Thermodynamics of Phosphate and Pyrophosphate Anions Binding by Polyammonium Receptors

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Received November 16, 1998. Revised Manuscript Received May 13, 1999

Abstract: The interactions of phosphate and pyrophosphate anions with polyammonium cations deriving from 14 polyamines (five polyazacycloalkanes, four polyazacyclophanes, and five acyclic polyamines) in aqueous solution have been studied by means of potentiometric, microcalorimetric, and NMR measurements in solution. Very stable 1:1 receptor-to-anion complexes are formed. The stability trends of such complexes are not strictly determined by electrostatic forces, hydrogen bond interactions being of considerable importance in the complex formation, the thermodynamic data being consistent with different hydrogen bonding modes. $\Delta H°-T\Delta S°$ compensatory relationships hold for such complexation reactions. The crystal structures of $(H_4\mathbf{L1})(H_2P_2O_7)_2\cdot 2H_2O$ and $(H_4\mathbf{L2})(H_2P_2O_7)_2\cdot 6H_2O$ (**L1** = 1,4,7,10,13,16-hexaazacyclooctadecane, **L2** = 1,10-dimethyl-1,4,7,-10,13,16-hexaazacyclooctadecane) have been solved by X-ray analysis, evidencing different substrate/anion binding characteristics.

Introduction

"Anion binding", the coordination of chemical species by virtue of their anionic nature, plays a central role in both inorganic and biological processes.[1] For instance, a large majority of substrates and cofactors engaged in biological processes are anions.[2] Despite this, the chemistry of anion binding has been rather slow to develop, and only in the past few years has it been recognized as a new area of coordination chemistry, stimulating the interest of many researchers.[1]

Among anionic substrates, phosphates are of special interest due to their ubiquitous presence in biological systems. Phosphate recognition by proteins has been recently illustrated by a well-resolved crystal structure, which allowed the unambiguous positioning of the anion, which is completely dehydrated and sequestered about 8 Å below the protein surface, where it forms 12 strong hydrogen bonds with protein groups.[3]

Several examples of phosphate anions binding by synthetic receptors, mostly of polyammonium type, have been reported.[4,5] Phosphate complexation by these synthetic receptors is not strictly representative of phosphate binding by proteins, since these natural receptors incorporate the anion in deep clefts protected from solvent and counterions, where the averaged dielectric constant is estimated to be in the 2−4 range, while the synthetic ligands present rather opened structures, allowing the phosphate complex to be in contact with the medium.

The effectiveness of hydrogen bonding in stabilizing anion complexes in water is not clearly understood, principally due to the difficulty of studying this type of binding interaction in such a solvent, which is a good donor and acceptor of hydrogen bonds, but also due to the lack of complete thermodynamic information ($\Delta G°$, $\Delta H°$, $T\Delta S°$) regarding the formation of such

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10.1021/ja983947y CCC: $18.00
Published on Web 07/14/1999

species.[6] Nevertheless, hydrogen bonding in anion coordination seems to be crucial also in water.[7]

A quantitative interpretation of the correlation between the bonding strength in N−H−O systems with the hydrogen bond N−O distance (r) and the dielectric nature of the medium has been recently furnished by ab initio molecular orbital calculations.[8] Using as an example the HCOOH/$NHCH_2$ model, the computed proton-transfer potentials indicate that, at relatively long r separations (3.5 Å), in the absence of any external influence (dielectric constant $\epsilon = 1$), the neutral complex HCOOH···$NHCH_2$ is largely more stable than the $HCOO^-$···$^+HNHCH_2$ ion pair. Upon the dielectric constant increasing, the hydrogen bonded ion pair is stabilized much more than the neutral complex, becoming more stable for relatively larger ϵ values ($\epsilon > 4$), while the electronic barrier to proton transfer decreases, vanishing for very short ($r = 2.5$ Å) hydrogen bonds.

These results furnish a key to the interpretation of thermodynamic data for the formation of anion complexes, since the formation of neutral complexes or hydrogen-bonded ion pairs from separated species is expected to be accompanied by quite different enthalpic and entropic contributions.

To get more insight into the nature of anion complexation in aqueous solution and, in particular of phosphate type anions, we have undertaken a thermodynamic study on phosphate and pyrophosphate anions binding by the polyammonium receptors deriving from the 14 synthetic polyamines[9] depicted in Chart 1, which are representative of three main classes of ligands (polyazacycloalkanes, acyclic polyamines, and polyazacyclophanes) employed in anion recognition. The set of $\Delta G°$, $\Delta H°$, and $T\Delta S°$ values determined in this study contains the first collection of microcalorimetrically measured enthalpic contributions to "anion binding" in solution. Although calorimetry alone cannot give definitive information regarding hydrogen bonding, the data herewith presented furnish a significant insight into the nature of hydrogen bonding in anion coordination.

Results and Discussion

Crystal Structures of $(H_4L1)(H_2P_2O_7)_2\cdot 2H_2O$ and $(H_4L2)(H_2P_2O_7)_2\cdot 6H_2O$ (L1 = 1,4,7,10,13,16-Hexaazacyclooctadecane, L2 = 1,10-Dimethyl-1,4,7,10,13,16-hexaazacyclooctadecane). The crystal structure of $(H_4\mathbf{L2})(H_2P_2O_7)_2\cdot 6H_2O$ consists of tetraprotonated cations $H_4\mathbf{L2}^{4+}$, $H_2P_2O_7^{2-}$ anions, and water solvent molecules. Figure 1 shows an ORTEP[10] drawing with atom labeling and crystal packing of the structure, omitting the crystallization water molecules. The crystal cell contains two independent macrocyclic $H_4\mathbf{L2}^{4+}$ cations, each one lying around a crystallographic inversion center (coordinates 0, 0, 0 and 0.5, 0.5, 0.5). Both independent cations, (a) and (b) in Figure 1, adopt similar flattened conformations (maximum deviation from the mean planes through the six nitrogen atoms of 0.106(4) Å for N3 and N3′ in (a), and 0.113(4) Å for N6 and N6′ in (b)), with almost elliptical shape (major and minor axes of about

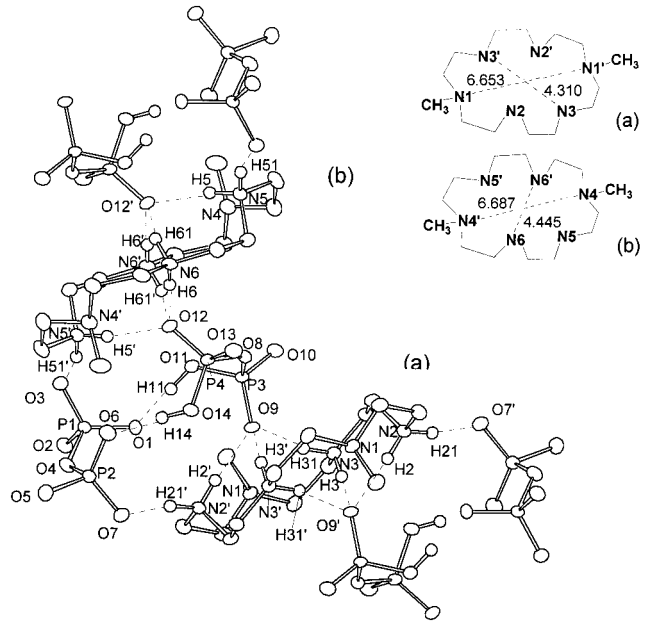

Figure 1. ORTEP[10] view of a portion of the crystal packing of $(H_4\mathbf{L2})(H_2P_2O_7)_2\cdot 6H_2O$, showing the $H_4\mathbf{L2}^{4+}$ cations (a) and (b) and the $H_2P_2O_7^{2-}$ anions together with the hydrogen bonds between them. Water molecules are not shown. Thermal ellipsoid are drawn at 30% probability.

