Modified Calix[4]pyrrole Receptor: Solution Thermodynamics of Anion Complexation and a Prelimenary Account on the Phosphate Extraction Ability of its Oligomer

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A modified calix[4]pyrrole, namely meso-tetramethyl-tetrakis-(4-hydroxyphenyl) calix[4]pyrrole, **1**, has been synthesized and characterized. ^{1}H NMR investigations in various deuterated solvents seems to indicate that this receptor interacts with acetone-d_6. The solution thermodynamics of **1** in various solvents is reported. Complexation studies in CD_3CN show that the NH and OH functionalities of **1** are the active sites of its interaction with the fluoride and the dihydrogen phosphate anions. The composition of the anion complexes was established through conductance measurements. In all cases, 1:1 complexes are formed. The thermodynamics of anion complexation in acetonitrile and *N*,*N*-dimethylformamide is discussed comparatively with previous reported data for the parent calix[4]pyrrole, **2**, and these anions in these solvents. The medium effect on anion complexation is discussed in terms of the solvation properties of the reactants and the product in acetonitrile and *N*,*N*-dimethylformamide. An oligomeric material containing **1** as anchor group was synthesized and characterized by mass spectrometry. Preliminary studies have been performed to assess the extracting properties of this oligomer for the removal of phosphates from aqueous solutions. The effects of pH, temperature on the extraction of this anion salt from water, as well as the kinetics of the process (fast) were investigated.

Introduction

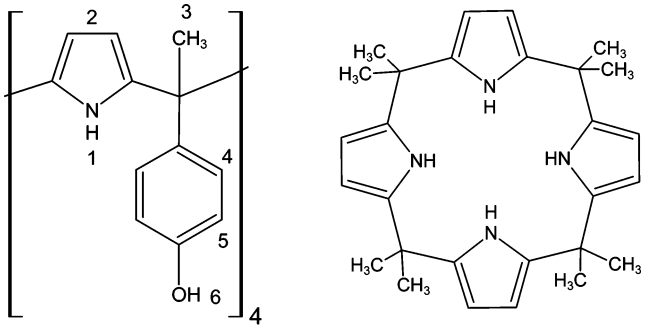
Calix[4]pyrroles are a class of hetero-calixarene analogues obtained as products of the condensation reaction of pyrrole and acetone in acidic medium.[1] These macrocycles have attracted much interest in recent years due to their easy synthesis and the wide range of applications[2−4] The thermodynamics of anion complexation of several calixpyrrole derivatives in nonaqueous media has been previously discussed by us.[5−7] Calix[4]pyrrole has three potential sites (the C-rim, the N-rim, and the meso-position) which can be used for the introduction of different functionalities.[8,9] In addition, the replacement of pyrrole by thiophene units has led to a series of calixthio[4]-pyrrole derivatives able to enter selective interaction with cations.[10,11] Detailed investigations on the thermodynamics of these systems have been reported recently.[10,11] The applications of calixpyrroles are versatile ranging from the attachment of these macrocycles to silica for anion extraction purposes to the most recent studies on the use of these macrocycles for the development of fluorescence and optical sensors.[12,13]

Based on Blasius and co-workers investigations[14] on the production of crown ether based resins obtained from the condensation of dibenzo-18-crown-6 and formaldehyde in formic acid, extensive studies were carried out by Danil de Namor and Sigstad[15] on the extraction of cations from water by these resins. A similar procedure for the preparation of calix-[4]pyrrole based resins was applied almost simultaneously by our group[16] and Kaledkowski and co-workers.[17]

In this paper, we report a detailed thermodynamic study on a calix[4]pyrrole derivative, namely, meso-tetramethyl-tetrakis-(4-hydroxyphenyl)calix[4]pyrrole, **1**, that resembles the calix-[4]arene. Thus the aim of this investigation is as follows:

(i) To compare these findings with those previously reported for calix[4]pyrrole, **2**, in order to build up a profile and thus gain information about the behavior of **1** in solution.

(ii) To proceed with the synthesis of a calix[4]pyrrole based resin and to assess its capacity to remove the phosphate anion from aqueous solutions.



1 **2**

Experimental Section

Chemicals. Pyrrole (99%), 4-hydroxyacetophenone, tetra-*n*-butylammonium hydroxide (15% in methanol), and methanesulfonic acid (99%) were all purchased from Aldrich Chemical Co.

Tetrahydrofuran, ethanol, methanol, and acetone (HPLC grade, Fisher) were used without further purification. Acetonitrile, MeCN (Aldrich), and dimethylsulphoxide (DMSO, Aldrich) were first refluxed in a nitrogen atmosphere with calcium hydride for several hours and then distilled.[18] *N*,*N*-Dimethylformamide (DMF; HPLC grade, Fisher U.K. Scientific International) was dried over 3 Å molecular sieves and subsequently distilled under reduced pressure. The middle fraction was

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collected.[18] Tetra-*n*-butylammonium halides (fluoride, chloride, bromide, and iodide), hydrogen sulfate, and dihydrogen phosphate (Aldrich) were dried over P_4O_{10} under vacuum for several days before use. The absence of a signal from the residual water in the ^{1}H NMR spectra of **1** with the anions in acetonitrile (CD_3CN) provided an indication that the anion salts used were anhydrous. Deuterated acetonitrile (CD_3CN), methanol (CD_3OD), acetone (d_6-acetone), and dimethylsulphoxide (d_6-DMSO) were purchased from Aldrich.

