Metal Chelate Compounds with Higher Rings. I. The Preparations and Some Properties of Copper(II) Complexes of ω-Aminocarboxylic Acids

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Introduction

It is well-known that chelation in metal chelate compounds is most favoured when the functional groups are in the 1,4 or 1,5 positions.

In fact, relatively few chelate rings containing more than six atoms have been prepared from bidentate compounds. But the formation of larger rings does not always seem to be difficult if the preparation is carried out in non-aqueous media such as alcohol, ether, or chloroform. Recently Pfeiffer[1,2], for instance, has succeeded in preparing 7-, 8-, and 9-membered rings by the reaction of tetra-, penta-, and hexa-methylenediamine, respectively, with some metal salts in organic solvents. In the case of dicarboxylic acid complexes, there have also been reported some other complexes containing 7- and 8-membered rings[3,4,5]. Those increasing examples of higher rings have led us to perform the further systematic researches of metal chelate compounds with higher rings. The chief purpose of this series of work is to establish experimental data concerning the relation between the stability and ring sizes.

First of all, we picked up copper(II) complexes of ω-aminocarboxylic acids which contain carbon atoms from C_2 to C_6, getting two new examples of higher rings and one new type of amino acid complex. They are copper(II) complexes of γ-aminobutyric*- and δ-aminovaleric-acid, and of ε-aminocaproic acid, respectively. This paper describes the preparations and some properties of those three new compounds with some discussion on their stabilities.

Experimental

General Method of Preparation.—Two methods were adopted for preparing copper(II) complexes of ω-aminocarboxylic acids. The one was a heterogeneous reaction, **(A)**, of a ligand with copper(II) perchlorate in an organic solvent, while the other was a homogeneous reaction, **(B)**, making use of the action of an overwhelming amount of a ligand in an aqueous solution. The product obtained by the method **(A)** necessitated to be recrystallized from a mixed solution of alcohol and water containing a large amount of the ligand. Therefore, the difference between the two methods was rather slight. When the preparation was performed on a small scale, however, the method **(A)** seemed to have much advantage over **(B)**.

Preparation of Bis-(γ-aminobutyrato)-copper(II), $[Cu(NH_2(CH_2)_3COO)_2]\cdot 2H_2O$.—The method **(A)** was applied to prepare this compound. To a suspension of 4 g. of γ-aminobutyric acid in chloroform, was added 3.5 g. of copper(II) perchlorate hexahydrate. The heterogeneous mixture was shaken vigorously till the light blue of the copper(II) perchlorate changed to deep blue or violet. To complete the reaction the mixture was preserved overnight. The viscous product was freed from chloroform by blowing dry air on it after decantation. Then the crude product was dissolved in a small quantity of water, and the resulting solution was filtered quickly. A large amount of alcohol was added carefully to the clear deep blue filtrate. Within a few days fine crystals of $[Cu(NH_2(CH_2)_3COO)_2]\cdot 2H_2O$ were obtained. The yield of the reaction was almost quantitative, and the compound was pure enough at least for spectrochemical studies. The results of the analyses were as follows.

Anal. Found: C, 31.54; H, 6.49; N, 9.29; H_2O, 11.55. Calcd. for $[Cu(NH_2(CH_2)_3COO)_2]\cdot 2H_2O$: C. 31.57: H, 6.56: N, 9.21: H_2O, 11.84%.

Preparation of Bis-(δ-aminovalerato)-copper(II), $[Cu(NH_2(CH_2)_4COO)_2]$.—This compound was prepared by the method **(A)**. In this case, however, there was provided twice the quantity of the ligand in mole ratio for the complex formation, since it was assumed that the complex might have less stability compared with bis-(γ-aminobutyrato)-copper(II). Other procedures for preparation were the same as those described above.

Anal. Found: C, 40.54; H, 7.09; N, 9.13. Calcd. for $[Cu(NH_2(CH_2)_4COO)_2]$: C, 40.60; H, 6.76; N, 9.47%.

Preparation of Tetrakis-(ε-carboxyamylamine)-copper(II) Perchlorate, $[Cu(NH_2(CH_2)_5COOH)_4](ClO_4)_2$.—To prepare this compound the method **(B)** was adopted as well as **(A)**. Copper(II)

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[1] P. Pfeiffer, E. Schmitz and A. Böhm. *Z. anorg. allg. Chem.*, **270**, 287 (1952).

