A Tale of Two Reactions: A Computational Study of Cyclopropyl Ring Opening Mechanisms Leading to 1,6-heptadiyne Isomers

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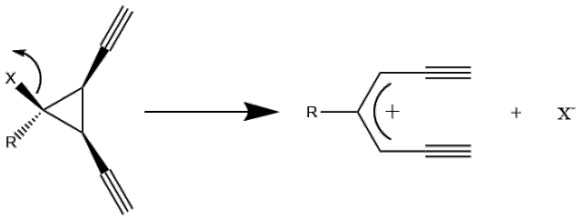
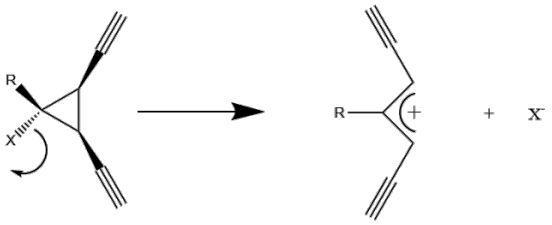
The energetics and reaction mechanisms of two cyclopropyl ring opening reactions (Scheme 1 and Scheme 2) were studied thoroughly using computational chemistry methods. Depending on the stereochemistry of the molecule and placement of the leaving group, the resulting 1,6-heptadiyne will be either an endo-endo or exo-exo isomer, due to the disroatatory nature of the reactions. The reactions were studied using Gaussian 03 and Gaussian 09, using both double- and triple-zeta basis sets with various DFT hybrid functionals. The effects of solvent, leaving group, and substituent group on the reaction energetics were also studied. The endo-endo isomer structure is oriented ideally to undergo a Bergman cyclization and form a tropylium diradical, whereas the exo-exo structure is not likely to undergo such a cyclization. Naturally-occurring diradicals are used commonly in cancer treatments because of their ability to strip hydrogens from DNA in cells, causing cell death. Accordingly, a major goal of this study was to determine whether the cyclopropyls would be viable as prodrugs to help treat cancer.



Scheme 1. *Endo-Endo Product Reaction*



Scheme 2. *Exo-Exo Product Reaction*