ORGANIC

UNDERGRADUATE EXPERIMENT

# Benchtop NMR Characterization and Electrocyclization of a Donor-Acceptor Stenhouse Adduct – Intuitive Photochromism Experiments for Undergraduate Laboratories

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## INTRODUCTION

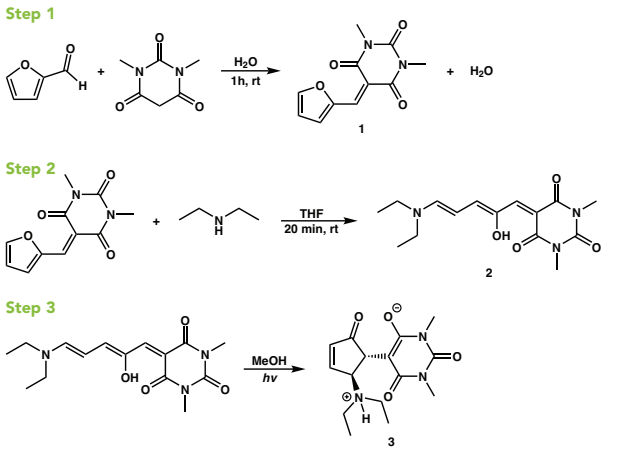
In most undergraduate curricula, the fundamental concepts taught in organic chemistry often culminate in the evaluation of multistep syntheses, where students are required to perform retrosynthetic analyses and make use of these early concepts.[1] Traditionally, multistep syntheses will be included in undergraduate lab sessions, where multiple products will be isolated and analyzed over the course of several weeks and in separate sessions. To ensure most students can successfully synthesize and study these multiple products, the transformations are often chosen such that they are easy to perform and the theory necessary to understand these is typically straightforward and involves concepts to which students have already been introduced. Unfortunately, many of these reactions and their subsequently isolated products are often colorless or off-white, meaning that the excitement of observing transformations via color changes in real-time is often lost on students. These more colorful reactions are typically reserved for introductory transition metal labs, and this is also when students will commonly be introduced to color theory as it pertains to chemistry.[2] To try and address this dearth of discussions about colors in organic chemistry labs, researchers such as Helmy *et al.* have published important work on subjects such as the multistep synthesis of donor-acceptor Stenhouse adducts, which afford a straightforward path towards the isolation and analysis of multiple reaction products using techniques such as ultraviolet-visible (UV-vis) spectroscopy, Fourier-transform infrared (FTIR) spectroscopy, and nuclear magnetic resonance (NMR) spectroscopy.[3]

While UV-vis and FTIR instruments are commonly made available for undergraduate students to use during their lab sessions, direct hands-on use of NMR instruments is often reserved for graduate students and researchers. The significant upfront and recurring costs of traditional high-field NMR spectrometers, combined with the requirements for expert staff and routine maintenance to ensure optimal performance of the instruments, mean that many institutions either can't afford these systems or can't allow undergraduate students to gain hands-on access to these, often relying on teaching assistants to collect the data or using printed handouts to provide students with data from a previously collected, idealized NMR spectrum. The advent and rise in popularity of benchtop NMR spectrometers over the last several years have allowed for the incorporation of this important analytical technique into an unparalleled number of underserved markets, addressing significant accessibility issues for many sectors, with

undergraduate labs and teaching settings being one such area.[4–7] Herein, we perform the multistep synthesis of donor-acceptor Stenhouse adducts as described by Helmy *et al.* in *The Journal of Chemical Education*[3] and analyze them using a 60 MHz benchtop NMR instrument, highlighting the powerful structural elucidation capabilities of this technique.

# RESULTS & DISCUSSION

The transformations performed in this work take place via three distinct steps, leading to the isolation and characterization of three unique products. The three steps and reaction conditions are shown in **Scheme 1**.




***Scheme 1.*** *Multistep synthesis of a donor-acceptor Stenhouse adduct, and subsequent cyclization, as performed in this study.*

In *Step 1*, a Knoevenagel condensation between furaldehyde and 1,3-dimethylbarbituric acid in water leads to the formation of **1**, which precipitates over the course of the reaction and can be conveniently isolated via filtration as a bright yellow solid (**Figure 1**).

