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A new macrocycle that forms pseudorotaxane-like complexes with dibenzylammonium ions

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Abstract—A new host molecule in which only one *diethylene glycol* chain (i.e., a loop possessing only three oxygen atoms) suitably positioned in a macroring recognizes a DBA^+ ion to form a 1:1 pseudorotaxane-like complex. To confirm unambiguously that the pseudorotaxane exists in solution, a corresponding interlocked rotaxane molecule was synthesized.

Although many elegant molecular switches[1] and actuators[2] based on interlocked molecular compounds and threaded supramolecular complexes have been developed in the past two decades, the number of recognition motifs that can be exploited for the preparation of these systems remains limited. Among these few recognition systems, the crown ether/dibenzylammonium ion (DBA^+) pair[3] is one of the most accessible systems for the construction of functional (supra)molecular entities, in which the nature of the complexation is very sensitive to the size and constitution of the crown ether. For example, DBA^+ ions form high-affinity pseudorotaxane-like[4] complexes with dibenzo[24]crown-8 (DB24C8) in relatively nonpolar solvents[5] (Fig. 1), but the slightly larger structural isomer of this crown ether, bis-*m*-phenylene[26]crown-8 (BMP26C8), displays a negligible binding affinity toward the DBA^+ ion.[6] In contrast, the significantly larger crown ether, bis-*p*-phenylene[34]crown-10 (BPP34C10), is capable of complexing two DBA^+ ions simultaneously and relatively strongly in nonpolar solvents.[7]

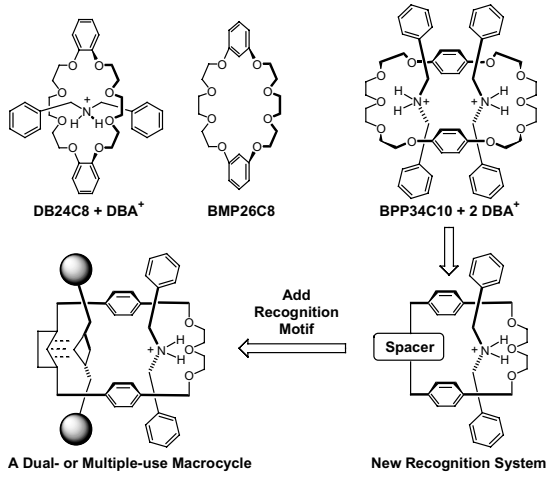

Figure 1.

In the latter 1:2 (host:guest) complex, both in solution and in the solid state, each DBA^+ ion binds to one of the tetraethylene glycol units of BPP34C10. This arrangement prompts an interesting question: would only one properly placed oligoethylene glycol chain in a macroring be sufficient to form 1:1 pseudorotaxane-like complexes with DBA^+ions?[8] If the answer is 'yes,' then the chemical skeletons of the macrocyclic oligoethers, which generally consist of two oligoethylene glycol chains for synthetic simplicity, could become much more varied in structure. Furthermore, it may become possible to prepare hosts that can recognize two (or more) different classes of guest molecules by linking together into a macrocycle an oligoethylene glycol loop and another recognition motif (Fig. 1). Such double-recognition macrocycles would have potential applications in, for example, the fine tuning of complexes, the construction of supramolecular catalytic systems, or the preparation of sensitive molecular switches. In this letter, we report a new host molecule in which only one *diethylene glycol* chain (i.e., a loop possessing only three

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oxygen atoms) suitably positioned in a macroring recognizes a DBA^+ ion to form a relatively strong 1:1 pseudorotaxane-like complex. To confirm unambiguously that the pseudorotaxane exists in solution, we have synthesized a corresponding interlocked molecular version of this complex, namely a [2]rotaxane.

Based on CPK molecular models and molecular mechanics calculations, we believed that positioning both *p*-xylene and diethylene glycol linkers between the phenolic rings of macrocycle **1** would position these two phenol units at a suitable π-stacking distance for guest reception. Moreover, the three oxygen atoms in the diethylene glycol chain of macrocycle **1** seemed to be located appropriately to provide a good reception site for two [N–H···O]-type hydrogen bonds with a threaded DBA^+ ion. In addition, the π-electron-rich phenolic rings are positioned appropriately for potential $N^+C–H\cdots\pi$,[9] $N^+–H\cdots\pi$[10] and/or cation–π[11] interactions with the guest's $CH_2NH_2^+CH_2$ center. We synthesized macrocycle **1** (Scheme 1) using a simple two-step approach: first reacting phenol **2** with α,α′-dibromo-*p*-xylene **3** to afford diol **4**[12] and then performing a [1+1] macrocyclization between **4** and ditosylate **5**.[13]

