Modeling chemical reaction mechanisms in nonaqueous solution by integral equation theory

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The prediction of thermodynamic and kinetic parameters of chemical reactions in solution is an important task in computational chemistry. Particularly challenging are situations where the commonly employed dielectric continuum models of solvation such as PCM (polarizable continuum model) fail due to the lack of directional solute-solvent interactions or due to the properties of nondipolar (quadrupolar or higher, or fully apolar) solvent species which cannot be adequately described. As an alternative, we have developed the embedded cluster reference interaction site model (EC-RISM) approach which combines statistical-mechanical 3D-RISM integral equation theory and quantum-chemical calculations in a self-consistent manner [1,2]. As a result of these calculations, we obtain the solvent-induced component of the free energy surface governing chemical reaction pathways along with the electronic polarization. Taken together, these data can be used to characterize reaction mechanisms quantitatively.

As an example, we here show the capabilities of the EC-RISM approach by studying an organocatalytic Michael addition in benzene and hexafluorobenzene solutions for which it has been shown experimentally that the two relatively similar solvents exhibit different stereoselectivities [3]. We show that the computed solvent distribution functions agree well with costly quantum-chemical calculations with ad hoc placement of single solvent molecules and that the resulting free energy data of the transition states correspond to observed product ratios.

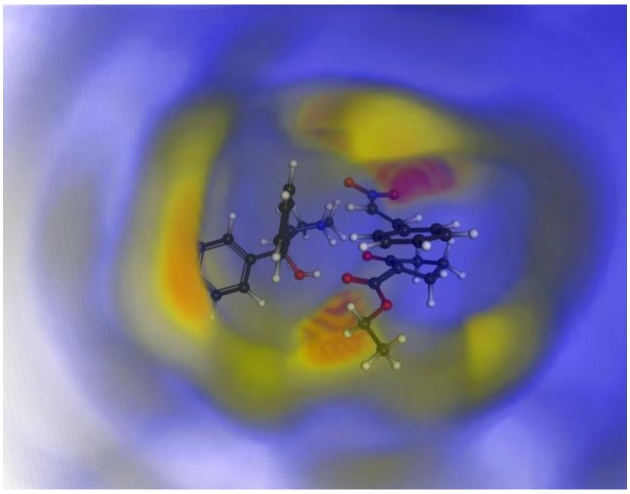

Fig. 1. Distribution of carbon atoms of hexafluorobenzene around the putative transition state of an organocatalytic Michael addition [3].

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[3] A. Lattanzi, C. De Fusco, A. Russo, A. Poater, L. Cavallo, *Chem. Commun.* **2012**, *11*, 1650-1652.