Natural Glycine Unidentate on Copper(II): A Novel Mode of Bonding†

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The compound of composition copper(II)-glycinate-picric acid-water (1/2/2/6) has been prepared and its crystal structure determined. It contains a centrosymmetric copper(II) ion, co-ordinated in a distorted octahedron by two water molecules in *trans* positions, two unidentate glycine moieties, linked to the metal in a *trans* arrangement *via* single carboxylate oxygens, and two more distant water molecules. The unidentate glycine species, probably zwitterions, represent an unexpected non-chelated form of the ligand. New similar compounds of (*S*)-alanine and (*S*)-lysine have also been prepared. The nature of the complexed ions in solution ('speciation') is considered.

Complex ions containing natural amino acids co-ordinated to copper(II) are common and important. Among them the copper(II)-glycine system is extremely well known and studied, and is an exemplar in aqueous co-ordination chemistry, and indeed in bioinorganic chemistry, where the copper(II) in the blue blood fraction and elsewhere is bound by amino acids. The first suggestions of the existence of chelation (by Ley,[2] who spoke of 'innere Komplexsalz') related to this very system.

The most common composition is bis(glycinato)copper(II). As is the case for several of the natural amino acids derived by hydrolysing proteins, both geometric isomers of this prototype bis complex with copper(II) are known[3] as solids, although, for glycine, only the *cis* isomer has repaid study[4] by X-ray diffraction: the limited structural information[5] on the *trans* isomer comes from electron diffraction.

Several adducts between phenols and copper(II) ions complexed by glycinate (glyO) are known: they include those[6] of stoichiometry $Cu(glyO)_2 \cdot 2L$ (L = phenol, *m*-cresol or *p*-cresol), originally isolated in early work[7] on paper chromatography, and a different type, where a single example[8] was known, of stoichiometry $Cu(glyO)_2 \cdot 2HOC_6H_2(NO_2)_3$-2,4,6$\cdot 6H_2O$. We have made two more of the latter type, containing (*S*)-alanine and -lysine, which differ in their hydration numbers (n = 4 and 2 respectively). Members of the first type readily lose their content of the phenol, leaving a residue of bis(glycinato)copper(II), apparently the *trans* isomer. We report on those elsewhere. The compound of the second type is made by adding a solution of picric acid $HOC_6H_2(NO_2)_3$-2,4,6 in the correct molar ratio to an aqueous solution of bis(glycinato)copper(II). The resulting solution from which the adduct crystallises has a pH around 2.5–3.0. The compound was first made[8] during work on specific precipitants for constituents of the products of protein hydrolysis, and its initially reported composition is indeed confirmed as $Cu(glyO)_2 \cdot 2L \cdot nH_2O$, where $n = 6$.

Results and Discussion

The remarkable structure of the glycine compound, determined by X-ray crystallography, is shown in Fig. 1. It contains two glycine residues, linked to the copper(II) ion in *trans* positions as unidentate ligands, each through an oxygen atom of its carboxylate function; Cu–O is 1.95 Å. Indeed, the copper ion is at a centre of symmetry. An approximate square of shorter oxygen–copper(II) contacts also contains two water ligands in mutually *trans* positions (Cu–O 2.011 Å). The distorted co-ordination octahedron involves two further water molecules at longer distances (2.299 Å). The units from picric acid and the remaining two water units form part of a weakly hydrogen-bonded network which completes the lattice. The strongest intermolecular hydrogen-bonded contact O(3W)···O(1b) is 2.723 Å (symmetry operator b $-x, -y, -z$). All other contacts are > 3.0 Å.

The stoichiometry is fully established but the location of some protons is not certain. For each copper(II) ion there are two glycinate residues ($glyO^-$), two picrate residues $[OC_6H_2(NO_2)_3]$ and two non-co-ordinated water molecules; two protons are located among them. Possible extreme tautomeric formulations are $[Cu(glyO^-)_2(OH_2)_4] \cdot 2HOC_6H_2(NO_2)_3 \cdot 2H_2O$ **a**, $[Cu(glyOH)_2(OH_2)_4][OC_6H_2(NO_2)_3]_2 \cdot 2H_2O$ **b** and $[Cu(glyO^-)_2(OH_2)_4][H_3O]_2[OC_6H_2(NO_2)_3]_2$ **c** and/or variants among them.

