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Wei Wang[a]; Angel E. Kaifer[a]
[a] Department of Chemistry, Center for Supramolecular Science, University of Miami, Coral Gables, FL, USA

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Transfer of cationic cucurbit[7]uril inclusion complexes from water to non-aqueous solvents†

Wei Wang and Angel E. Kaifer*

Department of Chemistry, Center for Supramolecular Science, University of Miami, Coral Gables, FL 33124-0431, USA

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The redox-active guests (ferrocenylmethyl)trimethylammonium (**2**$^+$) and methylviologen (**5**$^{2+}$) form stable complexes with the cucurbit[7]uril host (CB7) in aqueous solution. In this work, we report a method to transfer these cationic inclusion complexes – as their hexafluorophosphate salts – to less polar, non-aqueous solvents, such as CH_3CN, dimethylformamide and dimethylsulphoxide (DMSO). Both inclusion complexes were found to be stable in these solvents, although the determination of accurate equilibrium association constants was hampered by the low solubility of the free host. Voltammetric experiments show that the one-electron oxidation of the ferrocenyl residue in the CB7·**2**$^+$ complex increases its stability in CH_3CN and DMSO solutions, while the opposite effect was observed in aqueous media. These results provide valuable insight into the various roles played by hydrophobic interactions, solvation effects and ion–dipole interactions at stabilising CB7 inclusion complexes of cationic guests.

Keywords: host–guest complexes; cucurbiturils; electrochemistry; non-aqueous solvents

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Introduction

The recent expansion of the cucurbit[*n*]uril (CB*n*) host family is attracting considerable research attention to this class of molecular container receptors (*1–4*). While cucurbit[6]uril (CB6) has been known for a long time, the groups of Kim, Day and Isaacs have prepared and isolated a number of analogues with a range of interesting binding properties. The isolation of CB7 and CB8 was first reported in 2000 by the groups of Kim (*5*) and Day (*6*). A few years later, Isaacs and co-workers (*7*) isolated the much larger cavity host CB10 and investigated some of its binding properties. Isaacs and Kim (*8*) have reported the preparation of inverted CB hosts, and Isaacs (*9*) has recently prepared an interesting, dual-cavity host, designated as nor-seco-CB10. Some progress has also been made on the external functionalisation of these hosts (*10*, *11*), which will facilitate their immobilisation onto surfaces (*12*) and make possible the preparation of multivalent hosts and other derivatives.

The CB*n* hosts have shapes and sizes that are somewhat similar to those of the better known cyclodextrins (CDs) (*13*, *14*). For instance, β-CD has an average cavity diameter close to that of CB7 (*1*, *2*). However, the host binding properties of both receptors are quite different, as reflected by an examination of their binding affinities with ferrocenyl derivatives (*15*) (see Figure 1 for structures), such as hydroxymethylferrocene (**1**), (ferrocenylmethyl)trimethylammonium (**2**$^+$) and ferrocenecarboxylate (**3**$^-$). While the equilibrium association constants (K) of all three ferrocenyl derivatives with β-CD are in the range $1–5 \times 10^3\,M^{-1}$ in aqueous solution (*16*), CB7 shows a much greater level of selectivity. Thus, the inclusion complex between **1** and CB7 is extremely stable ($K = 3 \times 10^9\,M^{-1}$), guest **2**$^+$ is bound even more strongly ($K = 4 \times 10^{12}\,M^{-1}$), but anionic **3**$^-$ is not bound at all (*15*). The stability of the CB7 inclusion complex is extremely sensitive to the charge of the group directly attached to one of the cyclopentadienyl rings of the ferrocenyl guest. The lack of binding interactions between 3^- and CB7 has been attributed to electrostatic repulsions between the guest's carboxylate and the carbonyl oxygen-laced portal of the host cavity. The dicationic, symmetric guest **4**$^{2+}$ forms an extremely stable inclusion complex with CB7 (*17*), with an equilibrium association constant ($K \sim 10^{15}\,M^{-1}$) similar to that observed between the avidin–biotin host–guest pair (*18*). Thermodynamic analysis of the binding processes reveals that the binding affinity gain in going from guest **1** to guests **2**$^+$ and **4**$^{2+}$ is entirely due to the entropic term, with similar enthalpic contributions to the formation of all three inclusion complexes (*17*). The origin of the high binding affinity observed in the CB7·**2**$^+$ and CB7·**4**$^{2+}$ complexes is believed to rest on several factors: (1) the excellent fit

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*Corresponding author. Email: akaifer@miami.edu

†Dedicated to the memory of Prof Dmitry Rudkevic, a good friend and an excellent scientist.

