Molecular Devices

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Controlled Hydrogen-Bond Breaking in a Rotaxane by Discrete Solvation**

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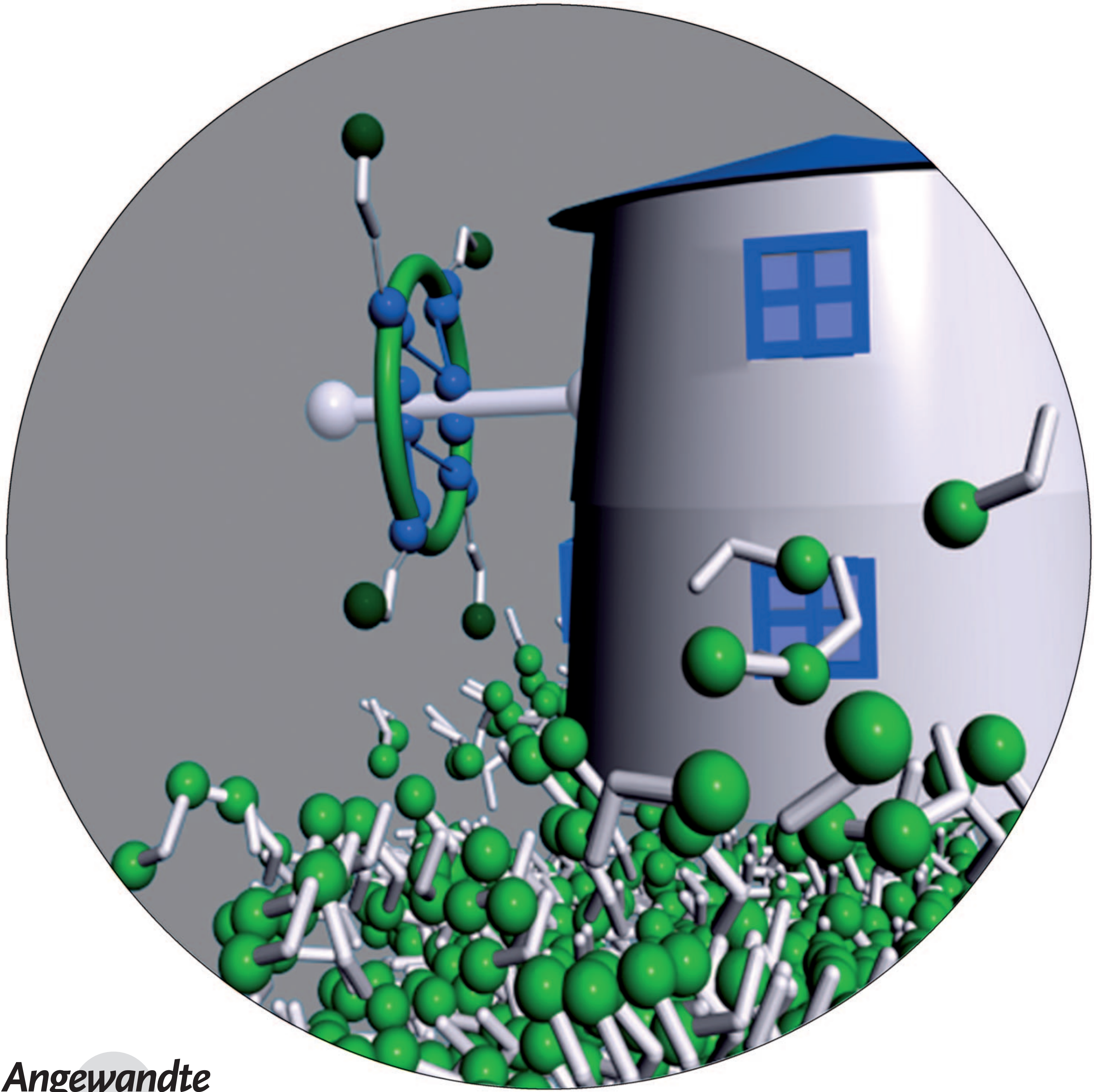

