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# Electrochemically Driven Formation of a Molecular Capsule around the Ferrocenium Ion

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The self-assembly of concave-shaped hosts into molecular capsules is a very active field of research in modern chemistry. The work of Rebek and co-workers has provided numerous examples.[1] In 1997, MacGillivray and Atwood demonstrated the self-assembly of a large capsule composed of six molecules of resorcinarene **1** (Chart 1) grouped in an octahedral arrangement and held together through hydrogen bonds by the upper rim OH groups and residual water molecules.[2] A similar supramolecular arrangement has been shown by a related resorcinarene.[3] These two reports are essentially concerned with molecular capsules formed in solution and investigated in the solid state after crystallization. Shivanyuk and Rebek have recently shown, using $^1$H NMR spectroscopy, that the self-assembly of resorcinarenes into molecular capsules can be driven in the solution phase by appropriately sized tetraalkylammonium and structurally related ions,[4] as well as $Bu_4SbBr$.[5] In this work, we describe the efficient formation of a robust molecular capsule of six resorcinarene hosts around an electrochemically generated ferrocenium ion, which acts as the nucleus of the assembly. As a result of the encapsulation, the electrochemical behavior of ferrocene changes drastically.

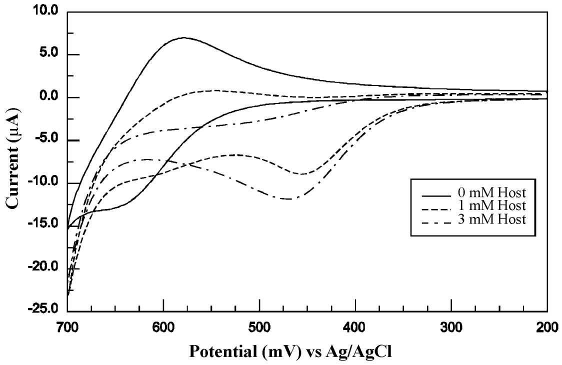
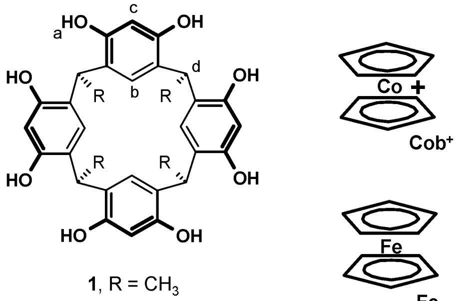


***Figure 1.*** Cyclic voltammetric response on a glassy carbon electrode (0.071 cm$^2$) of 0.5 mM ferrocene in 0.1 M $TDA^+{\cdot}Br^-/CH_2Cl_2$ in the presence of variable concentrations of host **2**. Scan rate: 0.1 V/s.

***Chart 1.*** Structures of Compounds Used in This Work



**1**, R = $CH_3$
**2**, R = $(CH_2)_{10}CH_3$

The resorcinarene hosts **1** and **2** were prepared according to reported procedures.[6] Because ferrocene (**Fc**) undergoes fast one-electron oxidation to its cationic form (**Fc**$^+$), we investigated its anodic electrochemical behavior in the presence of host **2** in $CH_2Cl_2$ solution. Because of the report of Shivanyuk and Rebek,[4] we initially avoided the use of tetrabutylammonium hexafluorophosphate, the most commonly utilized supporting electrolyte in nonaqueous solvents. With 0.1 M tetradodecylammonium hexafluorophosphate ($TDA^+{\cdot}PF_6^-$) as the supporting electrolyte, host **2** had a small effect on the **Fc**$^+$/**Fc** redox couple, which remained chemically and electrochemically reversible, at a half-wave potential that shifted gradually from its initial value (0.49 V vs Ag/AgCl) to less positive values, as the concentration of **2** was increased from 0 to 6 equiv (see Supporting Information). This voltammetric behavior reveals the relative stabilization of ferrocenium due to noncovalent interactions with host **2**.