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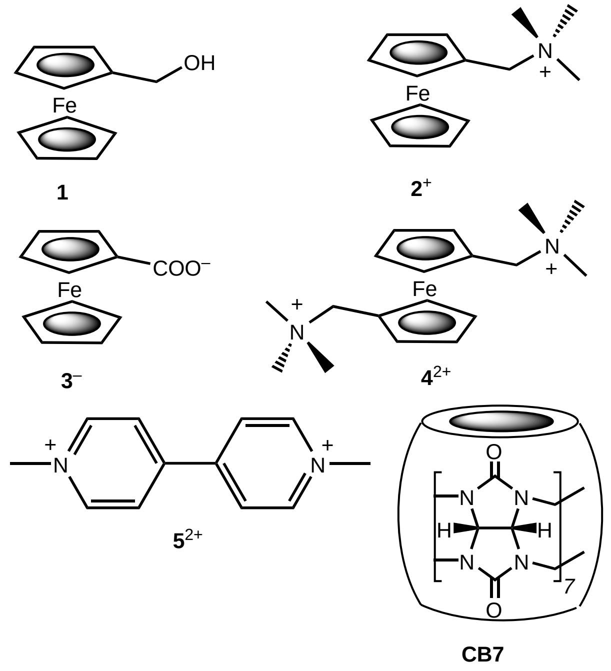
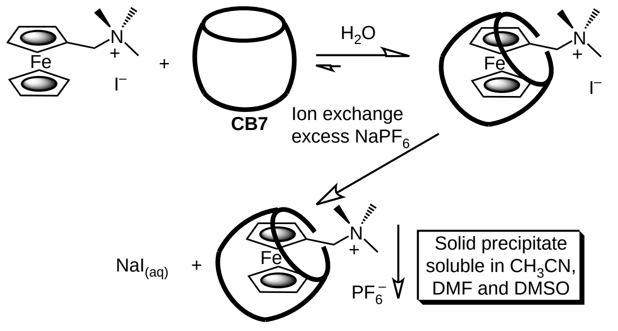


Figure 1. Structures of cucurbit[7]uril and relevant guests.

between the ferrocenyl group and the host cavity, (2) the rigid nature of both and (3) the substantial entropic contributions associated with the partial or full desolvation of the host portal(s) and the ammonium ion group(s) on the guest.

While their ability to form extremely stable inclusion complexes in aqueous solution is one of the most attractive properties of the CB hosts, we decided to investigate some of their binding properties in non-aqueous solutions, as a way to gauge the importance of aqueous solvation and the hydrophobic effect on the strong association between ferrocenyl guests and CB7. In non-aqueous solvents of intermediate polarity, such as acetonitrile (MeCN), dimethylformamide (DMF) or dimethylsulphoxide (DMSO), solvation and solvophobic effects are expected to play a more subdued role than in aqueous media. On the other hand, ion–dipole interactions between positively charged groups on the guest and the carbonyl oxygens on the host portals may be stronger in less polar media. A serious obstacle to this investigation is the extremely low solubility of CB hosts in solvents other than water. In order to overcome this limitation, we have developed a straightforward method to transfer positively charged CB7 inclusion complexes to solvents of intermediate polarity, which has allowed us to examine the properties of the CB7 complexes with ferrocenyl guest $\mathbf{2}^+$ and with methylviologen ($\mathbf{5}^{2+}$) in such media. The results of this study are reported here.



Scheme 1. Precipitation of the hexafluorophosphate salt of the CB7·$\mathbf{2}^+$ inclusion complex from the aqueous solution.

Results

In aqueous solution, the large *K* value for association between ferrocenyl guest $\mathbf{2}^+$ and host CB7 (*15*, *19*) gives rise to quantitative complexation when equal concentrations of both compounds are mixed at the millimolar level. Relying on the generally poor solubility of hexafluorophosphate salts of organic cations in aqueous media, we treated an aqueous solution containing the CB7·$\mathbf{2}^+$ complex (initially present as the iodide salt) with a concentrated aqueous solution of $NaPF_6$ in order to drive the precipitation of the cationic complex as its hexafluorophosphate salt (Scheme 1). The resulting yellow solid can be collected by filtration, dried and redissolved in MeCN, DMSO or DMF solution at millimolar concentrations. The same procedure can be applied to the CB7·$\mathbf{5}^{2+}$ complex with identical results. In other words, the solubility of the hexafluorophosphate salts of the CB7·$\mathbf{2}^+$ and CB7·$\mathbf{5}^{2+}$ complexes follows the same pattern as many other hexafluorophosphate salts of simple organic cations, allowing us to effectively transfer these complexes from aqueous to non-aqueous solutions by carrying out simple counterion exchange reactions.

