Introduction

In the past few years interlocked supramolecules have attracted a great deal of attention because of their interesting structures and potential application for supramolecular machines such as molecular switches, molecular wires, and information storage. Cucurbit[7]urils (CBs) can form very stable host-guest complexes with positively charged molecules such as bipyridinium, ammonium, imidazolium, and coordinatively unsaturated metal ions through charge−dipole, hydrogen-bonding, and hydrophobic interactions. As another class of macrocycles contrasting with CBs, cyclodextrins (CDs) have been widely used as wheels for supramolecular assemblies for their remarkable properties of forming inclusion complexes with a variety of guest molecules.
of small molecules or ions of appropriate size, \textsuperscript{7} 4,4'-Bipyridinium dication, commonly known as viologen, has been extensively utilized as a component of macrorings or axles due to its unique redox character and ability as an electron acceptor.\textsuperscript{7,8} Recently, Inoue and co-workers studied the 1:1:1 CB[6]–CD–dihexylammonium complex that mainly depended on the supramolecular positive cooperativity.\textsuperscript{9} The pH-controlled and electrochemically switchable pseudorotaxanes based on CB[7] and viologens (Chart 1) have also been reported by Kaifer’s group.\textsuperscript{10} Kim and Yui et al. studied pH-responsive movement of CB[7] in polypseudorotaxane containing dimethyl-\textbeta-CD and CB[7].\textsuperscript{11} However, the movement of one macrocyclic molecule controlled by another macrocyclic molecule is not involved. Therefore, we are motivated to investigate in detail the movement of CB[7] on the axles of the linear viologens driven by \textalpha-CD.

It is documented that the binding interactions between symmetrical viologens and CB[7] may lead to two different types of complexes: \textsuperscript{46} (a) \(N,N'\)-dimethyl-4,4'-bipyridinium (MV\textsuperscript{2+}) (Chart 1) or \(N,N'\)-diethyl-4,4'-bipyridinium (EV\textsuperscript{2+}) forms stable pseudorotaxane complexes with CB[7], in which CB[7] binds at the viologen nucleus; (b) \(N,N'\)- dibutyl-4,4'-bipyridinium (BV\textsuperscript{2+}) (Chart 1) or other viologens with longer aliphatic \(N\)-substituents favor the formation of external complexes with CB[7], in which CB[7] binds at the external docking points of viologens. In addition, \textalpha-CD hardly forms any complexes with dicaticonic guests such as viologens.\textsuperscript{12} On the contrary, its cavity can include small guest molecules possessing straight aliphatic chains.\textsuperscript{13} In the text, we respectively chose asymmetric \(N\)-methyl-\(N'\)-octyl-4,4'-bipyridinium (MVO\textsuperscript{2+}) and symmetrical MV\textsuperscript{2+}, BV\textsuperscript{2+}, \(N,N'\)-diocetyl-4,4'-bipyridinium (OV\textsuperscript{2+}), and \(N,N'\)-dibenzy-4,4'-bipyridinium (BnV\textsuperscript{2+}) as axles (Chart 1) and CB[7] and \textalpha-CD as wheels to build pseudorotaxanes. Our particular interest is to investigate how CB[7] moves on these viologen axles upon addition of \textalpha-CD.

