

Thermodynamic and Electrochemical Aspects of *p*-*tert*-Butylcalix[*n*]arenes (*n* = 4, 6, 8) and Their Interactions with Amines^{*}

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Abstract. Attention is drawn to the need of detailed thermodynamics in calixarene chemistry. The reasons for increasing efforts in this area are underlined and suggestions for new issues to be addressed are given. The solution thermodynamics of *p*-*tert*-butylcalix[*n*]arenes (*n* = 4, 6, 8) is discussed with particular reference to transfer Gibbs energies which reflect the selective solvation that the tetramer and the octamer undergo in the various solvents. This is followed by recent solution studies on amine-*p*-*tert*-butylcalix[*n*]arene (*n* = 4, 6, 8) in nitrobenzene and in benzonitrile at 298.15 K which indicate the lower acidic character of the tetramer relative to the hexamer and the octamer in these solvents. As an implication of these results, very low conductivities are observed in studies involving the interaction of the former with amines. Thus, thermodynamic studies suggest that *p*-*tert*-butylcalix[4]arene interacts with triethylamine in benzonitrile and in nitrobenzene through hydrogen bonding or ion-pair formation. A thermodynamic cycle is used to investigate the effect associated with the interaction of the amine with the tetramer in these solvents.

Key words: *p*-*tert*-Butylcalix[*n*]arenes, amines, thermodynamics, electrochemistry.

1. Introduction

Synthetic developments in the area of Supramolecular Chemistry are currently leading to a massive production of new macrocycles. The driving force for this continuous growth is the search for selective hosts to target a particular neutral or ionic species. There is no doubt that the impact produced by the discovery of macrocyclic ligands such as the crown ethers [1] and the cryptands [2] resulted from their cation complexation and this prompted us to consider the thermodynamic characterisation of these systems (mainly cryptands) which has been extensively reported [3–5]. Calixarenes, an important class of macrocyclic compounds, are products of the base-catalysed condensation reaction of *p*-substituted phenols and formaldehyde [6, 7]. These compounds are characterised by their low solubilities in most solvents, although until recently [8], no quantitative data has been reported. Functionalisation of the lower or upper rim of parent calix[*n*]arenes has

^{*} This paper is dedicated to the commemorative issue on the 50th anniversary of calixarenes.

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led to a number of interesting derivatives which are known to interact with metal cations in solution and stability constants for various calixarene derivatives and metal cations have been reported [9, 10]. As far as thermochemical studies are concerned, there are two communications based on research carried out mainly at the Thermochemistry Laboratory (Surrey) in which the first calorimetric (titration macrocalorimetry) data were reported on (i) calixarene esters and metal cations in two solvents (methanol and acetonitrile) [11] and (ii) parent calixarenes and amines in benzonitrile [12]. More recently, these two aspects of calixarene chemistry have been further considered [13–16]. Although the contributions so far made on the solution thermodynamics of calixarene chemistry have provided some useful insights, there are some aspects of the existing work that need to be examined and new issues should be addressed. In order to do so it is important to present a brief account on: (a) what can thermodynamicists contribute to the understanding of solution calixarene chemistry; (b) how far these issues have been addressed; and (c) what aspects of thermodynamics need to be considered.

In order to answer these questions it should be stressed that in our opinion, a detailed thermodynamic analysis should involve: (a) the solution thermodynamics of the host, the guest and if possible, the resulting complex (adduct) in the appropriate solvents; (b) the thermodynamic characterisation of the binding process in the same solvents. In both cases, the relevant parameters are Gibbs energy, enthalpy, entropy and heat capacity. As far as (a) is concerned, for a solid compound, solution data involve the contributions of the crystal lattice and that of solvation. The former can be eliminated by the calculation of transfer data from a reference solvent to another. These data reflect the difference in solvation of a solute between two solvents. Availability of these data are extremely useful, particularly in calixarene chemistry where the presence of hydrophobic regions gives unusual properties to these molecules to the extent that solute–solvent interactions often occur. These are likely to have implications on many processes, such as binding, choice of reaction media used for recrystallisation, solvent extraction technology, design of ion-selective electrodes, etc. Within this context, heat capacity data provide a thermodynamic probe of conformational changes taking place as a result of solute–solvent interaction.

Attention has been focussed on the possible applications of calixarene derivatives to mimic biological carriers. Although investigations carried out at the standard temperature are most encouraging since these compounds appear to fulfil the requirements for efficient carrier modelling in the sense that these are insoluble in water and their metal-cation complex stability is not very high, there are several aspects to be considered in order to place this interesting hypothesis on firmer grounds. The main ones are the kinetics and thermodynamics associated with these processes at the biological temperature.

From calixarene derivatives, through complexation with metal cation salts, new electrolytes are derived $[M^+ \text{Calix}]X^-$. Despite the fact that these new entities may find important applications in many aspects of research, not many efforts have

