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Three Protocols for the Formation of a [3]Pseudorotaxane *via* Orthogonal Cryptand-Based Host–Guest Recognition and Coordination-Driven Self-Assembly

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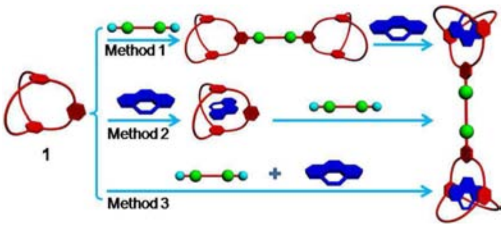
ABSTRACT



A novel bis(*m*-phenylene)-32-crown-10-based cryptand 1 with a pyridine nitrogen atom outside on the third arm was designed and synthesized. Subsequently, host–guest complexation between cryptand 1 and a selection of bipyridinium guests has been studied. More interestingly, the [3]pseudorotaxane $2\supset5_2$ was obtained in three methods by utilizing the noninterfering orthogonal nature of coordination-driven self-assembly and host–guest interactions.

The majority of known supramolecular architectures have been prepared merely employing a single recognition motif, while in nature, living creatures commonly exhibit multifunctionalities by elegantly integrating many recognition motifs in their biological processes.[1] Inspired by this, scientists have been trying to fabricate and construct artificial supramolecular systems based on orthogonal recognition motifs in which various noncovalent interactions facilitate multiple complementary components to self-assemble into complicated, hierarchically ordered supramolecular topological architectures with novel structures and superior properties.[2] Pseudorotaxanes, the basic building blocks for the preparation of advanced supramolecular topological structures, are self-assembled entities in which linear molecular components are encircled by macrocyclic components driven by many noncovalent interactions, such as hydrogen bonding, donor–acceptor, van der Waals forces, C–H$\cdots\pi$, *etc.*[3] Compared to these noncovalent interactions, strong and directional metal–ligand bonds have been proven to be an extremely important driving force for the construction of discrete 2D and 3D architectures with predetermined shapes, considerable stability, and inherent reversibility.[4] Undoubtedly,

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integration of general nondirectional noncovalent interactions and directional metal–ligand interactions into unified entities under the theme of orthogonal self-assembly will give the resultant architectures excellent adaptability and hierarchical complexity.[5] Therefore, we are interested in the fabrication of novel pseudorotaxane structures based on the combination of host–guest chemistry and metal–ligand bonding in an orthogonal way.[6]

Crown ether based cryptands are 3D bicyclic hosts with adequate cavities that are suitable for encapsulating ions and organic small molecules. There are many outstanding works contributed by Gibson, Huang, and others during the past two decades.[7] It has been well demonstrated that the introduction of additional binding sites (such as a N-atom) on the third arm and structural preorganization make them more powerful hosts for guest molecules than their crown ether precursors.[8] For example, from bis(*m*-phenylene)-32-crown-10 (BMP32C10) diol **7**[9a] to cryptand **8** (Figure 1), the association constants (K_a) between them and paraquat **3** increased about 9000 times in acetone.[9b] However, it is difficult to post-self-assemble on them on account of their structural characteristics, thereby limiting their further application in the construction of advanced topological structures.

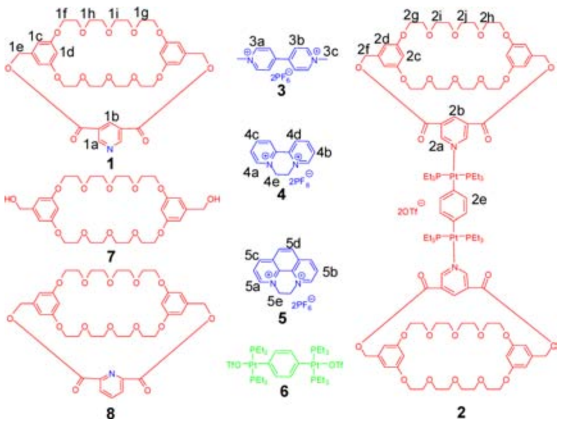
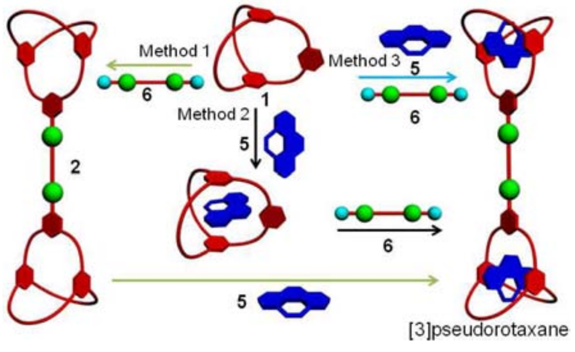


Figure 1. Compounds used in this study.

