Complexes of Aminophosphonates. Part 8.[1] Copper(II) Complexes of *N*-(Phosphonomethyl)amino Acids and Related Compounds†

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pH-Metric and spectroscopic (absorption and EPR) studies were made of the proton and copper(II) complexes of a series of ambidentate *N*-(phosphonomethyl)amino acids which contain both iminocarboxylate and iminophosphonate moieties. The stoichiometries and stability constants of the complexes formed were determined at 25 °C and at an ionic strength of 0.20 mol dm^{-3} (KCl). Stability data and spectroscopic measurements revealed that the first ligand molecule co-ordinates very strongly, forming a tridentate equimolar species, while the second one binds to the metal ion much less effectively in an axial-equatorial mode. The results were compared with those on the carboxylate analogues iminodiacetic acid and nitrilotriacetic acid.

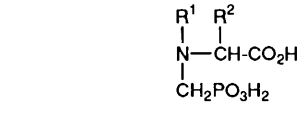
N-(Phosphonomethyl)glycine (Npm-Gly) is an active ingredient of Roundup®, a well-known herbicide,[2] which combines high activity with very low toxicity to animals, and short residence time in the soil.[3] It is therefore widely used against undesired plant growth in agriculture, forestry and fish ponds.[4] Its analogue *N*,*N*′-di(phosphonomethyl)glycine (Ndpm-Gly), an active component of Polaris®, is a plant growth regulator and also a herbicide used in high amounts.[5] On the other hand, aminophosphonic acids are very effective ligands for metal ions[1,6,7] and potent inhibitors of metalloenzymes, blocking the active metal centres.[8] There is growing interest in establishing an understanding of the influence of metal ions in soil biology and their impact on pesticide activity.[9,10]

The metal-binding ability of Npm-Gly has been studied towards various divalent (*e.g.* Cu^{2+}, Zn^{2+}, Ni^{2+}, Mn^{2+}, Ca^{2+} and Mg^{2+})[11-13] and trivalent (*e.g.* Fe^{3+}, Al^{3+} and La^{3+})[12] metal ions. The equimolar complex MA, most likely involving tridentate co-ordination of the ligand, was found to be the predominant species for all metal ions studied. Dhansay and Linder[14] recently reported similar results on the complexation of transition-metal ions by various phosphonic acid derivatives of iminodiacetic acid (H_2ida) and nitrilotriacetic acid (H_3nta).

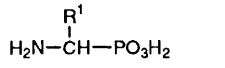
We report here the synthesis of some potentially tridentate aminophosphonic acids and a series of *N*-(phosphonomethyl)-amino acids and a study of their complex formation with copper(II) ion.

Experimental

N-Phosphonomethyl-L-threonine (Npm-Thr), -L-serine (Npm-Ser), -phenylglycine (Npm-Phg), -L-leucine (Npm-Leu) and glycine (Npm-Gly) were synthesised as in ref. 15. The reaction of the sodium salt of the appropriate amino acid, formaldehyde and diethyl phosphite was followed by hydrolysis with mineral acid. *N*-Phosphonomethyl-L-proline (Npm-Pro) and *N*,*N*′-di(phosphonomethyl)glycine (Ndpm-Gly) were synthesised from amino acid, crystalline phosphorus acid,



R^1 = H	R^2 = H	Npm-Gly
	$(CH_3)_2CHCH_2$	Npm-Leu
	Ph	Npm-Phg
	$HOCH_2$	Npm-Ser
	$CH_3(OH)CH$	Npm-Thr
R^1R^2 = $(CH_2)_3$		Npm-Pro
R^1 = $H_2PO_3CH_2$	R^2 = H	Ndpm-Gly



R^1 = $H_2N(CH_2)_4$	H_2L^1
$CH_3(OH)CH$	H_2L^2

formaldehyde solution and concentrated HCl as described earlier.[16,17]

The phosphono analogue of threonine, 1-amino-2-hydroxypropylphosphonic acid, was prepared as follows: diethyl 2-oxopropylphosphate was treated with benzenediazonium chloride at pH *ca.* 7, below 15 °C. The reaction mixture was then reduced with H_2–Raney nickel at 10^7 Pa. The resulting mixture was hydrolysed with concentrated aqueous HCl. Purification on Dowex resin gave 71% of final product, m.p. (uncorrected) 223–225 °C (Found: C, 23.10; H, 6.25; N, 8.80; P, 20.25. Calc. for $C_3H_{10}NO_4P$: C, 23.25; H, 6.50; N, 9.05; P, 20.00%). ^{1}H NMR (D_2O, 80 MHz): δ 1.2 (d, J = 6.4, CH_3C^2), 3.31 (dd, J_{HH} = 3.8, J_{HP} = 15 Hz) and 4.09–4.37 (m).

The phosphonate analogue of lysine, 1,5-diaminopentylphosphonic acid, was obtained by the following procedure: pimelic acid was converted into its acid chloride, which was then brominated and esterified with ethanol. The resulting product was treated with triethyl phosphite, then with hydrazine

† *Non-SI unit employed*: G = 10^{-4} T.

hydrate and nitrous acid, giving the azide, which was subjected to Curtius rearrangement. The crude product was purified on Dowex resin and then recrystallized. Yield: 21%, m.p. (uncorrected) 275–277 °C (Found: C, 32.80; H, 8.10; N, 15.20; P, 17.25. Calc. for $C_5H_{15}N_2O_3P$: C, 33.00; H, 8.30; N, 15.40; P, 17.05%). ^{1}H NMR (D_2O, 80 MHz): δ 1.27–2.02 (m, 6 H) and 2.82–3.37 (m, 4 H).

