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Eight-membered chelate-ring complexes of cobalt(III)-polyamine complexes of aminopolyphosphonates in aqueous solution

Kiyoshi Sawada,* Tomohide Ichikawa and Katsuhiro Uehara

Department of Chemistry, Faculty of Science, Niigata University, Niigata 950-21, Japan

The complex formation of *N*-methyliminodimethylenebis(phosphonic acid) [$MeN(CH_2PO_3H_2)_2$, H_4midmp] and nitrilotrimethylenetris(phosphonic acid) [$N(CH_2PO_3H_2)_3$, H_6ntmp] with cobalt(III)–polyamine complexes has been investigated by ^{31}P NMR and UV/VIS spectroscopies. The ^{31}P NMR spectra of the reaction mixtures were measured at 0 °C as a function of pH. The analysis of the pH dependence of the ^{31}P NMR signals revealed that two types of complexes were formed in the reaction of *cis*-$[Co(en)_2Cl_2]^+$ (en = ethane-1,2-diamine) with midmp: O-monodentate and O,O-bidentate having an eight-membered chelate ring. The N atom is not coordinated. The two types of complexes were separated by HPLC and characterized by ^{31}P NMR and UV/VIS spectrometry. The protonation constants and ^{31}P NMR chemical shifts of each protonated complex were determined and structures are proposed. The first protonation occurs on the imino nitrogen of midmp of the $Co(en)_2$ complexes. An intramolecular hydrogen bond plays an important role in the stability of the monoprotonated O-monodentate ligand complex. The complex *cis*-$[Co(en)_2(NH_3)Cl]Cl_2$ forms an O-monodentate ligand complex on reaction with midmp. The protonation constants and ^{31}P NMR chemical shifts of this complex corroborate the structure of the $Co(en)_2$ O-monodentate midmp complex. The complexes of the cobalt(III)–polyamines with ntmp have the same structures as those of the corresponding midmp complexes.

The aminopolyphosphonates, in which the carboxyl groups of aminopolycarboxylates are substituted by phosphonate groups, have been widely used for industrial purposes such as a scale inhibitor and for medical purposes such as a magnetic resonance imaging agent.[1-3] Many kinds of these compounds have been synthesized[4] and their complex formation has been studied.[5-10] The number of negative charges of aminopolyphosphonates is much higher than that of the corresponding aminopolycarboxylates, *e.g.* the charge of nitrilotrimethylenetris(phosphonate) is minus six ($ntmp^{6-}$), while that of nitrilotriacetate is minus three (nta^{3-}). Thus, the metal complexes of aminopolyphosphonates are easily protonated.

We have studied the formation and protonation of aminopolyphosphonate complexes with substitution-labile metal ions such as those of the alkaline-earth metals, divalent transition metals[11-14] and lanthanoid metals,[15] by means of potentiometry, NMR spectroscopy and calorimetry. The divalent transition-metal complexes of ntmp and their protonated species have an ordinal structure, *i.e.* ntmp co-ordinates as an N,O,O,O-tetradentate ligand. On the other hand, the structures of the protonated complexes of alkaline-earth and lanthanoid metals are unusual. That is, protonation occurs on the nitrogen atom of the ligand, rupturing the M–N bond and forming the O,O,O-tridentate ligand complex with eight-membered chelate rings.[11,12] In the case of methyliminodimethylenebis(phosphonate), midmp, some transition-metal complexes also have the O,O-bidentate (eight-membered chelate ring) structure.[13] Usually, eight-membered chelate rings are stable and no complex having such a chelate ring has been reported with an aminopolycarboxylate. Although eight-membered chelate complexes are formed at equilibrium, they have not been isolated.

The formation of inert metal complexes in which the sites available for the co-ordination are restricted to two, as in *cis*-$[Pt(NH_3)_2Cl_2]$ and *cis*-$[Co(en)_2Cl_2]^+$ (en = ethane-1,2-diamine), is particularly interesting, *e.g.* the reactions of *cis*-$[Pt(NH_3)_2Cl_2]$ are extensively investigated because of its anticancer properties.[16] The complexes *cis*-$[Co(en)_2Cl_2]^+$ and analogues accelerate hydrolysis of phosphate esters.[17,18] The formation of platinum(II) complexes with aminopolyphosphonates was reported by Appleton *et al.*[19] Although reaction products were reported, the detailed equilibria were not studied.

The complex formation of midmp and ntmp with cobalt(III)–polyamine complexes has now been investigated by means of ^{31}P NMR and UV/VIS spectroscopy. The number of sites on the cobalt (polyamine) available for co-ordination of aminopolyphosphonate is restricted to one {*cis*-$[Co(en)_2(NH_3)Cl]^{2+}$} or two {*cis*-$[Co(en)_2Cl_2]^+$}. The protonation equilibria and structures of the complexes and the NMR behaviour in aqueous solution were studied.

Experimental

Reagents

Cobalt(III)–polyamine complexes, *cis*-$[Co(en)_2Cl_2]Cl$ and *cis*-$[Co(en)_2(NH_3)Cl]Cl_2$, were synthesized according to literature procedures.[20] Nitrilotrimethylenetris(phosphonic acid) (H_6ntmp, H_6L) (Dojin Chemicals) was purified by recrystallization.[11] Methyliminodimethylenebis(phosphonic acid) (H_4midmp) was synthesized by the method described elsewhere.[4] The purity of H_6ntmp and H_4midmp was checked by ^{31}P NMR and pH titration methods.[11] Other chemicals were of reagent grade (Wako Pure Chemicals).

Sample preparation

Cobalt(III)–polyamine complex (0.15 mol dm^{-3}) was treated with an equimolar amount of aminopolyphosphonate at 50 °C and at various pH and times. The reaction was quenched by cooling the solution to 0 °C. The diaqua complex $[Co(en)_2(H_2O)_2]^{3+}$ was prepared by adding an equivalent amount of $AgNO_3$ to a $[Co(en)_2Cl_2]Cl$ solution at 50 °C for 30 min. After removing the precipitate of AgCl by centrifuging, the solution was treated with aminopolyphosphonate in the same manner as for the dichloro complex.

Complex separation

The mixture of the cobalt(III)–polyamine complex and aminopolyphosphonate was separated by HPLC (Tosoh CCPD dual pump, UV-8000 UV/VIS Detector) on a column (50 × 500 mm) packed with Toyopearl HW-40F (Tosoh). The sample loaded (10 cm^3) was eluted by 0.1 mol dm^{-3} sodium borate (pH 9.2) at a flow rate of 6 cm^3 min^{-1}. The fractions of eluent were freeze-dried just after collection. Sodium borate in the fraction was separated on the same column by eluting with distilled water. In the case of the $Co(en)_2$–midmp complex the chromatogram of the reaction mixture showed two peaks corresponding to midmp complexes and one to the cobalt(III) reactant. Owing to very poor peak separation, the complexes formed in the reaction with ntmp were not separated from the reactant complex.

pH Measurement

The pH measurements were carried out with a Denki Kagaku Keiki pHL-40 instrument. The glass electrode (DKK 6157) was calibrated by titration with nitric acid and potassium hydroxide at 0.0 ± 0.1 °C (I = 0.1 mol dm^{-3} KNO_3, pK_w = 14.98). The pH, *i.e.* the logarithm of the reciprocal of the hydrogen-ion concentration, was evaluated from the electromotive force using the calibration curve.