To further confirm that the solids obtained upon ion exchange in aqueous solution contain the corresponding 1:1 host–guest complex, the precipitates were redissolved in 1:1 (v/v) D_2O/ACN-d_3 mixtures to guarantee full solubilisation and their ^1H NMR spectra recorded after adding potassium acid phthalate as an internal standard for integration of proton signals. ^1H NMR integration of CB7 and guest protons confirmed that equimolar amounts of guest (either $\mathbf{2}^+$ or $\mathbf{5}^{2+}$) and host were present, providing strong support to the isolation of the 1:1 inclusion complex in the precipitate.

NMR spectroscopic studies

The ^1H NMR spectrum of CB7·$\mathbf{2}^+$ in CD_3CN solution (Figure 2(B)) shows the ferrocene and methylene protons of the guest in the region 3.4–3.8 ppm, strongly shifted upfield from the chemical shift region (4.2–4.5 ppm)

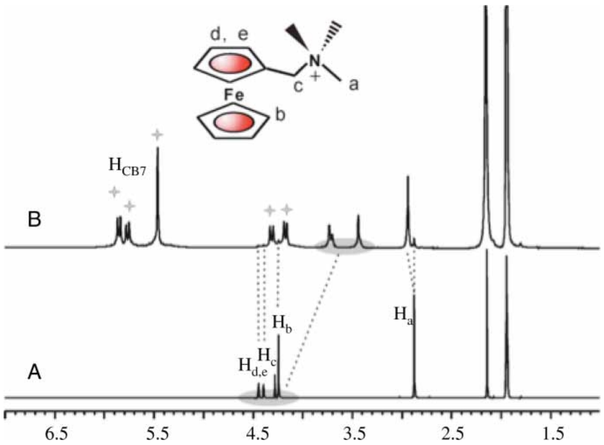


Figure 2. ^{1}H NMR spectra (500 MHz, CD_3CN) of guest $\mathbf{2}^+$ (A) in the absence and (B) in the presence of 1.0 equiv. of CB7. The 'cross' symbol marks host proton resonances.

where they resonate in the free guest (Figure 2(A)). This finding is consistent with the inclusion of the ferrocene groups inside the CB7 cavity (*15*, *19*). Careful inspection of the spectra in Figure 2(B) reveals the presence of residual resonances corresponding to the free guest in the 4.2–4.5 ppm region. Furthermore, the methyl protons of the guest in the complex appear at 2.93 ppm, but a smaller peak at 2.85 ppm is still visible. The latter clearly corresponds to the methyl protons of free guest $\mathbf{2}^+$. Therefore, the spectroscopic data show evidence for incomplete complexation in CD_3CN. Given that in aqueous medium, this complex is known to be highly stable, these findings lead to the inescapable conclusion that the stability of the complex is substantially reduced in CD_3CN solution. Since the equilibrium between the free and bound guest is in the slow exchange regime of the NMR timescale, we tried to use integral values for proton resonances in the free and complexed guests to estimate the corresponding equilibrium association constants. However, our best efforts to obtain reproducible values failed and we cannot report accurate *K* values at this time.

Further attempts to treat these NMR spectroscopic data by estimating the concentration of free CB7 host (in equilibrium with $\mathbf{2}^+$ and CB7·$\mathbf{2}^+$) from solubility measurements in CD_3CN also lead to inconsistent results. Similar problems were encountered in DMF and DMSO solutions.

The complexation of methylviologen ($\mathbf{5}^{2+}$) by CB7 in CD_3CN solution was also confirmed by ^{1}H NMR spectroscopy. Relevant spectra are shown in Figure 3. The pattern of CB7-induced shifts on the guest proton signals is essentially identical to that observed in aqueous solution (*20*, *21*). The β-aromatic protons of the guest undergo a pronounced upfield shift (8.35–7.30 ppm, along with considerable broadening) while the α-aromatic protons and the methyl protons move slightly downfield. In this case, the free and bound guests are in the fast exchange regime of the NMR timescale, so the observation of residual peaks for uncomplexed guest is not possible. Unfortunately, the determination of an accurate *K* value using titration data would require the use of [CB7]/[$\mathbf{5}^{2+}$] ratios that are not experimentally accessible.

