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Recognition of Biologically and Environmentally Important Phosphate Anions by Calix[4]pyrrole: Thermodynamic Aspects

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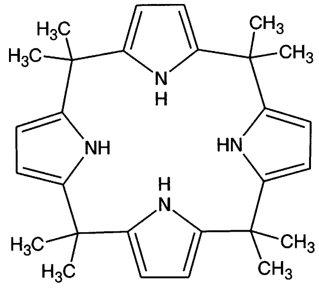
The complex formation of calix[4]pyrrole (**1**) and nonspherical anions in acetonitrile and *N,N*-dimethylformamide at 298.15 K has been investigated. ^{1}H NMR in CD_3CN at 298 K showed that, among the anions considered (dihydrogen phosphate, hydrogen pyrophosphate, dihydrogen pyrophosphate, hydrogen sulfate, perchlorate, nitrate, and trifluoromethane sulfonate), **1** interacts with $H_2PO_4^-$ and $HP_2O_7^{3-}$ in these solvents through hydrogen-bond formation. However, $H_2P_2O_7^{2-}$ is not sufficiently soluble in these solvents. Therefore, extraction experiments that were performed in the water:dichloromethane solvent system demonstrated that calix[4]pyrrole also interacts with this anion. Conductometric titrations were used to (i) determine the composition of the $H_2PO_4^-$ and $HP_2O_7^{3-}$ complexes with **1** and (ii) establish the concentration range at which the free and complex anion salts are predominantly in their ionic forms in acetonitrile and *N,N*-dimethylformamide. Titration microcalorimetry was used to determine the thermodynamics of complexation of these systems in these solvents. It is shown that, although **1** is able to form 1:1 (ligand:anion) complexes in acetonitrile and *N,N*-dimethylformamide, 2:1 complexes are formed with $H_2P_2O_7^{2-}$ in these solvents. The same complex stoichiometry is found for $H_2P_2O_7^{2-}$ and this ligand in water-saturated dichloromethane. The binding properties of the ligand for the $H_2PO_4^-$ are assessed in terms of the transfer thermodynamics of the reactants and the product from acetonitrile to *N,N*-dimethylformamide. Final conclusions are given.

1. Introduction

Anion recognition has been the subject of very interesting developments in the last two decades, with the synthesis of several macrocycles able to interact with these negatively charged species.[1,2] It was indeed the realization of the crucial role played by anions in biological systems that led to significant synthetic developments. As noted by Atwood and Steed,[3] a great percentage of enzyme substrates and co-factors are essentially anions. Within this context, phosphate residues are frequently found. Thus, the binding of proteins to phosphate and sulfate anions has been extensively studied. There is considerable crystallographic evidence that this interaction occurs through hydrogen-bond formation. Because of the amphiprotic character of hydrogen phosphate (HPO_4^{2-}) and dihydrogen phosphate ($H_2PO_4^-$) anions, they can behave as proton acceptors or donors. It has been shown that the (NH) groups of the protein have a significant contribution to anion coordination involving these amphiprotic anions. Besides the biological importance of phosphate anions is the fact that these are responsible for the eutrophication of rivers, which is due to the excessive use of fertilizers. Based on the aforementioned statements, it is important to consider the thermodynamics of anion complexation, including the characterization of the reactants and the product. The latter will allow establishment of the factors contributing to complexation in a given medium, relative to another. The selective recognition of spherical anions (fluoride, chloride, bromide) by calix[4]pyrrole in two dipolar aprotic solvents—namely, acetonitrile (MeCN) and *N,N*-dimethylformamide (DMF)—has been recently reported by us.[4] As far as nonspherical anions are concerned, research that has been conducted is limited to the complexation process involving the determination of stability constant data by ^{1}H NMR techniques in various solvents.[5−7] Also, the complexation of calix[4]pyrrole (**1**) with dihydrogen phosphate was investigated using titration calorimetry in acetonitrile at 30 °C.[8]



1 - Calix[4]pyrrole

This paper provides a detailed investigation not only on the ability of calix[4]pyrrole to recognize nonspherical anions such as dihydrogen phosphate ($H_2PO_4^-$), hydrogen pyrophosphate ($HP_2O_7^{3-}$), dihydrogen pyrophosphate ($H_2P_2O_7^{2-}$), hydrogen sulfate (HSO_4^-), perchlorate (ClO_4^-), nitrate (NO_3^-), and trifluoromethane sulfonate ($CF_3SO_3^-$) in MeCN and DMF but also on the solvation parameters of the reactants and the product (transfer Gibbs energy ($\Delta_t G°$), enthalpy ($\Delta_t H°$), and entropy ($\Delta_t S°$)) which control the complexation behavior of calix[4]pyrrole for a univalent anion ($H_2PO_4^-$) in one solvent, relative to another. Here, we report the following:

(1) ^{1}H NMR studies in CD_3CN, with the intent of investigating the presence of anion−ligand interactions and, if so, the active sites of the interaction of the macrocycle;

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(2) Conductometric studies to determine the complex composition in the appropriate solvent and the nature of the speciations present in these solvents;

(3) The thermodynamics of $H_2PO_4^-$ and $HP_2O_7^{3-}$ with calix[4]pyrrole in MeCN and DMF at 298.15 K;

(4) The extraction of $H_2P_2O_7^{2-}$ by calix[4]pyrrole in the water:dichloromethane solvent system; and

(5) The solution thermodynamics of the reactants and the product in MeCN and DMF.

