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Electrochemically Driven Clathration/Declathration of Ferrocene and Its Derivatives by a Nanometer-Sized Coordination Cage

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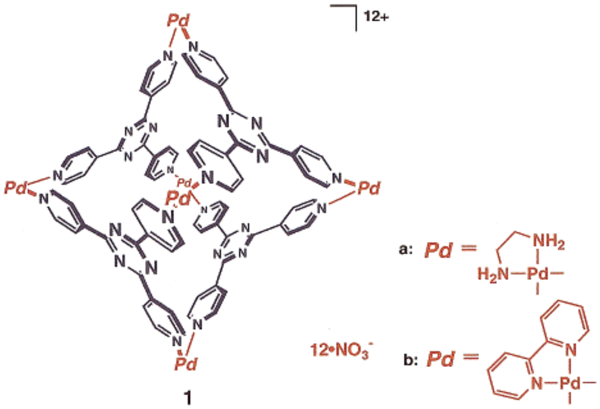
Previous studies of our and some other groups have demonstrated that hollow structures (cages, bowls, capsules etc.) with nanometer-sized cavities obtained by metal-directed self-assembly[1] have ability to encapsulate large guest molecules[2] and can regulate specific reactions[3] inside the cavity in aqueous media. Neutral molecules with suitable size can be encapsulated into the cavity via the noncovalent interactions due to the hydrophobic environment of the cavity.[2,3] However, if a cationic molecule is employed as a guest, no such encapsulation can be expected due to electrostatic repulsion, since these hollow structures with metal ions and pyridine-based ligands are also cationic.[4] Therefore, the encapsulated neutral molecules are expected to go outside when they are oxidized to cationic species. In other words, clathration and declathration of molecules by the cavity can be controlled by oxidation and reduction. In view of developing molecular-based switching systems, control of molecular motions by external stimuli is an attractive task of current chemistry.[5] As one approach of this idea, we have studied the host−guest interaction of Pd(II)-linked nanocage **1** with ferrocene and its derivatives (**2**, **3**, and **4**) as well as the corresponding ferrocenium ions ($\mathbf{2}^+$, $\mathbf{3}^+$, and $\mathbf{4}^+$).



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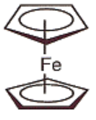

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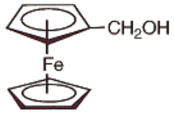

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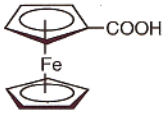

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When ferrocene (**2**) was saturated in aqueous solution of **1a**, the formation of $\mathbf{1a}\cdot(\mathbf{2})_n$ (n = ca. 3) was suggested by the upfield shift of **2** in NMR.[6] The voltammetric behavior of $\mathbf{1a}\cdot(\mathbf{2})_n$ complex was studied in water at 2.5 mM and compared with that of free **2**.[7,8] As shown in Figure 1A, the peak potential is positively shifted by 73 mV, and the peak currents are greatly enhanced by encapsulation. We suggest that the positive shift is caused by the cationic environment of the cage, while the peak current enhancement is simply caused by higher effective concentration of **2** within the cavity, as four molecules of **2** are crammed together.[9]

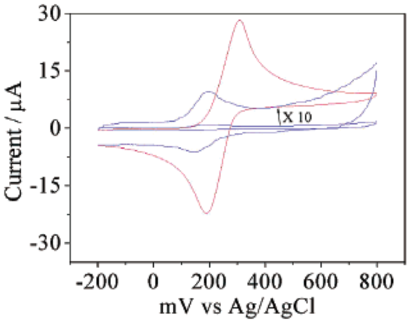

Figure 1. Cyclic voltammograms of saturated **2** in aqueous solution containing $NaNO_3$ (30 mM, blue line) and **1a** (2.5 mM, red line). Scan rate: 100 mV/s.