The symmetric nature of guest $\mathbf{5}^{2+}$ leads to a pattern of CB7 peaks in the complex (Figure 3(B)) that corresponds to the symmetry of the free host, that is, the methylene protons on the two portals of the host remain identical, showing two doublets (at 4.1 and 5.7 ppm) plus a singlet for the equatorial methyne protons. In strong contrast to this, the spectrum for the CB7·$\mathbf{2}^+$ complex (Figure 2(B)) clearly shows the effects of symmetry breakdown introduced by the monocationic ferrocenyl guest. In this spectrum, the top and bottom CB7 methylenes are clearly split into two different sets. One set of methylenes is near the guest's cationic ammonium group and the other set is at the opposite end of the complex. Therefore, we observe two sets of methylene host protons resonating as a total of four doublets (Figure 2(B)).

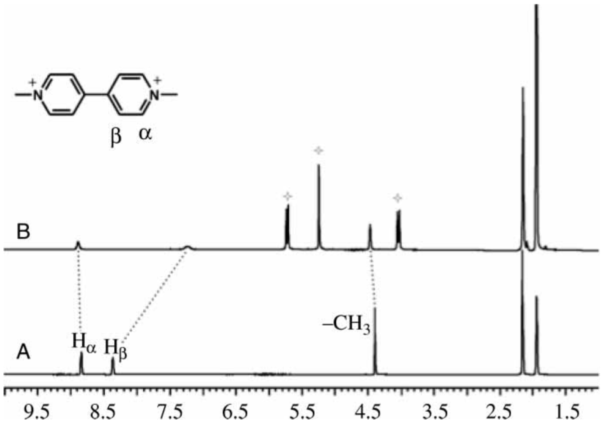


Figure 3. ^{1}H NMR spectra (500 MHz, CD_3CN) of guest $\mathbf{5}^{2+}$ (A) in the absence and (B) in the presence of 1.0 equiv. CB7. The 'cross' symbols mark host proton peaks.

Electrochemical studies

Ferrocene derivatives exhibit fast one-electron oxidation to their positively charged, ferrocenium form. The electrochemical behaviour of ferrocene derivatives is usually characterised by a reversible voltammetric wave corresponding to the ferrocene/ferrocenium redox couple (*19*). In aqueous media, the one-electron oxidation of the CB7·$\mathbf{2}^+$ complex exhibits a half-wave potential ($E_{1/2}$) that is ca. 110 mV more positive than that corresponding to the oxidation of the free guest in the same medium (*15*, *19*). This shift in the half-wave potential means that complexation by CB7 thermodynamically hampers the oxidation of the included ferrocenyl unit on the guest. Upon

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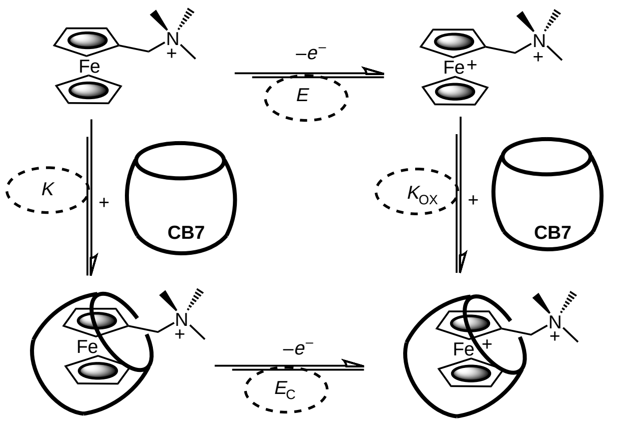

Scheme 2. Square scheme showing the relationship between the two complexation equilibria and the two electrochemical reactions involved in the one-electron oxidation of guest $\mathbf{2}^+$ in the presence of the CB7 host.

examination of the thermodynamic cycle that can be set up between the guest and its oxidised form, before and after CB7 complexation (Scheme 2), the relevant thermodynamic parameters are related through Equation (1):

$$\frac{K_{\mathrm{OX}}}{K} = \exp\left[\frac{F(E - E_{\mathrm{C}})}{RT}\right], \tag{1}$$

where all the symbols are defined in the scheme (*22*) (E and E_{C} represent formal potentials and are considered to be equal to the corresponding half-wave potentials measured in the voltammetric experiments). In aqueous solution, the observed CB7-induced shift in the half-wave potential implies that the CB7 complex is less stable upon oxidation, i.e. $K_{\mathrm{OX}} = 0.014\,K$. Of course, the CB7·$\mathbf{2}^+$ complex is so stable that the extent of stability lost upon oxidation of the ferrocenyl unit is only moderate and the complex still remains very stable. The loss of complex stability upon generation of a positive charge on the ferrocene nucleus of the guest also suggests the importance of hydrophobic interactions in reaching the high binding affinity shown by this complex.

