

Selective Recognition of Halide Anions by Calix[4]pyrrole: A Detailed Thermodynamic Study

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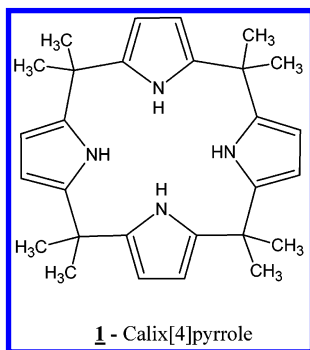
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Several analytical techniques (^1H NMR, conductance measurements, and titration calorimetry) have been used to assess the interaction of calix[4]pyrrole and halide anions in dipolar aprotic solvents (acetonitrile and *N,N*-dimethylformamide). Solubility data for calix[4]pyrrole in various solvents at 298.15 K were determined. These data were used to calculate the standard Gibbs energies of solution. Taking acetonitrile as the reference solvent, the transfer Gibbs energies of this ligand to various solvents were calculated. Chemical shift changes ($\Delta\delta$) of the pyrrole proton relative to the free ligand resulting from the addition of the anion salts to the ligand in CD_3CN at 298 K follow the sequence $\text{F}^- > \text{Cl}^- > \text{Br}^- > \text{I}^-$. Conductance measurements were performed (i) to establish the stoichiometry of the anionic calix[4]pyrrole complexes and (ii) to assess the range of concentration at which the free and complex anion salts are predominantly in their ionic forms in acetonitrile and *N,N*-dimethylformamide at 298.15 K. Titration calorimetry was used to determine the stability constant, K_s , (hence the standard Gibbs energy) and the enthalpy. Combination of Gibbs energy and enthalpy data yields the entropy of complexation. A linear correlation is found between the $\log K_s$ and the $\Delta\delta$ values. The results show that calix[4]pyrrole is able to recognize selectively the halide anions in these solvents. The selectivity of the ligand for one anion relative to another is quantitatively evaluated through the calculation of the selectivity factor. It is shown that the ligand behavior is representative of flexible ligands in which calix[4]pyrrole compete successfully with the solvent for the anion to an extent that the higher selectivity of the ligand is for the smallest anion (fluoride). The thermodynamics of complexation is discussed in terms of the solvation properties of the reactants and the products in acetonitrile and *N,N*-dimethylformamide.

Introduction

The chemistry of calix[4]pyrrole has been the subject of a number of interesting papers in recent years.¹ A detailed account of events that led to the synthesis of these macrocycles has been given by Gale et al. in 1998.² Despite that calix[4]pyrrole has found a considerable number of applications (ion selective electrodes, as anchor groups in solid supports for anion separation by high performance liquid chromatography, optical sensors) there is not a detailed study on the thermodynamics of these systems in solution. Stability constant data for **1** and



various anions (fluoride, chloride, bromide, and dihydrogen phosphate) in a variety of solvents, namely, dichloromethane³ (DCM), acetonitrile:chloroform (1:9),⁴ acetonitrile,⁵ and DMSO-*d*₆,⁶ have been reported in the literature. More recently,⁷ on the basis of direct calorimetric titrations, the selective behavior

previously observed for **1** and halides has been questioned. It was concluded that there is no preference of fluoride relative to chloride in dry acetonitrile at 303 K. We have previously demonstrated the role of solvation in complexation reactions involving macrocycles (crown ethers,⁸ cryptands,⁹ cyclodextrins,¹⁰ and calixarenes^{11,12}) and different neutral and ionic species in different media. In doing so, the transfer thermodynamics of the reactants and the product from a reference solvent to another were considered. In a recent review article¹¹ we emphasized the scope and limitations of the various methods used for the determination of stability constants. This paper discusses the thermodynamics of anion complexation of **1** and halide anions (fluoride, chloride, and bromide) in acetonitrile and *N,N*-dimethylformamide at 298.15 K. ^1H NMR measurements were performed to determine the sites of interaction of **1** and the halide anions in acetonitrile.

Experimental Section

Chemicals. Methanol (HPLC grade, Fisher UK Scientific International), ethanol (99%, HAYMAN Ltd), propylene carbonate (99.9%, Aldrich Chemical Co.), benzonitrile (99.9% HPLC grade, Aldrich Chemical Co.), and nitrobenzene (99.9% HPLC grade, Aldrich Chemical Co.) were used without further purification.

Acetonitrile¹³ (HPLC grade, Fisher UK Scientific International) was refluxed in a nitrogen atmosphere and distilled over calcium hydride. The middle fraction was collected.

N,N-Dimethylformamide¹³ (HPLC grade, Fisher UK Scientific International) was dried over 3 Å molecular sieves (which have been dried at 300 °C overnight for 72 h) and subsequently distilled under reduced pressure. The middle fraction was collected.

Deuterated acetonitrile (CD₃CN) and tetramethylsilane (TMS) were purchased from Aldrich Chemical Co.

Tetra-*n*-butylammonium Fluoride trihydrate (99%, Fluka Chemical Co.), tetra-*n*-butylammonium chloride (97%, Fluka Chemical Co.), tetra-*n*-butylammonium bromide (99%, Aldrich Chemical Co.), tetra-*n*-butylammonium iodide (99%, Aldrich Chemical Co.). These were dried over P₄O₁₀ under vacuum for several days before use.

Potassium chloride (KCl) (99%, Fisher UK Scientific International) was used without any further purification.

Tris(hydroxymethyl)aminomethane (THAM), ultrapure (99.9%, Aldrich Chemical Co.), was used without further purification.