Mechanically interlocked molecules are appealing nanoscale structures for the development of artificial molecular machinery components, such as switches,[1–7] actuators,[6] ratchets,[8–10] and motors.[11–14] Well-known examples are [2]rotaxanes,[14] which are composite molecular systems consisting of a macrocycle mechanically trapped onto a linear thread by bulky end groups ("stoppers"). The ability to reversibly control the relative orientation and position of the macrocycle with respect to the thread[1–14] is the key to their function. The way to induce large-amplitude internal motions is by influencing the non-covalent binding interactions between macrocycle and thread. However, understanding how such processes occur is very difficult to probe experimentally because bulk solvation involves many solvent molecules that can adopt numerous different arrangements of similar energies. Herein we demonstrate that these interactions can be addressed controllably and that a macrocycle can be unlocked from a thread by adding solvent molecules to a single [2]rotaxane one at a time.

The rotaxane studied consists of an amide macrocycle mechanically locked onto a succinamide-based thread by two bulky stoppers at either end (rotaxane **1**; Figure 1) and held in position by a network of hydrogen bonds. To eliminate environmental contributions, we started from isolated, internally cooled, molecular systems under collision-free conditions by seeding rotaxane **1** with laser desorption[15–17] into a supersonic expansion of argon mixed with methanol vapor. In the expansion, a distribution of rotaxane–methanol clusters formed that were probed with IR spectroscopy using an IR–UV ion-dip approach.[18–20] Methanol can act as a hydrogen-bond donor and acceptor, and may therefore form hydrogen bonds with either the free C=O groups of the macrocycle or compete with the intramolecular hydrogen bonds between thread and macrocycle. Microsolvation[21–24] thus enables a quasi continuous tuning of the hydrogen-bond interactions between thread and macrocycle to be achieved. As the frequencies of vibrational modes, such as amide A (NH stretch), amide I (C=O stretch), and amide II (NH bend) are highly sensitive to hydrogen-bond interactions,[25] IR spectroscopy provides a direct measure of (changes in) the interactions between thread and macrocycle, and between rotaxane and solvent molecules.[26,27] Herein, the mid-infrared region (1400–1750 cm^{-1}) was employed to probe the decoupling of the macrocycle from the thread (see Supporting Information for experimental details).

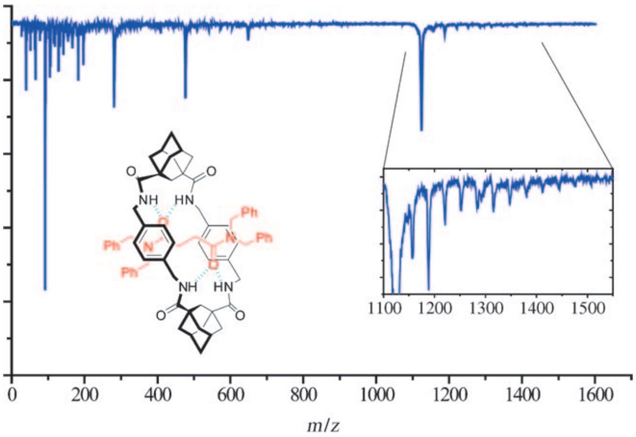

Figure 1. Photoionization mass spectrum of rotaxane **1** after two-photon ionization at 262 nm. The peak at m/z 1124 is of the molecular ion of the intact rotaxane. A progression of peaks is visible at higher masses (inset) with a regular spacing of 32 a.m.u. associated with rotaxane **1**-(MeOH)$_n$ clusters.

