The Solution Thermodynamics of Ethyl *p-Tert*-Butylcalix[4]arene Tetraacetate and its Alkali Metal Complexes in Acetonitrile and Methanol

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The first calorimetric studies of ethyl *p-tert*-butylcalix[4]arene tetraacetate and alkali metal cations in acetonitrile and in methanol are reported; the results suggest that acetonitrile enters the hydrophobic cavity of the ligand producing a synergistic effect which makes the hydrophilic cavity better preorganised to interact with cations in this reaction medium.

The thermodynamics of complexation and of transfer processes involving macrocyclic ligands, especially cryptands and metal cations, M^+, in different reaction media have contributed significantly to our understanding of the ion binding characteristics of these systems.[1–4] An important consequence of the binding process involving neutral ligands and metal salts is the generation of new types of electrolytes in solution. With the rapidly growing interest in the binding properties of calixarenes (Calix) there is now a need for details of the solution thermodynamics of the complexation process (eqn. 1) with these systems.

$$M^+(s) + \text{Calix}(s) \rightarrow M^+\text{Calix}(s) \qquad (1)$$

Thermodynamic studies so far have been limited to stability constant measurements of metal ion complexes of calixarene esters and amides in MeCN and MeOH[5–7] and complexation constants for esters, amides and some calixspherands in $CHCl_3$.[8,9]

Table 1 Thermodynamic parameters of complexation of ethyl *p-tert*-butylcalix[4]arene tetraacetate and alkali metal cations in acetonitrile and in methanol at 298.15 K

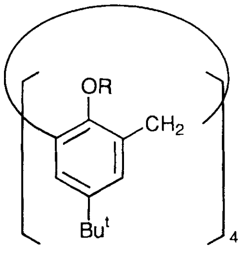
In acetonitrile cation	$\Delta_cG°$/ kJ mol^{-1} [a]	$\Delta_cH°$/ kJ mol^{-1}	$\Delta_cS°$/ JK^{-1}mol^{-1}	$\Delta_{solv}S°$/ JK^{-1}mol^{-1} [b]
Li^+	−36.53	−48.78	−41.1	−252.3
Na^+	−33.11	−61.55	−95.4	−214.8
K^+	−25.69	−43.85	−60.9	−187.0
Rb^+	−10.85	−18.67	−26.2	−174.0
Cs^+	−15.98	−11.48	15.1	−169.9
In methanol				
Li^+	−14.84	5.05	66.7	−240.2
Na^+	−28.54	−45.60	−57.2	−218.4
K^+	−13.70	−14.22	−1.7	−182.8

[a] From log K_s values (Ref. 5). [b] From refs. 10 and 11. [c] $\Delta_cH°$ values for Rb^+ and Cs^+ are too small to be measured by titration calorimetry. These are now being measured by titration microcalorimetry.

Table 2 Thermodynamic parameters of transfer of ethyl *p-tert*-butylethylcalix[4]arene tetraacetate and its sodium complex from methanol to acetonitrile at 298.15 K

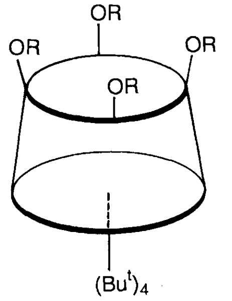
	$\Delta_tG°$/ kJ mol^{-1}	$\Delta_tH°$/ kJ mol^{-1}	$\Delta_tS°$/ JK^{-1} mol^{-1}
[EtCalix(4)]	−2.79[a]	−10.0[a]	−24.2
[Na^+EtCalix(4)]ClO_4^-	−4.03[a]	−31.71[a]	−92.8
[Na^+EtCalix(4)]	−2.53[b]	−16.56[b]	−47.2[b]

[a] Calculated from solution free energies (solubility data) and enthalpies (calorimetrically) in the appropriate solvents. [b] Single ion values (Ph_4AsPh_4B convention) calculated from the data for [Na^+EtCalix(4)]ClO_4^- and the single ion value for ClO_4^- (L. Ghousseini, PhD thesis University of Surrey, 1985)



1

R = CH_2CO_2Et



2

R = CH_2CO_2Et

For calixarene esters and amides, the thermodynamic behaviour of alkali metal calixarenates $(M^+Calix)X^-$ in solution is unknown.

