STUDIES ON THE SYNTHESIS AND REACTIVITY OF COPPER THIOLATE AND THIOAMIDE COMPLEXES

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ABSTRACT

In response to a clear need for a more systematic approach to the study of the interaction of copper with ligands containing the sulphhydryl group, or in thioamide tautomeric equilibrium with such, cuprous, cupric and mixed valence complexes of ligands containing a thiolate or thioamide moiety have been synthesised and characterised by spectroscopic, magnetic and crystallographic techniques. In certain cases their reactivity in aliphatic and aromatic nitrogen base solvents and nitromethane have been investigated.

Full names for the ligand abbreviations appear at the end of the abstract and ligand structures may be found in Figures at the beginning of the appropriate chapter.

The visible, esr and resonance Raman spectra of the type I, copper protein, azurin from Alcaligenes denitrificans, have been recorded and compared with other type I proteins. Through comparison with the spectral features of a series of cluster complexes $[Cu^{II}_2Cu^{I}_{10}(mmim)_{12}(Y)_4](X)_2$ (where Y = CH_3CN or H_2O, and X = BPh_4, ClO_4, PF_6, CH_3COO or OH), and $[Cu^{II}_6Cu^{I}_8(mea)_{12}Cl]Cl_5.7H_2O$, the so-called "unusual" spectroscopic features of the type I proteins have been re-interpreted as being normal phenomena of a Cu(II)-thiolate interaction coupled with specific geometrical requirements.

Investigation of the mbtH ligand system has led to the reformulation of a number of incorrectly formulated copper complexes as $[Cu(mbtH)_2Cl]$ or [Cu(mbt)] following successful removal of a disulphide contaminant. In support of such, similar cuprous compounds of general formula

$[Cu(LH)_2X]$ (LH = etmbtH, X = Cl, Br, I; LH = mbtH, X = Br, I; LH = mmimH, X = Cl), $[Cu(LH)X].xH_2O$ (LH = mbimH, mpyH, phmtzH, Ph_2PS_2H, X = Cl, Br; LH = mmimH; X = Br) and [Cu(L)] (L = bimet, dimtdz, dipmim etmbt, mpy, phmtz) have been prepared from similar ligand systems. The interaction of a number of these complexes with pyridine led to oxidation of organo-sulphur to sulphate with the production of $[Cu(py)_4SO_4].2H_2O$. This reaction is postulated to occur via two oxidising species $[Cu(py)_2OH)_2]$ or $[Cu(py)_xO]$ depending on whether halides are present or absent in the reaction solutions. Similar sulphato species are seen when quinoline and 3-ethylpyridine are used as solvents. However, compounds of general formula $[Cu(LH)_2X]$ and [Cu(LH)X] yield the complexes $[Cu(3\text{-}Mepy)_3Cl]$ and $[Cu(4\text{-}Mepy)_4Cl_2].H_2O$, from the solvents 3-methyl-pyridine and 4-methylpyridine respectively, which have been structurally characterised by X-ray crystallography.

The cupric and mixed valence complexes $[Cu(ttzH)_3X_2]$ (X = Cl, Br), $[Cu(ttzH)_2Br_2]$, $[Cu^{II}Cu^{I}{}_3(ttz)_5]$, $[Cu^{II}Cu^{I}(mmim)(mmimH)_2Cl_2]$, $[Cu^{II}Cu^{I}(mmimH)_2Cl_3]$, $[Cu(mbim)_2(H_2O)(NH_3)]$, $[Cu(mbim)_2(H_2O)]$, [Cu(dipmim)Cl] and [Cu(etu)OH] have been prepared and characterised by visible, infrared, and esr spectroscopy.

When $[Cu(ttzH)_3Br_2]$ is refluxed in nitromethane, a new cuprous complex [Cu(tztdz)Br] is produced in which modification of the ttzH ligand to produce the new organic moiety tztdz has occurred, confirmed by X-ray crystallography. Similarly the compounds [Cu(tztdz)Cl], $[Cu(tztdz)Cl_2]$ and $[Cu(mimmimz)Cl_2]$ are postulated from the interaction of $[Cu(ttzH)_3Cl_2]$ and $[Cu^{II}Cu^{I}(mmimH)_2Cl_3]$ with nitromethane.

With reference to well-defined literature examples the technique of

esr spectroscopy is shown to discriminate between equatorial donor atom sets of S_4, S_2O_2, S_2N_2, SO_3 and O_4 on the basis of lineshapes and position of fundamental parameters. The new compounds synthesised: $[Cu^{II}Cu^{I}_2(dimetH_2)(dimetH)_3Cl]$, $[Cu^{II}Cu^{I}_3(dimetH_2)_3(dimetH)(ClO_4)_4]$, $[Cu^{II}Cu^{I}_3(dimtolH)_5]$, $[Cu^{II}Cu^{I}_3(dimprolH)_5]$, $[Cu(mpoH_2)(mpoH)(ClO_4)]$, [Cu(phenylglyoxaldtsc)], [Cu(benzildtsc)] . H_2O and [Cu(3-n-heptoxy-2-oxobutyraldehydedtsc)] have been assigned donor sets on the basis of their respective esr signals. Similarly this has been done for a number of unisolatible species produced <u>in situ</u> from interaction of various cupric salts with a number of sulphhydryl and thioamide containing ligands.

Ligand abbreviations

bimetH	-	2-benzimidazoleethanethiol
dimtdzH	-	2,5-dimercapto-1,3,4-thiadiazole
dipmimH	-	4,5-diphenyl-2-mercaptoimidazole
$dimetH_2$	-	1,2-dimercaptoethane
$dimprolH_2$	-	2,3-dimercaptopropanol
$dimtolH_2$	-	3,4-dimercaptotoluene
dtsc	-	dithiosemicarbazide
etmbtH	-	6-ethoxy-2-mercaptobenzothiazole
etuH	-	2-mercaptothiazoline
mbimH	-	2-mercaptobenzimidazole
mbtH	-	2-mercaptobenzothiazole
meaH	-	cysteamine
mimmimz	-	3-(2,1-methylimidazolyl)-2,1-methylimidazoline thione
mmimH	-	2-mercapto-1-methylimidazole
$mpoH_2$	-	2-mercapto-3-pyridinol
$mpyH^2$	-	2-mercaptopyridine
phmtzH	-	2-mercapto-4-phenylthiazole
Ph_2PS_2H	-	diphenylphosphinodithioic acid
py	-	pyridine
ttzH	-	2-mercaptothiazoline
tztdz	-	3-(4,5-dihydro-2-thiazolyl)-2-thiazolidinethione

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GENERAL INTRODUCTION

Chemical experience indicates that in most cases cupric ions oxidise mercaptans to disulphides irreversibly(1,2):

$$2RS^- + Cu(II) \longrightarrow 2Cu(I) + RSSR \quad (A)$$

Although the mercapto-copper(II) bond is stable it has been postulated that a one electron reductive elimination can occur to produce copper(I) and a neutral mercapto radical(2):

$$[Cu^{II} - SR]^+ \rightleftharpoons Cu(I) + RS^\cdot \quad (B)$$

Complete reduction of Cu(II) is forced by radical coupling:

$$2RS^\cdot \longrightarrow RSSR \quad (C)$$

Nevertheless an increasing number of compounds have been prepared in which a thiolate-Cu(II) bond has been stabilised in normal or mixed-valence complexes (see Chapters 1, 5 and 6). The intermediate position of copper(II) in the Pearson "hard" and "soft" acids and bases classification(3) permits the binding of the soft base RS^- ; whereas with copper(I), regarded as a soft acid, binding to RS^- is preferred. In addition, in one case(4) reaction (A) has been reversed disputing its irreversible nature.

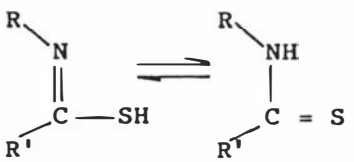
Two areas of copper(II) thiolate chemistry, the type I blue copper proteins and to a lesser extent chemotherapy, have strongly influenced the purpose and direction of research in the last two decades. The type I blue copper proteins are copper(II) containing proteins such as azurin, plastocyanin, stellacyanin, fungal laccases and ceruloplasmin which characteristically display a very intense optical absorption in the 600 nm region ($\varepsilon \approx 3500 - 5000$ l $mol^{-1} cm^{-1}$), extraordinarily

small esr copper hyperfine coupling ($|A_{11}|$ = 33-90 x 10^{-4} cm^{-1}) and high positive reduction potentials (E^{o} > +0.2V)(5). The elucidation, primarily by single crystal diffraction techniques, of the essentially distorted tetrahedral arrangement of ligands around copper(II) in two such proteins azurin(6) and plastocyanin(7), and the ubiquitous nature of the donor groups (two histidine nitrogens, a cysteine thiolato sulphur and a methionine thioether sulphur) has led to many serious attempts at producing small molecule thiolate analogues of the copper site. Great difficulty has been experienced in simulating successfully both geometrical and spectral features simultaneously, or either at all (see Chapter 1). In addition the often reactive nature of the copper(II) - thiolate interaction has led to few of these models being completely characterised by X-ray crystallography.

In the field of chemotherapy the success of the thiol containing drug D-penicillamine ($(CH_3)_2C(SH)CH(NH_2)COOH$) in the treatment of Wilson's disease(8), where a defect in the mechanism through which copper is excreted into the bile results in toxically high concentrations of copper in tissue; and its use (along with that of its copper complex) as an anti-inflammatory agent and in the treatment of rheumatoid arthritis(9), stimulated great interest in the basic chemistry of the copper-D-penicillamine interaction(10). Similarly with cancer research the discovery(11) that [Cu(KTS)] (KTS = 3-ethoxy-2-oxobutyraldehyde bis(thiosemicarbazone)) was a potent antitumour agent in rodents resulted in a resurgence of interest in the copper chemistry of thiosemicarbazide and its derivatives of α-ketoaldehydes and diketones (see Chapter 6).

The dictate of the "molecular roulette" approach adopted in the two areas outlined above, that is the pursuit of compounds which fulfil a particular function or possess special properties, has been at the expense of a systematic development of copper thiolate chemistry. It was apparent that a more orderly and further reaching approach was required to fully understand the area. Accordingly this research has been directed towards gaining an appreciation of copperthiolate chemistry as a whole, without the strict confines of bioinorganic modelling requirements. Nonetheless this tack has not deterred us from investigating model systems where ligand types proved suitable. Basically our aims were as follows:

1. to prepare new Cu(I), mixed valence, and Cu(II) compounds of ligands containing thiol functional groups or in tautomeric equilibrium with such a group:



in the hope of establishing trends and patterns for -

(a) the nature and stoichiometry of the product (Chapters 2 and 5)

(b) the requirements for the formation of Cu(II) and mixed valence compounds

(c) distinguishing spectral features, particularly esr, for compounds containing similar donor atoms. (Chapter 6).

2. to clarify anomalous results in the literature where they have coincided with our area of study. (Chapters 1,2 and 5)

3. to investigate the reactive nature of copper thiolate compounds

(Chapters 3,4 and 5)

4. to rationalise the "unusual" spectral properties of the type I blue copper proteins in terms of normal Cu(II) thiolate behaviour and wherever possible to provide model compounds for the system. (Chapter 1).

To achieve these aims a wide variety of ligand types have been used. A discussion of the nature of these ligands and their ability to stabilise the cupric state in relation to such factors as the pK_a of the sulphhydryl group, nucleophilicity, ligand ratio, order of mixing, solvents, the presence of co-ligands and steric bulk, is provided in the conclusion.

Fundamental Esr Theory (12-17)

Because of the importance of electron spin resonance (esr) spectrometry to this study an overview of the technique and its applicability to the investigation of cupric complexes is given here.

A prerequisite for esr study is that the compound have a magnetic moment, that is, it should possess one or more unpaired electrons. The technique is therefore confined to radical species and some transition metal complexes.

When placed in a magnetic field the degeneracy of the quantised electron spin states, $m_s = +1/2$ and $m_s = -1/2$, is broken, the lower energy or parallel state becoming more populated. According to the Planck relationship, $E = h\nu$, irradiation with the resonance frequency, ν will result in an electron transition to the higher energy state. In an

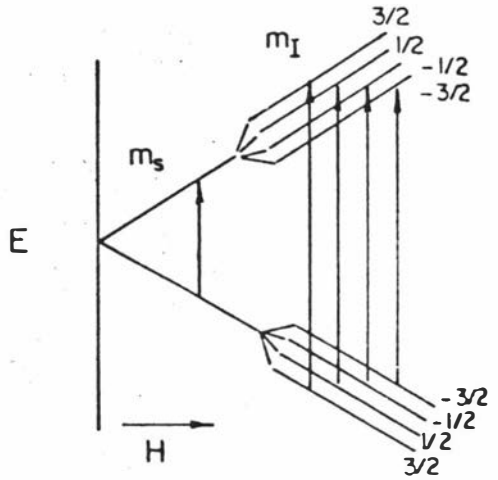
esr experiment the radiofrequency is maintained constant at ca 9 GHz (the so called X band frequency, used in this work), ca 35 GHz (Q band) or ca 3 GHz (K band), while the magnetic field is varied. The method of detection of resonance involves a small sinusoidal variation in external field. Thus only the change in absorption is detected, not the absorption itself. Consequently esr spectrometers usually plot the first derivative of the absorption.

In practice, the variable of interest in an esr experiment is not the resonance frequency, rather it is the 'g' value associated with the compound. This is related to ν by the equation

$$h\nu = g\mu_B B$$

where 'μ_B' is the electron Bohr magneton, 'B' the applied magnetic field and 'g' a proportionality constant. In instances where the electron spin is the only source of magnetism 'g' has the value 2.0023. Two phenomena which perturb the g value from the free electron value combine to make the technique a powerful one in the interpretation of transition metal geometry.

The first of these is the interaction of the electron with neighbouring nuclei. This causes a deviation as a result of the electron experiencing a magnetic field, 'B_I', arising from the nuclear magnetic moment, as well as the applied spectrometer field. Not only is 'g' shifted but the absorbance signal may also be split as a result of nuclear spins similarly being quantised. For a transition metal such as copper (for ^{63}Cu and ^{65}Cu the nuclear spin quantum number is 3/2) with nuclear spin states $m_I = \pm 3/2$ and $\pm 1/2$, the following energy level diagram may be drawn.



The selection rules $\Delta m_s = +1$ and $\Delta m_I = 0$ allow four transitions as shown above. In general for a nucleus with spin 'I' there are 2I+ 1 equally spaced hyperfine lines. The splitting, 'A', between adjacent lines is referred to as the hyperfine coupling constant and is indicative of the strength and type of bonding.

The second phenomenon, anisotropy, refers to the dependence of the g value on the orientation of the magnetic field. Conceivably three g values g_x, g_y or g_z may arise depending on whether the magnetic field is oriented along the x, y or z axes of the molecule. Associated with these will be the corresponding hyperfine coupling constants A_x, A_y and A_z. Together these values comprise the fundamental parameters obtained from an esr spectrum. In practice not all may be resolved as a result of symmetry. The majority of examples examined in this thesis have involved copper in an approximately axially symmetric environment where consequently $g_x \approx g_y$ and $A_x \approx A_y$ and the terms $g_\perp$ and $A_\perp$ are substituted, with g_{11} and A_{11} for the z component. $A_\perp$ is often ill resolved in the spectrum due to its relatively small size and occurrence in a position of maximum absorption. For reference a typical axial copper spectrum is shown in Fig 5.5a.

CHAPTER 1

SPECTROSCOPIC STUDIES OF AZURIN FROM *ALCALIGENES DENITRIFICANS* AND SMALL MOLECULE ANALOGUES OF ITS COPPER SITE

PART 1: AZURIN

Introduction

Azurins are relatively small (MW ≈ 14,000) proteins that contain a single copper atom. They are found mainly in bacteria of genera *Pseudomonas* and *Alcaligenes* or those closely related(18). Although the protein is thought to be involved in electron transfer, its exact cellular function is not entirely clear. It is generally thought that azurin mediates electrons between cytochrome c_{551} and cytochrome oxidase(19).

Azurins from a number of different sources have been isolated and studies of the electrochemical and spectroscopic properties have been carried out (Table 1.1). It should be noted that these proteins are not identical in structure. For instance, 35% of amino acid residues in *Alc. dentrificans* differ from those in *Ps. aeruginosa* azurin(20). The copper atom in azurin is known as type I. The three characteristic features of this designation of the blue copper proteins, that is intense blue colouration, low copper hyperfine splitting in the esr spectrum and high redox values, have been observed for all (Table 1.1)

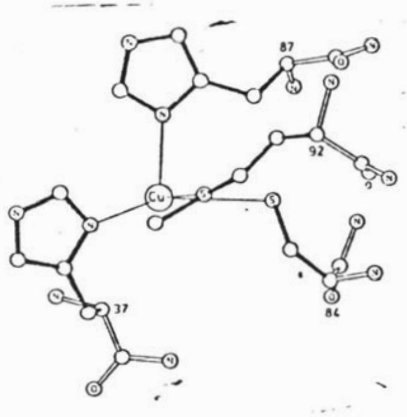
To date successful single crystal X-ray structural studies have

Table 1.1 Spectroscopic and redox properties of various azurins

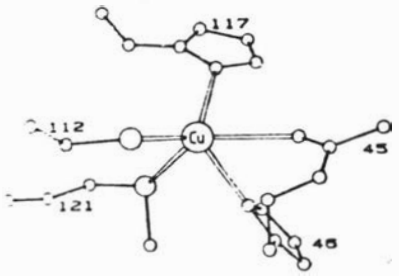
Azurin source(5)	ε at 625nm ($1\ mol^{-1}cm^{-1}$)	$\lvert A_{11} \rvert$ ($10^{-4}cm^{-1}$)	E^{o} (V)
Ps. aeruginosa	5 700	60	0.330
Ps. fluorescens	3 500	58	0.230
Ps. dentrificans	10 500	60	0.266
Bordetella bronchiseptica	3 500	60	0.395

been carried out on two azurin types, that isolated from *Ps. aeruginosa* (to a resolution of 2.7 Å) by Adman *et al.*(21) and that from *Alc. denitrificans* (to 2.0 Å) by Baker and co-workers(22) at Massey University. In addition the crystal structure of a related type I blue protein, *Populus nigra* plastocyanin, has been done by Freeman's group(23) (to 1.6 Å). The copper sites of the azurins and plastocyanin (Figure 1.1(a)) are similar. Four ligands are common to each. Three of these, thiolate sulphur from a cysteine and two histidyl nitrogen donor atoms, form an approximate plane with comparatively short bonding distances (Figure 1.1(c)). A fourth ligand, with a long bond to copper, methionine binding through thioether sulphur, occurs above this plane, giving overall a flattened tetrahedral stereochemistry (Figure 1.1(d)). A fifth ligand in *Alc. denitrificans*, the carbonyl oxygen of a glycine residue, is apparently within bonding distance of copper, although the bond at 3.17 Å would be considered very long. A similar glycine interaction was observed in an earlier 3 Å map of *Ps. aeruginosa*(24), although at a resolution of 2.7 Å only four ligands were considered to bind in a tetrahedral arrangement similar to plastocyanin(23). A distorted trigonal bipyramidal stereochemistry would be imposed, were the oxygen considered to be coordinating.

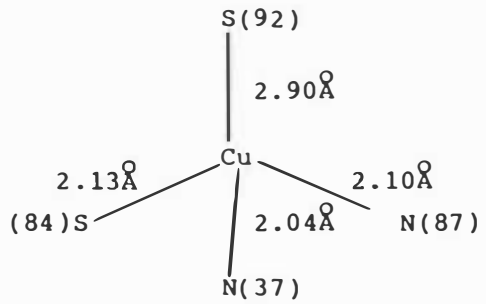
Although characterised by X-ray diffraction studies very little work has been done on the spectroscopic properties of the *Alc. denitrificans* azurin copper site. Apart from the desirability of obtaining this data for comparative purposes with other azurins, such a study could presumably indicate whether a similar ligand field to plastocyanin is experienced by copper in the protein, or whether the possible fifth ligand makes any significant contribution. Accordingly esr, electronic and resonance Raman spectra have been recorded for

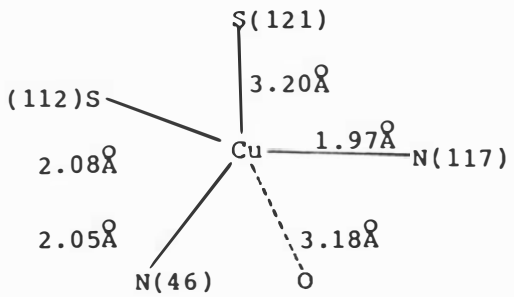


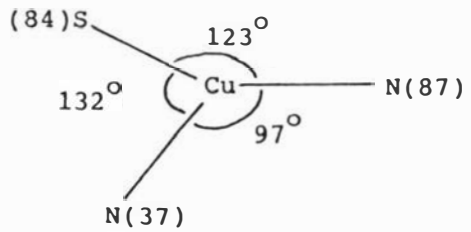
Populus nigra plastocyanin(23)

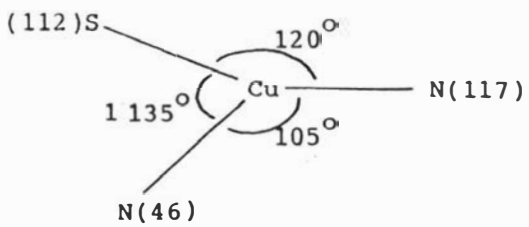


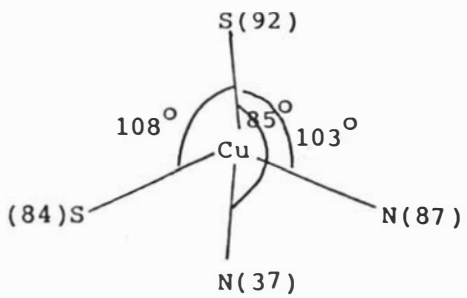
Alcaligenes denitrificans azurin(22)











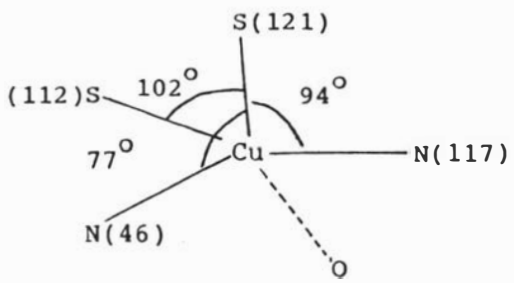


Figure 1.1 Dimensions of the copper site in azurin and plastocyanin.

Alc. denitrificans azurin.

1.1 EXPERIMENTAL

1.1.1 Source of Azurin

Azurin isolated from Alcaligenes denitrificans was a generous gift from Dr G.E. Norris. The procedure used for isolation and purification of the protein has been described elsewhere(25).

1.1.2 Instrumentation

Electronic spectra: In the range 350-900 nm the spectra were recorded on a Cary 219 spectrophotometer, while for the range 900-1100 nm a Shimadzu MPS 5000 spectrophotometer was used.

Resonance Raman spectra: Spectra were obtained by Dr T.M. Loehr and Dr J.E. Plowman, Oregon Graduate Centre, on an automatic Jarrell Ash 25-300 Raman spectrometer using a Spectra Physics 164 krypton ion laser and an R.C.A. photomultiplier with photon counting capability.

Electron spin resonance spectra: Frozen solution samples at 110 K were recorded using a Varian E-104A spectrometer equipped with a Varian E-257 variable temperature accessory. Spectral 'g' values were calibrated with a diphenylpicrylhydrazyl (DPPH) standard.

