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Complexes of Sulphur-Containing Ligands. III. Formation of Mixed Valence Complexes of Copper with L-Cysteine and its Derivatives

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A survey of the literature on the copper(II) complexes of sulphur-containing ligands reveals that the copper(II)–D-penicillamine system has been widely studied [1]. As a result of the redox and acid–base processes various products can be formed in this interaction. One of the most interesting compounds is the intense red-violet mixed valence complex of composition $[Cu(II)_6Cu(I)_8(PA)_{12}Cl]^{5-}$ [2]. In an earlier study Sugiura and Tanaka [3] concluded that copper can form mixed valence complexes with cysteine derivatives containing substituents on the β-carbon atom. Subsequently the formation of a mixed valence complex with a similar structure was described in the copper(II)–β,β-dimethyl-cysteamine system [4], and up to date there has been no experimental observation for the existence of the analogous compound with L-cysteine. In a study involving the copper(II)–L-cysteine system, however, Hanaki [5] found that intensely coloured intermediates were formed during the redox processes. This observation was explained by the formation of short-lived copper(II) complexes.

Recently Gergely and Sóvágó [6] came to the conclusion that the appearance of the mixed valence state is a function of the halide concentration in the copper(II)–D-penicillamine system. This result suggests that, in addition to the β-substituents, the formation of mixed valence complexes largely depends on the experimental conditions too, which is supported by the observations of Laurie and Prime [7]. It can also be assumed that the number of possible mixed valence complexes is much higher than those known in the literature.

The appearance of the mixed valence state as a function of the composition of the solution will be discussed in this communication.

Experimental

Chemicals were purchased from FLUKA and used without purification. Absorption spectra were recorded on a Beckman Acta M IV spectrophotometer.

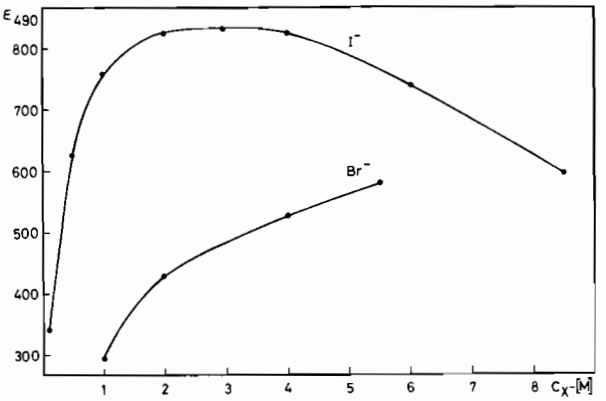

Fig. 1. Molar absorptivity of the solutions containing copper(II) and L-cysteine in 1:1.45 ratio at pH ~ 9 as a function of the halide concentrations.

JEOL MH-100 NMR spectrometer was applied for the measurement of magnetic susceptibility in water solutions. All experiments were performed under N_2 atmosphere.

Results and Discussion

The interactions of copper(II) with L-cysteine, L-cysteine methyl ester, N-acetyl-L-cysteine and glutathione were studied as functions of the halide concentration, the metal to ligand ratio and the pH. In the presence of high concentrations of halide ions a red complex with an intense charge transfer band at λ = 490 nm was formed with L-cysteine. The molar absorptivity of the solutions containing copper(II) and L-cysteine in 1:1.45 ratio at pH ~ 9 is shown as a function of the halide concentration in Fig. 1.

It is clear from Fig. 1 that the presence of 2 *M* KI or concentrated KBr makes the formation of the intense red complex possible. (The reactions were carried out in a three-necked test-tube to prevent the direct interaction of copper(II) with iodide ions.)

At a constant halide concentration the formation of the product depends on the ligand to metal ratio as shown in Fig. 2.

The λ_{490} *versus* Cys/Cu(II) plot has a maximum at a ligand to metal ratio of 1.45:1, which is in good agreement with the value obtained for the copper(II)–D-penicillamine system [6].

Magnetic measurements by the NMR method under N_2 atmosphere demonstrated that some 40% of the total copper in the solution is present as copper(II).