NMR Measurements

After adjusting the pH at 0 °C, ^{31}P NMR spectra of reaction mixtures or of separated complexes were recorded at 0 °C with a JEOL FX 90Q (36.23 MHz for ^{31}P) or GX400 Fourier-transform spectrometer (161.70 MHz) using sample tubes of 10 mm diameter and D_2O as external lock in a concentric tube (5 mm diameter). The ^{31}P NMR shifts were recorded against an external standard of 0.5% H_3PO_4 in D_2O and are reported as the values referenced to aqueous 85% H_3PO_4.

Electronic spectra

The UV/VIS spectra of the separated complexes at 0 °C were recorded at various pH by a Hitachi U-3400 spectrophotometer equipped with flow-cell system.[21]

Results

Protonation constants and ^{31}P NMR chemical shifts of midmp and ntmp

We have previously reported the protonation equilibria and the ^{31}P NMR behaviour of midmp and ntmp at 25 °C.[11,13] The protonation constants and chemical shifts were redetermined at 0 °C by means of potentiometry and ^{31}P NMR spectroscopy. The protonation constants (log K_n) obtained by pH titration are listed in Table 1. The values of log K_1 agree with those determined by ^{31}P NMR spectroscopy within experimental error.

The ^{31}P NMR chemical shifts of each species (δ_{H_nL}) determined by using these protonation constants are listed in Table 2. The values of the protonation constants at 0 °C are essentially the same as those at 25 °C, although a small difference is observed because of the change in the autoprotolysis constant, log K_w = 14.95 at 0 °C and I = 0.1 mol dm^{-3}. The quite large values of log K_1 and the large upfield chemical shifts indicate that the first protonation occurs on the nitrogen atom in both systems, ntmp and midmp. The small changes in chemical shift crossed by the succeeding protonations indicate protonations at oxygen atoms of the phosphonate groups.

Table 1 Logarithmic protonation constants (log K_n) of the aminopolyphosphonates at 0 °C *

	midmp	ntmp
log K_1	12.5 ± 0.2	13.1 ± 0.2
log K_2	6.6 ± 0.06	7.2 ± 0.06
log K_3	4.80 ± 0.05	5.62 ± 0.06
log K_4	< 1	4.00 ± 0.05
log K_5		< 1

* $K_n = [H_nL]/[H][H_{n-1}L]$, I = 0.1 mol dm^{-3} (KNO_3).

cis-$[Co(en)_2Cl_2]^+$–midmp system

^{31}P NMR measurements. The ^{31}P-{^1H} NMR spectrum of the reaction mixture adjusted at pH 10.5 at 0 °C is shown in Fig. 1(*a*), where $[Co(en)_2Cl_2]^+$ was treated with midmp at pH 4 and 50 °C for 3 h. There are four main peaks labelled (a)–(d). The change in the ^{31}P-{^1H} NMR spectrum upon change in pH is shown in Fig. 2. All the signals show a chemical shift change. They are broadened at pH 4–7 and (b) separates into two peaks in this region.

The change in the NMR spectrum of the reaction mixture was also studied as a function of reaction time. Just after the mixing of the solutions of $[Co(en)_2Cl_2]^+$ and midmp the spectrum shows only signal (d), which corresponds to unreacted

Table 2 Phosphorus-31 NMR chemical shifts of the aminopolyphosphonates at 0 °C

	δ	
	midmp	ntmp
L	15.9	17.3
HL	5.9	6.6
H_2L	6.4	6.8
H_3L	7.2	8.0
H_4L		7.2

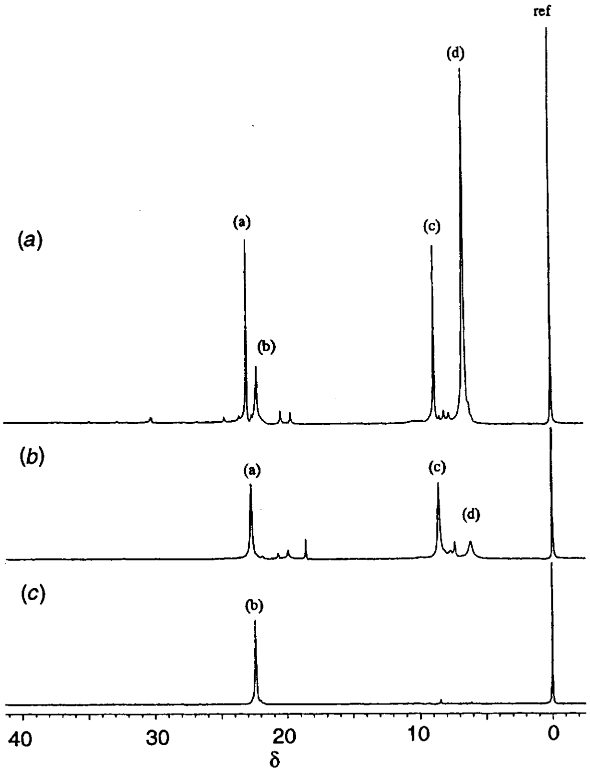


Fig. 1 The ^{31}P-{^1H} NMR spectra of (*a*) a mixture of $[Co(en)_2Cl_2]^+$–midmp at 0 °C at pH 10.5 which had been allowed to react for 3 h at 50 °C and pH 4, (*b*) first (pH 10.4) and (*c*) the second peak (pH 10.5) separated by HPLC

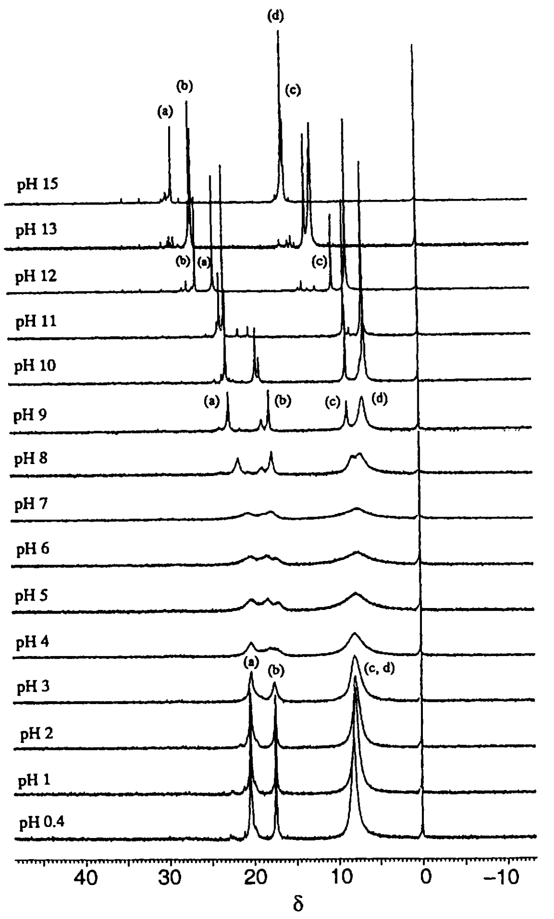


Fig. 2 The $^{31}P-\{^1H\}$ NMR spectrum of a $[Co(en)_2Cl_2]^+$–midmp mixture recorded at various pH at 0 °C