\textbf{Results and Discussion}

\textbf{\textsuperscript{1}H NMR Spectra.} The formation of the 1:1 or 1:2 complexes for viologen guests with CB[7] and the 1:1:1 or 1:1:2 complexes for MVO\textsuperscript{2+} or OV\textsuperscript{2+} with CB[7] and \textalpha-CD can be conveniently monitored by \textsuperscript{1}H NMR spectroscopy. We started our investigation with MVO\textsuperscript{2+}, CB[7], and \textalpha-CD. Figure 1A shows the \textsuperscript{1}H NMR spectra of MVO\textsuperscript{2+} in 0.2 M NaCl–D\textsubscript{2}O. Upon addition of 0.3 equiv of CB[7], the signals of aromatic protons are almost unchanged and those of the alkyl protons are broadened (Figure 1B). In the presence of 1.1 equiv of CB[7], the resonances of both the aromatic protons (\(\beta, \beta', \) and \(\alpha\)) and the alkyl protons shift to higher field (Figure 1C). This reveals that CB[7] is equilibrating between the bipyridinium and the octyl moieties in [MVO\textsuperscript{2+}CB[7]\textsuperscript{2+}], but mainly locates at the octyl moiety. Upon addition of 1.2 equiv of \textalpha-CD to the above mixed solution, the signals of \(\beta, \beta'\) aromatic protons exhibit a major upfield shift, and simultaneously those of octyl protons exhibit a downfield shift (Figure 1D). These observations indicate that CB[7] should bind at the bipyridinium moiety in the ternary complex [MVO\textsuperscript{2+}CB[7]\textsuperscript{2+}\textalpha-CD\textsuperscript{2+}]. The almost similar information of the chemical shifts of the aromatic and octyl protons in Figure 1E,F means that 3.0 equiv of \textalpha-CD can make all CB[7] locate at the bipyridinium moiety of MVO\textsuperscript{2+}. In the control experiment (Figure 1G), the addition of \textalpha-CD gives the signals of the octyl protons a minor downfield shift, but does not affect the chemical shift of the aromatic protons of MVO\textsuperscript{2+}, suggesting that \textalpha-CD just binds at the octyl moiety of MVO\textsuperscript{2+}. These combined observations confirm that CB[7] locates at the bipyridinium moiety of MVO\textsuperscript{2+} along with the addition of \textalpha-CD instead of shuttling between the octyl and bipyridinium moieties in [MVO\textsuperscript{2+}CB[7]\textsuperscript{2+}\textalpha-CD\textsuperscript{2+}]. The formation of the binary [MVO-CB[7]\textsuperscript{2+}] and the ternary [MVO-CB[7]\textsuperscript{2+}\textalpha-CD\textsuperscript{2+}] host–guest complexes is also evidenced by ESI-MS. The peaks at 723.8 and 1209.5 are
FIGURE 2. ESI-MS spectrum of a solution containing MVO$^2+$ (1.0 equiv), CB[7] (1.2 equiv), and α-CD (2.0 equiv) in water.

FIGURE 3. $^1$H NMR spectra (300 MHz, 0.2 M NaCl–D$_2$O, 298 K) of (A) OV$^2+$, (B) OV$^2+ + 0.5$ equiv of CB[7], (C) OV$^2+ + 1.2$ equiv of CB[7], and (D) OV$^2+ + 2.4$ equiv of CB[7].

We also chose the symmetrical OV$^2+$ guest to investigate the movement of CB[7] on viologen driven by α-CD. As shown in Figure 3B, the presence of 0.5 equiv of CB[7] splits every aliphatic proton signal of OV$^2+$ into two signals. In the presence of 2.4 equiv of CB[7], the aromatic proton signals are hardly changed, and the octyl ones obviously shift upfield (Figure 3D). These observations suggest that a 1:2 complex of [OV·2CB·7]$^{2+}$ is formed, and the two CB[7]'s are respectively docked at the two octyl moieties in [OV·2CB·7]$^{2+}$. The further NMR experiments of the addition of α-CD to [OV·2CB·7]$^{2+}$ reveal that α-CD cannot change the binding sites of CB[7] at OV$^2+$.14