Synthesis of Meso-tetramethyl-tetrakis-(4-hydroxyphenyl) calix[4]pyrrole, 1. The preparation of this derivative was achieved by modifying the procedure reported in the literature.[19,20] Thus, pyrrole (5 g, 75 mmol) was placed in a 250 mL round-bottom flask equipped with a magnetic stirrer and filled with methanol (100 mL). Methanesulfonic acid (1 mL) was then added to the mixture and stirred for 30 min. This was followed by the stepwise addition of a solution of *p*-hydroxyacetophenone (11 g, 80 mmol) in methanol (50 mL). The reaction mixture was monitored by TLC using dichloromethane:methanol (9.5:0.5) as the developing solvent and was left to stir overnight. It was then stopped by pouring the reaction mixture into distilled water (200 mL). An orange colored precipitate was obtained. The residue was filtered off and collected and then dissolved in diethyl ether (400 mL). The solution was filtered gravitationally to remove the black tar obtained. This was recrystallized from acetic acid and left to cool. Green crystals containing the αααα isomer of the calixpyrrole derivative, **1**, were obtained complexed with acetic acid. The acid was removed by further recrystallization with an acetonitrile:acetone mixture. White crystals in 65% yield were obtained. These were dried under vacuum at 90 °C. ^{1}H NMR (d_6-acetone, 300 MHz, 298 K, δ in ppm); 8.75 (s broad, 4H, NH); 8.22 (s, 4H, OH); 6.78 (d, 8H, ArH; $J = 9.3$ Hz); 6.66 (d, 8H, ArH, $J = 9.0$ Hz); 5.96 (d, 8H, PyH, $J = 2.7$ Hz); 1.81 (s, 12 H, CH_3).

Elemental analysis was carried out at the University of Surrey; Calculated % : C, 77.81; H, 5.99; N, 7.56; Found %: C, 77.60; H, 5.94; N ,7.51.

Synthesis of the Meso-tetramethyl-tetrakis-(4-hydroxyphenyl)-calix[4]pyrrole tetra-*n*-butylammonium fluoride (Bu_4N1F) and Di-hydrogen Phosphate ($Bu_4N1H_2PO_4$) Complexes. The preparation of these complexes were accomplished by mixing stochiometric amounts of the calix[4]pyrrole and the appropriate anion salt in acetonitrile. The mixture was swirled until all reactants were dissolved. Then the mixture was left overnight until crystals appeared.

Microanalysis was carried out at the University of Surrey; Bu_4N**1**F complex; $C_{48}H_{80}O_4N_4.C_{16}H_{36}FN$ Calculated % : C, 76.69; H, 8.04; N, 6.99. Found %: C, 76.33; H, 8.03; N, 6.90.

Bu_4N**1**H_2PO_4 complex; $C_{48}H_{80}O_4N_4.C_{16}H_{38}PO_4N$ Calculated %: C, 71.15; H, 7.68; N, 6.48. Found %: C, 70.99; H, 7.63; N, 6.40.

Preparation of Meso-tetramethyl-tetrakis-(4-hydroxyphenyl)-calix[4]pyrrole oligomer, R_1. The base-catalyzed phenol-formaldehyde procedure was used in the preparation of the calixpyrrole oligomeric material. Thus, meso-tetramethyl-tetrakis-(4-hydroxyphenyl) calix[4]pyrrole, **1**, (5 g, 6.75 mmol) was placed in a 250 mL round-bottom flask and dissolved with THF (100 mL). Formaldehyde (6.5 mL, 80.98 mmol) and tetra-*n*-butylammonium hydroxide (15% in methanol) were then added. The reaction mixture was left overnight under continuous stirring. The white precipitate obtained was collected, washed with THF, and dried under vacuum. The material was characterized by mass spectroscopy. The residual peaks found at *m*/*z* ratio between 2600 and 2800 indicate the formation of an oligomer (R_1) which is at least three times the molecular weight of the monomer, **1**.

Solubility Measurements. Solubility data were obtained in solvents in which the anion salts are predominantly as ionic species in solution as previously established.[5,6] Thus, these data are required to proceed with the experimental work on anion complexation studies as well as for assessing the medium effect on the thermodynamics associated to these processes.

Solubility measurements of **1** in protic (methanol, MeOH; ethanol, EtOH) and dipolar aprotic (acetonitrile, MeCN; *N*,*N*-dimethylformamide, DMF; dimethylsulfoxide, DMSO and propylene carbonate, PC) solvents were carried out at 298.15 K using the procedure previously described.[21] The amount of **1** in the saturated solution was determined gravimetrically by triplicate taking samples from the same equilibrium mixture. Several blank experiments were performed to ensure the absence of any nonvolatile material in the pure solvent. Solvate formation was checked by the de Ligny method.[21]

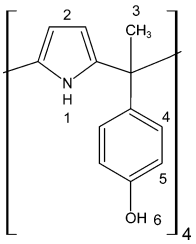
^{1}H NMR Measurements. ^{1}H NMR measurements were used to characterize the calix[4]pyrrole derivative and to provide information about its interaction with anions and whenever possible to establish the site(s) of interaction(s) of the ligand. All measurements were carried out at 298 K and conducted on a Bruker AC-300E pulsed Fourier transform NMR spectrometer. The operating conditions for proton measurements were as follow, "pulse" or flip angle of 30°, spectral frequency (SF) of 300.15 MHz, delay time of 1.60 s, acquisition time (AQ) of 1.819 s and line broadening (LB) of 0.55 Hz. The process of complexation was studied by adding the appropriate anion salt of known concentration (3.00×10^{-3} mol dm^{-3}) into the NMR tube (5 mm) containing a known amount of **1** (0.5 mL) (1×10^{-3} mol dm^{-3}) dissolved in the appropriate solvent. Tetramethylsilane (TMS) was used as internal reference.

Conductance Measurements. For these measurements, a Wayne-Kerr Autobalance Universal Bridge type B642 was used.[22] The conductivity cell constant was determined by the method of Jones and Bradshaw[23] as previously described. Conductometric titrations were carried out in a conductivity cell filled with a weighed volume of the solution containing the appropriate anion salt in the solvent of interest ($5.00 \times 10^{-5} - 1.00 \times 10^{-4}$ mol dm^{-3}) which was titrated with a solution of **1** (1.00×10^{-3} mol dm^{-3}) in the same solvent using a glass syringe connected to a calibrated automatic burette. Conductance readings at 298.15 K were recorded after each addition.

Calorimetric Measurements. Stability constant ($\log K_s$) and enthalpies of complexation of **1** with the anions at 298.15 K in MeCN and DMF were determined by direct calorimetric titrations using a Tronac 450.[24] The calibration of the machine was carried out using the standard reaction of protonation of an aqueous solution of tris-(hydroxymethyl)aminomethane (THAM) with an aqueous solution of hydrochloric acid (0.1 mol cm^{-3}) at 298.15 K. The value obtained (-47.33 kJ mol^{-1}) was in good agreement with that reported by Wilson and Smith[25] (-47.49 kJ mol^{-1}) at 298.15 K.

