Copper(I) and Copper(II) Complexes in Solution and the Crystalline State[1]

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ABSTRACT

Model studies on the copper-protein interaction that may catalyze lipid oxidation have been made by studying the copper complexes of glycyl-L-histidyl-glycine and ϵ-aminocaproic acid. The compositions of the complexes in solution were measured by emf methods. The structures of solid complexes were determined by x-ray diffraction techniques. The results indicate that all the solid complexes have their counterparts by species formed in solution.

It is well known that small amounts of copper play an important part in the development of oxidation defects in fat-containing food products (1). Of the copper ions present in foodstuffs, those bound in the form of complexes to nitrogen, oxygen and sulfur ligand atoms seem to catalyze the oxidation of lipids. However, no attempts have been made so far to identify a certain copper complex as being catalytically active. For such identification to be possible, it would be necessary to know the ranges of existences for the copper(I) and copper(II) complexes of the ligands.

In our laboratory we are investigating the copper complexes of a series of low molecular weight compounds intended as models for copper protein interaction.

COPPER COMPLEXES OF ϵ-AMINOCAPROIC ACID

The copper(II) complexes in 3.0 M $NaClO_4$ at 25 C were studied by emf methods using a glass electrode. The result is summarized in Figure 1. It shows the distribution of copper among different complexes. Mononuclear species having one and two ligands predominate (R. Osterberg and B. Toftgard, unpublished data). There are also two minor species, one binuclear and one having four ligands. This last complex has been isolated in the form of blue-violet crystals of composition $Cu(HA)_4(ClO_4)_2$. The crystal structure of this complex has been determined (2).

The copper(I) complexes of ϵ-aminocaproic acid in solution were investigated at the same conditions (R. Osterberg and B. Sjoberg, Contributions to Solution Chemistry in the Memory of Lars Gunnar Sillen. Edited by E. Hogfeldt, Stockholm 1971, in press.) The data were treated by first assuming the existence of homonuclear species (3) of the type Cu_pA_q. This gave: $P = 4 \pm 0.5$. In the next step we determine the prevailing value of q using the plot shown by Figure 2. Here, D denotes the total concentration of copper(I), and d and a the free concentrations of univalent copper and ligand, respectively. The data can be fitted to a straight line with slope 4. This corresponds to a single species, $Cu_4^IA_4$. From the intercept of the straight line we estimate $\log \beta_{44} = 42.8$.

In attempts to crystallize this univalent copper species we obtained four solid phases: one colorless, one green and two violet phases. The violet phases were formed by introducing the copper into the solution as copper(I) and then slowly oxidizing.

The results of our single crystal studies show that copper is eight coordinated in the blue-violet solid phase, $Cu(HA)_4(ClO_4)_2$. In this structure, copper is coordinated to a slightly distorted square formed by the carboxylate oxygen atoms of four different ligands (Cu-O = 1.97 A). The remaining oxygens of these carboxylic groups describe an elongated tetrahedron at 2.87 A from the copper (2).

The structure of one of the violet Cu(II) phases has also been determined. Here, the four closest ligand atoms are

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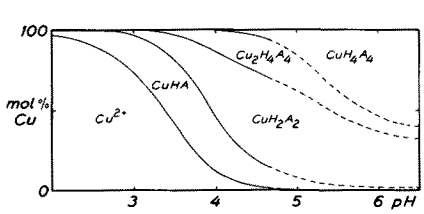

FIG. 1. Copper(II) complexes of ϵ-aminocaproic acid in 3.0 M $NaClO_4$ at 25 C. Distribution of Cu^{2+} among different complexes for total concentration of copper = 25 mM and total concentration of ligand = 1000 mM. For a certain pH the moles per 100 moles of Cu^{2+} present as a given species is represented by the segment of the vertical line falling within the coresponding range. Full drawn curves, experimental range; broken curves, extrapolated range.

