DALTON

Complexation properties of macrocyclic polyoxadiazadiphosphonates

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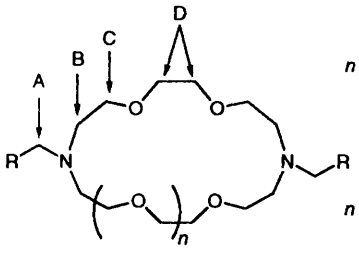
The macrocycle 1,4,10,13-tetraoxa-7,16-diazacyclooctadecane-7,16-diyldimethylenediphosphonic acid (H_4L^1), its bis(ethyl ester) (H_2L^3) and 1,4,10-trioxa-7,13-diazacyclopentadecane-7,13-diyldimethylenediphosphonic acid (H_4L^5) were prepared. The protonation constants of the macrocycles and the stability constants of their complexes with alkaline-earth-metal ions, lanthanide ions, Zn^{2+}, Cd^{2+} and Pb^{2+} were determined by pH-potentiometric titration. The phosphonate $(L^3)^{2-}$ forms only unprotonated complexes ML, while $(L^1)^{4-}$ and $(L^5)^{4-}$ form ML, monoprotonated complexes, M(HL), and diprotonated complexes, $M(H_2L)$. The trends in the stability constants through the lanthanide series are similar for all complexes: a weak maximum in log K is observed at around Pr^{3+}, Nd^{3+} and a minimum at about Tb^{3+}, Ho^{3+}. The chemical shifts of the non-labile protons of L^1 indicate that on protonation the first two protons are attached to the two nitrogens, the next two at one of the oxygen atoms of each phosphonate group. The equilibrium data and ^1H NMR spectra of the complexes $[LaL^1]^-$ and $[LuL^1]^-$ indicate the increasing role of the metal–phosphonate group interaction in the complexation through the lanthanide series from La^{3+} to Lu^{3+}. Attachment of the strongly co-ordinating phosphonate groups to the 15- and 18-membered ring macrocycles results in cessation of the size–match selectivity.

For the selective complexation of metal ions in aqueous solution a great number of functionalized macrocycles have been synthesized.[1–3] The complexes of 'hard' metal ions are sufficiently stable when the functional groups, most often attached to ring nitrogen atoms, possess negatively charged donor atoms. In the design of these macrocycles, it is expected that the selectivity attributed can be retained in the functionalized derivative. For some functionalized polyaza macrocycles, such as triazatriacetates or tetraazatetraacetates, the sizes of the cavities formed by the donor atoms of the ring and the pendant groups play a crucial role in determining the selectivity.[4–5]

The 18-membered ring 1,4,10,13-tetraoxa-7,16-diazacyclooctadecane ([18]aneN$_2$O$_4$) is known to be selective for large alkaline-earth-metal ions, although the stability constants of its complexes are relatively low (log K_{CaL} = 1.8, log K_{SrL} = 2.8 and log K_{BaL} = 2.65).[6] Its 7,16-bis(acetic acid) derivative H_2L^2 forms more stable complexes and to some extent maintains the selectivity for large metal ions.[7,8] The selectivity also holds for the large lanthanide ions (Ln^{3+}) and, as a result, the stability constants of the complexes $[LnL^2]^+$ decrease slightly from Gd^{3+} to Lu^{3+}, which is unusual for lanthanides.[7] An even more significant drop is observed in the stabilities of the complexes of Ln^{3+} with the corresponding 7,16-bis(malonic acid) (H_4L^4). The log K_{LnL} values decrease by about five orders of magnitude from Pr^{3+} to Lu^{3+}.[9] This unusual trend in stability constants would be of practical value in the separation of lanthanides, but the complexes $[LnL^4]^-$ dissociate too slowly at pH > 4, which prevents their successful application. The dissociation of the complexes is a proton-assisted process but unfortunately decarboxylation of the malonate group is also catalysed by H^+.[9]



n = 1, R = $PO(OH)_2$ — H_4L^1
CO_2H — H_2L^2
$PO(OH)OEt$ — H_2L^3
$(CO_2H)_2$ — H_4L^4

n = 0, R = $PO(OH)_2$ — H_4L^5
CO_2H — H_2L^6

The above examples indicate that the complexation properties of the functionalized derivatives of [18]aneN$_2$O$_4$ are very promising. Accordingly, we considered it useful to obtain more information on the complexation behaviour and selectivities of such compounds by synthesizing new derivatives. Since the open-chain polyaminopolyphosphonate ligands display interesting complexation properties, and several macrocyclic polyazapolyphosphonates have been synthesized,[10–13] it seemed worthwhile to study the bis(methylphosphonic acid) (H_4L^1) derivative. For a study of the effect of ring size on complexation, we also synthesized the corresponding 1,4,10-trioxa-7,13-diazacyclopentadecane ([15]aneN$_2$O$_3$) derivative (H_4L^5), and for comparison and in order to diminish the charge of the ligand the bis(methylphosphonic acid monoethyl ester) (H_2L^3) of [18]aneN$_2$O$_4$ was synthesized.

