Deep cavity $[CpFe(arene)]^+$ derivatized cyclotriveratrylenes as anion hosts

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Even in the absence of hydrogen bonding functionality, $[CpFe(arene)]^+$ derivatized cyclotriveratrylenes 5 will bind anionic substrates (*i.e.* $[PF_6]^-$, halides) deep within their preorganized molecular cavities. The crystal structure of 5b$[PF_6]_3\cdot(CH_3CH_2OCH_2CH_3)_{1.5}\cdot(H_2O)$ demonstrates the $[5b\subset(PF_6)]^{2+}$ complex and solution halide binding is monitored by ^1H NMR spectroscopy.

The development of receptor molecules for the specific complexation and/or detection of anions has over the years proven to be a formidable task. In consequence, a rather large and diverse array of supramolecular anion hosts has appeared.[1] Currently, work in our group is aimed at designing anion hosts by arranging positively charged organometallic moieties around the bowl shaped cavities of polyaromatic macrocycles such as calix[*n*]arenes and cyclotriveratrylene (CTV).[2] Similar organometallic anion receptors, including an amide functionalized $[CpFe(arene)]^+$ host,[3c] have been used extensively by Beer *et al.* for the sensing of anionic species with remarkable selectivity, although these hosts typically couple the function of charge pairing interactions with hydrogen bonding residues.[3] We have found that the tetrametallated calixarene $[\{(p\text{-cymene})Ru\}_4(\text{calix[4]arene} - 2H)]^{6+}$ **1**, the dimetallated CTV $[\{(p\text{-cymene})Ru\}_2CTV]^{4+}$ **2**, and related derivatives can function as anion receptors, despite the absence of hydrogen bonding functionality. The solution anion binding properties of hosts such as **1** and **2**, however, are typically complicated by the ability of the host to bind anions at sites exterior to the host cavity, as well as within.[2] We herein report new deep-cavity $[CpFe(arene)]^+$-based anion hosts whose upper rim charge preorganization allows binding of anions exclusively within the host cavity, and without the use of hydrogen bonding residues.

Racemic cyclotriveratrylene-based hosts **5** were synthesized as their $[PF_6]^-$ salts in good yield (75–85%) by S_NAr substitution of the respective $[CpFe(chloroarene)][PF_6]$**3a–c** complex with *rac*-cyclotriguaiacylene (CTG)[4] **4** in DMF containing excess K_2CO_3 (Scheme 1).[5] Neutralization of the reaction mixture with 2 M HCl(aq.) followed by addition of NH_4PF_6(aq.) and precipitation with water led to the products, which were further purified by passing through a short column of neutral alumina with acetone and reprecipitating with diethyl ether.

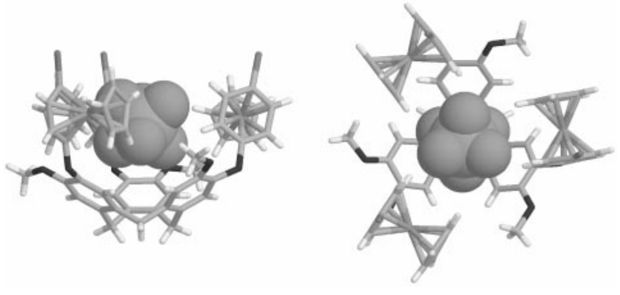
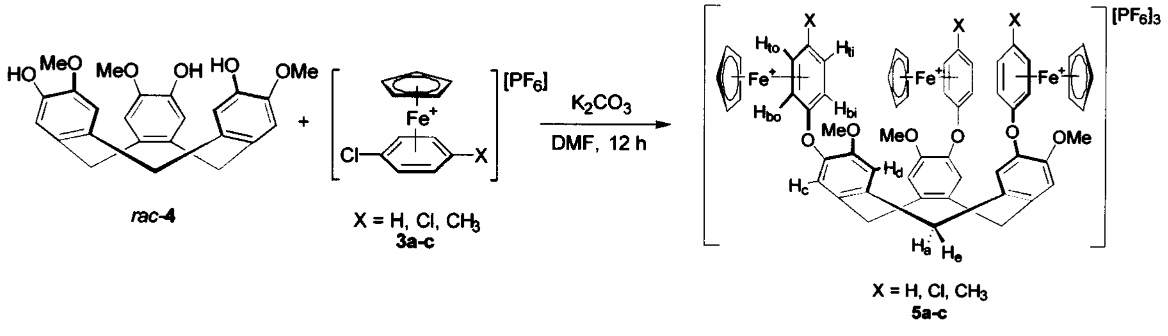


