

1-1-2013

The Use of Molecular Dynamics to Predict the Stability of Squaraine Rotaxanes

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Recommended Citation

Nelson, Ruth; Baumes, Jeffrey; Connell, Richard D.; Murgu, Ivan; Oliver, Allen; Smith, Bradley; and Johnson, Andrew, "The Use of Molecular Dynamics to Predict the Stability of Squaraine Rotaxanes" (2013). *Math & Science Department (SURI)*. Paper 8.
http://commons.cu-portland.edu/suri_msd/8

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Abstract / Introduction

Squaraine rotaxanes are fluorescent molecules comprised of two parts—a dumbbell-shaped squaraine dye threaded through a ring-shaped macrocycle—that are held together by hydrogen bonding, hydrophobic effects, and the size of the opening in the macrocycle¹. Since the squaraine is an extremely electrophilic species³, nucleophilic attack by water is possible when it slips out of the macrocycle. This results in a loss of fluorescence. These near-IR dyes have many applications, including effective labeling of bacterial cells⁴. Previous studies have shown that the unprotected squaraine dye is unstable, and the adamantyl rotaxane degrades over time while the isophthalamidyl and pyridinyl rotaxanes remain stable² (Fig. 2). In this study, we aim to determine if molecular dynamics (MD) is an effective method of ascertaining the relative stabilities of squaraine rotaxanes in solution.

