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Nature of the Copper(II) Complex Formed in the Reaction of Formaldehyde with Bis(glycinato)copper (II)

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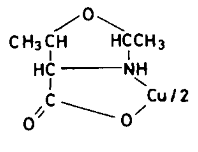
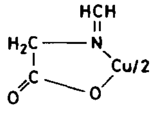
While the reactions of α-aminoacidato metal complexes with aldehydes have been extensively studied [1–9], much of the work involves bis(glycinato)-copper(II) and acetaldehyde. In most instances, the reaction mixtures are treated under acid conditions resulting in the isolation of the metal-free hydroxymethyl substituted amino acid rather than the metal-containing species. Recently [8] it has been shown that the reaction of glycine with acetaldehyde in alkaline medium in the presence of basic copper carbonate yields the compound, bis(2,5-dimethyloxazolidine-4-carboxylato)copper(II), shown schematically as *1*.



1

This important discovery led to mechanistic studies by Ichikawa and co-workers [7] who observed that formaldehyde cannot be easily condensed with bis(glycinato)copper(II). This behaviour has been explained on the assumption that the product in the first step of the condensation reaction of formaldehyde with bis(glycinato)copper(II) is the N-hydroxymethyl derivative, and it remains as such on account of the instability of the corresponding Schiff-base type intermediate, *2* (derived from the N-hydroxymethyl compound), under alkaline conditions. The formation of *2* is supposed to be base catalyzed.



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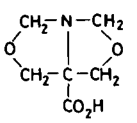
However, the preparation of bis(oxazolidine-4-carboxylato)metal(II) complexes has been carried out in the absence of a base [10]. Hence Ichikawa's argument must be viewed with some doubt. Moreover, a recent investigation [9] has shown that formaldehyde condenses readily with bis(L-serinato)-copper(II) at pH 7–9 resulting in the formation of the copper(II) complex of *3* [11].



3

It is therefore the objective of the present work to investigate the condensation reaction of formaldehyde with bis(glycinato)copper(II) with a view of obtaining an oxazolidine type compound. The reaction which was carried out in the presence of a base gave a deep blue crystalline product. The infra-red absorption spectrum of the compound is identical with that of the copper(II) complex of *3* (obtained by the base catalyzed reaction of formaldehyde with bis(L-serinato)copper(II)) (Fig. 1). This leads us to propose the same structure for the deep blue crystalline product. Furthermore microanalysis results agree closely with the proposed molecular formula. It is further observed that the reaction product is only slightly soluble in cold water and insoluble in the common organic solvents and when it is treated with H_2S, α-hydroxymethylserine is obtained. The same is observed for the copper(II) complex of *3* [12].

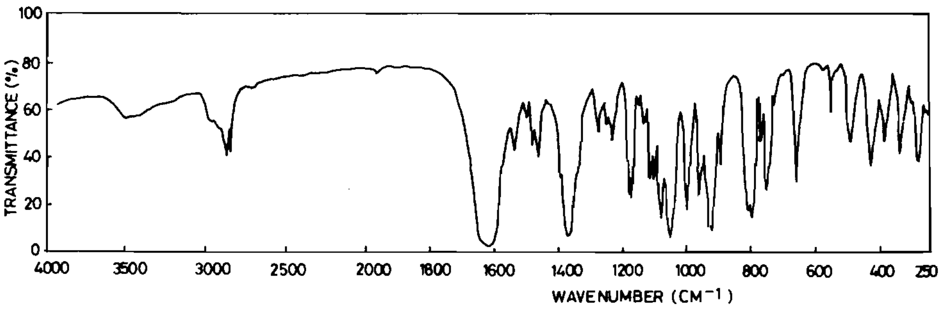


Fig. 1. Infra-red spectrum of the copper(II) complex of *3*.

The formation of N-substituted glycine complexes has been reported [13, 14]. However it was only recently that aldehydes have been shown to undergo condensation reactions with bis(α-aminoacidato)metal complexes to give oxazolidine type compounds [8, 9]. In the present work, the formation of the copper(II) complex of *3* indicates that the amino group of bis(glycinato)copper(II) is attacked by formaldehyde to form a mono-N-hydroxymethyl derivative. Attack by formaldehyde on the carbanion species formed under basic conditions also occurs and an oxazolidine is subsequently formed by cyclization. This is followed by further addition of hydroxymethyl groups on the α-carbon atom and the secondary nitrogen atom. Cyclization again occurs to give the copper(II) complex of *3*. The ready loss of protons (from the nitrogen atom as well as the α-carbon atom) which precedes electrophilic attack by formaldehyde is well known in metal glycine complexes [15–17].

Experimental

Bis(glycinato)copper(II) was prepared by previously reported procedures [18, 19]. A mixture consisting of bis(glycinato)copper(II) (1.9 g), formaldehyde (100 cm^3 of a 30% w/v solution) and sodium bicarbonate solution (100 cm^3 of a 0.1 *M* solution) was diluted to 500 cm^3 and thermostatted in a water bath at 40 °C (pH of the solution was 8.0).

The deep blue crystals which formed after 6 days were filtered and washed successively with distilled water, ethanol and diethyl ether and were finally dried under vacuum for 6 hours. Yield 2.2 g (71%). *Anal.* Found: C, 37,68; H, 4.38; N, 7.21. Calcd. for $C_{12}H_{16}N_2O_8Cu$: C, 37.95; H, 4.24; N, 7.37%.

The copper(II) complex of *3* was also prepared by a previously reported method [20] in order to compare its infrared absorption spectrum with that of the above reaction product.

Microanalyses were carried out by the Australian Microanalytical Service, CSIRO, Melbourne, Australia.

Infrared absorption spectra of the reaction product as well as the copper(II) complex of *3* were recorded using a Beckman IR 20A spectrophotometer (see Fig. 1). Samples were prepared as KBr discs.

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11 The systematic name for *3* is dihydro-1H,3H,5H-oxazolo-[3,4-c]-oxazole-7a-carboxylic acid.
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