The presence of 1.2 equiv of CB[7] makes the octyl signals split into three portions (Figure 4A). They should correspond with the 1:1 complex of [OV·CB·7]$^{2+}$ and 1:2 complex of [OV·2CB·7]$^{2+}$. From their integral areas, the dominating component between them is [OV·CB·7]$^{2+}$. Furthermore, upon stepwise addition of α-CD to the mixed solution of OV$^2+$ and 1.2 equiv of CB[7], the upfield displacement of the β aromatic protons is observed, and the signals of the alkyl protons are displaced downfield and broadened (from part B to part E of Figure 4). Upon addition of 12.0 equiv of α-CD, the resonance signals of the β aromatic protons shift upfield from 8.42 to 7.45 ppm, and those of the alkyl protons are similar to the signals of OV$^2+$ in the presence of 10.0 equiv of α-CD, as shown in Figure 4F. This pattern of complexion-induced shifts could be ascribed to CB[7] binding at the viologen nucleus, while α-CD includes the octyl chains in [OV·CB·7·α-CD]$^{2+}$. The [OV·CB·7]$^{2+}$, [OV·2CB·7]$^{2+}$, [OV·CB·7·α-CD]$^{2+}$, and [OV·CB·7·2α-CD]$^{2+}$ complexes are unambiguously detected by ESI-MS measurements.14 It should be noted that OV$^2+$ possesses two long alkyl chains, so a small quantity of α-CD cannot move CB[7] to the viologen nucleus. In light of the above NMR and MS experiments, we deduced that the movement of CB[7] is as follows: α-CD first binds at the free octyl moiety of [OV·CB·7]$^{2+}$, and then the binding of the second α-CD with another octyl chain of OV$^2+$ forces CB[7] to move from the octyl moiety to the bipyridinium moiety. In the process, both α-CDs play the roles of stoppers.

For comparison purposes, we investigated the binding interactions of other viologens (BV$^2+$, BnV$^2+$, and MV$^2+$) with CB[7] and α-CD by NMR spectroscopy.14 BV$^2+$ and BnV$^2+$ can form external inclusion complexes with CB[7] as OV$^2+$, in which the viologen nucleus is not engulfed by the CB[7].6b,c In sharp contrast, the addition of abundant α-CD cannot push CB[7] to the viologen nucleus. One possible reason is that both external butyl and benzyl groups are too short to be included by α-CD. For the case of MV$^2+$, CB[7] binds at the viologen nucleus directly,6b,c and the addition of α-CD cannot change the binding mode of [MV·CB·7]$^{2+}$.

(14) See the Supporting Information.

UV−Vis Spectra. UV−vis spectroscopic measurements were widely utilized to measure the binding constants between viologens and CB[7] because the molar absorptivity coefficients of their electronic absorption bands at ca. 260 nm were depressed when the viologen nucleus was included inside the cavity of CB[7]. In our experiments, the main parameters (λ_{max} and ε) of the UV absorption band of MVO_{2}^{2+} and OV_{2}^{2+} were not changed significantly by the increase of CB[7] or α-CD. Interestingly, the addition of α-CD showed a small hypochromic shift in the absorption band of MVO_{2}^{2+} in the presence of 1.0 equiv of CB[7] as shown in Figure 5, indicating the anticipated locomotion of CB[7] from the octyl moiety to the viologen nucleus. Analogous results were also obtained from the spectra of the addition of α-CD to the [OV•CB[7]]^{2+} aqueous Tris buffer solution. However, the main parameters (λ_{max} and ε) of [BnV•CB[7]]^{2+}, [BV•CB[7]]^{2+}, or [MBV•CB[7]]^{2+} were unchanged upon addition of α-CD. These results from the UV−vis spectra were in excellent agreement with the NMR experiments.

Microcalorimetric Titration. To investigate quantitatively the molecular recognition behavior of CB[7], α-CD with viologens, and their thermodynamic origins for the movement of CB[7] on viologens driven by α-CD, the isothermal titration calorimetry (ITC) experiments were performed in aqueous Tris buffers (pH 7.4). It should be mentioned that the protonated form of Tris can compete to some extent for CB[7] with the viologen dications. As can be seen from Table 1, the K_{S} value for the complexation of MVO_{2}^{2+} with CB[7] is 2 orders of magnitude larger than that with α-CD, leading to a large free energy change (ΔΔG° = −11.8 kJ mol⁻¹). The favorable free energy change results from the contributions of both the enthalpy term originating from ion−dipole interactions between the N⁺ groups of MVO_{2}^{2+} and the carbonyl groups of CB[7] (ΔΔH° = −4.7 kJ mol⁻¹) and the entropy term from the desolvation effect of the N⁺ groups (ΔΔS° = 7.1 kJ mol⁻¹). It is noted that the complex [MVO•CB[7]]^{2+} can interact further with α-CD to give the 1:1:1 [MVO•CB[7•α-CD]]^{3+} complex. If CB[7] exclusively locates at the bipyridinium moiety of MVO_{2}^{2+} originally, the thermodynamic parameters of α-CD with [MVO•CB[7]]^{2+} should be similar to those of the complexation of α-CD with MVO_{2}^{2+}. However, as shown in Table 1, the ΔG° value of the reaction is almost the same as that for complexation of MVO_{2}^{2+} with α-CD, but their enthalpy changes and entropy changes are distinctly different: the complexation of α-CD with MVO_{2}^{2+} mostly comes from the contribution of the enthalpy, while that with [MVO•CB[7•α-CD]]^{3+} is attributed to both favored enthalpy change and entropy change. It should be mentioned that the favored enthalpy change for the formation of [MVO•CB[7•α-CD]]^{3+} comes from not only the complexation of the octyl moiety with α-CD but also the hydrogen-bonding interactions.

