Influence of the Anion on the Stability of Second-Sphere Coordination of Ferrioxamine B with *cis*-Dicyclohexano-18-crown-6 in Chloroform

Ines Batinić-Haberle and Alvin L. Crumbliss*

Department of Chemistry, Duke University, Box 90346, Durham, North Carolina 27708-0346

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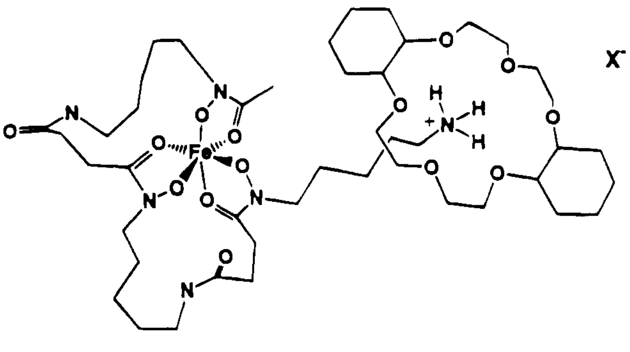
The influence of the anion X^- on the stability of the supramolecular assembly $FeHDFB^+,CE,X^-$ (**I**) where $FeHDFB^+$ is ferrioxamine B, CE is dicyclohexano-18-crown-6, and X^- is ClO_4^-, NO_3^-, Cl^-, or picrate was investigated. The formation constants for these host−guest adducts in wet chloroform at 25 °C were determined as follows: $K_a(ClO_4^-) = 1.77 \times 10^4$ M^{-1}, $K_a(NO_3^-) = 1.34 \times 10^2$ M^{-1}, $K_a(Cl^-) = 1.00 \times 10^1$ M^{-1}, K_a(picrate) $= 4.68 \times 10^3$ M^{-1}. Distribution constants (K_d) for the ion pairs between water and chloroform, as well as extraction constants (K_{ex}) for the corresponding crown ether separated ion pairs, were determined: $K_d(ClO_4^-) = 3.10 \times 10^{-4}$ M^{-1}, $K_d(NO_3^-) = 2.91 \times 10^{-4}$ M^{-1}, $K_d(Cl^-) = 3.00 \times 10^{-4}$ M^{-1} , K_d(picrate) $= 0.24$; $K_{ex}(ClO_4^-) = 5.50$ M^{-2}, $K_{ex}(NO_3^-) = 3.91 \times 10^{-2}$ M^{-2}, $K_{ex}(Cl^-) = 3.00{\cdot}10^{-3}$ M^{-2}, K_{ex}(picrate) $= 1.12 \times 10^3$ M^{-2}. Data are presented which support the assertion that crown ether intercalation into the $FeHDFB^+,X^-$ ion pair to form the supramolecular assembly in **I** provides a mechanism for the chloroform extraction process which is different from the distribution process. The importance of anion solvation in determining the stability of **I** is illustrated by a linear plot of log K_a *vs* anion hydration enthalpy. Comparison with our previously published data enable us to conclude that the stability of **I** is equally sensitive to hydration of the cation and the anion. We conclude that matching crown ether properties to the {cation,anion} combination in an ion pair may enhance host−guest interactions and optimize aqueous/organic phase extractions.

Introduction

Second-sphere interactions[1] between hydrophilic metal complexes and crown ethers leading to the formation of adducts offers the possibility of selective extraction of specific metal complexes into organic media.[2,3] Such second-sphere adducts may be formed with neutral[4−6] or charged[1,7−9] metal complexes which contain −NH, −OH, or −CH acidic ligands that are capable of hydrogen-bonding interactions. Most of the adducts formed with metal amine complexes show a structural analogy to the three-point hydrogen-bonding interaction of ammonium and substituted ammonium ions with crown ethers.[10] The interplay of hydrogen bonding forces and $\pi-\pi$ charge transfer interactions may serve to stabilize the host−guest adduct in a particular geometry.[10] Additional electrostatic charge−dipole interactions between a cationic complex and polyether oxygens serve to increase stability relative to adduct formation involving neutral species. Adducts are also possible where the crown ether serves as a simultaneous first- and second-sphere coordination ligand.[11−13]