The purities and the exact concentrations of the stock solutions of the ligands were determined pH-metrically by the Gran method.[18] The concentration of the metal chloride stock solution was measured gravimetrically *via* precipitation of the quinolin-8-olate.

The stability constants of the proton and the copper(II) complexes of the ligands were determined by pH-metric titration of 5 cm^3 samples. The concentration of the ligand in each sample was 0.004 mol dm^{-3} and the metal ion : ligand 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 pH range 3–11, with a carbonate-free KOH solution of known concentration (*ca.* 0.2 mol dm^{-3}).

The pH was measured with a Tacussel ISIS 2000 pH-meter, using a Radiometer GK2321C combined glass electrode. The electrode system was calibrated in hydrogen ion concentrations by the method of Irving *et al.*[19] In all cases, the temperature was 25 ± 0.1 °C.

To establish the bonding modes in the complexes formed spectroscopic measurements were performed. Absorption spectra were recorded on Beckman UV5240 and Cary 5 spectrophotometers. EPR spectral measurements were performed on a Radiopan SE/X spectrometer at the X-band (9.3 GHz) at 120 K in ethylene glycol–water (1 : 2 v/v) solutions.

The concentration stability constants $\beta_{pqr} = [M_pA_qH_r]/[M]^p[A]^q[H]^r$ were calculated with the aid of the PSEQUAD computer program.[20] Depending on the type of ligands the fully deprotonated forms have different charges. Thus, A^{2-} refers to aminophosphonates, A^{3-} to *N*-(phosphonomethyl)amino acid derivatives and A^{5-} to *N*,*N*′-di(phosphonomethyl)glycinate.

Results and Discussion

Aminophosphonic Acids.—Phosphonic acid analogues of threonine and lysine contain two or three dissociable protons within the measurable pH range. One of the two phosphonic protons dissociates at around pH ≈1 and does not take part in metal co-ordination equilibria. The fully deprotonated phosphonate group has a charge of 2−, and this elevates the p*K* of the ammonium group of simple aminophosphonic acids by ≈0.5 log unit as compared with their amino-carboxylate analogues.[7] A similar effect is observed for $[CH_3(OH)CH]CH(NH_2)PO(OH)_2$ and for both amino groups of $[H_2N(CH_2)_4]CH(NH_2)PO(OH)_2$ (see the last columns of Table 1). The alcoholic OH group in $[CH_3(OH)CH]CH(NH_2)PO(OH)_2$, similarly as in threonine, is very weakly acidic (pK > 14) and does not deprotonate in the pH range studied (2 < pH < 11).

Both $[CH_3(OH)CH]CH(NH_2)PO(OH)_2$ and $[H_2N(CH_2)_4]CH(NH_2)PO(OH)_2$ co-ordinate to Cu^{II} in a similar way to the simple bidentate alanine analogue $CH_3CH(NH_2)PO(OH)_2$. The stability constants of the complexes formed, together with derived equilibrium constants characteristic of some stepwise processes of complex formation, are listed in Table 1. For the sake of comparison, data on the copper(II) complexes of $CH_3CH(NH_2)PO(OH)_2$ and the corresponding amino-acid analogues are also included in this Table. As shown in the speciation diagram (see Fig. 1), there is a minor

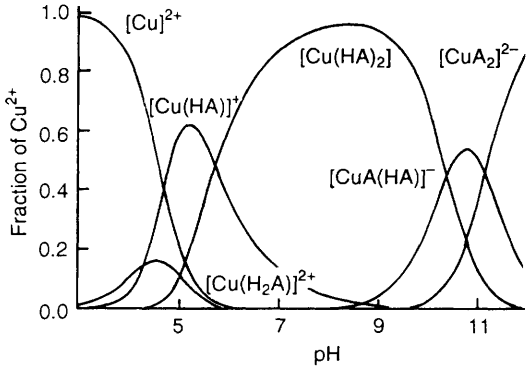


Fig. 1 Species distributions diagram for the Cu^{II}–$[H_2N(CH_2)_4]CH(NH_2)PO(OH)_2$ system; c_{Cu} = 0.002 mol dm^{-3}, c_L = 0.004 mol dm^{-3}

Table 1 Proton dissociation constants (pK) and copper(II) complex formation constants (log β) of amino acids and their corresponding phosphonic acid derivatives[a] at 25.0 ± 0.1 °C and I = 0.20 mol dm^{-3} (KCl)

