Redox control of host–guest recognition: a case of host selection determined by the oxidation state of the guest

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In the presence of β-CD, reduction of the strong complex between two cobaltocenium guests and the octaanionic form of calix[6]arene hexasulfonate leads to the formation of 1 : 1 complexes between cobaltocene and β-CD.

Redox conversions have been effectively used to control the strength of host–guest interactions. Typically, changes in the oxidation state of one of the interacting partners (either the host or the guest) lead to substantial modifications in the stability of the host–guest complex. Redox switchable hosts,[1] for instance, contain a redox subunit which can be acted upon (electrochemically or chemically) to alter their binding affinity for certain guests. Here, we extend these ideas to the concept of host selection. We describe a system composed of two redox inactive hosts and one redox active guest in which the oxidation state of the guest determines which of the two hosts is selected for complex formation.[2]

Fig. 1 shows the structures of the host and guest compounds used in this work. The solubilities of hosts and guests permit the investigation of this system in aqueous solution. The two hosts selected are the sulfonated calix[6]arene **1**$^{8-}$ and β-cyclodextrin (β-CD). The anionic character and conformational rigidity‡ of host **1**$^{8-}$ make it an excellent host for positively charged guests, while β-CD is well known to exhibit a strong binding affinity for suitably sized non-polar guests.[3] The two guests selected are cobaltocenium and carboxycobaltocenium. The cobaltocenium subunit undergoes a fast and reversible one-electron reduction to neutral cobaltocene. Very recently we have reported that, while β-CD does not interact appreciably with the positively charged cobaltocenium (Cob$^+$), it does form a stable 1 : 1 inclusion complex with the reduced form, cobaltocene (Cob).[4]

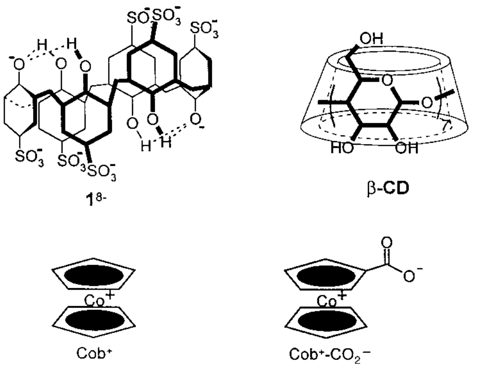


Fig. 1 Structures of calixarene hosts and molecular guests studied in this work

The voltammetric reduction of cobaltocenium yields the hydrophobic Cob form, which precipitates on the electrode surface. These precipitation effects distort the cyclic voltammogram [see Fig. 2(*a*)] from the otherwise anticipated nernstian, reversible shape. Addition of host **1**$^{8-}$ shifts the Cob$^+$–Cob voltammetric wave to more negative potentials but the distortions associated with deposition of the reduced form persist [Fig. 2(*a*)]. These findings are consistent with (*i*) complexation of Cob$^+$ by the anionic calixarene host and (*ii*) lack of substantial interaction between **1**$^{8-}$ and Cob. NMR titrations (^{1}H, 400 MHz) of buffered (pD = 7) D_2O solutions of **1**$^{8-}$ with increasing concentrations of Cob$^+$ produce strong evidence for the formation of a stable complex containing two Cob$^+$ guests bound to the anionic host.[5] The Cob$^+$-induced splitting patterns of both the aromatic proton and the methylene proton resonances of the calixarene (Fig. 3) constitute strong evidence for the formation of the 2 : 1 complex shown in Scheme 1. In 1992, Atwood *et al.* solved the crystal structure of the hydrated sodium salt of **1**$^{8-}$ (crystallized from neutral aqueous solution) and found that the calixarene adopts a double partial cone conformation exhibiting two clearly defined binding pockets.[6] To the best of our knowledge, our NMR data constitute the first unequivocal spectroscopic evidence for the adoption by host **1**$^{8-}$ of the same conformation in neutral aqueous solution. In the absence of Cob$^+$, the aromatic units of the calixarene undergo fast interconversions and, thus, only two proton resonances are observed (one for the methylene protons and another for the aromatic protons). In the presence of more than 2 equiv. of Cob$^+$, each one of these resonances splits into the patterns shown in Fig. 3. These resonances are consistent with a double partial cone conformation for the calixarene (see assignments in Fig. 3) and can only be rationalized by the formation of a complex in which one Cob$^+$ guest binds to each of the two cavity openings of the calixarene.§ Complexation of **1**$^{8-}$ to two Cob$^+$ guests slows down the otherwise fast averaging of the

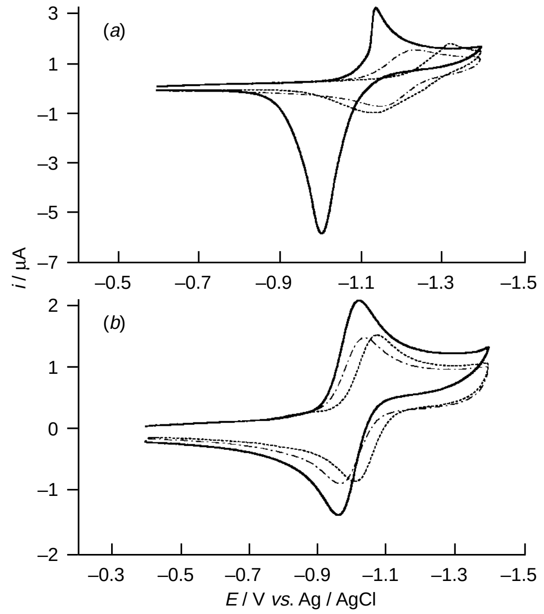


Fig. 2 (*a*) Voltammetric response on a glassy carbon electrode (0.008 cm^2) of a 1.0 mM solution of Cob$^+$ also containing 0.1 M phosphate buffer (pH = 7) in the absence of any host compound (——), in the presence of 4.0 mM **1**$^{8-}$ (------), and in the presence of 4.0 mM **1**$^{8-}$ and 4.0 mM β-CD (-·-·-·-). Scan rate = 0.1 V s^{-1}. (*b*) Same for 1.0 mM Cob$^+$–CO_2^- solution.