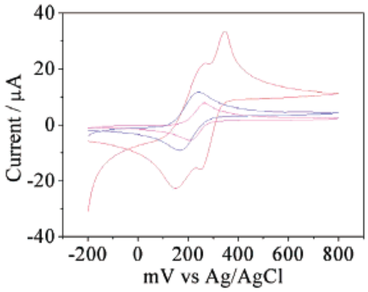

Figure 2. Cyclic voltammograms of **3** (2.5 mM) in aqueous solution containing 30 mM $NaNO_3$ (blue line) and 2.5 mM **1a** (magenta line). The red line shows the cyclic voltammogram of saturated **3** in aqueous solution containing 2.5 mM **1a**. Scan rate: 10 mV/s.

To compare the peak current at the same concentration, water-soluble ferrocene derivative **3** was used as a guest. Upon addition of **1a** (1 mol equiv), we observed ca. 40% decrease in the peak currents, in addition to the positive shift of peak potential (Figure 2, blue and magenta lines). The peak current is reduced by the slower diffusion of **3** when it is encapsulated.[9,10] Thus, both the positive shift in peak potential and the reduction in peak current are consistent with the efficient formation of encapsulation complex $\mathbf{1a}\cdot(\mathbf{3})_n$.[10] A positive shift in peak potential was also observed in the CV of **4** in the presence of **1a**, suggesting that this anionic guest is also encapsulated by **1a** (Supporting Information).

More interestingly, two redox couples were observed when excess **3** was added to the aqueous solution of **1a** (Figure 2, red line). The one with half-wave potential ($E_{1/2}$) at 209 mV, which is very close to 204 mV of **3** in the absence of **1a**, comes from free

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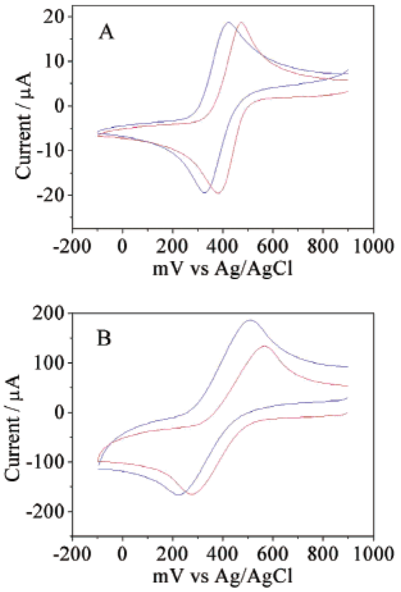

Figure 3. Cyclic voltammograms of **4**$\cdot PF_6$ (2.5 mM) in aqueous solution containing 30 mM $NaNO_3$ (blue line) and 2.5 mM **1a** (red line). Scan rate: 100 mV/s (A), 10 V/s (B).

Figure 4. Crystal structure of encapsulation complex **1b**$\cdot$(**2**)$_4$.

(uncomplexed) **3**, and the positively shifted one at 298 mV is from the encapsulated complex. The result demonstrates that the complexation between **1a** and **3** is strong enough to distinguish the complexed and uncomplexed species in the time scale of CV measurements (10−200 mV/s).

To investigate the interactions between host **1a** and a guest in the oxidized state that is, ferrocenium ion, the electrochemical studies of **2**$^+\cdot BF_4^-$, **3**$^+\cdot PF_6^-$, and **4**$^+\cdot PF_6^-$ were carried out in the absence and presence of **1a**.[11] For **3**$^+\cdot PF_6^-$ and **4**$^+\cdot PF_6^-$, whose reduced forms **3** and **4** are water soluble, their CV are reversible both in the absence and presence of **1a** (Figure 3A). In contrast to the decrease of peak currents in the CV of **3** and **4** (reduced state) upon addition of **1a** (Figure 2), the peak currents remain almost unchanged in CV of **3**$^+\cdot PF_6^-$ and **4**$^+\cdot PF_6^-$ upon addition of **1a** at scan rate of 100 mV/s (Figure 3A). This observation supports that the ferrocenium ion is free, that is, not encapsulated in the cavity of **1a**. However, when the scan rate is fast enough, for example, 10 V/s, the decrease in the anodic peak current was detected (Figure 3B). This may suggest that the reaction occurred in the reduction of **4**$\cdot PF_6$ following clathration of **4**.[12]