been devoted to their characterisation. In fact, these comments can be extended to the general area of supramolecular chemistry. A representative example of the applications of macrocyclic electrolytes is found in recent work carried out at Surrey [17] which demonstrate that the conductivities of some lithium coronate salts are greater than those observed for common lithium salts in dipolar aprotic media, a development likely to lead to a major contribution in the area of high energy lithium batteries and for which a detailed thermodynamic study made it possible to interpret the nature of these findings. As far as (b) is concerned, one of the most important questions regarding the interactions of calixarene derivatives with different guests in solution concerns selectivity. Therefore, if the factors controlling it are to be understood and rationalised, thermodynamics should be considered a priority area in calixarene chemistry. A direct implication of this statement is the need for accurate thermodynamic data, the derivation of which is largely dependent on the suitability of the methodology employed and this will be discussed in detail elsewhere [18]. However, it is important to mention that as far as stability constants are concerned, attempts should be made to check these data by different techniques since this information provides the guide for the isolation of metal-ion calixarene salts and the basis to establish a selectivity index in calixarene chemistry. This is particularly relevant for high stability complexes ($\log K_s > 5$) where new methodology needs to be developed. As far as enthalpies are concerned, calorimetry is by far the most suitable technique to derive these data particularly in view of the recent advances in microcalorimetry [19]. There are two reasons by which titration microcalorimetry offers advantages relative to classical macrocalorimetry; particularly for processes involving calixarenes. The first one is related to the lack of heat found when using the latter technique when some cations interact with calixarene derivatives in nonaqueous media [20]. Preliminary studies using titration microcalorimetry have shown that the failure to characterise thermodynamically the binding process between metal cations with these ligands by macrocalorimetry is not due to the fact that calorimetry is not a suitable reporter for molecular events but to kinetically slow processes being involved. It is well established that classical calorimetry is unsuitable to deal with these processes. The second reason is that in terms of accuracy, classical calorimetry cannot compete with the most sensitive calorimetric devices recently designed [21]. From the above discussion, it seems appropriate to state that the time has now come to characterise thermodynamically:

- (a) the effect of temperature on the solution properties of parent calixarenes and their derivatives in a large variety of solvents.
- (b) the factors governing selectivity as a function of temperature across a wide variety of calixarene derivatives and cations in different media. Particular emphasis should be placed on heat capacity measurements of the host, guest and the resulting complex.

These studies should be accompanied by ^1H - and ^{13}C -NMR evidence [22] and conductance studies. The latter should be carried out particularly in low permittivity media where the extent of ion-pair formation for these new electrolytes need to be investigated. No such studies have been undertaken in these media. We are carrying out extensive research on calixarene derivatives which are currently synthesised at Surrey using a new methodology developed by us [23] which increases their yields with respect to existing methods.

Although considerable progress has been made by our group on structural, thermodynamic and electrochemical aspects of these derivatives and metal cations in a wide variety of solvents, in this special commemorative volume on calixarenes, we consider it appropriate to discuss the 'parent compounds' and their interactions with amines in nitrobenzene and in benzonitrile. The background leading to this work has been described elsewhere by Danil de Namor and coworkers [13, 14] together with various aspects of calixarene-amine interactions in benzonitrile. Although a phase separation between nitrobenzene (or benzonitrile) in water can be achieved and therefore, this solvent can be also used in extraction processes, nitrobenzene ($\epsilon = 34.82$ at 298.15 K) offers a higher permittivity medium than benzonitrile ($\epsilon = 25.2$ at 298.15 K) [24] and this may have interesting implications on amine-calixarene interactions. Since the solution properties of *p*-*tert*-butylcalix[*n*]arene ($n = 4, 6, 8$) in nitrobenzene are unknown, these are discussed first.

2. Experimental

2.1. CHEMICALS

All chemicals were used as described previously [14]. The water content of nitrobenzene determined by Karl-Fischer titration was found to be less than 0.01% and its conductivity at 298.15 K was $7.98 \times 10^{-8} \text{ S cm}^{-1}$.

2.2. SOLUBILITY AND HEAT OF SOLUTION MEASUREMENTS

These were carried out as described elsewhere [25].

2.3. CONDUCTIMETRIC, POTENTIOMETRIC AND CALORIMETRIC TITRATIONS

Except for microcalorimetric titrations, readers are referred to the literature [14]. Microcalorimetric experiments at 298.15 K were carried out using the titration vessel of the 2277 Thermal Activity Monitor. The vessel was filled with 2.8 mL³ of a solution of *p*-*tert*-butylcalix[4]arene in benzonitrile ($5 \times 10^{-4} \text{ mol dm}^{-3}$) or in nitrobenzene (5×10^{-3} or $9 \times 10^{-3} \text{ mol dm}^{-3}$). Triethylamine solutions in the appropriate solvent (concentration range; 0.07–0.95 mol dm⁻³) were injected (16 injections; 0.015–0.025 mL for each run) from a 0.5 mL gas-tight Hamilton syringe, attached to a computer-operated syringe drive at 5 minute intervals. *p*-*tert*-Butylphenol solutions were 0.04 mol dm⁻³ in both solvents. A dynamic correction

TABLE I. Thermodynamic parameters of solutions of *p*-*tert*-butylcalix[*n*]arenes (*n* = 4, 6, 8) in nitrobenzene at 298.15 K. Derived parameters of transfer from benzonitrile.