Calix[4]pyrrole was synthesized at the Thermochemistry Laboratory according to the procedure reported in the literature.¹⁴

Solubility Measurements. Saturated solutions of calix[4]pyrrole were prepared by adding an excess amount of the solid to various organic solvents (acetonitrile, MeCN; ethanol, EtOH; methanol, MeOH; *N,N*-dimethylformamide, DMF; propylene carbonate, PC; benzonitrile, PhCN; nitrobenzene, PhNO₂). The mixture of each solvent was left in a thermostated bath at 298.15 K for several days until equilibrium was reached. Aliquots of the saturated solutions were taken and analyzed gravimetrically in triplicate. Blank experiments were carried out. Solvate formation was checked by exposing the solid to a saturated atmosphere of the solvent for several days, following the procedure described in the literature.¹⁵ The samples were weighed from time to time to check for any uptake of solvent. Solvate formation was observed in tetrahydrofuran, THF, dichloromethane, CH₂Cl₂, and chloroform, CHCl₃.

Conductance Measurements. For these measurements, a Wayne-Kerr model 7330 Automatic LCR Meter Conductivity Bridge at a frequency of 1 kHz was used. The conductance cell was a Russell type glass bodied electrode with a cell constant (determined using 0.10 mol·dm⁻³ aqueous KCl solution) of 1.009 ± 0.001 cm⁻¹. For these experiments, the vessel was filled with the halide anion as the tetra-*n*-butylammonium salt in the appropriate solvent (25 cm³) and the conductance of the solution was measured. Then, a known volume of solution of calix[4]pyrrole in the same solvent was added stepwise into the vessel and the conductance measured after each addition. The temperature of the vessel was kept at 298.15 K using a thermostat.

Conductance Measurements of the Halide Anion Complex Salts. For these experiments, the conductivity cell was filled with the appropriate solvent (25 cm³) and the conductance of the solvent was measured. The halide anion complex salt solution in the same solvent was added stepwise into the cell. After each addition, conductance readings at 298.15 K were recorded.

Calorimetric Titrations. Enthalpies of complexation of calix[4]pyrrole and halide anions in the appropriate solvents were determined by classical calorimetry (direct and competitive titrations) using a Tronac 450 calorimeter. The vessel was filled with the ligand solution (50 cm³) in the appropriate solvent and a solution of the halide anion in the same solvent was added from a 2 cm³ buret connected by a silicone tube to the reaction vessel. These experiments were repeated four times for each halide anion and each solvent. Blank experiments were carried out in all cases to account for heat of dilution effects resulting

from the addition of the halide anion as tetra-*n*-butylammonium salt to the solvent contained in the calorimetric vessel. The enthalpy of protonation of THAM (tris(hydroxymethyl)aminomethane) in an aqueous solution of hydrochloric acid (0.1 mol·dm⁻³), suggested as a standard thermochemical reaction,¹⁶ was used to check the accuracy and reproducibility of the equipment. The value obtained (-47.74 kJ·mol⁻¹) is in agreement with that reported by Wilson and Smith¹⁷ (-47.49 kJ·mol⁻¹) at 298.15 K.

For stability constant values lower than 10⁶ (log *K*_s = 6), direct calorimetric titrations were performed. A solution of the tetra-*n*-butylammonium salt of selected halide anion was prepared in the appropriate solvent, placed in the buret, and titrated into the vessel containing a solution of the free ligand prepared in the same solvent.

For log *K*_s values higher than 6, competitive calorimetric titrations were performed. A solution of the halide anion (tetra-*n*-butylammonium counterion) was prepared in the appropriate solvent, placed in the buret, and titrated into the vessel containing a solution of the calix[4]pyrrole complexed with a halide anion (X⁻) prepared in the same solvent (X⁻ = Br⁻ (MeCN), Cl⁻ (DMF); *n*_{X⁻} = 3*n*_{CP}, where *n*_{X⁻} and *n*_{CP} are the number of moles of the halide anion in the vessel and calix[4]pyrrole, respectively). The stability constant of the complex in the vessel was lower than that expected between calix[4]pyrrole and the halide anion under investigation placed in the buret, enabling the latter to compete and replace the halide anion of the complex in the vessel.

The whole system was then immersed in a thermostated water bath at 298.15 K and allowed to reach thermal equilibrium.

Corrections for the heat of dilution were also made by titrating the solution in the buret into the vessel with the appropriate solvent. An electrical calibration was carried out after each titration experiment.

In the case of iodide, titration microcalorimetry was used. The four-channel heat conduction microcalorimeter (Thermometric 2277) designed by Suurkuusk and Wadsö¹⁸ was used. Electrical (static and dynamic) and chemical calibrations were carried out to check the reliability of the equipment.¹⁹

The reaction vessel was charged with 2.8 cm³ of the calix[4]pyrrole in acetonitrile. The iodide anion (tetra-*n*-butylammonium counterion) was injected incrementally using a 0.5 cm³ gas tight motor driven Hamilton syringe. In each titration experiment, about 20 injections were made at time intervals of 30–45 min. Correction for the enthalpy of dilution of the titrant in the solvent was carried out. A computer program for TAM (Digitam 4.1 for windows from Thermometric AB and Scitech Software AB, Sweden) was used to calculate log *K*_s and Δ_c*H*^o values for the process under study.

Determination of Standard Enthalpies of Solution. Enthalpies of solution were carried out with the Tronac 450 calorimeter. To check the reliability of the solution calorimeter, the standard enthalpy of solution of THAM in an aqueous solution of 0.1 mol·dm⁻³ of HCl was determined. The value obtained (Δ_s*H*^o = -29.4 ± 0.2 kJ·mol⁻¹) is in good agreement with that of -29.71 kJ·mol⁻¹ given in the literature.²⁰

For the determination of the standard enthalpy of solution of the ligand and free and complex salts, glass ampoules were filled with an accurate amount of the compound and sealed. These were then placed in a calorimetric vessel containing the appropriate solvent (50 cm³). The system was placed in a thermostated bath until thermal equilibrium was reached. The ampoules were broken, and the resulting temperature changes were recorded. After each experiment an electrical calibration

