

Inherent Conformational Preferences of the Reactants Control Their Transannular Diels-Alder Reactivity!

by

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Transannular Diels Alder reaction (TADA), a combination of both intramolecular and Diels-Alder reactions, is a powerful synthetic organic reaction mechanism used in synthesizing polycyclic compounds with high degree of chemo-, regio- and stereospecificity. TADA reactions occur in $(x+y+2)$ -membered triene macrocycles, which contain both the diene and the dienophile moieties, to form A.B.C $[x+6+y]$ type tricyclic compounds. The TADA reactivity of a series of 14-membered macrocyclic rings have been studied using the density functional B3LYP level of theory. The reactants and the transition states are capable of existing in different conformations. The key conformers of the transition states were studied at the B3LYP level. We have done force field parameters for the trienes, and performed detailed replica exchange molecular dynamics simulations to identify all possible isomers of the reactants. We established a linear correlation between the activation energies and the extent of sampling of the reactants in certain conformational states. In this presentation, we also will present the effect of the lengths of the linkers (3 to 5 methylene units) connecting the diene and dienophile units on the TADA reactivities.

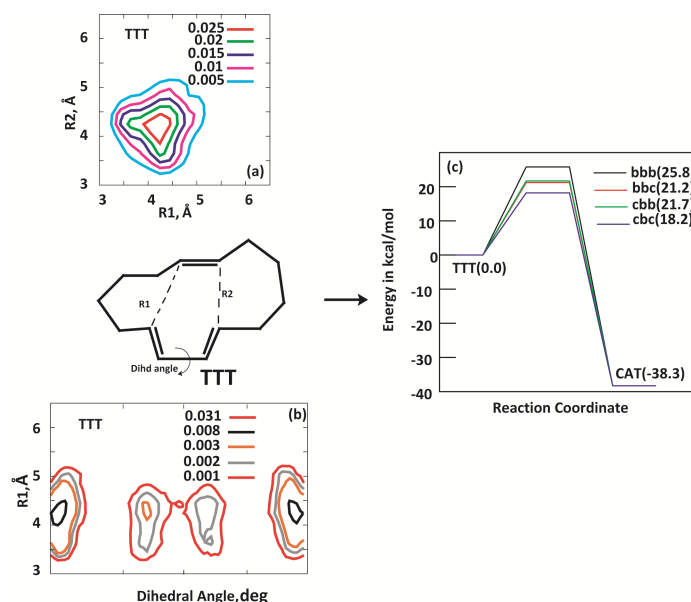


Fig: (a) Probability contours (a) with respect to the distances R1&R2, (b) the diene dihedral and the distance R1 and (c) energy profile of the TTT(C14) triene at B3LYP/cc-pVTZ level of theory.