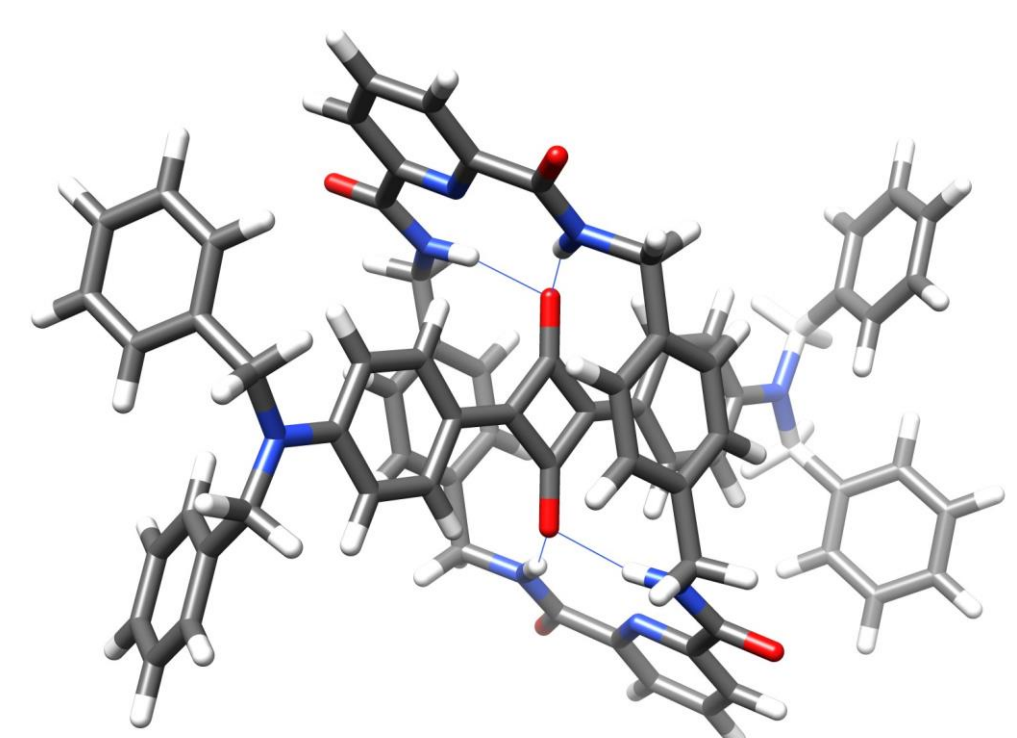


Figure 1- The Pyridinyl Rotaxane

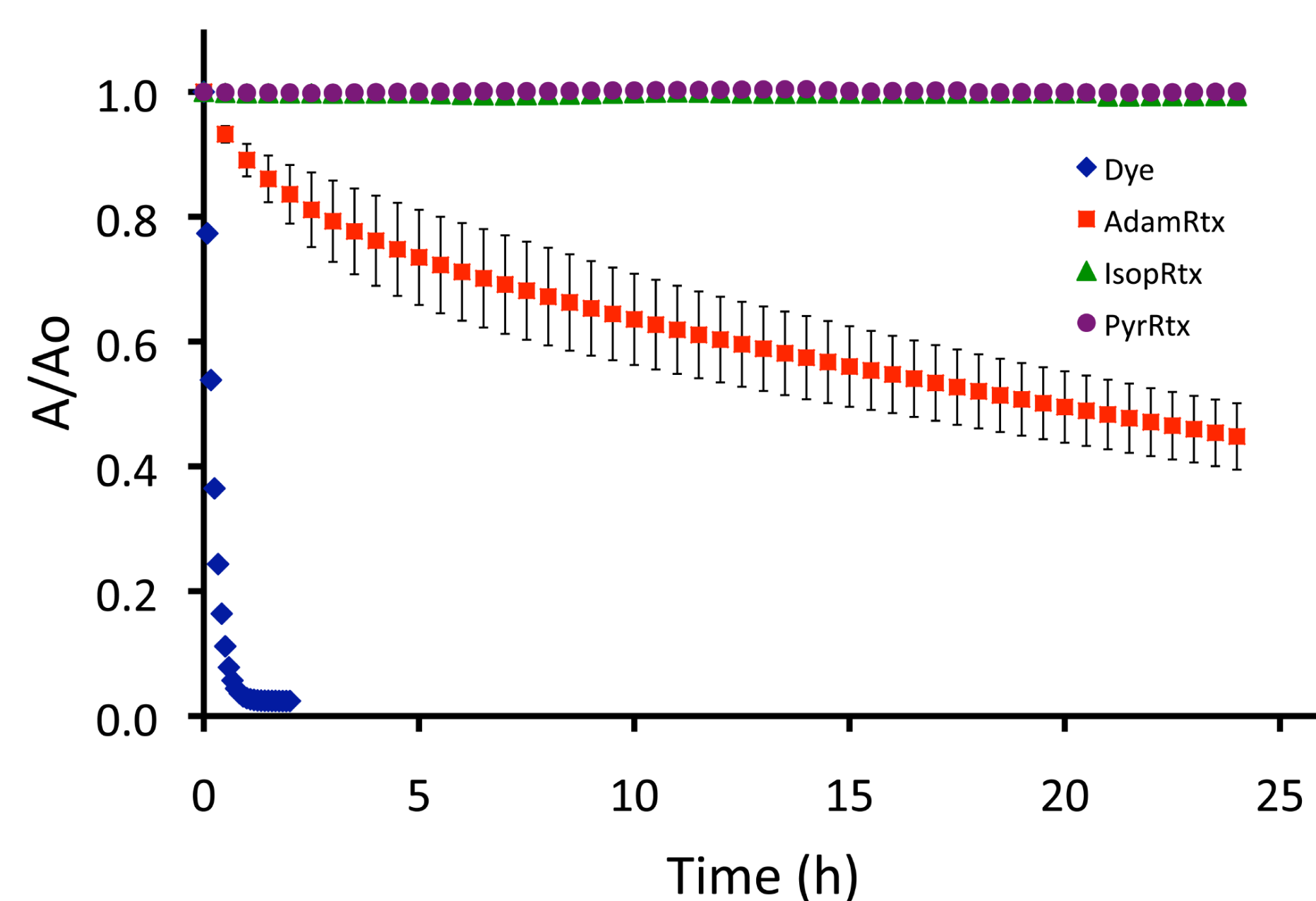


Figure 2- Rotaxane Stability vs. Time

Materials & Methods

Using the GAMESS software, the structures of the rotaxanes were optimized, and the charges were derived on HF optimized structures using the 6-31G* basis set. 100 ns MD trajectories were obtained using the NAMD program implementing the gaff force field at 300 K. The solvent was treated implicitly and a dielectric constant of 4.8 (chloroform) was chosen. The *ptraj* module of AmberTools 12 was used for all post-processing. Visualization was performed in Chimera.