midmp. In the early stage of the reaction signals (a) and (c) grow in a peak area ratio of 1 : 1, followed by signal (b). Upon prolonged reaction (> 10 h), signal (b) becomes the major peak and many others appear. Similar results were obtained for the reaction in acidic solutions, and the rate of complex formation decreases upon decreasing the pH. The complex formation in neutral and alkaline solution is quite slow. Owing to decomposition of midmp, the ^{31}P NMR spectra of the solutions at alkaline pH are quite complicated.

The $^{31}P-\{^1H\}$ NMR spectra of fractions separated by HPLC were measured as a function of pH. Those of the first and second peaks are shown in Fig. 1(*b*) and (*c*), respectively. The first peak fraction exhibits two major signals corresponding to (a) and (c) of the reaction mixture and shows the same pH dependence of chemical shifts as that of the reaction mixture. The ratio of the areas of the signals (a) : (c) is 1 : 1. These results indicate that (a) and (c) can be assigned to the same species. The fractions of the second peak show only one signal corresponding to (b) of the reaction mixture. Consequently, two types of complex are predominantly formed by the reaction of $Co(en)_2{}^{3+}$ with midmp, that is one corresponding to signals (a) and (c) and one to (b).

Protonation constants and chemical shifts of the complexes. The change in ^{31}P NMR chemical shifts are plotted as a function of pH in Fig. 3. The fact that the signals shift with change in pH without splitting indicates fast protonation equilibria. Consequently, the observed chemical shift for each signal, δ_{obs}, is a weighted average of the chemical shift of each protonated species of $Co(en)_2$–midmp complexes. Thus the calculated chemical shift is given by $\delta_{calc} = \Sigma\delta_{M(H_nL)}X_{M(H_nL)}$, where $\delta_{M(H_nL)}$ is the chemical shift of the protonated ($n \geqslant 1$) or unprotonated species ($n = 0$), $M(H_nL)$ and $M = Co(en)_2$; $X_{M(H_nL)}$ is the proportion of each species and is calculated from the solution pH by using the protonation constant $K_n = [M(H_nL)]/[H^+][M(H_{n-1}L)]$. The values of $\delta_{M(H_nL)}$ and K_n giving a minimum error-square sum of chemical shifts, $\Sigma(\delta_{obs} - \delta_{calc})^2$, were calculated by a non-linear regression with the aid of a microcomputer.[11] The logarithmic protonation constant, log K_n, and the chemical shift, $\delta_{M(H_nL)}$, of each protonated species obtained from plots of δ *vs.* pH (Fig. 3) are listed in Table 3. Solid lines in Fig. 3 are calculated curves obtained by using the values listed in Table 3 and show good agreement with the experimental results.

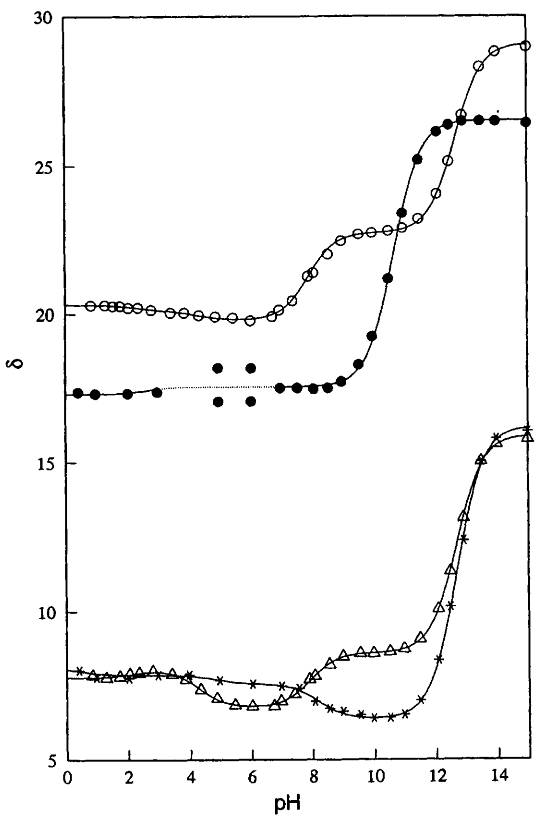


Fig. 3 The ^{31}P NMR chemical shifts of $Co(en)_2$–midmp complexes as a function of pH at 0 °C. Monodentate midmp complex: ○, co-ordinated phosphonate (*a*); △, unco-ordinated phosphonate (*c*). Bidentate midmp complex: ●, co-ordinated phosphonate (*b*). *, Unreacted midmp (*d*). Solid lines are calculated curves, see text

The plot of δ *vs.* pH for the signals (a) and (c) (Fig. 3) shows four inflection points and the protonation constants obtained from the signals (a) and (c) agree with each other (log K_1 = 12.7, log K_2 = 8.0, log K_3 = 4.3 and log K_4 = 2.2). This fact supports the assignment of these two peaks to the phosphonate groups in the same complex. It is reported that the co-ordination of phosphonate to an inert metal ion results in a downfield shift of the ^{31}P NMR signal.[19,22,23] Thus, signal (a) located downfield is assigned to the phosphonate group co-ordinated to Co^{III} and (c) located at high field is assigned to an unco-ordinated phosphonate group.

We have reported that the protonation of the nitrogen of an aminopolyphosphonate results in an upfield shift of the ^{31}P NMR signal of the phosphonate group.[11] Signals (a) and (c) show large upfield shifts (*ca.* 7 ppm) upon the first protonation (pH 12.7). This indicates that the first protonation of the complex occurs at the nitrogen atom of the imino group of midmp. The very high value of the protonation constant (log K_1 = 12.7) is in accord with this; protonation constants of the phosphonate oxygen atoms of co-ordinated midmp should be less than that of free midmp (log K_2 < 6.6). Thus the nitrogen atom is not co-ordinated to Co^{III}. Consequently, the complex corresponding to signals (a) and (c) is proposed to contain a

Table 3 Chemical shifts and logarithmic protonation constants[a] of *cis*-Co(en)$_2$–midmp and –ntmp complexes at 0 °C [M = Co(en)$_2$]

