

FRIEDEL-CRAFTS ACYLATION OF FERROCENE: SYNTHESIS OF ACETYLFERROCENE

In this experiment you will:

1. Synthesize acetylferrrocene via a Friedel-Crafts acylation reaction.
2. Isolate, purify and characterize the product using melting point determination and spectral analysis.
3. Analyze the methodology using the 12 principles of green chemistry.

THEORY

The Friedel-Crafts acylation is a reaction between an aryl compound and an acyl halide or anhydride to form an aryl ketone using a Lewis acid catalyst (such as AlCl_3). It is named after the young European chemist Charles Friedel and the American chemist, James Mason Crafts. The reaction begins with the Lewis acid abstracting the halide from the acyl halide to form an electrophilic acylium cation and a tetrasubstituted aluminum anion. The aromatic compound then attacks the acylium ion via an electrophilic aromatic substitution to give a cationic product with loss of aromaticity. Deprotonation with the aluminum anion results in the final aryl ketone and regeneration of the Lewis acid catalyst (Scheme 1).

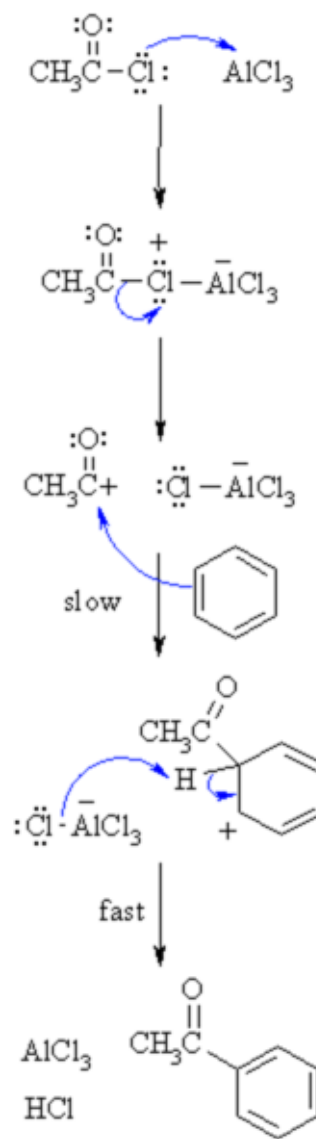
Friedel-Crafts alkylation reaction has serious limitations. The aromatic ring is activated by the presence of an alkyl substituent and leads to polyalkylation. The reaction is also prone to carbocation rearrangements leading to a mixture of products. Both of these limitations are eliminated in the Friedel Crafts acylation reaction. The acyl group deactivates the ring, so polyacylation does not occur. The acylium ion is resonance stabilized and is not prone to rearrangement reactions like a carbocation.

Step 1:
The acyl halide reacts with the Lewis acid to form a complex.

Step 2:
Loss of the halide to the Lewis acid forms the electrophilic acylium ion.

Step 3:
The p electrons of the aromatic **C=C** act as a nucleophile, attacking the electrophilic C+. This step destroys the aromaticity giving the cyclohexadienyl cation intermediate.

Step 4:
Removal of the proton from the sp³ C bearing the acyl- group reforms the **C=C** and the aromatic system, generating HCl and regenerating the active catalyst.



Scheme 1: Mechanism of the Friedel-Crafts Acylation Reaction

Textbooks of basic organic chemistry usually mention exclusively the use of reactive alkyl halides in combination with aromatics. However, alkenes, alkynes, alcohols, ethers, carbonyl compounds and so on, can also be effectively employed as alkylation agents. A range of molecular Lewis acids such as GaCl_3 , FeCl_3 , TiCl_4 , ZnCl_2 , BCl_3 , and Brønsted–Lowry acids (HF , H_3PO_4 , H_2SO_4) have proven efficient in accelerating this process. Figure 1 is an interesting journal article that highlights the history of this process.