A solution of the ligand ($10^{-4}-10^{-3}$ mol dm^{-3}) was placed in the vessel (50 cm^3) in the selected solvent and the anion salt ($10^{-3}-10^{-2}$ mol dm^{-3}) was placed in the same solvent in the syringe. The latter was added from a 2.5 cm^3 burette connected by a silicone tube to the reaction vessel once thermal equilibrium was reached. These experiments were performed in triplicate for each solvent. Blank experiments were carried out to account for dilution effects resulting from the addition of the fluoride anion salt solution to the solvent placed in the calorimetric vessel.

TABLE 1: ^{1}H NMR Data for 1 in Deuterated Methanol, Acetonitrile, and Acetone at 298 K



	δ (ppm)		
	CD_3OD	CD_3CN	d_6-acetone
1 (H_N)	9.06	--	8.22
2 ($H_{Pyrrole}$)	5.75	5.98	5.95
3 (CH_3)	1.87	1.82	1.82
4 (H_{Ar})	6.65	6.66	6.64
5 (H_{Ar})	6.90	6.76	6.79
6 (OH)		7.87	8.75

Determination of Standard Enthalpies of Solution. The enthalpies of solution, $\Delta_s H$ (kJ mol^{-1}), of **1** and its dihydrogen phosphate complex, $Bu_4N^+(\mathbf{1}H_2PO_4^-)$, at different concentrations (2×10^{-5} to 1×10^{-3} mol dm^{-3}) in MeCN and DMF at 298.15 K were determined calorimetrically using the Tronac 450 calorimeter. Thus glass ampoules (at least six) containing known quantities of the ligand were sealed. These were then placed on the holder at the end of the stirrer and immersed in the desired solvent in the reaction vessel. The system was then placed in a water bath until thermal equilibrium was attained. Ampoules were broken by means of the plunger that goes through the stirrer rod, and the resulting temperature changes were recorded. After each experiment, an electric calibration was performed. The total heat recorded was the sum of the heat of solution and the heat of ampule breaking. The latter was determined by breaking empty ampoules in the same solvent under investigation and recording the heat change. The heat of solution was calculated by subtracting the heat of breaking of the empty ampule from the total heat recorded.

Results and Discussion

^{1}H NMR Data of 1 in Different Deuterated Solvents at 298 K. Table 1 reports the proton chemical shifts observed in the ^{1}H NMR spectra of **1** in the "cone" conformation in three different deuterated solvents (CD_3OD, CD_3CN, and d_6-acetone) at 298 K. In a similar fashion to the parent compound, calix[4]pyrrole, the chemical shifts of the protons of **1** are affected by the solvent, particularly those of the OH and the NH functionalities. A more pronounced downfield shift is found for the NH proton in CD_3OD (protic solvent) relative to that in CD_3CN (dipolar solvent). This may be attributed to either the tendency of the former solvent to enter hydrogen bond formation with the OH and the NH functionalities or to the exchange of OH with OD in CD_3OD. However, a striking observation is the absence of the NH signal in the ^{1}H NMR spectrum of **1** in CD_3CN and its appearance in d_6-acetone. Taking into account that there are no dramatic changes in the chemical shifts of other protons in **1** in moving from one solvent to another, ^{1}H NMR titrations were performed to assess the effect of the solvent on the NH proton of **1**. Thus titrations were carried out by the addition of (i) known volumes of d_6-acetoneto a solution of **1** in CD_3CN and (ii) CD_3CN to a solution of **1** in acetone-d_6. Data are shown in Figure 1 in which δ values for the NH and the OH proton of **1** are plotted against the acetone-d_6:CD_3CN ratio at 298 K. It can be observed in this figure (from left to right) that, on addition of acetone-d_6 to a solution of this ligand in CD_3CN, the signals of the NH protons start to shift downfield.

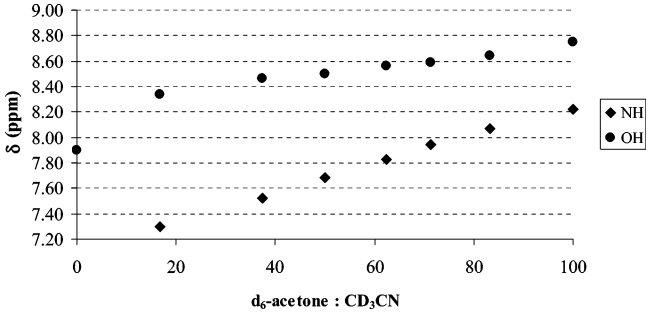


Figure 1. ^{1}H NMR plot of the chemical shift change, δ(ppm), of **1** in CD_3CN upon the addition of d_6-acetone at 298 K.

TABLE 2: Solubilities of 1 and 2 in Different Solvents, Standard Gibbs Energies of Solution, $\Delta_s G°$, and Transfer Gibbs Energies, $\Delta_t G°$, from Acetonitrile at 298.15 K

solvent[a]	solubility/ mol dm^{-3}	$\Delta_s G°$/kJ mol^{-1}	$\Delta_t G°_{(MeCN\rightarrow s)}$/ kJ mol^{-1}
	1[b]		
MeCN	$(9.45 \pm 0.04) \times 10^{-4}$	17.26	0.00
MeOH	$(7.52 \pm 0.02) \times 10^{-2}$	8.22	−9.04
EtOH	$(3.63 \pm 0.03) \times 10^{-2}$	6.41	−10.85
DMF	solvate formation		
DMSO	solvate formation		
PC	solvate formation		
	2[c]		
MeCN	$(1.39\pm) \times 10^{-2}$	10.60	0.00
MeOH	$(8.07\pm) \times 10^{-3}$	12.57	1.97
EtOH	$(6.27\pm) \times 10^{-3}$	11.95	1.35
DMF	$(1.36\pm) \times 10^{-2}$	10.65	0.05
DMSO	$(1.38\pm) \times 10^{-2}$	10.62	0.02
PC	$(1.40\pm) \times 10^{-2}$	10.58	−0.02

[a] Abbreviations: acetonitrile, MeCN; methanol, MeOH; ethanol, EtOH; *N*,*N*-dimethyl formamide, DMF; dimethylsulfoxide, DMSO; propylene carbonate, PC. [b] This work. [c] Reference 5.

