

## ORGANIC

### UNDERGRADUATE EXPERIMENT

#### Synthesis of a Cyalume Derivative for the Chemiluminescent Reaction



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## INTRODUCTION

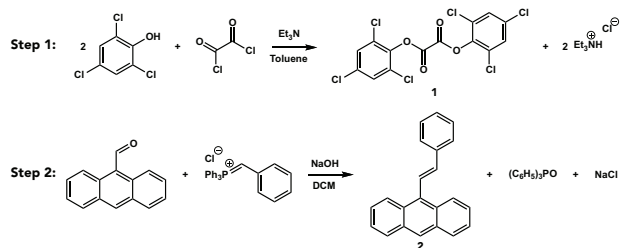
An undeniably important factor for teaching young, aspiring chemists is that of maintaining their interest in chemistry, whether through the theoretical material, which can sometimes be challenging, or using visual aids. One of the most popular types of reactions performed in undergraduate labs are chemiluminescent transformations. There are plenty of examples of chemiluminescence that many people have likely encountered in one way or another. A prime example of this are glow sticks, where the cracking of the glow stick initiates a chemiluminescent reaction, upon which light is emitted.<sup>1-2</sup> From a bioluminescence angle, fireflies emit light in the visible spectrum following a reaction between luciferin and adenosine triphosphosphate (ATP).<sup>1,3</sup> Generally, chemiluminescence results from a chemical reaction which produces light.<sup>1-4</sup>

An invaluable aspect of laboratory experiments for students is the hands-on experience they gain from the theory introduced to them in lectures. Specifically, students learn the underlying principles of spectroscopic characterization techniques (nuclear magnetic resonance (NMR) spectroscopy, infrared spectroscopy, etc.), but do not get to put these principles into practice until the laboratory

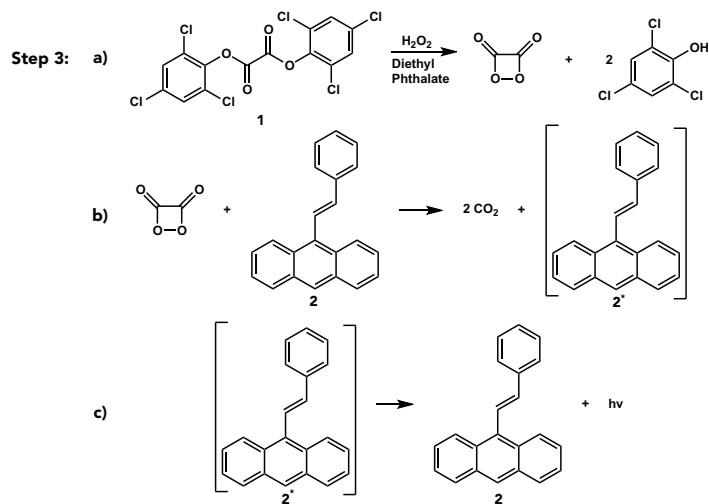
components of their courses. Here, we will focus on how NMR spectroscopy can be used to monitor reactions in a three-step chemiluminescent synthesis. During an undergraduate chemistry degree, students are not commonly exposed to the hardware and software used with NMR, arguably one of the most important characterization techniques in organic chemistry, until they are either in graduate school or working in a relevant industry. The biggest reason for this is in part due to most post-secondary institutions only having access to a high-field spectrometer, which have significant upfront and recurring costs, while also requiring extensive training and maintenance.<sup>5</sup> Due to these obstacles, a high-field spectrometer is usually entrusted to a specialist and is often used by graduate students, which leaves little to no time for undergraduates to garner any NMR experience. With the advent of benchtop NMR, students can gather experience early in their undergraduate degree and can use this to their advantage before entering graduate school or the industry, implementing the concepts learned in the classroom by directly using the instrument.