A specific type of second-sphere interaction between metal(III) complexes of a linear trihydroxamic acid (deferriferrioxamine B), $MHDFB^+$, and dicyclohexano-18-crown-6 has been observed and quantified in our laboratory.[14] In the case of transition metal amines, the crown ether interacts with an amine first-sphere ligand.[2,3] The deferriferrioxamine B metal complex has the distinct feature of a side chain bearing a substituted ammonium group that is not involved in the first coordination shell of the metal. The crown ether enters the second coordination shell of the metal complex where it recognizes the ammonium end of the ligand side chain as illustrated in **I** where



I

M = Fe(III). This supramolecular assembly may be viewed in the context of a second-sphere coordination of an iron siderophore complex and a first-sphere

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* Address correspondence to this author.

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interaction between an alkyl-substituted ammonium ion with a crown ether.

The assembly affords the opportunity to investigate an alkylammonium−crown ether host−guest complex using a chromophore attached to the alkylammonium guest.

The ammonium functionality in **I** bears a positive charge and exhibits both hydrogen-bonding and electrostatic forces with the crown ether oxygen atoms. The importance of the positive charge is illustrated by the fact that adduct formation is not observed when the metal complex is deprotonated.[15] The extraction of this stable supramolecular assembly, $\mathrm{MHDFB^+,CE,X^-}$ (**I**), into a chloroform medium was accomplished with an order of selectivity toward different M(III) complexes as follows: (Al(III) < Fe(III) < Ga(III) < In(III)). The observed selectivity order is consistent with metal ion radius dependent hydration effects which influence the primary coordination shell of the alkylammonium group.[14] Since the host−guest adduct stability and the chloroform extraction process are influenced by the nature of the cationic metal complex, they are also expected to be influenced by the nature of the accompanying anion.[16−32] Therefore, an investigation of the influence of the nature of the anion (X^-) on the stability and extractability of **I** was undertaken and is reported here. The influence of the crown ether structure[33−36] on the stability of the supramolecular assembly **I** in an organic medium, and therefore on the efficacy of the extraction, has been investigated as well.[37,38]

These results are relevant to gaining an understanding of the mechanism of deferriferrioxamine B mediated iron bioavailability.[39,40] In addition, an understanding of these extraction processes may lead to applications in trace and precious metal recovery,[41] as well as in the liquid membrane transport of industrial and biological materials.[42−49]

Experimental Section

Materials. The ferrioxamine B complex ($\mathrm{FeHDFB^+}$) was prepared as described previously.[14] A known amount of deferriferrioxamine B ($\mathrm{H_4DFB^+}$; Sigma) was diluted in a small volume of water, followed by the addition of iron(III) perchlorate, nitrate, or chloride stock solution. The iron(III) concentration of the stock solution was determined spectrophotometrically.[50] When nitrate was the anion, standardization was accomplished only after nitrate had been exchanged on an anion exchange resin (AG 1-X8, Bio-Rad; perchlorate form). The acid concentration of the iron(III) stock solution was determined by passing an aliquot through Dowex 50 W-X8 cation exchange resin, followed by titration with 0.1 M NaOH. The iron(III)−deferriferrioxamine B solution was adjusted to pH = 3.2 by the addition of solid $\mathrm{Mg(OH)_2}$ (98%). pH was measured using a Corning combined glass electrode. After the desired pH was reached, the solution was filtered and used in the extraction and distribution equilibrium experiments. *cis*-Dicyclohexano-18-crown-6 (DC-18-C-6), a mixture of approximately equal parts of *cis,syn,cis* and *cis,anti,cis* isomers, was used as obtained from Aldrich. Twice-distilled water was used throughout our experiments. Chloroform saturated with water was used in extraction and distribution experiments. Chloroform solutions of crown ether were made by dissolving appropriate amounts of DC-18-C-6 in a known volume of $\mathrm{CHCl_3}$. Ionic strength was kept at 0.1 M by $\mathrm{Mg(ClO_4)_2}$, $\mathrm{Mg(NO_3)_2}$, or $\mathrm{MgCl_2}$, formed by the neutralization of the corresponding acid by $\mathrm{Mg(OH)_2}$.

