

# A Heterowheel [3]Pseudorotaxane by Integrating $\beta$ -Cyclodextrin and Cucurbit[8]uril Inclusion Complexes

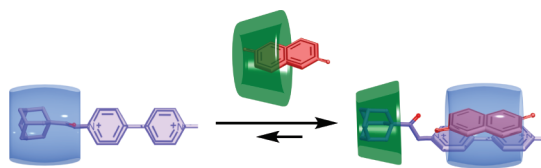
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## ABSTRACT



A heterowheel [3]pseudorotaxane was prepared by integrating two binary inclusion complexes of  $\beta$ -cyclodextrin-hydroxynaphthalene ( $\beta$ -CD·3) with a cucurbit[8]uril-viologen derivative (CB[8]·2), in which simultaneous molecular recognition of the adamantane moiety in 2 by  $\beta$ -CD and the charge-transfer interaction of 3 with the viologen nucleus of 2 in the cavity of CB[8] are two crucial factors for the formation of the quaternary complex.

In recent decades, much attention has been focused on pseudorotaxanes<sup>1</sup> because they not only are the supramolecular precursors of rotaxanes and catenanes<sup>2</sup> but also are viewed as prototypes of simple molecular machines.<sup>3</sup> Therefore, designing and synthesizing pseudorotaxanes

with novel topologies is desirable for both supramolecular chemistry and the construction of molecule-based devices. A general synthetic methodology for preparing pseudorotaxanes is that a/several cyclic wheel component(s) are threaded into a linear axle component to form stable host–guest pair(s).<sup>2,4</sup> Anion-templated,<sup>2d,5</sup> cation-templated,<sup>6</sup> and second-sphere coordination<sup>7</sup> routes

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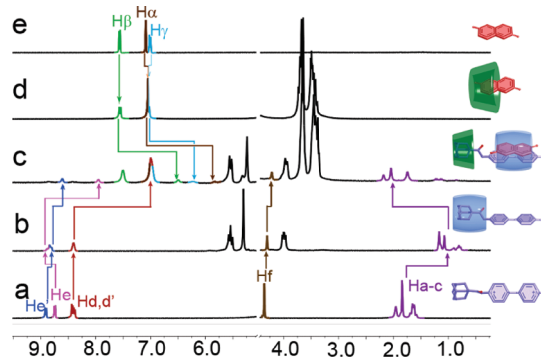
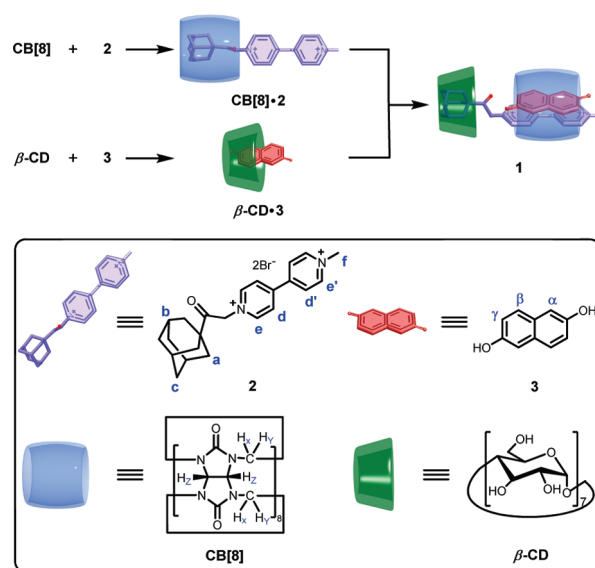
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are other efficient synthetic methodologies of pseudorotaxanes. Hydrogen bonding,<sup>2a–c</sup> halogen bonding,<sup>5a</sup> ion–dipole interactions,<sup>2c,f,8</sup> and the charge-transfer (CT) interactions<sup>6c,9</sup> are the main driving forces for the interpenetration of axle molecules into the cavity of wheel components to form pseudorotaxanes. Recently, we successfully constructed two heterowheel pseudorotaxanes by a macroring molecule ( $\alpha$ -cyclodextrin,  $\alpha$ -CD) driving another molecular wheel (cucurbit[7]uril, CB[7]) movement on a molecular axle.<sup>10</sup> The ion–dipole interaction of the axle molecule with CB[7] and the hydrophobic interactions of that with  $\alpha$ -CD/CB[7] are two critical driving forces to form the complex. In other pseudorotaxane-like plug-socket<sup>11</sup> and [3]rotaxane<sup>12</sup> systems, the ion–dipole interaction of 24-crown-8 with secondary dialkylammonium as well as the CT interaction between complementary anthracene/pyrene and naphthalenediimide provides impetus for the formation of these complexes. Herein, we report a new heterowheel [3]pseudorotaxane **1** by integrating two binary inclusion complexes of  $\beta$ -CD with hydroxynaphthalene **3** and CB[8] with viologen derivative **2**,<sup>13</sup> in which the driving forces come from simultaneous molecular recognition of adamantane by  $\beta$ -CD and the CT interaction of **3** with the viologen nucleus of **2** in the cavity of CB[8]. The formation of the quaternary complex is a bottom-up approach and a resulting guest-exchange process, as shown in Scheme 1.