In this sample experiment, a three-step chemiluminescent reaction

is performed and outlined in **Scheme 1** and **Scheme 2**. The transformations presented herein are based on work published by Williamson and Masters in Macroscale and Microscale Organic Experiments.<sup>1</sup> **Scheme 1** illustrates the synthesis of a peroxyoxalate (**1**) in **Step 1**, and a fluorescer (**2**) in **Step 2**. In **Scheme 2**, the chemiluminescent reaction is outlined, where **1** decomposes into an unstable 1,2-dioxetanedione, which further decomposes into carbon dioxide and releases energy, which is absorbed by the fluorescer (if there is no fluorescer present, the energy is released as heat), which promotes an electron into an excited state. The relaxation of this electron back to its ground state results in the emission of light.<sup>1-4</sup> Furthermore, the colour of the emitted light differs based on the fluorescer used. This is due to the difference in energy levels from the highest occupied molecular orbital (HOMO) and lowest unoccupied molecular orbital (LUMO), which can vary significantly across different molecules. Depending on that energy difference, the resultant light can span the visible light region, or even be outside of this range.



**Scheme 1.** First two steps of the three-step chemiluminescent reaction performed in this study. **Step 1:** synthesis of bis(2,4,6-trichlorophenyl) oxalate (**1**) from the reaction of 2,4,6-trichlorophenyl and oxalyl chloride in the presence of triethylamine in toluene. **Step 2:** synthesis of trans-9-(2-phenylethenyl)anthracene (**2**) from the reaction of benzyltriphenylphosphonium chloride and 9-anthraldehyde in dichloromethane using a 50% solution of sodium hydroxide as a catalyst.



**Scheme 2.** Final step of the chemiluminescent reaction, where oxalate **1** and fluorescer **2** are mixed in diethyl phthalate and treated with 30% hydrogen peroxide to promote an electron transfer, followed by relaxation and emission of visible light. The asterisk represents the molecule in an electronic excited state.

The <sup>1</sup>H and <sup>31</sup>P{<sup>1</sup>H} NMR spectra of the products in this work were acquired using a 60 MHz benchtop spectrometer, illustrating the benefits of incorporating this technology into undergraduate teaching labs for monitoring similar types of chemiluminescent reactions.

# PROCEDURE

## Materials

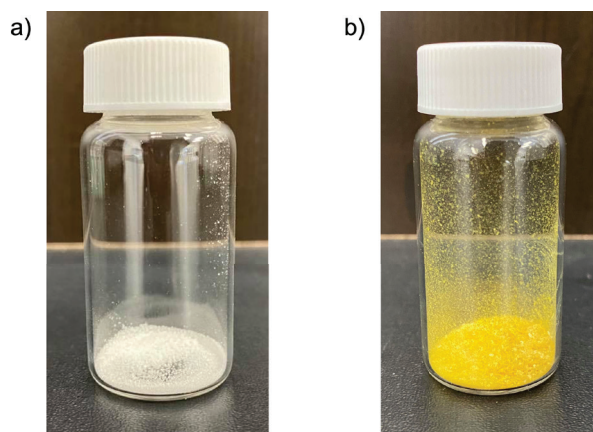
2,4,6-Trichlorophenol (≥97%), oxalyl chloride (≥99%), triethylamine (≥99%), toluene (anhydrous, 99.8%), hexanes (≥97%), 9-anthracenecarboxaldehyde (97%), benzyltriphenylphosphonium chloride (99%), dichloromethane (anhydrous, ≥99.8%), sodium hydroxide (pellets, ≥98%), magnesium sulfate (anhydrous, ≥99.5%), 1-propanol (≥99.9%), rhodamine B (purity not provided by supplier), hydrogen peroxide solution (30% w/w in water), diethyl phthalate (99.5%) and chloroform-*d* (99.8%) were purchased from MilliporeSigma and used without further purification.

## Instrumentation

All NMR data were obtained using a Nanalysis 60PRO instrument. The <sup>1</sup>H experiments were performed using the following parameters: spectral width, 20 ppm; spectral center, 5 ppm; number of points, 4096; number of scans, 16 for bis(2,4,6-trichlorophenyl) oxalate (**1**) (64 for trans-9-(2-phenylethenyl) anthracene (**2**)); dummy scans, 0; interscan delay, 1 second; pulse angle, 90°; receiver gain, auto. The <sup>31</sup>P{<sup>1</sup>H} experiments were performed using the following parameters: spectral width, 50 ppm; spectral center, 25 ppm; number of points, 4096; number of scans, 16; dummy scans, 0; interscan delay, 1 second; pulse angle, 67°; receiver gain, auto. All spectra were manually corrected for phase and baseline distortions using the MestReNova software (v14.2.1).

