Crystal Structure of Aqua(glycyl)-L-tryptophanatocopper(II) Dihydrate

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The crystal structure of the title compound has been determined by the heavy-atom method from a three-dimensional *X*-ray diffraction study. Least-squares refinement, based on 1 119 visually estimated independent reflections, has reduced *R* to 0.109. Crystals are orthorhombic, *a* = 7.74(4), *b* = 13.78(3), *c* = 14.81(3) Å, space group $P2_12_12_1$ and *Z* = 4.

In the complex the peptide molecule behaves as a terdentate chelate *via* its terminal amino-group, peptide nitrogen atom, and the carboxylate ion. The single peptide nitrogen is deprotonated. The Cu^{II} atom has co-ordination number 4, the peptide atoms and one water molecule forming an approximate square.

TRYPTOPHAN is one of the naturally occurring amino-acids. It is a precursor of neurochemically important compounds and chemically related to a group of psychopharmaca. Several structure determinations of tryptophan derivatives have been carried out.[1-5] The present *X*-ray analysis was undertaken since the title complex is the first-reported metal–peptide structure in which one of the peptide residues is tryptophan. A preliminary account has been published.[6]

EXPERIMENTAL

A deep blue solution of the title complex was prepared by reaction of equimolar amounts of either (*a*) freshly precipitated $Cu(OH)_2$ or (*b*) $CuCO_3$ with glycyl-L-tryptophan. The reactions were accelerated by warming. The complex separated as deep blue plate-like crystals.

Crystal Data.—$C_{13}H_{15}CuN_3O_4\cdot 2H_2O$, *M* = 376.9, Orthorhombic, *a* = 7.74(4), *b* = 13.78(3), *c* = 14.81(3) Å, U = 1 580 Å^3, D_m (by flotation) = 1.57, *Z* = 4, D_c = 1.58 g cm^{-3}, *F*(000) = 780. Space group $P2_12_12_1$. Cu-K_α radiation, λ = 1.5418 Å; μ(Cu-K_α) = 25.2 cm^{-1}. Unit-cell dimensions were determined from high-angle reflections on Weissenberg photographs.

Intensity data were collected for a crystal *ca.* 0.25 × 0.22 × 0.15 mm by use of Cu-K_α radiation and a Weissenberg camera. Layers 0—4*kl*, *h*0—7*l*, and *hk*0—3 were

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recorded by the equi-inclination technique. Intensities were estimated visually from multiple-film exposures by comparison with a calibrated wedge. Layers were scaled by hand using reflections common to more than one layer, resulting in 1 119 unique non-zero reflections. Data were corrected for Lorentz and polarization effects. For the non-zero layers the Phillips spot-shape correction was applied.[7]

Solution and Refinement of the Structure.—The structure was solved using programs of refs. 8 and 9 and refined using the program system '*X*-Ray '63 '.[9] Calculations were carried out in the earlier stages on an IBM 1130 and later on an Atlas computer.

A three-dimensional Patterson synthesis revealed the position of the copper atom, which was used in a structure-factor calculation for which R was 0.44. The remaining non-hydrogen atoms were located from successive difference syntheses. All atomic co-ordinates together with individual isotropic temperature factors, and the seventeen scale factors, were refined for three cycles of full-matrix least-squares and gave R 0.12. Three more cycles of refinement, computed with the copper atom assigned anisotropic temperature factors, gave R 0.11. In the final stages of refinement, a weighting scheme of the type suggested by Hughes[10] was used, where $w = 1$ for $F < F^*$ and $\sqrt{w} = F/F^*$ for $F > F^*$, with $F^* = 15$ found to be optimum. The final value of R was 0.108. The function minimised in the least-squares refinement was $\Sigma w(F_o - F_c)^2$. Atomic scattering factors were taken from ref. 11 and the real and imaginary parts of the anomalous dispersion correction for copper from ref. 12. A final difference-Fourier showed no significant peaks. Final atomic parameters are given in Table 1. Observed and calculated structure amplitudes are listed in Supplementary Publication No. SUP 21494 (5 pp., 1 microfiche).*