The reversible measurements (from right to left) led to upfield shifts in the signals of the NH protons. This finding suggests that acetone-d_6 is interacting with the NH proton, possibly through hydrogen bond formation through the carbonyl group of the solvent. To a lesser extent, the same trend is observed for the OH protons.

Solubility Measurements. Solubility data for **1** in various solvents are listed in Table 2. These are the result of several analytical measurements carried out on saturated solutions taken from the same equilibrium mixture. The standard deviations of the data are also included in Table 2. From solubility data, the standard Gibbs energies of the solution, $\Delta_s G°$ are calculated for cases in which the solid phase was not altered by solvation. These data are referred to the standard state of 1 mol dm^{-3}.

For comparison purposes, data for calix[4]pyrrole, **2**, are also included in Table 2. The results in this table show that **2** does not undergo selective solvation in these solvents since hardly any changes are observed in the $\Delta_t G°$ of this ligand from acetonitrile to the various solvents. However, the presence of phenol groups in **1** changes substantially the solvation of this ligand in the solvents investigated. Unlike calix[4]pyrrole, **1** undergoes solvate formation in various dipolar aprotic solvents (DMF, DMSO, and PC) and therefore prevented the calculation of $\Delta_s G°$ in these solvents, since this requires **1** to have the same composition in the solid state and in the saturated solution at equilibrium. On the other hand, **1** is better solvated in protic solvents relative to acetonitrile. This is concomitant with the outcome of ^{1}H NMR investigations of this ligand in CD_3OD. The results (i) demonstrate the versatile behavior of these ligands in different media and (ii) lead to the conclusion that, as far as

TABLE 3: Changes in the ^{1}H NMR Chemical Shifts for 1 and Anions Complexes in CD_3CN at 298 K

	H_N		OH	
	δ (ppm)	$\Delta\delta$ (ppm)	δ (ppm)	$\Delta\delta$ (ppm)
free ligand			7.87	
F^-			8.34	−0.47
Cl^-	9.15		7.83	−0.04
Br^-	8.20		7.85	−0.02
I^-			7.87	0.00
$H_2PO_4^-$	9.15		7.99	0.12
HSO_4^-			7.87	0.00

1 is concerned, its lower solvation in acetonitrile relative to methanol would contribute more favorably to the complex stability in the former than in the latter solvent. Having stated it, emphasis should be made about the fact that an accurate assessment of the medium effect on complexation also requires availability of transfer data not only for the ligand but also for the free and complex anion salts in these solvents,[26−28]and this will be discussed below.

^{1}H NMR Studies on the Interaction of 1 with Anions in CD_3CN at 298 K. Table 3 lists the relevant ^{1}H NMR chemical shift changes observed by the addition of anions (F^-, Cl^-, Br^-, I^-, HSO_4^-, and $H_2PO_4^-$) to calixpyrrole derivative, **1,** in CD_3CN at 298 K. The downfield chemical shifts of the pyrrolic protons indicate that the halide and the phosphate anions tend to interact with it, thus producing a deshielding effect of this proton. However, due to the low solubilities of **1** in CD_3CN, and the broadness of the NH signal, $\Delta\delta$ values for this proton could not be calculated.

In the case of fluoride, it was not possible to locate the NH signal in the NMR spectrum due to its broadness resulting from the low solubility of the fluoride complex in CD_3CN (even lower than that for the ligand) at 298 K. However, the considerable chemical shift changes of the OH protons indicate that F^- also interacts through the hydroxyl groups with **1**. On the other hand, the insignificant chemical shift changes found in the OH signals upon the addition of Cl^- and Br^- anion salts to **1** in CD_3CN indicate that the hydroxyl groups are not taking part in the complexation of this receptor with these anions. No significant chemical shift changes were observed upon the addition of I^- and HSO_4^- anion salts to **1** in this solvent suggesting the absence of interaction.

In conclusion, these findings provide a clear indication that **1** interacts with anions via hydrogen bond formation through the pyrrolic proton which shows different chemical shifts in the case of Cl^- and Br^- anions. Minor interactions from the OH were found with fluoride and dihydrogen phosphate anions which are absent when anions such as chloride, bromide, iodide, and hydrogen sulfate are considered.

Having established the active sites of interaction of **1** with the anions in CD_3CN at 298 K, conductance measurements were carried out in order to determine the composition of the anion complexes and to gain semiquantitative information regarding the strength of interaction of the ligand with a given anion in acetonitrile. The results are discussed in the following section.

Conductometric Titration. Conductometric titrations were carried out in acetonitrile and *N*,*N*-dimethylformamide at 298.15 K. Plots of molar conductance (Λ_m) against the ligand:anion concentration ratio involving **1** and halide, dihydrogen phosphate, and hydrogen sulfate anions in acetonitrile (Figure 2) revealed the following features. In all cases, a decrease in the molar conductance is observed. This is attributed to the lower

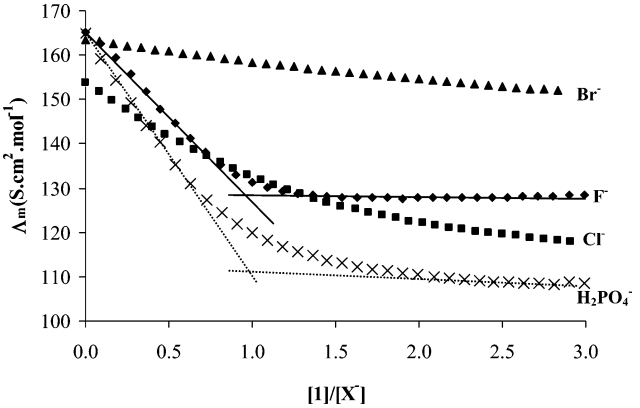


Figure 2. Conductometric titration curves of fluoride, chloride, bromide, and dihydrogen phosphate (as tetra-*n*-butylammonium) with **1** in MeCN at 298.15 K.

