Metal Complexs of Amino Acids. I. The Circular Dichroism of Copper(II) Complexes with Optically Active Amino Acids

By Takaji YASUI

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It is well known that copper(II) complexes show a broad absorption band, which is due to the d→d transition, in the visible region. There have been many reports[1,2] concerning the assignments of the absorption components of this band, but most of these studies have been made on the basis of the absorption spectrum.

Pfeiffer and Christeleit[3] have studied the optical rotatory dispersion (ORD) of copper(II) complexes with optically active amino acids; their ORD data suggest that the Cotton effect in the visible absorption region is only one. It may be expected from the recent circular dichroism (CD) studies by other workers[4] that the split components of the d→d transition of the copper(II) complexes with optically active amino acids may also be separated by the CD method.

In the present paper, the CD curves of [Cu(am)$_2$]-type complexes (am=L- and D-alanine, L-serine, L-valine, L-threonine, L-allothreonine, L-proline and L-hydroxyproline) have been reported in the region from 1000 to 400 mμ in aqueous solutions. A preliminary letter on this subject was published recently.[5]

Experimental

Measurements.—The CD curves were obtained by a Shimadzu QR-50 spectrophotometer with a CD attachment. All measurements were made at 10—12°C in the region from 1000 to 400 mμ. Saturated, 1/40 or 1/20 mol./l. solutions in water, pyridine or ethylene glycol were used. The cell length employed was 1 cm. The aqueous solutions of bis(DL-threoninato)copper(II) or bis(sarcosinato)copper(II) monohydrate were used as the reference solutions instead of water.

The absorption measurements were made by a Beckman DU spectrophotometer at room temperature.

Materials.—All of the copper(II) amino acid complexes were prepared from copper(II) hydroxide by a modification of the method of Abderhalden and Schnitzler.[6]

1) *Bis(L-alaninato)copper(II), [Cu(L-ala)$_2$].*—To a solution containing 4.5 g. of L-alanine in 30 ml. of warm water, 2.2 g. of copper(II) hydroxide was added; the mixture was then heated for a few minutes on a water bath. After the solution had been filtered, a small amount of alcohol was added drop-by-drop to the filtrate and the solution was cooled in an ice bath. The crystals which separated were collected and washed with alcohol and then ether. Recrystallization was carried out from an aqueous alcohol solution.

Found: C, 30.31; H, 4.91; N, 11.64. Calcd. for $Cu(C_3H_6NO_2)_2$: C, 30.06; H, 5.05; N, 11.69%.

2) *Bis(D-alaninato)copper(II), [Cu(D-ala)$_2$].*—This compound was prepared by the same procedure as was used in 1).

3) *Bis(L-serinato)copper(II), [Cu(L-ser)$_2$].*—One gram of copper(II) hydroxide was added to a solution containing 2.1 g. of L-serine in 30 ml. of warm water. The mixture was then filtered and left to stand at room temperature. When a proper amount of alcohol was added to the filtrate, blue crystals were deposited. They were washed with alcohol and then with ether. The complex was recrystallized from an aqueous alcohol solution.

Found: C, 26.75; H, 4.42; N, 10.19. Calcd. for $Cu(C_3H_6NO_3)_2$: C, 26.52; H, 4.46; N, 10.31%.

4) *Bis(L-valinato)copper(II) Monohydrate, [Cu(L-val)$_2$]·H$_2$O.* — The compound was obtained by a method similar to that used in 1). It forms bluish-violet crystals.

Found: C, 40.63; H, 6.95; N, 9.45; H_2O, 6.08. Calcd. for $Cu(C_5H_{10}NO_2)_2\cdot H_2O$: C, 40.60; H, 6.81; N, 9.47; H_2O, 5.74%.

5) *Bis(L-threoninato)copper(II) Monohydrate, [Cu(L-thr)$_2$]·H$_2$O.*—Bluish-violet crystals were separated by the method that was used in 3).

Found: C, 32.04; H, 5.39; N, 9.39; H_2O, 5.91. Calcd. for $Cu(C_4H_8NO_3)_2\cdot H_2O$: C, 32.05; H, 5.38; N, 9.35; H_2O, 5.67%.

6) *Bis(L-allothreoninato)copper(II) Monohydrate, [Cu(L-allothr)$_2$]·H$_2$O.*—The needle crystals of a bluish-violet color were separated by a method similar to that used in 3).

Found: C, 32.01; H, 5.48; N, 9.14; H_2O, 5.85. Calcd. for $Cu(C_4H_8NO_3)_2\cdot H_2O$: C, 32.05; H, 5.38; N, 9.35; H_2O, 5.67%.