| | <i>n</i> = 4 | <i>n</i> = 6 | <i>n</i> = 8 |
|--|----------------------------------|----------------------------------|----------------------------------|
| Solubility/mol dm ⁻³ (PhNO ₂) | $(1.83 \pm 0.04) \times 10^{-2}$ | $(2.26 \pm 0.03) \times 10^{-2}$ | $(2.57 \pm 0.06) \times 10^{-3}$ |
| $\Delta_s G^0$ /kJ mol ⁻¹ (PhNO ₂) | 9.92 ± 0.05 | 9.40 ± 0.03 | 14.78 ± 0.06 |
| $\Delta_s G^0$ /kJ mol ⁻¹ (PhCN) | 17.26 ^a | 12.88 ^a | 11.09 ^a |
| $\Delta_t G^0$ /kJ mol ⁻¹ (PhCN → PhNO ₂) | -7.34 | -3.48 | 3.69 |
| $\Delta_s H^0$ /kJ mol ⁻¹ (PhNO ₂) | -14.67 ± 2.88 | -34.85 ± 1.96 | -29.09 ± 1.50 |
| $\Delta_s H^0$ /kJ mol ⁻¹ (PhCN) | -14.20 ^a | -23.67 ^a | -45.90 ^a |
| $\Delta_t H^0$ /kJ mol ⁻¹ (PhCN → PhNO ₂) | -0.47 | -11.18 | 16.80 |
| $\Delta_s S^0$ /J K ⁻¹ mol ⁻¹ (PhNO ₂) | -82.5 ± 9.7 | -148.4 ± 6.6 | -147.1 ± 5.0 |
| $\Delta_s S^0$ /J K ⁻¹ mol ⁻¹ (PhCN) | -105.5 ^a | -122.6 ^a | -191.1 ^a |
| $\Delta_t S^0$ /J K ⁻¹ mol ⁻¹ (PhCN → PhNO ₂) | 23.0 | -25.8 | 44.0 |

^aFrom Reference [14].

based on Tian's equation [26, 27] was used to calculate the integrals from the microcalorimetric curve. Corrections for the thermal effect arising from dilution were applied. The reliability of the equipment was checked by carrying out the standard reactions suggested in the literature [28].

3. Results and Discussion

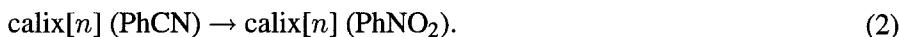
3.1. THERMODYNAMICS OF SOLUTIONS OF *p*-*tert*-BUTYLCALIX[*n*]-ARENES (*n* = 4, 6, 8)

Table I lists the solubility data, derived Gibbs energies, $\Delta_s G^0$, enthalpies, $\Delta_s H^0$ and entropies, $\Delta_s S^0$ of solutions of *p*-*tert*-butylcalix[*n*]arenes (*n* = 4, 6, 8) (calix *n*) in nitrobenzene (PhNO₂) at 298.15 K referred to the process



The standard deviation of the data are also included in Table I. Taking benzonitrile (PhCN) as the reference solvent, the thermodynamic parameters of transfer

($\Delta_t G^0$, $\Delta_t H^0$ and $\Delta_t S^0$) of these macrocycles to nitrobenzene (Equation 2) are calculated.

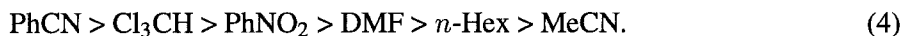


and these are reported in Table I.

As far as transfer Gibbs energies are concerned, as the size of the calixarene increases $\Delta_t G^0$ becomes more positive to the extent that the tetramer and the hexamer are better solvated in nitrobenzene than in benzonitrile while the converse is true for the cyclic octamer. Availability of $\Delta_s G^0$ values for *p*-*tert*-butylcalix[*n*]arenes ($n = 4, 8$) in various solvents at the same temperature allows the calculation of transfer Gibbs energies of these macrocycles to other media. Thus, for the cyclic tetramer, $\Delta_t G^0$ values from benzonitrile to various solvents [methanol, (MeOH); 1.17 kJ mol⁻¹; ethanol (EtOH); 2.61 kJ mol⁻¹; *N,N*-dimethylformamide (DMF); -0.37 kJ mol⁻¹; acetonitrile (MeCN); 7.43 kJ mol⁻¹; *n*-hexane(*n*-Hex); 3.71 kJ mol⁻¹; chloroform (Cl₃CH); -3.78 kJ mol⁻¹)] reflect the fact that *p*-*tert*-butylcalix[4]arene is more favourably transferred to nitrobenzene (see Table I) than to any of the solvents considered. The Gibbs energy term determines the equilibrium position associated with the transfer process and therefore, these results unambiguously demonstrate that this position is shifted considerably by changing the solvent to which *p*-*tert*-butylcalix[4]arene is transferred as to favour the medium which provides the macrocycle with the highest stability as a result of solvation. Consequently, the most striking feature of the transfer Gibbs energy data is the selective solvation that the tetramer undergoes with the various solvents to the extent that on the basis of $\Delta_t G^0$ values, a solvation selectivity index for *p*-*tert*-butylcalix[4]arene can be for the first time established. Thus, the capability of the medium to solvate *p*-*tert*-butylcalix[4]arene is reflected in the following sequence



Selective solvation is also observed for the cyclic octamer. Thus, $\Delta_t G^0$ values (kJ mol⁻¹) of 4.08, 16.17, 15.17 and 1.50 were found for the transfer of *p*-*tert*-butylcalix[8]arene from benzonitrile to DMF, MeCN, *n*-Hex and CHCl₃, respectively. These findings lead to a selectivity sequence for calix[8] in the order:



Much significance should be attributed to these results which provide clear evidence that the transfer Gibbs energy is a suitable reporter of molecular events related to solvation. Based on these data it is concluded that in calixarene chemistry, the role of the solvent is such that it could affect significantly their reactivity or indeed their host properties.