TABLE 1: Solubilities of Calix[4]pyrrole in Various Solvents and Standard Gibbs Energies of Solution, $\Delta_s G^\circ$, and Transfer, $\Delta_t G^\circ$, from Acetonitrile to Other Solvents at 298.15 K

solvent ^a	solubility (mol·dm ⁻³)	$\Delta_s G^\circ$ (kJ·mol ⁻¹)	$\Delta_t G^\circ$ (kJ·mol ⁻¹)
MeCN	$(1.39 \pm 0.05) \times 10^{-2}$	10.60	0.00
EtOH	$(6.27 \pm 0.08) \times 10^{-3}$	12.57	1.97
MeOH	$(8.07 \pm 0.03) \times 10^{-3}$	11.95	1.35
DMF	$(1.36 \pm 0.04) \times 10^{-2}$	10.65	0.05
PC	$(1.40 \pm 0.02) \times 10^{-2}$	10.58	-0.02
PhCN	$(2.63 \pm 0.04) \times 10^{-2}$	9.02	-1.58
PhNO ₂	$(3.20 \pm 0.09) \times 10^{-2}$	8.53	-2.07

^a Abbreviations used: MeCN, acetonitrile; EtOH, ethanol; MeOH, methanol; DMF, *N,N*-dimethylformamide; PC, propylene carbonate; PhCN, benzonitrile; PhNO₂, nitrobenzene.

was performed. The total heat was corrected for the heat associated with the breaking of empty glass ampules in the reaction vessel containing the solvent (50 cm³). The heat of solution was calculated by subtracting the heat of the empty ampule from the total recorded heat. For the determination of the enthalpies of solution of the fluoride and chloride complexes, these experiments were carried out in the presence of small excess of the ligand in the reaction vessel to ensure that no dissociation of the complex occurred during these measurements.

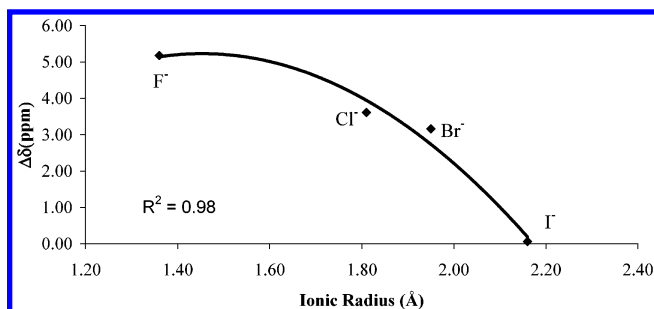
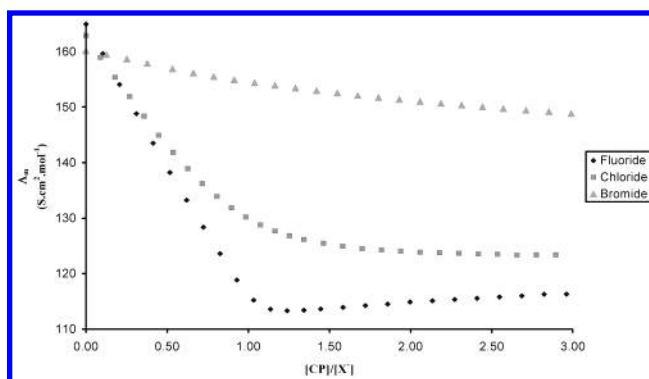
Preparation and Isolation of the Fluoride and Chloride Complexes Using Tetra-*n*-butylammonium (Counterion) Salts. This was accomplished by mixing stoichiometric amounts of the calix[4]pyrrole and the salt in acetonitrile. The mixture was swirled until all reactants are dissolved, then the mixture was left until crystals appeared. Microanalysis was carried out at the University of Surrey. Anal. Calcd for the salt C₂₈H₃₆N₄·C₁₆H₃₆FN: C, 76.58; H, 10.52; N, 10.15. Found: C, 76.30; H, 10.83; N, 9.90. Anal. Calcd for the salt C₂₈H₃₆N₄·C₁₆H₃₆ClN: C, 74.80; H, 10.27; N, 9.91. Found: C, 74.50; H, 10.67; N, 9.63.

Results and Discussion

Solubilities of Calix[4]pyrrole and Derived Standard Gibbs Energies of Solution. The solubilities of calix[4]pyrrole in various organic at 298.15 K are reported in Table 1. Gibbs energies of solution, $\Delta_s G^\circ$, referred to the standard state of 1 mol·dm⁻³ are listed in this table. Standard deviations of the data (average of analytical measurements carried out on the same saturated solution) are also included in Table 1. Taking acetonitrile as the reference solvent, the standard Gibbs energies of transfer, $\Delta_t G^\circ$, of calix[4]pyrrole to other solvents were calculated. The data reflect that the medium effect does not lead to significant variations on this parameter. Therefore, it is concluded that as far as these solvents are concerned the ligand does not undergo selective solvation.

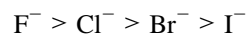
Solubility data and the kinetics associated with the dissolution processes are useful in assessing whether these pose a limitation in the experimental work required to investigate the structural, electrochemical, and thermodynamic characterization of this system and its interaction with anionic species. Thus ¹H NMR studies in CD₃CN at 298 K were carried out to assess the complexing ability of this ligand with the halide anions and, if so, to determine the active site of interaction and this is now discussed.

¹H NMR Measurements. Table 2 reports the chemical shift changes found by the addition of halide anions to calix[4]pyrrole at 298 K relative to the free ligand in CD₃CN. The most substantial changes are observed for the pyrrole proton, indicat-

**Figure 1.** Relationship between ionic radii of halide anions and $\Delta\delta$ values for the pyrrole proton at 298 K.**Figure 2.** Conductometric curves for the titration of halide anions (tetra-*n*-butylammonium counterion) with calix[4]pyrrole in acetonitrile at 298.15 K.**TABLE 2: ¹H NMR Chemical Shift Changes Found by the Addition of Halide Anions to Calix[4]pyrrole at 298 K Relative to the Free Ligand in CD₃CN at 298 K**

proton	δ (ppm) free ligand	$\Delta\delta$ (ppm)			
		F ⁻ complex	Cl ⁻ complex	Br ⁻ complex	I ⁻ complex
N-H	7.40	5.18	3.61	3.16	0.06
Ar-H	5.80	-0.28	-0.26	-0.24	0.02
CH ₃	1.48	0.15	0.24	0.27	0.05

ing that this provides the site of interaction between the ligand and the anions in acetonitrile. Thus the following sequence is observed.



