Structure and stability of cyclodextrin inclusion complexes with the ferrocenium cation in aqueous solution: ^{1}H NMR studies

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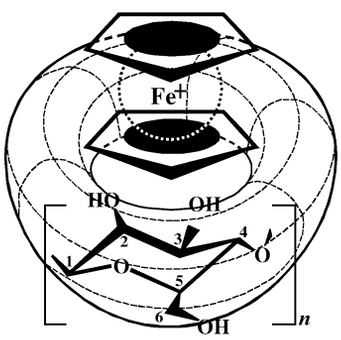
The interaction of the ferrocenium cation with cyclodextrins has been studied in aqueous and D_2O solutions by ^{1}H NMR spectroscopy. The 1 : 1 binding constants of the β- and γ-cyclodextrin complexes are 15 ± 3 and 18 ± 4 dm^3 mol^{-1}, respectively, whereas the binding of α-cyclodextrin is very weak. Although the values for the β- and γ-cyclodextrin complexes are very similar, the guest penetrates the cavity of the latter more deeply than that of the former. The results are compared with literature values of binding constants of ferrocene and substituted ferrocene and ferrocenium complexes of cyclodextrins in terms of the relative abilities of the different cyclodextrins to stabilise the Fe(II) oxidation state with respect to Fe(III).

Introduction

Cyclodextrins are cyclic oligosaccharides produced enzymatically from starch.[1a] They consist of a number of α-(1,4) linked D-glucopyranose units, forming a toroidal truncated cone. In α-, β-, and γ-cyclodextrins the number of glucopyranose units is 6, 7 or 8, respectively. There is considerable interest in the interaction of cyclodextrins and ferrocenes and their derivatives as redox switches for nanomolecular reactors and sensors.[1b,1c,2,3] The interaction of ferrocenium and other metallocenium cations and cyclodextrins is often assumed to be negligible.[4–7] β-Cyclodextrin accelerates the electrocatalytic oxidation of NADH by ferrocene derivatives including ferrocenecarboxylic acid in aqueous solution, however, and this suggests that ferrocenium–cyclodextrin complexes exist and that they are effective oxidants.[8,1c] Ferrocenes react with peroxides to form ferrocenium cations, which are highly reactive toward free radicals.[9] The interaction of ferrocenium and cyclodextrins is relevant to our interest in peroxide–cyclodextrin interactions.[10]

We report a study of inclusion complexes of cyclodextrins with the ferrocenium cation using NMR shift titrations. NMR studies of cyclodextrins and their host–guest complexes are the subject of numerous reviews.[11–14] NMR titration, measuring the cyclodextrin proton shifts as the concentration of the guest is varied, yields the binding constant of the complex and at the same time provides insight into its conformation and definitive evidence of inclusion. The cyclodextrin structure is shown in Scheme 1. The secondary hydroxy groups in the 2 and 3 positions, HO(2) and HO(3), are located at the wider rim of the cyclodextrin cavity with the corresponding H(2) toward the outside of the cavity and H(3) toward the inside. The H(4) proton is located on the outside of the molecule. The narrower end of the cavity is made up of the primary hydroxy groups HO(6), with H(5) on the inside. The simplest structural inference with regard to cyclodextrin inclusion complexes is that if only H(3) undergoes a change in chemical shift in the presence of a guest then the cavity penetration is shallow, whereas if H(5) also undergoes a change in shift then the cavity penetration is deep. Paramagnetic species, including ferrocenium cations, have been characterised by ^{1}H NMR spectroscopy.[15–17]



Scheme 1 A representation of the ferrocenium–cyclodextrin complex (without accounting for the orientation of the ion).

Experimental

Cyclodextrins were of the best commercially available quality: α-cyclodextrin (Sigma, cyclohexaamylose, 99%, HPLC; Aldrich, α-cyclodextrin hydrate), β-cyclodextrin (Fluka, ≥99%, HPLC), and γ-cyclodextrin (Sigma, ≥99%). Ferrocenium salts were purchased from Aldrich ($FcBF_4$ and $FcPF_6$) or prepared by oxidation of ferrocene (Fluka, ≥98%) by $AgNO_3$ (Aldrich) in aqueous H_2SO_4 solution. In the latter case, and for $FcPF_6$ that proved difficult to dissolve completely in water, the concentration of ferrocenium was determined spectrophotometrically. All ferrocenium solutions contained 0.025 mol dm^{-3} H_2SO_4 to stabilise the cation. D_2O, 99.9%, and $NaBF_4$, analytical grade, were purchased from Aldrich and methyl α-D-glucopyranoside and methyl β-D-glucopyranoside (≥99%, HPLC) were purchased from Fluka. All chemicals were used as supplied.

