Indole Glycoside Synthesis

PROJECT ID:

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Introduction

- Melatonin is a hormone the body uses to regulate body cycles, especially the cycles revolving around sleep. Commercial melatonin pills are widely available over the counter for people who may need it.
- There are also analogs to melatonin on the market, like ramelteon, presenting a similar chemical structure that interacts with the same neurotransmitters melatonin affects.
- In interest of synthesizing a related compound, a carbohydrate attached to an indole came to mind, like how an amide is in melatonin.
- Indole was made reactive following a textbook electrophilic substitution with bromine at the C3 (Wade & Simek 2017).
- A procedure by Rhoke and Bhate (2017) protected glucose so that it had only one reactive hydroxyl group.
- The results of the two procedures would be combined to synthesize an indole glycoside.

Methods

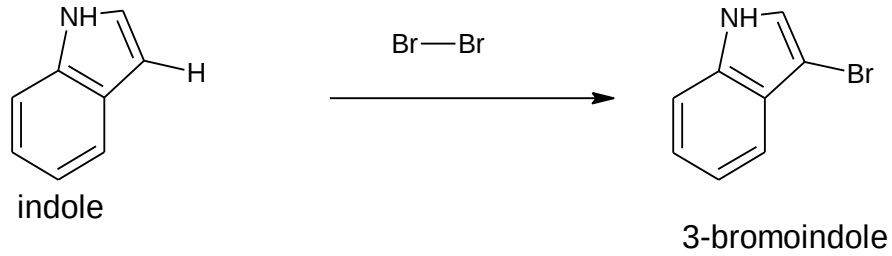
Substituting Indole

Following the textbook was only in concept.

Indole and bromine were combined in a test tube.

Different forms of bromine in different solvents were used.

The precipitate would be identified by its melting point.



Creating Deep Eutectic Solvent (DES)

Measure out choline chloride and malonic acid in a 2:3 mass ratio (adjusting for the amount wanted)

Place in a beaker and heat to 70-80°C for a few hours

Keep covered and store until use

Protecting Glucose

Rokade and Bhate's procedure was followed (2017)

10 g of glucose and 20 mL of acetone were dissolved in 15 g of DES

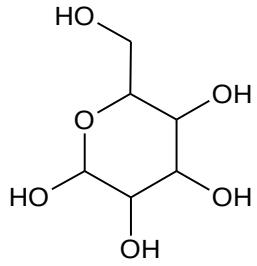
The mixture is refluxed at 50°C

Wash with an organic polar solvent

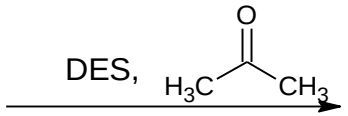
- Original recipe called for ethyl acetate
- Acetonitrile was also tried

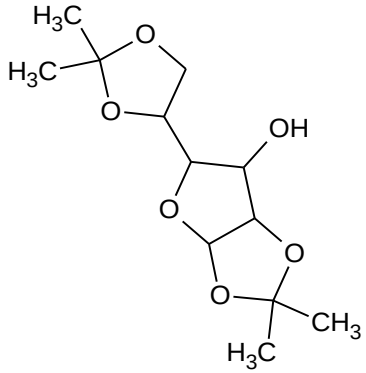
Collect this polar layer and vacuum distill the solvent

Use FTIR analysis to identify products



glucose

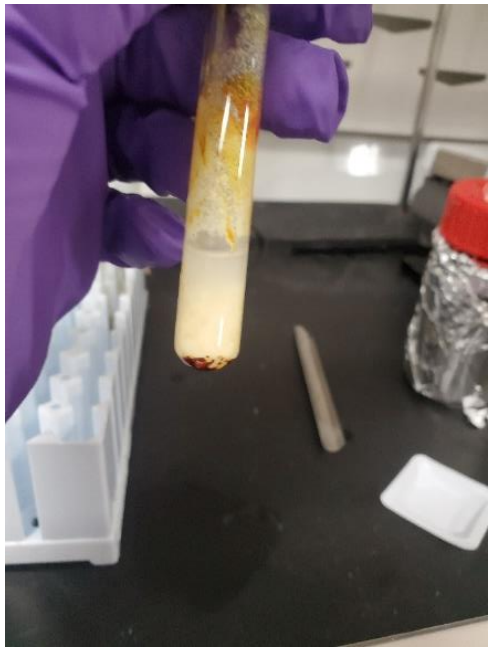




Diacetone-d-glucose

Results and Discussion

	Brominated Indole Melting Point (°C)
Attempt 1	107
Attempt 2	140
Attempt 3	170
Expected	60



Images taken by presenter

Substituted Indole

The resulting powder was mostly white with a yellow tint. Samples left in air for some time turned yellower.

The table to the left lists melting points for different attempts across different solvents for bromine.

They were notably higher than ChemSpider's listen melting point of 60°C (n.d.)

Overbromination was the likely cause. Bromine at other locations on indole would raise the MP. The exact locations would not be worth finding as only 3-bromoindole was of interest.

