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Electrochemically Switchable Cucurbit[7]uril-Based Pseudorotaxanes

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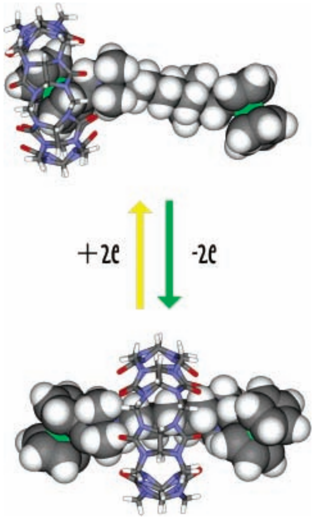
ABSTRACT



The binding location of cucurbit[7]uril can be controlled via redox conversions in these novel, structurally simple pseudorotaxanes.

From the development of the first molecular shuttle by Stoddart and co-workers in 1991,[1] interest in "molecular machine" systems has grown rapidly because they hold promise for unprecedented device miniaturization via the bottom-up approach to nanotechnology.[2] A great deal of attention has centered on molecular systems that exhibit reversible structural changes in response to external stimuli, in the form of heat,[3] light,[4] pH changes,[5] ion additions,[6] polarity changes,[7] or electrochemical/chemical control of oxidation states.[8,9] Rotaxanes are simple mechanically interlocked molecules that contain two noncovalently bound components: a macrocycle or "wheel" threaded by a long "axle" component terminated on bulky stopper groups that prevent wheel dissociation.[10] Bistable or switchable rotaxanes contain at least two functional residues or stations along the axle. The strength of the interactions between each axle station and the wheel macrocycle can be controlled by external stimuli. As a result, controlled motions of the wheel along the axle become possible and two or more different states of the molecule, corresponding to different relative

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10.1021/ol061128+ CCC: $33.50

positions of the macrocycle, can be identified. Since the preparation of larger-cavity cucurbit[*n*]uril hosts ($n > 6$) by Kim and co-workers in 2000,[11] considerable attention has been focused on the properties of these hosts, which have also been utilized as wheel components in rotaxanes (Figure 1).[12,13]

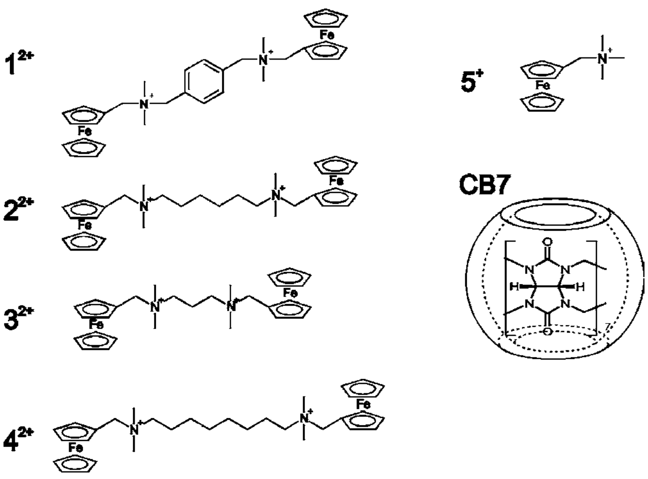

Figure 1. Structures of the guests used in this work and the **CB7** host. All guests were utilized as their bromide salts.

In this work, we report the preparation and properties of novel, structurally simple pseudorotaxanes with electrochemically switchable structures. These compounds are prepared around the binding interactions between the cucurbit[7]uril host (**CB7**) and the dicationic axle guests $\mathbf{1}^{2+}$ and $\mathbf{2}^{2+}$, which exhibit a central binding site (between two quaternized, positively charged nitrogens) and two terminal binding sites (on the electroactive ferrocenyl residues). The switching of the main **CB7** binding location is the result of a delicate balance between the stability of **CB7** on the two types of binding sites (terminal or central) as a function of the oxidation state of the ferrocenyl centers.

