

1-Hydroxyalkane-1,1-diylidiphosphonates as potent chelating agents for metal ions. Potentiometric and spectroscopic studies of copper(II) co-ordination

Marcin Dyba,^a Malgorzata Jezowska-Bojczuk,^a Erzsebet Kiss,^b Tamas Kiss,^b Henryk Kozlowski,^{*a} Yves Leroux^c and Driss El Manouni^c

^a Institute of Chemistry, University of Wroclaw, F. Joliot-Curie 14, 50383 Wroclaw, Poland

^b Department of Inorganic and Analytical Chemistry, Kossuth University, H-4010 Debrecen, BOB 21, Hungary

^c Laboratoire de Chimie Structurale Biomoleculaire, URA CNRS 1430, University Paris-Nord, 93012 Bobigny Cedex, France

Potentiometric and spectroscopic (EPR and absorption) studies have shown that two phosphonic groups bound to the same carbon atom serve as a very powerful binding site for Cu^{2+} ion in spite of the very high negative charge centred on these groups. The steric effects as well as a high negative charge enforce unusual geometries around the metal ion and the formation of 1:2 complexes is less favourable. These features of the diphosphonic moiety mean that alkoxo-bridged dimer formation *via* the adjacent hydroxyl groups is less likely.

Our recent works on aminophosphonic acid co-ordination ability have shown that amino acids and their various derivatives are very effective binder molecules for Cu^{2+} ions.^{1,2} The organic diphosphonic acids are potentially very powerful chelating agents used in metal extractions³ and are tested by the pharmaceutical industry for use as efficient drugs preventing calcification and inhibiting bone resorption. Diphosphonic acids are used in the treatment of Paget disease, osteoporosis and tumoral osteolysis. The high affinity of diphosphonates for bones allows their application in nuclear medicine as ligands for $^{99\text{m}}\text{Tc}$. Several diphosphonates were commercially developed by pharmaceutical companies. The P-C-P bond system of the acidic form has low toxicity and high thermostability. It should also be mentioned that the P-C-P motif is very resistant to enzymatic degradation. Thus, a large number of diphosphonates have been synthesised and tested clinically. The very high ability to bind various metal ions results from the mobility and flexibility of neighbouring phosphonate functions which can accommodate a large number of ionic radii.⁴⁻¹¹ X-Ray crystallography indicates that diphosphonates may form very stable chelates with various metal ions from Na^+ to Cu^{2+} . In the case of copper(II) complexes, solid-state studies have shown that substitution of the methyl group in 1-hydroxyethane-1,1-diylidiphosphonic acid by aminopropyl or aminopentyl leads to considerable modification of the co-ordination sphere around the metal ion.^{10,11} In this work we present spectroscopic and potentiometric results obtained for Cu^{2+} with three hydroxydiphosphonate and one dihydroxytetraphosphonate ligand (L^1 – L^4) in solution.

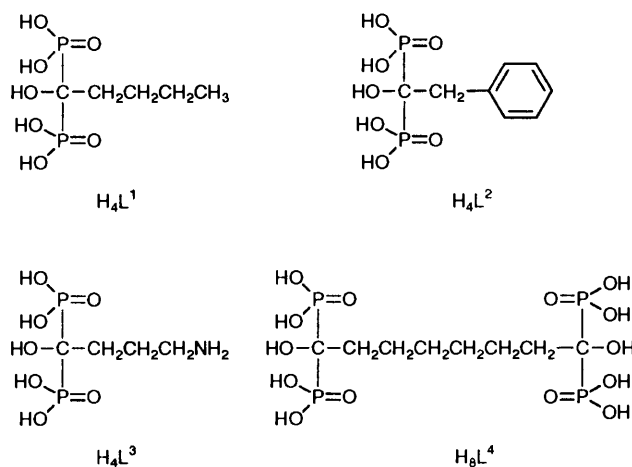
Experimental

Ligand synthesis

The detailed ligand synthesis is given in refs. 3, 12 and 13.

