Synthesis, Crystal Structures, and Solution Properties of *N*-Methylene(phenyl)phosphinic Acid Derivatives of Cyclen and Cyclam

Jan Rohovec,[a] Mojmír Kývala,[a] Pavel Vojtíšek,[a] Petr Hermann,[a] and Ivan Lukeš*[a]

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Two phenylphosphinic acid derivatives of tetraaza macrocycles, (1,4,7,10-tetraazacyclododecanetetrayl)tetrakis(methylene)tetrakis(phenylphosphinic acid)] (H_4L^1) and (1,4,8,11-tetraazacyclotetradecanetetrayl)tetrakis(methylene)tetrakis(phenylphosphinic acid)] (H_4L^2), were synthesised and the crystal structures of H_4L^2 and its bis(1-adamantylammonium) salt were determined. In both the structures, the ring conformation is virtually the same and is stabilised by hydrogen bonds. Protonation constants of the acids and stability constants of their Zn^{2+} and Cd^{2+} complexes were determined pH-metrically at 25 °C and at an ionic strength of 0.1 mol dm^{-3} (KNO_3). The pK_A values found for both the compounds are lower than those for their carboxylic analogues and correspond to the expected electron-withdrawing ability of the $-P(Ph)O_2H$ moiety. The value pK_1 of the last dissociation constant of H_4L^1 is surprisingly high. The complexes of Zn^{2+} and Cd^{2+} with $(L^1)^{4-}$ and $(L^2)^{4-}$ are less stable than those with other similar ligands, which is in accordance with lower overall basicity of H_4L^1 and H_4L^2. A pronounced drop in the stability of the complexes of H_4L^2 can be explained by partial coordination of the ligand to the metal ions. The solution properties of the ligands were also investigated by ^{31}P-NMR spectroscopy. The spectra observed suggest stable (on the NMR time scale) conformations of the protonated ligands in solution. A comparison of NMR spectra in solution and CP/MAS-NMR spectra indicates that the structures of the conformers roughly correspond to the structures observed in the solid state. The conformations are stabilised by intramolecular hydrogen bonds and by hydrophobic interactions of phenylphosphinic moieties. The conformers are stable even at 90 °C, but not in the presence of complexing metal ions.

A large number of derivatives of 12- and 14-membered tetraazamacrocycles, “cyclen” and “cyclam”, have been described. The macrocycles are usually substituted on the nitrogen atoms by four identical pendant groups. The selectivity of complexation (i.e. the stability of the complexes) of such ligands towards various metal ions can be tuned by adjusting the ring size, the number or kind of coordinating atoms in the ring and the type of side chain.[1] Tetraazacycles with acetate side chains and their complexes are the most thoroughly studied substances of this kind.[2] They form thermodynamically very stable complexes, the most stable being generally those formed with di- and trivalent metals.[1][2] Some of the complexes formed are kinetically inert; e.g. with lanthanides.[3] These complexes have been widely tested because of their use, e.g. as contrast substances in MRI,[4] for labelling antigenic antibodies using metal radioisotopes[4c,5] for both diagnostic and therapeutic purposes, and also as catalysts for the splitting of nucleic acids.[6]

Some years ago, a study of aza cycles with side chains containing a methylenephosphonic[7–9] ($-CH_2-PO_3H_2$) or methylenephosphinic[7a,10–16] [$-CH_2-P(R)O_2H$] groups was begun, in a search for ligands with properties different from those containing acetic acid groups. Variation of the R group should also contribute to a change in the ion selectivity and properties of the macrocyclic compounds. Therefore, we studied the influence in a series of simple aminomethylphosphinic acids $H_2NCH_2P(R')O_2$ H, where R′ = H, methyl, phenyl, or *tert*-butyl.[17] Changes in complexing properties of the simple acids were surprisingly large, the formation constants increasing from phenyl to methyl, *tert*-butyl and hydrogen substituents. Except for R′ = H, the order follows that of the increasing basicity of the acids. Thus, we focused on the study of the influence of the methylene(phenyphosphinic acid) substituent on complexing properties of the 12- and 14-membered tetraazacycles. We have reported on the synthesis of 1,4,7-triazacyclononane and 1,4,7,10-tetraazacyclododecane functionalised with methylenephosphinic pendant groups [R = $-CH_2-P(H)O_2H$].[18] In the present paper, we report the synthesis, structure and solution properties of two polyazamacrocycle ligands; the previously described[19] (1,4,7,10-tetraazacyclododecanetetrayl)tetrakis(methylene)tetrakis(phenylphosphinic acid)] (H_4L^1), and the new ligand (1,4,8,11-tetraazacyclotetradecanetetrayl)tetrakis(methylene)tetrakis(phenylphosphinic acid)] (H_4L^2). The formulae of both the ligands studied, together with those of analogous ligands known from the literature and mentioned in the discussion, are shown in the following scheme.

Results and Discussion

Synthesis

Compounds H_4L^1 and H_4L^2 were synthesised by the Mannich reaction of 1,4,7,10-tetraazacyclododecane tetra-

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[a] Department of Inorganic Chemistry, Universita Karlova (Charles University),
Albertov 2030, 128 40 Prague 2, Czech Republic

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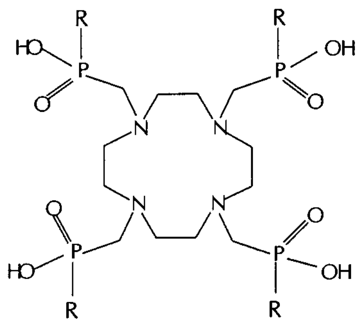

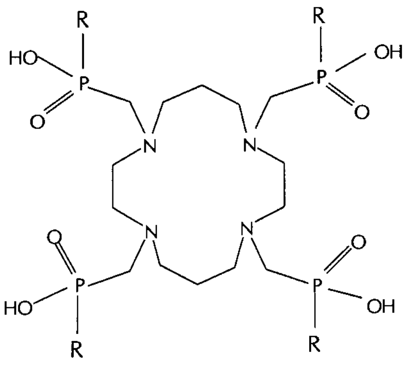

R = Ph H_4L^1

R = H H_4L^3

R = Et H_4L^4

R = OH H_8L^5

H_4L^2

H_8L^6

hydrochloride and 1,4,8,11-tetraazacyclotetradecane tetrahydrochloride, respectively, with paraformaldehyde and phenylphosphinic acid in aqueous HCl. The reaction conditions, i.e. concentration of HCl, rate of the addition of paraformaldehyde and temperature in the range 50−110 °C, were optimised for both the syntheses and the best conditions are described in the Experimental Section. The ligand H_4L^2 precipitated from the reaction mixture as $H_4L^2 \cdot n\,HCl$ ($n = 3-4$) and was purified by recrystallisation from methanol containing propylene oxide to give the free acid. The ligand H_4L^1 was isolated as an oily ammonium salt after ion-exchange chromatography of the reaction mixture and was subsequently converted into the free acid by acidification. In some cases, the acid contained traces of HCl, which were usually removed in high vacuum over KOH. Samples of the ligands for potentiometric measurements were recrystallised from MeOH solution containing propylene oxide to remove any traces of HCl. Elemental analysis, thin layer chromatography, ^{31}P-CP/MAS-NMR spectra of the bulk materials, and X-ray analysis of H_4L^2 indicate that both the compounds were obtained in the pure form.