	Lys[b]	H_2L^1	Thr	H_2L^2	Ala[c]	H_2L^3	ΔLys	ΔThr	ΔAla
pK(ε-NH_3^+)	10.66	11.08(3)	—	—	—	—	0.42	—	—
pK(α-NH_3^+)	9.20	9.70(2)	8.91(2)	9.28(2)	9.68	10.11	0.50	0.37	0.45
pK(PO_3H^-)	—	5.40(1)	—	5.40(1)	—	5.55	—	—	—
pK(CO_2H/PO_3H_2)	2.15	1.0	2.15	1.0	2.35	1.0	—	—	—
$Cu(H_2A)$	—	23.71(3)	—	—	—	—			
Cu(HA)	18.33	19.44(2)	—	12.13(2)	—	12.29			
$Cu(HA)_2$	35.40	37.64(2)	—	—	—	—			
CuA(HA)	25.32	27.16(4)	—	—	—	—			
CuA	—	—	7.91	8.17(1)	8.04	8.29			
CuA_2	14.81	16.12(2)	14.52	14.97(2)	14.73	14.94			
CuA_2H_{-1}	—	—	4.68	4.23(4)	—	—			
CuA_2H_{-2}	—	—	−6.05	−7.03(3)	—	—			
$pK_{Cu(H_2A)}$	4.27	—	—	—	—	—			
$pK_{Cu(HA)}$	—	—	—	3.96	—	4.00			
$pK_{Cu(HA)_2}$	10.08	10.48	—	—	—	—	0.40		
$pK_{CuA(HA)}$	10.51	11.04	—	—	—	—	0.53		
pK_{CuA_2}	—	—	9.84	10.74	—	—	—	0.90	
$pK_{CuAH_{-1}}$	—	—	10.73	11.26	—	—	—	0.53	
$\log(K_{Cu(HA)}/K_{Cu(HA)_2})$	1.26	1.24	—	—	—	—	—	—	
$\log(K_{CuA}/K_{CuA_2})$	—	—	1.30	1.37	1.35	1.64	—	—	
$\log K_{Cu(HA)} - \Sigma pK$	−3.68	−6.74	—	—	—	—	−3.06	—	
$\log K_{Cu(HA)_2} - \Sigma pK$	−4.94	−7.98	—	—	—	—	−3.33	—	
$\log K_{CuA} - \Sigma pK$	—	—	−3.15	−6.41	−3.99	−7.37	—	−3.26	−3.42
$\log K_{CuA_2} - \Sigma pK$	—	—	−4.45	−7.78	−5.34	−9.01	—	−3.33	−3.67

[a] H_2L^1 = $[H_2N(CH_2)_4]CH(NH_2)PO(OH)_2$, H_2L^2 = $[CH_3(OH)CH]CH(NH_2)PO(OH)_2$, H_2L^3 = $CH_3CH(NH_2)PO(OH)_2$. [b] Ref. 21. [c] Ref. 6.

monodentate phosphonate co-ordinated species, $[Cu(HA)]^+$ for $[CH_3(OH)CH]CH(NH_2)PO(OH)_2$ and $[Cu(H_2A)]^{2+}$ for $[H_2N(CH_2)_4]CH(NH_2)PO(OH)_2$, at around pH 4, but this cannot be detected by spectroscopy because of its low concentration. Two chelates, with one or two ligand molecules co-ordinated *via* the phosphonate group and the α-amino group, are the predominant species. This is clearly confirmed by spectroscopic methods. The spectral parameters of these chelates (Table 2) are characteristic of 1N- and 2N-species. The stoichiometries of the complexes are [CuA] or $[CuA_2]^{2-}$ for $[CH_3(OH)CH]CH(NH_2)PO(OH)_2$, and $[Cu(HA)]^+$ and $[Cu(HA)_2]$ for $[H_2N(CH_2)_4]CH(NH_2)PO(OH)_2$, as the terminal amino group of $[H_2N(CH_2)_4]CH(NH_2)PO(OH)_2$ is protonated in the pH range in which these complexes are formed.

As shown by the basicity-adjusted stability constants log $K_n - \Sigma pK$, listed in the final rows of Table 1, PO_3^{2-}/CO_2^- substitution has a similar effect on the relative stability of the 1:1 and 1:2 complexes of all three ligands, including $CH_3CH(NH_2)PO(OH)_2$. The stability increase due to the increase in basicity of the co-ordinating donor groups (*cf.* the log β values of the complexes of the aminophosphonates and their corresponding aminocarboxylate analogues) is over-compensated by steric and electrostatic effects.[8] This results in a decrease in the basicity-adjusted stability constants amounting to about three orders of magnitude.

At pH > 10 the complex $[Cu(HA)_2]$ of $[H_2N(CH_2)_4]CH(NH_2)PO(OH)_2$ undergoes stepwise deprotonation, but this is not accompanied by significant changes in the spectral data (see Table 2). This indicates that deprotonation of the lateral ammonium groups does not result in any changes in the co-ordination sphere of the metal ion. Similarly, the increase in basicity of the non-co-ordinated lateral NH_2 group due to PO_3^{2-}/CO_2^- substitution is about the same as for the free ligand (see Table 1: $\Delta pK = 0.4$–0.5 log unit), indicating no involvement of this group in the co-ordination.

For $[CH_3(OH)CH]CH(NH_2)PO(OH)_2$, two deprotonation processes of $[CuA_2]^{2-}$ could also be detected by potentiometry. Formation of the deprotonated species $[CuA_2H_{-1}]^{3-}$ and $[CuA_2H_{-2}]^{4-}$ could be interpreted as proton dissociation from the alcoholic OH group of the ligand or from one of the axially bound water molecules. The very slight changes in the spectral parameters on formation of these deprotonated species suggests minor changes in the co-ordination pattern. This is in accordance with the assumption made for the copper(II) complexes of serine[22] that at least one of the alcoholic OH groups is weakly co-ordinated to the Cu^{II} *via* an axially bound water molecule in the complex $[CuA_2]^{2-}$. Thus, loss of a proton from this part of the complex (*i.e.* neither water ionization nor alcoholic-OH deprotonation) will hardly affect any spectroscopic properties due to the copper(II)–ligand interaction. The increase in the respective pK value by 0.9 log unit (see Δ Thr for pK_{CuA_2} in Table 1) is in agreement with the stronger electron-releasing effect of the dinegative PO_3^{2-} group. This effect can be felt on the alcoholic OH, again indicating some involvement of the latter group in the deprotonation process. However, the PO_3^{2-}/CO_2^- substitution has practically no effect on the second proton release, suggesting that this process can rather be attributed to ionization of the axially bound water molecule which is not hydrogen bonded to the alcoholic-OH group.

