The Synthesis and Crystal Structure of Bis(cyclo-L-histidyl-L-histidyl)copper(II) Perchlorate Tetrahydrate

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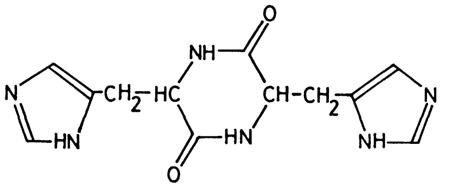
The title compound was prepared, and its structure then determined by X-ray structure analysis. The crystal is trigonal with the space group $P3_221$, $a=8.450(3)$, $c=42.00(6)$Å, and $Z=3$. The crystal structure has been determined from the diffractometer data and refined by a least-squares method to an R value of 0.103 for 1349 independent reflections with $I>3\sigma(I)$. The cyclo-L-histidyl-L-histidyl is coordinated to the Cu atom *via* the N atoms of the respective imidazolyl groups. The coordination of Cu is not planar but distorted toward the tetrahedral configuration, the interplanar angle between $\mathrm{Cu}{<}^{\mathrm{N}}_{\mathrm{N}}$ planes being 29°. The complex has virtually D_2 symmetry: there are two pseudo two-fold axes and one crystallographically imposed two-fold axis which relates two chelate rings. The chelate rings assume the δ conformation, and the ligating cyclo-L-histidyl-L-histidyl is of a folded form with a bowsprit-boat 2,5-piperazinedione ring. The electronic and circular dichroism spectra in the visible region are presented.

Histidine and its cyclic dipeptide play an important role in biological systems. Langenbeck *et al.* found that these substances catalyze the oxidation of DOPA and that the addition of the Cu^{2+} ion to the reaction system accerelates the oxidation.[1] As structural information is indispensable for an understanding of the function of the L-histidine residue in a biological process, we have attempted to make a structural investigation of cyclo-L-histidyl-L-histidyl [=(3*S*,6*S*)-bis(4-imidazolylmethyl)-2,5-piperazinedione, hereafter abbreviated as cyhis], and its metal chelates. Two of the present authors (Y. K. and K. M.) previously reported the crystal structure of aquabis(cyclo-L-histidyl-L-histidylato)dicopper(II) perchlorate hydrate,[2] which had been obtained from the reaction of $Cu(ClO_4)_2$, cyhis, and LiOH in a 1 : 1 : 1 mole ratio. The reaction of $Cu(ClO_4)_2$ with twice as many moles of the cyhis in methanol yielded a violet compound which was analysed to be $Cu(cyhis)_2(ClO_4)_2\cdot 4H_2O$. This compound has been characterized by means of X-ray structure analysis and its visible and circular dichroism (CD) spectra.



cyhis

Experimental

Preparation of $Cu(cyhis)_2(ClO_4)_2\cdot 4H_2O$. A suspension of $Cu(ClO_4)_2\cdot 6H_2O$ (0.371 g, 1 mmol) and the cyhis·$2H_2O$ (0.585 g, 2 mmol) in methanol was stirred at room temperature until these compounds were completely dissolved. The violet crystals were then separated out and recrystallized from hot water. Yield, 0.590 g (67%).
Found: C, 32.73; H, 4.11; N, 19.12%. Calcd for $Cu(C_{12}H_{14}N_6O_2)_2(ClO_4)_2\cdot 4H_2O$: C, 32.64; H, 4.11; N, 19.03%.
The compound is different in color from $Cu(cyhis)_2SO_4\cdot 5H_2O$(blue), which was prepared by Losse *et al.*[1]

Spectral Measurements. The absorption and CD spectra in an aqueous solution were recorded at room temperature on a Hitachi EPS 3T Recording Spectrometer and a JASCO J-20 Automatic Recording Spectrometer respectively.

X-Ray Data Measurements. *Crystal Data*: $C_{24}CuCl_2H_{36}N_{12}O_{16}$, Trigonal, $a=8.450(3)$, $c=42.00(6)$Å, $U=2597.7(2)$ Å^3, $D_m=1.68$, $D_c=1.67$ g/cm^3, $Z=3$, $\mu(\mathrm{Cu}\,K\alpha)=32.0$ cm^{-1}, space group $P3_221$. The Laue symmetry, space-group extinctions, and approximate unit-cell dimensions were obtained from Weissenberg and precession photographs. The cell dimensions were refined by the leasts-quares analysis of 22 θ values measured on a Philips PW1100 diffractometer by the use of Cu $K\alpha$ radiation. The space group was determined on the basis of the configuration (*S*) of the asymmetric carbon atom in the cyhis ligand.

