The Preparation and Properties of N-Salicylideneglycinato-aquo-copper(II), Sodium N-Salicylideneglycylglycinato-cuprate(II) and Related Compounds

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It was demonstrated by Eichhorn and Marchand[1] that the coordination of copper(II) ion with the Schiff base produced from salicylaldehyde and glycine results in a stabilization of the >C=N-double bond under conditions that would promote its rupture in the absence of the metal. However, the formation of the copper(II) chelate of salicylideneglycine was observed only in a solution on the basis of a spectroscopic investigation; and the composition of the complex was deduced from an extension of the method of continuous variation to a three component system, copper : salicylaldehyde : glycine. In the present work the same compound, *N*-salicylideneglycinato-aquo-copper(II), **A**, was isolated in the crystalline state and investigated as to its properties. Sodium *N*-salicylideneglycylglycinato-cuprate(II), **B**, was also prepared and investigated as to its structure.

Experimental

Preparation of Copper(II) Chelates.—*N-Salicylideneglycinato-aquo-copper(II).*— To a solution of 6 g. of glycine in 100 ml. water was added 10 g. of salicylaldehyde. The resulting mixture was stirred and heated at about 60°C.

Upon the addition of 16 g. of crystalline cupric acetate, a dark-green solution was formed. A yellowish-green crystalline solid of *N*-salicylideneglycinato-aquo-copper(II) was then gradually deposited within half an hour. The reaction mixture was allowed to cool and filtered by suction. The additional crude product was also obtained by evaporating the filtrate. The yield, in total, was almost quantitative. Recrystallization from a large amount of water gave acicular crystals which decomposed at 240°C.

Anal. Found: C, 32.46; H, 5.39; N, 4.21; H_2O, 26.9. Calcd. for tetrahydrate of **A**: C, 32.60; H, 5.14; N, 4.23; H_2O, 27.2%.

In the above procedure cupric sulfate in place of acetate was observed to give the same result. Furthermore, the same compound was prepared also by reactions between: (1) bis-glycinato-copper(II) and bis-salicylaldehyde-copper(II) in 1:1 molar ratio; (2) bis-glycinato-copper(II) and salicylaldehyde in 1:2 molar ratio; (3) glycine and bis-salicylaldehyde-copper(II) in 2:1 molar ratio.

However, the yield of reaction 2) or 3) was only half of that of 1), since the copper was not sufficient to give the same amount of the product.

The compound is soluble in water, methanol and ethanol, though the solubility is comparatively small, especially in the latter two solvents.

Sodium N-salicylideneglycylglycinato-cuprate(II).— To a solution of 5.3 g. of glycylglycine and 3.2 g. of sodium hydroxide in 100 ml. water was added 8 g. of crystalline cupric acetate. After heating the resulting mixture on a water bath, a deep-blue solution characteristic of copper(II) chelates of peptides was gradually formed. Upon the addition of 5 g. of salicylaldehyde the color of the solution changed to violet. The solution was stirred and heated for thirty more minutes, and was then filtered. The filtrate was concentrated to a small volume and allowed to stand, whereupon beautiful violet needles were obtained. These were recrystallized from their concentrated aqueous solution by adding alcohol or acetone.

Anal. Found: C, 30.69; H, 5.02; N, 6.32; H_2O, 25.8. Calcd. for hexahydrate of **B**: C, 30.81; H, 4.91; N, 6.54; H_2O, 25.2%.

A complete dehydration of the compound was performed by heating the crystals in vacuo at 56°C.

Anal. Found: C, 41.00; H, 3.04; N, 8.89. Calcd. for **B**: C, 41.2; H, 2.81; N, 8.75%.

As described above, an aqueous solution of the compound is violet, but reversibly changes to green in an acid solution.

Potassium salt of the same copper(II) chelate was also obtained in the same way by employing potassium hydroxide instead of sodium hydroxide.

In order to identify the potassium salt, a precipitation of potassium hexanitro-cobaltate(III) was ascertained.