7) *Bis(L-prolinato)copper(II) Dihydrate, [Cu(L-prol)$_2$]·2H$_2$O.*—To a solution containing 3 g. of L-proline in 20 ml. of water, 1.2 g. of copper(II) hydroxide was added; then a sufficient amount of

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[1] J. Bjerrum, C. J. Ballhausen and C. K. Jørgensen, *Acta Chem. Scand.*, **8**, 1275 (1954).

[2] C. K. Jørgensen, ibid., **10**, 887 (1956).

[3] P. Pfeiffer and W. Christeleit, *Z. physiol. Chem.*, **245**, 197 (1937).

[4] B. E. Douglas, R. A. Haines and J. G. Brushmiller, *Inorg. Chem.*, **2**, 1194 (1963).

[5] T. Yasui, J. Hidaka and Y. Shimura, *J. Am. Chem. Soc.*, **87**, 2762 (1965).

[6] E. Abderhalden and E. Schnitzler, *Z. physiol. Chem.*, **163**, 94 (1927).

acetone was added to the solution until crystals deposited. These crystals were collected and washed with acetone. The needle crystals were obtained in blue by recrystallizing them from an aqueous acetone solution. The complex prepared by the method of Pfeiffer and Christeleit³⁾ was hygroscopic, but the crystals separated by the present method were not so.

Found: C, 41.57; H, 5.53; N, 9.53; H_2O, 11.06. Calcd. for $Cu(C_5H_8NO_2)_2\cdot 2H_2O$: C, 41.16; H, 5.53; N, 9.60; H_2O, 10.99%.

The anhydrous compound was prepared by the dehydration of bis(L-prolinato)copper(II) dihydrate in a vacuum oven at 75°C.

8) Bis(L-hydroxyprolinato)copper(II) Trihydrate, [Cu(L-hydprol)₂]·3H₂O.—The compound, obtained by the same method as was used in 7) was trihydrate and blue plates.

Found: C, 37.02; H, 5.04; N, 8.58; H_2O, 14.95. Calcd. for $Cu(C_5H_8NO_3)_2\cdot 3H_2O$: C, 37.08; H, 4.99; N, 8.65; H_2O, 14.31%.

Results and Discussion

The CD and absorption data in an aqueous solution are shown in Figs. 1—3 and in Table I. As is shown in Fig. 1, the absorption curve of $[Cu(L\text{-}ala)_2]$ shows a simple broad band, while the CD curve shows three bands in the region (namely, a positive band at about 730 mμ and two negative band, at 630 and 565 mμ). The CD curve of the copper complex with D-alanine is also plotted for the comparison. The CD curve of $[Cu(L\text{-}ser)_2]$ is similar to that of $[Cu(L\text{-}ala)_2]$ on the whole; namely, it has a small positive peak at about 730 mμ, a negative band at 595 mμ, and a negative shoulder at about 640 mμ. However, another small positive shoulder (about 820 mμ) is observed on the longer wavelength side of the positive peak at about 730 mμ. Similar trends are also observed in the curves of $[Cu(L\text{-}thr)_2]$, $[Cu(L\text{-}val)_2]$, and $[Cu(L\text{-}allothr)_2]$ (Figs. 1 and 2). These facts suggest that the broad positive bands in the 900—700 mμ region are composed of two weak positive CD components. As may be seen in Fig. 1, it also seems likely that the observed broad negative bands of $[Cu(L\text{-}thr)_2]$ and $[Cu(L\text{-}val)_2]$ are caused by the superposition of two negative CD bands.

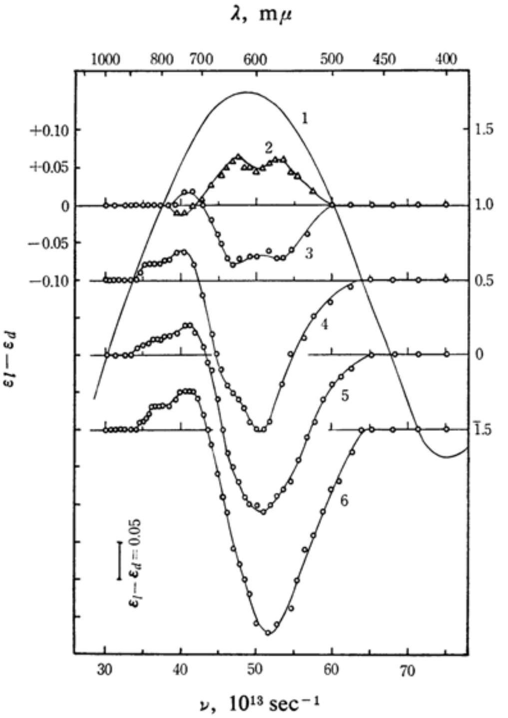

Fig. 1. Absorption curve of (1) $[Cu(L\text{-}ala)_2]$ and CD curves of (2) $[Cu(D\text{-}ala)_2]$, (3) $[Cu(L\text{-}ala)_2]$, (4) $[Cu(L\text{-}ser)_2]$, (5) $[Cu(L\text{-}thr)_2]\cdot H_2O$ and (6) $[Cu(L\text{-}val)_2]\cdot H_2O$ in aqueous solutions.