Data Collection: The intensity data were collected on the diffractometer using graphite-monochromated Cu $K\alpha$ radiation. The specimen size was $0.20\times0.20\times0.18$ mm^3. A scan speed of 0.033 s^{-1} and a scan width of $(0.8+0.2\tan\theta)°$ in ω were chosen. The background was counted for 10 s at each end of scan range. Of the independent reflections collected in the $2\theta\leq120°$ range, 1349 reflections with $I>3\sigma(I)$ were used for the structure analysis. The number of reflections corresponds to *ca.* 70% of the total number of independent reflections within the range. No appreciable decay was observed in the intensities of the standard reflections monitored every 5 h throughout the data collection. Intensity data were also corrected for Lp factor.[3] A spherical absorption correction ($r=0.10$ mm) was applied.

Structure Determination and Refinement. The crystal structure was solved by the heavy-atom method. The positional and thermal parameters were refined by the block-diagonal least-squares method, anisotropic temperature factors being used for the Cu and Cl atoms. The minimized function was $\sum w(F_o-|F_c|)^2$. The weighting scheme of $w=1.0$ for $F_o\leq F_{max}$ and $w=(F_{max}/F_o)^2$ for $F_o>F_{max}$ was used. The F_{max} value of 30.0 was found to be best for making $w(\Delta F_o)^2$ relatively constant over the whole range of F_o. The final R value was 0.103 ($R'=[\sum w(F_o-|F_c|)^2/\sum wF_o^2]=0.139$). In the final cycle of refinements, all the parameter shifts were less than 0.2σ. The large temperature factors of the O atoms in the ClO_4^- ions are indicative of a disorder in the arrangement of ClO_4^-. The atomic parameters are listed in Table 1. A table of the observed and calculated structure factors is preserved by the Chemical Society of Japan (Document No. 7912). The atomic scattering factors for Cu^0, Cl,$^-$ O, N, and C atoms were taken from Ref. 4, with corrections for

TABLE 1. POSITIONAL AND THERMAL PARAMETERS

	x	y	z	B/Å^2
Cu	0.7547(4)	1	2/3	a)
O(1)	0.592(2)	0.344(2)	0.7601(2)	3.4(2)
O(2)	0.562(2)	0.897(2)	0.8161(2)	3.6(2)
N(1)	0.506(2)	0.468(2)	0.6961(3)	3.0(2)
N(2)	0.592(2)	0.747(2)	0.6817(3)	2.5(2)
N(3)	0.422(2)	0.635(2)	0.7880(3)	2.6(2)
N(4)	0.737(2)	0.626(2)	0.7818(3)	3.0(2)
N(5)	0.816(2)	1.153(2)	0.7602(2)	2.3(2)
N(6)	0.835(2)	1.072(2)	0.7110(2)	2.3(2)
C(1)	0.602(2)	0.601(2)	0.6752(3)	2.8(3)
C(2)	0.474(2)	0.701(2)	0.7074(3)	2.5(2)
C(3)	0.419(2)	0.529(2)	0.7173(3)	2.2(2)
C(4)	0.300(2)	0.414(2)	0.7436(3)	2.7(3)
C(5)	0.402(2)	0.467(2)	0.7762(3)	1.7(2)
C(6)	0.591(2)	0.481(2)	0.7731(3)	2.3(2)
C(7)	0.745(2)	0.769(2)	0.8026(3)	2.7(3)
C(8)	0.568(2)	0.774(2)	0.8034(3)	2.5(2)
C(9)	0.903(2)	0.961(2)	0.7934(3)	2.3(2)
C(10)	0.870(2)	1.020(2)	0.7624(3)	1.8(2)
C(11)	0.880(2)	0.975(2)	0.7314(3)	2.0(2)
C(12)	0.795(2)	1.180(2)	0.7288(3)	2.4(2)
Cl(1)	0	0.4811(7)	5/6	a)
Cl(2)	0.2649(8)	1	2/3	a)
O(3)	−0.161(4)	0.333(4)	0.8213(5)	11.7(7)
O(4)	0.058(3)	0.606(3)	0.8071(5)	10.1(5)
O(5)	0.324(2)	0.930(2)	0.6420(3)	5.6(3)
O(6)	0.098(3)	0.855(3)	0.6780(4)	8.8(5)
O(7)	0.087(2)	0.690(2)	0.7430(4)	7.8(4)
O(8)	0.330(2)	0.989(2)	0.7791(3)	5.8(3)