In fact, a relationship is found between the $\Delta\delta$ values for pyrrole protons and the ionic radius for these anions (Figure 1) where the most significant change is observed for the smallest anion. Very small chemical shift changes are observed for this ligand and the iodide anion.

Having established the site of interaction of this ligand and these anions, we proceeded with conductometric titrations and these are now discussed.

Conductometric Titrations. The aim of these titrations was to determine the stoichiometry of the anion complexes in acetonitrile and in *N,N*-dimethylformamide at 298.15 K.

Thus plots of molar conductances (Λ_m° , S·cm²·mol⁻¹) against the ligand:anion (CP/X⁻) molar ratio in acetonitrile and *N,N*-dimethylformamide at 298.15 K are shown in Figures 2 and 3, respectively, for the fluoride, chloride, and bromide anions and calix[4]pyrrole in these solvents.

As previously stated,²¹ the variation of the electrical conductivity with the ligand:anion mole ratios can be classified under three main groups:

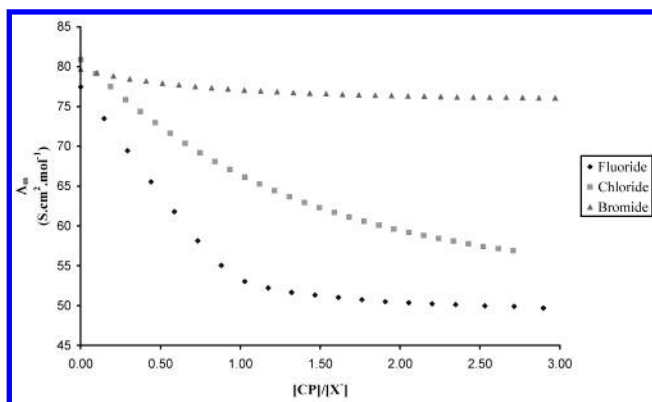


Figure 3. Conductometric curves for the titration of halide anions (tetra-*n*-butylammonium counterion) with calix[4]pyrrole in *N,N*-dimethylformamide at 298.15 K.

(i) plots with a slight (or nonexistent) slope and without any indication of a change in slope at any given mole ratio (these plots reflect very little or no complexation),

(ii) plots with a well-defined change in the curvature at the stoichiometry of the reaction, which indicates an intermediate strength of complexation, and

(iii) plots formed by two straight lines intersecting at the stoichiometry of the complex, which corresponds to the formation of a highly stable complex.

In accordance with the chemical shift changes observed in the ^1H NMR spectra by the addition of these anion salts to the ligand in CD_3CN , conductance measurements indicate that the ligand is able to discriminate among the halide anions following the same sequence as observed by ^1H NMR measurements. For the iodide anion, the conductometric titration curve in acetonitrile shows the pattern described under (i). Indeed, if there is interaction between this ligand and the iodide anion, this must be very weak, to the extent that it is hardly detected by ^1H NMR or indeed by conductivity measurements.

Further remarks regarding the conductometric titration curves are as follows:

(i) The Λ_m values at a ligand/anion ratio of zero, corresponding to the molar conductance of the salt (where the anion is in its free form), are within the expected values for this salt at the starting concentrations, as assessed from their Λ° values reported in the literature.²⁰

(ii) The decrease observed in the Λ_m° upon complexation is attributed to the larger size of the complex relative to the free anion.

Having established the complex composition, we performed conductance measurements at different anion salt concentrations to determine the range of concentrations at which the anion complex salt is predominantly dissociated in solution. A representative example is given in Figure 4 for the complex anion salt in acetonitrile where data for the molar conductance against $c^{1/2}$ at 298.15 are shown. The linear relationship found provides evidence that these electrolytes are predominantly in their ionic forms in acetonitrile. The same behavior was observed for these salts in *N,N*-dimethylformamide at 298.15 K. As far as the free anion salt in these solvents are concerned, ion-pair formation constants of tetra-*n*-butylammonium salts (bromide–iodide) in acetonitrile at the standard temperature have been reported.²² The data reflect that these salts are predominantly dissociated in these solvents. Data obtained by us for the chloride and fluoride salts in these solvents also reflect that ionic species are predominantly in solution. A representative example is shown in Figure 4 for tetra-*n*-butylammonium

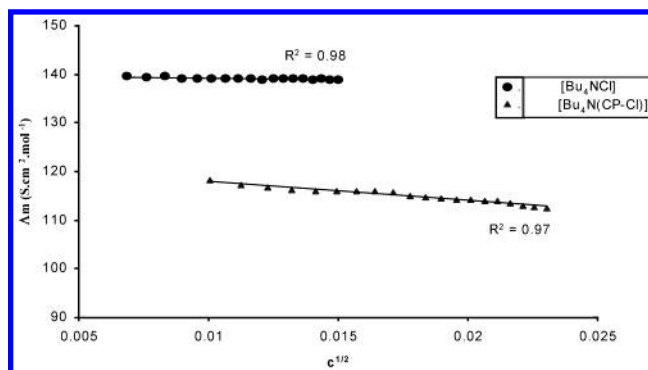


Figure 4. Molar conductances of Bu_4NCl and $\text{Bu}_4\text{N}(\text{CP-Cl})$ complex as a function of the square root of molar concentrations in acetonitrile at 298.15 K.