[2] P. Pfeiffer, *Naturwiss.*. **35**, 190 (1948).

[3] J. C. Duff, *J. Chem. Soc.*, **119**, 385, 1982 (1921); **123**, 560 (1923).

[4] T.S. Price and S.A. Brazier, ibid., **107**, 1367 (1915).

[5] T. S. Price and J. C. Duff, ibid., **117**, 1071 (1920).

* Although there are some descriptions of the complex formation of bis-(γ-aminobutyrato)-copper (II), the compound has never been isolated in the crystalline state up to date.

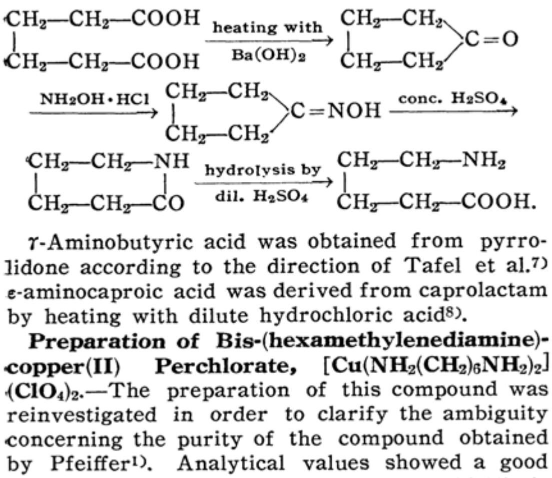
perchlorate hexahydrate was added to an aqueous solution which contained an over-whelming amount of ε-aminocarboxylic acid. After filtration of the deep blue solution, beautiful violet crystals were obtained. Within a couple of hours the deposition of the complex ended. The yield of the reaction was almost quantitative. The analyses of the compound were as follows.

Anal. Found: C, 36.52; H, 6.52; N, 7.02; Cu, 7.87; Cl, 9.39. Calcd. for $[Cu(NH_2(CH_2)_5COOH)_4](ClO_4)_2$: C, 36.62; H, 6.62; N, 7.12; Cu, 8.08; Cl, 9.01%.

The compound prepared by the method (**B**) was ascertained to be identical with that obtained by the method (**A**). However, (**B**) was much more convenient than (**A**), when the preparation was carried out on a large scale.

Preparation of Bis-(glycinato)-copper(II), $[Cu(NH_2CH_2COO)_2]\cdot H_2O$, and Bis-(β-alaninato)-copper(II), $[Cu(NH_2(CH_2)_2COO)_2]\cdot 6H_2O$.—Although there are some known methods, the above described method, (**A**), was also applied for preparing these two complexes. It was confirmed that there was no difference between the known and the present method.

Syntheses of the Ligands.—The synthesis of δ-aminovaleric acid was carried out by the method of Wallach[6] as shown in the following scheme:



γ-Aminobutyric acid was obtained from pyrrolidone according to the direction of Tafel et al.[7] ε-aminocaproic acid was derived from caprolactam by heating with dilute hydrochloric acid[8].

Preparation of Bis-(hexamethylenediamine)-copper(II) Perchlorate, $[Cu(NH_2(CH_2)_6NH_2)_2](ClO_4)_2$.—The preparation of this compound was reinvestigated in order to clarify the ambiguity concerning the purity of the compound obtained by Pfeiffer[1]. Analytical values showed a good agreement with each other as follows: Pfeiffer's analyses (crude substance): Cu, 12.74; N, 11.34. Analysis in this work (pure crystal): N, 11.09. Calcd. for $[Cu(NH_2(CH_2)_6NH_2)_2](ClO_4)_2$: Cu, 12.85; N, 11.32%.

The recrystallization of Pfeiffer's crude substance was performed in the same way as that used in the preparation of bis-(γ-aminobutyrato)-copper(II).

