Experiment 6 & 7

Pyrylium Synthesis and Alcohol oxidation via photoreaction

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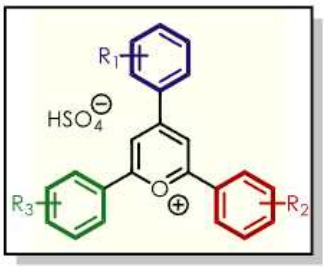
PURPOSE OF THE EXPERIMENT

Conduct pyrylium synthesis and alcohol oxidation using pyrylium via photo-oxidation. Use laboratory instrumentation and interpret resulting data including an NMR spectrometer, UV-Vis spectrometer, and CV.

BACKGROUND INFORMATION[1]

In the past decade, photoredox catalysis has emerged as a valuable tool for developing novel organic reactions, often via mechanistic pathways inaccessible by traditional synthetic methods. Polypyridyl complexes of iridium and ruthenium, which absorb visible light possess well-understood photophysical properties and are commonly employed in photoredox transformations. Additionally, various organic dyes have been utilized as catalysts in photoredox methodologies. The utilization of transition metal-free organic photoredox catalysts is advantageous due to the absence of toxic and expensive metal-based catalysts. One class of these catalysts comprises 2,4,6-triarylpyrylium salts (Figure 1). These salts act as potent single electron oxidants in their corresponding singlet excited state, possessing excited state reduction potentials often exceeding 1.5 V vs. SCE, enabling new reaction pathways to become energetically favorable. Through carefully designed reaction pathways, the process can be completed using catalytic amounts of photooxidants. The photophysical properties, including the excited-state reduction potential (E* 1/2), of these catalysts are influenced by the electronics of the substituents along the pyrylium core. E* 1/2 is derived from the sum of the ground-state reduction potential (E1/2) and the excited-state energy (E0,0). Consequently, the excited-state reduction potential can vary dramatically depending on the identity of the substituents on the triarylpyrylium motif.



Pyrylium salts are brightly colored molecules that have found utility in the developing field of photoredox catalysis. Photoredox catalysis is a method through which chemists harness light energy to synthesize

molecules more efficiently. The efficacy of photoredox catalysts arises from their capacity to absorb visible light and transition into higher energy excited electronic states (denoted on a chemical structure by *). In these excited states, the salts function as potent oxidizing agents, capable of extracting an electron from (oxidizing) organic molecules. This process generates highly energetic organic intermediates with distinct reactivity compared to the initial materials.

EXPERIMENT **Pyrylium Synthesis and alcohol oxidation**

Reagents and Properties

substance	*quantity*	*molar mass (g/mol)*	equiv.	*mp* (^oC)	bp (^oC)	*density (g/mL)*
Acetophenone A	14.4 mmol		1			
Acetophenone B	5.4 mmol					
Benzaldehyde	14.4 mmol		1			
EtOH	15 mL					
4M NaOH	4.5 mL					
Conc. H_2SO_4	0.5 mL					
$LiNO_3$	17 mg					
1-phenylethanol	30 uL (0.25 mmol)					

PROCEDURE

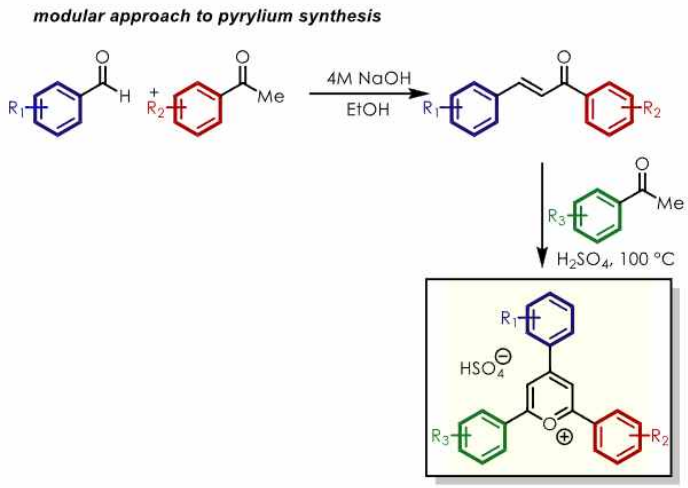
Caution: Wear lab coats and safety goggles at all times while in the lab. Many chemicals are potentially harmful. Prevent contact with your eyes, skin, and clothing. Wearing contact lens is strictly prohibited.