These data are used to assess the effect of solvation of the participating species on the anion binding of calix[4]pyrrole in one medium, relative to another. Solution and transfer thermodynamics data are obtained only for monovalent anions, because of the complexity involved with multiple charged anions.

2. Experimental Section

2.1. Chemicals. Benzonitrile (99.9% HPLC grade, Aldrich Chemical Co.) was used without further purification. Acetonitrile[9] (HPLC grade, Fisher UK Scientific International) was refluxed in a nitrogen atmosphere and distilled over calcium hydride. The middle fraction was collected.

N,N-Dimethylformamide[9] (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. The water contents of the solvents, as analyzed via Karl Fisher titration, was not greater than 0.02%.

Dichloromethane (HPLC grade, Fisher UK Scientific International) was used without further purification. Deuterated acetonitrile (CD_3CN) and tetramethylsilane (TMS) were purchased from Aldrich Chemical Co.

Tetra-*n*-butylammonium dihydrogen phosphate, hydrogen sulfate, nitrate, perchlorate, trifluoromethanesulfonate (99%), tris(tetra-*n*-butylammonium)hydrogen pyrophosphate (99%), and sodium pyrophosphate dibasic (98%) were purchased from Aldrich Chemical Co. These were dried over P_4O_{10} under vacuum for several days before use.

Potassium chloride (KCl) (99%, Fisher UK Scientific International) was used without 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.[10]

2.2. Solubility Measurements. Saturated solutions of tetra-*n*-butylammonium dihydrogen phosphate were prepared by adding an excess amount of the solid to the solvent. The mixtures were left in a thermostat 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 performed. 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.[11] The samples were weighed from time to time to check for any uptake of solvent.

Solvate formation was checked for all the salts and $HP_2O_7^{3-}$ was observed to solvate in these solvents. $H_2P_2O_7^{2-}$ was determined to have very low solubility in the organic solvents investigated.

2.3. Conductance Measurements. *2.3.1. Conductometric Titrations of Dihydrogen Phosphate and Hydrogen Pyrophosphate Anions with Calix[4]pyrrole.* 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 anion as the tetra-*n*-butylammonium salt in the appropriate solvent (25 cm^3) and the conductance of the solution was measured. A known volume of solution of **1** in the same solvent then 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.

2.3.2. Conductance Measurements of the Dihydrogen Phosphate Anion Complex Salts. For these experiments, the conductivity cell was filled with the appropriate solvent (25 cm^3) and the conductance of the solvent was measured. The dihydrogen phosphate ($H_2PO_4^-$) 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.

2.4. Calorimetric Titrations. Enthalpies of complexation of calix[4]pyrrole with dihydrogen phosphate ($H_2PO_4^-$) and hydrogen pyrophosphate ($HP_2O_7^{3-}$) anions (with tetra-*n*-butylammonium as the counter ion) in the appropriate solvents were determined by titration microcalorimetry. The four-channel heat conduction microcalorimeter (Thermometric 2277) designed by Suurkuusk and Wadsö[12] was used. Electrical (static and dynamic) and chemical calibrations were performed to check the reliability of the equipment.[13]

The reaction vessel was charged with 2.8 cm^3 of the calix[4]pyrrole in acetonitrile. The phosphate anion (with tetra-*n*-butylammonium as the counter ion) was injected incrementally using a 0.5 cm^3 gas-tight motor-driven Hamilton syringe. In each titration experiment, ~20 injections were made at time intervals of 30−45 min. Correction for the enthalpy of dilution of the titrant in the solvent was performed. A computer program for TAM (Digitam 4.1 for Windows from Thermometric AB and Scitech Software AB, Sweden) was used to calculate the stability constant (log K_s) and the enthalpy of complexation ($\Delta_c H°$) for the process under study.

2.5. Extraction of $Na_2H_2P_2O_7$ in the Water−Dichloromethane Solvent System in the Presence of Calix[4]pyrrole at 298.15 K. The investigation of the interaction between calix[4]pyrrole and disodium dihydrogen pyrophosphate by conductometric and calorimetric techniques was not feasible, because of the low solubility of the salt in the organic solvents of interest (MeCN and DMF). Extraction experiments were conducted to show the ability of the ligand to interact with $H_2P_2O_7^{2-}$ and show the stoichiometry of this interaction.

For the distribution experiments in the absence of the ligand, a series of solutions containing different concentrations of $Na_2H_2P_2O_7$ (1.0×10^{-5}−1.0×10^{-4} mol dm^{-3}) in water (saturated with dichloromethane) were prepared. Known volumes (10 cm^3) of these solutions were mixed with equal volumes of dichloromethane (saturated with water) and shaken for a period of 15 min. The tubes were left in a thermostated bath at 298.15 K for a period of 24 h. After equilibrium was reached, the phases were separated and aliquots of the aqueous solution were analyzed for phosphate using UV−Vis spectrophotometry (Cecil model 8000).

Distribution experiments in the presence of the calixpyrrole were performed in a similar way; however, in this case, the concentration of $H_2P_2O_7^{2-}$ in the aqueous solution was kept constant (~1×10^{-4} mol dm^{-3}) whereas different concentrations of the ligand (2.2×10^{-3}−2.2×10^{-4} mol dm^{-3}) were used in the organic phase.

In all cases, distribution experiments and analysis of samples were performed in triplicate.

