Crystal Structure of the Copper(II) Chloride Complex of 3,5-Diiodo-L-tyrosine

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The crystal structure of the copper(II) chloride complex of the thyroid hormone precursor, 3,5-diiodo-L-tyrosine, ($C_9H_9I_2NO_3 \cdot CuCl$) was determined by the X-ray diffraction method. The space group is $P2_12_12_1$, with cell dimensions $a = 8.405(2)$, $b = 20.694(3)$ and $c = 7.532(3)$ Å. The structure was refined to $R = 0.064$ for 1374 reflections ($I > 3\sigma(I)$). The Cu(II) ion is six-coordinated by interaction with one amino nitrogen, two carboxyl oxygens and one chlorine atom in a square plane, and the phenol iodine and oxygen atoms in axial positions. Three-dimensional arrangement of the molecules are stabilized by two hydrogen bonds of O–H(phenol)··O(carboxyl), and N–H(amino)··O(carboxyl).

Keywords crystal structure; 3,5-diiodo-L-tyrosine–Cu(II) complex; thyroid hormone precursor; 3,5-diiodo-L-tyrosine; Cu(II) chelate compound

Introduction

Human blood serum contains about 73—149 μg/100 ml of Cu(II) ions,[1] 0.5—1.0 μg/100 ml of monoiodo-L-tyrosine plus 3,5-diiodo-L-tyrosine, 3.0—7.4 μg/100 ml of thyroxine and 96—170 ng/100 ml of 3,5,3′-triiodo-L-thyronine.[2] Because of the biological importance, the interaction of the thyroid hormone, thyroxine and its analogues such as 3,5-diiodo-L-tyrosine with Cu(II) ions has been studied in solution using ultraviolet and/or visible spectra, nuclear magnetic resonance (NMR), circular dichroism and electron paramagnetic resonance spectra.[3-5] Many possible structural models for thyroxine- and its analogue–Cu(II) complexes have been proposed, but to data the crystal structures of the complexes are still unknown because of the difficulty in crystallizing the complexes. Here, we succeeded in obtaining single crystals of 3,5-diiodo-L-tyrosine–Cu(II) complex, and the crystal structure of this chelate complex was determined by X-ray diffraction method.

Experimental

Crystals of the 3,5-diiodo-L-tyrosine–Cu(II) complex were obtained from a 50% ethanol solution of a 1 : 5 mixture of 3,5-diiodo-L-tyrosine (Sigma Chemical Co., St. Louis) and $CuCl_2 \cdot 2H_2O$ by slow evaporation of the solution kept at 20 °C. Dark-blue platelet crystals were obtained within a few days. A single crystal with approximate dimensions of $0.2 \times 0.2 \times 0.1$ mm³ was used for the X-ray diffraction data collection. The intensities were measured with a Rigaku AFC5R automated four circle diffractometer with graphite-monochromated Mo K_α radiation. Lattice parameters were determined from 2θ values of 25 reflections ($28.1 < 2\theta < 35.4°$). A total of 1768 independent reflections within $2\theta = 55.0°$ was collected in the ω–2θ scan method with a peak range of $(1.63 + 0.30 \tan\theta)°$ and an arbitrary maximum scan speed of 32.0° min⁻¹ in ω; the ratio of peak counting time to background counting time was 2 : 1. One thousand three hundred seventy-four reflections having intensities greater than 3.0 times their standard deviations were used for the analysis. The data were corrected for Lorenz, polarization and absorption factors. The maximum and minimum transmission factors were 0.75 and 1.11, respectively. Crystal data are given in Table I. The structure was solved by direct methods with MITHRIL[6] and DIRDIF[7] and refined by a full-matrix least squares method with anisotropic thermal parameters for nonhydrogen atoms. Hydrogen atoms of the phenol ring were shown on difference Fourier maps, and were included in further refinement with isotropic thermal parameters. Refinement was carried out to minimize $\sum w(|F_O| - |F_C|)^2$, where $|F_O|$ and $|F_C|$ were observed and calculated structure amplitudes, respectively. The weight (w) used for the refinement was $w = 4|F_O|^2/\sigma^2(|F_O|^2)$. The final $R(=\sum(|F_O| - |F_C|)/\sum|F_O|)$, $R_w(=[\sum w(|F_O| - |F_C|)^2/\sum w|F_O|^2]^{1/2})$ and $S(=[\sum w(|F_O| - |F_C|)^2/(M-N)]^{1/2}$, where M, the number of reflections, is 1374, and N, the number of variables, is 144, 0.064, 0.096 and 3.04, respectively. The H-atom positions were included for calculating R and R_w. The residual fluctuations on the difference Fourier map were in a range of -1.52 to $1.83 e$ Å^{-3}. Final atomic coordinates are listed in Table II.[8] The atomic scattering factors were taken from International Tables for X-Ray Crystallography.[9] All numerical calculations were performed by using TEXSAN crystallographic software package.[10]