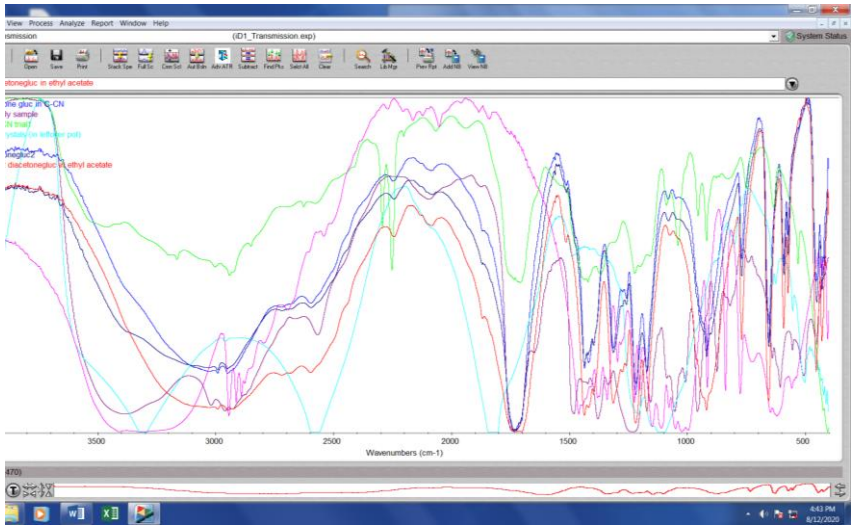


Image and screenshot taken by presenter

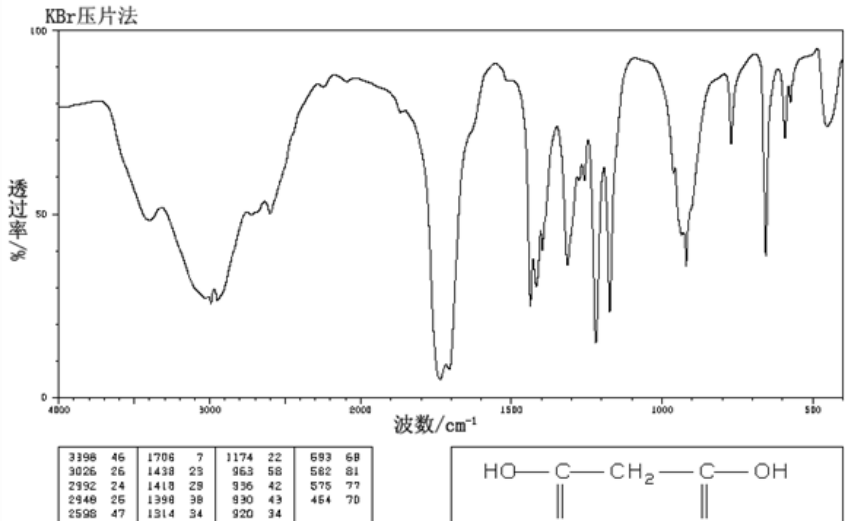
Protected Glucose

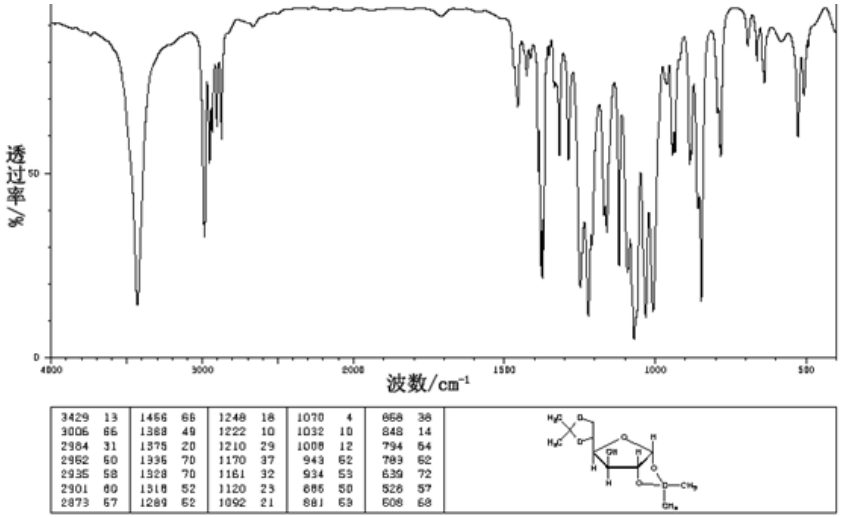
White crystals deposited after the vacuum distillation

FTIR spectra were obtained from multiple attempts

Most matched identifiers for malonic acid but one spectrum had protected glucose character as well.

Prevalent malonic acid likely due to bad DES. This could be improved with more time. The small amount of protected glucose does prove the procedure works.





Reference Spectra

These two spectra from Chemical Book (n.d.) for malonic acid on top and protected glucose (diacetone-d-glucose) on the bottom

Spectra sourced from https://www.chemicalbook.com/SpectrumEN_141-82-2_IR2.htm and https://www.chemicalbook.com/SpectrumEN_582-52-5_IR2.htm

References

- *3-bromoindole*. (n.d.). ChemSpider. http://www.chemspider.com/Chemical-Structure.2043966.html
- *Diacetone-d-glucose*. (n.d.). Chemical Book. https://www.chemicalbook.com/SpectrumEN_582-52-5_IR2.htm
- *Malonic acid* [Chemical Book]. (n.d.). https://www.chemicalbook.com/SpectrumEN_141-82-2_IR2.htm
- Rokade, S. M., & Bhate, P. M. (2017). Practical preparation of mono- and di-O-isopropylidene derivatives of monosaccharides and methyl 4,6-O-benzylidene glycosides from free sugars in a deep eutectic solvent. *Journal of Carbohydrate Chemistry*, *36*(1), 20-30. https://doi.org/10.1080/07328303.2017.1347262
- Wade, L. G., & Simek, J. W. (2017). *Organic chemistry* (9th ed.). Prentice Hall.

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