Previous work has shown that cationic derivatives of (ferrocenylmethyl)dimethylamine display remarkably high association constants with **CB7** ($K > 10^{12}$ M^{-1}).[14] At absolute concentrations above the micromolar level, complexation is quantitative between any of these guest molecules and **CB7**, with very slow dissociation rates, so no bulky stopper groups are required to keep the host bound to the axle guest. In $\mathbf{1}^{2+}$ and $\mathbf{2}^{2+}$, the xylylene and hexylene units terminated in quaternary nitrogens are also very stable binding sites for **CB7** as they are capable of hydrophobic interactions with the inner cavity of **CB7**. In both cases, the distance between the positively charged nitrogens is ideal for the development of strong ion−dipole interactions with the electron-rich carbonyl portals of **CB7**, adding to the overall stability of the complex. Isaacs and co-workers have reported relatively high binding constants between 1,6-hexylenediammonium and **CB7** ($K = 9 \times 10^{7}$ M^{-1}) and xylylenediammonium and **CB7** ($K = 1.8 \times 10^{9}$ M^{-1}).[15] In guests $\mathbf{3}^{2+}$ and $\mathbf{4}^{2+}$, the propylene and octylene spacers are either too short or too long, respectively, for optimization of the ion−dipole interactions with the **CB7** portals, diminishing the importance of the central site as a **CB7** binding station. Therefore, these two guests were used as control compounds for comparison purposes.

We first investigated the binding interactions between guests $\mathbf{1}^{2+}$−$\mathbf{4}^{2+}$ and host **CB7** by ^{1}H NMR spectroscopy. We observed pronounced upfield shifts of all the ferrocenyl proton resonances upon addition of **CB7** to a D_2O/NaCl solution of any of the guests (Figure 2 shows the data for guest $\mathbf{1}^{2+}$). This experimental finding clearly indicates the inclusion of the ferrocenyl residue inside the cavity of **CB7**. When less than 2.0 equiv of **CB7** is present, two sets of peaks are observed corresponding to the **CB7**-bound and free ferrocenyl units. In other words, the chemical exchange of host molecules among the available ferrocenyl residues is slow on the NMR time scale. Binding saturation occurs after the addition of 2.0 equiv of **CB7**, indicating that the guests are capable of forming both 1:1 and 2:1 (host−guest) complexes with **CB7**. The 1:1 complexes are stable and remain soluble indefinitely, whereas the less-soluble 2:1 complexes precipitate easily. The binding interactions between the **CB7** host and the ferrocenyl units of all four guests were found to follow a similar pattern.

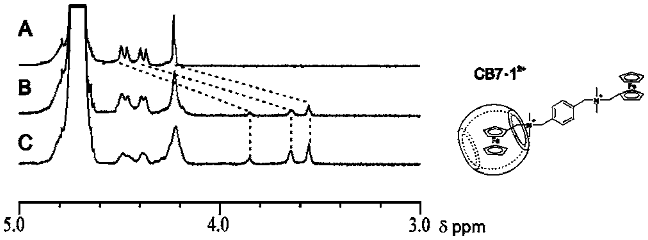

Figure 2. ^{1}H NMR partial spectra (400 MHz, 0.2 M NaCl/D_2O) of $\mathbf{1}^{2+}$ in the presence of (A) 0 equiv, (B) 0.5 equiv, and (C) 1 equiv of **CB7**. Inset shows location of **CB7** binding around the ferrocenyl group.

Quite recently, we have shown that the voltammetric behavior of the (ferrocenylmethyl)trimethylammonium cation ($\mathbf{5}^{+}$) is very sensitive to the presence of **CB7**.[14] Basically, a new voltammetric wave is observed for the **CB7**·$\mathbf{5}^{+}$ complex, which undergoes oxidation at a half-wave potential ($E_{1/2}$)