	O-Monodentate ligand			O,O-Bidentate ligand			
(*a*) midmp							
Complex	δ(a)	δ(c)	log K_n	Complex	δ(b)		log K_n
M(OH)L	29.1	15.9		ML	26.5		
			12.7 ± 0.2^a				10.7 ± 0.1^b
M(OH)(HL)	22.7	8.6		M(HL)	17.6		
			8.0 ± 0.1^c				2.6 ± 0.2^{b,d}
M(H_2O)(HL)	19.8	6.8		M(H_2L)	17.3		
			4.3 ± 0.2^e				
M(H_2O)(H_2L)	20.1	8.0					
			2.2 ± 0.2^{d,e}				
M(H_2O)(H_3L)	20.3	7.8					
(*b*) ntmp							
	δ(e)	δ(g)	log K_n		δ(f)	δ(h)	log K_n
M(OH)L	31.5	18.6		ML	28.4	17.3	
			13.1 ± 0.2^a				11.7 ± 0.1^b
M(OH)(HL)	23.4	9.5		M(HL)	18.9	8.3	
			9.4 ± 0.1^c				
M(H_2O)(HL)	19.8	7.5					

[a] K_n = [M(OH)(HL)]/[M(OH)L][H$^+$]. [b] K_n = [M(H_nL)]/[M($H_{n-1}L$)][H$^+$]. [c] K_n = [M(H_2O)(HL)]/[M(OH)(HL)][H$^+$]. [d] Evaluated from UV/VIS spectroscopy. [e] K_n = [M(H_2O)($H_{n-1}L$)]/[M(H_2O)($H_{n-2}L$)][H$^+$].

monodentate aminopolyphosphonate, co-ordinating through an O atom.

The downfield shift of signal (b) compared with that of free midmp indicates that a phosphonate oxygen is co-ordinated to Co^{III}. The fact that no other signal is observed [Fig. 1(*c*)] suggests that both phosphonate groups are equivalent, *i.e.* both are co-ordinated to Co^{III}. The large value of the first protonation constant (log K_1 = 10.7) and the large upfield shift upon protonation indicate that the nitrogen atom of midmp is not co-ordinated. Consequently, signal (b) is assigned to a complex containing an O,O-bidentate ligand.

The minor ^{31}P NMR signals which occur upon prolonged reaction are assigned to decomposition products of midmp and its complexes with Co(en)$_2$. It has been reported that decomposition of a phosphate ester is promoted in the presence of a cobalt(III) complex.[24]

The ^{31}P NMR spectra and their changes with pH of the complexes obtained by reaction of [Co(en)$_2$(H_2O)$_2$]$^{3+}$ with midmp are the same as those found for the reaction of [Co(en)$_2$Cl$_2$]$^+$.

The pH region at which the line broadening occurs in the ^{31}P NMR spectrum (Fig. 2) does not exactly correspond to that of protonation of the complexes. The signal of free midmp is also broadened in the same pH region. This indicates that this broadening is not caused by slow proton exchange on the complexes, rather it suggests some interaction between the complexes and free midmp. It is difficult to deduce a reasonable explanation for this interaction from the experimental data obtained so far.

UV/VIS spectroscopy. The UV/VIS spectra of the complexes of O-monodentate and O,O-bidentate midmp separated by HPLC were measured at various pH at 0 °C. Some spectra of the complex of O-monodentate midmp at representative pH are shown in Fig. 4. The absorbances of both peaks (348 and 520 nm) decrease with decreasing pH. Similar spectra changes were observed for the O,O-bidentate midmp complex. The changes in molar absorption coefficients (ε) of both complexes are shown in Fig. 5 as a function of pH. The plots were analysed in a similar manner to those of δ(^{31}P) *vs.* pH. The solid lines were calculated using the protonation constants in Table 3 and are in accord with the experimental values.

The second protonation constant of the O,O-bidentate midmp complex was obtained from the analysis of ε. In the case of the ^{13}P NMR measurement the change in chemical shift at this protonation step is very small, so the protonation constant was not obtained.

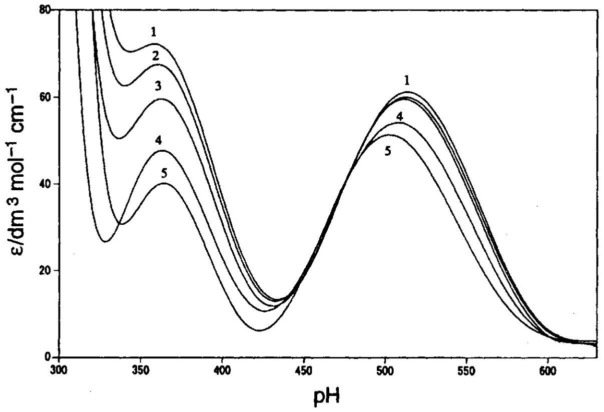


Fig. 4 The UV/VIS spectra of the O-monodentate midmp complex of Co(en)$_2$ at pH 12.5 (1), 11.6 (2), 9.2 (3), 7.2 (4) and 2.5 (5)

cis-[Co(en)$_2$Cl$_2$]$^+$–ntmp system

The ^{31}P-{^{1}H} NMR spectrum of a solution of [Co(en)$_2$Cl$_2$]$^+$ treated with ntmp at pH 4 and 50 °C for 12 h is shown in Fig. 6. There are five main peaks labelled (e)–(i). Signal (i) corresponds to the unreacted midmp. In the early stage of the reaction signals (e) and (g) grow, followed by (f) and (h). At any reaction time the peak area ratio of (e) and (g) is 1 : 2, and of (f) and (h) is 2 : 1. The ^{31}P-{^{1}H} NMR spectra of the reaction mixture were measured at various pH and the chemical shifts of the peaks are plotted as a function of pH in Fig. 7. Owing to broadening of the peaks, no signals can be observed in the acidic region (pH < 7). All the signals show downfield shifts with decreasing pH. Using the same analysis of the chemical shift as for the midmp system, the logarithmic protonation constants, log K_n, and the chemical shifts, $\delta_{M(H_nL)}$, were obtained for each signal. The results listed in Table 3 indicate that ntmp co-ordinates to Co(en)$_2$ in the same manner as that of midmp, that is as an O-monodentate ligand in one complex and as an O,O-bidentate ligand in another. The quite large value of the first protonation constant (log K_1 = 13.1) and the corresponding large upfield shifts (Δδ = 8–9 ppm) of signals (e) and (g) indicate