Herein, we designed a novel BMP32C10-based cryptand **1** (Figure 1) with its pyridine nitrogen atom outside the third arm in order to realize post-self-assembly on it by metal coordination. Subsequently, host–guest complexation of cryptand **1** with guests **3**, **4**, and **5** was studied. Furthermore, we successfully obtained bis-cryptand host **2** by metal-coordination interaction with 180° diplatinum(II) acceptor **6**, which complexes with guest molecules (for example guest **5**) to form [3]pseudorotaxanes (Scheme 1, method 1). Alternatively, [2]pseudorotaxane $\mathbf{1}\supset\mathbf{5}$ also coordinates with **6** to form [3]pseudorotaxane (Scheme 1, method 2). More interestingly, the [3]pseudorotaxane can be synthesized from five precursors *via* multiple, orthogonal noncovalent interactions in one simple self-assembly step (Scheme 1, method 3).

Compounds **3**–**6** were synthesized according to literature procedures.[10] Equimolar acetone solutions (5.00 mM) of cryptand **1** with guests **3**–**5** are yellow, which originates from charge-transfer (CT) interactions between the electron-rich aromatic rings of the cryptand host and the electron-poor pyridinium rings of the guests, good evidence for host–guest complexation. Furthermore, 1:1 stoichiometry between cryptand-based host **1** and three bipyridinium guests in acetone was confirmed by Job plots[11] (Figure S15) and electrospray ionization mass spectrometry (ESI-MS): m/z 1057.5 for $[\mathbf{1}\supset\mathbf{3} - \mathrm{PF_6}]^+$ and 456.3 for $[\mathbf{1}\supset\mathbf{3} - 2\mathrm{PF_6}]^{2+}$ (Figure S22), m/z 1055.6 for $[\mathbf{1}\supset\mathbf{4} - \mathrm{PF_6}]^+$ and 455.4 for $[\mathbf{1}\supset\mathbf{4} - 2\mathrm{PF_6}]^{2+}$ (Figure S23), and m/z 1079.4 for $[\mathbf{1}\supset\mathbf{5} - \mathrm{PF_6}]^+$ and 467.3 for $[\mathbf{1}\supset\mathbf{5} - 2\mathrm{PF_6}]^{2+}$ (Figure S24). In addition, peaks with other stoichiometries were not observed in the mass spectra. The association constants (K_a) were determined in acetone by using a UV–vis titration method to be $(6.39 \pm 0.73) \times 10^3\ \mathrm{M}^{-1}$ for $\mathbf{1}\supset\mathbf{3}$, $(2.69 \pm 0.84) \times 10^3\ \mathrm{M}^{-1}$ for $\mathbf{1}\supset\mathbf{4}$, and $(1.13 \pm 0.14) \times 10^4\ \mathrm{M}^{-1}$ for $\mathbf{1}\supset\mathbf{5}$ (Figures S16–S18).

Scheme 1. Cartoon Representation of the Formation of [3]Pseudorotaxane $\mathbf{2}\supset\mathbf{5}_2$ by Three Different Methods



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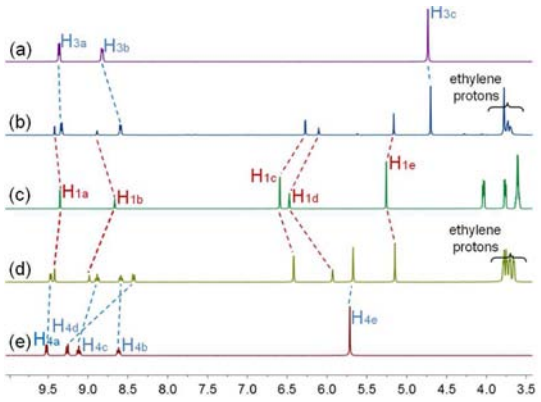

Figure 2. Partial ^{1}H NMR spectra (400 MHz, acetone-d_6, 293 K): (a) 5.00 mM **3**; (b) 5.00 mM **1** + 5.00 mM **3**; (c) 5.00 mM **1**; (d) 5.00 mM **1** + 5.00 mM **4**; (e) 5.00 mM **4**.