The electrochemical behaviour of the ferrocenyl guest $\mathbf{2}^+$ and its CB7 complex in acetonitrile solution is shown in Figure 4. Notice that complexation by CB7 decreases the level of current associated with the electrochemical oxidation wave, as anticipated from the larger size and lower diffusivity of the complex compared to the free guest. In addition to this, a small CB7-induced shift of the half-wave potential to more negative values is also visible in the data. In this case, $\Delta E_{1/2} = -30$ mV, which suggests that oxidation increases the stability of the complex ($K_{\mathrm{OX}} = 3.5\,K$). Similarly, we can also conclude that complexation by CB7 eases thermodynamically the oxidation of the ferrocene nucleus while included in the host cavity. The effect of CB7 in this medium is thus exactly opposite to our previously reported observations in aqueous media (*15*, *19*). All the electrochemical potentials measured in MeCN, DMF and DMSO are collected in Table 1.

In DMSO solution, the electrochemistry is similar to that recorded in acetonitrile solution, but the $E_{1/2}$ value for the complex is 180 mV less positive than for free $\mathbf{2}^+$, which indicates a much larger relative stabilisation of the complex upon one-electron oxidation of the ferrocene centre ($K_{\mathrm{OX}} = 1.1 \times 10^3\,K$). In fact, transfer from water to DMSO appears to result in a very pronounced inversion of the relative stabilities of the oxidised and reduced forms of the CB7·$\mathbf{2}^+$ complex. We decided to examine the electrochemical behaviour of this complex in a series of H_2O–DMSO mixtures to investigate this inversion behaviour in more detail. As supporting electrolyte in these experiments, we used either tetrabutylammonium chloride (in water-rich solutions) or tetrabutylammonium hexafluorophosphate (in DMSO-rich solutions). However, we carried out control experiments in solutions of intermediate composition (70% DMSO by vol.), in which both supporting electrolytes are soluble, and

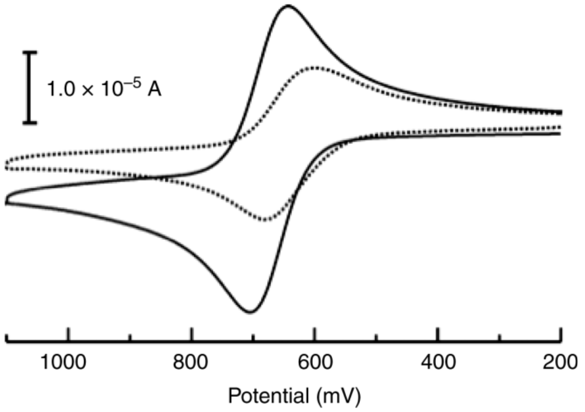

Figure 4. Cyclic voltammetric behaviour on glassy carbon ($0.071\,\mathrm{cm}^2$) of 1.0 mM $\mathbf{2}^+$ in the absence (continuous line) and in the presence (discontinuous line) of 1.0 equiv. CB7. Scan rate: $0.1\,\mathrm{V\,s^{-1}}$.

Table 1. Half-wave potentials (V vs. Ag/AgCl) for the one-electron oxidation of guest $\mathbf{2}^+$ and its CB7 complex in CH_3CN containing 0.1 M $TABPF_6$ as supporting electrolyte.

Solvent	$E_{1/2}$ (guest)	$E_{1/2}$ (complex)	$\Delta E_{1/2}$ (mV)
H_2O^a	0.43	0.54	+110
CH_3CN	0.67	0.64	−30
DMF	0.72	0.57	−150
DMSO	0.66	0.48	−180

[a] Values taken from reference (*19*).

