Ternary interaction between copper(II), imidazolinone herbicides and glycylglycine

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The ternary interaction between Cu^{II}, (±)-2-(4-isopropyl-4-methyl-5-oxo-2-imidazolin-2-yl)-5-ethyl-nicotinic or (±)-2-(4-isopropyl-4-methyl-5-oxo-2-imidazolin-2-yl)nicotinic acid and glycylglycine, was studied in aqueous solution.

Keywords: copper(II), imidazolinone herbicides, glycylglycine

The study of the complexes of Imazapyr, (±)-2-(4-isopropyl-4-methyl-5-oxo-2-imidazolin-2-yl)nicotinic acid (Imz, Scheme 1) highlighted the ligand behaviour of imidazolinone herbicides.[7–9] Of particular interest was to find that metal ions induce the deprotonation of the lactam group in the physiological pH range. The process makes the ligand strong and efficient through a donor set consisting of the pyridine and the N(1) nitrogen atoms, although other tautomeric forms of the ligand could be involved. We have investigated the ternary interaction of Imazapyr and Imazethapyr, (±)-2-(4-isopropyl-4-methyl-5-oxo-2-imidazolin-2-yl)-5-ethyl-nicotinic acid (Imzt) in the presence of Gly-Gly.

Imz Imzt

Scheme 1

The pK_a values of Imzt (H_3A^+) are very close to those of Imz (Table 1). The pK_a values of *ca* 2 and 3.8 are assigned to the imidazole and the carboxylic sites, respectively. The third dissociation process (pK_a = 10.8) is distinctive of the lactam group.

Imzt exhibits a behaviour similar to that of Imz and yields $[CuAH]^+$, $[CuA_2H_2]$, $[CuA_2H]^-$, $[CuA_2]^{2-}$, and $[CuAH_{-2}]^{2-}$ (Table 1). In HA- the ligand has undergone dissociation at the carboxylic group and does not have a proton on the imidazole nitrogen. These two donors, however, cannot coordinate simultaneously a single metal ion because of sterical reasons. EPR substantiates that the ligand chelates copper(II) through the imidazole (N_{im}) and pyridine (N_{py}) nitrogens. A logK value of 5.1 is calculated for the reaction $Cu^{2+} + HA^- \rightleftharpoons [CuAH]^+$. The value is notably lower in comparison with that (8.11) found for the 2,2′-bipy complex,[10,11] but greater than that of the 1:1 species formed by simple imidazole (4.30)[12] which is monodentate. For the reaction $Cu^{2+} + 2\ HA^- \rightleftharpoons [CuA_2H_2]$ logK = 10.0 is calculated. The corresponding equilibria with imidazole and 2,2′-bipy exhibit values of 7.85 and 13.66, respectively.[10–12]

The lactam groups (N_{lact}) dissociate sequentially and replace the imidazole donors to yield $[CuA_2H]^-$ and $[CuA_2]^{2-}$ (pK_a 6.6 and 7.6, respectively). EPR indicates five-co-ordinate species with a geometry intermediate between the square pyramid and trigonal bipyramid.[13] The intermediate $[CuA_2H]^-$ species is not observed distinctly because of the coexistence of $[CuA_2H_2]$ and $[CuA_2]^{2-}$. $[CuAH_{-2}]^{2-}$ is a monomeric dihydroxo species involving two hydroxo groups, besides the pyridine and lactam nitrogens, in co-ordination.

Table 1 Proton (log K) and Cu^{II} (log β) stability constants at I = 0.10 mol/dm^3 KNO_3 and t = 25 °C.

Species	Imz	Imzt
$logK_{COO-}$	3.60(2) 3.60[a]	3.83(2)
$logK_{N(im)}$	1.9(1) 2.2[a]	2.0(1)
$logK_{N-(lact)}$	10.8(1) 10.8[a]	10.8(1)
$[CuAH]^+$	15.61(9)	15.95(9)
$[CuA_2H_2]$	30.78(3)	31.65(3)
$[CuA_2H]^-$	24.18(3)	25.04(2)
$[CuA_2]^{2-}$	16.57(3)	17.41(2)
$[CuAH_{-2}]^{2-}$	–7.3(1)	–7.8(1)
[CuABH]	21.59(8)	22.18(7)
$[CuAB]^-$	15.22(7)	15.73(8)
$[CuABH_{-1}]^{2-}$	6.61(5)	7.27(11)

[a]Ref. 7.