Copper(II) chelate of N-salicylideneglycineethylester.—This compound, **F**, was prepared according to the direction of Pfeiffer et al.[2] by treating the copper(II) complex of salicylaldehyde with hydrochloride of glycineethylester in the presence of sodium acetate in alcohol. It was also confirmed that a reaction in an aqueous suspension between bis-salicylaldehyde-copper(II) and hydrochloride

1) G. L. Eichhorn and N. D. Marchand, *J. Am. Chem. Soc.*, **78**, 2688 (1956).

2) P. Pfeiffer, W. Offermann and H. Werner, *J. prakt. Chem.*, **159**, 313 (1942).

of glycineethylester in the presence of sodium hydroxide is more convenient than the previously reported one[2]. After recrystallization from pyridine or ethanol olive-green crystals were obtained, which decomposed at 200°C, showing a good agreement with the previous datum[2].

Glycylglycinato-aquo-copper(II)[3]. — Freshly precipitated cupric hydroxide was treated in an aqueous suspension with a slight excess of glycylglycine. The resulting deep-blue solution was filtered and concentrated to a small volume, and was then filtered again. The filtrate was allowed to stand for several days over sodium hydroxide, whereupon deep-blue prisms were obtained. These were recrystallized from their concentrated aqueous solution by adding alcohol.

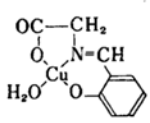
Anal. Found: C, 20.99; H, 4.53; N, 12.09; H_2O, 14.73. Calcd. for monohydrate of **C**: C, 20.85; H, 4.35; N, 12.18; H_2O, 15.65%.

Measurements. — The visible and ultraviolet absorption spectra were determined with a Beckman DU Spectrophotometer at room temperature. The concentration of the solutions varied from 10^{-2} to 10^{-5} F/1.

The infrared spectra were obtained by a Hilger H 800 Infrared Spectrophotometer using a sodium chloride prism. The potassium bromide disk method was employed.

Discussion

The result of analyses and other small tests described in the preceding section afford good reasons to assign structures **A** and **B** for the copper(II) chelate of *N*-salicylideneglycine and that of *N*-salicylideneglycylglycine, respectively. Structure **A** is exactly the same as that postulated by Eichhorn and Marchand[1] on the basis of a spectroscopic investigation. Though they reported also on the formation of 1 : 2 : 2 copper : salicylaldehyde : glycine complex at pH 5, no such compound was isolated in the present investigation even under conditions that would favor its formation. For example, in the case of the reaction between bis-glycinato-copper(II) and salicylaldehyde or between glycine and bis-salicylaldehyde-copper(II) a 1 : 2 : 2 ratio of copper, salicylaldehyde and glycine was employed in a neutral solution, but the reaction product was only the 1 : 1 : 1 complex, **A**. The disagreement might be understood by taking the low solubility of **A** into consideration, since there might be an equilibrium between 1 : 1 : 1- and 1 : 2 : 2-complex in the system.



A

Inspection of the chemical quations of the reactions used in this work reveals that the formation of **A** is accompanied by a liberation of acid:

$$CuSO_4 + C_6H_4\langle^{OH}_{CHO} + NH_2CH_2COOH \rightarrow \mathbf{A} + H_2SO_4$$

$$Cu(CH_3COO)_2 + C_6H_4\langle^{OH}_{CHO} + NH_2CH_2COOH \rightarrow \mathbf{A} + 2CH_3COOH$$

In fact, it was ascertained that the solution was considerably strong acid when the reaction was over. Thus, the present work supports the previous conclusion[1] that the cordination of copper(II) with salicylideneglycine stabilizes >C=N- double bond to such an extent that the Schiff base complex is capable of existence even in acid media, where the uncomplexed Schiff base is dissociated.

It may further be speculated that the tremendous effect of this kind, of metal, may play an important role also in the case of the non-enzymatic transamination reaction of pyridoxal[4-6].