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ca. 110 mV more positive than the free guest. Thus, the **CB7** complex is significantly destabilized (by ca. 2.5 kcal/mol) upon oxidation of the ferrocene center.[16] This destabilization is rationalized by the increased hydrophilicity of the oxidized guest formed within the hydrophobic cavity of the host, along with the inability of the host to adapt to the spatial arrangement of the two charges. Cyclic voltammetric experiments with guests $\mathbf{1}^{2+}$–$\mathbf{4}^{2+}$ (in the absence of **CB7**) show that the two ferrocenyl groups behave as independent redox subunits because their reversible oxidation to the positively charged ferrocenium form takes place at roughly the same potential. This result is completely within expectations because the two terminal ferrocenyl groups are spatially separated and their degree of electronic coupling is anticipated to be negligible. For guests $\mathbf{1}^{2+}$ and $\mathbf{2}^{2+}$, in the presence of 1.0 equiv of **CB7**, two oxidation waves are observed in the anodic scan, which correspond to the **CB7**-bound and free ferrocenyl groups, in agreement with the NMR spectroscopic data. However, on the reverse (cathodic) scan, only one wave was observed at a potential that corresponds to the reduction of the unbound ferrocenium center (Figure 3A, bottom). The absence of a voltammetric peak for the reduction of the bound ferrocenium center reveals that, after electrochemical oxidation, the ferrocenium group is no longer encapsulated by **CB7**. In clear contrast to this behavior, $\mathbf{3}^{2+}$ and $\mathbf{4}^{2+}$ showed two oxidation waves and two clear reduction waves corresponding to **CB7**-bound and unbound ferrocenium centers (Figure 3B, bottom). The voltammetric behavior of the latter two guests is thus typical of cationic derivatives of (ferrocenylmethyl)dimethylamine, for which oxidation to the ferrocenium form does not lead to dissociation of **CB7**.

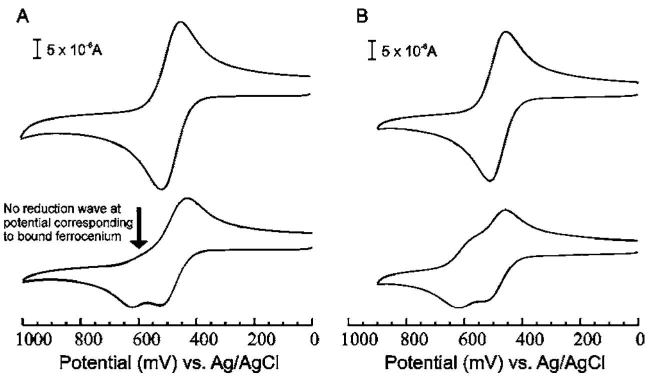

Figure 3. CV responses recorded on a glassy carbon electrode (0.071 cm^2) in 0.1 M NaCl of (A) 1.0 mM $\mathbf{1}^{2+}$ in the absence (top) and in the presence of 1 equiv of **CB7** (bottom) and (B) 1.0 mM $\mathbf{3}^{2+}$ in the absence (top) and in the presence of 1 equiv of **CB7** (bottom). Scan rate: 0.1 V/s.

Simple dissociation between **CB7** and the guests does not explain the voltammetric data because there is no reason for oxidation-induced dissociation between the host and the guest to take place with $\mathbf{1}^{2+}$ and $\mathbf{2}^{2+}$ and not with $\mathbf{3}^{2+}$ and $\mathbf{4}^{2+}$. The observation of a voltammetric cathodic peak for the **CB7**-encapsulated ferrocenium center with guests $\mathbf{3}^{2+}$ and $\mathbf{4}^{2+}$ and its absence with $\mathbf{1}^{2+}$ and $\mathbf{2}^{2+}$ strongly suggest that the presence of a suitable binding site in the center of the axle may attract the **CB7** host after oxidation of the ferrocenyl residue because oxidation is known to decrease the stability of the complex between **CB7** and the terminal binding sites. To further explore this idea, we performed cyclic voltammetric experiments with solutions containing ca. 2 equiv of **CB7** and guest $\mathbf{1}^{2+}$. In this situation, both ferrocenyl groups are included by **CB7** and cyclic voltammetry shows that both groups are oxidized at the higher potential expected for the inclusion complex. However, the corresponding reduction peak for the ferrocenium inclusion complex is clearly visible on the reverse scan (Figure 4A, bottom). This is due to the presence of two **CB7** hosts bound to guest $\mathbf{1}^{2+}$, as neither macrocycle can now move to the central binding position upon oxidation because the resulting proximity of the second **CB7** host would give rise to strong repulsions between the negatively charged carbonyl rims on their cavity openings. Therefore, the oxidation-induced motion of **CB7** only takes place in the 1:1 complexes (with guests $\mathbf{1}^{2+}$ and $\mathbf{2}^{2+}$) and is impossible in the 2:1 complexes.