Methods. Distribution Equilibria of Ferrioxamine B. The distribution of ferrioxamine B, accompanied by different anions, between an aqueous and a chloroform phase was accomplished by mixing 40 mL of a ferrioxamine B solution with 40 mL of chloroform. The chloroform solution, 35 mL, was evaporated to dryness and the residue dissolved in 1 mL of water. The concentration of ferrioxamine B was determined by UV/vis spectroscopy at 425 nm ($\epsilon_{425} = 2600$ $\mathrm{M^{-1}\,cm^{-1}}$).[51]

Distribution Equilibrium of *cis*-Dicyclohexano-18-crown-6. The distribution of crown ether between an aqueous and an organic phase has been previously determined by its re-extraction with potassium picrate into the organic phase.[14,52] The molar absorptivity of $\mathrm{(K^+,DC\text{-}18\text{-}C\text{-}6,pic^-)_{CHCl_3}}$, $\epsilon = 1.59 \times 10^4$ $\mathrm{M^{-1}\,cm^{-1}}$ at 366 nm used for our calculations, was determined in a separate experiment as described previously.[14]

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Extraction Equilibria. The extraction of ferrioxamine B in the presence of DC-18-C-6 was performed as described previously.[14] The concentration of ferrioxamine B in the chloroform phase was determined after it had been re-extracted with 0.1 M KNO_3 into the aqueous phase. The concentration of ferrioxamine B in the aqueous phase was calculated from the difference between the initial concentration (0.015 M) and the concentration in the chloroform phase. The concentration of crown ether varied from 0.05 to 0.20, 0.20 to 0.40, and 0.43 to 0.55 M when the anion (initially 0.06 M) was perchlorate, nitrate, and chloride, respectively.

All spectrophotometric determinations were performed using a Hewlett Packard 8451A diode array spectrophotometer. All reported values are based on three to five independent determinations ,and the errors are within 10%, except for ferrioxamine B distribution data which are within 25%.

Results

The overall experimental approach to determining host–guest association constants in chloroform in the presence of various anions involves determining extraction and distribution equilibria. An overall extraction equilibrium for the systems reported here is shown in eq 1, where $FeHDFB^+$ is ferrioxamine B, CE is DC-18-C-6, and X^- is ClO_4^-, NO_3^- or Cl^-. Data previously reported[14] in the presence of picrate anion will also be included in our discussion for the purposes of comparison. The function of the magnesium salt is to permit all experiments to be carried out at a constant ionic strength ($I = 0.1$). As elaborated on below, the Mg^{2+} cation provides negligible competition for the crown ether cavity.

$$FeHDFB^{+}_{aq} + Mg^{2+}_{aq} + 3X^{-}_{aq} + 2CE_{org} \overset{K_{overall}}{\rightleftharpoons} (FeHDFB^{+},CE,X^{-})_{org} + (Mg^{2+},CE,2X^{-})_{org} \quad (1)$$

The overall extraction experiment may be conceptually broken down into two extraction equilibria involving $FeHDFB^+$ (eqs 2 and 3) and Mg^{2+} (eqs 4 and 5). The overall extraction constant ($K_{overall}$) may then be expressed as the product of the extraction constants for the individual equilibria of interest as shown in eq 6.

$$FeHDFB^{+}_{aq} + X^{-}_{aq} + CE_{org} \rightleftharpoons (FeHDFB^{+},CE,X^{-})_{org} \quad (2)$$

$$K_{ex}^{FeHDFB^{+}CE,X^{-}} = [(FeHDFB^{+},CE,X^{-})]_{org}/\{[FeHDFB^{+}]_{aq}[X^{-}]_{aq}[CE]_{org}\} \quad (3)$$

$$Mg^{2+}_{aq} + 2X^{-}_{aq} + CE_{org} \rightleftharpoons (Mg^{2+},CE,2X^{-})_{org} \quad (4)$$

$$K_{ex}^{Mg^{2+},CE,2X^{-}} = [(Mg^{2+},CE,2X^{-})_{org}]/\{[Mg^{2+}]_{aq}[X^{-}]_{aq}^{2}[CE]_{org}\} \quad (5)$$

$$K_{overall} = (K_{ex}^{FeHDFB^{+},CE,X^{-}})(K_{ex}^{Mg^{2+},CE,2X^{-}}) \quad (6)$$