Potentiometric measurements

The stability constants of the proton and copper(II) complexes of diphosphonic acids were determined by pH-potentiometric titrations of 5 cm³ samples at 25 °C. The diphosphonic acid concentration in each sample was 0.002



mol dm⁻³ and the metal ion to acid ratio was 0:1, 1:1, 1:2 or 1:4. The ionic strength was adjusted to 0.20 mol dm⁻³ with KCl in each case. The titrations were performed over the range pH 3–11, with carbonate-free KOH solution of known concentration (*ca.* 0.2 mol dm⁻³). The pH was measured with a Radiometer PHM 84 instrument equipped with a GK 2322C combined glass electrode, calibrated for hydrogen-ion concentration according to the procedure of Irving *et al.*¹⁴ The pK_w , calculated from strong acid titrations was 13.76. The concentration stability constants, $\beta_{prq} = [\text{M}_p\text{H}_r\text{L}_q]/[\text{M}]^p[\text{H}]^r[\text{L}]^q$, were calculated with the aid of the PSEQUAD computer program.¹⁵

Spectroscopic measurements

The EPR spectra were recorded on a Bruker ESP 300E spectrometer at X-band frequency (9.3 GHz) at 120 K; Mn^{2+} in MgO and diphenylpicrylhydrazyl (dpph) were used as the standards for *g*-value calculations. Absorption spectra were recorded on a Beckman DU 650 spectrophotometer. The metal-to-ligand ratios were 1:1 and 1:2 and the metal concentration was 5×10^{-3} mol dm⁻³.

Table 1 Stability constants of the proton ($\log K$) and copper(II) complexes ($\log \beta$) of 1-hydroxyalkane-1,1-diylidiphosphonic acids at 25 °C and $I = 0.2 \text{ mol dm}^{-3}$ (KCl)

	$\begin{array}{c} \text{PO}_3\text{H}_2 \\ \\ \text{C}(\text{OH})(\text{CH}_2)_3\text{CH}_3 \\ \\ \text{PO}_3\text{H}_2 \end{array}$	$\begin{array}{c} \text{PO}_3\text{H}_2 \\ \\ \text{C}(\text{OH})\text{CH}_2\text{Ph} \\ \\ \text{PO}_3\text{H}_2 \end{array}$	$\begin{array}{c} \text{PO}_3\text{H}_2 \\ \\ \text{C}(\text{OH})(\text{CH}_2)_3\text{NH}_2 \\ \\ \text{PO}_3\text{H}_2 \end{array}$
$\log K(\text{HL})$	10.81(2)	11.64(2)	12.04(6)
$\log K(\text{H}_2\text{L})$	6.72(2)	6.53(2)	10.77(2)
$\log K(\text{H}_3\text{L})$	2.47(4)	2.44(2)	6.21(2)
$\log K(\text{H}_4\text{L})$	≈ 1	≈ 1	2.16(3)
$\log K(\text{H}_5\text{L})$	—	—	≈ 1
$[\text{Cu}(\text{H}_3\text{L})]^+$	—	—	32.70(8)
$[\text{Cu}(\text{H}_2\text{L})]$	21.80(4)	21.96(6)	28.92(3)
$[\text{Cu}(\text{HL})]^-$	17.83(4)	18.01(5)	24.24(3)
$[\text{CuL}]^{2-}$	12.77(4)	12.64(6)	15.70(7)
$[\text{CuH}_{-1}\text{L}]^{3-}$	2.54(9)	2.36(6)	4.62(6)
$[\text{CuH}_{-2}\text{L}]^{4-}$	-7.68(6)	—	—
$[\text{CuH}_2\text{L}_2]^{4-}$	—	—	40.49(17)
$[\text{CuL}_2]^{6-}$	16.96(11)	18.35(13)	—
$[\text{Cu}_2\text{L}]$	—	—	23.62(23)
$[\text{Cu}_2\text{H}_1\text{L}]^-$	12.76(9)	12.64(10)	—
Fitting*	0.0039	0.0039	0.0058
No. points	211	231	302
$\log K(\text{CuH}_2\text{L}_2)$	—	—	16.25
$\log K(\text{CuL}_2)$	4.19	5.71	—
$\log(K_1/K_2)$	8.58	6.93	7.99
$\text{Cu}^{2+} + \text{H}_3\text{L}^- \rightleftharpoons [\text{Cu}(\text{H}_2\text{L})] + \text{H}^+$	1.80	1.35	—
$\text{Cu}^{2+} + \text{H}_4\text{L} \rightleftharpoons [\text{Cu}(\text{H}_3\text{L})]^+ + \text{H}^+$	—	—	1.52

* The average difference in the experimental and calculated titration curves expressed in cm^3 of the titrant.