Analysis of the enthalpy and entropy contributions to the transfer process reflects the different origins of the favourable (negative) Gibbs energies of the tetramer

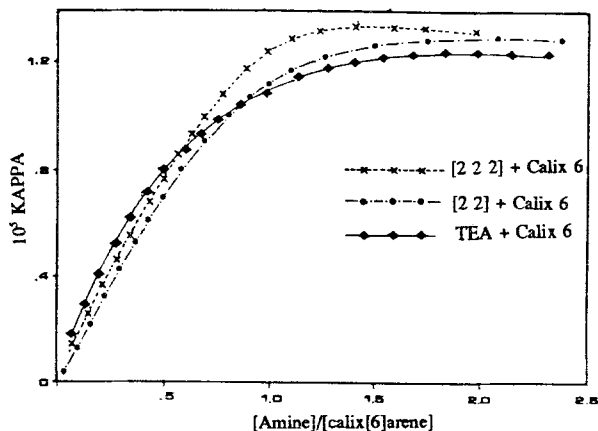


Fig. 1. Conductimetric titrations curves of *p*-tert-calix[6] and amines in nitrobenzene at 298.15 K.

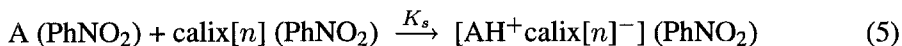
(entropy controlled) relative to the hexamer (enthalpy controlled). For the octamer, the positive entropic contribution is not favourable enough to overcome the energy barrier (endothermic process) and therefore, the net result (positive $\Delta_t G^0$) is that the cyclic octamer is better solvated in benzonitrile and therefore, reluctant to transfer to nitrobenzene. However, an interesting feature of these results is that shown by the hexamer since its transfer to nitrobenzene occurs with heat release (exothermic process) accompanied by a considerable loss in entropy. This pattern is similar to that found by Danil de Namor and coworkers for the transfer of (a) cyclodextrins from water to *N,N*-dimethylformamide [29], (b) an ester derivative of *p*-tert-butylcalix[4]arene from methanol to acetonitrile, where in both cases the receiving media are believed to enter specific interactions with the ligand. These data suggest that the hexamer exhibits significant interactions with nitrobenzene and this is now being further investigated.

3.2. AMINE-CALIXARENE INTERACTIONS. CONDUCTANCE STUDIES

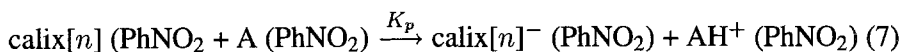
In order to establish whether or not ions are formed as a result of the interaction of *p*-tert-butylcalix[*n*]arene ($n = 6, 8$) and amines ($A =$ triethylamine, cryptand 22 and cryptand 222) in nitrobenzene, conductance measurements were carried out at 298.15 K. A representative example is given in Figure 1 in which the conductimetric titration curves for the hexamer and the different amines in PhNO₂ at the standard temperature are shown.

Since the starting solution contains a nonelectrolyte (calixarene; nonconducting species), the increase in conductance by the addition of the amine results from the formation of a 1 : 1 electrolyte resulting from the transfer of the proton from the calixarene to the amine. The initial portion of the titration curve was used to calculate the thermodynamic equilibrium constants for the formation of the adduct;

K_s , (Equation 5) and for the ion-pair (association) process, K_a (Equation 6),



following the procedure described elsewhere [14]. Table II lists the limiting molar conductances, Λ^0 , of the ammonium calixarene salts; $\log K_s$ (Equation 5) and $\log K_a$ (Equation 6) of *p-tert*-butylcalix[*n*]arene ($n = 6, 8$) and amines in nitrobenzene at 298.15 K. Equilibria data (Equations 5 and 6) are combined to derive corresponding values for the proton transfer reaction (Equation 7).



and these data are also included in Table II.

As far as Λ^0 values are concerned, these are the results of the anion and cation contributions. Unfortunately, very few conductance studies for electrolyte in nitrobenzene have been reported and the data available are mostly referred to the tetra-*n*-alkylammonium salts [30]. Values for these salts in this solvent at the standard temperature vary from approximately 20 to 40 S cm² mol⁻¹. Interestingly, a Λ^0 value of 22.31 S cm² mol⁻¹ in nitrobenzene at 298.15 K has been reported for Bu₄NPh₄B, an electrolyte constituted by a cation larger than Et₃NH⁺ and an anion smaller than calix[6]⁻ or indeed calix[8]⁻. Therefore, the values given in Table II for the triethylammonium *p-tert*-butylcalix[*n*]arene ($n = 6, 8$) electrolytes in this solvent seem reasonable. To our knowledge no values have been reported for the ionic conductivities, λ^{0+} , of protonated amines in nitrobenzene as to derive the λ^{0-} for the *p-tert*-butylcalix[*n*]arene ($n = 6, 8$) anions. However, the anion effect can be assessed by considering the differences in Λ^0 values for a given cation and the two different anions. Thus, in moving from calix[6]⁻ to calix[8]⁻, a decrease in the limiting conductance of about 0.3 S cm² mol⁻¹ (average value) is observed which is likely to be attributed to the size increase of the anion. It should be emphasised that this difference is relatively small and may reflect the higher solvation of the hexamer relative to the octamer in nitrobenzene as discussed above. However, this is difficult to assess since the solvation of the conjugated base (anion) would differ from that of the parent calixarene.

Similarly, for a given calixarene anion (common anion), the cation effect is reflected in the different Λ^0 values obtained for the various electrolytes. Thus, the limiting conductance decreases significantly (~ 6.5 S cm² mol⁻¹) from the triethylammonium containing electrolyte to the protonated cryptand salt. This drop in conductance for the latter relative to the former electrolyte is likely to be the result not only of the considerable size increase of the cation but also to the shielding effect of the cryptands on the proton which will undoubtedly reduce the electric field in the vicinity of the ion.

