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MOLECULAR ASSOCIATION OF THE 1:2 COMPLEXES OF COPPER(II) WITH AMINO ACIDS IN AQUEOUS MEDIA

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The ESR experiments show that the 1:2 complexes of copper(II) with amino acids are present in frozen aqueous solution as a kind of aggregates, whose structures are different from those in crystals, and the aggregates disperse into dimers and monomers in the frozen aqueous solutions containing alcohols, protein denaturants, or certain inorganic salts.

The 1:2 complexes of copper(II) with amino acids are mononuclear and inner complex salts. The ESR experiments described in this paper establish the new fact that the complex molecules are present as a kind of aggregates in frozen aqueous solution and, furthermore, the dimers and monomers of them are produced in the frozen aqueous solutions containing alcohols, protein denaturants, or certain inorganic salts. This fact is particularly interesting, for it is apparently similar to the phenomena of hydrophobic interactions.[1,2] The first-derivative X-band ESR spectra were measured in the range of 0 to 6,000 gauss for frozen solutions in liquid nitrogen. Most experiments were performed for the solutions at a concentration of 1.0×10^{-2} M of the complexes, and no concentration dependence of the ESR results were observed over the whole range of concentration from 1×10^{-4} to 0.1 M.

The ESR spectra of the 1:2 complexes of copper(II) with L-alanine, DL-alanine, DL-α-amino-n-butyric acid, L-serine, DL-serine, and DL-valine were measured in both polycrystalline powder and frozen aqueous solution; several of them are shown in Fig. 1. For all the complexes, the ESR line shapes in both states are quite different from each other. It is characteristic of any of the ESR spectra observed in frozen aqueous solution that there is only a single and symmetrical absorption in the whole field range, and, for all the complexes employed here, the parameters of the absorption, which are illustrated in Fig. 1 (A), were as follows; g_0 = 2.110 – 2.119 (± 0.001), ΔH_{msl} = 94 – 130 (± 3) gauss, and (I_L/I_H) = 0.90 – 0.96 (± 0.01) (the reproducibility of the data was very good, and the errors are shown in parentheses). It seems quite unlikely that these symmerical absorptions are due to the monomerically dispersed molecules of the complexes, since Jahn-Teller distortions are decisively present in frozen solution at about - 200°C [3], and since it is difficult to consider a special kind of solvent effects only at the low temperature for such stable complexes as the copper(II) complexes of α-amino acids. It is, furthermore, shown by a simple analysis of line shape that the absorption of the solid line in

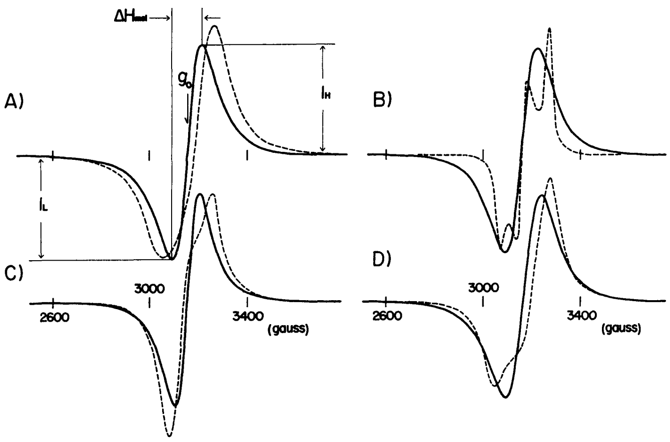

Fig. 1. The X-band ESR spectra of the copper(II) complexes of amino acids (———: frozen aqueous solution at 77°K, ---------: polycrystalline powder at room temperature).

(A): Bis-(L-alaninato)-Cu(II).
(B): Bis-(DL-alaninato)-Cu(II) monohydrate
(C): Bis-(L-serinato)-Cu(II)
(D): Bis-(DL-valinato)-Cu(II).

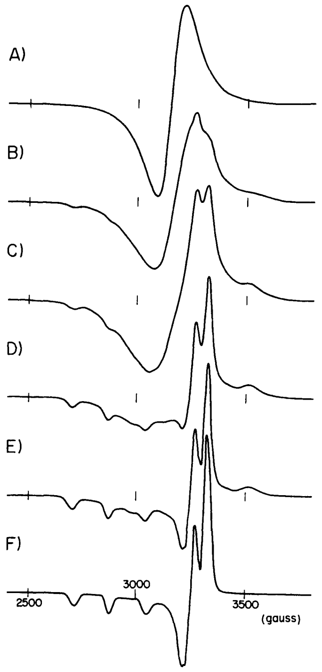

Fig. 2. The X-band ESR spectra (at 77°K) of bis-(L-alaninato)-Cu(II) in frozen water-methanol solvents (the following numbers represent the mole fractions of methanol).