Since the p*K* values of free glycine are[9] 2.36 and 9.57, that of O-co-ordinated glycine is probably about 9; picric acid, with[10] its pK_a of 0.33 at 25 °C, is far more acidic. Consequently, if we were concerned solely with equilibria in solution, formulation **b** would be the more likely.

We therefore describe the structure in terms of the units of O-co-ordinated glycine (as its zwitterion), picrate ion and water of crystallisation, *i.e.* $[Cu(glyOH)_2(OH_2)_4][OC_6H_2(NO_2)_3]_2 \cdot 2H_2O$, but it is conceivable that the protons may be in differing positions of glycinate, picric acid or H_3O^+. For **b** the lattice energy of a crystal formed from formally charged units (a doubly positive copper complex cation with singly anionic picrates) may be advantageous. These putative ions are both large, reducing the force of this consideration. However, the IR spectrum of the crystals shows some unusual features and merits further study in detail. It is suggestive of zwitterionic glycine, supporting our formulation **b**.

Many solid compounds containing α-amino acids and copper(II) ions have known structures. Non-chelated structures involving natural amino acids like glycine are very rare, whatever the metal ion. With copper(II) the present case is the first. There are, of course, unnatural amino acids where the pattern of substitution precludes chelation. Typically, these include the *N*-substituted glycines, like *N*-toluene-*p*-sulfonylglycine. Here, Menabue and co-workers have shown unidentate co-ordination of the highly sterically obstructed ligand through

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† The Isomers of α-Amino Acids with Copper(II). Part 8.[1]

Supplementary data available: see Instructions for Authors, *J. Chem. Soc., Dalton Trans.*, 1995, Issue 1, pp. xxv–xxx.