TABLE 1: ^{1}H NMR Chemical-Shift Changes Observed via the Addition of Nonspherical Anions to Calix[4]pyrrole at 298 K, Relative to the Free Ligand in CD_3CN at 298 K

proton	free ligand (ppm)	Δδ (ppm)					
		$H_2PO_4^-$	$HP_2O_7^{3-}$	HSO_4^-	NO_3^-	ClO_4^-	$CF_3SO_3^-$
N−H	7.40	3.80	4.47	1.26	1.94	0.03	0.01
Ar−H	5.80	−0.38	−0.30	−0.11	−0.16	−0.09	0.00
CH_3	1.48	0.15	0.15	0.04	0.06	0.00	0.00

2.6. Determination of Standard Enthalpies of Solution. Enthalpies of solution were performed 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 ($\Delta_s H^\circ = -29.4 \pm 0.2$ kJ/mol) is in good agreement with that given in the literature (−29.71 kJ/mol).[14,15]

For the determination of the standard enthalpy of solution of the free ligand, dihydrogen phosphate, and complex salts, glass ampules were filled with accurate amounts of the appropriate compound and sealed. These were then placed in a calorimetric vessel containing the appropriate solvent (50 cm^3). The system was placed in a thermostated bath until thermal equilibrium was reached. The ampules were broken, and the resulting temperature changes were recorded. An electrical calibration was performed after each experiment. The total heat was corrected for the heat associated with the breaking of empty glass ampules in the reaction vessel containing the solvent (50 cm^3). 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 dihydrogen phosphate complex, these experiments were performed in the presence of a small excess of the ligand in the reaction vessel, to ensure that no dissociation of the complex occurred during these measurements.

2.7. Preparation and Isolation of the Dihydrogen Phosphate Complex Using Tetra-*n*-butylammonium Salts as the Counterion. This was accomplished by mixing stoichiometric amounts of the calix[4]pyrrole and the salt in acetonitrile. The mixture was swirled until all reactants were dissolved; the mixture then was left until crystals appeared. Microanalysis was performed at the University of Surrey. Anal. Calcd for the salt, $C_{44}H_{74}N_5O_4P$: C, 68.81; H, 9.71; N, 9.1. Found: C, 68.52; H, 9.93; N, 8.91.

3. Results and Discussion

3.1. ^{1}H NMR Studies. Among the nonspherical anions considered, four of them are characterized by a tetrahedral shape ($H_2PO_4^-$, HSO_4^-, ClO_4^-, and $CF_3SO_3^-$), whereas the nitrate anion has a trigonal planar geometry. ^{1}H NMR studies in CD_3CN at 298 K (Table 1) show that, among these anions, significant chemical shift changes in the NH protons are observed via the addition of $H_2PO_4^-$ and $HP_2O_7^{3-}$ to the ligand in this solvent. The addition of increasing amounts of HSO_4^-, ClO_4^-, $CF_3SO_3^-$, and NO_3^- to **1** did not show any significant chemical-shift changes, relative to the free ligand in this solvent. In an attempt to corroborate the outcome of ^{1}H NMR measurements and establish the complex composition in the solvents investigated, we proceeded with conductometric studies, and these are discussed in the following section.

3.2. Conductometric Studies. *3.2.1. Conductometric Titrations.* These studies corroborated the ^{1}H NMR data in acetonitrile, in that the conductometric titration curve of tetra-*n*-butylammonium dihydrogen phosphate with **1** shows a significant break in both solvents (MeCN and DMF) at 1:1 (ligand:anion) stoichiometry. On the other hand, the conductometric titration curve of tris(tetra-*n*-butylammonium) hydrogen pyrophosphate with **1** shows a clear break in MeCN at 2:1 (ligand:anion) stoichiometry. In both solvents, the conductometric titration curves show the expected decrease in molar conductance in moving from the free to the complex anion. Note that, for $Bu_4NH_2PO_4$, the Λ_m values observed at zero ligand concentration in MeCN and DMF are within those expected for 1:1 electrolytes in these solvents,[16] whereas the Λ_m value for $(Bu_4N)_3HP_2O_7$ is that expected for 3:1 electrolytes in the appropriate solvent. No changes in the molar conductances were observed by the addition of **1** to tetra-*n*-butylammonium salts containing HSO_4^-, ClO_4^-, $CF_3SO_3^-$, and NO_3^- anions.

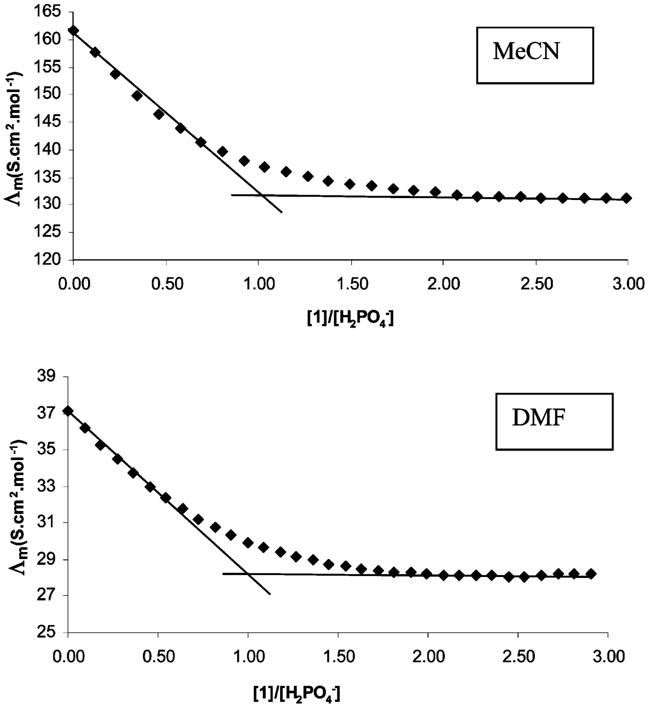

Figure 1. Conductometric curves for the titration of the dihydrogen phosphate anion (with tetra-*n*-butylammonium as the counter ion) with calix[4]pyrrole in acetonitrile and *N,N*-dimethylformamide at 298.15 K.

