

[3]Pseudorotaxane-Like Complexes Formed between Bipyridinium Dications and Bis-*p*-xylyl[26]crown-6

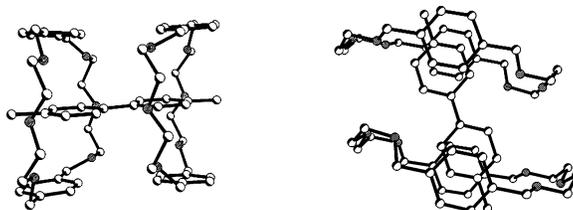
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ABSTRACT



The crown ether BPX26C6 forms a [3]pseudorotaxane-like complex with the *N,N'*-dimethyl-4,4'-bipyridinium dication both in solution and in the solid state. The facile one-pot synthesis of a [2]rotaxane from neutral precursors—BPX26C6, 4,4'-dipyridyl, and 3,5-di-*tert*-butylbenzyl bromide—suggests that BPX26C6 may bind to (mono)pyridinium cations in a [2]pseudorotaxane-like manner.

The synthesis of functional interlocked molecules continues to attract much attention because these machine-like molecules¹ have been demonstrated to have potential applicability in mesoscale molecular electronic devices.² Many functional supramolecular systems take advantage of the structural simplicity and redox activity of alkyl pyridinium salts; for example, *N,N'*-dialkyl-4,4'-bipyridinium dications are often studied as guest moieties for synthetic host molecules, such as cucurbiturils,³ cyclophanes,⁴ calixarenes,⁵ cryptands,⁶ and crown ethers.⁷ Many synthetic interlocked molecules, such as rotaxanes,⁸ comprise bipyridinium ion and crown ether

[e.g., bis-*p*-phenylene[34]crown-10 (BPP34C10)] components.⁹ In these syntheses, the bipyridinium dication units have generally been preinstalled within the guest component as recognition sites for crown ethers prior to the formation of the final interlocked rotaxanes, but the requirement for

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bipyridinium dication-containing thread-like components sometimes can complicate the synthetic procedures toward such interlocked molecules. A conceptually simpler approach relies upon the crown ether moiety complexing with (mono)pyridinium cations (e.g., the 1-methyl-4-pyrid-4-ylpyridinium cation). If a host macrocycle can recognize a single pyridinium ion to form a [2]pseudorotaxane-like complex¹⁰ in solution, then the synthesis of a molecular rotaxane from a neutral bipyridine should be quite straightforward: the initial alkylation of one of the pyridine moieties activates the recognition site, which then binds the crown ether, and subsequent alkylation of the second pyridine unit interlocks the two components (Figure 1).¹¹

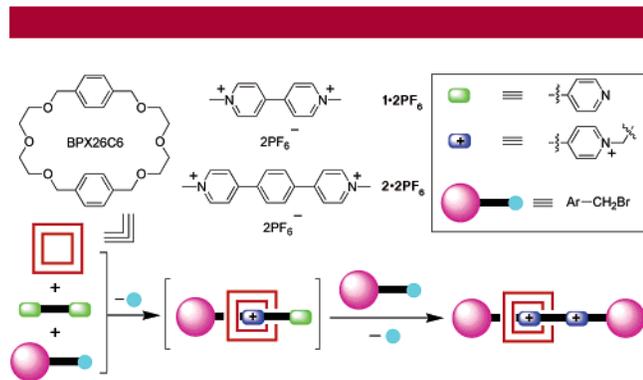


Figure 1.

Although the 1:1 complexation between sizable crown ethers, such as BPP34C10, and bipyridinium dications has been known for almost 2 decades,^{7b} the recognition of (mono)pyridinium cations by crown ethers remains a challenging task.¹² In this paper, we report that the crown ether bis-*p*-xylyl[26]crown-6 (BPX26C6, Figure 1) is capable of binding to the *N,N'*-dimethyl-4,4'-bipyridinium dication to form [3]pseudorotaxane-like complexes both in solution and in the solid state.¹³ This result suggested that BPX26C6 may be able to complex to (mono)pyridinium cations in a [2]-

pseudorotaxane-like fashion in solution. Taking advantage of the possible crown ether/(mono)pyridinium ion recognition system, we synthesized two [2]rotaxanes in one-pot reactions from nonionic starting materials.