Experimental

Synthesis of the macrocycles

The compound [18]aneN$_2$O$_4$ (Kryptofix 2.2), [15]aneN$_2$O$_3$ (Kryptofix 2.1) (Merck), sodium, benzene, diethyl ether, hydrochloric acid (Reanal), paraformaldehyde, diethyl phosphite and anhydrous phosphorous acid (Aldrich) of the highest available purity were used without further purification. Methanol was freshly distilled from sodium methoxide solution immediately before use. Except when noted, all experiments were carried out in standard laboratory glassware without an inert-gas atmosphere.

7,16-Bis(diethyl methylphosphonate) of [18]aneN$_2$O$_4$. The compound [18]aneN$_2$O$_4$ (700 mg, 2.668 mmol) was dissolved in benzene (5 cm^3) and diethyl phosphite (0.72 cm^3) added. The mixture was heated to boiling and dry paraformaldehyde (200 mg) added in small portions during 60 min. After refluxing for 45 min, hydrochloric acid (3 cm^3, ≈3 mol dm^{-3}) was added and the mixture shaken thoroughly. The benzene phase was separated and the aqueous solution extracted with diethyl ether (10 cm^3). The aqueous solution was cooled in ice, made alkaline first with potassium hydroxide solution (3 mol dm^{-3}, 6 cm^3) and then saturated with solid potassium carbonate. A yellowish oil separated and was extracted by chloroform (3 × 6 cm^3). The

chloroform solution was dried with anhydrous sodium sulfate, filtered and evaporated under reduced pressure to give a viscous oil. This was dissolved in diethyl ether (20 cm^3), filtered and the filtrate evaporated to give a clear oil (1261 mg, 2.241 mmol, 84%).

H_2L^3. The above tetraester (1192 mg, 2.119 mmol) was suspended in water (5 cm^3), potassium hydroxide solution (3.137 mol dm^{-3}, 2.03 cm^3) added and the mixture refluxed for 5 h. The solution was evaporated to dryness, redissolved in absolute ethanol and evaporated again to a glassy solid which was taken up in diethyl ether, where it solidified upon stirring. The solid was filtered off, washed with diethyl ether and dried under nitrogen to constant weight. The product H_2L^3 was a white hygroscopic solid (1031 mg, 1.769 mmol, 83.5%), m.p. > 182 °C.

H_4L^1. The compound [18]aneN_2O_4 (1006 mg, 3.835 mmol) was dissolved in water (15 cm^3), and anhydrous phosphorous acid (1260 mg, 19.52 mmol) and then concentrated hydrochloric acid (0.5 cm^3) were added. The reaction mixture was brought to boiling and paraformaldehyde (350 mg, 11.67 mmol, calculated as monomer HCHO) was added during 60 min, after which the solution was refluxed for 60 min. Absolute ethanol (100 cm^3) and concentrated hydrochloric acid (0.5 cm^3, ≈6 mol dm^{-3}) were added. The resulting mixture was concentrated to 20 cm^3 under reduced pressure. The solid which settled out was filtered off, washed with absolute ethanol (2 × 5 cm^3) and diethyl ether (2 × 5 cm^3) and dried to constant weight in a nitrogen atmosphere at 50 °C. The product was H_4L^1·HCl (1605 mg, 3.297 mmol, 86%), m.p. 102 °C [Found (Calc.): C, 33.25 (34.55); H, 6.85 (6.80); N, 5.35 (5.75); P, 11.50 (12.70)%].

H_4L^5. The compound [15]aneN_2O_3 (1666 mg, 7.63 mmol) was dissolved in a mixture of water (3.7 cm^3), anhydrous phosphorous acid (2450 mg, 14.93 mmol) and hydrochloric acid (37%, 3.0 cm^3) and the solution heated to reflux. Under constant boiling, paraformaldehyde (682 mg, calculated as 22.71 mmol monomer HCHO) was added during 60 min, and boiling was maintained for 60 min. The reaction mixture was concentrated to one-third volume under reduced pressure, and co-evaporated first with absolute ethanol (50 cm^3) then with a mixture of concentrated hydrochloric acid (1 cm^3) and absolute ethanol (50 cm^3). Isopropyl alcohol (25 cm^3) was added to the residue, which resulted in the formation of a sticky white solid. The solvent was decanted off and the solid extracted into hot absolute ethanol (50 cm^3). After cooling in ice, anhydrous diethyl ether (100 cm^3) was added which led to the precipitation of a white solid. The solvent was decanted off and the solid stirred in anhydrous ether (50 cm^3) for several days. The precipitate was filtered off, washed with diethyl ether and dried to constant weight over P_4O_{10} at 80 °C in high vacuum. The product (H_4L^5·HCl) was a very hygroscopic white solid (1181 mg, 4.12 mmol, 54%), which starts to decompose above 202 °C [Found (Calc.): C, 32.05 (32.55); H, 6.25 (6.55); N, 6.05 (6.35); P, 13.00 (14.00)%].