Unlike for halide anions, benzonitrile does not provide a complexation medium for $H_2PO_4^-$, as shown by the conductance data in this solvent. It seems that the ligand is unable to compete effectively with the solvent for the anion and, therefore, no complexation occurs. Conductance measurements were also performed in an attempt to assess the nature of the speciations in solution, and these are now discussed.

3.2.2. Conductance Measurements as a Function of the Ionic Strength of the Free and Complex Salts. To ensure that ions rather than ion pairs are the predominant species for both, the free and complex dihydrogen phosphate salts (with tetra-*n*-butylammonium as the counter ion) in MeCN and DMF, conductance measurements at different concentrations were performed at 298.15 K.

Figures 1−4 show the molar conductances of these electrolytes versus the square root of the ionic strength. The linear behavior observed provides an indication that the ionic species

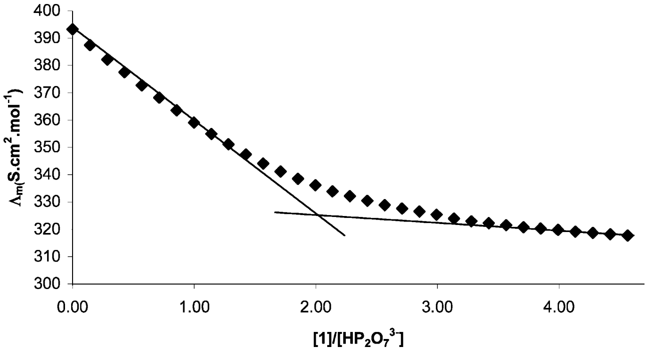

Figure 2. Conductometric curve for the titration of hydrogen pyrophosphate anion (with tetra-*n*-butylammonium as the counter ion) with calix[4]pyrrole in acetonitrile at 298.15 K.

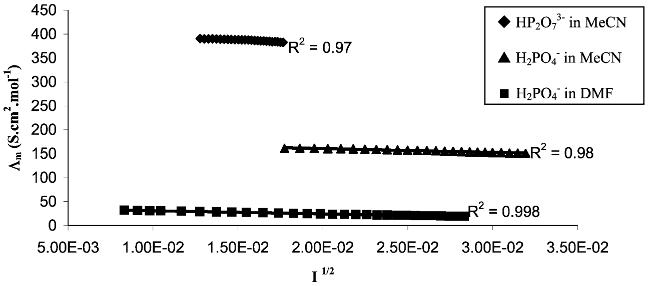

Figure 3. Molar conductances (in units of S cm^2 mol^{-1}) of $H_2PO_4^-$ and $HP_2O_7^{3-}$, as a function of the square root of ionic strength in acetonitrile and *N*,*N*-dimethylformamide at 298.15 K.

predominate in solution. The same procedure was applied for the tris(tetra-*n*-butylammonium) pyrophosphate in MeCN at 298.15 K.

Having established (i) the complex composition and (ii) that ions are predominantly in solution, in the working range of concentrations, we proceeded with the thermodynamics of complexation of **1** with $H_2PO_4^-$ and $HP_2O_7^{3-}$ in MeCN and DMF at 298.15 K, and this is now discussed.

3.3. Thermodynamics of Complexation. Titration microcalorimetry was the technique used to determine the stability constant (expressed as log K_s) and the enthalpy of complexation ($\Delta_c H°$) of **1** with $H_2PO_4^-$ and $HP_2O_7^{3-}$ in MeCN and DMF at 298.15 K. These data, together with the Gibbs energy ($\Delta_c G°$) and entropy ($\Delta_c S°$) for the processes described in eqs 1a and 1b are shown in Tables 2a and 2b, respectively.

$$H_2PO_4^-(s) + \mathbf{1}(s) \rightarrow \mathbf{1}H_2PO_4^-(s) \tag{1a}$$

$$HP_2O_7^{3-}(s) + 2[\mathbf{1}](s) \rightarrow \mathbf{1}_2{-}HP_2O_7^{3-}(s) \tag{1b}$$

The standard deviation of the data are also included in these tables. As far as the stability of the complex of $H_2PO_4^-$ and **1** in these two solvents is concerned, similar values are observed, as inferred in the log K_s values and derived standard Gibbs energies ($\Delta_c G°$). However, in acetonitrile, the process is enthalpically controlled, whereas in *N*,*N*-dimethylformamide, both the enthalpy and entropy contribute favorably to complex stability.