Because of the possibility of counterion effects,[4] we decided to also perform voltammetric experiments with tetradodecylammonium *bromide* ($TDA^+{\cdot}Br^-$) as the supporting electrolyte. The presence of a large concentration of bromide ion was underscored by the large background oxidation wave observed at potentials slightly more positive than those necessary to drive the reversible oxidation of ferrocene (~0.6 V, see Figure 1). However, the electrochemical behavior of ferrocene was severely affected by the presence of host **2**. The addition of 1 equiv of **2** gives rise to the appearance of a new anodic wave for ferrocene oxidation at a peak potential of 0.44 V. The oxidized species generated at this potential does not undergo reduction back to ferrocene in the potential range surveyed. Addition of increasing amounts of **2** led to increasing currents for the new ferrocene oxidation wave at the expense of the original wave. Upon the addition of 6 equiv of **2**, the original **Fc**$^+$/**Fc** wave fully disappeared, and the new wave attained full development (Figure 1). This unusual electrochemical behavior reveals that: (1) addition of **2** leads to a very substantial stabilization of the ferrocenium cation, as reflected by the lower potential observed for ferrocene oxidation, and (2) the stabilization of **Fc**$^+$ is of such nature that its reduction back to **Fc** requires an overpotential of approximately 500 mV. This point was confirmed in CV experiments using extended cathodic scans (see Supporting Information), in which a broad and poorly defined reduction wave was observed starting around −0.1 V. The stoichiometry of the binding interactions between host **2** and ferrocenium is clearly revealed by the electrochemical data as *six molecules of host to one ferrocenium cation* (**Fc**$^+{\cdot}$**2**$_6$), in excellent agreement with previous reports on the self-assembly of these resorcinarenes.[2−5]

We also conducted voltammetric experiments in $CH_2Cl_2$ solutions containing supporting electrolytes with smaller tetraalkylammonium

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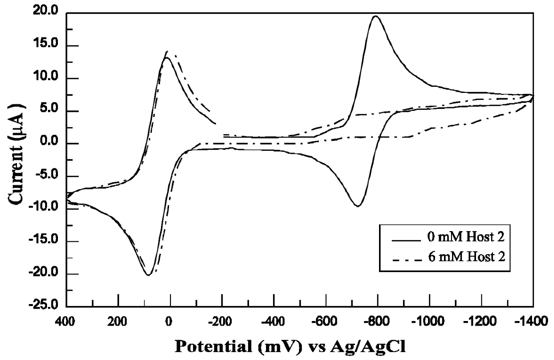

***Figure 2.*** Cyclic voltammetric response on a glassy carbon electrode (0.071 $cm^2$) of 1.0 mM decamethylferrocene and 1.0 mM $\mathbf{Cob}^+{\cdot}PF_6^-$ in 0.1 M $TBA^+{\cdot}Br^-/CH_2Cl_2$ in the absence and in the presence of 6 mM host **2**. Scan rate: 0.1 V/s.

ions, which can also mediate the self-assembly of resorcinarenes, according to Shivanyuk and Rebek.[4] However, the voltammetric results were strikingly similar using tetrabutylammonium, tetrahexylammonium, or tetradodecylammonium salts. This suggests that ferrocenium is much more efficient than tetraalkylammonium ions as a “nucleating agent” for the resorcinarene self-assembly process. In contrast to the insensitivity of our results to the nature of the cation, we observed some strong counterion effects; that is, the use of bromide (or chloride) supporting electrolytes results in encapsulation of the electrogenerated ferrocenium, while perchlorate, tetrafluoroborate, and hexafluorophosphate salts prevent it.

