of interest. If the compound moves too rapidly, a less polar solvent should be tried, whereas if it moves too slowly a more polar solvent is appropriate. The trend of polarity (increasing from the top of this list to the bottom) of some common chromatographic solvents is shown as follows:

light petroleum, pentane, hexane, and the like
 carbon tetrachloride
 toluene
 benzene
 dichloromethane
 chloroform
 ethyl ether
 ethyl acetate
 acetone
 ethanol
 methanol
 water

At this point it is probably obvious that the successful choice of adsorbent and solvent is an art that is learned largely by doing chromatographic separations. The references at the end of this experiment do offer, however, many hints on how to use these techniques more effectively.

Column Chromatography

Having established the solvent or solvent mixture that will separate the sample on TLC plates, it is hoped that the same solvent can be used to separate larger quantities of the sample on a silica gel chromatography column. Generally this is possible. It is necessary, however, to use a much larger silica gel particle size for column chromatography (80-200 mesh) than that used in TLC (finer than 200 mesh). This necessitates using a different source of silica gel, which may or may not have the same adsorption characteristics as that used in TLC. Fortunately, silica gels are frequently similar enough that a mixture can be separated on a column using the same solvent that was used successfully on the TLC plates. Initially, it is reasonable to assume that this is possible.

A simple burette may be used for the chromatography column (Fig 4). First a small glass wool plug is pushed to the bottom of the column, and a 5 mm layer of washed sand is added. Make up a slurry of the silica gel in the solvent to be used in the separation and pour it onto the sand. After draining the column until the solvent level is the same as the top of the silica gel, add a slurry of the sample and silica gel in a few milliliters of the solvent to the column. Then add a 5 mm layer of sand to the top of the silica gel. (Instead of adding the sample as a slurry, it may be dissolved in a small volume of the solvent and added to the column.)

Then the liquid level is lowered to the top of the silica gel. Never allow the solvent level to fall below the top of the silica gel, for channels in the column will result, and solution will pass down the channels without properly percolating through the adsorbent. The eluting solvent is added to the column, and the elution of the compounds begins. The flow-rate will depend upon the separation, but slow flow-rates give better separations than do high flow-rates.

If the compounds are colored, it is easy to determine what fractions should be collected to obtain the products. If the compounds are colorless, fractions may have to be collected at regular volume intervals and examined for the presence of compounds spectrophotometrically or by other techniques. While the initial eluting solvent may elute one or more of the compounds, other compounds may require (as noted by TLC) more polar solvents to move them down the column. If a change in solvent is required, it is best to introduce it gradually by using first a mixture of the initial and the subsequent solvent and then finally the pure solvent. Sometimes a direct change of solvent involves a large evolution of heat when the new solvent adsorbs to the silica gel. This causes the solvent to expand, and channels are formed in the adsorbent that destroy the efficiency of the column.

The fractions eluted from the column that contain the desired compounds may simply be evaporated to dryness to give the pure compound. Evaporation sometimes does not give a crystalline solid, and recrystallization of the material usually gives a better looking product.

Column chromatography has numerous variations. Although silica gel and alumina (" Al_2O_3 ") are the most common adsorbents, many others have also been used. For materials that decompose at room temperature, chromatographic separations have been carried out in cooled, jacketed columns. Air-sensitive compounds have been chromatographed in an atmosphere of nitrogen or argon. All of these variations, however, are basically chromatography, and it is these basics that will be practiced in this experiment.

The separation of $\text{Fe}(\text{C}_5\text{H}_5)_2$ (mp, 173-4°C) and $\text{Fe}(\text{C}_5\text{H}_5)(\text{C}_5\text{H}_4\text{COCH}_3)$ (mp, 83-5°C) is a relatively, easy) one. There is more than one solvent or solvent combination that will provide the desired separation. It is the student's task to determine at least one solvent system that will work. Having separated the compounds, the eluted products must then be identified by their melting points and their infrared and NMR spectra.

