559f Molecular Modeling of Catalysis in Molecular Square Nanocavities

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In recent years, self-assembly techniques have yielded a growing number of large molecules that have well-defined nanometer-sized cavities within them. For example, "molecular squares" can be synthesized with $Re(CO)_3Cl$ corner units linked by dipyridyl organic groups. Reactant molecules bind within the cavities of such squares in solution, and this can be exploited, for example, to catalyze acyl transfer reactions. A wide variety of squares can be synthesized, starting from a series of similar building blocks. We are developing molecular modeling techniques to select and design the most appropriate nanocavity for a particular reaction, as well as to elucidate the behavior of such systems.

To test the simulation force fields, we first determined the conformations adopted by representative molecular squares and compared the results to experimental, wide-angle, solution X-ray scattering data. Quantum mechanical calculations were performed to determine some aspects of the force field, with other parameters taken from the literature. Simulated annealing identified minimum-energy structures that compare well with the X-ray data, providing confidence in the force field. Building on this approach, we can determine the free energy difference between the free and bound states of a catalyst-reagent complex using molecular dynamics simulations in which both reagent and catalyst are completely flexible. From the free energy differences, we can calculate binding constants and compare them with experiment. In the catalysis of the acyl transfer reaction, the molecular square (catalyst) must flex in order to optimally bind the various transition-state analogues tested. Such "induced fit" behaviour is characteristic of enzymes, but rare in artificial systems.