The two-photon ionization mass spectrum of rotaxane **1** and its solvent clusters, rotaxane **1**-(MeOH)$_n$ with n up to 12, obtained at 37550 cm^{-1} (the maximum of the unresolved UV excitation spectrum) is shown in Figure 1. By monitoring the signal at the mass of each of the rotaxane **1**-(MeOH)$_n$ clusters ($n = 1$–6) as a function of the IR wavelength, we obtained IR spectra for each of the clusters. The IR spectrum of the bare rotaxane **1** is depicted in Figure 2a. In the amide I region, two strong peaks are present that were assigned to the C=O stretch of free carbonyl groups in the macrocycle (C=O$_{\mathrm{mc}}$, 1677 cm^{-1}), and the C=O stretch of carbonyl groups in the thread hydrogen-bonded to NH groups of the macrocycle (CO$_{\mathrm{thr}}\cdots$HN$_{\mathrm{mc}}$, 1620 cm^{-1}). In the amide II region, a single peak is observed at 1525 cm^{-1} associated with the NH bend of hydrogen-bonded NH groups in the macrocycle. IR absorption experiments on the isolated thread and macrocycle show that the amide I frequency of the free C=O of the thread and the amide II frequency of the free NH of the macrocycle are 1660 and 1504 cm^{-1}, respectively.[27] The absence of bands in the spectrum shown in Figure 2a that have an appreciable intensity at these frequencies thus indicates that conformations with free C=O groups in the thread or free NH groups in the macrocycle are not abundant under our experimental conditions.

This conclusion is confirmed by calculations on the conformational structures and energy minima of rotaxane **1** with a procedure that combines molecular dynamics, Monte

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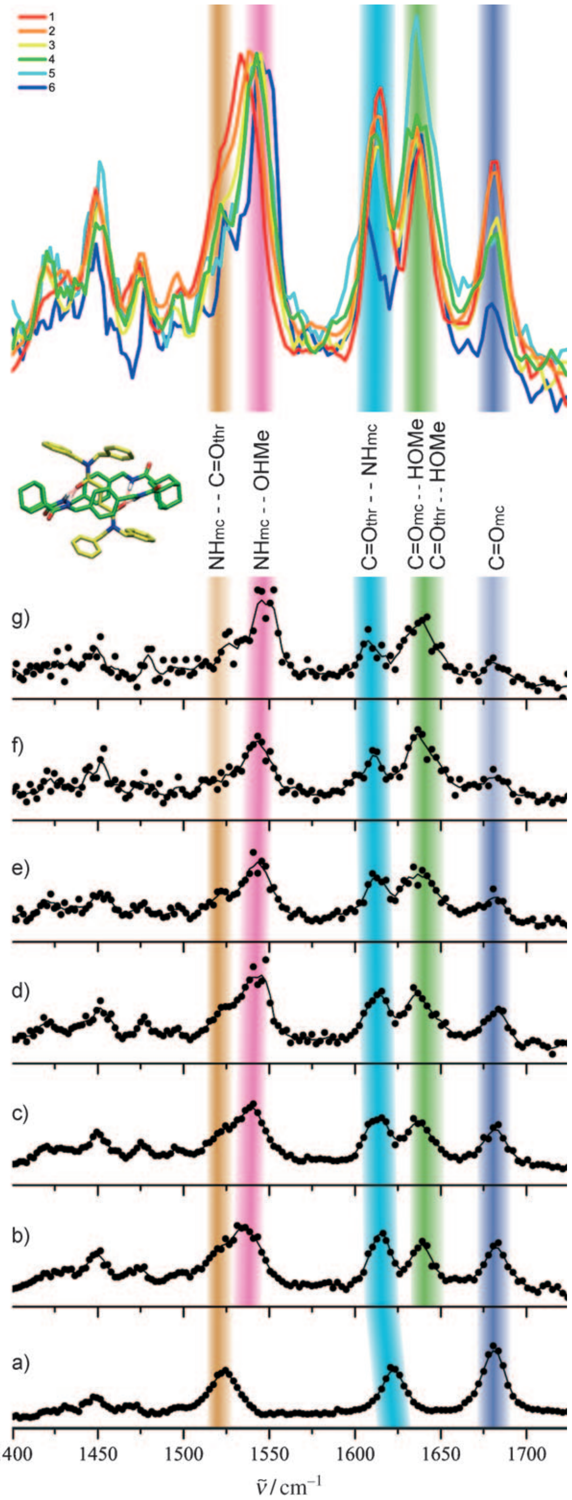