The formation of an in intensely coloured compound was also characteristic for the copper(II)–

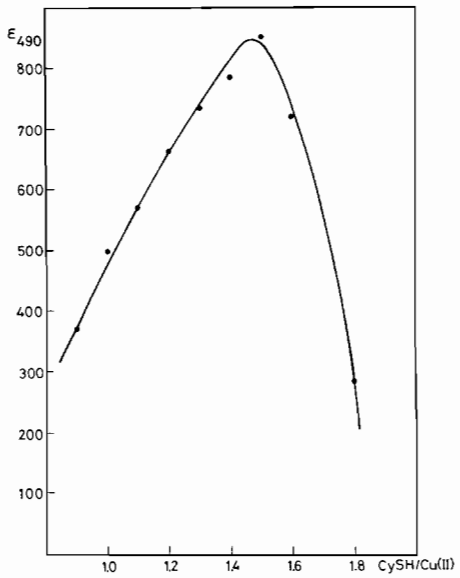

Fig. 2. Molar absorptivity of the solutions containing copper(II) and L-cysteine as a function of the metal to ligand ratio. pH ~ 9; C_{KI} = 2 mol·dm^{-3}.

L-cysteine methyl ester system. The best parameters are similar to those of L-cysteine, but λ_{max} = 500 nm and its formation requires the presence of 0.5 *M* KBr.

Comparing the magnetic and spectral behaviour of the intensely coloured complexes of L-cysteine and L-cysteine methyl ester with those of D-penicillamine [6], we can conclude that mixed valence complexes are formed with L-cysteine and L-cysteine methyl ester too. This means that a mixed valence state can develop with ligands which do not contain substituents on the β-carbon atom. It is also clear that the appearance of the mixed valence state of copper requires the presence of halide ions. 0.2 *M* KCl, 0.5 *M* KBr and 2 *M* KI are the best values for D-penicillamine, L-cysteine methyl ester and L-cysteine, respectively. The oxidative stability of the complexes, however, by and largely decreases in the same sequence. This reveals that the formation of mixed valence complexes with sulphur-containing ligands is connected with the presence of halide ions, but their stability is a function of the substituents which prevent the hydration of the copper(I) atoms [4].

In contrast with the above, intensely coloured compounds were not formed with N-acetyl-L-cysteine and glutathione at any metal to ligand ratio, even in the presence of halide ions. Similarly certain B-ligands also preclude the formation of mixed valence complexes. Namely, in the presence of an excess of L-histidine, histamine and 2,2′-bipyridyl (containing aromatic-N donors) or glycylglycine, glycylglycylglycine, carnosine or glycylasparagine (containing peptide-N donors) the intense red-violet complex of D-penicillamine did not develop.

The lack of formation of the mixed valence complexes shows the role of the $Cu(II)A_2$ intermediate complexes. The $[Cu(II)_6Cu(I)_8(PA)_{12}Cl]^{5-}$ structure contains six $Cu(II)A_2$ units, which should be present in the first step of the parallel redox and acid–base reactions [7]. The short-lives (S,N)-coordinated $Cu(II)A_2$ molecules can be formed with D-penicillamine, L-cysteine and L-cysteine methyl ester, which leads to the formation of mixed valence complexes. If steric hindrance or other reasons rule out the existence of 1:2 complexes, as is the case with glutathione and N-acetyl-L-cysteine, the mixed valence state can not be stabilized. Consequently, in the presence of B-ligands which can form stable mixed ligand complexes, the intermediate CuAB also precludes the appearance of the mixed valence state. Since the aromatic and peptide nitrogen donors are present in all of the biological systems, the biochemical significance of the various mixed valence complexes is probably limited [7].

References

1 A. Gergely and I. Sóvágó, 'Metal IOns in Biological Systems', Vol. 9, Chapter 3, H. Sigel, ed., Marcel Dekker Inc., New York and Basel (1979).
2 P. Birker and H. C. Freeman, *J. Am. Chem. Soc., 99,* 6890 (1977).
3 Y. Sugiura and H. Tanaka, *Chem. Pharm. Bull, 18,* 368 (1970).
4 H. J. Schugar, C. Ou, J. A. Tich, J. A. Potenza, R. A. Lalancette and W. Furey, Jr., *J. Am. Chem. Soc., 98,* 3047 (1976).
5 A. Hanaki, *Chem. Phar. Bull., 22,* 2491 (1974).
6 A. Gergely and I. Sóvágó, *Bioinorg. Chem., 9,* 47 (1978).
7 S. H. Laurie and D. M. Prime, *J. Inorg. Biochem., 11,* 229 (1979).
8 A. Braithwaite, M. Goldberg, H. Merkle, I. Pecht and P. Kroneck, *Proceedings II of the XIX. Int. Conference on Chemistry,* p. 20, Prague (1978).