Results and Discussion

1-Hydroxyalkane-1,1-diylidiphosphonic acids H_4L^1 and H_4L^2

These diphosphonic derivatives contain four dissociable protons (H_4L) in the measurable pH range, two at each phosphonic function. The alcoholic hydroxyl group according to expectations is very weakly acidic and does not deprotonate below pH 13. The acid-base properties of the diphosphonic acids differ considerably from those of simple monophosphonates. The latter have two protonation constants with $\log K_{\text{HL}} \approx 5-6$ and $\log K_{\text{H}_2\text{L}} \approx 1$.^{1,2} In the case of diphosphonates the basicity of the second phosphonic group increases distinctly due to fairly strong electronic interactions between the two nearby groups (Table 1). Accordingly, the $\log K_{\text{HL}}$ value is above 10.

Both potentiometric and spectroscopic results obtained for the copper(II)-diphosphonic acid (H_4L^1 and H_4L^2) systems suggest the formation of 1:1 and 1:2 complex species. The co-ordination of the second ligand is, however, hindered by the strong interphosphonate electrostatic interactions of four strongly charged groups. Two fully deprotonated diphosphonate ligands would bring together a charge of 8- around Cu^{2+} . The strong repulsive interactions between two phosphonic (in $[\text{CuL}]^{2-}$ complexes) and four phosphonic (in $[\text{CuL}_2]^{6-}$ species) groups bound to a metal ion are reflected in the very low and rather unusual symmetry of the complexes as observed in the EPR spectra. The formation of protonated equimolar species, $[\text{Cu}(\text{H}_2\text{L})]$ and $[\text{Cu}(\text{HL})]^-$, has only slight impact on the absorption and EPR spectra when compared to aqua metal ion species (Table 2). However, the complete deprotonation of the equimolar complex and formation of $[\text{CuL}]^{2-}$ species shifts distinctly the d-d transition to about 730 nm and changes completely the g pattern in the EPR spectra, from the usual axial spectrum with $g_{\parallel} > g_{\perp}$ (unpaired electron on $d_{x^2-y^2}$) via orthorhombic g_1, g_2, g_3 for $[\text{Cu}(\text{HL})]^-$ ($\text{L} = \text{L}^2$) to a spectrum with $g_{\perp} > g_{\parallel}$ for $[\text{CuL}]^{2-}$ (unpaired electron on d_{z^2}). This clearly indicates that even in the equimolar complex the bulky and highly charged phosphonic groups have considerable

impact on the geometry around the metal ion. An increase in pH above 8 and formation of the $[\text{CuL}_2]^{6-}$ species leads to another drastic change in the EPR spectrum (Table 2) while the d-d transitions shift to around 700 nm. The $g_{\parallel} \approx 2.4$ and small A_{\parallel} values may suggest that in the $[\text{CuL}_2]^{6-}$ complex strong interphosphonic interactions between the four highly charged and bulky groups cause distinct geometry distortion around the metal ion. The unfavourable conditions for the formation of the $[\text{CuL}_2]^{6-}$ complex are also clearly seen in the high values of $\log(K_{\text{CuL}}/K_{\text{CuL}_2})$ (Table 1). It is worthwhile mentioning that the bis(ligand) complex formation is somewhat less hindered with H_4L^2 having a terminal phenyl ring. In this case the likely stacking interactions between the aromatic rings may partly compensate the unfavourable effect of the electrostatic repulsions. The formation of the $[\text{CuL}_2]^{6-}$ complexes and the considerable distortions around the metal ion in these species are confirmed by the solid-state structures.^{10,11}