Results

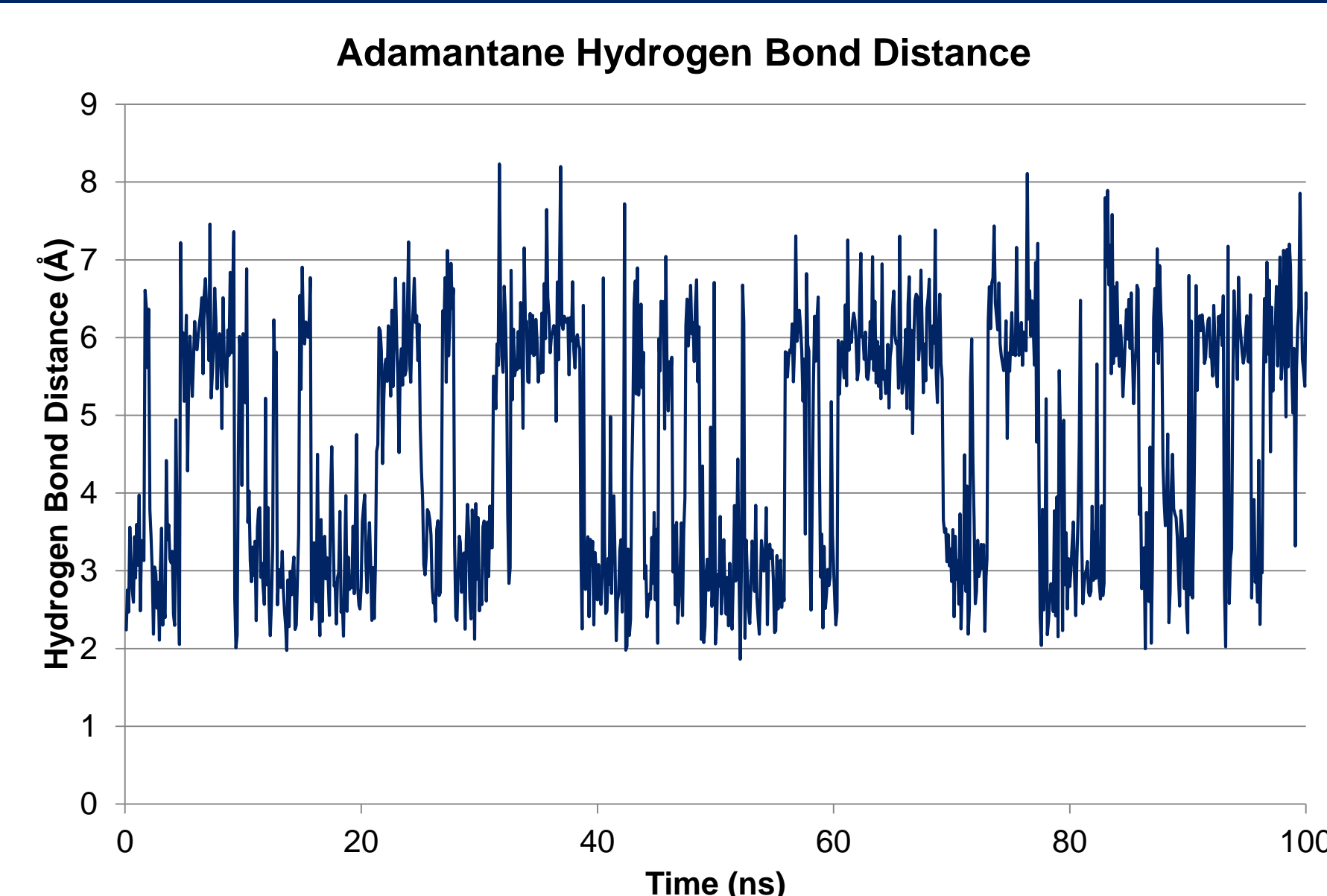


Figure 3- Squaraine-macrocycle hydrogen bond distance vs. time for adamantyl rotaxane