The formation of two 1:1 complexes of CB[8]·**2** and  $\beta$ -CD·**3** can be conveniently monitored by <sup>1</sup>H NMR spectroscopy. As can be seen from Figure 1a, b, upon the addition of CB[8], the proton signals of H<sub>a–c</sub> in **2** shift to higher field and those of aromatic protons (H<sub>e</sub>) of adjacent adamantane exhibit a downfield shift and are split into two signals, while other aromatic protons are almost unchanged. These observations suggest that the

**Scheme 1.** “Bottom-up” Approach of [3]Pseudorotaxane **1**



**Figure 1.** Partial <sup>1</sup>H NMR spectra (400 MHz, D<sub>2</sub>O, 298 K) of (a) **2** (2.1 mM), (b) CB[8]·**2** (1.8 mM), (c) CB[8]·**2** (1.8 mM) + 2 equiv of  $\beta$ -CD·**3**, (d) CD·**3** (2.1 mM), and (e) **3** (2.1 mM).

adamantane moiety of **2** is included in the cavity of CB[8], and the viologen moiety is near one of its portals, as the right illustration shown in Figure 1b. On the other hand, upon the addition of  $\beta$ -CD, the signals of H <sub>$\gamma$</sub>  protons in **3** shift to lower field, while those of H <sub>$\alpha$</sub>  go to a higher field, which indicates that **3** is included in the cavity of  $\beta$ -CD (Figure 1d). The formation of the 1:1 CB[8]·**2** and 1:1  $\beta$ -CD·**3** complexes is also evidenced by ESI-MS. The peaks at 838 and 1295 are assigned to [CB[8]·**2** – 2Br]<sup>2+</sup> and [ $\beta$ -CD·**3** + H]<sup>+</sup> respectively (Figures S3 and S4 Supporting Information).

When 2 equiv of  $\beta$ -CD·**3** complex were added to the D<sub>2</sub>O solution of CB[8]·**2**, all aromatic proton signals of **2** and **3** are significantly shifted to higher field, and those of nonaromatic protons of **2** exhibit a remarkable downfield shift (Figure 1c). In the 2D NMR spectrum of the quaternary

