Synthesis, Purification, and Characterization of Guest molecules for Inclusion in Cucurbit[n]urils

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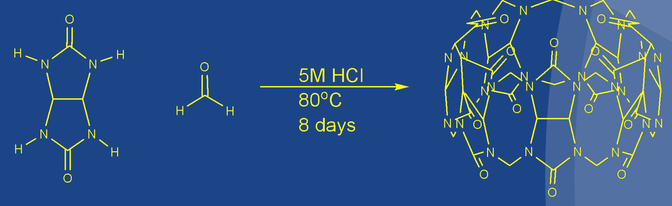
Abstract

Cucurbit[n]uril (CB[n]) is a unique macrocycle that can bind small molecules with promising potential applications in drug delivery, molecular machines, and smart materials. This work focuses on the supramolecular equilibrium binding modes and the equilibrium binding constants of CB[n] with a variety of viologens, pyridinium species which have not previously been studied. The synthesis, purification and characterization of these guest species will be presented. The knowledge gained from the study of physical properties of these host guest systems which will aid in the future development of more complex systems.

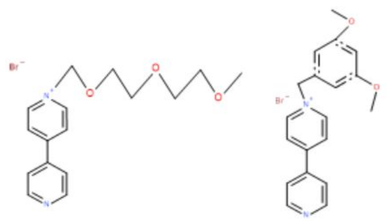
Background and Aims

Cucurbutrils are commonly known as CB[n], where n is the number of glycouril units which are linked by methylene bridge. These can be synthesize by heating glycouril with formaldehyde. CB[n] are interesting compounds because they are host for wide range of the cationic and anionic species and bind with abnormally high binding constant in the range of 10^5 to 10^12 M^-1. These could be used for various applications in drug delivery, asymmetric synthesis molecular switching and protecting dyes from photooxidation. Viologens are organic compounds which are dipyridinum derivatives and their tendency to form host-guest complex could be key to molecular machines. The main goal of this research is the synthesis of viologens. We can study their binding modes by H^1 NMR chemical shift data and binding constant with CB[7] and CB[8] by H^1NMR competition studies. Potential applications of studying these binding modes and binding constants are in molecular machines, such as shuttles and sensors where we can involve host-guest chemistry. CB[7] acts as the shuttle allowing the communication between receptor group and signaling group of a molecular receptor. Before the receptor interacts with any type of biomarkers it is encapsulated by CB[7] with high binding constant . If a small amount of CB[7] shuttles down the axle of molecular sensor to weaken binding site, then the biomarker gets the opportunity to interact with receptor. At this point the binding constant of CB[7] and receptor might be reduced by the steric bulk and electronic interaction from the surface of the biomarker and weaker binding site triggers the an event of fluorescence. The fluorescence increase from the baseline could be measured with high sensitivity for each type of cancer.

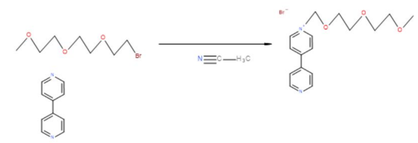
Synthesis of CB[7]



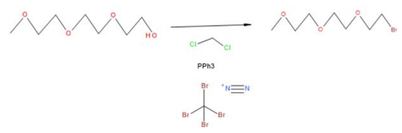
Viologen guests proposed in this study



Synthesis of 1-bromo-2-(2-(2-methoxyethoxy)ethoxy)ethane



Synthesis of 1-(2-(2-(2-methoxyethoxy)ethoxy)ethyl)-4-(pyridin-4-yl)pyridinium



Synthetic Procedure

The viologen and dipyridyl compounds were chosen for this study contained several features in common. First, each compound had at least one end that was sterically open on at least one side to allow the threading of CB[7] onto the axle. Second, the end groups on the axle were chosen to destabilize the binding by incorporating electronegative elements such as ether groups. Compounds triethylene glycol bromides were synthesis from triethylene glycol monomethyl ether by the Appel reaction. As for the dipyridine and triethylene glycol bromides, those compounds were synthesized from SN2 substitution. The reactions were carried out in an experimentally optimized organic solvent, ensuring that the starting material would completely react and the resulting product would precipitate out upon completion of the reaction. This experiment was started by dissolving triethylene glycol monomethyl ether and tetrabromide in methylene chloride then adding the mixture in a round–bottom flask along with a stir bar. The round-bottom flask was cooled to 0 degree Celsius in an ice bath and allowed it to stir until all solids dissolved before adding triphenylphosphine in solution dropwise. The sample was stirred and allowed to warm up to room temperature for a few hours. The sample was then taken out of solution by attaching the round-bottom flask to the rotary evaporator to yield a light orange viscous liquid. Afterward, the sample was split in half. One half was taken to produce an IR spectrum, then will be triturated with ether and purified on a reverse thin-layer chromatography.

The other half will be dissolved in ethanol in an Erlenmeyer flask. Then the solution will be heated and stirred while adding zinc chloride dissolved in ethanol. Then the mixture was allowed to cool to room temperature before being filtrated and evaporated. Then it was triturated with ether. Lastly, both samples will be added in acetonitrile and refluxed. Acetonitrile is evaporated and distilled water was added to the crude mixture. Excess 4,4-dipyridine precipitated from solution and was filtered out and discarded. The remaining filtrate was washed three times with toluene and three times with ether. The water layer was then evaporated. NMR spectra will then be used to confirm the purity of the sample.

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Conclusion

Due to short time during the experiment and lack of results no conclusive conclusion could be made at the time. However, the sample was taken an FT-IR was taken to check the purity of the synthesis. The FT-IR spectra confirmed that the synthesis of 1-bromo-2-(2-(2-methoxyethoxy)ethoxy)ethane was successful. However, a small broad peak around 3500 showed that a little of the starting reagent did not wholly react. The solution will be weighed, and part two of the synthesis will be started. The 1-bromo-2-(2-(2-methoxyethoxy)ethoxy)ethane will then be reacted with 4 4-bipyridine forming 1-(2-(2-(2-methoxyethoxy)ethoxy)ethyl)-4-(pyridin-4-yl)pyridinium as the final product.

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Acknowledgements

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