From these results, it is concluded that the $[Cu(L\text{-}am)_2]$ complex shows *four* CD components of the d→d transitions, which are related to the magnetic dipole-allowed transitions under the symmetry of C_2. The signs of these CD components of the L-amino acid complexes are (+), (+), (−) and (−), listing from longer to shorter wavelengths. The single ORD inversion observed by Pfeiffer and Christeleit³⁾ may be thought to be a superposition of four Cotton effects.

The CD and absorption curves of the $[Cu(L\text{-}thr)_2]$ and $[Cu(L\text{-}allothr)_2]$ complexes are shown in Fig. 2. The L-threonine or L-allothreonine

TABLE I. CIRCULAR DICHROISM AND ABSORPTION DATA OF $[Cu(am)_2]$ IN AQUEOUS SOLUTIONS

Complex	CD Band ν, 10^{13} sec^{-1} ($\{\varepsilon_l-\varepsilon_d\}_{max}$)				Absorption band ν, 10^{13} sec^{-1}(log ε)
$[Cu(L\text{-}ala)_2]$		41.1(+0.02)	47.6(−0.07)	53.1(−0.07)	48.78(1.75)
$[Cu(D\text{-}ala)_2]$		40.5(−0.01)	47.6(+0.06$_5$)	53.1(+0.06)	48.78(1.75)
$[Cu(L\text{-}ser)_2]$	sh ca. 36.1(+0.02)	40.0(+0.03$_5$)	sh ca. 46.9(−0.15)	50.4(−0.20)	48.50(1.71)
$[Cu(L\text{-}val)_2]\cdot H_2O$	sh ca. 36.6(+0.03)	41.1(+0.05)		51.7(−0.27)	49.16(1.77)
$[Cu(L\text{-}thr)_2]\cdot H_2O$	sh ca. 36.1(+0.02)	41.1(+0.04)		50.9(−0.21)	49.50(1.72)
$[Cu(L\text{-}allothr)_2]\cdot H_2O$	36.6(+0.02$_5$)	39.5(+0.02)	sh ca. 46.9(−0.30)	49.6(−0.35)	48.39(1.66)

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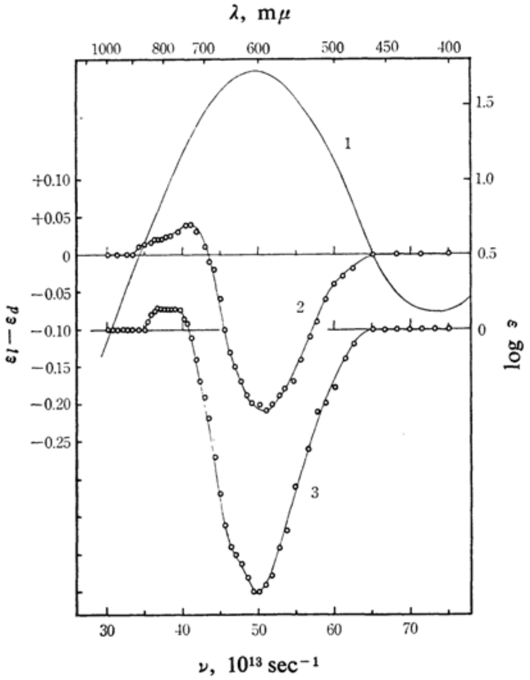

Fig. 2. Absorption curve of (1) [Cu(L-thr)$_2$]·H_2O and CD curves of (2) [Cu(L-thr)$_2$]·H_2O and (3) [Cu(L-allothr)$_2$]·H_2O in aqueous solutions.

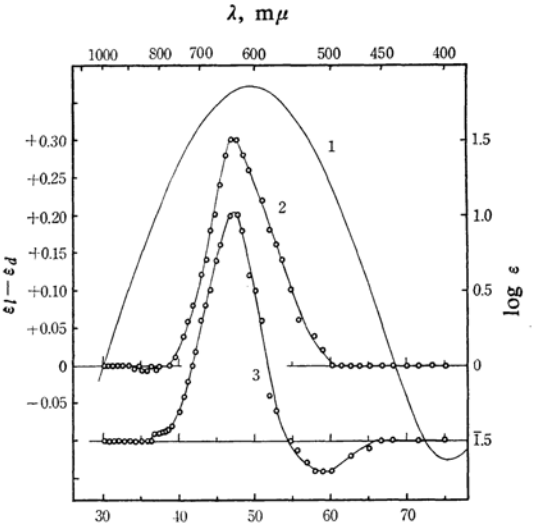

Fig. 3. Absorption curve of (1) [Cu(L-prol)$_2$]·$2H_2O$ and CD curves of (2) [Cu(L-hydprol)$_2$]·$3H_2O$ and (3) [Cu(L-prol)$_2$]·$2H_2O$ in aqueous solutions.

