Copper(II) Co-ordination by Oxime Analogues of Amino Acids and Peptides

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Complexes formed by the *N*-pyruvoylamino acid oximes $CH_3C(=NOH)CONHCHRCO_2H$, where R = H, Me, CH_2Ph or $(CH_2)_2SMe$, and 2-hydroxyiminopropanoic acid [alanine oxime, $CH_3C(=NOH)CO_2H$] and some derivatives with H^+ and Cu^{2+} have been studied in aqueous solution using a combination of pH-metric titrations, UV/VIS and EPR spectroscopy. The oxime group was able to bind to Cu^{2+} through both the N and O donors from about pH 5 upwards with extensive formation of binuclear complexes, which dominated the equilibria in equimolar solutions.

N-Pyruvoylamino acid oximes [$CH_3C(=NOH)CONHCHRCO_2H$, where R is an amino acid side chain] and 2-hydroxyiminocarbonic acids [$RC(=NOH)CO_2H$] are structural analogues of dipeptides and 2-amino acids respectively. Pyruvoylamino acids are similar in their structure to dipeptides and differ from them by containing oxime fragments C(=NOH) in place of the terminal amino groups $CH(NH_2)$. The two groups form a class of interest in models of metal–protein interaction and the possible mobilisation of metal ions in biological systems and contaminated natural waters. Solid-state studies[1–3] have shown that they can act as ambidentate ligands which can be present in different ionic forms. The co-ordination properties of *N*-pyruvoylamino acid oximes are, to a large extent, governed by the presence of a planar $CH_3C(=NOH)CONH$ framework which allows them to form several different chelate rings with transition-metal ions such as Cu^{2+}; for example *N*(oxime), *N*(deprotonated amide) co-ordination can take place with virtually no change in conformation[4] and *N*(oxime), *O*(carbonyl) co-ordination can take place on reorganisation of the ligand by changing the hydroxyimino group from a '*trans*' to a '*cis*' position with respect to the amide carbonyl group. In addition there is the possibility of binding through the deprotonated O^- donor of the oxime group. While synthetic and structural investigations of their solid-state complexes have been reported, no solution equilibria studies have been reported. Other studies have shown that oximes also co-ordinate to Pd^{II} *via* the oxime N, with the oxime OH free[5] and, in non-aqueous solution, it has been shown that both aryl and alkyl oximes exist with a small but significant concentration of the NH nitrone ($=NH^+-O^-$).[6]

Modification of either the amino or the carboxylate terminal groups of amino acids or peptides may lead to a considerable variation in their binding abilities. For example, modification of the poorly co-ordinating carboxylate to form a hydroxamic moiety leads to one of the most effective donors[7] found in natural ligands, *e.g.* in siderophores such as deferrioxamine. The amino group is usually a much more effective binding site than carboxylate, especially to transition-metal ions, and its modification would be expected to have a marked effect on the overall binding ability of the ligand.

Organic chelating ligands containing the oxime functional group have been extensively used in analytical chemistry for the detection and separation of metal ions.[8] Hydroxyoxime ligands have been the most widely studied since they are used in analytical chemistry and as commercial reagents in extractive metallurgy. Unlike the amino group, the hydroxyimino group is not basic, protonation occurring only under very acidic conditions. On the other hand, the proton of a hydroxyimino group dissociates readily in alkaline solutions, with corresponding pK values in the range 10–12 for aliphatic oximes. These can be several orders in magnitude lower in the case of oximes containing an electron-withdrawing group in the α position (*e.g.* cyanoximes[9]). Therefore, depending on the pH and the nature of the metal ion in solution, the oxime group can act both as a neutral or a deprotonated group, binding to a metal ion *via* nitrogen (usually with d metals, either as a neutral and deprotonated group), *via* oxygen (mostly with p-block metals, only on deprotonation), and in a N,O bridging fashion. Modification of an amino group into an oxime can, therefore, critically alter the binding ability and specificity of biologically important amino acids and peptides.

Interest in oxime-containing compounds is increasing in connection with the understanding of their biological function especially as possible intermediates in the biosynthesis of nitric oxide and in the marked bioactivity of several different oximes, the transition-metal complexes of which can show varying types of bioactivity. We report the results of a pH-metric and spectroscopic study of proton and copper(II) complexes of *N*-pyruvoyl-amino acid oximes and -amino acid amide oximes.