N-(Phosphonomethyl)amino Acids.—This group of ligands consists of amino acids substituted on the amino nitrogen by a phosphonomethyl group. All these ligands, *i.e.* Npm-Gly, Npm-Leu, Npm-Phg, Npm-Pro, Npm-Ser and Npm-Thr, have similar co-ordination patterns. The complexes [Cu(HA)], $[CuA]^-$, $[Cu(HA)_2]^{2-}$ and $[CuA(HA)]^{3-}$ are species with one nitrogen atom (1N) co-ordinated to Cu^{II}, while in the species $[CuA_2]^{4-}$ as well as in the other two deprotonated complexes $[CuA_2H_{-1}]^{5-}$ and $[CuA_2H_{-2}]^{6-}$ of Npm-Ser and Npm-Thr two nitrogens (2N) are bound in the equatorial plane of the Cu^{II} ion. This assumption can be made on the basis of the spectroscopic results given in Table 3 and is supported by the stability data obtained from pH-metric titrations and listed in Table 4. The proposed bonding modes of the complexes formed are presented in Scheme 1.

Table 2 Spectral parameters (ESR, visible) for copper(II) complexes of lysine (Lys), threonine (Thr) and their phosphonic acid derivatives

	$A_{\parallel}$/G	$g_{\parallel}$	λ_{max}/nm (ε/dm³ mol⁻¹ cm⁻¹)
ML type complexes			
Lys	162	2.30	725 (29)
H_2L^1	144	2.33	705 (39)
Thr	161	2.30	730 (30)
H_2L^2	153	2.32	713 (43)
ML_2 type complexes (neutral pH)			
Lys	176	2.26	625 (56)
H_2L^1	164	2.27	647 (52)
Thr	177	2.27	620 (66)
H_2L^2	164	2.27	640 (65)
ML_2 type complexes (high pH)			
Lys	176	2.26	615 (65)
H_2L^1	168	2.27	635 (57)
Thr	190	2.24	608 (40)
H_2L^2	168	2.27	625 (68)

Table 3 Spectral parameters (ESR, visible) for copper(II) complexes of *N*-(phosphonomethyl)amino acids

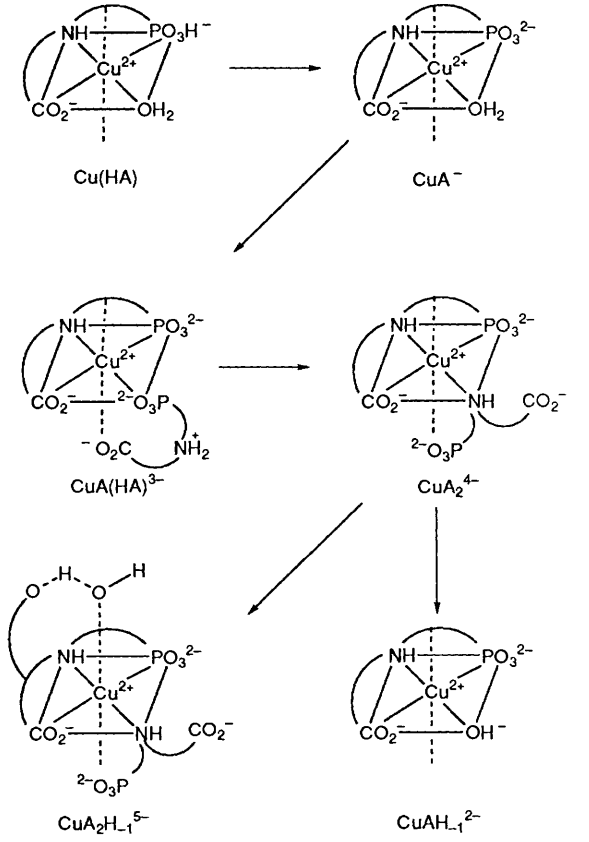
	$A_{\parallel}$/G	$g_{\parallel}$	λ_{max}/nm (ε/dm³ mol⁻¹ cm⁻¹)
1N type complexes			
Npm-Gly	149	2.32	725 (58)
Npm-Leu	156	2.31	717 (55)
Npm-Phg	155	2.31	715 (72)
Npm-Pro	156	2.31	712 (57)
Npm-Ser	155	2.31	698 (55)
Npm-Thr	157	2.31	700 (56)
2N type complexes			
Npm-Gly	170	2.27	708 (79)
Npm-Leu	165	2.27	709 (83)
Npm-Phg	160	2.28	674 (98)
Npm-Pro	176	2.27	689 (85)
Npm-Ser	162	2.28	695 (82)
Npm-Thr	164	2.28	695 (79)