a) Anisotropic thermal parameters ($\times 10^4$) in the form $\exp[-(B_{11}h^2+B_{22}k^2+B_{33}l^2+B_{12}hk+B_{13}hl+B_{23}kl)]$.

	B_{11}	B_{22}	B_{33}	B_{12}	B_{13}	B_{23}
Cu	153(7)	97(6)	1.0(1)	0	0	4(1)
Cl(1)	159(12)	80(10)	2.4(2)	0	9(3)	0
Cl(2)	142(12)	180(13)	4.0(3)	0	0	16(3)

the anomalous scattering for Cu and Cl atoms. All computations were carried out by using programs in the UNICS.5)

In order to confirm the structure, further least-squares calculations were performed, anisotropic temperature factors being used for all the atoms. The R and R' values reached 0.070 and 0.108 respectively. The difference Fourier map showed no peaks greater than 0.4 e/Å^3.

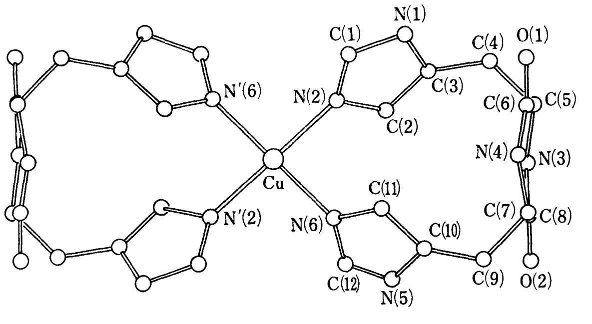


Fig. 1a. The structure of the complex viewed along the a axis.

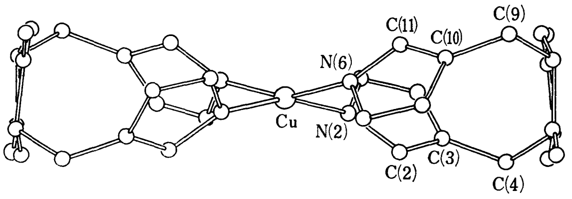


Fig. 1b. An elevation of the complex.

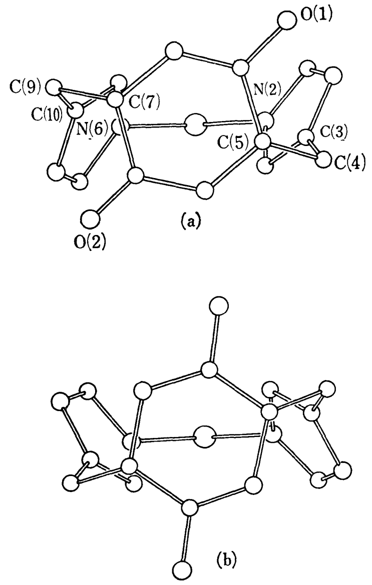


Fig. 2. (a) An elevation of the chelate ring (δ conformation. (b) λ chelate ring.

Results and Discussion

Figures 1a and b show the projection and elevation of the complex. Another elevation (half of the complex) is presented in Fig. 2(a). The complex has a crystallographically imposed two-fold axis; it is parallel to the a axis, runs through the Cu atom, and bisects the N(2)–Cu–N′(2) angle as well as the N(6)–Cu–N′(6) angle. Moreover, there are two pseudo two-fold axes. One bisects the N(6)–Cu–N′(2) (and N(2)–Cu–N′(6)) angle (Fig. 1b), and the other passes through the Cu atom and the center of the 2,5-piperazinedione ring (DKP ring) composed of N(3), C(5), C(6), N(4), C(7), and C(8). These three axes perpendicularly intersect one another at the position of the Cu atom; hence, the complex virtually possesses a D_2 symmetry.