## Synthesis of bis(2,4,6-trichlorophenyl) oxalate (**1**)

2,4,6-Trichlorophenol (802 mg, 4.1 mmol) was dissolved in toluene (6 mL) and triethylamine (0.56 mL, 4.0 mmol) was added to a 25 mL round-bottom flask equipped with a magnetic stirring bar. The flask was placed in an ice bath and allowed to cool for 10 minutes. Oxalyl chloride (0.20 mL, 2.3 mmol) was added to the flask dropwise over 5 minutes. Upon addition of oxalyl chloride, the formation of a precipitate was immediately observed. The reaction mixture was refluxed for 30 minutes, then allowed to cool to room temperature and the solid was filtered and washed with cold hexanes. The solid was dried *in vacuo* and collected in a 20 mL vial. 10 mL of water were added to the vial, which was then shaken vigorously to dissolve any remaining hydrochloride impurities. The solid was filtered and dried again *in vacuo*. A minimal amount of toluene was added, the solution was heated to dissolve the product, and the mixture was allowed to recrystallize. The final product was isolated as a fine white solid (shown in Figure 1a).



**Figure 1.** Final purified products of oxalate **1** (a, left) and fluorescer **2** (b, right).

## Synthesis of *trans*-9-(2-phenylethenyl) anthracene (**2**)

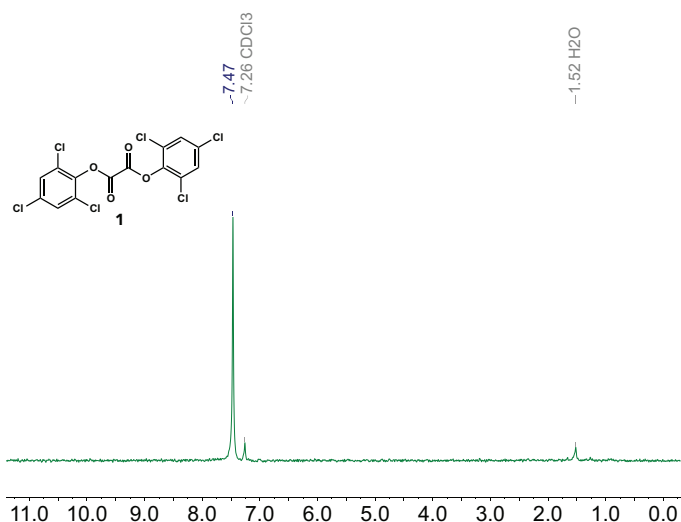
9-Anthracenecarboxaldehyde (577 mg, 2.8 mmol) and benzyltriphenylphosphonium chloride (1.00 g, 2.6 mmol) were added to a 25 mL round-bottomed flask equipped with a magnetic stirring bar and dissolved using dichloromethane (3 mL). To the mixture, a 50% w/w aqueous solution of sodium hydroxide (1.30 mL, 28.7 mmol) was added and stirred for 30 minutes. The reaction was monitored using  $^{31}\text{P}$  NMR and appeared to be complete within 5 minutes, however, the reaction was allowed to stir for 30 minutes to ensure optimal conversion.<sup>1</sup> To the mixture, dichloromethane (7 mL) and water (7 mL) were added, and the resulting biphasic solution was stirred for another 15 minutes. The aqueous layer was washed 3 times with dichloromethane and the organic layers were collected and combined into a 25 mL Erlenmeyer flask. The dichloromethane washes were dried with anhydrous magnesium sulfate and filtered. The filtrate was then concentrated *in vacuo* and dissolved in hot 1-propanol (5 mL). The solution was left to cool to recrystallize, and the purified product was collected by vacuum filtration. The final product was isolated as a fine, crystalline, yellow solid (shown in Figure 1b).