The first complex formed at around pH 3 is [Cu(HA)]. Its high stability constant compared with those of simple aminophosphonate or aminocarboxylate complexes (*cf.* the data given in Tables 1 and 3) suggests tridentate co-ordination involving three donor groups: CO_2^-, PO_3H^- and imino-NH. Assuming only bidentate iminocarboxylate, NH, CO_2^--type co-ordination, the derived equilibrium constants for the reaction $Cu^{2+} + [AH_{PO_3H^-}]^{2-} \rightleftharpoons [Cu(HA)]$ are about two orders of magnitude higher than that for *N*-methylglycine (log $\beta_{CuA} = 7.94$).[23] The d–d transition energy around 720 nm and the EPR parameters correspond well to 1N co-ordination.[24] Above pH 4 a proton dissociates from the phosphonic group in [Cu(HA)], yielding a stable complex $[CuA]^-$, which predominates up to pH ≈ 9 even with a ligand excess (see Fig. 2, which illustrates the concentration distribution curves of the complexes formed in the Cu^{II}–Npm-Ser system). In agreement with Motekaitis and Martell,[12] the bonding mode in this complex is tridentate with participation of all the donor groups of the ligands. This is clearly reflected in the basicity-adjusted stability constants (log $K_n - \Sigma pK$), which are about one order of magnitude larger than those for the bidentate $[CH_3(OH)CH]CH(NH_2)PO(OH)_2$ or $[H_2N(CH_2)_4]CH(NH_2)PO(OH)_2$ (*cf.* the data in Tables 1 and 3). It should also be mentioned that the larger

Table 4 Proton dissociation constants (pK) and copper(II) complex formation constants (log β) of *N*-(phosphonomethyl)amino acids at 25.0 ± 0.1 °C and I = 0.20 mol dm^{-3} (KCl)

	Npm-Gly	Npm-Leu	Npm-Phg	Npm-Pro	Npm-Ser	Npm-Thr
pK(NH_3^+)	10.03	9.79	9.42	11.57	9.52	9.26
pK(PO_3H^-)	5.37	5.40	5.33	5.36	5.27	5.27
pK(CO_2H)	1.88	2.06	1.98	1.74	1.87	1.87
Cu(HA)	15.35(1)	15.43(1)	15.30(6)	16.88(2)	15.61(1)	15.30(1)
CuA	11.68(1)	11.62(1)	11.59(1)	13.23(2)	11.90(1)	11.51(1)
$CuAH_{-1}$	2.16(8)	2.11(2)	2.17(7)	3.29(3)	3.36(2)	2.63(3)
$Cu(HA)_2$	29.37(4)	28.9(1)	28.6(1)	32.2(2)	29.08(7)	28.69(5)
CuA(HA)	24.61(3)	24.16(7)	23.80(8)	27.64(8)	24.44(4)	23.90(4)
CuA_2	16.42(3)	15.58(5)	15.58(7)	18.37(6)	16.33(4)	16.08(4)
CuA_2H_{-1}					6.01(4)	6.26(4)
CuA_2H_{-2}					−4.84(4)	−4.24(4)
$pK_{Cu(HA)}$	3.85	3.81	3.71	3.65	3.71	3.79
pK_{CuA}	9.52	9.51	9.42	9.94	8.54	8.88
$pK_{Cu(HA)_2}$	4.76	4.74	4.80	4.56	4.64	4.79
$pK_{CuA(HA)}$	8.19	8.58	8.22	9.27	8.11	7.82
pK_{CuA_2}					10.32	9.82
$pK_{CuA_2H_{-1}}$					10.85	10.50
log K_{CuA} − ΣpK	−5.60	−5.63	−5.14	−5.44	−4.76	−4.92
log K_{CuA_2} − ΣpK	−12.54	−13.29	12.74	−13.53	−12.23	−11.86
log (K_{CuA}/K_{CuA_2})	6.94	7.66	7.6	8.09	7.47	6.94
$Cu + HA_{PO_3H^-} \rightleftharpoons Cu(HA)$ [a]	10.16	10.03	9.97	11.52	10.52	10.00
$CuA + HA_{NH_2^+} \rightleftharpoons CuA(HA)$ [b]	2.90	2.75	2.79	2.84	3.02	3.13

[a] log K = log $\beta_{Cu(HA)}$ − $pK_{PO_3H^-}$. [b] log K = log $\beta_{CuA(HA)}$ − log β_{CuA} − $pK_{NH_2^+}$.



Scheme 1 Proposed structures of complexes formed by *N*-(phosphonomethyl)amino acids with Cu^{II}

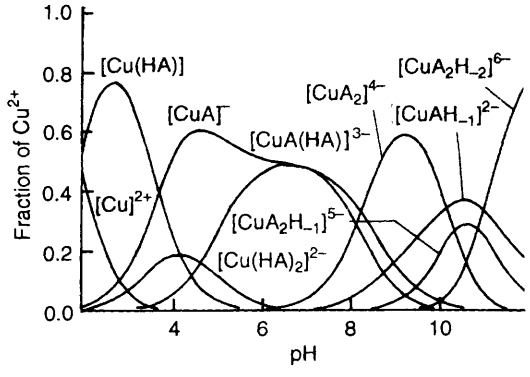


Fig. 2 Species distributions diagram for the Cu^{II}–Npm-Ser system; c_{Cu} = 0.002 mol dm^{-3}, c_L = 0.004 mol dm^{-3}

overall stability of the proline derivative vanished on basicity adjustment as it was solely attributed to the much higher basicity of the cyclic imino-NH.