$^1H$ NMR spectroscopy indicates that there is no interaction between ferrocene (**Fc**) itself and host **2**, but the paramagnetic character of $\mathbf{Fc}^+$ hampered the use of NMR spectroscopy in this oxidation state. Therefore, we utilized the structurally similar, diamagnetic cobaltocenium ion ($\mathbf{Cob}^+$) as an excellent model for $\mathbf{Fc}^+$ in NMR experiments. In $CD_2Cl_2$ solution, the cobaltocenium protons of $\mathbf{Cob}^+{\cdot}PF_6^-$ appear as a sharp singlet at 5.64 ppm. In the presence of 1−5 equiv of host **2**, this singlet broadens, and a new resonance appears at 4.03 ppm (see Supporting Information). The integrated intensity of the latter peak (bound $\mathbf{Cob}^+$) increases with the concentration of **2** at the expense of the original (free) $\mathbf{Cob}^+$ proton resonance. In the presence of 6 equiv of **2**, the resonance at 4.03 ppm reaches full development, and the original resonance disappears. Similar results were obtained with $\mathbf{Cob}^+{\cdot}Br^-$ in $CDCl_3$ solution. This behavior is clearly consistent with the encapsulation of $\mathbf{Cob}^+$ by six molecules of host **2**. We also investigated the effects of **2** on the reversible electrochemical reduction of $\mathbf{Cob}^+$ to neutral **Cob** in $CH_2Cl_2$ solution. In excellent agreement with the results obtained with the $\mathbf{Fc}^+/\mathbf{Fc}$ couple, we found that the usually reversible, one-electron reduction of $\mathbf{Cob}^+$ (at ca. −0.8 V) is inhibited in the presence of 6 equiv of **2** (Figure 2) when using $TBA^+{\cdot}Br^-$ as the supporting electrolyte. The cyclic voltammogram of the figure also shows the reversible wave for the decamethylferrocenium/decamethylferrocene redox couple (at ca. 0.04 V), as a clear demonstration that the working electrode surface remains accessible to other redox couples (decamethylferrocenium appears to be too large for encapsulation by **2**). Clearly, the observed inhibition of $\mathbf{Cob}^+$ reduction does not originate from coverage and/or fouling of the electrode surface by host **2**. Furthermore, the use of $TBA^+{\cdot}PF_6^-$ as supporting electrolyte gives rise to voltammetric data inconsistent with encapsulation (see Supporting Information) and similar to the results obtained with the $\mathbf{Fc}^+/\mathbf{Fc}$ redox couple in this medium.

The results reported here illustrate a remarkable example of electrochemically driven self-assembly.[7] In bromide and chloride supporting electrolytes, the electrochemical behavior of ferrocene in the presence of **2** is clearly consistent with its encapsulation upon oxidation. In other words, removal of a single electron from ferrocene starts a very efficient process in which six resorcinarene molecules form a large capsule around the oxidized ferrocenium cation. Noncovalent interactions between the central cation and the inner $\pi$ surfaces of the resorcinarenes drive the formation of this kinetically stable assembly, which is held together and further stabilized by numerous hydrogen bonds.[8] Our voltammetric data also indicate the encapsulation of the structurally similar $\mathbf{Cob}^+$ ion. Electrochemical experiments with hexafluorophosphate, tetrafluoroborate, and perchlorate supporting electrolytes clearly reveal that these anions hinder the formation of the molecular capsules around $\mathbf{Fc}^+$ or $\mathbf{Cob}^+$. Although the total inner volume of the $\mathbf{2}_6$ capsule[2] (~1375 $Å^3$) is large enough to accommodate the ion pair formed by $\mathbf{Fc}^+$ (or $\mathbf{Cob}^+$) and every anion surveyed, the high concentration of counterions present in the electrochemical experiments may give rise to higher-order ion pairs which may not fit in the inner volume of the molecular capsule. In the $^1H$ NMR spectroscopic experiments with $\mathbf{Cob}^+$, the results suggest encapsulation with both $Br^-$ and $PF_6^-$, but these counterions are present at much lower concentrations, as supporting electrolytes are not required in the NMR experiments. Further work to clarify counterion effects is currently underway in our laboratory.

Another important finding in this work is that encapsulation of ferrocenium or cobaltocenium inside the $\mathbf{2}_6$ molecular capsule drastically slows the kinetics of their electrochemical reduction, because the cation is shielded and kept away from the electrode surface by the surrounding molecules of **2**.[9] The large kinetic stability and size of this molecular assembly provide a rationalization for these findings.

In conclusion, we present evidence in this work for a unique example of electrochemically driven, molecular self-assembly around the ferrocenium cation. These results open a number of interesting possibilities for the interactive control of large supramolecular structures.

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**Supporting Information Available:** Additional electrochemical and spectroscopic data mentioned in the text (PDF). This material is available free of charge via the Internet at http://pubs.acs.org.

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