In our continued quest for macrocycles that can recognize different types of guests,¹⁴ we found that BPX26C6 not only is capable of forming pseudorotaxane-like complexes with dialkylammonium ions but also can recognize *N,N'*-dimethyl-4,4'-bipyridinium bis(hexafluorophosphate) (**1**·2PF₆). We observed significant shifts in the signals in the ¹H NMR spectrum (298 K) of an equimolar (10 mM) mixture of BPX26C6 and **1**·2PF₆ in CD₃CN (Figure 2). The splitting

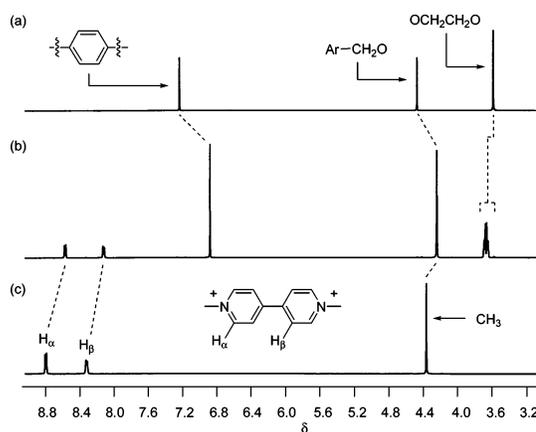


Figure 2. Partial ¹H NMR spectra (400 MHz, CD₃CN, 298 K) of (a) BPX26C6, (b) an equimolar mixture of BPX26C6 and **1**·2PF₆ (10 mM), and (c) **1**·2PF₆.

of the originally overlapping signals for the protons of the diethylene glycol unit's two methylene groups in BPX26C6 into a multiplet at δ 3.63–3.74 in the presence of **1**²⁺ suggests that [C–H···O] hydrogen bonding probably occurs between the host and guest moieties. The resonances of the xylyl and bipyridinium aromatic protons shifted upfield (to δ 6.89, 8.14, and 8.59) from their original positions (δ 7.25, 8.34, and 8.79, respectively); these shifts are characteristic of the existence of aryl–aryl interactions and suggest that the complexation between BPX26C6 and **1**²⁺ in solution is likely to have the geometry of a pseudorotaxane.

Using continuous variation methods,¹⁵ the stoichiometry for the binding between BPX26C6 and **1**²⁺ seemed to be 2:1 (Figure 3a). Interestingly, the solid-state structure that we obtained from single crystals of the complex, grown through slow evaporation of a CH₃CN solution containing a

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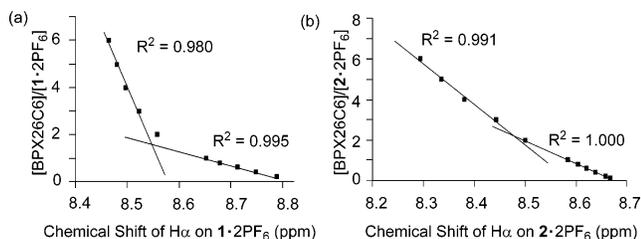


Figure 3. Molar ratio plots (CD_3CN) for (a) BPX26C6 and $1\cdot 2\text{PF}_6$ and (b) BPX26C6 and $2\cdot 2\text{PF}_6$.

1:1 mixture of BPX26C6 and $1\cdot 2\text{PF}_6$, reveals a [3]pseudorotaxane-like geometry, $[(\text{BPX26C6})_2\supset 1]\cdot 2\text{PF}_6$ (Figure 4).

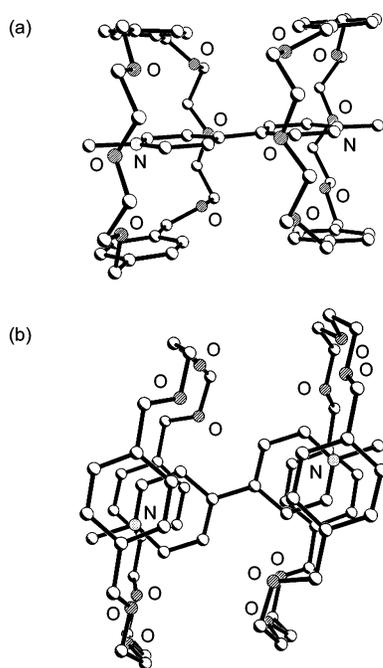


Figure 4. Ball-and-stick representations of the solid-state structure of the [3]pseudorotaxane-like complex $[(\text{BPX26C6})_2\supset 1]^{2+}$: (a) side view; (b) top view.