The formation of the bis complexes is generally hindered [see for example the very high values of log(K_{CuA}/K_{CuA_2}) in Table 4] because of the tridentate co-ordination of the first ligand and the electrostatic repulsion occurring when the second ligand molecule co-ordinates. The relatively low energy of the d–d transition and also the EPR parameters in Table 3 suggest that in the complex $[CuA_2]^{4-}$ the Cu^{II} is five-co-ordinated, with the second ligand molecule bound in an equatorial–axial manner to the tridentate species $[CuA]^-$. The crystal structure of the copper(II) complex of Npm-Gly supports such five-co-ordination around the Cu^{II}.[25] This tridentate + bidentate bonding mode also explains the fact that a pH increase above ≈9 leads to the formation of a mixed hydroxo species $[CuAH_{-1}]^{2-}$. The displacement of one ligand molecule by OH^- indicates its weaker binding to the metal ion. Such a process is generally not observed for the bidentate aminophosphonate or aminocarboxylate complexes, in which two five-membered chelate rings are formed in the equatorial plane around Cu^{II}.[1,6,7]

In the protonated bis complexes, only the bonding mode of the second ligand changes. The species $[CuA(HA)]^{3-}$ loses a proton with pK of ≈8.5, which suggests the presence of a protonated imino group in this complex. Thus, the bonding mode of the second ligand molecule is monodentate PO_3^{2-} with weak axial involvement of the carboxylate function *via* the formation of an eight-membered chelate ring {see the equilibrium constants for the process $[CuA]^- + [HA_{NH_2^+}]^{2-} \rightleftharpoons [CuA(HA)]^{3-}$ in Table 4}. The relatively low stability of the double protonated species $[Cu(HA)_2]^{2-}$, which is a minor complex at pH ≈ 4, suggests weak binding of the

second ligand, most likely *via* oxygen donor(s) of the CO_2^- and/or PO_3H^- functions.

For Npm-Ser and Npm-Thr the major species above pH ≈ 10 are $[CuA_2H_{-1}]^{5-}$ and $[CuA_2H_{-2}]^{6-}$. The deprotonation processes indicate a slightly different co-ordination mode of the ligands containing β-hydroxy groups, which are most likely involved in metal-ion binding in both complexes. Alcoholate co-ordination is even more likely in the complex $[CuAH_{-1}]^{2-}$ of Npm-Ser and Npm-Thr, which is formed at a pH about 0.5–1 unit lower for the other Npm derivatives (see Table 4 and Fig. 2). In this case, the deprotonation process is accompanied by a significant blue shift of the d–d transition from ≈ 700 nm (ε = 56 dm^3 mol^{-1} cm^{-1}) to ≈660 (50) as the pH is increased from ≈8 to ≈11.5.

Npm-Gly *and* Ndpm-Gly *and their Carboxylic Analogues*, H_2ida *and* H_3nta.—Iminodiacetic acid differs from Npm-Gly only in containing a carboxylic group instead of a phosphonic group. Apparent differences in speciation (see Fig. 3 and Table 5) result from the presence of an extra dissociable proton on each phosphonic group, which does not take part in the co-ordination equilibria, but gives the possibility for the formation of protonated complexes. If allowance is made for this, the two systems behave similarly in spectroscopy and potentiometry (see Tables 5 and 6). However, H_2ida is a more effective chelating agent than Npm-Gly. This is reflected in the much higher basicity-adjusted stability constants (log K_n − ΣpK), and also in the pH value of complexation of 50% of Cu^{II}, which is 1.7 for H_2ida and 2.8 for Npm-Gly (see Fig. 3). The reason for this difference is in the larger space requirement and the higher charge of the PO_3^{2-} group. The charge neutralization favours formation of the complex [CuA] for H_2ida, but not for Npm-Gly. For similar reasons, co-ordination of the second ligand molecule, which is hardly favoured for H_2ida [log(K_{CuA}/K_{CuA_2}) = 4.72; Table 5], is even more hindered for Npm-Gly [log(K_{CuA}/K_{CuA_2}) = 6.94]. In the latter case, the resulting bis complex [CuA_2] has a charge of 4−.

Another pair of analogous ligands are Ndpm-Gly and H_3nta. The presence of two phosphonic groups instead of carboxylic groups makes the differences in co-ordination between the two ligands much larger than observed for H_2ida and Npm-Gly. Nitrilotriacetic acid forms 1N-and 2N-complexes (see the spectral parameters in Table 6). Although the carboxylate function is a relatively weak donor for Cu^{II}, the presence of three such functions, combined with the strong metal binder N donor, allows the simultaneous formation of three five-membered chelate rings, which makes H_3nta a very effective chelating agent.[23]

The relatively rigid structure of a bound nta molecule enforces deviation of the complex geometry from planarity if the co-ordination of all potential donors is assumed. Such deviation

Table 5 Proton dissociation constants (pK) and copper(II) complex formation constants (log β) of *N*,*N*-di(phosphonomethyl)glycine (Ndpm-Gly) and related compounds at 25.0 ± 0.1 °C and I = 0.20 mol dm^{-3} (KCl)

	H_2ida *	Npm-Gly	H_3nta *	Ndpm-Gly
pK(NH_3^+)	9.34	10.03	9.67	11.49
pK(PO_3H^-)	—	5.37	—	6.28
pK(PO_3H^-)	—	—	—	4.85
pK(CO_2H)	2.6	2.13	2.52	1.76
pK(CO_2H)	1.8	—	1.9	—
pK(CO_2H)	—	—	1.0	—
$Cu(H_2A)$	—	—	—	24.67(7)
Cu(HA)	12.9	15.53(1)	14.8	21.14(6)
CuA	10.56	11.68(1)	13.1	15.97(5)
$CuAH_{-1}$	2.0	2.16(8)	3.9	5.56(6)
$Cu(HA)_2$	—	29.37(4)	—	—
CuA(HA)	—	24.61(3)	—	—
CuA_2	16.4	16.42(3)	17.5	
$pK_{Cu(H_2A)}$	—	—	—	3.50
$pK_{Cu(HA)}$	2.3	3.85	1.6	5.17
pK_{CuA}	8.5	9.52	9.2	10.41
log K_{CuA} − ΣpK	−3.18	−5.91	−3.99	−8.41
log K_{CuA_2} − ΣpK	−7.9	−12.85	−12.69	—
log K_{CuA}/K_{CuA_2}	4.72	6.94	8.7	—

* Ref. 23.

