Synthesis of Bioactive *p*-Indolequinones

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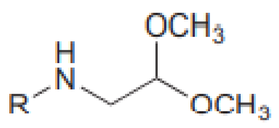
Abstract

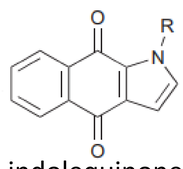
Indolequinones has been known to be an anticancer agent and is used in many medication for cancer patients. Our lab figured out a new method to synthesize *p*-indolequinones from α-aminoacetals and 1,4-naphtoquinone. In this experiment we will increase the substrate scope and check for their bioactivity to make a better drug.

Introduction

Indolequinones are of high interest due to their bioactivity against cancer cells as well as their use for synthesis of compounds. Our lab figured out how to synthesize *p*-indolequinones using α-aminoacetals and 1,4-naphtoquinone. The compounds we used to synthesize the α-aminoacetals are benzaldehyde and 1-naphthylaldehyde which will lead into the creation of their corresponding indolequinone. So far only 1-benzyl benzo [*f*]p-indolequinone has been made and the 1-naphthylaldehyde is still in the process of becoming an indolequinone. Once the compounds have been synthesized then it will then be experimented on to expand its substrate range.



α-aminoacetals



p-indolequinones

Acknowledgement

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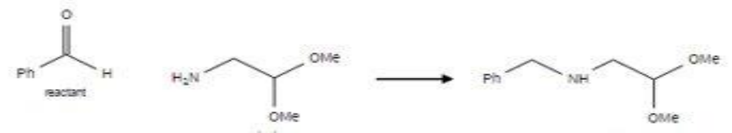
•The University of Texas Rio Grande Valley

Methods

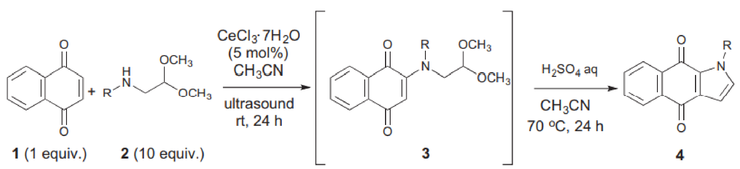
Synthesis of α-aminoacetals

Amino acetaldehyde dimethyl and acetal benzaldehyde/1-naphthylaldehyde was reacted in ethyl acetate. To that solution sodium borohydride is added and 3 drops of water as well. The mixture was then extracted and evaporated at low pressure. The compound was then purified through column chromatography and confirmed through NMR.

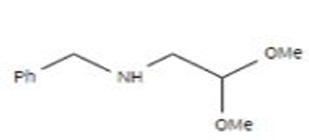


Synthesis of 1-benzyl benzo [*f*]p-indolequinone

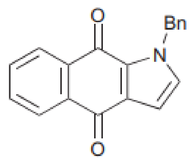
1,4-napthoquinone and α-aminoacetals made from the benzaldehyde were reacted with $CeCl_3 \bullet H_2O$ and CH_3CN in the sonicator. 1M H_2SO_4 and CH_3CN was added at high temperatures before finalizing the reaction. The compound was then purified through column chromatography and confirmed through NMR.



Results



23% yield



42% yield

Discussion

The synthesis of the 1 benzyl benzo[*f*]indole-4,9-diones was confirmed through NMR while the 1-naphthylmethylene aminoacetal has still not been confirmed to continue synthesis to indolequinone. The yield from the benzyl amino acetal was not achieved at the best yield as well as the indolequinone and this is probably due to my mistake in the column chromatography.

Conclusion

In conclusion, the correct compound was created but at a yield that is a lot less then what it should be. With the compound left, it will be used to proceed to future work.

Future Work

•Proceed with the next reaction using the *p*-indolequinones created in order to remove the R and replace it with a different substrate.
•Learn how to increase yield from the synthesis of both compounds.

Citations

1. Phillips R. M., et al,. (1999) Bioreductive activation of a series of indolequinones by human DT-diaphorase: structure-activity relationships
2. Luu Q.H., et al., (2016) Ultrasound assisted one-pot synthesis of benzo-fused indole-4, 9-dinones from 1,4-naphthoquinone and α-aminoacetals
3. Yan, C., et al.,(2009). Potent activity of indolequinones against human pancreatic cancer: identification of thioredoxin reductase as a potential target. *Molecular pharmacology*, *76*(1), 163–172.