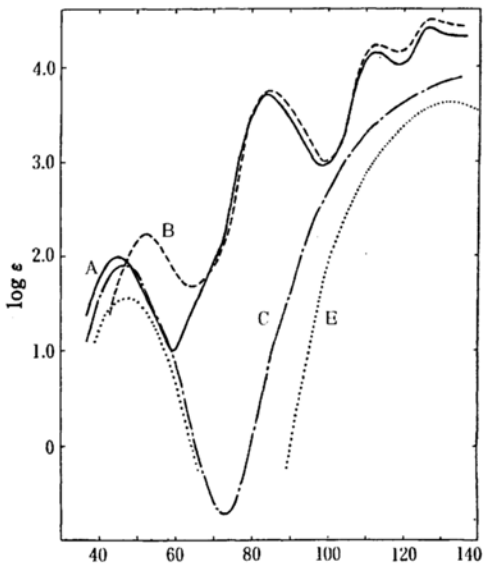


Fig. 1. Visible and ultraviolet absorption spectra of: **A**, *N*-salicylideneglycinato-aquo-copper(II); **B**, sodium *N*-salicylideneglycylglycinato-cuprate (II); **C**, glycylglycinato-aquo-copper(II); **E**, bis-glycinato-copper(II), in aqueous solutions.

3) A. R. Manyak, C. B. Murphy and A. E. Martell, *Arch. Biochem. Biophys.*, **59**, 373 (1955).
4) F. Schlenk and A. Fischer, *Arch. Biochem.*, **12**, 69 (1947).
5) D. E. Metzler, M. Ikawa and E. E. Snell, *J. Am. Chem. Soc.*, **76**, 648 (1954).
6) J. B. Longenecker and E. E. Snell, *Proc. Natl. Acad. Sci.*, **42**, 221 (1956).

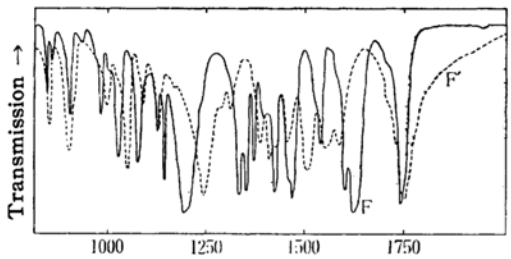


Fig. 2. Infrared absorption spectra of: **F**, copper(II) chelate of *N*-salicylideneglycineethylester; **F'**, hydrochloride of glycineethylester.

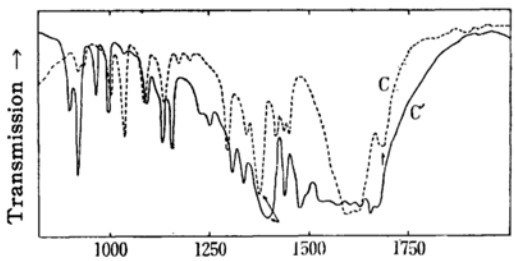


Fig. 3. Infrared absorption spectra of: **C**, glycylglycinato-aquo-copper; **C'**, glycylglycine.

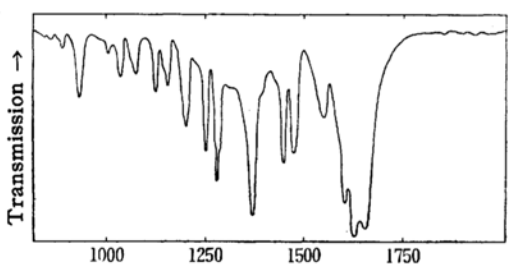


Fig. 4. Infrared absorption spectrum of *N*-salicylideneglycinato-aquo-copper(II), **A**.

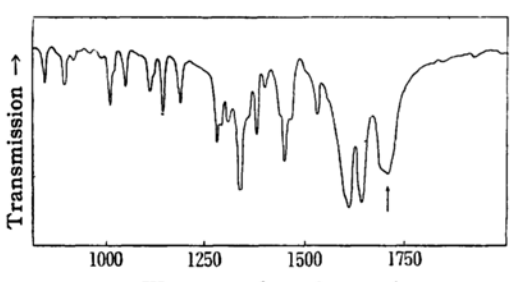
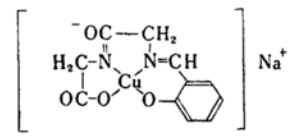


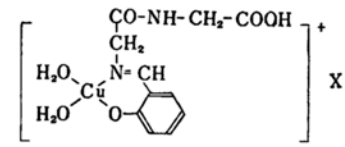
Fig. 5. Infrared absorption spectrum of sodium *N*-salicylideneglycylglycinatocuprate(II), **B**.