The purity of the macrocyles was checked by ^1H NMR spectroscopy and found to be higher than 99.5%. The proton chemical shifts for a 0.01 mol dm^{-3} H_4L^1·HCl solution were δ 3.45 (d, NCH_2P), 3.70 (t, NCH_2), 3.78 (s, OCH_2CH_2O) and 3.93 (t, OCH_2). The spectrum of H_4L^5·HCl solution is more complicated due to the non-symmetric structure. On the basis of the pH-dependent changes in the chemical shifts some signals were assigned: δ 3.47 (d, NCH_2P), 3.70 (t, NCH_2), 3.76 (s, OCH_2CH_2O), 3.88 (t) and 3.96 (t).

Equilibrium and NMR studies

For the preparation of solutions of $CaCl_2$, $SrCl_2$, $BaCl_2$, $ZnCl_2$, $Cd(NO_3)_2$ and $Pb(NO_3)_2$, the salts used were of the highest analytical grade. The concentrations of the solutions were determined by complexometric titration with standardized K_2H_2(edta) (H_4edta = ethylenediamine tetraacetic acid), with Eriochrome Black T or methylthymol blue as indicator. The $LnCl_3$ solutions were prepared from lanthanide oxides; Ln_2O_3 (99.9%, Fluka) was dissolved in 1 : 1 HCl and the excess of HCl was evaporated off. Their concentrations were determined by complexometry with xylenol orange as indicator.

The concentrations of H_4L^1, H_2L^3 and H_4L^5 solutions were determined by pH-potentiometry, on the basis of the titration curves obtained in the absence and presence of an excess of $CaCl_2$.

The pH-potentiometric titrations were carried out in vessels thermostatted at 25 °C, with a Radiometer PHM 85 pH-meter, an ABU80 autoburette, and G202B glass and K401 calomel electrodes. The titrated solutions (15–20 cm^3) were stirred with a magnetic stirrer and, to avoid the effect of CO_2, nitrogen gas was bubbled through the samples. The concentrations of ligand, MCl_2 and $LnCl_3$ solutions were around 1×10^{-3}–2×10^{-3} mol dm^{-3}. To avoid the hydrolysis of metal ions a 5–10% excess of macrocycle was applied.

The protonation and stability constants were determined at constant ionic strength, in 0.1 mol dm^{-3} NMe_4Cl (pK_w = 13.90) or 0.1 mol dm^{-3} KNO_3 (pK_w = 13.86) (Pb^{2+} and Cd^{2+}) solutions. The hydrogen-ion concentration was calculated from the measured pH values by a known procedure.[14] To obtain reliable equilibrium data two to four parallel titrations were carried out. Each titration curve contained 25–30 usable data points, that is for the calculation of the protonation and stability constants 50–100 data points were used in one fitting procedure. The titration data for the calculations were obtained in a broad interval of pH, which was about 2.5–9 for the lanthanides and 5–10 for the alkaline-earth metal ions.

For calculation of the protonation and stability constants, the program PSEQUAD was used.[15] The reliability of the calculated equilibrium constants was characterized by the standard deviation and the 'fitting parameter', *i.e.* the difference in the volumes of base (cm^3) used and that calculated with the stability constants to obtain a given pH value. The protonation or stability constant was accepted when this 'parameter' was less than 0.01 cm^3.

Proton NMR spectroscopic measurements were carried out in D_2O with a Bruker WP 200 SY spectrometer, using sodium 4,4-dimethyl-4-silapentane-1-sulfonate as internal standard. The pD values were calculated from the measured pH values *via* the known[16] equation pD = pH − 0.4. The ^{31}P NMR spectra were recorded at 81 MHz. Chemical shifts are referred to 85% H_3PO_4 as external standard.

Results and Discussion

Protonation of macrocycles

The protonation constants of open-chain polyaminopolyphosphonates are regularly higher than their polyaminopolycarboxylate analogues.[17] A similar conclusion can be drawn by comparing the protonation constants of $(L^1)^{4-}$ and $(L^5)^{4-}$ with those of $(L^2)^{2-}$ and $(L^6)^{2-}$, presented in Table 1. This is probably a consequence of the higher negative charge of the phosphonate derivatives, since the monoester, $(L^3)^{2-}$, possessing an identical charge to that of $(L^2)^{2-}$, has lower protonation constants. Protonation constants are defined as K_i^H = $[H_iL]/[H_{i-1}L][H^+]$, where i = 1–4. The standard deviation of the protonation constants is lower than 0.05.

