**Precise Facial Control in Threading Guests into a Molecular Cage and the Formation of a Turtelike Supramolecular Complex**

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The synthesis of functional interlocked molecules continues to attract attention because these machinelike molecules[1] have potential applicability in mesoscale molecular electronic

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devices.[2] On the other hand, some interlocked molecules are of considerable interest not for their specific function but as synthetic challenges or for their aesthetic appeal.[3] Although many different macrocycles, including crown ethers,[4] cyclophanes,[5] and cyclodextrins,[6] have been used for the construction of a range of interlocked molecules, their molecular structures are quite similar in that they present only two open faces for guest penetration. In contrast, molecular cages[7] containing internal voids may possess more than two openings for the threading of rodlike components. Conceptually, different [2]pseudorotaxane complexes can be generated from a cubic molecular cage[8] by threading the guest species through its different faces, but such supramolecular systems have not been constructed previously, possibly because of synthetic difficulties (e.g., the number of macrocyclization reactions required) and the less-predictable nature of guest complexation by the host.

Recently, we demonstrated that molecular cage 1 forms an extremely stable supramolecular complex with the dimethyl diazapyrenium (DMDAP) ion (Scheme 1).[9] Herein, we report that two different thread components are capable of selectively penetrating 1 through its two different sets of open faces (namely, the 24-[10] and 34-membered rings, respectively) to result in two different [2]pseudorotaxane-like complexes. The mixture of these two thread components and 1 represents a new type of molecular machinery: the two thread components alternate between their corresponding [2]pseudorotaxane complexes upon threading through the different faces of the molecular cage under the control of K+ ions. A small tetrasubstituted macrocycle forms a unique turtle-like supramolecular complex with 1; in this complex, the four substituent groups penetrate through the four opening faces of the molecular cage.

Previously, we demonstrated that the methyl and α-pyridinium protons of the DMDAP dication form multiple C/H−O hydrogen bonds with the oxygen atoms in the ethylene glycol chains of 1. Based on this finding, we synthesized the rod-shaped salt 2·2PF6 by reaction of commercially available 1,2-bis(4-pyridyl)ethane and 1-bromopentane. We expected that 2·2PF6 ions would form [2]pseudorotaxane complexes with 1 upon the threading of two pentyl groups through the two 24-membered ring faces of 1. This complex should be stabilized not only through C−H−O hydrogen bonds between the α-pyridinium protons and the oxygen atoms of the ethylene glycol chains but also through π stacking of the two pyridinium rings with the concave aromatic surfaces of the molecular cage (Scheme 2).[11]

The 1H NMR spectrum of an equimolar mixture of 1 and thread 2·2PF6 in CDCl3/CD3CN (9:1, 3 mM) at room temperature displays significant changes in the chemical shifts of the protons of the complex relative to those of its free components (Figure 1). To confirm that the disappearance of the signals of the free species in the spectrum is due to complete complexation of the two components, rather than being the result of fast rates of exchange for the complexation/decomplexation processes under these conditions, we obtained the 1H NMR spectrum of a non-stoichiometric mixture of 1 (2 mM) and 2·2PF6 (3 mM) in CDCl3/CD3CN (9:1). We observed two sets of signals, which integrated in a 2:1 ratio, with the weaker absorption set corresponding to the signals of free 2·2PF6 (see the Supporting Information). This result suggests that the binding stoichiometry of 1 to 2·2PF6 is 1:1 and that the exchange rates for their complexation and decomplexation are slow under these conditions. We did not observe any signals of the free species in the 1H NMR spectra upon diluting equimolar mixtures of 1 and 2·2PF6 from 1 mM

\[ \text{Scheme 1. Complexation of molecular cage 1 with DMDAP.} \]

\[ \text{Scheme 2. Complexation of molecular cage 1 with 2·2PF}_6. \]

\[ \text{Figure 1. Partial 1H NMR spectra (400 MHz, CDCl}_3/\text{CD}_3\text{CN (9:1), 298 K) of a) 1, b) an equimolar mixture of 1 and 2·2PF}_6 (3 mM), and c) 2·2PF}_6.} \]
to 20 μm (see the Supporting Information), thus suggesting that the binding between 1 and 2·2PF₆ is extremely tight.

The spectrum of the complex displays shifts downfield of the signals of the methylene protons Hₓ adjacent to the pyridinium center and the α-pyridinium protons Hᵧ of 2·2PF₆ (Figure 1), in conjunction with weak, but discernable, shifts in the signals of the ethylene glycol protons of 1. These shifts suggest the existence of C–H···O hydrogen bonds in the complex. The considerable upfield shifts of signals for aromatic protons of both components (namely, Hₐ and Hₜ) and of the ethylene protons of 2·2PF₆ (Hₖ) imply that π stacking of the aromatic rings occurs in the complex. We grew single crystals suitable for X-ray crystallography through liquid diffusion of isopropyl ether into an equimolar solution of 1 and 2·2BF₄ in CH₃CN.