Synthesis of phosphinic acid derivatives of azamacrocycles by the Mannich reaction in acid aqueous solution seems to be a convenient reaction; however, the reaction conditions for each phosphinic acid and azamacrocycle have to be optimised to reduce *N*-methylation of the cycle.[20] In accordance with the literature,[20][21] we can confirm that the side reactions are suppressed by a lower temperature, higher acidity, higher concentration of reagents than is usually recommended and by the use of paraformaldehyde, instead of an aqueous solution of formaldehyde, and its slow addition.

Structure

In solving the structure of $H_4L^2 \cdot 4\,H_2O$ we wanted to confirm the protonation and conformation of the $(H_2L^2)^{2-}$ anion. Only bis(1-adamantylammonium) salt $(AdNH_3)_2(H_2L^2) \cdot 6\,H_2O$ was found to form crystals suitable for X-ray analysis. Structures of both the compounds are shown with the numbering scheme in Figures 1 and 2. Tables 1 and 2 list selected bond lengths and angles. Superposition of the molecular structures of H_4L^2 and $(H_2L^2)^{2-}$ is projected in Figure S1 (see Supplementary Material).

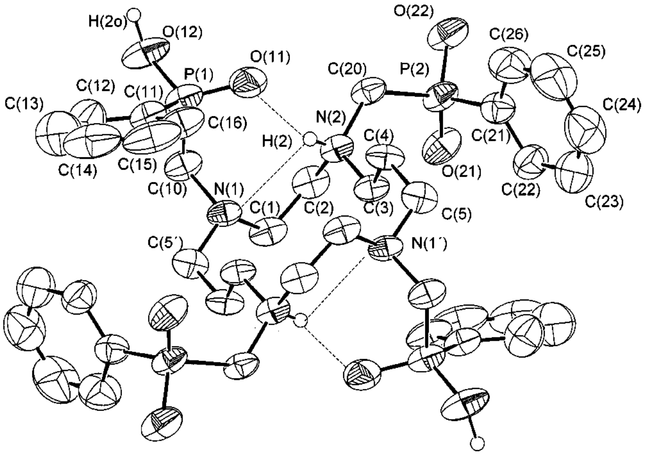

Figure 1. View of $H_4L^2 \cdot 4\,H_2O$ with the atom numbering scheme. The hydrogen bonds are denoted with primed lines

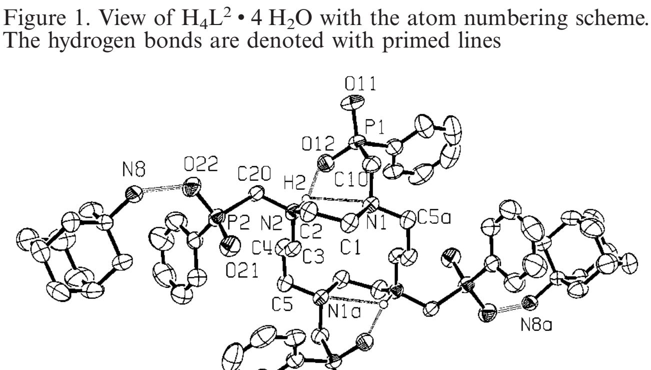

Figure 2. View of $(AdNH_3)_2(H_2L^2) \cdot 6\,H_2O$ with the atom numbering scheme. The hydrogen bonds in the structure of the $(H_2L^2)^{2-}$ anion are denoted with primed lines

Table 1. Selected bond lengths [Å], bond angles [°], and structure of $H_4L^2 \cdot 4\ H_2O$

The geometry of phosphorus atoms

P(1)−O(11) 1.491(2)	O(11)−**P(1)**−O(12) 117.3(1)	O(12)−**P(1)**−C(11) 108.4(1)
P(1)−O(12) 1.520(2)	O(11)−**P(1)**−C(10) 108.8(1)	C(11)−**P(1)**−C(12) 109.3(1)
P(1)−C(10) 1.801(2)	O(11)−**P(1)**−C(11) 108.1(1)	
P(1)−C(11) 1.785(3)	O(12)−**P(1)**−C(10) 104.8(1)	
P(2)−O(21) 1.478(2)	O(21)−**P(2)**−O(22) 115.3(1)	O(22)−**P(2)**−C(21) 107.8(1)
P(2)−O(22) 1.527(2)	O(21)−**P(2)**−C(20) 112.9(1)	C(21)−**P(2)**−C(22) 107.6(1)
P(2)−C(20) 1.819(3)	O(21)−**P(2)**−C(21) 110.5(1)	
P(2)−C(21) 1.788(3)	O(22)−**P(2)**−C(20) 102.3(1)	

The geometry of atoms C(10) and C(20)

C(10)−P(1) 1.801(3)	P(1)−**C(10)**−N(1) 112.0(2)	P(1)−**C(10)−N(1)**−C(1) 124.2(2)
C(10)−N(1) 1.480(3)		P(1)−**C(10)−N(1)**−C(5)[a] −10.4(2)
C(20)−P(2) 1.819(3)	P(2)−**C(20)**−N(2) 119.6(2)	P(2)−**C(20)−N(2)**−C(2) 71.7(3)
C(20)−N(2) 1.502(3)		P(2)−**C(20)−N(2)**−C(3) −59.6(3)

The geometry of the symmetrically independent part of the macrocyclic ring

N(1)−C(1) 1.460(3)	C(5)[a]−**N(1)**−C(1) 111.7(2)	C(5)[a]−**N(1)−C(1)**−C(2) −170.6(2)
C(1)−C(2) 1.504(4)	N(1)−**C(1)**−C(2) 113.5(2)	N(1)−**C(1)−C(2)**−N(2) 46.1(3)
C(2)−N(2) 1.506(3)	C(1)−**C(2)**−N(2) 113.3(2)	C(1)−**C(2)−N(2)**−C(3) 59.7(3)
N(2)−C(3) 1.492(3)	C(2)−**N(2)**−C(3) 113.4(2)	C(2)−**N(2)−C(3)**−C(4) −166.8(2)
C(3)−C(4) 1.509(3)	N(2)−**C(3)**−C(4) 112.2(2)	N(2)−**C(3)−C(4)**−C(5) 179.1(2)
C(4)−C(5) 1.514(3)	C(3)−**C(4)**−C(5) 112.7(2)	C(3)−**C(4)−C(5)**−N(1)[a] −68.2(3)
C(5)−N(1)[a] 1.460(3)	C(4)−**C(5)**−N(1)[a] 115.0(2)	C(4)−**C(5)−N(1)**[a]−C(1)[a] −75.7(3)

The geometry of the hydrogen bonds

O(12)−O(22)[b]	2.402(4)	O(12)−H(20)−O(22)[b]	165(2)
N(2)−O(11)	2.675(4)	N(2)−H(2N)−O(11)	160(2)
N(2)−N(1)	2.888(3)	N(2)−H(2N)−N(1)	116(1)
O(8)−O(12)	2.795(6)	O(8)−H(81 W)−O(12)	156(2)

[a] $-x + 1, -y + 1, -z + 2$. − [b] $-x, -y + 1, -z + 1$.