Chart 1

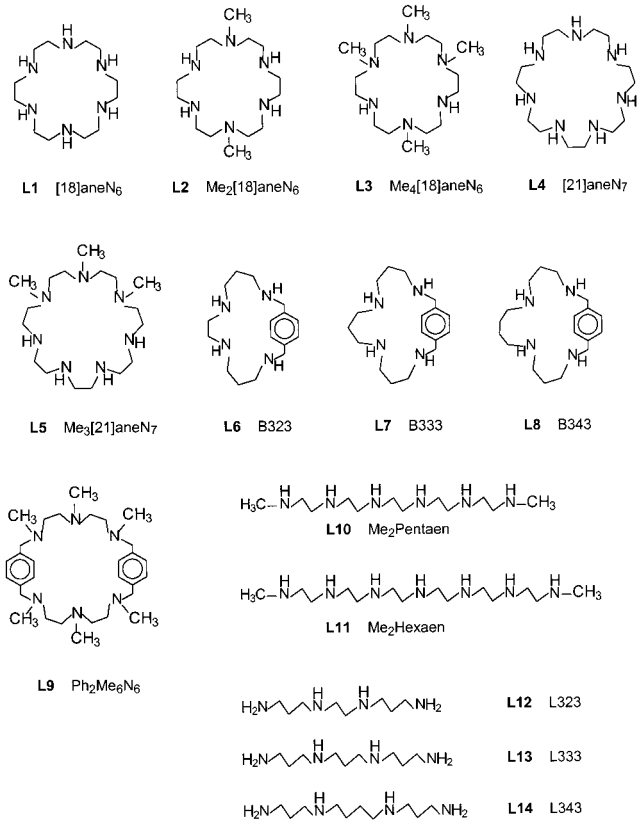

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Table 1. Hydrogen Bond Contacts for $[H_4\mathbf{L1}](H_2P_2O_7)_2\cdot 2H_2O$ and $[H_4\mathbf{L2}](H_2P_2O_7)_2\cdot 6H_2O$

	r (Å)		*r* (Å)	symmetry operation
		$[H_4\mathbf{L1}](H_2P_2O_7)_2\cdot 2H_2O$		
N3′···O2	2.86(1)	H3A′···O2	1.96(6)	$-x, -y, -z$
N2···O2	2.77(1)	H2B···O2	1.94(9)	
N2′···O1	2.85(1)	H2A′···O1	1.8(1)	$-x, -y, -z$
N3···O5	2.72(1)	H3B···O5	2.0(1)	
		$[H_4\mathbf{L2}](H_2P_2O_7)_2\cdot 6H_2O$		
N6···O12	3.037(5)	H6···O12	2.34(5)	
N6′···O12	2.732(5)	H61′···O12	1.70(8)	$1-x, 1-y, 1-z$
N5′···O12	2.777(6)	H5′···O12	1.85(8)	$1-x, 1-y, 1-z$
N3···O9	2.945(5)	H31···O9	2.01(6)	
N3′···O9	2.839(5)	H3′···O9	2.02(6)	$-x, -y, -z$
N2′···O9	2.831(5)	H2′···O9	1.92(6)	$-x, -y, -z$
N5′···O3	2.835(5)	H51′···O3	1.82(8)	$1-x, 1-y, 1-z$
N2′···O7	2.710(6)	H21′···O7	1.70(9)	$-x, -y, -z$
O11···O1	2.477(6)	H11···O1	1.57(8)	
O14···O6	2.553(6)	H14···O6	1.66(8)	

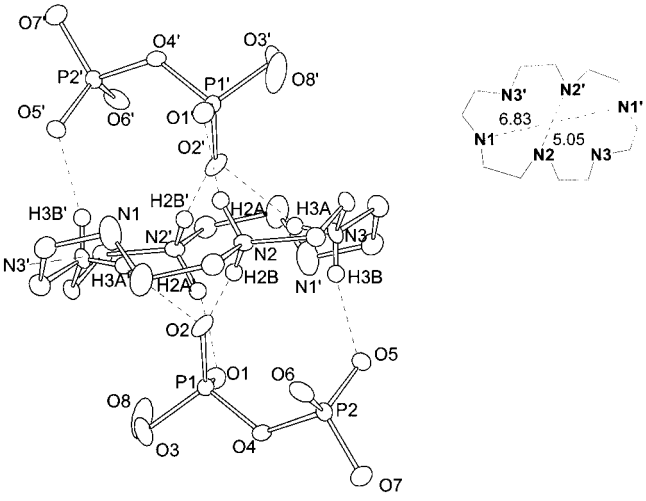

Figure 2. ORTEP[10] view of $(H_4\mathbf{L1})(H_2P_2O_7)_2$ complex. Thermal ellipsoid are drawn at 30% probability.

6.7 and 4.3 Å). All nitrogen atoms of these molecules are in *endo* conformation. It is noteworthy that the charged ammonium groups are localized near the minor axis of the ellipsoid, where they experience greater electrostatic repulsion. This particular charge distribution can be ascribed, considering the overall crystal packing, to the bridging interaction via strong hydrogen bonds of two oxygen atoms of different dihydrogen pyrophosphate anions with the closest symmetry-related nitrogens in each $H_4\mathbf{L2}^{4+}$ cation.

Two $H_2P_2O_7^{2-}$ anions, linked together via hydrogen bonding (Table 1), are intercalated between almost parallel $H_4\mathbf{L2}^{4+}$ cations, interacting via hydrogen bonds with such anion couples, giving rise to hydrogen-bonded polymeric chains constituting the crystal packing (Figure 1).

The crystal structure of $(H_4\mathbf{L1})(H_2P_2O_7)_2\cdot 2H_2O$ consists of discrete $(H_4\mathbf{L1})(H_2P_2O_7)_2$ hydrogen-bonded species (Figure 2) and water solvent molecules.

Also in this structure, the protonated macrocycles, which lies around a crystallographic inversion center, adopts an almost planar arrangement (maximum deviation from the mean plane defined by the six nitrogen atoms being 0.19(1) Å for N1 and N1′), with the nitrogen atoms in *endo* conformation. In the present case, with N···N′ intramolecular distances falling in the range 5.05(1)−6.83(1) Å, $H_4\mathbf{L1}^{4+}$ assumes a more circular and expanded conformation than that observed for $H_4\mathbf{L2}^{4+}$ in the previous structure.

This different conformation may be connected with the binding mode of the dihydrogen pyrophosphates, which are facially bound to the protonated cations in a sandwich-like fashion, forming long N3−H···O−P−O−P−O···H−N3′ and N2−H···O−P−O···H−N2′ hydrogen-bonded bridges (Table 1), in contrast to the shorter N−H···O···H−N bridges found in $(H_4\mathbf{L2})(H_2P_2O_7)_2\cdot 6H_2O$.

The only other interactions in the packing involve the water solvent molecules and the dihydrogen pyrophosphate anions, belonging to different units.

Interesting comparisons can be done with two crystal structures recently reported by Martell et al.[4f,h] In these structures, $H_2P_2O_7^{2-}$ forms adducts with ditopic hexaazacycloalkanes, giving rise to anion complexes in which the dihydrogen pyrophosphate is partly[4f] or deeply[4h] enclosed in the macrocyclic cavity. The anion inclusion into the macrocyclic cavity is facilitated by the larger dimensions of such ligands (approximately 8 Å × 8 Å for both structures) with respect to **L1** and **L2**. However, the N−H···O hydrogen bond distances found for $(H_4\mathbf{L1})(H_2P_2O_7)_2\cdot 2H_2O$ and $(H_4\mathbf{L2})(H_2P_2O_7)_2\cdot 6H_2O$ (Table 1), which are comparable with those reported by Martell et al.[4f,h] (2.64−2.93 and 2.60−2.75 Å), demonstrate that tight association of polyammonium cations with pyrophosphate can occur independently of anion inclusion.

Interesting crystal structures of phosphate complexes with protonated forms of sapphyrins were recently reported by Sessler et al.[4j]

Stability of Anion Complexes. Computer analysis of potentiometric data furnished the overall equilibrium constants of the complexes formed by phosphate and pyrophosphate (A) with the ligands **L1**−**L14** (L), according to the general reaction

$$A + L + mH = ALH_m$$

where charges are omitted for simplicity.

An interesting point concerns the identity of the reacting species in the complex. The overall equilibrium constants do not furnish any information about the location of the H^+ ions in the adducts, and, in principle, there is no reason to assume that the same proton location found in the isolated reagents is maintained in the complex.

