Observing invisible machines with invisible light: The mechanics of molecular machines

Panman, M.R.

Citation for published version (APA):
Summary

Over the past few decades, chemists have designed and constructed a large variety of artificial molecular machines. Understanding the fundamental principles behind motion at the molecular scale is key to the development of such molecular machines. Motion at the molecular level is very different from that in the macroscopic world: molecular devices have to operate in constant thermal noise and must therefore make use of the specificity of chemical reactions or external stimuli to produce work. In this thesis we have investigated how non-covalent interactions between the components of molecular machines govern their operation. The principal technique we use to investigate mechanics at the molecular level is time-resolved vibrational spectroscopy.

The molecular machines studied in this thesis are based on the so-called rotaxane architecture. A rotaxane is a supramolecular system comprising a ring-like component (macrocycle) mechanically interlocked onto an axle-like component (thread). The thread is capped at both ends with bulky stoppers, which prevent the ring from slipping off. The axle is usually functionalized with one or more chemical groups which form points of interaction (called stations) to which the macrocycle can bind. The most simple rotaxanes contain a single-station thread. In such wheel-and-axle systems the inter-component motion is restricted to the circumrotation of the ring around the axle (pirouetting). The next level of complexity in rotaxane design is the incorporation of a second station, the system is then referred to as a molecular shuttle. In such a system, the ring can be made to translate from one station to the other (shuttling). The wheel-and-axle and molecular shuttle make it possible to specifically investigate the rotational and translational motion that are being addressed in such molecular machines.

We use a photochemically-switchable two-station molecular shuttle, the components of which are held together by hydrogen bonds between amide and imide groups. Shuttling motion from one station to the other is initiated by exciting the second station with a short pulse of ultraviolet (UV) light. The CO groups of the macrocycle and stations are spectrally separated and can therefore be individually monitored with time-resolved infrared spectroscopy during the shuttling (chapter 3). Detailed knowledge of the photochemical steps and the infrared signature of the molecular shuttle provided us with the means to unravel its operation mechanism (chapter 4). By measuring the temperature dependence of the shuttling rate, we
determined that the activation enthalpy for shuttling matches the energy required to break four hydrogen bonds. This suggests that the rate limiting step is the separation of the macrocycle from the initial station. We also find a negative entropy of activation which suggests that a certain amount of ordering is necessary for the ring to escape. The next step in the operation mechanism is the translational motion of the macrocycle over the thread. To investigate this motion, we varied the length of the axle between the initial and final station. The dependence of the shuttling rate on this length was found to be well described by a biased one-dimensional random walk. The bias was, unexpectedly, in favor of the initial station. The operation mechanism of the molecular shuttle can be compared to a game show where the macrocycle is a contestant and the thread an obstacle course. All the contestants begin at one end of the course, the initial station. The object of the game is to reach the final station. As the race starts (initiated by the UV-laser pulse), the contestants try to scramble up a slippery hill, which represents the enthalpy of activation. The few contestants that make it to the top find they need to pass through a hoop to reach the other side. Maneuvering through the hoop requires the participant to arrange their body in a specific manner, which represents the free-energy cost caused by the loss in entropy in the transition state. Those that managed to squeeze through the hoop find themselves in a maze which either leads to the end, the final station, or back towards the start. In the latter case, the contestants slip right back to where they started and have to begin the race from scratch. The maze represents the random walk the macrocycle makes when traveling over the thread, and the game being a cruel one, means that more paths through the maze lead back to the beginning than to the end. If by chance a contestant reaches the end, they stay there, exhausted and content to have made it. This analogy is meant to show that, unlike microscopic machinery, the motion of molecular devices is intrinsically random and that a large uncertainty exists in the timing of their operation.

During our experiments, we found, quite by accident, that water strongly accelerates the rate of translational and rotational motion of a macrocycle in a molecular shuttle and wheel-and-axle, respectively (chapter 5). Other protic liquids had a smaller or even contrary effect on the rate of operation. From the time-resolved infrared spectra of the shuttle we deduced that water interacts directly with the CO groups of the components. The temperature dependence of the operational rates of both devices revealed that addition of water does not decrease the enthalpy of activation (the height of the slippery hill) but increases the number of successful attempts at crossing the free-energy barrier. Water thus effectively decreases the uncertainty in the operation of the molecular devices. From the above observations, the following molecular picture of how water lubricates molecular machines emerges. Upon breaking the hydrogen bonds between the macrocycle and the first station, the NH and CO groups of both components are left dangling. Because of its small size and fourfold hydrogen bonding capability, water is able to effectively stabilize these dangling groups and reduces the probability that the macrocycle rebinds to the initial station. In view of the importance of water for the operation of biomolecular machines, studies of how water affects the mechanics of artificial molecular machines are of direct relevance for understanding the role of water in biological systems.

We investigated whether isotopic substitution of the NH groups involved in the hydrogen-bonded components of molecular machines would influence their rate of operation (chapter 6). We measured the rate of operation between the isotopologues of a molecular shuttle
and wheel-and-axle. We found that rotational motion occurred at a higher rate in the deuterated wheel-and-axle than in the protonated variant. However, for the translational motion of the molecular shuttle no measurable difference was found. These apparently contradictory results can be explained by the difference in zero-point vibrational energies between isotopologues and solvent interactions with the components which reduce these differences. The observation of an isotope effect constitutes definitive proof that the rate determining step of the pirouetting and shuttling motions of the macrocycle is breaking of the hydrogen bonds between the macrocycle and the station to which it is bound.

In chapter 7 we demonstrate how 2DIR spectroscopy can be used to determine the conformation of a supramolecular catalyst. The system is composed of two CO ligands, one hydride, and a bi-dentate phosphine ligand coordinated to a rhodium ion. The catalyst is fluxional, and can therefore adopt two rapidly interchanging conformations in solution. We use two-dimensional infrared spectroscopy (2DIR) to determine the spatial orientation of the CO and the hydride ligands in both conformations of the catalyst. We find that in one of the conformations the angle between the ligands deviates significantly from what would be expected. Using the results of DFT calculations, we can ascribe this discrepancy to an attractive Van der Waals interaction between the CO ligands and the bi-dentate phosphine ligand. Furthermore, we see that 2DIR is a suitable method for capturing rapidly evolving conformational changes in solution.

In the last chapter, we apply this method to study the dynamics of a molecular machine. We used the time-resolved 2DIR spectrum of the CO groups in each of the components of the molecular shuttle along with complementary DFT calculations to investigate the time-dependent conformation. We found that the macrocycle adopts a chair-like configuration when it is bound to the initial station, and a boat-like structure when it resides at the final station. We also confirmed the positional discrimination of the macrocycle for the initial station when the shuttle is in the resting state, and the final station when it has switched. In order to obtain structural parameters of the initial state of the molecular shuttle, we devised a new method capable of selectively measuring the 2DIR spectrum of a specific part of a molecular system. This method provides an elegant and widely applicable technique to unravel congested 2DIR spectra.