Availability of Λ^0 values for the same electrolytes at the same temperature in benzonitrile (see Table II, values in brackets) allows comparison between the

TABLE II. Limiting molar conductances, Λ^0 of *p*-*tert*-butylcalixarene salts and equilibria data of *p*-*tert*-butylcalix[*n*]arene (*n* = 6, 8) and amines in nitrobenzene at 298.15 K. Comparison with corresponding data in benzonitrile.

| Amine | calix[6] | | | calix[8] | | |
|---------------|---|-----------------------------|-----------------------------|---|-----------------------------|-----------------------------|
| | Λ^0/S cm ² mol ⁻¹ | log K_s | log K_a | Λ^0/S cm ² mol ⁻¹ | log K_s | log K_a |
| Triethylamine | 22.79 ± 0.03 (31.07) ^a | 1.69 (3.19) ^a | 1.36 (2.44) ^a | | | |
| | | | 0.33 (0.75) ^a | (30.66) ^a | (3.98) ^a | (3.23) ^a |
| Cryptand 22 | 16.32 ± 0.06 (23.86) ^a | 2.06 (3.04) ^a | 1.13 (1.88) ^a | 15.82 ± 0.07 (23.03) ^a | 2.30 (3.24) ^a | 1.21 (2.62) ^a |
| Cryptand 222 | 16.95 ± 0.04 (24.70) ^a | 3.20 (3.18) ^a | 2.13 (1.73) ^a | 16.79 ± 0.04 (24.37) ^a | 2.74 (3.70) ^a | 1.94 (2.52) ^a |
| | | | (1.45) ^a | | | (1.18) ^a |

^aFrom Reference [14].

two sets of data. Thus, for a given electrolyte, the differences in the limiting conductances in benzonitrile relative to nitrobenzene are within the experimental error, constant. The Λ^0 values in the former solvent are about $7.5 \text{ S cm}^2 \text{ mol}^{-1}$ higher than in the latter and this is attributed to the lower viscosity of benzonitrile ($\eta = 0.0124 \text{ p}$ at 298.15 K) [24] relative to nitrobenzene ($\eta = 0.0186 \text{ p}$) [24]. This statement is based on the suggestion put forward by Walden [31] ($\Lambda_1^0, \eta_1, -\Lambda_2^0\eta_2$) which enables the calculation of approximate values of limiting conductances for electrolytes constituted by large ions in a given solvent from known Λ^0 for the same electrolyte in another solvent. Despite the complexity of the systems involved, Walden's rule works reasonably well for the cryptands. Thus, using the Λ^0 for $[22\text{H}^+ \text{ calix}[6]^-]$ in benzonitrile, a corresponding value of $15.96 \text{ S cm}^2 \text{ mol}^{-1}$ is calculated for this electrolyte in nitrobenzene which does not differ significantly from the value of $16.32 \text{ S cm}^2 \text{ mol}^{-1}$ reported in Table II. Similar agreement is found for other cryptand containing electrolytes.

Equilibria data ($\log K_s$) for the process represented in Equation 5 result from the contribution of (i) the ion-pair formation between the protonated amine and the calixarene anion ($\log K_a$) and (ii) the proton transfer reaction ($\log K_p$). The data shown in Table II for the overall process (Equation 5) shows that this is less favoured in nitrobenzene than in benzonitrile (values in brackets). Judging from $\log K_s$ values, the selectivity pattern observed for the octamer in nitrobenzene (cryptand 222 > cryptand 22 > Et_3N) differs from that found in benzonitrile (Et_3N > cryptand 222 > cryptand 22). Regarding $\log K_s$ values for the hexamer in benzonitrile, these data reflect that this ligand is unable to selectively recognise among these amines. In nitrobenzene, the selectivity sequence for the hexamer and the different amines follows the same pattern to that found for the octamer. However, the lower stability ($\log K_s$) in nitrobenzene is mainly attributed to the weaker acidic and basic behaviour of *p-tert*-butylcalix[*n*]arene ($n = 6, 8$) and these amines respectively; in this solvent relative to benzonitrile as assessed from potentiometric (qualitative) studies in nitrobenzene. However, an interesting aspect of these results is that in benzonitrile, the formation of ion-pairs is more favoured for the electrolyte containing the smaller cation. Thus, $\log K_a$ values decrease in going from $\text{R}_3\text{NH}^+\text{calix}[n]^-$ ($n = 6, 8$) to $\text{Cry}\cdot\text{H}^+\text{calix}[n]^-$. Considering that the proton is more likely to be exposed in the former than in the latter, where ^{13}C -NMR studies [14] have revealed that the cation is likely to be sitting in the cavity (cryptand 222) or in the hole (cryptand 22), these results are somehow expected. However, this is not the pattern observed in nitrobenzene. It should be emphasized that transfer Gibbs energies from benzonitrile to nitrobenzene reflect the fact that triethylamine is slightly better solvated in nitrobenzene than in benzonitrile (as discussed below). In an attempt to gain further understanding on these systems we are now proceeding with ^{13}C -NMR studies and with the calculation of transfer data for the protonated amines in these two solvents [32].

In summary, as far as amine-*p*-*tert*-butylcalix[*n*]arene (*n* = 6, 8) interactions are concerned, conductance studies provided information regarding

- (a) the nature of these interactions
- (b) the stoichiometry of the reaction
- (c) the behaviour of the calixarenate anion (delocalised charge) in these solvents [14]
- (d) the extent of ion-pair formation
- (e) the limiting conductances for these new electrolytes in these solvents
- (f) the factors contributing to the overall interaction of calixarenes with amines including the solvent effect on the ability of *p*-*tert*-butylcalix[*n* = 6, 8]arene to selectively recognise amines [14].