mobility of the ions in solution due to the conversion of the anion from the free to the complex state. In the case of fluoride, the conductometric curve shows a well-defined change in the curvature at the stoichiometry of the reaction resulting from the combination of two linear segments suggesting the formation of a relatively strong complex. However the slope of the curvature is gradually changing for chloride and bromide suggesting the formation of relatively weak complexes. Their stoichiometries are determined by extrapolating the slopes of the curves at high and low host−guest concentration ratios. In a similar fashion to that observed for the fluoride anion, the dihydrogen phosphate conductometric plot shows a well defined change (but less marked than that for the fluoride anion) in curvature at the 1:1 (ligand:anion) concentration ratio. No changes in conductance were found in the titration of iodide and hydrogen sulfate anions with this ligand in acetonitrile suggesting that hardly any interaction takes place between **1** and these anions in this solvent and this is the reason why these data were not included in Figure 2. The selectivity trend for this ligand and these anions that may be inferred from conductometric studies in acetonitrile is as follows:

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

With the aim of assessing the medium effect on the anion−ligand interactions, conductometric titrations of anions with **1** at 298.15 K were carried out in *N*,*N*-dimethylformamide. This solvent is considered a protophilic dipolar aprotic solvent and as such is a poor solvating medium for the anions and consequently it is expected to be a suitable complexation medium. However, solvate formation was observed when **1** was exposed to a saturated atmosphere of DMF (see Table 2). Therefore, the anion will have to compete with the solvent to complex with this ligand. The results showed that while fluoride and dihydrogen phosphate anions were able to compete favorably (although the curve broadness and the vague break observed are indicative of weak complexation) other anions such as chloride, bromide, iodide, and hydrogen sulfate were not.

Having established the composition of the anion complexes and knowing the concentration range at which the free anion salts are predominantly as ions in these solvents, we proceeded with the thermodynamic characterization of the complexation process of **1** and these anions in these solvents, and this is now discussed.

Thermodynamics of Complexation. The thermodynamic parameters of complexation of **1** and several anions (as tetra-*n*-butylammonium salts) in acetonitrile and *N*,*N*-dimethylfor-

TABLE 4: Thermodynamic Parameters of Complexation of 1 and Anions as Tetra-*n*-butylammonium Counter-Ion in Acetonitrile and *N*,*N*-Dimethylformamide at 298.15 K

anion	log K_s	$\Delta_c G^{o\prime}$/ kJ mol^{-1}	$\Delta_c H^o$/ kJ mol^{-1}	$\Delta_c S^o$/ J mol^{-1} K^{-1}
		Acetonitrile		
		1		
F^-	5.44 ± 0.08	−31.1 ± 0.4	−32.4 ± 0.6	−5
Cl^-	3.82 ± 0.02	−21.8 ± 0.1	−20.5 ± 0.5	5
Br^-	3.20 ± 0.09	−18.2 ± 0.5	−15.4 ± 0.3	9
$H_2PO_4^-$	4.82 ± 0.04	−27.5 ± 0.2	−32.1 ± 0.7	−15
		2		
F^-	6.21 ± 0.03[a]	−35.4 ± 0.2[a]	−43.5 ± 0.3[a]	−27[a]
Cl^-	4.70 ± 0.07[a]	−26.8 ± 0.4[a]	−44.7 ± 0.9[a]	−60[a]
Br^-	3.65 ± 0.06[a]	−20.8 ± 0.3[a]	−30.7 ± 0.9[a]	−33[a]
$H_2PO_4^-$	5.00 ± 0.08[b]	−28.5 ± 0.5[b]	−48.1 ± 0.1[b]	−66[b]
		N,*N*-Dimethylformamide		
		1		
F^-	4.23 ± 0.05	−24.2 ± 0.3	−17.8 ± 0.6	22
$H_2PO_4^-$	4.81 ± 0.06	−27.4 ± 0.3	−18.9 ± 0.2	29
		2		
F^-	6.8 ± 0.3[a]	−39.0 ± 0.5[a]	−26.2 ± 0.5[a]	43[a]
$H_2PO_4^-$	4.8 ± 0.1[b]	−27.4 ± 0.6[b]	−18.8 ± 0.3[b]	29[b]

[a] Reference 5. [b] Reference 6.

mamide determined by direct titration calorimetry (unless otherwise stated) are reported in Table 4, and these are referred to the process described in eq 1

$$\mathbf{1}(s) + X^-(s) \rightarrow \mathbf{1}X^-(s) \quad (1)$$

Inspection of stability constant data (expressed as log K_s) shows that this ligand interacts selectively with anions in acetonitrile following the sequence

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

This behavior is reversed in DMF as far as the fluoride and dihydrogen phosphate anions are concerned. Indeed in this solvent, **1** shows higher selectivity for the $H_2PO_4^-$ relative to the fluoride anion. In both solvents, the process is enthalpically controlled. However, the lower enthalpic stability in *N*,*N*-dimethylformamide than in acetonitrile which is accompanied by a gain in entropy in the former relative to the latter solvent is indicative of a higher desolvation upon complexation in DMF relative to MeCN which may be partially attributed to the higher energy required to overcome the strong ligand-solvent interaction which appears to occur when the medium is DMF. It should also be noted that the stability of the **1**−$H_2PO_4^-$ complex is not altered in moving from MeCN to DMF as a result of a remarkable enthalpy−entropy compensation effect. For comparison purposes, thermodynamic data for the parent calix[4]-pyrrole, **2**, and these anions are also included in Table 4. As far as the halide anions are concerned, the stability of **1**−anion complexes in both solvents is lower than that of **2** and these anions. This decrease may be attributed to the presence of the phenol groups at the bridge between the pyrrole rings which may either (i) lead to steric effects by which the phenol units may form rigid walls restricting the easy access of the anions to interact with the pyrrolic protons or (ii) to electronic effects, since the aromatic phenol rings may form an induced magnetic field which may act as a repulsive force for these anionic guests. In fact, the ligand effect is clearly reflected in the selectivity factor, $S_{2/1} = K_s^\theta(\mathbf{2})/K_s^\theta(\mathbf{1})$ shown in Table 5. These data provide a quantitative assessment of the selective behavior of **2** relative to **1** for a given ion in a given solvent. Such effect is not observed in the interaction of $H_2PO_4^-$ with either ligand in each of these solvents. In fact the stability of complex formation is not altered by moving from one ligand to another or from one solvent to another for this anion. Consequently, $S_{2/1} = 1$ in both solvents. Although in acetonitrile, the similar stability of the complexes formed between $H_2PO_4^-$ and ligands **1** and **2** results from different enthalpic and entropic contributions, in *N*,*N*-dimethylformamide, these two parameters remain essentially unchanged. In conclusion, the interaction of **1** and **2** with the $H_2PO_4^-$ anion in MeCN is enthalpically favored and entropically destabilized. However in DMF, both, the enthalpy and entropy contribute favorably to the stability of the complex.