A JEOL EX 270 MHz spectrometer was used to record the proton NMR spectra of samples in distilled water or D_2O, containing 0.025 mol dm^{-3} H_2SO_4. The concentration of cyclodextrin in solution was 2.0×10^{-3} mol dm^{-3} unless stated otherwise. The concentration of ferrocenium in solution was varied from 5.0×10^{-4} to 8.0×10^{-3} mol dm^{-3}. Spectra were recorded as soon as possible after mixing of solutions; this was particularly important for mixtures with high ratios of ferrocenium ion to cyclodextrin because of the oxidation of the latter (see results). A Pharmacia Biotech Ultraspec 2000 spectrophotometer equipped with a thermostatic cell holder was used to determine ferrocenium concentrations using an extinction coefficient at λ_{max} 618 nm determined from $FcBF_4$ solutions.

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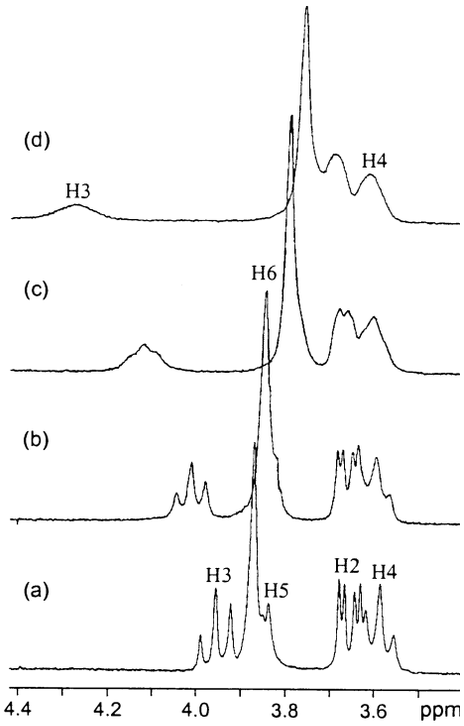

Fig. 1 Partial NMR spectra of 2.0×10^{-3} mol dm^{-3} β-cyclodextrin (a) alone; and in the presence of (b) 1.0×10^{-3} mol dm^{-3}, (c) 3.0×10^{-3} mol dm^{-3} and (d) 5.0×10^{-3} mol dm^{-3} ferrocenium tetrafluoroborate. Chemical shifts are in ppm downfield of external TMS. Proton assignments are shown.

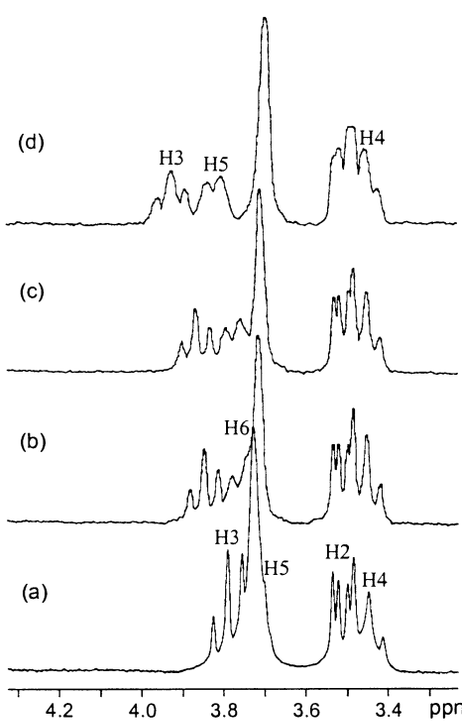

Fig. 2 Partial NMR spectra of 2.0×10^{-3} mol dm^{-3} γ-cyclodextrin (a) alone; and in the presence of (b) 3.0×10^{-3} mol dm^{-3}, (c) 4.0×10^{-3} mol dm^{-3} and (d) 7.0×10^{-3} mol dm^{-3} ferrocenium tetrafluoroborate.