**FIGURE 5.** UV−vis spectra of 50.0 μM [MVO•CB[7]]^{2+} in the presence of increasing concentrations (0−8.0 mM, in the direction of the arrow) of α-CD in Tris buffer (pH 7.4) at 298 K.

**FIGURE 6.** Partial 1H ROESY spectrum of a mixture of MVO_{2}^{2+} (5 mmol/L), CB[7] (5 mmol/L), and α-CD (6 mmol/L) in D_{2}O at 298 K with a mixing time of 250 ms.

<table>
<thead>
<tr>
<th>complexation reaction</th>
<th>K_{S}</th>
<th>−ΔG°</th>
<th>−ΔH°</th>
<th>−ΔS°</th>
</tr>
</thead>
<tbody>
<tr>
<td>MVO_{2}^{2+} + CB[7] ↔ [MVO•CB[7]]^{2+}</td>
<td>33800 ± 8000</td>
<td>31.56 ± 0.06</td>
<td>24.1 ± 0.2</td>
<td>7.5 ± 0.2</td>
</tr>
<tr>
<td>MVO_{2}^{2+} + α-CD ↔ [MVO•α-CD]^{2+}</td>
<td>2940 ± 40</td>
<td>19.80 ± 0.04</td>
<td>19.4 ± 0.2</td>
<td>0.4 ± 0.2</td>
</tr>
<tr>
<td>[MVO•CB[7]]^{2+} + α-CD ↔ [MVO•CB[7•α-CD]]^{3+}</td>
<td>2180 ± 20</td>
<td>19.06 ± 0.03</td>
<td>8.0 ± 0.2</td>
<td>11.1 ± 0.2</td>
</tr>
<tr>
<td>OV_{2}^{2+} + CB[7] ↔ [OV•2CB[7]]^{2+}</td>
<td>516000 ± 20000</td>
<td>32.60 ± 0.09</td>
<td>21.7 ± 0.2</td>
<td>10.9 ± 0.3</td>
</tr>
<tr>
<td>OV_{2}^{2+} + 2α-CD ↔ [OV•2α-CD]^{2+}</td>
<td>2360 ± 24</td>
<td>19.24 ± 0.03</td>
<td>22.25 ± 0.06</td>
<td>−3.08 ± 0.09</td>
</tr>
<tr>
<td>[OV•CB[7]]^{2+} + α-CD ↔ [OV•CB[7•α-CD]]^{2+}</td>
<td>5640 ± 250</td>
<td>21.4 ± 0.1</td>
<td>14.8 ± 0.2</td>
<td>6.6 ± 0.1</td>
</tr>
<tr>
<td>[OV•CB[7•α-CD]]^{2+} + 2α-CD ↔ [OV•CB[7•2α-CD]]^{3+}</td>
<td>626 ± 16</td>
<td>16.0 ± 0.1</td>
<td>19.2 ± 0.4</td>
<td>−3.3 ± 0.5</td>
</tr>
</tbody>
</table>

*a* The net reaction heat in this run was calculated by the “one set of binding sites” model in ORIGIN software. *b* The net reaction heat in this run was calculated by the “1:2 sequential binding sites” model in ORIGIN software.
between CB[7] and α-CD. These observations suggest that CB[7] in the complex [MVO-CB[7]]\(^{2+}\) should mainly locate at the octyl moiety of MVO\(^{2+}\), and the addition of α-CD pushes CB[7] from the octyl moiety to the bipyridinium moiety.