Experimental

Synthesis of Oximes.—The oximes were synthesised by standard methods, as described elsewhere,[2] purity being checked by elemental analysis and NMR spectroscopy. It was also checked by pH-metric titration which showed the oximes to be near 100% pure and an excellent fit was obtained between calculated and experimental titration curves with alkali over the whole pH range.

Metal Solutions.—Solutions of Cu^{2+} were prepared from either the nitrate (Hopkins and Fisons analytical grade reagents) or the chloride salt (Reanal p.a. quality) using distilled deionised water. Concentrations were checked gravimetrically *via* the quinolin-8-olate

Potentiometric Studies.—All the oximes were sufficiently water soluble. Two independent techniques were used, performed in different laboratories, to check the speciation present in the equilibria. The technique employed for most titrations involved an ionic background of 0.1 mol dm^{-3} KNO_3, oxime concentrations of 0.001 mol dm^{-3} and a Cu:L ratio of 1:2. Stability constants for the complexes of H^+ and Cu^{II} were calculated from titrations carried out using total volumes of 1–2 cm^3. Alkali was added from a 0.25 cm^3 micrometer syringe which had been calibrated by weight titrations and the titration of standard materials. The pH-metric titrations were performed at 25 °C using a MOLSPIN automatic titration system with a microcombined glass–calomel electrode calibrated in hydrogen-ion concentration using HNO_3.[10] Titrations were performed in triplicate and the SUPERQUAD computer program was used for stability-constant calculations.[11]

To confirm the presence of dimeric complexes, potentiometric data for 2-hydroxyiminopropanoic acid (or pyruvic acid-2-oxime), 2-hydroxyiminopropanamide (or pyruvamide 2-oxime) and *N*-2-hydroxyiminopropanoylglycine (pyruvoylglycine oxime) were checked by repeating titrations independently at an ionic background of 0.2 mol dm^{-3} (KCl), oxime concentration of 0.004 mol dm^{-3} and metal ion-to-oxime ratios of 1:4, 1:2 and 1:1. The total volume of the samples was 5 cm^3. In these titrations the pH was measured with a Radiometer pHM 84 instrument with a GK 2322C combined electrode calibrated in hydrogen-ion concentration.[10] The concentration stability constants $\beta_{pqr} = [M_pH_qL_r]/[M]^p[H]^q[L]^r$ were calculated with the aid of the PSEQUAD computer program.[12] Standard deviations quoted were computed by SUPERQUAD or PSEQUAD and refer to random errors only. They are, however, a good indication of the importance of a particular species in the equilibrium.

Spectroscopic Studies.—The EPR spectra were recorded on a Bruker ESP 300E spectrometer at X-band frequency (9.3 GHz) at 120 K. Manganese(II) ions and diphenylpicrylhydrazyl (dpph) were used as standards for the calculations of *g*. Absorption spectra were recorded on a Beckman DU 650 spectrophotometer. The metal-to-oxime molar ratios were 1:1 and 1:2 and the metal concentration was 5×10^{-3} mol dm^{-3}.

Results and Discussion

Protonation Constants.—Calculated cumulative and stepwise protonation constants are presented in Table 1. The data for 2-aminopropanoic acid (α-alanine) and 2-aminopropanamide are also shown for comparison. The pyruvoylamino acid oximes have two protonation constants. The first, starting at high pH, corresponds to protonation of the hydroxyimino group $C{=}NO^-$ (log K_{NOH} = 10.1–10.2), while the other represents protonation of the carboxyl group (log K_{CO_2H} = 3.1–3.5). The oxime nitrogen is protonated only at very low pH; hence its protonation constant was not within the experimental range. The close similarity within each group of constants shows that they are only marginally affected by the nature of the amino group side chain. The protonation constants of 2-hydroxyiminopropanoic acid amides [log *K*(HL) = 9.9–10.3] are lower than that of 2-hydroxyiminopropanoic acid (log *K* = 11.6) as a result of the inductive effect of the electron-withdrawing amide group in the α position.