Results

Fig. 1 shows examples of NMR spectra of β-cyclodextrin in the presence of increasing concentrations of ferrocenium tetrafluoroborate. The chemical shift of proton H(3) exhibits a pronounced downfield movement whereas those of H(4) and H(5) remain virtually constant. The peaks exhibit considerable

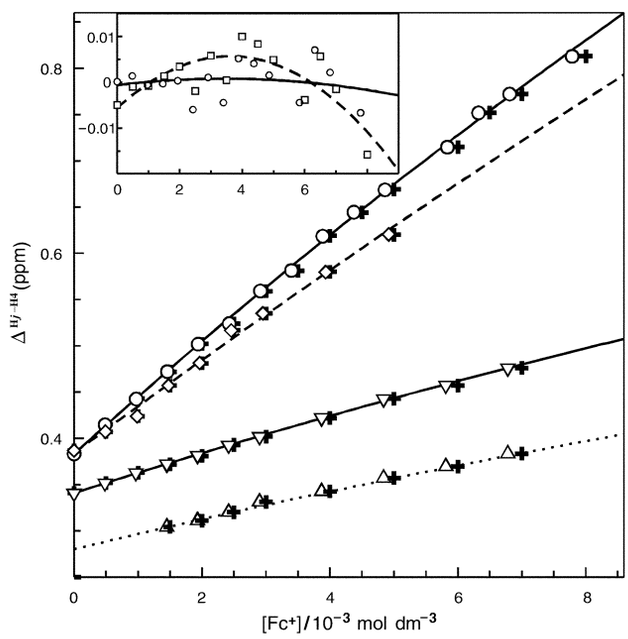

Fig. 3 Plot of the difference in chemical shifts, Δ^{Hj-H4}, at 25 ± 1 °C, against free ferrocenium concentration, calculated according to eqn. (5), used for the determination of the stability constants according to eqn. (2). The lines show the calculated best-fit dependence according to eqn. (2). Circles and diamonds represent $j = 3$ for β-cyclodextrin in D_2O and water, respectively. Inverted triangles and triangles represent $j = 3$ and 5, respectively, for γ-cyclodextrin solutions in D_2O. Crosses are the corresponding values for the total ferrocenium ion concentration, $[Fc^+]_0$. Inset: residual plots for $j = 3$ for β-cyclodextrin in D_2O: circles, according to eqn. (2): squares, according to a linear equation, *i.e* eqn. (2) with the denominator set to unity. The lines are polynomials that show the trends of the residuals: the full line shows no systematic deviation from eqn. (2) whereas the dashed line indicates a systematic deviation from the linear form.

broadening. Fig. 2 shows that the spectral changes for γ-cyclodextrin are significantly different in certain respects. As with β-cyclodextrin, the chemical shift of H(4) remains virtually constant with increasing concentrations of ferrocenium tetrafluoroborate, but, in contrast, both the H(3) and H(5) chemical shifts move downfield. The peaks do not broaden to such an extent as with β-cyclodextrin, and neither is the H(3) shift so pronounced. The difference between the chemical shifts of cyclodextrin protons H(3) and H(4), Δ^{H3-H4}, as shown in Fig. 3, was taken as a measure of binding of ferrocenium ion to the cyclodextrins. Fig. 3 also shows Δ^{H5-H4} for γ-cyclodextrin and that the effect of ferrocenium ion concentration on Δ^{H3-H4} for β-cyclodextrin solutions is similar in D_2O and water. The NMR spectrum of 2.0×10^{-3} mol dm^{-3} α-cyclodextrin, Δ^{H3-H4} is 0.402 ppm at 25 °C, was not significantly affected by ferrocenium tetrafluoroborate at all concentrations tested (up to 4×10^{-3} mol dm^{-3}, results not shown).

Although desirable for a more precise determination of binding constants, it was not possible to obtain accurate results when the concentration of ferrocenium was above 8.0×10^{-3} mol dm^{-3}, because a light yellow precipitate formed before a satisfactory spectrum could be recorded. In the case of β-cyclodextrin the precipitate was collected, rinsed with ice–water, carefully dried, dissolved in DMSO and identified by ^{1}H NMR as a 1 : 1 complex of cyclodextrin and ferrocene.