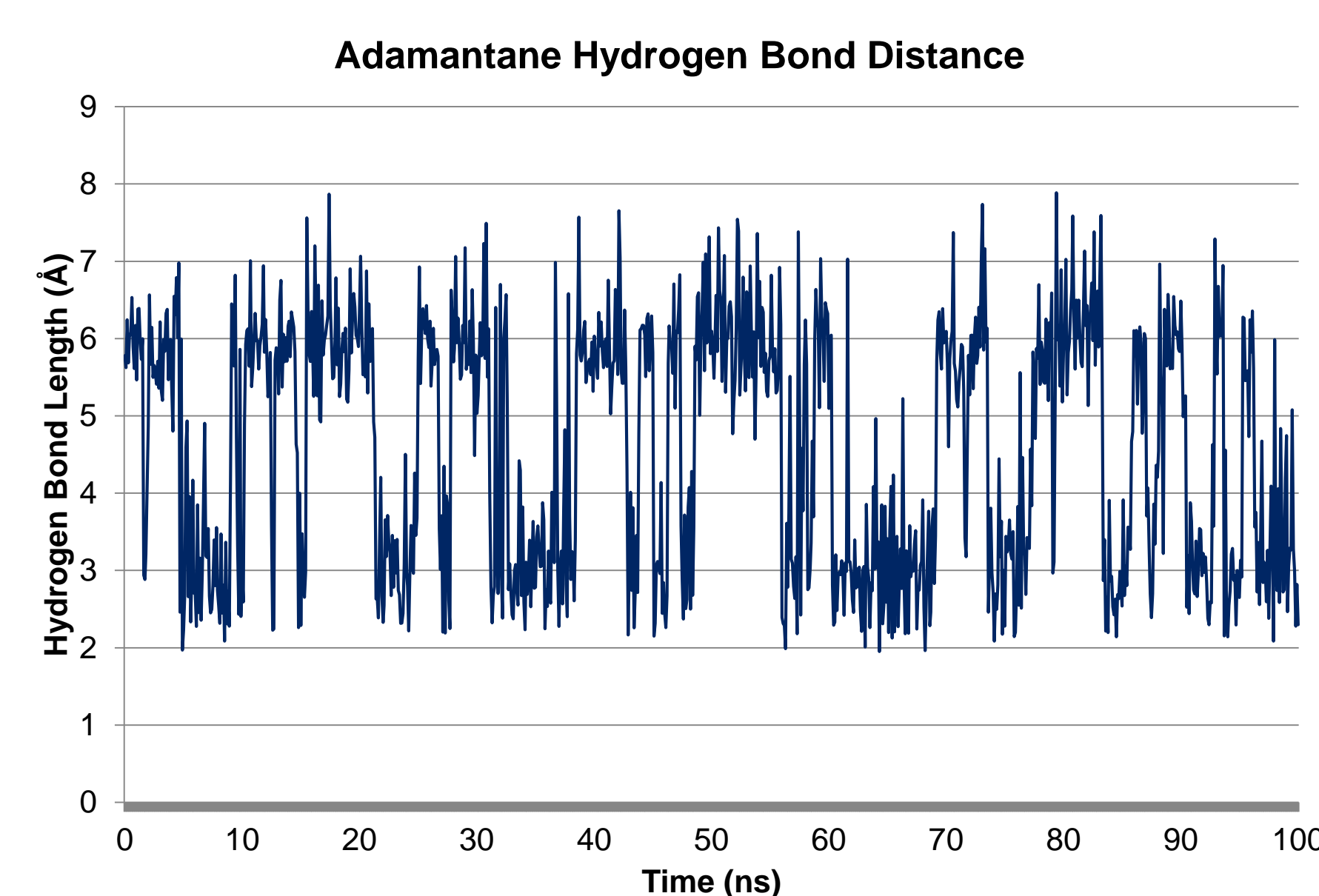


Figure 4- Flipped squaraine-macrocycle hydrogen bond distance vs. time for adamantyl rotaxane