In summary, in moving from acetonitrile to *N*,*N*-dimethylformamide, there is an enthalpy–entropy compensation[18] effect. Comparison of log K_s values with those previously reported for halide anions in these solvents [4] clearly shows the selective recognition of this ligand for anions. Thus, the following sequence is observed:

$$F^- > H_2PO_4^- > Cl^- > Br^-$$

TABLE 2: Thermodynamic Parameters of Complexation of (a) 1 and Dihydrogen Phosphate and (b) 1 and Hydrogen Pyrophosphate (Each with Tetra-*n*-butylammonium as the Counter Ion) in Acetonitrile and *N*,*N*-Dimethylformamide at 298.15 K[a]

(a) **1** and Dihydrogen Phosphate

$H_2PO_4^-$	log K_s	$\Delta_c G°$ (kJ/mol)	$\Delta_c H°$ (kJ/mol)	$\Delta_c S°$ (J K^{-1} mol^{-1})
MeCN	5.00 ± 0.08	−28.5 ± 0.5	−48.1 ± 0.1	−66
DMF	4.8 ± 0.1	−27.4 ± 0.6	−18.8 ± 0.3	29

(b) **1** and Hydrogen Pyrophosphate

$HP_2O_7^{3-}$ (ligand:anion)		log K_s	$\Delta_c G°$ (kJ/mol)	$\Delta_c H°$ (kJ/mol)	$\Delta_c S°$ (J K^{-1} mol^{-1})
MeCN	1:1	4.17 ± 0.02	−23.8 ± 0.1	−89.5 ± 0.1	−220
	2:1	4.44 ± 0.02	−25.3 ± 0.1	−184.2 ± 0.2	−533
DMF	1:1	4.08 ± 0.02	−23.3 ± 0.1	−22.95 ± 0.03	+1
	2:1	5.04 ± 0.07	−28.8 ± 0.4	−39.91 ± 0.07	−37

[a] MeCN = acetonitrile; DMF = *N*,*N*-dimethylformamide.

As far as enthalpies and entropies of complexation are concerned, note that a basic, protophilic dipolar aprotic solvent such as DMF is likely to interact more strongly with $H_2PO_4^-$ than acetonitrile. Unlike the halide anions, $H_2PO_4^-$ can behave as a proton donor anion. Therefore, $H_2PO_4^-$ is expected to be more solvated in DMF than the halides. Anion desolvation upon complexation will lead to a decrease in enthalpic stability and an entropy increase. This is indeed reflected in the data shown in Table 2a.

To corroborate this statement, the transfer thermodynamics of reactants and product is investigated. These data are derived from standard Gibbs energies ($\Delta_s G°$), enthalpies ($\Delta_s H°$), and entropies ($\Delta_s S°$) of solution of the free and complex anion salts and the ligand in DMF and MeCN, and these are discussed later in this paper.

The behavior of **1** with $HP_2O_7^{3-}$ in MeCN and DMF at 298.15 K (see Table 2b) is striking. In both solvents under investigation, two calixpyrrole molecules are complexing with one unit of pyrophosphate, and the data obtained in each solvent are now discussed.

3.3.1. In Acetonitrile. The thermodynamic data listed in Table 2b show that, upon titration of the anion into the microcalorimetric vessel containing an excess of the ligand, the reaction proceeds by the complexation of one molecule of the anion, taking up two molecules of the ligand simultaneously, because the hydrogen pyrophosphate is a symmetrical diphosphate molecule with a monovalent negative charge on one side and a bivalent charge on the other. Upon addition of an excess volume of the anion, the 2:1 (ligand:anion) complex seems to release one of the two ligand molecules that is already associated with the monovalent side of the anion to complex with the excess free anion that has a free bivalent site. This is clearly reflected in the enthalpy values obtained where the value for the 2:1 (ligand:anion) process is approximately twice the value for the 1:1 (ligand:anion) process. This finding explains the lower loss in entropy in the 1:1 process, relative to the 2:1 (ligand:anion) process. It is indeed the higher enthalpic stability of the ligand for the bivalent side of the anion that induces one unit of the ligand from the 2:1 complex. As a result, a higher degree of disorder in the system is produced, as reflected in the entropy increase observed in moving from the 2:1 complex to the 1:1 complex.

3.3.2. In N,N-Dimethylformamide. The complexation process in *N*,*N*-dimethylformamide proceeds in a fashion similar to that in acetonitrile, as far as enthalpy and entropy are concerned, in

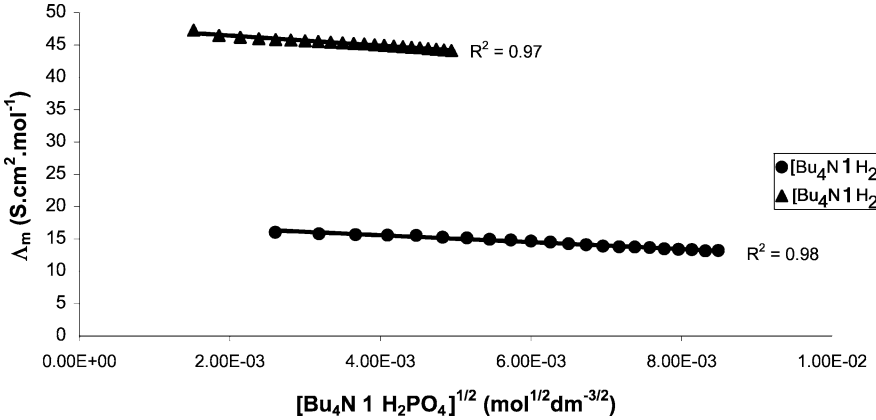

Figure 4. Molar conductances (in units of S cm^2 mol^{-1}) of $Bu_4NH_2PO_4^-$ (**1**) complex as a function of the square root of molar concentrations in acetonitrile and *N,N*-dimethylformamide at 298.15 K.