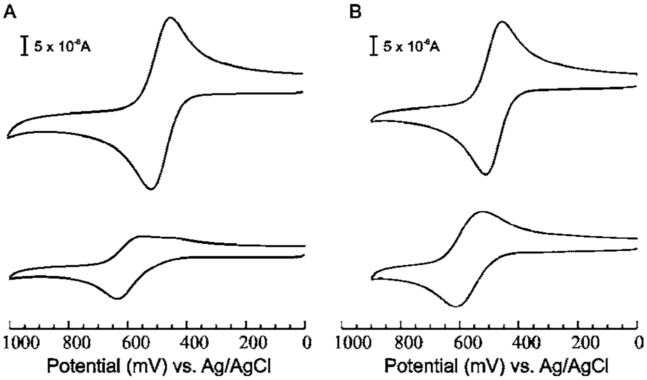

Figure 4. CV responses recorded on a glassy carbon electrode (0.071 cm^2) in 0.1 M NaCl of (A) 1.0 mM $\mathbf{1}^{2+}$ in the absence (top) and in the presence of ca. 2 equiv of **CB7** (bottom) and (B) 1.0 mM $\mathbf{3}^{2+}$ in the absence (top) and in the presence of 2 equiv of **CB7** (bottom).

To verify the movement of **CB7** to the central binding site of guests $\mathbf{1}^{2+}$ and $\mathbf{2}^{2+}$, the ferrocene units were quantitatively oxidized to their ferrocenium forms using nitrosonium tetrafluoroborate, and ^{1}H NMR spectroscopy was used to determine the new binding positions for the **CB7** host. The paramagnetic character of the ferrocenium residues broadens and shifts some of the proton resonances, but the proton signals of the xylylene unit in $\mathbf{1}^{4+}$ and the hexylene chain in $\mathbf{2}^{4+}$ were still clearly observable. Addition of **CB7** to oxidized $\mathbf{1}^{4+}$ and $\mathbf{2}^{4+}$ confirmed that the **CB7** now binds around the xylylene and hexylene units, as shown by the disappearance of the xylylene proton resonances in $\mathbf{1}^{4+}$ and, much more clearly, by the upfield shift of the methylene

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[16] Kaifer, A. E.; Gómez-Kaifer, M. *Supramolecular Electrochemistry*; Wiley-VCH: Weinheim, Germany, 2000.

proton resonances of **2**$^{4+}$ (Figure 5). This is strong evidence in support of **CB7** shuttling along **1**$^{2+}$ and **2**$^{2+}$ (from one of the terminal binding sites to the central binding site) upon oxidation to **1**$^{4+}$ and **2**$^{4+}$. In strong contrast to this, ^{1}H NMR experiments with **3**$^{4+}$ and **4**$^{4+}$ demonstrate that **CB7** showed no shuttling effect, and no binding around the propylene and octylene spacers was detected.