TABLE 5: Selectivity Factor $S_{2/1}$ of Calix[4]pyrrole, 1, for the Fluoride Anion Relative to 2 in Acetonitrile (MeCN) and *N*,*N*-Dimethylformamide (DMF) at 298 K

	$S_{2/1}$	
anion	MeCN	DMF
F^-	4	115
Cl^-	8	
Br^-	4	
$H_2PO_4^-$	1	1

TABLE 6: Enthalpies of Solution of 1 and Its Tetra-*n*-butylammonium Dihydrogen Phosphate Complex in Acetonitrile and *N*,*N*-Dimethylformamide at 298.15 K

	$\Delta_s H^\circ$/kJ mol^{-1}	
	acetonitrile	*N*,*N*-dimethylformamide
1	46.0 ± 0.6[a]	−45.7 ± 0.5[a]
$Bu_4N^+(\mathbf{1}H_2PO_4^-)$	62.9 ± 0.2[b]	163.3 ± 0.5[b]

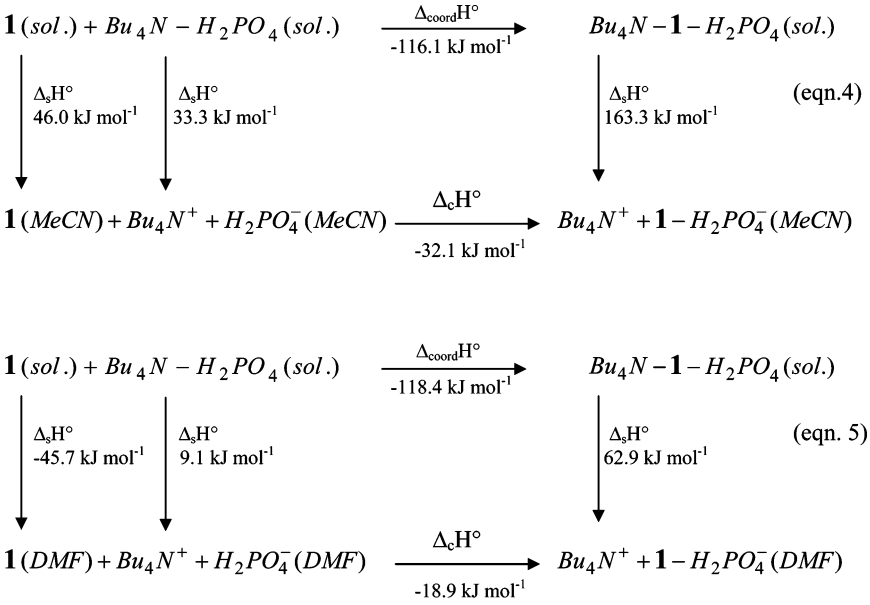
[a] Average of several measurements. [b] Extrapolated value at $c = 0$.

To asses the factors contributing to the stability of the complex in one solvent relative to another (medium effect), we proceeded with the determination of the enthalpies of solution of these ligands and their anionic complexes in these solvents. We were unable to analyze these data in terms of Gibbs energies given that either the free anion salt or the ligand undergoes solvation in DMF. Enthalpies of solution of the calix-[4]pyrrole derivative, **1**, and its anionic complexes are now discussed.

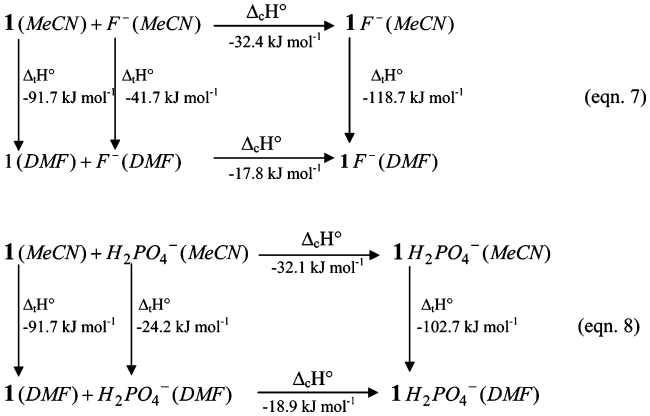
Enthalpies of Solution. The standard enthalpies of solution, $\Delta_s H^\circ$, of **1** and its complex with dihydrogen phosphate anion in MeCN and DMF at 298.15 K determined calorimetrically are those shown in Table 6. These values were calculated from $\Delta_s H$ values at different molar concentrations of the ligand in the appropriate solvent. In cases where no systematic variation in the $\Delta_s H$ values was found by altering the concentration of the appropriate compound, the standard enthalpy of solution, $\Delta_s H^\circ$, was taken as the average of the various data. When $\Delta_s H$ values vary with changes in the electrolyte concentration, the $\Delta_s H^\circ$ value was calculated from the intercept at $c^{1/2} = 0$ of a plot of $\Delta_s H$ against the square root of the concentration. This method was used for the calculation of the standard enthalpies of solution of **1**−$H_2PO_4^-$ in MeCN and DMF.