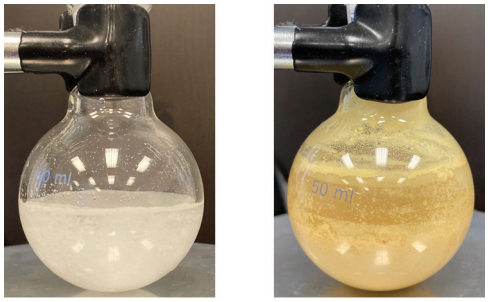



***Figure 1.*** *Left: suspension of furaldehyde in water prior to addition of 1,3-dimethylbarbituric acid. Right: precipitation of 1 as a bright yellow solid after addition of 1,3-dimethylbarbituric acid.*

In *Step 2*, the donor-acceptor Stenhouse adduct (**2**) is formed by reaction of **1** with diethylamine in THF. Dropwise addition of the base leads to an immediate color change from bright yellow to pink/red, and quickly to very dark purple (**Figure 2**). This product is also isolated via simple filtration.

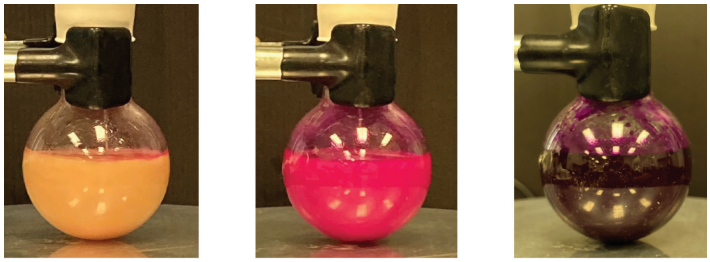


***Figure 2.*** *Left: suspension of **1** in THF immediately following addition of first drops of diethylamine. Middle: persistent pink/red color observed upon introduction of additional diethylamine. Right: final dark purple color caused by the formation of **2**.*

Finally, in *Step 3*, the electrocyclization of **2** is performed by exposing it to light in methanol, leading to the formation of a mostly colorless compound that precipitates over the course of the reaction (**Figure 3**).

***Figure 3.*** *Left: solution of **2** in methanol with LED setup for cyclization reaction. Right: suspension of **3** in methanol with pink/red color caused by presence of minimal amounts of unreacted starting material.*

The isolated products were all analyzed using a 60 MHz benchtop NMR spectrometer. The $^1$H spectrum of **1** is presented in **Figure 4**, along with the molecular structure and assigned peaks. The singlet at 3.39 ppm corresponds to the two equivalent methyl groups of the barbituric acid fragment, which don't exhibit coupling to other protons. The alkenyl proton on the carbon linking the furan and barbituric acid groups gives rise to a singlet at 8.42 ppm, as it also does not couple to other protons. The furan protons responsible for the two doublets centered around 7.8 ppm and 8.6 ppm both couple to the remaining furan proton, which gives rise to the broad doublet of doublets centered around 6.7 ppm. This $^1$H spectrum provides an opportunity to elaborate on concepts such as *J*-coupling, multiplicity, and symmetry. Integrations provide clues for students, who can use these in conjunction with the molecular structure to assign peaks to specific functionalities.

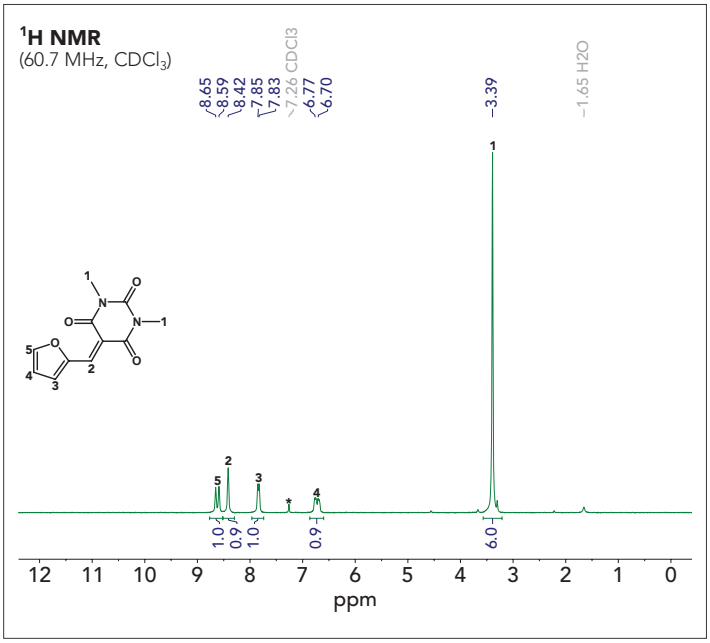



***Figure 4.*** *$^1$H (60.7 MHz) NMR spectrum of **1** with assigned peaks. The asterisk represents the residual solvent peak for chloroform-d.*