Copper(II) Complexes with N-Pyruvoylamino Acid Oximes.—*N*-Pyruvoylamino acid oximes are similar to dipeptides, differing only in having the oxime fragment RC(=NOH)– in place of the terminal amino group $RCH(NH_2)$–. Hence their complexation with Cu^{II} would be expected to be similar to that of peptides. In particular Cu^{II} would be expected to be able to deprotonate and bind to the amide nitrogen in a weakly acidic medium, *e.g.* around pH 5. The equilibria between Cu^{II} and the oximes proved surprisingly complicated. In 1:2 Cu:L mixtures good fits between experimental and calculated titration curves over the region pH 6.0–11.0 were obtained by assuming only monomeric mono- and bis-complexes. However the inclusion of dimeric species in the models gave fits over the range pH 3.5–10.7 within experimental error.

To confirm the presence of dimers, titrations with *N*-pyruvoylglycine oxime were repeated independently with an ionic background of 0.2 mol dm^{-3} KCl. These titrations involved fewer data points than those using 0.1 mol dm^{-3} KNO_3 but covered Cu:L ratios of 1:1 to 1:4; hence the standard deviations are a little larger. Good agreement was found between the two sets of titrations; the major species present in the 'best-fit' models were the same and the stability constants reassuringly consistent so that closely similar species-distribution curves were calculated from each study. Solutions of the oximes with Cu^{II} became distinctly green above pH 5 suggesting oxime O to Cu bonding. The presence of dimers was confirmed by spectroscopic studies.

Calculated stability constants are given in Table 2 and the species-distribution curves for 1:1 Cu:pyruvoylglycine oxime is shown in Fig. 1. The behaviour of all four *N*-pyruvoylamino acid oximes studied was closely similar, with virtually identical species-distribution curves. Hence discussion will be centred on the simplest, *N*-pyruvoylglycine oxime.

Since the oximes studied were analogues of peptides, spectroscopic measurements were performed on pyruvoylglycine oxime in an attempts to assign the structures to the complexes based on the known spectra of peptide complexes, and assuming that spectra would be closely comparable. Spectroscopic data are reported in Table 3. These give

Table 1 Protonation constants for the pyruvoylamino acid oximes, 2-hydroxyiminopropanoic acid and its amides at 25 °C and I = 0.1 mol dm^{-3} (KNO_3)

Compound	log β(HL)	log β(H_2L)	log *K*(H_2L)
2-Hydroxyiminopropanoic acid (H_2L)	11.608(7)	14.853(8)	3.25
	11.28(2)[a]	14.49(2)[a]	3.21[a]
2-Hydroxyiminopropanamide (HL)	9.868(2)		
	9.82(1)[a]		
2-Hydroxyimino-*N*-methylpropanamide (HL)	10.204(1)		
N-2-Aminoethyl-2-hydroxyiminopropanamide	10.32(1)	19.51(2)	9.19
N-Pyruvoylglycine oxime (H_2L)	10.130(4)	13.623(6)	3.49
	10.05(1)[a]	13.48(2)[a]	3.43[a]
N-Pyruvoyl-L-alanine oxime (H_2L)	10.174(2)	13.711(3)	3.54
N-Pyruvoyl-L-phenylalanine oxime (H_2L)	10.19(1)	13.33(1)	3.14
N-Pyruvoyl-L-methionine oxime (H_2L)	10.123(2)	13.336(3)	3.21
2-Aminopropanoic acid (α-alanine) (HL)[b]	9.72	12.05	2.33
2-Aminopropanamide[c]	8.18		

[a] Determined at I = 0.2 mol dm^{-3} (KCl). [b] Ref. 13. [c] Ref. 14.

Table 2 Copper(II) complex-formation constants at 25 °C and I = 0.1 mol dm^{-3} KNO_3

	log β			
Ligand	[CuL]	[$CuH_{-2}L$]	[$Cu_2H_{-1}L_2$]	[$Cu_2H_{-2}L_2$]
N-Pyruvoylglycine oxime	8.49(2)	−7.73(4)	13.94(5)	8.65(4)
	8.36(2)*	−8.14(4)*	14.11(4)*	8.29(3)*
N-Pyruvoylalanine oxime	8.64(1)	−7.97(2)	14.20(3)	9.07(2)
N-Pyruvoylphenylalanine oxime	8.34(1)	−8.25(2)	13.97(2)	8.78(1)
N-Pyruvoylmethionine oxime	8.37(1)	−7.60(2)	14.10(2)	8.99(2)

* Determined at I = 0.2 mol dm^{-3} (KCl).