The electrospray ionization (ESI) mass spectrum recorded from an equimolar mixture of $1\cdot 2\text{PF}_6$ and BPX26C6 reveals peaks at m/z 1163 and 747, which correspond to 2:1 and 1:1 complexes, respectively, that have each lost one PF_6^- ion.

Having determined that BPX26C6 and $1\cdot 2\text{PF}_6$ can form stable [3]pseudorotaxane-like complexes in solution, in the gas phase, and in the solid state, we turned our attention toward the estimation of the association constants (K_1 and K_2) to determine whether cooperativity exists between the first and second binding events. Figure 5a displays the nonlinear Scatchard plot that we obtained for the binding of BPX26C6 and $1\cdot 2\text{PF}_6$ after determining the extent of complexation (p) of the bipyridinium units from the ^1H NMR data for proton H_α of $1\cdot 2\text{PF}_6$.¹⁶ From this Scatchard plot,

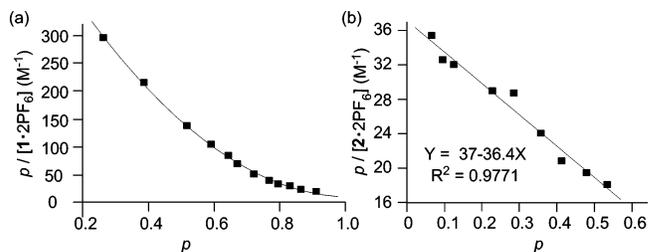


Figure 5. Scatchard plots (CD_3CN , 298 K) for the complexation of BPX26C6 with (a) $1\cdot 2\text{PF}_6$ ($[1\cdot 2\text{PF}_6]_0 = 0.5$ mM) and (b) $2\cdot 2\text{PF}_6$ ($[2\cdot 2\text{PF}_6]_0 = 0.5$ mM); p defines the fraction of bound guest. The second-order polynomial fitting line in (a) is presented merely to guide the eye.

we estimated K_1 and K_2 to be 700 ± 80 and 60 ± 25 M^{-1} , respectively.¹⁷ The ratio of K_2 to K_1 is 0.086; this value is significantly lower than the value (0.25) expected¹⁸ for statistical complexation and suggests negative cooperativity¹⁹ during the binding of the second crown ether unit, presumably because of steric factors. To test this hypothesis, we synthesized 1,4-bis(1-methylpyridinium)phenylene bis(hexafluorophosphate) $2\cdot 2\text{PF}_6$, an analogue of $1\cdot 2\text{PF}_6$ in which the two N -methylpyridinium units are separated via a p -phenylene unit, and dissolved it in CD_3CN in the presence of an equimolar (10 mM) amount of BPX26C6. We observed shifts in the signals in the ^1H NMR spectrum of this mixture (see Supporting Information) that are similar to those of the BPX26C6/ $1\cdot 2\text{PF}_6$ system. We determined, using the molar ratio method, that a 2:1 binding stoichiometry also exists between BPX26C6 and $2\cdot 2\text{PF}_6$ (Figure 3b). The Scatchard plot of the complexation is linear (Figure 5b), which suggests independent (i.e., noncooperative) binding of the two N -methylpyridinium ions in $2\cdot 2\text{PF}_6$ by the BPX26C6 units. We determined the association constants K_1 and K_2 (72 ± 8 and 18 ± 2 M^{-1} , respectively) from the slope of this line.²⁰ Interestingly, the association constant for the first binding

(16) We used the Benesi–Hildebrand method (ref 15), based on a series of ^1H NMR spectroscopy experiments with constant $[1\cdot 2\text{PF}_6]$ or $[2\cdot 2\text{PF}_6]$ and various values of $[\text{BPX26C6}]$, to determine the differences in δ values (Δ_0 for the α -proton of the uncomplexed and fully complexed $1\cdot 2\text{PF}_6$). Thus, $p = \Delta/\Delta_0$, where Δ is the chemical shift change relative to that of the free species (see ref 6a). We fitted the values of Δ using a nonlinear least-squares method (WinEQNMR) to obtain the values of K_1 and K_2 (990 ± 240 and 32 ± 10 M^{-1} , respectively). For WinEQNMR software, see: Hynes, M. J. *J. Chem. Soc., Dalton Trans.* **1993**, 311.