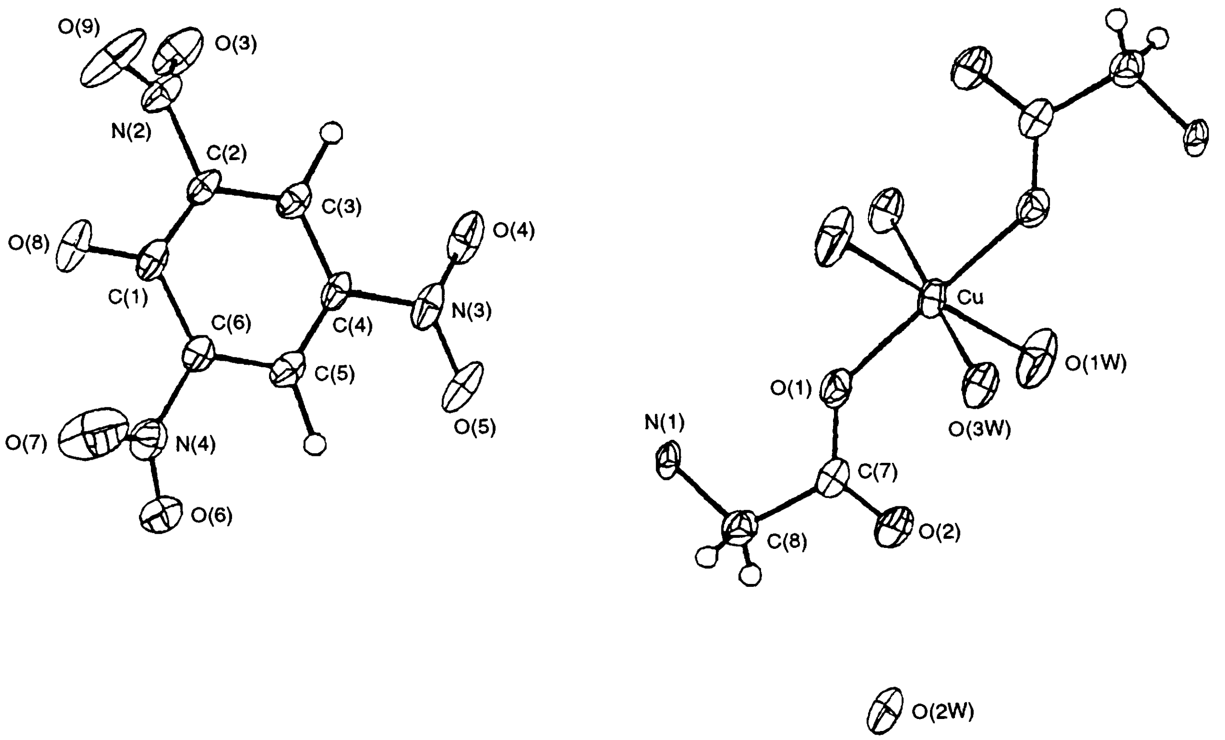

Fig. 1 Atom numbering and relative arrangements of the centrosymmetric $Cu(OH_2)_4(glyO)_2$ unit and the picric acid and water molecules in $Cu(glyO)_2{\cdot}2HOC_6H_2(NO_2)_3$-2,4,6·$6H_2O$. Important bond lengths are: Cu–O(1) 1.950(4), Cu–O(1W) 2.299(5), Cu–O(3W) 2.016(4), C(7)–O(1) 1.260(5), C(7)–O(2) 1.245(5) and C(1)–O(8) 1.257(5) Å

its carboxylate moiety, in the compound aquabis(4-methylpyridine)bis(*N*-toluene-*p*-sulfonylglycinato)copper(II),[11] and a related species[12] bis(μ-*N*-toluene-*p*-sulfonylglycinato-*O*)-bis-[(2,2′-bipyridine)(*N*-toluene-*p*-sulfonylglycinato-*O*)copper(II)]. In view of the steric demands of the toluenesulfonyl substituent, the failure of the substituted glycinate to form a chelate ring in these solids is predicted. With less sterically demanding *N*-substituents, bidentate ligation may be observed. The *trans*-bis isomer is of course favoured over the *cis* for such hindered systems with tertiary amines in the amino acid. Examples are square-planar[13] *trans*-bis[*N*,*N*-diethyl(*S*)-alaninato]copper(II) and five-co-ordinated[14] *trans*-aqua bis-(*N*,*N*-dimethylglycinato)copper(II).

The mere existence of a metastable picrate-containing copper(II) ion is itself noteworthy, in view of the renowned hazard in mixing the two (this, of course, caused the premature explosion of many defect shells in the Great War). There are few other crystalline compounds of copper(II) containing picric acid or picrate. These include the adducts[15] with complexes of tetradentate Schiff bases which are possibly akin to a number of intercalated adducts between picric acid and other flat co-ordination compounds, chiefly of 8-hydroxyquinolinate.[16] (Acetylacetonato)diaquacopper(II) picrate,[17] made by carefully displacing a chelated acetylacetonate (acac, pentane-2,4-dionate) from bis(acetylacetonato)copper(II) with moist picric acid, seems to be the only other compound anything like the present one. In that compound, studied initially using photographic detection,[17a] and later, on the same crystal, with a diffractometer, the copper ion has[17b] a quasi-octahedral environment. Four shorter bonds in plane (Cu–O of acac, 1.891 Å: Cu–O of water, 1.963 Å) are augmented by long bonds in the perpendicular axis to the phenoxide of the next layer (Cu–O 2.784 Å) and a short contact to the central carbon atom of the β-diketonate (Cu–C 3.13 Å). Most remarkably,[17b] the phenoxide oxygen of picrate is bent quite severely out of its aromatic plane toward the copper ion, again indicating a bonding interaction. This conformation of a picric acid moiety is consistent with the relatively non-aromatic character of such highly nitrated molecules.