The presence of two phosphonate groups in the ligand molecules and their dinegative charge strongly favours complex protonation. The $[\text{Cu}(\text{H}_2\text{L})]$ complex is very likely to have monodentate phosphonate co-ordination, or a six-membered chelated arrangement of the two phosphonic functions, each being monoprotonated. This is seen in the crystal structures of copper(II) complexes of these phosphonic ligands having different substituents on the quaternary carbon atom: each phosphonate group binds *via* one oxygen atom forming a six-membered chelate ring.^{10,11} The very slight effect seen in the absorption and EPR spectra of these complexes in solution at $\text{pH} < 4$ (Table 2), however, may indicate the monodentate binding mode. Not surprisingly, Cu^{2+} binds to both ligands, H_4L^1 and H_4L^2 , with a similar strength indicated clearly by the similar value of the basicity-adjusted formation constant referring to the reaction $\text{Cu}^{2+} + \text{H}_3\text{L}^- \rightleftharpoons [\text{Cu}(\text{H}_2\text{L})] + \text{H}^+$ (Table 1). The stepwise deprotonation constants of $[\text{Cu}(\text{H}_2\text{L})]$ and $[\text{Cu}(\text{HL})]^-$ species can easily be assigned to the bound PO_3H^- groups or the non-bound PO_3H_2 group, that of $[\text{CuL}]^{2-}$ to the ionisation of a bound water molecule. The $\text{p}K$ of this latter reaction is rather high (≈ 10) due to the high negative charge density of the co-ordinated phosphonate

Table 2 Spectroscopic parameters for copper(II) complexes formed by 1-hydroxyalkane-1,1-diphosphonic acids and 1,8-dihydroxyoctane-1,1,8,8-tetrilytetraphosphonic acid

Acid	Species	EPR		UV/VIS, λ/nm (ϵ/dm^3 $\text{mol}^{-1} \text{cm}^{-1}$)
		A_{\parallel}	g	
H_4L^1	$[\text{Cu}(\text{H}_2\text{L})]$	124	$g_{\parallel} = 2.41$	792(27)
	$[\text{Cu}(\text{HL})]^-$	121	$g_{\parallel} = 2.41$	785(31)
	$[\text{CuL}]^{2-}$	—	$g_{\parallel} = 2.06$ $g_{\perp} = 2.18$	730(38)
H_4L^2	$[\text{CuH}_{-1}\text{L}]^{3-}$	123	$g_{\parallel} = 2.38$	705(52)
	$[\text{Cu}(\text{H}_2\text{L})]$	124	$g_{\parallel} = 2.41$	793(25)
	$[\text{Cu}(\text{HL})]^-$	—	$g_{\parallel} = 2.41$ $g_2 = 2.15$ $g_3 = 2.08$	781(29)
	$[\text{CuL}]^{2-}$	—	$g_{\parallel} = 2.06$ $g_{\perp} = 2.18$	731(34)
H_4L^3	$[\text{CuL}_2]^{6-}$ and $[\text{CuH}_{-1}\text{L}]^{3-}$	128	$g_{\parallel} = 2.39$	707(40)
	$[\text{Cu}(\text{H}_3\text{L})]^+$	123	$g_{\parallel} = 2.43$	797(24)
	$[\text{Cu}(\text{HL})]^-$	—	$g_{\parallel} = 2.05$ $g_{\perp} = 2.18$	720(124) ^a
H_8L^4	$[\text{CuL}]^{2-}$	122	$g_{\parallel} = 2.38$	729(43)
	$[\text{CuH}_{-1}\text{L}]^{3-}$	130	$g_{\parallel} = 2.38$	711(46)
	$[\text{Cu}(\text{H}_4\text{L})]^{2-}$	121	$g_{\parallel} = 2.41$	798(31)
	$[\text{Cu}(\text{H}_3\text{L})]^{3-}$	116	$g_{\parallel} = 2.42$	—
	$[\text{CuL}]^{6-}$	129	$g_{\parallel} = 2.38$	—
	$[\text{Cu}_3\text{H}_{-1}\text{L}]^{3-b}$	—	—	805(43)
	$[\text{Cu}_4\text{L}_2]^{8-b}$ $[\text{Cu}_4\text{H}_{-2}\text{L}_2]^{10-b}$	—	—	778(41) 714(44)

^a Some precipitation is observed. ^b EPR silent.

functions, which will extend towards the Cu^{2+} -bound water molecule making it less acidic.

At $\text{pH} > 10$ the EPR spectrum becomes classical ($g_{\parallel} > g_{\perp}$) suggesting tetragonal symmetry around Cu^{2+} . This fits very well with the potentiometric model indicating hydrolysis of the species $[\text{CuL}]^{2-}$ and $[\text{CuL}_2]^{6-}$ to $[\text{CuH}_{-1}\text{L}]^{3-}$. In the latter complex the chelation of two phosphonic groups is accompanied by co-ordination of the small, though effective hydroxyl group which leads to simple tetragonal geometry around the metal ion.