molecule has two asymmetric carbon atoms, located in α- and β-positions. The CD behavior of [Cu(L-thr)$_2$] is, on the whole, almost the same as that of [Cu(L-allothr)$_2$] except for a small difference in their intensities. These facts suggest that the vicinal effect caused by the α-asymmetric carbon atom, which is located in the five-membered chelate ring containing a central copper atom, is more effective than that of the β-asymmetric atom, which is located in the side chain of the chelate ring. Similar work concerning the α- and β-asymmetry of optically active amino acids has been reported on the basis of ORD study in another wavelength region,⁷⁾ but it resulted in no definite conclusion.

As may be seen in Fig. 3, the CD curve of [Cu(L-prol)$_2$] is considerably different from those of the other amino acid complexes. This may be attributed to the stereospecific activation of the nitrogen atom in the coordinated ligand, because the construction of the molecular models of the complexes shows that the nitrogen atom of the coordinated L-proline takes a forced asymmetric configuration, and that of the coordinated D-proline, the enantiomorphous configuration. This was also supported by the X-ray analysis of the [Cu(L-prol)(D-prol)]·$2H_2O$ crystal.⁸⁾ The [Cu(L-hydprol)$_2$] may be said to have the same conditions as [Cu(L-prol)$_2$] in view of the similarity of their CD behavior. These CD behavior will suggest that the vicinal effect from the activated nitrogen atom will be more effective than that from the α-asymmetric carbon atom, since the nitrogen atom is directly

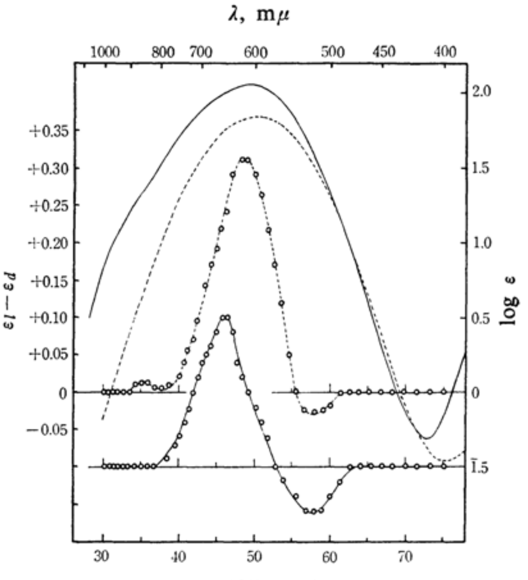

Fig. 4. Absorption and CD curves of [Cu(L-prol)$_2$] in ethylene glycol (----) and in pyridine (——).

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7) N. Izumiya, M. Winitz, S. M. Birnbaum and J. P. Greenstein, *J. Am. Chem. Soc.*, **78**, 1602 (1956).

8) A. M. Mathieson and H. K. Welsh, *Acta Cryst.*, **5**, 599 (1952).

attached to the copper atom, while the carbon atom is attached indirectly.

The CD and absorption data of [Cu(L-prol)$_2$] in pyridine or ethylene glycol are shown in Fig. 4. This complex can be kept in these solvents without decreasing its optical activity. The absorption maxima of this complex in these solvents are almost the same as that in an aqueous solution, though the absorption intensity is slightly higher in pyridine than in the other two solvents. On the other hand, the intensity of the CD band in pyridine is less than that in ethylene glycol or in water. It may be considered, however, that these differences in behavior in these different solvents do not suggest any essential differences in the CD components.

Summary

On the basis of the CD measurements of the complexes of the [Cu(L-am)$_2$] type, four CD components have been observed in the region of the d→d absorption band, namely, (+), (+), (−) and (−), listing from longer to shorter wavelengths. The L-configuration of the amino acids determines the signs of these CD components.

Judging from the CD curves of the copper(II) complexes with L-threonine and with L-allothreonine, it has been suggested that the vicinal effect caused by the α-asymmetric carbon atom is stronger than that caused by the β-asymmetric one.

It has also been suggested that, when L-proline or L-hydroxyproline is coordinated to copper, the nitrogen atoms of these ligands are activated by the configurational stereospecificity.

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Depatment of Chemistry
Faculty of Science
Osaka University
Toyonaka, Osaka