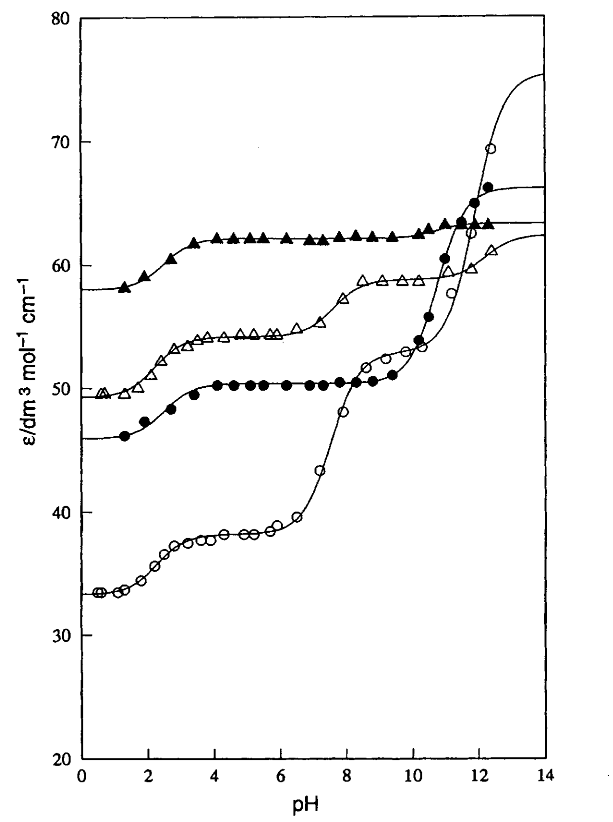


Fig. 5 Changes in molar absorption coefficients (ε) of separated Co(en)$_2$–midmp complexes as a function of pH. Monodentate midmp complex: ○, 348; △, 520 nm. Bidentate midmp complex: ●, 370; ▲, 515 nm

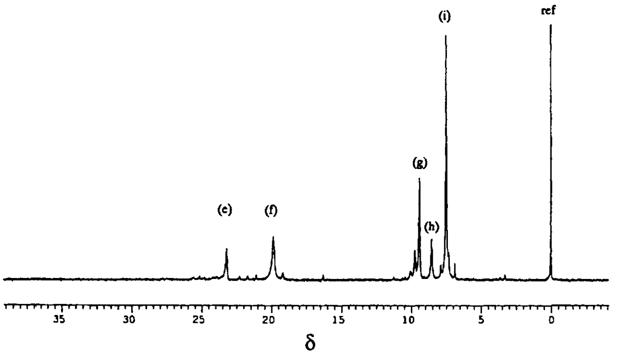


Fig. 6 The ^{31}P-{^{1}H} NMR spectrum of a [Co(en)$_2$Cl$_2$]$^+$–ntmp reaction mixture at 0 °C at pH 11 which had been allowed to react for 3 h at 50 °C and pH 4

protonation of the imino nitrogen, that is, this atom does not co-ordinate to the metal ion. The peak area ratio of the signal of co-ordinated phosphonate (e) to that of unco-ordinated phosphonate (g), 1:2, is consistent with the formation of an O-monodentate ntmp complex. The protonation constant (log K_1 = 11.7) and the change in chemical shift of signals (f) and (h) also indicate that the nitrogen atom is not co-ordinated. The peak ratio of (f) (co-ordinated) and (*h*) (unco-ordinated phosphonate) = 2:1 is consistent with an O,O-bidentate ntmp complex.

cis-[Co(en)$_2$(NH$_3$)Cl]$^{2+}$–midmp system

In the case of *cis*-[Co(en)$_2$(NH$_3$)Cl]$^{2+}$ only one site is available for co-ordination of midmp. The ^{31}P-{^{1}H} NMR spectrum of a midmp solution treated with *cis*-[Co(en)$_2$(NH$_3$)Cl]Cl$_2$ for 36 h at 50 °C is shown in Fig. 8(*a*). Two main signals (j) and (k) are observed except for that of free midmp (l). The peak area ratio of signals (j) and (k) is 1:1 at any reaction time. The solution

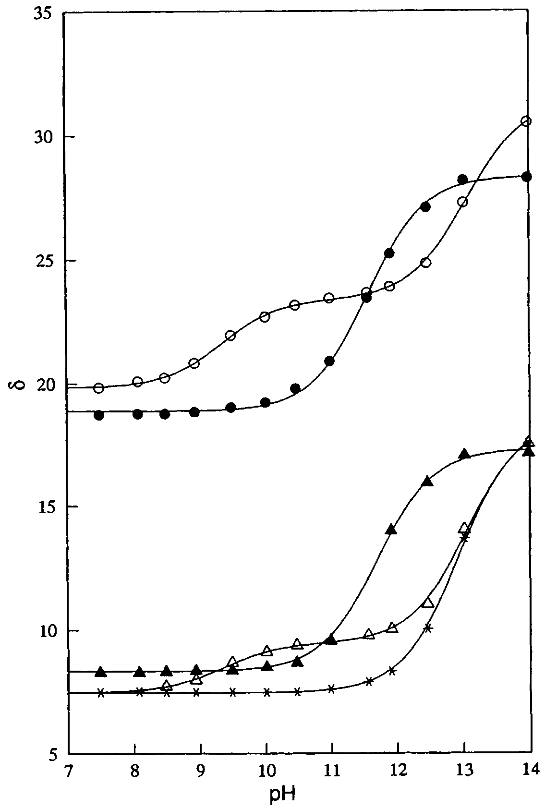


Fig. 7 The ^{31}P NMR chemical shifts of a [Co(en)$_2$Cl$_2$]$^+$–ntmp reaction mixture as a function of pH at 0 °C. Monodentate ntmp complex: ○, co-ordinated phosphonate (e); △, unco-ordinated phosphonate (g). Bidentate ntmp complex: ●, co-ordinated phosphonate (f); ▲, bidentate phosphonate (h). *, Unreacted ntmp (i)

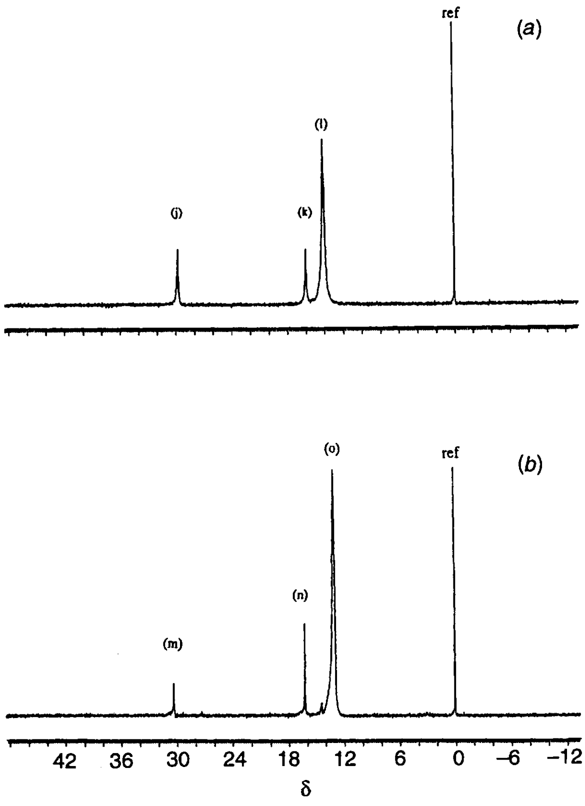


Fig. 8 The ^{31}P-{^{1}H} NMR spectra of mixtures of (*a*) [Co(en)$_2$(NH$_3$)Cl]$^{2+}$–midmp and (*b*) [Co(en)$_2$(NH$_3$)Cl]$^{2+}$–ntmp at 0 °C at pH 13 which had been allowed to react for 36 h at 50 °C and pH 4