In the present compound the framework of the picric acid moiety is undistorted and seems to serve merely to stabilise the lattice. While its 4-nitrophenoxide moiety is essentially planar, the nitro-groups in its 2 and 6 positions are canted equally relative to the plane. King's compounds[18] $Cu(py)_n[OC_6H_2(NO_2)_3]_2$ (py = pyridine; $n = 2$, light green; $n = 5$, deep green) are true ionised picrates and their properties are given in the Experimental section. Whether the picrate is a gegenion or a ligand to copper(II) is not clear. Dipyridinecopper(II) picrate is made by adding ammonium picrate in stoichiometric amounts to an aqueous dilute solution of $CuCl_2$, in the presence of an excess of pyridine. The dark green pentapyridinecopper(II) picrate is made by recrystallising the dipyridine compound from boiling pyridine. Complex ions with more than four pyridine ligands on any metal ion are similarly unusual, so it seems probable that at least one molecule of pyridine in the pentakis compound is merely 'solvent of crystallisation'.

Solution Equilibria.—The present copper(II) cation may be regarded as an intermediate in the formation or dissociation of chelated glycine. Structures of this kind are not commonly invoked in solution equilibria, because of the expected dominance of the chelate effect. There are a few examples, like $[Pt(glyO)_4]^{2-}$ (all seem to be *N*-bonded), of unidentate amino acids in kinetically inert systems, isolated as metastable intermediates with long half-lives. Particularly striking in the picrate is the presence of two unidentate ligands in a compound isolated from a kinetically labile system. Kinetic studies of the mechanism of acid dissociation of chelated amino acids have occasionally suggested the intermediacy of unidentate ligands, but it is rare that they can be studied in isolation.

Irving and Pettit[9] measured log β_{111} for reaction (1) (alaO =

$$Cu^{2+} + (S)\text{-alaO}^- + H^+ \longrightarrow [Cu\{(S)\text{-alaO}\}(H)]^{2+} \quad (1)$$

Table 1 Analyses of the copper picrates (calculated values in parentheses)

	Analysis (%)				
Complex[a]	C	H	N	Cu	Ref.
$Cu(glyO)_2 \cdot 2HOC_6H_2(NO_2)_3 \cdot 6H_2O$	24.3 (24.7)	3.4 (3.35)	14.4 (14.4)	8.2 (8.15)	*b*, *c*
$Cu(glyO)_2 \cdot 2HOC_6H_2(NO_2)_3$	28.4 (28.65)	2.15 (2.10)	16.95 (16.75)	9.35 (9.50)	8
$Cu[(S)\text{-}alaO]_2 \cdot 2HOC_6H_2(NO_2)_3 \cdot 4H_2O$	28.0 (28.1)	2.9 (3.40)	14.4 (14.55)	8.3 (8.25)	*b*
$Cu[(S)\text{-}lysO]_2 \cdot 2HOC_6H_2(NO_2)_3 \cdot 2H_2O$[d]	33.6 (34.0)	4.5 (4.30)	16.2 (16.5)	7.6 (7.50)	*b*
$Cu(py)_2[OC_6H_2(NO_2)_3]_2$	37.4 (39.0)	2.0 (2.10)	16.5 (16.55)	8.9 (9.35)	*b*
				9.6	18
$Cu(py)_5[OC_6H_2(NO_2)_3]_2$	44.9 (48.55)	2.9 (3.20)	16.7[e] (16.85)	6.7 (6.95)	*b*
				6.95	18

[a] The formulae denote stoichiometries rather than structural elements: as discussed in the text, the first compound is almost certainly $Cu(glyOH)[OC_6H_2(NO_2)_3]_2 \cdot 6H_2O$. [b] This work. [c] Ref. 8 reports 'water of crystallisation' 13.95 (Calc. 13.90)%. The other analyses of ref. 8 quoted here are for the anhydrous residue. [d] lysO = Lysinate. [e] The mass loss of this compound on standing corresponds closely to three molecules of pyridine.

alaninate). The corresponding potentiometric value seems not to have been determined for glycine. The above 1 : 1 : 1 product was a solution species of unknown structure, but it was pointed out,[9] in that connection, that it would be 'not very stable since it is no longer able to form a chelate'. This remark applies with more force to our case, since here the species is not 1 : 1 : 1, with one chelate ring lost, but 1 : 2 : 2 with two chelate rings lacking.

