MAGNETIC PROPERTIES OF DL-PENICILLAMINE-Cu(I,II) COMPLEX

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The complex, DL-penicillamine-Cu(I,II), was investigated by ESR
in solution. The spin Hamiltonian parameters determined are $g_{||}$ =
2.414, $g_{\perp}$ = 2.080, and $A_{||}$ = 123 G. The paramagnetic susceptibility
of the solid complex measured from 77°K to 230°K followed the
Curie-Weiss law with a Curie constant of 0.45°Kemu/mol, a Weiss
constant of -1.5°K. A spin concentration is obtained to be 99 %
as pure doublet, S = 1/2, based on the molecular composition
proposed by Sugiura.

DL-penicillamine (Pen) has been used as a noble drug for the oral treatment
of Wilson's disease, which is caused by the abnormal metabolism of copper.
Since the preliminary isolation and identification were reported by Sugiura
(Y.S.),[1] there have been several works on the Pen-Cu complex and various chemi-
cal structures have been proposed. Y.S. reported that the complex is composed of
one Cu(II) chelating with the thiol and amino groups of Pen, and of the other two
Cu(I) binding with the thiol group. Recently, a polymeric Pen-Cu complex with
mixed valence Cu_2L_2 repeating unit has been also presented.[2] On the other hand,
the ternary complex between some peptide-Cu(II) complex and D-Pen was investi-
gated[3] by ESR parameters, but the identification of the complex was not described
in details.
One of the difficulties of the studies arises from the complexed redox reaction of

Cu(II) and ligand thiol during the complex formation, and in addition the complex
is fairly sensitive to the air oxidation. In the present studies, the complex was
carefully isolated and recrystallized under anaerobic atmosphere. The measurements
of the paramagnetic susceptibilities were performed for the pure solid in the
continuous temperature range, and spin state was determined from Curie constant.

The ESR observation was carried out in solution and the Hamiltonian parameters
were estimated. Based on the experimental magnetic moment and ESR parameters, the
bonding nature of the paramagnetic site was investigated.

In the same manner as reported by Y.S.,[1] the red-violet complex was prepared
under nitrogen atmospher, or in vacuo to avoid the side oxidation;

Anal. calcd. for $C_{10}H_{18}O_4N_2S_2Cu_3 \cdot 2H_2O$: C,23.05; H,4.26; N,5.38; Cu,36.59.

Found: C,22.64; H,4.68; N,5.01; Cu,37.37.

The red-violet complex dissolved in the Michelis buffer (PH=6.2) shows the charac-
teristic absorption at 517 nm with the extinction coefficient, 3×10^3 $cm^{-1}M^{-1}$.

Magnetic susceptibilities were measured in the continuous temperature range from
77°K to 230°K using a Shimadzu MB-2 type magnetic torsion balance, equipped with a
low temperature cryostat. Manganese Tutton salt was used for the calibration of
the thermometers and field gradient. The correction for the diamagnetic contri-
bution (χ_{dia} = -0.236×10^{-3} emu/mol) was tentatively calculated by Pascal's
method using the chemical structure proposed by Y.S. and by the contribution of Cu
ions estimated from that of Zn(II).

The ESR measurements were carried out at 77°K using a JES-ME-3X spectrometer
operating with 10C KHz magnetic field modulation. The ESR operating frequency was
measured with a Takeda-Riken microwave frequency counter, and g values were
determined taking Li-TCNQ (g = 2.0026) as a standard. The magnetic fields were
calibrated by the splitting of Mn(II) in MgO (ΔH_{3-4} = 86.9 G).

The temperature dependence on the inverse molar susceptibility of this complex
is plotted in Fig. 1. The susceptibility showed an excellent accordance with the
Curie-Weiss law, with a Curie constant of 0.45 ± 0.02 °Kemu/mol and a Weiss
constant -1.5 ± 2 °K. The susceptibility measurement demonstrated that the spin
state of this complex is nearly in the pure doublet, (S = 1/2) and that its con-
centration is nearly 100 % within the limit of experimental accuracy. No impor-
tant deviation from the straight line can be detected on the $1/\chi$-T plot throughout
the present temperature range. The possibility of the strong inter-molecular spin

exchange interaction occuring in the spin cluster or in the spin chain can be

negligible with referrence to small values of Weiss constant. It has been known

that[4,5] most of the Cu(II) complexes with ionic or rather weak covalent bonds

take the value of the effective magnetic moment, μ_{eff} between 1.9 and 2.2, and that

those with strong covalent bonds reduce the value to 1.72 - 1.82 B.M. We have

calculated the effective magnetic moment, μ_{eff} by the following expression:[6]

$$\mu_{eff} = 2.828 \sqrt{\chi \cdot T}$$

In the experimental temperature range, the effective magnetic moment (μ_{eff} = 1.89