Useful information about proton location in the anion complexes can be obtained from NMR measurements. The protonation patterns of the receptors considered in this work, except for **L1** and **L4**, were determined in previous studies[9b−f] by following the pH dependence of the ^1H and ^{13}C NMR signals of ligand solutions in the absence of phosphate and pyrophosphate anions, allowing the protonation sites to be known at each protonation step. Analogous studies performed in the presence of phosphate and pyrophosphate evidence that the interaction with such coordinating anions does not alter the protonation patterns and the topology of the charged groups, and, with the exception of $Ph_2Me_6N_6$ (**L9**), complexation does not modify significantly the overall conformation of the protonated receptors. Only a modest, general displacement of NMR signals corresponding to the increase of ligand basicity, brought about by anion complexation, is observed. These observations are strongly indicative of the fact that, in the formation of such anion complexes, the interacting partners maintain their identity, and no significant redistribution of protons occurs; that is, under our experimental conditions, hydrogen-bonded ion pairs are favorably formed. In the case of $Ph_2Me_6N_6$, some ligand rearrangement occurs upon complexation of phosphate and pyrophosphate, although the ligand maintains its protonation pattern. Figure 3 displays the pH dependence of the ^1H NMR

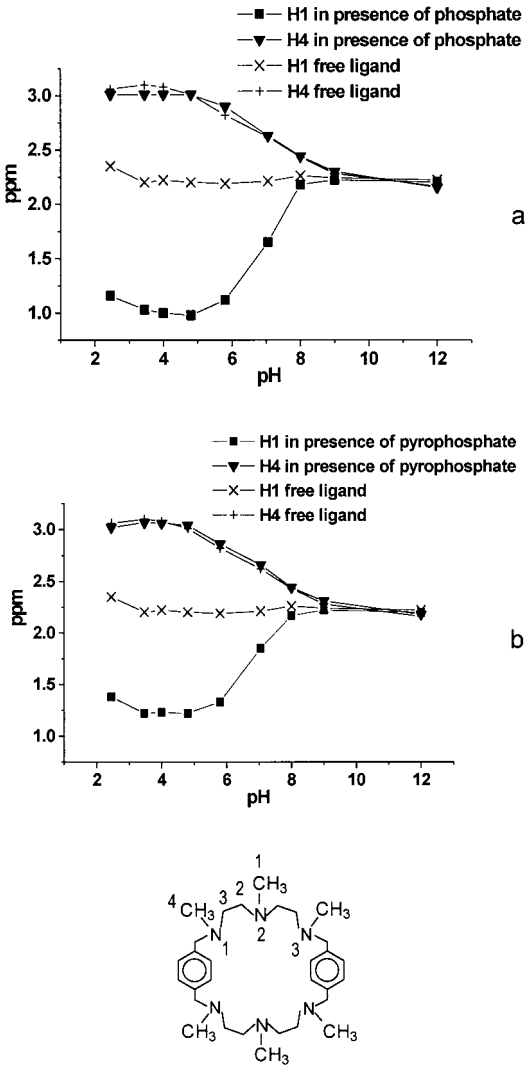

Figure 3. Experimental ^{1}H chemical shifts of H1 and H4 protons of $Ph_2Me_6N_6$ as a function of pH measured in the absence and in the presence of phosphate (a) or pyrophosphate (b).

signals for the methyl groups on the ligand nitrogen atoms in the absence of interacting anions and in the presence of phosphate (Figure 3a) and pyrophosphate (Figure 3b); these signals are very sensitive to nitrogen protonation. The complete ^{1}H and ^{13}C NMR study of $Ph_2Me_6N_6$ protonation in the absence of complexing anions, defining the protonation pattern of the ligand, was reported in a previous paper.[9f] The ^{1}H NMR signal of the protons (H1) belonging to the C1 methyl groups keeps constant from alkaline pH down to pH 3, while in the same pH range the signal for the C4 protons (H4) experiences an evident downfield shift, manifesting that the first four protons bind to the benzylic nitrogens; in more acidic solution, the H4 signal keeps constant while the H1 one shifts downfield according to a fifth protonation step taking place on the N2 atoms. In the presence of phosphate (Figure 3a) and pyrophosphate (Figure 3b), the H4 signal displays the same behavior observed in the absence of interacting anions, confirming the previous protonation pattern; on the other hand, the H1 signal undergoes a marked upfield shift in the pH range 8−2.5, the maximum shift corresponding to the presence of complexes with $H_4\mathbf{L9}^{4+}$. This behavior can be ascribed to a rearrangement of the ligand, brought about by anion binding, which maintains the overall conformation around the benzylic ammonium groups but pushes the methyl groups bearing H1 toward the benzene π electron clouds, determining the observed shielding of H1 protons. A similar ligand arrangement was found in the crystal structure of the perchlorate complex of $H_4\mathbf{L9}^{4+}$.[9f]

On the other hand, it has been shown,[9b] by means of NMR studies, that in the cases of **L1** and **L4** there is no observable charge localization in the successive protonation steps, due to the equivalence of the secondary amino groups. This means that in solution, on the NMR time scale, the overall positive charge has a mediate homogeneous distribution over all the nitrogen atoms of the ligands. So, independently of pH, all the ligand atoms remain magnetically equivalent, both in the absence and in the presence of interacting anions, and consequently NMR experiments do not furnish helpful information regarding the number of H^+ ions bound to the ligands. Similarly, also ^{31}P NMR experiments do not give clear information about the protonation state of the phosphate anions in these systems. Hence, taking into account the observation that, in the formation of the anion complexes with all the other receptors, the interacting partners maintain their identity, we have assumed this applies also for **L1** and **L4**. As a matter of fact, the anion complex $(H_4\mathbf{L1})(H_2P_2O_7)_2\cdot 6H_2O$, containing $H_4\mathbf{L1}^{4+}$ and $H_2P_2O_7^{2-}$, crystallizes under pH conditions (pH 3.5) in which these species are the main forms of **L1** and pyrophosphate in solution. However, despite these considerations, we cannot exclude the presence in solution of anion complexes with equal stoichiometry but different protonation states of the ligand and anion.

Once the number l of protons bound to the ligand in the general ALH_m complex is known, we can write the complexation reactions according to the actual protonation state:

$$H_{(m-l)}A + H_lL = H_lL\cdot H_{(m-l)}A$$

and calculate the relevant equilibrium constants collected in Tables 2−4.

However, we can correctly expect these equilibria to describe the formation of the main complexed species present in solution, although, especially in the cases of **L1** and **L4**, the presence of minor anion complexes characterized by equal stoichiometry but different protonation states cannot be excluded.

As far as the stability of the complexes is considered, it is to be noted first that, despite the different sizes, molecular architecture, and number of binding groups in the ligands, only complexes with 1:1 anion/receptor stoichiometry are found in solution with both phosphate and pyrophosphate. Although electrostatic attraction is the driving force in anion interactions with polyammonium receptors, the stability trends of such complexes are not strictly determined by electrostatic contributions, in contrast with the general trend of increasing stability with increasing charge of receptors and anions previously observed for the complexes of these ligands with other inorganic anions, such as $Fe(CN)_6^{4-}$, $Co(CN)_6^{3-}$, and $Pt(CN)_4^{2-}$.[11] For instance, the stability of the complexes formed by HPO_4^{2-} with the mono-, di-, and triprotonated forms of B343 decreases with increasing charge on the ligand (Table 3), while the stability of the complexes formed by $H_4Ph_2Me_6N_6^{4+}$ with $HP_2O_7^{3-}$, $H_2P_2O_7^{2-}$, and $H_3P_2O_7^-$ increases with decreasing charge on the anion (Table 3). Many other examples of the same type can be found in Tables 2−4. Similar behavior has never been reported before and can be ascribed, as discussed later on, to

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Table 2. Thermodynamic Parameters[a] for the Formation of Hexa- and Heptaaza Macrocyclic Polyamine Complexes with PO_4^{3-} (A^{3-}) and $P_2O_7^{4-}$ (B^{4-}) Determined in 0.15 mol dm^{-3} $NaClO_4$ at 298.1 ± 0.1 K