Table 3 The UV/VIS and EPR data for copper(II)–pyruvoylglycine oxime

		EPR	
Species (bonding modes)	UV/VIS λ/nm (ε/dm^3 mol^{-1} cm^{-1})	$10^4A/T$	g
[CuL] (N_{ox}, N^-, CO_2^-)	666(78)[a]	160	2.259
[$CuH_{-2}L$] (N_{ox}, N^-, CO_2^-, OH^-)	617(134)[a]	160	2.220
[$Cu_2H_{-1}L_2$]	642(115)[a]	*b*	
[$Cu_2H_{-2}L_2$] (N_{ox}, N^-, CO_2^-, O^-)	609(213)[a]	*b*	
	360(1280)[c]		

[a] d–d Transition. [b] Not observed. [c] $O^- \rightarrow Cu^{II}$ charge-transfer transition.

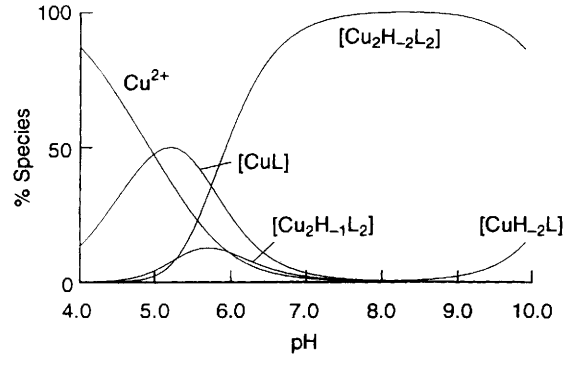

Fig. 1 Species distribution curves for 1:1 Cu:*N*-pyruvoylglycine oxime (0.001 mol dm^{-3})

additional and conclusive evidence for the formation of dimers. The EPR spectra were silent in the pH regions over which the existence of dimeric species had been predicted from the speciation calculations (see Fig. 2) and an intense charge-transfer band was present at about 360 nm from about pH 5, so accounting for the clear green colour noted during potentiometric titrations. Assignments of the spectroscopic data for the copper(II)–pyruvoylglycine system are given in Table 3. Based on the copper(II)–peptide scheme,[15,16] d–d bands at λ_{max} 666 (ε = 78) and 617 nm (ε = 134 dm^3 mol^{-1} cm^{-1}) can be assigned to the co-ordination of two nitrogen atoms to Cu^{II}; peptide complexes with one nitrogen co-ordinated generally have d–d bands in the region of 730 nm. The [CuL] species is therefore co-ordinated *via* the oxime and deprotonated amide nitrogens and, presumably, the carboxylate O, with the oxime oxygen protonated, Fig. 2(*a*). The [$CuH_{-2}L$] complex forms only above pH 9.5 (see Fig. 1). This pH is typical for the ionisation of a co-ordinated water molecule and it can be assumed that the structure of [$CuH_{-2}L$] would be similar to that in Fig. 2(*a*) but with both the oxime O and co-ordinated water molecule deprotonated. The species-distribution curves show that dimerisation commenced as low as pH 5 with the [CuL] complex going rapidly to [$Cu_2H_{-2}L_2$] with the loss of two protons and, between pH 6 and 10, [$Cu_2H_{-2}L_2$] was virtually the only species present. Dimerisation would result from the high affinity between Cu^{II} and a deprotonated oxime O and the inability of the oxime N and O both to co-ordinate to the same

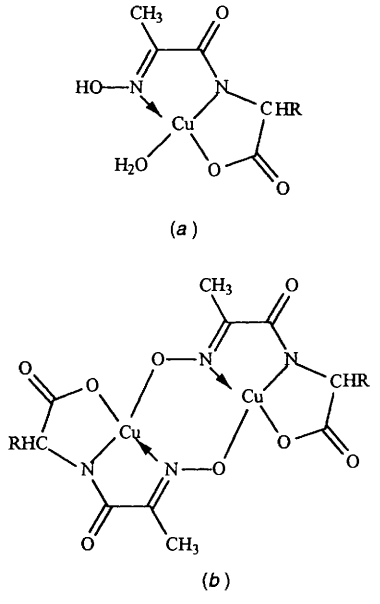

Fig. 2 Proposed structure for (*a*) [CuL] and (*b*) [$Cu_2H_{-2}L_2$] complexes of pyruvoylamino acid oximes

metal ion, resulting in the probable structure for [$Cu_2H_{-2}L_2$] shown in Fig. 2(*b*).