Table 2. Selected bond lengths [Å], bond angles [°], and structure of $(AdNH_3)_2 \cdot (H_2L^2) \cdot 6\ H_2O$

The geometry of phosphorus atoms

P(1)−O(11) 1.491(1)	O(11)−**P(1)**−O(12) 118.77(8)	O(12)−**P(1)**−C(11) 108.96(8)
P(1)−O(12) 1.508(1)	O(11)−**P(1)**−C(10) 107.80(9)	C(11)−**P(1)**−C(12) 105.75(8)
P(1)−C(10) 1.825(2)	O(11)−**P(1)**−C(11) 107.98(9)	
P(1)−C(11) 1.805(2)	O(12)−**P(1)**−C(10) 106.85(8)	
P(2)−O(21) 1.466(1)	O(21)−**P(2)**−O(22) 119.12(8)	O(22)−**P(2)**−C(21) 108.94(8)
P(2)−O(22) 1.486(1)	O(21)−**P(2)**−C(20) 109.95(7)	C(21)−**P(2)**−C(22) 5.48(8)
P(2)−C(20) 1.842(2)	O(21)−**P(2)**−C(21) 108.62(8)	
P(2)−C(21) 1.810(2)	O(22)−**P(2)**−C(20) 103.87(8)	

The geometry of atoms C(10) and C(20)

C(10)−P(1) 1.825(2)	P(1)−**C(10)**−N(1) 112.6(1)	P(1)−**C(10)−N(1)**−C(1) 127.3(1)
C(10)−N(1) 1.474(2)		P(1)−**C(10)−N(1)**−C(5)[a] −105.9(1)
C(20)−P(2) 1.842(2)	P(2)−**C(20)**−N(2) 117.3(1)	P(2)−**C(20)−N(2)**−C(2) 71.3(2)
C(20)−N(2) 1.505(2)		P(2)−**C(20)−N(2)**−C(3) −56.9(2)

The geometry of the symmetrically independent part of the macrocyclic ring

N(1)−C(1) 1.459(2)	C(5)[a]−**N(1)**−C(1) 111.8(1)	C(5)[a]−**N(1)−C(1)**−C(2) −170.8(2)
C(1)−C(2) 1.519(2)	N(1)−**C(1)**−C(2) 112.8(1)	N(1)−**C(1)−C(2)**−N(2) 45.2(2)
C(2)−N(2) 1.509(2)	C(1)−**C(2)**−N(2) 113.4(1)	C(1)−**C(2)−N(2)**−C(3) 63.3(2)
N(2)−C(3) 1.495(2)	C(2)−**N(2)**−C(3) 112.9(1)	C(2)−**N(2)−C(3)**−C(4) −171.4(1)
C(3)−C(4) 1.512(2)	N(2)−**C(3)**−C(4) 112.7(1)	N(2)−**C(3)−C(4)**−C(5) 177.5(1)
C(4)−C(5) 1.524(2)	C(3)−**C(4)**−C(5) 111.9(1)	C(3)−**C(4)−C(5)**−N(1)[i] −66.2(2)
C(5)−N(1)[a] 1.467(2)	C(4)−**C(5)**−N(1)[a] 114.0(1)	C(4)−**C(5)−N(1)**[a]−C(1)[a] −73.5(2)

The geometry of the hydrogen bonds

N(2)−O(12)	2.702(3)	N(2)−H(2)···O(12)	166(1)
N(8)−O(11)[b]	2.691(5)	N(8)−H(81)···O(11)[b]	162(2)
N(8)−O(22)	2.800(4)	N(8)−H(82)···O(22)	170(2)
N(8)−O(99)[c]	2.913(5)	N(8)−H(83)···O(99)[c]	165(3)
O(97)−O(22)[d]	2.917(4)	O(97)−H(972)···O(22)[d]	174(3)
O(98)−O(21)[d]	2.711(4)	O(98)−H(981)···O(21)[d]	170(4)
O(98)−O(12)[a]	2.794(4)	O(98)−H(982)···O(12)[a]	170(3)
O(99)−O(22)	2.922(4)	O(99)−H(991)···O(22)	175(2)
O(99)−O(98A)[e]	2.479(5)	O(99)−H(992)···O(98A)[e]	148(4)
O(99)−O(98)[e]	2.729(5)	O(99)−H(992)···O(98)[e]	171(4)

[a] $-x, -y, -z$. − [b] $-x, -y - 1, -z$. − [c] $-x + 1, -y - 1, -z$. − [d] $-x + 1, -y, -z$. − [e] $x, y - 1, z$.

In the crystalline state, both the compounds exist as zwitterions with two protonated nitrogen atoms in the rings and their structures contain the centres of symmetry. A comparison of bond lengths and angles in the rings shows that the ring conformation is virtually the same for both structures. This is also evident from the superposition of the two molecules, as shown in Figure S1 in the Supplementary Material available (see footnote on the first page). The ring conformations are stabilised by hydrogen bonds N2−H2···O11 (2.67 Å) in $H_4L^2 \cdot 4\ H_2O$ and N2−H2···O12 (2.70 Å) in $(AdNH_3)_2(H_2L^2) \cdot 6\ H_2O$. The bond lengths of N2−N1 are 2.88 Å and 2.89 Å respectively, which would point to additional hydrogen bonds, although the angles N2−H2.N1 are about 110° and, hence, we assume only a weak interaction.

The coordination around the P atoms significantly departs from the regular tetrahedron. In both the structures, the P−O distances are strongly influenced by hydrogen bonds and in $H_4L^2 \cdot 4\ H_2O$ also by protonation. In the structure of $H_4L^2 \cdot 4\ H_2O$, the molecules are linked through a very short hydrogen bond (2.4 Å) between P(1)−O(12)−H(20)···O(22)−P(2) to give a polymeric structure with the P−O distances virtually the same due to the strong hydrogen bond. The P(1)−O(11) and P(2)−O(21) distances are also very similar and are linked by hydrogen bonds with an H_2O molecule [P(2)−O(21)] or with the N(2)−H(2) bond [P(1)−O(11)]. In the structure of $(AdNH_3)_2(H_2L^2) \cdot 6\,H_2O$ the P−O distances are shorter than in $H_4L^2 \cdot 4\,H_2O$. All oxygen atoms are linked through hydrogen bonds of 2.8−2.9 Å with the nitrogen of adamantylammonium or with molecules of water (Table 2). The changes in the geometry on C10 and C20 atoms also correspond to the protonation of phosphinic acid groups. The longest C−P and the shortest C−N distance was found for N1−C10−P1 (the phosphinic acid group is protonated) in H_4L^2.