(17) The slope of the first four data points for low values of p gave the value of $2K_2 - K_1$. The slope of the last four data points (high values of p) gave the value of $-2K_2$. See: Perlmutter-Hayman, B. *Acc. Chem. Res.* **1986**, *19*, 90. We calculated the errors of the association constants on the basis of the error of the slope.

(18) In a system possessing two identical binding sites for its complementary partner, with association constants K_1 and K_2 , respectively, $K_1 = 4K_2$ if the binding sites operate independently. A system is positively cooperative if K_2/K_1 is greater than 0.25 and negatively cooperative if K_2/K_1 is smaller than 0.25; see: (a) Chang, T.; Heiss, A. M.; Cantrill, S. J.; Fyfe, M. C. T.; Pease, A. R.; Rowan, S. J.; Stoddart, J. F.; Williams, D. J. *Org. Lett.* **2000**, *2*, 2943. (b) Reference 15. (c) Reference 17.

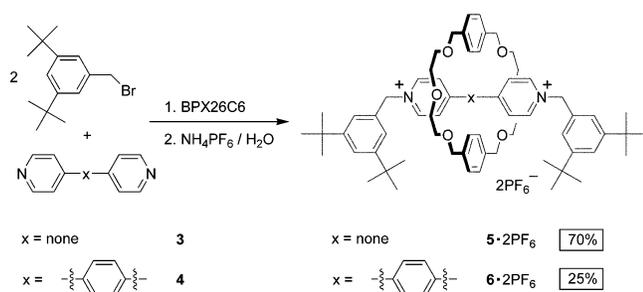
(19) The linearity of the data points in the Scatchard plot also provides information regarding the cooperativity; see: Gibson, H. W.; Yamaguchi, N.; Hamilton, L.; Jones, J. W. *J. Am. Chem. Soc.* **2002**, *124*, 4653.

(20) The value of the slope is -36 , which equals the values of both $-2K_2$ and $2K_2 - K_1$ simultaneously. We calculated the errors of the association constants on the basis of the error of the slope.

event (K_1) during the complexation of $1 \cdot 2PF_6$ with BPX26C6 is ca. 10 times higher than that of $2 \cdot 2PF_6$, presumably because increased delocalization of positive charges in the extended π system of 2^{2+} .

The fact that BPX26C6 binds to $2 \cdot 2PF_6$ in 2:1 stoichiometry suggests that it may also recognize (mono)pyridinium ions in [2]pseudorotaxane-like geometries in solution. If so, it would open up the possibility of using such systems for the facile syntheses of [2]rotaxanes. We suspected that BPX26C6, 3,5-di-*tert*-butylbenzyl bromide, and 4,4'-dipyridyl could undergo two-step reactions in one pot to generate the corresponding [2]rotaxanes: (1) N-alkylation of dipyrindyl with the benzyl bromide to generate a monoalkyl pyridinium ion, which is then encircled by a BPX26C6 unit to form the corresponding [2]semirotaxane,²¹ followed by (2) a second N-alkylation of the remaining pyridine unit of the thread component with another equivalent of the benzyl bromide; this second reaction would interlock the BPX26C6 moiety along the rodlike unit of the dumbbell-shaped component of the [2]rotaxane. Gratifyingly, we used this approach for the successful syntheses of the [2]rotaxanes $5 \cdot 2PF_6$ (isolated yield 70%) and $6 \cdot 2PF_6$ (25%)²² (Scheme 1) from the

Scheme 1. One-Pot Syntheses of [2]Rotaxanes $5 \cdot 2PF_6$ and $6 \cdot 2PF_6$



reactions of BPX26C6, 3,5-di-*tert*-butylbenzyl bromide, and the bipyridines **3** and **4**, respectively, in CH_3CN . We used vapor diffusion of isopropyl ether into a CH_3CN solution of $5 \cdot 2PF_6$ to obtain single crystals that were suitable for X-ray crystallographic analysis, and the solid-state structure (Figure 6) reveals the expected [2]rotaxane.