The extraction of Mg^{2+} into the organic phase was found to be neglible relative to that of $FeHDFB^+$.[14] Thus the concentration of the Mg^{2+},CE,$2X^-$ assembly in the organic phase was neglected in the overall extraction equilibrium given by eq 1. $K_{ex}^{FeHDFB^{+},CE,X^{-}}$ may be expressed as follows:

$$K_{ex}^{FeHDFB^{+},CE,X^{-}} = D_{FeHDFB^{+}}/\{[X^{-}]_{aq}[CE]_{org}\} \quad (7)$$

where

Table 1. Extraction (K_{ex}), Distribution (K_d), and Host–Guest Association (K_a) Equilibrium Constants for Ferrioxamine B ($FeHDFB^+$,X^-) ($X^- = ClO_4^-$, NO_3^-, Cl^-, Picrate; $I = 0.1$ M) and *cis*-Dicyclohexano-18-crown-6 in Chloroform at 25 °C and Hydration Enthalpies, ΔH_{hydr}

X^-	K_d, M^{-1}	K_{ex}, M^{-2}	K_a, M^{-1}	ΔH_{hydr},[a] kJ mol^{-1}
ClO_4^-	3.10×10^{-4}	5.50	1.77×10^{4}	−209
NO_3^-	2.91×10^{-4}	3.91×10^{-2}	1.34×10^{2}	−297
Cl^-	3.00×10^{-4}	3.00×10^{-3}	1.00×10	−331
picrate^{-}[b]	2.40×10^{-1}	1.12×10^{3}	4.68×10^{3}	−226

[a] Anion hydration enthalpy as defined in eq 13; ref 53. [b] Data from ref 14.

$$D_{FeHDFB^{+}} = [FeHDB^{+},CE,X^{-}]_{org}/[FeHDFB^{+}]_{aq} = [K_{overall}/K_{ex}^{Mg^{2+},CE,2X^{-}}][X^{-}]_{aq}[CE]_{org} = [K_{ex}^{FeHDFB^{+},CE,X^{-}}][X^{-}]_{aq}[CE]_{org} \quad (8)$$

$K_{ex}^{FeHDFB^{+},CE,X^{-}}$ values were obtained from the slopes of linear plots of $D_{FeHDFB^{+}}$ *vs* $[X]_{aq}[CE]_{org}$, where $[X^-]_{aq}$ and $[CE]_{org}$ were taken as their initial concentrations in the aqueous and chloroform phases, due to their being present in excess and the lack of competition for CE from Mg^{2+}. The linearity of these plots also serve to confirm the 1:1 stoichiometry of the host–guest complex as shown in eq 2. Values for $K_{ex}^{FeHDFB^{+},CE,X^{-}}$ are listed in Table 1.

In order to use extraction equilibrium data to calculate host–guest association constants in chloroform in the presence of various anions, $K_{ex}^{FeHDFB^{+},CE,X^{-}}$ must be corrected for the distribution of the ion pair $FeHDFB^+$,X^- between the aqueous and chloroform phases in the absence of crown ether. Distribution equilibria (K_d) between the aqueous and chloroform phases were determined at constant ionic strength by carrying out the overall extraction experiment in the absence of DC-18-C-6. The distribution of MgX_2 into the chloroform phase was negligibly small so that K_d values for $FeHDFB^+$ were readily determined from measurements of $[FeHDFB^{+},X^{-}]_{org}/[FeHDFB^{+}]_{aq}$ at a fixed $[X^-]_{aq}$ as shown in the following equations:

$$FeHDFB^{+}_{aq} + X^{-}_{aq} \rightleftharpoons (FeHDFB^{+},X^{-})_{org} \qquad K_d \quad (9)$$

$$K_d = [FeHDFB^{+},X^{-}]_{org}/\{[FeHDFB^{+}]_{aq}[X^{-}]_{aq}\} \quad (10)$$

K_d values for ferrioxamine B with perchlorate, nitrate, and chloride as counterions are compiled in Table 1.

