Calixarene-facilitated transfer of alkali metal ions across the polarised liquid–liquid interface

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The transfer of sodium and potassium ions across the water–1,2-dichloroethane interface by the neutral ionophore tetraethyl-*p-tert*-butyl calix[4]arene tetraacetate has been investigated using voltammetric methods. The electrochemical data has been used to determine the stoichiometry of the metal : ligand complex and the appropriate association constants between the metal ions and the ligand in the organic phase. This data is correlated with structural studies, including the crystal structure of the Na+-calixarene complex, which is reported for the first time.

The calixarenes,[1] macrocyclic products of phenol-formaldehyde condensations, are well known ionophoric materials with properties that can be tailored through the substituents appended to the phenolic oxygens.[2,3] The ionophoric nature of the calixarenes has made them attractive reagents for applications in electrode[4] and sensor[5] devices. Analytical investigations have sought to couple calixarene "recognition" behaviour with potentiometric,[6,7] modified electrode voltammetric,[8] visible absorbance[9] and fluorescence[10,11] measurements. The most widespread investigations have been targetted[3–5] towards Na+, employing tetrameric calixarene esters and amides. Likewise, potentiometry at polyvinyl chloride-supported liquid membrane electrodes has been the most widely employed measurement method. Potentiometric selectivity coefficients for Na+ over K+ of the order of 100 and Nernstian responses have been reported, making such devices attractive for the clinical monitoring of Na+ in serum.[4,5] Higher selectivity coefficients have been obtained with bridged "calix-crown" complexes.[12]

The study of calixarene–metal ion interactions is generally carried out in the solution phase using spectrophotometry,[13] NMR spectroscopy[14] or calorimetry,[15] yielding information on stability constants. Simulations of metal ion complexation by calixarenes have also been performed using molecular dynamics methods.[16] The technique of ionophore-facilitated ion-transfer voltammetry at the interface between two immiscible electrolyte solutions (ITIES) has allowed study of ion transfer processes[17] and has yielded quantitative information on the extent of association between the ionophore and metal ions. The ITIES has been suggested as a model system for the study of biological interfaces.[18] Likewise, calixarenes have been proposed as models for bio-membrane transport components (*e.g.*, the calix[4]arene amide[19]) and the ability of calixarene esters to transport ions across phospholipid bilayers has been reported recently.[20] Despite the wide availability of calixarenes and the increasing interest in voltammetry at the ITIES as a means of studying ion-transfer reactions, we are not aware of any previous investigations of calixarene-facilitated ion transfer at the ITIES. To date, the transfer of metal ions across the ITIES using ligands such as crown ethers,[21,22] thio-ethers[23] and natural antibiotics such

as valinomycin[24] has been investigated in a similar manner. The dual ionophoric and hydrophobic host areas of calixarene esters add an extra dimension of interest to the nature of the interfacial ion transfer process. Recently Mareček *et al.* reported the adsorption of the calixarene tetraesters at the ITIES but no facilitated ion transfer was observed.[25]

As noted above, calixarenes have been employed previously in transport studies across bilayer membranes, however the complexity of the solution|membrane|solution system means that a voltammetric study of calixarene–metal binding at a simpler interface would be of interest. For example, in the recently reported phospholipid bilayer study,[20] only the relative ionic permeability coefficients were obtained from the current–voltage data.

Analysis of the voltammetric response of the ITIES to a facilitated ion transfer allows the stoichiometry of the active metal : ligand complex(es) and the mechanism of the charge-transfer process to be determined.[21,23,26] The Galvani potential difference at the water–organic interface, $\Delta_o^w\phi$, governs the partition of an ion between the aqueous and organic phases:[17]

$$\Delta_o^w\phi = \Delta_o^w\phi_{M^{z+}}^{o'} + \left(\frac{RT}{zF}\right)\ln\left(\frac{c_{M^{z+},\,x=0}^o}{c_{M^{z+},\,x=0}^w}\right) \quad (1)$$

where $\Delta_o^w\phi^{o'}$ represents the formal transfer potential for the ion M^{z+} (which can be determined by voltammetric experiments at the ITIES where an "extra-thermodynamic" assumption is made to relate the observed transfer potentials to a standard scale[27]), the c terms represent the interfacial ($x = 0$) concentration of the ion in the organic and aqueous phases (o and w respectively) and the other symbols have their usual meanings. "Anion-free" organic phase association constants can be defined between the metal ion and the ligand (L),

$$M_{(o)}^+ + jL_{(o)} \rightleftharpoons ML_{j(o)}^+$$
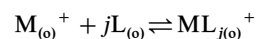
with the constants given by:

$$\beta_j^o = \left(\frac{c_{ML_j^{z+}}^o}{c_{M^{z+}}^o(c_L^o)^j}\right) \quad (2)$$

where β_j^o allows for the existence of complexes of differing stoichiometry. Combination of eqn. (1) and (2) yields:

$$\Delta_o^w\phi = \Delta_o^w\phi_{M^{z+}}^{o'} + \left(\frac{RT}{zF}\right)\ln\left(\frac{c_{ML_j^{z+}, x=0}^o}{c_{M^{z+}, x=0}^w(c_{L, x=0}^o)^j\beta_j^o}\right) \quad (3)$$