Comparing the structure of $H_4L^2 \cdot 4\,H_2O$ with structures of $H_4teta \cdot 6\,H_2O$[22] (H_4teta = 1,4,8,11-tetraazacyclotetradecane-1,4,8,11-tetraacetic acid) and $H_4dotp \cdot 7\,H_2O$[23] (H_4dotp = 1,4,8,11-tetraazacyclotetradecane-1,4,8,11-tetrapropionic acid), it is clear that orientation of the acetic groups in H_4teta is completely different from that of phosphinic acid groups in H_4L^2 and the conformations of both the rings also show small differences. On the other hand, the molecular structure of H_4dotp is very similar to that of H_4L^2, and that of $Na_2H_2dotp \cdot 16\,H_2O$[24] is similar to $(AdNH_3)_2(H_2L^2) \cdot 6\,H_2O$. In the structures, the orientation of two pendant arms towards protonated nitrogen atoms of the ring and formation of the same motif of hydrogen bonds and conformation were found. The similarity of H_4dotp to H_4L^2 probably results from better flexibility of the propionic acid arms in contrast to the short acetic acid moiety.

Differences in protonation of both phosphinate groups and amine of the ring were also observed in ^{31}P-CP/MAS-NMR spectra. In the spectrum of $H_4L^2 \cdot 4\,H_2O$, two signals at δ = 33.2 and 20.4 were observed and in the spectrum of $(AdNH_3)_2(H_2L^2) \cdot 6\,H_2O$, signals at δ = 23.5 and 15.6 were observed. From the solution NMR titration curves of (aminoalkyl)phosphinic[25−27] and (aminoalkyl)phosphonic[28] acids, it is known that the minimum of the curve corresponds to a system with protonated amine and deprotonated phosphorus acid groups. Therefore, in the ^{31}P-CP/MAS-NMR spectrum of $H_4L^2 \cdot 4\,H_2O$ the signal at δ = 33.2 should correspond to $N{-}CH_2{-}P(Ph)O_2H$ and that at δ = 20.4 to $NH^+{-}CH_2{-}P(Ph)O_2^-$ moieties, while in the spectrum of $(AdNH_3)_2(H_2L^2){\cdot}6H_2O$ the signal at δ = 23.5 corresponds to $N{-}CH_2{-}P(Ph)O_2^-$ and that at δ = 15.6 to $NH^+{-}CH_2{-}P(Ph)O_2^-$ moieties. The value of the chemical shift of the $NH^+{-}CH_2{-}P(Ph)O_2^-$ system is higher for H_4L^2 than for $(H_2L^2)^{2-}$ and this is probably due to the strong intermolecular hydrogen bond mentioned previously. The assignment of phosphorus signals confirms the values found in the ^{31}P-CP/MAS-NMR spectra of a simple (aminomethyl)(phenyl)phosphinic acid $H_3N^+CH_2P(Ph)O_2^-$ (δ = 20.8) and its sodium salt (δ = 27.8). In the spectrum of the solid H_4L^1, two phosphorus signals at δ = 24.0 and 26.7 were also observed, and thus a similar way of protonation is assumed.

Potentiometry

The calculated values of the protonation and stability constants are given in Table 3. The computed standard deviations seem to be inadequately small. This fact mainly points to a high precision and good reproducibility of the measurements, the use of a suitable calibration function with many degrees of freedom and also to a large number of experimental points. However, the real accuracy is substantially lower (and the real standard deviations are substantially larger). According to the conclusions of several inter-laboratory tests the real standard deviations of the determined protonation and stability constants are at least 0.05−0.1 units on the logarithmic scale,[29] which is discussed in the Supplementary Materials.

A comparison of pK_A values determined for H_4L^1 and H_4L^2 with the values for cyclen, cyclam and their acetic acid, methylenephosphinic acid, and methylenephosphonic acid derivatives is shown in Table 4. From the comparison, it is clear that the protonation scheme of both the acids H_4L^1 and H_4L^2 corresponds to the protonation of the other ligands. The first two protonations occur in the alkaline region and reflect protonations of two opposite nitrogen atoms of the ring. On the basis of protonation of $H_4L^2 \cdot 4\,H_2O$ and $(AdNH_3)_2(H_2L^2) \cdot 6\,H_2O$ in the solid state and on comparison of the constants in Table 4, we assume that the next protonations occur on phosphinic moieties.

Table 3. Protonation constants of H_4L^1 and H_4L^2 and stability constants of their Zn^{2+} and Cd^{2+} complexes at 25°C and $I = 0.1$ mol dm^{-3} (KNO_3); the values in parentheses are standard deviations given by the programme

Ion	Species	log β_{pqr}	
		H_4L^1	H_4L^2
H^+	HL^{3-}	11.436(7)	9.85(1)
	H_2L^{2-}	18.71(1)	19.793(5)
	H_3L^-	21.46(2)	21.639(9)
	H_4L	22.91(2)	
Zn^{2+}	ZnH_2L	21.06(5)	21.92(5)
	$ZnHL^-$	18.61(4)	
	ZnL^{2-}	15.92(1)	9.79(1)
	Zn_2L	18.32(5)	
	$Zn(H_{-1}L)^{3-}$	4.16(2)	
	$Zn_2(H_{-2}L)^{2-}$	3.45(2)	−3.24(3)
	$Zn_2(H_{-4}L)^{4-}$		−26.11(4)
Cd^{2+}	CdH_2L		22.05(5)
	$CdHL^-$	20.96(2)	
	CdL^{2-}	18.24(2)	9.91(2)
	Cd_2L	21.32(3)	12.99(4)

The last dissociation constant (pK_1) of H_4L^1 is unexpectedly higher than the values for H_4L^3 and H_4L^4, probably due to steric hindrance and hydrophobic interactions, which are discussed in the NMR section, and is not as strongly influenced by the electron-withdrawing $-P(R)O_2^-$ group[17] as the next protonation steps. The values for the other steps (pK_2, pK_3) indicate that the $-P(Ph)O_2^-$ group is more electron-withdrawing than $-CO_2^-$ and $-PO_3^{2-}$, as was expected from the well-known order observed for simple aminophosphinic, phosphonic, and carboxylic acids.[17]

Table 4. Comparison of the protonation constants and of H_4L^1 and H_4L^2 and of the stability constants of their complexes with the constants of their analogues

		cyclen[a]	H_4dota[b]	H_4L^1[g]	H_4L^3[c]	H_4L^4[d]	H_8L^5[e]	cyclam[f]	H_4teta[b]	H_4L^2[g]	H_8L^6[e]
log β_1	pK_1	10.6	12.6	11.44	10.41	10.94	13.7	11.29	10.52	9.85	13.4
log β_2 − log β_1	pK_2	9.6	9.70	7.27	6.84	8.24	12.2	10.19	10.17	9.94	12.8
log β_3 − log β_2	pK_3	(1.5)	4.50	2.75	1.97	3.71	9.28	1.61	4.09	1.85	8.82
log β_4 − log β_3	pK_4	(0.7)	4.14	1.45			8.09	1.91	3.35		7.75
log β_5 − log β_4	pK_5		2.32				6.12				6.25
log β_6 − log β_5	pK_6						5.22				5.42
Zn^{2+} log β_{101}		16.2	21.10	15.92	14.60	15.8		15.5 [a]	16.40	9.79	
Cd^{2+} log β_{101}		14.3	21.31	18.24	17.34	16.65		11.7 [a]	18.02	9.91	

[a] Ref.[39] – [b] Refs.[2a,2b] (0.1 M NMe_4Cl or NMe_4NO_3). – [c] Ref.[18] (0.1 M KNO_3). – [d] Ref.[11] (0.1 M KNO_3). – [e] Refs.[8,9a] (0.1 M NMe_4NO_3). – [f] Ref.[30] (0.1 M KCl). – [g] This work.