TABLE 3: Thermodynamics of Complexation of Calix[4]pyrrole and Halide Anions in Acetonitrile and *N,N*-Dimethylformamide at 298.15 K

anion	$\log K_s$	$\Delta_c G^\circ$ ($\text{kJ}\cdot\text{mol}^{-1}$)	$\Delta_c H^\circ$ ($\text{kJ}\cdot\text{mol}^{-1}$)	$\Delta_c S^\circ$ ($\text{J}\cdot\text{mol}^{-1}\cdot\text{K}^{-1}$)
Acetonitrile				
fluoride	6.21 ± 0.03^a	-35.4 ± 0.2	-43.5 ± 0.3^a	-27
			-39.1 ± 0.7	
chloride	4.70 ± 0.07^b	-26.8 ± 0.4^b	-44.7 ± 0.9^b	-60^b
	4.74 ± 0.08^c	-27.0 ± 0.5^c	-45.2 ± 0.7^c	-61^c
bromide	3.65 ± 0.06^b	-20.8 ± 0.3^b	-30.7 ± 0.9^b	-33^b
	3.67 ± 0.06^d	-20.8 ± 0.3^d	-31.3 ± 0.9^d	-35^d
iodide	1.55 ± 0.06^e	-8.8 ± 0.3^e	-4.0 ± 0.5^e	15^e
<i>N,N</i>-Dimethylformamide				
fluoride	6.8 ± 0.3^a	-39.0 ± 0.5	-26.2 ± 0.5	43
chloride	4.2 ± 0.1	-24.0 ± 0.6	-14.5 ± 0.1	32
bromide	3.4 ± 0.1	-19.1 ± 0.7	-9.2 ± 0.9	33

^a From competitive calorimetry. ^b Tetra-*n*-butylammonium as counterion. ^c Tetra-*n*-methylammonium as counterion. ^d Tetra-*n*-ethylammonium as counterion. ^e From microcalorimetry titrations.

chloride in acetonitrile at 298.15 K. The same applies to the tetra-*n*-butylammonium salts in *N,N*-dimethylformamide.

The following section discusses the thermodynamics of complexation of calix[4]pyrrole and halide anions in acetonitrile and *N,N*-dimethylformamide at 298.15 K.

Thermodynamics of Complexation. Having established from conductance measurements (i) the stoichiometry of the complexes in acetonitrile and *N,N*-dimethylformamide at 298.15 K and that (ii) the free and complex salts are in their ionic forms in both solvents, an equation representative of the binding process can be formulated (eq 1) for the interaction of calix[4]pyrrole (CP) and the halide anions ($\text{X}^- = \text{F}^-, \text{Cl}^-, \text{Br}^-, \text{I}^-$) in nonaqueous solvents ($s = \text{MeCN}$ or DMF) to give the anionic complex, CPX^- .



Stability constants (expressed as $\log K_s$) and derived standard Gibbs energies, $\Delta_c G^\circ$, enthalpies, $\Delta_c H^\circ$, and entropies, $\Delta_c S^\circ$, for this ligand and halide anions in acetonitrile and *N,N*-dimethylformamide at 298.15 K are listed in Table 3.

Titration calorimetry was used to obtain $\log K_s$ and $\Delta_c H^\circ$ values. Direct titrations were performed for the complexation process involving chloride and bromide anions whereas the competitive method was used to derive the $\log K_s$ and $\Delta_c H^\circ$ values for the fluoride anion. For the binding reaction involving the fluoride anion, the $\Delta_c H^\circ$ value was also obtained by direct calorimetry. Excellent agreement was found between the two sets of data. As previously shown in eq 1., the stability constant

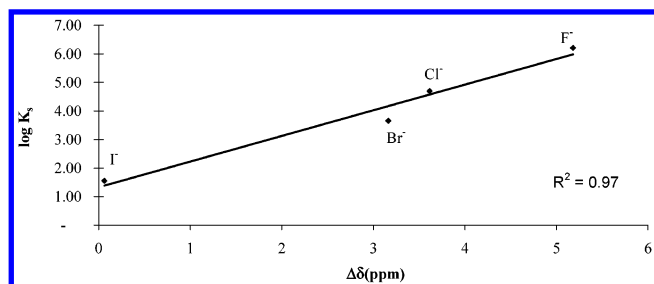
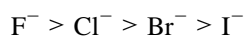


Figure 5. Linear relationship between $\log K_s$ and $\Delta\delta$ values for the pyrrole proton at 298 K.

and hence $\Delta_c G^\circ$, $\Delta_c H^\circ$, and $\Delta_c S^\circ$ values should be independent of the cation. If these are cation dependent, then other processes are taking place in solution and therefore the value obtained is not the true stability constant. This statement was corroborated by using as anion source other salts such as tetra-*n*-methylammonium and tetra-*n*-ethylammonium salts. These data are also included in Table 3. Good agreement was found between these sets of data.

The striking feature of the data is the selective behavior of the ligand for the halide anions in both solvents, acetonitrile and *N,N*-dimethylformamide. Indeed, the ligand is able to recognize selectively these anions in the following sequence:



This is in accord with the chemical shift changes observed in the ^1H NMR spectra for the pyrrole proton. This statement is corroborated by the linear relationship ($r^2 \approx 0.97$) found between the stability constants (expressed as $\log K_s$) of calix[4]pyrrole and halide anions in acetonitrile at 298.15 K and the chemical shift changes ($\Delta\delta$, ppm) for the pyrrole proton, as shown in Figure 5.

Calculation of the selectivity factor, $S(K_s(\text{F}^-)/K_s(\text{X}^-))$ leads to a quantitative assessment of the affinity of calix[4]pyrrole for the fluoride relative to other anions in acetonitrile. It is therefore concluded that this ligand is more selective for fluoride relative to chloride, bromide, and iodide by factors of 32, 363, and 45684, respectively.

Similar considerations in *N,N*-dimethylformamide show that in this solvent, S increases to 398 and 2512 for fluoride relative to chloride and bromide, respectively. As far as fluoride and chloride are concerned, the stability constants in these solvents follow the behavior observed in the solid state in that the fluoride anion is more tightly bound to the pyrrole proton (1.64 Å) than to the chloride anion (2.221 Å), as shown by X-ray diffraction studies.²³

In an attempt to assess the monatomic size dependence of the stability constant, a plot of $\log K_s$ against the reciprocal of the anion radius is shown in Figure 6.