For OV\(^{2+}\) possessing two octyl chains, the 2:1 and 2:1:1 inclusion complexes are respectively formed between CB[7] (α-CD) and OV\(^{2+}\) and between α-CD and [OV-CB[7]]\(^{2+}\). The binding constants (\(K_\alpha\)) and the relevant thermodynamic parameters obtained are shown in Table 1. The \(K_\alpha\) values for the complexation of CB[7] or α-CD with OV\(^{2+}\) approximate those with MVO\(^{2+}\), but their enthalpy changes and entropy changes are different. In comparison to the latter, the complexation of CB[7] with OV\(^{2+}\) gives a favorable entropy change (\(\Delta T\Delta S^\sigma = 3.4 \text{ kJ mol}^{-1}\)) and a less unfavorable enthalpy change (\(\Delta H^\sigma = 2.4 \text{ kJ mol}^{-1}\)). Contrarily, the complexation of α-CD and OV\(^{2+}\) is enthalpically favorable (\(\Delta H^\sigma = -2.8 \text{ kJ mol}^{-1}\)) and entropically unfavorable (\(\Delta T\Delta S^\sigma = -3.5 \text{ kJ mol}^{-1}\)). Further, the binding constant for the formation of the 1:1 complex of α-CD and [OV-CB[7]]\(^{2+}\) (5640 ± 250 M\(^{-1}\)) is larger than that of α-CD and OV\(^{2+}\) (2360 ± 24 M\(^{-1}\)). This should be ascribed to the OV\(^{2+}\) charge density decreasing with the binding of CB[7] and resulting in α-CD easily binding at the octyl moiety.

The above NMR experiments have clarified that CB[7] just binds at the octyl moiety of [OV-CB[7]]\(^{2+}\), while CB[7] does at the viologen nucleus of MV\(^{2+}\). The binding constant of CB[7] with OV\(^{2+}\) is slightly larger than that with MV\(^{2+}\) (\(K_\alpha = 2.24 \times 10^5 \text{ M}^{-1}\)). That is to say, the affinity of CB[7] toward the octyl moiety of OV\(^{2+}\) should be slightly stronger than that toward its bipyridinium moiety. Therefore, it is a natural process that the weaker binding of α-CD with OV\(^{2+}\) can compete with very strong binding of CB[7] to force it to move from the octyl moiety to the bipyridinium moiety.

**Two-Dimensional NMR Experiments.** To investigate the interactions among MVO\(^{2+}\), CB[7], and α-CD, 2D NMR experiments were employed upon addition of 1.2 equiv of α-CD to a solution of [MVO-CB[7]]\(^{2+}\). As shown in Figure 6, the ROESY spectrum of the ternary system exhibits clear NOE cross-peaks between the H\(_8\) protons of the octyl in MVO\(^{2+}\) and H3 and H5 of α-CD (peaks A and B), which demonstrate that the octyl chain is completely included in the cavity of α-CD. The cross-peak between H\(_8\) and H5 (peak C) further confirms that the primary side of α-CD locates at the portal of MVO\(^{2+}\). Meanwhile, clear NOE cross-peaks between H\(_8\) and H3 (peak D) as well as between the H\(_8\) protons of CB[7] and H2 and H3 of α-CD provide strong evidence for not only α-CD penetrating into the octyl chain from its secondary side, but also the two macrocycles being closely located in the ternary complex, which suggests hydrogen-bonding interactions between CB[7] and α-CD. That is, CB[7] is moved to the nucleus, and α-CD correspondingly perches on the octyl moiety in [MVO-CB[7]·α-CD]\(^{2+}\). Furthermore, we also carried out molecular dynamics simulation\(^{(17)}\) on the system, and four snapshots are shown in Figure 7, which are consistent with our experimental results.

