Synthesis of 4,3'-Dihydroxy Chalcone

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Abstract

Our goal this quarter was to synthesize 4,3'-dihydroxychalcone, using the lab skills we acquired throughout the Organic Chemistry series taught at Whatcom Community College. The goal of synthesizing 4,3'-dihydroxychalcone was to provide the General Chemistry students with a new chalcone to use in their antibiotic CURE research. We obtained pure 4,3'-dihydroxychalcone with a workable percent yield that can be used in future research.

Introduction

Chalcones are naturally-occurring chemicals found in high concentrations in all vascular plants and are extracted for their antibiotic effects in pharmaceuticals and medicinal chemistry (Zhuang *et. al.*, 2017). For example, the plant *Crotalaria orixensis* produces Crotaorixin, a hydroxychalcone used inhibiting the growth of the *P. Falciparum* malaria strain at concentrations of 50 and 10 µg/mL (Villa *et. al.*, 2024). By producing an untested variant, we hope that future General Chemistry students will be able to test these antibiotic effects.

The process of synthesizing chalcones requires a solid understanding of Organic Chemistry lab techniques and mechanistic knowledge, primarily through using Thin-Layer Chromatography (TLC) and IR Spectroscopy to test the purity of our chemical.

Methods

Materials

Provided by Whatcom Community College:

4-hydroxybenzaldehyde, 3'-hydroxyacetophenone, Methanol, 6.0M Hydrochloric Acid, 6.0M 60% Sodium Hydroxide.

97% pure 4'-hydroxychalcone provided by Matrix Scientific.

Instrumentation

Shimadzu FTIR Spectroscopy Software - LabSolutions IR

Column Chromatography glassware and funnel

Model UVGL-58 Mineralight© Lamp 115Volts

Mel-Temp II Laboratory Devices USA

Procedure

1) Mix 0.2 grams of 4-hydroxybenzaldehyde to 3'-hydroxyacetophenone.

2) Combine in 5ml conical vial and add 1ml of methanol. Gently heat 1-3 minutes until dissolved.

3) Cool to room temperature, then add 0.3ml of NaOH. Stir and cool for 3-5 minutes. Wait for a few minutes to 24 hours for a precipitate to form.

4) Add HCl for 30 seconds to 1 minute until acidic.

5) Filter through Hirsch funnel with small amounts of cold methanol and allow solid to dry.

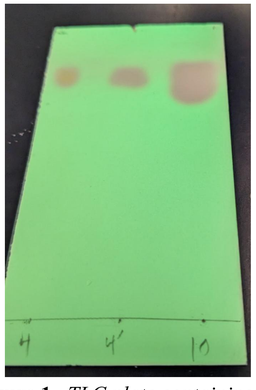
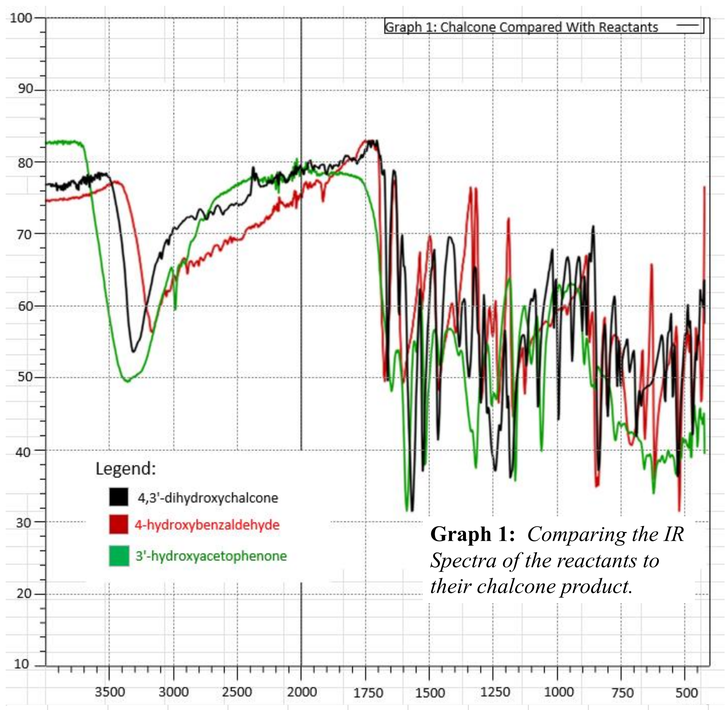
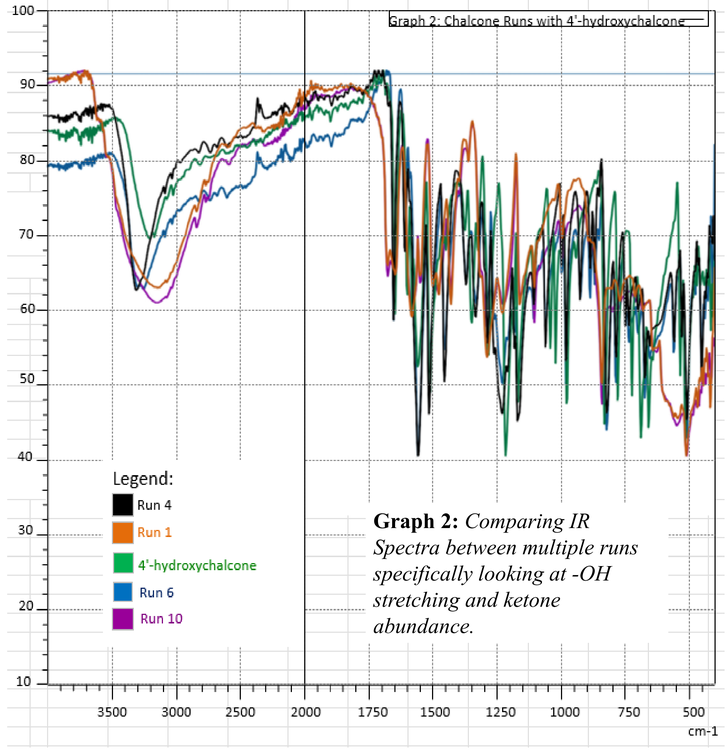