### Chemiluminescent Reaction

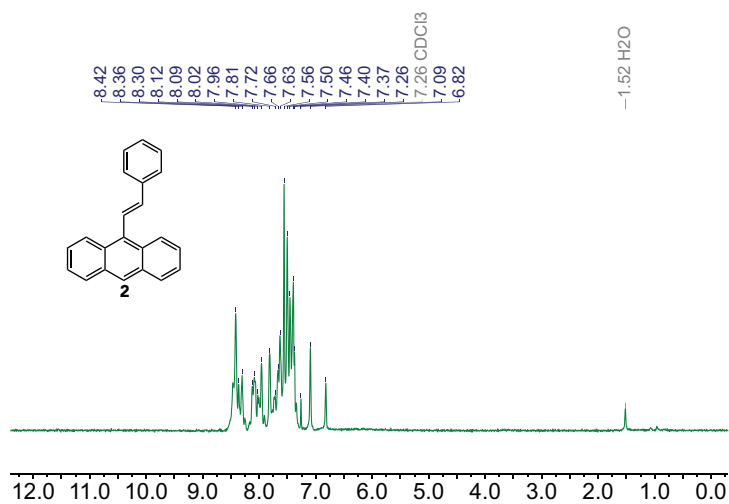
To a 20 mL vial, cyalume **1** (53.2 mg, 0.12 mmol) and fluorescer **2** (3.67 mg, 0.013 mmol) were dissolved in diethyl phthalate (5 mL) with stirring and heating in an oil bath. In a separate Erlenmeyer flask, 30% hydrogen peroxide (0.2 mL) and diethyl phthalate (5 mL) were mixed, yielding an emulsion. The peroxide emulsion was added to the cyalume solution using a pipette. In a dark room, the chemiluminescence was observed. Importantly, the wavelength of the light emitted is dependent on the structure of the fluorescer, due to the different energy level differences between the excited states and the ground states.<sup>1,3</sup>

## Results and Discussion

The  $^1\text{H}$  NMR spectra of oxalate **1** and fluorescer **2** were obtained and are shown in Figures 2 and 3, respectively.



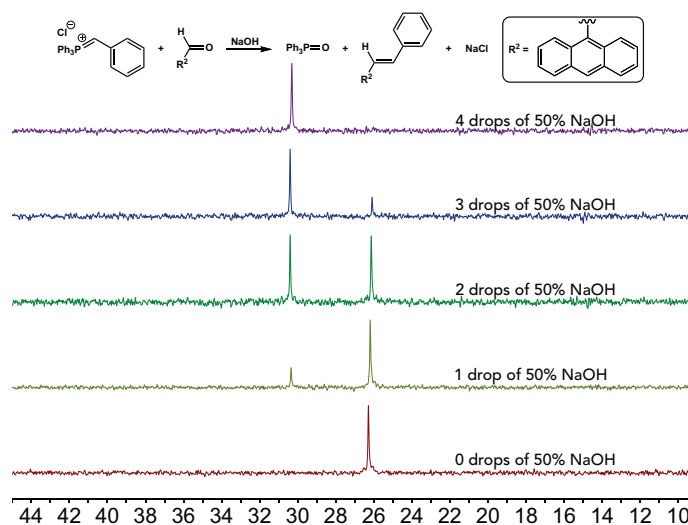
**Figure 2.**  $^1\text{H}$  (60 MHz) NMR spectrum of bis(2,4,6-trichlorophenyl) oxalate (**1**) in  $\text{CDCl}_3$ .



**Figure 3.**  $^1\text{H}$  (60 MHz) NMR spectrum of *trans*-9-(2-phenylethenyl) anthracene (**2**) in  $\text{CDCl}_3$ .

In the  $^1\text{H}$  spectrum in Figure 2, a singlet is observed since each hydrogen atom is in the same chemical environment. In contrast, the  $^1\text{H}$  spectrum in Figure 3 is more complex, as all 10 chemically unique hydrogen atoms in **2** are  $\text{sp}^2$  hybridized and are observed from 6.5 ppm to 9 ppm, which is characteristic for these aromatic and alkene chemical environments.