We have completed a preliminary thermodynamic study of the complexation and transfer processes with a representative calix[4]arene tetraester and its alkali metal complexes in methanol and acetonitrile and we now report the first data on (*a*) enthalpies, (by titration calorimetry) and entropies of complexation (eqn. 1) with ethyl *p-tert*-butylcalix[4]arene tetraacetate **1** [EtCalix(4)] and (*b*) free energies, $\Delta_tG°$, enthalpies, $\Delta_tH°$, and entropies, $\Delta_tS°$ of transfer of the ligand and of its sodium complex [Na^+EtCalix(4)]ClO_4^- from methanol (reference solvent) to acetonitrile. The complexation data (Table 1) shows that the process is enthalpically more stable ($\Delta_CH°$ more negative) in MeCN than in MeOH. An exothermic maximum is observed for sodium and the tetraester in both solvents. Interestingly, the $\Delta_CH°$ values for Na^+ and **1** are the same (within experimental error) as those reported for this cation and cryptand 222 in MeCN ($\Delta_CH° = -60.96$ kJ mol^{-1})[10] and MeOH ($\Delta_CH° = -44.64$ kJ mol^{-1}).[11] The complexation process is enthalpy controlled for all alkali metal cations in both solvents with the exception of Li^+ in methanol where the stability is entropy controlled, a difference attributable to desolvation of both ligand and Li^+ ion upon complexation.

The higher stability observed in complexation in MeCN relative to MeOH may be analysed in terms of the thermodynamic parameters related to solvation of the cation (entropies of solvation, $\Delta_{solv}S°$)[11] and that of the ligand (transfer data). For the cations, $\Delta_{solv}S°$ (Table 1) becomes more positive along the series Li^+ to Cs^+. Accordingly, if these cations are likely to loose most of their solvation shell on complexation, $\Delta_CS°$ values would be expected to become progressively more negative along the series Li^+ to Cs^+. This trend is observed for Li^+ and Na^+ only; thereafter $\Delta_CS°$ values follow the same trend as $\Delta_{solv}S°$. This observation may indicate that the larger cations are not fully desolvated in the complex or more likely, that these cations are not completely shielded by the ligand and, therefore, are partly exposed to the solvent. Turning now to the ligand (Table 2) a particularly notable property of calix[4]arene esters in the cone conformation **2** is the presence of two cavities; one hydrophobic lying between the aromatic residues and a second of a hydrophilic character created by the encircling oxygen atoms of the $-OCH_2CO_2Et$ moieties.

The thermodynamic data of transfer of this ligand are striking, particularly the $\Delta_tH°$ and $\Delta_tS°$ values which clearly reflect that quite different interactions take place in MeCN relative to MeOH.[8] In fact, these data are atypical of the behaviour observed for the transfer of cryptands between these solvents but are similar to the transfer data for cyclodextrins from water to *N*,*N*-dimethylformamide, a solvent in which specific interactions are believed to occur.[12] The loss of enthalpy and entropy for the transfer of **1** from MeOH to MeCN reflect a specific interaction between the ligand and MeCN. This conclusion is supported by NMR data. Whereas the ^1H chemical shifts of **1** in CD_3OD are essentially identical with those in $CDCl_3$, the spectrum in CD_3CN shows a significant downfield shift (0.18 ppm) for the aromatic protons. Similar shifts have been observed in cation complexation and have been attributed to a slight conformational reorganisation concomitant with reception of the guest,[13] suggesting that the interaction of **1** with acetonitrile may be similar to that of calix[4]arene tetracarbonate derivative with MeCN, where X-ray diffraction has confirmed the formation of a 1 : 1 complex with the guest MeCN molecule residing in the hydrophobic cavity.[12] The implication of our findings is that there exists a synergistic effect whereby the hydrophilic cavity is better preorganised to interact with alkali metal cations in MeCN than in MeOH. Accordingly, stabilities in the former medium are higher than in the latter (Table 1). This is further corroborated by the single ion transfer data for [Na^+EtCalix(4)] from MeOH to MeCN (Table 2). These data refer to the transfer of a large complexed cation with an essentially empty hydrophobic cavity which attracts a guest when transferred to MeCN. The effect is particularly reflected in the entropy loss of the complexed cation which is greater than that of the ligand and may be attributed to the higher loss of conformational freedom of this cation (with a guest in both cavities) relative to that of the ligand (with a single guest). The very similar $\Delta_t G^\circ$ values found for the ligand and the complexed cation, a measure of their differences in solvation in these two solvents, are a strong indication that the sodium cation in the complex must be essentially shielded by the ligand.

Our principal conclusion is that interactions in the hydrophobic cavity of calixarene esters (and probably in related derivatives) induce conformational changes of a cooperative nature which, in the case of acetonitrile, make the hydrophilic cavity more receptive to cationic guests and may even alter cation selectivity.

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