Results

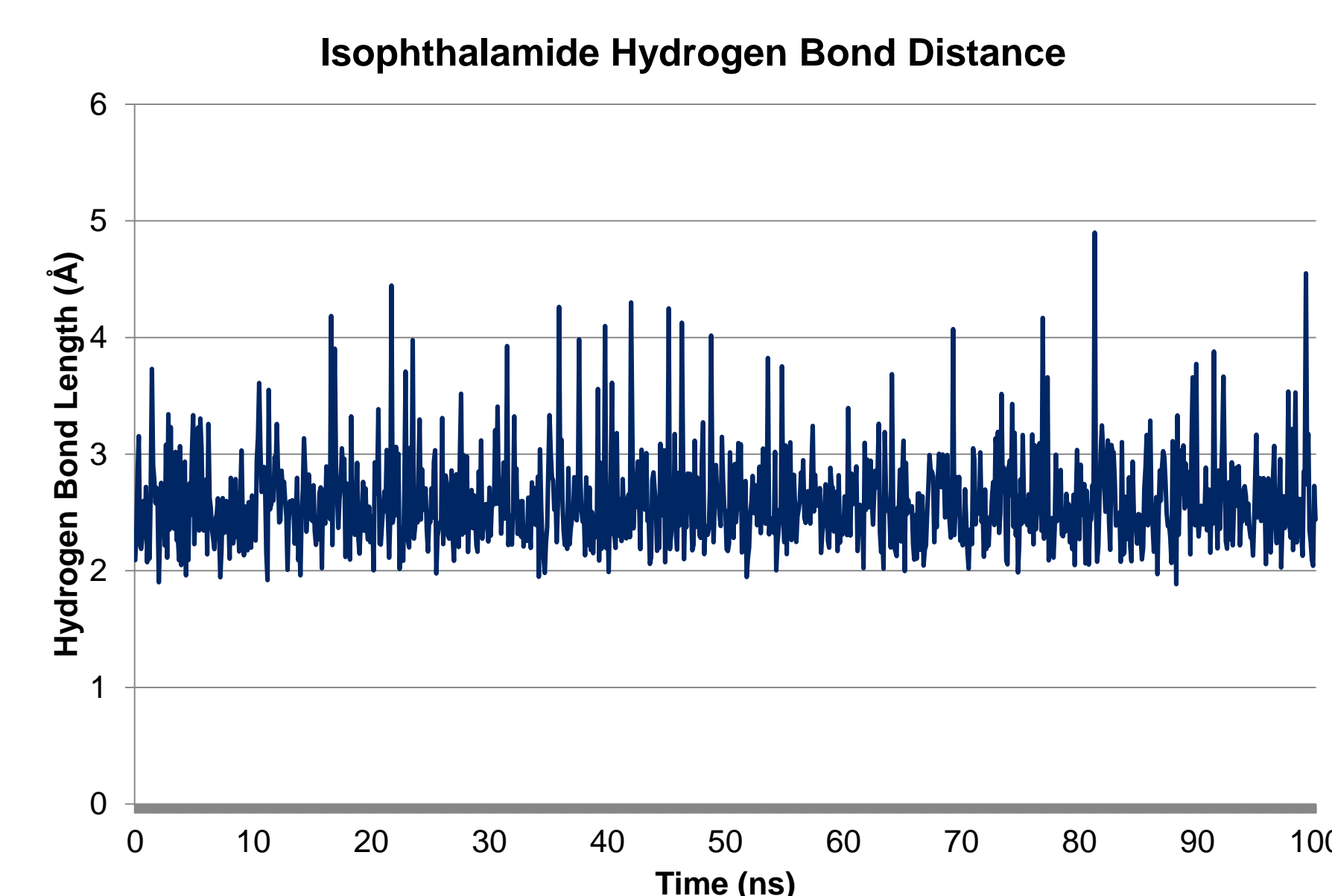


Figure 5- Squaraine-macrocycle hydrogen bond distance vs. time for isophthalamidyl rotaxane