The protonation sequence of open-chain polyaminopolyphosphonates may differ from that of the polyaminopolycarboxylates because protonation of some phosphonate groups can take place before protonation of nitrogen atoms.[17] The protonation sequence of L^1 was studied by ^1H and ^{31}P NMR spectroscopy. The chemical shifts of the non-labile protons and

Table 1 Protonation constants (log K_i^H) of the macrocycles (25 °C, 0.1 mol dm^{-3} NMe_4Cl)

	log K_1^H	log K_2^H	log K_3^H	log K_4^H
L^1	10.69	9.35	5.76	4.89
	9.96[a]	9.17	5.61	4.68
L^2[b]	8.45	7.80	2.90	—
L^5	10.82	9.81	5.96	4.73
	9.80[a]	8.77	5.28	4.55
L^6[b]	9.02	8.79	2.95	—
L^3	8.25	6.42	1.9	—

[a] In 0.1 mol dm^{-3} KNO_3. [b] Ref. 18.

the phosphorus atom of the phosphonate groups are shown in Fig. 1 as a function of pD. To interpret the chemical shifts we assume that protonation of the PO_3^{2-} group predominantly affects the chemical shift of the NCH_2P (A) protons, while protonation of the nitrogens influences the chemical shifts of both the NCH_2CH_2O (B and C) and NCH_2P protons. The signal of the A protons is a doublet due to coupling between the proton and phosphorus spins. The chemical shifts of the A protons shown in Fig. 1 are given as the centre of the doublet.

In the interval 4 < pD < 8 only the chemical shifts of the A protons exhibit any change. Those of the protons B–D change only when pD > 8. These data indicate that, on decrease of the pD from about 12 to 8, protonation occurs at the nitrogen atoms, while a further decrease of from pD 8 to 4 results in protonation of an oxygen atom of the phosphonate groups. The ^{31}P chemical shifts of the phosphonate groups exhibit changes in the same interval of pD as do the proton signals. These variations indicate protonation of the PO_3^{2-} groups in the interval 4 < pD < 8 and of the nitrogen atoms at 8 < pD < 12.

On the basis of the results obtained for L^1, it can be assumed that the protonation sequences for the other two phosphonate derivatives, L^3 and L^5, are similar, that is the nitrogen atoms are protonated first, followed at lower pD by protonation of one of the oxygen atoms of the PO_3^{2-} groups. Further protonation of PO_3H^- groups occurs only in strongly acidic solutions (pD < 1).

Stability constants of complexes

The stability constants of the complexes were calculated from the results of pH-potentiometric titration of the macrocycles in the presence of metal ions. Some typical titration curves of L^1 and L^5 are shown in Figs. 2 and 3. The equilibrium pH values as a function of the number of added equivalents of base indicate the formation of the diprotonated $M(H_2L)$, monoprotonated M(HL) and unprotonated ML complexes. In the calculations of the stability constants the best fits of the data were obtained when the formation of these species was assumed. The stability constants of the complexes are defined by $K_{M(H_iL)} = [M(H_iL)]/[M][H_iL]$, where i = 0–2. The values are listed in Table 2.

The compositions of the complexes formed with the phosphonate derivatives differ considerably from those of the acetate derivatives, since in the case of L^2 and L^6 only the formation of unprotonated species ML was observed.[7,18] This difference originates in the different complex-forming properties of the carboxylate and phosphonate groups. A dinegative phosphonate group in general forms more stable complexes than a carboxylate. The coordination of a carboxylate is particularly weak when a protonated nitrogen atom is situated in proximity, as is the case with protonated α-amino acids. However, the phosphonate group of aminomethylphosphonic acids protonated at nitrogen can be coordinated to 'hard' metal ions such as Ca^{2+}.[17,19] Taking into account the protonation sequence of L^1 and L^5 and the considerations mentioned above, we assume that in the mono- and di-protonated complexes the

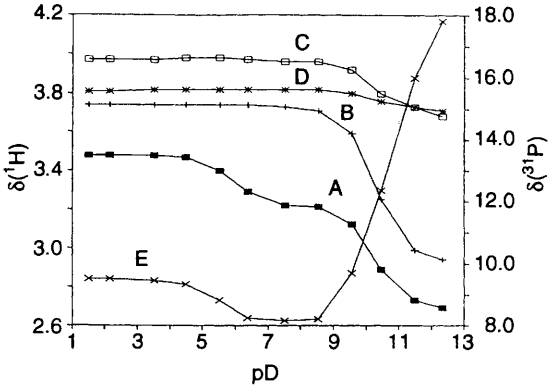


Fig. 1 Proton and ^{31}P NMR shifts of the non-labile protons (A–D) and the phosphorus atoms (E) of the ligand L^1