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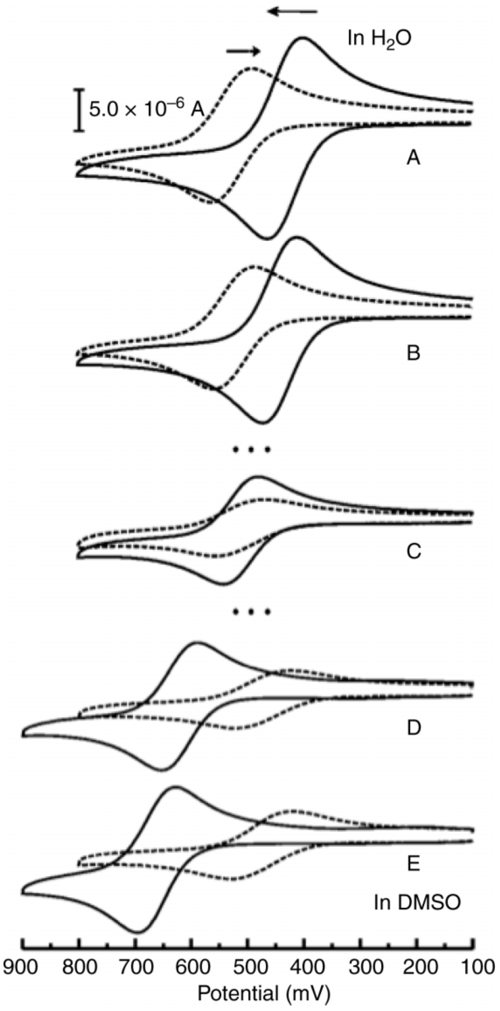

Figure 5. Cyclic voltammetric response on glassy carbon ($0.071\,cm^2$) of 1.0 mM $\mathbf{2}^+$ in the absence (continuous lines) and in the presence (discontinuous lines) of 1.0 equiv. CB7 in (A) pure H_2O, (B) 10% DMSO:90% H_2O (v/v), (C) 50% DMSO:50% H_2O (v/v), (D) 90% DMSO:10% H_2O (v/v) and (E) pure DMSO. All solutions contain either 0.1 M $TBAPF_6$ or TBACl as supporting electrolyte. Scan rate: $0.1\,V\,s^{-1}$.

confirmed that the nature of the anion does not affect the recorded electrochemical potentials. Figure 5 shows some of the relevant voltammetric data and Table 2 collects the corresponding half-wave potentials. The data clearly show that, in going from aqueous to DMSO solution, the half-wave potential for oxidation of the complex shifts gradually towards more negative values. In water-rich solutions, the complex is oxidised at an $E_{1/2}$ value more positive than that observed for the oxidation of the free guest, while the opposite is true in DMSO-rich solutions. The crossing point, at which both half-wave potentials are the same, occurs at a composition of ca. 50% (v/v) DMSO–H_2O, which corresponds to a 0.203 molar fraction for DMSO. Although electrochemical potentials in different solvent systems cannot be correlated directly, it is still instructive to note that the rate of variation of the potential of the free guest is much more pronounced than that of the complex (Table 2). This finding suggests that the inclusion of the ferrocenyl nucleus by CB7 shields it to a large extent from environmental effects and gives rise to an encapsulated organometallic centre which is not very sensitive to the media in which it is dissolved, as evidenced by the small changes observed in the $E_{1/2}$ value for its one-electron oxidation. In contrast to this, the half-wave potential for the free guest $\mathbf{2}^+$ is much more sensitive to the solvent composition. Therefore, we conclude that the cross-over of the half-wave potentials observed in going from pure water to pure DMSO is mostly due to solvation effects on the half-wave potential for the oxidation of the free guest, while the oxidation of the CB7 complex depends to a much smaller extent on the nature of the solvent molecules.

We also investigated the voltammetric behaviour of methylviologen ($\mathbf{5}^{2+}$) and its CB7 complex in DMSO solution in order to compare it to the reported data obtained in aqueous solution (*20*). In DMSO, the first one-electron reduction process ($\mathbf{5}^{2+}/\mathbf{5}^{+}$) shifts to more negative potentials upon addition of 1.5 equiv. of CB7 host, while the second reduction ($\mathbf{5}^{+}/\mathbf{5}$) is almost unaffected (Figure 6). The magnitude of the CB7-induced shift on the $E_{1/2}$ value for the first reduction process is ca. $-60\,mV$, which is moderately larger than the value reported in aqueous solution (*20*). In contrast to this, the second reduction process is strongly affected by the

Table 2. Half-wave potentials (V vs. Ag/AgCl) for the oxidation of free guest $\mathbf{2}^+$ and the CB7·$\mathbf{2}^+$ complex in solutions of variable composition.

