Non-Adiabatic Nanoreactor (NANR): A Novel Tool for in silico Photoreaction Discovery Applied to Woodward Hoffmann Ring Opening of Cis/Trans-3,4-Dimethylcyclobutene

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Light is a promising alternative to traditional reagents for synthesis due to its reduced environmental toxicity, ease of control, and lowered cost. Moreover, photochemisty's ability to create complex molecules and properties inaccessible through ground-state, thermal pathways adds to light's value in medicinal chemistry and organic synthesis. However, the immense dimensionality and lack of selectivity in photoreactions create an intractable number of possible pathways and outcomes. Novel computational tools are therefore required for fast, systematic high-throughput screening and design of optimal synthetic routes. A preliminary effort to address this issue is the development of the Non-adiabatic Nanoreactor (NANR): a simulation tool for automated, blackbox photodiscovery. In my study, I test NANR by examining the discrepancy between the theoretical stereospecificity and experimental non-stereospecificity of photochemical Woodward-Hoffmann (WH) ring-opening of cis/trans-3,4-dimethylcyclobutene. I then enhance NANR by developing a robust photoproduct yield prediction model. NANR identified 5 of 6 experimental WH products, proving initial disrotation then s-cis/s-trans isomerization to minimize steric hindrance. By applying 3 different models, I determined that running a combination of the Arrhenius and velocities models for 1000 femtoseconds generated the most accurate photoproduct yields with improvements of 52% & 66% for cis & trans, respectively. Applying cis ratios to a missing trans product raised the improvement to 96%. The demonstrated success proves that these models offer deeper insight for any photochemical reaction, paving the way for a future of rapid, green, low-cost chemical engineering, drug development, and explorations of theoretical photochemistry.

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