Ferrocenium, prepared from ferrocene and silver nitrate in water, and ferrocene hexafluorophosphate in D_2O caused identical chemical shifts, within experimental error, to those shown in Fig. 3 at all of the several concentrations tested. Sodium tetrafluoroborate had no effect on the NMR spectra of the cyclodextrins at equimolar and other concentrations tested. Sulfuric acid had no effect on the NMR spectra of the cyclodextrins. Sodium tetrafluoroborate, added at equimolar or

Table 1 Stability constants, K_{11}/dm^3 mol^{-1}, for cyclodextrin complexes of ferrocene and ferrocenium derivatives

Cyclodextrin	Fc	Fc^+	^-OOCFc	$^-OOCFc^+$	$Me_3N^+CH_2Fc$	$Me_3N^+CH_2Fc^+$
α	140 [ab]	<2 [c]	100 [d]	4.4 [d]	150 [e]	10 [f]
β	4100 [g]	15 [c]	2200 [d]	37 [d]	4800 [e]	150 [f]
γ	900 [a]	18 [c]	200 [d]	8.8 [d]	500 [e]	Nd [f,h]

[a] Ref. 26, 25 °C, water. [b] K_{12}, 2400 dm^3 mol^{-1}. [c] Present work, 25 °C, 0.025 mol dm^{-3} H_2SO_4 in D_2O. [d] Ref. 29, 18 ± 3 °C, 0.2 mol dm^{-3} Na_2HPO_4 in water. [e] Ref. 30, 25 °C, 0.025 mol dm^{-3} phosphate buffer pH 6.68 in D_2O. [f] Ref. 30, 25 °C, 0.1 mol dm^{-3} $HClO_4$ in water. [g] Ref. 20, temperature not given, 0.1 mol dm^{-3} $LiClO_4$ in water. [h] Not determined, see discussion.

higher concentrations, had no effect on the chemical shift produced by an equimolar concentration of ferrocenium on the respective cyclodextrins. Ferrocenium at 2×10^{-3} mol dm^{-3} and at 1.5 and 2 times this concentration had no effect on the NMR spectra of 2×10^{-3} mol dm^{-3} and 1.4×10^{-2} mol dm^{-3}, respectively, of both methyl α-D-glucopyranoside and methyl β-D-glucopyranoside (results not shown).

Assuming 1 : 1 complex formation between cyclodextrin, CD, and ferrocenium, Fc^+, according to eqn. (1), K_{11}, the binding

$$CD + Fc^+ \overset{K_{11}}{\rightleftharpoons} CD,Fc^+ \quad (1)$$

constant of the cyclodextrin–ferrocenium complex, CD,Fc^+, is given by the modified Hildebrand–Benesi equation [eqn. (2)],

$$\Delta^{H3-H4} = \frac{\Delta_{CD}^{H3-H4} + \Delta_{CD,Fc}^{H3-H4} K_{11}[Fc^+]}{1 + K_{11}[Fc^+]} \quad (2)$$

where Δ_{CD}^{H3-H4} is the difference between chemical shifts of protons H(3) and H(4) in cyclodextrin in the absence of ferrocenium and $\Delta_{CD,Fc}^{H3-H4}$ is the corresponding quantity for the cyclodextrin–ferrocenium complex. Because the experiments were not performed with a large excess of ferrocenium the mass balance eqns. (3) and (4) are taken into account in order to calculate the free ferrocenium concentration according to eqn. (5). The data

$$[CD] = [CD]_0 - [CD,Fc^+] \quad (3)$$

$$[Fc^+] = [Fc^+]_0 - [CD,Fc^+] \quad (4)$$

$$[Fc^+] = (1/2K_{11})(K_{11}[Fc^+]_0 - K_{11}[CD]_0 - 1 + \sqrt{(K_{11}[CD]_0 - K_{11}[Fc]_0 + 1)^2 + 4K_{11}[Fc]_0}) \quad (5)$$