Two limiting cases may be defined, one where the organic phase ligand is in excess over the aqueous phase metal concentration, the second where the opposite condition is met. In the latter case, eqn. (3) may be rewritten for a 1 : 1 metal : ligand complex as:

$$\Delta_o^w\phi = \Delta_o^w\phi_{M^{z+}}^{o'} - \left(\frac{RT}{zF}\right)\ln(c_{M^{z+}, bulk}^w\beta_j^o)$$
$$+ \left(\frac{RT}{zF}\right)\ln\left(\frac{c_{ML_j^{z+}, x=0}^o}{c_{L, x=0}^o}\right) \quad (4)$$

where the interfacial concentration of the aqueous phase metal ion has been approximated by the bulk value, due to the high excess of metal ion. If the ligand is assumed to remain largely in the organic phase (*i.e.*, its organic–water partition coefficient $\gg 1$), then its interfacial concentration will determine the transfer equilibrium. At the applied potential difference corresponding to the "half-wave" potential difference, the concentrations of the potential-determining species are equal, hence eqn. (4) reduces to:

$$\Delta_o^w\phi^{1/2} = \Delta_o^w\phi_{M^{z+}}^{o'} - \left(\frac{RT}{zF}\right)\ln(c_{M^{z+}, bulk}^w\beta_j^o) \quad (5)$$

Analogous equations have been derived for general conditions by Reymond *et al.* for cyclic voltammetry at the ITIES[23] and Matsuda *et al.* for dropping-electrolyte polarography.[21] Consequently, expressions of the form of eqn. (5) have been used to determine the association constants of 1 : 1 metal : ligand complexes by analysis of the dependence of the half-wave potential on the metal ion concentration.

The versatility of potentiometric methods in general for the quantification of complexation processes has been noted,[15] since the potential responds to the logarithm of the concentration (or, formally, the activity), whereas measurements based on conductance or spectroscopy depend on the concentration. Thus, potentiometric measurements have an extended range and are less likely to be limited to the placement of a lower bound on the equilibria measured. As Danil de Namor *et al.* have noted,[15] many of the parameters previously quoted for the liquid–liquid extraction of metal ions by calixarenes are open to some interpretation, since the transfer of the cation across a non-electrified interface will require an associated partition of an anion from the aqueous solution to the organic medium. Alternatively, facilitated transfer using ionisable ligands is possible, however, this leads to complications due to the resultant pH-dependence of the transfer process.

In this article, we report the voltammetric transfer of sodium and potassium ions across the water–1,2-dichloroethane (DCE) interface using the neutral calixarenes tetraethyl-*p-tert*-butyl calix[4]arene tetraacetate, **1**. The conclusions drawn from the voltammetric study are correlated with the solid-state structure of the Na$^+$-complex of **1**, obtained using X-ray diffraction.

Experimental

Voltammetric studies of calixarene-facilitated ion transfer at the ITIES were carried out using a purpose-built four-electrode potentiostat. A glass cell, similar to designs previously reported,[28] was employed with two Luggin capillaries to accommodate the reference electrodes. The cross-sectional area of the cell was 0.785 cm^2. Water, of resistivity 18 MΩ cm, was obtained from a Millipore Milli-Q system. DCE (99% + purity) was purchased from Lancaster Synthesis (Lancaster, UK). Both of the solvents used in the cell were

mutually saturated prior to experimentation. The silver–silver chloride and silver–silver sulfate reference electrodes were prepared by electrolysis of a 0.125 cm diameter silver wire, immersed in 0.1 M solutions of potassium chloride and potassium sulfate, respectively. Pt gauze (Advent, Eynsham, UK) was employed as the counter electrode in each phase. The salts used as the aqueous phase electrolyte and the organic reference solution were obtained from Aldrich (Gillingham, UK). The organic phase electrolyte, bis(triphenylphosphoranylidene)ammonium tetraphenylborate (BTPPATPB) was prepared by metathesis of BTPPA chloride (Aldrich, 97%) and sodium tetraphenylborate (Lancaster, 99%), using a published procedure.[29] Compound **1** was synthesised according to the procedure originally described by McKervey *et al.*[30,31] ^{1}H NMR spectra were consistent with the expected product and in agreement with the published NMR spectrum of **1**.[31] The general cell composition is given below:

Ag(s)	AgCl(s)	10^{-3} M BTPPACl 10^{-2} M LiCl (aq)	0.025 M BTPPATPB a M **1** (DCE)	(b/2) M M$_2$SO$_4$(aq)	Ag$_2$SO$_4$(s)	Ag(s)

Cell 1

where the interface polarised by the application of the potential difference has been indicated by the double bar and the variables a and b represent the molar bulk concentrations of **1** and metal ions added to the DCE and aqueous phases, respectively. All electrochemical experiments were carried out at room temperature (293 $\pm$ 2 K).