Inspection of this plot shows that as the ionic radius of the anion decreases, the stability of complex formation increases. This behavior is typical of ligands that are flexible enough to arrange themselves around the anion, and in doing so, these can successfully compete with the solvent for the anion to the extent that the gain in binding energy is greater for the smallest ion. In conclusion, the stability constants follow the pattern observed for the transfer Gibbs energies, $\Delta_t G^\circ$,²⁴ of these anions from a dipolar aprotic solvent to a protic solvent in that the strength of hydrogen bond formation increases as the charge density of the anion increases. This is indeed the case for this ligand and these anions in these solvents given that in the complexation process the anion is transferred from a dipolar

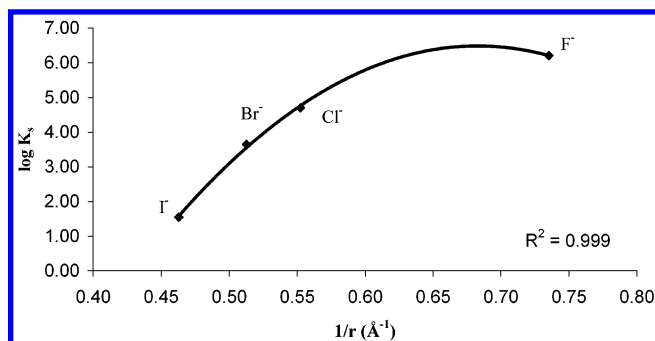


Figure 6. Dependence of $\log K_s$ values with the reciprocal of the anion radius.

aprotic solvent to a receiving medium (the ligand) with the capability of entering hydrogen bond formation. This statement is corroborated by the very weak complexation observed for this ligand and the halide anions in methanol. In this medium the ligand is unable to compete with the solvent for the anion.

As far as enthalpies and entropies of complexation are concerned, the higher stability of the fluoride anion in acetonitrile relative to chloride is mainly attributed to the less unfavorable entropy change of the former relative to the latter given that enthalpy values for these two anions do not differ significantly. In acetonitrile, the complexation process is enthalpically controlled whereas in *N,N*-dimethylformamide, both the enthalpy and entropy of complexation contribute favorably to the Gibbs energy associated to these processes. To assess the contribution of the reactants and the product to the complexation process in these two solvents, we proceeded with the determination of the enthalpies of solution of the ligand and their anionic complexes and these are now discussed.

Enthalpies of Solution. The standard enthalpies of solution, $\Delta_s H^\circ$, of the tetra-*n*-butylammonium calix[4]pyrrole fluoride [$\text{Bu}_4\text{N}^+(\text{CPF}^-)$] and chloride [$\text{Bu}_4\text{N}^+(\text{CPCl}^-)$] salts in acetonitrile and *N,N*-dimethylformamide at 298.15 K are reported in Table 4. Also reported in this table are the $\Delta_s H^\circ$ values for the calix[4]pyrrole (CP) in these solvents.

These values were obtained from calorimetric measurements carried out at different concentrations (c) of the appropriate compounds. The standard values are the intercept at $c = 0$ of a plot of solution enthalpies ($\Delta_s H^\circ$) as a function of $c^{1/2}$. In cases where no variation was found in the $\Delta_s H^\circ$ with the concentration, the $\Delta_s H^\circ$ is the average of several measurements. The concentration range ($\text{mol}\cdot\text{dm}^{-3}$) and number of measurements (n) are as follows,

CP: MeCN, 1.15×10^{-4} to 9.52×10^{-4} , $n = 9$;
DMF, 2.1×10^{-4} to 6.8×10^{-4} , $n = 6$

Bu_4NCPF : MeCN, 1.5×10^{-4} to 7.4×10^{-4} , $n = 9$;
DMF, 5.8×10^{-4} to 1.4×10^{-3} , $n = 5$

Bu_4NCPCl : MeCN, 7.4×10^{-4} to 1.8×10^{-3} , $n = 5$;
DMF, 6.5×10^{-4} to 2.1×10^{-3} , $n = 10$

Bu_4NF : MeCN, 8×10^{-5} to 2×10^{-4} , $n = 5$;
DMF, 8.5×10^{-4} to 1.6×10^{-3} , $n = 6$

Combination of these data and those reported in the literature²⁴ for Bu_4NCl in acetonitrile and *N,N*-dimethylformamide at 298.15 K with complexation enthalpies reported in Table 3 allows the calculation of the enthalpy of coordination, $\Delta_{\text{coord}} H^\circ$, referred

TABLE 4: Enthalpies of Solution ($\Delta_s H^\circ$) of Calix[4]pyrrole and Its Tetra-*n*-butylammonium Complex Salts (Fluoride and Chloride) in Acetonitrile and in *N,N*-Dimethylformamide at 298.15 K in kJ mol⁻¹

	acetonitrile	<i>N,N</i> -dimethylformamide
CP	21.6 ± 0.7 ^a	31 ± 1 ^b
Bu ₄ N ⁺ (CPF ⁻)	33.2 ± 0.5 ^a	13.7 ± 0.3 ^b
Bu ₄ N ⁺ (CPCl ⁻)	3.8 ± 0.1 ^a	39.5 ± 0.8 ^b
Bu ₄ NF	39.0 ± 0.5 ^b	-2.7 ± 0.5 ^a

^a Extrapolated value at $c = 0$. ^b Average of several measurements (see text).