The host–guest association equilibrium of interest in chloroform solution is described in eq 11. Values for host–guest association constants, K_a, may be calculated from $K_{ex}^{FeHDFB^{+},CE,X^{-}}$ and K_d according to eq 12, provided that the crown ether is present only in the chloroform phase. This was established experimentally by determining the distribution equilibrium of *cis*-dicyclohexano-18-crown-6 between chloroform and water (DC-18-C-$6_{org} \rightleftharpoons$ DC-18-C-6_{aq}), $K_d' = 6.3 \times 10^{-4}$.[14] Host–guest association constants (K_a) for $FeHDFB^+$,CE,X^- in the presence of perchlorate, nitrate, and chloride anions, together with a previously obtained value in the presence of picrate,[14]

$$(FeHDFB^{+},X^{-})_{org} + CE_{org} \rightleftharpoons (FeHDFB^{+},CE,X^{-})_{org} \qquad K_a \quad (11)$$

$$K_a = (K_{ex}^{FeHDFB^{+},CE,X^{-}})/K_d \quad (12)$$

are listed in Table 1. As indicated in the Experimental Section, the thermodynamic quantities given here relate to a mixture of *syn* and *anti* crown ether isomers.

Discussion

Distribution Equilibria. There is no observable distribution of the potassium salts of the hydrophilic anions used in our study ($X^- = ClO_4^-$, NO_3^-, Cl^-) between an aqueous phase and a chloroform[16] or dichloroethane[25] phase. From our data reported in Table 1, it is evident that, once hydrophilic K^+ is replaced with the more lipophilic ferrioxamine B cation, the ion pair $FeHDFB^+,X^-$ will distribute between chloroform and water in the absence of crown ether on a low, but detectable, level. However, the distribution does not vary with changes in the hydrophilic anions studied. We propose that the K_d values for $FeHDFB^+,X^-$ are insensitive to X^- because the *effective* charge density on $X(H_2O)_n^-$ taken with its solvation shell is relatively constant for ClO_4^-, NO_3^-, and Cl^-. This has been described by Zavâda and co-workers in terms of a balance between concordant and discordant solvation, which results in constant activity coefficients for the different anions X^-.[22] Hence, if the hydrated anions (ClO_4^-, NO_3^-, Cl^-) are considered as entities, we may expect similar hydrophilicities for such units.

Distribution data (K_d) for the picrate anion are included in Table 1 for $FeHDFB^+,pic^-$.[14] These results show a 3 order of magnitude increase in K_d for picrate over that observed for the hydrophilic anions. The organic picrate anion is soft and has a hydrophobic core. Therefore, even as a hydrated ion, it favors entering chloroform, relative to the other three hydrophilic, hard bases investigated. Since no correlation between K_d and ΔH_{hydr} for the anion exists, we conclude that softness and hydrophobicity of the anion are more important than dehydration in the distribution process.

While K_d is unaffected for $FeHDFB^+,X^-$ when the anion is changed from ClO_4^- to NO_3^- to Cl^- , changing the cation for $MHDFB^+,pic^-$ influences K_d significantly in the order M(III) = Al(III) < Ga(III) < Fe(III) < In(III), as evidenced by the linearity of a log K_d *vs* $\Delta H_{hydr}(M(H_2O)_6{}^{3+}{}_g)$ plot reported previously.[14] This $MHDFB^+$ cation influence on K_d is not unexpected since the cation, $MHDFB^+$, differs significantly from the hard anion X^-, its character being much closer to that of the soft and hydrophobic picrate anion. K_d increases for $MHDFB^+,pic^-$ monotonically with increasing ionic radius of M(III).[14] We propose that the water molecules in the second coordination shell of the metal complex, the number of which is influenced by the charge density on M(III), are carried with the metal complex entering the organic phase and therefore influence its lipophilicity.

Extraction Equilibria. Contrary to K_d, the extraction constant K_{ex} varies by 3 orders of magnitude with changes in the hydrophilic anion ($X^- = ClO_4^-$, NO_3^-, or Cl^-; see Table 1). Apparently the presence of the crown ether permits the fundamental differences among ClO_4^-, NO_3^-, and Cl^-, which are lost or neutralized in the distribution process, to be expressed. When the picrate anion is included in the comparison, K_{ex} is seen to vary by 6 orders of magnitude with variation in the anion.