Table 4 Chemical shifts and logarithmic protonation constants* of *cis*-$Co(en)_2(NH_3)$–midmp and –ntmp complexes at 0 °C [$M = Co(en)_2$]

	Monodentate midmp			Monodentate ntmp		
Complex	δ(j)	δ(k)	log K_n	δ(m)	δ(n)	log K_n
$M(NH_3)L$	29.7	16.0		31.0	16.8	
			10.7 ± 0.1			11.9 ± 0.2
$M(NH_3)(HL)$	18.9	6.8		18.9	6.9	
			4.9 ± 0.1			6.2 ± 0.1
$M(NH_3)(H_2L)$	18.2	8.2		18.4	6.8	
			2.2 ± 0.2			3.4 ± 0.1
$M(NH_3)(H_3L)$	20.1	7.8		19.2	7.8	
						1.4 ± 0.2
$M(NH_3)(H_4L)$				20.3	7.2	

* $K_n = [M(NH_3)(H_nL)]/[M(NH_3)(H_{n-1}L)][H^+]$.

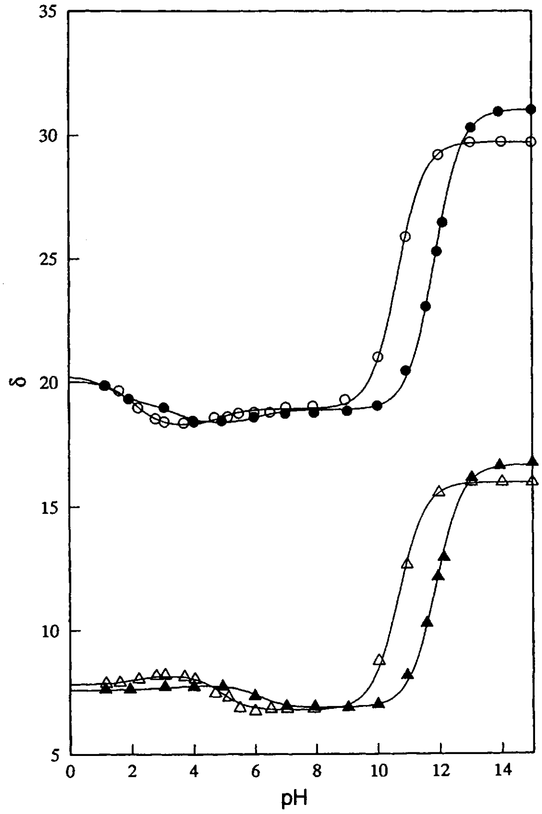


Fig. 9 The ^{31}P NMR chemical shifts of the $Co(en)_2(NH_3)$–midmp and –ntmp complexes as a function of pH at 0 °C. midmp complex: ○, co-ordinated phosphonate (j); △, unco-ordinated phosphonate (k). ntmp complex: ●, co-ordinated phosphonate (m); ▲, unco-ordinated phosphonate (n)

separated by HPLC shows a pair of signals corresponding to peaks (j) and (k) with peak area ratio 1 : 1. These results indicate signals (j) and (k) originate from one complex. As only one site is available for co-ordination, the formation of an O-monodentate midmp complex is anticipated. The low-field signal (j) is assigned to a phosphonate group co-ordinated *via* an oxygen atom and the high-field signal (k) to the unco-ordinated group.

Plots of the ^{31}P NMR chemical shifts of the signals as a function of pH are shown in Fig. 9. The change in chemical shift was analysed in the same manner as that for the *cis*-$Co(en)_2$ system. The protonation constants (log K_n) and the chemical shifts $\delta_{M(H_nL)}$ thus obtained are listed in Table 4. The calculated curves obtained by using these constants are shown in Fig. 9 as solid lines. The protonation constants obtained from signals (j) and (k) agreed with each other. The facts that the first protonation constant (log K_1 = 10.7) is much larger than that of the phosphonate oxygen atom (log K_2 = 6.6) of the ligand and that these signals show a large upfield shift upon protonation are consistent with a structure in which the imino nitrogen atom of the ligand is not co-ordinated to the metal ion.

cis-$[Co(en)_2(NH_3)Cl]^{2+}$–ntmp system

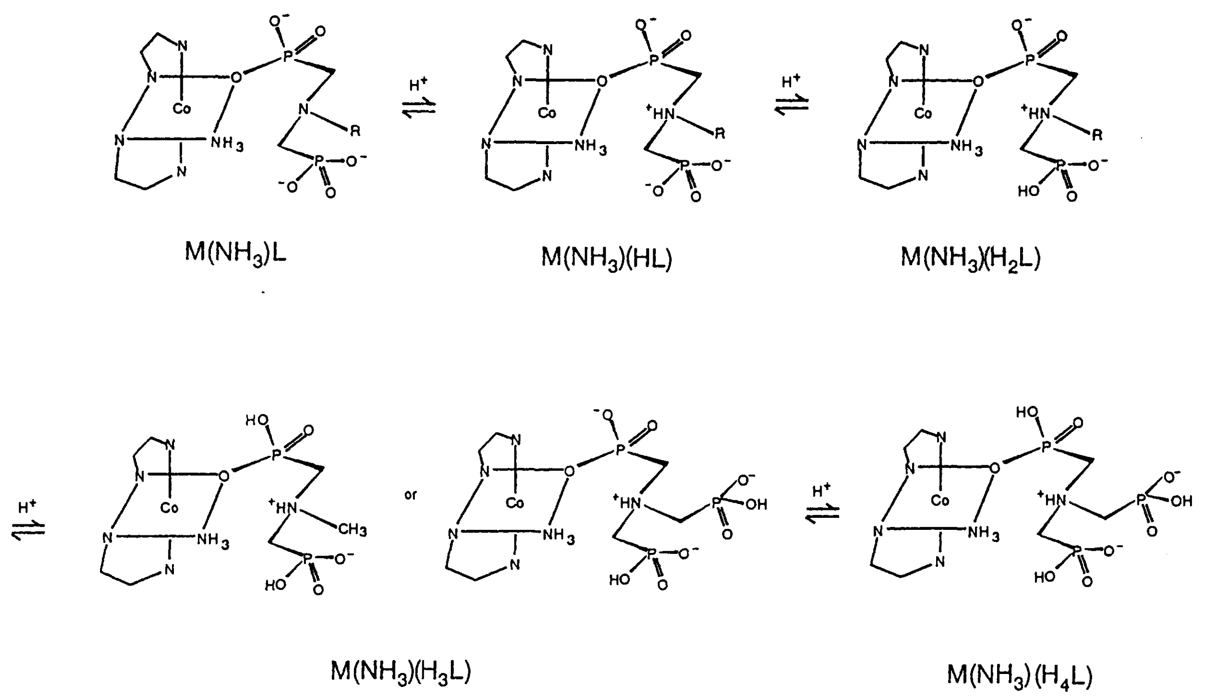
The ^{31}P-{^1H} NMR spectrum of a solution of $[Co(en)_2(NH_3)Cl]^{2+}$ treated with ntmp for 36 h is shown in Fig. 8(*b*). The changes in chemical shifts as a function of pH are shown in Fig. 9. The protonation constants and chemical shifts of each signal obtained from the data in Fig. 9 are listed in Table 4. The ^{31}P NMR spectra and their change by pH are quite similar to those of the midmp-system, except for the peak area ratio of signals (m) and (n), 1 : 2. This ratio indicates the formation of an O-monodentate ntmp complex, that is one phosphonate group co-ordinates *via* an oxygen atom and the other two are unco-ordinated.