Although we have now completed a thermodynamic study on amine-*p*-*tert*-butylcalix[*n*]arene (*n* = 6, 8) in nitrobenzene, in the remaining part of this paper we address new issues related to *p*-*tert*-butylcalix[4]arene–amine interactions in benzonitrile and in nitrobenzene.

3.2. AMINO *p*-TERT-BUTYLCALIX[4]ARENE INTERACTIONS IN BENZONITRILE AND IN NITROBENZENE

Unlike calix[6] and calix[8], very low conductivities were obtained in the titration of *p*-*tert*-butylcalix[4]arene and these amines in benzonitrile and nitrobenzene. The relatively low conductances observed in the titration of the tetramer and amines in these solvents do not necessarily imply that these two species are unable to interact in solution. Essentially, these findings reflect the fact that very few ions are formed in solution. These could be attributed to an extensive formation of ion-pairs or to a process in which hydrogen bonding rather than a proton-transfer (ion) reaction predominates. These two possibilities are feasible since benzonitrile and, to a lesser extent nitrobenzene, are media of lower permittivity than acetonitrile (the solvent commonly used to study calixarene–amine interactions). Therefore, electrolytes will have a greater tendency to undergo ion-pair formation in PhCN or PhNO₂ than in MeCN. On the other hand, hydrogen bond formation is known to occur between the monomer (*p*-*tert*-butylphenol) and amines and the thermodynamics of phenol–amine interactions have been reported [33]. In order to identify which of these processes are responsible for *p*-*tert*-butylcalix[4]arene–amine interactions in solution it is necessary to have information regarding the acid and basic strengths of the species involved. It must be a condition that for a proton (ion formation) transfer reaction to occur, the amine should be basic enough to be able to remove the proton from the calixarene. The dissociation constants (pK_a) of various amines in benzonitrile at 298.15 K were previously reported [14].

Thus, Figure 2 shows the potentiometric curve (and its first derivative) for the titration of *p*-*tert*-butylcalix[4]arene in benzonitrile at 298.15 K. For comparison

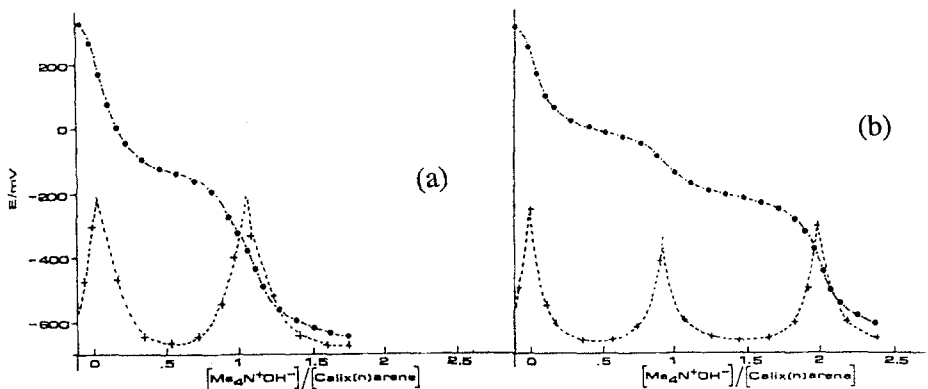
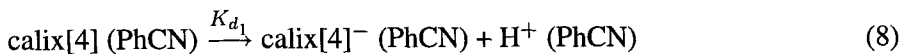
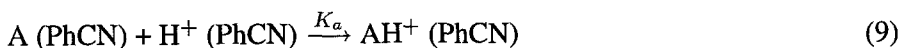


Fig. 2. Potentiometric titrations of (●) *p*-*tert*-butylcalix[*n*]arene (*n* = 4, 6) with tetramethylammonium hydroxide in benzonitrile at 298.15 K (a) calix[4], (b) calix[6]. (+) First derivative of titration curve.

purposes, the corresponding titration curve for calix[6] in the same solvent and at the same temperature is included. It should be noted that unlike the cyclic octamer (four inflection points) and the hexamer (two inflection points) [14] only one proton is removed for *p*-*tert*-butylcalix[4]arene in benzonitrile. The potentiometric titration data were analysed using a MINIQUAD program [34]. The dissociation constant (expressed as pK_{d1}) for the process



in benzonitrile ($pK_{d1} = 19.33$) is combined with pK_a values for the various amines (Equation 9).



so data for the proton transfer reaction (Equation 7) from *p*-*tert*-butylcalix[4]arene to the various amines in benzonitrile can be obtained and these are reported in Table III. Also included in this table are the derived Gibbs energies, $\Delta_p G^0$ for this process.

These data show that unlike calix[6] and calix[8] (negative $\Delta_p G^0$), the proton transfer reaction for *p*-*tert*-butylcalix[4]arene and these amines in benzonitrile is much less favoured (positive $\Delta_p G^0$) and these findings explain the low conductivities observed for these systems. Unfortunately, some experimental difficulties are found in measuring the pK_d values for *p*-*tert*-butylcalix[4]arene in nitrobenzene and we were unable to obtain quantitative data on this system.

