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Synthesis and Analysis of 1-Propionylferrocene: An Organometallic Approach to Structure Elucidation

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INTRODUCTION

Ferrocene remains one of the most versatile learning tools for introductory organometallic chemistry classes, both in terms of in-classroom theory and hands-on lab experiments.¹ It is commonly students' introduction to metal complexes bearing cyclopentadienyl ligands and serves as a useful platform for teaching concepts such as ligand field theory, σ - and π -bonding, molecular orbital diagrams, symmetry groups, as well as the synthesis and reactivity of organometallic species.²

An air- and water-stable bright orange solid, ferrocene is soluble in most common organic solvents and is an important building block for further reactivity, as well as being a standard in electrochemistry. Ferrocenium salts, such as ferrocenium tetrafluoroborate, are widely used one-electron oxidants, made attractive by the inherent stability of ferrocene, the reduced product.³

One of the most important reactions included in the undergraduate curriculum for organometallic chemistry is the synthesis of acetylferrocene via Friedel-Crafts acylation of ferrocene.^{4,5} Recently, work was published to provide options

beyond the routine synthesis of acetylferrocene,⁶ opting instead for an educational approach focusing on various alkanoylferrocene derivatives, based on previously prepared experimental protocols.⁷ Herein, we elaborate on the synthesis of 1-propionylferrocene, as presented by Donahue et al.,⁶ and discuss how the 60 MHz benchtop NMR instrument can be incorporated into undergraduate labs to assist with the analysis of this molecule.

EXPERIMENTAL

Materials

Ferrocene (98%), propionic anhydride (97%), boron trifluoride diethyletherate (46%-51% BF₃ basis), and chloroform-*d* (99.8%) were purchased from MilliporeSigma and used without further purification.

Synthesis

All manipulations were performed under an inert argon (nitrogen is also suitable) atmosphere using standard Schlenk techniques. The synthesis of 1-propionylferrocene is accomplished using a modified literature procedure, and proceeds via the reaction scheme in Figure 1. This reaction can be performed on a multi-gram scale using commercially available and inexpensive reagents.

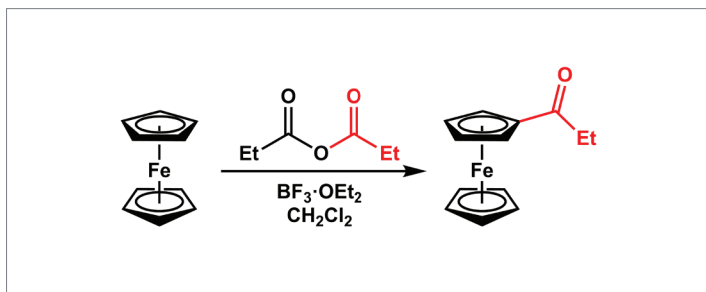


Figure 1. Reaction scheme for the preparation 1-propionylferrocene.

Ferrocene (5.00 g, 26.9 mmol) and propionic anhydride (6.90 mL, 7.00 g, 53.8 mmol) are suspended in DCM (40 mL) in a 250 mL round bottom Schlenk flask and cooled to 0 °C with an ice bath. Boron trifluoride diethyletherate (30 mL) is added via syringe over 10-15 minutes and the reaction is allowed to return to room temperature. The deep red mixture is stirred at this temperature for 2-3 hours, then poured over ice water (100 mL). The resulting solution is transferred to a 500 mL separatory funnel and the layers are separated. In a 500 mL beaker, the organic layer is washed with a saturated NaHCO_3 solution (100 mL) and stirred vigorously for 5 minutes. **Caution: NaHCO_3 washing can be violent if reaction is performed on a large scale and the saturated solution must be added slowly. Care must be taken to ensure bubbling subsides fully before transferring to the separatory funnel, and appropriate venting is necessary to avoid pressure buildup.** The mixture is carefully transferred to a 500 mL separatory funnel and the layers are separated. The NaHCO_3 washings are repeated two additional times and the organic layer is dried over Na_2SO_4 and filtered. The solvent is removed under reduced pressure, affording impure 1-propionylferrocene as a dark red oil. The product is purified using flash chromatography and is mounted on the column with a minimal amount of DCM. A mixture of cyclohexane/ethyl acetate (8:2) is used as eluent, initially affording an orange band, followed by a dark red band (the 1-propionylferrocene). A dark purple-red band remains on the column after the separation. The combined fractions containing the second dark red band are evaporated under reduced pressure, affording pure product as a dark orange-red powder.

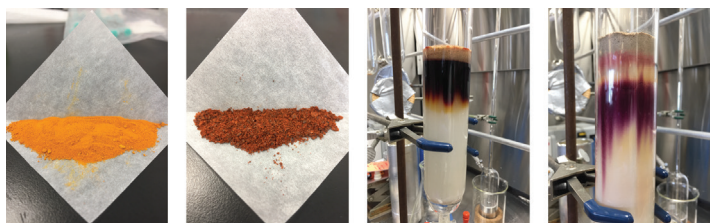


Figure 2. From left to right: ferrocene, 1-propionylferrocene, initial separation of orange and dark red bands, leftover dark purple-red band.