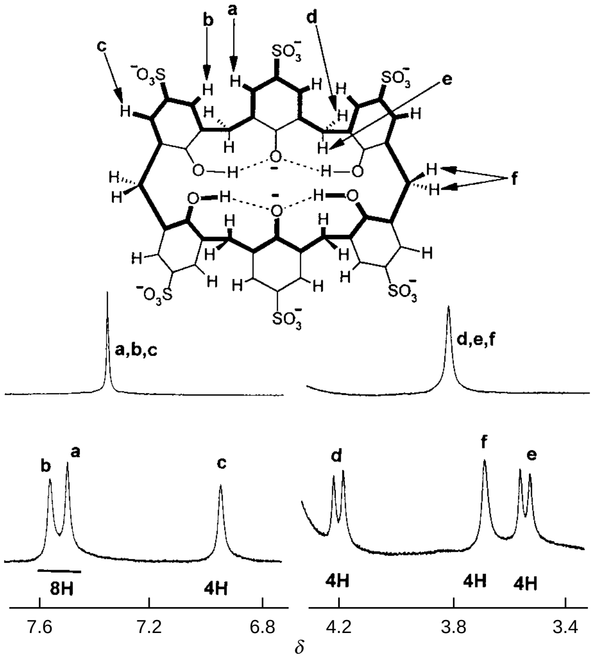
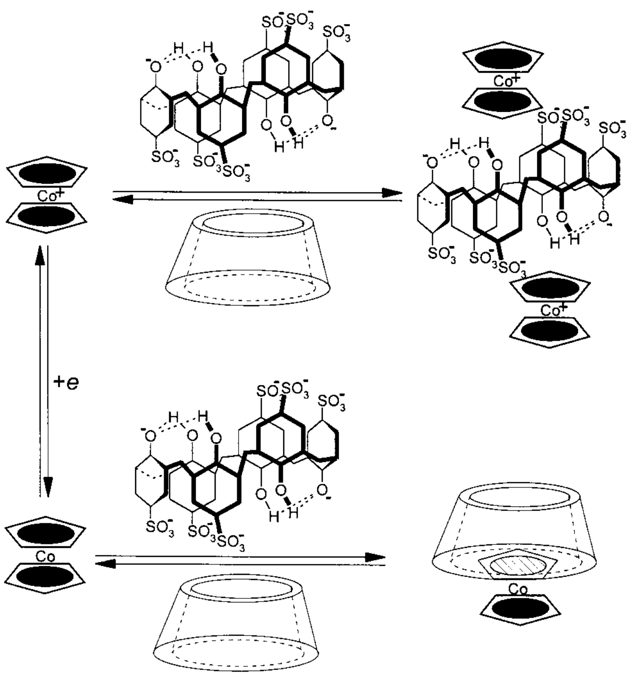


Fig. 3 ^{1}H NMR (400 MHz) of a 2.0 mm solution of $\mathbf{1}^{8-}$ in D_2O also containing 0.1 M phosphate buffer (pD = 7) in the absence (top) and in the presence (bottom) of 6.0 mm Cob^+

host's proton resonances, giving rise to the distinctive splitting patterns shown in Fig. 3.

The $\mathbf{1}^{8-}$–Cob^+ host–guest system is further affected by the addition of β-CD to the medium [Fig. 2(*a*)]. In the presence of this neutral host, the precipitation effects associated with the generation of the hydrophobic Cob form (which is not effectively complexed by $\mathbf{1}^{8-}$) completely disappear, revealing that Cob forms a stable 1 : 1 inclusion complex with the β-CD host, as anticipated from our previous work.[4] Therefore, we must conclude that, while Cob^+ forms a stable 2 : 1 complex with the anionic calixarene host $\mathbf{1}^{8-}$, its reduced form, Cob, is preferentially bound by β-CD. Since the binding interactions between the Cob^+–β-CD and Cob–$\mathbf{1}^{8-}$ pairs are indeed quite weak, the electrochemical reduction of Cob^+ has a profound effect not only on the selection of host by this redox active guest but also on the stoichiometry of the resulting complex as represented in Scheme 1. The voltammetric results obtained with the more water soluble Cob^+–COO^- guest are shown in Fig. 2(*b*). No precipitation of the reduced Cob–CO_2^- form is observed, but the shifts recorded in the $E_{1/2}$ values upon addition of $\mathbf{1}^{8-}$ and β-CD indicate that similar host selection phenomena also take place with this guest.

We have shown here that the redox chemistry of cobaltocenium guests can be used to select the appropriate host between calixarene $\mathbf{1}^{8-}$ and β-CD. These results add to the arsenal of mechanisms and schemes by which redox conversions can be used to control molecular recognition interactions.



Scheme 1

The authors are grateful to the US National Science Foundation for the support of this work (to A. E. K. CHE-9633434) and Cerestar for continued and generous gifts of cyclodextrins.

Notes and References

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‡ For more details on the solution conformation of this calixarene host, see the preceding communication in this same issue.

§ From our NMR data we estimate that the association constant for the overall equilibrium 2 Cob^+ + $\mathbf{1}^{8-}$ = $\mathbf{1}\cdot(Cob)_2^{6-}$ is at least 2 × 10^6 dm^6 mol^{-2}.

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Received in Columbia, MO, USA; 30th January 1998; 8/00845K