Crystals of the NaTPB complex with **1** were obtained by vapour diffusion, whereby an equimolar amount of NaTPB and **1** were dissolved in ethanol (Aldrich, HPLC grade). The open vial containing the ethanolic solution was left to stand in the dark in a sealed vial of *n*-hexane (Lancaster, 99% +) for 48 h. The resultant crystals were removed and analysed by ^{1}H NMR (300 MHz, 298 K, CDCl$_3$). The peaks due to the calixarene concurred with those reported in the literature for other salts of this ion.[31] Additional peaks due to the TPB anion were present at δ 7.50 (br d, 8H, *ortho*), 7.22 (t, 8H, *meta*) and 7.05 (t, 4H, *para*). ^{11}B NMR (64.3 MHz, 298 K, CDCl$_3$) gave a single sharp peak at δ -6.5, again corresponding with the literature value of the tetrabutylammonium salt in the same solvent.[32]

The crystals were also analysed by X-ray diffraction. A needle was selected direct from the mother liquor, coated in perfluoropolyether oil, mounted on a glass fibre and placed in the cold nitrogen stream of a Nonius Mach 3 single crystal diffractometer. Crystal data: $C_{60}H_{80}O_{12} \cdot C_{24}H_{20}BNa \cdot C_2H_5OH$. Monoclinic, $a = 16.500(1)$, $b = 28.983(3)$, $c = 17.292(2)$ Å, $\beta = 109.52(1)°$, $U = 7794.1(14)$ Å^3, $Z = 4$, $D_c = 1.176$ Mg m^{-3}, Mo-Kα radiation, $\lambda = 0.71069$ Å, $\mu = 0.082$ mm^{-1}, space group $P2_1/c$. Intensity data were collected in the range $1.48 < \theta < 24.98°$ using the $\varpi/2\theta$ technique. Of the 14179 reflections collected, 13674 were unique ($R_{int} = 0.0341$). All were used in the solution and refinement, using the SHELXS-98 and SHELXL-98 suite of programs (G. Sheldrick, University of Göttingen). All heavy atoms were allowed to refine anisotropically, with all hydrogens in calculated positions. A disordered ethanol solvent molecule was located in the upper rim of the calixarene. This was modelled as possessing a two-fold disorder; its (O)–H atom was not located, and it was not considered chemically meaningful for its position to be calculated. There were further two-fold disorders in one of the *t*-butyl groups and in one of the ethyl ester groups of the calixarene, both of which were successfully modelled. Refinement on F^2 converged to a conventional $R_1 = 0.0799$

[for 5390 reflections with $I > 2\sigma(I)$], $wR_2 = 0.1631$ (for all data, based on F^2, not F).

CCDC reference number 440/163. See http://www.rsc.org/suppdata/nj/a9/a908257c/ for crystallographic files in .cif format.

Results and discussion

In the absence of ligand **1** (*i.e.*, $a = 0$), polarisation of the water–DCE interface in Cell 1 gave rise to the voltammogram shown in Fig. 1 (top), with M = Na$^+$ ($b = 0.1$ M). The potential window was limited at the positive end by the transfer of TPB$^-$ ions from DCE to water, as demonstrated in earlier studies.[29] Introduction of **1** to Cell 1 led to the appearance of a new current wave in the centre of the voltammogram, as shown in Fig. 1 (bottom). The sign of the new wave is indicative of a transfer of positive charge from the aqueous phase to the organic phase, or alternatively of the transfer of negative charge from the organic phase to the aqueous phase. The current was consequently attributed to the transfer of sodium ions facilitated by **1**, based on the known ability of calixarene esters (such as **1**) to form complexes with alkali metal ions.[31] Furthermore, the separation of the peak potentials of the forward and reverse scans was close to 60 mV, the value expected for a complex of 1:1 stoichiometry.[26] Analogous voltammetric behaviour was also observed when the aqueous phase contained potassium sulfate, in the presence of **1** in the organic phase.