RESULTS AND DISCUSSION

The 1-propionylferrocene is perfectly suited for analysis using the benchtop NMR spectrometer. A 60 MHz ^1H spectrum (Figure 3, top) can be acquired in only a few minutes and provides immediate insight into the structure of the final product, making it a very useful teaching tool. The presence of an ethyl fragment is confirmed by the triplet and quartet resonances, produced by the methyl and methylene groups, respectively. Both splitting patterns have a matching coupling constant, $J_{\text{H-H}} = 7.10$ Hz, and their relative integrations are consistent with CH_2 and CH_3 fragments.

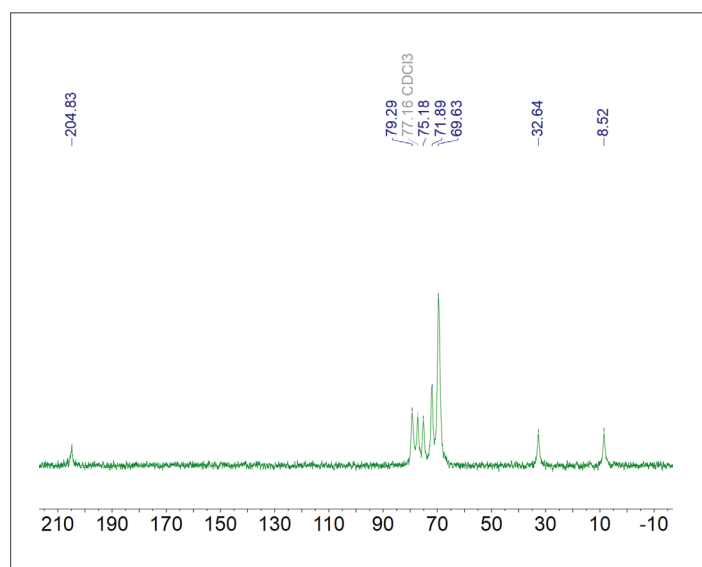
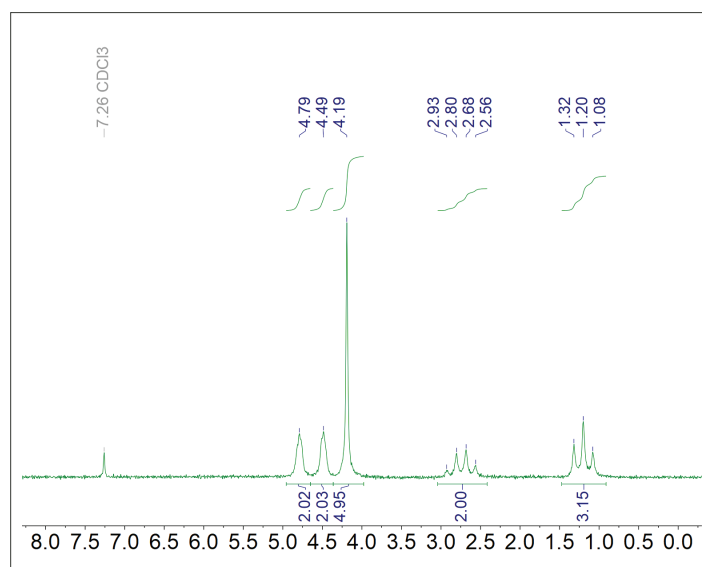


Figure 3. ^1H (top) and $^{13}\text{C}\{^1\text{H}\}$ (bottom) NMR spectra of 1-propionylferrocene in CDCl_3 . The residual solvent peak for chloroform-d is represented by an asterisk.

The region between 4-5 ppm reveals 3 signals, all caused by the cyclopentadienyl (Cp) protons. Since these broad signals don't exhibit splitting patterns, the integration values can be used to help assign the resonances. The intense signal at 4.19 ppm integrates to 5 protons and can be attributed to the unsubstituted Cp ring. The two remaining signals at 4.49 ppm and 4.79 ppm each integrate to 2 protons and are thus related

to the propionyl-substituted Cp ring. The presence of 2 signals for this ligand can be explained by the fact that the protons in positions 2 and 5 on the ring are equivalent to each other, being closer to the substituted carbon, while positions 3 and 4 are further from the substituted carbon.