Fig. 1 X-Ray crystal structure of **5b**$[PF_6]_3\cdot(CH_3CH_2OCH_2CH_3)_{1.5}\cdot(H_2O)$† depicting side and top views of $[\mathbf{5b}\subset(PF_6)]^{2+}$ (see http://www.rsc.org/suppdata/cc/1998/2109 for full colour version of this figure)

The crystal structure of **5b** $[PF_6]_3\cdot(CH_3CH_2OCH_2CH_3)_{1.5}\cdot(H_2O)$† demonstrates an approximate C_3 symmetric host conformation, with all of the $[CpFe(arene)]^+$ substituents directed up from the rim of the CTG moiety, and exemplifies the ability of these new hosts to complex large anions deep within their cavities (Fig. 1). One $[PF_6]^-$ ion is located central to the host cavity with its three-fold symmetry axis matching that of the pseudo three-fold axis of the host cation. The depth of cavity penetration is highlighted by the fact that the phosphorus atom lies approximately 0.6 Å below the plane defined by the iron atoms. Short P···Fe distances of 5.16, 5.14, and 5.08 Å to the three iron atoms of the host are representative of significant charge pairing interactions between the included $[PF_6]^-$ anion and all three metal centers of the host, whereas the other two $[PF_6]^-$ anions each only exhibit similar close contacts to one iron atom at 5.09 and 5.12 Å respectively.

The solution anion binding properties of hosts **5** become evident upon examination of the ^1H NMR spectrum of $[\mathbf{5b}][PF_6]_3$. In NO_2CD_3 the *para* substituted aromatic rings of the upper rim $[CpFe(arene)]^+$ moieties appear as a typical AB pattern, indicative of fast rotation of this group on the NMR timescale. Addition of $[NBu_4]Br$ results in the concomitant splitting of this AB pattern into two separate patterns as the rotation of the $[CpFe(arene)]^+$ moieties is slowed as a consequence of bromide binding. Thus, separate signals are observed for sets of protons on the inside and outside of the molecular cavity of **5b**. In acetone-d_6,‡ **5b** displays inhibited $[CpFe(arene)]^+$ rotation even in the absence of bromide,