Contrary to the case of *N*-salicylideneglycine which is coordinated to copper(II) ion as a terdentate chelate ligand even at a low pH value, *N*-salicylideneglycylglycine behaves as a quadridentate ligand in neutral or basic media and perhaps as a bidentate in acid media.

Formula **B** corresponds to the structure of the copper(II) chelate in neutral or basic media, while **D** would correspond to that in acid media.



B



D

Though there is no decisive reason for the latter the fact that it is green in acid media seems to favor the formula, **D**, in which the peptide nitrogen and carboxylate oxygen are detached from the copper.

As to the process of the formation of **A** the first step may be the coordination of copper(II) with glycinate ion, since a deep-blue solution characteristic of copper(II) chelates of amino acids was first observed before any other marked change occurred, regardless of the methods of preparation employed in this investigation. A chelate ligand in coordination very often increases its reactivity on account of the effect of the metal[7]. Therefore, it may be considered that the glycinate ligand in coordination gains greater activity and becomes easier to form the Schiff base with salicylaldehyde. In contrast with this type of reactions, Sato et al.[8] already reported that bis-glycinato-copper(II) reacts with acetaldehyde in a basic solution to give threonine in a very good yield. The difference between the above two reactions may be attributed to the effect of the -OH group in the molecule of salicylaldehyde.

Visible and Ultraviolet Absorption Spectra.—

7) A. E. Martell and M. Calvin, "Chemistry of the Metal Chelate Compounds", New York Prentice-Hall, Inc., New York (1952) p. 336.

8) M. Sato, K. Okawa and S. Akabori, This Bulletin, **30**, 937 (1957).

TABLE I. ABSORPTION MAXIMA OF COPPER(II) COMPLEXES IN THE VISIBLE REGION

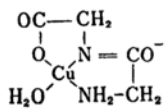
Compounds	Solvent	ν_{max} 10^{13} sec^{-1}	log ε_{max}	Type of complexes with respect to the kind of donor atoms
$CuSO_4 \cdot 5H_2O$*	water	36.5	1.09	4O
$(NH_4)_4[CuO_6Mo_6O_{18}H_6] \cdot 5H_2O$*,a)	〃	37.1	1.06	
$[Cusalgly(H_2O)] \cdot 4H_2O$, **A**	〃	45.3	1.98	1N3O
$CuSO_4 \cdot en \cdot 3H_2O$*	1/4 F en·2$HClO_4$ solution	45.3	1.51	2N2O
$[Cugly_2] \cdot H_2O$, **E**	water	48.0	1.54	
$[Cuala_2] \cdot H_2O$	〃	48.8	1.54	
$[Cu(C_5H_{10}O_2N)_2] \cdot 2H_2O$*b)	1/100 F ligand solution	49.5	2.04	
$[Cuglygly(H_2O)] \cdot H_2O$, **C**	water	46.5	1.89	
$Na[Cusalglygly] \cdot 6H_2O$, **B**	〃	52.2	2.20	
$[Cu(NH_3)_4]SO_4 \cdot H_2O$*	$(NH_4)_2SO_4 + NH_3$ solution	49.2	1.76	4N
$[Cuen_2]SO_4 \cdot 2H_2O$*	water	54.0	1.85	

* Reported by H. Ito[9].

a) Ammonium hexa-molybdato-cuprate(II).

b) Di-α-methylamino-isobutyrato-copper(II).