Figure 2. IR spectra of rotaxane **1** and rotaxane **1**-(MeOH)$_n$ clusters detected by IR–UV ion-dip spectroscopy. a) Spectrum of the bare rotaxane, b–g) spectra of clusters with one (b) to six (g) methanol molecules. Colored bars indicate the vibrational bands, where mc = macrocycle, thr = thread. Blue: free $C{=}O_{mc}$ stretching mode, green: $C{=}O_{mc}\cdots HOMe$ and $C{=}O_{thr}\cdots HOMe$ stretch, cyan: $C{=}O_{thr}\cdots HN_{mc}$ stretch, pink: NH bend of $NH_{mc}\cdots OHMe$, orange: NH bend of $NH_{mc}\cdots O{=}C_{thr}$. Upper panel: overlay of the same IR spectra normalized on the intensity of the $NH_{mc}\cdots OHMe$ band. Numbers in color scheme indicate number of MeOH molcules.

Carlo search, and geometry optimization (see the Supporting Information for details). These show that geometry optimization leads to three different classes of minima that differ primarily in the number of internal hydrogen bonds (4, 2, or 0). Within each class, the geometries vary by and large in the orientation of the phenyl rings of the thread, and have fairly similar energies. Therefore, only the relative energies of the lowest-energy geometry within each class are given in Figure 3.[28] The most stable class, I, has two sets of bifurcated hydrogen bonds between thread and macrocycle; conformations in class II have two single hydrogen bonds owing to the rotation of one or more amide groups of the macrocycle, and for the least-stable class, III, thread and macrocycle are not connected at all by internal hydrogen bonds (Figure 4a). The presence of only three peaks in the 1700–1500 cm^{-1} region is therefore in perfect agreement with the prediction that primarily class I conformations are present in our molecular beam.

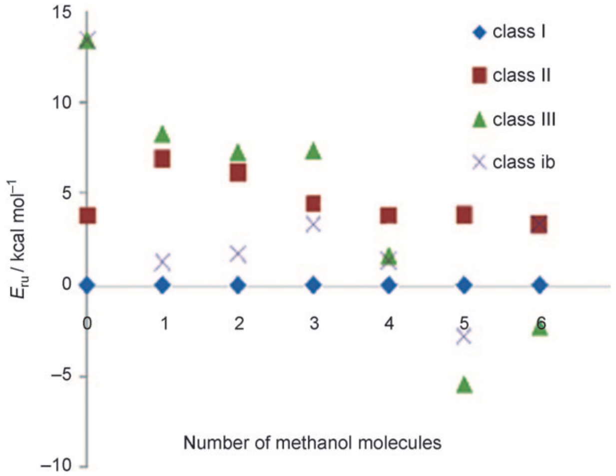

Figure 3. Relative energies E_{rel} of classes of isolated rotaxane conformations and of rotaxane conformations solvated by up to six methanols with respect to most stable class I conformation. The various classes are distinguished by the number of intramolecular hydrogen bonds between thread and macrocycle (4 for class I, 2 for class II, and 0 for class III and ib conformations).

The IR spectrum of the complex of rotaxane **1** and one single methanol solvent molecule is shown in Figure 2b. Comparison with the spectrum of the non-solvated system (Figure 2a) reveals a number of distinct changes. In the amide I region, the $C{=}O_{mc}$ peak at 1677 cm^{-1} remains at the same position, but its relative intensity is reduced. A new peak appears at 1635 cm^{-1} that is assigned to the C=O stretch of one of the carbonyl groups in the macrocycle hydrogen-bonded to methanol ($C{=}O_{mc}\cdots HOMe$). The hydrogen bond between methanol and macrocycle indirectly affects the hydrogen bonds between thread and macrocycle,[27,29] and the $CO_{thr}\cdots HN_{mc}$ stretch is accordingly shifted to lower frequency.[30] Methanol clustering also has a striking effect on the amide II region. The peak associated with the NH bend of the macrocycle remains at the same position as in the bare rotaxane (1525 cm^{-1}), but the most prominent feature is now