Similar ligands in which the phosphonic groups are replaced by carboxylic or amino functions, such as malic acid, isoserine (3-amino-2-hydroxypropanoic acid) or 1,3-diaminopropan-2-ol, readily form dimeric $[\text{Cu}_2\text{H}_{-2}\text{L}_2]^{2-}$ complexes with alcoholate groups bridging the two metal ions.¹⁶ In the case of the acids discussed here having phosphonic functions of unfavourable shape (tetrahedral phosphonate compared to planar carboxylate) and high negative charge, the formation of dimeric species involving the hydroxyl group on the adjacent carbon seems to be rather hindered. However, the assumption of a dinuclear species, $[\text{Cu}_2\text{H}_{-1}\text{L}]^-$, which can be a monoalcoholate-bridged complex with the formation of two joint five-membered chelate systems, improved the fitting of experimental potentiometric data by about 20%. Thus, this species was also included in speciation (Fig. 1, Table 1). The formation of oligonuclear complexes with diphosphonic ligands is a common feature in the solid state. X-Ray studies of copper(II) complexes of such ligands revealed various dinuclear or chain-like oligonuclear structures, although the bridging units were the phosphonic functions rather than the alkoxy groups.^{10,11} However, such pronounced di/oligonuclear complex formation could not be detected by EPR spectroscopy in solution.

4-Amino-1-hydroxybutane-1,1-diylidiphosphonic acid H_4L^3

Compared to H_4L^1 and H_4L^2 , this compound has one dissociable proton more on the amino group (H_5L^+). The most likely protonation constant of this group is the highest one, log

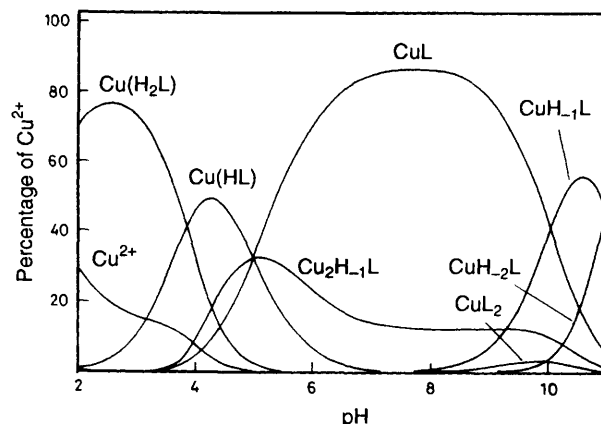


Fig. 1 Species distribution curves for the Cu^{2+} - H_4L^1 system; metal concentration 1 mmol dm^{-3} , phosphonic acid concentration 2 mmol dm^{-3}

$K = 12.04$ (Table 1), although some overlap with the first proton uptake by the phosphonate functions cannot be excluded.

Both the potentiometric and spectroscopic data indicate that there is no major difference in the Cu^{2+} -binding ability of compounds H_4L^1 - H_4L^3 (Tables 1 and 2). Thus, the distant amino site is of minor importance for metal ion co-ordination over the whole pH range studied. Assuming the ligand form HL^{3-} (with protonated terminal amino group) as the complexing agent, the respective equilibrium constants (log β) derived in this way $[\text{CuH}_2(\text{HL})]$, 20.66; $[\text{CuH}(\text{HL})]$, 16.88; $[\text{Cu}(\text{HL})]$, 12.2; $[\text{CuH}_{-1}(\text{HL})]$, 3.66; $[\text{Cu}(\text{HL})_2]$, 16.41; $[\text{Cu}_2\text{H}_{-1}(\text{HL})]$, 11.58] agree fairly well with those of H_4L^1 and H_4L^2 (see Table 1). Similarly, the basicity-adjusted stability constants for the equimolar species agree very well with each other (Table 1).