The solid-state structure reveals a [2]pseudorotaxane-like molecular geometry for the complex [1·2]₂⁺ (Figure 2) in which the rodlike component 2⁺ penetrates through the two 24-membered rings of the molecular cage.

As indicated in Figure 3b, the signals of the protons of an equimolar mixture of 1 and anthraquinone (3) in CDCl₃/CD₂CN (50:1, 5 mM) at room temperature do not undergo significant shifts relative to those of the free species. This observation suggests that the binding affinity between the two species is negligible under these conditions. After the addition of two equivalents of KPF₆ to the solution, however, the ¹H NMR spectrum displays significant shifts for the signals of both of the organic components (Figure 3c). In particular, the upfield shifts of the signals of the aromatic protons of both components imply that stacking of the aromatic rings occurs within this supramolecular complex.

We grew single crystals suitable for X-ray crystallography through liquid diffusion of isopropyl ether into a solution of 1, KPF₆, and 3 (1:2:1) in CH₃CN. The solid-state structure (Figure 4) reveals the expected [2]pseudorotaxane binding.
The rodlike 3 penetrates the two 34-membered rings, whereas the two oxygen atoms coordinate to the two K$^{+}$ ions. Thus, we can form pseudorotaxane complexes from 1 with precise facial control (namely, threading through either the 24- or 34-membered rings) by using the rod-shaped salt 2·2PF$_6$ or a combination of K$^{+}$ ions and 3.

Because K$^{+}$ ions not only template the formation of the [2]pseudorotaxane complex [3·1·K$_2$]$^{2+}$ but also cause dissociation of complex [1·2]$^{2+}$ in solution, the addition and removal of K$^{+}$ ions from a solution of 1, 2·2PF$_6$, and 3 could be used to mediate an unprecedented type of machinelike molecular motion, in which the rodlike components penetrate the molecular cage alternately through its different faces (Figure 5).

The $^1$H NMR spectrum of an equimolar mixture of 1, 2·2PF$_6$, and 3 in CDCl$_3$/CD$_3$CN (9:1) indicates the formation of the [2]pseudorotaxane complex [1·2]$^{2+}$ exclusively (Figure 6a). The addition of four equivalents of K$^{+}$ ions to this solution not only leads to the dissociation of most of the [1·2]$^{2+}$ but also to the generation of the other [2]pseudorotaxane complex [3·1·K$_2$]$^{2+}$ (Figure 6b). The subsequent addition of [2,2,2]cryptand (4 equiv), which is a very strong binder of K$^{+}$ ions, to the solution leads to the disappearance of the signals that are diagnostic of [3·1·K$_2$]$^{2+}$ and the reappearance of the signals of [1·2]$^{2+}$. Thus, sequential addition of K$^{+}$ ions and [2,2,2]cryptand to a mixture of 1, 2·2PF$_6$, and 3 in solution controls the mechanical threading of the different rodlike components within the molecular cage through selective formation of [1·2]$^{2+}$ and [3·1·K$_2$]$^{2+}$ (Figure 5).

Having proven that precise facial control is achievable in the formation of [2]pseudorotaxane complexes from 1 and that machinelike molecular motion can occur with these supramolecular systems, we turned our attention to the construction of a supramolecular complex in which each of the four macrocyclic openings in 1 encircles a rodlike unit. We synthesized the four-armed salt 5·2PF$_6$ through the reaction of the bipyridine 4 with 1-bromopropane. We expected that the complexation of 5·2PF$_6$ with 1 would lead to the formation of a symmetrical complex [1·5·(PF$_6$)$_2$], in which each of the four substituting groups of 5·2PF$_6$ would thread through a different opening of the 1 (Scheme 4).

The $^1$H NMR spectrum (see the Supporting Information) of an equimolar mixture (2.6 mm) of 1 and 5·2PF$_6$ in CDCl$_3$/CD$_3$CN (3:17) displays three sets of resonances—one set for free 1, one for free 5·2PF$_6$, and one for the 1:1 complex formed between 1 and 5·2PF$_6$—which suggests that the rates of complexation and decomplexation are both slow on the $^1$H NMR timescale at 400 MHz and 298 K. Using a single-
point method we determined the association constant ($K_a$) of this system at 298 K to be 300 M$^{-1}$ in CDCl$_3$/CD$_3$CN (3:17).

We grew single crystals suitable for X-ray crystallography through liquid diffusion of isopropyl ether into an equimolar solution of 1 and 5·2PF$_6$ in CH$_3$CN$^{[13]}$. The solid-state structure reveals a binding geometry for the complex [1·5]$^{[+]}$ in which the n-propyl groups penetrate through the 24-membered rings and the two tosyl groups emerge from the 34-membered rings of 1 (Figure 7). The structure of [1·5]$^{[+]}$ is unique, which may be correlated to a turtle’s four legs protruding from its hard shell.