that (i) the enthalpy value for the formation of the 2:1 complex is much higher than that for the 1:1 complex and (ii) there is an entropy loss in moving from the 1:1 complex to the 2:1 complex. However, the enthalpic stability and the loss in entropy in *N,N*-dimethylformamide is much lower than that in acetonitrile. This may be attributed to the higher solvation of the ligand in this solvent. Indeed, crystallographic evidence of this ligand has shown that DMF interacts with the ligand through hydrogen bond formation with the pyrrolic (NH) protons.[5] On the other hand, the (OH) group in the $P_2O_7^{3-}$ anion may act as a proton donor in a protophilic aprotic solvent such as DMF. Desolvation of the ligand or the anion or both will lead to a decrease in the enthalpic stability and an increase in entropy in this solvent, relative to acetonitrile, as shown in the thermodynamic data in the former solvent, relative to the latter solvent.

3.3.3. Charge Effect. Comparison of thermodynamic data for the monovalent anion, relative to the trivalent anion, reflects the charge effect in moving from $H_2PO_4^-$ to $HP_2O_7^{3-}$, particularly in acetonitrile. Indeed, the $\Delta_cH°$ value for $H_2PO_4^-$ is almost half of the $HP_2O_7^{3-}$ for the formation of the 1:1 complex. However, the complex stability of the monovalent anion and **1** in MeCN is higher than that of the trivalent anion and this ligand. This is attributed to the much higher entropy loss of the latter, relative to the former, in this solvent.

In *N,N*-dimethylformamide, the gain in entropy upon complexation of **1** with $H_2PO_4^-$, relative to $HP_2O_7^{3-}$, overcomes the higher enthalpic stability of the latter anion and this ligand. As a result, 1:1 complexes between this ligand and the monovalent anion are more stable than those involving the trivalent anion in these solvents.

Because of the limited solubility of $H_2P_2O_7^{2-}$ in these solvents, we were unable to proceed with the thermodynamic characterization of the binding process involving this anion and **1** in these media. Therefore, we perform distribution experiments in the water–dichloromethane solvent system to determine whether interaction between **1** and the bivalent anion occurs and, if it does occur, the composition of the complex formed. Those are now discussed.

3.4. Extraction Data. Figure 5 shows the extraction percentages of extraction of $H_2P_2O_7^{2-}$ from the aqueous phase to dichloromethane (both phases are mutually saturated) in the presence of calix[4]pyrrole against the ligand:anion ratio. The pronounced break observed at $[CP]/[H_2P_2O_7^{2-}] = 2$ clearly demonstrate that, similar to the $HP_2O_7^{3-}$ anion, two units of **1** are interacting with the bivalent anion in the water-saturated organic phase. The shape of the extraction curve is well-defined, and this finding is indicative that the interaction of **1** and this anion is relatively strong.

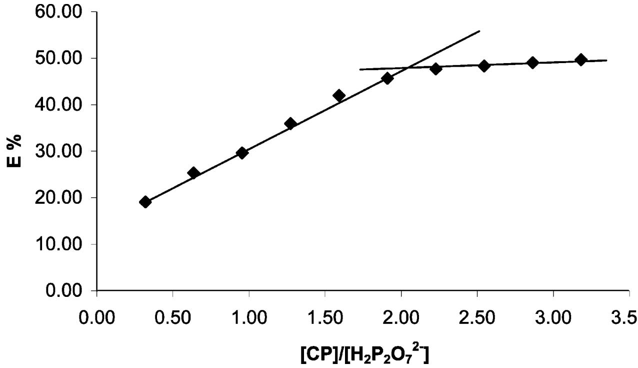

Figure 5. Percentages of $H_2P_2O_7^{3-}$ extracted by **1** in dichloromethane (saturated with water) as a function of the ligand:anion concentration ratios at 298.15 K.

3.5. Solution and Transfer Thermodynamics of Reactants and Product. We have previously reported[4] the $\Delta_tG°$ value for **1** from acetonitrile to DMF. This value was calculated from the $\Delta_sG°$ value of this ligand in both solvents through solubility measurements. Given that tetra-*n*-butylammonium dihydrogen phosphate and its complex salt, tetra-*n*-butylammonium calix[4]pyrrole dihydrogen phosphate salts, in MeCN and DMF are predominantly in their ionic forms, the thermodynamic solubility product (eq 2) was calculated directly from solubility data and the mean molar activity coefficient (eq 3). lacking a better approximation, the latter was calculated through the extended Debye–Hückel equation. Solubility data referenced in the process described by eqs 4 and 5 are listed in Table 3.

$$K_{sp}^{o} = [Bu_4N^+][H_2PO_4^-]\mathscr{P}_{\pm}^{\,2} \tag{2}$$

$$\log \mathscr{P}_{\pm} = \frac{-Az_+z_-\sqrt{I}}{1 + a°B\sqrt{I}} \tag{3}$$

$$Bu_4NH_2PO_4(sol) \rightarrow Bu_4N^+(s) + H_2PO_4^-(s) \tag{4}$$

$$Bu_4N\mathbf{1}H_2PO_4(sol) \rightarrow Bu_4N^+(s) + \mathbf{1}H_2PO_4^-(s) \tag{5}$$