The first two deprotonation constants of the $[\text{Cu}(\text{H}_3\text{L})]^+$ complex of H_4L^3 can be assigned to deprotonation of the phosphonic groups promoted by the metal-ion binding, while

Table 3 Stability constants of the proton ($\log K$) and copper(II) complexes ($\log \beta$) of 1,8-dihydroxyoctane-1,1,8,8-tetryltetraphosphonic acid at 25 °C and $I = 0.2 \text{ mol dm}^{-3}$ (KCl)

	$\log K(\text{HL})$	$\log K(\text{H}_2\text{L})$	$\log K(\text{H}_3\text{L})$	$\log K(\text{H}_4\text{L})$	$\log K(\text{H}_5\text{L})$	$\log K(\text{H}_6\text{L})$	$\log K(\text{H}_7\text{L})$	$\log K(\text{H}_8\text{L})$
	12.14(3)	10.98(3)	7.28(3)	6.42(3)	3.06(3)	2.21(4)	≈ 1	< 1
$[\text{Cu}(\text{H}_5\text{L})]^-$	43.70(6)	43.71(6)	43.71(6)	43.70(6)				
$[\text{Cu}(\text{H}_4\text{L})]^{2-}$	41.29(6)	41.30(2)	41.29(1)	41.29(1)				
$[\text{Cu}(\text{H}_3\text{L})]^{3-}$	37.19(9)	36.56(22)	36.68(18)	37.12(3)				
$[\text{Cu}(\text{H}_2\text{L})]^{4-}$	31.67(10)	—	—	—				
$[\text{Cu}(\text{HL})]^{5-}$	24.62(12)	—	—	—				
$[\text{CuL}]^{6-}$	14.74(13)	15.04(4)	15.02(4)	15.03(5)				
$[\text{CuH}_{-1}\text{L}]^{7-}$	3.42(6)	3.37(7)	3.16(11)	3.00(12)				
$[\text{CuH}_2\text{L}_2]^{12-}$	40.65(16)	—	—	—				
$[\text{CuHL}_2]^{13-}$	29.99(14)	—	—	—				
$[\text{Cu}_2(\text{H}_2\text{L})]^{2-}$	—	37.43(11)	37.40(12)	—				
$[\text{Cu}_2(\text{HL})]^{3-}$	—	32.83(7)	32.70(9)	32.5(2)				
$[\text{Cu}_2\text{L}]^{4-}$	—	26.51(7)	26.41(8)	—				
$[\text{Cu}_2\text{H}_{-1}\text{L}]^{5-}$	—	16.53(11)	16.58(9)	—				
$[\text{Cu}_2\text{H}_{-2}\text{L}]^{6-}$	—	5.65(18)	—	—				
$[\text{Cu}_3\text{H}_{-1}\text{L}]^{3-}$	—	—	27.66(15)	28.3(1)				
$[\text{Cu}_3\text{HL}_2]^{9-}$	—	—	—	42.0(5)				
$[\text{Cu}_3\text{H}_{-2}\text{L}_2]^{12-}$	—	—	23.59(13)	24.1(3)				
$[\text{Cu}_4\text{L}_2]^{8-}$	—	—	—	56.3(2)				
$[\text{Cu}_4\text{H}_{-2}\text{L}_2]^{10-}$	—	—	—	37.3(2)				
$[\text{Cu}_4\text{H}_{-4}\text{L}_2]^{12-}$	—	—	14.70(23)	15.3(4)				
Fitting*	0.004 90	0.004 62	0.004 62	0.004 60				
No. points	397	397	397	397				

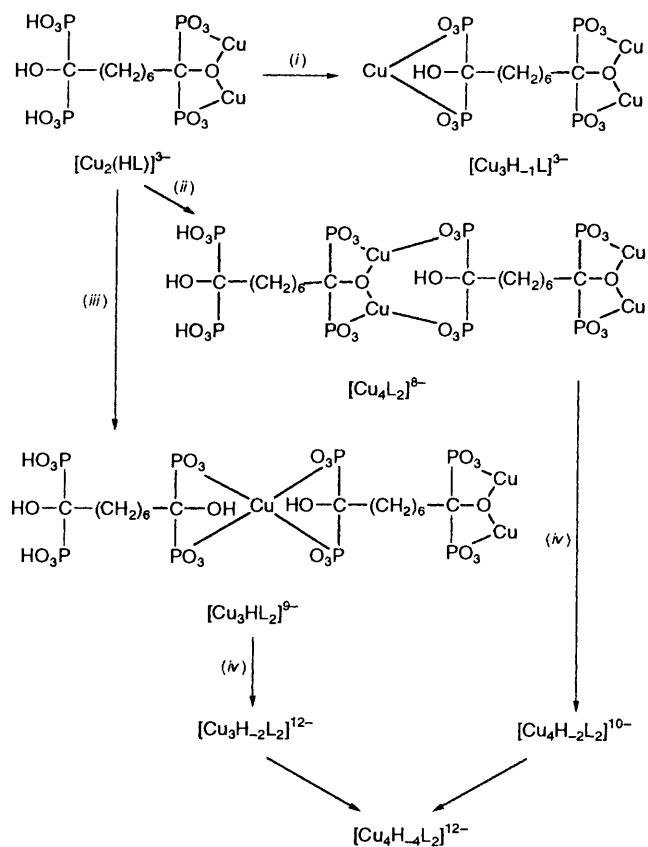
* The average difference in the calculated and the experimental titration curves expressed in cm^3 of the titrant.