The Cu atom is surrounded by 4 N atoms of the respective imidazolyl groups. The disposition of the 4 N atoms is not planar, but distorted toward a tetrahedral configuration (Fig. 1b), the interplanar angle between [N(2), Cu, N(6)] and [N′(2), Cu, N′(6)] planes being 29°. The two Cu–N bond lengths are substancially identical and are in agreement with those in the sulfate6) and perchlorate7) of tetrakis(imidazole)copper(II), and with the Cu(B)–N(5) distance in the aquabis(cyclo-L-histidyl-L-histidylato) dicopper (II) perchlorate hydrate.2) Above and below the Cu atom (Fig. 1b) there are no atoms within 3.4 Å. The bond lengths and angles are listed in Table 2.

As has been described above, the chelate ring has a

TABLE 2. INTERATOMIC DISTANCES AND BOND ANGLES

Bond lengths (l/Å)			
Cu–N(2)	1.98(1)	Cu–N(6)	1.97(1)
N(1)–C(1)	1.34(2)	N(5)–C(12)	1.37(2)
N(1)–C(3)	1.41(2)	N(5)–C(10)	1.41(2)
N(2)–C(1)	1.31(2)	N(6)–C(12)	1.35(2)
N(2)–C(2)	1.39(2)	N(6)–C(11)	1.37(2)
C(2)–C(3)	1.35(2)	C(11)–C(10)	1.37(2)
C(3)–C(4)	1.48(2)	C(10)–C(9)	1.47(2)
C(4)–C(5)	1.56(2)	C(9)–C(7)	1.55(2)
N(3)–C(5)	1.43(2)	N(4)–C(7)	1.46(2)
C(5)–C(6)	1.55(2)	C(7)–C(8)	1.52(2)
C(6)–N(4)	1.28(2)	C(8)–N(3)	1.37(2)
C(6)–O(1)	1.28(2)	C(8)–O(2)	1.20(2)
Cl(1)–O(3)	1.40(3)	Cl(2)–O(5)	1.40(2)
Cl(1)–O(4)	1.43(3)	Cl(2)–O(6)	1.41(3)
Bond angles (ϕ/°)			
N(2)–Cu–N(6)	89(1)		
Cu–N(2)–C(1)	128(1)	Cu–N(6)–C(12)	125(1)
Cu–N(2)–C(2)	125(1)	Cu–N(6)–C(11)	124(1)
N(1)–C(1)–N(2)	111(2)	N(5)–C(12)–N(6)	109(1)
N(2)–C(2)–C(3)	111(2)	N(6)–C(11)–C(10)	110(1)
C(1)–N(1)–C(3)	108(1)	C(12)–N(5)–C(10)	109(1)
N(1)–C(3)–C(4)	122(1)	N(5)–C(10)–C(9)	121(1)
C(2)–C(3)–C(4)	134(2)	C(11)–C(10)–C(9)	134(1)
N(1)–C(3)–C(2)	104(1)	N(5)–C(10)–C(11)	105(1)
C(1)–N(2)–C(2)	106(1)	C(12)–N(6)–C(11)	107(1)
C(3)–C(4)–C(5)	112(1)	C(10)–C(9)–C(7)	111(1)
C(4)–C(5)–N(3)	112(1)	C(9)–C(7)–N(4)	112(1)
C(4)–C(5)–C(6)	110(1)	C(9)–C(7)–C(8)	109(1)
C(5)–N(3)–C(8)	129(1)	C(7)–N(4)–C(6)	126(2)
C(5)–C(6)–O(1)	116(1)	C(7)–C(8)–O(2)	121(2)
C(5)–C(6)–N(4)	120(1)	C(7)–C(8)–N(3)	117(1)
N(3)–C(5)–C(6)	110(1)	N(4)–C(7)–C(8)	113(1)
O(1)–C(6)–N(4)	124(2)	O(2)–C(8)–N(3)	123(2)
Possible hydrogen bonds (l/Å)			
N(1)···O′(5)[a]	3.01(2)	H[N(1)][b]···O′(5)	2.05
N(3)···O(4)	3.07(3)	H[N(3)]···O(4)	2.22
O(1)···O′(8)	2.81(2)		
O(2)···O(8)	2.89(2)		
O(6)···O(7)	3.05(3)		
O(7)···O(8)	2.78(3)		

a) The primed atoms refer to the unprimed ones at the equivalent position ($x, y-1, z$). b) The coordinates of the H atoms were calculated on the assumption that the N–H distance is 1.00 Å.