1.2 RESULTS AND DISCUSSION

1.2.1 Electronic Absorption Spectroscopy

Samples were run in aqueous solution (pH 6.0) over the range 400-1100 nm. Extinction coefficients were calculated on the basis of

moles copper present, determined immediately after running the spectra, by atomic absorption. Figure 1.2 shows the region of interest, and in Table 1.2 band positions and possible assignments are listed. Data for Populus nigra plastocyanin and Ps. aeruginosa azurin are included for comparison.

An intense absorbance responsible for the vivid blue colour of the protein occurs at 619 nm flanked by weaker bands at 460 nm and 780 nm (a broad shoulder). A long absorption tail runs into the near infrared from this latter band. Absorbance assignments are based on those of Penfield et al.(26) and Solomon et al.(27). The hypothesis that the major bands are of d-d origin, the intensities of which have been enhanced via "borrowing" mechanisms in a noncentric structure, has been disputed. Detailed studies of the visible spectra of nickel(II), manganese(II) and cobalt(II) substituted proteins, as well as small molecule complexes(28-32) favour a charge transfer assignment. Accordingly the bands at 619 and 780 nm are considered to be $\sigma(S^-) \rightarrow d_{x^2-y^2}$ and $\pi(S^-) \rightarrow d_{x^2-y^2}$ ligand to metal charge transfer bands respectively, arising from the copper-cysteine interaction. The absorbance at 460 nm has been assigned to a π(N, from histidine)$\rightarrow d_{x^2-y^2}$ charge transfer type. Gaussian analysis of the major 618 nm peak in Ps. aeruginosa azurin revealed an additional band at about 560 nm. This was attributed(26) to another $\sigma(S^-) \rightarrow d_{x^2-y^2}$ charge transfer transition rather than σ(S Methionine)$\rightarrow d_{x^2-y^2}$ favoured by McMillin and Morris(33) as the long Cu-Met bond and the poor orientation of the $d_{x^2-y^2}$ orbital should result in an absorption at higher energy and presumably lower intensity. Also small molecule compounds with long apical copper-thioether bonds have been shown to absorb in the range 300-400 nm(34,35). A d-d absorption

.2 Electronic absorption spectrum of Alc. denitrificans azurin.

Table 1.2 Electronic band maxima[a] for Alc. denitrificans and Ps. aeruginosa azurins and Populus nigra plastocyanin

Alc. denitrificans azurin	Ps. aeruginosa azurin[11]	Populus nigra plastocyanin[10]	Assignment
460 (580)	481 (198)	467 (300)	$\pi(N) \rightarrow d_{x^2-y^2}$
-	567[b] (504)	559[b] (1163)	$\sigma(S^-)(\alpha S + \beta pz) \rightarrow d_{x^2-y^2}$
619 (5100)	631 (3798)	606 (4364)	$\sigma(S^-) \rightarrow d_{x^2-y^2}$
ca 780sh (ca 1040)	779 (686)	749 (1289)	$\pi(S^-) \rightarrow d_{x^2\ y^2}$
ca 900	980	893	d → d band

Notes: a. units nm, extinction coefficients (1 $mol^{-1} cm^{-1}$) in brackets

b. via Gausian analysis

c. sh = shoulder

has been estimated to be in the region 900 nm, but near infrared C.D. and M.C.D. spectral studies are needed to help resolve the spectrum. Analysis of Table 1.2 shows that the spectra of the two azurins and plastocyanin are inherently similar.

1.2.2 Resonance Raman Spectroscopy

Resonance Raman spectra were recorded for aqueous samples of approximately 0.9 mM concentration at 277 K and 77 K. The spectrum of Alc. denitrificans at 77 K in the frequency ranges 540-240 cm^{-1} and 840-640 cm^{-1} is shown in Figure 1.3. A relatively strong set of peaks are observed around 400 cm^{-1}, and, as has been observed with Ps. aeruginosa(36), a second weak set occurs from 750-800 cm^{-1}.

Thamann et al.(37) have conducted a normal coordinate analysis of the azurin copper centre based on data from Ps. aeruginosa and considered a number of possible stoichiometries including trigonal bipyramidal, square planar, tetrahedral and trigonal. The latter two models proved the most successful in matching theoretical and observed bands. To a first approximation the structure of Alc. denitrificans copper site can be regarded as trigonal, so assignments have been based accordingly. Band maxima and assignments are shown in Table 1.3. Ps. aeruginosa azurin and plastocyanin data are provided for comparison.

For the prinicipal bands at 374, 410 and 429 cm^{-1} the calculated assignments show mixing of vibrational contributions, to which the Cu-S (cysteine) coordinate always donates. The intensity enhancement of the observed bands is thus neatly rationalised on the basis that resonance is achieved by excitation within the (cysteine S^{-})$\rightarrow d_{x^2-y^2}$ charge transfer transition(38). Further support for the hypothesis that the

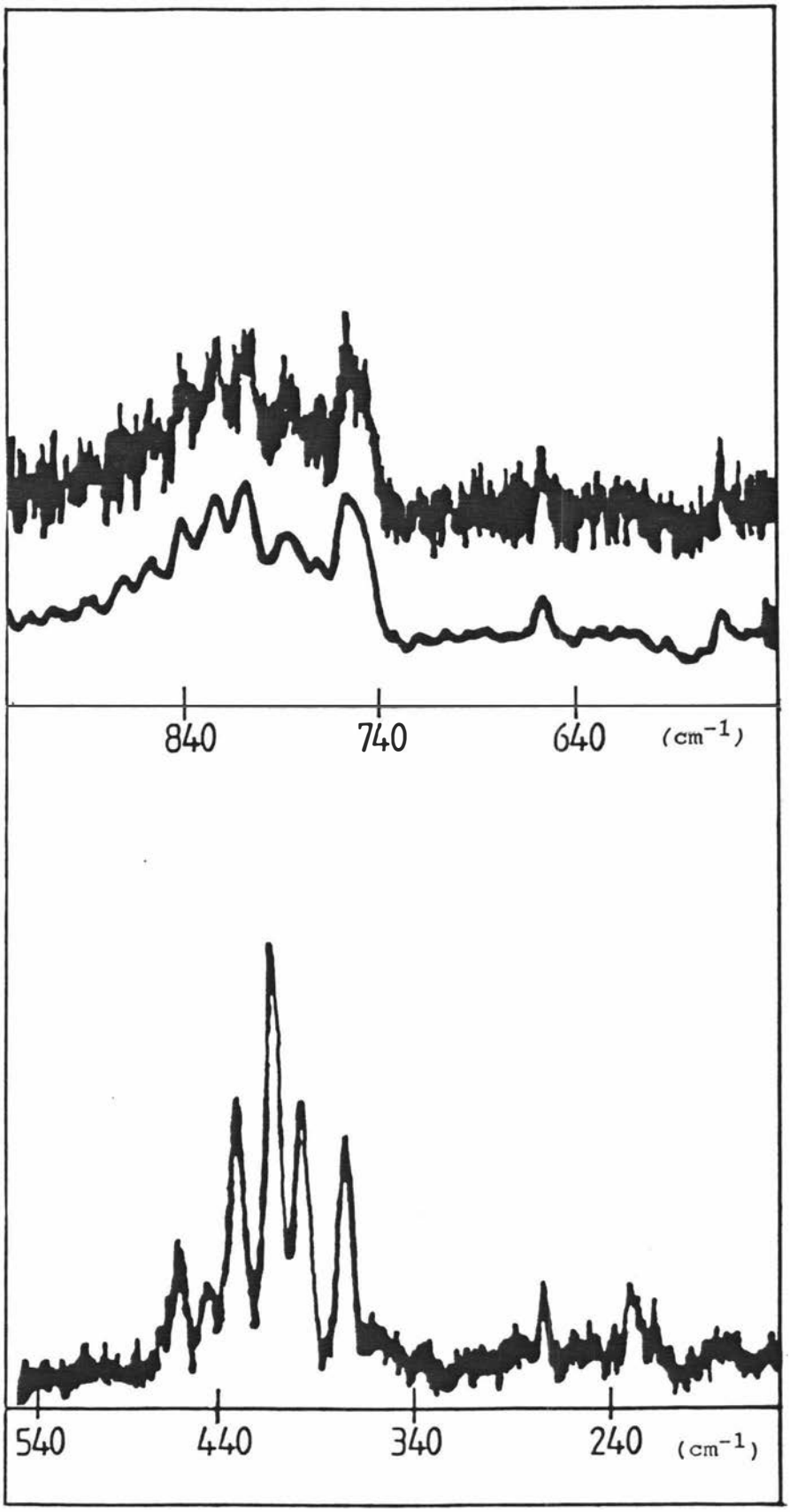


Figure 1.3 Resonance Raman spectrum of Alcaligenes denitrificans azurin

Table 1.3 Resonance Raman frequencies, relative intensities and possible assignments of the proteins between 260 and 500 cm^{-1}.

Alc. denitrificans azurin		Ps. aeruginosa azurin(36)		Tentative assignment(37)	Plastocyanin(36)	
ν (cm^{-1})	I_{rel}[a]	ν(cm^{-1})	I_{rel}		ν(cm^{-1})	I_{rel}
273	0.3	260	-	92% ∂(S-Cu-N)	262	-
374	0.6	373	0.4	57% ν(Cu-S)+35% ν(Cu-N)	377	0.7
396	0.7	400	0.4(sh)		387	0.5
410	1.0	409	1.0	67% ν(Cu-N)+30% ν(Cu-S)	393	0.4
429	0.7	428	0.5	93% ν(Cu-N)+3% ν(Cu-S)	407	0.5
446	0.3	441	0.1		425	1.0
459	0.4	455	0.07		442	0.6
					480	0.1

Notes: a. The strongest peak in each spectrum is given as 1.0.
All other peak intensities are given as fractions of the strongest peak.
sh. shoulder

four vibrations at 374, 396, 410 and 429 cm^{-1} contain a significant Cu-S(cysteine) contribution is provided by an analysis of the bands in the region 740-860 cm^{-1}. These bands can be assigned as overtone and combination frequencies of the vibrations in the low frequency region, as is shown in Table 1.4. Normally overtone bands are only seen for fundamental vibrations involving the resonance source.

The band at 273 cm^{-1} is common to all type I copper proteins so far investigated(37). This has been assigned by Ferris et al.(39) to a Cu-S(Met) vibration. However, the length of the copper-methionine bond (3.20Å in Alc. denitrificans)(22), the fact that the vibration remains when methionine is replaced by selenomethionine in Ps. aeruginosa azurin(37), the presence of the vibration in the spectrum of stellacyanin which lacks methionine altogether(37) and the inability of EXAFS spectral studies on plastocyanin to detect the copper-methionine bond(40) bring this assignment into dispute. Normal coordinate analysis proposes a δ(S-Cu-N) vibration to account for this band.

The predominantly Cu-N(His) vibration, from normal coordinate analysis data, occurs for Alc. denitirificans at 429 nm. This assignment in the type I copper proteins has proved controversial to date as the postulated frequencies (usually ca. 400 cm^{-1}) are thought by some(36) to be unusually high when it is considered that the vibration in the copper proteins haemocyanin and tyrosinase has been assigned to bands in the frequency region 220-320 cm^{-1}(41). Recently, Woodruff et al.(36) have argued that only one of the metal-ligand stretching modes of the blue copper chromophore is actually expected to be near 400 cm^{-1}, i.e. ν(Cu-S), and assign the remainder of the resonance enhanced modes to internal motions of the coordinated ligands, including

Table 1.4 Resonance Raman combination and overtone frequencies of azurin from Alcaligenes denitrificans

Observed frequency (cm^{-1})	Predicted frequency (cm^{-1})	Assignment
748	748	overtone (2 x 374 cm^{-1})
768	770	combination (374 + 396 cm^{-1})
787	784	combination (374 + 410 cm^{-1})
	792	overtone (2 x 396 cm^{-1})
	803	combination (374 + 429 cm^{-1})
809	806	combination (396 + 410 cm^{-1})
	820	overtone (2 x 410 cm^{-1})
824	825	combination (396 + 429 cm^{-1})
841	839	combination (410 + 429 cm^{-1})
858	858	overtone (2 x 429 cm^{-1})

the histidine imidazole rings. However, support for ν(Cu-N) in the 400 cm^{-1} region comes from the resonance Raman spectra of small molecule thiolate compounds. For instance the mixed valence compound $[Cu^{II}_2Cu^{I}_{10}(mmim)_{12}(H_2O)_4]^{2+}$ (mmim = 2-mercaptomethylimidazolate) has a band at 439 cm^{-1} which may be assigned to ν(Cu-N) (see p. 39). An elegant analysis of the spectra of [Cu(diethyldithiocarbamate)$_2$] and $[Cu^{II}_6Cu^{I}_8(D\text{-penicillamine})_{12}Cl]^{5-}$ by Tosi and Garnier(43) has led to the assignment of the band at 425 cm^{-1} in the latter to being mostly ν(Cu-N). Similarly in the type I model compound p-nitrobenzenethiolato-(hydrotris (3,5 dimethyl-1- pyrazolyl)borato)copper(II) with an N_3S coordination site in constrained tetrahedral geometry, the assigned ν(Cu-N) vibrations at 339, 360 and 385 cm^{-1} are also approaching the azurin region(1).

One of the most significant features of the spectrum of Alc. denitrificans is the presence of a new band at 396 cm^{-1}. This vibration has not been previously observed in type I proteins, although recently a low temperature study by Woodruff(36) revealed a shoulder at 400 cm^{-1} in the spectrum of Ps. aeruginosa. At the moment there is no satisfactory explanation for this new band.

On inspecting Table 1.3 it can be seen that the resonance Raman spectra of the two azurins are very similar in terms of band position and intensity. However, the spectrum of plastocyanin shows significant differences, with respect to the intensity profile and the appearance of a new band at 387 cm^{-1}. If it is considered that the band positions are a reflection of the strengths of the respective bond components and that their intensities are a function of the bond dipole moment, the differences in the spectra may be interpreted as lending support to the

hypothesis that the copper site in azurin and plastocyanin is significantly different.

1.2.3 Electron Spin Resonance Spectroscopy

The esr spectrum of Alc. denitrificans is shown in Figure 1.4. The spin Hamiltonian parameters have been evaluated assuming axial symmetry giving $g_{\perp} = 2.059$, $g_{11} = 2.255$ and $|A_{11}| = 60 \times 10^{-4} cm^{-1}$. Data for other azurins and plastocyanins is listed in Table 1.5 for comparison. It can be seen that the parameters for Alc. denitrificans adhere closely to the values found for other proteins.

Striking features of the spectrum are the low value of $|A_{11}|$, observed in the region 2800-2950 G, and the overall axial appearance. Considering the latter, the first derivative plot as shown in Figure 1.4 shows little sign of broadening in the $g_{\perp}$ region (3150-3200 G). This lack of rhombic character may indicate that the long bonded axial ligands, glycine 45 and methionine 121, contribute very little to the copper ligand field giving an approximately C_{2v} geometry. Alternatively, as suggested by Solomon et al.(44), an axial symmetry of D_{2d} or C_{3v} character is also plausible, derived from a distorted tetrahedron of ligands.

Possible factors contributing to the low value of $|A_{11}|$ are discussed in Part 2.

An esr experiment was conducted in order to investigate the stability of the copper site to variation in pH. The study revealed that it retains its character over quite a large pH range. In the alkaline region breakdown was observed above pH 10.9 after which a

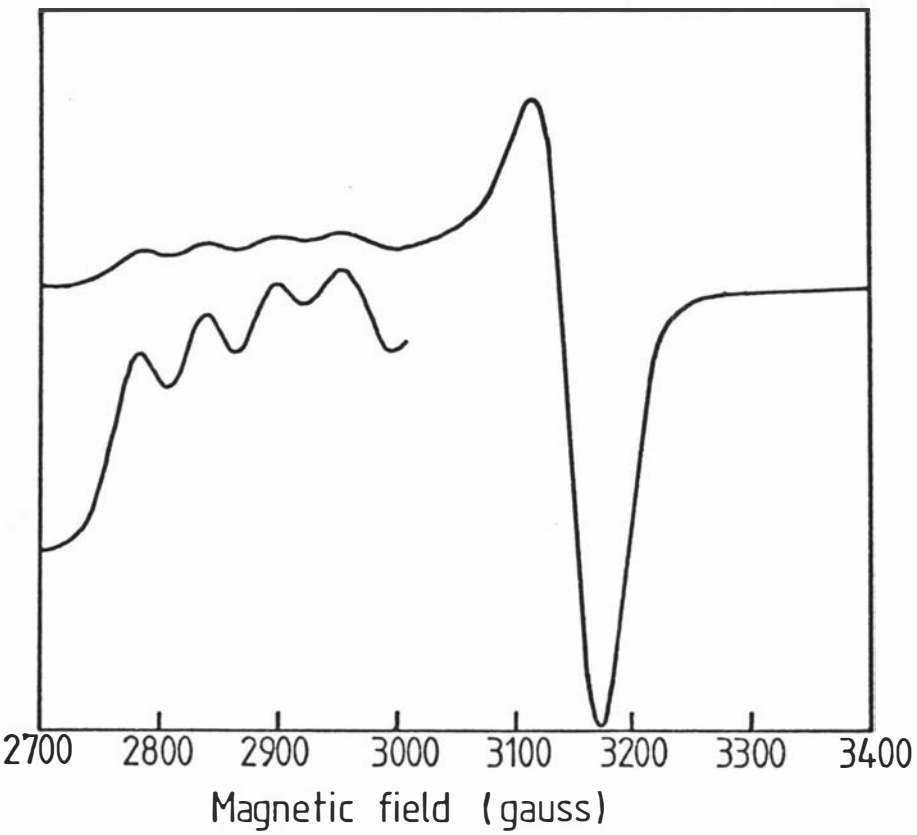


Figure 1.4 Esr spectrum of Alc. denitrificans azurin.

Table 1.5 Esr parameters for azurin types

Source	$\lvert A_{11} \rvert$ (10^{-4} cm^{-1})	g_{11}	$g_{\perp}$	Ref
Alcaligenes denitrificans azurin	60	2.255	2.059	this work
Pseudomonas fluorescens azurin	58	2.261	2.052	(5)
Pseudomonas aeruginosa azurin	60	2.260	2.056	(5)
Pseudomonas denitrificans azurin	60	2.260	2.055	(5)
Bordetella bronchiseptica azurin	60	2.273	2.049	(5)
Cucumus sativus plastocyanin	60	2.226	2.060	(5)
Cucurbita pepo plastocyanin	60	2.230	2.050	(5)

spectrum was obtained with parameters $|A_{11}| = 220 \times 10^{-4} cm^{-1}$, $g_{11} = 2.18$ and $g_{\perp} = 2.05$ indicating that copper had moved to a non-specific site(45). In the acid region colour and esr signal were stable to pH 3.4, below which the blue colour disappeared, and new species were observed for which the parameters of the major were $|A_{11}| = 128 \times 10^{-4} cm^{-1}$, $g_{11} = 2.43$, and $g_{\perp} = 2.089$ allowing it to be assigned to $[Cu(H_2O)_6]^{2+}$(46).

Summary

Azurin from Alcaligenes denitrificans shows an electronic spectrum with maxima at 460, 619 and 780 nm, and an esr spectrum with parameters $g_{\perp} = 2.059$, $g_{11} = 2.255$, $|A_{11}| = 0.060\ cm^{-1}$ similar to that observed for Pseudomonas aeruginosa azurin and Populus nigra plastocyanin. The resonance Raman spectrum of Alcaligenes denitrificans azurin shows bands attributable to copper(II)-ligand interactions as well as combination and overtone frequencies of the fundamental vibrations. The spectrum is similar to that of Pseudomonas aeruginasa azurin but Populus nigra plastocyanin shows significant differences.

PART 2: SMALL MOLECULE MODELS FOR THE TYPE I COPPER PROTEINS

Introduction

One of the most compelling arguments for the study of low molecular weight synthetic analogues of the blue copper proteins is that such compounds would allow reactivity and modification studies not possible with a molecule as complex and fragile as a metalloprotein(1). Although research into the structural nature of these proteins has met with considerable success, questions such as the modes of action of the proteins and even their role, in some instances, in cellular activity remain largely unanswered. Representative model systems would no doubt prove of great use in the elucidation and hypothesis testing of such matters.

From the results of research on the type I proteins a representative model would have to fulfil the following requirements:

(i) possess a considerably distorted four or five coordinate ligand geometry involving thiolate and nitrogen base ligands stablising Cu(II).

(ii) low copper hyperfine splitting in the esr spectrum ($|A_{11}| < 100 \times 10^{-4} cm^{-1}$)

(iii) an intense absorption in the 600 nm region of the visible spectrum.

(iv) high positive E^{o} values.

As was mentioned in the general introduction there has been little success in attempts to meet the above requirements. This is in contrast

to the success achieved in modelling iron sulphur proteins and haemoglobin. Solomon(44) has rationalised this anomaly on the basis that the latter contain "extrinsic" active sites capable of existing as well-defined entities independent of the protein. On the other hand all known active sites in copper proteins are "intrinsic"; that is they are formed only through the intimate interaction of the copper ions with the ligating protein residues. A copper site is thus generated which differs, both in geometry and ligation, from small molecule copper complexes. Nonetheless a few(1,47-51) model systems have succeeded in mimicking at least some of the properties of the protein copper site. The more successful are listed in Table 1.6, and shown in Figure 1.5.

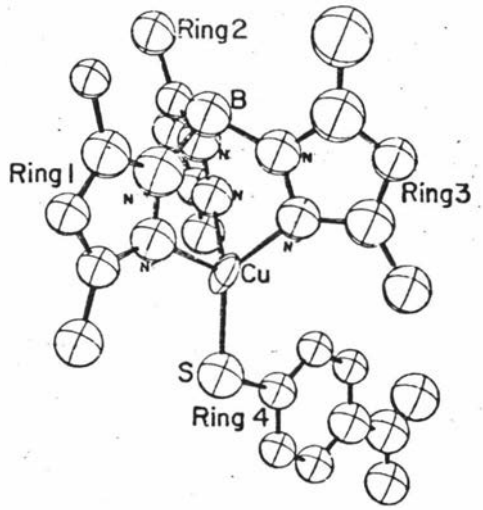
Barring copper substituted horse liver alcohol dehydrogenase which itself is a metalloprotein, it can be seen from Table 1.6 that the mixed valence compound of copper and 2-mercapto-1-methylimidazole (mmimH) fulfils most of the requirements for a type I copper model.

