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The Reaction of CuO with L-lysine

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Abstract

The reaction of CuO with L-lysine in boiling water results in the formation of the unusual product [bis(3,4,5,6-tetrahydropicalinate)Cu(II)]$\cdot$8H$_2$O. The complex, $C_{12}H_{32}CuN_2O_{12}$, $M_r = 459.9$, crystallizes in the triclinic space group $P\bar{1}$ with $Z = 1$. Cell dimensions are: $a = 10.713(5)$, $b = 7.321(4)$, $c = 6.907(4)$ Å, $\alpha = 107.66(5)$, $\beta = 90.55(5)$, $\gamma = 95.85(5)°$, $V = 513.0$ Å^3. The structure was refined to $R = 0.038$ and $R_w = 0.051$. The complex is centrosymmetric with the copper atom at the (0, 0, 0) inversion center. The geometry around the copper atom is essentially (4 + 2)-elongated octahedron. The ligand 3,4,5,6-tetrahydro picolinic acid which is obtained by oxidation of L-lysine to the corresponding α-keto acid followed by cyclization, adopts the expected half-chain conformation. The water molecules of hydration adopt an unusual hexagonal arrangement.

Introduction

The complexation of Cu(II) by amino acids has been extensively studied. Many copper–amino acids complexes have been prepared and structurally characterized [1].

We have been studying the complexation of Cu(II) by L-lysine and have found that different products can be obtained, depending on the starting copper salt and on the pH of the reaction mixture. In this paper we wish to report on an unusual product which is obtained from the reaction of CuO with L-lysine in boiling water.

Experimental

Synthesis of Bis(3,4,5,6-tetrahydropicolinate)copper(II)-8-water

5 g of L-lysine and 2.5 g of CuO in 20 ml of distilled water were refluxed for 6 h. The mixture was then cooled to room temperature and filtered. Slow evaporation of the resulting blue–green solution gave good quality crystals of the titled compound. The complete stoichiometry was obtained from the solution of the structure. The compound can be recrystallized from hot ethanol*.

Crystallography and Structure Determination

A suitable dark green crystal of dimensions 0.33 X 0.17 X 0.33 mm was mounted on a glass fiber with epoxy cement and placed on a Philips 1100/20 four-circled automated diffractometer. Accurate cell parameters were obtained from 25 carefully centered reflections. Details of data collection and crystal parameters are summarized in Table I.

Intensities were collected with graphite-monochromated Mo Kα radiation. Apparatus and crystal stabilities were monitored by three reference reflections. No fluctuations higher than 5% were detected.

The structure was solved by the heavy atom method. The copper atom was located by a Patterson map at (0, 0, 0) and the remaining light atoms by successive difference Fourier maps. Calculations were performed by the SHELX 77 package [2]. Scattering factor tables for C, O and N were taken from Cromer and Mann [3], for H from Davidson and Simpson [4], and for Cu from International Tables for X-ray Crystallography, Vol. IV. The correct assignment of the various atoms of the ligand was possible only at the final stages of the refinement. Hydrogen atoms were placed at their correct positions after all the nonhydrogen atoms were refined anisotropically. The structure was further refined by allowing the hydrogen atoms to shift isotropically. Unit weights were introduced initially, and statistical weights at the final stages of the refinement. A difference Fourier map at $R = 0.039$ showed no electron densities higher than 0.4 e Å^{-3}. Final atomic coordinates are listed in Table II**.

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*Recrystallization from hot ethanol leads to the titled compound but with only two water of hydration. *Anal.* Calc. for $C_{12}H_{20}O_6N_2Cu$: C, 40.96; H, 5.69; N, 7.96. Found: C, 41.70; H, 6.01; N, 7.57%.