in Fig. 3 were treated by initially approximating $[Fc^+]$ as the concentration of ferrocenium salt added, $[Fc^+]_0$, and determining the best fit values of Δ_{CD}^{H3-H4}, the product $\{\Delta_{CD,Fc}^{H3-H4} K_{11}\}$ and K_{11} by non-linear regression using eqn. (2). The best fit value of K_{11} was substituted into eqn.(5) to calculate improved values of $[Fc^+]$. The regression using eqn. (2) and subsequent re-calculation of $[Fc^+]$ was repeated three or four times until the difference between successive best fit K_{11} values was less than 0.001%. This iterative procedure yields values ± standard deviation for K_{11}, Δ_{CD}^{H3-H4}, and $\Delta_{CD,Fc}^{H3-H4}$, the latter calculated from the quotient of $\{\Delta_{CD,Fc}^{H3-H4} K_{11}\}$ and K_{11}. In D_2O these are, respectively, for β-cyclodextrin, 15 ± 3 dm^3 mol^{-1}, 0.383 ± 0.001 ppm, and 4.5 ± 1.0 ppm, and for γ-cyclodextrin, 18 ± 4 dm^3 mol^{-1}, 0.341 ± 0.001 ppm, and 1.6 ± 0.3 ppm. The open symbols and lines in Fig 3 show the concentrations of free ferrocenium obtained from the iterative procedure, and the best fit dependencies of Δ^{H3-H4} on these concentrations. The inset to Fig. 3 shows that the residuals are randomly distributed. On the other hand, a linear fit (not shown) to a reduced form of eqn. (2) with the denominator set to unity, *i.e.* assuming $[Fc^+] \ll K_{11}^{-1}$, showed systematic deviations as demonstrated by the squares in the inset. Δ^{H5-H4} for γ-cyclodextrin was not used in the determination of the binding constant because of uncertainties in its value at low ferrocenium concentrations. Nevertheless values at higher concentrations together with the binding constant determined from Δ^{H3-H4} allow the determination of $\Delta_{CD,Fc}^{H3-H4}$. The dotted line in Fig. 3 shows the dependence of Δ^{H5-H4} calculated for γ-cyclodextrin using values of Δ_{CD}^{H3-H4} and $\Delta_{CD,Fc}^{H3-H4}$ of 0.280 and 1.2, respectively. In water the value of $\{\Delta_{CD,Fc}^{H3-H4} K_{11}\}$ for β-cyclodextrin is 54 ± 11 ppm dm^3 mol^{-1} compared to its value of 68.6 ± 2.4 ppm dm^3 mol^{-1} in D_2O. This small difference is probably significant. Due to the inherently less precise measurements of the NMR shift in water the standard deviation of K_{11} was so large, however, that it is impossible to determine which of the factors in $\{\Delta_{CD,Fc}^{H3-H4} K_{11}\}$ contributes the most to the difference. Consideration of the errors involved in the measurements of chemical shifts suggests that the value for K_{11} for the ferrocenium α-cyclodextrin complex shown in Table 1 is a reasonable upper limit.

In the case of 1 : 1 and 2 : 1 binding of cyclodextrin and ferrocenium according to eqns. (1) and (6), the equation for the difference in chemical shift of the H(3) and H(4) protons is given by eqn. (7) where $\Delta_{CD_2,Fc}^{H3-H4}$ is the difference in chemical shifts

$$CD + CD,Fc^+ \overset{K_{12}}{\rightleftharpoons} CD_2,Fc^+ \quad (6)$$

$$\Delta^{H3-H4} = \frac{\Delta_{CD}^{H3-H4} + (\Delta_{CD,Fc}^{H3-H4} K_{11} + \Delta_{CD_2,Fc}^{H3-H4} K_{11}K_{12}[CD])[Fc^+]}{1 + (K_{11} + 2K_{11}K_{12}[CD])[Fc^+]} \quad (7)$$

for the 2 : 1 complex. Eqn (7) has exactly the same form as eqn. (2) at constant [CD], which is the condition that approximately applies to the data in Fig. 3 where the apparent 1 : 1 binding constant is small compared to $[Fc^+]$ so that [CD] approximates to $[CD]_0$. Under these conditions Connors has pointed out that the best test for 2 : 1 binding is to vary $[CD]_0$, whose increase will lead to a corresponding increase in the proportion of the 2 : 1 complex and a change in measured chemical shift.[18] Increasing the concentration of β-cyclodextrin from 2.0×10^{-3} mol dm^{-3} up to 0.016 mol dm^{-3} in steps of 2.0×10^{-3} mol dm^{-3} had no significant effect on Δ^{H3-H4} for solutions containing 4.0×10^{-3} mol dm^{-3} ferrocenium ion (results not shown). This is conclusive evidence that 2 : 1 binding is insignificant compared to 1 : 1.