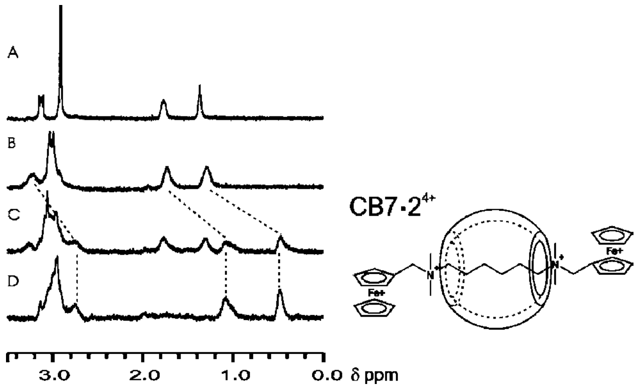
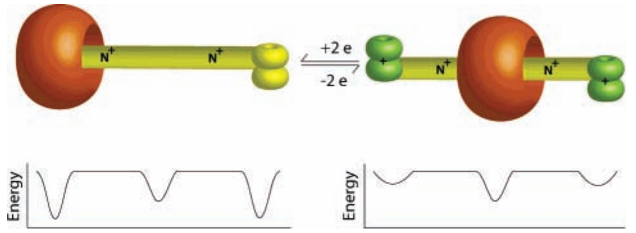


Figure 5. ^{1}H NMR partial spectra (400 MHz, 0.2 M NaCl/D_2O) of (A) **2**$^{2+}$, (B) after oxidation with NO^+ BF_4^- to **2**$^{4+}$, (C) in the presence of 0.6 equiv and (D) 1.2 equiv of **CB7**. Inset shows **CB7** binding around the central hexylene chain.

Cyclic voltammetric experiments also showed no changes in voltammetric behavior after multiple repeated scans for the switchable pseudorotaxane complexes formed upon mixing of guest **1**$^{2+}$ (or **2**$^{2+}$) with 1.0 equiv of **CB7**. The reproducibility of the voltammetric behavior cycle after cycle demonstrates that these systems are stable and capable of a large number of reversible oscillations.

The principle of operation of these two switchable pseudorotaxanes, **CB7·1**$^{2+}$ and **CB7·2**$^{2+}$, involves the electrochemical destabilization of the complex around the ferrocenyl units coupled with the presence of a suitable secondary binding site with a high affinity for **CB7** along the axle component. It is interesting to note that the known values for the stability of the **CB7** complexes with the individual binding sites (as found in simple guests) do not fully explain the switching behavior in the **CB7** complexes of **1**$^{2+}$ and **2**$^{2+}$. The $\Delta G°$ value for **CB7** complexation of **5**$^{+}$ has been reported as −16.8 kcal/mol,[14] and the corresponding $\Delta G°$ values for complexation of 1,6-hexylenediammonium and 1,4-xylylenediammonium are −10.9 and −12.6 kcal/mol, respectively.[15] Therefore, the loss of stability calculated for the **CB7·5**$^{+}$ complex upon one-electron oxidation[14] (2.5 kcal/mol) is not enough to explain the switching of **CB7** from the ferrocenium site to the central binding site between the two positively charged nitrogens. This fact is not completely unexpected because the stability of **CB7** inclusion complexes may be strongly affected by medium effects,[17] as well as by structural or charge features on the guest, regardless of whether these features are included in the host cavity or proximal to the host. In any instance, the experimental results reported here reveal an energetic landscape that fits the potential energy curves shown in Scheme 1.

Scheme 1. Pictorial Representation of Electrochemical Control on the **CB7** Binding Location in the **CB7·1**$^{2+}$ and **CB7·2**$^{2+}$ Pseudorotaxanes and Estimated Relative Potential Energies Associated to Wheel Movement along the Axle



Overall, we have demonstrated the operation of structurally simple **CB7** pseudorotaxanes under redox control. Our group recently reported another **CB7**-based pseudorotaxane under pH control.[5] An unusual characteristic of these systems is their operation as reversible switchable molecules in aqueous media, in contrast to most other reported bistable rotaxanes and pseudorotaxanes. The systems reported here take advantage of hydrophobic, ion−dipole, and electrostatic forces in controlling the shuttling movement of **CB7** and constitute the first example of electrochemically controlled pseudorotaxanes based on **CB7**.

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Supporting Information Available: Synthetic details and NMR spectroscopic data (6 pages). This material is available free of charge via the Internet at http://pubs.acs.org.

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