Properties of the Three Amino Acid Complexes.—The crystal of bis-(γ-aminobutyrato)-copper(II) is very small and prismatic, and shows a remarkable dichroism on the prism face, that is, deep violet and almost colourless. Tetrakis-(ε-carboxyamylamine)-copper(II) perchlorate also shows a clear dichroism on the well-developed face of the acicular crystal, that is, violet and blue. In the case of bis-(δ-aminovalerato)-copper(II), no optical properties were observed cleary because the crystal was extremely small. All the three compounds are stable in the crystalline state but quite unstable in water, and decompose over 180°C.

It is impossible to get the 0.01 M-solution of bis-(γ-aminobutyrato)-copper(II) on account of its decomposition even in an aqueous solution containing 0.08 M of the ligand. In water containing over 1.5 M of the ligand, however, clear solutions of the complex are obtainable without any detectable decomposition. δ-Aminovalerato-complex resembles the γ-aminobutyrato-complex in many respects, but the former is still more unstable in water than the latter. Although the three complexes show different colours from one another in the crystalline state, it is impossible to discriminate one from the others when they are dissolved in water with a large amount of the respective ligand. With respect to their infrared spectra, only the ε-aminocaproic acid complex shows a widely different curve, suggesting a different type of structure[9].

Results and Discussion

In this work three new complexes were obtained as shown in the experimental part. They were bis-(γ-aminobutyrato)-copper(II), bis-(δ-aminovalerato)-copper(II) and tetrakis-(ε-carboxyamylamine)-copper(II) perchlorate. As is clear from the analytical values of those compounds the former two complexes must be metal chelate compounds of the bis-(glycinato)-copper(II) type in structure. (Fig. 1). On the other hand, the last complex must have a structure which corresponds to an amminederivative complex, containing four unidentate ligands, as is seen in Fig. 2.

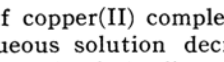


Fig. 1. Chelate-type.

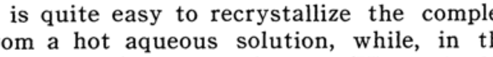


Fig. 2. Unidentate-type.

It is of interest to notice here that the stabilities of copper(II) complexes of ω-amino acids in aqueous solution decrease with an increasing length of the ligands. For example, bis-(glycinato)-copper(II) is so stable that it is quite easy to recrystallize the complex from a hot aqueous solution, while, in the case of bis-(β-alaninato)-copper(II), it is difficult to recrystallize the complex from a hot solution without any detectable decomposition. The comparison of the stabilities of β-alaninato- and γ-aminobutyrato-complex is

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[6] O. Wallach, *Ann.*, **312**, 179 (1900).

[7] J. Tafel and M. Stern, *Ber.*, **33**, 2230 (1900).

[8] J. C. Eck, Org. Syn., **17**, 7 (1937).

[9] To be submitted later.

the same as that of glycinato- and β-alaninato-complex, that is, the former is less unstable than the latter. This tendency is well-observed in the comparison of γ-aminobutyrato- and δ-aminovalerato-complex, too.

Judging from this tendency, it may be supposed that ε-aminocaproato-complex would be extremely unstable, if it would coördinate to a copper atom as a chelate ligand. In fact, ε-aminocaproic acid does not behave as a chelate ligand but coördinates to a copper atom as an unidentate ligand, as was already shown in the preceding section.

Thus, we may conclude that 8-ring is the highest ring for the formation of metal chelate compounds, so far as the copper(II) complexes of ω-aminocarboxylic acids are concerned. On the other hand, Pfeiffer has succeeded in preparing a 9-membered ring by the reaction of hexamethylenediamine with copper(II) perchlorate according to the same method*. This indicates directly that hexamethylenediamine is more favoured than ε-aminocaproic acid in forming the chelate ring. In other words, those bidentate ligands which have two nitrogen atoms in the functional end groups can form more stable copper(II) chelate compounds than can those having one nitrogen and one oxygen atom. With respect to the ligand, ε-aminocaproic acid, there are two possible ways in coördinating to a copper atom as an unidentate ligand. The one corresponds to the case in which the nitrogen attaches directly to the copper atom, and the other the case in which the oxygen plays the part of the donor atom. In the present case, however, the former is more likely than the latter in many respects. For example, the color of the complex quite resembles that of the ammine-complex. Spectroscopic studies also support the above interpretation, and show the presence of free carboxyl groups[9)]. Therefore, the structure of the copper(II) complex of ε-aminocaproic acid should coincide with that shown in Fig. 2, and the nomenclature of the complex should be " tetrakis-(ε-carboxyamylamine)-copper(II) perchlorate " taking the copper-nitrogen linkage into consideration. *In consequence, we reach a conclusion that nitrogen has a greater affinity than oxygen for copper.* In the case of chromium(III) complexes with amino acids[10)], oxygen seems to be more favoured than nitrogen in uniting with chromium contrary to the case with copper.

