

# Two-step synthesis and oxidizing power assessment of novel pyrylium

**Jingyun Wu**

Department of Chemistry, University of North Carolina at Chapel Hill, Chapel Hill, NC, USA

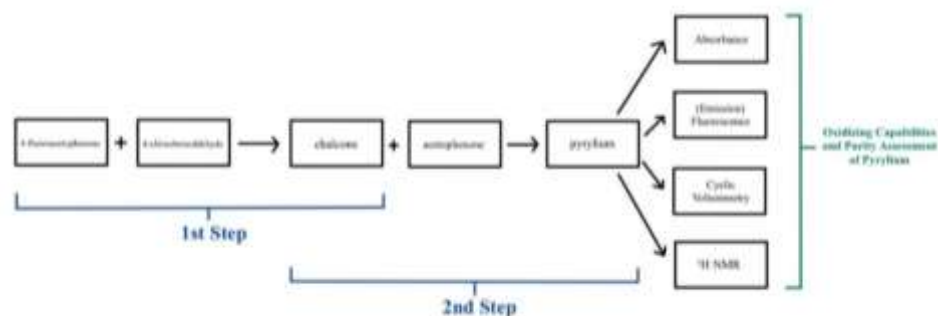
jingyun@live.unc.edu

**Abstract.** Photoredox catalysis is a relatively new concept, and it involves the absorption of light for more productive use of lower energy radiation and to catalyze selective reactions. Traditionally, catalysts used for oxidation or reduction reactions were metal catalysts, such as iridium. However, these metal catalysts are not environmentally friendly and are expensive, prompting the use of organic catalysts. Pyrylium salt, an organic catalyst, can be used as a catalyst. However, the oxidizing ability of basic pyrylium is not that good and can still be improved. In this project, a pyrylium salt with substituents that include fluorine and chlorine (halogens) was synthesized to boost its oxidizing ability in an alcohol oxidation reaction due to its electron-withdrawing groups. Despite unsuccessful oxidation, there is still much research to prove that it can substitute for metal catalysts.

**Keywords:** Pyridium salt, photoredox catalyst, alcohol oxidation, oxidizing agent.

## 1. Introduction

Photoredox chemistry relies on the ability of metal complexes or organic dyes to convert light energy into chemical energy by engaging in single-electron transfer. During this redox process, the catalyst enters the excited state and becomes the solid oxidizing agent that generates high-energy intermediates[1]. Photoredox catalyst can increase the reaction rate while not being consumed. They are reduced and then re-oxidized in photoredox reactions and, therefore, are frequently applied as oxidizing agent in organic synthesis. Photoredox catalysts are known for their different capabilities of developing new reaction mechanisms and enabling the construction of new bonds or intermediates that were previously challenging to make. For example, the generation of alkyl radicals in the hydroxymethylation of heteroaromatic bases is made possible under room temperature by photoredox catalysis [2]. The Nicewicz lab utilizes photoredox chemistry to catalyze the biosynthesis of cyclobutane lignans, which are lead compounds for developing antifungal, antiviral, and anticancer drugs [3]. The development and analysis of photoredox catalysts is essential because it opens doors to new possibilities for synthesizing novel and complex compounds while minimizing wastes of energy and resources. Organic photoredox dyes are vital as they are cheaper, more environmentally friendly, more readily available, and non-toxic than other metal catalysts.



**Figure 1.** Overall two-step synthesis and assessments of Pyrylium.

In this experiment, pyrylium salt, a type of photoredox catalyst, is generated using a two-step synthesis to allow for different substituents in the salt. The absorbance and emission profiles and its excited state properties (with cyclic voltammetry) will be characterized to assess its capabilities as an oxidizing agent, and its reactivity in an alcohol oxidation reaction will be measured.