the last two $\log K$ values correspond to overlapping deprotonation processes of the side-chain NH_3^+ group and the co-ordinated water molecule.

1,8-Dihydroxyoctane-1,1,8,8-tetryltetraphosphonic acid, H_8L^4

In this molecule two $\text{C}(\text{OH})(\text{PO}_3\text{H}_2)_2$ moieties are linked together by an alkane chain and the two diposphonic functions are well separated by six methylene groups. However, the stepwise protonation constants (H_8L , Table 3), unambiguously indicate significant, 'through-space' interactions (*via* water molecules) between the two diposphonic terminals. Assuming that both protonation sites are completely separated and purely statistical effects govern the protonation process, the difference between the corresponding pairs of protonation constants for identical functional groups ($\log K_{\text{K}(\text{HL})}$, $\log K_{\text{K}(\text{H}_2\text{L})}$, etc.) should be 0.6 log unit. Instead it is between 0.85 and 1.16 log units.

Binding of Cu^{2+} to this 'tetrafunctional' ligand starts at one end of the molecule, as in the cases discussed above for the 'difunctional' ligands having two phosphonic groups bound to one carbon atom. The basicity-adjusted stability constant, $\log K = 1.61$ for the reaction $\text{Cu}^{2+} + \text{H}_6\text{L}^{2-} \rightleftharpoons [\text{Cu}(\text{H}_5\text{L})]^- + \text{H}^+$ agrees well with those of the corresponding 1:1 complexes of the diposphonic derivatives (see Table 1), which confirms this assumption. The EPR and absorption spectra also support the formation of complexes similar to those discussed above for the other acids (Table 2). At $\text{pH} > 4$ the EPR spectra broaden and then vanish (clearly seen for 1:1 molar ratio solutions). This strongly suggests the formation of oligomeric



Scheme 1 (i) Cu^{2+} ; (ii) $[\text{Cu}_2(\text{HL})]^{3-}$; (iii) $[\text{Cu}(\text{H}_2\text{L})]^{4-}$; (iv) cyclisation

species, *i.e.* binding of Cu^{2+} ions at both diposphonic terminals of H_8L^4 . Formation of oligonuclear complexes is also supported by potentiometric measurements. Accurate measurements could not be performed for solutions having an excess of Cu^{2+} because of precipitation in the range $\text{pH} 3\text{--}6$. Even at a 1:4 metal ion-to-ligand ratio slight precipitation was observed. The precipitate is most likely an oligonuclear $\text{Cu}^{2+}\text{--H}_8\text{L}$ complex(es); it cannot be $\text{Cu}(\text{OH})_2$ as no precipitation occurred with any of the hydroxydiposphonic acids, which indicates their ability to bind Cu^{2+} strongly enough to prevent precipitation of the hydroxide. In order to obtain reliable pH-metric data over as wide a pH range as possible, back titrations with 0.2 mol dm^{-3} HCl starting from $\text{pH} 11$ were also carried out. In this way the precipitation down to $\text{pH} 3$ could be avoided even in equimolar solutions, probably due to formation of oversaturated solutions.

On the basis of the above-mentioned spectral findings, indicating formation of oligonuclear species, pH-metric titration curves were evaluated by assuming various speciation models. Some of the results of model selection are listed in Table 3. The data show some slight improvement of the fit between the experimental and the calculated titration curves, when various chain-like and cyclic oligomeric species are also included in the speciation model (*cf.* data in column 1 with those in the other columns). The proposed binding modes of the complexes are given in Scheme 1. Potentiometric and spectroscopic data suggest a higher extent of oligomerisation with this tetraphosphonic acid having tridentate chelating functions at both ends of the molecule, as compared with that of the diposphonic acid derivatives ($\text{H}_4\text{L}^1\text{--H}_4\text{L}^3$). Each oligonuclear species cannot be identified exactly on the basis of our measurements; we can only suggest that the species are formed *via* alcoholate and phosphonate bridges (see Scheme 1 and Fig. 2).