**See also 'Supplementary Material'.

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TABLE I. Crystallographic Data and Refinement Details

Formula	$Cu(C_6H_8O_2N)_2 \cdot 8H_2O$
Formula weight	459.9
$F(0, 0, 0)$	243
a (Å)	10.713(5)
b (Å)	7.321(4)
c (Å)	6.907(4)
α (deg)	107.66(5)
β (deg)	90.55(5)
γ (deg)	95.85(5)
V (Å^3)	513.0
Z	1
Space group	$P\bar{1}$
D_m (in syn-tetrabromoethane + toluene) (g cm^{-3})	1.480
D_c (g cm^{-3})	1.489
Radiation	Mo Kα
μ(Mo Kα) (cm^{-1})	11.62
Scan mode	$\omega/2\theta$
Scan speed (° ω min^{-1})	1.5
Scan width (° ω)	1.15
Angular range (2θ deg)	5–50
Monitored reflections	(110), ($\bar{2}$00), (10$\bar{1}$)
Background time at each side of the peak (s)	10
No. of unique reflections	1793
No. of unobserved reflections	108
No. of reflections at the final refinement stage	1685
Criterion for omission of F_{obs}	$F_o > 1.5\sigma(F_o)$
Number of refined parameters	196
R^a	0.038
$R_w{}^b$	0.051
Weighting scheme	$2.255/(\sigma^2(F_o) + 0.0002(F_o)^2)$

$^aR = \Sigma|\Delta|/\Sigma|F_o|$. $^bR_w = \Sigma(w^{1/2}|\Delta|)/\Sigma w^{1/2}F_o$.

TABLE II. Final Fractional Coordinates for Nonhydrogen Atoms are $\times 10^4$ and for Hydrogens $\times 10^3$. Equivalent Temperature Factors $(U_{eq})^a$ are $\times 10^4$ and Isotropic Temperature Factors $\times 10^2$. e.s.d.s are shown in Parentheses

Atom	x	y	z	U_{eq}
Cu	0	0	0	393(1)
O(1)	1079(2)	2450(2)	630(3)	413(4)
O(2)	1020(2)	5584(3)	2047(3)	487(5)
N(1)	−1222(2)	1675(3)	1487(3)	361(5)
C(1)	−831(2)	3465(3)	2027(4)	340(5)
C(2)	−1576(3)	5056(4)	3038(5)	461(7)
C(3)	−2925(4)	4361(6)	3126(9)	799(13)
C(4)	−3141(4)	2508(6)	3376(9)	812(14)
C(5)	−2490(3)	1013(5)	1891(7)	502(8)
C(6)	528(2)	3915(4)	1550(4)	365(5)
OW(1)	836(2)	−479(3)	3387(4)	508(5)
OW(2)	3757(3)	3633(5)	1391(5)	710(8)
OW(3)	3464(4)	839(7)	3708(9)	745(10)
OW(4)	4966(4)	−2391(4)	2415(6)	803(9)
				U_{iso}
H(21)	−151(3)	598(5)	227(5)	6(1)
H(22)	−120(4)	559(6)	436(7)	9(1)
H(31)	−342(4)	524(6)	395(6)	8(1)
H(32)	−338(8)	398(12)	163(12)	24(3)
H(41)	−341(2)	252(3)	204(4)	2(1)
H(42)	−418(4)	205(7)	322(7)	10(1)
H(51)	−241(3)	2(5)	235(5)	6(1)
H(52)	−281(4)	49(6)	80(7)	8(1)
HW(11)	87(4)	−160(7)	316(6)	8(1)
HW(12)	25(7)	−1(9)	340(10)	15(3)
HW(21)	299(5)	342(7)	114(7)	10(2)
HW(22)	386(6)	464(9)	149(10)	13(3)
HW(3A)	367(8)	165(13)	306(13)	7(3)
HW(3B)	231(14)	23(18)	380(19)	16(4)
HW(3C)	330(9)	20(14)	248(14)	8(3)
HW(3D)	354(16)	17(21)	408(27)	10(3)
HW(41)	442(5)	−238(7)	169(7)	9(2)
HW(42)	550(5)	−253(8)	134(9)	13(2)

$^aU_{eq} = \frac{1}{3}\Sigma_i\Sigma_j U_{ij}a_i{}^*a_j{}^*(a_ia_j)$.

Results and Discussion

An ORTEP [5] diagram of the complex is shown in Fig. 1, and a stereoscopic view of the packing of the unit cell is shown in Fig. 2. Important bond distances and bond angles are listed in Table III.