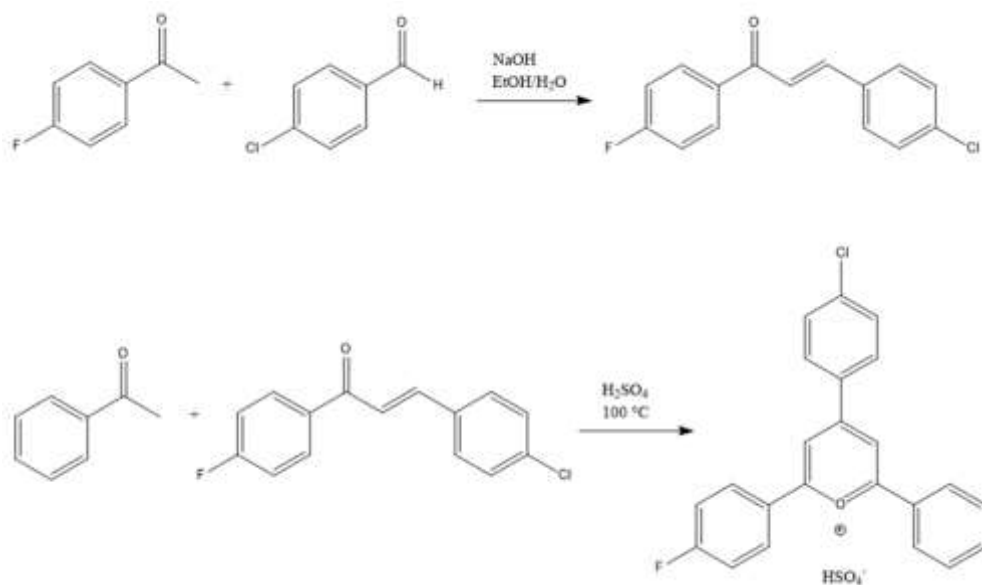
**Figure 2.** Generic Pyrylium structure.

## 2. Methods

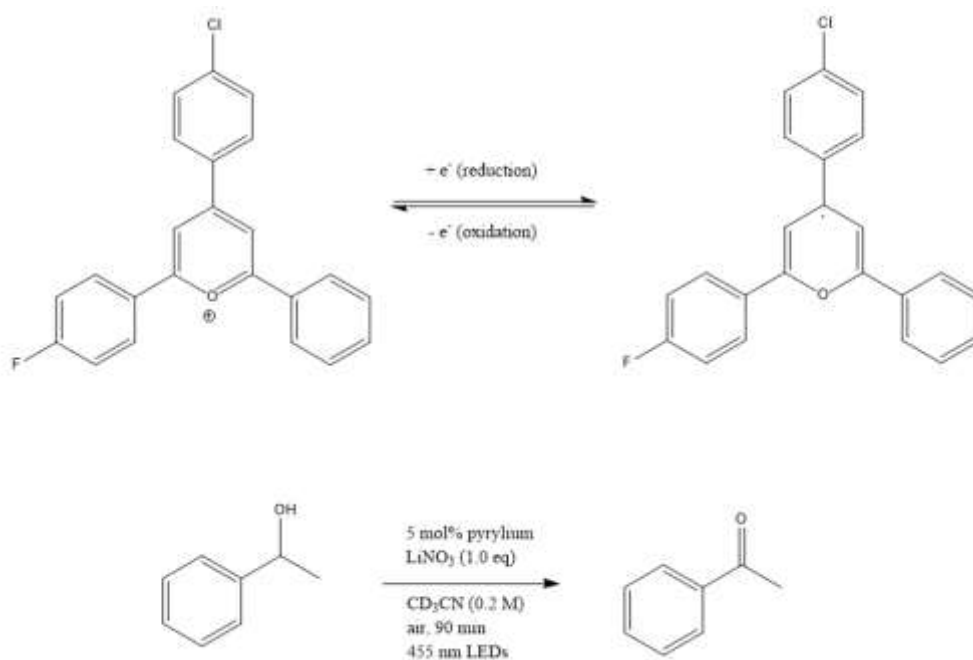
A 1:1 (20 mmol) ratio of 4-fluoroacetophenone (2.763 g) and 4-chlorobenzaldehyde (2.800 g) were mixed with 21 mL NaOH to produce 4-chloro-4'-fluorochalcone by adding 6.4 mL of 4M NaOH dropwise, placing in an ice bath, and filtering the solution using suction filtration with 10 mL distilled water and cold EtOH. Then, 5.6 mmol of this chalcone (1.460 g) and 5.6 mmol of acetophenone (0.649 g) were mixed with 0.5 mL H<sub>2</sub>SO<sub>4</sub> under heat for 45 minutes to produce 4-(4-chlorophenyl)-2-(4-fluorophenyl)-6-phenylpyrylium. The solution was then purified using suction filtration with 2 rinses of 10 mL cold EtOAc and crystal recrystallization with methanol.