Solution enthalpy data for the free ligand and its dihydrogen phosphate complex deserve some comments. Given that (i) the $\Delta_s H^\circ$ values result from the contribution of corresponding data for the crystal lattice, $\Delta_{cl} H^\circ$ (endothermic) and solvation, $\Delta_{solv} H^\circ$, (exothermic) processes and (ii) for a given compound, $\Delta_{cl} H^\circ$ is the same, it follows that the enthalpies of solution of the ligand is more stable in DMF than that in acetonitrile by ∼92 kJ mol^{-1}, whereas the dissolution of the complex is more endothermic in DMF than in MeCN. These results demonstrate that the introduction of the phenol groups in **2** to give **1** alters

SCHEME 1



SCHEME 2



significantly the solvation properties of these ligands and their complexes in these solvents.

Solution enthalpies were used for two purposes, the calculation of coordination enthalpies, $\Delta_{coord}H°$ and to assess the medium effect as discussed below.

Coordination Enthalpies. As previously stated[5,6] for a given system, $\Delta_{coord}P°(P° = G°, H°, S°)$ should be the same, independently of the solvent from which the data are derived. Therefore these data are useful to check the accuracy of the solution and complexation enthalpies reported in this paper. The $\Delta_{coord}H°$ refers to the process in which reactants and product are in their pure physical state (in this case in the solid, sol., state). As a representative example, the process involving **1** and $Bu_4NH_2PO_4$ is considered (eq 2)

$$\mathbf{1}(\text{sol}) + Bu_4NH_2PO_4(\text{sol}) \xrightarrow{\Delta_{coord}H°} \mathbf{1}Bu_4NH_2PO_4\,(\text{sol}) \qquad (2)$$

Coordination enthalpies are calculated from solution and complexation data in the appropriate solvent, *s* (*s* = MeCN and DMF) at 298.15 K (eq 3)

$$\Delta_{coord}H°(\text{s}) = \Delta_sH°(Bu_4N^+H_2PO_4^-)(\text{s}) + \Delta_sH°(\mathbf{1})(\text{s}) + \Delta_cH°(\text{s}) - \Delta_sH°(Bu_4N^+\mathbf{1}H_2PO_4^-)(\text{s}) \qquad (3)$$

Equation 3 is now expressed in the form of a thermodynamic cycle where the enthalpy values for the various processes involved in acetonitrile (eq 4, in Scheme 1) and *N*,*N*-dimethyl formamide (eq 5, in Scheme 1) are involved.The agreement found between the $\Delta_{coord}H°$ values derived from acetonitrile (-116.1 kJ mol^{-1}) and *N*,*N*-dimethylformamide (-118.4 kJ mol^{-1}) demonstrates the accuracy of the solution and complexation data reported in this paper.

Medium Effect on the Complexation Process. Taking into account that the medium effect on the complexation process is controlled by the differences in the solvation of the reactants and the product participating in the process involving these two solvents as shown in the following relationship (eq 6)

$$\Delta_cH°(\text{MeCN}) - \Delta_cH°(\text{DMF}) = \Delta_tH°(\mathbf{1})(\text{MeCN} \rightarrow \text{DMF}) + \Delta_tH°(\text{X}^-)(\text{MeCN} \rightarrow \text{DMF}) - \Delta_tH°(\mathbf{1}\text{X}^-)(\text{MeCN} \rightarrow \text{DMF}) \qquad (6)$$

it follows that the most favorable complexation medium is that which is a poor solvator for the reactants and a good solvator for the product. Equation 6 is now illustrated in terms of a thermodynamic cycle where the 1-fluoride (eq 7, in Scheme 2) and 1-$H_2PO_4^-$ (eq 8, in Scheme 2) systems are now considered.The upper and lower parts of eqs 7 and 8 refer to the enthalpies of complexation of **1** with F^- and $H_2PO_4^-$ respectively in acetonitrile and *N*,*N*-dimethylformamide. These data are given in Table 4. The enthalpy of transfer of **1** from MeCN to DMF was calculated from the standard enthalpies of solution of this ligand obtained calorimetrically in acetonitrile and *N*,*N*-dimethylformamide (Table 6). The Δ_tH° values of the F^- and the $H_2PO_4^-$ anions from acetonitrile to DMF (data based on Ph_4AsPh_4B convention) are those from the literature.[5,6,8] The Δ_tH° of the complex anion salt is calculated through rearrangement of eq 6. For both systems, the higher enthalpic stability in MeCN relative to DMF is attributed to the lower interaction of the reactants in the former solvent which overcomes the higher solvation of the complex (favorable for complexation in DMF) in DMF.

Extraction Experiments Using a Resin Containing 1 as Anchor Groups. The calix[4]pyrrole derivative, **1**, is character-

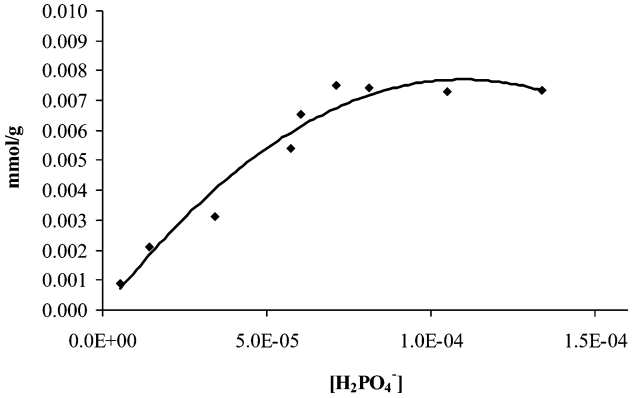


Figure 3. Uptake isotherm for $H_2PO_4^-$ anion from aqueous solution by a calix[4]pyrrole based resin at 298.15 K.