Discussion

The lack of a significant effect of ferrocenium tetrafluoroborate on the NMR spectrum of α-cyclodextrin is conclusive evidence that no appreciable interaction takes place between these species (just as is the case with both methyl α-D-glucopyranoside and methyl β-D-glucopyranoside) and the binding is very weak. The broadening of the γ-cyclodextrin, and more so the β-cyclodextrin, peaks induced by the paramagnetic ferrocenium ion has also been reported for β-cyclodextrin with paramagnetic Fe^{III} tetrakis(4-sulfonatophenyl)porphyrin and indicates spatial proximity.[19] The use of Δ^{H3-H4} as a measure of binding of the ferrocenium ion to the cyclodextrins in the present work obviates the requirement for an internal standard to obtain precise chemical shift measurements, and so eliminates any uncertainty with regard to possible interaction between the cyclodextrin and the internal standard. The changes in chemical shifts induced in cyclodextrins by guest

Table 2 Ratios of stability constants for cyclodextrin complexes of ferrocene and ferrocenium derivatives

Cyclodextrin(s)	Fc/Fc^+	$^-OOCFc/^-OOCFc^+$	$Me_3N^+CH_2Fc/Me_3N^+CH_2Fc^+$
α	>70	23	15
β	273	60	32
γ	50	23	
β/α	<3.9	2.8	2.1
β/γ	5.5	2.6	

molecules can be interpreted in terms of the structure of the host–guest complex.[11–13] The value of $\Delta_{CD,Fc}^{H3–H4}$ for β-cyclodextrin is about three times larger than it is for γ-cyclodextrin. For γ-cyclodextrin, $\Delta_{CD,Fc}^{H5–H4}$ is about the same size as $\Delta_{CD,Fc}^{H3–H4}$, whereas it is insignificant for β-cyclodextrin. These results suggest that ferrocenium penetrates only the wider end of the β-cyclodextrin cavity, whereas it penetrates more deeply into the larger γ-cyclodextrin cavity, but, in a time-averaged sense, is not as close to any one part of the latter cavity as it is to the wider end of the β-cyclodextrin. The binding constants for ferrocenium and β- and γ-cyclodextrin are quite similar suggesting that in β-cyclodextrin the ferrocenium is in closer contact with the smaller host cavity and that stronger ion–dipole, ion-induced dipole, and dispersion forces are manifest, whereas the weaker intermolecular forces because of the larger γ-cyclodextrin cavity are offset by the greater conformational entropy. We have demonstrated that in aqueous solution the counter ions PF_6^- and BF_4^- have no effect on the stability of ferrocenium inclusion complexes of cyclodextrins.

While the present results were being prepared for publication, values of the ferrocenium–β-cyclodextrin binding constant of 65 dm^3 mol^{-1} from conductivity measurements and 36 dm^3 mol^{-1} from changes in the ferrocenium chemical shift were reported.[20] The former value is subject to a number of assumptions and the latter is based on very small changes. The binding constants ± standard deviations for the ferrocenium–β- and γ-cyclodextrin complexes reported in the present work, 15 ± 3 dm^3 mol^{-1} and 18 ± 4 dm^3 mol^{-1} are obtained by non-linear regression analysis of the very large changes in the cyclodextrin chemical shift shown in Fig. 3. The analysis of residuals in the inset to Fig. 3 confirms the validity of the data treatment and additional measurements at varying cyclodextrin concentrations show the absence of 2 : 1 binding. The very large changes in the cyclodextrin chemical shift upon binding of ferrocenium enables a very small upper limit, <2 dm^3 mol^{-1} to be placed on the binding constant for α-cyclodextrin.