TABLE 3. DEVIATIONS (Δd) OF ATOMS FROM LEAST-SQUARES PLANES AND INTERPLANAR ANGLES (ϕ)

Plane (1) [Cu,N(2),N(6)]
Plane (2) [N(2), C(1), N(1), C(3), C(2)]
(Δd/Å); N(2) −0.02, C(1) 0.02, N(1) −0.01, C(3) 0.00, C(2) 0.01
Plane (3) [N(6), C(12), N(5), C(10), C(11)]
the d's are less than 0.003 Å.
Plane (4) [C(3), C(4), C(5)]
Plane (5) [C(10), C(9), C(7)]
Plane (6) [C(5), C(6), N(4), C(7), C(8), N(3)]
(Δd/Å); C(5) −0.08, C(6) −0.02, N(4) 0.12, C(7) −0.11, C(8) −0.02, N(3) 0.11, O(1) −0.06, O(2) −0.02

Interplanar angles

	ϕ/°
Plane (1)—Plane (2)	58
Plane (1)—Plane (3)	58
Plane (2)—Plane (4)	78
Plane (3)—Plane (5)	75
Plane (6)—Plane (2)	65
Plane (6)—Plane (3)	71

TABLE 4. TORSION ANGLES (deg) CONCERNING THE DKP RING[a]

ϕ_1[C(8), N(3), C(5), C(6)]	−18°
ψ_1[N(3), C(5), C(6), N(4)]	2
ω_1[C(5), C(6), N(4), C(7)]	18
ϕ_2[C(6), N(4), C(7), C(8)]	−23
ψ_2[N(4), C(7), C(8), N(3)]	7
ω_2[C(7), C(8), N(3), C(5)]	13
χ_1^1[N(3), C(5), C(4), C(3)]	74
χ_1^2[C(5), C(4), C(3), N(1)]	101
χ_2^1[N(4), C(7), C(9), C(10)]	68
χ_2^2[C(7), C(9), C(10), N(5)]	105

a) The conventions of the IUPAC-IUB Commission are followed.[b] b) IUPAC-IUB Commission on Biological Nomenclature, *Biochem.*, **9**, 3471 (1970).

pseudo two-fold axis. Every pair of bonds related to each other by the axis agrees well in length. This is also the case for such a pair of bond angles. The bond lengths and angles in the imidazole moieties are comparable to those in the imidazole at −150 °C[8] and the tetrakis(imidazole)copper(II) complexes.[6,7] The Cu–N bond does not lie on the imidazole plane; the Cu–N(2) bond makes an angle of 12° with the [N(2), C(1), N(1), C(3), C(2)] plane, while the Cu–N(6) bond deviates from the [N(6), C(12), N(5), C(10), C(11)] plane by 17°. Several important interplanar angles are listed in Table 3, where the deviations of atoms from least-squares planes are also given.

The DKP ring is slightly buckled toward a boat conformation. The torsion angles (Table 4) rather resemble those of the DKP ring in cyclo(L-alanyl-L-alanyl), which was found to be the bowsprit-boat conformation.[9] The C(5)–C(4) and C(7)–C(9) bonds are quasi-equatorial with respect to the ring. As indicated by χ^1 values, both imidazolylmethyl side chains have a folded conformation. The ligating cyhis molecule thus assumes a folded form with a bowsprit-boat DKP ring. The structural parameters of the DKP ring are comparable to those in cyclo(L-threonyl-L-histidyl) dihydrate.[10]