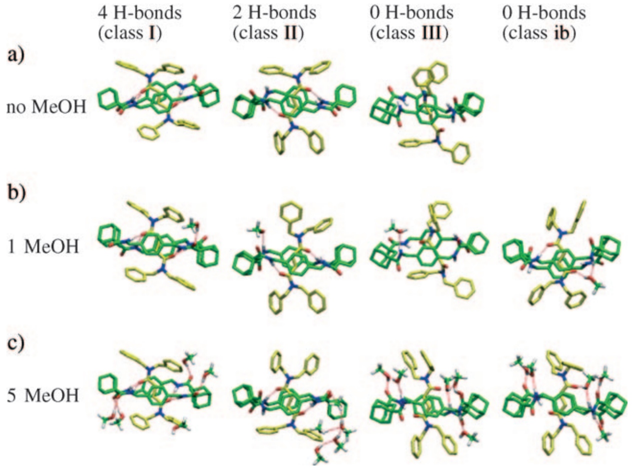

Figure 4. Structure of rotaxane **1** under a) non-solvated, b) monosolvated, and c) pentasolvated conditions for class I, II, III, and ib conformations. (For an animated version of the changes that are induced in conformation and intramolecular hydrogen bonding upon stepwise solvation, see the Supporting Information.)

a peak shifted by about 10 $\mathrm{cm^{-1}}$ to higher frequencies. This peak is assigned to the NH bend of the macrocycle with methanol attached to NH ($\mathrm{NH_{mc}\cdots OHMe}$), with methanol in this case acting as a hydrogen-bond acceptor. The new C=O stretch and NH bend peaks imply that there are two types of rotaxane–methanol conformations present in the molecular beam: one that retains the two bifurcated hydrogen bonds, and one in which one or more hydrogen bonds between thread and macrocycle are broken.

Upon further addition of methanol molecules (Figure 2 b–g), the IR spectrum of each rotaxane **1**-$(\mathrm{MeOH})_n$ cluster is subject to systematic changes, albeit that these changes now manifest themselves predominantly as changes in the relative intensities of vibrational bands, and only to a minor extent in their positions (Figure 2, upper panel). Each additional methanol molecule reduces the peak intensity of the free C=O stretch of the macrocycle and increases the intensity of the $\mathrm{C{=}O_{mc}\cdots HOMe}$ band, in line with the decreasing number of free C=O groups in the macrocycle. At the same time, the intensities of the C=O and NH bands associated with vibrations of groups involved in hydrogen bonds between thread and macrocycle decrease steadily. This feature indicates that the population distribution over class I and non-class I rotaxanes gradually shifts in favor of the latter one.

Although each additional methanol molecule gradually changes the appearance of the IR spectrum, by the time rotaxane **1** is solvated with five methanol molecules (Figure 2 f), the spectrum has become fundamentally different. In fact, the relative intensities of the marker bands discussed above demonstrate that in such complexes the macrocycle is effectively not locked to the thread; that is, there are no longer hydrogen bonds between thread and macrocycle to hold the macrocycle in place. This effect is manifested most noticeably in the amide II region, where the peak at 1525 $\mathrm{cm^{-1}}$, associated with the NH bend of NH groups in the macrocycle that are hydrogen-bonded to C=O groups in the thread, disappears in the pentasolvated spectrum. The absence of intramolecular hydrogen bonds between ring and thread is confirmed by the decrease of the $\mathrm{CO_{thr}\cdots HN_{mc}}$ and the concomitant increase of the $\mathrm{C{=}O_{mc}\cdots HOMe}$ carbonyl stretching peaks. Remarkably, we find that the relative intensity of the latter peak still increases for $n>4$ clusters when all C=O binding sites on the macrocycle are occupied. IR spectra of methanol clusters of the separate thread and macrocycle (see Supporting Information) show that the C=O stretch of hydrogen-bonded carbonyl groups in the macrocycle ($\mathrm{C{=}O_{mc}\cdots HOMe}$) and thread ($\mathrm{C{=}O_{thr}\cdots HOMe}$) appear at about the same frequency (ca. 1635 $\mathrm{cm^{-1}}$). The spectra in Figure 2 therefore strongly suggest that methanol complexation of carbonyl groups in the thread is an additional solvating mechanism that becomes important for larger clusters.