Copper(II) Complexes with 2-Hydroxyiminopropanoic Acid and its Amides.—The equilibria between Cu^{II} and 2-hydroxyiminopropanoic acid and its analogues were also complicated. Using a Cu:L ratio of 1:2, the potentiometric titration data could fit two different stoichiometric models, one involving bis complexes and the other dimeric species. The goodness of fit when using 1:1 ratios was significantly in favour of more complicated equilibria involving dimers, and covered a greater pH range. Excellent agreement was obtained between experimental and calculated titration curves over the range pH 2.5–10 by assuming equilibria to form the mixture of mono- and bis-complexes shown in Table 5. Similar results were found with the amide and *N*-methylamide analogues.

As with the pyruvoylamino acid oximes, the titrations were repeated independently with an ionic background of 0.2 mol

Table 4 Copper(II) complex-formation constants for 2-hydroxyiminopropanoic acid and its analogues at 25 °C and I = 0.1 mol dm^{-3} KNO_3

	Ligand[a]					
	1	1[b]	2	2[b]	3	4
$\beta(CuH_2L_2)$	31.76(6)	31.39(38)				
$\beta(CuHL_2)$	29.00(5)	28.95(19)				22.67(7)?
$\beta(CuL_2)$	18.84(14)	18.68(24)				13.42(5)?
$\beta(Cu_2L_2)$	27.15(7)	27.78(24)				
$\beta(Cu_2H_{-1}L_2)$	21.64(7)	21.70(23)	12.30(3)	12.98(4)	11.32(2)	
$\beta(Cu_2H_{-2}L_2)$	11.67(8)	11.19(23)	5.66(3)	6.00(6)		
$\beta(CuHL)$		16.16(14)				15.91(1)
$\beta(CuL)$			7.87(1)	7.82(2)	7.99(1)	10.01(1)
$\beta(CuH_{-1}L)$					0.78(1)	−0.84(3)
$\beta(CuH_{-1}L_2)$			5.66(2)	5.42(4)	3.81(1)	
$\beta(CuH_{-2}L_2)$			−4.74(2)	−5.08(5)	−6.67(1)	

[a] 1, 2-Hydroxyiminopropanoic acid; 2, 2-hydroxyiminopropanamide; 3, 2-hydroxyimino-*N*-methylpropanamide; 4, *N*-2-aminoethyl-2-hydroxyiminopropanamide. [b] Determined at I = 0.2 mol dm^{-3} (KCl).

Table 5 The UV/VIS and EPR data for the copper(II) complexes of 2-hydroxyiminopropanoic acid and its amide

		EPR	
Species (bonding mode)	UV/VIS λ/nm (ε/dm^3 mol^{-1} cm^{-1})	$10^4 A_{\parallel}$/T	$g_{\parallel}$
(*a*) 2-Hydroxyiminopropanoic acid			
[Cu(HL)] (N, CO_2^-)	715(22)[a]	150	2.340
[$CuHL_2$] 2(N, CO_2^-)	598(110)[a]	185	2.230
[CuL_2] 2(N, CO_2^-)	611(127)[a]	186	2.232
[Cu_2L_2] 2(N, CO_2^-, O^-)	623(51)[a]	*b*	
	350 (sh)[c]		
[$Cu_2H_{-1}L_2$]	662(95)[a]	*b*	
[$Cu_2H_{-2}L_2$]	649(99)[a]	*b*	
	337(1463)[c]		
(*b*) 2-Hydroxyiminopropanamide			
[CuL] (N_{ox}, N_{amine})	688(54)[a]	185	2.240
[$CuH_{-1}L_2$]	613(129)[a]		
[$CuH_{-2}L_2$] 2(N_{ox}, N_{amine})	505(138)[a]	202[d]	2.186
	649 (sh)(86)[a]		
[$Cu_2H_{-1}L_2$]	662(98)[a]	*b*	
[$Cu_2H_{-2}L_2$] 2(N_{ox}, N_{amine}, O^-)	629(145)[a]	*b*	
	350 (sh)(1444)[c]		