Years ago, careful potentiometric and calorimetric work by Letter and Bauman[19] supported the opinion of Pearlmutter and Stuehr[20] that amino-acid zwitterions do not interact with copper(II) (*i.e.* that the amino acid does not function as a unidentate ligand). This conclusion has held sway since. However, the present work shows the need to modify it. Gotsis and Fiat,[21] using ^{17}O and ^{14}N paramagnetic relaxation rates, did include the following species in their description of the copper(II)–glycine system (G = glycinate anion), $CuHG^{2+}$, $CuHG_2^{+}$ and $CuHG_3$, but said that '$Cu(HG)_2^{2+}$ was not considered as a major species, and there was no compelling evidence to the contrary'. The existence and nature of the present solid copper(II) salt, which contains that very ion, suggests that natural amino acids unidentate on metal ions may well need incorporating into a revised view of the complex compounds actually present in equilibria in aqueous solution.

The present picrate is (quite apart from its unidentate ligands) also of interest as the first unsubstituted *trans*-bis(glycinato)copper(II) species the structure of which has been solved by X-ray diffraction, although we have recently made the novel adduct of formula $[Cu(glyO)_2] \cdot 2AgNO_3$, which contains *trans*-bis(chelated glycinato)copper(II), as opposed to the unidentate glycine zwitterion here. The geometric isomers of such species as $[CuH(glyO)_2]^+$ or $[Cu(glyO)_3]^-$ are, perhaps surprisingly, not considered in most solution studies.

Experimental

Analyses are given in Table 1. Copper was determined by electrodeposition from a mildly acidic solution.

trans-*Diaquabis(glycine)copper*(II) *Picrate Hydrate*.—The complex $Cu(glyO)_2 \cdot 2HOC_6H_2(NO_2)_3 \cdot 6H_2O$ was made following the detailed directions of Selim *et al.*[8] The similar compounds with other natural α-amino acids of Table 1 were made in the same way. The transmission IR spectrum of a single crystal (recorded using a Nicolet FTIR microscope) showed major absorptions (in cm^{-1}) at 3200vs (vbr), 2520vvw, 2501vvw, 2440vw, 2291w, 2280wm, 2230w (br), 2106vw, 2094vw, 1874w, 1840m, 1595vs, 1491s, 1452s, 1378s, 1346vs, 1301 (sh), 1284s, 1179m, 1112m, 1099m, 1018m and 905s.

$Cu(py)_2[OC_6H_2(NO_2)_3]_2$.—To a stirred aqueous solution (100 cm^3) of copper(II) chloride dihydrate (5 g, 0.03 mol) was added pyridine (20 g, 0.25 mol). Picric acid (14.7 g, 0.064 mol), which had previously been converted into its ammonium salt in water (1300 cm^3), was added to the blue suspension. Dipyridinecopper(II) picrate separated immediately in excellent yield, and was filtered off and stored in a desiccator over P_2O_5.

$Cu(py)_5[OC_6H_2(NO_2)_3]_2$.—Pentapyridinecopper(II) picrate was prepared by dissolving the dipyridine salt obtained above in four times its own weight of boiling pyridine. The filtered deep green solution was left in a desiccator over concentrated sulfuric acid overnight, after which large deep green plates had separated. Once the crystals are removed from their mother liquor they start to decompose, and a sample was quantitatively converted into the blue dipyridinecopper(II) picrate by standing in air for 24 h. A known mass of pentapyridinecopper(II) picrate (0.071 g) was left open to the air and its decomposition followed for 24 h. The final mass was 0.053 g, corresponding to a loss of 25.6% [calc. 26% for three pyridines, as in equation (2)]. After

$$Cu(py)_5[OC_6H_2(NO_2)_3]_2 \longrightarrow Cu(py)_4[OC_6H_2(NO_2)_3]_2 \longrightarrow Cu(py)_2[OC_6H_2(NO_2)_3]_2 \quad (2)$$

1 h the residual mass was 0.0656 g, and after 5 h, 0.0653 g. This would correspond to the loss of one pyridine (7.1%).