B.M.) of this complex indicates that of the Cu(II) is of rather weak covalency. An

effective $\bar{g}$ value ($\bar{g}$ = 2.18) thus calculated from μ_{eff} as a pure doublet shows

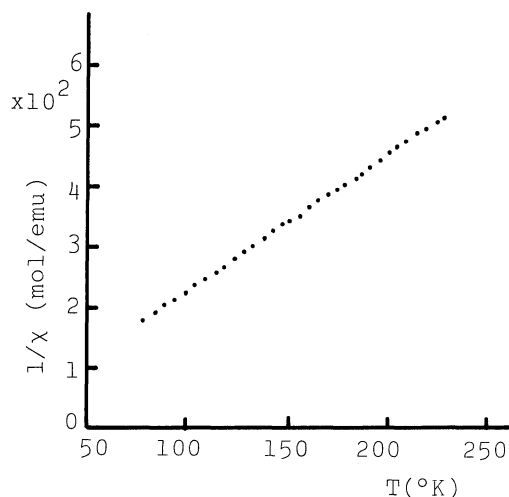a good accordance with the averaged g value ($\bar{g}$ = 2.19) determined by ESR.

Fig.1. Inverse molar susceptibilities
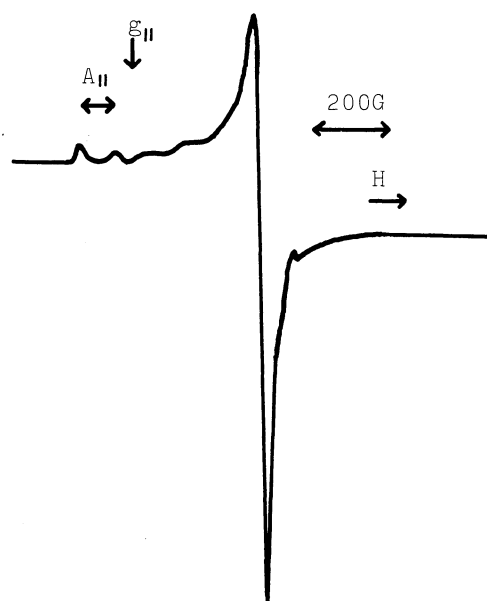of Pen-Cu(I,II) complex vs temperature.

Fig.2. ESR spectrum of
Pen-Cu(I,II) complex at 77°K.

The ESR spectrum of the complex in a frozen matrix shown in Fig. 2, exhibits a

typical hyperfine patterns with the axial symmetry, i.e. ($g_x \simeq g_y$). The ESR para-

meters determined are $A_{\parallel}$ = 123 $\pm$ 3 G, $g_{\parallel}$ = 2.414 $\pm$ 0.004, and $g_{\perp}$ = 2.080 $\pm$ 0.002

respectively. The absorption at g = 4 (ΔM_s = 2) due to the triplet dimer has

never been detected. The complex is fairly stable in vacuo, and no important

change is recognized for a week. It should be noteworthy, however, that the ESR

spectrum lost the hyperfine structure and altered to the broadened single absorp-

tion upon a long exposure to air, nevertheless no remarkable changes were detected

in the visible absorption spectrum. A broadening of the ESR spectrum is probably

due to the formation of the polymer, but its identification claims further inves-

tigations. The spectroscopic data of Pen-Cu(I,II) complex are compared with those

of sulfur- or histidine-containing peptide-Cu(II) complexes in Table 1.

Table 1. Spectroscopic Parameters for Pen-Cu(I,II) and Peptide-Cu(II) Complexes

	$g_{\parallel}$	$g_{\perp}$	$-A_{\parallel}$	α^2	ε
Pen-Cu(I,II)	2.414	2.080	123	0.87	3000
α-Mercaptopropionylglycine-Cu(II)[7]	2.259	2.040	82	0.52	300
Acetylglycylglycyl-L-histidine-Cu(II)[8]	2.179	2.045	201	0.80	60

The bonding parameter of Pen-Cu(I,II) complex, $\alpha^2 = 0.87$ calculated by the

following expression[9] means that the bonding nature is of rather weak covalency,

consistent with the result of the susceptibility measurement.

$$\alpha^2 = -A_{\parallel}/P + (g_{\parallel} - 2) + 3/7(g_{\perp} - 2) + 0.04 \qquad (P = 0.036 \text{ cm}^{-1})$$

A weak covalence of the paramagnetic site is rather surprising as compared with

the case of α-Mercaptopropionylglycine-Cu(II) complex. With the anomalous high

extinction coefficient in the visible absorption, a reduction of the covalent

nature suggests that some modification of the ligand geometry will be probable in

this complex. The further investigations are under way.

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