Equimolar (5.00 mM) acetone solutions of host **1** with guests **3**–**5** (Figures 2 and 4) were all examined by proton ^{1}H NMR experiments. After complexation between **1** and **3**, protons H_{1c}, H_{1d}, and H_{1e} of **1** and H_{3b} of **3** shifted upfield, while H_{1a} and H_{1b} of **1** moved downfield (Figure 2, spectra a–c). Similar chemical shift changes were also observed for the cases of **1**⊃**4** and **1**⊃**5** (Figures 2 and 4). It is worth noting that protons H_{5e} on **5** split into two peaks after it was mixed with **1** (Figure 4). It might be because the H_{5e} protons on one face of **5** are interacting with the host **1** in a different manner compared to the H_{5e} protons on the opposite face.

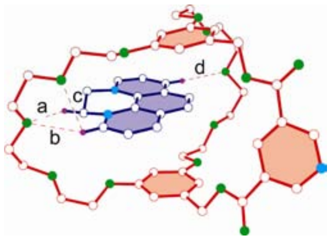

Figure 3. Ball-and-stick view of the X-ray structure of **1**⊃**5**. Cryptand **1** is red, guest **5** is blue, hydrogens are purple, oxygens are green, and nitrogens are sky blue. PF_6^- counterions and hydrogens except the ones involved in hydrogen bonding were omitted for clarity. Hydrogen bond parameters are as follows: C···O distance (Å), H···O distance (Å), C–H···O angles (deg): (a) 3.30, 2.38, 153.4; (b) 3.33, 2.49, 147.5; (c) 3.09, 2.70, 104.9; (d) 3.57, 2.62, 176.9.

The successful preparation of cryptand-based [2]-pseudorotaxane **1**⊃**5** was further unambiguously confirmed by X-ray analysis of a yellow single crystal with a 1:1 stoichiometry grown by vapor diffusion of pentane into an acetone solution of **1**⊃**5**. In the solid state, [2]-pseudorotaxane **1**⊃**5** is stabilized by four hydrogen bonds and π–π stacking interactions between the phenyl rings of the host **1** and the pyridinium units on the guest **5** (Figure 3). Three oxygen atoms on host **1** and three hydrogen atoms on guest **5** are involved in these hydrogen bonding interactions. Importantly, from the crystal structure, we can confirm that the pyridine nitrogen atom on the third arm of cryptand **1** is located outside of the cavity, which facilitates the further self-assembly of the cryptand-based topological structures by metal coordination.

Furthermore, we synthesized the metal-coordination-driven bis-cryptand host **2** by mixing crypand **1** (10.0 μM) and 180° diplatinum(II) acceptor **6** (5.00 μM) in a 2:1 ratio in CD_2Cl_2 at room temperature for 30 min. Multinuclear NMR (^{1}H and ^{31}P) analysis of the reaction mixture confirmed the formation of bis-cryptand host **2**. The $^{31}P\{^{1}H\}$ NMR spectrum of **2** showed a sharp single peak at *ca.* 12.95 ppm with concomitant ^{195}Pt satellites corresponding to a single phosphorus environment (Figure S12). This peak shifted upfield from the starting diplatinum(II) acceptor **6** by *ca.* 6.08 ppm (Figures S5 and S12), indicating the formation of host **2**. In the ^{1}H NMR spectrum of host **2**, the obvious downfield shifts of the H_{2a} and H_{2b} pyridyl protons on host **2** were observed because of the loss of electron density that occurs upon coordination of the pyridyl *N*-atom to the Pt(II) metal center (Figure 4, spectra a and e). The formation of host **2** was further confirmed by ESI-MS: *m*/*z* 1196.9 for $[\mathbf{2} - 2OTf]^{2+}$ (Figure S25).

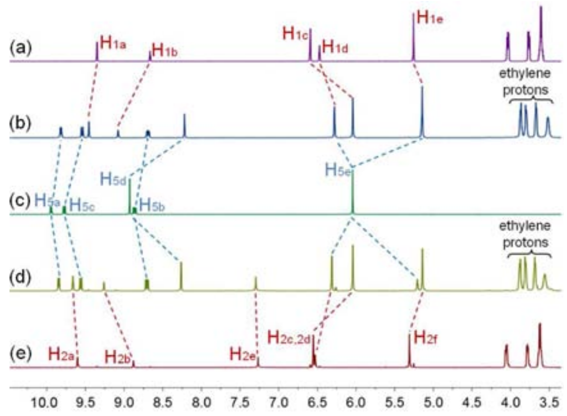

Figure 4. Partial ^{1}H NMR spectra (400 MHz, acetone-d_6, 293 K): (a) 5.00 mM **1**; (b) 5.00 mM **1** + 5.00 mM **5**; (c) 5.00 mM **5**; (d) 2.50 mM **2** + 5.00 mM **5**; (e) 2.50 mM **2**.