Dobry-Duclaux and Perichon(53) were the first to report cupric compounds of this ligand, formulating two forms of complex - $[Cu(mmim)_2]$ and $[Cu^{II}Cu^{I}_5(mmim)_6]X$ (X = mmim or ClO_4) - although only the latter was isolated from solution. Almost simultaneously work was being conducted in this laboratory leading to the isolation of the postulated products $[Cu^{II}Cu^{I}_5(mmim)_6]X$ (X = ClO_4, PF_6 or CH_3COO)(54). These mixed valence compounds have been reformulated in this work as $[Cu^{II}_2Cu^{I}_{10}(mmim)_{12}(H_2O_4]X_2$ as a result of a timely crystallographic investigation by Agnus et al.(50) of the analogous mixed valence system $[Cu^{II}_2Cu^{I}_{10}(mmim)_{12}(CH_3CN)_4](BPh_4)_2$. Here also the series has been extended to include $[Cu^{II}_2Cu^{I}_{10}(mmim)_{12}(H_2O)_4](OH)_2$ and the earlier $[Cu(mmim)_2]$ formulation of Dobry-Duclaux(53) has been reinterpreted

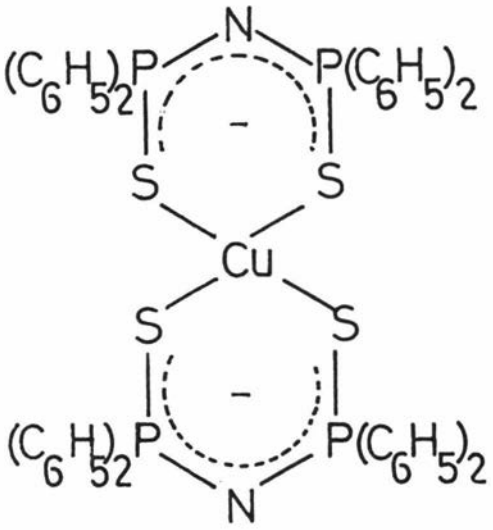
Table 1.6 The best models to date for type I blue proteins.

	Compound	Suspected Geometry	Donor Atoms	Band max(nm)[a]	$\lvert A_{11} \rvert$ $10^{-4}cm^{-1}$	E^{o}/ V	Ref
I	$[Cu(HB(3,5\text{-}Me_2pz)_3(mnb)$	elongated tetrahedral	N_3S	588 (3900)	171	-	1
II	$[Cu(SPh_2PNPPh_2S)_2]$	distorted tetrahedral	S_4	575 (3610)	121	-	47
III	$[Cu(mpg)]^-$	square planar	NSO_2	605 (300)	82	-	48
IV	$[Cu(cyclam)(2\text{-mercaptopropane})]^+$	square pyramidal	N_4S	364 (9800)	-	-	49
V	$[Cu^{II}_2Cu^{I}_{10}(mmim)_{12}(CH_3CN)_4]^{2+}$	distorted square pyramidal	N_3S_2	635 (3800)	65	-0.205	50
VI	copper-doped horse alcohol dehydrogenase	distorted tetrahedral	S_2NO	620 (2000)	30	-	52

Notes: a. extinction coefficient (1 mol cm^{-1}) in parentheses.



(I)



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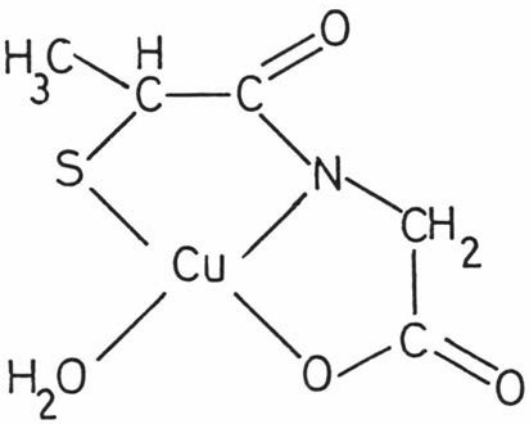

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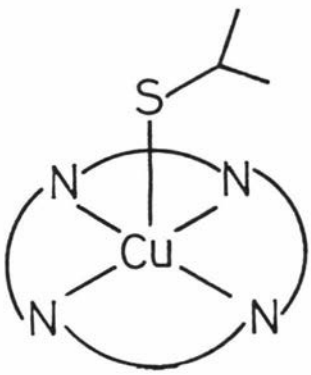

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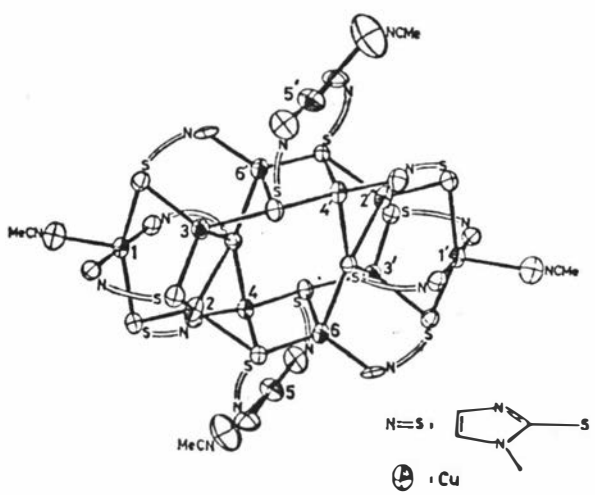
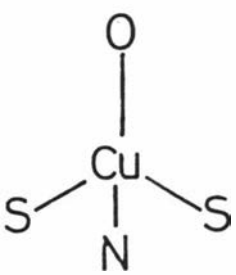


(V)



(VI)

Figure 1.5 Structures of the best type I models.

as $[Cu^{II}_2Cu^{I}_{10}(mmim)_{12}(H_2O)_4](CH_3COO)_2$

The remarkable spectral features of the Cu-2-mercapto -1-methylimidazole system have not been exploited to full advantage in the light of its suitability as a type I blue copper model. Accordingly in this section a detailed electronic, esr and resonance Raman spectral study is conducted. The electronic and esr spectra of one other new suitable model complex, $[Cu^{II}_6Cu^{I}_8mea_{12}Cl](NO_3)_2Cl_5.7H_2O$ are also investigated. Finally an attempt is made to rationalise the physical requirements for the unusual spectral features found in the blue proteins on the basis of evidence presented here and from other relevant compounds in the literature.

1.3 SYNTHESIS OF THE COMPLEXES

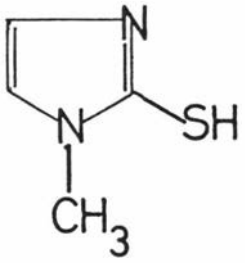
Full preparative details may be found in the experimental section (1.7.1).

$[Cu^{II}_2Cu^{I}_{10}(mmim)_{12}(H_2O)_4]$ $(OH)_2.2H_2O$ was obtained from addition of an ammoniacal aqueous solution of 2-mercapto-1-methylimidazole to copper sulphate. Found(%): C,25.9; H,3.0; N,14.9. $C_{48}H_{74}Cu_{12}N_{24}O_8S_{12}$ requires: C,25.9; H,3.2; N,15.1.

$[Cu^{II}_6Cu^{I}_8(mea)_{12}Cl](NO_3)_2(Cl)_5.7H_2O$ was prepared by adding $Cu(NO_3)_2.3H_2O$ to 2-mercaptoethylammonium chloride and raising the solution pH to 9 with NH_4OH. Found(%): C,12.6; H,3.3; N,8.1; Cl,9.7. $C_{24}H_{86}Cl_6Cu_{14}N_{14}O_{13}S_{12}$ requires: C,12.7; H,3.8; N,8.65; Cl,9.4.

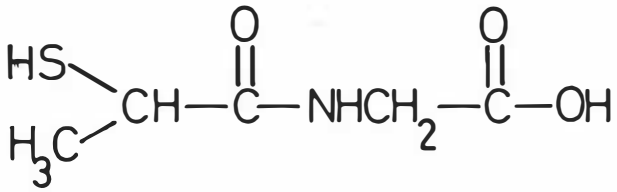
$[Cu^{II}_2Cu^{I}_{10}(mmim)_{12}(H_2O)_4]X_2$ ($X = ClO_4$, CH_3COO, PF_6) and

Figure 1.6 Structures and abbreviations of ligands appearing in this section.

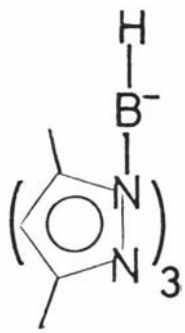


2-mercapto-1-methylimidazole (mmimH)

4-nitromercaptobenzene (mnbH)



N-2-mercaptopropionyl glycine ($mpgH_3$)



hydrotris(3,5-dimethyl-1-pyrazolyl) borato ($HB(3,5\text{-}Me_2pz)_3$) ion

Note: In concordance with common usage, where appropriate ligands have been named and drawn in the thiol rather than the thione form, although the latter predominates in most cases. This helps in simplifying the systems and emphasises the primal reactive role of the sulphhydryl group in the coordination chemistry of copper.

$[Cu^{II}_2Cu^{I}_{10}(mmim)_{12}(CH_3CN)_4](BPh_4)_2$ were prepared according to the methods of Kermode(54) and Agnus(50) respectively.

1.4 RESULTS AND DISCUSSION

1.4.1 Infrared spectra

The spectrum of $[Cu^{II}_2Cu^{I}_{10}(mmim)_{12}(H_2O)_4]$ $(OH)_2.2H_2O$ as may be expected is very similar to that of the compounds where the hydroxyl group is replaced by ClO_4,PF_6 or CH_3COO(54) with the exception of the characteristic bands shown by these anions. A strong ν(OH)(55(a)) vibration is observed at 3390 cm^{-1}, to which presumably both aquo and hydroxy ligands contribute. ∂(HOH)(55(a)) is present at 1630 cm^{-1}.

For $[Cu^{II}_6Cu^{I}_8(mea)_{12}Cl]$ $(NO_3)_2(Cl)_5.7H_2O$ vibrations attributable to ν(NO)(55(b)) stretches are observed at 1430 and 1340 cm^{-1} consistent with the presence of ionic nitrate. The medium band intensity is also confirmation of the low percentage of nitrate since these bands are normally quite strong. The ν(OH) absorptions of water appear at 3400 cm^{-1}, the ν(NH) absorptions from the amino group at 3230 and 3100 cm^{-1} and the NH bending mode occurs at 1585 cm^{-1}(55(c)).

1.4.2 Electronic spectra

Data for the complexes run in solution, or where insolubility prevented, as nujol mulls, are presented in Table 1.7.

Compounds involving the cluster $[Cu^{II}_2Cu^{I}_{10}(mmim)_{12}(Y)_4]$ X_2 (where Y = acetonitrile or water, X = BPh_4,ClO_4,PF_6,CH_3COO,OH) show almost identical spectral features. A moderately intense band or shoulder appearing at 410 nm has been assigned as a π(N)→Cu(II) charge

Table 1.7 Electronic spectra for small molecule analogues.

Compound	Solvent	Band max (nm)	Assignment	Ref
$[Cu^{II}_2Cu^{I}_{10}(mmim)_{12}(MeCN)_4](BPh_4)_2$	CH_3CN	410 (1200) 635 (3800) 880 (1800)	$\pi(N)\rightarrow Cu(II)$ $\sigma(S^-)\rightarrow Cu(II)$ $\pi(S^-)\rightarrow Cu(II)$	(50)
$[Cu^{II}_2Cu^{I}_{10}(mmim)_{12}(H_2O)_4](ClO_4)_2$	CH_3NO_2	437(sh)(1070) 625(sh)(3500) 693 (3910)	$\pi(N)\rightarrow Cu(II)$ $\sigma(S^-)\rightarrow Cu(II)$ $\pi(S^-)\rightarrow Cu(II)$	(54)
$[Cu^{II}_2Cu^{I}_{10}(mmim)_{12}(H_2O)_4](ClO_4)_2$	CH_3CN	430(sh) 620 ca730(sh)	$\pi(N)\rightarrow Cu(II)$ $\sigma(S^-)\rightarrow Cu(II)$ $\pi(S^-)\rightarrow Cu(II)$	(C)
$[Cu^{II}_2Cu^{I}_{10}(mmim)_{12}(H_2O)_4](PF_6)_2$	CH_3NO_2	433(sh)(1050) 625(sh)(3300) 695 (3680)	$\pi(N)\rightarrow Cu(II)$ $\sigma(S^-)\rightarrow Cu(II)$ $\pi(S^-)\rightarrow Cu(II)$	(54)
$[Cu^{II}_2Cu^{I}_{10}(mmim)_{12}(H_2O)_4](PF_6)_2$	CH_3CN	430(sh) 638(br) 730(sh)	$\pi(N)\rightarrow Cu(II)$ $\sigma(S^-)\rightarrow Cu(II)$ $\pi(S^-)\rightarrow Cu(II)$	(C)
$[Cu^{II}_2Cu^{I}_{10}(mmim)_{12}(H_2O)_4](CH_3COO)_2.2H_2O$	CH_3NO_2[b]	625(sh)(2800) 698 (3125)	$\sigma(S^-)\rightarrow Cu(II)$ $\pi(S^-)\rightarrow Cu(II)$	(54)
$[Cu^{II}_2Cu^{I}_{10}(mmim)_{12}(H_2O)_4](CH_3COO)_2.2H_2O$	CH_3CN	410 634 730(sh)	$\pi(N)\rightarrow Cu(II)$ $\sigma(S^-)\rightarrow Cu(II)$ $\pi(S^-)\rightarrow Cu(II)$	(C)

Table 1.7 contd

Compound	Solvent	Band max (nm)	Assignment	Ref
$[Cu^{II}_2Cu^{I}_{10}(mmim)_{12}(H_2O)_4]OH_2.2H_2O$	CH_3CN[b]	625 735(sh)	$\sigma(S^-)\rightarrow Cu(II)$ $\pi(S^-)\rightarrow Cu(II)$	(C)
	nujol mull[b]	630 750(sh,br)	$\sigma(S^-)\rightarrow Cu(II)$ $\pi(S^-)\rightarrow Cu(II)$	(C)
$[Cu(mmimH)_2Cl]$(resulting blue soln)	H_2O[b]	625 (2850) 750(sh)(2550)	$\sigma(S^-)\rightarrow Cu(II)$ $\pi(S^-)\rightarrow Cu(II)$	(C)
$[Cu^{II}_6Cu^{I}_8(mea)_{12}Cl](NO_3)_2(Cl)_5.7H_2O$	nujol mull	597	$(S^-)\rightarrow Cu(II)$	(C)

Notes a. extinction coefficient bracketed (units 1 $mol^{-1}cm^{-1}$)

b. band at ca 400nm obscured

C. this work

sh. shoulder

transfer. The absorbance responsible for the intense blue colour at about 650 nm is actually two bands which show some solvent dependence for their position and intensity. This property is a feature of charge transfer transitions and has been observed in the spectra of copper phenolate compounds(56). In nitromethane a distinct band at ca. 700 nm is observed flanked by a shoulder at 625 nm, whereas in acetonitrile a reversal occurs, the main band appearing about 630 nm and a shoulder at 730 nm. The intense nature of these bands and their solvent dependence are supportive of a charge transfer assignment. The absorbance is most likely $\sigma(S^-) \rightarrow Cu(II)$, with the 730 nm transition assigned as $\pi(S^-) \rightarrow Cu(II)$. Comparison with the electronic spectrum of Alc. denitrificans azurin (Table 1.2) shows a remarkable similarity between band positions, which may denote the similarity of the environment of the copper atom in both cases.

When the white solid $[Cu^{I}(mmimH)_2Cl]$ (see Chapter 2) is dissolved in water, a strikingly intense blue colour develops within seconds which has a spectrum identical to the above cluster compounds lending credence to the suggestion that a new soluble compound $[Cu^{II}_2Cu^{I}_{10}(mmim)_{12}(H_2O)_4]Cl_2$ is being formed.

The nujol mull spectrum of $[Cu^{II}_6Cu^{I}_8(mea)_{12}Cl](NO_3)_2(Cl)_5.7H_2O$ showed a single band at 597 nm which has been assigned as a $S \rightarrow Cu(II)$ charge transfer transition.

1.4.3 Esr spectra

Parameters for the complexes may be found in Table 1.8. An almost

Table 1.8 Esr parameters for the complexes

Compound	Solvent	$g_\perp$	g_{11}	$\|A_{11}\|(10^{-4}cm^{-1})$
$[Cu^{II}_2Cu^{I}_{10}(mmim)_{12}(CH_3CN)_4](BPh_4)_2$	CH_3NO_2	2.067	2.281 2.238[a]	64 64[a]
	CH_3CN	2.081	2.281 2.238[a]	64 64[a]
$[Cu^{II}_2Cu^{I}_{10}(mmim)_{12}(H_2O)_4](ClO_4)_2$	CH_3NO_2	2.069	2.281 2.238[a]	64 64[a]
$[Cu^{II}_2Cu^{I}_{10}(mmim)_{12}(H_2O)_4](PF_6)_2$	CH_3NO_2	2.069	2.281 2.238[a]	64 64[a]
$[Cu^{II}_2Cu^{I}_{10}(mmim)_{12}(H_2O)_4](CH_3COO)_2.2H_2O$	CH_3NO_2	2.074	2.281 2.238[a]	64 64[a]
$[Cu^{II}_2Cu^{I}_{10}(mmim)_{12}(H_2O)_4](OH)_2.2H_2O$	CH_3NO_2	2.082	2.281 2.238[a] 2.274[b]	64 64[a] 179[b]
$[Cu^{II}_6Cu^{I}_8(mea)_{12}Cl](NO_3)_2(Cl)_5.7H_2O$	H_2O	2.074[c] ca2.054[d]	2.247[e]	183[f]

Notes: a. second species b. third species c. g_2 d. g_3

e. g_1 f. A_1

identical lineshape is produced for compounds of the type $[Cu^{II}_2Cu^{I}_{10}(mmim)_{12}(Y)_4](X)_2$ (where Y = CH_3CN, H_2O and X = BPh_4, ClO_4, PF_6, CH_3COO and OH). Henry et al.(57) were only able to obtain a quasi isotropic lineshape for "$[Cu^{II}Cu^{I}_5(mmim)_6](ClO_4)$" ($[Cu^{II}_2Cu^{I}_{10}(mmim)_{12}(H_2O)_4](ClO_4)_2$). Agnus et al.(50) succeeded in resolving the spectrum of $[Cu^{II}_2Cu^{I}_{10}(mmim)_{12}(CH_3CN)_4](BPh_4)_2$, however the interpretation of it as being due to a single axially symmetric species is in retrospect too simplistic. Figure 1.7 shows the spectrum of the compound run in nitromethane. The copper hyperfine peaks are clearly asymmetric and an extra hyperfine absorbance occurs at 2743 G. It appears that the spectrum is composed of two species which have similar parameters. An attempt has been made to substitute parameters for these (Table 1.8), however, a computer simulation experiment is required to properly evaluate those with best fit. Nonetheless the predicted $|A_{11}|$ value of $64\times10^{-4}cm^{-1}$ for the species mimicks that of the type I blue proteins ($\approx60\times10^{-4}cm^{-1}$) extraordinarily well.

On ageing of $[Cu^{II}_2Cu^{I}_{10}(mmim)_{12}(H_2O)_4](CH_3COO)_2.2H_2O$, but even for freshly prepared $[Cu^{II}_2Cu^{I}_{10}(mmim)_{12}(H_2O)_4](OH)_2.2H_2O$, a third species was observed in the esr spectrum. This showed a number of nitrogen superhyperfine lines suggesting that the compound may have a disulphide ligand with ligating nitrogens, resulting from oxidation of the cluster.

The spectrum of the in situ species $[Cu(mmim)_2]$ of Henry et al.(57) generated by addition of cupric acetate to ligand in ethanol shows a similar spectrum to that of the $[Cu^{II}_2Cu^{I}_{10}(mmim)_{12}(H_2O)_4]^{2+}$ cluster supporting the suggestion that it be better formulated as $[Cu^{II}_2Cu^{I}_{10}(mmim)_{12}(H_2O)_4](CH_3COO)_2$. Such a compound has been isolated from a solution of this composition.(54).

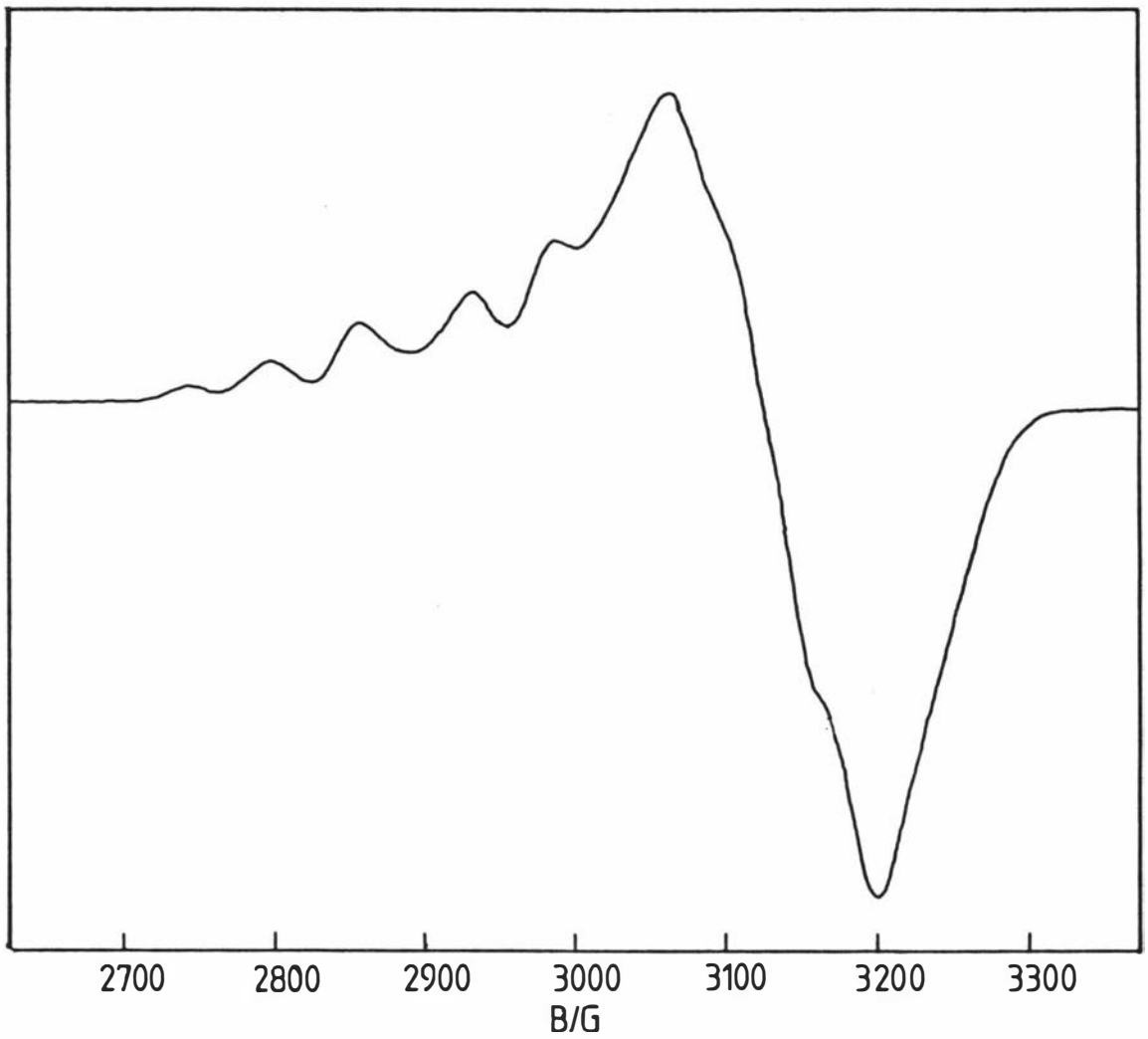


Figure 1.7 Esr spectrum of $[Cu^{II}_2Cu^{I}_{10}(mmim)_{12}(CH_3CN)_4](BPh_4)_2$ in nitromethane.

The spectral lineshape of $[Cu^{II}_6Cu^{I}_8(mea)_{12}Cl](NO_3)_2Cl_5.7H_2O$ shows rhombic character - two absorbances appearing in the $g_\perp$ region. Bencini et al.(58) have observed similar behaviour in the spectrum of square pyramidal complexes.