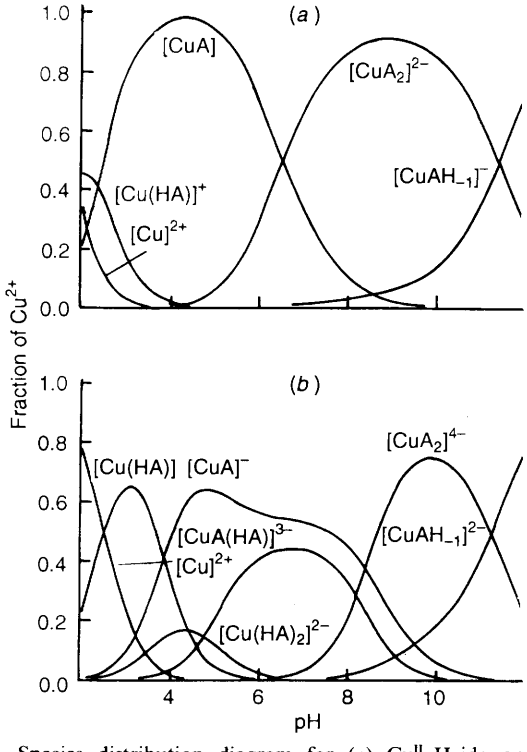


Fig. 3 Species distribution diagram for (*a*) Cu^{II}–H_2ida and (*b*) Cu^{II}–Npm-Gly; c_{Cu} = 0.002 mol dm^{-3}, c_L = 0.004 mol dm^{-3}

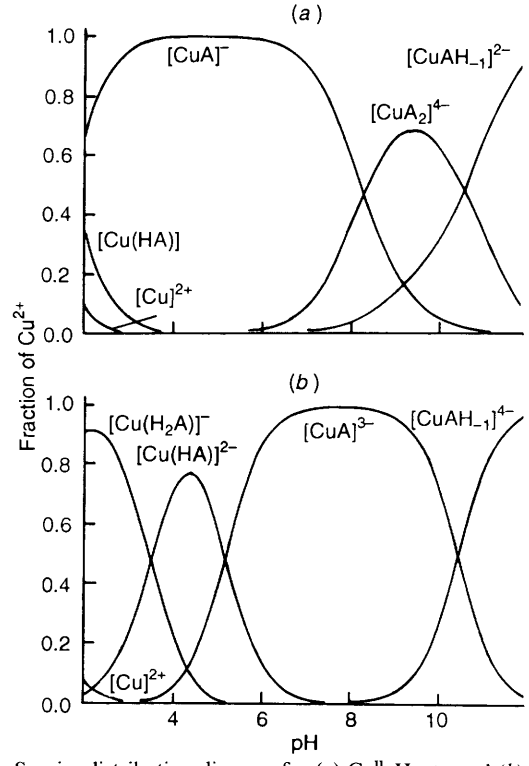


Fig. 4 Species distribution diagram for (*a*) Cu^{II}–H_3nta and (*b*) Cu^{II}–Ndpm-Gly; c_{Cu} = 0.002 mol dm^{-3}, c_L = 0.004 mol dm^{-3}

Table 6 Spectral parameters (ESR, visible) for copper(II) complexes of *N*,*N*-di(phosphonomethyl)glycine (Ndpm-Gly) (see Table 3), H_3nta and H_2ida

		$A_{\parallel}$/G	$g_{\parallel}$	λ_{max}/nm (ε/dm^3 mol^{-1} cm^{-1})
1N type complexes				
$Cu(H_2A)$	Ndpm-Gly	141	2.34	950 (sh) (46), 820 (63)
Cu(HA)	Ndpm-Gly	153	2.31	950 (sh) (67), 820 (80)
	Npm-Gly	149	2.32	740 (63)
	H_3nta	153	2.30	775 (63)
CuA	Ndpm-Gly	126	2.32	965 (90), 820 (sh) (70)
	Npm-Gly	149	2.32	725 (58)
	H_3nta	145	2.33	900 (sh) (68), 810 (75)
	H_2ida	150	2.30	722 (58)
$CuAH_{-1}$	Ndpm-Gly*	$A_1 = 48$	$g_1 = 2.279$	940 (125), 820 (120)
		$A_2 = 42$	$g_2 = 2.202$	
		$A_3 = 11$	$g_3 = 2.047$	
	Npm-Gly	Not detected		
	H_3nta	168	2.29	915 (90), 750 (87)
	H_2ida	173	2.26	675 (68)
2N type complexes				
	Npm-Gly	170	2.27	708 (79)
	H_3nta	173	2.27	670 (60)
	H_2ida	166	2.27	663 (63)

* Values obtained through the simulation of the spectrum; sh = shoulder.