Host–Guest Equilibria. As can be seen from eq 12, the overall extraction process is composed of two independent and different processes, distribution and association. Eliminating distribution from extraction, we obtain data that represent the pure association of $FeHDFB^+,X^-$ with the crown ether. Therefore, the apparent discrimination among hydrophilic anions, within 3 orders of magnitude, in the overall extraction process is ascribed to their different associations with the $FeHDFB^+,CE$ assembly, as quantified by the association constant K_a. The advantage in the distribution that picrate gained over perchlorate through its lipophilicity (log $K_d = -0.62$ *vs* -3.54) has been partly lost in the association process. Nevertheless picrate still remains the most efficient anion in the overall extraction process.

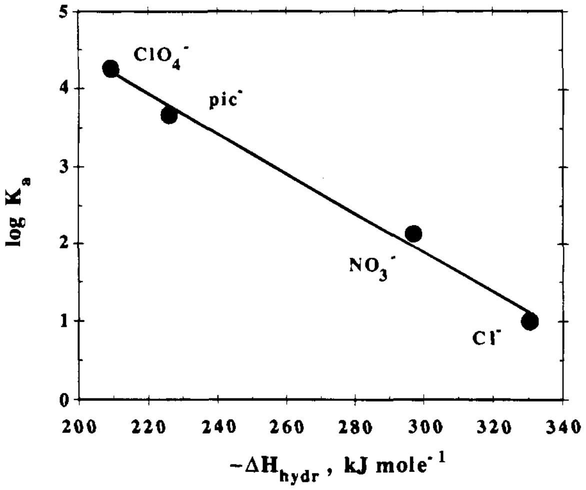

Figure 1. Plot of log host–guest complex formation constant (log K_a) for $FeHDFB^+,CE,X^-$ as a function of hydration enthalpy (ΔH_{hydr})[53] for $X^- = ClO_4^-$, NO_3^-, Cl^-, and picrate. Data were collected in chloroform at 25 °C, $I = 0.1$ M (MgX_2).

The three hydrophilic anions under investigation have widely different enthalpies of hydration. Figure 1 is a plot of the log of the host–guest association constant for $FeHDFB^+,CE,X^-$ (log K_a; eqs 11 and 12) as a function of the hydration enthalpy for X^-. The ΔH_{hydr} data used in Figure 1 and Table 1 are defined by the process given by eq 13 and have all been taken

$$\text{anion}^-{}_g \rightleftharpoons \text{anion}^-{}_{aq} \qquad \Delta H_{hydr} \tag{13}$$

from Yatsimirskii's publication.[53] (These data differ slightly from similar data available from multiple sources[54–56] as a result of slight differences in methods of calculation and experimental methods.) The same trend given in Figure 1 is observed if log K_a data are plotted *vs* ΔG_{hydr}, where ΔG_{hydr} data are taken from Rakhman'ko *et al.* [55] and from Marcus.[57] Data for the picrate anion fit the linear correlation between log K_a and ΔH_{hydr} given in Figure 1. Apparently, picrate behaves like the other three anions studied in forming the supramolecular assembly (**I**) in chloroform. The differences in hydrophilicity/hydrophobicity that account for their different distributions do not play a role in the association process. The association of anion with crown ether, which parallels $FeHDFB^+$ association, may be considered as the competition of crown ether with water molecules for the anion first hydration shell in order to intercalate between the protonated amine cation and anion. That is, supramolecular assembly formation requires the removal of water molecules from the anion hydration shell, as well as the cation hydration shell. Thus, it may be expected, as suggested from Figure 1,

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(54) Vasil'ev, V. P.; Zolotarev, E. K.; Kapustinskii, A. F.; Mishchenko, K. P.; Podgornaya, E. A.; Yatsimirskii, K. B. *Zh. Fiz. Khim.* **1960,** *34,* 1763; *Russ. J. Phys. Chem. (Engl. transl.)* **1960**, *34,* 840.