1.4.4 Resonance Raman Spectra

The resonance Raman spectrum of the compound $[Cu^{II}_2Cu^{I}_{10}(mmim)_{12}(H_2O)_4](ClO_4)_2$ was recorded in the range 200 to 600 cm^{-1} in nitromethane, and from 1100 to 1500 cm^{-1} in acetonitrile. A 676.5 nm laser was used as the excitation source. Regions of interest are presented in Figure 1.8. An absorbance at 330 cm^{-1} has been assigned to ν(CuS), with the band at 439 cm^{-1} interpreted as ν(CuN). The peak at 478 cm^{-1} is due to solvent and the remaining bands in this region are unassigned. For the high frequency area, bands at 1145,1283,1318,1361,1413 and 1452 cm^{-1} are all associated with ring stretching modes of the mmim ligand. The peak at 1374 cm^{-1} is due to the CH_3CN solvent.

1.5 STRUCTURE OF THE MODEL COMPLEXES

The single crystal X-ray structure for $[Cu^{II}_2Cu^{I}_{10}(mmim)_{12}(CH_3CN)_4](BPh_4)_2$ was reported by Agnus et al.(50). The two Cu(II) atoms of the cluster occupy identical sites, the geometry of which is shown in Figure 1.9.

Around copper there is a trans S_2N_2 donor set with Cu-N bond distances of 1.960 and 1.934 Å and Cu-S bonds of 2.464 and 2.466 Å; N-Cu-N and S-Cu-S angles are 175.4° and 150.9° respectively. A fifth

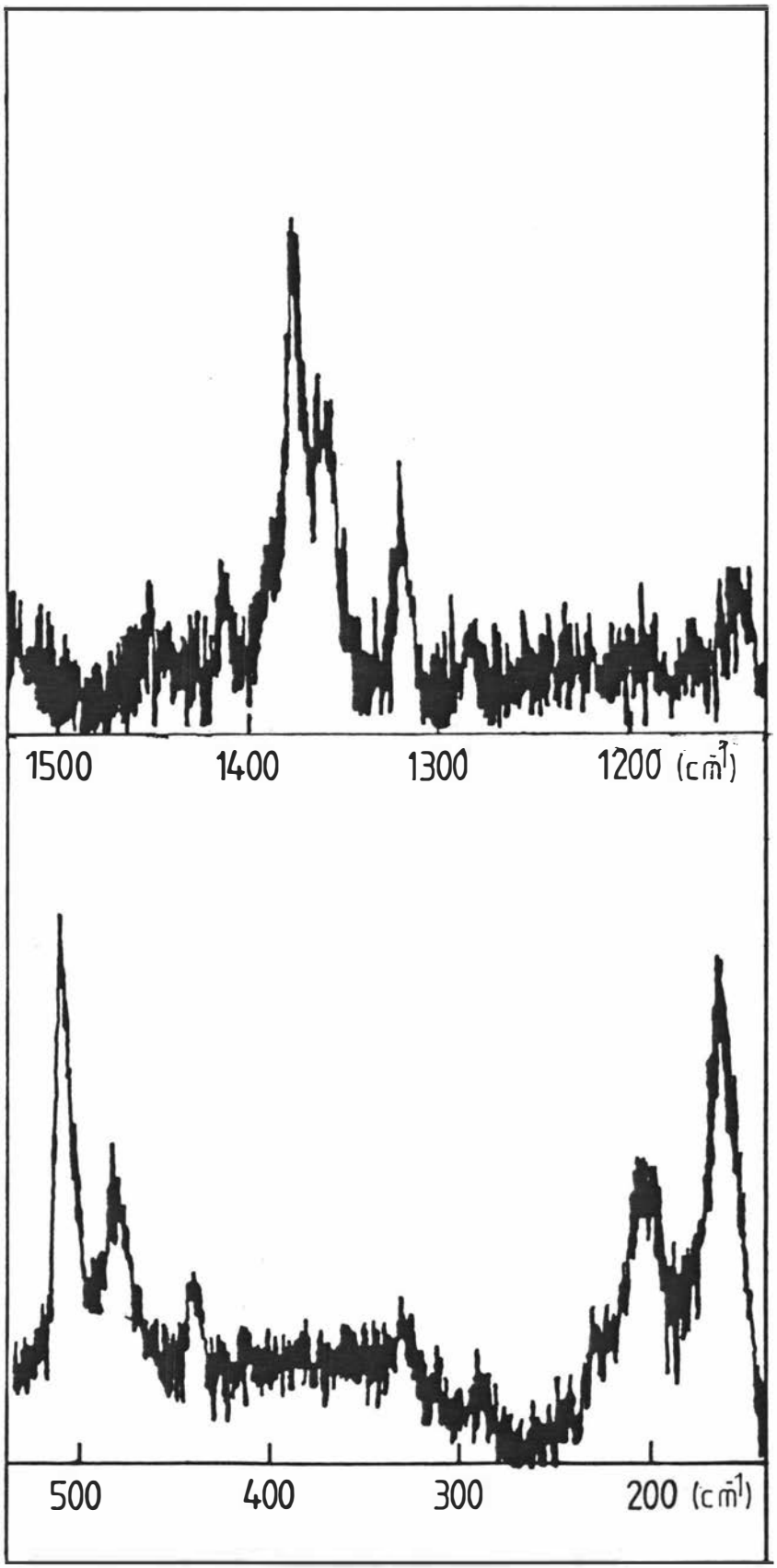


Figure 1.8 Resonance Raman spectrum of $[Cu^{II}_{2}Cu^{I}_{10}(mmim)_{12}(H_2O)_4]^{2+}$.

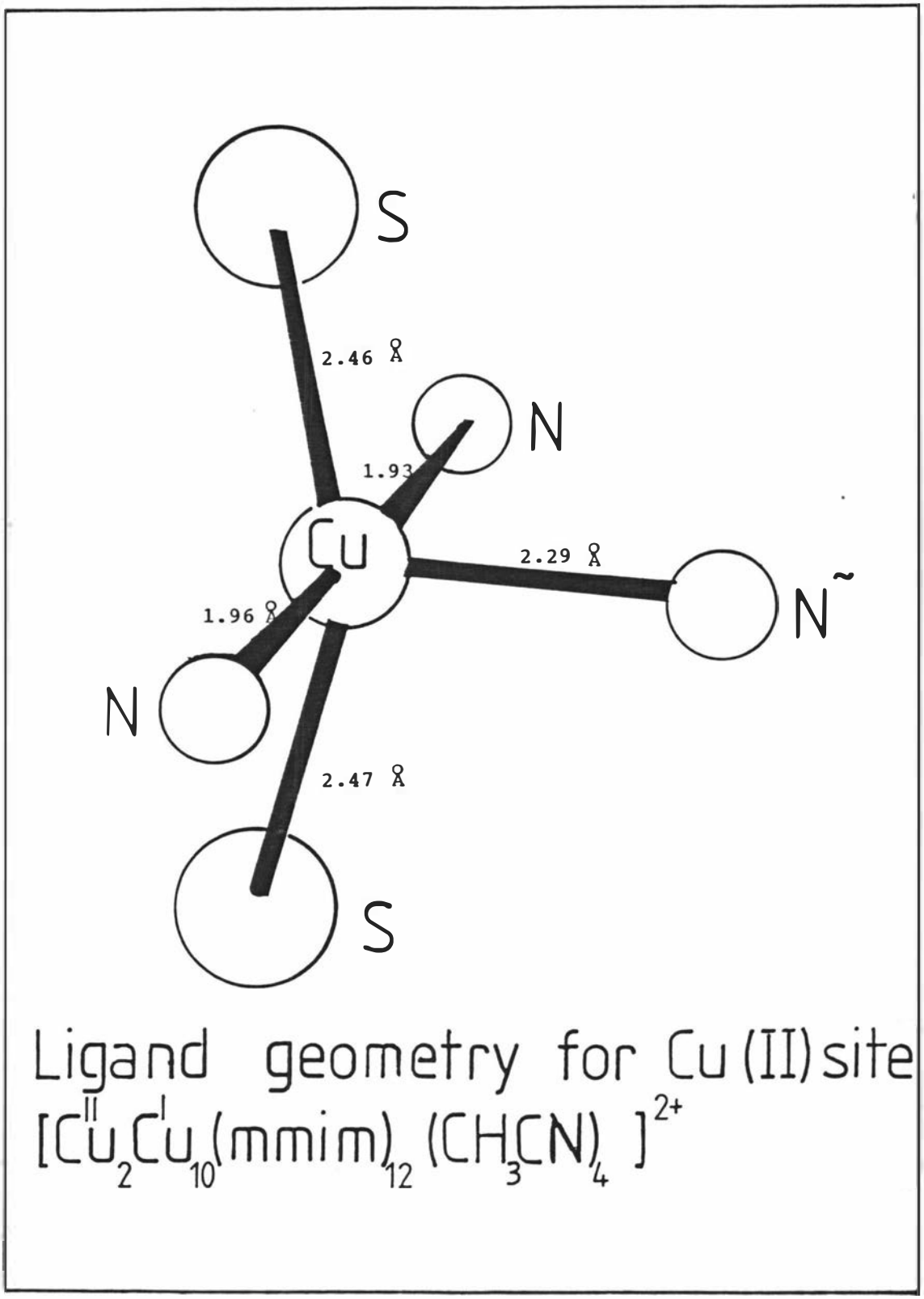

S
2.46 Å
N
1.93
Cu
2.29 Å
N~
1.96 Å
N
2.47 Å
S
Ligand geometry for Cu(II) site
[Cu(II)2 Cu(I)10 (mmim)12 (CH3CN)4]2+

Figure 1.9

ligand, CH_3CN binding through nitrogen, has a longer Cu-N bond of 2.295 Å and occupies an axial position. It is possible to interpret the copper environment in three ways. Firstly, as described by Agnus et al. (50), the S_2N_2 donor set forms an approximate equatorial plane, leading to an overall distorted square pyramidal stereochemistry when the axial acetonitrile ligand is taken into account. However, on closer examination the structure may be interpreted in terms of two other geometries based on a trigonal ligation approach. In this way the three nitrogen ligands can be seen to occupy a plane, with the two sulphurs in distorted axial positions. Alternatively a similar trigonal outlook can be achieved by placing the two sulphur ligands and the acetonitrile in a plane having long bonds; with the two remaining nitrogen ligands occupying short bonded axial positions.

The similarity of the spectral features of the compounds $[Cu^{II}_2Cu^{I}_{10}(mmim)_{12}(H_2O)_4](X)_2$ (where X = OH, ClO_4, PF_6 and CH_3COO] suggests that the same structural framework is present, with ligating acetonitrile molecules replaced by water molecules.

The blue complex $[Cu^{II}_6Cu^{I}_8(mea)_{12}Cl](NO_3)_2Cl_5.7H_2O$ was formulated on the basis of the structure revealed by Birker and Freeman(10) for the complex formed with the ligand penicillamine (pen) with copper. X-ray analysis showed a structure involving the cluster $[Cu^{II}_6Cu^{I}_8(pen)_{12}Cl]^{5-}$ with the Cu(II) atoms corodinated by S_2N_2 chelates in a square planar stereochemistry. In solution a solvent ligand may coordinate in an equatorial position to give the apparently 5-coordinate esr spectrum.

1.6 AN INTERPRETATION OF THE STRUCTURAL REQUIREMENTS NECESSARY FOR THE PRODUCTION OF THE DISTINCT SPECTRAL FEATURES OF THE TYPE I BLUE COPPER PROTEINS

An attempt is made here to explain which features are essential in both protein and model to produce the intense charge transfer absorption at ca 600 nm and the low value of $|A_{11}| \approx 60 \times 10^{-4} cm^{-1}$ for the esr spectrum.

As more Cu(II) thiolate compounds are synthesised evidence seems to suggest that the two properties are separable. Bands which may be assigned to $\sigma(S) \rightarrow Cu(II)$ charge transfer transitions occur over a wide range of energies in the visible spectrum, from 330 nm in biscysteinato Cu(II)(59) to 630 nm in the case of $[Cu^{II}_2Cu^{I}_{10}(mmim)_{12}(CH_3CN)_4](BPh_4)_2$ (50). However for a number of Cu(II) and mixed valence thiolato compounds the bands are observed in the region 500-650 nm (10,60,Table 1.6) where the type I proteins predominantly absorb. The blue bands observed for the proteins then should not be regarded as a phenomenon of the particular nature and geometry of the ligands found in the type I site. Compounds have been prepared (See Table 1.6) which can satisfactorily match electronic band position and intensity, but which have distinctly different esr properties. Rather the transition should be interpreted as being a normal interaction of Cu(II) with a thiolate ligand.

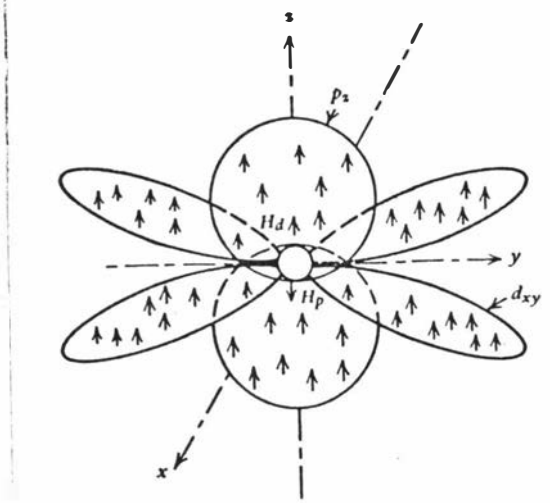
The problem of interpreting esr parameters is more complicated and much effort has been directed towards providing an explanation based on structural considerations. The paucity of well characterised compounds exhibiting low copper hyperfine ($|A_{11}| < 100$ G) has proved a severe

hindrance in the development of ideas. The g_{11} and $g_{\perp}$ parameters of the type I proteins are considered "normal" in that they can be matched by model compounds with similar ligands(1) however the wide range of $g_{||}$ values (2.19-2.31) is greater than has yet been observed for synthetic analogues with a constant ligand set(1).

Early attempts at rationalising the low values of $|A_{11}|$ attributed them to the tetrahedral nature of the copper site. It has been observed for some years that distortion from a square planar stereochemistry to a more tetrahedral one invariably results in a decrease in the value of $|A_{11}|$(61,62). It was thought that sufficient distortion towards tetrahedral coordination could lower $|A_{11}|$ to the "blue" region. Indeed studies of γ irradiated $[Cu(CH_3CN)_4ClO_4]$ (63) and Cu(II) doped crystals of $[ZnHg(SCN)_4]$(64), both imposing N_4 tetrahedral geometries resulted in $|A_{11}|$ values of 80 and 78 $\times 10^{-4}cm^{-1}$ respectively. The crystal structure of plastocyanin(23) indicating a pseudotetrahedral ligand arrangement was consistent with this theory. However inconsistencies in this trend, such as in $[Cu(HB(3,5\text{-}Me_2pz)_3)(mnb)]$(1), where although the geometry is thought to be elongated tetrahedral, "normal" $|A_{11}|$ values were observed; but more particularly that geometries other than tetrahedral could give rise to appropriately low values of $|A_{11}|$(48) (e.g. $[Cu^{II}_2Cu^{I}_{10}(mmim)_{12}CH_3CN)_4]^{2+}$, (50) and [Cu(mpg)])(48), indicated that the problem was more complex.

A plausible mechanism for copper hyperfine reduction was proposed by Bates et al.(65,66) and Sharnoff(67), who investigated a series of complexes of copper(II) with distorted tetrahedral environments. The reason for the low values of $|A_{11}|$ observed ($\lesssim 50 \times 10^{-4}cm^{-1}$), if hyperfine was seen at all, was attributed to admixture of a 4p

contribution into the $3d_{xy}$ ground state wave function (from hole formalism) of copper. It was thought that $|A_{11}|$ is lowered as a result of the small total magnetic field experienced at the nucleus. This arises because the magnetic moment from the p_z distribution produces a magnetic field at the nucleus which is in the opposite direction to that of the d_{xy} distribution. Provided that a sufficient amount of p-type wave function is built into the ground state, it is possible to have such a low total magnetic field at the nucleus that a collapsed magnetic hyperfine structure results. The figure below shows schematically the distribution of spin angular momentum over d_{xy} and p_z wave functions, and the resultant cancelling effect of the fields H_d and H_p at the nucleus.



Furthermore Sharnoff(67) suggests that the greater the covalency in complexes, the more admixture of 4p orbitals into primarily 3d wavefunctions will occur. Thiolate ligands which are considered to have highly covalent interactions(68) are therefore presumably well favoured in their ability to promote $|A_{11}|$ reduction.

It should be noted also that mixing of p orbitals can give rise to enhanced $|A_{11}|$ values when a particular geometry is present. For instance in copper doped zinc oxide(66), copper(II) is present in a trigonally distorted tetrahedral environment, that is, one of the Cu-O bond distances is shorter than the other three. Here the spin contributions from the p and d wavefunctions to the total magnetic moment add, contributing to the enhancement of $|A_{11}|$ to 195 x 10^{-4} cm^{-1}

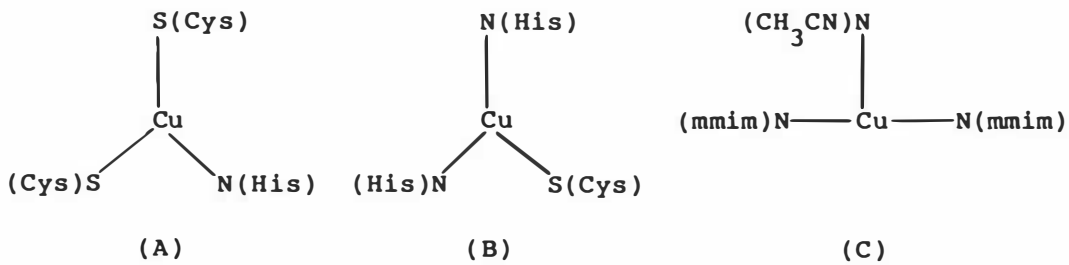
Recently, however, Bencini and Gatteschi(69) have inferred that covalency effects, in particular a relatively small Fermi contact term, are responsible for the low value of $|A_{11}|$ in the pseudotetrahedral $Cs_2[CuCl_4]$ complex, rather than 4p metal orbital mixing into the ground state.

Turning our attention towards the blue proteins and their synthetic analogues again; if mixing of d and p orbitals is a requirement a.priori for the reduction of $|A_{11}|$, structures promoting mixture are favoured. Immediately a regular octahedral field is ruled out, as mixing is forbidden for such stoichiometries(65). Furthermore from Table 1.6 it is evident that a regular elongated tetrahedral system with C_{3v} symmetry is also incapable of providing the right environment. What then are the cosmopolitan structural and geometrical features present in compounds exhibiting low $|A_{11}|$? A promising stratagem would be to compare the structures of compounds giving rise to this property in the hope of finding the prerequisite requirements.

A feature common to each, if all possible ligands are considered, is a high degree of irregularity or rhombicity in their structures. The proteins azurin, plastocyanin and horse liver alcohol dehydrogenase

contain one or more axial ligands bound at irregular angles to an approximate plane containing 3 ligands, one of which is different. In $[Cu^{II}_2Cu^{I}_{10}(mmim)_{12}(CH_3CN)_4]^{2+}$ a buckled trans-oriented plane containing four donor atoms is axially bound by a fourth hetero-ligand.

Another structural theme, that of trigonal ligation, is evident if only the strongly binding ligands are considered. For instance in both azurin and plastocyanin the three strongest ligands, the two histidines and the cysteine are found in an approximate planar arrangement. Similarly with alcohol dehydrogenase two cysteines and a histidine form a plane of strongly interacting ligands, and this is so also, as has been discussed, for $[Cu^{II}_2Cu^{I}_{10}(mmim)_{12}(CH_3CN)_4]^{2+}$



(A) (B) (C)

Trigonal ligation for (A) horse liver alcohol dehydrogenase
(B) azurin and plastocyanin
(C) $[Cu^{II}_2Cu^{I}_{10}(mmim)_{12}(CH_3CN)_4]^{2+}$

From the above diagram it can be seen that in each case C_{2v} symmetry, or C_2 if copper is out of the plane, can be assigned. Justification for the neglect of the axial ligands in azurin has been discussed previously, but it is also interesting to note that in a recent study of the system trans[Cu(cyclam)$(SC_6F_5)_2$](70), in which pentafluorothiophenolate ligands bind axially with bond lengths of 2.94 Å,

comparable with the axial methionine in plastocyanin and azurin, little effect was produced on the characteristic optical and esr spectra of $[Cu(cyclam)]^{2+}$.

The postulation that C_{2v} symmetry, or alternatively a symmetry of C_s if all ligands are considered, is important in promoting d-p mixing is at first glance apparently in contention with what are generally regarded as the more authoritative symmetry models for the type I proteins. A theoretical approach based on ligand field calculations for plastocyanin conducted by Solomon et al.(27) favoured a higher symmetry, that of D_{2d} corresponding to a tetragonally flattened tetrahedron. Elongated and compressed trigonal bipyramidal symmetry (D_{3h}) and a compressed four coordinate pseudotetrahedral structure with C_s symmetry were discounted because of poor agreement of theoretical and observed g values.

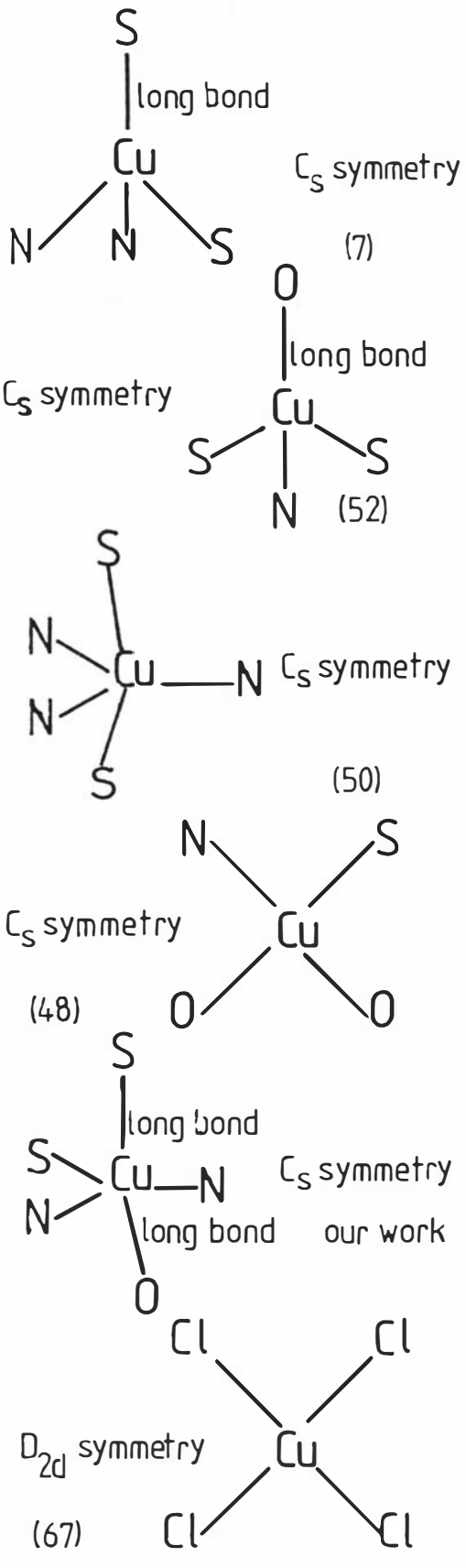
Further calculations are required for the five coordinate structure of the azurin from Alc. denitrificans incorporating C_s symmetry, and also the limiting trigonal structure with C_{2v} symmetry. Penfield and coworkers(26) have also performed spectroscopic studies on plastocyanin single crystals and favour a description corresponding to elongated C_{3v} with significant rhombic distortions. It sould be noted that the ground state for this symmetry is not d_{xy} but $d_{x^2-y^2}$, as it is also for D_{2d}.