Absorption curves of **A** and **B**, and of the copper(II) chelate of glycine, **E**, and glycylglycine, **C**, are shown in Fig. 1. The curves of **C** and **E** consist of two each

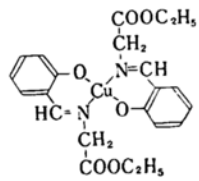


C

of typical absorption bands, whereas both **A** and **B** contain some additional absorption bands in the ultraviolet region. These additional bands apparently belong to the specific absorption bands, being due to the salicylaldimino group of the ligand in coordination. On the other hand, the small absorption bands on each curve in the visible region are the characteristic band of copper(II) complexes. Their numerical data together with those of some other copper(II) complexes are tabulated in Table I. Inspection of Table I reveals that the absorption maximum of **B** is hypsochromically shifted to a considerable degree compared with those of the same type of complexes with respect to the kind of donor atoms. In fact, the color of **B** rather resembles that of bis-ethylenediamine-copper(II) complex, in which all the four donor atoms are nitrogens. From this point of view, it may be supposed[9] that *N*-salicylideneglycylglycinato-cuprate(II), **B**, belongs to a typical dsp^2-type complex.

Infrared Absorption Spectra. — Infrared absorption curves of **A**, **B**, **C**, and of the copper(II) chelate of *N*-salicylideneglycine-ester, **F**, are shown in Figs. 2—5.

From a comparison of the spectrum of **A** with that of **F**, in which two carboxylate groups of the ligand are protected from coordination by being bound to ethyl groups, it may be concluded that the carboxylate group of **A** is apparently coordinates to copper(II). This is owing to the fact that there is no very strong absorption band in the region of 1700～1740 cm^{-1} on the curve of **A**, contrary to the case of **F**.



E

The carbonyl peak of the carboxylate groups is usually shifted toward lower frequencies upon coordination[10,11]. In the present case, however, the carbonyl peak which is expected to shift toward lower frequencies can not be assigned, since there are some very strong absorptions of salicylaldimino group of the ligand in the expected region.

In the case of the curve, **C**, the carbonyl peak of the coordinated carboxyl group

9) H. Ito, *J. Chem. Soc. Japan, Pure Chem. Sec.* (*Nippon Kagaku Zasshi*), **78**, 1395 (1956).

10) D. H. Busch and J. C. Bailar, Jr., *J. Am. Chem. Soc.*, **75**, 4574 (1953).

11) S. Kirschner, ibid., **78**, 2372 (1956).

is observed at about 1600 cm^{-1}. Not only the anti-symmetric C–O stretching band, but also the shifting of the symmetric stretching band from 1400 to 1370 cm^{-1} affords an additional evidence for the structure with a coordinated carboxyl group[12].

Of interest is a weak absorption at 1680 cm^{-1}, which is supposed to be concerned with the carbonyl group of the peptide link. The concerned band in the free peptide molecule normally appears at about 1655 cm^{-1} [13].

However, the coordination of copper(II) with the nitrogen atom of peptide may shift the band to some extent. Richard and Thompson[14] have pointed out, for example, that electrophilic substituents on the nitrogen atom can give rise to an increase in the frequency up to 1680 cm^{-1}.

The same kind of shifting of the peptide carbonyl band is more effectively presented in **B**. In this case, however, the absorption band is much stronger than that of **C**; and the degree of shifting is even greater. This fact may indicate that the linkage between copper(II) and peptide nitrogen is stronger in **B** than in **C**, and is consistent with the conclusion that **B** might be a typical dsp^2-type complex.

12) K. Nakamoto, J. Fujita, S. Tanaka and M. Kobayashi, ibid., **79**, 4904 (1957).
13) L. J. Bellamy, "The Infra-red Spectra of Complex Molecules", John Wiley & Sons, Inc., New York (1954), p. 192.
14) R. E. Richards and H. W. Thompson, *J. Chem. Soc.*, **1947**, 1248.

Summary

The two new compounds, *N*-salicylideneglycinato-aquo-copper(II) and sodium *N*-salicylideneglycylglycinato-cuprate(II) were prepared and investigated as to their structure.

Their infrared, visible and ultraviolet absorption spectra together with those of some related compounds were measured and discussed.

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