TABLE 1

Final fractional co-ordinates (×10^4) and thermal parameters, with estimated standard deviations in parentheses

Atom	x	y	z	B/Å^2
Cu	163(3)	382(2)	1 787(1)	*
O(1)	−640(13)	1 571(8)	4 217(6)	2.9(2)
O(2)	−2 384(14)	494(8)	1 268(7)	3.3(2)
O(3)	−4 999(18)	1 088(10)	1 530(8)	4.0(2)
O(4)	825(18)	−245(10)	715(9)	4.5(2)
O(5)	4 193(19)	−748(11)	708(10)	5.0(3)
O(6)	868(19)	3 316(11)	5 082(11)	5.6(3)
N(1)	2 111(19)	329(12)	2 563(10)	3.8(3)
N(2)	−966(17)	1 101(11)	2 750(8)	3.1(2)
N(3)	−758(21)	3 414(12)	398(10)	4.4(3)
C(1)	1 692(20)	791(20)	3 462(10)	2.8(3)
C(2)	−131(21)	1 189(11)	3 485(9)	2.5(2)
C(3)	−2 792(19)	1 434(13)	2 616(10)	2.9(3)
C(4)	−3 460(18)	991(13)	1 773(10)	2.8(3)
C(5)	−2 867(19)	2 564(13)	2 515(9)	2.7(2)
C(6)	−1 814(21)	3 000(14)	1 791(12)	3.4(3)
C(7)	−2 160(26)	3 076(16)	878(13)	4.4(4)
C(8)	621(19)	3 565(12)	1 010(9)	2.6(2)
C(9)	2 278(23)	3 951(15)	856(11)	3.7(3)
C(10)	3 355(22)	3 960(15)	1 587(12)	3.9(4)
C(11)	2 824(20)	3 655(14)	2 432(11)	3.1(3)
C(12)	1 147(19)	3 307(13)	2 592(10)	2.9(3)
C(13)	19(20)	3 284(12)	1 846(9)	2.9(2)

* Anisotropic tmperature factors (×10^4) in the form [exp $-(\beta_{11}h^2 + \beta_{22}k_2 + \beta_{33}l^2 + 2\beta_{12}hk + 2\beta_{13}hl + 2\beta_{23}kl)$], with standard deviations given in parentheses, and parameters:

Atom	β_{11}	β_{22}	β_{33}	β_{12}	β_{23}	β_{23}
Cu	144(3)	48(1)	34(1)	9(3)	9(2)	−4(1)

DESCRIPTION OF THE STRUCTURE AND DISCUSSION

The molecular structure is shown in Figure 1.[13] The complex is monomeric and the central copper atom has square-planar co-ordination. The peptide molecule behaves as a terdentate chelate *via* its terminal amino group, peptide nitrogen atom, and carboxylate group, the fourth position being occupied by a water molecule. The single peptide nitrogen N(2) is deprotonated, and planar (see Table 2). There are other examples of Cu^{II} peptide complexes with square-planar co-ordination.[14,15] The

TABLE 2

Molecular geometry

(*a*) Bond lengths (Å)

Cu–O(2)	1.960(11)	C(9)–C(10)	1.37(2)
Cu–O(4)	1.935(13)	C(10)–C(11)	1.38(2)
Cu–N(2)	1.879(13)	C(11)–C(12)	1.40(2)
Cu–N(1)	2.039(14)	C(12)–C(13)	1.41(2)
O(2)–C(4)	1.31(2)	C(13)–C(8)	1.38(2)
C(4)–O(3)	1.25(2)	C(8)–C(9)	1.41(2)
C(4)–C(3)	1.48(2)	C(8)–N(3)	1.42(2)
C(3)–N(2)	1.50(2)	N(3)–C(7)	1.38(3)
N(2)–C(2)	1.27(2)	C(7)–C(6)	1.38(3)
C(2)–O(1)	1.27(2)	C(6)–C(13)	1.47(2)
C(2)–C(1)	1.51(2)	C(6)–C(5)	1.48(2)
C(1)–N(1)	1.51(2)	C(5)–C(3)	1.57(3)