%DMSO (by volume)	0	0.10	0.20	0.30	0.40	0.50	0.60	0.70	0.80	0.90	1.0
X_{DMSO}	0	0.028	0.06	0.098	0.145	0.203	0.276	0.372	0.504	0.696	1.0
$E_{1/2}$ (V)[a] Free $\mathbf{2}^+$	0.43	0.44	0.45	0.47	0.49	0.51	0.54	0.57			
$E_{1/2}$ (V)[a] CB7·$\mathbf{2}^+$	0.53	0.53	0.52	0.52	0.51	0.51	0.51	0.51			
$E_{1/2}$ (V)[b] Free $\mathbf{2}^+$								0.57	0.59	0.62	0.66
$E_{1/2}$ (mV)[b] CB7·$\mathbf{2}^+$								0.51	0.49	0.47	0.48
$\Delta E_{1/2}$ (mV)[c]	96	84	67	44	25	0	−21	−56	−102	−148	−186

[a] Supporting electrolyte: 0.1 M TBACl.
[b] Supporting electrolyte: 0.1 M $TBAPF_6$.
[c] Calculated as $E_{1/2}$ (complex) − $E_{1/2}$ (free guest).

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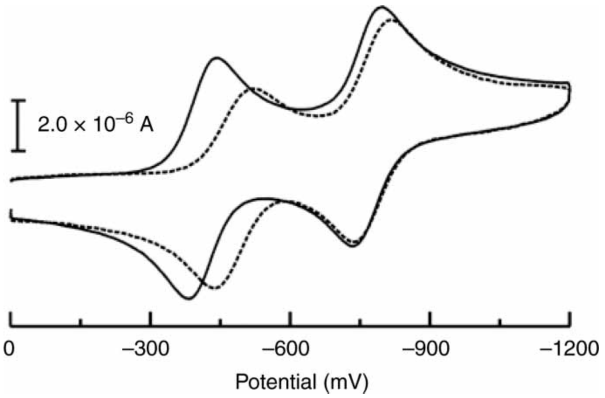

Figure 6. Cyclic voltammetric response on glassy carbon (0.071 cm^2) of 0.5 mM $\mathbf{5}^{2+}$ in the absence (continuous line) and in the presence (discontinuous line) of 1.5 equiv. CB7 in DMSO.

presence of CB7 in aqueous media (*20*), while it is almost unaffected in DMSO solution.

Discussion

The experimental results reported in this work clearly delineate two distinct types of CB7 complexes. First, the CB7·$\mathbf{2}^+$ complex, which is extremely stable in aqueous media ($\Delta G^0_\mathrm{w} \sim -70\,\mathrm{kJ\,mol^{-1}}$) and loses a large fraction of its thermodynamic stability upon transfer to intermediate polarity solvents, such as DMSO or CH$_3$CN. The loss in stability may be equivalent to a decrease in the *K* value of approximately eight orders of magnitude (from $\sim 10^{12}$ to $\sim 10^4\,\mathrm{M^{-1}}$), judging qualitatively from the results of this work, such as the finding of incomplete complex formation when equivalent amounts of host and guest are mixed at millimolar concentrations in CD$_3$CN solution. However, the problems that we found to determine accurate *K* values in non-aqueous solvents prevent a more quantitative assessment. Second, the CB7·$\mathbf{5}^{2+}$ complex, which exhibits a moderately high stability in aqueous media ($\Delta G^0_\mathrm{w} \sim -30\,\mathrm{kJ\,mol^{-1}}$) and stands transfer to DMSO or CH$_3$CN while undergoing a comparatively small loss in thermodynamic stability, based again on a qualitative evaluation of the data reported here. The pronounced contrast between these two complexes must correlate with structural differences between the guests (Figure 7). The cationic ferrocenyl derivative ($\mathbf{2}^+$) appears to be an optimal guest for CB7. A key factor is the hydrophobic character of the ferrocenyl centre and its excellent, tight fit inside the host cavity. The presence of a single positive charge on this guest suggests that ion–dipole interactions may not play a very pronounced role in giving rise to the thermodynamic stability of the CB7·$\mathbf{2}^+$ complex. A good fraction of the binding affinity with CB7 must result from hydrophobic interactions and changes in solvation by water molecules from the free host and free guest to the complex. As a result of the predominant role played by hydrophobic forces and water solvation in stabilising this host–guest complex, its transfer to a less polar, non-aqueous environment results in a substantial decrease in host–guest binding affinity.