By adding 2 equiv of guest **5** to an acetone-d_6 solution of host **2** (Scheme 1, method 1), [3]pseudorotaxane **2**⊃$\mathbf{5}_2$ was successfully obtained. Upon the addition of guest **5**, the solution quickly became yellow due to CT interactions

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between the electron-rich aromatic rings of host **2** and the electron-poor pyridinium rings of guest **5**. Compared to host **2**, the $^{31}P\{^{1}H\}$ NMR spectrum of $\mathbf{2}\supset\mathbf{5}_2$ does not show any significant change, indicating that the incorporation of guest **5** does not substantially change the chemical environment of the phosphorus atoms. The ^{1}H NMR spectrum of $\mathbf{2}\supset\mathbf{5}_2$ (Figure 4d), however, exhibited characteristic shifts associated with the complexation of guest **5**, for example, H_{2c}, H_{2d}, and H_{2f} of **2** moved upfield and the signal of proton H_{5e} on guest **5** also split into two signals, as observed in the case of $\mathbf{1}\supset\mathbf{5}$ (Figure 4b). A Job plot (Figure S15d) demonstrated that the host–guest complex between **2** and **5** was of 1:2 stoichiometry in acetone. In addition, the structure of $\mathbf{2}\supset\mathbf{5}_2$ was confirmed by ESI-MS: m/z 468.0 for $[M - 2OTf - 4PF_6]^{6+}$ and m/z 1080.5 for $[M - 2OTf - PF_6]^{3+}$ (Figure S26). The average association constant (K_{av}) was determined in acetone by using a UV–vis titration method to be 470 M^{-1} for $\mathbf{2}\supset\mathbf{5}_2$ (Figures S19–S20). It is worth noting that the binding constant between **2** and **5** decreased about 25 times compared to that of **1** and **5**. The poor affinity of bis-cryptand **2** for guest **5** may arise from the following three reasons. First, the charge repulsion between the cationic host **2** and the cationic guest **5** can obviously weaken the binding abilities between them. Second, since the pyridine atom on the third arm of cryptand coordinates with Pt, the electron-withdrawing platinum atom can reduce the electron density of the pyridine rings of **2**, thereby weakening the π–π stacking and CT interactions between phenylene rings of **2** and the pyridinium rings of **5**. Third, the presence of triflate counterions can also reduce the binding affinity due to the ion effect.[12]

The [3]pseudorotaxane $\mathbf{2}\supset\mathbf{5}_2$ can also be prepared by an alternative stepwise method (Scheme 1, method 2). Stirring a 1:1 mixture of host **1** and guest **5** in acetone-d_6 yielded [2]pseudorotaxane $\mathbf{1}\supset\mathbf{5}$. Then, the addition of 0.500 equiv of **6** resulted in the formation of [3]pseudorotaxane $\mathbf{2}\supset\mathbf{5}_2$. Multinuclear NMR ($^{1}H$ and ^{31}P) analysis of the reaction mixtures showed the same features as those observed in the spectra of $\mathbf{2}\supset\mathbf{5}_2$ prepared by method 1, thus confirming the formation of the same species by this alternative stepwise procedure. However, the best demonstration of the power of this orthogonal procedure is to employ a third method of self-assembly. Just mixing a 2:2:1 ratio of three different components **1**, **5**, and **6** (Scheme 1, method 3) also produces [3]pseudorotaxane $\mathbf{2}\supset\mathbf{5}_2$ which was characterized by multinuclear NMR (^{1}H and ^{31}P) analysis.

In summary, we designed and synthesized a BMP32C10-based cryptand with its pyridine nitrogen atom outside the third arm, which was confirmed by X-ray analysis. It not only can complex with guests **3**, **4**, and **5** to form [2]-pseudorotaxanes but also can be further post-self-assembled by metal-coordination interactions. The [3]-pseudorotaxane $\mathbf{2}\supset\mathbf{5}_2$ was obtained by three methods by utilizing the noninterfering orthogonal nature of coordination-driven self-assembly and host–guest interactions. The methodology presented here demonstrates that the complexed supramolecular topological architectures can be prepared from multiple, different precursors under the theme of orthogonal noncovalent interactions in a simple self-assembly way. Our current efforts are focused on extending this strategy by combining coordination-driven self-assembly with cryptand-based molecular recognition to fabricate supramolecular polymers and other advanced supramolecular architectures.

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Supporting Information Available. Synthetic details, determination of stoichiometries and binding constants (K_a), ESI-MS, X-ray crystallographic file (CIF) for $\mathbf{1}\supset\mathbf{5}$ (CCDC 947846), and other materials. This material is available free of charge via the Internet at http://pubs.acs.org.

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The authors declare no competing financial interest.