(A): 0 (B): 0.003,
(C): 0.007, (D): 0.024
(E): 0.057, (F): 0.2 or above.

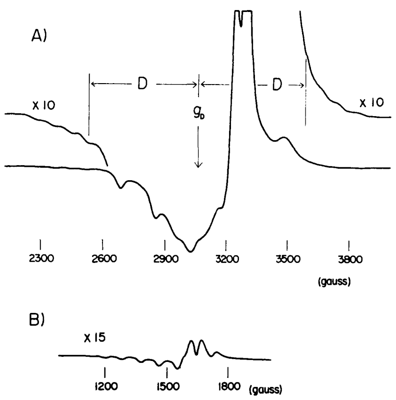

Fig. 3. The enlarged X-band ESR spectrum (at 77°K) of bis-(L-alaninato)-Cu(II) in a frozen water-methanol solvent (the mole fraction of methanol: about 0.03, the spectrum of (B) is the half-field one due to the $\Delta M = 2$ transitions, and g_D and D are the magnetic parameters of triplet dimers).

Fig. 1 (A) is close to a Lorentzian curve rather than to a Gaussian one, since the values of $\Delta H_{1/2}/\Delta H_{msl}$ are 1.60, 1.732, and 1.382 respectively. All these facts suggest that the symmetrical absorptions observed in frozen aqueous solution are due to a kind of aggregates of the complex molecules, called ⟨P⟩ hereafter, in which there are barely enough spin-exchange interactions to smear out the magnetic anisotropies.[4] Ayscough et al. studied the ESR spectra of α,α-diphenyl-β-picrylhydrazyl in various frozen organic solvents in connection with the effect of micro-crystal formation.[5] Although the possibility can not denied that the above-mentioned aggregates may be equal to micro-crystals of the complexes, the aggregates are quite different in structure from the usually obtained crystals, as is shown in Fig. 1 and as will be mentioned later.

The ESR line shapes were changed drastically by the addition of small amounts of methanol to the aqueous solution, as are shown in Fig. 2. Such was the case with other alcohols, isopropanol, ethyleneglycol, glycerin, and methyl cellosolve. The spectrum in Fig. 2 (A) is due to ⟨P⟩ , and the absorption line shape shown in Fig. 2 (F) is the representative one due to monomerically dispersed molecules of the copper(II) complexes.[6] It is, furthermore, understood from a consideration of ESR line shapes that the absorptions which appear at both about 3,500 and 2,950 gauss, as are shown in Fig. 2 (C) – (E), are due to the triplet dimers[7,8]; the half-field spectrum due to the $\Delta M = 2$ transitions is observed as soon as the absorption at about 3,500 gauss appears, and an enlarged spectrum in such case is shown in Fig. 3. It is, accordingly, clear that the ESR spectra shown in Fig. 2 (B) – (E) are made up of the proper superposition of three spectra due to the monomers, the triplet dimers, and ⟨P⟩ ; the three species coexist at the equilibrium depending upon the solvent compositions.

The magnetic parameters in the case of Fig. 2 were as follows; the dimers: $g_D = 2.164$, $D = 532 \times 10^{-4}$ cm^{-1}, the monomers: $g_{\parallel} = 2.264$, $g_{\perp} = 2.06$, $|A_{\parallel}| = 181 \times 10^{-4}$ cm^{-1}, where g_D and D are defined in Fig. 3. The Cu-Cu atomic distance, R, of the triplet dimers can be calculated from the above-determined values of g_D and D, using the equation $R_{calcd} = (0.650\, g_D^2/D)^{1/3}$, [7,9] and the R value was calculated to be about 3.85 Å, from which we can estimate the structure of the dimers. It has been reported that the R values are about 5.5 Å for the hydrate crystals of the copper(II) complexes of amino acids and about 4.8 Å for the anhydrous ones.[10] All these R values indicate that the dimers under discussion are quite different from the crystals in molecular configuration. The most probable structure of the dimers could be estimated to be as follows; monomeric halves are joined by two copper-oxygen bonds of about 3.2 Å, where the oxygen atoms are the ones directly coordinated to copper in each of the halves, and this gives a square pyramidal configuration for each copper. If ⟨P⟩ be made up by stacking these dimers, it will be reasonable that ⟨P⟩ shows a symmetrical ESR absorption line, since ⟨P⟩ is much smaller in the R value than the crystals and, therefore, is more effective in the spin-exchange