***You will be synthesizing **TWO DIFFERENT** Pyrylium salts during this experiment and conducting alcohol oxidation reactions using both of them.

Week 1

Part A

1. Chalcone Synthesis



Caution: Ultraviolet radiation can cause severe damage to the eyes. Do not look directly into the UV lamp. Sodium hydroxide is corrosive. Use it under the fume hood.

To a 50 mL Erlenmeyer flask containing a stir bar, add 14.4 mmol of your assigned acetophenone, 14.4 mmol of your assigned benzaldehyde and 15 mL absolute ethanol (EtOH). To this solution, while stirring, add 4.5 mL of 4 M NaOH dropwise over one minute.

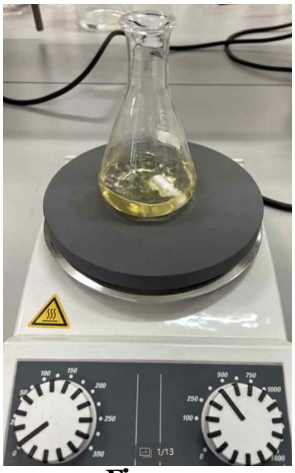


Fig. 1

Allow the solution to stir for 30 minutes and then place the flask in an ice bath for 10 minutes.

2. Isolating Product

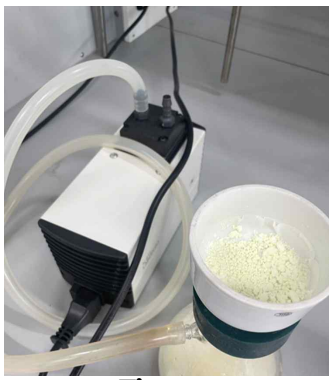


Fig. 2

Filter the suspension using suction filtration, then rinse the precipitate with 10 mL distilled water followed by 10 mL cold EtOH and pull suction to allow the product to dry. Transfer your product to a tared watch glass for additional drying.

3. Characterizing the Product

During the following lab period, record your yield and obtain a 1H NMR spectrum of your sample in approximately 500 µL deuterated chloroform. Save your product for PART B.

Part B

4. Synthesis of pyrylium bisulfate derivatives

Caution: Ultraviolet radiation can cause severe damage to the eyes. Do not look directly into the UV lamp. Sodium hydroxide is corrosive. Use it under the fume hood.

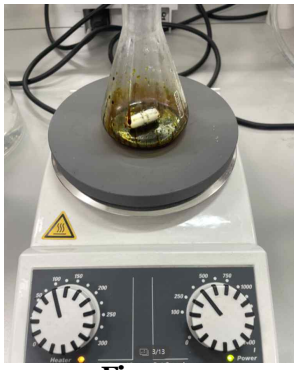


Fig. 3

Preheat the stir plate to 120’ C. To a scintillation vial, add 5.6 mmol of your synthesized chalcone. Break apart any chunks with a spatula to evenly distribute the chalcone in the vial. Then add 5.4 mmol of the selected acetophenone. With a micropipette, carefully add 0.5 mL concentrated H2SO4 to the flask and place the flask on the hot plate for 45 minutes.

5. Isolating Product

Caution: Ultraviolet radiation can cause severe damage to the eyes. Do not look directly into the UV lamp. Use every reagent under the fume hood.