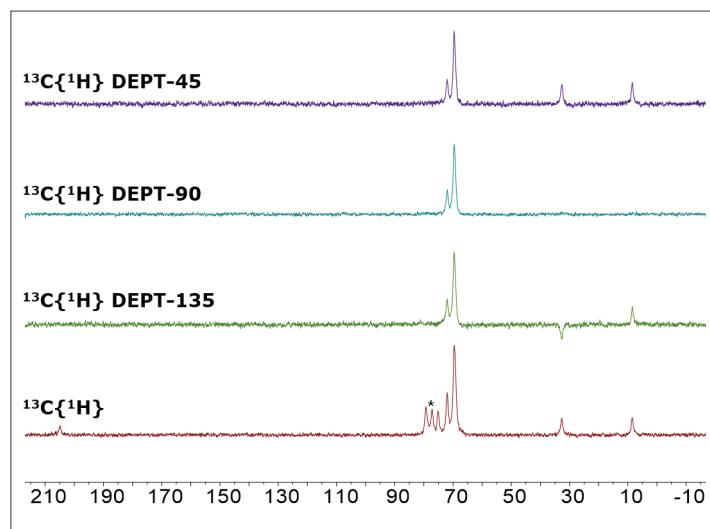


Figure 4. Stacked plot of $^{13}\text{C}\{^1\text{H}\}$, DEPT-135, -90 and -45 NMR spectra of 1-propionylferrocene in CDCl_3 . The residual solvent peak for chloroform- d is represented by an asterisk. DEPT experiments do not show quaternary carbons. DEPT-135 shows $-\text{CH}$ and $-\text{CH}_3$ resonances with positive intensities and $-\text{CH}_2$ resonances with negative intensities. DEPT-90 shows only $-\text{CH}$ resonances with positive intensities. DEPT-45 shows all $-\text{CH}$, $-\text{CH}_2$ and $-\text{CH}_3$ signals with positive intensities.

The 15 MHz $^{13}\text{C}\{^1\text{H}\}$ spectrum of 1-propionylferrocene (Figure 3, bottom) displays the expected resonances for the $-\text{C}=\text{O}$, $-\text{CH}_2$ and $-\text{CH}_3$ functional groups. However, the cyclopentadienyl signals are a little more convoluted, as one of the $-\text{CH}$ resonances on the substituted Cp ring overlaps with the signal for the unsubstituted Cp ring at 69.63 ppm. In addition, the quaternary carbon on the substituted Cp ring overlaps with the residual solvent signal for CDCl_3 . DEPT-135, -90 and -45 experiments can help assign some of the more convoluted signals and provides an additional teaching opportunity to elaborate upon the structural elucidation capabilities of multinuclear NMR spectroscopy (Figure 4). Importantly, these experiments do not show quaternary carbons, and the DEPT-90 experiment confirms that some of the substituted Cp resonances are overlapping with others, as described above. Note that the signals in the spectra shown in this study are slightly broadened, likely due to the presence of a trace amount of a paramagnetic Fe(III) impurity, which was not completely removed during chromatography.

The synthesis and characterization of 1-propionylferrocene in the undergraduate laboratory by NMR provides opportunities to touch upon a wide variety of subjects, both from experimental and theoretical angles. From an experimental perspective, this synthesis allows students to experience fundamental organometallic synthetic skills firsthand, such as the proper techniques to add air- or moisture-sensitive reagents to a reaction (in this case, $\text{BF}_3 \cdot \text{OEt}_2$) and how to carry out a reaction under an inert atmosphere. Additionally, students are introduced to one of the most exciting aspects of transition metal chemistry: color changes. The use of column chromatography to purify the final product expands on these color changes, as knowing that the product is dark orange-red makes it easier to track the separation and serves as an effective visual aid. In addition, students must prepare TLC plates and determine their optimal eluent mixture, which builds upon key concepts learned in

introductory organic chemistry classes. From a theoretical viewpoint, this experiment allows to elaborate upon concepts such as structural elucidation/confirmation using basic NMR, asymmetry in molecules leading to inequivalent NMR signals, coupling constants and splitting patterns, as well as ligand field theory (e.g., why does substitution of a single Cp ring create a change in color of the Fe complex from bright orange to dark orange-red?) and electron counting for transition metal species.

Importantly, this experiment is not limited to the preparation of 1-propionylferrocene but can be expanded to include a number of alkanoylferrocene compounds by changing the acid anhydride.⁶ Additionally, bis(alkanoyl)ferrocene complexes can be prepared using a different approach. Finally, if time permits, additional reactivity of the alkanoylferrocene molecules can be explored, building on the fundamental organometallic synthesis skills learned in this experiment.⁷

CONCLUSION

The synthesis of 1-propionylferrocene as described by Donahue et al.⁶ is elaborated upon and serves as a useful introduction for students to basic organometallic synthetic techniques and the analysis of molecules using NMR spectroscopy for structural elucidation. The NMReady-60 is perfectly suited to an undergraduate environment by allowing high quality ^1H data to be collected within minutes. In addition, ^{13}C experiments can also be performed, allowing for further characterization of this Fe(II) complex. The relatively simple NMR spectra acquired during this experiment are a great introduction to fundamentals such as splitting patterns, coupling constants and the usefulness of integrations.

References

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— Dr. Filip Bureš, Professor Ing.,
University of Pardubice