The extremely low solubility of calixarenes such as **1** in water, and the high solubility of related ligands[15] in DCE leads us to propose that the observed charge transfer mechanism proceeds *via* a complexation of the metal ions with the ligand either in the organic phase, or at the water–DCE interface (respectively, "TOC" and "TIC" mechanisms, using the notation of Girault *et al.*[33]). As noted in the Introduction, the half-wave potential dependence of the ion-transfer current may be used to determine complex stoichiometry and association constants. Accordingly, the half-wave potential of calixarene-facilitated Na$^+$ transfer was determined for various excess metal ion concentrations (0.01 M $< b < 0.75$ M), using ligand concentrations, a, of 2×10^{-3} M (see Fig. 2). A similar series of experiments was performed for the K$^+$ transfer process. The gradient of the $\Delta_o^w\phi^{1/2}$ *vs.* logarithm of the aqueous phase metal concentration plot was 21 ± 9 mV in the case of Na$^+$ and 25 ± 4 mV in the case of K$^+$ (see Fig. 2). The
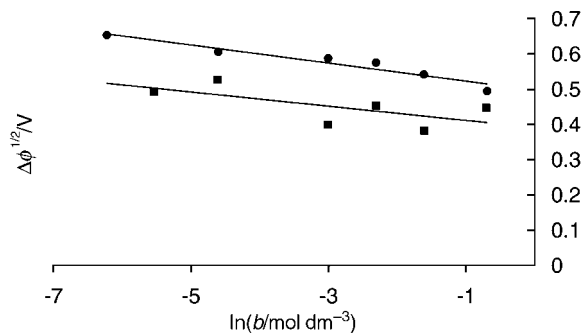
Fig. 2 $\Delta\phi^{1/2}$ *vs.* ln(conc/M) plots for (●) K$^+$ and (■) Na$^+$, with $a = 2 \times 10^{-3}$ M.

idealised slope expected for a 1:1 complex is 25 mV, on the basis of eqn. (5).

Furthermore, the intercepts from Fig. 2 may be used in conjunction with the formal potentials of Na$^+$ and K$^+$ transfer to determine preliminary values of the association constant, β_1^0, of each metal with the ligand in DCE [see eqn. (5)]. The potentials obtained experimentally from Cell 1 were transposed to the generally employed tetraphenylarsonium tetraphenylborate scale[27] by comparing the experimentally observed half-peak transfer potential for the tetramethylammonium ion ($+0.64$ V) to the standardised formal transfer potential value for this ion[34,35] of $+0.16$ V (this approximation is valid if the diffusion coefficients of the ion in each phase are treated as equal). Transposition of the observed $\Delta_o^w\phi$ at the x-axis intercepts from Fig. 2 gave values of -0.10 V and $+0.01$ V as the calixarene-facilitated formal transfer potentials of molar sodium and potassium ions, respectively, on the tetraphenylarsonium tetraphenylborate scale. The $\Delta_o^w\phi^{o'}$ value for Na$^+$ has been quoted[29,36] as $+0.58$ V, while that for K$^+$ has been reported[29,36,37] as $+0.49$ V. Substitution of these values into eqn. (5) gives β_1^0 values of $5 \pm 0.6 \times 10^{11}$ and $2 \pm 0.1 \times 10^8$ M^{-1} for the association of **1** with Na$^+$ and K$^+$ in DCE, respectively. The smaller relative error for K$^+$ reflects the lower standard deviation of the potassium data.

Ion-pairing effects have not been included in the preliminary analysis presented above. It should be noted that in a medium with a relatively low dielectric constant, such as DCE, it is likely that the metal–calixarene complex is at least partially ion-paired.[15,38] The anions in this case (denoted A$^-$) are derived from the supporting electrolyte added to the DCE. Ion-pairing between the metal ion and its aqueous phase counter-ion need not be considered since the latter species is not co-transported to the organic phase under these conditions. Moreover, if β_j^0 is large, ion-pairing between the non-complexed metal ion and the organic phase supporting electrolyte may be neglected, since the organic phase concentration of the non-complexed metal will be extremely low. Hence, a further equilibrium can be written:

$$\text{ML}_{(o)}^+ + \text{A}_{(o)}^- \rightleftharpoons \text{MLA}_{(o)}$$

with an ion-pair formation constant, K^a, defined as:

$$K^a = \left(\frac{c_{\text{MLA}}^o}{c_{\text{ML}^{z+}}^o c_{\text{A}^{z-}}^o} \right) \qquad (6)$$