Several attempts to determine the crystal structure failed because the crystals decomposed: one crystal encapsulated in araldite on a glass fibre did yield the cell dimensions a = 12.6256, b = 15.3529, c = 17.7002 Å, α = 100.218, β = 95.342 and γ = 94.519°, but it was not possible to proceed with a data collection.

Structure Determination of trans-*Diaquabis(glycine)copper*(II) *Picrate Hydrate*.—*Crystal data*. $C_{16}H_{26}CuN_8O_{24}$, M_r = 777.965, triclinic, space group $P\bar{1}$, a = 6.441(5), b = 7.931(6), c = 15.233(10) Å, α = 104.27(1), β = 92.16(1), γ = 107.23(1)°, U = 715.1(9), Z = 1, D_c = 1.806 g cm^{-3}, μ(Mo-Kα) = 7.96 cm^{-1}, F(000) = 399, T = 291 K, crystal dimensions 0.10 × 0.12 × 0.18 mm.

5876 Data were recorded using a FAST TV area detector diffractometer[22] with Mo-Kα radiation (λ = 0.710 69 Å). 2832 Data were unique (R_{int} = 0.035), of which 2372 were observed [$F_o > 3\sigma(F_o)$]. The structure was solved by direct methods,[23] and refined *via* full-matrix least squares.[24] Non-hydrogen atoms were anisotropic, organic hydrogens isotropic, but water, carboxylate and phenol H atoms were not located. The final R value (unit weights) was 0.0437. The data were corrected for absorption using the DIFABS method[25] with minimum and maximum absorption corrections of 0.915 and 1.091. Final atomic fractional coordinates are listed in Table 2.

Table 2 Fractional atomic coordinates (× 10^4) for $[Cu(glyOH)_2(OH_2)_4][OC_6H_2(NO_2)_3]_2 \cdot 2H_2O$

Atom	*x*	*y*	*z*
Cu	0	0	0
O(1)	2 788(4)	1 516(3)	723(1)
O(2)	2 896(4)	4 302(3)	605(2)
O(3)	7 269(5)	−4 569(3)	5 427(2)
O(4)	6 838(5)	−1 530(4)	3 109(2)
O(5)	7 813(5)	1 424(4)	3 495(2)
O(6)	10 618(5)	4 582(3)	6 617(2)
O(7)	8 686(7)	3 708(5)	7 617(2)
O(8)	7 595(4)	−5(3)	7 349(1)
O(9)	5 832(7)	−3 707(4)	6 631(2)
N(1)	6 362(5)	2 613(4)	1 851(2)
N(2)	6 706(5)	−3 410(4)	5 963(2)
N(3)	7 368(4)	−36(4)	3 688(2)
N(4)	9 237(5)	3 424(4)	6 858(2)
C(1)	7 607(5)	4(4)	6 525(2)
C(2)	7 064(5)	−1 644(4)	5 773(2)
C(3)	6 990(4)	−1 664(4)	4 869(2)
C(4)	7 470(4)	−26(4)	4 638(2)
C(5)	8 198(5)	1 644(4)	5 300(2)
C(6)	8 263(5)	1 631(4)	6 203(2)
C(7)	3 628(5)	3 231(4)	898(2)
C(8)	5 749(5)	4 047(4)	1 539(2)
O(1W)	−1 265(5)	−430(5)	1 346(2)
O(2W)	4 073(4)	8 017(3)	1 183(2)
O(3W)	−1 234(4)	2 104(3)	197(2)

Additional material available from the Cambridge Crystallographic Data Centre comprises H-atom coordinates, thermal parameters and remaining bond lengths and angles.

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