Figure 1. *TLC plate containing solute dots for Run 4 of our chalcone, 4'-hydroxychalcone, and Run 10 of our chalcone (listed left to right).*



Graph 1: *Comparing the IR Spectra of the reactants to their chalcone product.*



Graph 2: *Comparing IR Spectra between multiple runs specifically looking at -OH stretching and ketone abundance.*

Discussion

By the end of our research, we were able to successfully synthesize pure 4,3'-dihydroxychalcone. Our main struggle through the process was maintaining consistency from run to run. We were first able to verify purity with a TLC that compared our samples to a pure sample of a similar chalcone (4'-hydroxychalcone). We were then able to take an IR spectra of our compounds to identify key structures such as -OH groups.

We knew it would be important to use an anhydrous solvent as the use of H2O would hinder the reaction progress. H2O is one of our final products and excess would lower our overall yield significantly. We also found that bringing the reaction to the correct temperatures during the synthesis played a large role in our workable yield, with rushed steps leading to significant changes to our yield. During our first three runs, we were successful at creating our chalcone but struggled with maintaining purity as unreacted 4-hydroxybenzaldehyde and 3'-hydroxyacetophenone were still present as indicated by the IR spectra and Mel-Temp results. After adding NaOH, our precipitate took anywhere from a few minutes to 24 hours to form.

To increase both purity and yield, we consulted with another lab group and decided to incorporate an acid workup step to push the reaction to completion. By using HCl to add a protonation step, When we looked at our Runs 4 and 6, our chalcone showed a noticeable change in the IR spectra and varied melting points as well as in our TLC. These changes led us to believe we had an increase in purity compared to our 4' hydroxychalcone sample. Throughout our experiment, we tried both re-crystallization and column separation in hopes of finding a way to better purify our sample with little to no successes.

Although we had errors in our synthesis, we hope our findings will be useful in synthesizing our chalcone. We suggest pursuing further purification steps utilizing crystallization and column separation. We also hope that future General Chemistry CURE projects can utilize our chalcone for their own antibiotic research.

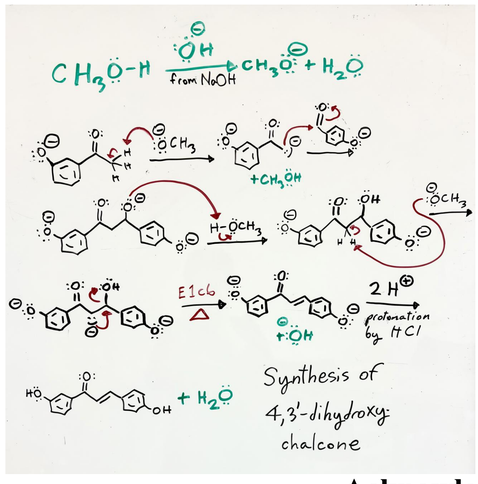


Figure 2. *Proposed synthetic mechanism of 4,3'-dihydroxychalcone using NaOH as a basic catalyst in a solution of methanol and methoxide.*

Acknowledgements

We would like to thank Professor Steve Deroy for guiding us through the synthesis and providing the education we needed to progress through our experiment. We would also like to express our gratitude to Mark Price for guiding us through the IR Spectra and its software as well as being able to setup the IR for us to use outside of class. To confirm the purity of our experimental results. We would also like to thank Alan Hernandez Zavala for his help and inspiration with our synthesis and poster. Lastly, we would like to thank Matrix Scientific for their punctual delivery and service of their 4'-hydroxychalcone, which we used to compare with the purity of our 4,3'-dihydroxychalcone.

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