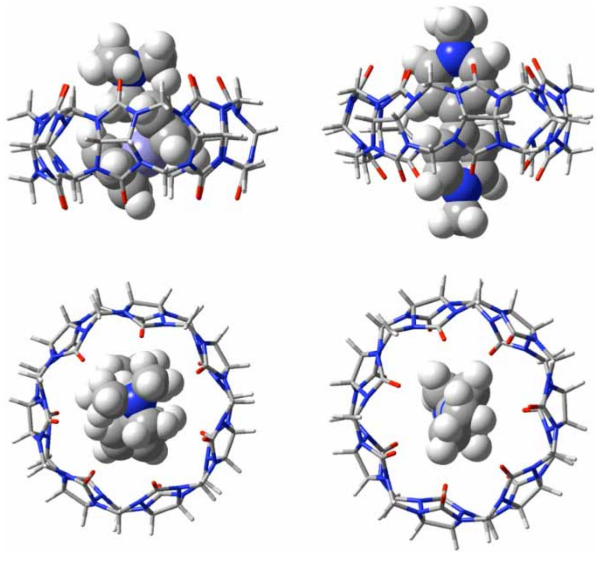

Figure 7. Side and top views of the minimised structures (PM3 method) of the CB7 inclusion complexes with guest $\mathbf{2}^+$ (left) and guest $\mathbf{5}^{2+}$ (right).

The methylviologen guest ($\mathbf{5}^{2+}$) is certainly a good guest for CB7, but the thermodynamic stability of this complex in aqueous media, albeit high, is only moderate compared to that of the CB7·$\mathbf{2}^+$ complex. One important reason for this is that the shape of the hydrophobic portion of $\mathbf{5}^{2+}$ does not provide a tight fit inside the host cavity (*23*). Therefore, although hydrophobic interactions and solvation changes do play a role in the formation of the CB7·$\mathbf{5}^{2+}$ complex, ion–dipole interactions have a greater impact than in the case of the CB7·$\mathbf{2}^+$ complex. This is consistent with the two positive charges of methylviologen, primarily located on the two quaternised nitrogens and perfectly positioned to interact with the two carbonyl rims on the cavity portals of the host (Figure 7, top right). Transfer from water to DMSO or CH$_3$CN may result in stability losses associated with solvation issues, but these are much less important than for the CB7·$\mathbf{2}^+$ complex and partially compensated in the less polar solvents by the increased stabilisation brought about by the ion–dipole interactions at both ends of the complex.

Similar arguments can be put forward to discuss and rationalise the electrochemical potential data. More specifically, the fact that one-electron oxidation of the ferrocenyl centre decreases the stability of the CB7·$\mathbf{2}^+$ complex in aqueous media, whereas the same electrochemical conversion results in enhanced stability in non-aqueous solutions. In aqueous media, oxidation leads to a less hydrophobic guest, which attenuates the main driving force for complex formation. In less polar, non-aqueous solvents, solvophobic effects are minor, while the additional charge created by the oxidation process probably increases ion–dipole interactions between the guest and the host. For the CB7·$\mathbf{5}^{2+}$ complex, one-electron reduction in the guest removes one positive charge and decreases the stabilisation due to ion–dipole interactions. This effect is expected to be less important in water than in non-aqueous media, in agreement with the observed relative CB7-induced shifts on the half-wave potential for the first reduction process.

In conclusion, we have described a simple method to transfer CB7 inclusion complexes of cationic guests from aqueous to non-aqueous solutions, where their thermodynamic stabilities can be investigated and compared to those in aqueous media. Our findings suggest that ferrocenyl and viologen guests behave in different ways. The cationic ferrocenyl guest $\mathbf{2}^{+}$ gives rise in aqueous media to an extremely stable complex with CB7, which loses a large fraction of its stability upon transfer to DMSO and CH_3CN solutions. In contrast, methylviologen is bound by CB7 to form a complex of moderately high stability in water, which can be transferred to DMSO and CH_3CN solutions with relatively minor stability losses. These findings reflect the remarkable binding properties of CB7 and other CB*n* hosts, which, combined with the special solvent properties of water, suggest interesting possibilities for the design of structurally simple, synthetic host–guest pairs with very high binding affinities, quite similar to those exhibited by biological receptor–ligand systems.

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Experimental

The CB7 host was prepared as reported before (*6*). Its effective molecular weight was obtained from titration with cobaltocenium hexafluorophosphate in aqueous solution. The end point of this titration was determined by monitoring the absorbance of the cobaltocenium cation at 261 nm (*24*). The electrochemical experiments were performed in a single-compartment cell fitted with a glassy carbon working electrode ($0.071\ cm^2$), platinum auxiliary electrode and Ag/AgCl reference electrode. The working electrode was polished with a 0.05 μm alumina powder/water slurry on a felt surface. The electrolysis solution was purged with purified nitrogen before the voltammetric experiments and kept under a nitrogen atmosphere throughout.

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