

DFT CALCULATIONS ON AZIRIDINES WITHIN THE SUPERMOLECULE APPROACH

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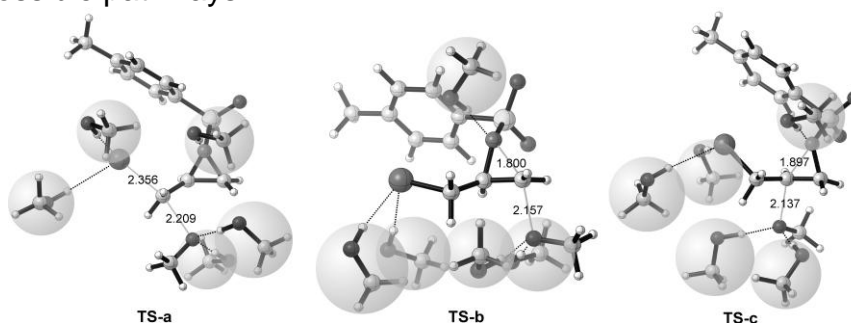


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Aziridines are useful synthetic intermediates for the preparation of a variety of ring-opened and ring-expanded amines. The key element in the design of a strategy based on the use of aziridium intermediates is the control of regio- and stereoselectivity in ring opening, which is dependent on the substrate, the type of nucleophile and the solvent environment. All three factors have been studied by means of DFT-based computational studies.

The difference in reactivity between activated and non-activated aziridines with respect to sodium methoxide in methanol was analyzed. Since nucleophilic substitution reactions are known to be influenced by reaction conditions, the pathways were modeled with a proper solvent environment. As explicit solvent interactions are present, discrete solvent molecules were placed around the chemically active species to form a so-called "supermolecule" structure. Furthermore, the energetics that arise from this explicit solvent approach were critically evaluated. It was found that for the chemical problems at hand, where the solvent is able to make explicit hydrogen bonds with the reacting substrate, the supermolecule approach gives a fair representation of the molecular environment. On the other hand, explicit accounting for the methanol environment was found to be essential to acquire an adequate representation of the free energy surface and the competition between the possible pathways.¹



Furthermore, the experimentally observed solvent-dependant reactivity of aziridines toward different nucleophiles was investigated. DFT calculations were employed to elucidate the extraordinary selective formation of aziridines in dimethylformamide and azetidines in acetonitrile. The difference in the observed selectivity in DMF and MeCN was unexpected, since both solvents are polar and aprotic, and have very similar dielectric constants. However, different close-packing of the nucleophiles, the nucleophile and the bicyclic aziridinium intermediate by DMF and MeCN was found to be very important for the extent of the nucleophiles mobility and attack capacity as well as the nucleophile capacity to leave.²

¹H. Goossens, K. Vervisch, S. Catak, S. Stanković, M. D'hooghe, F. De Proft, P. Geerlings, N. De Kimpe, M. Waroquier and V. Van Speybroeck, *J. Org. Chem.* **2011**, *76*, 8698.

²S. Stanković, H. Goossens, S. Catak, M. Tezcan, M. Waroquier, V. Van Speybroeck, M. D'hooghe and N. De Kimpe, *J. Org. Chem.* **2012**, *77*, 3181.