[a] d–d transition. [b] Not observed. [c] $O^- \rightarrow Cu^{II}$ charge-transfer transition. [d] Nine superhyperfine lines of 4N.

dm^{-3} KCl to confirm the presence of dimers. Good agreement was found between the two sets of titrations; the major species present in the 'best-fit' models were the same and the stability constants reassuringly consistent so that closely similar species-distribution curves were calculated from each study. Again solutions became distinctly green as the pH was increased, suggesting oxime O^- to Cu bonding. Calculated stability constants from both studies are given in Table 4 and spectroscopic data in Table 5.

In equimolar mixtures of 2-hydroxyiminopropanoic acid and Cu^{II}, 0.001 mol dm^{-3}, dimeric complexes are the major species from below pH 5 as shown in Fig. 3(*a*). Dimers are much less important species when the ratio is 2:1 or higher and, in this case, [$CuHL_2$]$^-$ is the major species up to pH 9 [Fig. 3(*b*)].

Table 5 shows the assignment of λ_{max} values in the UV/VIS spectra for species in the Cu^{2+}–2-hydroxyiminopropanoic acid and –2-hydroxyiminopropanamide systems. Values for λ_{max} in the region of 650 nm and $A_{\parallel}$ values in the region of 185 × 10^{-4} T are typical of 2N co-ordination. This suggests that, with 2-hydroxyiminopropanoic acid, the bis complexes (both protonated and unprotonated) have 2N co-ordination, involving bonding to the oxime N and carboxyl O^- donors with the oxime O not co-ordinated. Both would be protonated in [CuH_2L_2]. These bis complexes are very stable species, forming below pH 4. As the pH is raised, however, Cu^{II} can deprotonate the oxime OH group and bind to form an $O^- \rightarrow Cu^{II}$ bond but co-ordination of both the oxime N and O^- can only take place if dimers are formed. The EPR over the region in which dimers predominate was virtually silent (characteristic of dimer formation) and there was a very strong charge-transfer band at 337 nm (ε = 1463 dm^3 mol^{-1} cm^{-1}), characteristic of $O^- \rightarrow Cu^{II}$ bonding. In the dimer each copper(II) ion would have a co-ordinated water molecule which can be deprotonated to give the probable structure for the fully deprotonated dimer of 2-hydroxyiminopropanoic acid [$Cu_2H_{-2}L_2$]$^{2-}$, shown in Fig. 4.

Fitting experimental data for 2-hydroxyiminopropanamide proved even more difficult than for the parent acid and the equilibria were studied independently using a range of Cu:amide ratios. From potentiometry very good fits between experimental and calculated pH-metric data were obtained using a variety of models; in particular either the dimer [Cu_2L_2]$^{2+}$ or the monomer [CuL]$^+$ (but not both) could be included at lower pH while deprotonated dimers were clearly present at higher pH. At pH 5 the mononuclear complex, [CuL]$^+$, was unambiguously detected by EPR spectroscopy and this was therefore included in the evaluation of the titration data in solutions of both equimolar and 1:2 metal–amide ratios. This monomer dimerises above pH 5 and dimers were shown to be present from both potentiometric titrations and spectroscopy, as demonstrated in Tables 4 and 5. From UV/VIS spectroscopy, O^-–Cu^{II} bonding was clearly present in the dimeric complexes (see Table 5). 2-Hydroxyimino-*N*-methyl-