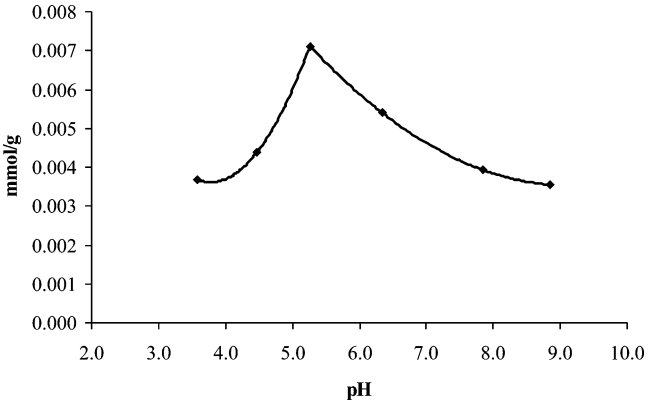


Figure 4. Effect of pH on the uptake of $H_2PO_4^-$ anion from aqueous solution by a calix[4]pyrrole based resin at 298.15 K.

ized by the presence of phenol groups which are fused into the bridge between the pyrrole rings. Unlike **2**, the phenol groups in **1** make this receptor prone to oligomerization at this site to produce a oligomeric material suitable for the extraction of anions from water. In this paper, we discuss the capacity of this material to uptake the dihydrogen phosphate salts from aqueous solutions containing different concentrations of $H_2PO_4^-$. A plot of the mmoles of $H_2PO_4^-$ taken up per gram of dry resin against the equilibrium concentration of $H_2PO_4^-$ in water is shown in Figure 3. This is a typical extraction isotherm which clearly demonstrates that the maximum capacity of the material to extract $H_2PO_4^-$ from water at 298.15 K is $\sim 7 \times 10^{-3}$ mmol/g. This amount is expected to increase significantly when this anion is extracted from a protophobic aprotic solvent such as acetonitrile given that the anion−solvent interaction decreases significantly. However, the solubility of phosphates in acetonitrile or indeed *N*,*N*-dimethylformamide is very low as to proceed with these experiments. Studies carried out to assess the pH effect on the extraction process showed that the optimum pH for extraction of $H_2PO_4^-$ was found at about 5.3 (Figure 4). Taking into account the pK_a values for the dissociation of phosphates in water, it is estimated that, at this pH, the $H_2PO_4^-$ predominates in solution relative to HPO_4^{2-}. In fact at this pH the amount of $H_2PO_4^-$ extracted is approximately equal to the capacity of this material to uptake this anion. Although the above experiments were carried out at 298.15 K, we found that the optimum temperature for the extraction of $H_2PO_4^-$ from water was 303.15 K. At this temperature, the maximum capacity of the material to take up this anion is close to 1×10^{-2} as shown in Figure 5 where the kinetics of the process was assessed. The results lead us to the conclusion that the full capacity is reached

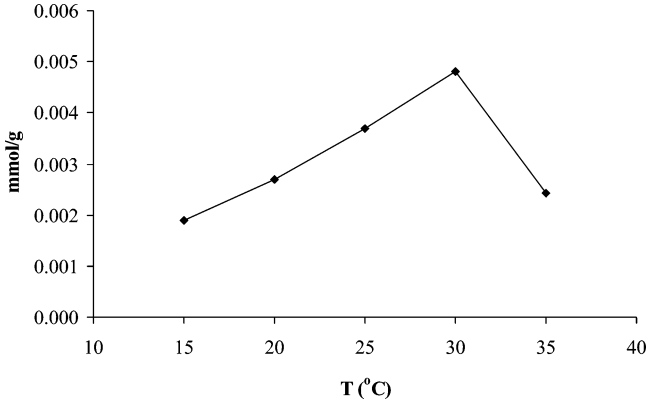


Figure 5. Effect of temperature (°C) on the uptake of $H_2PO_4^-$ anion from aqueous solution by a calix[4]pyrrole based resin at 298.15 K.

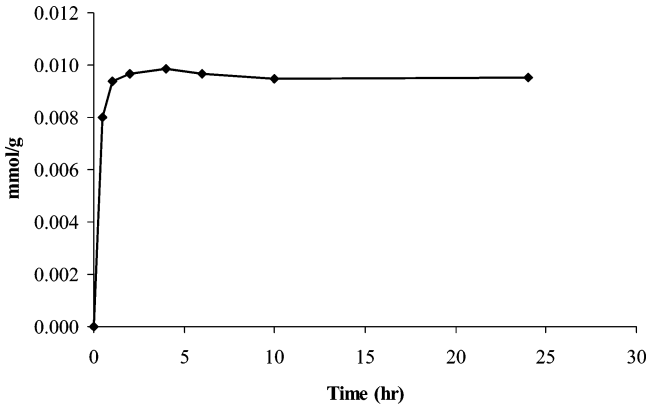


Figure 6. Determination of the optimum time for the uptake of $H_2PO_4^-$ anion from aqueous solution by a calix[4]pyrrole based resin at 298.15 K.

in a few minutes, and therefore, the process is considered to be relatively fast.

Conclusions

From the above discussion the following conclusions are drawn:

1. ^{1}H NMR measurements in CD_3CN at 298 K show that **1** interacts with the halide (spherical) and dihydrogen phosphate (nonspherical) anions through the NH groups of the pyrrole ring. The OH functionalities are also participating in the complexation of **1** with fluoride and dihydrogen phosphate anions. Conductance measurements demonstrated that in MeCN and DMF 1:1 complexes are formed between **1** and anions.

2. In acetonitrile and *N*,*N*-dimethylformamide, **1** can recognize selectively the anions as shown through the various approaches undertaken in this work. The selectively trend of calixpyrrole **1** has not changed from that of **2** in acetonitrile. The impact of introducing the phenol groups at the meso-position of **2** was revealed in the lower stability constants for the anion complexes of **1**.

3. Solution thermodynamics of **1** and its complexes (fluoride and dihydrogen phosphate) in acetonitrile and *N*,*N*-dimethyformamide were determined at 298.15 K. The enthalpies of coordination for both complexes were then calculated in both solvents and enthalpies of transfer of the reactants and the product from acetonitrile to DMF were evaluated in order to gain some insight about the medium effect on the complexation process.

4. The results of extraction studies indicate that the calixpyrrole resin is suitable for the removal and recovery of $H_2PO_4^-$

ions from aqueous media. The uptake of $H_2PO_4^-$ ions by this material was influenced by experimental parameters such as initial anion and resin concentrations, pH, and temperature. The optimum time for $H_2PO_4^-$ ions removal from aqueous medium was determined as less than 1 h, and the observed capacity is $\sim 7 \times 10^{-3}$ mmol/g. This value combined with the amount of calixpyrrole units in 1 g of resin led to an estimated percentage of accessible sites in the material (83%) from which 0.85% seem to bind the phosphate anions.

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