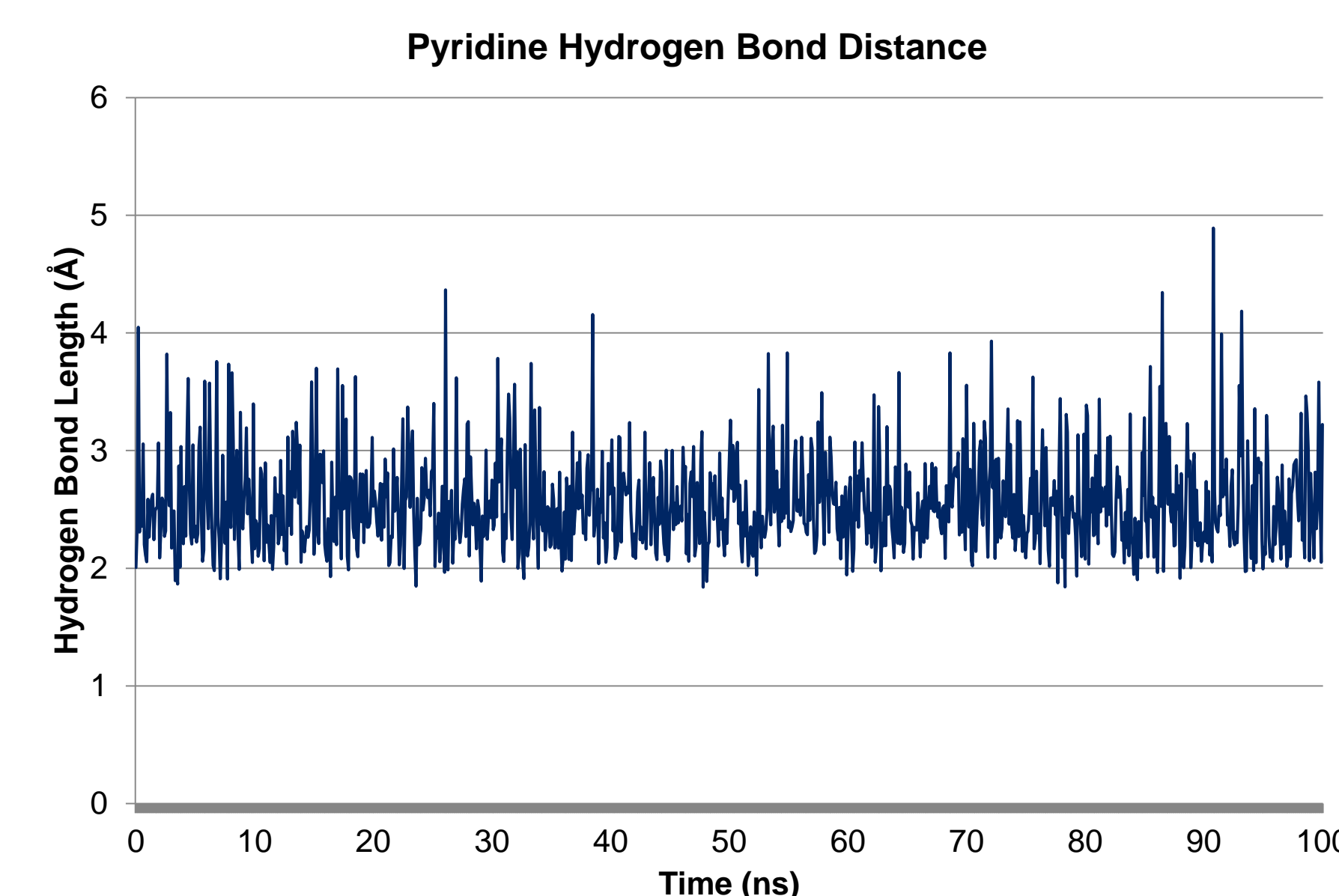


Figure 6- Squaraine-macrocycle hydrogen bond distance vs. time for pyridinyl rotaxane