However, in an attempt to gain further insight on these processes, we proceeded with the thermodynamics associated with the interactions of the cyclic tetramer and amines in benzonitrile and in nitrobenzene at the standard temperature. For these purposes, titration microcalorimetry was the technique used since inconsistent data were obtained by the use of classical macrocalorimetry mainly due

TABLE III. Equilibria data for the proton-transfer reaction from *p*-*tert*-butylcalix[4]arene and amines in benzonitrile at 298.15 K. Derived Gibbs energies (molar scale).

| Amine | $\log K_p^a$ | $\Delta_p G^0/\text{kJ mol}^{-1}$ |
|-------------------------|--------------|-----------------------------------|
| atropine | -1.62 | 9.25 |
| cryptand 22 | -1.54 | 8.79 |
| cryptand 222 | -0.93 | 5.31 |
| triethylamine | -1.35 | 7.71 |
| <i>tert</i> -butylamine | -1.54 | 8.79 |

^aObtained from a combination of pK_a values of *p*-*tert*-butylcalix[4]arene (see text) and amines (References [14]) in benzonitrile at 298.15 K.

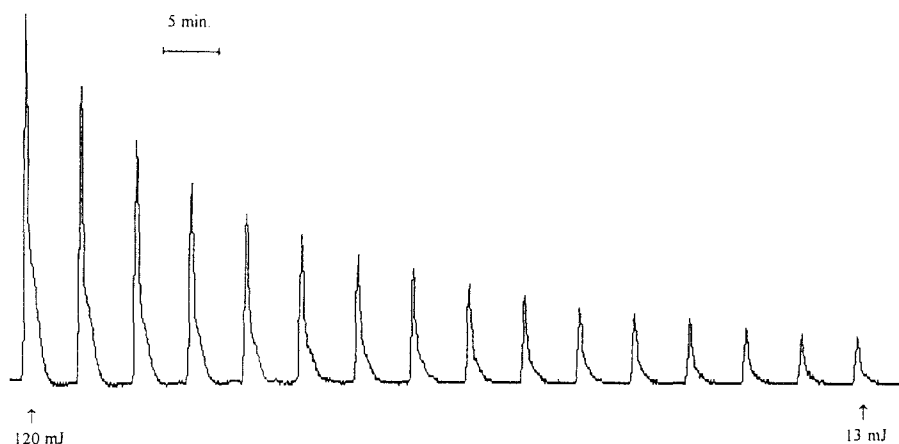
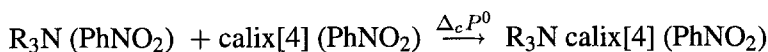
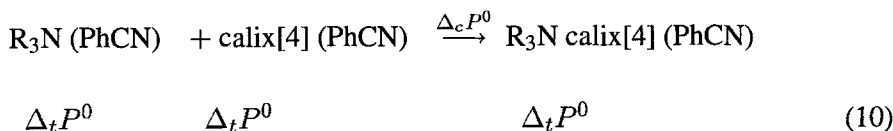


Fig. 3. Microcalorimetric recorded graph for the titration of *p*-*tert*-butylcalix[4]arene and triethylamine in nitrobenzene at 298.15 K.

to the low sensitivity of the latter relative to the former technique. Since there are no published data in nonaqueous media originated from the Thermal Monitor Analyser (microcalorimeter, see Experimental) we consider it appropriate to show a typical microcalorimetric recorded graph (Figure 3) for the titration of *p*-*tert*-butylcalix[4]arene and triethylamine in nitrobenzene at 298.15 K. In this figure, the integral values for the first (120 mJ) and the last (13 mJ) areas in the plot are indicated. Also included is the time interval (5 min) at which samples were introduced in the calorimetric vessel. Similar titration graphs were obtained in benzonitrile. From these data, equilibrium constants and enthalpy changes were calculated using a nonlinear least squares procedure based on Marquardt's method, including an algorithm in which linear parameters are eliminated [35]. Uncertainties for the K_s and $\Delta_c H$ values were obtained from the diagonal of the variance-covariance matrix [36]. Calorimetric data were consistent with a model assuming

1 : 1 amine-*p-tert*-butylcalix[4]arene interaction. It must be noted that despite the small formation of ions observed for this system in these solvents, this stoichiometry was also found in the conductance measurements. Table IV lists $\log K_s$ and derived Gibbs energies, enthalpies and entropies for the interaction of triethylamine and *p-tert*-butylcalix[4]arene in benzonitrile and in nitrobenzene at 298.15 K. For comparison purposes, corresponding values for *p-tert*-butylphenol (monomer) and the same amine in these solvents at the same temperature are also included in this table. The medium effect is clearly reflected in the thermodynamic data. Although the process involving the tetramer is enthalpically more stable ($\Delta_c H^0$ more negative) in nitrobenzene than in benzonitrile, the loss of entropy is greater in the former relative to the latter. These results seem to suggest that there is a greater loss of translational freedom upon interaction of these species in nitrobenzene than in benzonitrile. The outcome of enthalpy and entropy contributions makes the process more favoured ($\Delta_c G^0$ more negative) in PhCN than in PhNO₂. Note that the opposite is found for the monomer and triethylamine in these solvents.

Medium effects on adduct formation are best analysed by considering the solvation properties of the species involved. Thus, using transfer thermodynamic data for *p-tert*-butylcalix[4]arene (Table I), corresponding values for triethylamine from benzonitrile to nitrobenzene ($\Delta_t G^0 = -1.11 \text{ kJ mol}^{-1}$, $\Delta_t H^0 = 1.67 \text{ kJ mol}^{-1}$ and $\Delta_t S^0 = 9.3 \text{ J K}^{-1} \text{ mol}^{-1}$) combined with the complexation data in these solvents given in Table IV, the thermodynamic parameters for the transfer of the triethylamine-*p-tert*-butylcalix[4]arene adduct [R₃N·calix[4]] between these two solvents are calculated by inserting the appropriate quantities in the following cycle, where P = G, H or S.