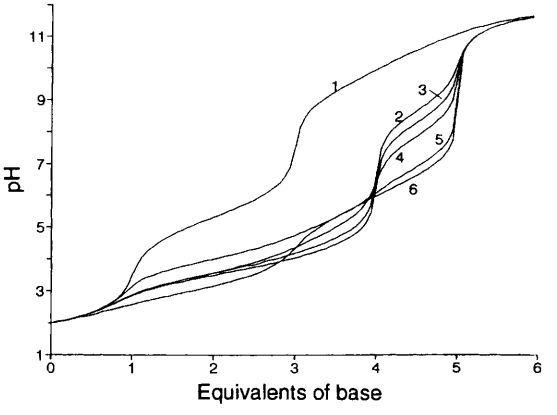


Fig. 2 Titration curves of H_4L^1 in the absence (1) and presence of metal ions Gd^{3+} (2), Sm^{3+} (3), Ho^{3+} (4), La^{3+} (5) and Lu^{3+} (6). The macrocycle and metal-ion concentrations were each 0.0013 mol dm^{-3}

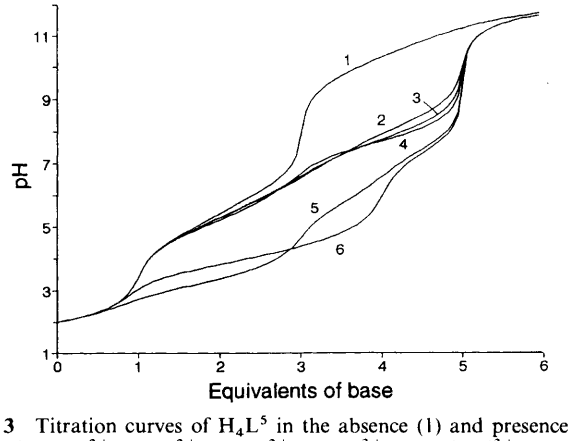


Fig. 3 Titration curves of H_4L^5 in the absence (1) and presence of metal ions Ca^{2+} (2), Sr^{2+} (3), Ba^{2+} (4), Lu^{3+} (5) and Nd^{3+} (6). The macrocycle and metal-ion concentrations were each 0.0013 mol dm^{-3}

protons are attached to the nitrogen atom(s), while the two phosphonate groups are co-ordinated to the metal ion at one side of the bent ring.

Like the acetate derivatives, the monoester derivative L^3 forms only unprotonated complexes. This similarity results from the strong acidity of the phosphonic acid ester groups, PO(OR)OH, which leads to the relatively low stability constants of complexes of L^3.

The stability constants, log K_{ML}, of the unprotonated complexes ML formed between the alkaline-earth-metal ions, Zn^{2+}, Cd^{2+} and Pb^{2+} and L^1 and L^5 (Table 2) are quite similar to the log K_{ML} values of the respective L^2 and L^6 complexes.[7,18] A comparison of the stability constants reveals that both the phosphonate and acetate derivatives of the 15-membered macrocycle, L^5 and L^6, form more stable complexes with Zn^{2+} and Cd^{2+} than those of the 18-membered ring, L^1 and L^2.[7,18]

Table 2 Stability constants (log K) of the complexes (25 °C, 0.1 mol dm^{-3} NMe_4Cl)

	L^1			L^5			L^3
M^{z+}	ML	M(HL)	$M(H_2L)$	ML	M(HL)	$M(H_2L)$	ML
Ca^{2+}	7.45	5.54	2.15	7.81	5.27	2.18	5.43
Sr^{2+}	7.05	4.62	2.34	8.05	5.13	2.11	5.33
Ba^{2+}	8.56	4.95	1.74	8.22	4.81	2.31	5.74
Zn^{2+}	9.78	6.45	3.43	13.25	6.66	5.56	—
Cd^{2+} *	10.73	8.97	4.46	10.93	7.53	4.02	—
Pb^{2+} *	13.06	10.95	6.81	11.78	8.61	4.98	—
La^{3+}	12.90	9.10	4.96	13.65	9.62	4.85	7.60
Ce^{3+}	13.45	9.73	5.29	14.06	10.37	5.01	7.68
Pr^{3+}	13.39	10.16	5.37	13.98	10.45	5.14	7.80
Nd^{3+}	13.07	10.46	5.50	14.36	10.74	5.44	7.74
Sm^{3+}	13.43	11.08	5.92	14.01	10.63	5.79	7.78
Eu^{3+}	13.08	10.96	5.97	13.76	10.48	5.72	7.65
Gd^{3+}	12.71	10.73	5.85	13.38	10.10	5.66	7.30
Tb^{3+}	12.74	10.64	5.95	13.14	10.00	5.60	7.12
Dy^{3+}	12.95	10.54	6.01	12.48	9.64	5.53	7.10
Ho^{3+}	13.12	10.33	5.89	12.98	9.75	5.59	6.82
Er^{3+}	12.81	9.74	5.66	13.31	9.91	5.60	6.40
Tm^{3+}	13.77	10.24	6.11	13.80	10.22	5.86	6.47
Yb^{3+}	14.08	10.27	6.48	13.70	10.38	6.32	6.55
Lu^{3+}	14.91	10.80	6.83	14.16	10.65	6.55	6.64

* In 0.1 mol dm^{-3} KNO_3.