The crystal structure of bis(3,4,5,6-tetrahydropicolinate)Cu(II) consists of centrosymmetric units with the copper atom residing on the (0, 0, 0) inversion center of the unit cell. The copper atom is bonded to two centrosymmetrically related ligand molecules via the heterocyclic nitrogens N(1) and carboxyl oxygens O(1). Bond distances and bond angles in this structure are quite normal [1]. The six-membered heterocyclic ring with the double bond located between C(1) and N(1), exists in the expected half-chair conformation, and the carboxylate group is coplanar with the ring portion defined by the atoms C(2), C(1) and N(1). Two water molecules OW(1) which are related by the (0, 0, 0) inversion center occupy octahedral sites above and below the complex plane at a relatively long distance of 2.630 Å from the metal atom.

The crystal contains eight water molecules per formula unit, of which six are involved in an uncommon hydrogen bonded pattern as depicted in Fig. 3. This pattern can be described as ribbons of hexagons extending along the c axis. Each hexagon of water molecules is generated by the inversion center at (1/2, 0, 0). Each hexagon of water molecules is further hydrogen bonded to an adjacent hexagon which is related to it by the inversion center at (1/2, 0, 1/2). Some ambiguity as to the role of the various water molecules as hydrogen bond donors or acceptors results from the fact that the hydrogen atoms of OW(3) were found to be dis-

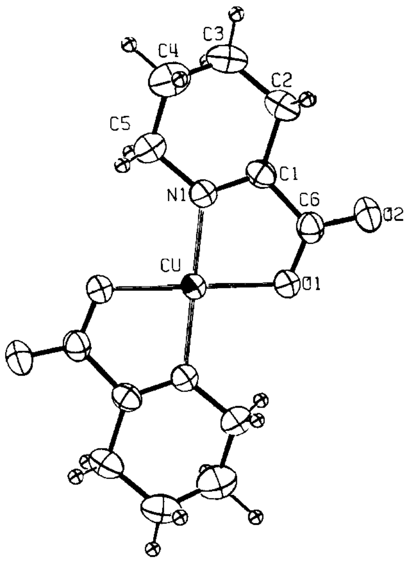

Fig. 1. Molecular structure of bis(3,4,5,6-tetrahydropicolinate)Cu(II).

TABLE III. Noteworthy Bond Lengths (Å) and Angles (deg). e.s.d.s are shown in Parentheses

Lengths			
Cu–O(1)	1.959(1)	C(4)–H(41)	0.96(2)
Cu–N(1)	1.965(1)	C(4)–H(42)	1.12(4)
O(1)–C(6)	1.274(2)	C(5)–H(51)	0.89(4)
O(2)–C(6)	1.225(2)	C(5)–H(52)	0.79(4)
N(I)–C(1)	1.274(2)	OW(1)–HW(11)	0.79(4)
N(1)–C(5)	1.453(3)	OW(1)–HW(12)	0.74(7)
C(1)–C(2)	1.480(3)	OW(2)–HW(21)	0.83(5)
C(1)–C(6)	1.521(3)	OW(2)–HW(22)	0.72(6)
C(2)–C(3)	1.490(5)	OW(3)–HW(3A)	0.9(1)
C(3)–C(4)	1.415(7)	OW(3)–HW(3B)	1.3(1)
C(4)–C(5)	1.492(5)	OW(3)–HW(3C)	0.84(8)
C(2)–H(21)	0.97(4)	OW(3)–HW(3D)	0.6(1)
C(2)–H(22)	0.94(4)	OW(4)–HW(41)	0.77(5)
C(3)–H(31)	0.93(4)	OW(4)–HW(42)	0.93(6)
C(3)–H(32)	1.08(8)		
Angles			
O(1)–Cu–N(1)	82.53(8)	C(2)–C(3)–C(4)	114.6(3)
C(1)–N(1)–C(5)	120.9(2)	C(3)–C(4)–C(5)	113.7(4)
N(1)–C(1)–C(2)	125.7(2)	N(1)–C(5)–C(4)	114.3(3)
N(1)–C(1)–C(6)	114.4(2)	O(1)–C(6)–O(2)	124.5(2)
C(2)–C(1)–C(6)	119.9(2)	O(1)–C(6)–C(1)	115.1(2)
C(1)–C(2)–C(3)	112.1(3)	O(2)–C(6)–C(1)	120.4(2)