The thermodynamic solubility product is referenced to the standard state of 1 mol dm^{-3} for the reactants and the product. The corresponding standard Gibbs energy of solution ($\Delta_sG°$) for these dissociated electrolytes in MeCN and DMF at 298.15 K are shown in Table 3. Taking MeCN as the reference solvent, the $\Delta_tG°$ value of Bu_4N^+ (MeCN → DMF), based on the Ph_4AsPh_4B convention[17] (−3.35 kJ/mol), is used to derive the single

TABLE 3: Thermodynamic Solubility Product of Tetra-*n*-butylammonium Dihydrogen Phosphate in Acetonitrile and *N,N*-Dimethylformamide and Derived Standard Gibbs Energies of Solution ($\Delta_sG°$) and Transfer ($\Delta_tG°$) from Acetonitrile to *N,N*-Dimethylformamide at 298.15 K

				MeCN → DMF	
solvent[a]	solubility (mol dm^{-3})	K_{sp}	$\Delta_sG°$ (kJ/mol) [$Bu_4NH_2PO_4$]	$\Delta_tG°$ (kJ/mol) [$Bu_4NH_2PO_4$]	$\Delta_tG°$ (kJ/mol) [$H_2PO_4^-$][b]
MeCN	$2.74 \times 10^{-1} \pm 0.01 \times 10^{-1}$	1.58×10^{-2}	+10.28	0.00	0.00
DMF	$1.32 \times 10^{-1} \pm 0.01 \times 10^{-1}$	4.67×10^{-3}	+13.30	+3.02	−1.58

[a] Abbreviations used: MeCN = acetonitrile; DMF = *N,N*-dimethylformamide. [b] Data based on the Ph_4AsPh_4B convention at 298.15 K.

TABLE 4: Enthalpies and Entropies of Solution of Calix[4]pyrrole and Its Dihydrogen Phosphate Complex Salt (with Tetra-*n*-butylammonium as the Counter Ion) in Acetonitrile and *N,N*-Dimethylformamide at 298.15 K

	$\Delta_sH°$ (kJ/mol)		MeCN → DMF	
	acetonitrile	*N,N*-dimethyl-formamide	$\Delta_tH°$ (kJ/mol)	$\Delta_tS°$ (J mol^{-1} K^{-1})
1	21.6 ± 0.7[a]	31 ± 1[a]	9.4[a]	31[a]
$Bu_4NH_2PO_4$	33.3 ± 0.6[c]	9.0 ± 0.5[c]	−24.2	−76
Bu_4N **1** H_2PO_4	14.0 ± 0.4[c]	28.6 ± 0.2[c]	14.6	50

[a] From ref 4. [b] Extrapolated value at $c = 0$. [c] Average of several measurements.

ion $\Delta_tG°$ value for $H_2PO_4^-$. The derivation of $\Delta_sG°$ values requires that the composition of the solid is the same as that in the saturated solution. This is not the case for the complex salt. Indeed, exposure of this salt to a saturated atmosphere of these solvents shows that, in both solvents, the complex salt undergoes solvation; therefore, the $\Delta_tG°$ value for the complex cation was calculated via eq 6.

$$\Delta_cG°(\mathrm{MeCN}) - \Delta_cG°(\mathrm{DMF}) = \Delta_tG°(\mathbf{1})(\mathrm{MeCN} \rightarrow \mathrm{DMF}) + \Delta_tG°(\mathrm{H_2PO_4}^-)(\mathrm{MeCN} \rightarrow \mathrm{DMF}) - \Delta_tG°(\mathbf{1}\mathrm{H_2PO_4}^-)(\mathrm{MeCN} \rightarrow \mathrm{DMF}) \quad (6)$$

In an attempt to analyze the factors that contribute to the similar stabilities of complex formation in these solvents, as reflected in the $\Delta_cG°$ values, ΔG values are inserted in the following thermodynamic cycle (eq 7).

$$\begin{tikzcd}
\underline{1}\ (MeCN) \arrow[d, "\Delta_tG° \ 0.05\ kJ.mol^{-1}"] & + H_2PO_4^-\ (MeCN) \arrow[r, "\Delta_cG°", "-28.5\ kJ.mol^{-1}"'] \arrow[d, "\Delta_tG° \ -1.58\ kJ.mol^{-1}"] & \underline{1}-H_2PO_4^-\ (MeCN) \arrow[d, "\Delta_tG° \ -0.43\ kJ.mol^{-1}"] \\
\underline{1}\ (DMF) & + H_2PO_4^-\ (DMF) \arrow[r, "\Delta_cG°", "-27.4\ kJ.mol^{-1}"'] & \underline{1}-H_2PO_4^-\ (DMF)
\end{tikzcd} \quad (7)$$

The individual parameters of transfer show that the slightly higher solvation of the anion in DMF, relative to that in MeCN, is compensated by the $\Delta_tG°$ of the complex anion from DMF to MeCN and, therefore, taking into account eq 6, it follows that the extent of solvation of the reactants and the product in these solvents is approximately the same. As a result, hardly any change is observed in the stability of the complex by altering the medium from MeCN to DMF.