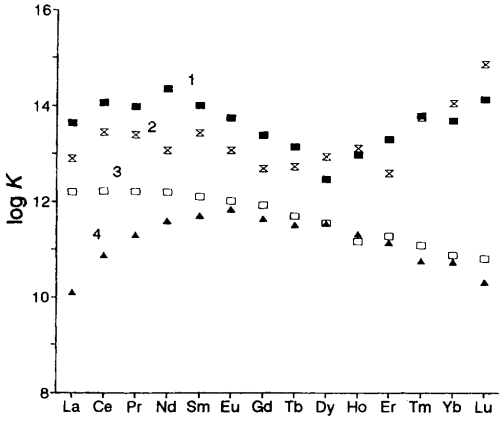


Fig. 4 Stability constants (log K_{ML}) of the lanthanide complexes of the ligands L^5 (1), L^1 (2), L^2 (3) and L^6 (4)

The stability constants of the di-, mono- and un-protonated complexes formed between the lanthanide ions and L^1 and L^5 exhibit an unusual trend with increase in atomic number. A similar trend was observed for the complexes of L^3 (Table 2). The log $K_{M(H_iL)}$ values (i = 0–2) exhibit a weak maximum at around Pr^{3+}, Nd^{3+}, a minimum at about Tb^{3+}, Ho^{3+} and then an increase again till Lu^{3+}. In Fig. 4 the stability constants, K_{ML}, of the unprotonated complexes $[LnL^5]^-$ and $[LnL^1]^-$ are compared with those of $[LnL^6]^+$ and $[LnL^2]^+$. The trend for the phosphonate derivatives differs considerably from that for the acetate derivatives. The complexes of lanthanides with the 15-membered ring L^5 are slightly more stable than those with the 18-membered ring L^1 (except for the last few Ln^{3+}). For the complexes of the acetate derivatives L^2 and L^6, the situation is reversed: the 18-membered ring L^2 forms the more stable complexes. Fig. 4 shows that the log K_{ML} values of the complexes $[LnL^2]^+$ are practically constant for the lighter elements, but decrease from Gd^{3+} to Lu^{3+}. The complexes $[LnL^6]^+$ display the highest stability in the middle of the Ln^{3+} series. In the interpretation of these trends the different cavity sizes of the 15- and 18-membered ligands were taken into consideration. The larger Ln^{3+} fit better into the 18-membered macrocycle, while the smaller 15-membered ring prefers the medium-sized Ln^{3+}.[7,18]

The trend in the stability constants of the complexes of the phosphonate derivatives cannot be interpreted in a like manner. In spite of the difference in the ring sizes of L^1 and L^5 the trends in the log K_{ML} values of the complexes are similar. This holds for the protonated complexes too. To interpret these similar trends we have to assume that the interactions between Ln^{3+} and the phosphonate groups play a significant role in the formation of these complexes. Unfortunately, too few data have been published on the stability constants of the Ln^{3+}–polyaminopolyphosphonates to permit a comparison, particularly for the whole series of lanthanides.[17]

For an interpretation of the equilibrium data a knowledge of the structures of the complexes would be essential. Unfortunately, even for the acetate derivatives, only the structure of $[CuL^2]$ has been studied by X-ray diffraction. This complex has a *trans*-carboxylate configuration. The two nitrogen and two acetate oxygen atoms are co-ordinated in a plane perpendicular to that of the four ring oxygens.[20,21] Since the cavity of the 15-membered ring is too small for Ln^{3+} (cavity diameter *ca.* 160 pm[21]), for the co-ordination of L^5 we assume a *cis*-phosphonate configuration. A *cis*-carboxylate configuration was proposed for the structure of $[LnL^6]^+$.[18] If the functional groups are co-ordinated in a *cis* configuration the donor atoms of the bent ring and the phosphonate oxygens form a cage. The position of Ln^{3+} in the cage depends on the relative strength of its interaction with the ring oxygens and the phosphonate groups. In the protonated complexes $[Ln(HL^5)]$ and $[Ln(H_2L^5)]^+$, where the interactions between Ln^{3+} and the PO_3^{2-} groups predominate, Ln^{3+} is located closer to the phosphonate groups.

