# The Preparation and Properties of Dipotassium Bis(glycylglycinato)cuprate(II)

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In a previous communication¹⁾ we reported the preparation of dipotassium bis(diketopiperazinato)cuprate(II). The investigation was, there after, continued in an attempt to obtain more detailed information on the structure of that novel compound; contrary to our expectations, we reached the conclusion that the complex we had isolated before was bis(glycylglycinato)cuprate(II) instead of bis(diketopiperazinato)cuprate(II). Our results do, however, seem worth reporting because the isolation of dipotassium bis(glycylglycinato)cuprate(II) is still new, and it does contribute to the knowledge in this field. In fact, all the papers previously published dealing with the bis(glycylglycinato)cuprate(II) complex were concerned only with the complex formation in solution.²⁾ The purpose of the present paper is not only to rectify the erroneous conclusion in the previous communication, but also to describe the preparation and properties of the dipotassium bis(glycylglycinato)cuprate(II).

## Experimental

**Dipotassium Bis(glycylglycinato)cuprate(II).**—A mixture of 11.4 g. (0.1 mol.) of diketopiperazine and 8.4 g. (0.15 mol.) of potassium hydroxide was dissolved in 150 ml. of water. To the solution there was added about 4 g. of freshly precipitated cupric oxide with a rapid agitation at about 25°C. Though the solution had been red-purple at the beginning of the reaction, it gradually became blue-purple. The reaction was completed within a few hours. After it had been filtered, the solution was evaporated to dryness in vacuo to give a red-purple, crystalline product. The product was repeatedly recrystallized from water by adding a large amount of acetone. The same compound was also prepared, employing the same procedure, from glycylglycine instead of diketopiperazine.

Although the thoroughly-purified crystal is fairly stable in a dry atmosphere, it is quite unstable to moisture; hence, it is impossible to obtain a red-purple aqueous solution without the coexistence of a large quantity of glycylglycinate ions. M. p. 113—120°C (decomp.). The results of the elemental analysis of the non-dehydrated crystal were as follows:

Found: K, 15.66; Cu, 12.75; C, 19.08; H, 5.00; N, 10.96; $H_2O$, 22.6. Calcd. for $K_2[Cu(C_4H_6N_2O_3)_2]\cdot 6H_2O$: K, 15.31; Cu, 12.43; C, 18.83; H, 4.71; N, 10.98; $H_2O$, 21.2%.

On the other hand, the results of the analysis of a completely dehydrated crystal were as follows:

Found: C, 24.12; H, 3.22; N, 13.15. Calcd. for $K_2[Cu(C_4H_6N_2O_3)_2]$: C, 23.88; H, 2.94; N, 13.90%.

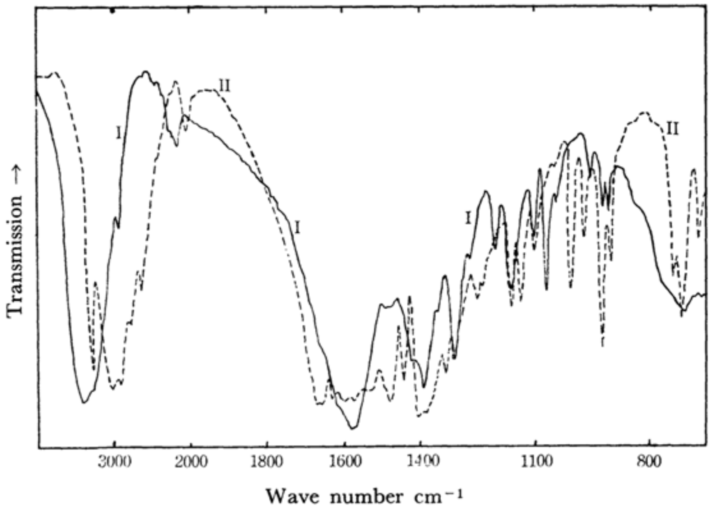

Fig. 1. Infrared absorption spectra of: I, dipotassium bis(glycylglycinato)cuprate(II); II, glycylglycine.

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1) A. Nakahara, K. Sakurai, K. Suzuki and Y. Nakao, This Bulletin, **38**, 1051 (1965).

2) H. Dobbie and W. O. Kermack, *Biochem. J.*, **59**, 246 (1955); S. P. Datta and B. R. Rabin, *Trans. Faraday Soc.*, **52**, 1117 (1956); F. R. N. Gurd and P. E. Wilcox, "Advances in Protein Chemistry," Academic Press, New York (1956), p. 311; W. L. Koltun, R. H. Roth and F. R. N. Gurd, *J. Biol. Chem.*, **238**, 124 (1963).

**Diketopiperazine (2, 5-Piperazinedione)** was prepared according to the directions of Sannié,[3] while in preparing glycylglycine we applied the method of Fischer et al.[4]

**Measurements.**—The infrared spectra were obtained by a Hitachi EPI-2 Infrared Spectrophotometer. The measurements were made at room temperature using the pressed potassium bromide disk technique in the wave number range from 700 to 4000 $cm^{-1}$ with a rock-salt prism. The spectra are shown in Fig. 1.

The visible and ultraviolet spectra were obtained with a Shimadzu Spectrophotometer, Type QB-50. Since the bis(glycylglycinato)cuprate(II) complex was readily dissociated in an aqueous solution, a solution containing 1F of potassium glycylglycinate was employed as the solvent.

