



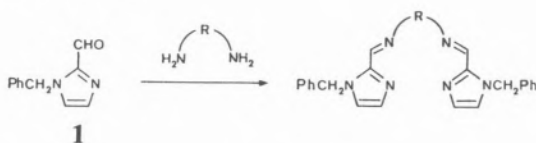
PS4.20 — TH

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### IMIDAZOLE-CONTAINING SCHIFF BASE LIGANDS AS VERSATILE MODELS FOR COPPER PROTEIN ENVIRONMENTS

The active sites of cuproproteins, for which crystal structures are available, contain copper(II) ion bound by one or more histidine imidazole groups [1]. Consequently it is of interest to prepare complexes of ligands containing imidazole groups as small molecule models for these copper(II) sites.

The condensation of 1-benzylimidazole-2-carboxaldehyde, **1**, with primary diamines leads to ligands able to complex a central metal ion in an  $N_4$  donor set:



Visible spectroscopy of the copper(II) complexes of these ligands has been used to examine the effect of the length and nature of the ligand backbone (R) on the geometry of the central metal ion. The crystal structure of the copper(II) complex where  $R = (CH_2)_4$ ,  $Cu(Bzic_2tmd)(ClO_4)_2$ , has been solved, (Figure).

4-Methyl-5-[(2-aminoethyl)thiomethyl]imidazole, **2**, (an intermediate in the production of the antiulcer drug cimetidine [2]), and related amino-thioetherimidazoles, have been employed in the design and synthesis of Schiff Base chelates capable of providing  $N_3S$ ,  $N_2S_2$ , or  $N_2SO$  donor sets around a central metal ion.

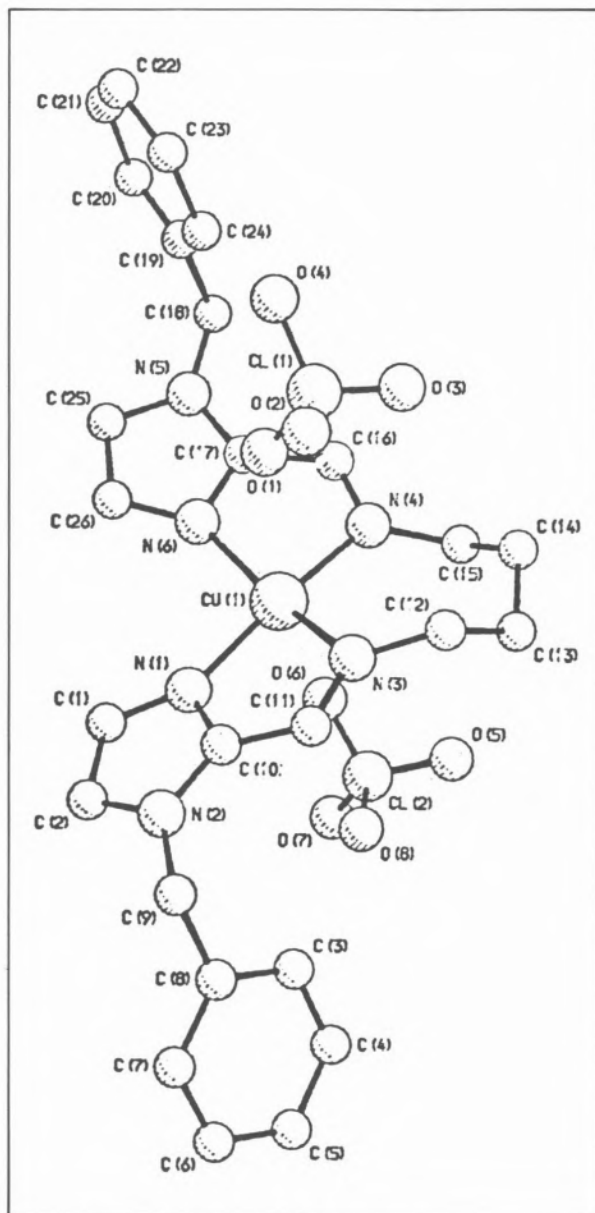
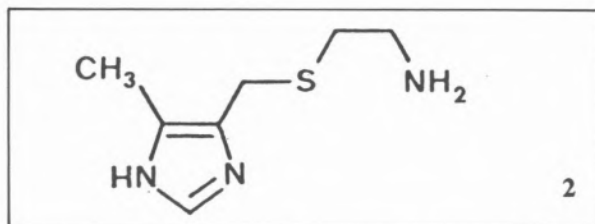


