

Mechanistic and Regioselectivity Analysis on the Intra- and Intermolecular [2+2] Photocycloaddition Reactions

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1. Introduction

The [2+2] photocycloaddition of α,β unsaturated enones to alkenes leads to the formation of cyclobutane, which is a precursor for the synthesis of natural products. The major disadvantage of the photocycloaddition reactions is their low regioselectivity and/or strange regioselectivity-inversion in some reactions. The regioselectivity preference and the mechanism of these reactions have been a topic of great interest.

The [2+2] photocycloadditions of cycloenone to alkene have been widely investigated from mechanistic point of view. The mechanistic information on these reactions is obtained experimentally; nevertheless, modern computational studies are very rare. Computational chemistry serves as a good tool in predicting the reaction mechanism, regioselectivity preference or even locating the transition state of the reaction, which is impossible to locate experimentally.

2. Results and Discussions

Inversion in the regioselectivity of the intra- and intermolecular [2+2] photocycloaddition reactions was successfully elucidated by transition state (TS) analysis at various levels of calculation. The TS leading to the formation of biradical intermediate plays an important role in controlling the regioselectivity of the product. The computed trend agreed qualitatively with experiment. Single point energy calculation on semiempirical PM5 geometries is a perfect choice for

TS computation. The TS structures analysis showed that some electrostatic factors played a role in controlling the TS energies.

In the intermolecular reaction the main factor was the existence of hydrogen bonding. These factors drive the reaction to undergo the lowest energy route. Moreover, the deformation energies of the reactants are believed to play a main role in controlling the reaction products. It was found that the $\Delta E^{\text{def-hf}}$ of the enone sharply increases with the increment of the alkenes ring in the hh reactions, and sharply decrease in the ht reactions. The stationary points at the triplet potential energy surface were estimated using PM5 method of computation, which perfectly described the PES. Other methods exaggerate or underestimate some stationary point on the PES. The suggested mechanism for the intra- and intermolecular reactions involves a two-step process via the formation of biradical intermediate. The regioselectivity preference in the intramolecular reaction was also determined by the TS of the biradical producing step. The biradical intermediate analysis showed that the so-called "rule of five" has no impact on the regioselectivity preference.

3. Conclusions

Inversion in the regioselectivity of the inter- and intra-molecular [2+2] photocycloaddition reactions were successfully elucidated by transition state TS analysis at several levels of calculations. The computed trend agreed qualitatively with experiment. The TS structures analysis showed that some electrostatic factors played a role in controlling the energy of TS.