Earliest History of the Friedel-Crafts Reaction¹

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INTEREST in the use of aluminum chloride as a reagent for bringing about chemical reactions on a commercial scale has been growing rapidly during the past ten years. New methods for manufacturing the chloride have led to a product at a figure attractive to industry. In 1923 a little over 5000 tons were manufactured in the United States, while during 1926 the quantity produced reached 16,750 short tons and at a marked decrease in price per ton over that for 1925. Success in the commercial production of aluminum chloride has stimulated a number of industrial processes. The formation of toluene from xylenes has been shown to be feasible by Moore and Egloff.² Cheaper aluminum chloride has made possible the manufacture of anthraquinone, which is better for vat dyes than that recovered from coal tar.³ Probably the most outstanding commercial application has been in the cracking of petroleum for gasoline.⁴

The advent of the summer of 1927 marks the fiftieth anniversary of the announcement of the Friedel-Crafts reaction, which has now become of so much interest to the industrial world. It has been one of the most fruitful and far-reaching reactions known to organic chemistry. Indeed, Elbs said: "The Friedel-Crafts synthesis is the one most commonly used. It serves for the preparation of hydrocarbons, ketones, acids, keto acids, and phenols, especially phenol ethers."⁵ Had Elbs been writing at a somewhat later date, just so certainly would he have included in his praises the action of aluminum chloride as an agent for cracking hydrocarbons.

To American chemists the discovery of the reaction possesses peculiar interest for, contrary to the belief of many, James Mason Crafts was one of our own fellow citizens. He was born of American parents in the city of Boston in 1839 and there received his early education. He pursued graduate studies in chemistry under Bunsen in Heidelberg and under Wurtz in Paris. After returning home he became the first professor of chemistry at Cornell University. Three years later he went to the Massachusetts Institute of Technology, where he remained until impaired health made him resign active teaching in 1874. He then returned to the laboratory of Wurtz and there he worked for the next seventeen years, much of the time in collaboration with Prof. Charles Friedel. When he came back to America in 1891, he was again associated with the Massachusetts Institute of Technology, serving in turn as a member of the corporation, professor of organic chemistry, head of the department of chemistry, and finally as president of the Institute. In 1900 he resigned the presidency, devoting the rest of his years and strength to scientific work. He died in June, 1917.

The discovery of the Friedel-Crafts synthesis "sprang from an accidental observation on the action of metallic aluminum on chloride of amyl."⁶ It is very interesting to note that the commonly accepted statement that an attempt was being made to convert amyl chloride into the iodide by means of aluminum and iodine made its first appearance seven years after the original paper.⁷ In spite of the great handicap

under which the work was done, the early development of the reaction proceeded with dramatic speed. "The discoverers had at that time only a very small laboratory, with no place for students, and not even provided with the convenience of running water."⁸ The first paper was presented to L'Academie des Sciences on June 11, 1877. Peligot was president and the papers were sponsored by Wurtz.⁹ "The experiments which demonstrated the wide scope of the reaction were so easy of execution that those described in the first three papers were carried out in the course of five or six weeks."⁸ The first paper is a classic for clearness and simplicity in presenting an account of an important discovery. In honor of the fiftieth anniversary of its presentation to L'Academie des Sciences and for the value it may have for readers of English, it is presented here translated from the original French.

The First Observations

In a research which we undertook together we were led to study the action of metallic aluminum in thin plates or leaves on various organic chlorides. We observed that the reaction, slow at first and initiated only by the aid of heat, afterwards accelerated to the point of becoming tumultuous when it was necessary to control it by cooling. The addition of a very small quantity of iodine provoked the reaction, which was always accompanied by an abundant evolution of hydrogen chloride. In the case of certain chlorides, such as amyl chloride, it was accompanied by the formation of numerous gaseous and liquid hydrocarbons, certain of which boiled at a very high temperature. The reaction seemed the more active if a considerable proportion of aluminum chloride was formed.

Aluminum Chloride the Activating Agent

This last circumstance led us to find out if the principal reaction ought not be attributed to the metallic chloride instead of to the metal, as we supposed at first.

It was easy to assure ourselves that such was indeed the case. For example, when a little aluminum chloride was added to amyl chloride we saw at once a vigorous evolution of gas, even in the cold. The gas was composed of hydrogen chloride accompanied by gaseous hydrocarbons not absorbed by bromine. In the midst of the amyl chloride in which the first portions of the aluminum chloride dissolved small droplets were formed. Shortly a layer of dense brown liquid developed and the reaction appeared to pass principally to the interface between the two liquids. We had noticed a similar circumstance in the reaction with aluminum, when a similar brown liquid was produced.

When the reaction had continued long enough, with the aid of a gentle heat to complete it at the end, a quantity of hydrogen chloride could be recovered which corresponded to nearly all the chlorine originally contained in the amyl chloride. An extremely varied series of hydrocarbons, from gases to products boiling above the boiling point of mercury, was also recovered. The residue consisted of aluminum chloride, which sublimed in hexagonal plates or in a crystalline crust when sufficiently heated in a current of an inert gas.