The cavity in the 18-membered ring [18]aneN_2O_4 is large enough for Ln^{3+}. In the complexes $[Ln([18]aneN_2O_4)][NO_3]_3$ synthesized by Desreux *et al.*[22] the macrocycle adopts a non-planar conformation. In $[LnL^2]^+$ a *trans*-acetate configuration was proposed[7] and a similar *trans*-phosphonate co-ordination can be assumed for $[LnL^1]^-$ (particularly in the case of the larger Ln^{3+}). However, in the protonated complexes $[Ln(HL^1)]$ and $[Ln(H_2L^1)]^+$, where the nitrogen(s) is protonated and hence the interactions between Ln^{3+} and the ring oxygens are not significant, practically only the phosphonate groups participate in the complexation. Owing to the presence of the protonated nitrogen(s), the phosphonate groups can be co-ordinated at one side of the ring, when again a *cis*-phosphonate configuration is created.

The increasing role of the phosphonate groups in complex formation for the heavier lanthanides can be depicted in the

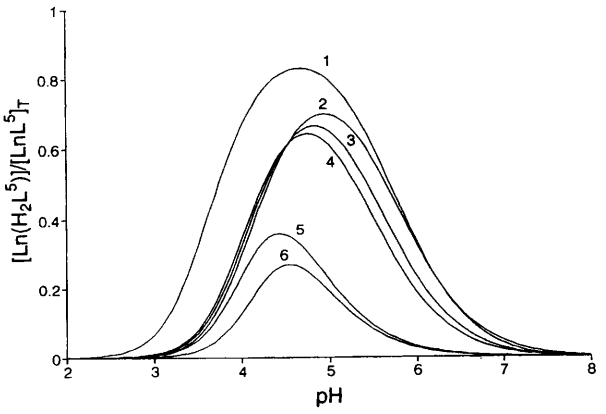


Fig. 5 Concentration distribution of the diprotonated complexes $[Ln(H_2L^5)]$ of Lu^{3+} (1), Er^{3+} (2), Gd^{3+} (3), Dy^{3+} (4), Nd^{3+} (5) and Ce^{3+} (6)

concentration distribution curves of the diprotonated complexes $[Ln(H_2L^5)]^+$, presented in Fig. 5. In these complexes, only the phosphonate groups are co-ordinated, due to the electrostatic repulsion between Ln^{3+} and the protonated nitrogens. The concentration of diprotonated complexes increases with increasing atomic number, indicating the higher extent of interaction between the phosphonate groups and the heavier lanthanides. For the larger ions of lower atomic number elements the interaction with the ring oxygen-donor atoms is stronger, which leads to deprotonation and a lower concentration of the diprotonated complexes.

^{1}H NMR spectra of complexes

The ^{1}H NMR spectra of the complexes of L^1 and L^5 with the diamagnetic La^{3+} and Lu^{3+} are very complicated in a broad interval of pD (5–10) due to the splitting and overlapping of signals. In these spectra the doublet of the $NCH_2PO_3^{2-}$ (A) protons can be identified and the chemical shifts established (or estimated). Fig. 6 shows the spectra of $[LaL^1]^-$ at different pD. For comparison the distribution of species formed in the La^{3+}–L^1 system is shown in Fig. 7. At lower pD (3–5), where the diprotonated species $[La(H_2L^1)]^+$ predominates, the exchange between the co-ordinated and free macrocycle is rapid (the complexation is not complete as is seen in Fig. 7). The spectra of $[LuL^1]^-$ at pD < 5 are similar to those of $[LaL^1]^-$. The chemical shifts of the A protons of L^1 and the complexes $[LaL^1]^-$ and $[LuL^1]^-$ at different pD are given in Table 3.

The data in Table 3 indicate that the chemical shifts (δ) of the A protons in the complexes are somewhat lower than those of the protons in the free macrocycle at about pD < 6, where the protonated complexes predominate. Deprotonation of the complexes results in a larger drop in δ, particularly in the case of $[LaL^1]^-$. At about pD > 7.5 the chemical shifts for $[LaL^1]^-$ are constant and this value of δ 2.74 is quite close to that for the fully deprotonated macrocycle (δ 2.69). The difference in the δ values of the macrocycle and the complex $[LuL^2]^+$ is significantly larger at pD > 7. Since the chemical shift of the A protons depends on the extents of co-ordination of both the nitrogen and phosphonate oxygen-donor atoms, the larger difference may be a result of a stronger interaction between the phosphonate groups and Lu^{3+}. While phosphonate oxygens are more strongly co-ordinated to Lu^{3+}, the interactions between these donor atoms and La^{3+} are weak, which is manifested in the small difference in the δ values of the A protons of the macrocycle and the complex $[LaL^1]^-$. The weak La^{3+}–phosphonate interaction is probably a consequence of the relatively strong co-ordination of the ring donor atoms to the large La^{3+}. This interpretation is not correct if the ligand may adopt different conformations, when the observed chemical shifts are average values of the different conformers.