If the ion-pairing equilibrium is introduced into eqn. (4), the following expression for the potential difference is obtained:

$$\Delta_o^w\phi \approx \Delta_o^w\phi_{\text{M}^{z+}}^{o'} - \left(\frac{RT}{zF} \right) \ln(c_{\text{M}^{z+}, \text{ bulk}}^w \beta_j^o)$$

$$+ \left(\frac{RT}{zF} \right) \ln \left(\frac{c_{\text{MLA}, x=0}^o}{c_{\text{L}, x=0}^o c_{\text{A}^{z-}, x=0}^o K^a} \right) \qquad (7)$$
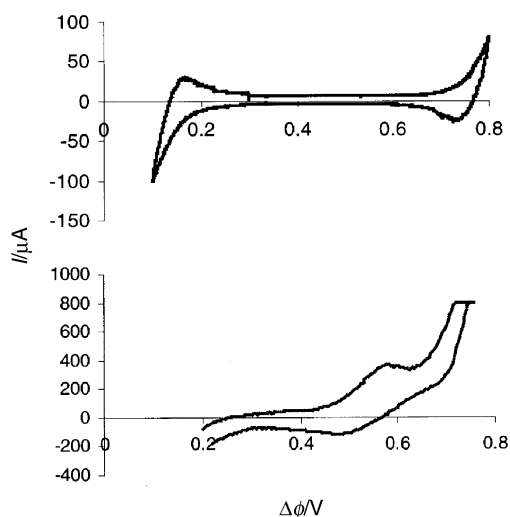

Fig. 1 Top: cyclic voltammogram obtained using Cell 1, $a = 0$, $b = 0.1$ M (Na$^+$ present in aqueous phase). The interfacial 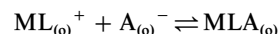potential difference was swept at a rate of 0.05 V s^{-1}. Bottom: cyclic voltammogram obtained using Cell 1, $a = 2 \times 10^{-3}$ M, $b = 0.1$ M (Na$^+$ present in aqueous phase). The interfacial potential difference was swept at a rate of 0.05 V s^{-1}.

Previous reports of two-phase extraction of metal ions by calixarenes using non-polarised interfaces have used picrate counter-ions, which are believed to associate strongly with calixarene-complexed cations in the organic phase (estimated K^a values in benzonitrile exceed 10^6 M^{-1}).[38] By contrast, the counter-ion used in this study—tetraphenylborate—has less pronounced co-ordinating properties. A much lower K^a value (ca. 10^2 M^{-1}) has recently been determined in DCE extracted from water for BTPPATPB, the organic phase electrolyte employed in this work.[39] Similar K^a values can also be expected for the calixarene-complexed alkali metal cations and tetraphenylborate. Comparison of eqn. (4) and (7) shows that the half-wave potential is defined by the point where the organic phase interfacial concentrations of the ion pair and the ligand (rather than the complexed ion and the ligand) are equal, with an additional logarithmic term including the K^a value and the free interfacial anion concentration. Substitution of approximate values based on the experimental conditions employed (respectively, 10^2 M^{-1} and 10^{-4} M, since the anion is partly associated with BTPPA) suggest that correcting for the ion-pairing effect lowers the $\Delta_o^w \phi^{1/2}$ value by around 0.1 V. To a first approximation, this effect is independent of the metal ion concentration and leads to corrected β_1^0 values of $9 \pm 2 \times 10^9$ and $3 \pm 0.4 \times 10^6$ M^{-1} for the association of **1** with Na$^+$ and K$^+$ in DCE, respectively. The uncertainties in the data used to account for ion-pairing introduce a larger relative error into the corrected β_1^0 values.

It is worth noting that the association between Na$^+$ and **1** in 50 : 50 mixtures of acetonitrile and chloroform has been investigated using NMR spectroscopy.[14] No evidence of interaction between the tetraphenylborate counter-ion and the complexed Na$^+$ was observed in the NMR data, whilst a value of 1×10^5 M^{-1} was given as a lower bound on β_1^0. Our own NMR measurements in chloroform confirm this finding (vide infra). It was also reported that, where the ligand concentration was in excess relative to the metal (i.e., $a \ll b$), a 1 : 2 complex of Na$^+$: **1** could be formed, probably as an intermediate between the rapidly equilibrating ion and ligand. There are also literature reports describing the use of absorption spectroscopy to probe the interaction between alkali metal cations and **1** in tetrahydrofuran.[40] The complex stoichiometry was 1 : 1 under the conditions employed experimentally. An association constant (including ion-pairing between the cations and the picrate counter-ions) of the order of 10^4 M^{-1} was calculated. The spectroscopic data suggested that a tight ion pair was formed between Na$^+$ and the picrate anion in THF, but that a solvent-separated ion pair was formed following association with **1**, due to the strength of the interaction between Na$^+$ and **1**. Other reports have quantified the formation of complexes between alkali metal cations and **1**. Values ranging from 10^5 to 10^8 M^{-1} have been quoted for the formation of the 1 : 1 complex between Na$^+$ and **1** in polar organic solvents.[15] These equilibrium constants apply to more polar organic solvents and thus are believed to be free of the effects of ion-pairing. Equilibrium constants 2 to 3 orders of magnitude lower have been reported for the formation of the 1 : 1 complex between K$^+$ and **1** under similar conditions. The variation seen in the values of the constants reported is partly due to the sensitivity of the strength of the interactions between **1** and metal ions to the nature of the organic solvent.[41] By analogy with studies of cryptands, it has been suggested that the ligand–metal binding is likely to be enhanced when the metal is poorly solvated by the organic phase; this is likely to be the case for a solvent such as DCE and may explain why higher association constants have been observed in this study.