	L1	L2	L3	L4	L5		L1	L2	L3	L4	L5
						log *K*					
$HL^+ + HA^{2-} =$ $(HL\cdot HA)^-$		2.87(5)			3.43(3)	$HL^+ + B^{4-} =$ $(HL\cdot B)^{3-}$		2.33(9)			2.19(7)
$H_2L^{2+} + HA^{2-} =$ $(H_2L\cdot HA)$		3.16(3)	2.74(5)		3.65(3)	$H_2L^{2+} + B^{4-} =$ $(H_2L\cdot B)^{2-}$		2.45(6)			2.77(3)
$H_3L^{3+} + HA^{2-} =$ $(H_3L\cdot HA)^+$	2.69(6)	3.70(3)	3.24(5)		4.31(3)	$H_3L^{3+} + B^{4-} =$ $(H_3L\cdot B)^-$	2.94(3)	3.47(4)	3.49(5)	2.74(4)	3.24(3)
$H_3L^{3+} + H_2A^- =$ $(H_3L\cdot H_2A)^{2+}$	3.71(5)	4.21(3)	3.40(4)	2.70(2)	4.78(3)	$H_3L^{3+} + HB^{3-} =$ $(H_3L\cdot HB)$	3.27(3)	3.79(3)	2.52(6)	3.93(2)	3.49(2)
$H_4L^{4+} + H_2A^- =$ $(H_4L\cdot H_2A)^{3+}$	5.02(6)	5.20(5)	3.83(5)	2.14(3)	5.32(3)	$H_4L^{4+} + HB^{3-} =$ $(H_4L\cdot HB)^+$	5.69(3)	6.33(3)		7.50(3)	4.96 (2)
$H_5L^{5+} + H_2A^- =$ $(H_5L\cdot H_2A)^{4+}$	5.53(7)			3.11(2)	6.42(4)	$H_3L^{3+} + H_2B^{2-} =$ $(H_3L\cdot H_2B)^+$	4.04(3)	4.29(3)			4.46(2)
$H_6L^{6+} + H_2A^- =$ $(H_6L\cdot H_2A)^{5+}$				4.61(3)	6.93(4)	$H_4L^{4+} + H_2B^{2-} =$ $(H_4L\cdot H_2B)^{2+}$	4.37(4)	4.53(4)		5.16(2)	4.71(2)
						$H_5L^{5+} + H_2B^{2-} =$ $(H_5L\cdot H_2B)^{3+}$	4.11(6)			6.53(2)	6.14(2)
						$H_6L^{6+} + H_2B^{2-} =$ $(H_6L\cdot H_2B)^{4+}$				8.29(3)	7.10(2)
						$\Delta H°$ (kcal mol^{-1})					
$HL^+ + HA^{2-} =$ $(HL\cdot HA)^-$		−0.2(3)			0.5(2)	$HL^+ + B^{4-} =$ $(HL\cdot B)^{3-}$		0.9(2)			0.3(4)
$H_2L^{2+} + HA^{2-} =$ $(H_2L\cdot HA)$		0.8(2)	0.3(1)		1.9(2)	$H_2L^{2+} + B^{4-} =$ $(H_2L\cdot B)^{2-}$		0.1(1)			1.9(2)
$H_3L^{3+} + HA^{2-} =$ $(H_3L\cdot HA)^+$	1.1(3)	0.3(2)	0.8(1)		1.3(2)	$H_3L^{3+} + B^{4-} =$ $(H_3L\cdot B)^-$	1.2(2)	0.5(1)	1.1(2)	0.2(2)	2.3(2)
$H_3L^{3+} + H_2A^- =$ $(H_3L\cdot H_2A)^{2+}$	−2.9(3)	−6.0(2)	−1.3(1)	−12.11(6)	-2.2(3)	$H_3L^{3+} + HB^{3-} =$ $(H_3L\cdot HB)$	−6.6(2)	−9.71(7)	−1.0(2)	−9.32(8)	−5.6(2)
$H_4L^{4+} + H_2A^- =$ $(H_4L\cdot H_2A)^{3+}$	0.3(3)	−2.1(2)	−0.8(1)	−12.5(1)	1.8(3)	$H_4L^{4+} + HB^{3-} =$ $(H_4L\cdot HB)^+$	2.3(2)	0.4(2)		−2.8(1)	0.2(2)
$H_5L^{5+} + H_2A^- =$ $(H_5L\cdot H_2A)^{4+}$	−5.4(3)			−4.7(1)	2.3(3)	$H_3L^{3+} + H_2B^{2-} =$ $(H_3L\cdot H_2B)^+$	−9.7(2)	−11.82(8)			−10.0(2)
$H_6L^{6+} + H_2A^- =$ $(H_6L\cdot H_2A)^{5+}$				−6.53(1)	1.7(2)	$H_4L^{4+} + H_2B^{2-} =$ $(H_4L\cdot H_2B)^{2+}$	−1.3(2)	−1.4(1)		−8.92(8)	−5.3(2)
						$H_5L^{5+} + H_2B^{2-} =$ $(H_5L\cdot H_2B)^{3+}$	1.4(3)			−8.71(8)	−2.8(2)
						$H_6L^{6+} + H_2B^{2-} =$ $(H_6L\cdot H_2B)^{4+}$				−6.43(7)	2.2(2)
						$T\Delta S°$ (kcal mol^{-1})					
$HL^+ + HA^{2-} =$ $(HL\cdot HA)^-$		3.7(3)			5.2(2)	$HL^+ + B^{4-} =$ $(HL\cdot B)^{3-}$		4.1(2)			3.3(4)
$H_2L^{2+} + HA^{2-} =$ $(H_2L\cdot HA)$		5.1(2)	4.0(1)		6.8(2)	$H_2L^{2+} + B^{4-} =$ $(H_2L\cdot B)^{2-}$		3.4(1)			5.7(2)
$H_3L^{3+} + HA^{2-} =$ $(H_3L\cdot HA)^+$	4.8(3)	5.3(2)	5.2(1)		7.2(2)	$H_3L^{3+} + B^{4-} =$ $(H_3L\cdot B)^-$	5.2(2)	5.2(1)	5.9(2)	3.9(2)	6.7(2)
$H_3L^{3+} + H_2A^- =$ $(H_3L\cdot H_2A)^{2+}$	2.1(3)	−0.3(2)	3.3(1)	−8.4(1)	4.3(3)	$H_3L^{3+} + HB^{3-} =$ $(H_3L\cdot HB)$	−2.1(2)	−4.5(1)	2.4(2)	−3.9(1)	−0.8(2)
$H_4L^{4+} + H_2A^- =$ $(H_4L\cdot H_2A)^{3+}$	7.1(3)	5.0(2)	4.4(1)	−9.6(1)	9.1(3)	$H_4L^{4+} + HB^{3-} =$ $(H_4L\cdot HB)^+$	10.1(2)	9.0(1)		7.4(1)	7.0(2)
$H_5L^{5+} + H_2A^- =$ $(H_5L\cdot H_2A)^{4+}$	2.1(3)			−0.5(1)	11.1(3)	$H_3L^{3+} + H_2B^{2-} =$ $(H_3L\cdot H_2B)^+$	−4.2(2)	−5.9(1)			−3.9(2)
$H_6L^{6+} + H_2A^- =$ $(H_6L\cdot H_2A)^{5+}$				−0.2(1)	11.2(3)	$H_4L^{4+} + H_2B^{2-} =$ $(H_4L\cdot H_2B)^{2+}$	4.7(2)	4.8(1)		−1.9(1)	1.1(2)
						$H_5L^{5+} + H_2B^{2-} =$ $(H_5L\cdot H_2B)^{3+}$	7.0(3)			0.2(1)	5.6(2)
						$H_6L^{6+} + H_2B^{2-} =$ $(H_6L\cdot H_2B)^{4+}$				4.9(1)	11.9(2)

[a] Values in parentheses are standard deviations on the last significant figure.

the particular ability of phosphate species to behave as acceptors and donors of hydrogen bonds.

Considering the stability of the complexes formed by phosphate and pyrophosphate in a given protonation degree, with the same receptor, one can observe that no strict trends are found, and, in contrast to electrostatic expectations, once again the less charged anion can form more stable complexes. However, in a general sense, pyrophosphate displays a greater propensity to form complexes, in particular with greater ligands in high protonation degrees and especially with open-chain ligands. As a matter of fact, phosphate does not form complexes with Me_2hexaen and L323. This behavior seems to be connected with the ability of pyrophosphate to involve one or two phosphate moieties in the interaction with a single polyammonium cations, as depicted by the crystal structures in Figures 1 and 2, availing of localized anchorage in small receptors and separated binding groups in greater ligands.

Enthalpic and Entropic Contributions. According to a simple electrostatic model, the formation of ion pairs between rigid cations and anions (hard sphere with embedded point charges) in an ideal structureless, homogeneous solvent is expected to be accompanied by slightly unfavorable $\Delta H°$ contributions and largely favorable entropic terms, principally deriving from the desolvation of the interacting species determined by the charge neutralization occurring in the pairing process.[12]

Tables 2−4 collect the enthalpic and entropic contributions

(12) Bianchi, A.; Garcia-España, E. In *Supramolecular Chemistry of Anions*; Bianchi, A., Bowman-James, K., Garcia-España, E., Eds.; Wiley-VCH: New York, 1997; 217−275.