Discussion

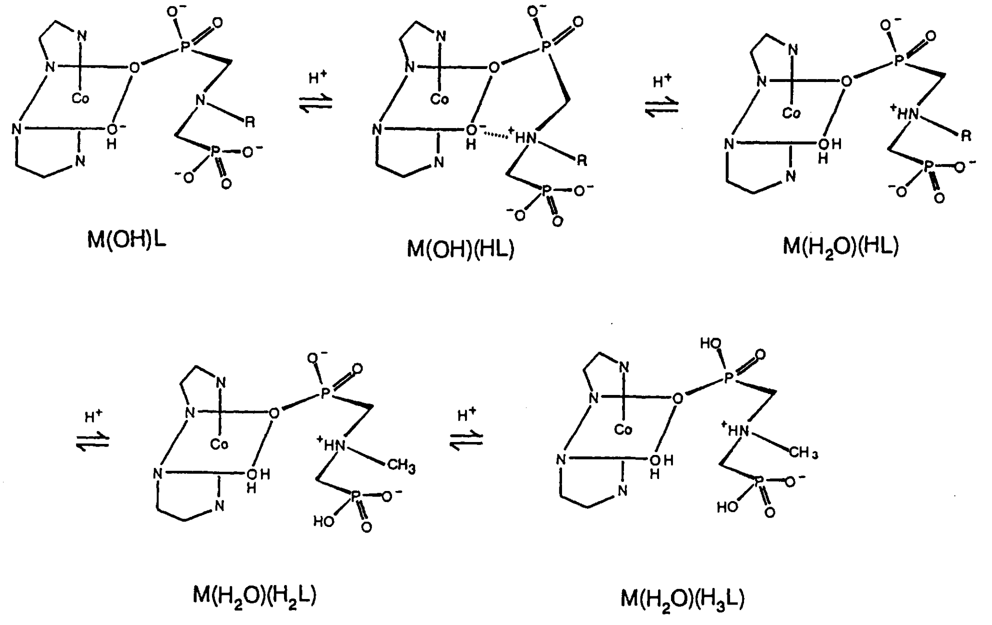
Structure of $Co(en)_2(NH_3)$ O-monodentate ligand complexes

As only one phosphonate oxygen atom is co-ordinated in the O-monodentate ligand complexes of $Co(en)_2(NH_3)$, the structure of the unprotonated complex is that of $M(NH_3)L$ in Scheme 1, where $M = Co(en)_2{}^{3+}$ and $L = midmp^{4-}$ or $ntmp^{6-}$. The first protonation of the complex occurs at the nitrogen atom of the imino group, to give $M(NH_3)(HL)$. The chemical shifts of the unco-ordinated phosphonate of the unprotonated complexes, $\delta_{M(NH_3)L}$ 16.0 [midmp, (k)] and 16.8 [ntmp, (n)] (Table 4), are very similar to those of the free phosphonates [δ_L 15.9 (midmp) and 17.3 (ntmp), Table 2]. The chemical shifts of the monoprotonated complexes, $\delta_{M(NH_3)(HL)}$, are also very similar to those of the corresponding free phosphonates, δ_{HL}. The first protonation constants of the complexes [log K_1 = 10.7 (midmp) and 11.9 (ntmp), Table 4] are relatively smaller than those of the phosphonates (log K_1 = 12.5 and 13.1, Table 1). Thus, the basicity of the nitrogen atom of the imino group is lowered by co-ordination to the cationic species, $Co(en)_2(NH_3)^{3+}$.

The second protonation occurs on an unco-ordinated phosphonate oxygen, to give $M(NH_3)(H_2L)$ in Scheme 1. The very small change in the chemical shift is consistent with this. The corresponding protonation constants of the complexes [log K_2 = 4.9 (midmp) and 6.2 (ntmp), Table 4] are very similar to those of the phosphonates (log K_3 = 4.8 and 5.6, Table 1). The quite small values of the third protonation constant of the (midmp) complex, $M(NH_3)(H_3L)$ (log K_3 = 2.2), and the fourth protonation of the ntmp complex, $M(NH_3)(H_4L)$ (log K_4 = 1.4) are consistent with protonation on the phosphonate oxygen atom co-ordinated to Co^{III}.



Scheme 1 $R = CH_3$ or $CH_2PO_3{}^{2-}$, $M = Co(en)_2$



Scheme 2 $R = CH_3$ or $CH_2PO_3{}^{2-}$, $M = Co(en)_2$

Structure of $Co(en)_2$ O-monodentate ligand complexes

The complex *cis*-$[Co(en)_2Cl_2]^+$ also forms an O-monodentate ligand complex on reaction with midmp or ntmp. However, the chemical shifts and protonation constants of the midmp complex (Table 3) are significantly different from those of the $Co(en)_2(NH_3)$ complexes (Table 4). This can be explained by the structures shown in Scheme 2. The co-ordinated chloride in $[Co(en)_2Cl_2]^+$ is substituted by water molecules within 30 min at 50 °C.[25] Thus, one site of the O-monodentate ligand complex is occupied by a phosphonate oxygen atom and another is substantially substituted by a water molecule.

The water molecule of complexes $[Co(en)_2X(H_2O)]^{2+}$ has a relatively high acidity, $pK_a = 8.12$ for *cis*-$[Co(en)_2(OH)(H_2O)]^{2+}$ and $pK_a = 7.13$ for *cis*-$[Co(en)_2Cl(H_2O)]^{2+}$.[26] Thus, the co-ordinated water in the O-monodentate ligand complex must be deprotonated at high pH, *i.e.* the structure of the unprotonated species is that of M(OH)L, Scheme 2. As the basicity of the imino nitrogen of L is much higher than that of the OH^- in $Co(en)_2X(OH)$ or phosphonate oxygen, the first protonation of the complex, M(OH)L, occurs on the ligand imino nitrogen atom, M(OH)(HL) in Scheme 2. The first protonation constants [$\log K_1 = 12.7$ (midmp) and 13.1 (ntmp), Table 3] are larger than those of $Co(en)_2(NH_3)$ O-monodentate ligand complexes ($\log K_1 = 10.7$ and 11.9, Table 4) and are comparable to those of the free phosphonates. The changes in chemical shifts accompanying the first protonation ($\Delta\delta = ca.$ 7 ppm) are smaller than that of the $Co(en)_2(NH_3)$ complex ($\Delta\delta = ca.$ 10 ppm). These facts may indicate that the monoprotonated complexes are stabilized by an intramolecular interaction, *i.e.* hydrogen bonding between OH^- and ^+HN as shown in Scheme 2.