![Figure 7. Ball-and-stick representation of the solid-state structure of [1·5]$^{[+]}$: a) side and b) top views. C gray, O red, N blue, S yellow.](image)

We have demonstrated that two different types of thread component (based on a bispyridinium ion and quinone) can be applied to molecular cage 1 to generate different [2]pseudorotaxane-like complexes with precise facial control. A mixture of the two threading components and 1 in solution undergoes a new type of molecular motion, powered through the addition and removal of K$^+$ ions and [2,2,2]cryptand units, in which the rodlike components penetrate the molecular cage alternately through its different faces. In addition, the four-armed macrocyclic guest 5·2PF$_6$ forms a complex with 1, in which each of the limbs of the guest protrudes from a unique macrocyclic face of the host to result in a turtlelike supramolecular complex. We believe that the molecular recognition properties of this molecular cage will be useful in various fields, such as the construction of molecular machinery, supramolecular polymers, and supramolecular catalytic systems, which we are presently investigating.

**Experimental Section**

2·PF$_6$: 1-Bromopentane (403 µL, 3.2 mmol) was added to a solution of 1,2-di(4-pyridyl)ethane (100 mg, 0.54 mmol) in DMF (2 mL) at ambient temperature. The solution was stirred for 12 h before being poured into CH$_2$Cl$_2$ (5 mL) to provide a precipitate, which was collected and dissolved in CH$_3$CN (10 mL). Saturated aqueous NH$_4$PF$_6$ (10 mL) was added, and then the organic solvent was evaporated under reduced pressure. The precipitate was collected, washed with H$_2$O (20 mL), and dried to give 2·PF$_6$ as a pale-yellow solid (246 mg, 74%).

$^1$H NMR (400 MHz, CD$_3$CN): $\delta$ = 0.91 (t, J = 7 Hz, 6H), 1.23–1.42 (m, 8H), 2.08–2.21 (m, 4H), 3.28 (s, 4H), 4.45 (t, J = 7 Hz, 4H), 7.85 (d, J = 6 Hz, 4H), 8.54 ppm (d, J = 6 Hz, 4H).

$^{13}$C NMR (100 MHz, CD$_3$CN): $\delta$ = 14.0, 22.6, 28.5, 31.3, 35.0, 61.8, 128.3, 143.9, 160.3 ppm; HR-MS (FAB): C$_2$H$_8$F$_4$N$_2$P$_2$F$_4$ $^{[+]}$ ([2PF$_6$]$^{[+]})$ calc m/z 779.2363; found m/z 779.2403.

5·2PF$_6$: 1-Bromopropane (50 µL, 0.53 mmol) was added to a solution of the dipyrine 4 (25 mg, 0.05 mmol) in DMF (1 mL) at ambient temperature. The solution was stirred at 90°C for 12 h before being poured into diethyl ether (10 mL) to give a precipitate, which was dissolved in CH$_3$CN (10 mL). Saturated aqueous NH$_4$PF$_6$ (10 mL) was added, and then the organic solvent was evaporated under reduced pressure. The precipitate was collected, washed with H$_2$O (20 mL), and dried to give 5·2PF$_6$ as a pale-yellow solid (41 mg, 98%).

$^1$H NMR (400 MHz, CD$_3$CN): $\delta$ = 0.84 (t, J = 7 Hz, 6H), 1.77–1.85 (m, 4H), 2.51 (s, 6H), 4.29 (t, J = 7 Hz, 4H), 4.66 (s, 8H), 7.54 ppm (d, J = 8 Hz, 4H), 7.88 (d, J = 8 Hz, 4H), 8.27 (s, 4H), 8.75 ppm (s, 2H).

$^{13}$C NMR (100 MHz, CD$_3$CN): $\delta$ = 10.6, 21.7, 25.1, 51.1, 64.1, 127.4, 130.7, 135.6, 137.5, 143.2, 145.4, 147.7 ppm; HR-MS (FAB): C$_4$H$_8$F$_4$N$_2$O$_2$P$_2$F$_4$ $^{[+]}$ ([5PF$_6$]$^{[+]})$ calc m/z 779.2289; found m/z 779.2305.

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Chem. Eur. J., DOI: 200600090. The 1H NMR spectra displayed similar shifts of signals when macrocycle I was mixed with the PF6 or BF4 salt of this guest under the same conditions (see the Supporting Information).

Crystal data for [1·2·MeCN·0.5CHCl3·0.5CH3CN: [C98H124O20N6S2][BF4]2, M1 = 1787.34, monoclinic, space group P21/n, a = 20.3900(10), b = 16.3152(3), c = 19.0614(5) Å, V = 9784.30(3) Å3, μ(MoKα) = 2.52 mm−1, T = 295(2) K, light-yellow plates; 15996 independent measured reflections, F2 refinement, Rs = 0.1308, wR2 = 0.3733.

Crystal data for [3·1·K+]·2MeCN·0.5CHCl3·H2O·2PF6: [C98H124O20N6S2][BF4]2, M1 = 1787.34, monoclinic, space group P21/n, a = 31.5200(4), b = 16.3152(3), c = 19.0614(5) Å, V = 9784.30(3) Å3, μ(MoKα) = 2.52 mm−1, T = 295(2) K, deep-yellow plates; 11101 independent measured reflections, F2 refinement, Rs = 0.1235, wR2 = 0.3002.

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