(*b*) Bond angles (°)

O(2)–Cu–O(4)	92.2(5)	C(1)–N(1)–Cu	108(1)
O(2)–Cu–N(2)	85.1(5)	C(9)–C(10)–C(11)	122(2)
N(2)–Cu–N(1)	84.2(6)	C(10)–C(11)–C(12)	122(1)
N(1)–Cu–O(4)	98.8(6)	C(11)–C(12)–C(13)	117(1)
Cu–O(2)–C(4)	114(1)	C(12)–C(13)–C(8)	199(1)
O(2)–C(4)–C(3)	118(1)	C(13)–C(8)–C(9)	124(1)
O(2)–C(4)–O(3)	120(1)	C(8)–C(9)–C(10)	116(2)
C(3)–C(4)–O(3)	122(1)	C(13)–C(8)–N(3)	106(1)
C(4)–C(3)–C(5)	108(1)	C(8)–N(3)–C(7)	108(1)
C(4)–C(3)–N(2)	109(1)	N(3)–C(7)–C(6)	112(2)
C(5)–C(3)–N(2)	110(1)	C(7)–C(6)–C(13)	103(1)
C(3)–N(2)–Cu	114(1)	C(6)–C(13)–C(8)	111(1)
C(3)–N(2)–C(2)	125(1)	C(12)–C(13)–C(6)	130(1)
Cu–N(2)–C(2)	121(1)	C(9)–C(8)–N(3)	130(1)
N(2)–C(2)–O(1)	128(2)	C(13)–C(6)–C(5)	127(1)
N(2)–C(2)–C(1)	115(1)	C(7)–C(6)–C(5)	129(2)
O(1)–C(2)–C(1)	117(1)	C(6)–C(5)–C(3)	117(1)
C(2)–C(1)–N(1)	112(1)		

(*c*) Selected intramolecular contacts (Å)

C(3) ··· O(1)	2.90	C(5) ··· O(3)	3.00
C(5) ··· O(2)	3.42	C(13) ··· N(2)	3.37
N(1) ··· O(5)	3.51	C(2) ··· C(12)	3.35
C(12) ··· N(2)	3.45	C(12) ··· C(6)	2.62
C(5) ··· C(12)	3.27	O(1) ··· C(5)	3.35
C(3) ··· C(13)	3.54	O(4) ··· O(2)	2.81
C(4) ··· C(7)	3.32	C(6) ··· O(2)	3.57
N(2) ··· C(6)	3.04	C(3) ··· C(7)	3.46
C(4) ··· C(6)	3.05	N(1) ··· O(4)	3.02
C(2) ··· C(5)	3.18		

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* See Notice to Authors No. 7, in *J.C.S. Dalton*, 1974, Index issue (items less than 10 pp. are supplied as full-size copies).

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copper(II)-ligand bond lengths and also the angles at the bonded ligand atom in this complex agree well with those in other Cu^{II} peptides.[16] Calculation of the least-squares plane through the four ligand atoms (Table 3) shows the co-ordination plane to have a slight tetrahedral distortion. The bond distances and angles in the chelate rings are normal.[16] The peptide group C_α–CO–N–C_α[1] and the carbonyl groups are planar. The geometry of the tryptophan residue is in agreement with the values found for the free acid,[2-5] but the C(8)–N(3) distance [1.42(2) Å] does not agree with that (1.31 Å) reported by Pasternak.[1]