A detailed analysis of the thermodynamics of alkali metal extraction by **1** under two-phase conditions has been reported,[38] using UV absorption methods to determine the distribution of alkali metal picrates between water and benzonitrile.

Parameters describing the various equilibria (ion-pairing, distribution, etc.) were calculated and used to determine an overall equilibrium constant, describing the "extraction" of the aqueous phase ions by the organic phase ligand:

$$K^{ex} = \frac{c_{MLA}^o}{c_{M^{z+}}^w + c_{A^{z-}}^w \cdot c_L^o} \tag{8}$$

K^{ex} values of 6.2×10^7 and 1.6×10^6 mol^{-2} dm^6 were determined for Na$^+$ and K$^+$, respectively: a "selectivity" factor (the ratio of the K^{ex} values for Na$^+$ to K$^+$) of 39 was thus calculated. In the case of the ITIES data reported herein, an extraction equilibrium constant can be obtained by combination of the complex formation constant, β_1^0 [eqn (2)], with the equilibrium constant describing the distribution of the metal ion between the organic and aqueous phases (K^t):

$$M_{(w)}^+ \xrightleftharpoons{K^t} M_{(o)}^+ + L_{(o)} \xrightleftharpoons{\beta_1^o} ML_{(o)}^+$$
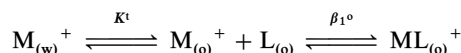
The K^t values for Na$^+$ and K$^+$ may be obtained from their free energies of transfer;[29] combination with the corrected β_1^0 values determined above gives an "anion-free" extraction constant, $K^{ex'}$, for each metal:

$$K^{ex'} = \frac{c_{ML^{z+}}^o}{c_{M^{z+}}^w \cdot c_L^o} = K^t \beta_1^o \tag{9}$$

The $K^{ex'}$ values determined were 1.4 and 0.02 M^{-1} for Na$^+$ and K$^+$, respectively, which gives a Na$^+$/K$^+$ "selectivity" factor of 70 ± 23 for **1** in the water–DCE system.

The peak current of the forward portion ($I_{p, forward}$) of the voltammetric data was analysed as a function of the voltage sweep rate (v) employed. A linear dependence of I_p on the square root of v was observed for excess metal ions relative to **1** (i.e., $b \gg a$), indicative of a diffusion-controlled process. Under conditions where the concentration of metal ions was vastly in excess of the ligand concentration (0.5 and 2×10^{-3} M, respectively), the ion transfer current would normally be limited solely by the diffusion of **1** in DCE.[23,26] Peak current data is presented as a function of $v^{1/2}$ for both K$^+$ and Na$^+$ in Fig. 3. For a complex of 1 : 1 stoichiometry the standard Randles–Sevčik equation should describe the peak current.[23] Substitution of the appropriate terms into this equation and comparison with the gradient of Fig. 3 yields a diffusion coefficient value of $4.0 \pm 0.3 \times 10^{-6}$ cm^2 s^{-1}, which can be equated to the diffusion of **1** in the DCE phase.

The NMR studies confirmed that the cone conformation of **1** is retained upon complexation, and concurred with the previously suggested "encapsulation" of the sodium cation by **1**.[14,31] There was no evidence of any interaction between **1·**Na$^+$ and the TPB anion in solution: the high symmetry of the TPB species was retained on the NMR timescale, as shown by the sharpness of the ^{11}B NMR resonance. This confirms earlier work in CDCl$_3$–CH$_3$CN mixtures.[14] However, it is interesting to note that no crystallographic evidence of such sodium encapsulation has yet been reported, in spite of the now widely accepted co-ordination mode, and numerous attempts by other groups. A solid-state structure of the 1,3-alternate conformer of **1·**Na$^+$ is known,[42] but since the conformers are not interchangeable the two molecules are essentially quite different. It is notable, however, that although the
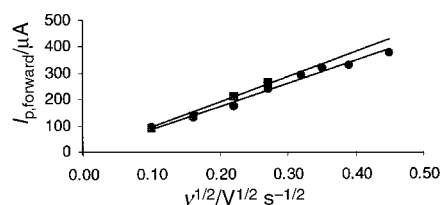

Fig. 3 $I_{p, forward}$ vs. $v^{1/2}$ data from Cell 1 for (●) K$^+$ and (■) Na$^+$, with the conditions given in the text.

co-ordination number of the sodium is lower in the 1,3-alternate conformer, the association constant of the picrate salt of the complex in THF is reported to be slightly higher;[43] this was attributed to the greater degree of pre-organisation of 1,3-alternate **1** over the cone form of **1**.