Figure  
The crystal structure of  $Cu(Bzic_2tmd)(ClO_4)_2$



Mononuclear copper(II) complexes of these ligands can be related to Type I copper protein environments, while homo- and hetero-binuclear

imidazolate-bridged complexes can be prepared as models for the bimetallic active sites of metallo-proteins such as superoxide dismutase.

## REFERENCES

- [1] E.I. SOLOMON, K.W. PENFIELD, D.E. WILCOX, *Struct. Bonding (Berlin)*, **53**, 1 (1983).
- [2] G.J. DURANT, J.C. EMMETT, C.R. GANELLIN, *British Patent*, 1 338 169 (1973).



PS4.21 — MO

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## MODELS FOR COPPER PROTEINS

Copper proteins are widespread in biology, performing many functions related to oxygen metabolism; and binding and activation of dioxygen by hemocyanin and tyrosinase have attracted much recent attention [1]. In many respects, this focussed interest has largely ignored the rich inorganic chemistry of the binuclear active-site in hemocyanin which encompasses reactions of the reduced form of the protein with carbon monoxide, nitric oxide, and other small ligands; generation of mixed-valence derivatives; and reactions of the oxidized form of the protein with small anionic ligands.

We have pursued studies in several directions with the aim of exploring the chemistry, spectroscopy, and physical properties of mono- and binuclear copper complexes. Much of this work involves the synthesis of multidentate ligands that are able to chelate the copper ion in an environment that mi-

mics the structural features of the hemocyanin active site.

We prepared the binucleating ligand bpeac (2,6-bis{bis[2-(1-pyrazolyl)ethyl]amino}-*p*-cresol) and both its copper(II) [2] and copper(I) [3] derivatives. The copper(II) complex thus formed contains two Cu(II) ions bridged by a phenolate group and bound by three nitrogen donors each. In addition, another anionic ligand (acetate or azide) bridges the two copper ions, completing the coordination sphere. The azide derivative is especially interesting since the two copper(II) ions are antiferromagnetically coupled, and the singlet-triplet splitting,  $2J$ , is equal to  $-1800 \text{ cm}^{-1}$ , rendering the complex diamagnetic at room temperature. Other spectroscopic properties of this azido-bridged dimer are similar to those for the azido derivative of hemocyanin, strengthening the proposals for the structure of its active site. The copper(I) derivative of bpeac represents one of only two phenolato-bridged copper(I) dimers having no other bridging group. However, the reaction of this compound with  $\text{O}_2$ , even at low temperature, results in irreversible oxidation of the copper(I) ions and illustrates the possible importance for isolation of the active site by the protein in hemocyanin in order to eliminate intermolecular interactions. Studies of the copper(I) derivatives of more hindered analogs of bpeac will be reported.

The unusual luminescence of the carbonyl derivative of hemocyanin has provided us with another interesting lead to follow to understand the structure of the hemocyanin active site [4]. We have prepared a number of mononuclear copper(I) complexes and examined their absorption spectra and luminescence properties both in the absence and presence of carbon monoxide. The results of these investigations will be reported, and their implications discussed.

## REFERENCES

- [1] E.I. SOLOMON, in T.G. SPIRO (ed.), «Copper Proteins», John Wiley & Sons, Inc., New York, 1981, chapter 2.
- [2] T.N. SORRELL, C.J. O'CONNOR, O.P. ANDERSON, J.H. RIEBENSPIES, *J. Am. Chem. Soc.*, in press.
- [3] T.N. SORRELL, A.S. BOROVNIK, *J. Chem. Soc., Chem. Commun.*, 1489-1490 (1984).
- [4] A. FINAZZI-AGRO, L. ZOLLA, L. FLAMIGNI, H.A. KUIPER, M. BRUNORI, *Biochemistry*, **21**, 415-418 (1982).