The concentration of the complex used varied from $10^{-2}$ to $10^{-3}$F. The spectra are shown in Fig. 2.

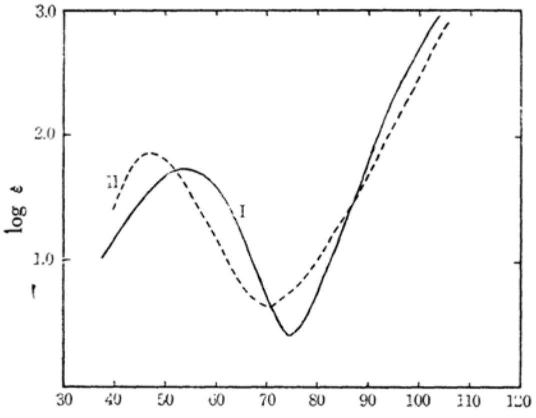
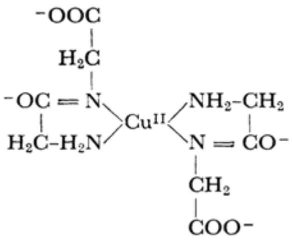


Fig. 2. Visible and ultraviolet absorption spectra of I, dipotassium bis-(glycylglycinato)cuprate(II) in water solution containing 1F of glycylglycine and 2F of potassium hydroxide; II, the same complex in water.

## Results and Discussion

It will, first of all, be necessary to correct our previous communication, which reported the successful preparation of bis(diketopiperazinato)-cuprate(II). The diketopiperazinatocuprate(II) structure was finally negated by the following two facts. First, it has been disclosed that the complex derived from glycylglycine is identical with that derived from diketopiperazine. Second, it has also been found that the results of the elemental analysis of the perfectly dehydrated complex eliminate the possibility of diketopiperazinato-cuprate(II) structure. The second fact may be supposed to be particularly important because the analytical values of the constituent elements in the non-dehydrated complex are expected to be same (except for the value of the water of crystallization) in the case of either the octahydrate of diketopiperazinatocuprate(II) or the hexahydrate of bis(glycylglycinato)cuprate(II). Thus, we may conclude that the complex prepared from the reaction between a mixture of potassium hydroxide and diketopiperazine and cupric oxide is not diketopiperazinatocuprate(II) but the bis(glycylglycinato)cuprate(II) complex.

The formation of this complex in solution has been investigated by several chemists.[2] They have presented a structure in which copper(II) links to the glycylglycinate anion only through the terminal amino group and the nitrogen of the peptide linkage. In other words, the carboxylate group is not involved in the coordination. The present work strongly supports the above proposal, giving more evidence for the structure I.



Structure I. The Bis(glycylglycinato)cuprate(II) Ion.

For example, all the four donor atoms (apart from the further coordination sites of copper(II)) are apparently nitrogen, judging from the color of the crystal and the location of the ligand field absorption band of the complex in solution, as is clear from Fig. 2. Indeed, the absorption maximum of the complex in the presence of an excess of glycylglycinate ions, $54 \times 10^{13}$ $sec^{-1}$, nearly coincides with that of bis(ethylenediamine)copper(II), suggesting its $Cu(N)_4$-type structure.

The proposal that the carboxylate group is not involved in the coordination can also reasonably be accepted, since there is estimated to be a considerable strain in the structure which contains the additional links of the carboxylate oxygens to the $Cu(N)_4$-type planar complex. As to the geometrical isomerism, the trans configuration, which has been suggested by Gurd and Wilcox,[2] is positively supported, because X-ray study* has recently shown that there is a center of symmetry in the complex.

The complex is readily dissociated in water, without the aid of a large quantity of glycylglycinate ions, to give a blue solution which may be considered to correspond to a $Cu(N)_3(O)_1$- or $Cu(N)_2(O)_2$-type structure.[5] This may be seen as the result of a displacement of peptide nitrogen in the coordination by water molecules. Indeed, the absorption

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[3] C. Sannié, *Bull. Soc. Chim. France*, **9**, 487 (1942).

[4] E. Fischer and E. Fourneau, *Ber.*, **34**, 2868 (1901).

* Private communication from Dr. Yoshio Sasada of the Institute for Protein Research, Osaka University.

[5] A. Nakahara, This Bulletin, **32**, 1195 (1959).

maximum of the complex alone in water appears in the region of considerably longer wavelengths, as is shown in Fig. 2, suggesting the validity of the above consideration.

Thus, the hygroscopic nature of this particular complex crystal does not imply the simple dissolution of the complex in the absorbed water, but it does imply the partial dissociation of the complex in the absorbed water. On the other hand, the water molecules which displaced the peptide nitrogen from the coordination sites can be expelled by a large amount of acetone to give the $Cu(N)_4$-type structure again. The recrystallization of the present complex using water and acetone may proceed by means of such a mechanism.

## Summary

The previous conclusion has been corrected as follows. The complex prepared from the reaction of cupric oxide with a mixture of potassium hydroxide and diketopiperazine is not diketopiperazinatocuprate(II) but bis(glycylglycinato)-cuprate(II).

The preparation and some properties of dipotassium bis(glycylglycinato)cuprate(II) have been described. As to the structure of the complex, it has been concluded, from powerful evidence, that two glycylglycinate anions are coordinated around copper(II) in the trans configuration only through the terminal amino group and the nitrogen in the peptide linkage.

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