Table 3. Thermodynamic Parameters[a] for the Formation of Paracyclophane Complexes with PO_4^{3-} (A^{3-}) and $P_2O_7^{4-}$ (B^{4-}) Determined in 0.15 mol dm^{-3} $NaClO_4$ at 298.1 ± 0.1 K

	L6	L7	L8	L9		L6	L7	L8	L9
					log *K*				
$HL^+ + HA^{2-} = (HL{\cdot}HA)^-$	2.89(2)	2.88(2)	3.42(2)	2.45(1)	$H_2L^{2+} + B^{4-} = (H_2L{\cdot}B)^{2-}$	2.60(3)	3.69(2)	4.42(3)	
$H_2L^{2+} + HA^{2-} = (H_2L{\cdot}HA)$	3.31(2)	3.61(2)	3.02(2)	2.47(2)	$H_2L^{2+} + HB^{3-} = (H_2L{\cdot}HB)^-$	3.28(3)	4.24(4)	5.16(3)	
$H_3L^{3+} + HA^{2-} = (H_3L{\cdot}HA)^+$	3.88(2)	4.21(2)	2.49(3)	2.54(4)	$H_3L^{3+} + HB^{3-} = (H_3L{\cdot}HB)$	3.55(3)	4.57(3)	5.35(3)	2.63(4)
$H_3L^{3+} + H_2A^- = (H_3L{\cdot}H_2A)^{2+}$	3.87(2)	4.20(5)	2.58(4)	2.11(5)	$H_4L^{4+} + HB^{3-} = (H_4L{\cdot}HB)^+$		5.39(4)	5.62(2)	2.55(3)
$H_4L^{4+} + H_2A^- = (H_4L{\cdot}H_2A)^{3+}$	6.08(3)	4.41(4)		1.74(3)	$H_3L^{3+} + H_2B^{2-} = (H_3L{\cdot}H_2B)^+$	4.15(4)			
					$H_4L^{4+} + H_2B^{2-} = (H_4L{\cdot}H_2B)^{2+}$	5.41(4)	4.93(4)	5.79(3)	2.77(5)
					$H_4L^{4+} + H_3B^- = (H_4L{\cdot}H_3B)^{3+}$				3.17(4)
					$\Delta H°$ (kcal mol^{-1})				
$HL^+ + HA^{2-} = (HL{\cdot}HA)^-$	−1.09(2)	−1.44(3)	−0.66(3)	2.83(2)	$H_2L^{2+} + B^{4-} = (H_2L{\cdot}B)^{2-}$	1.15(1)	1.00(2)	2.66(1)	
$H_2L^{2+} + HA^{2-} = (H_2L{\cdot}HA)$	−1.07(3)	−0.65(3)	−0.43(3)	2.43(2)	$H_2L^{2+} + HB^{3-} = (H_2L{\cdot}HB)^-$	−3.54(1)	−5.03(2)	−2.98(1)	
$H_3L^{3+} + HA^{2-} = (H_3L{\cdot}HA)^+$	0.58(6)	1.36(5)	0.82(5)	6.61(3)	$H_3L^{3+} + HB^{3-} = (H_3L{\cdot}HB)$	−2.59(2)	−3.36(2)	−0.89(1)	1.94(2)
$H_3L^{3+} + H_2A^- = (H_3L{\cdot}H_2A)^{2+}$	−0.81(6)	−1.78(6)	−8.34(7)	11.71(4)	$H_4L^{4+} + HB^{3-} = (H_4L{\cdot}HB)^+$		1.49(2)	4.97(2)	2.25(3)
$H_4L^{4+} + H_2A^- = (H_4L{\cdot}H_2A)^{3+}$	−1.42(8)	−0.79(6)		9.00(7)	$H_3L^{3+} + H_2B^{2-} = (H_3L{\cdot}H_2B)^+$	−5.39(2)			
					$H_4L^{4+} + H_2B^{2-} = (H_4L{\cdot}H_2B)^{2+}$	−1.09(2)	0.02(2)	1.50(2)	0.93(4)
					$H_4L^{4+} + H_3B^- = (H_4L{\cdot}H_3B)^{3+}$				−6.20(5)
					$T\Delta S°$ (kcal mol^{-1})				
$HL^+ + HA^{2-} = (HL{\cdot}HA)^-$	2.85(3)	2.49(3)	4.01(4)	6.17(3)	$H_2L^{2+} + B^{4-} = (H_2L{\cdot}B)^{2-}$	4.69(4)	6.03(2)	8.69(1)	
$H_2L^{2+} + HA^{2-} = (H_2L{\cdot}HA)$	3.43(4)	4.27(3)	3.69(5)	5.81(4)	$H_2L^{2+} + HB^{3-} = (H_2L{\cdot}HB)^-$	0.93(3)	0.75(3)	4.06(3)	
$H_3L^{3+} + HA^{2-} = (H_3L{\cdot}HA)^+$	5.92(3)	7.10(5)	4.22(5)	10.09(4)	$H_3L^{3+} + HB^{3-} = (H_3L{\cdot}HB)$	2.25(3)	2.87(3)	6.41(3)	5.54(2)
$H_3L^{3+} + H_2A^- = (H_3L{\cdot}H_2A)^{2+}$	4.51(4)	4.03(4)	−4.82(5)	12.00(8)	$H_4L^{4+} + HB^{3-} = (H_4L{\cdot}HB)^+$		8.75(3)	12.63(3)	5.74(2)
$H_4L^{4+} + H_2A^- = (H_4L{\cdot}H_2A)^{3+}$	6.93(4)	5.22(4)		11.38(9)	$H_3L^{3+} + H_2B^{2-} = (H_3L{\cdot}H_2B)^+$	0.27(4)			
					$H_4L^{4+} + H_2B^{2-} = (H_4L{\cdot}H_2B)^{2+}$	6.29(3)	6.74(4)	9.39(4)	4.71(2)
					$H_4L^{4+} + H_3B^- = (H_4L{\cdot}H_3B)^{3+}$				−1.87(2)

[a] Values in parentheses are standard deviation on the last significant figure.

to the formation of the anion complexes studied in this work in aqueous solution. As can be seen, many complexation reactions are almost athermic, or endothermic, and are promoted by favorable entropic contributions ($T\Delta S° > 0$), in agreement with the ideal electrostatic model, although there is also a considerable number of reactions promoted by large favorable enthalpy changes ($\Delta H° < 0$) and accompanied by evident entropy loss.

Phosphate, pyrophosphate anions, and polyammonium receptors can be involved in the formation of many hydrogen bonds in which both the anions and the receptors can act as acceptors or donors. Hydrogen bonding is largely determined by electrostatic attraction (dipole−dipole, charge−dipole), although significant contributions are also furnished by charge-transfer, dispersive, and covalent forces.[12] In particular, when hydrogen bonding takes place between chemical species characterized by marked acid/base properties, such as amine, ammonium, phosphate, and protonated phosphate compounds, contributions from proton transfer (charge transfer) from the donor to the acceptor groups may be of considerable importance. There are four possible modes of hydrogen bonding (type 1) involving amine or ammonium groups as donors, and just one (type 2) involving the amine groups as acceptors in the formation of the anion complexes considered in the present study:

$$-N-H^+\cdots{}^-O- \qquad \Delta H° > 0,\ T\Delta S° > 0 \qquad (1.1)$$

$$-N-H^+\cdots OH- \qquad \Delta H° > 0,\ T\Delta S° \approx 0 \qquad (1.2)$$

$$-N-H\cdots{}^-O- \qquad \Delta H° > 0,\ T\Delta S° \approx 0 \qquad (1.3)$$

$$-N-H\cdots OH- \qquad \Delta H° > 0,\ T\Delta S° < 0 \qquad (1.4)$$

$$-N|\cdots H-O- \qquad \Delta H° < 0,\ T\Delta S° < 0 \qquad (2)$$

The binding mode 1.1, leading to the formation of hydrogen-bonded ion pair interactions, is of principal importance in such association processes since it furnishes synergetic hydrogen bonding and electrostatic attraction and represents a preferred association scheme, especially in solvents with high dielectric constants such as water. Type 1.2 hydrogen bonds should be effective only in very acidic solution, where both the anion and the receptors are extensively protonated. On the other hand, type 1.3 bonds are favored in alkaline media, where both the receptors and the anions are extensively deprotonated; they seem not to be very important since, under similar pH conditions, anion complexes are not formed. Modes 1.4 and 2 are the possible hydrogen bonds occurring between amines and compounds bearing −OH groups, but as known,[13] type 1.4 bonds are largely weaker than type 2 ones, which give the major contribution.