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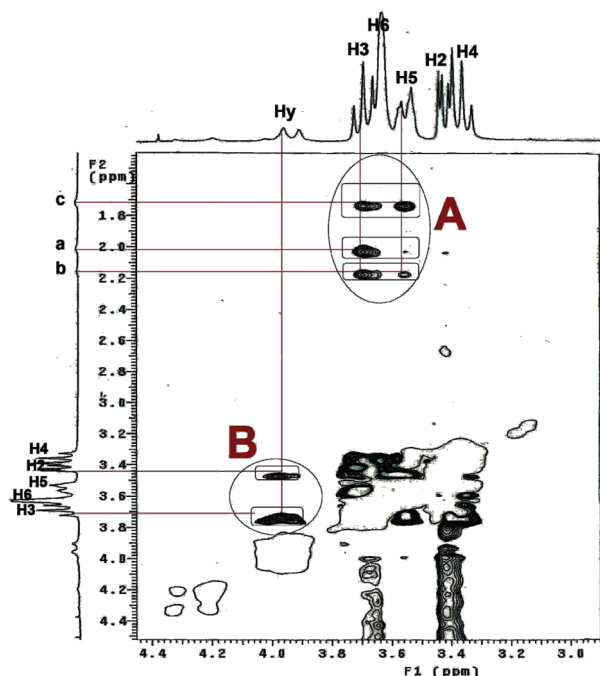
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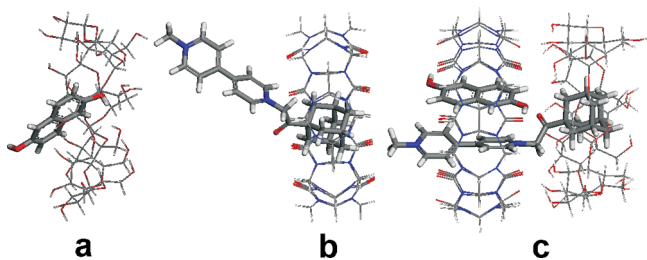
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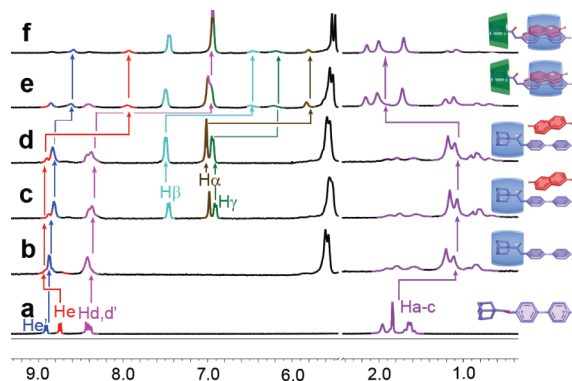


**Figure 2.** Partial  $^1\text{H}$  ROESY spectrum of a 1:1 mixture of  $\text{CB}[8]\cdot 2$  (1 mM) and  $\beta\text{-CD}\cdot 3$  (1.2 mM) in  $\text{D}_2\text{O}$  at 298 K with a mixing time of 250 ms.

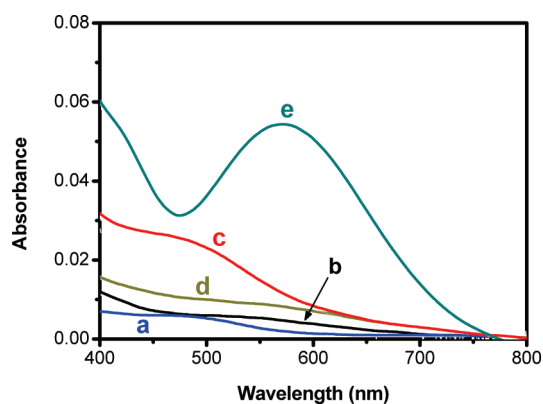


**Figure 3.** Optimized structures of (a)  $\beta\text{-CD}\cdot 3$ , (b)  $\text{CB}[8]\cdot 2$ , and (c)  $[3]\text{pseudorotaxane } 1$ .

mixture **2**, **3**,  $\text{CB}[8]$ , and  $\beta\text{-CD}$  (Figure 2), we can easily find NOE cross-peaks between the protons of adamantane and  $\text{H}_3$  and  $\text{H}_5$  of  $\beta\text{-CD}$  (peaks A), indicating that the adamantane moiety of **2** is included in the cavity of  $\beta\text{-CD}$ .<sup>13</sup> Meanwhile, NOE cross-peaks between the  $\text{H}_y$  protons of  $\text{CB}[8]$  and  $\text{H}_2$  and  $\text{H}_3$  of  $\beta\text{-CD}$  (peaks B) provide strong evidence for not only  $\beta\text{-CD}$  enfolding the adamantane part but also the two macrocycles being closely located in the quaternary complex. That is,  $\text{CB}[8]$  is moved to the viologen moiety facilitating the formation of the stable CT complex between **2** and **3**, and  $\beta\text{-CD}$  correspondingly perches on the adamantane moiety in the quaternary complex. Furthermore, we also carried out molecular energy minimization on the system, and two snapshots are shown in Figure 3. The formation of  $[3]\text{pseudorotaxane } 1$  was also evidenced by ESI-MS (Figure S5, Supporting Information).



