

Stereochemistry

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Regio and stereoselectivity in 1,3-dipolar cycloadditions: Activation strain analyses for reactions of hydrazoic acid with substituted alkenes

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1,3-dipolar cycloaddition reactions are versatile in organic synthesis, among others, because they can be used to form a wide range of compounds in only one experimental step. 1,3-dipolar cycloadditions constitute a type of reaction which a 1,3-dipolar molecule ("dipole") reacts with a dipolarophile molecule forming a five-membered heterocyclic cycloadduct. The stereoselectivity in 1,3-dipolar cycloaddition and Diels-Alder reactions favour the formation of the endo cycloadduct, although this is sterically less favourable with the bulkier groups located on the same side. In this study, we have quantum chemically analyzed 1,3-dipolar cycloadditions of hydrazoic acid HN_3 with various substituted alkenes $\text{H}_2\text{C}=\text{CHR}$ ($\text{R} = \text{CH}_3, \text{OH}, \text{OCH}_3, \text{NH}_2, \text{CN}$ and NO_2) using dispersion-corrected DFT at WB97XD/6-311++(d,p) level. The activation strain model (ASM) with energy decomposition analysis (EDA) were used to explore the reactivity, regio- and stereo-selectivity in the reactions. For a dipolarophile containing an electron donating group, the pathway involves the interaction $\text{HOMO}_{\text{dipolarophile}}\text{-LUMO}_{\text{dipole}}$, resulting in a 1,5-cycloaddition. On the other hand, when dipole reacts with a dipolarophile containing electron withdrawing groups, the interaction is $\text{HOMO}_{\text{dipole}}\text{-LUMO}_{\text{dipolarophile}}$ causing a low distortion of dipole fragment along the reaction coordinate. The energy difference between endo and exo transition states was attributed to the Pauli repulsion term of the interaction energy. In the reaction with nitroethene, mainly electrostatic and polarization terms of the interaction energy favouring the highest endo stereoselectivity was observed ($1.6 \text{ kcal mol}^{-1}$). The presence of substituent with multiple bonds (CN and NO_2), not only the electrostatic but the polarization term seem to lead to the preferential endo stereopreference.

Biography

Felipe de S Vilhena has completed his PhD in 2013, and after that has been dedicated to explore the the regio and stereochemistry of pericyclic reactions. He published four articles during his Doctoral period and has been writing and submitted some manuscripts using activation strain model and energy decomposition analysis to investigate the regio and stereochemistry of several 1,3-dipolar cycloaddition reactions.

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