TABLE I. Crystal Data 3,5-Diiodo-L-tyrosine Copper (II) Chloride

Chemical formula	$C_9H_9I_2NO_3 \cdot CuCl$
Molecular weight	531.98
Space group	$P2_12_12_1$
a (Å)	8.405 (2)
b (Å)	20.694 (3)
c (Å)	7.532 (3)
V (Å³)	1309.9 (6)
Z	4
D (mesd) (g·cm⁻³)	2.697 (2)
D (calcd) (g·cm⁻³)	2.697
μ (MoK_α) (cm⁻¹)	65.39
F (000)	984
T (K) (°)	296

TABLE II. Atomic Coordinates for Non-H Atoms with e.s.d.'s in Parentheses and in the Form of $B_{eq} = 4/3 \sum_i \sum_j \boldsymbol{a}_i \boldsymbol{b}_j B_{ij}$

Atom	x	y	z	B_{eq} (Å²)
I(1)	1.0478 (2)	0.2636 (1)	0.8310 (3)	2.67 (8)
I(2)	0.4020 (2)	0.3910 (1)	0.7436 (3)	2.80 (8)
Cu(1)	0.4409 (4)	−0.0031 (2)	1.0221 (5)	2.2 (1)
Cl(1)	0.6243 (9)	−0.0102 (4)	1.235 (1)	3.6 (4)
O(1)	0.792 (2)	0.3735 (9)	0.810 (3)	3 (1)
O(2)	0.294 (2)	0.001 (1)	0.814 (3)	2.6 (9)
O(3)	0.203 (2)	0.072 (1)	0.610 (3)	2.4 (4)
N(1)	0.532 (3)	0.075 (1)	0.912 (3)	3 (1)
C(1)	0.581 (3)	0.200 (2)	0.662 (4)	3 (1)
C(2)	0.746 (3)	0.204 (1)	0.711 (3)	2 (1)
C(3)	0.809 (3)	0.260 (2)	0.758 (4)	3 (1)
C(4)	0.718 (3)	0.318 (2)	0.758 (4)	3 (1)
C(5)	0.558 (3)	0.307 (2)	0.714 (4)	3 (1)
C(6)	0.490 (3)	0.248 (2)	0.664 (4)	4 (1)
C(7)	0.510 (4)	0.134 (2)	0.617 (4)	3 (1)
C(8)	0.422 (3)	0.103 (1)	0.785 (3)	1.0 (4)
C(9)	0.299 (3)	0.057 (1)	0.735 (4)	2 (1)

Results and Discussion

The bond lengths and angles for nonhydrogen atoms as well as the hydrogen bonds are listed in Table III. The torsion angles for the molecular conformation are listed in Table IV. The 3,5-diiodo-L-tyrosine molecules surrounding the Cu(II) ions are shown in Fig. 1 with hydrogen bonding and the atomic numbering scheme. The Cu(II) ion of the complex is surrounded by four 3,5-diiodo-L-tyrosine molecules. It is coordinated to the oxygen atom of the carboxyl group (O(2)) and the nitrogen atom of the amino group (N(1)) of one 3,5-diiodo-L-tyrosine molecule, the oxygen atom of the carboxyl group (O(3)) of another neighboring molecule and one chlorine atom (Cl(1)) in a square planar environment, and one each phenol iodine and oxygen atom (I(2) and O(1)) of the other two 3,5-diiodo-L-tyrosine molecules by axial interaction. Because of the chlorine atom, the crystal structure of the 3,5-diiodo-L-tyrosine–Cu(II) complex is neither typical *trans* nor *cis*-ligand configuration, which is the usual configuration of amino acid–Cu(II) chelate compounds. The geometrical relation between two oxygen atoms (O(2) and O(3)) of the 3,5-diiodo-L-tyrosine–Cu(II) complex corresponds, rather to, the *cis* configuration. Walker *et al.*[5] reported that the results of ^{1}H-NMR studies for 3,5-diiodo-L-tyrosine and other tyrosine analogues in dimethyl sulfoxide containing $CuCl_2$ could be explained by assuming some interaction between the phenol oxygen atom and the Cu(II) ion as well as between the iodine atom and the Cu(II) ion. Their explanation was confirmed by the crystal structure of 3,5-diiodo-L-tyrosine–Cu(II) complex in this study. The distances between the iodine atom and the Cu(II) ion, and between the phenol oxygen and the Cu(II) ion are 3.248(4) Å and 3.22(2) Å, respectively. These distances are about 1 Å longer than those between the Cu(II) ion and the Cl(1), N(1), O(2), O(3) in a square plane coordination. This result indicates that a relatively weak interaction occurs between the phenol iodine and/or oxygen atoms and the Cu(II) ion. The present crystal structure also suggests the possibility of a third electrically negative element in the system like a chlorine atom contributing to the Cu(II) ion. Models of