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that dehydration dominates the magnitude of the association process. It also suggests that partial hydration in the organic phase is an important factor in affecting the stability of the host–guest interaction shown in **I**. Apparently, the anion hydration shell imposes a steric hindrance to the approach of the crown ether-protonated amine supramolecular assembly. Additionally, specific steric requirements of the bulky picrate anion may affect the stability of the assembly.

To test the relative influence of the anion hydration shell and the $FeHDFB^+$ cation hydration shell on the stability of the supramolecular assembly shown in **I**, we shall also consider the K_a values for the metal complex series $MHDFB^+$ (M = Al(III), Fe(III), Ga(III), In(III)).[14] By varying M in this way, we change the charge density at the metal center and therefore the second coordination shell hydration. Changes in ferrioxamine B second coordination shell hydration influence the first coordination shell of the alkylammonium guest ion. A measure of the *changes* in the second coordination shell hydration is the variation of the hydration shell enthalpy (ΔH_{hydr}) for $M(H_2O)_6{}^{3+}{}_g$ with M, where ΔH_{hydr} is defined in eq 14. We

$$M(H_2O)_6{}^{3+}{}_g \rightleftharpoons M(H_2O)_6{}^{3+}{}_{aq} \qquad \Delta H_{hydr} \qquad (14)$$

can use the Born equation to calculate the solvation enthalpies for this process (ΔH_{hydr}), taking into account that the entropy change for this process is negligible at room temperature.[58,59] Since we are considering only relative *changes* in cation complex hydration shell, it is important to note that, on changing from In(III), to Fe(III), to Ga(III), to Al(III), there is only an 8% increase in ΔH_{hydr} for $M(H_2O)_6{}^{3+}{}_g$. As expected, this is a much smaller variation than the 58% change in anion hydration enthalpy on changing from ClO_4^-, to picrate, to NO_3^-, to Cl^-.

Figure 2 illustrates that a single linear correlation exists between log K_a and the relative changes in hydration shell for both the cation and the anion, where relative hydration shell changes are measured by the percent change in ΔH_{hydr} for the anion (relative to ClO_4^-) and cation (relative to $InHDFB^+$). The fact that data for changes in M(III) and changes in X^- fall on the same line suggests that the stability of the supramolecular complex shown in **I** depends to the same extent on the hydration shell surrounding the cation $MHDFB^+$ and anion X^-. Thus we conclude that anion and cation solvation are equally important in determining host–guest interactions. By matching crown ether properties to the {cation,anion} combination in an ion pair, one may optimize host–guest interactions.

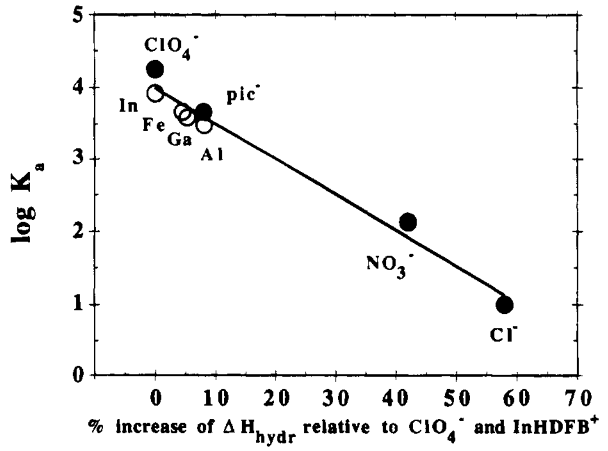

Figure 2. Plot of log host–guest complex formation constant (log K_a) for $FeHDFB^+$,CE,X^- (X^- = ClO_4^-, NO_3^-, Cl^-, picrate) as a function of the change in hydration enthalpy (ΔH_{hydr})[53] for $X^-{}_g$ relative to ClO_4^- (closed circles) and plot of log host–guest complex formation constant (log K_a) for $MHDFB^+$,CE,picrate$^-$ (M = In(III), Fe(III), Ga(III), Al(III))[14] as a function of the change in hydration enthalpy (ΔH_{hydr})[58,59] for $M(H_2O)_6{}^{3+}{}_g$ relative to In(III) (open circles). See text.

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