Summary

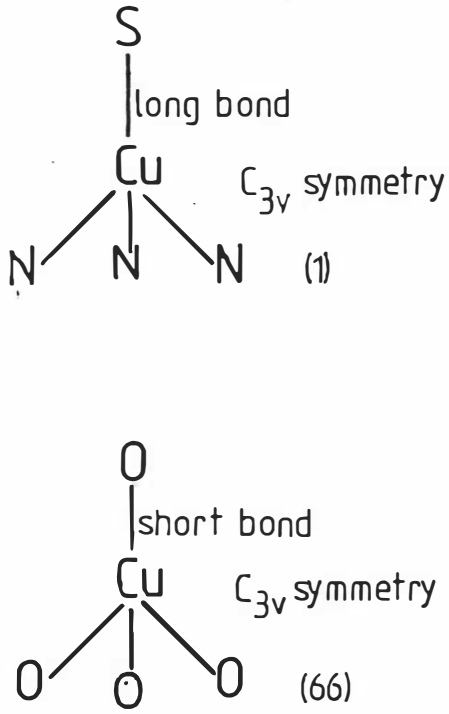
1. X-ray crystallographic, resonance Raman and esr evidence favour an essentially trigonal coordination sphere for copper in the active site

Figure 1.10 Relation of copper geometry and the size of the $|A_{11}|$ esr parameter

Structures producing low values of $|A_{11}|$ ($<100\times10^{-4}cm^{-1}$)



Structures producing high values of $|A_{11}|$ ($>150\times10^{-4}cm^{-1}$)



of Alc. denitrificans.

2. The intense blue absorption in the electronic spectrum of the type I proteins can be attributed to a normal phenomenon of the thiolate-Cu(II) interaction, and is not a unique feature of the type I site.

3. The low $|A_{11}|$ values observed for the type I copper proteins results from mixing of p orbital character into the d orbitals of copper. Perfect or distorted tetrahedral, trigonal C_{2v} or a symmetry of C_s appear to promote this mixing, with subsequent reduction of the magnetic field at the nucleus and collapse of A_{11}. C_{3v} symmetry results in an increase of the nuclear magnetic field with resulting enhancement of A_{11}.

4. These studies indicate that pertinent small models for the copper azurin site may be based on a trigonal planar geometry with C_{2v} symmetry. Such systems, up to this time, have been impossible to synthesise as coordination number three is unknown in simple copper(II) chemistry. However, five coordinated models with long axial bonds may be useful alternatives.

1.7 EXPERIMENTAL

1.7.1 Instrumentation

Instruments used were as for part 1 except that the Shimadzu MPS 5000 only was used for electronic spectra. Solid state electronic spectra were often run as nujol mulls on Whatman filter paper, with a nujol filter paper blank in the reference compartment. A Pye Unicam

SP3-300 was used to record infrared spectra which were run as nujol mulls on CsI plates. A Cahn Farraday balance No. 7550 was used to determine magnetic susceptibilities.

1.7.2 Preparation of the complexes

$$[Cu(II)_2Cu(I)_{10}(mmim)_{12}(H_2O)_4](OH)_2.2H_2O$$

To 25 cm^3 of a 1% aqueous solution of mmimH was added 14 drops concentrated NH_4OH or alternatively n-butylamine. This solution was added dropwise to $CuSO_4.5H_2O$ in water (20cm^3). A blue-black precipitate apeared almost immediately which was collected and washed with water. Yield 0.09g (60%).

$$[Cu(II)_6Cu(I)_8(mea)_{12}Cl](NO_3)_2Cl_5.7H_2O$$

$Cu(NO_3)_2.3H_2O$ (1.2g, 5mmol) in water (20cm^3) was added dropwise to 2-mercaptoethylammonium chloride (0.81g, 7mmol) in water (20cm^3) upon which a white compound was precipitated. The pH of the solution was slowly raised to 8-9 with 2M NH_4OH during which the white precipitate changed to a red colour and finally a blue-purple. This compound was collected and washed with water and acetone. Yield: 60%.

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CHAPTER 2

THIOLATE AND THIOAMIDE COMPLEXES OF COPPER(I)

Introduction

In most cases where a cupric salt interacts with a sulphhydryl containing ligand, reduction to copper(I) occurs with oxidation of ligand to the disulphide. Excess ligand may then stabilise the cuprous state by formation of a complex. Where the coordinating sulphur atom is in the thiolate form, polymeric species involving clusters of bridged copper atoms are commonly observed such as in $[Cu_4(C_6H_5S)_6]^{2-}$(1) $[Cu_5(C_6H_5S)_7]^{2-}$(2) and $[Cu_5((CH_3)_3CS)_6]^{-}$(3). However where tautomerism between thiol and thioketo forms is possible for the ligand (see Figure 2.1) neutral thione sulphur may coordinate in conjunction with an anion, particularly when the anion is a halide

thiol form thioketo or thione form

Figure 2.1 Thiol-thioketo tautomerism for imidazole (Y=NH) and thiazole (Y=S) skeletons

The ability for the ligand to form such a tautomeric equilibrium is conferred when the thiol group is attached to an imidazole or thiazole-type skeleton. In most cases the thioketo form predominates for the free ligand in the solid state(4). In the thioketo form the ligand is referred to as a thioamide compound.

Thioamide compounds are normally solids at room temperature, and for the most part odourless, making them popular choices as ligands with which to study the interaction of copper with sulphur. Studies, particularly in the case of the ligands 2-mercaptothiazoline(5,6), 2-mercaptoimidazoline(7) and 2-mercaptobenzoxazole,(8,9,10) have often been extensive, nonetheless there has been little attempt to elucidate emerging trends in compound synthesis. In addition, in some instances, results for copper-thioamide systems exist in a state of disarray due to conflicting and contradicting formulations from different authors.

Such a case is typified by the 2-mercaptobenzothiazole system. The ligand itself is of great industrial importance, tonnes being used annually in the vulcanisation of rubber(11). In the field of corrosion inhibitors 2-mercaptobenzothiazole has proved especially suitable for protection of metals such as copper(12). It is also important medicinally, through its ability to cause partial reversal of the Crabtree effect, that is, it discourages excessive glycolytic oxidation in tumour cells(13). All of these processes are believed to be promoted by metal ligand interactions, and although copper may not be specifically involved in each case, it is essential that the true nature of the interaction be documented for legitimate comparisons between it and more applicable metals.

The formulations that have been presented to date for the addition of neutral ligand to cupric salt are presented in Table 2.1. As will be demonstrated only two specific compounds $[Cu(mbtH)_2Cl]$ and [Cu(mbt)], are formed, depending on the solvent used.

To support these formulations and to further extend knowledge on the

Table 2.1 Proposed formulations of the Cu-2-mercaptobenzothiazole (mbtH) system

Year		Cu(II) source CuX_2	Solvent	Formulation	Ref
1935	G. Spacu and M. Kuras	X = $\frac{1}{2}SO_4$	aqueous ethanol	[Cu(II)$(mbt)_2$]	14
1975	I. Kuhllar and U. Agarwala	X = Cl	ethanol	[Cu(II)$(mbt)_2$]	15
1977	M.F. El-Shazly et al.	X = Cl	ethanol	[Cu(II)$(mbt)_2$]	16
1977	F. Pruchnik et al.	X = $\frac{1}{2}SO_4$	aqueous ethanol	[Cu(II)$(mbt)_2$]	17
1979	T. Yoshida et al.	X = $\frac{1}{2}SO_4$, NO_3 Cl, CH_3COO	aqueous ethanol	[Cu(I) mbt(mbt-mbt)$\frac{1}{2}$]	18
		X = Cl	ethanol	[Cu(I)$(mbtH)_2$(mbt-mbt)$\frac{1}{2}$Cl]	
1982	S.E. Livingstone et al.	X = Cl	aqueous ethanol	[Cu(I)(mbtH)(mbt)]	13
1983	This work	X = Cl, $\frac{1}{2}SO_4$	aqueous ethanol	[Cu(I)mbt]	
		X = Cl	ethanol	[Cu(I)$(mbtH)_2$Cl]	

nature of the cuprous-thioamide-thiolate interaction, the reactions of copper(II) salts, with compounds structurally analogous to 2-mercaptobenzothiazole, have been studied (See Figure 2.2).

2.1 SYNTHESIS OF THE COMPOUNDS

Details for the preparation of the complexes found in this chapter may be located in the experimental section. The proposed empirical formulae and microanalytical results, consistent with these formulations, are presented in Table 2.2.

The reaction stoichiometries for the synthesis of the compounds can be represented by three general equations.

(1) $CuX_2 + 3LH \rightarrow [Cu(LH)_2X] + \frac{1}{2}L\text{-}L + HX$

(LH = mbtH, etmbtH; X = Cl,Br: LH=mmimH; X = Cl)

(2) $CuX_2 + 2LH \rightarrow [Cu(LH)X] + \frac{1}{2}L\text{-}L + HX$

(LH = mbimH, mpyH, phmtzH, Ph_2PS_2H; X = Cl,Br: LH = mmimH; X = Br)

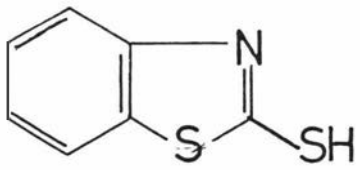
(3) $CuX_2 + 2LH \rightarrow [CuL] + \frac{1}{2}L\text{-}L + HX$

(LH = mbtH, etmbtH, phmtzH, mpyH, dimtdzH, dipmimH, bimetH;

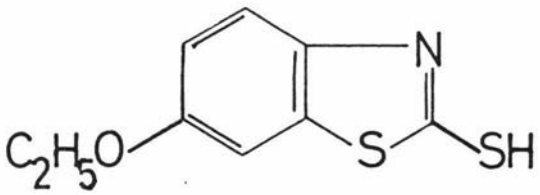
X = ClO_4, NO_3 or $\frac{1}{2}SO_4$).

In all cases, as well as the desired compound, a disulphide co-product (L-L) and an acid (HX) are produced. The latter does not participate in any further reaction, but has been used in instances to verify the number of ligands coordinating via its titration with base(5). The disulphide, however, poses a real threat as a contaminant for the legitimate product if it lacks solubility in either the

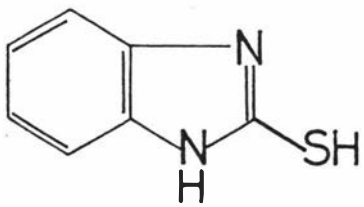
Figure 2.2 Structures of the ligands used in this Chapter and their abbreviations



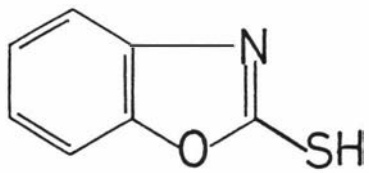
2-mercaptobenzothiazole
(mbtH)



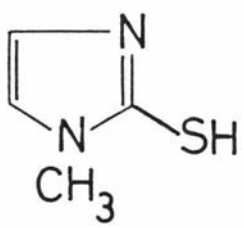
6-ethoxy-2-mercaptobenzothiazole
(etmbtH)



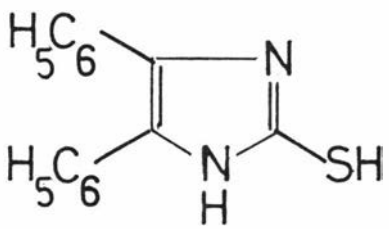
2-mercaptobenzimidazole
(mbimH)



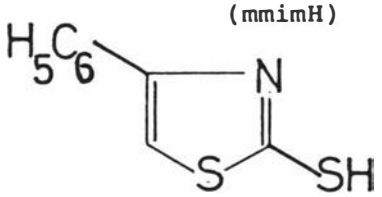
2-mercaptobenzoxazole
(mboH)



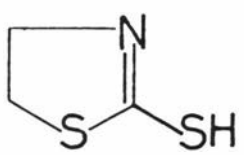
2-mercapto-1-methylimidazole
(mmimH)



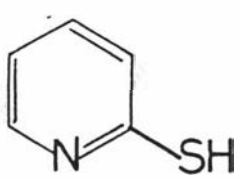
4,5-diphenyl-2-mercaptoimidazole
(dipmimH)



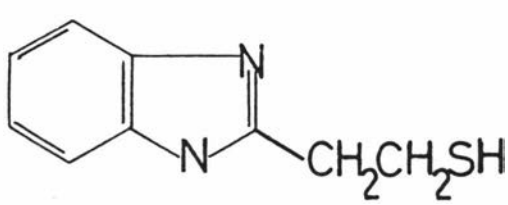
2-mercapto-4-phenylthiazole
(phmtzH)



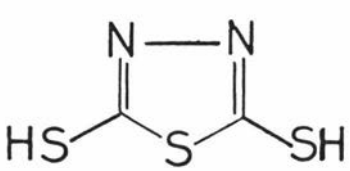
2-mercaptothiazoline
(ttzH)



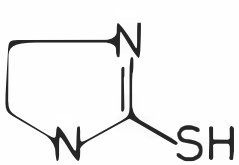
2-mercaptopyridine
(mpyH)



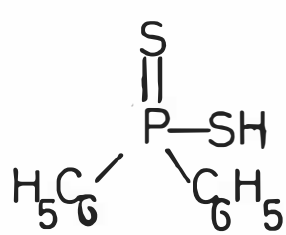
2-benzimidazoleethanethiol
(bimetH)



2,5-dimercapto-1,3,4-thiadiazole
(dimtdzH)



2-mercaptoimidazoline
(etuH)



diphenylphosphinodithioic acid
(Ph_2PS_2H)

Table 2.2 Analytical data for the complexes

Compound	Colour	%C	%H	%N	Other
$[Cu(mbtH)_2Cl]$	pale yellow	39.3 (38.8)	2.7 (2.10)	6.7 (6.5)	8.4[a] (8.2)
$[Cu(mbtH)_2Br]$	yellow	34.2 (35.3)	2.2 (1.9)	5.7 (5.9)	-
$[Cu(mbtH)_2I]$	buttercup yellow	33.0 (32.0)	2.35 (1.9)	5.3 (5.3)	23.6[b] (24.2)
[Cu(mbt)][e]	orange	36.75 (36.6)	1.9 (1.8)	(6.1) (6.1)	-
$[Cu(etmbtH)_2Cl]$	tan	42.45 (41.45)	3.75 (3.5)	5.4 (5.35)	5.55[a] (6.8)
$[Cu(etmbtH)_2Br]$	cream	38.3 (38.2)	3.6 (3.2)	4.7 (4.95)	14.8[c] (14.1)
$[Cu(etmbH)_2I]$	pale yellow	37.7 (35.3)	3.0 (3.0)	4.8 (4.6)	22.2[b] (20.7)
[Cu(etmbt)]	orange	39.3 (39.3)	3.0 (2.9)	5.1 (5.1)	-
$[Cu(mmimH)_2Cl]$	white	29.5 (29.35)	4.0 (3.7)	17.3 (17.1)	-
[Cu(mmimH)Br]	yellow	18.1 (18.6)	2.5 (2.35)	10.7 (10.9)	-

Table 2.2 contd

Compound	Colour	%C	%H	%N	Other
[Cu(phmtzH)Cl].1/2H_2O	yellow green	35.4 (35.9)	2.4 (2.7)	4.6 (4.65)	11.8[a] (11.8)
[Cu(phmtzH)Br].H_2O	yellow green	30.4 (30.55)	2.3 (2.4)	3.8 (4.0)	24.4[c] (23.8)
[Cu(phmtz)]	white	42.4 (42.25)	2.2 (2.4)	5.4 (5.5)	-
[Cu(mpyH)Cl]	orange yellow	29.5 (28.6)	3.0 (2.4)	6.5 (6.7)	17.7[a] (16.9)
[Cu(mpyH)Br].1/2H_2O	orange	22.7 (22.8)	2.25 (2.3)	5.3 (5.3)	32.6[c] (30.3)
[Cu(mpy)][f]	yellow	34.3 (34.6)	2.7 (2.3)	8.1 (8.1)	-
[Cu(Ph_2PS_2H)Cl]	white	41.0 (41.3)	3.75 (3.2)	8.6[d] (8.9)	9.2[a] (10.15)
[Cu(Ph_2PS_2H)Br]	white	36.7 (36.6)	3.3 (2.8)	-	7.2[d] (7.9)
[Cu(mbimH)Cl].1/2H_2O	off white	32.55 (32.6)	2.9 (2.7)	10.5 (10.85)	12.6[a] (13.7)
[Cu(mbimH)Br].1/2H_2O	off white	28.5 (27.8)	2.6 (2.3)	8.7 (9.3)	-

Table 2.2 contd

Compound	Colour	%C	%H	%N	Other
[Cu(dimtdz)]	yellow brown	11.8 (11.2)	0.8 (0.9)	13.75 (13.75)	-
[Cu(dimtdz)]	yellow brown	11.8 (11.2)	0.8 (0.9)	13.75 (13.75)	-
[Cu(dipmim)]	yellow	57.2 (57.2)	3.85 (3.5)	8.6 (8.9)	-
[Cu(bimet)]	light green	43.0 (43.3)	3.3 (4.0)	10.8 (11.2)	-

Notes: a. %Cl, b. %I, c. %Br, d. %P, e. prepared previously Ref. 19

f. prepared previously Ref. 20

reaction or wash solvents. Failure to acknowledge this fact may lead to erroneous analysis results and has largely contributed to the number of anomalous formulations for the 2-mercaptobenzothiazole system (Table 2.1). Ideally the solubility properties of each disulphide should be evaluated, requiring their preparation or isolation. This has been the approach taken in this work for compounds where formulation or infrared inconsistencies indicated that contamination was possible or where literature evidence did not preclude this possibility. (Mass spectral details of the disulphide species isolated from the reactions of the ligands 6-ethoxy- and 2-mercaptobenzothiazole and 2-mercapto-4-phenyl-thiazole are presented in the Appendix).

Chloroform was found to be a solvent in which most disulphide species have high solubility and for dibenzothiazol-2-yl disulphide, experiments in which the amount of disulphide extracted was weighed indicated that the wash process was quantitative. Accordingly chloroform has been used as a wash solvent in all the preparations listed.

The enigma surrounding the mbtH system is simplified when it is considered that in no previous preparation has any author effectively removed the contaminating disulphide. Details of elemental analysis for anomalous proposed formulations and for alternative formulations where disulphide is removed are presented in Table 2.3

As is evident from Table 2.3 the only possible compounds from the starting materials are $[Cu(mbtH)_2Cl]$ and [Cu(mbt)]. Yoshida *et al*(18) have acknowledged the overall stoichiometry of the reaction with formulations containing disulphide, however, the authors

Table 2.3 Elemental analysis figures for various Cu(II)-2-mercaptobenzothiazole(mbtH) preparations

CuX_2	Solvent	Formulation without $CHCl_3$ wash	Analyses[a] C	H	N	Ref	Formulation with $CHCl_3$ wash	Analyses C	H	N	Ref
X=Cl	ethanol	$[Cu^{II}(mbt)_2]$	42.4 (42.5)	1.9 (2.0)	7.2 (7.1)	15					
X=Cl	ethanol	$[Cu^{I}(mbtH)_2(mbt\text{-}mbt)^{b}_{\frac{1}{2}}Cl]$	42.4 (42.1)	2.2 (2.3)	7.0 (7.0)	18	$[Cu^{I}(mbtH)_2Cl]$	39.3 (38.8)	2.7 (2.1)	6.7 (6.5)	c
X=Cl	aqueous ethanol	$[Cu^{I}(mbtH)(mbt)]$	42.6 (42.4)	2.2 (2.0)	7.1 (7.0)	13					
X=Cl	aqueous ethanol	$[Cu^{I}(mbt)(mbt\text{-}mbt)^{b}_{\frac{1}{2}}]$	42.3 (42.5)	2.0 (2.0)	7.1 (7.1)	18	$[Cu^{I}(mbt)]$	36.75 (36.6)	1.9 (1.8)	6.1 (6.1)	c
X= SO_4	aqueous ethanol	$[Cu^{II}(mbt)_2]$	-	-	-	14					

Notes: a. calculated values given in parenthesis

b. (mbt-mbt) is the disulphide

c. this work

were mistaken in believing that the disulphide is coordinated.

As well as quantitative production of disulphide, proof that the copper is in the cuprous state comes from X-ray photoelectron studies(18).

Similar product contamination with disulphide was encountered in trial reactions of the ligands 6-ethoxy-2-mercaptobenzothiazole and 2-mercapto-4-phenylthiazole where our initial $[Cu(LH)_xLCl]$ and $[CuL_2]$ formulations were adjusted to $[Cu(LH)_xCl]$ and [CuL] respectively once an efficient wash solvent was adopted. The probable removal of disulphide has allowed the reformulation of $[Cu(mpyH)_2Br_2]$ prepared by Wilkinson and Evans(21) as [Cu(mpyH)Br] and the obtention of satisfactory analytical figures for [Cu(mpyH)Cl].

Special mention should be made at this stage of the compounds $[Cu(Ph_2PS_2H)Cl]$ and $[Cu(Ph_2PS_2H)Br]$. The ligands here do not fall into the thioamide category, however, it is likely that structural similarities will occur, due to a thione sulphur moiety being present. The complexes are unusual in that this is the first recorded instance of a dialkyldithiophosphinic acid ligand coordinating to copper(I) in the neutral state. More commonly compounds of the form $[R_2PS_2Cu]_4$ in which the ligand is deprotonated, are observed(22).

2.2 INFRARED SPECTRAL ANALYSIS

Because the cuprous state has a $3d^{10}$ configuration the techniques available to the coordination chemist to aid in the struct-

ural deduction of his product are limited. In the ideal situation an X-ray crystal structure provides definitive evidence. However, with the exception of [Cu(etmbt)], all compounds prepared in this chapter proved amorphous and insoluble in a wide variety of solvents, precluding the growing of suitable crystals. In such a situation one of the few spectroscopic techniques available, infrared spectroscopy, assumes a special significance for the assignment of structures.

The presence of a ν(NH) stretching vibration in the range 3050-3300 cm^{-1} for compounds containing the thiazole group, and postulated as LH, is confirmation that the ligand is indeed neutral and that the thione tautomeric form is present. Where the ligand is thought to be deprotonated this absorbance is absent as is expected. Authors who have misformulated $[Cu(mbtH)_2Cl]$(15,16) have often missed the ν(NH) vibration, or alternatively if preparing "[Cu(mbtH)(mbt)]"(13) have confused a sharp band occuring at ca 3060 cm^{-1} (ν(CH)) in the disulphide for ν(NH).