An <sup>1</sup>H NMR spectrum was gotten for the chalcone and the products of the alcohol oxidation reaction. In addition, a UV-Vis spectrum, emission spectrum, and cyclic voltammetry trace were also obtained for the pyrylium.

To test the oxidation ability of the pyrylium, 0.0125 mmol (0.00452 g) of pyrylium and 0.25 mmol (17 mg) of LiNO<sub>3</sub> were mixed with 0.25 mmol (30 μL) of 1-phenylethanol and 1 mL deuterated acetonitrile. The solution was then placed in a light box for 90 minutes, and 0.47 mmol (10 μL) HMDSO internal standard was added. <sup>1</sup>H NMR was then taken of the product.



**Figure 3.** Two synthesis reaction steps and products.



**Figure 4.** Oxidation reaction.

### 3. Results and discussion

The pyrylium salt synthesis in this experiment has two steps: the first step of chalcone synthesis includes 4-fluoroacetophenone and 4-chlorobenzaldehyde as starting materials; the second step is the reaction of the chalcone product with acetophenone. For the pyrylium salt to be a potent oxidizing agent, the more electron deficient it is, the bigger its tendency to receive electrons during photoredox reactions. Therefore, the substituents selected in this pyrylium synthesis are electron withdrawing groups, such as fluoro and chloro, which have large electronegativity values. In addition to the type of substituents, their location on the benzene rings is also selected to be 1,4 instead of 1,2 to minimize the negative effects of

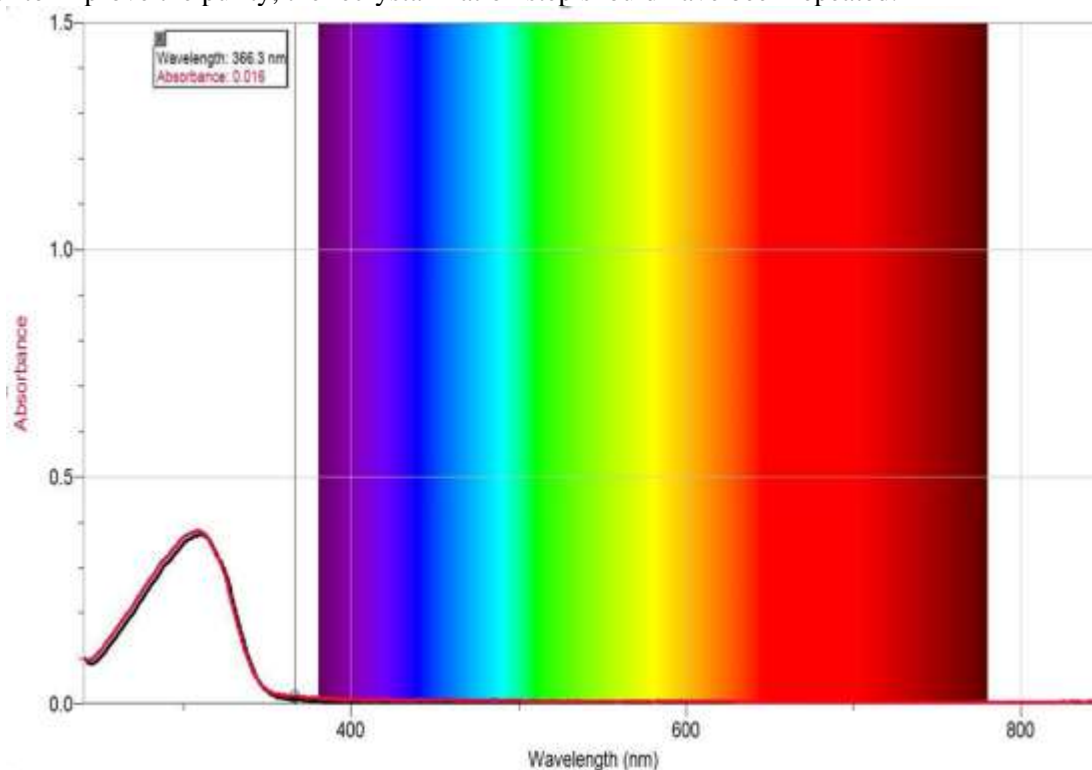
hindrance on reactions. This experiment included an elevated amount of starting materials, leading to a higher pyrylium product for subsequent analyses. The crude pyrylium salt product weighed 0.525 g. The purified product, 2-fluorophenyl-4-chlorophenyl-6-phenylpyrylium, weighed 0.200 g (5.53 mmol, 10% yield; 38% recovery from crude) [4].