In this study, suitable crystals of **1**·NaTBP·EtOH were grown and subjected to crystallographic analysis. The possibility that a phenyl group from TPB⁻ would co-operatively occupy the upper rim of **1** as the lower rim bound the Na⁺ cation (as has been noted previously)[14] had to be considered in view of the number of known calix[4]arene hosts incorporating aromatic guests in the upper rim cavity, including one in which the lower rim simultaneously accommodates a Na⁺ cation.[44] The crystal structure shows no evidence of such a specific anion recognition event. The Na⁺ cation occupies the lower rim cavity, and is indeed encapsulated by the four ether and four carbonyl oxygen atoms, as postulated based upon earlier NMR studies.[14,31,45] The upper rim is occupied by a loosely held ethanol solvent molecule. Much of this is lost on standing the crystals in air. The anion occupies holes in the cation lattice with no significant close contacts. Its structural parameters are unremarkable. The molecular structure of the cation–ligand complex is depicted in Fig. 4. It has an almost totally symmetrical cone conformation, again as predicted based upon NMR measurements.[14,31,45] Co-ordination arrests the breathing motion of the pinched-cone free ligand. A geometry almost exactly conforming to the mid-point between the two pinched-cone conformers is attained, as judged by the angles made between opposite pairs of phenyl rings of the calixarene. In free calixarene **1**, these angles are reported to be 1.9 and 94.8°.[31] The mean of these values, 48.4°, is very close to the mean of the corresponding values in **1**·Na⁺ of 46.1 and 50.9° (mean 48.5°).

Further information on the extent of deviation from the ligand's preferred geometry upon complexation comes from an analysis of O–O distances in free and metal-bound states: the ether O–O distances in free **1** range from 3.10 to 3.28 Å;[31] in **1**·Na⁺ they range from 3.14 to 3.18 Å, again a more limited range with a similar mean. It would seem that only the car-

bonyl oxygen atoms have to re-organise significantly upon complexation of **1** with Na⁺; the calixarene cavity is in this instance a "perfect fit" for Na⁺. Comparisons of ether O–Na⁺ data are also pertinent; in the *p-tert*-butyl methoxycalix[4]arene complex of Na⁺,[44] these distances averaged 2.30 Å; in **1**·Na⁺ they average 2.42 Å (see Table 1). This lengthening is ascribable to the higher co-ordination number of the cation in **1**·Na⁺. In fact, the ether O–Na⁺ distances in **1**·Na⁺ are shorter than the ester carbonyl O–Na⁺ distances (mean 2.55 Å), a somewhat surprising feature indicating a degree of strain in the side-arm co-ordination, which would explain the modest stability constant of **1**·Na⁺ in comparison with, for example, cryptands,[46] despite the high specificity of the ligand **1** for Na⁺.

An interesting analogy can be drawn between **1** and nonactin, a natural ionophore antibiotic that also co-ordinates Na⁺ and K⁺ through four ether and four ester carbonyl oxygen atoms. Nonactin-facilitated Na⁺ transfer across the water–nitrobenzene interface has been investigated voltammetrically;[47] β_1^0 values of the order of 10^7 M^{-1} have been determined for this system. In this case the carbonyl oxygen–cation bonds (mean 2.42 Å for Na⁺)[48] are shorter than those of the ether oxygens (mean 2.77 Å for Na⁺) for both Na⁺ and K⁺.[49] However, the structural analogy does not extend to a functional one: nonactin is selective for K⁺ over Na⁺; this difference can perhaps be ascribed to the differences in the co-ordination polyhedron: this is depicted in Fig. 5 for **1**·Na⁺. The four ether oxygens O(1)–O(4) define one plane, while the four carbonyl oxygens O(5)–O(8) define another. In nonactin complexes, the two groups of chemically related oxygens define two interpenetrating tetrahedra. While the two planes of oxygens in **1**·Na⁺ are slightly twisted, the overall co-ordination polyhedron most approximately matches that
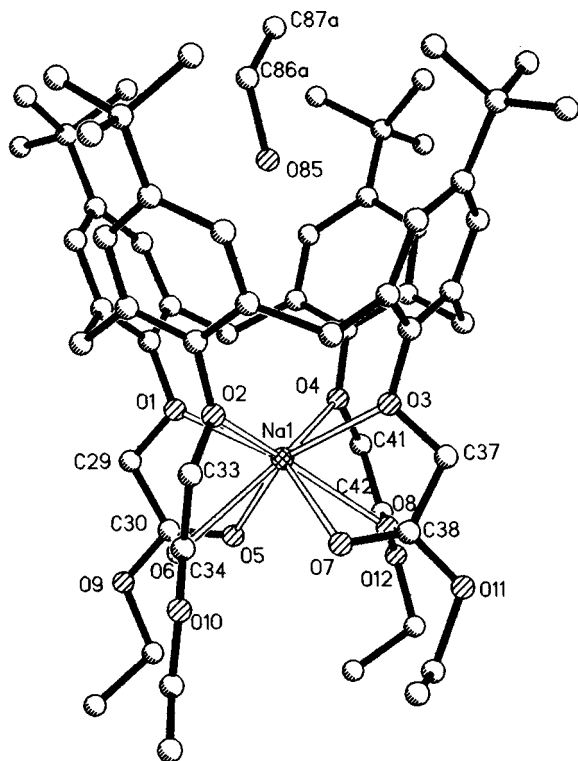
Table 1 Selected bond lengths (Å) and angles (°) in **1** · Na⁺ · EtOH