Our first attempt at isolating **2** from *Step 2* initially seemed successful, leading to the isolation of a very dark purple, almost black solid. However, $^1$H NMR analysis revealed the presence of a possible ethyl-containing impurity, the peaks for which are highlighted in the zoomed inset in **Figure 5**. While the rest of the

spectrum looks mostly as expected, this impurity proved very difficult to remove, and did not appear to be volatile. In addition, it is likely that this impurity would carry over in *Step 3* and possibly interfere with the reaction. This result, though unexpected, demonstrates the power of NMR towards the identification and characterization of mixtures. It would be difficult to confirm the presence of this type of impurity via more traditional analytical approaches that do not always provide a clear picture of everything in solution, such as UV-vis spectroscopy or FTIR spectroscopy. Typically, experiments providing the highest degree of confidence in students' success are chosen for undergraduate labs. However, in recent years, there has been a push towards highlighting the importance of understanding that reactions don't always proceed as planned, and that this can be a positive event if time is taken to understand why this occurs under certain circumstances (*e.g.*, reaction with adventitious water, pH, temperature fluctuations, rate of addition, competing pathways, etc.). Importantly, researchers such as Morrison *et al*. have recently published relevant work on the development and incorporation of multioutcome experiments (MOEs),[6,8] highlighting the advantages of increasing the possible number of outcomes from undergraduate experiments to encourage students in the utilization of various analytical techniques to confirm the identity of their products.

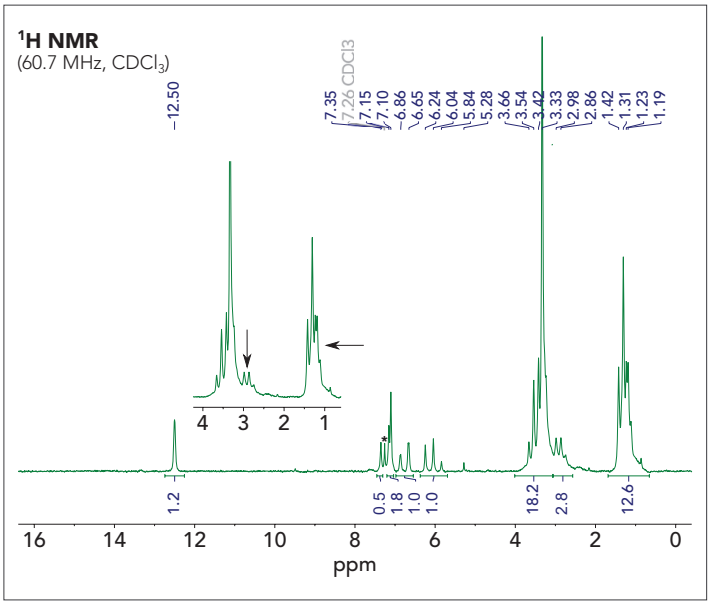



***Figure 5***. *$^1$H (60.7 MHz) NMR spectrum of **2** with possible ethyl-containing impurity highlighted by arrows in the zoomed inset. The asterisk represents the residual solvent peak for chloroform-d.*

Repeating the *Step 2* experiment with slower addition of the base led to the isolation of a pure sample of **2**, the $^1$H spectrum of which is presented in **Figure 6**, along with the molecular structure and assigned peaks. Note that the peak at 7.33 ppm is part of a doublet, the second peak for which overlaps with the resonance at 7.13 ppm. However, integrations provide some insight by revealing that 1.5 protons are being represented by the peak at 7.13 ppm and approximately 0.5 protons are being represented by the peak at 7.33 ppm. While the signal centered around 6.75 ppm is easily identifiable as a doublet of doublets, the one at 6.0 ppm serves as a good example of a doublet of doublets that seems like a triplet at first glance, especially before students have been introduced to these types of splitting patterns.

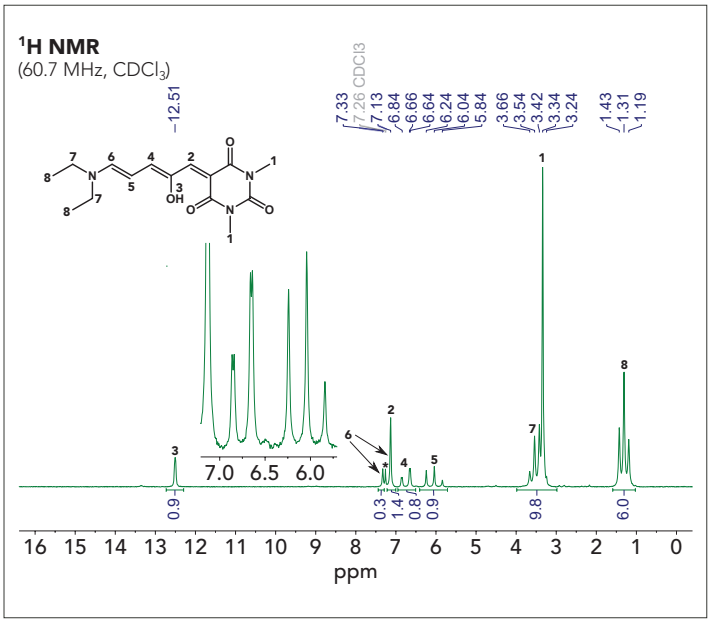



***Figure 6***. *$^1$H (60.7 MHz) NMR spectrum of **2** with assigned peaks. The asterisk represents the residual solvent peak for chloroform-d.*

