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Copper and Zinc Complexes of Schiff Base Ligands Containing Penicillamine

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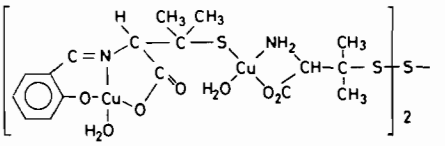
Schiff base amino acid complexes of copper and zinc are believed to be key intermediates in the non-oxidative transformation of pyridoxal-dependent enzymes [1]. However, little work has been reported on the formation of this type of complex using thiol-containing amino acids, possibly because the products obtained tend to be complex. For example, preparation of the ligands can lead to the formation of a thiazolidene ring [2]. In a model study, using salicylaldehyde or 2-hydroxy-1-naphthaldehyde and penicillamine with copper or zinc acetate, we have isolated stoechiometric products which give some insight into the complexities of these systems.

In the case of copper, constituent combination of the reactants in ethanol, using a minimum amount of water to ensure solubility of the amino acid, produced complex products. However, when this reaction, using salicylaldehyde, was carried out under nitrogen, a compound, N-salicylidene penicillamine$_2$-copper$_2$·½H_2O (A) could be crystallised out. N-salicylidene penicillamine and 2-hydroxy-1-naphthilidene penicillamine can be prepared in aqueous ethanol and subsequent reaction of these ligands with copper(II) acetate in ethanol produced crystals of N-salicylidene penicillamine copper 1·5H_2O (B) and 2-hydroxynaphthilidene-1-penicillamine copper-·2H_2O. In the case of zinc, only N-2-hydroxy-1-naphthilidene penicillamine zinc·2H_2O was characterised. Analysis of the products for sulphur and copper as well as CH and N confirmed the formulae. Thermal belance measurements further confirmed these results and suggested that the water molecules are chemically bonded in the complexes.

Infrared spectra and chemical tests using Ellman's method indicate that the ligand contained free thiol groups but none could be detected in the compounds. Anti-Stokes Raman spectra of the ligand and zinc complex suggested that the sulphur was coordinated in the zinc complex and that there was no disulphide bond in either compound. Raman spectra of the copper compounds were not obtained due to absorption of the incident radiation by the complexes. The infrared spectrum of the ligand 2-hydroxy-1-naphthilidene penicillamine in the 1600 cm^{-1} region consisted of two bands at 1630 cm^{-1} and 1580 cm^{-1}. The Raman spectrum of this ligand was of low sensitivity due to fluorescence but one band at 1585 cm^{-1} was detected. In the zinc complex there was one rather broad band in both the infrared ($\nu \cong 1610$ cm^{-1}) and Raman spectra ($\nu \cong 1615$ cm^{-1}). It seems most likely, on the basis of the relative intensities of the infrared and Raman spectra, that the ligand exists in a zwitterionic form in the solid, with the azomethine band at a lower frequency than usual due to the positive charge. Formation of the Schiffs base complex would lower the carboxylate and raise the azomethine frequency so that they are probably unresolved in the spectra of the complex.

It seems likely that the zinc complex and possibly the copper complex (B) are five coordinate. Thermal balance studies on the copper complex (A) indicate two separate water losses of one molecule of water per formula unit each. The second water loss is followed immediately by a very rapid ligand decomposition. A possible structure consistent with the above observation would be:



It is suggested, therefore, that dipenicillamine is formed quickly and acts as a bridging ligand. Copper ions are well known to catalyse the formation of disulphide bridges from free thiols, whereas zinc ion would not be expected to do so. It would appear that, in this case, the rate of formation of the dimer is competitive with that of the template reaction. However, the rate of this reaction will be solvent-, pH- and oxygen-dependent and consequently any potential reaction of penicillamine *in vivo* involving the pyridoxal enzyme systems may be critically dependent on the micro-environment in which the reaction occurs.

References

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