Organic compounds containing the thioamide H-N-C=S chromophore have been attributed a number of vibrations(23). Where the thioamide is secondary, as is the case for the ligands used here, four principal bands are observed in the region 1600-650 cm^{-1}. These bands are not often assignable to any single vibration, rather they are a combination of the various modes present in the thioamide skeleton. According to the terminology of Rao et al.(23) the bands have been designated as I-IV with decrease in frequency. The proposed constitutions(24) and their approximate positions are:

Band I - $\partial(CH) + \partial(NH) + \nu(CN)$ (near 1500 cm^{-1})

Band II - $\nu(CH) + \nu(CS) + \partial(NH) + \partial(CH)$ (ca 1200-1300 cm^{-1})

Band III - $\nu(CN) + \nu(CS)$ (near 1000 cm^{-1})

Band IV - mainly $\nu(CS)$ (between 650-850 cm^{-1})

The vibrations tend to be broad and strong facilitating their identification. On binding of a thioamide ligand to a metal atom, shifts observed for these bands have proved useful in identifying coordinating atoms(7,25) , as conceivably binding may occur through sulphur or nitrogen or both atoms simultaneously.

Interpretations of the effect of coordination on the individual components of the various bands has led to the following conclusions (24,25) summarised in Table 2.4.

One other vibration associated with the thioamide entity, the pure $\nu(NH)$ mode is also useful in pinpointing binding atoms. However, interpretation of band movements is complicated by hydrogen bonding effects(10). When the ligands are run in the solid state hydrogen bonding causes bands around 3100-3200 cm^{-1} to be observed, whereas for a dilute solution of ligand in an aprotic solvent such as chloroform, this effect is minimised and the $\nu(NH)$ vibration is seen as a sharp peak at ca 3300 cm^{-1} (4). The broad peaks seen in the spectra of the complexes indicate that hydrogen bonding is occuring there also, making comparison with the free vibrations unrealistic. An admittedly approximate comparison with the solid state ligand (i.e. nujol mull) value may prove more valid for distinguishing trends on atom coordination. In a simlar vein, then, coordination through sulphur only should see a blue shift of $\nu(NH)$ whereas in the case of simultaneous

Table 2.4 Infrared spectral changes with respect to the free ligand on coordination of sulphur and nitrogen(24,25).

Thioamide Band	Atom(s) coordinating S	N	S and N
I	Blue Shift	Red Shift	Red[a] shift
II	Blue shift	Red Shift	Blue[b] shift
III	Red shift	Slight blue shifts or none at all are likely	Small blue shift and/or considerable lowering of intensity.
IV	Red shift	as above	Red shift

Note (a) Singh and Thakur(24) favour a red shift for this band, however Jeannin et al.(26) caution that although coordination through nitrogen should result in a frequency decrease, the increased C---N double bond character caused by sulphur binding should have a converse effect. It is difficult to determine which of the two effects will prevail.

(b) as for (a), but a blue shift is favoured(24).

coordination through sulphur and nitrogen, or binding through nitrogen only, red shifts should be observed.

Band assignments for the thioamide ligands and the new positions observed on coordination are presented in Table 2.5. It should be emphasised that due to the error involved in assigning frequencies to bands (± 2 cm^{-1}) only differences greater than $10cm^{-1}$ can be considered as significant. Also to achieve internal consistency bands recorded in Table 2.5 for the ligands were exactly as they appeared in the spectra, although where possible literature references were used to locate the approximate position of the absorption. Evaluation of band movements has allowed the following proposals.

Complexes of 2-mercaptopyridine and 2-mercapto-1-methylimidazole all show a distinct blue shift of their broad ν(NH) band on complexation suggesting nitrogen is not bound. Confirmation of this is seen in compounds of the former ligand where thioamide I moves significantly to higher frequency. Conversely red shifts of thioamide IV for both systems implicate coordination by sulphur atom. Accordingly ligation by thione sulphur only is proposed for the complexes of these ligands. A similar coordination is predicted for compounds of 2-mercaptobenzimidazole although interpretation of ν(NH) band shifts are complicated by the presence of additional ν(NH) and ν(OH) vibrations in the molecules. Nonetheless sulphur coordination is intimated by red shifts of bands III and IV.

The remaining compounds have proved a little more difficult to determine, due to the insensitive nature of some of the thioamide bands

Table 2.5 Thioamide band positions[a]

Compound	Thioamide I (cm^{-1})	Thioamide II (cm^{-1})	Thioamide III (cm^{-1})	Thioamide IV (cm^{-1})	ν(NH) (cm^{-1})
2-mercaptobenzothiazole	1495[b]	1319[b]	1043[b]	675	3050
$[Cu(mbtH)_2Cl]$	1485	1330	1028	665	3110
$[Cu(mbtH)_2Br]$	1492	1330	1039	675	3105
$[Cu(mbtH)_2I]$	1493	1333	1043	676	3110
6-ethoxy-2-mercaptobenzothiazole	1487	1225	1020	695(sh)	3100
$[Cu(etmbtH)_2Cl]$	1480	1220	1020	687	3100
$[Cu(etmbtH)_2Br]$	1490(sh)	1230	1015	682	3130
$[Cu(etmbtH)_2I]$	1480	1225	1010	690	3100
2-mercapto-4-phenylthiazole	1480	1335	1030	692	3040
$[Cu(phmtzH)Cl].1/2H_2O$	-	1310	1026	690	3080(sh)[d]
$[Cu(phmtzH)Br].H_2O$	1479	1305	1025(sh)	682	3050[d]
2-mercaptopyridine	1460(sh)	1270	980	740	3140
[Cu(mpyH)Cl]	1510	1270	1002	720	3165
$[Cu(mpyH)Br].1/2H_2O$	1506	1264	1000	725	3160

Table 2.5 (contd)

Compound	Thioamide I (cm^{-1})	Thioamide II (cm^{-1})	Thioamide III (cm^{-1})	Thioamide IV (cm^{-1})	ν(NH) (cm^{-1})
2-mercapto-1-methylimidazole	1457[c]	1277[c]	1080[c]	770[c]	3115
$[Cu(mmimH)_2Cl]$	1450	1282	1080	754	3190
[Cu(mmimH)Br]	-	1278	1080	748	3220
2-mercaptobenzimidazole	1500	1176	1017	710	3160[e]
$[Cu(mbimH)Cl].1/2H_2O$	1490	1173	1005	675(sh)	3100[d,e]
$[Cu(mbimH)Br].1/2H_2O$	1498	1177	1010	688	3100[d,e]

Notes: a. nujol or hexachlorobutadiene mulls

b. ref. 15

c. ref. 27

d. band complicated by νOH absorption

e. two ν(NH) vibrations occur in this molecule

sh. shoulder

to change on coordination. Nonetheless, some tentative assignments can be made for shifts which were observed. Complexes of 2-mercaptobenzothiazole and its 6-ethoxy derivative show some similarity in spectral changes as might be expected. A significant move of thioamide IV to lower frequency in the complexes of the latter and in $[Cu(mbtH)_2Cl]$ is consistent with sulphur coordination. This is confirmed by a red shift in thioamide III for some of the compounds. Blue shifting of thioamide II is suggestive of a free imino group, however, ν(NH) values do not appear at significantly higher frequencies. Coordination by thione sulphur only is probably favoured for these systems, although simultaneous nitrogen-sulphur binding cannot be discounted.

2.3 STRUCTURAL ASPECTS OF THE PREPARED COMPOUNDS

2.3.1 Cuprous thioamide compounds

X-ray crystallographic studies of cuprous compounds of thioamide ligands and their thiolate analogues are not common. Nonetheless those compounds which have been studied show a number of different types of binding modes which provide useful models for the potential structures of the new compounds.

For thioamide ligands, a trigonal planar stereochemistry is commonly observed. Monomeric structures in which three thione sulphurs bind to copper in this arrangement have been found for $[Cu(mpyH)_3](NO_3)$(28) and $[Cu(etuH)_3]_2SO_4$(29), whereas in Cu[(N,N,-dimethylimidazolidine -2-thione)$_2$Cl](30) a chloro group substitutes one of the sulphurs. For the dimeric species $[Cu_2(6\text{-mercaptopurinium})_2Cl_4]$(31) an essentially trigonal copper is bound by two chlorines and a thione sulphur with a

long fourth bond (2.73Å) between copper and sulphur of adjacent molecules.

A tetrahedral coordination geometry is also seen for this ligand type. For instance in $[Cu(etuH)_4](NO_3)$(32) four thione sulphurs bind to copper in a regular tetrahedral arrangement. Similarly this stereochemistry is found in the cluster $[Cu_4(etuH)_9](NO_3)_4$(33) where again thione sulphur is the sole ligating atom. Here four sulphur atoms bridge two coppers, four are non-bridging and one central sulphur atom bridges all four copper atoms. In the dimer $[Cu_2(etuH)_4Cl_2]$ one thione sulphur bridges trigonal and tetrahedrally coordinated coppers. The latter has a ligand sphere of three sulphurs and one chlorine and the former two sulphur and one chlorine(32).

These examples, then, show exclusive binding of thione sulphur, the endocyclic nitrogen of the thioamide ligand playing little part in coordination. With polymeric species the sulphurs may bridge copper superceeding the bridging role of the halides. Table 2.6 summaries the cystallographic information for cuprous thiomide complexes.

Considering the structures of the new cuprous thioamide complexes prepared in this chapter, on the basis of infrared evidence, and crystallographic information to hand, coupled with knowledge of the compounds insolubility, the following structures are considered plausible for the various complex types:

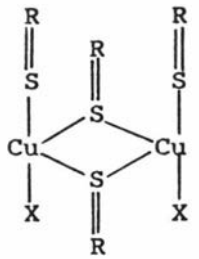
Table 2.6 The geometry of various cuprous thioamide complexes

Compound	Character	Stereochemistry	Coordinating atoms/Cu	Bridging atoms	Ref
$[Cu(mpyH)_3]NO_3$	monomeric	trigonal planar	three thione sulphurs	-	28
$[Cu(etuH)_3]SO_4$	monomeric	trigonal planar	three thione sulphurs	-	29
[Cu(N,N'-dimethylimidazolidine-2-thione)$_2$Cl$_2$]	monomeric	trigonal planar	two thione sulphurs one chlorine	-	30
[Cu$_2$(6-mercaptopurinium)$_2$Cl$_4$]	dimeric	trigonal plannar	one thione sulphur two chlorines	sulphur	31
$[Cu(etuH)_4]NO_3$	monomeric	tetrahedral	four thione sulphurs	-	32
$[Cu_4(etuH)_9(NO_3)_4$	tetrameric	tetrahedral	four thione sulphurs	sulphur	33
$[Cu_2(etuH)_4(Cl)_2]$	dimeric	1.tetrahedral	three thione sulphurs, one chlorine	sulphur	32
		2.trigonal plannar	two thione sulphurs, one chlorine	sulphur	32

compounds of the type

$[Cu(LH)_2X]$

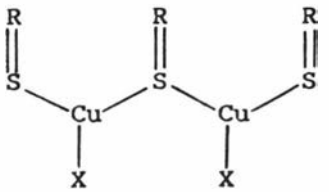
X = Cl or Br



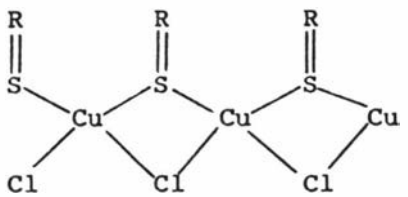
Compounds of the type

[Cu(LH)X]

X = Cl or Br



or



2.3.2 Cuprous thiolate compounds

To date there has been only one structural analysis of a cuprous thiolate compound derived from a thioamide ligand, occuring in the mixed valence cluster $[Cu^{II}_2Cu^{I}_{10}(mmim)_{12}(CH_3CN)_4]^{2+}$(34). Two geometries are observed here - a linear arrangement where copper is bound by two nitrogens, and two forms of tetrahedral geometry where copper is either bound to an S_4 donor set or one involving SN_3. In all cases the ligands bridge different copper atoms. Crystals of [Cu(6etmbt)] have been grown and are awaiting diffraction studies. If successful the compound would provide a basis for interpretation of many of the [CuL] compounds prepared here. In the meantime it is necessary to consider structures with central metal atoms other than copper to obtain a full picture of the potential modes of coordination for deprotonated thioamide ligands.

The mbtH system has been well characterised in this respect and Figure 2.3 illustrates a number of ways in which the thiolate form of mbtH may coordinate.

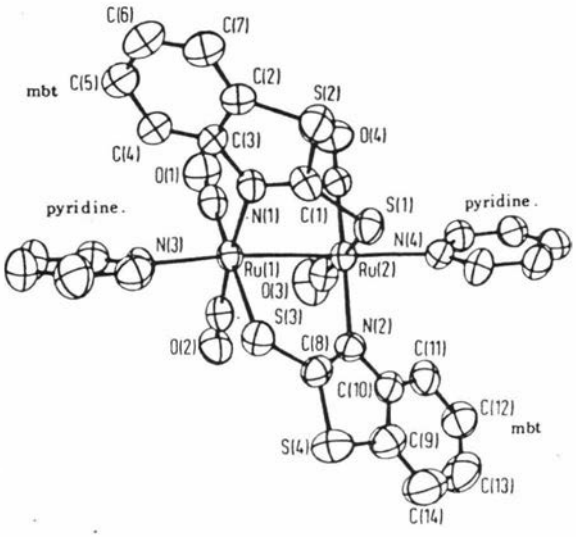
2.4 TRENDS IN THE FORMATION OF COMPLEXES

In conjunction with one of the fundamental aims of this study of thiols, an attempt is made here to elucidate trends and patterns for the synthesis of cuprous complexes from cyclic thioamide ligands and their thiolato-form analogues and to rationalise any particular requirements for their formation. The compounds prepared in this chapter have largely involved the thioamide entity contained in an unsaturated (benzo)thiazoline or (benz)imidazoline skeleton. On the other hand most literature studies have been based on the saturated imidazolidine and thiazolidine structures. Thus a wide range of compound types are at hand for comparative purposes.

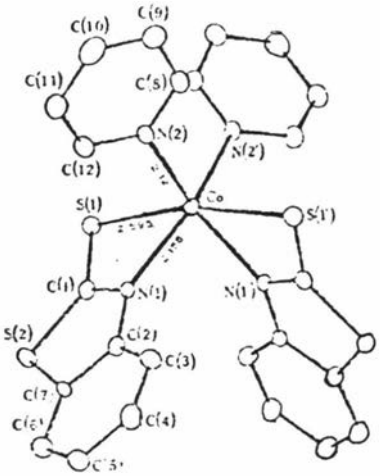
Table 2.7 lists the proposed compound stoichiometries for the reaction of neutral ligand with the specified copper salt in ethanol or methanol. On its inspection the following generalisations can be made:

(1) When a cupric halide salt is used the halide ion is incorporated into the complex structure and the ligand remains neutral, coordinating normally in a Cu-ligand ratio of 2:1.

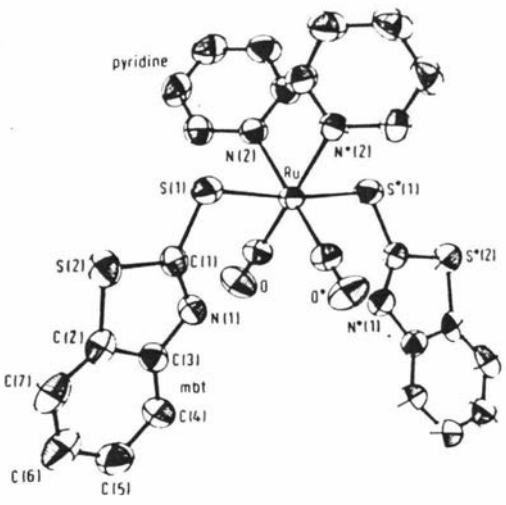
(2) The interaction of the unsaturated thioamides with salts containing more weakly coordinating ions such as ClO_4^- and NO_3^- results in the formation of [CuL] type compounds. Conversely with the saturated



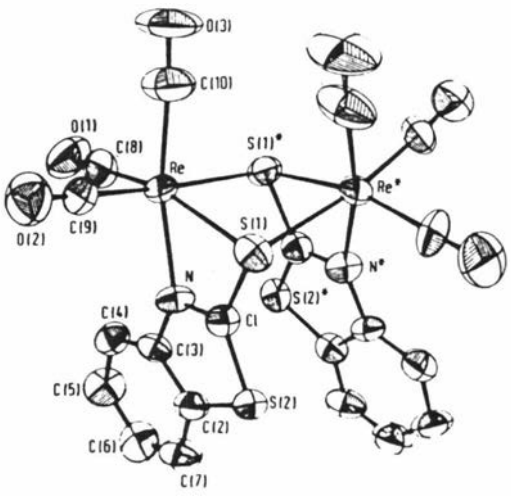
I



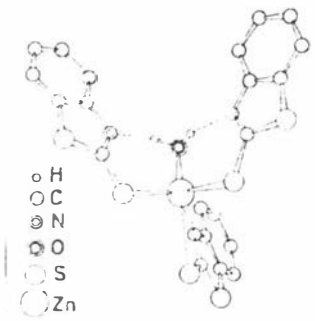
II



III



IV



V

I $[Ru_2(mbt)_2(py)_2(CO)_4]$(38

II $[Co(mbt)_2(py)_2]$(39)

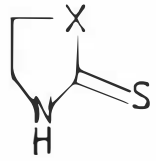
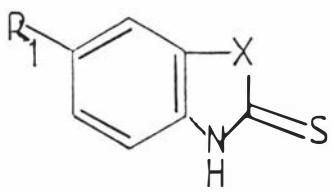
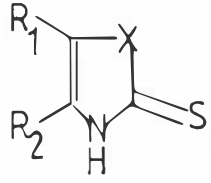
III $[Ru(mbt)_2(py)_2(CO)_2]$(37)

IV $[Re_2(mbt)_2(CO)_6]$(35)

V $[Zn(mbt)_3(OH)_2]^-$(36)

Figure 2.3 Some coordinating modes of the mbt ligand.

Table 2.7 Nature of the product formed from the interaction of a thioamide ligand and the respective cupric salt

General formula for ligand (LH)	X	R_1	R_2	Product from $CuCl_2.2H_2O$	$CuBr_2$	$Cu(No_3)_2.2H_2O$ $Cu(ClO_4)_2.6H_2O$	Ref.
	CH_2			$Cu(LH)_2Cl$	$Cu(LH)_2Br$	$Cu(LH)_3NO_3$	6
	O			$Cu(LH)_2Cl$	$Cu(LH)_2Br$	$Cu(LH)_3NO_3$	6
	NH			Cu(LH)Cl	Cu(LH)Br	$Cu(LH)_2NO_3$	7,6
	NCH_3			$Cu(LH)_2Cl$	$Cu(LH)_2Br$	$Cu(LH)_3NO_3$	7,6
	NCH_2CH_3			$Cu(LH)_2Cl$	$Cu(LH)_2Br$	$Cu(LH)_3NO_3$	7,6
	S			$Cu(LH)_3Cl$ $Cu(LH)_2Cl$	$Cu(LH)_3Br$ $Cu(LH)_2Br$	$Cu(LH)_3NO_3$	5,6
	S	H		$Cu(LH)_2Cl$	$Cu(LH)_2Br$	CuL	c
	S	OCH_2CH_3		$Cu(LH)_2Cl$	$Cu(LH)_2Br$	CuL	c
	NH	H		Cu(LH)Cl	Cu(LH)Br	-	c
	O	H		b	$Cu(LH)_2Br$	CuL	8,9
	S	C_6H_5	H	Cu(LH)Cl	Cu(LH)Br	CuL	c
	N	C_6H_5	C_6H_5	b	b	CuL	c
	S	N	SH	CuL	"CuL"	CuL	c
	NCH_3	H	H	Cu(LH) Cl	Cu(LH)Br	"CuL"	c

Notes: a. water of crystallisation excluded for clarity b. Cu(II) compound formed

c. this work

ligands the neutral thioamide form is mantained normally in a ligand to copper ratio of 3:1.

Considering trend (1), the binding of halide ion can be rationalised on the basis of the Pearson(40) concept of hard and soft acids and bases. Copper(I) is regarded as "soft" in such a classification and binds preferentially to "soft" ligands in which category chloride and bromide fall. Similarly the adoption of the formulation $[Cu(LH)_2Cl]$ instead of the possible [CuL] allows, as has been shown crystallographically and from infrared evidence, also coordination of the "soft" thione group.

With respect to trend (2) there is crystallographic evidence to suggest that copper in the saturated compounds can attain a stable trigonal planar environment involving three thione sulphur atoms. That such a form is not adopted for the less saturated ligands may be due to factors such as solubility, increased nucleophilocity of coordinating atoms and resonance stability.

It will be noticed from Table 2.7 that there are occasional exceptions to the listed trends particularly in the case of the ligand system 2-mercaptobenzimidazole. Devillanova et al(5) postulate that the different behaviour of such ligands may be due to different packing determined by the hydrogen bonding availability among H, N, the thioketonic sulphur, the group X and the halogen. Another possibility is raised by Evans and Wilkinson(21) who suggest that in some cases reduction of copper may well occur after coordination of the ligand to the metal, so that the stoichometry adopted by the complex reflects more the reaction of a Cu(II) species. Certainly in the case of the

$CuCl_2$-mbimH reaction cupric species can be detected prior to obtention of the cuprous complex (see Chapter 5).

Summary

1. Interaction of the ligands (LH) mbtH, etmbtH, mmimH, mbimH, mpyH, Ph_2PS_2H and phmtzH with cupric chloride or bromide salts in ethanol produced compounds of the form $[Cu(LH)_xX]$ (x=1 or 2).

Use of cupric nitrate or perchlorate resulted in the formation of complexes of the type [CuL] for the ligands mbtH, etmbtH, phmtzH, mpyH, dimtdzH, dipmimH and bimetH in ethanol.

2. Failure to remove the disulphide co-product in the above reactions has led to the postulation of erroneous formulations in the literature. New stoichiometries have been presented where the disulphide contaminant has been effectively removed.

3. Infrared spectral analysis of compounds containing the thioamide entity suggests that for such ligands binding through thione sulphur only is prevalent.

2.5 EXPERIMENTAL

2.5.1 Instrumentation: This was as described in 1.7.1.

2.5.2 Preparation of the complexes:

Compounds of the type $[Cu(LH)_2X]$

(LH = mbtH, X = Cl,Br; LH = mmimH and etmbtH, X = Cl).

These compounds were prepared by adding CuX_2 (5 mmol) in ethanol (X = Cl, 50 cm^3; X = Br, 100 cm^3) dropwise to the appropriate ligand (15 mmol) in ethanol, (mbtH, 100 cm^3; etmbtH, 350 cm^3; mmimH, 150 cm^3). The products were collected and washed thoroughly with ethanol then chloroform. $[Cu(etmbtH)_2Br]$ was simlarly prepared except the ligand to copper ratio was adjusted to 6:1. Yields were typically about 70%.

Compounds of the type $[Cu(LH)X].xH_2O$

(LH = mpyH, phmtzH, mbimH; X = Cl,Br).

CuX_2 (2.5 mmol) in ethanol (X = Cl, 50 cm^3; X = Br, 80 cm^3) was added dropwise to the ligand (5 mmol) in ethanol (mpyH, 50 cm^3; mbimH, 100 cm^3; phmtzH, 250 cm^3). The compounds were recovered on quantitative addition and washed thoroughly with ethanol and chloroform. $Cu(mbimH)Cl.\frac{1}{2}H_2O$ decolourised on drying in vacuo.

(LH = Ph_2PS_2H, X = Cl,Br).

CuX_2 (5 mmol) in ethanol (X = Cl, 50 cm^3; X = Br, 100 cm^3) was added dropwise to a solution of ligand (12.25 mmol) in acetone/ethanol (100 cm^3 acetone and 150 cm^3 ethanol). The resulting precipitates were washed thoroughly with ethanol, acetone and chloroform.