As far as Gibbs energies are concerned, the $\Delta_t G^0$ values reveal the differences in solvation of these species in these solvents. Thus, nitrobenzene while stabilising both *p-tert*-butylcalix[4]arene and triethylamine better than benzonitrile ($\Delta_t G^0$ negative) it weakens the acidic properties of the tetramer and the basic character of the amine. This statement is based on comparative potentiometric studies carried out with this system in these solvents. This is further corroborated by the decrease observed in the stability of the adduct in nitrobenzene relative to benzonitrile as shown in the $\Delta_c G^0$ values listed in Table V. Therefore, the role of the solvent is such that conclusions drawn for the same (or similar) process in the solid state are not necessarily applicable to solution processes [37]. It should be emphasised that the most interesting feature of the data shown in Table V are observed in the enthalpy and entropy contributions to the Gibbs energy of the process. Thus,

TABLE IV. Thermodynamic parameters for the interaction of *p*-*tert*-butylcalix[4]arene and *p*-*tert*-butylphenol with triethylamine in benzonitrile and in nitrobenzene at 298.15 K.

| Compound | $\log K_s$ | $\Delta_c G^0/\text{kJ mol}^{-1}$ | $\Delta_c H^0/\text{kJ mol}^{-1}$ | $\Delta_c S^0/\text{J K mol}^{-1}$ |
|-------------------------------------|-----------------|-----------------------------------|-----------------------------------|------------------------------------|
| Benzonitrile | | | | |
| calix[4] | 2.39 ± 0.04 | -13.65 ± 0.20 | -27.33 ± 0.02 | -45.9 ± 0.7 |
| <i>p</i> - <i>tert</i> -butylphenol | 0.70 ± 0.01 | -3.99 ± 0.03 | -21.72 ± 0.06 | -59.5 ± 0.2 |
| Nitrobenzene | | | | |
| calix[4] | 1.57 ± 0.01 | -8.97 ± 0.03 | -40.25 ± 0.01 | -105.0 ± 0.1 |
| <i>p</i> - <i>tert</i> -butylphenol | 1.18 ± 0.01 | -6.73 ± 0.04 | -29.09 ± 0.01 | -75.0 ± 0.1 |

TABLE V. Thermodynamic parameters for the transfer of triethylamine-*p*-*tert*-butylcalix[4]arene adduct from benzonitrile to nitrobenzene at 298.15 K.

| $\Delta_c G^0$ (PhCN) ^a kJ mol ⁻¹ | $\Delta_c G^0$ (PhNO ₂) ^a kJ mol ⁻¹ | $\Delta_t G^0$ (PhCN → PhNO ₂)/kJ mol ⁻¹ | | |
|---|---|--|-----------------------|--|
| | | Et ₃ N ^b | calix[4] ^c | R ₃ N·calix[4] ^d |
| -13.65 | -8.97 | -1.11 | -7.34 | -3.77 |
| $\Delta_c H^0$ (PhCN) ^a kJ mol ⁻¹ | $\Delta_c H^0$ (PhNO ₂) ^a kJ mol ⁻¹ | $\Delta_t H^0$ (PhCN → PhNO ₂)/kJ mol ⁻¹ | | |
| | | Et ₃ N ^b | calix[4] ^c | R ₃ N·calix[4] ^d |
| -27.33 | -40.25 | 1.67 | -0.47 | -11.72 |
| $\Delta_c S^0$ (PhCN) ^a J K ⁻¹ mol ⁻¹ | $\Delta_c S^0$ (PhNO ₂) ^a J K ⁻¹ mol ⁻¹ | $\Delta_t S^0$ (PhCN → PhNO ₂)/J K ⁻¹ mol ⁻¹ | | |
| | | Et ₃ N ^b | calix[4] ^c | R ₃ N·calix[4] ^d |
| -45.9 | -105.0 | 9.3 | 23.0 | -26.7 |

^aFrom Table IV. ^bSee text. ^cFrom Table I. ^dCalculated via cycle (Equation 10).

for triethylamine and the tetramer, their favourable transfer to nitrobenzene is entropy driven, while for the adduct, the process is enthalpy controlled and takes place with a loss of entropy. Since the transfer enthalpy for triethylamine ($\Delta_t H^0 = 0.67 \text{ kJ mol}^{-1}$), these findings unambiguously demonstrate that the difference observed in the $\Delta_c H^0$ values in these solvents (Table V) is mainly attributed to the higher enthalpic stability of the adduct in nitrobenzene relative to benzonitrile.

It is therefore concluded that the interaction of *p*-*tert*-butylcalix[4]arene and triethylamine in these solvents occurs predominantly through hydrogen bonding or ion-pair formation. So far for the tetramer, the thermodynamic data fits a one step process which do not distinguish between hydrogen bonding or ion-pair formation. However, due to the increased acidity of the hexamer and the octamer relative to the tetramer in these solvents, their interactions with amines result in the formation of ions and ion-pairs. Thus, for *p*-*tert*-butylcalix[4]arenes ($n = 6, 8$) and this amine thermodynamic data fit a two-step process where the formation of ions are

considered and these will be shortly reported. We are now proceeding with heat capacity measurements in order to gain further information on these systems.

Finally, it must be said that in this paper discussion on previous work carried out with these (or similar) systems [22, 38–40] in different media has been deliberately omitted since the behaviour of amines and mainly calixarenes depends crucially upon the medium and for the purpose of useful comparison, potentiometric, conductimetric and thermodynamic data in the relevant solvents are required.

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