**Figure 4.** Partial  $^1\text{H}$  NMR spectra (400 MHz,  $\text{D}_2\text{O}$ , 298 K) of (a) **2** (2.1 mM), (b)  $\text{CB}[8]\cdot 2$  (2.1 mM), (c)  $\text{CB}[8]\cdot 2$  (1.8 mM) + 1 equiv of **3**, (d)  $\text{CB}[8]\cdot 2$  (1.8 mM) + 2 equiv of **3**, (e)  $\text{CB}[8]\cdot 2$  (1.8 mM) + 2 equiv of **3** + 1 equiv of  $\beta\text{-CD}$ , and (f)  $\text{CB}[8]\cdot 2$  (1.8 mM) + 2 equiv of **3** + 2 equiv of  $\beta\text{-CD}$ .



**Figure 5.** Absorption spectra of (a) **2** (1 mM), (b) **3** (1 mM), (c) **2** (1 mM) + **3** (1 mM), (d)  $\text{CB}[8]\cdot 2$  (1 mM) + **3** (1 mM), and (e)  $\text{CB}[8]\cdot 2$  (1 mM) + **3** (1 mM) +  $\beta\text{-CD}$  (1 mM) in  $\text{H}_2\text{O}$ , at 298 K.

It has been well demonstrated that  $\text{CB}[8]$  can facilitate effectively the formation of the stable CT complex between viologen derivatives and hydroxynaphthalenes.<sup>9</sup> There is also a CT complex of **2** with **3** in the above quaternary system. Unexpectedly, if  $\beta\text{-CD}$  is not in this system, the **2**·**3** CT complex would hardly exist. NMR spectra and UV–vis spectroscopic experiments can validate the effect of  $\beta\text{-CD}$  on the formation of the stable CT complex. As can be seen from Figure 4c, d, the addition of 1 equiv (even 2 equiv) of **3** to  $\text{CB}[8]\cdot 2$  does not change the NMR signals of  $\text{CB}[8]\cdot 2$ , which indicates that **3** does not enter the cavity of  $\text{CB}[8]$  to form the CT complex. When 2 equiv of  $\beta\text{-CD}$  were added to the solution of  $\text{CB}[8]\cdot 2$  and **3**, all aromatic proton signals in **2** and **3** are significantly shifted to higher field, while those of nonaromatic protons in **2** go downfield (Figure 4e, f). This observation is consistent with that in Figure 1c, suggesting the formation of  $[3]\text{pseudorotaxane } 1$ .

Figure 5 shows the absorption experiments on **2**, **3**, a mixture of equivalent **2** and **3**, a mixture of equivalent

CB[8]·**2** and **3**, and a mixture of equivalent CB[8]·**2**, **3**, and  $\beta$ -CD. An unremarkable absorption band around 470 nm is observed in the spectrum of [**2** + **3**] relative to the free **2** and **3**, indicating the presence of a fractional CT complex in the mixture of **2** and **3**.<sup>9i</sup> However, no obvious interaction was observed between CB[8]·**2** and **3** (Figure 5, line d). This observation should be attributed to CB[8] including the adamantane moiety of **2** to prevent the free **3** from becoming close to the viologen nucleus of **2**. Significantly, when equivalent  $\beta$ -CD was added to the aqueous solution of CB[8]·**2** and **3**, a distinctly different photophysical behavior was observed. A strong CT band emerges at about 580 nm. The result leads to the solution color changing from colorless to purple. In addition, the remarkable fluorescence quenching of the quaternary system relative to the free **3**, [**2** + **3**], and [**2** + **3** + CB[8]] is also evidence for the formation of the CT complex (Figure S6, Supporting Information).