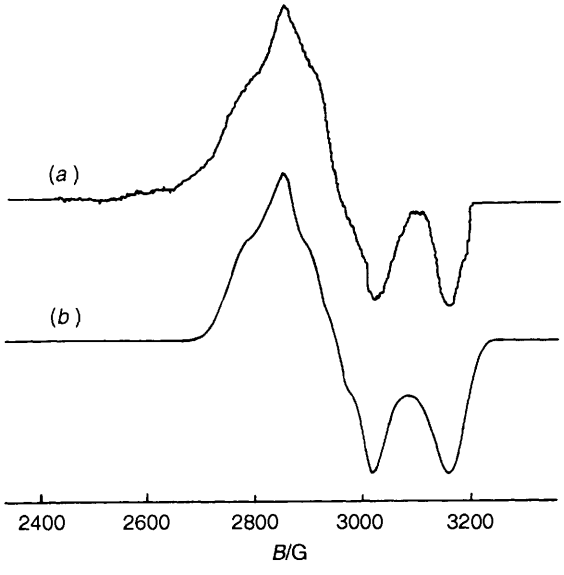
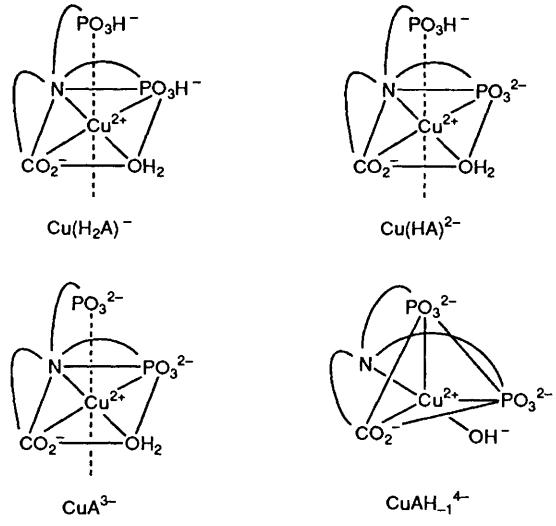


Fig. 5 Experimental (*a*) and simulated EPR spectra (*b*) of the Cu^{II}–Ndpm-Gly system at a 1 : 1 metal ion : ligand ratio, pH ≈ 8, and 120 K



Scheme 2 Proposed structures of complexes formed by *N*,*N*-di(phosphonomethyl)glycine with Cu^{II}

is seen in the complexes $[CuA]^-$ and $[CuAH_{-1}]^{2-}$ of H_3nta. The complex $[CuA]^-$ is formed from [Cu(HA)] at pH ≈1.5, and by pH 2 it is the predominant species in solution. This process involves deprotonation of a carboxylic group and is accompanied by a decrease in $A_{\parallel}$ and a slight increase in $g_{\parallel}$ in the EPR spectrum. A profound change is seen in the electronic spectra, *i.e.* a significant red shift and splitting of the d–d band (see Table 6). Such changes are characteristic of deviation from tetragonal symmetry towards a distorted square pyramid.[26,27] The complex $[CuA_2]^{4-}$ of H_3nta is a typical 2N species. It is a predominant complex at around pH 9–10. The species $[CuAH_{-1}]^{2-}$ is a hydrolytic product of $[CuA_2]^{4-}$, when the weakly co-ordinated second ligand molecule is replaced by an OH^- ion (see above). Its geometry is similar to that of $[CuA]^-$, with an OH^- in place of a water molecule. The much higher electron-donating ability of OH^- relative to that of H_2O is responsible for the changes in the EPR parameters.

Owing to the larger space requirement and higher charge deriving from the phosphonate groups, Ndpm-Gly forms only equimolar complexes. The charge of the bis complex would be 8−. Despite the presence of two bulky phosphonate groups, the chelating ability of this ligand in the 1 : 1 complexes is high. It is a weaker chelating agent than H_3nta, but more effective than H_2ida (see Figs. 3 and 4). In the protonated species $[Cu(H_2A)]^-$ the bonding mode is ter- or tetra-dentate, with strong N, CO_2^- co-ordination and some involvement of the protonated $-PO_3H^-$ moieties. The deprotonation processes leading to the formation of $[CuA]^{3-}$ correspond to the stepwise liberation of two protons from the weakly co-ordinated PO_3H^- group, which then becomes more strongly bound to the Cu^{II}. Deviation from tetragonal symmetry is observed for all these complexes. The complexes $[Cu(H_2A)]^-$ and $[Cu(HA)]^{2-}$ exhibit splitting and low energy of the d–d transition (see Table 6), while their axial-like EPR spectra suggest approximately planar geometry with $d_{x^2-y^2}$ as the orbital having the unpaired electron in the ground state.[28,29] Formation of the complex $[CuA]^{2-}$ results in distinct changes in the EPR and absorption spectra. The EPR spectrum reveals rhombic distortion, demonstrated by a large increase in $A_{\parallel}$ and broadening of the perpendicular part of the spectrum. This further decrease in complex symmetry results

from the electrostatic repulsion between the negatively charged phosphonate groups. At around pH 10.5, a co-ordinated water molecule loses a proton and the species $[CuAH_{-1}]^{4-}$ is formed. This complex exhibits a fully rhombic EPR spectrum (Fig. 5) and twin-peaked blue-shifted d–d bands. These spectroscopic features are characteristic of heavily distorted geometry between a square pyramid and a trigonal bipyramid.[30] The value of $R(=1.71)$ calculated from the EPR spectrum [$R = (g_2 - g_1)/(g_3 - g_2)$ is characteristic of involvement of the d_{z^2} orbital in the ground state of the Cu^{II} ion] is normally associated with trigonal symmetry. Thus, the complex $[CuAH_{-1}]^{4-}$ should have two of the five bonds (*i.e.* Cu–N and Cu–OH^-) distinctly shorter. Formation of such a structure in solution is facilitated by the very high negative charge density, 6−, around the metal ion forming an electrostatic cage (see Scheme 2).

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