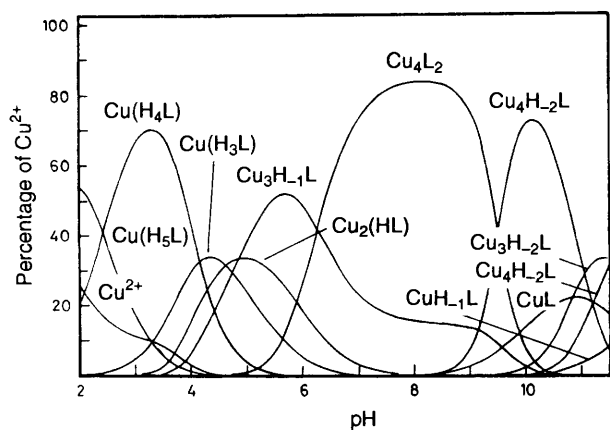


Fig. 2 Species distribution curves for Cu^{2+} -D system for stability constants collected in the fourth column of Table 3; metal concentration 1 mmol dm^{-3} , ligand concentration 2 mmol dm^{-3}

Acknowledgements

This work was supported by the Hungarian Academy of Sciences (Project No. OTKA T7458/93) and University of Wrocław (2015/W/ICH/95/2).

References

1 T. Kiss, M. Jezowska-Bojczuk, H. Kozłowski, P. Kafarski and K. Antczak, *J. Chem. Soc., Dalton Trans.*, 1991, 2275.

2 M. Jezowska-Bojczuk, T. Kiss, H. Kozłowski, P. Decock and J. Barycki, *J. Chem. Soc., Dalton Trans.*, 1994, 811.
 3 A. Tromelin, D. El Manouni and R. Burgada, *Phosphorus Sulfur Relat. Elem.*, 1986, **27**, 301.
 4 B. L. Barnett and L. C. Strickland, *Acta Crystallogr., Sect. B*, 1979, **35**, 1212.
 5 V. A. Uchtman, *J. Phys. Chem.*, 1972, **76**, 1304.
 6 J. P. Silvestre, N. El Messbahi, R. Rochdaoui, Nguyen Quy Dao, M. R. Lee and A. Neuman, *Acta Crystallogr., Sect. C*, 1990, **46**, 986.
 7 R. Rochdaoui, J. P. Silvestre, Nguyen Quy Dao, M. R. Lee and A. Neuman, *Acta Crystallogr., Sect. C*, 1990, **46**, 2083.
 8 P. Charpin, M. Lance, M. Nierlich, D. Vigner, M. R. Lee, J. P. Silvestre and Nguyen Quy Dao, *Acta Crystallogr., Sect. C*, 1988, **44**, 990.
 9 J. P. Silvestre, I. Bkouche-Waksman, G. Heger and Nguyen Quy Dao, *New J. Chem.*, 1990, **14**, 29.
 10 A. Neuman, A. Safsaf, H. Gillier, Y. Leroux and D. El Manouni, *Phosphorus Sulfur Silicon Relat. Elem.*, 1992, **70**, 273.
 11 Y. Leroux, A. Neuman, H. Gillier, D. El Manouni, Z. Abkhar and Th. Prangé, *Supramol. Chem.*, 1995, **5**, 267.
 12 Y. Leroux, D. El Manouni, A. Safsaf, A. Neuman and H. Gillier, *Phosphorus Sulfur Silicon Relat. Elem.*, 1991, **63**, 181.
 13 M. Kanaan and R. Burgada, *Phosphorus Sulfur Relat. Elem.*, 1988, **37**, 217.
 14 H. Irving, M. G. Mills and L. D. Pettit, *Anal. Chim. Acta*, 1967, **38**, 475.
 15 L. Zékány and I. Nagypál, in *Computational Methods for the Determination of Stability Constants*, ed., D. Leggett, Plenum, New York, 1985.
 16 T. Kiss, Cs. Simon and Zs. Vachter, *J. Coord. Chem.*, 1987, **16**, 1987.

Received 4th September 1995; Paper 5/05832E