

Diastereoselectivity in Diels-Alder Reactions: a Theoretical Chemistry Approach

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Diels-Alder reaction is a well-know process discovered by Diels and Alder almost 100 years ago which is pivotal in organic synthesis. It is at the basis of many fundamental processes, like de-aromatization, as well as in the synthesis of specific drugs. One important point is that the cycloaddition can give rise to endo and/or exo forms, which is related to possible different stereochemistry. The possibility of controlling the endo/exo ratio is thus pivotal in organic synthesis.

Such selectivity can be controlled in different ways, here we will discuss two interesting possibilities: (i) using specific solvents; (ii) performing the reaction at high-pressure.

We begun a theoretical study to clarify this aspect using a combination of accurate but fast density functional theory calculations and molecular dynamics simulations. Both classical, polarizable and QM/MM approaches were used at this end.

In particular, we will show how QM/MM simulations can explain on a simple Diels-Alder reaction how the intermolecular interactions can be crucial in selecting the reaction pathways. This coupled with a correct description of transition state energies (and more importantly the endo/exo energy difference) will be an important starting point to study a wider classes of Diels-Alder and, more in general, cycloaddition reactions.

References:

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