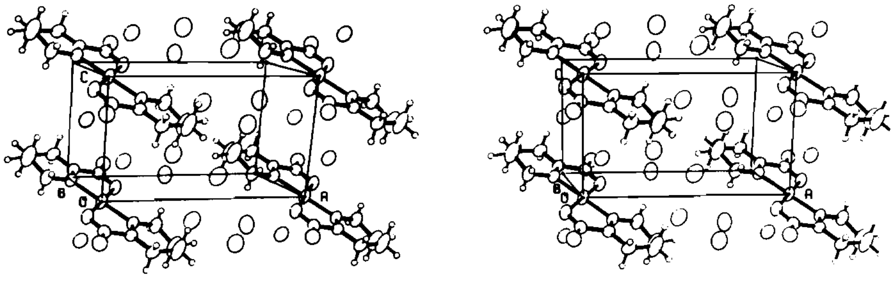

Fig. 2. ORTEP stereoscopic drawing of the crystal structure viewed approximately along the *b* axis. Ellipsoids are of 50% probability.

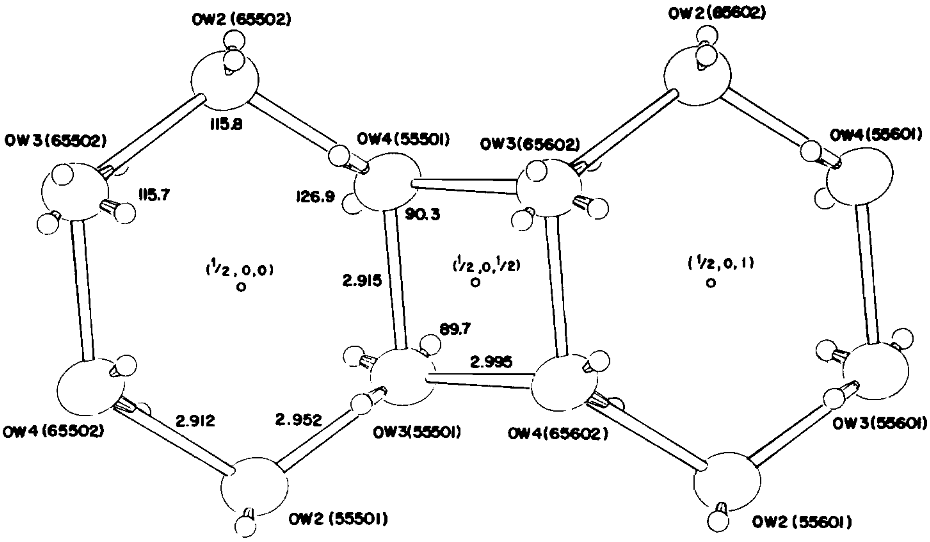

Fig. 3. Geometry of the hydrogen bonded pattern of water molecules. The atoms involved in hydrogen bonds are denoted by ORTEP codes shown in parentheses.

tributed among several possible sites. The hydrogen bonded hexagons of water molecules are packed together with the complex units mainly by van der Waals contacts. However, a possible hydrogen bond exists between OW(3) and OW(1) (d(OW(1)–OW(3)) = 2.866 Å).

The heterocyclic ligand 3,4,5,6-tetrahydro picolinic acid is of particular interest since it is implicated as an intermediate in the convention of L-lysine to acetoacetyl–CoA. It is believed [6] that L-lysine is first oxidized to the corresponding α-keto acid by L-amino acid oxidase and then cyclized to 3,4,5,6-tetrahydro picolinic acid. Thus it is reasonable to suggest that in an analogous way, CuO first oxidized L-lysine to the corresponding α-keto acid, which is then cyclized and trapped as the heterocyclic ligand by the copper atom. This ligand was previously prepared [7] by reacting L-lysine with hydrogen peroxide under strongly basic conditions in the presence of catalytic amounts of copper. It should be noted, that from this reaction under slightly acidic conditions one isolates bis(L-lysine)-Cu(II) as the major product [8].

Supplementary Material

Tables of anisotropic temperature factors and observed *versus* calculated structure factors are available from the author on request.

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