In comparison with the phosphinic acid derivatives of cyclen, we can also observe an influence of the substituent on the phosphorus atom. The values increase in the order $H_4L^3 < H_4L^1 < H_4L^4$, i.e. from H to phenyl and ethyl substituents. The same order was observed for phosphinic analogues of glycine.[17] The pK_A values of H_4L^1 and other phosphinic acids were also reported in a short communication[26] and were discussed for similar azacyclic phosphinic acid ligands in ref.[27] We agree with Sherry's[27] opinion; therefore, the pK_A values found for H_4L^1 from potentiometry and NMR titration published previously[26] are incorrect. A reverse order of pK_1 and pK_2 found for H_4L^2 is discussed in the Supplementary Material.

Systems with the diamagnetic metal ions Zn^{2+} and Cd^{2+} were also studied in order to obtain information on whether solution conformations influence of the coordination ability of the ligands (see NMR section). Results are presented in Table 3 and are compared with the constants of the related ligands in Table 4. In the system with Zn^{2+}, H_4L^1 forms species $[ZnH_2L^1]$, $[ZnHL^1]^-$, $[ZnL^1]^{2-}$, $[Zn_2L^1]$, $[ZnH_{-1}L^1]^{3-}$ and $[Zn_2H_{-2}L^1]^{2-}$. The protonated species were found at a pH of around 3 with a low abundance. The anion $[ZnL^1]^{2-}$ is the predominant species in the neutral region (molar ratio M/L = 1:1). In the alkaline region, hydroxo complexes $[ZnH_{-1}L^1]^{3-}$ (molar ratio M/L = 1:1) and $[Zn_2H_{-2}L^1]^{2-}$ (molar ratio M/L = 2:1) were observed. In the system with Cd^{2+}, H_4L^1 forms species $[CdHL^1]^-$, $[CdL_1]^{2-}$ and $[Cd_2L^1]$. Hydroxo complexes were not found.

In contrast to H_4L^1, H_4L^2 forms species $[ZnH_2L^2]$, $[ZnL^2]^{2-}$, $[Zn_2H_{-2}L^2]^{2-}$, and $[Zn_2H_{-4}L^2]^{4-}$ in the system with Zn^{2+} and $[CdH_2L^2]$, $[CdL^2]^{2-}$, and $[Cd_2L^2]$ in the system with Cd^{2+}. The species $[MH_2L^2]$ have the same number of protons as $(H_2L^2)^{2-}$ and, thus, evidence for their existence can be provided by potentiometry only indirectly; however, its inclusion into the chemical model significantly improved the goodness of fit. For the protonated complexes, we suggest protonation of two nitrogen atoms of the ring. The almost simultaneous deprotonation of both the nitrogen atoms is similar to the process observed for the free H_4L^2. Interactions of the metal ions with the ligands in the acid region were confirmed by NMR measurements (see below).

As expected, the stability constant values of H_4L^1 with Zn^{2+} and Cd^{2+} (15.92 and 18.24) are lower than those of H_4dota (21.10 and 21.31) due to the lower overall basicity of the ligand caused by the electron-withdrawing effect of the phosphinic acid group. On the other hand, the stability constant of H_4L^1 with Cd^{2+} is higher than that for Zn^{2+}, probably due to the larger size of the cadmium ion, which may enable coordination of more pendant arms than for Zn^{2+}, in an analogous way to that observed for 1,4,8,10-tetraazacyclododecane-1,4,8,10-tetrakis(acetamide).[31] Azacycles with methylenephosphinic acid pendant arms seem to be selective to larger ions.[18] For $[ML^1]^{2-}$, we can assume coordination of all nitrogen atoms of the ring as is the case in other cyclene derivatives (e.g. H_4dota). The pK_A values of the $[MHL^1]^-$ for both the metal ions (2.69 for Zn^{2+} and 2.72 for Cd^{2+}) are close and could be attributed to protonation of phosphinic acid pendant arms.

In contrast to H_4L^1 systems, the stability constant values of H_4L^2 for complexes with both of the cations (9.79 for Zn^{2+} and 9.91 for Cd^{2+}) are much lower (Table 4) than the values for H_4teta (16.40 and 18.02, respectively). These lower values could result from differences in the size of the ring for H_4L^1 and H_4L^2, from the lower overall basicity of H_4L^2 in comparison with other ligands and, mainly, from a different bonding mode of the ligand. If we compare the stability constant values for H_4L^2 and H_4teta, we can see that the values for H_4L^2 are about half (on the logarithmic scale) that for H_4teta. This points to the fact that only a part of H_4L^2 is coordinated in $[ML^2]^{2-}$ complexes. The suggestion could be supported by formation of complexes with the ratio M/L = 2:1.

NMR Spectroscopy

Contrary to our expectation, extremely broad signals in the ^{1}H-NMR spectra of both the compounds and the presence of several signals in the ^{31}P-NMR spectra were found, and these roughly correspond to the spectra of the compounds in the solid state. Some ^{31}P-NMR spectra of both the compounds in dependence on pD are shown in Figure 3. From Figure 3, it is evident that coalescence of the signals occurs only in the strong alkaline region after full deprotonation of the compounds. The coalescence of the signals in the neutral region does not occur, even at a temperature of 90°C. In our opinion, the hydrophobic phenyl groups surround protonated amines in H_4L^1 or H_4L^2 molecules and thus protect them against attack by bulk water. Consequently, the hydrogen bonds N(2)−H(2)···O(11) in H_4L^2 and in $(H_2L^2)^{2-}$ and analogous hydrogen bonds in $(H_2L^1)^{2-}$ are stable in solution and, therefore, can stabilise some ligand conformations. After complete deprotonation, the structures are not stabilised by hydrogen bonds, fast conformation changes occur and only one sharp signal is observed in ^{31}P-NMR spectra. The conformations can also be stabilised by hydrophobic interactions between phenyl groups and/or phenyl-propylene/ethylene chains. Analogous changes in the ^{31}P-NMR spectra were observed for 1,2-diaminoethane-*N,N,N′,N′*-tetrayl-tetramethylene-tetrakis-(phenylphosphinic acid).[25a] Two peaks in the ^{31}P-NMR spectrum at low temperature were also observed in a solution of H_8L^5, which is in accordance with the molecular structure of the compound in the solid state.[32]