As may be seen in Fig. 2 (a), the chelate ring has δ chirality. That the crystals comprise solely a (δ,δ)-conformer is indicative of the selective formation of this isomer. The λ chelate ring (Fig. 2 (b)) can be derived from the cyhis ligand of the δ conformation (Fig. 2 (a)) in the following way: i) counter-clockwise rotation (72°)[11] of the C(4)–C(3)–imidazole and C(9)–C(10)–imidazole fragments about the C(5)–C(4) and C(7)–C(9) bonds respectively, followed by ii) the rotation (180°) of the respective imidazole rings about the C(4)–C(3) and C(9)–C(10) bonds, and iii) linking the Cu atom to N(2) and N(6). These operations can be performed without changing the bond lengths and angles. A comparison of the scaled models of δ and λ chelate rings indicates that there is no appreciable difference between the nonbonded interaction energy in the δ ring and that in the λ ring. However, the δ ring is different from the λ one in the dispositions of the imidazole ring and the polar N(imidazole)–H bond relative to the C=O bond of the DKP ring, which might be partly responsible for the selective formation of the (δ,δ)-conformer.

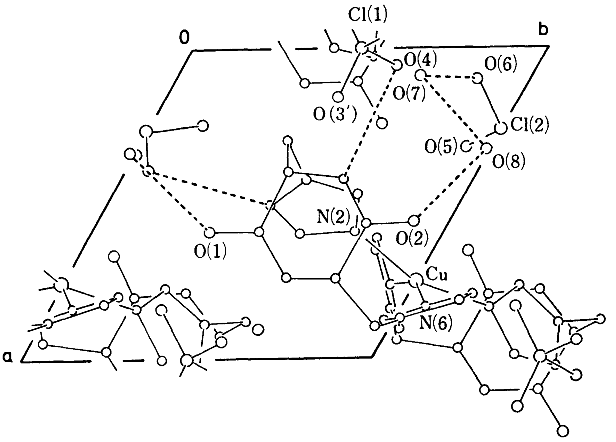


Fig. 3. The bounded projection (z=0.52—0.92) of crystal structure viewed down the c axis. The O(3) at $(-x, y-x, 1\frac{2}{3}-z)$ equivalent position is shown by O(3′).

A part of the crystal structure is shown in Fig. 3, where the broken lines indicate hydrogen bonds, the data of which are summarized in Table 2.

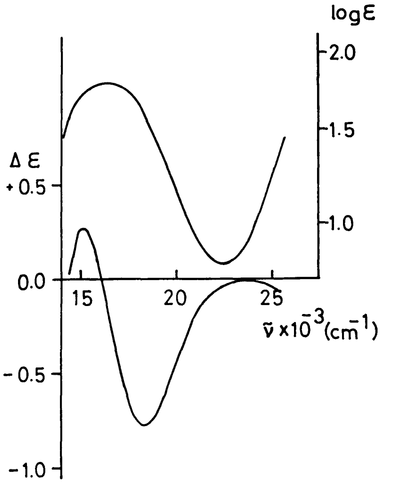


Fig. 4. Absorption (top) and CD (bottom) spectra.

Figure 4 shows the absorption and CD spectra. No appreciable variation in the CD curve was observed within 24 h. The absorption band at 16500 cm^{-1} is assignable to d→d transition. Although, in the crystal structure, the disposition of the 4 N atoms around the Cu atom deviates significantly from a planar configuration toward a tetrahedral one, the intensity and energy of the band are similar to those of tetragonal [Cu(R-pn)$_2$](ClO$_4$)$_2$;[12] but different from those of the bis(dipyrromethene)copper(II) complex,[13] in which 4 N donor atoms have a flattened tetrahedral configuration (the interplanar angle between $\mathrm{Cu}\!\left\langle\begin{matrix}\mathrm{N}\\ \mathrm{N}\end{matrix}\right.$ planes is 68°).[14] By analogy with the CD of [Cu(R-pn)$_2$](ClO$_4$)$_2$ the major CD band at 18300 cm^{-1} may be assigned to d_{xz}, $d_{yz}\rightarrow d_{x^2-y^2}$ transition.[12] The minor band at 15500 cm^{-1} can be regarded as arising from the $d_{xy}\rightarrow d_{x^2-y^2}$ transition, since the $d_{z^2}\rightarrow d_{x^2-y^2}$ transition is magnetically forbidden in D_2 symmetry. As the asymmetric C atoms in the present complex are distant from the Cu atom, the chiral disposition of four imidazolyl groups may be mainly responsible for the d electron optical activity.

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