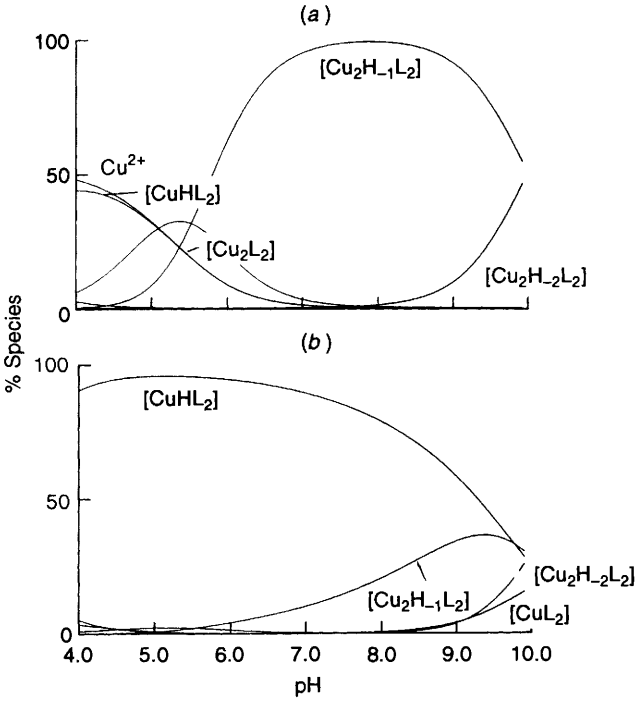

Fig. 3 Species distribution curves for 2-hydroxyiminopropanoic acid:copper(II) mixtures (total Cu = 0.001 mol dm^{-3}), (*a*) 1:1 and (*b*) 2:1

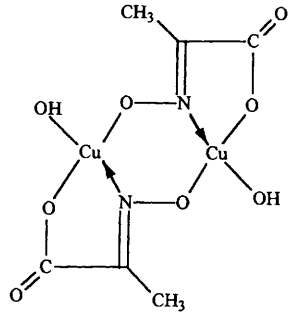

Fig. 4 Suggested structure for the $[Cu_2H_{-2}L_2]$ complex of 2-hydroxyiminopropanoic acid

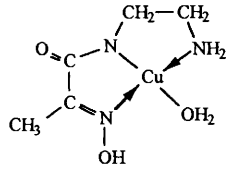

Fig. 5 Suggested structure for the $[CuL]^+$ complex of *N*-2-aminoethyl-2-hydroxyiminopropanamide

propanamide behaved in an almost identical fashion, as expected, giving very similar species-distribution curves.

In all cases with 1:1 mixtures, dimeric complexes were the only significant species above pH 5.5. The complex $[CuL]^+$ formed below this pH is clearly a 2N species with co-ordination through the oxime N and the deprotonated amide NH. As the oxime O is still protonated at this pH the composition of the complex can be written more precisely as $[CuH_{-1}(HL)]^+$. Once this complex is formed it dimerises rapidly as a result of copper(II)-promoted deprotonation and binding to the oxime O^-, with the oxime acting as a tridentate ligand. Bonding to both the oxime N and O can only occur in polynuclear complexes, so accounting for both the EPR-silent spectra and the green colour. In the presence of an excess of amide, amide-type co-ordination becomes more favoured and, by pH 10, a 4N species with $2(NO^-,NH^-)$ co-ordination becomes predominant, which is unambiguously demonstrated by the electronic absorption and EPR spectral parameters (Table 5).

N-2-Aminoethyl-2-hydroxyiminopropanamide behaved very differently. There was no evidence of dimer formation and the potentiometric data gave an excellent fit for the species $[Cu(HL)]^{2+}$, $[CuL]^+$ and $[CuH_{-1}L]$. In 1:2 Cu:L mixtures the species $[CuHL_2]^+$ and $[CuL_2]$ were detected, but with very low concentrations. In 1:1 mixtures the $[CuL]^+$ complex was predominant between pH 6.5 and 10.5. The ligand has an additional amino group compared to the other hydroxyimino-propanoic acids studied and can therefore co-ordinate in a tridentate manner; this would discourage strongly the formation of dimeric complexes. A probable structure for $[CuL]^+$ is shown in Fig. 5. Above pH 9.5 this deprotonates to form $[CuH_{-1}L]$ with a deprotonation constant of log $K = -10.85$, characteristic of the ionisation of a co-ordinated water molecule. A $[CuH_{-2}L]^-$ species was also detected at high pH. This was formed in only small quantities at the maximum pH studies (10.5) so is not included in Table 4. These overlapping deprotonations would correspond to deprotonation of the co-ordinated water molecule and the oxime OH. Hence both species would have structures similar to that in Fig. 5.

Conclusion

The results show that all the oximes studied, both peptide and amino acid analogues, are able to form stable soluble complexes with Cu^{2+} with extensive dimer formation above pH 5. This binuclear complex formation results from the two alternative donor centres (N and O) in the ligands which both have a high affinity for Cu^{II} and cannot both co-ordinate to the same metal ion.

Acknowledgements

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