First Conclusions

We have not yet completed the study of the numerous products, the first members of which appear to be in the series of hydrocarbons C_nH_{2n+2} and the higher members of which are much poorer in hydrogen. For the present we wish to make the following observations: First, organic chlorides are attacked by aluminum chloride; second, the greater part of the products formed, which contain a large proportion of saturated hydrocarbons, could not be produced by a simple polymerization of amylene resulting from the subtraction of hydrogen chloride from amyl chloride; third, it seems much more likely that the hydrogen chloride which disengages itself is formed at the expense of two molecules, of which one furnishes the chlorine and the other the hydrogen, and the two parts then unite.

⁸ Friedel and Crafts, *Compt. rend.*, **84**, 1292, 1450 (1877); **85**, 74 (1877).

¹ Adapted from a paper under the title "James Mason Crafts" presented before the Section of History of Chemistry at the 73rd Meeting of the American Chemical Society, Richmond, Va., April 11 to 16, 1927.

² *Chem. Met. Eng.*, **17**, 61, 128 (1917).

³ Phillips, *Ibid.*, **33**, 173 (1926).

⁴ McAfee, *This Journal*, **7**, 737 (1915); Egloff, *Ibid.*, **15**, 581 (1923).

⁵ "Synthetischen Darstellungs Methoden," Vol. II, p. 144 (1891).

⁶ Crafts, *J. Chem. Soc. (London)*, **77**, 1006 (1900).

⁷ Friedel and Crafts, *Ann. chim. phys.*, [VI], **1**, 449 (1884).

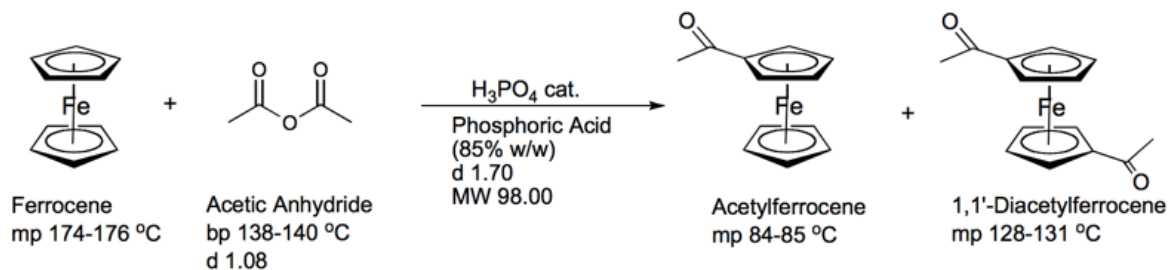
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Figure 1: Journal Article: The Friedel-Crafts Reaction

Greening the Reaction:

1. One of the primary problems in the traditional acylation method is the use and handling of aluminum chloride as a Lewis acid catalyst. Lewis acids such as AlCl_3 have great affinity for water and produce burns when come in contact with skin. The side product of this reaction is aluminum chloride trihydrate, a waste to be dealt with. This byproduct is usually removed during workup and the final byproduct waste is aluminum hydroxide. In this greener acylation experiment, phosphoric acid is used as the catalyst instead of AlCl_3 .
2. Traditional methods of acylation also involve the use of solvents. Solvents are common to laboratory processes and are indispensable to synthetic organic chemistry. Several billion pounds of solvent waste are generated by the chemical processes and discharged into streams. Many of these solvents are detrimental to our ecosystems, deplete the ozone layer and are cancer-causing. While contained use of these solvents may reduce the environmental and health hazards, reducing or eliminating the use of solvents is a better route. No solvent is used in this reaction. Acetic anhydride is used in excess, functions as both the acylating reagent and a solvent.

In this laboratory, you will acylate ferrocene (Scheme 2). Ferrocene is an organometallic compound, which behaves like an aromatic compound. 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.



Scheme 2: Green 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.