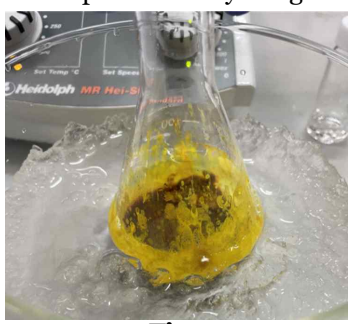
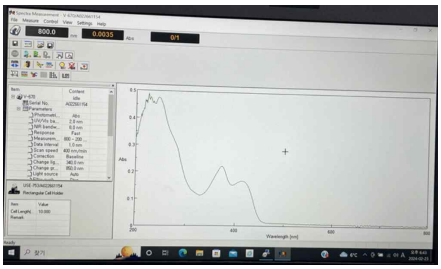


Fig. 4

Allow the flask to cool to room temperature, then place in an ice bath for 5 min before adding 6 mL ethyl acetate (EtOAc). Swirl the flask to loosen solids and scrape any residue off the bottom of the flask. Filter the suspension via suction filtration and rinse the solid with 2 rinses of 10 mL cold EtOAc. Next, you will recrystallize your impure product in methanol as follows. Pre-heat methanol to boil on your hotplate and use a boiling chip to prevent any bumping of the solvent. Place your impure pyrylium in a separate 250 mL Erlenmeyer flask with a stir bar and add a minimal amount of hot methanol, while stirring on your hotplate, until the crude pyrylium is completely dissolved. Remove the solution from the hotplate and cool to room temperature, then cool at 0°C for 15 minutes. You should see a significant amount of the precipitated product. If not, ask your TA if adding cold water is appropriate to aid in precipitation. After cooling, collect the pure pyrylium using vacuum filtration with a Büchner funnel. Store the product on a pre-weighed watch glass until next lab period. Remember to obtain the yield when you return. SAVE YOUR PRODUCT!

6. Characterizing the Product

During the following lab period, record your yield and obtain a 1H NMR spectrum of your sample in approximately 500 µL deuterated chloroform. You will be measuring the absorbance and emission of your pyrylium. Obtain an UV-Vis spectrum of the 16 µM solution and record any absorbance peaks (λ) you observe. (TA will instruct how to use Uv-Vis instrument)



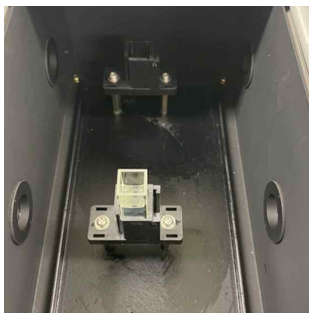
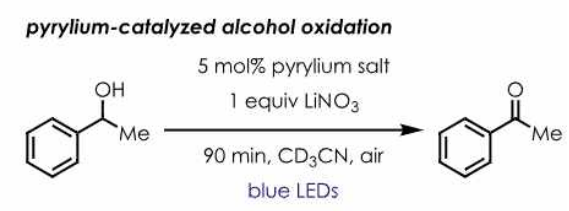


Fig. 5, 6

SAVE your product for NEXT WEEK!

Week 2

1. Alcohol Oxidation



To a 2 mL vial equipped with a stir bar, add 17 mg (0.25 mmol) LiNO3 and 0.05 equiv (5 mol%) of your synthesized pyrylium. Using a microliter pipet, add 30 µL (0.25 mmol) of 1-phenylethanol to the vial, followed by 1 mL of deuterated acetonitrile. Cap the vial and place in the light box. Allow the reaction to stir for 90 minutes under irradiation.

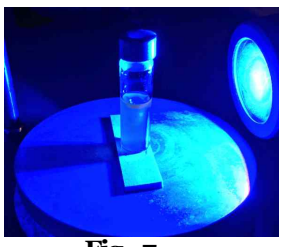


Fig. 7

After 90 minutes, vial is removed from the light box. Crude mixture is dried under reduced pressure.

2. Preparing the Column (Wet-pack Method)

Using a utility clamp, attach the column to a support stand. Use a glass rod to push the cotton at the bottom of the column. Be careful not to make the plug too tight or the eluent flow will be limited. Make sure the column is vertical. If the clamp is too large to firmly hold the column, use paper towels or a split stopper to hold the column in the clamp

tightly. Add a small amount of sea sand on the cotton.
Slowly add hexane to the beaker containing silica gel and mix until the mixture become slurry. Make sure that stopcock is closed, and then pour the slurry of silica gel into the column using funnel. The height of the packed silica gel in column should be ~13 cm high. Open the stopcock and wash the inside of the column with additional hexane. Allow the solvent to be drained through the column until its level is slightly above the the silica gel. (***CAUTION*** : No cracks and bubbles should be formed.) Then, pour a little amount of sea sand on the silica gel to make thin layer (<5mm) of sea sand above the silica gel.

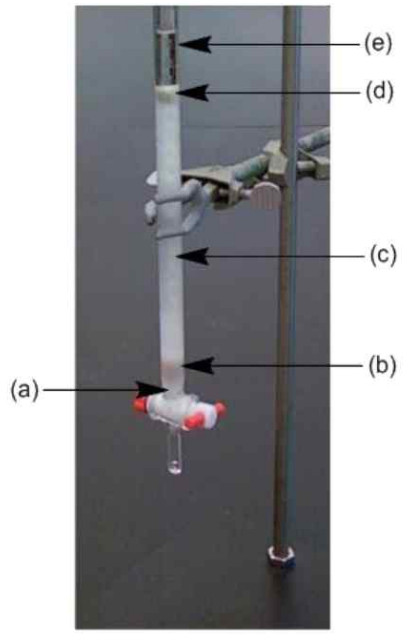


Figure 8. Prepared chromatography column
a: cotton, b: sand, c: silica gel, d: sand. e: mobile phase

3. Choosing the eluent using TLC experiment

According to the experimental TLC, develop the TLC. Choose the appropriate solvent system based on the result from TLC experiment.

Note. It is possible to change the polarity of the solvent system during separation, by changing the ratio of the solvent. Generally, the polarity of the solvents should be changed gradually from a less-polar to a more-polar solvent. (So-called gradient column chromatography)

4. Load the Sample to the Column

Load dried crude mixture. Make sure that the surface of the column is flat while loading the sample. Then add small amount of sea sand above the loaded sample.

5. Running the Column

Caution: Once the column chromatography has started, it should not be stopped or allowed to run dry for any reason! You should monitor the column and collect fractions, and prepare the necessary eluting solvent well in advance of its use.

Number the 20 ml vials as 1,2,3,...,n. These vials will be used to collect the components (fractions) of the mixtures as they are eluted from the column.

Carefully transfer the appropriate eluent, consisting of ethyl acetate and hexane, into the column. Make sure not to disturb the silica layer when adding the eluent.

Continuously collect fractions and re-fill the eluent until all of the compounds came out from the column. It can be monitored by TLC.
If you separate one compound from the mixture, you can use a more polar solvent mixture as eluent.

6. Characterizing the Product

Gather the product and dry under reduced pressure. Weigh the mass of final product. During the following lab period, record your yield and obtain a 1H NMR spectrum of your sample in approximately 500 µL deuterated chloroform.

Pre-Laboratory Questions

Week 1

1. Summarize all MSDS's of chemicals used in this experiment.

2. How would R groups attached to pyrylium affect the oxidation potential?

3. How can the excited state energy of pyrylium, $E_{0,0}$, be measured, and what does it equivalent to?

Week 2

1. Summarize all MSDS's of chemicals used in this experiment.

2. Draw the photoinduced alcohol oxidation reaction mechanism.

3. Which of your pyrylium would oxidize alcohol better, why?

Post-Laboratory Questions

Week 1

1. Assign peaks in ^{1}H NMR spectrum to confirm the product. You should provide proper logic for peak assignment. (Integrals, coupling pattern, and chemical shift)

2. According to your Uv-Vis data, what would be the best light source for your alcohol oxidation reaction?

Week 2

3. Assign peaks in ^{1}H NMR spectrum to confirm the product. You should provide proper logic for peak assignment. (Integrals, coupling pattern,

and chemical shift)

4. Identify product and calculate the yield.