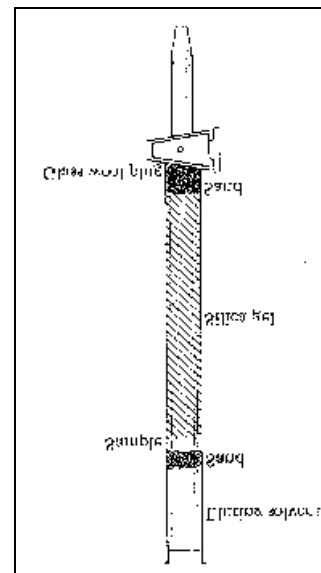


Fig. 4

EXPERIMENTAL PROCEDURE

The reactant, $\text{Fe}(\text{C}_5\text{H}_5)_2$, and product, $\text{Fe}(\text{C}_5\text{H}_5)(\text{C}_5\text{H}_4\text{COCH}_3)$, are stable solids in both air and water at room temperature.

Acetylcyclopentadienyl-(cyclopentadienyl)-iron(II), $\text{Fe}(\text{C}_5\text{H}_5)(\text{C}_5\text{H}_4\text{COCH}_3)$

Add 1 ml of 85 per cent phosphoric acid dropwise with constant stirring to a mixture of 1.5 g (8.05 mmoles) of ferrocene and 5 ml (5.25 g, 87 mmoles) of acetic anhydride in a small Erlenmeyer flask. Protect the mixture with a CaCl_2 drying tube. Heat the reaction mixture on a steam bath (or in a boiling water bath) for 10 minutes. Then pour the mixture onto about 20 g of ice in a tall beaker. When the ice has melted, neutralize the mixture by adding solid NaHCO_3 until CO_2 is no longer evolved. (This will require a fairly large amount of NaHCO_3 .) Cool the mixture in an ice bath for 30 minutes to ensure complete precipitation of the ferrocenes from solution. Suction-filter the solid on a coarse frit and wash it with water until the filtrate is pale orange. Air-dry the solid on the frit for 15 minutes. This solid largely contains $\text{Fe}(\text{C}_5\text{H}_5)_2$ and $\text{Fe}(\text{C}_5\text{H}_5)(\text{C}_5\text{H}_4\text{COCH}_3)$, but other impurities are also present.

Thin Layer Chromatography, TLC

Using TLC, determine which solvent system will allow you to separate $\text{Fe}(\text{C}_5\text{H}_5)(\text{C}_5\text{H}_4\text{COCH}_3)$ from the product mixture by column chromatography.

Prepare the TLC plates by placing two microscope slides (2.5 x 7.5 cm) back to back and dipping them into a stirred chloroform slurry of TLC silica gel (approximately 40 g of silica gel per 100 ml of CHCl_3). Withdraw them slowly and touch them to the edge of the container to allow them to drain. Separate the slides, remove excess silica gel on the edges with your fingers, and allow the slides to air-dry on a horizontal surface for about 5 minutes. Handle the slides carefully to keep the silica gel layer intact. (Keep the slurry bottle closed when not in use because silica is hygroscopic.)

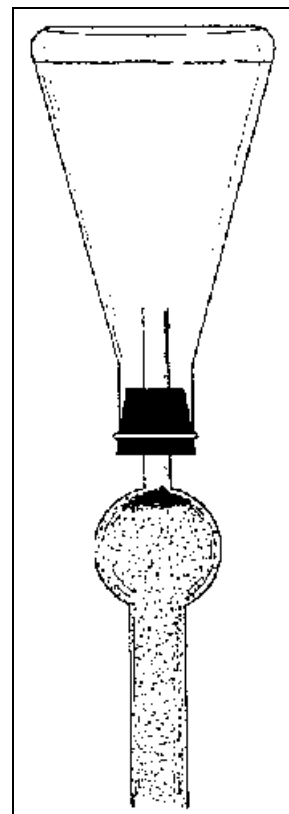


Fig. 5

With a very small portion of the ferrocene mixture, prepare a concentrated benzene solution for use in the TLC trial separations. A very small amount of this solution will be spotted on the silica gel 8 to 10 mm from the bottom of the microscope slide. Since the best separations are achieved when this spot is the smallest, the benzene solution should be applied with a very small capillary. It can be prepared by heating the middle of a melting point capillary tube over a low flame and quickly pulling the ends of the tube apart before the tube is sealed off. Scratch the capillary with a sharp file and break the tube into two applicators. Dip an applicator into the benzene solution of the mixture and touch it to the slide, giving a spot that is not larger than 4 mm in diameter. Allow the benzene to evaporate, and then make a second application of the solution to the same spot.