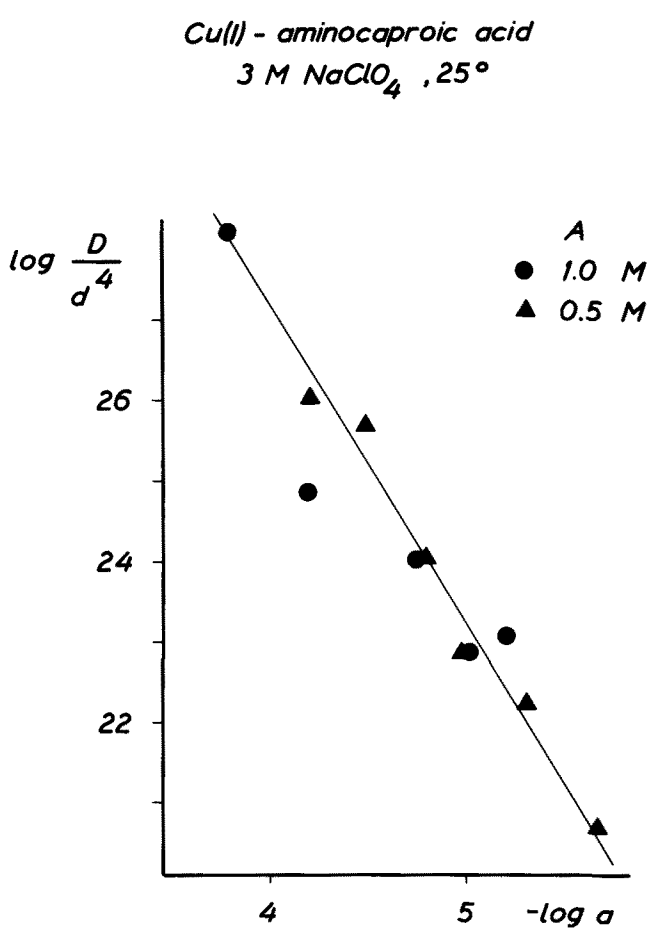

FIG. 2. Copper(I) complexes of ϵ-aminocaproic acid in 3.0 M $NaClO_4$ at 25 C. Determination of prevailing values of q, assuming species of the general composition $Cu_4^IA_q$. The slope of the straight line gives q = 4. The intercept corresponds to $\log \beta_{44} = 42.8$.

Cu(II) - GlyHisGly

3 M $NaClO_4$, 25°

-log h = 4.5 : Cu_2L , CuL , CuL_2 , $Cu_{15}L_{16}$

-log h = 7.0 : CuL_2 , $L(Cu_3L_3)_n$; n = 1 , 2 , 3, ...

-log h = 10.0 : $Cu_3L_4(Cu_2L_2)_n$, $(CuL_2)_n$; n = 1 , 2 , 3, ...

FIG. 3. Copper(II) complexes of glycyl-L-histidylglycine in 3.0 M $NaClO_4$ at 25 C. Summary of the result obtained by titration at constant pH.

two carboxylic oxygens and two nitrogen atoms (2). The ligand atoms come from four different ligands. There are two weak interactions through the other oxygens of the carboxylic groups, and as a consequence copper has coordination number six.

COPPER(II) COMPLEXES OF GLYCYLHISTIDYLGLYCINE

Figure 3 summarizes our solution data for this system. They were obtained by using both glass and copper amalgam electrodes. Since we worked at constant levels of pH we need not for each set of pH static data consider the number of protons in the complexes during the calculations (L denotes the ligand and includes all the protonated forms that may enter the complexes). Titrations were carried out for pH 4.5, 7.0 and 10.0. The results obtained at pH 4.5 indicate the formation of Cu_2L, CuL, CuL_2 and a polynuclear complex. The best fit to experimental data was obtained by assuming the polynuclear complex to be $Cu_{15}L_{16}$ (4). At pH 7 and 10 we have attempted to describe the data by infinite series of complexes using a modified version of the program Letagrop (5). At pH 7 the best fit was obtained assuming one single species CuL_2 and an infinite series of $L(Cu_3L_3)_n$ species; n = 1,2,3 . . . . At pH 10 the best agreement with the experimental data was

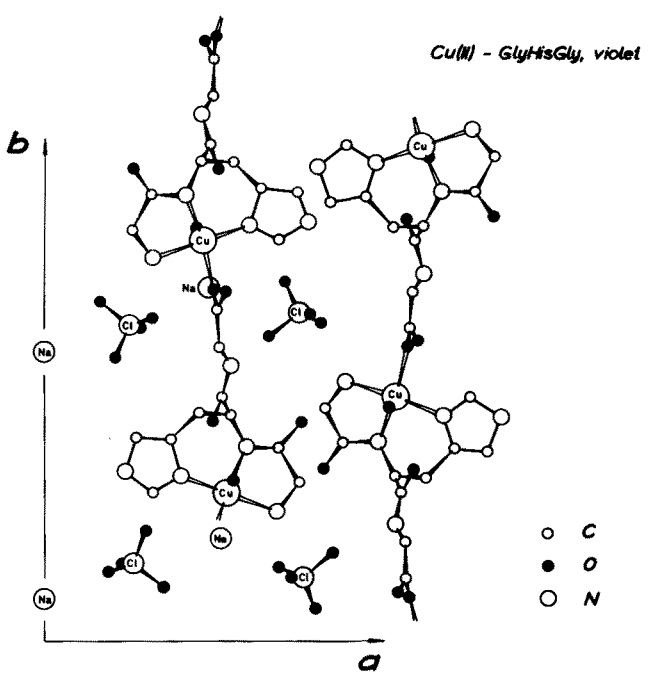

FIG. 4. Sodium glycyl-L-histidylglycinatocopper(II) perchlorate hydrate, packing of the -copper-ligand-copper- chains.

Cu(II) - GlyHisGly, violet

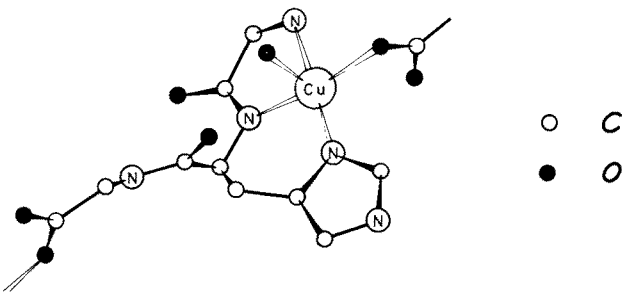

FIG. 5. Sodium glycyl-L-histidylglycinatocopper(II) perchlorate hydrate, coordination of copper.

obtained by assuming two infinite series of species.

This system is obviously very complicated and in order to obtain some independent information we have started a series of single crystal studies. Thus three solid phases have been prepared: one blue-violet, one light blue and one violet phase. The structure of the violet phase is shown in Figure 4. It consists of infinite peptide-copper chains, running parallell to the b axis (R. Osterbert and B. Sjoberg, unpublished data). Figure 5 shows the coordination of copper. It is bound to one peptide molecule via the α-amino, amide and imidazole nitrogens and to a second peptide molecule via the carboxylic oxygen. The fifth position is occupied by the oxygen of a water molecule. Also in this structure there is a weak interaction to the second oxygen of the carboxylic group indicating coordination number six.

A comparison between our findings in solution and in the crystalline state for Cu(II)-glycylhistidylglycine is shown in Figure 6. The blue-violet crystals formed from solutions at pH 7 have CuL as the asymmetric unit. Its counterpart in solution is polynuclear $(L(Cu_3L_3)_n$ species. Also, the violet crystals having infinite -copper-ligand-copper- chains compare with species of the type $L(CuL)_n$ found in solution. It is tempting to regard these latter species, $L(CuL)_n$, as fragments of the chains present in the crystal.

REFERENCES

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Cu(II) - GlyHisGly

Colour	Asymmetric unit	Space group	Solution
Blue-violet	$CuL(H_2O)_x$	$P4_12_12$	$L(Cu_3L_3)_n$
Violet	$CuL(NaClO_4 \cdot H_2O)$	$P2_12_12_1$	$L(CuL)_n$

FIG. 6. Copper(II) glycyl-L-histidylglycine in 3.0 M $NaClO_4$ solutions and in the crystalline state.