TABLE III. Bond Length (Å) and Angles (°) between Non-H Atoms, and Hydrogen Bonds (Å)

Bond	Distance (Å)	Bond	Distance (Å)
I(1)–C(3)	2.09 (2)	C(1)–C(2)	1.44 (4)
I(2)–C(5)	2.19 (3)	C(1)–C(6)	1.27 (5)
Cu(1)–Cl(1)	2.231 (8)	C(1)–C(7)	1.52 (4)
Cu(1)–O(2)	2.00 (2)	C(2)–C(3)	1.31 (4)
Cu(1)–O(3)	1.97 (2)	C(3)–C(4)	1.42 (4)
Cu(1)–N(1)	1.97 (3)	C(4)–C(5)	1.41 (4)
O(1)–C(4)	1.37 (3)	C(5)–C(6)	1.39 (5)
O(2)–C(9)	1.31 (4)	C(7)–C(8)	1.60 (3)
O(3)–C(9)	1.27 (3)	C(8)–C(9)	1.45 (3)
N(1)–C(8)	1.45 (3)		

Bond	Angle (°)	Bond	Angle (°)
Cl(1)–Cu(1)–O(2)	174.2 (6)	C(2)–C(3)–C(4)	122 (2)
Cl(1)–Cu(1)–O(2)	97.7 (6)	O(1)–C(4)–C(3)	118 (2)
Cl(1)–Cu(1)–N(1)	95.1 (8)	O(1)–C(4)–C(5)	129 (3)
O(2)–Cu(1)–O(3)	85.2 (8)	C(3)–C(4)–C(5)	112 (3)
O(2)–Cu(1)–N(1)	82.7 (9)	I(2)–C(5)–C(4)	115 (2)
O(3)–Cu(1)–N(1)	164.9 (9)	I(2)–C(5)–C(6)	118 (2)
Cu(1)–O(2)–C(9)	112 (2)	C(4)–C(5)–C(6)	126 (3)
Cu(1)–O(3)–C(9)	118 (2)	C(1)–C(6)–C(5)	117 (2)
Cu(1)–N(1)–C(8)	111 (2)	C(1)–C(7)–C(8)	112 (2)
C(2)–C(1)–C(6)	122 (3)	N(1)–C(8)–C(7)	113 (2)
C(2)–C(1)–C(7)	120 (3)	N(1)–C(8)–C(9)	112 (2)
C(6)–C(1)–C(7)	118 (3)	C(7)–C(8)–C(9)	113 (2)
C(1)–C(2)–C(3)	120 (3)	O(2)–C(9)–O(3)	121 (3)
I(1)–C(3)–C(2)	119 (2)	O(2)–C(9)–C(8)	119 (3)
I(1)–C(3)–C(4)	119 (2)	O(3)–C(9)–C(8)	120 (3)

Donor (D) at x, y, z	Acceptor (A)	Distance D···A (Å)	Symmetry code
O(1) (phenol)	O(2) (carboxyl)	2.89 (3)	$-x$, $1/2+y$, $1/2-z$
N(1)	O(1)	3.09 (3)	$1/2+x$, $1/2-y$, $-2-z$

TABLE IV. Selected Torsion Angles with e.s.d.'s in Parentheses

Bond sequence	Angle (°)
Cu(1)–O(2)–C(9)–O(3)	−173 (2)
Cu(1)–O(2)–C(9)–C(8)	10 (3)
Cu(1)–N(1)–C(8)–C(7)	−145 (2)
Cu(1)–N(1)–C(8)–C(9)	−16 (3)
Cl(1)–Cu(1)–O(2)–C(9)	−84 (7)
Cl(1)–Cu(1)–N(1)–C(8)	−168 (2)
O(2)–Cu(1)–N(1)–C(8)	17 (2)
O(3)–Cu(1)–O(2)–C(9)	155 (2)
O(3)–Cu(1)–N(1)–C(8)	−20 (5)
N(1)–Cu(1)–O(2)–C(9)	−15 (2)

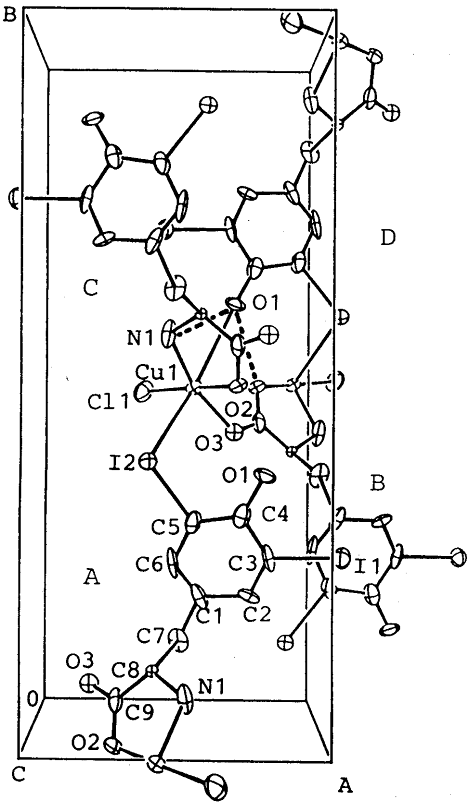

Fig. 1. Crystal Structure of $C_9H_9I_2NO_3\cdot CuCl$ Showing Surrounding Cu(II) Ion with the Hydrogen Bonding Scheme

Symmetry operation codes: (A) x, y, z; (B) $1/2+x$, $1/2-y$, $1-z$; (C) $1-x$, $1/2+y$, $3/2-y$; (D) $3/2-x$, $1-y$, $-1/2+z$.

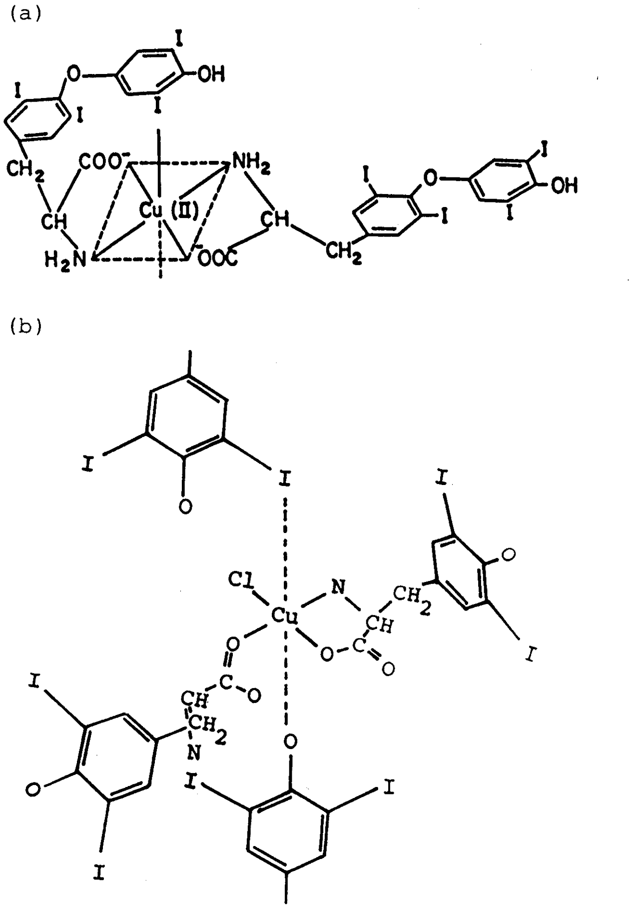

Fig. 2. (a) The Model of Thyroxine–Cu(II) Complex Appearing in Ref. 5, and (b) Schematic Representation Around Cu(II) Ion of 3,5-Diiodo-L-tyrosine–Cu(II) Complex

thyroxine–Cu(II) complex were previously constructed as shown in Fig. 2, but the phenolic hydroxyl group had not been taken into consideration as the axial ligand.[3–5] The coordination scheme clarified in this study may be useful for considering other thyroid hormone metabolites complexed with Cu(II) ions in future studies. Three-dimensional molecular packings of 3,5-diiodo-L-tyrosine molecules are stabilized by two hydrogen bonds, in which the phenol O(1) is bonded to the carboxyl O(2) and the amino N(1) atoms. The hydrogen atoms of both amino- and carboxyl-groups were not be revealed on a difference Fourier map, and consequently the protonation or deprotonation of these groups was not confirmed in this study.

References and Notes

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