Potentiometric data could be fitted only by the assumption of mixed species (Fig. 3). In the fully protonated form H_2B^+, Gly-Gly is assumed to be diprotic. Over the pH range 4–8 a ternary species [CuABH] is formed by the (N_{py}, N_{im}) coordination of the HA^- form of Imzt (or Imz). Gly–Gly is in the B^- form which binds the metal ion *via* the (NH_2, CO) chelating set. [CuABH] is not observed distinctly by EPR because of species overlap. Two proton dissociation processes occur stepwise. $[CuAB]^-$ shows up above pH 5. The proton could be removed from either the lactam ring of the imidazolinone molecule or the amide group of Gly-Gly. From a comparison of the spectral data of this system with those of Cu^{II}/Imzt/Gly-Sar – the secondary amide group of Gly-Sar cannot be ionised – we conclude that the proton is released by the lactam ring. The pK_a value of the process is 6.45, more than four log units lower than in the free ligand. Therefore, Imzt (or Imz) switches its co-ordination mode and the resulting species exhibits the [(N_{py}, N_{lact}) (NH_2, CO)] donor set.

Above pH 8 $[CuABH_{-1}]^{2-}$ is formed by the deprotonation and co-ordination of the amide group of Gly-Gly, whilst Imzt (or Imz) retains its binding mode. The amide pK_a in the

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ternary Cu^{II}/Imzt/Gly-Gly system is 8.46 (8.61 with Imz), noticeably higher than for binary Cu^{II}/oligopeptide systems.[14]

$[CuABH_{-1}]^{2-}$ is five-coordinate with donor sets (N_{py}, N_{lact}) and (NH_2, N^-, COO^-) from Imtz (or Imz) and Gly-Gly, respectively. The geometry is essentially of the square pyramidal type, in which Gly-Gly fills three of the equatorial positions and one nitrogen of the additional ligand is in the equatorial plane, whereas the other occupies a tilted apical site. EPR spectroscopy suggests a geometry derived from the square pyramid, as a $d_{x^2-y^2}$ ground state is substantiated. The rather low value for the Cu^{II} hyperfine constant ($A_{||}$ = $145–148 \times 10^{-4}$ cm^{-1}) could indicate a strong axial interaction of the lactam nitrogen. Most likely, this binding mode is an effect of the sterical hindrance due to the substituents in the position 4 of the imidazolinone ring.

On the whole, stable complexes are formed by imidazolinone ligands with copper(II) in the physiological pH region through the adoption of a 2,2′-bipy-like type of co-ordination that takes advantage of a donor as strong as the lactam nitrogen. The donor set anchors effectively the metal ion and makes the herbicides very competitive toward other ligands. Even an effective bioligand like Gly-Gly is unable to detach the metal ion once bound to Imz or Imz, at least in equimolar solution. Stable mixed complexes can be therefore formed with the participation of the herbicide and oligopeptides.

Techniques used: pH-potentiometry; EPR, Absorption spectroscopy.

Table 2 Spectral parameters for binary and ternary Cu^{II} complexes.

References: 20.

Schemes: 2

Figure 1: Species distribution diagram for Cu^{II}/Imzt system; $c_{Cu(II)}$ = 0.001 M, c_{ligand} = 0.002 M.

Figure 2: EPR spectrum of the $[CuA_2]^{2-}$ species of Imzt (a) and its simulation with the parameters listed in Table 2 (b).

Figure 3: Species distribution diagram for Cu^{II}/Imzt/Gly-Gly system at the molar ratio 1:1:1, $c_{Cu(II)}$ = 0.001 M.

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