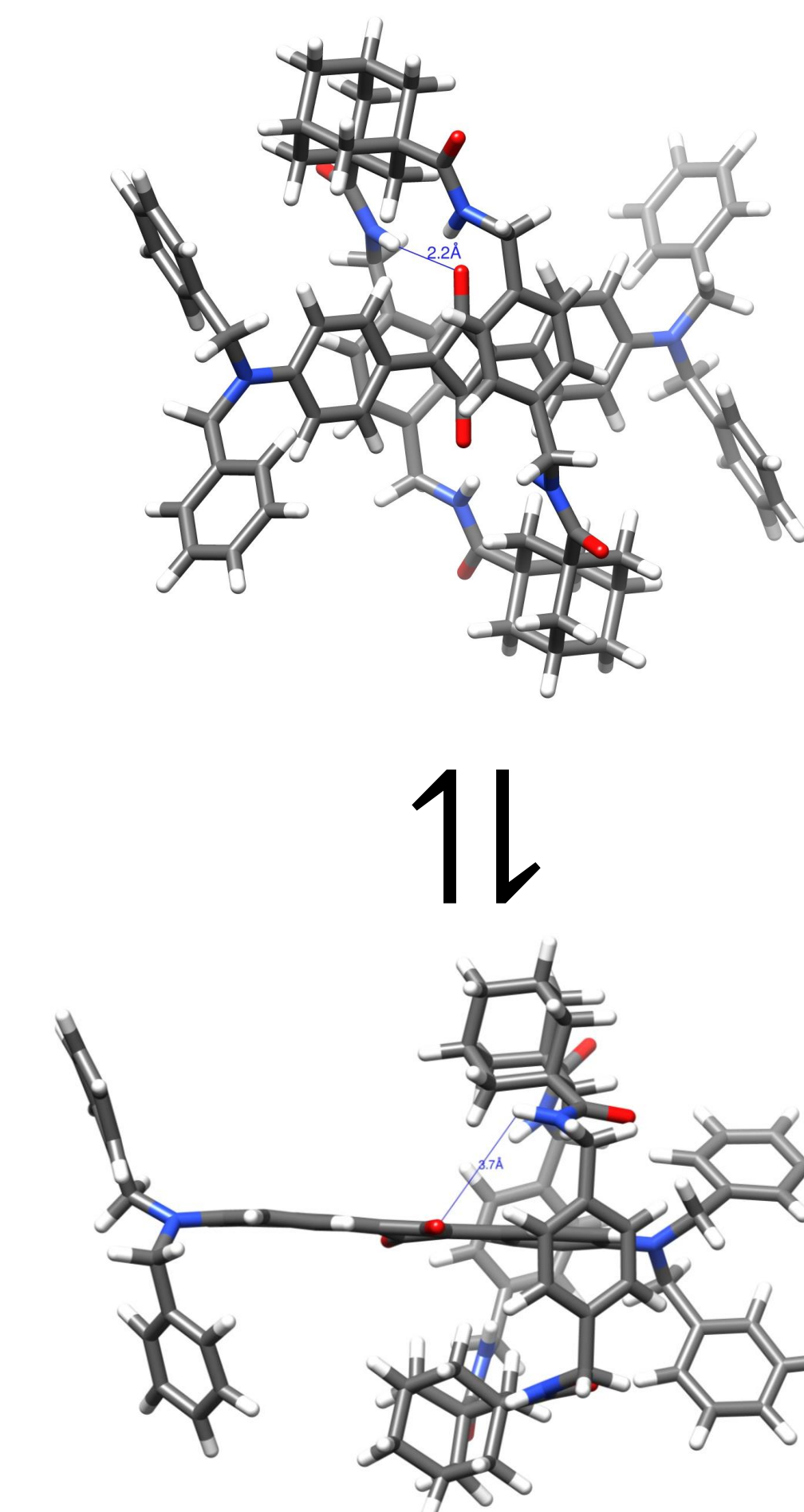


Figure 7- Visualization of the rotation of the squaraine dye within the adamantyl macrocycle

Conclusions

Our results along with previous experimental findings demonstrate that the isophthalamidyl and pyridinyl macrocycles are able to protect the squaraine dye from nucleophilic attack in solution. MD simulations show that over the course of the trajectory the squaraine dye does not slip out of the macrocycle often, leading to the observed stabilities in solution. However, the squaraine dye is able to rotate and slip out of the adamantyl macrocycle. These results are consistent with the NMR data and solution stability experiments performed by the Smith group². This proof of concept study aimed to determine if MD could be used to determine solution stability of squaraine rotaxane dyes. Our results indicate that a straightforward and theoretical treatment of these supramolecular systems is possible, and that the methods used in this study may be implemented as an effective and efficient way to design new rotaxane systems in the future.

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Acknowledgements

Funding was provided by the Concordia University Faculty Development Grant.