

Investigation of 1,3-dipolar cycloaddition mechanism: which orbital is active?

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1,3-dipolar cycloaddition (1,3-DC) is a type of reaction that occurs between a 1,3-dipole and a dipolarophile yielding 5-membered heterocycles. It became very popular and important in organic synthesis due to its versatility, once there are many suitable types of 1,3-dipoles and dipolarophiles. Recently, much advance in asymmetric 1,3-DC has been accomplished, enhancing even more the interest in it [1]. Since its discovery in the late 19th century, studies focused on understanding the mechanism have been developed. Currently the proposal made by Huisgen is the most accepted by the scientific community: a concerted, often asynchronous, pericyclic cycloaddition [2], involving a symmetry-allowed $\pi^4 s + \pi^2 s$ six-electron transition state (TS) in which the extent of the reactivity of the 1,3-dipole is directly influenced by the frontier molecular orbitals (FMO). However, our observations indicate that not always a π -electron system is involved in the TS and σ non-bonded electrons can take relevant part in the reaction.

The aim of the present work is to correlate the orbital's symmetries of different 1,3dipoles with bond formation to ethene, as well as the energetic profile. The dipoles were divided into 3 groups: allyl-type centered on N; allyl-type centered on O; and allenyltype. Geometry optimizations and MO calculations of 1,3-dipoles were made with the post-Hartree-Fock MP2 method and the 6-31G(d) basis set. Natural bond orbital (NBO) analysis was employed to determine the structure with major contribution to the hybrid and to describe the symmetry of the FMO between σ (orbitals in the molecular plane) and π (out of plane orbitals). Initial complexes (IC), TS and products were optimized. Frequencies were calculated to characterize the nature of the stationary points. Kinetic and thermodynamic data are shown in **Scheme 1**.

For allyl cases, π orbitals are involved in bond formation. The FMO related with adequate symmetries are HOMO/LUMO, except for the dipoles with less favorable energetic profiles (nitro compound and ozone). In those cases, the LUMO shows the right π symmetry, while HOMO-2 and HOMO-3, less accessible electronic states, have the right symmetry. For azomethine imine, azimine and nitrosimine, π interaction between atoms 1 and 3 of the dipole was observed. Those dipoles also showed the lowest activation barriers and highest negative values of ΔE and ΔG , indicating a high instability of the starting material.



Scheme 1. Kinetic and thermodynamic data for 1,3-DC of different dipoles at 298 K.

Key-words: 1,3-dipolar cycloaddition, 1,3-dipole, transition state, symmetry. **Support:** This work has been supported by FAPERJ, CNPq and PPGQ-UFF.

References:

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