The ^1H NMR spectrum (Fig. 2b) of an equimolar mixture of macrocycle **1** and $DBA{\cdot}PF_6$ in $CDCl_3/CD_3CN$ (1:1) displays three sets of resonances: one set for free **1** (Fig. 2a), one for free $DBA{\cdot}PF_6$ (Fig. 2c), and one for the 1:1 complex formed between macrocycle **1** and the DBA^+ ion. The presence of both free and complexed species in equilibrium implies that the rates of complexation and decomplexation are both slow on the ^1H NMR timescale at 400 MHz and 298 K.[14] The splitting of the originally overlapping signals for the protons of the diethylene glycol unit's two methylene groups in macrocycle **1** into two separate multiplets—one shifted upfield to δ 3.06 and the other downfield to δ 3.59—in the presence of the salt suggests that hydrogen bonding probably takes place between the host and guest, but the most remarkable shift occurs for the methylene protons adjacent to the ammonium center. When uncomplexed, these protons resonate at ca. 4.17 ppm, but this signal experiences an upfield shift of >2 ppm (to δ 1.95) upon complexation with **1**, which suggests that the NH_2^+ center is positioned in the shielding zone between the two phenol units of **1**, as would be expected when [N–H···O] hydrogen bonds exist.[15] Unfortunately, we were not able to detect the signal for the resonance of the NH_2^+ protons, which we expect to also undergo a significant upfield shift, possibly because of severe broadening. The resonances of the phenolic protons shift upfield to 6.60 and 6.74 ppm from their original positions (δ 6.74 and 7.06, respectively), which suggests the existence of possible aryl–aryl interactions caused by the threading of the DBA^+ ion into the cavity of macroring **1**. Thus, these shifts suggest that the complexation between macrocycle **1** and the DBA^+ ion in solution is likely to have the geometry of a [2]pseudorotaxane. Using a single-point method,[16] we determined the association constant (K_a) of this system to be 550 M^{-1} in $CDCl_3/CD_3CN$ (1:1) and 15,000 M^{-1} in CD_3NO_2; that is, the binding strength is comparable to those of crown ether-containing complexes.[5–7,17]

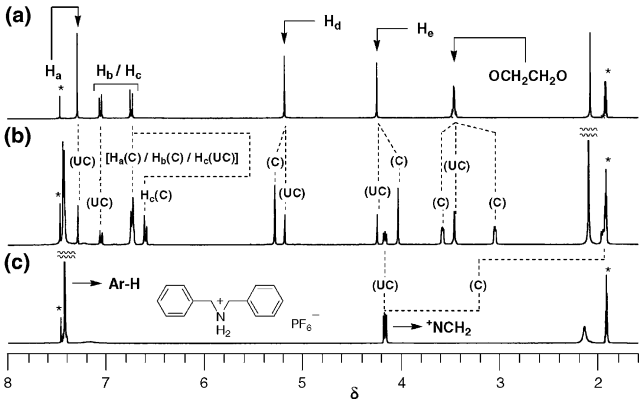
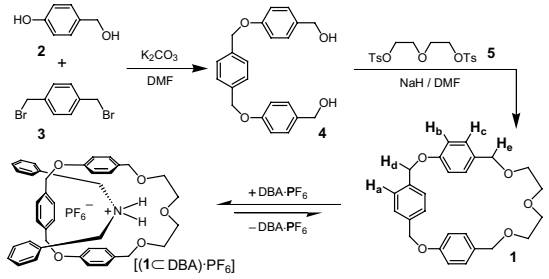


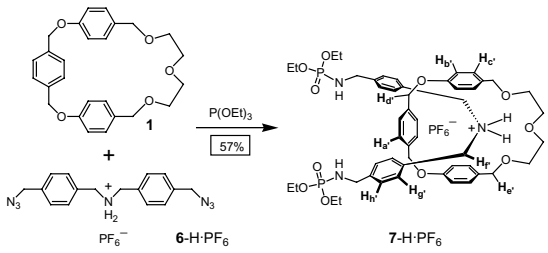
Figure 2. Partial ^1H NMR spectra [400 MHz, $CDCl_3/CD_3CN$ (1:1), 298 K] of (a) macrocycle **1**, (b) an equimolar mixture of **1** and $DBA{\cdot}PF_6$ (10 mM), and (c) $DBA{\cdot}PF_6$. The descriptors (c) and (uc) refer to complexed and uncomplexed states of the components.

To prove unambiguously that a [2]pseudorotaxane complex forms between macrocycle **1** and the DBA^+ ion in solution, we chose to stopper such a complex to form a corresponding [2]rotaxane. From a CPK molecular model, it appeared that because compound **1** is a 25-membered-ring macrocycle that incorporates three rigid benzene rings, diethyl phosphoramidate groups[18] would be suitable stoppers. Thus, we added triethyl phosphite (200 mM) to a solution of benzylic azide **6**-H·PF_6 (100 mM) and macrocycle **1** (150 mM) in CH_2Cl_2 and isolated the corresponding [2]rotaxane **7**-H·PF_6 in 57% yield after silica gel column chromatography (Scheme 2).[19]

The ^1H NMR spectrum (Fig. 3a) of the [2]rotaxane **7**-H·PF_6 recorded in CD_3CN displays an upfield shift in



Scheme 1.



Scheme 2.