PROCEDURE

Set up a hot water bath in a well-ventilated hood. Add 1.5 g of ferrocene in a 20 mL round bottom flask and add a magnetic stir bar. Add 5.0 mL of acetic anhydride followed by 1 mL of 85% phosphoric acid to the flask. Attach a water-cooled condenser to the flask, making sure the water hoses are securely clamped (as shown in figure 1). Attach a drying tube to the water condenser.¹ Clamp the flask in the boiling water bath and stir the mixture. The mixture will turn dark red. Continue stirring until all ferrocene dissolves. You can infer this by the dissolving of yellow ferrocene solid. After ferrocene has dissolved, reflux the mixture for an additional 10 minutes.

Turn off the heat and allow the set up to cool. Pour the reaction mixture (with the magnetic stir bar) over 25 g ice in a 125 mL beaker. Rinse the flask with 10 mL of room temperature water and add this to the beaker. Transfer the stir bar to the mixture. Stir the red-brown mixture on a stir plate. **Make sure that the heat is not turned on.** Slowly add 37.5 mL of 3M NaOH solution. Check the pH of the mixture. Check the pH by placing a small drop on a pH paper. Do not immerse the pH paper into the contents. The pH is usually very basic. If this is not the case, add solid sodium bicarbonate in small portions until the pH is basic. Considerable fizzing can occur in this step. The amount of NaHCO_3 can vary with each reaction set up. Collect the crude product by

¹ Insert some cotton in the drying tube (available in microkit). Then add several spatulas of anhydrous calcium chloride to fill the tube halfway. Add cotton to secure the open end of the tube.

suction filtration. Save a small portion of the crude product for TLC analysis and use the remaining solid for recrystallization.

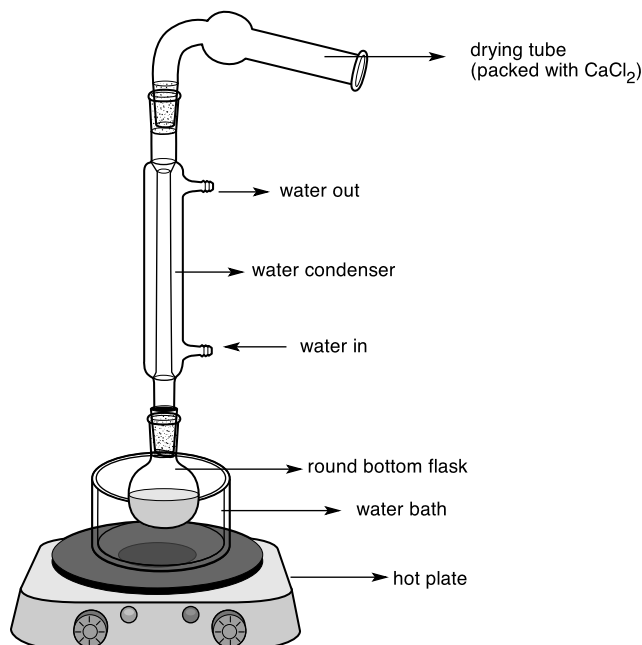


Figure 2: Set up for Acetylation of Ferrocene

Recrystallization

Add 20 mL of hexanes to the product. Add some boiling stones and boil the solution on a hot plate (medium heat) to dissolve the product. A black tar will stay at the bottom of the flask. **Quickly** transfer the clear but colored solution using a pipet plugged with cotton. If tar contaminates the transfer, **a hot gravity filtration may be necessary.** **Check with your instructor to assist you.** Allow the flask to cool slowly to room temperature, and then cool in an ice bath for ~ 10 minutes. Acetylferrocene crystallizes as dark red needles. Suction filter the product.

Drying

Dry the product under a heating lamp for 30 minutes. Alternately, you may leave the product to dry until the next lab period.

Product Characterization

Determine the yield and the melting point of acetylferrocene. Calculate the % yield for the reaction. Run an IR spectrum of ferrocene and acetyl ferrocene and confirm the formation of the acetylated product. Run ^1H NMR spectra on ferrocene and the product obtained. Compare and make a note of the differences in the spectra. Analyze the spectra for both compounds.

DATA:

Mass of Ferrocene: 1.5215 g

Moles of Ferrocene:

Volume of acetic anhydride: 5.0 mL

Moles of acetic anhydride:

Limiting Reactant is:

Calculation of Theoretical yield (show set up):

Crude yield of acetyl ferrocene: 1.2350 g

Weight of sample used for purification: 1.0512 g

Weight of purified acetyl ferrocene:

% of acetyl ferrocene in the sample:

% of acetyl ferrocene in the total crude product:

% yield of acetyl ferrocene: