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# Stiff, and Sticky in the Right Places: Binding Interactions in Isolated Mechanically Interlocked Molecules Probed by Mid-Infrared Spectroscopy

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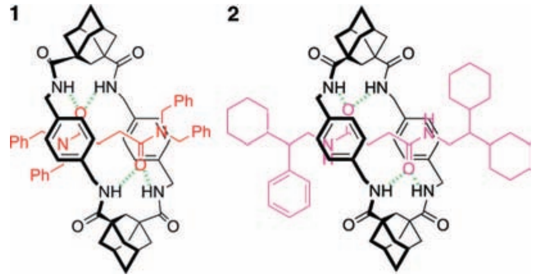
Mechanically interlocked molecules are promising structures for realizing the concept of artificial molecular machinery.[1] Well-known examples are hydrogen-bonded [2]rotaxanes,[2] molecular systems that consist of a macrocycle locked onto a thread by hydrogen bonds and trapped by two bulky stoppers. The unique advantage these architectures offer is that the large-amplitude submolecular motions of macrocycle with respect to thread can be relatively easily controlled by manipulation of the hydrogen bond interactions. To fully exploit the potential of these molecules and for the design of molecules with improved functionality, a full elucidation and characterization of their intrinsic structural properties and intercomponent interactions is mandatory. High-resolution spectroscopy on isolated molecules would be the natural approach to obtain this information, but has so far remained out of reach for representative multicomponent systems of interest—or for that matter for any realistic supramolecular system—because of their size and complexity. Here we report on the first gas-phase IR spectroscopic studies of isolated [2]rotaxanes, and their constituting threads and macrocycles, that provide such a detailed picture.

***Chart 1.*** Chemical Structure of Rotaxane **1** and **2**



The rotaxanes studied consist of an adamantalic amide macrocycle that is mechanically locked onto a succinamide-based thread. The macrocycle is held in position by four intramolecular hydrogen bonds, while two bulky end groups prevent the macrocycle from slipping off the thread (see Chart 1). The two rotaxanes have the same macrocycle and succinamide binding motif, but differ in the finer details of the composition of the thread. The thread of rotaxane **1** consists of a tertiary amide and four phenyl groups as bulky stoppers, while the thread of rotaxane **2** has a secondary amide and one phenyl group plus three cyclohexane groups as stoppers.

Isolated and rovibrationally cooled rotaxanes **1** and **2**, as well as their separate macrocycle and thread components, were produced by seeding laser-desorbed molecules into a supersonic expansion of argon.[3] To record IR absorption spectra, IR−UV ion-dip spectroscopy was applied employing FELIX,[4] a free electron laser, as IR light source. The use of FELIX is essential since it provides high laser fluences over a broad wavelength region that covers both the C═O stretch and NH bend, as well as the fingerprint region. The first region gives a direct view on the hydrogen bond interactions, and thus shows how macrocycle and thread are connected, while the latter region affords a detailed structural analysis as has been amply demonstrated in our previous steady-state[5] and time-resolved[6] IR studies in solution.

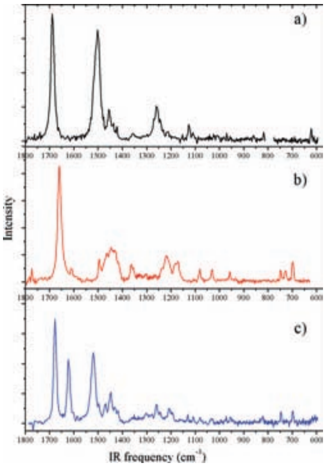


***Figure 1.*** IR absorption spectrum of (a) macrocycle, (b) the thread of **1**, and (c) rotaxane **1**.

Figure 1 shows the IR absorption spectra of the free macrocycle (top), the thread of **1** (middle), and rotaxane **1** (bottom). In the 1800−600 cm$^{-1}$ region the spectra display a wealth of well-resolved absorption bands. The width of these peaks is determined by the bandwidth of the infrared laser at those particular wavelengths; it ranges from 3 to 5 cm$^{-1}$ in the low energy region to a width of 9 cm$^{-1}$ around 1800 cm$^{-1}$ (about 0.5% of the IR frequency). In this paper we only focus on the most intense bands in the 1800−1450 cm$^{-1}$ range (amide I and II).

Comparison of the amide I and II frequencies in the three systems offers a sensitive probe for the binding geometry and interactions in the rotaxane. In the macrocycle the C═O stretch and NH bending modes are found as prominent peaks at 1687 and 1504 cm$^{-1}$, respectively. As thread **1** contains a tertiary amide, its IR spectrum shows only one dominant peak at 1660 cm$^{-1}$ associated with the C═O stretch vibration. The IR spectrum changes significantly when thread and macrocycle are mechanically interlocked in rotaxane **1**. The spectrum now displays two amide I bands due to the two types of C═O groups. We assign the band at 1677 cm$^{-1}$ to the four free C═O groups in the macrocycle, while the two hydrogen-bonded

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C═O groups in the thread are assigned to the 1620 $\mathrm{cm}^{-1}$ band. We can thus conclude that the isolated rotaxane dominantly adopts the conformation drawn in Chart 1.

The bifurcated hydrogen bonds between the C═O groups of the thread and the NH groups in the macrocycle do not only decrease the C═O frequency of the thread by about 40 $\mathrm{cm}^{-1}$, but also lead to a red shift of the non-hydrogen-bonded C═O frequency in the macrocycle by $\sim$10 $\mathrm{cm}^{-1}$. The latter decrease is in line with predictions based on a model that treats the hydrogen bonding interaction in a donor−acceptor approach.[7] However, to the best of our knowledge an experimental confirmation for representative systems under isolated conditions has not been reported yet.[8] The effects of turning on the interaction between thread and macrocycle in the rotaxane are further reflected in the NH bend mode of the macrocycle, of which the frequency increases by $\sim$16 $\mathrm{cm}^{-1}$ when the macrocycle is incorporated into the rotaxane. The presence of a single amide II band in the spectrum of rotaxane **1** once more confirms that conformations with non-hydrogen-bonded NH groups are not detected in our experiments.

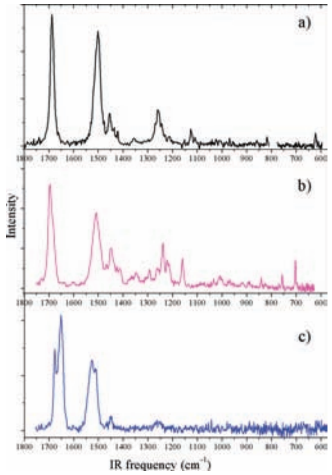

***Figure 2.*** IR absorption spectrum of (a) macrocycle, (b) the thread of **2**, and (c) rotaxane **2**.

The effects of changing binding motif and stoppers on the intramolecular binding interactions become evident from the IR spectra of rotaxane **2** and its components (Figure 2). The spectrum displays the same features as observed for rotaxane **1**, although some of the peaks are slightly shifted. In the amide I region the free C═O groups of the macrocycle appear at the same frequency as in rotaxane **1**, but the hydrogen-bonded C═O groups of the thread are now found at 1652 $\mathrm{cm}^{-1}$. In addition, the spectrum shows two closely spaced peaks in the amide II region associated with the NH bend mode of the free NH of the thread (1512 $\mathrm{cm}^{-1}$) and the hydrogen-bonded NH of the macrocycle (1525 $\mathrm{cm}^{-1}$). Comparison with the frequencies of the amide I of the bare thread of **2** (1693 $\mathrm{cm}^{-1}$) and the amide II of the isolated macrocycle (1504 $\mathrm{cm}^{-1}$) leads to the conclusion that the relative shift due to hydrogen bonding upon rotaxanation is identical for both rotaxanes. That is, the absolute frequencies of the C═O stretch as well as the NH bend mode participating in the hydrogen bonding clearly depend on the rotaxane building blocks, but their relative shift is independent of the rotaxane composition. Separate experiments on a slightly modified version of rotaxane **2** in which the phenyl group in the thread of **2** is replaced by a cyclohexyl group confirm that the bonding characteristics are not affected by the changes in the end groups.

The observed frequency changes upon rotaxanation provide a direct measure of the strengths and geometric details of the hydrogen bonds between thread and macrocycle. Theoretical studies of analogous binding geometries with one amide acceptor forming hydrogen bonds with an isophtalic amide donor have shown that the IR frequencies in the complexes are well correlated with their binding energies.[9] Using the relation derived in these studies and the shift observed here for the C═O frequency of the thread (−40 $\mathrm{cm}^{-1}$) leads to a hydrogen bond interaction energy of about 9−10 kcal/mol, in fair agreement with $\Delta G^{\ddagger}_{298}$ values found for pirouetting of the macrocycle as derived from temperature-dependent NMR experiments on similar systems.[10]

Summarizing, we have shown for the first time that it is possible to perform detailed spectroscopic studies of isolated mechanically interlocked molecular assemblies, thereby enabling us to elucidate their structural properties in the absence of the interfering contribution of interactions with solvent molecules. We have demonstrated that IR absorption spectra of prototypical [2]rotaxanes and their associated threads and macrocycles provide a direct view on the effects of interlocking the macrocycle on the thread, and offer a straightforward approach to study their structural properties. We believe that application of this approach to switchable systems as is presently being performed in our laboratories will lead to an unrivaled insight into—and ultimately control over—the functioning of these molecular devices.

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