Type 1 hydrogen bonds determine a partial deprotonation of the amino group and a partial protonation of a phosphate oxygen. As known,[14] deprotonation of an amino group is a strongly endothermic reaction, while protonation of HPO_4^{2-}, $H_2PO_4^-$, and pyrophosphate anions is athermic or weakly endothermic (see also Supporting Information). Altogether, charge transfer in type 1 hydrogen bonds is accompanied by an unfavorable enthalpic contribution ($\Delta H° > 0$), while from the entropic point of view different contributions are expected, mostly depending on the effect the process has on the separation of charge. Hence, an entropy gain is expected for type 1.1 bonds, due to the release of solvent molecules determined by charge neutralization, while an entropy loss should accompany charge transfer in type 1.4) bonds, and no evident entropic effects should be determined by types 1.2 and 1.3, which are expected not to alter significantly the charge separation. Conversely, the formation of type 2 hydrogen bonds, which consists of partial protonation of an amino group and partial deprotonation of a phosphate oxygen, is promoted by negative enthalpy changes, the entropic terms being unfavorable.

As observed above, 1.1, 1.2, and 2 are expected to be the principal hydrogen binding modes. In any case, the extent of such contributions is strictly connected with the extent of proton transfer in the hydrogen bond formation, which depends, as already discussed (see Introduction), on the N−O separation and the dielectric constant of the medium. The difference

(13) Jeffrey, G. A. *An Introduction to Hydrogen Bonding*; Oxford University Press: New York, 1997.

(14) Smith, R. M.; Martell, A. E. *NIST Critical Stability Constants Database*, version 4, 1997.

Table 4. Thermodynamic Parameters[a] for the Formation of Acyclic Polyamine Complexes with PO_4^{3-} (A^{3-}) and $P_2O_7^{4-}$ (B^{4-}) Determined in 0.15 mol dm^{-3} $NaClO_4$ at 298.1 ± 0.1 K

	L10	L11	L12	L13	L14		L10	L11	L12	L13	L14
						log *K*					
$H_2L^{2+} + HA^{2-} =$ $(H_2L\cdot HA)$	2.80(5)					$H_3L^{3+} + HB^{3-} =$ $(H_3L\cdot HB)$	3.73(3)	3.77(2)	3.00(2)	3.64(1)	3.47(4)
$H_3L^{3+} + HA^{2-} =$ $(H_3L\cdot HA)^{+}$	2.47(7)					$H_4L^{4+} + HB^{3-} =$ $(H_4L\cdot HB)^{+}$	4.41(4)	3.88(3)	3.91(4)	3.34(1)	2.56(3)
$H_4L^{4+} + HA^{2-} =$ $(H_4L\cdot HA)^{2+}$				2.28(4)	2.23(4)	$H_4L^{4+} + H_2B^{2-} =$ $(H_4L\cdot H_2B)^{2+}$	4.27(4)	4.67(3)	3.02(3)	2.90(1)	2.15(4)
						$H_5L^{5+} + H_2B^{2-} =$ $(H_5L\cdot H_2B)^{3+}$	4.62(5)	5.23(6)			
$H_3L^{3+} + B^{4-} =$ $(H_3L\cdot B)^{-}$	2.47(4)		2.38(3)	2.79(2)		$H_6L^{6+} + H_2B^{2-} =$ $(H_6L\cdot H_2B)^{4+}$	4.27(6)	5.74(6)			
$H_4L^{4+} + B^{4-} =$ $(H_4L\cdot B)$		3.87(2)			3.62(4)	$H_7L^{7+} + H_2B^{2-} =$ $(H_7L\cdot H_2B)^{5+}$		5.74(6)			
						$\Delta H°$ (kcal mol^{-1})					
$H_2L^{2+} + HA^{2-} =$ $(H_2L\cdot HA)$	8.05(6)					$H_3L^{3+} + HB^{3-} =$ $(H_3L\cdot HB)$	−9.47(3)	−10.98(2)	−6.20(1)	−7.83(1)	−3.16(4)
$H_3L^{3+} + HA^{2-} =$ $(H_3L\cdot HA)^{+}$	9.28(6)					$H_4L^{4+} + HB^{3-} =$ $(H_4L\cdot HB)^{+}$	−5.96(2)	−6.64(3)	1.20(2)	2.82(1)	10.22(8)
$H_4L^{4+} + HA^{2-} =$ $(H_4L\cdot HA)^{2+}$				1.09(5)	2.02(5)	$H_4L^{4+} + H_2B^{2-} =$ $(H_4L\cdot H_2B)^{2+}$	−11.38(5)	−12.84(6)	0.74(2)	2.26(1)	12.03(4)
						$H_5L^{5+} + H_2B^{2-} =$ $(H_5L\cdot H_2B)^{3+}$	−6.02(5)	−10.07(7)			
$H_3L^{3+} + B^{4-} =$ $(H_3L\cdot B)^{-}$	0.32(2)		0.51(1)	3.83(1)		$H_6L^{6+} + H_2B^{2-} =$ $(H_6L\cdot H_2B)^{4+}$	2.13(5)	−4.91(5)			
$H_4L^{4+} + B^{4-} =$ $(H_4L\cdot B)$		−0.21(3)			8.69(3)	$H_7L^{7+} + H_2B^{2-} =$ $(H_7L\cdot H_2B)^{5+}$		2.22(4)			
						$T\Delta S°$ (kcal mol^{-1})					
$H_2L^{2+} + HA^{2-} =$ $(H_2L\cdot HA)$	11.88(7)					$H_3L^{3+} + HB^{3-} =$ $(H_3L\cdot HB)$	−4.38(2)	−5.83(2)	−2.10(3)	−2.87(3)	1.58(3)
$H_3L^{3+} + HA^{2-} =$ $(H_3L\cdot HA)^{+}$	12.66(8)					$H_4L^{4+} + HB^{3-} =$ $(H_4L\cdot HB)^{+}$	0.06(2)	−1.34(2)	6.53(3)	7.37(3)	13.71(3)
$H_4L^{4+} + HA^{2-} =$ $(H_4L\cdot HA)^{2+}$				4.20(6)	5.07(6)	$H_4L^{4+} + H_2B^{2-} =$ $(H_4L\cdot H_2B)^{2+}$	−5.55(2)	−6.46(2)	4.86(4)	6.21(4)	14.96(4)
						$H_5L^{5+} + H_2B^{2-} =$ $(H_5L\cdot H_2B)^{3+}$	0.28(2)	−2.93(2)			
$H_3L^{3+} + B^{4-} =$ $(H_3L\cdot B)^{-}$	4.30(2)		3.76(1)	7.63(1)		$H_6L^{6+} + H_2B^{2-} =$ $(H_6L\cdot H_2B)^{4+}$	7.95(2)	2.92(2)			
$H_4L^{4+} + B^{4-} =$ $(H_4L\cdot B)$		5.07(2)			13.62(2)	$H_7L^{7+} + H_2B^{2-} =$ $(H_7L\cdot H_2B)^{5+}$		10.05(2)			

[a] Values in parentheses are standard deviation on the last significant figure.

between hydrogen bonding in the ion pairs and in the neutral complexes vanishes for short separations, while the neutral complex is favored by low dielectric constants. In the case of phosphate and pyrophosphate complexes with polyammonium ligands, the strong electrostatic attraction brings the anion and the receptor in contact with each other. Under these conditions, both types of hydrogen bonds can be formed, depending on the complex structure and the protonation degree of the reacting species. As a matter of fact, in the crystal structures of the **L1** and **L2** complexes with $H_2P_2O_7^{2-}$ described above, only type 1.1 hydrogen bonds are formed between the anion and the receptors, while in a previous $H_2P_2O_7^{2-}$ complex,[4f] also type 2 bonds were observed. Upon increasing the ligand protonation, also its donor properties are enhanced, favoring the formation of type 1 hydrogen bonds, while type 2 bonds are favored by increasing anion protonation.