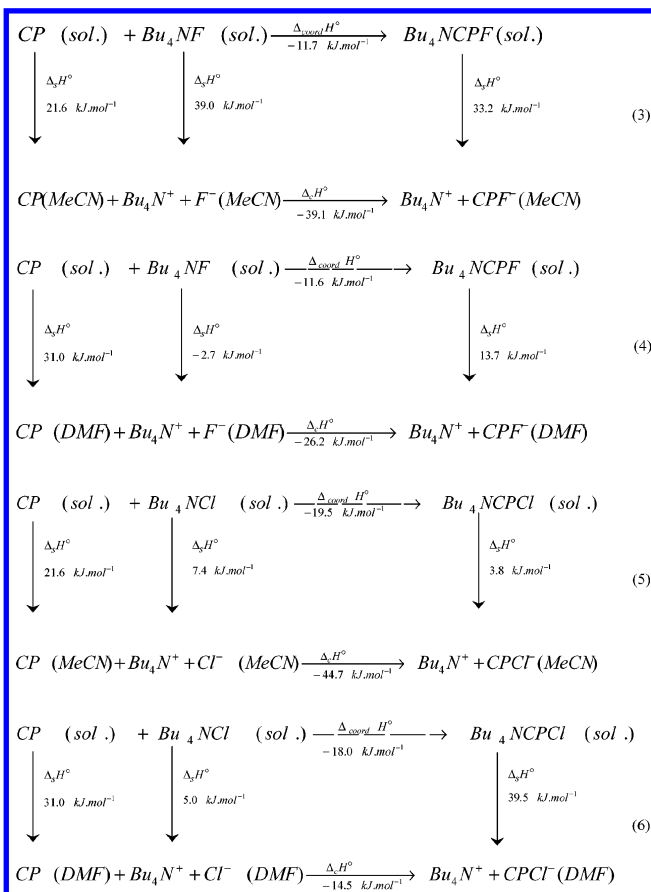
to the process where the reactants and the product are in the solid state (eq 2). All data are in kJ·mol⁻¹.

$$\Delta_{\text{coord}}H^\circ = \Delta_s H^\circ(\text{Bu}_4\text{N}^+\text{X}^-)(\text{s}) + \Delta_s H^\circ(\text{CP})(\text{s}) + \Delta_s H^\circ(\text{s}) - \Delta_s H^\circ(\text{Bu}_4\text{N}^+\text{CPX}^-)(\text{s}) \quad (2)$$

As previously stated, coordination data are useful parameters to check the accuracy of the complexation and solution enthalpies. Thus for a given system, $\Delta_{\text{coord}}P^\circ$ ($P^\circ = G^\circ, H^\circ, S^\circ$) should be the same independently of the solvent from which these data are derived.

We were unable to calculate the standard Gibbs energy of solution, $\Delta_s G^\circ$, of the halide complex salts from solubility measurements. Its calculation requires the same composition for the solid in equilibrium with the saturated solution. This is not the case for these salts because both undergo solvation when exposed to a saturated atmosphere of acetonitrile or *N,N*-dimethylformamide. As a result, the standard Gibbs energies of coordination for these systems could not be calculated.

As far as coordination enthalpies are concerned, eq 3 shows that for the fluoride system the value derived from acetonitrile ($\Delta_{\text{coord}}H^\circ = -11.7$ kJ·mol⁻¹) is in excellent agreement with



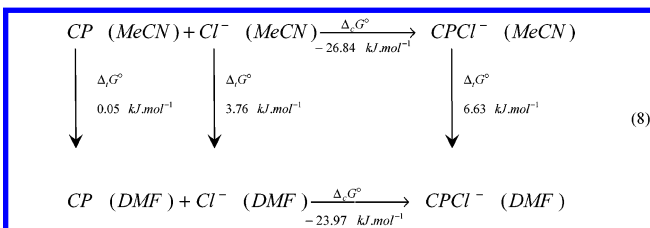
that calculated from *N,N*-dimethylformamide ($\Delta_{\text{coord}}H^\circ = -11.6$ kJ·mol⁻¹) (eq 4). The same conclusions are drawn for the chloride system. Indeed, good agreement is found from data obtained from acetonitrile ($\Delta_{\text{coord}}H^\circ = -19.5$ kJ·mol⁻¹) (eq 5) and *N,N*-dimethylformamide ($\Delta_{\text{coord}}H^\circ = -18.0$ kJ·mol⁻¹) (eq 6). While in solution, the thermodynamic data for ionic complexation should be independent of the counterion, this is not the case in the solid state, and this is reflected in the $\Delta_{\text{coord}}H^\circ$ for the fluoride relative to the chloride system. The slightly higher $\Delta_{\text{coord}}H^\circ$ of the chloride relative to the fluoride system can be explained in terms of the anion polarizability that is expected to be slightly greater for the calix[4]pyrrole–chloride complex than for the fluoride complex, and therefore the former is able to interact slightly better with the highly bulky organic cation.

Having checked the reliability of the enthalpy data reported in this paper, the effect of the medium on the complexation process is discussed.

The Medium Effect. Equation 7 shows that the medium effect upon complexation is controlled by the solvation properties of the reactants and the product in any two given solvents.

$$\Delta_c P^\circ(\text{s}_1) - \Delta_c P^\circ(\text{s}_2) = \Delta_t P^\circ(\text{CP})(\text{s}_1 \rightarrow \text{s}_2) + \Delta_t P^\circ(\text{X}^-)(\text{s}_1 \rightarrow \text{s}_2) - \Delta_t P^\circ(\text{CPX})(\text{s}_1 \rightarrow \text{s}_2) \quad (7)$$

Equation 7 is best illustrated through a thermodynamic cycle (eq 8). This is now discussed in terms of Gibbs energies using the chloride system as an illustrative example. Thus the



appropriate quantities [$\Delta_c G^\circ$ values from Table 3, $\Delta_t G^\circ(\text{CP})$ –(MeCN→DMF) from Table 1, $\Delta_t G^\circ(\text{Cl}^-)$ from the literature,²⁴ and $\Delta_t G^\circ(\text{CPCl})(\text{s} \rightarrow \text{s}_2)$ calculated via the cycle] are inserted in this cycle. The latter two $\Delta_t G^\circ$ values are based on the Ph₄AsPh₄B convention.