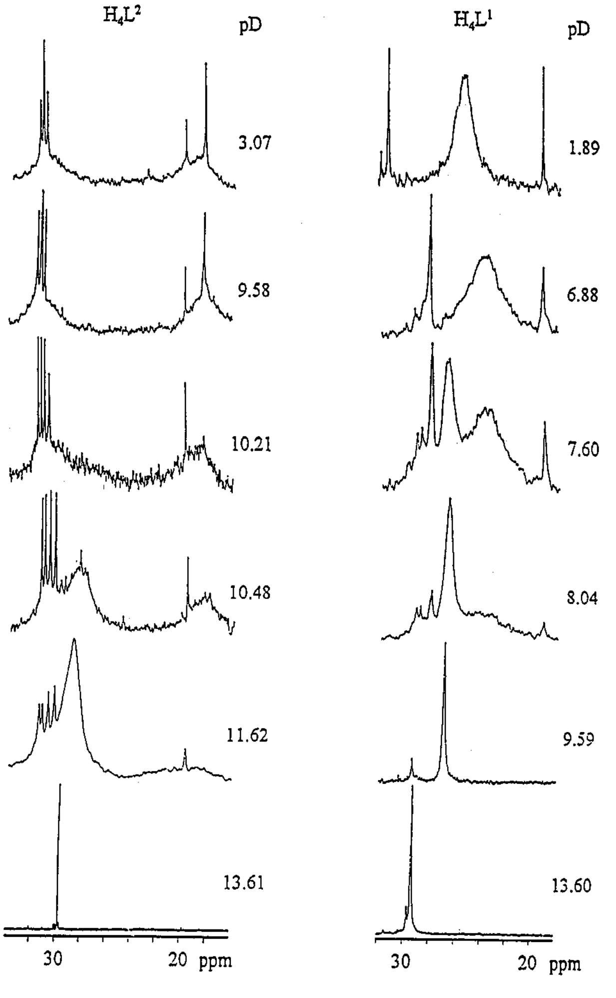

Figure 3. The ^{31}P-NMR spectra of H_4L^1 (right) and H_4L^2 (left) in dependence on pD

The ^{31}P-NMR spectra of H_4L^1 show the same features as the spectra of H_4L^2; however, the conformation of $(H_2L^1)^{2-}$ does not seem to be as rigid as that of $(H_2L^2)^{2-}$. In the spectra in the region of pD = 1.89−6.88 (pH ≈ 2.6−6.5), two sharp signals at $\delta = 19$ corresponding to the pendant arm with the protonated amine and at $\delta = 30$ corresponding to the pendant arm with the deprotonated amine were observed. In addition to the signals at $\delta = 19$ and 30, the spectrum contains a broad signal at about $\delta = 25$. Fast protonation of a phosphinic acid pendant arm occurs, as can be illustrated by the changes in the chemical shifts of the peaks in the acid region. The broad signal probably reflects a number of conformers in which all phosphorus atoms are equivalent with respect to the site of protonation. On the other hand, the sharp signals belong to a conformer with nonequivalent phosphorus atoms. The sharp peak at $\delta = 30$ changes its position with pD significantly whereas the other one changes only negligibly. Thus, it is evident that the former peak corresponds to a phosphinic group where the third protonation takes place. Near the pD value corresponding to the pK_2 = 7.27 (pD = 7.6, pH ≈ 7.2), a strong sharp signal at about $\delta = 27$ appears and reflects the $(HL^1)^{3-}$ species. The spectrum looks like a superposition of the spectra at lower and higher pD values. This is a consequence of a slow exchange (dissociation) of protons in $(H_2L^1)^{2-}$ and differences in the structure of conformers belonging to $(H_2L^1)^{2-}$ and $(HL^1)^{3-}$species. The signal at $\delta =$ 27 is dominant in the spectra over the range of pD 7.5−10.5. With the last deprotonation (pD = 10.9−13.6), the signal becomes increasingly sharp and continuously moves to $\delta = 29$, which confirms the fast proton exchange in the $(HL^1)^{3-}$ anion.

The acid pK's determined from the ^{31}P-NMR titration in the range of $-\log[H^+]$ 1.0−2.5 under the conditions of the potentiometric titrations correspond to the values found from potentiometry. The changes in the ^{31}P-NMR spectra indicate the unsymmetrical protonations of phosphinic acid groups as the peaks at about $\delta = 19$ and 30 are shifted to different pH values.

H_4L^2 exhibits virtually the same spectrum in the range of pD 3.07−9.58. This range of pD corresponds to conformers of a species $(H_2L^2)^{2-}$ in which two nitrogen atoms are protonated [see the crystal structure of $(AdNH_3)_2(H_2L^2) \cdot 6\,H_2O$]. As mentioned above, the ^{31}P-NMR titration curves of (aminoalkyl)phosphinic and (aminoalkyl)-phosphonic acids point to the fact that the minimum of the curve corresponds to a system with protonated amine and deprotonated phosphorus groups.[25−27] Therefore, signals in the region $\delta = 18{-}20$ reflect $NH^+{-}CH_2{-}PPhO_2^-$ pendant arms and signals in the region $\delta = 30{-}32$ reflect $N{-}CH_2{-}PPhO_2^-$ pendant arms bound by hydrogen bonds to the other nitrogen atoms of the ethylenediamine chains (see the crystal structure of the adamantylammonium salt). The broad peak observed in the spectrum of H_4L^1 at about $\delta = 25$ was not found in the spectrum of H_4L^2, probably due to the presence of propylene chains in H_4L^2 dividing the molecule into two almost independent parts each stabilised by the hydrogen bond. The spectra in the region above pD 10.21, i.e. pH 9.8, (Figure 3) reflect the first and second deprotonations of the ring. A new signal at $\delta = 28$ is seen and this belongs to $(HL^2)^{3-}$ and $(L^2)^{4-}$ species in almost fast conformation changes with the fast deprotonation of the last proton as indicated by a continuous change of the chemical shift from $\delta = 28$ to 30 and by a sharpening of the signal. At pD = 13.61, the deprotonation is complete and only one sharp signal is observed in the spectrum. Unfortunately, full interpretation of all observed changes in the ^{31}P-NMR spectra of the ligand is more complicated than for H_4L^1.

We wanted to know whether the ligand conformations are influenced by the presence of complexing ions and thus ^{31}P-NMR spectra of both the ligands in the presence of Zn^{2+} or Cd^{2+} were measured. The NMR spectra are very sensitive to complexation. Only one sharp signal at about $\delta = 27$ is observed in the spectra of the solutions containing H_4L^1 with Zn^{2+} or Cd^{2+} in the L:M molar ratio 1:1 in the wide region of pH from 1.8 to 12. The signal is observed even in the acid region where formation of protonated complexes starts. Similarly, H_4L^2 in the M/L ratio 1:1 gives a sharp peak ($\delta = 26$) in the neutral region and a very broad unresolved peak ($\delta = 18-32$) in acidic solution (pH 2.0). This behaviour confirms the presence of metal ion/ligand interactions and, therefore, complexes $[MH_2L^2]$ should be present in acidic solutions. We assume that nitrogen atoms are protonated in the species and metal ion/ligand interactions occur through phosphinic acid groups. These results indicate a fast exchange of a metal ion between ligand molecules. On the other hand, H_4L^1 or H_4L^2 in the presence of noncoordinating ions such as Li^+ or K^+ (concentration of LiCl or KCl solutions was about 3 mol·dm^{-3}) in the neutral region give virtually the same spectra as the solutions with a low ionic strength. These results suggest that complexation of metal ions with ligands through phosphinic acid group(s) and/or nitrogen atom(s) breaks the system of hydrogen bonds that stabilise conformations of free ligands.