Actually, the binding reactions involving the fully deprotonated pyrophosphate anions, which forms only type 1.1 hydrogen bonds, are accompanied by unfavorable enthalpic and favorable entropic contributions (Tables 2−4). Also, the stability decrease previously highlighted for the complexes formed by HPO_4^{2-} with the mono-, di-, and triprotonated forms of B343 (Table 3) can be interpreted in terms of increasing hydrogen bond donor properties (type 1 bonds) of the receptors, leading to unfavorable enthalpic contributions. On the other hand, the stability increase of the complexes formed by pyrophosphate and $H_4Ph_2Me_6N_6^{4+}$, as the charge on the anion decreases from $HP_2O_7^{3-}$ to $H_3P_2O_7^{-}$ (Table 5), can be attributed to the greater donor ability of the more protonated anions (type 2 bonds) determining more favorable enthalpic and less favorable entropic contributions.

Table 5. Slope (α) and Intercept (*I*)[a] of the $\Delta H°-T\Delta S°$ Plots for 1:1 Complexation Reactions with Various Receptors and Substrates in Solution.

host	guest	α	*I* (kcal/mol)	ref
podands	metal cations	0.86	2.3	15a
crown ethers	metal cations	0.76	2.4	15a
cryptands	metal cations	0.51	4.0	15a
cyclophanes/calixarenes	neutral molecules	0.78	3.4	15f
cyclodextrins		0.90	3.1	15e
modified cyclodextrins	neutral molecules	1.07	5.0	15f
metalloporphyrins	neutral molecules	0.61	1.6	15f
quinone receptor porphyrins	neutral molecules	0.60	0.0	15f,g
polyammonium cations deriving from polyazacycloalkanes and polyazacyclophanes	HPO_4^{2-}, $H_2PO_4^{-}$, $P_2O_7^{4-}$, $HP_2O_7^{3-}$, $H_2P_2O_7^{2-}$, $H_3P_2O_7$-	0.92(4)	5.3(1)	*b*
polyammonium cations deriving from acyclic polyamines	HPO_4^{2-}, $P_2O_7^{4-}$, $HP_2O_7^{3-}$, $H_2P_2O_7^{2-}$	0.89(3)	4.7(1)	*b*

[a] Numbers in parentheses are standard deviations on the last significant figures. [b] This work.

As observed before, dealing with the stability trends of the

studied complexes, several other examples of this type can be found in Tables 2−4.

Enthalpy−Entropy Compensation. The examples presented in the previous section evidence some compensation between the enthalpy and entropy changes for the relevant complexation reactions. Considering the complete set of thermodynamic data obtained in this work for the interaction of phosphate and pyrophosphate with the nine macrocycles and the five acyclic ligands, good linear $\Delta H°-T\Delta S°$ correlations (correlation coefficients (R) of 0.96 and 0.98, respectively) are obtained for both cyclic (92 data points) and acyclic (29 data points) receptors.

Similar $\Delta H°-T\Delta S°$ compensatory relationships hold in general for complexation reactions involving weak interactions, i.e., van der Waals, hydrogen bonding, dipole−dipole, and ion−dipole interactions, and have been used to get quantitative estimations of the ligands' conformational changes resulting from complex formation, according to the general observation that the slope α of the $\Delta H°-T\Delta S°$ plots ($T\Delta S° = \alpha\Delta H° + I$) decreases with increasing ligand rigidity.[15] A significant example of this trend is given by the α values reported in Table 5 for the binding of alkaline and alkaline-heart cations by podand, crown ether, and cryptand ligands. However, in such complexation reactions, the "ligand rigidity" has to be interpreted in terms of adaptability of the ligand binding sites to the specific substrates. Actually, the high α values (0.90−1.07, Table 5) found for reactions of substrates' inclusion into cyclodextrins and modified cyclodextrins contrast with the considerable rigidity of the skeleton of such molecules, but this apparently surprising behavior is explained by the well-known ability of cyclodextrins in reorganizing their internal hydrogen bond network upon inclusion complexation.[15e]

From this point of view, also the polyammonium cations studied in this work display considerable adaptability, i.e., high α values (0.92(4) and 0.89(3) for macrocyclic and acyclic receptors, respectively), in the binding of phosphate and pyrophosphate anions, despite the ligand stiffening occurring upon accumulation of positive charge on the ligands. It is interesting to note that no significant difference in the fitting parameters (slope α and intercept I) is found when treating separately the $\Delta H°-T\Delta S°$ data for polyazacycloalkanes and polyazacyclophanes, indicating that, although the insertion of aromatic benzene spacers in macrocyclic polyamines gives rise to more rigid molecular skeletons, whose effects are observed for instance in metal ions coordination,[16] the adaptability of these receptors in the binding of the considered anionic substrates is determined not by the ligand rigidity but by the receptor ability in organizing hydrogen bonds and salt bridges in the complexes. Furthermore, also the α parameter obtained for the acyclic polyammonium receptors is almost identical, within experimental errors (Table 5), to that found for cyclic ones, evidencing that the adaptability of such receptors in the present anion binding processes is not strictly connected with their cyclic or acyclic structures.

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Table 6. Crystal Data and Structure Refinement for $(H_4\mathbf{L1})(H_2P_2O_7)_2\cdot 2H_2O$ and $(H_4\mathbf{L2})(H_2P_2O_7)_2\cdot 6H_2O$

	$(H_4\mathbf{L1})(H_2P_2O_7)_2\cdot 2H_2O$	$(H_4\mathbf{L2})(H_2P_2O_7)_2\cdot 6H_2O$
formula	$C_{12}H_{42}N_6O_{16}P_4$	$C_{14}H_{54}N_6O_{20}P_4$
FW	650.4	750.51
dimensions (mm^3)	0.07 × 0.25 × 0.3	0.2 × 0.15 × 0.1
crystal system	monoclinic	triclinic
color, shape	colorless, prismatic	colorless, prismatic
space group	$P2_1/n$	$P\bar{1}$
unit cell dimensions	a = 9.201(8) Å	a = 11.009(2) Å
	α = 90°	α = 110.71(2)°
	b = 12.617(7) Å	b = 13.286(2) Å
	β = 104.59(6)°	β = 112.830(10)°
	c = 11.838(9) Å	c = 13.450(2) Å
	γ = 90°	γ = 90.820(10)°
V (Å^3)	1330(2)	1669.6(5)
Z	2	2
ρ_{calcd} (g cm^{-3})	1.624	1.493
T (K)	298	298
goodness-of-fit on F^2	0.996	1.055
final R indices [$I > 2\sigma(I)$][a]	$R1$ = 0.1010	$R1$ = 0.0670
	$wR2$ = 0.2452	$wR2$ = 0.1907
R indices (all data)[a]	$R1$ = 0.1428	$R1$ = 0.0731
	$wR2$ = 0.2698	$wR2$ = 0.1990

[a] $R1 = ||F_o| - |F_c||/|F_o|$; $wR2 = [w(F_o^2 - F_c^2)^2/wF_o^4]^{1/2}$.

On the other hand, interesting information on the receptor nature is given by the intercept parameter I. This parameter can be considered a common contribution to the stability of all complexes of the considered class of ligands ($\Delta G° = (1 - \alpha)\Delta H° - I$). Indeed, the I value is 4.7(1) kcal mol^{-1} for acyclic receptors and 5.3(1) kcal mol^{-1} for cyclic ones, indicating a greater "intrinsic" contribution to the stability of complexes with the second type of ligands, which form, thanks to their cyclic nature, protonated species of higher charge densities, producing stronger electrostatic interactions with anionic substrates.

An interesting trend of I values is found as far as the cyclic receptors in each protonation degree are concerned. The slope α of the fitting curves is identical, within experimental values, for all ligand protonation states, indicating that the adaptability of such receptors for such anions is not strictly connected with the protonation state of receptors. On the other hand, the intercept I increases considerably from 3.9(2) to 6.4(4) kcal mol^{-1} with increasing charge on the ligands for HL^+ to H_4L^{4+}, accounting for a greater intrinsic contribution (I) to the stability of complexes with more charged receptors.

Experimental Section

Materials. Ligands **L2**−**L6** and **L9**−**L11** were synthesized according to previously described procedures.[9] **L1** and **L12**−**L14** were purchased from commercial sources and purified as hydrochloride salts. **L7** and **L8** were prepared from 1,5,9,13-tetraazatridecane or 1,5,10,-14-tetraazatetradecane and 1,4-bis(bromomethyl)-benzene, by the general procedure reported for related polyaza[n]paracyclophanes.[9g] High-purity $Na_2HPO_4\cdot 2H_2O$ and $Na_4P_2O_7\cdot 10H_2O$, employed in the potentiometric measurements and in the synthesis of the crystalline complexes, were purchased from Merck.