Theoretical yield (g) = (0.0054 mol acetophenone)  $\times$  (1/1)  $\times$  361.82 g/mol = 1.954 g mmol product = 0.200g / (361.82g/mol) = 0.000553 mol = 5.53 mmol

$$\% \text{ yield} = (0.200 \text{ g}) / (1.954 \text{ g}) \times 100\% = 10\%$$

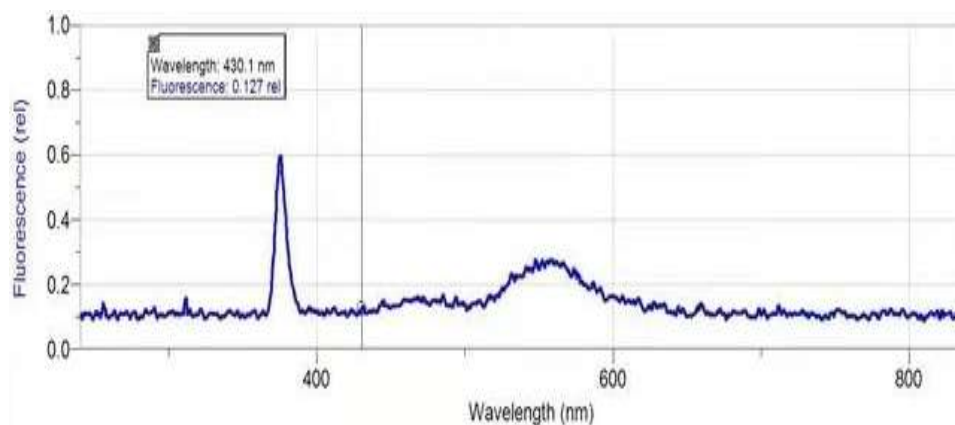
$$\% \text{ recovery} = (0.200 \text{ g}) / (0.525 \text{ g}) \times 100\% = 38\%$$

The UV-Vis spectrum of the synthesized pyrylium salt has a maximum absorbance peak of 0.4. at the approximate wavelength of 320 nm ( $\lambda_{\text{maxabs}}$ ). This wavelength value is not within the visible light region as expected for pyrylium salt, indicating the absence of pure product yielded or a low concentration of pyrylium in the measured sample. The low absorbance wavelength signifies a low conjugation and, therefore, poor oxidizing ability of the product due to impurity or low yield. Therefore, a slightly more concentrated pyrylium sample should be made for the UV-Vis measurement, and in order to improve the purity, the recrystallization step should have been repeated.



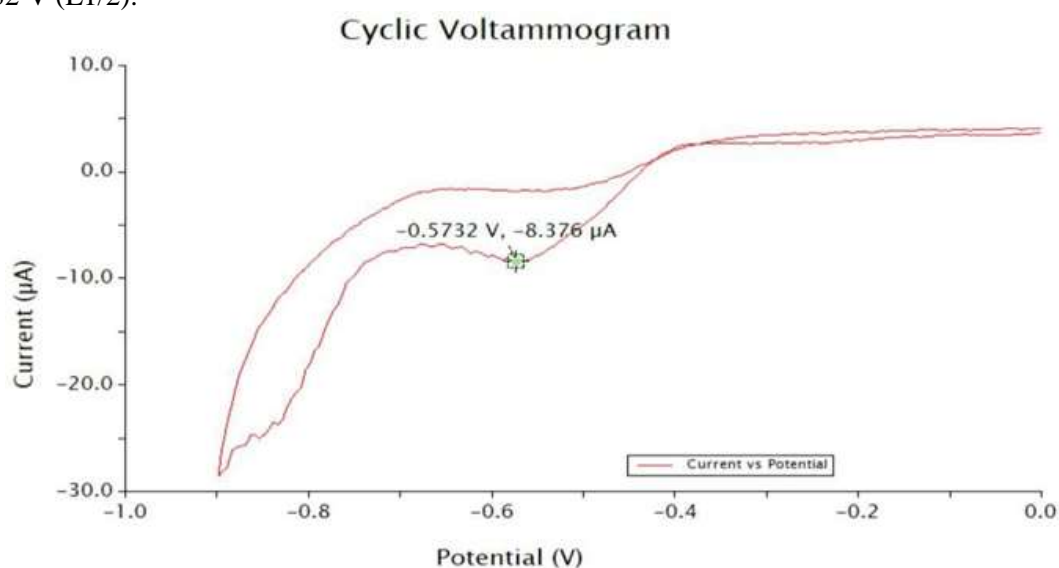
**Figure 5.** UV-VIS spectrum of Pyrylium.

The fluorescence spectrum of the synthesized pyrylium salt has a maximum emission peak at the approximate wavelength of 380 nm ( $\lambda_{\text{maxem}}$ ). As expected for pyrylium salt, this emission wavelength is slightly lower, indicating impurity and low concentration. Since the sample used for fluorescence is the same as that used to acquire the UV-Vis spectrum (Figure. 1), the improvement methods discussed for UV-Vis can also apply here.



**Figure 6.** Fluorescence spectrum of Perylium.

The cyclic voltammery trace of synthesized perylium salt has a ground state reduction potential of -0.5732 V (E1/2).



**Figure 7.** Cyclic voltammery of Perylium.

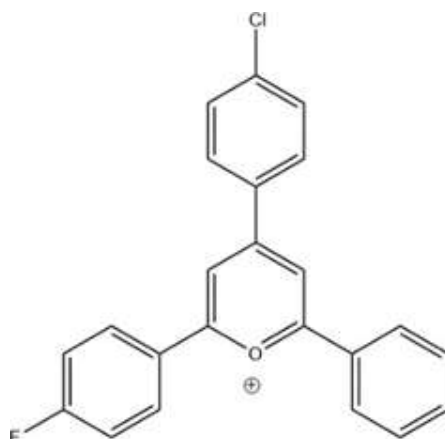
The perylium salt's excited state energy,  $E_{0,0}$ , is calculated using its maximum absorption wavelength (320 nm) determined from the UV-Vis spectrum (Figure. 1) and its maximum emission wavelength (380 nm) determined from the fluorescence spectrum (Figure. 2). The ground state reduction potential,  $E_{1/2}$ , is determined from the CV trace (Figure. 3). The corresponding excited state reduction potential,  $E^*_{1/2}$ , is calculated using both  $E_{0,0}$  and  $E_{1/2}$ , and is used to quantify the ability of electron transferring of perylium as an oxidizing agent [5].

Sample calculation for perylium salt synthesized in this experiment:

$$E_{0,0} = (1230 V \times nm) / ((\lambda_{abs} + \lambda_{em}) / 2) = (1230 V \times nm) / ((320 nm + 380 nm) / 2) = 3.514 V$$

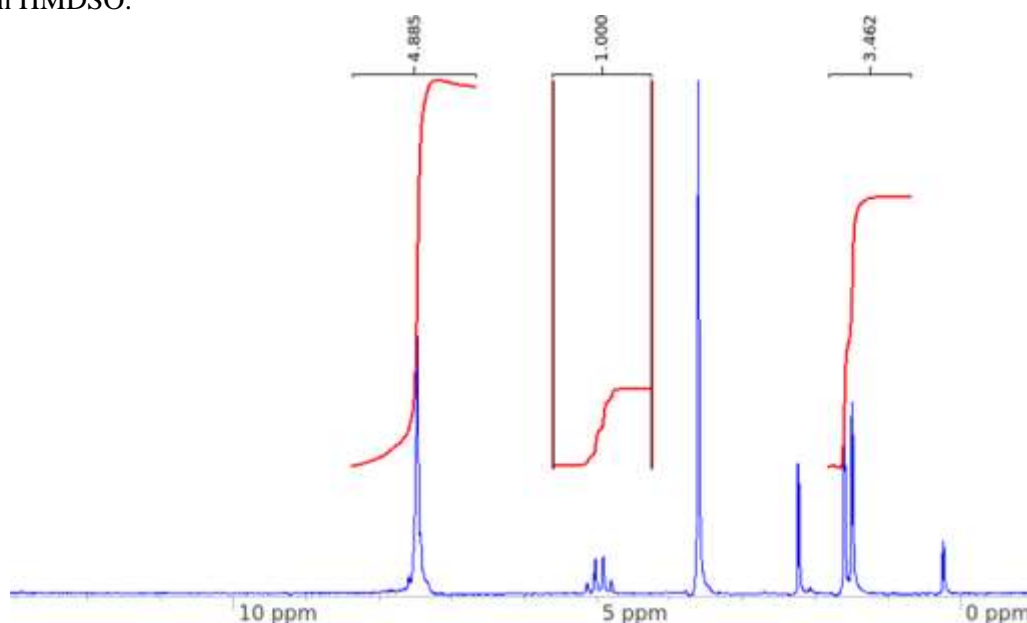
$$E^*_{1/2} = E_{1/2} + E_{0,0} = -573.2 mV + 3.514 V = -0.5732 V + 3.514 V = 2.941 V$$

The absorption absorbance, the emission absorbance, and the potential reduction values are determined for the following six perylium salts (A1 to A3, B1 to B3) and for the perylium salt synthesized in this experiment. The structure of 2-fluorophenyl-4-chlorophenyl-6-phenylperylum is shown using ChemDraw.



**Figure 8.** Novel Pyrylium product.

The  $^1\text{H}$  NMR diagram of the reaction mixture after the alcohol oxidation reaction is obtained at 60 MHz in HMDSO.



**Figure 9.**  $^1\text{H}$  NMR of post-alcohol oxidation mixture.

To assess the efficacy of the synthesized pyrylium, it is used as a photoredox catalyst in the oxidation of 1-phenylethanol to acetophenone. However, the resulted NMR diagram does not show any yield of the product acetophenone, because the 3Hs on acetophenone's methyl group should have a singlet shown at 2.60 ppm, according to the literature [6]. However, this NMR shows a singlet at the aromatic region, a multiplet at five ppm, and a doublet at the methyl region, indicating the presence of the starting material, 1-phenylethanol. The reaction mixture should have been heated for more time. It is also possible that the pyrylium catalyst solution is not effective enough due to impurities, which are also observed in the NMR. More recrystallizations or other purification methods could have been applied to purify the pyrylium. The pyrylium synthesis and the alcohol oxidation reaction could be repeated more times to reduce uncertainties caused by systematic errors, such as inaccurate reading, loss of chemicals during transferring or heating, and contaminations of experimental instruments.

#### 4. Conclusion

Overall, the results of this project were not very successful. The percent yield of chalcone was not very high, with a 28.2% yield. Also, although pyrylium was generated, it was very little, with only a 10%

yield. Additionally, although the percent recovery was higher (38%), it was still not very high. The UV-Vis and fluorescence spectra indicated that this value was likely to be lower as they showed the presence of impurities.

Furthermore, the oxidation of the alcohol could not be completed due to low amounts of pyrylium and the short reaction time, resulting in 0% yield of acetophenone. Although the results of these chemical reactions were insignificant, some things can be learned from the synthesized pyrylium. The pyrylium synthesized in this project had lower conjugation and oxidizing activity based on the spectra; however, its  $E^*_{1/2}$  was relatively high, suggesting that it might be a more potent oxidizing agent. These contrasting results most likely came from the skewed analysis due to impurities and the low yield of pyrylium. Broadly, pyrylium salts with EWGs should result in a more potent oxidizing agent as these have high electronegativity values and make the center of the pyrylium more unstable.

Since barely any pyrylium was generated and no alcohol was oxidized, future experiments would include changes to synthesize more pyrylium and acetophenone. This can include increasing the reagents for the synthesis of pyrylium, repeating the recrystallization step for better purification, and heating the pyrylium and the alcohol more during the alcohol oxidation step. Taking these changes would allow for successful oxidation and, therefore, a better analysis of the pyrylium regarding how substituents change its properties and efficacy. Successful analysis and oxidation would then provide this pyrylium as an alternative to metal catalysts used in oxidation reactions, as the substituents were halogens, which are EWGs.

## Reference

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