(LH = mmimH, X = Br)

mmimH (14.6 mmol) in ethanol (100 cm^3) was added dropwise to $CuBr_2$ (10 mmol) in ethanol (100 cm^3). The resulting yellow product was washed with ethanol and chloroform. Yields for the compounds $[Cu(LH)X].xH_2O$ were in the range 40-70%.

[Cu(mpy)]

$Cu(NO_3)_2.3H_2O$ (0.725 g, 3 mmol) in ethanol (100 cm^3) was added dropwise to mpyH (0.67 g, 6 mmol) in ethanol/DMSO (200 cm^3/30 cm^3) upon which the orange product precipitated and was collected and washed with ethanol and DMSO. Yield 0.2 g (50%).

[Cu(etmbt)]

$Cu(NO_3)_3.3H_2O$ (0.725 g, 3 mmol) in ethanol (100 cm^3) was added dropwise to etmbtH (1.27 g, 6 mmol) in ethanol/DMSO (200 cm^3/30 cm^3), after which the solution was stirred for 1 hour. The resulting solid was collected washed with DMSO and ethanol and dissolved in CH_2Cl_2. On slow evaporation of this solution over a period of days, orange crystals of product were deposited which were carefully isolated from a disulphide co-precipitant.

[Cu(mbt)]

mbtH (1.6 g, 10 mmol) in ethanol (120 cm^3) was added dropwise to $CuSO_4.5H_2O$ (1.2 g, 4.5 mmol) in water (40 cm^3). A transient green precipitate appearing initially changed to a more orange colour as the stoichiometric amount of ligand was added. The precipitate was collected and washed with water, ethanol and chloroform. Yield 0.223 g (20%).

[Cu(phmtz)]

$[Cu(CH_3CN)_4](ClO_4)$ (1.0 g, 3 mmol) in acetonitrile was added dropwise to ligand (0.6 g, 3 mmol) in ethanol (150 cm^3). The white precipitate was collected and washed with acetonitrile and ethanol. Yield 0.58 g (78%).

[Cu(dipmim)]

$Cu(ClO_4)_2.6H_2O$ (0.37 g, 1 mmol) in ethanol (50 cm^3) was added to a solution containing dipmimH (0.50 g, 2 mmol) in ethanol (50 cm^3). The resulting yellow precipitate was recovered and washed with ethanol. Yield 0.28 g (80%).

[Cu(bimet)]

$Cu(CH_3COO)_2.3H_2O$ (0.40 g, 2 mmol) in methanol (40 cm^3) was added dropwise to a solution of bimetH (0.356 g, 2 mmol) in MeOH (50 cm^3). The resulting product was washed with ethanol.

[Cu(dimtdz)]

$CuBr_2$(0.50 g, 2.2 mmol) in ethanol (100 cm^3) was added dropwise to ligand (1.0 g, 6.6 mmol) in ethanol (100 cm^3). The yellow precipitate appearing was washed thoroughly with ethanol and chloroform. Yield 0.42 g (84%).

$[Cu(mbtH)_2I]$, $[Cu(etmbtH)_2I]$

$[Cu(LH)_2Cl]$ (1 mmol) was added to a solution of KI (5 mmol) in water (50 cm^3). The slurry was refluxed for 2-3 hours during which time the colour of the original complex perceptibly grew more intense. The compounds were collected and washed with water, ethanol and chloroform.

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CHAPTER 3

REACTIVITY STUDIES OF CUPROUS THIOAMIDE AND THIOLATE COMPLEXES IN ORGANIC BASES

Introduction

With a few exceptions the compounds prepared in Chapter 2 were exclusively insoluble in the traditional organic solvents. However El-Shazly et al.(1) have noted that "$[Cu(mbt)_2]$" (more correctly $[Cu(mbtH)_2Cl]$) is soluble in pyridine and picolines and postulated the formation of the adduct "$[Cu(mbt)_3py]$" for the product from pyridine. Similarly Kuchen(2) has observed that the tetrameric cuprous dialkyldithiophosphinato complexes have some solubility in pyridine and that new compounds corresponding to the formulation "$[R_2P(S)S.Cu(OH).-(py)_4]$" can be produced. Initially our interest was drawn to the compound "$[Cu(mbt)_3py]$" as its suspected S_3N coordination, deep blue colour and crystalline properties augured well for a valuable cupric thiolate crystallographic study. However our subsequent re-examination of the reaction revealed that the compound represented as $[Cu(mbt)_3py]$ had been seriously misformulated, and that a far more extensive series of reactions were occurring in which a product completely divorced from the original starting material had been produced - namely $[Cu(py)_4SO_4].2H_2O$. Intrigued by the unusual nature of the reaction a range of similar organic nitrogen bases were used as solvents for $[Cu(mbtH)_2Cl]$. A surprisingly diverse range of compounds, in which the thioamide ligand has been substituted by solvent molecules of 2-,3-, and 4-methylpyridine, 2- and 3-chloropyridine, and 1,2-diaminoethane to give both cupric and cuprous complexes with sulphato, chloro and even

2-mercaptobenzothiazolato counter ions, has been observed. Similarly surprising, has been the observation that such reations are not restricted to $[Cu(mbtH)_2Cl]$ alone, but may occur for a wide variety of copper(I) complexes involving a thiolate or thioamide ligand.

This chapter, then, is concerned with the reactvity of cuprous thiolate and thioamide compounds in pyridine and its picoline analogues, and the characterisation of the resulting products.

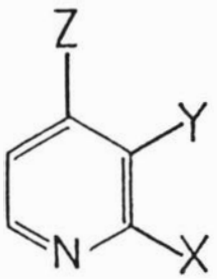
3.1 RESULTS AND DISCUSSION

3.1.1 Reactions in neat pyridine

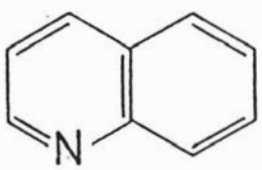
On dissolution of $[Cu(mbtH)_2Cl]$ in pyridine a transient yellow product, attributed by its fluorescent properties to $[Cu(py)_3Cl]$(3) quickly disappeared to give a yellow-green solution. Within 12-36 hours vivid blue needles were produced. From a simlar experiment El-Shazly et al.(1) isolated the product assigned as "$[Cu(mbt)_3py]$". Suspicions were raised as to the plausibilty of this formulation from inconsistencies appearing in both the published and our own infrared spectra. This and subsequent reanalysis of the compound proved critical to its reassignment as $[Cu(py)_4SO_4].2H_2O$. Microanalysis parameters were found to differ significantly from those found by El-Shazly et al.(1) and were no longer tenable with a formulation of "$[Cu(mbt)_3py]$" (see Table 3.1).

The infrared spectrum of the compound over the range 1650 cm^{-1} to 400 cm^{-1} is shown in Figure 3.2a. The intense broad band appearing in the 1100 cm^{-1} region is difficult to rationalise on the basis of the

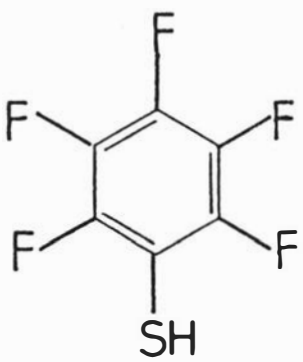
Figure 3.1 Structures and nomenclature for Chapter 3 ligand



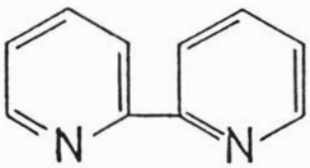
X	Y	Z	Name
H	H	H	pyridine (py)
Cl	H	H	2-chloropyridine (2-Clpy)
H	H	H	3-methylpyridine (3-Mepy)
H	CH_2CH_3	H	3-ethylpyridine (3-Etpy)
H	Cl	H	3-chloropyridine (3-Clpy)
H	H	Cl_3	4-methylpyridine (4-Mepy)



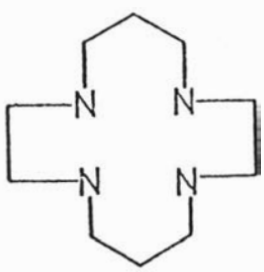
quinoline



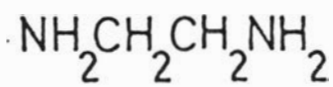
pentafluorothiophenol (pftpH)



2,2'-bipyridyl (bipyridyl)



1,4,8,11-tetraazocyclotetradecane (cyclam)



1,2-diaminoethane (en)

The remaining ligands can be found in Figure 2.2

Table 3.1 Analytical Figures for the Compounds Produced from Reactivity Studies

Compound	%C	%H	%N	Other	Ref[c]
$[Cu(3\text{-Mepy})_3Cl]$	57.1 (57.1)	5.6 (5.6)	11.3 (11.1)	8.6[a] (9.4)	3
$[Cu(3\text{-Clpy})_2Cl_2]$	33.7 (33.2)	2.4 (2.2)	7.5 (7.5)		
$[Cu(2\text{-Clpy})_2Cl_2]$	34.0 (33.2)	2.2 (2.2)	7.8 (7.5)		6
$[Cu(4\text{-Mepy})_4Cl_2].H_2O$	54.0 (54.9)	6.3 (5.8)	10.7 (10.7)	12.6[a] (12.6)	
$[Cu(4\text{-Mepy})_2Cl_2]$	45.5 (44.9)	4.4 (4.4)	8.6 (8.7)		6
$[Cu(py)_4SO_4].2H_2O$	46.7 (46.9)	4.5 (4.7)	10.7 (10.9)		7
$[Cu(py)_3SO_4].21/2H_2O$	40.5 (40.8)	3.5 (4.6)	9.5 (9.5)		7
$[Cu(3\text{-Etpy})_2SO_4].2H_2O$	40.8 (41.0)	5.4 (5.4)	7.0 (6.8)		
$[Cu(quinoline)_2SO_4]$	51.9 52.0[b] (51.7)	3.9 3.7[b] (3.4)	6.8 6.8[b] (6.7)		7
$[Cu(quinoline)_2SO_4].31/2H_2O$	44.5 (44.95)	3.9 (4.4)	5.8 (5.8)		7
$[Cu(3\text{-Mepy})_2SO_4].2H_2O$	38.1 (37.7)	4.9 (4.75)	7.4 (7.3)		
$[Cu(en)_2(mbt)_2].H_2O$	40.9 (40.5)	4.6 (4.9)	15.7 (15.7)		
$[Co(3\text{-Mepy})_2(mbt)_2]$	53.8 (54.1)	3.9 (3.8)	9.7 (9.7)		

Notes: a. %Cl, b. compound prepared from $CuSO_4.5H_2O$+ quinoline,

c. reference to a previous preparation.

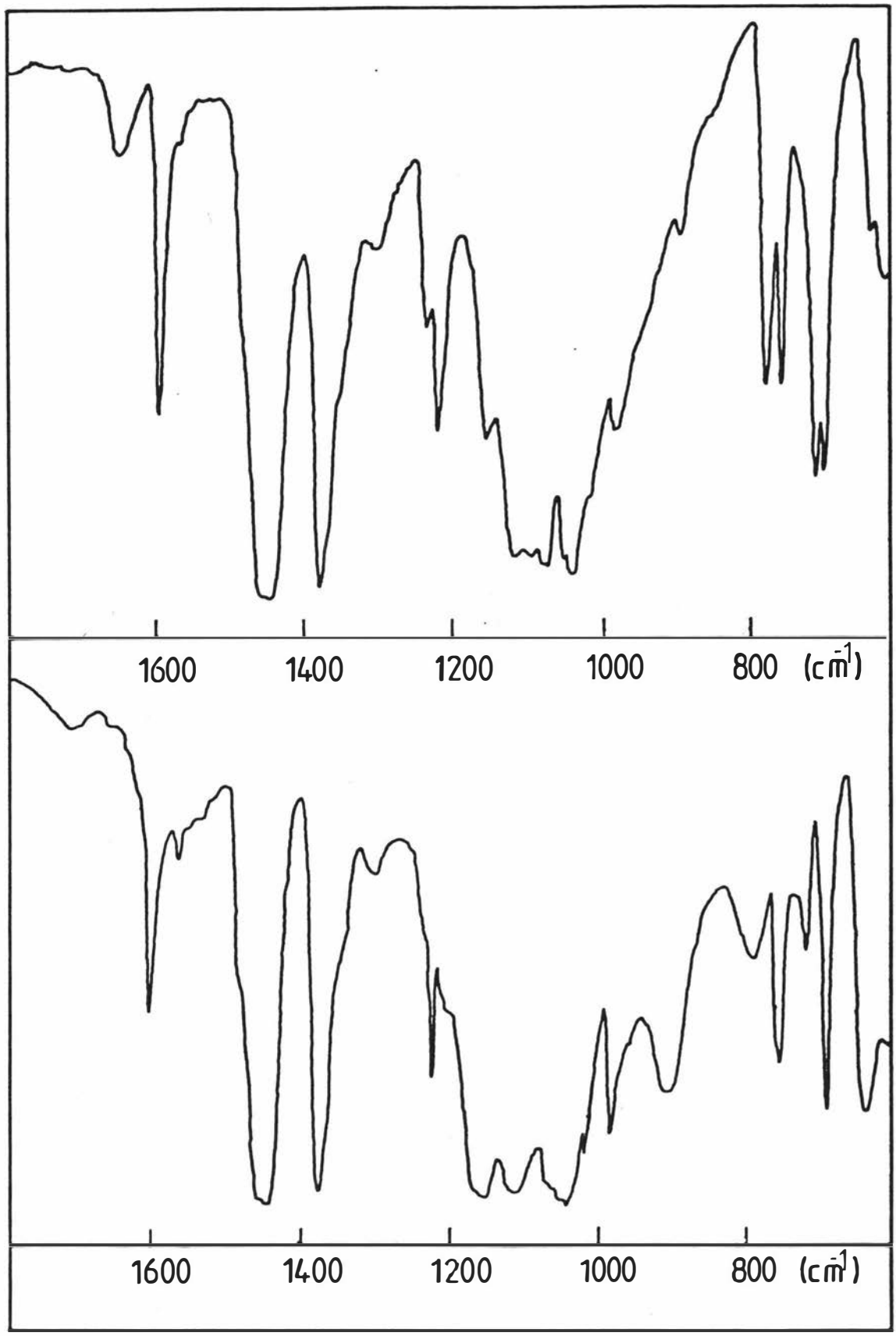
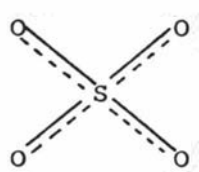


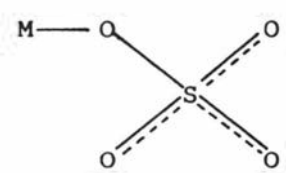
Figure 3.2 Infrared spectra of (a) $[Cu(py)_4SO_4].2H_2O$ and (b) $[Cu(py)_3SO_4].2\frac{1}{2}H_2O$ in nujol.

proposed ligands for "$[Cu(mbt)_3py]$". Furthermore, on exposure to moist air, within one day the dark blue crystals became light blue in colour and amorphous. The infrared spectrum of this new complex showed a distinct splitting of the broad band at 1100 cm^{-1}, as is shown in Figure 3.2b. Intense broad bands in the region 1400-1100 cm^{-1} are characteristic of inorganic anions such as nitrate, sulphate and perchlorate. This splitting behaviour and the position of the bands is typical of sulphate coordination and lends credence to the reformulation of "$[Cu(mbt)_3py]$" as $[Cu(py)_4SO_4].2H_2O$ and the corresponding pale blue compound as $[Cu(py)_3SO_4].2\frac{1}{2}H_2O$. Elimination of one pyridine molecule from $[Cu(py)_4SO_4].2H_2O$ to form $[Cu(py)_3SO_4].2\frac{1}{2}H_2O$ was further confirmed by elemental analysis data (Table 3.1) and weight loss studies.

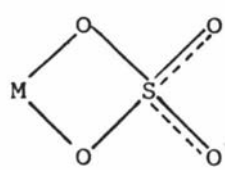
The differences in infrared spectra of compounds containing sulphate are well established and have been discussed by Nakamoto(4) and Chia et al.(5) The sulphate radicle may be present as a free ion or as a coordinated group. The types of linkage, and the symmetry assignment associated with each mode are displayed below.



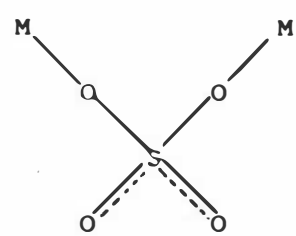
Free ion : T_d



Unidentate : C_{3v}



Bidentate : C_{2v}



Bridging : C_{2v}

Free sulphate ion belongs to the high symmetry point group T_d, but of the four fundamentals predicted by Group theory, only the vibrations ν_3 and ν_4 occuring at ca 1100 and 610 cm^{-1} respectively are infrared active. On coordination of the sulphate, symmetry is lowered and splitting of the degenerate modes occurs, with new bands also appearing in the spectrum corresponding to Raman active bands in the free ion. The change in selection rules and the removal of degeneracy are shown in Table 3.2.

Table 3.2 Infrared and Raman active bands for various symmetries of SO_4^{2-} radicle

point group	ν_1 symmetric stretch	ν_2 symmetric bend	ν_3 asymmetric stretch	ν_4 asymmetric bend
T_d	$A_1(R)$	$E(R)$	$T_2(I,R)$	$T_2(I,R)$
C_{3v}	$A_1(I,R)$	$E(I,R)$	$A_1(I,R)+E(I,R)$	$A_1(I,R)+E(I,R)$
C_{2v}	$A_1(I,R)$	$A_1(I,R)+A_2(R)$	$A_1(I,R)+B_1(I,R)+B_2(I,R)$	$A_1(I,R)+B_1(I,R)+B_2(I,R)$

I = Infrared active R = Raman active

Considering Figure 3.2, although some fine structure due to pyridine ligand vibrations complicate the spectrum, the single band (ν_3) occurring over the region 980-1120 cm^{-1} is consistent with ionic sulphate for $[Cu(py)_4SO_4].2H_2O$. Splitting of this mode to give two bands at 1050 cm^{-1} and 1160 cm^{-1}, and the infrared activation of ν_1, at 905 cm^{-1} is indicative of unidentate sulphate coordination in $[Cu(py)_3SO_4].2\frac{1}{2}H_2O$.

Further confirmation that sulphate is indeed the new counter-ion in the product was provided by the independent preparation of $[Cu(py)_4SO_4].2H_2O$ by addition of pyridine to an aqueous solution of $CuSO_4.5H_2O$. The product has identical spectral properties to the compound produced on reaction of $[Cu(mbtH)_2Cl]$ with pyridine.

The production of $[Cu(py)_4SO_4].2H_2O$ from reaction in pyridine is not restricted to $[Cu(mbtH)_2Cl]$ alone. The compound has been similarly prepared and identified from $[Cu(etmbtH)_2Cl]$, [Cu(phmtzH)Cl], [Cu(etuH)Cl], $[Cu(mbimH)Cl].\frac{1}{2}H_2O$ and $[Cu(Ph_2PS_2H)Cl]$. With [Cu(mbt)] and [Cu(pftp)], where the compounds are less soluble, the complex is produced more slowly. These compounds represent a cosmopolitan selection of cuprous thiolate and thioamide complexes, and provide support for the contention that the reaction is one of a general nature for such compounds.

The source of sulphur in the production of sulphate ion clearly must originate from the thiol or thiolate ligand. It is apparent that as well as $[Cu(py)_4SO_4].2H_2O$, new organic compounds with a deficiency in sulphur must also be produced. The key to their identification was provided in an experiment where $[Cu(etmbtH)_2Cl]$ was dissolved in pyridine. The sulphate complex (40% yield) was produced within 24 hours, but continued to appear slowly over some weeks. Slow evaporation of the mother liquor over a period of months allowed the crystallisation of needles of an organic product. The mass (see Appendix) and infrared spectra indicated that the compound was di-6-ethoxybenzothiazol-2-yl sulphide. It is thus possible to draw a reaction stoichiometry for compounds of the type $[Cu(RSH)_2Cl]$:

$$[Cu(RSH)_2Cl] + 4 \text{ pyridine} + 4\text{"O"} \Rightarrow [Cu(py)_4SO_4] + R\text{-}S\text{-}R + 2HCl$$

Table 3.3 Sulphate complexes and principal infrared bands

Compound	ν(OH)	Sulphate		ν(CuN)	Proposed coordination of sulphate ion
		ν_1	ν_3		
$[Cu(py)_4SO_4].2H_2O$	3380(br)	980	1080(br)	245	Ionic
$[Cu(py)_3SO_4].21/2H_2O$	3200(br)	910	1160 1040	275	Unidentate
$[Cu(3\text{-}Etpy)_2SO_4]$	3180(br)	937	1157 1096 1050	-	Bridging or Chelating
$[Cu(quinoline)_2SO_4]$	3400	930	1200 1130 1020	275	Bridging or Chelating
$[Cu(3\text{-}Mepy)_2SO_4]$	3150(br)	955	1150 1110 1060	270	Bridging or Chelating

Note: br. broad

3.1.2 Reactions in neat quinoline and 3-ethylpyridine

Similar sulphato products may be isolated using quinoline, 3-ethylpyridine and 3-methylpyridine as the neat bases. When [Cu(mbimH)Cl].$\frac{1}{2}H_2O$ was added to 3-ethylpyridine blue-green crystals of a compound with microanalysis figures corresponding to [Cu(3-ethylpyridine)$_2SO_4$].$2H_2O$ were produced. Likewise [Cu(mbtH)$_2$Cl] dissolved in quinoline produced blue crystals analysing as [Cu(quinoline)$_2SO_4$]. This was identical to the product obtained by dissolving crushed $CuSO_4.5H_2O$ in neat quinoline. Three fold splitting of the ν_3 sulphate vibration in the infrared of these compounds indicates that the sulphate is bridging or chelating (see Table 3.3).

Interestingly, on immediate contact of [Cu(mbtH)$_2$Cl] with quinoline a brown product is produced with an infrared spectrum consistent with [Cu(mbt)] - so in actual fact the reactant may be [Cu(mbt)] in this case rather than [Cu(mbtH)$_2$Cl]. [Cu(mbt)] also reacts with 3-methylpyridine giving the chelating/bridging sulphato complex [Cu(3-Mepy)$_2SO_4$].$2H_2O$.

3.1.3 Reactions in neat 3-methylpyridine

On refluxing [Cu(mbtH)$_2$Cl] in neat 3-methylpyridine for fifteen minutes yellow green crystals were seen to appear on cooling. Elemental analyses indicated that a formulation of [Cu(3-Mepy)$_3$Cl] was likely for the compound (see Table 3.1). Fortunately the crystals proved suitable for X-ray diffraction studies and the structure was accordingly investigated by Dr K.G. Brown, DSIR, Wellington.