Table 3 Chemical shifts (δ) of the methylene protons A

pD	L^1	$[LaL^1]^-$	$[LuL^1]^-$
3.5	3.48	3.48	3.45
4.5	3.47	3.45	3.45
5.5	3.40	3.4	3.4
6.4	3.29	3.3	2.9–3.1
7.4	3.22	2.74	2.9–3.1
8.5	3.21	2.74	2.9–3.1
9.5	3.12	2.74	2.9–3.1
12.3	2.69	—	—

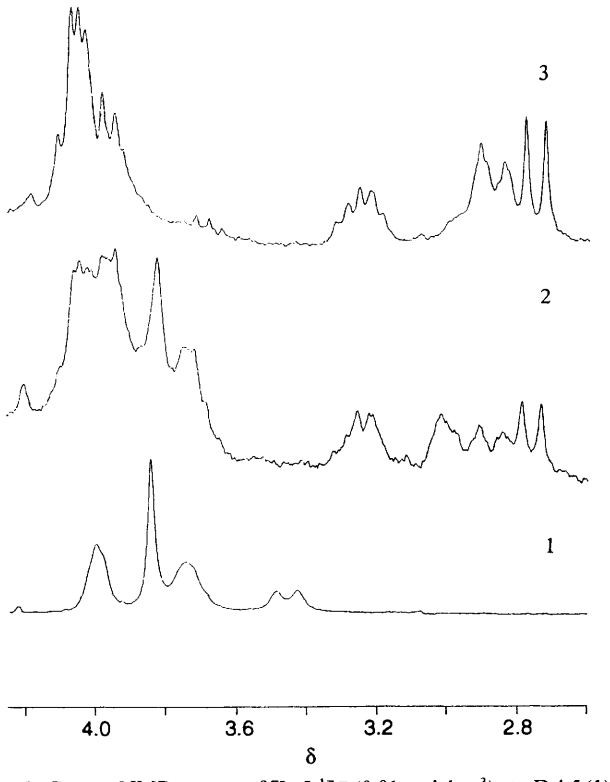


Fig. 6 Proton NMR spectra of $[LaL^1]^-$ (0.01 mol dm^{-3}) at pD 4.5 (1), 7.5 (2) and 9.0 (3)

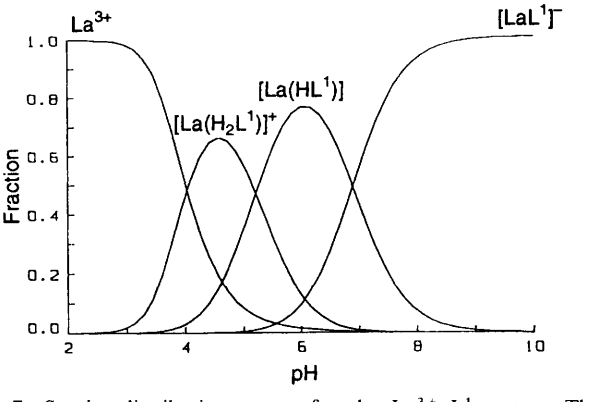


Fig. 7 Species distribution curves for the La^{3+}–L^1 system. The protonation and stability constants used for the calculation are in Tables 1 and 2. The concentrations of La^{3+} and L^1 were 0.01 mol dm^{-3}

However, the effect of the strong La^{3+}–ring donor atom interaction, which we assumed, is also reflected in the ^{1}H NMR spectrum of $[LaL^1]^-$ at pD 9 (Fig. 5). The split signal pattern appearing between δ 3.4 and 2.8 is similar to those for $[LaL^4]^-$ and $[BaL^4]^{2-}$.[9,23] The spectra of [18]aneN$_2$O$_4$ bis(malonate) complexes were interpreted by assuming a rigid structure of the co-ordinated ring, with a long lifetime of the metal ion–donor atom bonds on the NMR time-scale. This rigidity results in

spin–spin coupling of the NCH_2CH_2O protons, which leads to the appearance of a complex AA'XX' spectral pattern.[24] The weak interaction between the phosphonate and La^{3+} and the strong co-ordination of the ring donor atoms suggest a *trans*-phosphonate configuration for $[LaL^1]^-$, as for $[LaL^4]^-$ and $[BaL^4]^{2-}$.[9,23] While the ^1H NMR spectrum of $[LaL^1]^-$ suggests a *trans*-phosphonate configuration, this is not the case for $[LuL^1]^-$. The spectrum of the latter indicates a stronger interaction between Lu^{3+} and the phosphonate oxygens. However, the existence of this neither proves nor precludes the possibility of a structural change, and the formation of a *cis*-phosphonate configuration for $[LuL^1]^-$.

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