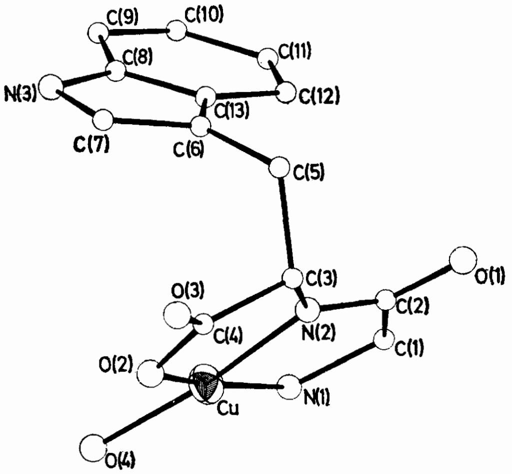

FIGURE 1 The molecular structure [free water molecules O(5) and O(6) are omitted]

A significant feature of this structure is the sandwiching of the copper square-plane by two tryptophan residues, one from the same molecule and one from a neighbouring molecule (Figure 2).[13] The angle between the square plane and the plane of the tryptophan residue from the same molecule is 50°; that between the square plane and that of the tryptophan residue from the neighbouring molecule is, however, only 13°, and the planes are quite close, the shortest approach to copper being Cu ··· C(12) 3.12 Å (Table 4). Similar intermolecular contacts Cu ··· C(Ph) (3.01—3.27 Å) have been found.[17-19] It has been suggested that a weak interaction exists between the Cu^{2+} ions and the aromatic rings of the tyrosine groups,[17,19] and a similar effect could occur in the present complex: the sum of the van der Waals radii, estimated to be between 3.5 and 4.1 Å, is significantly larger than the observed shortest contact (3.12 Å).

TABLE 3

Equations of planes through various atoms in the form $Ax + By + Cz = D$, with deviations (Å) of relevant atoms from the planes in square brackets

	A	*B*	*C*	*D*
Plane (*A*): O(2), O(4), N(1), N(2)	2.177	11.993	−5.987	−0.609
[O(2) −0.077, O(4) 0.066, N(1) −0.071, N(2) 0.083, Cu −0.007]				
Plane (*B*): N(3), C(6)—(13)	−2.377	12.856	2.780	−4.726
[N(3) −0.046, C(6) 0.059, C(4) −0.014, C(8) −0.010, C(9) 0.050, C(10) 0.008, C(11) −0.023, C(12) −0.027, C(13) 0.004]				
Plane (*C*): Cu, O(2), N(2), C(3), C(4)	2.191	11.457	−7.081	−0.857
[Cu 0.015, O(2) 0.001, N(2) −0.031, C(3) 0.035, C(4) −0.022]				
Plane (*D*): Cu, N(1), N(2), C(1), C(2)	2.626	11.910	−5.499	−0.501
[Cu −0.044, N(1) 0.038, N(2) 0.057, C(1) −0.017, C(2) −0.034]				
Plane (*E*): O(1), N(2), C(1)—(3)	2.616	12.274	−4.501	−0.140
[O(1) 0.003, N(2) 0.012, C(1) −0.005, C(2) −0.003, C(3) −0.008]				

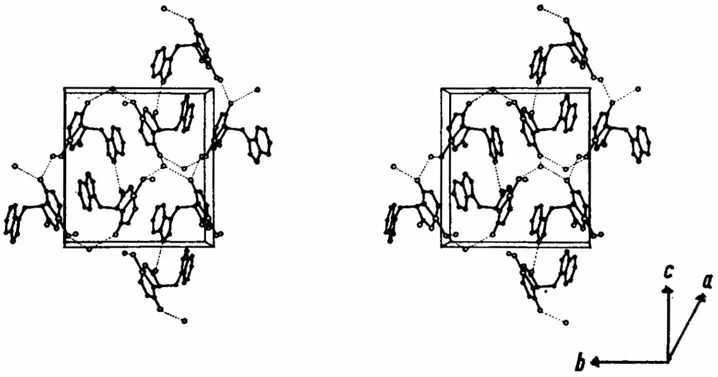

FIGURE 2 A stereoscopic view showing the packing

There also appears to be extensive hydrogen bonding in the structure (Figure 2). No attempt was made to locate hydrogen atoms but their presence in hydrogen bonds has been inferred by consideration of interatomic