The $^1$H spectrum of **3** is presented in **Figure 7**, along with the molecular structure and assigned peaks. Although more overlapping is observed in this sample, the light-driven transformation is very clean and integrations once again play an important role in assigning key resonances. The characteristic triplet signal at 1.37 ppm from the methyl groups on the diethylamine fragment remains, but the corresponding quartet at 3.45 ppm overlaps with the barbituric acid methyl groups at 3.30 ppm in a similar fashion as in **2**. The protons attached to the two $sp^3$ carbons in the cyclopentanone fragment in **3** are observed at 3.95 ppm and 4.92 ppm, but the latter overlaps slightly with the residual solvent signal for water. Finally, the two alkenyl protons on the cyclopentanone fragment are observed at characteristically high chemical shifts, around 6.79 ppm and 7.89 ppm.

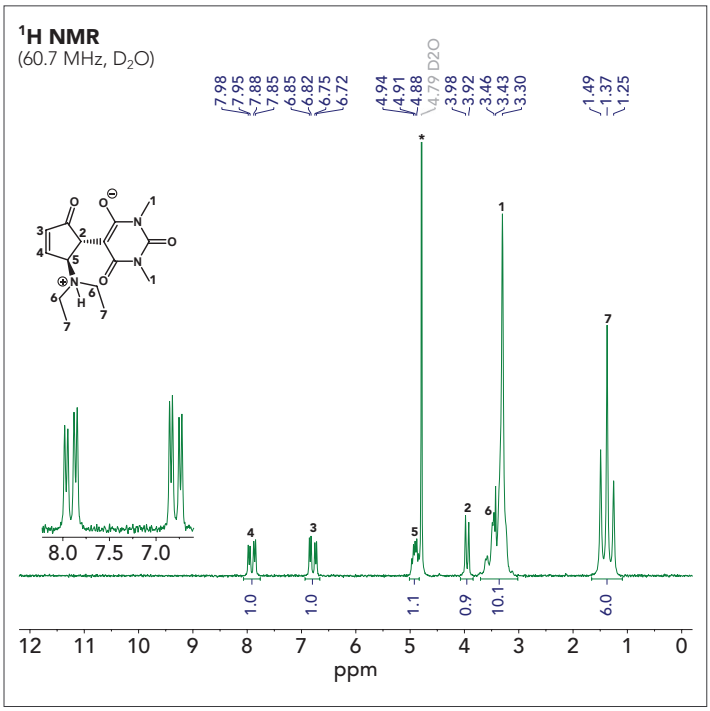



***Figure 7***. *$^1$H (60.7 MHz) NMR spectrum of **3** with assigned peaks. The asterisk represents the residual solvent peak for $D_2O$.*

The $^{1}$H NMR spectra presented herein demonstrate the advantages of hands-on access to NMR technology, where students can acquire and analyze their own spectra. The products isolated in these experiments all give rise to spectra which can be challenging, but also rewarding for students to decipher. Since the data can be collected in a few minutes for each sample, this allows students to compare results and attempt to explain why their own spectra might contain additional or fewer signals than their colleagues. For an especially thorough theoretical discussion of all the transformations described in this work, including reaction mechanisms and orbital arrays pertinent to electrocyclization reactions, the reader is highly encouraged to read the original publication and relevant supporting information by Helmy and coworkers.[3]

# Conclusions

Three unique products were synthesized and isolated in a straightforward multistep process, followed by $^{1}$H benchtop NMR analysis. The reactions all proceed through striking color changes, which serve as a visual cue for students to discuss some of the theoretical concepts underlying these transformations. These types of donor-acceptor Stenhouse adducts offer a great approach towards the introduction of key ideas related to photochromism in the undergraduate organic chemistry lab. In conjunction with analytical techniques to which students are more commonly afforded hands-on access, such as UV-vis and FTIR, benchtop NMR technology allows them to gather their own data without needing to rely on facility managers, teaching assistants, or printed handouts for access to data.

# References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