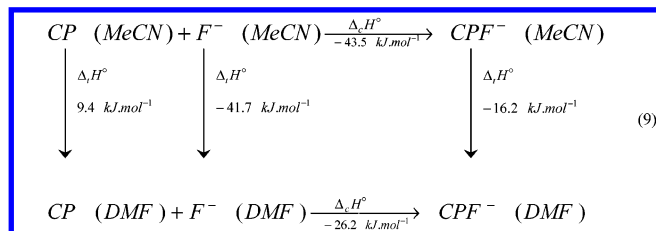
It is noteworthy that the similar $\Delta_c G^\circ$ values for this ligand and the chloride ions in acetonitrile and in *N,N*-dimethylformamide result from the rather small difference in the solvation properties of the reactants and the product in these two solvents. A similar situation is found with the fluoride anion and this ligand in these two solvents.

Equation 7 is now discussed in terms of enthalpy for both anions.

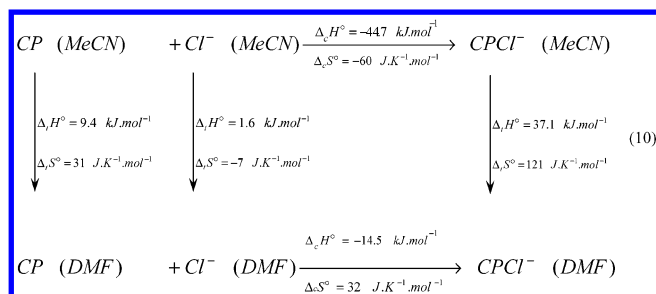
Thus for the fluoride system, $\Delta_c H^\circ$ values in MeCN and DMF are from Table 3, whereas the $\Delta_t H^\circ(\text{CP})(\text{MeCN} \rightarrow \text{DMF})$ was calculated from the enthalpies of solution of this ligand in these solvents (Table 4). As for the single ion $\Delta_t H^\circ$ values for the free and complex anions, these were calculated from the solution enthalpies for the salts given in Table 4. The $\Delta_t H^\circ$ value for the Bu₄N⁺ cation from MeCN to DMF based on the Ph₄AsPh₄B convention is that reported in the literature.²⁴ It should be noted that ΔH values for the entire cycle should be 0 kJ·mol⁻¹. However, the small variation observed is within the experimental error expected from the contribution of the various processes involved.

The result shows (see eq 9) that the higher enthalpic stability of the complexation process in MeCN relative to DMF is attributed to the favorable contribution of the free anion

overcoming those for the ligand and its complex (unfavorable for complexation in MeCN). Another interesting aspect of the data is the decrease in the enthalpic stability of the complex relative to the free anion in moving from MeCN to DMF. This observation could be explained in terms of the partial shielding of the anion by the ligand. It seems to correlate well with the X-ray crystallographic study on this complex, which shows that there is scope for the calix[4]pyrrole fluoride anion to interact with the solvent.²



As far as the chloride system is concerned (eq 10), the enthalpy values for the individual process are as follows, the $\Delta_c H^\circ(\text{Cl}^-)(\text{MeCN} \rightarrow \text{DMF})$ is that from the literature²⁴ whereas



that for the complex anion was calculated from the $\Delta_c H^\circ$ values of the appropriate salt in these solvents (Table 4) and the single ion $\Delta_c H^\circ$ value for the Bu_4N^+ cation from $\text{MeCN} \rightarrow \text{DMF}$.²⁴ These data are based on the $\text{Ph}_4\text{AsPh}_4\text{B}$ convention. The $\Delta_c H^\circ$ values in acetonitrile and *N,N*-dimethylformamide are those from Table 3.

The results in terms of enthalpy for this system sharply contrast with that for the fluoride system. Indeed, the highly enthalpic stability observed for the chloride–calix[4]pyrrole system in acetonitrile (although quite close to that of the fluoride system) is mainly attributed to the favorable contribution of the anionic complex given that, in this case, the contributions of both the ligand and the free anion (both unfavorable, see eq 7) are not significant.

In terms of entropy, the differences in the $\Delta_c S^\circ$ values of the chloride anion with this ligand in acetonitrile (unfavorable $\Delta_c S^\circ$) relative to *N,N*-dimethylformamide are again mainly attributed to the substantial gain in entropy of the anionic complex in moving from MeCN to DMF. It is indeed the magnitude of the entropy change for the transfer of the calix[4]pyrrole chloride complex that contributes to the entropically favorable complexation process observed in DMF relative to MeCN. It should be also noted that the favorable $\Delta_c S^\circ$ value of the complex anion from MeCN to DMF is in accord with those observed for hydrophobic ions in transfers involving these two solvents,²⁴ although for the latter ions, the $\Delta_c S^\circ$ are significantly lower.

Final Conclusions

We claim that this is the first detailed thermodynamic study on the calix[4]pyrrole–anion complexation process where every

step has been taken to ensure that the thermodynamic data are representative of the process taking place in solution.

From the above discussion we conclude the following:

(I) Calix[4]pyrrole is able to recognize selectively the halide anions in acetonitrile and *N,N*-dimethylformamide, as demonstrated by ¹H NMR, conductance measurements, and titration calorimetry. Thus a relationship has been found between the stability constants and the chemical shift changes of the pyrrole protons.

(II) The behavior of the ligand is typical of highly flexible ligands able to arrange themselves around the anion. In doing so, the ligand competes successfully with the solvent for the anion to an extent that the gain in binding energy is greater for the smallest anion. Thus, the stability constants follow the pattern observed for the transfer Gibbs energies of halide anions from a dipolar aprotic to a protic solvent in that the strength of hydrogen bond formation increase with an increase of the charge density of the anion.

(III) For a given anion, the strength of complexation with this ligand does not vary significantly in these two solvents. Therefore, the $\Delta_c G^\circ$ values are relatively close as a result of a considerable enthalpy–entropy compensation effect²⁵ in moving from acetonitrile to *N,N*-dimethylformamide.

(IV) The factors that contribute to the selective behavior of this ligand for the anion have been analyzed in terms of the solvation properties of reactants and product in these solvents.

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