Scheme 1 Synthesis of deep cavity $[CpFe(arene)]^+$-based hosts **5**

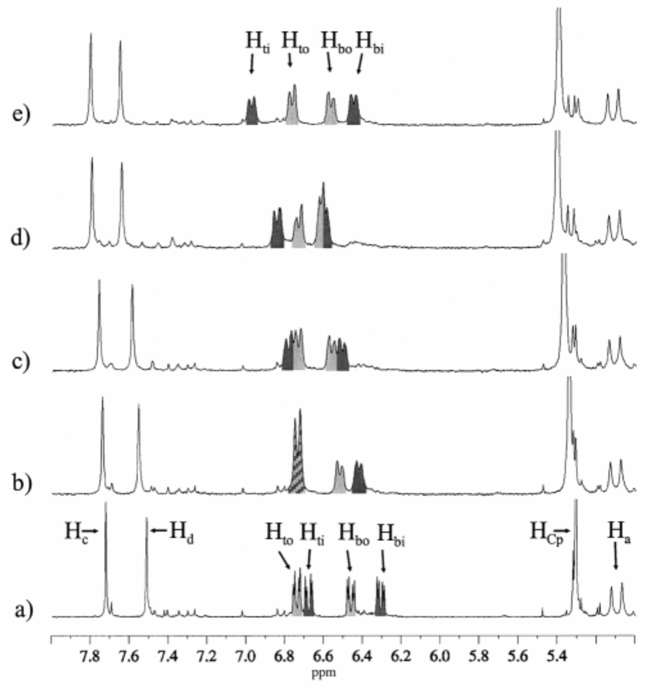


Fig. 2. ^{1}H NMR spectrum of **5b**[PF$_6$]$_3$ (acetone-d_6, 2.5 mM) with: (a) 0; (b) 0.35; (c) 0.60; (d) 1.00 equivalent of added NBu$_4$Br; (e) 1.00 equivalent of added NBu$_4$Cl

probably indicating binding of the [PF$_6$]$^-$ anion in a fashion similar to that observed in the crystal structure. A ^{1}H–^{1}H NOESY experiment allows assignment of the four unique protons according to Scheme 1 (*e.g.* H$_{\text{top,inside}}$ = H$_{\text{ti}}$). Although, from this experiment, it is not possible to determine which set of top (H$_{\text{t\_}}$) and bottom (H$_{\text{b\_}}$) protons (dark or light shaded) correspond to the inside (H$_{\text{\_i}}$) of the cavity and which correspond to the outside (H$_{\text{\_o}}$), ^{1}H NMR titration experiments with [NBu$_4$]Br make this apparent. Fig. 2 shows that as up to one equivalent of bromide is added, the chemical shifts of one top/bottom set (dark shaded) of protons are more dramatically affected than the other ($\Delta\delta_{\max}$ = 0.17, 0.29 ppm for H$_{\text{ti}}$ and H$_{\text{bi}}$). This behavior is indicative of the difference in [PF$_6$]$^-$ and bromide binding and these protons are thus assigned as those corresponding to the inside of the molecular cavity (H$_{\text{ti}}$ and H$_{\text{bi}}$). Similar effects are observed with the addition of NBu$_4$Cl ($\Delta\delta_{\max}$ = 0.30, 0.14 ppm for H$_{\text{ti}}$ and H$_{\text{bi}}$) although the magnitude of the chemical shift change is larger for H$_{\text{ti}}$ than H$_{\text{bi}}$. Conversely, addition of iodide affects H$_{\text{bi}}$ more than H$_{\text{ti}}$ and also more than the addition of bromide ($\Delta\delta_{\max} \geqslant 0.07$, 0.35 ppm for H$_{\text{ti}}$ and H$_{\text{bi}}$). No changes in chemical shifts are observed with the addition of [NBu$_4$][PF$_6$].

In all instances precipitation of **5b**[X]$_3$ onsets when any amount greater than one equivalent of halide is added and association constants could not be determined due to these constraints. This in itself is a significant feature of hosts **5**, however, since typical non-preorganized [CpFe(arene)]$^+$ cations are acetone soluble and display essentially no ^{1}H chemical shift changes even in the presence of a large excess of halide. Furthermore, the near linear dependence of the chemical shifts of H$_{\text{\_i}}$ on the amount of added halide suggests large association constants and extremely efficient complexation of halides (*vs.* [PF$_6$]$^-$) by the host in this solvent. That precipitation onsets when more than one equivalent of halide is present is indicative of a soluble [**5b**$\subset$X]$^{2+}$ (X = Cl$^-$, Br$^-$, I$^-$) species which will precipitate in the presence of significant concentrations of unbound halide. It is difficult to interpret the differences in chemical shift behavior of H$_{\text{ti}}$ and H$_{\text{bi}}$ with the different halides but it is likely an artifact of the relative differences in host conformations of [**5b**$\subset$(PF$_6$)]$^{2+}$ and the [**5b**$\subset$X]$^{2+}$ species. On the basis of these data, the relative preference of **5b** for the different sized halides cannot be definitively established, but the overall greater changes in chemical shift for iodide complexation may suggest a preference for the larger halide.