The bulk electrolysis (BE) of **1a**$\cdot$(**2**)$_n$ complex was also examined (applied potential of 500 mV versus Ag/AgCl, 1.5 h) to confirm whether **2** goes out from the cage by oxidation. When the CV before and after BE were compared (Figure S1 in Supporting Information), the increase (ca. 50%) in peak currents was observed implying that the oxidized species (**2**$^+$) can diffuse more easily to the electrode than the reduced state (**2**). On the other hand, the CV after BE of **1a**$\cdot$(**2**)$_n$ was exactly the same to that of **2**$^+\cdot BF_4^-$, in the presence of **1a** both in the peak current and potential. These results strongly suggest that guest **2** encapsulated in **1a** goes outside of the cage after it is electrochemically oxidized to **2**$^+$.

The direct evidence for the encapsulation was provided by crystal structure analysis. We succeeded in obtaining single crystals for the encapsulated complex of **2** and **1b** (an analogue of **1a** with 2,2′-bipyridine as protecting group instead of ethylenediamine). The crystallographic results clearly indicate the encapsulation of four molecules of **2** inside the cavity of **1b** (Figure 4).[13] Crystallization from **1b** + **2**$^+\cdot PF_6^-$ solution was also examined, but the crystallographic analysis always demonstrated the inclusion of no ferrocenium ion in **1b**; only anion exchange occurred (several NO_3^- of **1b** were replaced by PF_6^-).

Supporting Information Available: Experimental procedures, CV of **2**, **2**$^+BF_4^-$, **4** in the presence/absence of **1a**, ^1H NMR spectra, and the details of the X-ray diffraction study of **1b**$\cdot$(**2**)$_4$ (PDF). An X-ray crystallographic file in CIF format. This material is available free of charge via the Internet at http://pubs.acs.org.

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(6) For example, **2** (4 mol equiv) was suspended in D_2O solution of **1a** and stirred overnight to give a clear solution. The ^1H NMR signal of **2** was observed at 2.92 ppm (Supporting Information), while the signal of **2** in the absence of **1a** in $CDCl_3$ appeared at 4.16 ppm. The large upfield shift of the ^1H NMR signal of **2** confirms the encapsulation of **2** inside the **1a**.[3b] Although the *n* value in solution is lower than that in solid,[13] this is probably due to rapid equilibration between **1b**$\cdot$(**2**)$_4$ (75%) and empty **1b** (25%) rather than to the selective formation of **1b**$\cdot$(**2**)$_3$ because we have previously found the cooperative effect in the complexation that makes **1**$\cdot$**G**$_4$ much more stable than **1**$\cdot$**G**$_n$ (n = 1, 2, or 3).

(7) Experimental procedures: see Supporting Information.

(8) The **2** itself is almost insoluble in water and gives very weak peak currents and poor reversibility of cyclic voltammogram (CV).

(9) Positive shifts in the peak potential were observed for inclusion complex of ferrocene and its derivatives in CD. (a) Kaifer, A. E. *Acc. Chem. Res.* **1999**, *32*, 62. (b) Cardona, C. M.; Mendoza, S.; Kaifer, A. E. *Chem. Soc. Rev.* **2000**, *29*, 37.

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(13) Crystallographic data of **1b**$\cdot$(**2**)$_4\cdot(H_2O)_{79}$: $C_{172}H_{294}N_{48}O_{115}Pd_6Fe_4$, $M = 5736.35$, tetragonal, space group $P4_12_12$, $a = b = 28.918(7)$ Å, $c = 30.428(11)$ Å, $V = 25445(13)$ Å^3, $Z = 4$. Final R indicates ($I > 2\sigma(I)$): R1 = 0.1094, wR2 = 0.2664. X-ray crystallographic details are provided in Supporting Information.

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