The Relation between Chelate Formation and Ring Sizes.—As is clear from the above described facts the greater the separation of the carboxyl and amino groups the less the tendency for chelate formation. In an aqueous solution, therefore, it is considered to be difficult to obtain a metal chelate compound which has a larger ring on account of the strong solvolytic aquation[11,12,13,14)]. In this respect, the heterogeneous reaction method adopted in this work is quite suitable for the study of the metal chelate compounds with higher ring, since there are very few interrupting factors in the reaction system. But yet the 9-membered ring was too unstable to be included in this work. In connexion with this fact, it seems to be desirable to afford some elucidation concerning the reason why the stablities of metal chelate compounds decrease with an increasing number of ring members.

Firstly, we propose steric effects. With very few exceptions the recognized examples of steric influences on stability are based on qualitative observations which usually involve formation or non-formation of the metal complexes. In the present case, however, that is not the way to consider the subject, since it is clear through the examinations of models that there is hardly expected any remarkable difference between the steric condition of δ-aminovalerato-chelate and that of ε-aminocaproato-chelate. Judging from their lactam forms, the amino and carboxyl groups in the free molecules of δ-amino- and ε-aminocarboxylic acid are accessible to each other without any serious distortion. Therefore, it seems to be easy for both the ligands to arrange their functional groups about a central metal atom so that the respective metal chelate complex can be formed. Such being the case, the stability of higher rings is not fully explained from the standpoint of the steric effect, though it is considered to be a very important factor.

Secondly, electronic influences induced with the separation of the two functional groups probably play another important role for the chelate formation. According to the work of Ley[15)], the acidity of ω-aminocarboxylic acid decreases with an increasing distance between carboxyl and amino groups, and there is the opposite inclination with respect-

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* Pfeiffer's 9-membered ring seemed to be unreliable, since the reaction product obtained by heterogeneous reaction had not been recrystallized. According to our reinvestigation, however, the analytical value of the pure crystal which was obtained by the present authors showed a good agreement with that of Pfeiffer's product.

10) R. W. Green and K. P. Ang, *J. Am. Chem. Soc.*, **77**, 5482 (1955).

11) A. Werner, *Ber.*, **40**, 15 (1907).

12) L. Tschugaeff, ibid., **39**, 3190 (1906); *J. Prakt. Chem.*, [2] **75**, 159 (1907).

13) P. Pfeiffer and M. Haimann, *Ber.*, **36**, 1063 (1903).

14) P. Pfeiffer and E. Lübbe, *J. prakt. Chem.*, [2] **136**, 321 (1933).

15) H. Ley, *Ber.*, **42**, 354 (1909).

to the basicity. Thus, it is quite natural to expect a different affinity for a metal with the separation of the two functional groups.

It may be considered that the stability of higher chelate rings is mainly influenced by the above two factors. Probably accumulations of slight steric constraints and electronic influences may prevent the ε-aminocaproic acid from the chelate formation with copper. We are continuing the study of the stability of higher chelate rings from another point of view.

Summary

Three new compounds, bis-(γ-aminobutyrato)-copper(II), bis-(δ-aminovalerato)-copper (II), and tetrakis-(ε-carboxyamylamine)-coppe(II) perchlorate, have been prepared. The first and the second compound belong to the bis-(glycinato)-copper(II) type, having a 7- and 8-membered ring, respectively. The last compound has a structure of ammine-derivative complex. In all cases preparations were carried out in non-aqueous media such as ether and chloroform.

It has been concluded that the 8-membered ring is the highest ring for the formation of metal chelate compounds, so far as the copper(II) complexes of ω-aminocarboxylic acids are concerned.

Stability of higher chelate rings was considered as the functions of steric constraints and electronic influences which may be induced with the separation of the two functional groups.

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