Our experiments unambiguously show that conformations in which the intramolecular hydrogen bonds that originally linked the macrocycle to the thread are broken have become dominant for rotaxane **1**-$(\mathrm{MeOH})_n$ clusters with $n \geq 4$–5. At the same time, the IR spectra of the larger clusters show that the intensity of the $\mathrm{C{=}O_{mc}}$ and $\mathrm{CO_{thr}\cdots HN_{mc}}$ carbonyl stretch bands does not completely disappear. Under our experimental conditions other types of conformations still appear to be present in the molecular beam, albeit in minor concentrations, which implies that the energy differences between the various solvent binding configurations are small. As shown below, these conclusions are confirmed by calculations.

The experimentally observed unlocking of the macrocycle is reflected in the calculated stabilities of rotaxane **1**-$(\mathrm{MeOH})_n$ clusters for the three different classes of rotaxane conformations. Figure 4 b and c show the lowest-energy conformation of the mono- and pentasolvated clusters, respectively, for each of these classes. In the monosolvated class I cluster, methanol binds to one of the four free C=O groups in the macrocycle, leaving the intramolecular hydrogen bonds intact. In contrast, for class II and III conformers, methanol is first hydrogen-bonded to one of the free NH groups of the macrocycle, in agreement with the higher stability of the NH···OHMe bond compared to the C=O···HOMe bond by about 2 $\mathrm{kcal\,mol^{-1}}$. Apart from these configurations where methanol binds either to the thread or the macrocycle, the calculations show that it can also be bound in a configuration in which it forms a bridge between the NH of the thread and the C=O group of the macrocycle, a configuration designated in the following as class ib. The class I conformation for the rotaxane–$(\mathrm{MeOH})_1$ cluster is energetically favored over class II and III, with class ib being only slightly higher in energy than III (Figure 3), and it is thus expected to be present as well. This conclusion perfectly reproduces the experiment, in which two conformations are observed, one with two bifurcated hydrogen bonds, and one in which at least one hydrogen bond between thread and macrocycle is broken.

Solvation proceeds in a straightforward manner up to the tetrasolvated cluster. For class I conformations, methanol binds to the free C=O groups of the macrocycle; for class II it binds to the previously added methanol, forming a methanol drop attached to one of the NH groups of the macrocycle, whereas for class III, binding occurs to one of the remaining free NH groups of the macrocycle. For class ib conformations, one methanol forms a bridge between the macrocycle and the thread. For steric reasons, no conformations are found with more than two methanol molecules bridging macrocycle and thread. All structures are shown in the Supporting Information, Figure S1.

Most importantly, the calculations predict that for class III, another stable configuration is possible after adding four methanol molecules. In this configuration two methanol molecules link to each other and form a $C{=}O_{mc}\cdots HO\cdots HO\cdots HN_{mc}$ bridge between an NH and C=O group on opposite sides of the macrocycle (Figure 4c). For the tetrasolvated cluster, these conformations have about the same energy as class I conformations, but they become the most stable species for larger clusters with increasing energy differences (Figure 3). This result is in excellent agreement with our experimental observations that reveal that after adding five and more methanol molecules to rotaxane **1**, macrocycle and thread have become independent moieties and are no longer coupled by intramolecular hydrogen bonds.

In summary, the present study has shown that it is possible to gain detailed control over intramolecular interactions in a prototypical mechanically interlocked molecular assembly. By adding one solvent molecule at a time to the bare molecular system, we have induced conformational changes that uncouple the separate components from each other. Disengaging the macrocycle from the thread is an essential step in functions that rely on influencing the equilibrium between the various co-conformations by external stimuli. A similar control over these rotational and translational motions, as demonstrated herein for binding interactions, that allows molecular motion to be probed in the gas phase has therefore now come within reach.

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