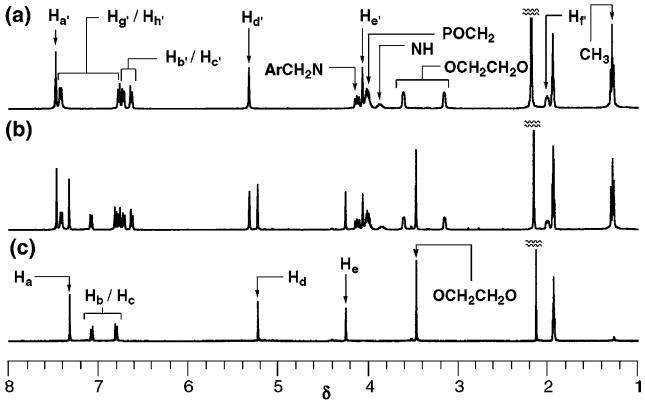


Figure 3. Partial ^{1}H NMR spectra (400 MHz, CD_3CN, 10 mM, 298 K) of (a) [2]rotaxane **7**-H·PF_6, (b) an equimolar mixture of rotaxane **7**-H·PF_6 and macrocycle **1**, and (c) macrocycle **1**.

the position of the signal of the resonance of the methylene protons adjacent to the ammonium center and those of the ethylene protons of the encircled macrocyclic component of **7**-H·PF_6, relative to the positions of these signals in its free components, which confirms that the interactions between these components in the rotaxane are similar to those present in the initial complex. The ^{1}H NMR spectrum (Fig. 3b) of an equimolar mixture of **7**-H·PF_6 and macrocycle **1** (10 mM each) in CD_3CN at 298 K corresponds to a superimposition of the two spectra (Fig. 3a and c) of the separate components. These spectra establish that no exchange occurs between the macrocycle and dumbbell components in solution and, therefore, proves the constitutional integrity of the [2]rotaxane.[20]

The fact that it is possible to generate [2]pseudorotaxane complexes in solution from the interaction of DBA^+ ions with a macrocycle **1** that contains just three oxygen atoms suggests that the cooperative effect of the five to eight oxygen atoms found in the recognition sites of most of the crown ethers that have been used previously to complex DBA^+ ions is not a necessary prerequisite for efficient binding. Indeed, it appears that N^+C–H$\cdots\pi$, N^+–H$\cdots\pi$ and/or cation–π interactions can be induced to play extremely important roles in stabilizing such macrocycle–ammonium ion complexes. We are now investigating the complexation behavior of macrocycle **1** toward electron-deficient aromatic molecules in addition to constructing related macrocycles possessing double-recognition properties.

Acknowledgements

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12. Typical procedure for the synthesis of diol **4** and its selected spectral data: A mixture of 4-hydroxybenzyl alcohol **2** (3.72 g, 30 mmol), α,α′-dibromo-*p*-xylene **3** (2.63 g, 10 mmol), and K_2CO_3 (10 g, 72.4 mmol) in DMF (50 ml) was heated at 50 °C for 2 days. The reaction mixture was cooled to room temperature and the organic solvent was evaporated under reduced pressure. The residue was washed with CH_2Cl_2 (500 ml), H_2O (500 ml), and MeOH (150 ml) to afford the desired product **4** as a brown solid (3.14 g, 90%). ^{1}H NMR (400 MHz, CD_3SOCD_3): $\delta = 4.40$ (s, 4H), 5.08 (s, 4H), 6.94 (d, $J = 8$ Hz, 4H), 7.21 (d, $J = 8$ Hz, 4H), 7.43 (s, 4H). ^{13}C NMR (100 MHz, CD_3SOCD_3): $\delta = 62.4$, 68.7, 113.9, 127.0, 127.3, 134.1, 136.0, 156.2. MS (FAB): *m/z* 389.1 for $[M+K]^+$.
13. Typical procedure for the synthesis of macrocycle **1** and its selected spectral data: Diethylene glycol ditosylate **5**

(5.95 g, 14.4 mmol) was added slowly to a solution of diol **4** (5.0 g, 14.4 mmol) and NaH (1.75 g, 42.8 mmol) in DMF (700 ml) and the resulting mixture was stirred at room temperature for 7 days. The reaction was quenched by the addition of MeOH (10 ml) and then the organic solvent was evaporated under reduced pressure. The residue was partitioned between H_2O (500 ml) and CH_2Cl_2(500 ml); the organic layer was collected, dried ($MgSO_4$), and concentrated to afford a crude product, which was then purified by column chromatography (SiO_2; EtOAc/Hexanes, 3:7) to give macrocycle **1** as a white solid (183 mg, 3%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.50 (m, 4H), 3.60 (m, 4H), 4.39 (s, 4H), 5.17 (s, 4H), 6.65 (d, J = 8 Hz, 4H), 7.06 (d, J = 8 Hz, 4H), 7.27 (s, 4H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 69.1, 69.6, 70.5, 72.6, 115.6, 127.0, 129.0, 130.3, 136.8, 157.0. MS (FAB): m/z 421.2 for $[M + H]^+$.

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