Na(1)–O(4)	2.412(3)	Na(1)–O(5)	2.469(3)
Na(1)–O(3)	2.417(3)	Na(1)–O(7)	2.514(4)
Na(1)–O(2)	2.425(3)	Na(1)–O(8)	2.574(4)
Na(1)–O(1)	2.434(3)	Na(1)–O(6)	2.653(4)
O(4)–Na(1)–O(3)	81.08(10)	O(5)–Na(1)–O(7)	107.65(12)
O(4)–Na(1)–O(2)	133.83(1)	O(4)–Na(1)–O(8)	64.91(11)
O(3)–Na(1)–O(2)	82.24(10)	O(3)–Na(1)–O(8)	79.50(11)
O(4)–Na(1)–O(1)	80.87(10)	O(2)–Na(1)–O(8)	150.91(12)
O(3)–Na(1)–O(1)	134.25(11)	O(1)–Na(1)–O(8)	127.93(12)
O(2)–Na(1)–O(1)	80.75(10)	O(5)–Na(1)–O(8)	71.57(11)
O(4)–Na(1)–O(5)	83.69(11)	O(7)–Na(1)–O(8)	72.77(12)
O(3)–Na(1)–O(5)	150.88(12)	O(4)–Na(1)–O(6)	151.10(12)
O(2)–Na(1)–O(5)	125.54(12)	O(3)–Na(1)–O(6)	127.50(11)
O(1)–Na(1)–O(5)	66.49(11)	O(2)–Na(1)–O(6)	63.61(10)
O(4)–Na(1)–O(7)	129.87(12)	O(1)–Na(1)–O(6)	80.33(11)
O(3)–Na(1)–O(7)	65.51(11)	O(5)–Na(1)–O(6)	68.73(11)
O(2)–Na(1)–O(7)	79.11(11)	O(7)–Na(1)–O(6)	69.57(11)

Fig. 4 Molecular structure of **1** · Na⁺ · EtOH. Hydrogen atoms and minor contributors to disorder are omitted for clarity.
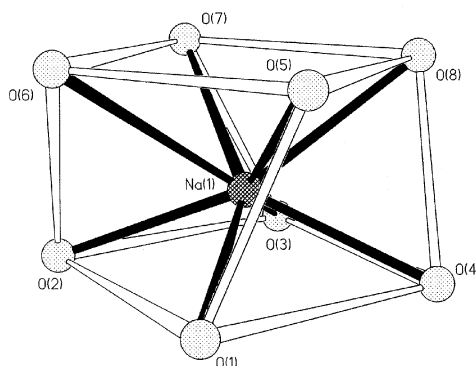

Fig. 5 Co-ordination polyhedron of **1** · Na⁺.

of a cube rather than an antiprism, and in this feature is again analogous to nonactin.[48,49] The resultant co-ordination polyhedra give good "fits" for their respective cations: the difference between the mean metal–oxygen bond length and the sum of the van der Waals radii is 0.10 Å for the K$^+$ complex with nonactin, and 0.13 Å for $1 \cdot$ Na$^+$.[49]

Conclusion

Voltammetry at the ITIES has been used to obtain quantitative information on the interaction between the calixarene, **1**, and sodium and potassium ions. Equilibrium constants for the formation of 1 : 1 complexes between **1** and these cations in DCE have been obtained and compared with results reported for the same species in different solvent systems. The voltammetric data indicated that a 1 : 1 metal : ligand complex was formed under the conditions employed in this study. This conclusion was supported by crystallographic data describing the structure of the Na$^+$ complex. Analysis of this data revealed minimal changes to the calixarene core upon Na$^+$ complexation.

Acknowledgements

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