3.6. Enthalpies and Entropies of Transfer. Calorimetry was the technique used to determine the standard enthalpies of solution ($\Delta_sH°$) of Bu_4N H_2PO_4 and Bu_4N **1** H_2PO_4 in MeCN and DMF at 298.15 K, and these data are also included in Table 4. These are the result of enthalpies of solution measured at different concentrations. The standard enthalpy of solution for these dissociated electrolytes in these solvents is the intercept at $c = 0$ of a plot of solution enthalpy against the square root of the ionic strength of the solution. Combination of $\Delta_sH°$ values for each electrolyte in these solvents led to the calculation of their standard enthalpy of transfer from MeCN to DMF. Taking the $\Delta_tH°$ value of Bu_4N^+ from MeCN to DMF, based on the Ph_4AsPh_4B convention[17] at 298.15 K, the single-ion $\Delta_tH°$ values for $H_2PO_4^-$ and **1** $H_2PO_4^-$ from MeCN to DMF were calculated, as shown in Table 4. By inserting the appropriate $\Delta_cH°$ values in MeCN and DMF (Table 2) and $\Delta_tH°$ values for the ligand, $H_2PO_4^-$, and **1**−$H_2PO_4^-$ from MeCN to DMF (Table 4) in the thermodynamic cycle (eq 8), the factors that contribute to the higher enthalpic stability of complex formation in MeCN, relative to DMF, can be clearly elucidated.

$$\begin{tikzcd}
\underline{1}\ (MeCN) \arrow[d, "\Delta_tH° = 9.4\ kJ.mol^{-1} \ \Delta_tS° = 31\ J.mol^{-1}.K^{-1}"] & + H_2PO_4^-\ (MeCN) \arrow[r, "\Delta_cH° = -48.1 kJ.mol^{-1}", "\Delta_cS° = -66\ J.mol^{-1}.K^{-1}"'] \arrow[d, "\Delta_tH° = -24.2\ kJ.mol^{-1} \ \Delta_tS° = -76\ J.mol^{-1}.K^{-1}"] & \underline{1}-H_2PO_4^-\ (MeCN) \arrow[d, "\Delta_tH° = +14.6\ kJ.mol^{-1} \ \Delta_tS° = 50\ J.mol^{-1}.K^{-1}"] \\
\underline{1}\ (DMF) & + H_2PO_4^-\ (DMF) \arrow[r, "\Delta_cH° = -18.8 kJ.mol^{-1}", "\Delta_cS° = 29\ J.mol^{-1}.K^{-1}"'] & \underline{1}-H_2PO_4^-\ (DMF)
\end{tikzcd} \quad \text{(eqn. 8)}$$

The data in the cycle show that both the ligand and its complex are enthalpically more stable in MeCN than in DMF. The opposite is true for the free anion, thus corroborating the statement made previously in that $H_2PO_4^-$ behaves as a proton donor species in a protophilic aprotic solvent such as DMF.

Taking into account eq 6, expressed in terms of enthalpies, it follows that the higher enthalpic stability associated with the complexation of $H_2PO_4^-$ and **1** in MeCN is mainly attributed to the $\Delta_tH°$ of this anion from MeCN to DMF. Considering that binding (exothermic) and desolvation (endothermic) are the two processes that predominantly contribute to the $\Delta_cH°$ values, the higher energy input required to desolvate the anion (partially or totally) from DMF will reduce the stability (in enthalpic terms) in this solvent, relative to MeCN, as shown in the thermodynamic cycle (eq 8).

Combination of Gibbs energy and enthalpy data allows the calculation of the transfer entropies of the reactants and the product from MeCN to DMF, and these are shown in the aforementioned cycle. Complexation entropies in MeCN and DMF are those from Table 2.

Entropy data corroborate the aforementioned discussion, in terms of enthalpy, in that the higher enthalpic stability of the ligand and the complex in MeCN, relative to DMF, is accompanied by a gain in entropy for these species in their transfer to the latter medium. On the other hand, the entropy loss observed for the free anion is in accord with the suggestion that solvent−anion interactions are greater in DMF than in MeCN. Taking into account eq 6, it follows that the unfavorable entropy (negative $\Delta_cS°$ value) in MeCN, relative to that in DMF (entropically favorable), upon complexation of **1** with $H_2PO_4^-$ results from the entropic contribution for the transfer of both the free anion (MeCN → DMF) and the complex (DMF → MeCN), which overcomes that of the ligand to DMF.

Conclusions

From the above discussion, we conclude the following:

(1) Among the nonspherical anions investigated, calix[4]pyrrole is able to interact with $H_2PO_4^-$ and $HP_2O_7^{3-}$ in MeCN and DMF. The stoichiometry of the complexes with $H_2PO_4^-$, as revealed by conductance and calorimetric measurements, is 1:1 (ligand:anion), whereas that for $HP_2O_7^{3-}$ is 2:1 (ligand: anion). The same stoichiometry was also observed for $H_2P_2O_7^{2-}$ and **1** from extraction experiments in the water:dichloromethane solvent system.

(2) The selective behavior of this ligand for halides is now extended to nonsphericals anions, and this is, for the first time, quantitatively demonstrated.

(3) The thermodynamics of complexation of the $H_2PO_4^-$ and $HP_2O_7^{3-}$−**1** systems have been reported for the first time in acetonitrile and in *N*,*N*-dimethylformamide. The interaction between the monovalent anion and **1** has been interpreted in terms of the differences in solvation of the reactants and the product in these media. The results obtained demonstrate the role of solvation in complexation processes involving macrocycles and guest species.

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