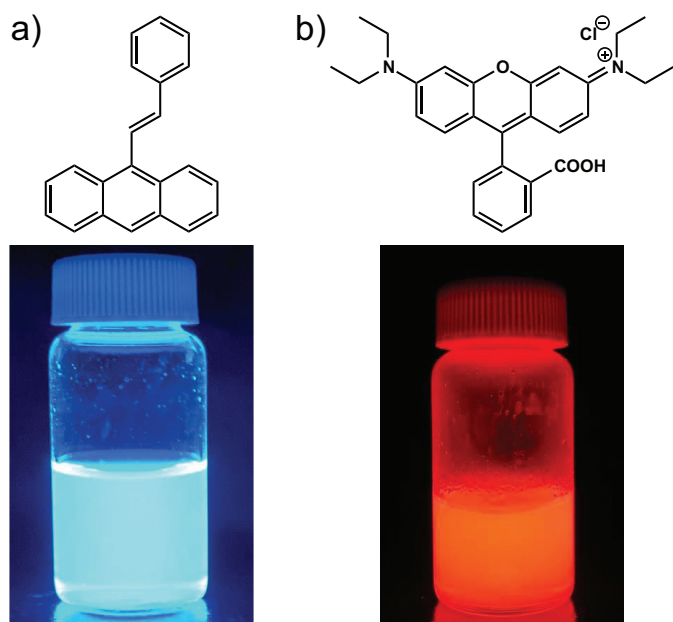
In addition to  $^1\text{H}$  NMR, the benchtop NMR spectrometer is also capable of heteronuclear  $^{31}\text{P}\{^1\text{H}\}$  NMR spectroscopy. The Wittig reaction performed during the synthesis of fluorescer **2** was monitored by  $^{31}\text{P}$  NMR (Figure 4).



**Figure 4.**  $^{31}\text{P}\{^1\text{H}\}$  (24.3 MHz) stacked spectra plot for the monitoring of the benzyltriphenylphosphonium chloride (Wittig reagent) transformation upon dropwise addition of 50% NaOH.

The  $^{31}\text{P}$  monitoring was performed as a separate experiment and was conducted in a 5 mm NMR tube using approximately 100 mg (0.03 mmol) of Wittig reagent. At the starting point, before adding any NaOH (red trace), a singlet is observed at approximately 26 ppm, which is the starting Wittig reagent. After adding a drop of NaOH (lime trace), the by-product triphenylphosphine oxide is observed at the characteristic chemical shift of approximately 30 ppm. With the additional drops (green and blue traces), the triphenylphosphine oxide peak grows in intensity as the Wittig reagent decreases until it is finally completely converted with the addition of 4 drops of NaOH (purple trace).

After conducting the final step of the chemiluminescent reaction in a dark room (Scheme 2) as described in the Procedure section, a characteristic glow was observed (Figure 5).



**Figure 5.** Completed chemiluminescent reaction showing the glowing solution upon addition of hydrogen peroxide. **a)** Reaction of oxalate **1** with fluorescer **2**. **b)** Reaction of oxalate **1** with rhodamine B fluorescer.

The two different colours observed in this chemiluminescent reaction (blue and red) stem from the HOMO-LUMO energy gap. This HOMO-LUMO energy gap is equivalent to the energy that is required for an electron to be promoted from the HOMO to the LUMO. With a larger gap, more energy is required to promote an electron and when it relaxes, it will emit a higher energy photon (closer to blue on the visible light spectrum). Contrarily, the smaller the HOMO-LUMO energy gap, the lower the energy it takes to promote that electron and therefore, a lower energy photon will be emitted upon relaxation (closer to red on the visible light spectrum). In the reaction flask, the oxalate decomposes into 2,4,6-trichlorophenol and an unstable 1,2-dioxetanedione, which further decomposes into carbon dioxide and transfers an electron to an acceptable donor (in this case a fluorescer) or as heat if there is no suitable molecule.<sup>1,3</sup> In **Figure 5a**, the blue light comes from the reaction done with *trans*-9-(2-phenylethenyl)anthracene, whereas **Figure 5b** is the chemiluminescent reaction done with rhodamine B. This allows us to conclude that rhodamine B has a smaller HOMO-LUMO gap than *trans*-9-(2-phenylethenyl)anthracene.

## Conclusion

Using benchtop NMR spectroscopy, students can directly work with an NMR spectrometer in their labs to obtain multinuclear NMR data. Specifically, students can gather <sup>1</sup>H data, but they also have the tools to monitor their reactions (in this case <sup>31</sup>P NMR). In this sample experiment, a three-step chemiluminescent reaction is conducted, resulting in the observance of a chemiluminescent reaction. The observation of blue light with *trans*-9-(2-phenylethenyl)anthracene (**2**) and red light with rhodamine B serves as a useful teaching tool for the concepts of HOMO-LUMO gaps and conjugated systems. With NMR being one of the most powerful analytical tools available to chemists, this experiment shows that NMR can be included into undergraduate labs not only for its structural elucidation capabilities, but also for its ability to monitor reactions.



## References

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