The second protonation constant of M(OH)(HL) [$\log K_2 = 8.0$ (midmp) and 9.4 (ntmp), Table 3] is much larger than those of the $Co(en)_2(NH_3)(HL)$ complexes [log $K_2 = 4.9$ (midmp) and 6.2 (ntmp)] and close to the value for protonation of OH^- in $[Co(en)_2X(OH)]^+$. Thus, the diprotonated species is assigned as $M(H_2O)(HL)$ (Scheme 2). It is reasonable that the chemical shifts of the diprotonated species $Co(en)_2(H_2O)(HL)$ [δ 19.8 (a), 6.8 (c) for midmp, Table 3] are closer to those of the monoprotonated species $Co(en)_2(NH_3)(HL)$ [δ 18.9 (k), 6.8 (n) for midmp, Table 4]. The third and fourth protonations may occur on the unco-ordinated and co-ordinating phosphonates, respectively. The values of log K_3 and log K_4 for the $M(H_2O)$–midmp are very similar to log K_2 and log K_3 of the $M(NH_3)$ system. These facts support the protonation sequence in Scheme 2.

The UV/VIS spectra of the $Co(en)_2$ O-monodentate midmp complex (Fig. 5) also provide support for Scheme 2. The large changes in the absorption accompanying the first (≈pH 13) and second (≈pH 8) protonations indicate these occur near to cobalt(III) centre, that is formation of an $OH^- \cdots HN^+$ hydrogen bond and protonation of OH^-. The third protonation occurs on the unco-ordinated phosphonate group far from the metal centre, and the corresponding change in absorbance is negligible (Fig. 5, pH 4.3). The change in absorbance accompanying the fourth protonation (pH 2.2) is consistent with protonation of the phosphonate group co-ordinated to Co^{III}.

In the case of the O-monodentate ligand complexes formed by the reaction of $[Co(en)_2Cl_2]^+$ it is anticipated that a co-ordinated water molecule is substituted by the chloride ion. The diaqua complex $[Co(en)_2(H_2O)_2]^{3+}$ was treated with midmp under the same experimental conditions for the $[Co(en)_2Cl_2]^+$ system. There was no difference in the ^{31}P NMR spectra and protonation constants between these two systems. Thus, the contribution of Cl^- ion to the complex formation of the $Co(en)_2$ systems is not significant.

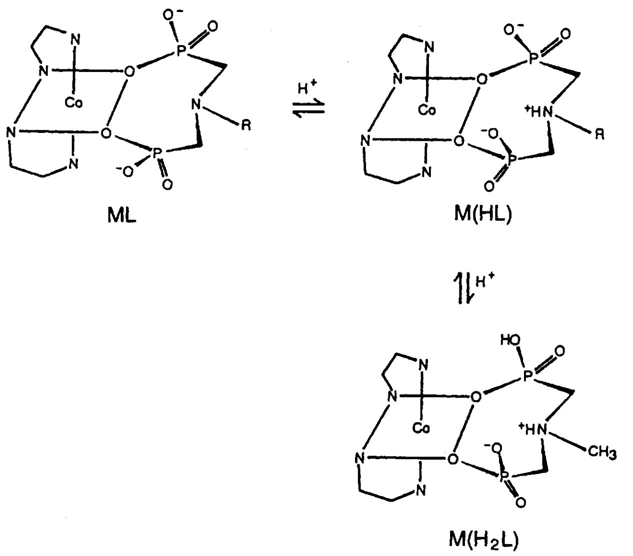
Structure of O,O-bidentate ligand complex

As shown above, the imino nitrogen of the O,O-bidentate ligand complexes is not co-ordinated to the metal. Thus, the midmp and ntmp in these complexes co-ordinate by forming an eight-membered chelate ring (Scheme 3). We have previously reported the formation of such chelate rings in protonated labile metal complexes of aminopolyphosphonate,[11–13] however, they were not isolated. The eight-membered chelate ring is thought to be an unstable structure, and has never been reported for aminopolycarboxylate complexes, although the α,γ-triphosphate complexes of Co^{III} [27] and Pt^{II} [28] were isolated.

The protonation equilibria of the O,O-bidentate ligand complexes are rather simple as shown in Scheme 3. The first protonation on the imino nitrogen [M(HL)] results in an upfield shift of about 10 ppm (Table 3). The first protonation constants of the complexes [log $K_1 = 10.7$ (midmp) and 11.7 (ntmp)] are comparable to those of $Co(NH_3)(HL)$. The second protonation constant of the $Co(en)_2$–midmp complex (log $K_2 = 2.6$, Table 3), estimated from the UV/VIS measurement, is comparable to that for the co-ordinated phosphonate group in O-monodentate ligand complexes. The change in the UV/VIS absorption spectra at around pH 3 is quite similar to that of the O-monodentate ligand complex $M(H_2O)(H_3L)$. These findings are consistent with protonation near to the metal centre, $M(H_2L)$ in Scheme 3.

Dinuclear complexes

Another possibility for the O,O-bidentate ligand complex is a dinuclear structure with bridging diphosphonate ligands, ML_2M, in which the two nitrogen atoms are not co-ordinated and four phosphonate groups are equivalent. Since the bridging ligands are in close proximity, the basicity of the second nitrogen atom would be significantly lowered by the first protonation. From the pH titrations and ^{31}P NMR chemical shift changes, a two-step protonation is not observed in the alkaline region. In order to form a dibridged complex appreciable amounts of monobridged complexes must be formed as intermediate species. There was no evidence for such complexes either in the HPLC separation or the ^{31}P NMR spectra of the reaction mixture under any experimental conditions. Thus, the formation of dinuclear complexes is unlikely.



Scheme 3 R = CH_3 or $CH_2PO_3^{2-}$, M = $Co(en)_2$

Four-membered chelate-ring complex

Four-membered chelate-ring complexes in which two oxygen atoms of one phosphonate group are co-ordinated to the metal ion are formed by the reaction of orthophosphate with *cis*-$[Co(en)_2(H_2O)_2]^{3+}$ [23,29] and *cis*-$[Pt(NH_3)_2Cl_2]$.[30] This type of co-ordination is much more common in acetate complexes.[31,32] On formation of the four-membered chelate ring, the phosphonate ^{31}P or carbonyl ^{13}C resonance of the bidentate group shows a larger downfield shift than that of the corresponding monodentate group.[23,29,32] In the present study no downfield signal was observed in the ^{31}P NMR spectra of any systems. Consequently, no species having a four-membered chelate ring is formed in the $Co(en)_2$–aminopolyphosphonate systems under the experimental conditions.

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Received 2nd *February* 1996; *Paper* 6/00787B