**Conclusion**

In summary, we have presented the controlled wheel-molecular movement on a molecular axle driven by another macroring molecule. The binding constants and the thermodynamic parameters obtained in this study reveal that the exothermic enthalpy changes of the complexation between the axle molecules and α-CD afford an impetus to push CB[7] from the octyl moiety to the bipyridinium moiety of the viologen. This work should not only be useful for supramolecular control of molecular behavior, but also provide insight into designing locomotive molecular devices that are driven by another molecule.

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(17) A 100 ps MD simulation is performed by using the NVT ensemble with a time step of 1 fs at 298 K using the Dreiding force field (Mayo, S. L.; Olafson, B. D.; Goddard, W. A., III. *J. Phys. Chem.* 1990, 94, 8897). The cutoff distance is 9 Å with a buffer length of 0.5 Å.
Experimental Section

Materials. All chemicals were of the highest purity commercially available and were used without further purification. BV$_2^{2+}$ and BnV$_2^{2+}$ were synthesized according to refs 18 and 19, respectively. The syntheses of MVO$_2^{2+}$ and OV$_2^{2+}$ are described in the Supporting Information.

Isothermal Microcalorimetric Titration. All calorimetric experiments were performed using a thermostated and fully computer-operated VP-ITC calorimeter purchased from a commercial supplier. In this study, all microcalorimetric titrations were performed in an aqueous Tris buffer solution (pH 7.4) at atmospheric pressure and 298 K. Each solution was degassed and thermostated using a ThermoVac accessory before titration. Each microcalorimetric titration experiment consisted of 25 or 29 successive injections. A constant volume (10 µL/injection for α-CD or CB[7]) of host solution (2.87–9.93 mM for each host) in a 0.250 mL syringe was injected into the reaction cell (1.4227 mL) charged with MVO$_2^{2+}$, OV$_2^{2+}$, [MVO-CB[7]]$_2^{2+}$, or [OV-CB[7]]$_2^{2+}$ solution (0.12–0.32 mM) in the same buffer solution.

A control experiment to determine the heat of dilution was carried out with each run by performing the same number of injections with the same concentration of host compound as used in the titration experiments into a pure buffer solution without the guest compound. The dilution enthalpies determined in control experiments were subtracted from the enthalpies measured in the titration experiments to obtain the net reaction heat.

ORIGIN software, which was used to simultaneously compute the equilibrium constant ($K_S$) and standard molar enthalpy of reaction ($\Delta H^\circ$) from a single titration curve, gave a standard deviation based on the scatter of the data points in the titration curve. The net reaction heat in each run was calculated by the “one set of binding sites” model unless noted otherwise. Additionally, the first point was removed from the titration curve, acknowledging that the concentration of guest in the cell far exceeded the concentration of the host. A typical titration curve and the fitted results for the complexation of CB[7] with MVO$_2^{2+}$ are shown in Figure 8. The isothermal calorimetric titration curve obtained by the addition of α-CD to the [OV-CB[7]]$_2^{2+}$ solution is analyzed by using the equation for the simultaneous formation of the 1:1 and 1:2 complexes (sequential binding sites model). The knowledge of the binding constant ($K_S$) and molar reaction enthalpy ($\Delta H^\circ$) enabled calculation of the standard free energy of binding ($\Delta G^\circ$) and entropy changes ($\Delta S^\circ$), according to the equation

$$\Delta G^\circ = -RT \ln K_S = \Delta H^\circ - T\Delta S^\circ$$

where $R$ is the gas constant and $T$ is the absolute temperature.

Multiple independent titration runs ($N = 2$) were performed to afford self-consistent thermodynamic parameters, and the averaged values are reported in Table 1. The uncertainties in the thermodynamic parameters reported for host–guest complexation are 2 standard deviations of the mean value.

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Supporting Information Available: Additional 1D and 2D NMR, ESI-MS, and UV–vis spectra and an ITC titration curve as mentioned in the text. This material is available free of charge via the Internet at http://pubs.acs.org.