To gain more insight on the position of CB[8] on **2**, CV measurements were carried out for **2**, CB[8]·**2**, CB[8]·**2** + **3**, and CB[8]·**2** +  $\beta$ -CD·**3** (Figure S10, Supporting Information). The reduction potentials of CB[8]·**2** and CB[8]·**2** + **3** only slightly change (Figure S10, lines a, b, and c) compared to the reduction potentials of **2** (−0.54 and −0.77 V). This observation should be attributed to CB[8] including the adamantane moiety of **2** and the reduction potentials of the viologen unit was not significantly affected by the cavity of CB[8], while the [3]pseudorotaxane exhibits a large shift for the reduction peaks (−0.89 and −1.22 V) compared to **2**. This large shift indicates the formation of a CT inclusion complex in the cavity of the CB[8].<sup>9i</sup> To further understand the roles of  $\beta$ -CD in the formation of the stable CT complex, we determined the binding constants ( $K_S$ ) of CB[8] with **2**, and the quaternary system by NMR titration. Comparing the  $K_S$  value ( $5.5 \times 10^5 \text{ M}^{-1}$ ) of [CB[8] + **2**] with those reported for [CB[8] + MV<sup>2+</sup>] ( $1.1 \times 10^5 \text{ M}^{-1}$ , MV = methylviologen)<sup>14</sup> as well as [ $\beta$ -CD + **2**] ( $1.3 \times 10^4 \text{ M}^{-1}$ ),<sup>13</sup> we deduce reasonably that CB[8] will include preferably **2** relative to  $\beta$ -CD. This deduction is also well validated by the observation of the changeless CB[8]·**2** NMR signals upon the addition of  $\beta$ -CD (Figure S7, Supporting Information). The larger  $K_S$  value for [CB[8] + **2**] relative to [CB[8] + MV<sup>2+</sup>] suggests that a majority of CB[8]

should bind the adamantane moiety of **2**, not its viologen nucleus, which has been proved by previous NMR experiments. In Kim's CB[8]/MV/hydroxynaphthalene systems, the preorganization of CB[8] with the viologen nucleus can greatly facilitate hydroxynaphthalene into the cavity of CB[8], forming the stable ternary CT complex.<sup>9i</sup> In the present system, CB[8]s mostly bind the adamantane moiety of **2**, which makes the cavity of CB[8] not work for the formation of the stable CT complex of **2** with **3**. However, upon the addition of  $\beta$ -CD in the solution of CB[8], **2**, and **3**,  $\beta$ -CD will bind competitively the adamantane moiety of **2**, making partial CB[8] molecules move onto the viologen nucleus of **2**. This not only leads to the formation of the stable CT complex between **2** and **3** but also impels more CB[8] to move onto the viologen nucleus. The  $K_S$  value of the quaternary system is about  $3.5 \times 10^{10} \text{ M}^{-3}$  (Table S11, Supporting Information). This is the driving force for the formation of the heterowheel [3]pseudorotaxane **1**.

In conclusion, a novel heterowheel [3]pseudorotaxane **1** has been constructed by integrating two binary complexes of  $\beta$ -CD·**3** with CB[8]·**2**. The collaborative contributions of the ion–dipole interaction between the axle molecule **2** and CB[8], the hydrophobic interactions of **2/3** with  $\beta$ -CD/CB[8], and the CT interaction of **2** with **3** are the main driving forces for the formation of this [3]pseudorotaxane. Distinctly differing from the reported conclusion about the stable CT complex between viologen derivatives and hydroxynaphthalenes in the cavity of CB[8], the present viologen derivative **2** and hydroxynaphthalene **3** cannot form any CT complex in the presence of CB[8]. The molecular recognition of the adamantane moiety in **2** by  $\beta$ -CD is a crucial factor to pushing CB[8] onto the viologen nucleus of **2**, resulting in the formation of the **2**·**3** CT complex. The present heterowheel [3]pseudorotaxane not only enriches the world of supramolecular architectures but also provides a novel approach to design highly unsymmetrical supramolecular architectures with different blocks.

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**Supporting Information Available.** 1D and 2D NMR, ESI-MS, emission spectra, CV curves and determination of binding constants. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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