Fill five weighing bottles with the trial solvents listed below to a depth of 4 mm or less, such that the level is below your spot when the microscope slide is inserted.

1. petroleum ether, 60 °C to 70 °C boiling fraction
2. benzene
3. ethyl ether
4. 10 per cent ethyl acetate and 90 per cent petroleum ether (by volume)
5. ethyl acetate

Insert a spotted slide into each bottle and replace the cover. Allow the solvent to rise about three-fourths

of the way up the slide and then remove it and allow it to dry. Do this for each of the five slides, carefully recording what solvent was used for each slide. Although $\text{Fe}(\text{C}_5\text{H}_5)_2$ and $\text{Fe}(\text{C}_5\text{H}_5)(\text{C}_5\text{H}_4\text{COCH}_3)$ are colored, they may hardly be visible in the low concentrations on the plate. Their presence can be unequivocally established by placing each of the slides in a closed weighing bottle containing a few crystals of iodine. The volatile iodine will adsorb to the plate where compounds are located.

Make a drawing in your research notebook of the location of the spots for each of the five attempts. To establish which spot is ferrocene, prepare another TLC slide, spotting it first with the benzene solution of the mixture and then in an adjacent position with a benzene solution of pure ferrocene. Develop the slide in one of the solvents that gave a good separation of spots, and establish which spot of the mixture is ferrocene by comparing it with the known ferrocene spot.

From the five TLC trials you should select a solvent for the column chromatographic separation. You may select a solvent in which one of the components moves rapidly and the other more slowly. Such a solvent should give a good separation on the column. Alternatively, one might choose an initial solvent in which only one component moves while the other remains at the starting point. The first component could then be washed off the column, and then a more polar solvent that moves both materials could be added to elute the other component. Regardless of your choice, it should be based on the separation achieved on the TLC slides.

Column Chromatography

A 25 ml burette (9 mm, i.d.) may be used. Push a wad of glass wool to the bottom of the burette with a glass rod. Then pour in enough washed sand to give a 5 mm layer. Make a slurry of silica gel (80-200 mesh) in the solvent that you initially plan to use in the separation, and pour it into the column until the silica gel column height is about 30 cm. (Keep the stock bottle of silica gel closed when not in use. Dry silica gel is very hygroscopic and will become deactivated if exposed to atmospheric humidity.) Drain the burette until the solvent level is the same as the silica gel level. (*Do not* allow the solvent level to drop below the top of the silica gel.) Then pour a slurry of silica gel and about 0.4 g of the ferrocene mixture in a few milliliters of the initial solvent onto the column. (Depending upon which solvent you choose, the sample may or may not dissolve. Even if it does not dissolve, a good separation should result if you have selected your solvents correctly.) Lower the solvent again at the top of the adsorbent and add another 5 mm layer of washed sand to prevent the silica gel bed from being disturbed when the eluting solvent is added. Then gently fill the burette with the initial eluting solvent, being careful not to agitate the silica gel. Carry out the elution, using a flow rate of approximately 1 drop per second. Since ferrocenes decompose somewhat in light, the column should be loosely wrapped with aluminum foil. The progress of the separation can be noted by momentarily opening the foil. The color of the two ferrocenes should allow you to collect separately solutions of $\text{Fe}(\text{C}_5\text{H}_5)_2$ and $\text{Fe}(\text{C}_5\text{H}_5)(\text{C}_5\text{H}_4\text{COCH}_3)$. Transfer each solution to a small filter-flask. Stopper the top of the flask and evaporate the solution to dryness under water aspiration (Figure 6-3). Weigh each of the solids. The tar that remains at the top of the column should be discarded along with the rest of the used silica gel.

The two colored products that are collected must be identified and characterized. Measure their melting points. Record the infrared spectrum of each compound in CCl_4 solution. Obtain the nmr spectrum of the two compounds in CDCl_3 or benzene- d_6 solution. Having identified the $\text{Fe}(\text{C}_5\text{H}_5)(\text{C}_5\text{H}_4\text{COCH}_3)$, calculate the percentage yield of the product and the percentage recovery of unreacted ferrocene.