Experimental Section

Chemicals: Cyclen hydrochloride[33] and cyclam hydrochloride[34] were synthesised using known procedures. Other chemicals used were from commercial sources and were of the best quality available.

Crystallography: Crystals of $H_4L^2 \cdot 4\,H_2O$ and $(AdNH_3)_2(H_2L^2) \cdot 6\,H_2O$ suitable for X-ray diffraction were obtained from methanol/water solutions. For unit-cell and space-group determinations and for data collections, crystals of both the compounds were mounted at random orientations on glass fibres using an epoxy glue and were coated with a thin paraffin film. An Enraf−Nonius CAD4 diffractometer was used for measurements at 293(2) K with Mo-K_α radiation (λ = 0.71073 Å). Unit-cell dimensions were determined from angular settings of every twenty-five high-order (θ from 14 to 15° and from 13.5 to 14.5°, respectively) reflections using the CAD4 centring routines. Selected crystallographic and other relevant data for both compounds are listed in Table 6.

Intensities were collected using variable scan speeds to assure constant statistical precision. Three standard reflections measured every hour were used to confirm the stability of the crystal and of the experimental conditions. The orientation of the crystal was checked by measuring five standards every 100 reflections. The data were corrected for Lorenz polarisation, but not for absorption. The extinction correction was applied only in the case of $(AdNH_3)_2(H_2L^2) \cdot 6\,H_2O$ using the procedure included in SHELXL97.[35] The structure was solved by a combination of Patterson and Fourier methods (SHELXS86,[36] SHELXL97) and refined by full-matrix least-squares techniques (SHELXL97). Scattering factors for neutral atoms used were included in the program SHELXL97. The hydrogen atoms were found (with the exception of two hydrogen atoms of the water molecules in the structure of H4L2···4 H_2O) on the difference maps and refined isotropically. The partially disordered water molecules in the crystal lattice of H4L2···4 H_2O were described as two oxygen atoms [O(8) and O(8A)] in two close positions [distance O(8)···O(8A) 0.81(1) Å]. The refined total occupancy of this water molecule converged to unity within experimental error and the final relative ratio of the individual position was 0.69:0.31.

Table 6. Experimental data for the X-ray diffraction studies

Parameter	$(AdNH_3)_2\,H_2L^2 \bullet 6\,H_2O$	$H_4L^2 \bullet 4\,H_2O$
Empirical formula	$C_{58}H_{86}N_6O_8P_4 \bullet 6\,H_2O$	$C_{38}H_{52}N_4O_8P_4 \bullet 4\,H_2O$
M	1227.30	888.78
T/K	293(2)	293(2)
λ/Å	0.71073	0.71073
Crystal system	triclinic	monoclinic
Space group	$P\bar{1}$ (no. 2)	$P2_1/c$ (no. 14)
a/Å	8.6179(7)	8.5729(8)
b/Å	14.0002(7)	24.449(3)
c/Å	14.9305(10)	10.873(3)
α /°	67.892(5)	−
β /°	79.452(6)	108.38(1)
γ /°	85.790(6)	−
V/Å^3	1640.7(2)	2162.7(7)
Z	1	2
D_c/g•cm^{-3}	1.242	1.365
μ/mm^{-3}	0.179	0.239
F(000)	660	944
Crystal habit and colour	plate, colourless	rod, colourless
Crystal size/mm	0.6 ± 0.9 ± 0.2	0.35 ± 0.3 ± 0.7
Scan mode	$\omega - 2\theta$	$\omega - 2\theta$
θ range for data collection/°	1.49−24.98	1.67−27.22
Index ranges	$-10 \le h \le 10$ $-15 \le k \le 16$ $0 \le l \le 17$	$0 \le h \le 11$; $0 \le k \le 31$; $-13 \le l \le 13$
Reflections collected	5773	5117
Reflections observed $[I \ge 2\sigma(I)]$	4907	3403
Independent reflections	5773	4809 (R_{int} = 0.0335)
Coefficients in weighting scheme[a]	0.0541; 0.4778	0.0757; 1.0441
Data, restrains, parameters	5773; 0; 577	4809; 0; 388
Goodness-of-fit on F^2	1.076	1.043
Final R, R' indices $[I \ge 2\sigma(I)]$[b]	0.0365; 0.0978	0.0510; 0.1380
Maximum shift/e.s.d.	0.008 (H atom)	0.065 (H atom)
Largest differ. peak and hole /eÅ^{-3}	0.43; −0.40	0.35; −0.43

[a] $R = \Sigma|F_o - F_c|/\Sigma|F_c|$ $R' = [\Sigma w(F_o^2 - F_c^2)^2/\Sigma w(F_o^2)^2]^{1/2}$ (SHELXL97; ref.[35]). − [b] $w = 1/[\sigma^2(F_o^2) + (A \bullet P)^2 + B \bullet P]$ (SHELXL97, see ref.[36])

Crystallographic data (excluding structure factors) for the structures reported in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC-118658 $[(AdNH_3)_2(H_2L^2) \cdot 6\,H_2O]$ and -118659 $(H_4L^2 \cdot 4\,H_2O)$. Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB21EZ, UK [Fax: (internat.) +44(1223)336-033; E-mail:deposit@ccdc.cam.ac.uk].

Chemicals and Stock Solutions for Potentiometric Titrations: Stock solutions of the individual metal cations were prepared by dissolving appropriate nitrates recrystallised from aqueous solutions. The metal contents in the solutions were determined by titration with Na_2H_2edta solution. Nitric acid was prepared by passing aqueous potassium nitrate solution through a Dowex 50 W-8 column in the H^+ form because of traces of NO and NO_2 present in the concentrated acid. KOH solution was standardised against potassium hydrogen phthalate and HNO_3 solution against the KOH solution. Stock solutions of the ligands were prepared by dissolving solids in a standard KOH solution ($\approx$ 1.8 equivalents) followed by addition of water. Analytical concentrations of the ligands were determined by pH-metric end-point titrations. Four protons of H_4L^1 in the presence of an equivalent amount of $Cu(NO_3)_2$ and two protons of H_4L^2 were titrated using a potassium hydroxide solution of known analytical concentration.