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TABLE 4

(*a*) Possible hydrogen bonded contacts (Å) X ·· H ··· Y

Atom X		Atom Y		Atom X		Atom Y	
O(5)	···	O(4)	2.70	O(1)	···	O(5$^{\mathrm{II}}$)	2.72
O(6)	···	O(1)	2.96	N(3)	···	O(3$^{\mathrm{IV}}$)	2.99
O(5)	···	O(3$^{\mathrm{I}}$)	2.88	O(6)	···	O(4$^{\mathrm{V}}$)	2.65
N(1)	···	O(3$^{\mathrm{I}}$)	2.91	O(6)	···	O(1$^{\mathrm{VII}}$)	2.90

(*b*) Bond angles at hydrogen-bond donors and acceptors (°)

O(5) ··· O(4)–Cu	117	C(2)–O(1) ··· O(5$^{\mathrm{II}}$)	113
O(6) ··· O(1)–C(2)	126	N(3) ··· O(3$^{\mathrm{IV}}$)–C($^{\mathrm{IV}}$)	119
O(5) ··· O(3$^{\mathrm{I}}$)–C(4$^{\mathrm{I}}$)	104	O(6) ··· O(4$^{\mathrm{V}}$)–Cu$^{\mathrm{V}}$	122
N(1) ··· O(3$^{\mathrm{I}}$)–C(4$^{\mathrm{I}}$)	123	O(1) ··· O(6) ··· O(1$^{\mathrm{VII}}$)	124
O(5) ··· O(4) ··· O(6$^{\mathrm{IV}}$)	106		

(*c*) All other van der Waals distances less than 3.60 Å

O(5) ··· C(4$^{\mathrm{I}}$)	3.40	C(6) ··· N(1$^{\mathrm{V}}$)	3.36
O(5) ··· O(2$^{\mathrm{I}}$)	3.26	C(11) ··· C(4$^{\mathrm{V}}$)	3.46
O(5) ··· C(1$^{\mathrm{III}}$)	3.40	Cu ··· C(13$^{\mathrm{VI}}$)	3.53
O(5) ··· C(2$^{\mathrm{III}}$)	3.43	Cu ··· C(12$^{\mathrm{VI}}$)	3.12
C(9) ··· O(2$^{\mathrm{IV}}$)	3.25	O(4) ··· C(12$^{\mathrm{VI}}$)	3.55
C(11) ··· Cu$^{\mathrm{V}}$	3.40	O(2) ··· C(12$^{\mathrm{VI}}$)	3.58
C(11) ··· O(2$^{\mathrm{V}}$)	3.20	N(1) ··· C(13$^{\mathrm{VI}}$)	3.38

Superscripts refer to the following transformations of the atomic co-ordinates x,y,z: I $1 + x,y,z$; II $\frac{1}{2} - x, -y, \frac{1}{2} + x$; III $\frac{1}{2} - x, -y, -\frac{1}{2} + z$; IV $\frac{1}{2} + x, \frac{1}{2} - y, -z$; V $-x, \frac{1}{2} + y, \frac{1}{2} - z$; VI $-x, \frac{1}{2} + y, \frac{1}{2} - z$; VII $\frac{1}{2} + x, \frac{1}{2} - y, 1 - z$.

distances and angles. Chains of molecules lie parallel to the *ac* plane at $y = 0$ and $y = \frac{1}{2}$. The co-ordinated water acts as a hydrogen donor to the other two water molecules, each of which bond also to the carbonyl oxygen atoms. Further hydrogen bonding also occurs between the peptide and tryptophan nitrogen atoms and the carbonyl oxygen of the carboxyl group. Details of these interactions are listed in Table 4. These hydrogen bond distances and angles are similar to those found previously.[20-23]

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[5/319 *Received*, 17*th February*, 1975]

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