The new anion hosts reported represent a new class of anion receptor molecules whose binding properties are a direct consequence of only appropriately arranged sites of positive charge in the molecule. **5a–c** have distinct advantages over molecules such as **1** and **2** in that they do not possess significant binding sites exterior to the molecular cavity. We anticipate that the reactive chlorine substituents at the upper rim of **5b** will allow extension of the host cavity. Moreover, we are currently investigating the distinct possibility of synthesizing new metallated cryptophane[6] host molecules by capping off **5b** with another cyclotriguaiacylene moiety. Finally, the chiral nature of **4**, which can be resolved into its two optically active forms,[4] may provide a unique opportunity to investigate enantio-selective binding of anionic species using chiral hosts similar to **5**.

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Notes and References

† *Crystal data* (173 K, Siemens SMART CCD diffractometer): [C$_{57}$H$_{48}$O$_6$Cl$_3$Fe$_3$][PF$_6$]$_3$·(CH$_3$CH$_2$OCH$_2$CH$_3$)$_{1.5}$·(H$_2$O), orange–brown, M = 1667.02, monoclinic, $P2_1/c$ (no. 14), a = 17.791(1), b = 21.858(1), c = 18.178(1) Å, β = 103.456(1)°, V = 6874.8(7) Å^3, Z = 4, D_c = 1.61 g cm^{-3}, μ(Mo-Kα) = 9.14 cm^{-1}, G.O.F. = 1.05, wR_2(all data) = 0.199, $R_1[I > 2\sigma(I)]$ = 0.0652, 9468 independent reflections. Manipulations were performed using the program RES2INS.[13] CCDC 182/975.

‡ ^{1}H NMR data (acetone-d_6, 250 MHz, J/Hz) for **5a**: δ 7.73 (s, 3H, H$_c$), 7.53 (s, 3H, H$_d$), 6.29–6.39 (m, 9H, [CpFe(*arene*)]$^+$), 6.23 (t, 6H, ^3J = 5.4, [CpFe(*arene*)]$^+$), 5.18 (s, 15H, Cp), 5.10 (d, 3H, ^2J = 13.8, H$_a$), 3.93 (d, 3H, ^2J = 13.8, H$_e$), 3.79 (s, 9H, OMe); for **5b**: δ 7.72 (s, 3H, H$_c$), 7.52 (s, 3H, H$_d$), 6.74 (dd, 3H, ^4J = 1.9, ^3J = 6.9, H$_{\text{to}}$), 6.68 (dd, 3H, ^4J = 12.3, ^3J = 6.9, H$_{\text{ti}}$), 6.46 (dd, 3H, ^4J = 1.9, ^3J = 6.9, H$_{\text{bo}}$), 6.31 (dd, 3H, ^4J = 2.3, ^3J = 6.9, H$_{\text{bi}}$), 5.31 (s, 15H, Cp), 5.10 (d, 3H, ^2J = 13.8, H$_a$), 3.91 (d, 3H, ^2J = 13.8, H$_e$), 3.78 (s, 9H, OMe); for **5c**: δ 7.71 (s, 3H, H$_c$), 7.51 (s, 3H, H$_d$), 6.22–6.31 (m, 9H, [CpFe(*arene*)]$^+$), 6.11 (dd, 3H, ^4J = 2.0, ^3J = 5.8, [CpFe(*arene*)]$^+$), 5.13 (s, 15H, Cp), 5.09 (d, 3H, ^2J = ???, H$_a$) 3.82 (d, 3H, ^2J = 13.9, H$_e$), 3.78 (s, 9H, OMe), 2.44 (s, 9H, CH$_3$).

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