Potentiometric Titrations: Titrations were carried out in a vessel thermostatted at 25±0.1 °C, at an ionic strength of $I\,(KNO_3) = 0.1$ mol·dm^{-3} and in the presence of an excess of HNO_3 in the region $-\log[H^+] = 1.8-12$ [except for the titrations where precipitation of $Zn(OH)_2$ and $Cd(OH)_2$ was detected] using a PHM 240 pH-meter, a 2 cm^3 capacity Radiometer ABU 900 automatic piston burette and a GK 2401B combined electrode (Radiometer). The initial volume was 5 cm^3 and concentration of both the ligands was 0.002 mol.dm^{-3} due to their low solubility in the acid region. The metal:ligand ratios were 2:1, 1:1 and 1:2. Titration for each ratio was carried out at least three times. Each titration consisted of about 40 points. An inert atmosphere was ensured by constant passage of argon saturated with the solvent vapor during measurements. The stability constants for $M^{2+} - OH^-$ systems included in the calculations and $pK_w = 13.78$ were taken from the literature.[37] The protonation and stability constants β_{pqr} are concentration constants and are defined by $\beta_{pqr} = [M_pH_qL_r]/[M]^p\cdot[H]^q\cdot[L]^r$. The constants and the analytical concentrations were calculated using the program OPIUM.[38] The program minimises the criterion of the generalised least squares method using the calibration function where the additive term E_0 contains standard potentials of the electrodes used and contributions of inert ions to the liquid-junction potential, S corresponds to the Nernstian slope, the value of which should be close to the theoretical value and $j_1[H^+]$ and $j_2[OH^-]$ terms are contributions of the H^+ and OH^- ions to the liquid-junction potential. It is clear that j_1 and j_2 cause deviation from a linear dependence between E and $-\log[H^+]$ only in strongly acidic and strongly alkaline solutions.

$$E = E_0 + S\cdot\log[H^+] + j_1[H^+] + j_2(K_W/[H^+])$$

NMR Spectra: NMR spectra were obtained with a Varian Inova Plus instrument, ^1H (400 MHz) at 25 °C with sodium 4,4-dimethyl-4-silapentane-1-sulfonate as an internal standard, $^{31}P\{^1H\}$ (161,.9 MHz) with 85% H_3PO_4 as an external standard. The ^{31}P-NMR titration experiments were performed in D_2O at concentrations of the ligands of 0.01 mol·dm^{-3} and at room temperature. The pD values (pD = pH + 0.40; electrode calibration in pH scale using standard buffers) were adjusted by addition of KOD or DCl solutions. Solutions for ^{31}P-NMR titrations in the acidic region ($-\log[H^+] = 1.0-2.5$) and the measurements in the presence of metals were run under the same conditions as the potentiometric measurements in H_2O with D_2O in the coaxial capillary for the lock. ^{31}P-CP/MAS-NMR spectra were measured at 161.9 MHz, spinning 4 kHz, contact time 0.5 ms and repetition time 8 s with $CaHPO_4$ as external standard.

Synthesis of $H_4L^1 \cdot 4\,H_2O$: To a stirred suspension of cyclen hydrochloride (1.0 g, 3.14 mmol) and phenylphosphinic acid (2.75 g, 19.3 mmol) in 20 mL of aqueous HCl (1:1, v/v) was added paraformaldehyde (0.85 g, 28.3 mmol) in portions at 100 °C over 7 h. A clear solution was formed after addition of the first portion of paraformaldehyde [***Caution:*** Formation of carcinogenic $(ClCH_2)_2O$ cannot be excluded, work in an efficient fumehood]. The reaction mixture was held at the same temperature for 2.5 h. The volatiles were removed using a rotary evaporator and the resulting yellow oily residue was co-distilled three times with water. The residue was dissolved in an H_2O/EtOH mixture (1:1, v/v) and loaded onto Dowex 50 W8 cation exchange resin in the H^+ form. The resin was washed with H_2O and the product was subsequently eluted with 10% aqueous NH_3. Fractions containing H_4L^1 as its ammonium salt were evaporated. The oily product obtained was dissolved in 7 mL of an H_2O/EtOH mixture (1:1, v/v) and acidified with 1 mol dm^{-3} HCl to pH $\approx$ 1. H_4L^1 started to crystallise after scratching of the flask wall and standing overnight. The product was filtered off, washed with water, and dried at 100 °C over solid KOH under vacuum (1.33 kPa). The solution was filtered (S4), evaporated, and the product precipitated by addition of water. Yield 1.7 g (65%). M.p. 200−203 °C (dec.). Elemental analysis: found (calcd.) C 50.2 (50.2); H 6.1 (6.5); N 6.6 (6.5). − ^1H NMR (0.1 M KOD/D_2O): δ = 2.51 (s, 16 H, NCH_2), 2.91 (d, 8 H, $^2J_{PH}$ = 6.4 Hz, NCH_2P), 7.5−7.9 (m, 20 H, aryl H). − $^{31}P\{^1H\}$ NMR (0.1 M KOD/D_2O): δ = 29.38. A sample used for potentiometric measurements was recrystallised from refluxing MeOH containing propylene oxide.

Synthesis of $H_4L^2 \cdot 4\,H_2O$: To a stirred suspension of cyclam hydrochloride (0.8 g, 1.9 mmol) and phenylphosphinic acid (2.0 g, 14 mmol) in 7.5 mL of aqueous HCl (1:1, v/v) was added paraformaldehyde (0.9 g, 30 mmol) in portions at 65 °C over 2 h [***Caution:*** Formation of carcinogenic $(ClCH_2)_2O$ cannot be excluded, work in an efficient fumehood]. A clear solution formed during addition of paraformaldehyde and a white precipitate of the product began to separate after addition of approximately half of the amount. The mixture was stirred for 3 h at 65 °C to complete the reaction. A white precipitate of $H_4L^2 \cdot n\,HCl$ (n = 3−4) was filtered off, washed with 5% aqueous HCl, acetone, and dried over KOH. The hydrochloride was converted into H_4L^2 by dissolution in a large volume of boiling methanol and addition of an excess of propylene oxide (2 mL) to trap HCl. The solution was concentrated to about 1/4 volume and crystallisation started after addition of water. The isolated product was dried to constant weight under vacuum (1.33 kPa) over KOH at 100 °C in an Abderhalden apparatus. Yield 1.3 g (75%). M.p. 221−224 °C (dec.). − Elemental analysis: found (calcd.) C 51.6 (51.4); H 6.6 (6.8); N 6.5 (6.3). − ^1H NMR (0.1 M KOD/D_2O): δ = 0.82 (bp, 4 H, $CH_2CH_2CH_2$), 1.87 (s, 8 H, NCH_2CH_2N), 2.07 (bt, 8 H, N$CH_2CH_2CH_2$N), 2.32 (d, 8 H, NCH_2P, $^2J_{PH}$ = 9.4 Hz), 7.3−7.5 (m, 20 H, aryl H). − $^{31}P\{^1H\}$ NMR (0.1 M KOD/ D_2O): δ = 29.8, s.

Synthesis of $(AdNH_3)_2(H_2L^2) \cdot 6\,H_2O$: To a stirred MeOH/$H_2O$ (1:1, v/v, 10 mL) solution of $H_4L^2.4H_2O$ (0.89 g, 1 mmol) was added a methanolic solution (10 mL) of 1-adamantylamine (0.30 g, 2 mmol). The product crystallised from the solution during a few days. Yield 0.65 g (53%). M.p. 207−209 °C (dec.). Elemental analysis: found (calcd.) C 56.9 (56.7), H 7.8 (8.0), N 6.9 (6.8).

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