It is worthwhile to compare the structural features and stability of the cyclodextrin complexes of the ferrocenium cation deduced from the present NMR study to those of related systems. Crystalline inclusion complexes, 2 : 1, 1 : 1, and 1 : 1, respectively, of α-, β-, and γ-cyclodextrins and ferrocene were prepared by Harada and co-workers by stirring fine crystals of ferrocene in an aqueous solution of the cyclodextrin.[21,22] Docking calculations[23] successfully predicted the structure of the 2 : 1 α-cyclodextrin complex, with a tilted ferrocene, obtained from X-ray crystallography.[24] The same calculations were unable to distinguish between axial and equatorial orientations in β- and γ-cyclodextrin complexes but showed that the degree of insertion of ferrocene in the former is much less (the iron at the level of the secondary oxygen atoms) than in the latter. Crystalline inclusion complexes of α- and β-cyclodextrin with the hexafluorophosphate salt of $[(\eta^5C_5H_5)Fe(\eta^6\text{-}C_6H_6)]^+$ have been prepared and both show 2 : 1 stoichiometry with this slightly larger transition metal complex.[25] Evidence for 2 : 1 inclusion in solution is only seen for the ferrocene α-cyclodextrin system.[26] Because the ferrocenium ion has a significantly larger volume than that of ferrocene[27,28] it might be possible that 2 : 1 complexation could occur between it and β-cyclodextrin. Our results show unequivocally that this is not the case.

Table 1 includes the stability constants of cyclodextrin complexes of ferrocene and ferrocenium, and their derivatives with charged substituents. The binding constant for ferrocene and β-cyclodextrin obtained by cyclic voltammetry is taken from ref. 20. The other ferrocene binding constants were obtained from solubility measurements.[26] Ferrocene and ferrocenium carboxylate complexes were measured by cyclic voltammetry.[29] $Me_3N^+CH_2Fc$ complexes were measured using the chemical shift of the ferrocene protons and those of $Me_3N^+CH_2Fc^+$ from the rate of electron transfer from ascorbic acid to the metal centre.[30] The upper limit, <1, of the stability constant for the $Me_3N^+CH_2Fc^+$ γ-cyclodextrin complex assigned by the original authors does not conform to the general pattern of results shown in Table 1. This low upper limit is based on the fact that the rate of reaction between ascorbic acid and the transition metal complex is unaffected by the presence of γ-cyclodextrin. This is not proof of lack of binding but may be due to the rate constant for the reaction of the unbound reactant being very similar to that of the bound reactant. We have observed this with cyclodextrin and with a surfactant system.[31] Table 1 shows that, with the exception of ferrocenium with β- and γ-cyclodextrins, the stability of the host–guest complexes with any particular metal complex decreases in the order β-cyclodextrin > γ-cyclodextrin > α-cyclodextrin. Also the stability of the ferrocene complexes is significantly greater than that of the ferrocenium complexes. Taking into account the problem with the interpretation of the kinetic data for $Me_3N^+CH_2Fc^+$ and γ-cyclodextrin, the data in Table 1 are consistent with the doubly charged trimethylammonium ferrocenium derivatives binding to the cyclodextrins more strongly than the ferrocenium cation itself. This is in agreement with the results of Kataky and Parker and co-workers who have demonstrated size-matched binding of alkyltrimethylammonium cations and modified cyclodextrins.[32] The first part of Table 2 shows the ratio of equilibrium constants corresponding to the exchange reaction, eqn. (8), for each of the cyclodextrins with each Fc/Fc^+ couple. The second part of Table 2 shows ratios corresponding to the exchange reactions in eqns. (9) and (10).

$$CD,Fc^+ + Fc \rightleftharpoons CD,Fc + Fc^+ \quad (8)$$

$$\beta\text{-}CD,Fc^+ + \alpha\text{-}CD,Fc \rightleftharpoons \beta\text{-}CD,Fc + \alpha\text{-}CD,Fc^+ \quad (9)$$

$$\beta\text{-}CD,Fc^+ + \gamma\text{-}CD,Fc \rightleftharpoons \beta\text{-}CD,Fc + \gamma\text{-}CD,Fc^+ \quad (10)$$

This approach essentially factors out the different solvation energies of the cyclodextrins and the very great difference in the solvation energies of the ferrocenes and ferrocenium cations and reflects the host–guest interactions and the interactions of the host–guest complexes and the solvent.[14] Hence Table 2 shows that β-cyclodextrin stabilises the ferrocenes with respect to the ferrocenium ions about 2–4 times more effectively than does α-cyclodextrin and 2–6 times more effectively than does γ-cyclodextrin.

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