$(H_4L1)(H_2P_2O_7)_2\cdot 2H_2O$ and $(H_4L2)(H_2P_2O_7)_2\cdot 6H_2O$. Crystals of these compounds suitable for X-ray analysis were obtained by slow diffusion of acetone into aqueous solutions containing the ligand and the anion in 1:1 molar ratio at pH 3. Satisfactory elemental analyses were obtained for all samples.

X-ray Crystallography. General Procedures. Experimental details of the X-ray analyses are provided in Table 6. Single-crystal X-ray data for $(H_4\mathbf{L1})(H_2P_2O_7)_2\cdot 2H_2O$ (A) and $(H_4\mathbf{L2})(H_2P_2O_7)_2\cdot 6H_2O$ (B) were collected on an Enraf-Nonius CAD4 diffractometer which uses an equatorial geometry, with graphite-monochromated Mo Kα (A) and Cu Kα (B) radiations, at room temperature. Cell parameters were

determined by least-squares refinement of diffractometer setting angles for 25 carefully centered reflections. The intensities of two standard reflections per compound were monitored during data collections to check the stability of the diffractometer and of the crystals; no loss of intensity was recognized.

Total of 2046 (θ range from 2.52 to 24.97°, $\pm h,k,l$) and 4863 (θ range from 3.61 to 59.95°, $h,\pm k,\pm l$) reflections were collected for A and B, respectively. Intensity data were corrected for Lorentz and polarization effects, and an absorption correction was applied once the structures were solved by the Walker and Stuart method.[17]

The structures were solved by the direct method,[18] and the refinements were performed by means of the full matrix least-squares method of the SHELXL-93[19] program that uses the analytical approximation for atomic scattering factors and anomalous dispersion corrections for all atoms from ref 20. The function minimized was $\sum w(F_o^2 - F_c^2)$, with $w = 1/[\sigma^2(F_o^2) + (aP)^2 + bP]$ and $P = (F_o^2 + 2F_c^2)/3$, where a and b are adjustable parameters calculated by the program.

(A) $(H_4L1)(H_2P_2O_7)_2\cdot 2H_2O$. The compound crystallizes in the monoclinic family, space group $P2_1/n$ ($Z = 2$). All non-hydrogen atoms were anisotropically refined, with the hydrogen atoms in idealized positions (final value for the isotropic thermal parameter, 0.054 Å^2). Disorder was found for a moiety of the macrocyclic molecule: in particular, C2, C2′, N1, and N1′ were introduced using population parameters 0.8 (C2, N1) and 0.2 (C2′, N1′). The hydrogen atoms belonging to the four ammonium groups of H_4**L1**$^{4+}$ were localized in the final ΔF map. These hydrogen atoms were introduced in the calculation and isotropically refined.

For 187 refined parameters, the final agreement factors were $R1 = 0.1010$ (for 1336 reflections with $I > 2\sigma(I)$) and $wR2 = 0.2698$.

(B) $(H_4L2)(H_2P_2O_7)_2\cdot 6H_2O$. Crystals of this compound belong to the triclinic family, space group $P\bar{1}$ ($Z = 2$). All non-hydrogen atoms were anisotropically refined. The methylic and methylenic hydrogen atoms were introduced in idealized positions and their coordinates refined accordingly to those of the linked atoms, with overall thermal parameters refined up to 0.052 (methylenic) and 0.074 Å^2 (methylic). Double positions were found (positional parameters used 0.6 and 0.4) for a water molecule. The ΔF map carried out in the final refinement step allowed us to localize the hydrogen atoms belonging to the four ammonium groups of H_4**L2**$^{4+}$ and to a pyrophosphate anion. These hydrogen atoms were introduced in the calculation and isotropically refined.

For 450 refined parameters, the final agreement factors were $R1 = 0.067$ (for 4315 reflections with $I > 2\sigma(I)$) and $wR2 = 0.1990$.

Potentiometric Measurements. All pH-metric measurements (pH $= -\log [H^+]$) employed for the determination of protonation constants were carried out in 0.15 mol dm^{-3} $NaClO_4$ solutions at 298.1 ± 0.1 K, by using the equipment and the methodology that has been already described.[21] The combined Ingold 405 S7/120 electrode was calibrated as a hydrogen concentration probe by titrating known amounts of HCl with CO_2-free NaOH solutions and determining the equivalent point by Gran's method,[22] which allows one to determine the standard potential $E°$ and the ionic product of water ($pK_w = 13.73(1)$ at 298.1 ± 0.1 K in 0.1 mol dm^{-3} $NaClO_4$). At least five measurements (about 100 data points each) were performed for each system in the pH ranges 2.5−10.5. In all experiments, the ligand concentrations [L] were 5×10^{-4}, 1×10^{-3}, and 5×10^{-3} mol dm^{-3}. In the complexation experiments, the anion concentration was varied in the range $[L] \leq [\text{anion}] \leq 2[L]$, except for measurements with $[L] = 5 \times 10^{-3}$ mol dm^{-3}, when equimolar anion concentrations were used. The computer program HYPERQUAD[23] was used to calculate the equilibrium constants from emf data. Protonation constants of **L1**−**L6**, **L9**−**L11**, PO_4^{3-}, and $P_2O_7^{4-}$ employed in the calculations were determined in previously works.[5a,9] Successive protonation constants of **L7**, **L8**, and **L12**−**L14** determined in 0.15 mol dm^{-3} $NaClO_4$ at 298.1 ± 0.1 K are as follow: log K = 10.59(2), 9.62(2), 7.72(2), 6.08(2) for **L7**; log K = 10.39(2), 9.54(2), 7.54(2), 6.64(2) for **L8**; log K = 10.36(5), 9.86(2), 8.40(4), 5.65(6) for **L12**; log K = 10.27(4), 9.93(2), 8.60(3), 7.29(3) for **L13**; log K = 10.35(9), 10.24(3), 8.97(5), 7.99(5) for **L14**.

Great care was taken in the selection process for the equilibrium models, as described before.[24]

Microcalorimetric Measurements. The enthalpies of ligand protonation and anion complexation were determined in 0.15 mol dm^{-3} $NaClO_4$ solution by means of an automated system composed of a Thermometric AB thermal activity monitor (model 2277) equipped with a perfusion−titration device and a Hamilton pump (model Microlab M) coupled with a 0.250 cm^3 gastight Hamilton syringe (model 1750 LT). The measuring vessel was housed in a 25 dm^3 water thermostat, which was maintained at the chosen temperature within $\pm 2 \times 10^{-4}$ K. The microcalorimeter was checked by determining the enthalpy of reaction of strong base (NaOH) with strong acid (HCl) solutions. The value obtained, −13.55(5) kcal mol^{-1}, was in agreement with the literature values.[25] Further checks were performed by determining the enthalpies of protonation of ethylenediamine.

In a typical experiment, an NaOH solution (0.15 mol dm^{-3}, addition volumes 15.00 ± 0.03 μL) was added to acidic solutions of the ligands (5×10^{-3} mol dm^{-3}, 1.5 cm^3) containing equimolar quantities of the anion in the complexation experiments. Corrections for the heats of dilution were applied. Complexation experiments were designed to determine at most three enthalpy changes per calorimetric titration. The measurements were repeated at least three times. About 120 data points (at least one point per 0.1 pH unit) were obtained for each system. Further measurements were performed by adding anion solutions to ligand solutions in order to get independent confirmations of the enthalpy changes obtained for specific complexed species. Independent measurements were performed to determine ligand protonation and complexation enthalpy changes.

The enthalpies of reaction were determined from the calorimetric data by means of the AAAL program.[26]

Tables of thermodynamic data for the protonation of PO_4^{3-}, $P_2O_7^{4-}$, and **L1**−**L14** are available as Supporting Information.

Supporting Information Available: Tables of crystal data, structure solution and refinement, atomic coordinates, bond lengths and angles, anisotropic and isotropic displacement parameters for non-hydrogen atoms, and isotropic displacement parameters for hydrogen atoms for $(H_4$**L1**$)(H_2P_2O_7)_2\cdot 2H_2O$ and $(H_4$**L2**$)(H_2P_2O_7)_2\cdot 6H_2O$, and thermodynamic parameters (log K, $\Delta H°$, $T\Delta S°$) for protonation of ligands, phosphate, and pyrophosphate (PDF). This material is available free of charge via the Internet at http://pubs.acs.org.

JA983947Y

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