The syntheses of these [2]rotaxanes prove unambiguously that [2]pseudorotaxane-like complexes can exist between

(21) A semirotaxane has been defined as a pseudorotaxane possessing a stoppering unit at one terminus of the rodlike component. See: (a) Collin, J.-P.; Gaviña, P.; Sauvage, J.-P. *New J. Chem.* **1997**, *21*, 525. (b) Seel, C.; Parham, A. H.; Safarowsky, O.; Hübner, G. M.; Vögtle, F. *J. Org. Chem.* **1999**, *64*, 7236.

(22) At the reaction concentration (240 mM), 4,4'-dipyridyl (**3**) was completely soluble in MeCN, but the bipyridine **4** was not; thus, the relatively lower yield of the [2]rotaxane $6 \cdot 2PF_6$ may arise either from the low reaction concentration of the (mono)pyridinium intermediate from **4** or from its weaker association with BPX26C6.

(23) In addition to the small values of K_2 for the binding of BPX26C6 to $1 \cdot 2PF_6$ and $2 \cdot 2PF_6$, we determined that complex formation between BPX26C6 and *N*-methyl-4-methylpyridinium hexafluorophosphate in CD_3CN at 25 °C occurred with a binding constant of $16 \pm 2 M^{-1}$.

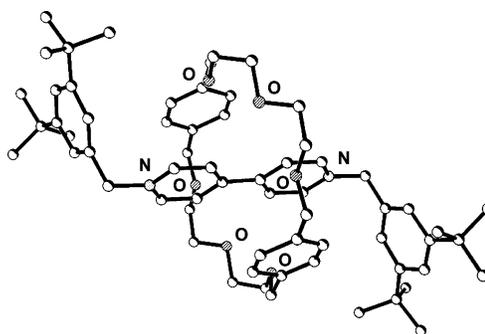


Figure 6. Ball-and-stick representation of the solid-state structure of the [2]rotaxane $5 \cdot 2PF_6$.

BPX26C6 and (mono)pyridinium ions in solution. Because (mono)pyridinium recognition sites for BPX26C6 can be established in situ, one-pot [2]rotaxane syntheses can be performed from readily available reagents without the need to use ionic starting materials possessing preinstalled recognition sites. Even though association constants for the interactions of BPX26C6 with (mono)pyridinium ions are small,²³ the yields of the [2]rotaxanes were surprisingly high. This result suggests that a relatively high concentration of (mono)pyridinium ions is generated in solution to facilitate the formation of the corresponding [2]semirotaxanes with BPX26C6. The weaker nucleophilicity of the nitrogen atom in the more electron-deficient (mono)pyridinium ion, relative to those in the neutral bipyridyls, may be responsible for the production of substantial amount of (mono)pyridinium ion in solution. It is also possible that the encircling crown ether donates some of its electron density (i.e., through charge transfer) to the thread component of the [2]semirotaxane to enhance the nucleophilicity of the nitrogen atom of the remaining pyridine unit, which facilitates the production of the [2]rotaxane rather than the dumbbell-shaped bipyridinium salt.

BPX26C6 is capable of forming [2]pseudorotaxane-like complexes with (mono)pyridinium ions; this property results in BPX26C6 forming [3]pseudorotaxane complexes with bipyridinium ions both in solution and in the solid state. This unique recognition behavior allows [2]rotaxanes to be prepared in one-pot reactions of BPX26C6, bipyridine derivatives, and moderately bulky benzyl bromides.

Acknowledgment. We thank the National Science Council (Taiwan) for financial support (NSC-94-2113-M-002-011).

Supporting Information Available: Synthetic procedures and characterization data for BPX26C6, $5 \cdot 2PF_6$, and $6 \cdot 2PF_6$, including CIF files. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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