REPORT

Include the following:

1. Percentage yield of $\text{Fe}(\text{C}_5\text{H}_5)(\text{C}_5\text{H}_4\text{COCH}_3)$ and percentage recovery of $\text{Fe}(\text{C}_5\text{H}_5)_2$.
2. Melting points of $\text{Fe}(\text{C}_5\text{H}_5)(\text{C}_5\text{H}_4\text{COCH}_3)$ and $\text{Fe}(\text{C}_5\text{H}_5)_2$.
3. Infrared spectra of $\text{Fe}(\text{C}_5\text{H}_5)(\text{C}_5\text{H}_4\text{COCH}_3)$ and $\text{Fe}(\text{C}_5\text{H}_5)_2$. Point out differences and similarities.
4. NMR spectra of $\text{Fe}(\text{C}_5\text{H}_5)(\text{C}_5\text{H}_4\text{COCH}_3)$ and $\text{Fe}(\text{C}_5\text{H}_5)_2$ and interpretation.

QUESTIONS

1. Was $\text{Fe}(\text{C}_5\text{H}_5)(\text{C}_5\text{H}_4\text{COCH}_3)$ or $\text{Fe}(\text{C}_5\text{H}_5)_2$ eluted first? Why?
2. Why was the reaction to form $\text{Fe}(\text{C}_5\text{H}_5)(\text{C}_5\text{H}_4\text{COCH}_3)$ protected with a CaCl_2 drying tube?
3. What might be the tar that remained at the top of the chromatography column?
4. Account for the different chemical shifts of the H's in the acetylated ring of $\text{Fe}(\text{C}_5\text{H}_5)(\text{C}_5\text{H}_4\text{COCH}_3)$ as compared to that of the H's in the nonacetylated ring.
5. Write a complete mechanism for the formation of acetylferrocene by the reaction used in this experiment.
6. The rates at which ferrocene derivatives elute from a silica gel column depend upon any pre-treatment of the silica gel. Would acetylferrocene move down a column made of silica gel that had been heated at 150° under vacuum for 8 hours faster or slower than it would on a column using silica gel that had been sitting open in the laboratory for a few days? Explain.
7. What methods might be used to detect the elution of colorless compounds from a column?
8. A mixture of *cis* and *trans* isomers of the neutral complex $\text{Cr}(\text{CO})_4[\text{P}(\text{C}_6\text{H}_5)_3]_2$ is loaded onto a column and eluted with CHCl_3 . Which isomer would elute first, and why?

INDEPENDENT STUDIES

- A. Analyze the $\text{Fe}(\text{C}_5\text{H}_5)_2$ - $\text{Fe}(\text{C}_5\text{H}_5)(\text{C}_5\text{H}_4\text{COCH}_3)$ reaction mixture for the amounts of each of these compounds, using *gas chromatography*. (O. E. Ayers, T. G. Smith, J. D. Burnett, and B. W. Ponder, *Anal. Chem.*, **1966**, *38*, 1606.)
- B. Measure the mass spectra of $\text{Fe}(\text{C}_5\text{H}_5)_2$ and/or $\text{Fe}(\text{C}_5\text{H}_5)(\text{C}_5\text{H}_4\text{COCH}_3)$ and make assignments to all peaks.
- C. Separate the $\text{Fe}(\text{C}_5\text{H}_5)_2$ - $\text{Fe}(\text{C}_5\text{H}_5)(\text{C}_5\text{H}_4\text{COCH}_3)$ reaction mixture, using dry-column *chromatography*. (J. C. Gilbert and S. A. Monti, *J. Chem. Educ.*, **1973**, *50*, 369.)
- D. Prepare and characterize ferricinium picrate, $[\text{Fe}(\text{C}_5\text{H}_5)_2]^+ [\text{C}_6\text{H}_2\text{O}_7\text{N}_3]^-$. (D. W. Johnson and G. W. Rayner-Canham, *J. Chem. Educ.*, **1972**, *49*, 211.)
- E. Synthesize and characterize nickelocene, $\text{Ni}(\text{C}_5\text{H}_5)_2$. (K. W. Barnett, *J. Chem. Educ.*, **1974**, *51*, 422.)

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