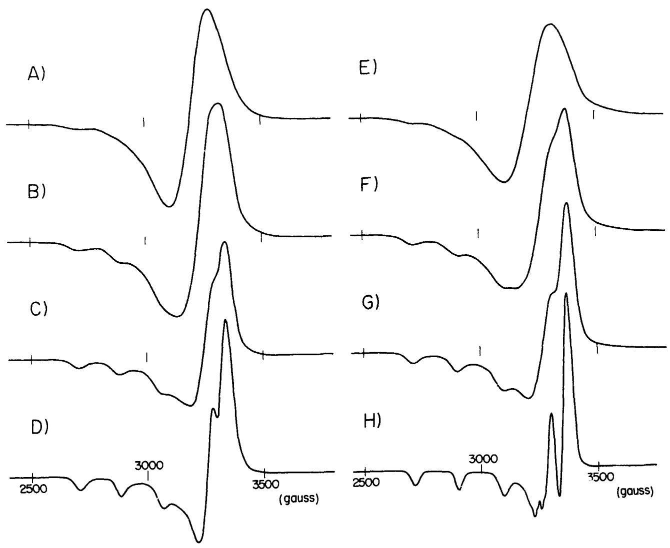

Fig. 4. The X-band ESR spectra (at 77°K) of bis-(L-alaninato)-Cu(II) in the frozen aqueous solutions containing the following substances (mol/l).

guanidine hydrochloride	(A):	0.025
	(B):	0.050
	(C):	0.100
	(D):	0.251
sodium perchlorate	(E):	0.021
	(F):	0.046
	(G):	0.100
	(H):	0.997

interaction.

Guanidine hydrochloride and urea are the representatives of protein denaturants. The symmetrical absorptions observed in frozen aqueous solution were changed into the spectra due to the monomers by the addition of these agents, as are shown in Fig. 4 (A) — (D) in case of guanidine hydrochloride. Interestingly, the same spectral changes also took place on addition of small amounts of certain inorganic salts, as are shown in Fig. 4 (E) — (H) in case of sodium perchlorate. There is no evidence indicating the direct interaction between these inorganic ions and the complex molecules in low concentrations. It has been reported that such inorganic salts as sodium perchlorate cause a breaking down of water structure.[11)] On the other hand, the symmetrical absorptions observed in frozen aqueous solution were kept almost unchanged by the addition of various amounts of such aprotic solvents as acetonitrile and acetone.

All the experimental facts above-mentioned indicate that the 1:2 complexes of copper(II) with amino acids are present in frozen aqueous solution as a special kind of aggregates, whose structures are different from those in the usually obtained crystals, and the aggregates disperse into dimers and monomers by the addition of alcohols, urea, guanidine hydrochloride, or certain inorganic salts. This behavior of the complex molecules in frozen solution may depend upon the water structure and is apparently similar to the phenomena of hydrophobic interactions.

REFERENCES

1) C.Tanford, P.K.De, and V.G.Taggart, J.Amer.Chem.Soc., 82, 6028 (1960); C.Tanford, ibid., 84, 4240 (1962); R.E.Weber and C.Tanford, ibid., 81, 3255(1959).

2) A.Kurono and K.Hamaguchi, J.Biochem., 56, 432 (1964); K.Hamaguchi, Nippon Kagaku Zasshi, 87, 893 (1966).

3) H.C.Allen, Jr., G.Kokoszka, and R.G.Inskeep, J.Amer.Chem.Soc., 86, 1023 (1964); G.Kokoszka, C.Reimann, H.C.Allen, Jr., and G.Gordon, Inorg.Chem., 6, 1657 (1967).

4) J.H.Van Vleck, Phys.Rev., 74, 1168 (1948); H.Kumagai, K.Ono, I.Hayashi, H.Abe, and J.Shimada, J.Phys.Soc.Japan, 9, 369 (1954).

5) P.B.Ayscough, H.E.Evans, and A.P.McCann, Nature, 203, 1378 (1964).

6) R.H.Sands, Pyhs.Rev., 99, 1222 (1955); T.Vänngård and R.Aasa, Proc. 1st Intern. Congr. "Paramagnetic Resenance," Jerusalem, 1962, ed. by W.Low, Academic Press, New York (1963), p. 509.

7) N.D.Chasteen and R.L.Belford, Inorg.Chem., 9, 169 (1970).

8) J.F.Boas, R.H.Dunhill, J.R.Pilbrow, R.C.Srivastava, and T.D.Smith, J.Chem.Soc. (A), 1969, 94.

9) M.Chikira and T.Isobe, to be published.

10) H.C.Freeman, "The Biochemistry of Copper," ed. by J.Peisach, P.Aisen, and W.E. Blumberg, Academic Press, New York (1966), p. 77.

11) H.S.Frank and M.W.Evans, J.Chem.Phys., 13, 507 (1945); H.S.Frank and W.Y.Wen, Discussions Faraday Soc., 24, 133 (1957).

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