The crystal structure revealed that copper was tetrahedrally coordinated by the three 3-methylpyridine and single chlorine ligands. The stereochemistry of the compound is shown in Figure 3.3 and bond

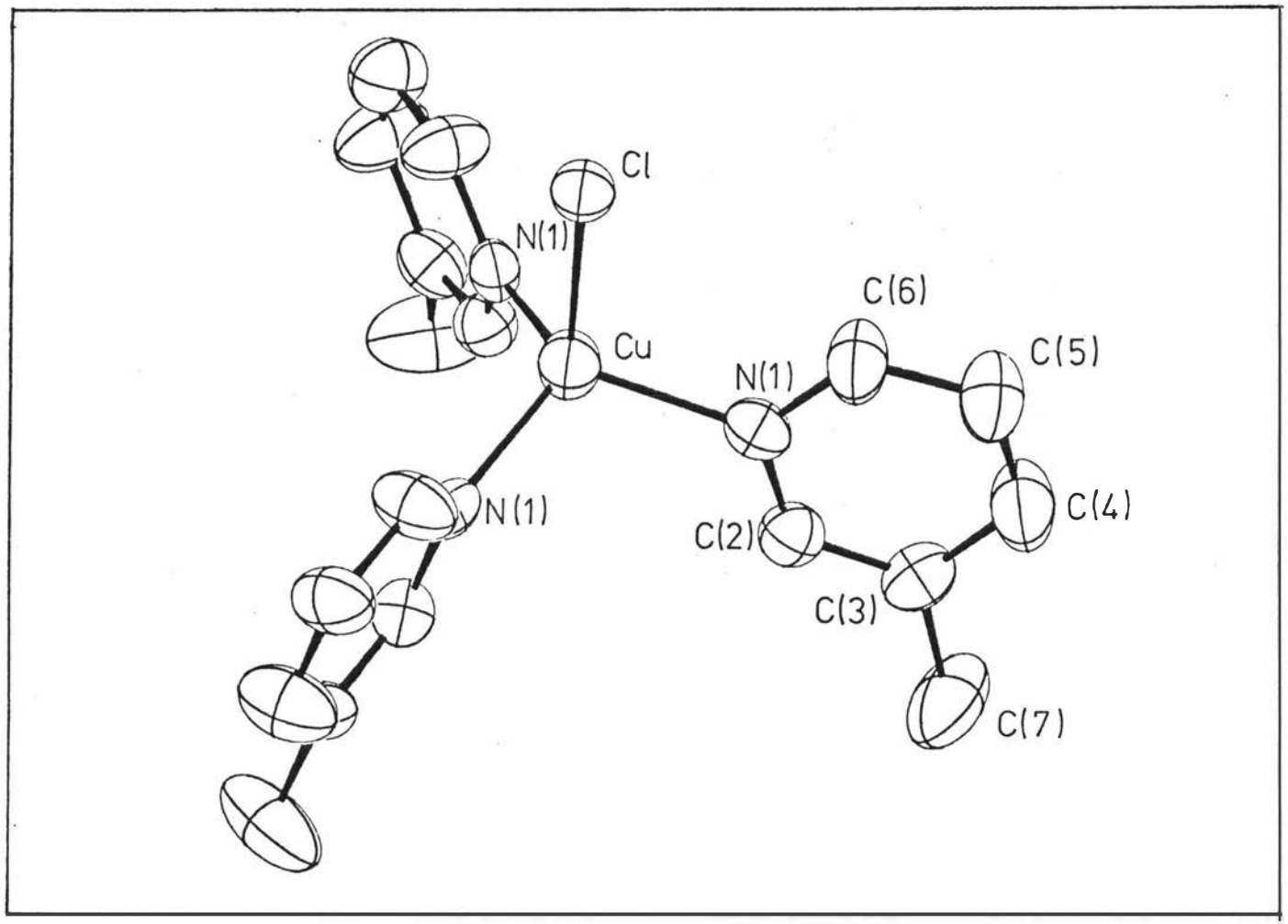


Figure 3.3 Structure of $[Cu(3\text{-Mepy})_3Cl]$

Table 3.4 Bond lengths (Å) and angles (°) for $[Cu(3\text{-Mepy})_3Cl]$ with estimated standard deviations in parentheses

(a) Bond lengths			
Cu -Cl	2.458(2)	C(3)-C(4)	1.389(13)
Cu -N(1)	2.021(5)	C(3)-C(7)	1.507(11)
N(1)-C(2)	1.338(8)	C(4)-C(5)	1.345(13)
N(1)-C(6)	1.329(9)	C(5)-C(6)	1.398(11)
C(2)-C(3)	1.366(10)		
(b) Bond angles			
Cl -Cu -N(1)	105.4(1)	C(2)-C(3)-C(4)	117.9(7)
N(1)-Cu -N(1)	113.2(3)	C(2)-C(3)-C(7)	120.7(7)
Cu -N(1)-C(2)	124.6(4)	C(4)-C(3)-C(7)	121.4(8)
Cu -N(1)-C(6)	120.0(4)	C(3)-C(4)-C(5)	118.8(7)
C(2)-N(1)-C(6)	115.4(6)	C(4)-C(5)-C(6)	119.2(7)
N(1)-C(2)-C(3)	125.2(6)	C(5)-C(6)-N(1)	123.6(6)

lengths and angles are given in Table 3.4. Interestingly, infinite linear Cu-Cl---Cu chains are formed from the particular stacking of the [Cu(3-Mepy)$_3$Cl] units. This phenomenon is shown in Figure 3.4. The coordination geometry of the CuN_3Cl unit is only slightly distorted from tetrahedral. The Cu-N bond distances are within the range normally found for cuprous complexes with pyridine and substituted pyridine ligands(8). The Cu-Cl distance at 2.458(2) Å, however, falls slightly outside the expected range of 2.24-2.40 Å for a terminal Cu(I)-Cl bond(9). A steric factor may contribute to the lengthening of this bond, as, in all, nine contacts of less than 3 Å are made between each chlorine and surrounding hydrogen atoms. Three contacts are made from the ortho hydrogens H(6) within the molecule, three others are of an inter-molecular nature from H(2) on an adjacent molecule and the final three are provided by the para hydrogens of ligands on an adjacent chain. A stereodiagram depicting chlorine-hydrogen contacts is shown in Figure 3.5.

Discussion

All compounds of the type [Cu(LH)Cl] and [Cu(LH)$_2$Cl] prepared in Chapter 2 produced [Cu(3-Mepy)$_3$Cl] on addition of cold 3-methyl-pyridine, suggesting that the reaction is quite general for cuprous compounds containing a neutral thiol or thioamide ligand. That the reaction is one of simple substitution was shown in an experiment in which the mother liquor of the reaction involving [Cu(mbimH)Cl]$\cdot \frac{1}{2}H_2O$ was evaporated to near dryness on a rotary evaporator. On standing a white crystalline compound appeared which was shown to be 2-mercaptobenzimidazole by mass and infrared spectroscopy. The reaction then can be represented simply as:

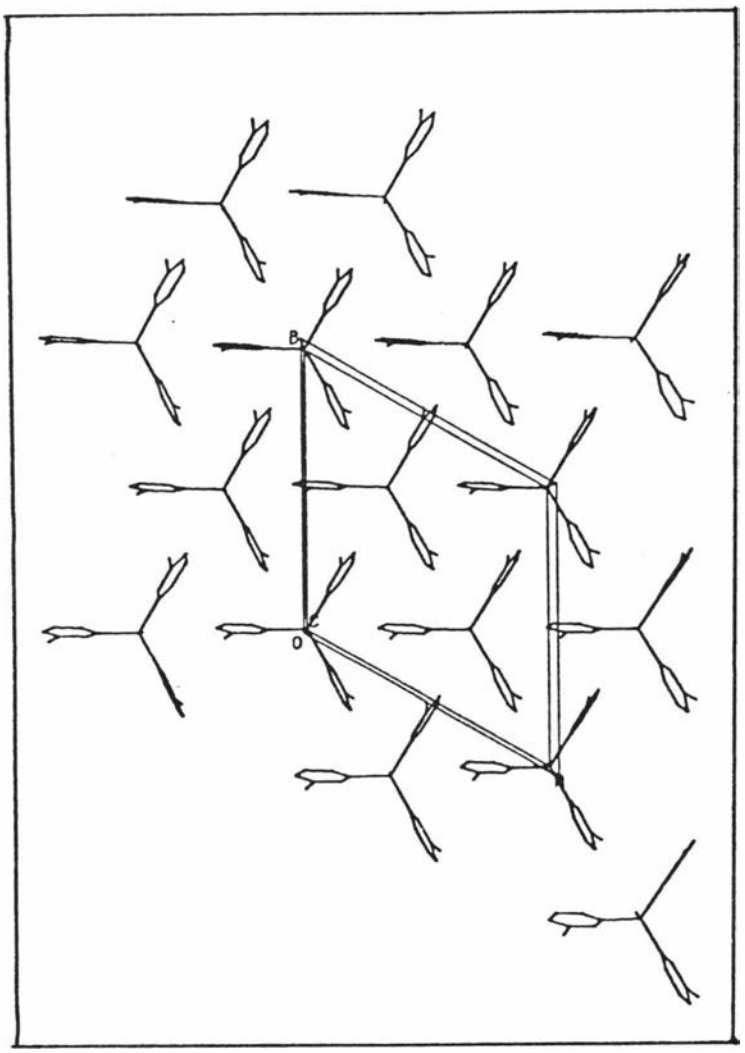


Figure 3.4 Diagram showing infinite linear Cu-Cl---Cu chains in $[Cu(3\text{-Mepy})_3Cl]$

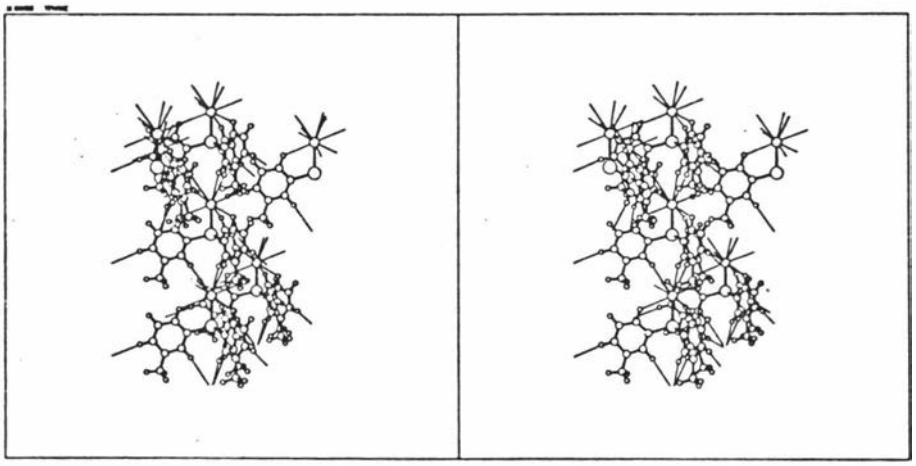


Figure 3.5 A stereoscopic view of $[Cu(3\text{-Mepy})_3Cl]$ chains showing Cl.....H distances less than 3Å

$[Cu(LH)_xCl] + 3(3\text{-Mepy}) \longrightarrow [Cu(3\text{-Mepy})_3Cl] + xLH$

(LH = mbtH, etmbtH, etuH, mmimH, phmtzH, mpyH, Ph_2PS_2H, mbimH)

$[Cu(3\text{-Mepy})_3Cl]$ is the first compound of the type $[CuL_3X]$ (where L = pyridine or a picoline and X = Cl or Br) to have been definitively characterised by X-ray crystallography and it is quite likely that analogous structures should exist for other members of the set. Prior to this study structural characterisation of such compounds had been limited to information obtainable from infrared spectral analysis(10). In fact interest had focussed chiefly on their fluorescent properties(3). Specifically $[Cu(3\text{-Mepy})_3Cl]$ displays an absorption at 360 nm assigned as a $3d^{10} \rightarrow 3d^9\pi^*$ metal to ligand charge transfer transition, the source of an intense yellow fluorescence(11). This property can be used to advantage for quick qualitative tests for chloride or bromide in a cuprous thioamide compound prior to elemental analysis. On addition of neat 3-methylpyridine to the appropriate $[Cu(LH)_xX]$ complex $[Cu(3\text{-Mepy})_3Cl]$ or $[Cu(3\text{-Mepy})_3Br]$ is immediately formed if halogen is present and facilely detected by their fluorescence in ultra-violet light (360 nm).

3.1.4 Reactions in neat 2-chloro- and 3-chloropyridine

On refluxing $[Cu(mbtH)_2Cl]$ in 2-chloro and 3-chloropyridine blue green microcrystalline compounds appeared on cooling. Microanalysis figures suggested the formulations $[Cu(2\text{-Clpy})_2Cl_2]$ and $[Cu(3\text{-Clpy})_2Cl_2]$ (see Table 3.1).

These were confirmed by infrared spectra which showed vibrations attributable to the pyridine ligands.

3.1.5 Reactions in neat 4-methylpyridine

A dark blue amorphous powder was produced on refluxing [Cu(mbtH)$_2$-Cl] in 4-methylpyridine, however, in moist air the compound rapidly changed to a pale blue colour. This latter complex was analysed and a fit consistent with the formulation [Cu(4-Mepy)$_2$Cl$_2$] was obtained (see Table 3.1). Using a method in which the compound [Cu(ethanethiol)Cl] was prepared *in situ* and allowed to react with excess 4-methylpyridine, plate-like crystals of the dark blue compound were grown. The infrared spectrum confirmed that organic ligands other than 4-methylpyridne were absent. A strong band at 3400 cm^{-1} due to ν(OH) suggested water of crystallisation is present. The electronic spectrum run as a nujol mull showed a single band at 624 nm and the powder esr spectrum displayed two g values with g_{11} = 2.228 and $g_{\perp}$ = 2.063. The compound was successfully analysed for C,H,N and Cl prior to turning light blue, however two possible basic formulations may be proposed based on figures received if the halogen analysis is interpreted liberally. They are [Cu(4-Mepy)$_4$-Cl$_2$].H$_2$O (I) and [Cu(4-Mepy)$_5$Cl$_2$].3H$_2$O (II). Figures found for the dark blue crystals were : C, 54.0; H, 6.3; N, 10.7; Cl, 12.6. Calculated for $C_{24}H_{30}N_4Cl_2CuO$ (I): C, 54.9; H, 5.8; N, 10.7; Cl, 12.6; and for $C_{30}H_{41}N_5Cl_2CuO$ (II): C, 55.1; H, 6.3; N, 10.7; Cl, 10.8. The compound's physical properties were unable to distinguish between the two possibilities. Furthermore Langfelderova *et al.*(12) reported the synthesis of [Cu(4-Mepy)$_5$Cl$_2$] from addition of CuCl$_2$.2H$_2$O to 4-methylpyridine in 1:9 ratio in aqueous solution. The proposed compound has similar electronic and esr spectral parameters to the dark blue crystals.

Because of this apparent anomaly, and also due to the fact that there have been no crystallographic studies of compounds of the type

[Cu(pyridine or picoline)$_x$Cl$_2$] where $x > 2$ it was decided to determine the structure by X-ray diffraction.

Structure of [Cu(4-Mepy)$_4$Cl$_2$].H$_2$O.

The crystal structrue determination was performed by Drs E.N. Baker and B.F. Anderson of Massey University, with myself assisting in refinement of the data. R is currently 21%. The structure has not been fully refined so far, because the Cu atoms are located on crystallographic 2-fold axes, and although the molecules are thus required to have 2-fold symmetry, they do in fact have pseudo-4-fold symmetry. This has so far prevented proper refinement of the positions of the atoms in the picoline rings, although it should not affect the Cu-N or Cu-Cl distances. The structure of the complex is shown in Figure 3.6. It is apparent that the copper is five coordinate. The geometry may best be regarded as distorted square pyramidal. Four 4-methylpyridine ligands occupy an approximate plane with the copper atom raised slightly above. A chlorine atom occurs in an axial position with a Cu-Cl bond distance of 2.49 Å. The remaining chlorine atom is non-bonding and is found at a distance of 4.19 Å from copper in the alternate axial position.

Only two other crystallographic examples of a tetrakis monodentate pyridine or picoline copper complex with two anionic groups have been determined - those of [Cu(py)$_4$](CF$_3$COO)$_2$(13) and [Cu(3-Mepy)$_4$(H$_2$O)$_2$]-(ClO$_4$)$_2$(14). Both structures were found to involve a tetragonally elongated octahedral arrangement of ligands, with the four pyridine or picoline ligands in a plane containing copper(II) at bond distances of 2.03-2.05 Å. The two axial trifluoroacetate oxygen atoms in

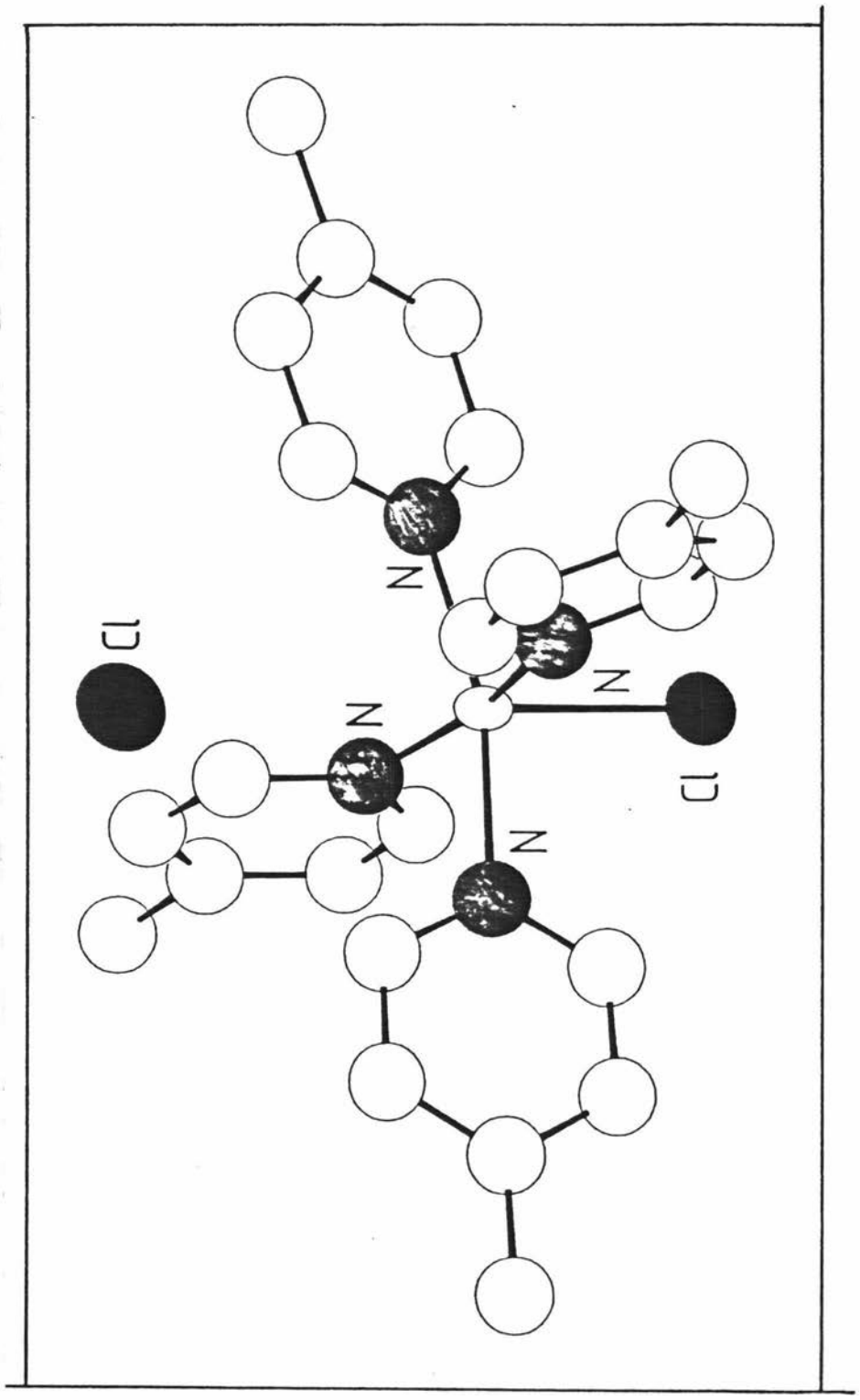


Figure 3.6 Structure of $[Cu(4\text{-Mepy})_4Cl_2].H_2O$.

$[Cu(py)_4](CF_3COO)_2$ were found 2.37 Å from copper(II), whereas the aquo Cu-O bond lengths in $[Cu(3\text{-}Mepy)_4(H_2O)_2](ClO_4)_2$ were 2.49 Å.

The paucity of data for tetrakis systems can most likely be attributed to the instabilty of these complexes. For a more objective comparison it is necessary to turn to a more stable system such as is found for the ligand bipyridyl which acts like a bidentate chelating pyridine. The structures of a series of compounds of the type $[Cu(bipyridyl)_2X]^+$ (where X = Cl, Br and I) have been determined for which $[Cu(bipyridyl)_2Cl]$ (15) proves in many respects analogous to $[Cu(4\text{-}Mepy)_4Cl]$ having a distorted five coordinate stereochemistry but more nearly related to trigonal bipyramidal than to square pyramidal. The structure is shown in Figure 3.7.

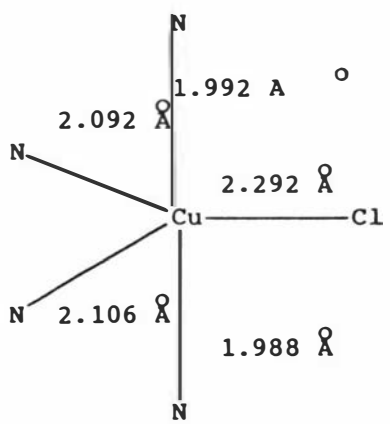


Figure 3.7 Ligand environment of $[Cu(bipyridyl)_2Cl]_2S_5O_6.6H_2O$.

Where Cl is replaced by Br and I(16) the structures are very similar with Cu-halogen bond lengths of 2.419 Å and 2.675 Å respectively.

3.1.6 Reactions in neat 1,2-diaminoethane

Yet another facet of reactivity is seen if an aliphatic base is used as a neat solvent. When $[Cu(mbtH)_2Cl]$ is refluxed in

1,2-diaminoethane blue needle-like crystals appear as the solution cools. The infrared of these indicate not only the presence of the base as ligands, but also 2-mercaptobenzothiazole in the thiolate form. Analytical figures are consistent with a formulation of $[Cu(en)_2(mbt)_2]$. H_2O. The esr spectrum of the compound in dimethylformamide (Figure 3.8) shows a line shape and parameters representative of an N_4(17) donor system suggesting that the thiolate ligands are axial and that their interaction with copper, if any at all, is weak. This is supported by the absence of bands attributable to charge transfer transitions in the visible spectrum; there being only a single absorbance at 620 nm in the reflectance spectrum ascribed to a d-d absorbance. As was mentioned in Chapter 1 a similar compound [Cu(cyclam)(pentafluorothiophenolate)$_2$] has been prepared and crystallographically characterised by Addison et al.(18). It was found that the pentafluorothiophenolate ligands, axially bound with bond lengths of 2.94 Å which were considered as weak, similarly had little effect on the characteristic spectral features of $[Cu(cyclam)]^{2+}$.

3.1.7 Reactions of other transition metal ions

The cobalt(II) and nickel(II) complexes analogous to $[Cu(mbtH)_2Cl]$-$[Co(mbt)_2]$ and $[Ni(mbt)_2]$ display reactions with pyridines and picolines of a more conventional nature, forming adducts with the base involved. For instance Dance and Isaac(19) interacted $[Co(mbt)_2]$ with pyridine and obtained the compound $[Co(mbt)_2(py)_2]$. Similarly the series of compounds $[Ni(mbt)_2L_2]$ (where L = 2-Mepy, 3-Mepy, 4-Mepy and n-butylamine) are produced when $[Ni(mbt)_2]$ was dissolved in an excess of base(1).

The cobalt reaction was extended to include the base 3-methyl-

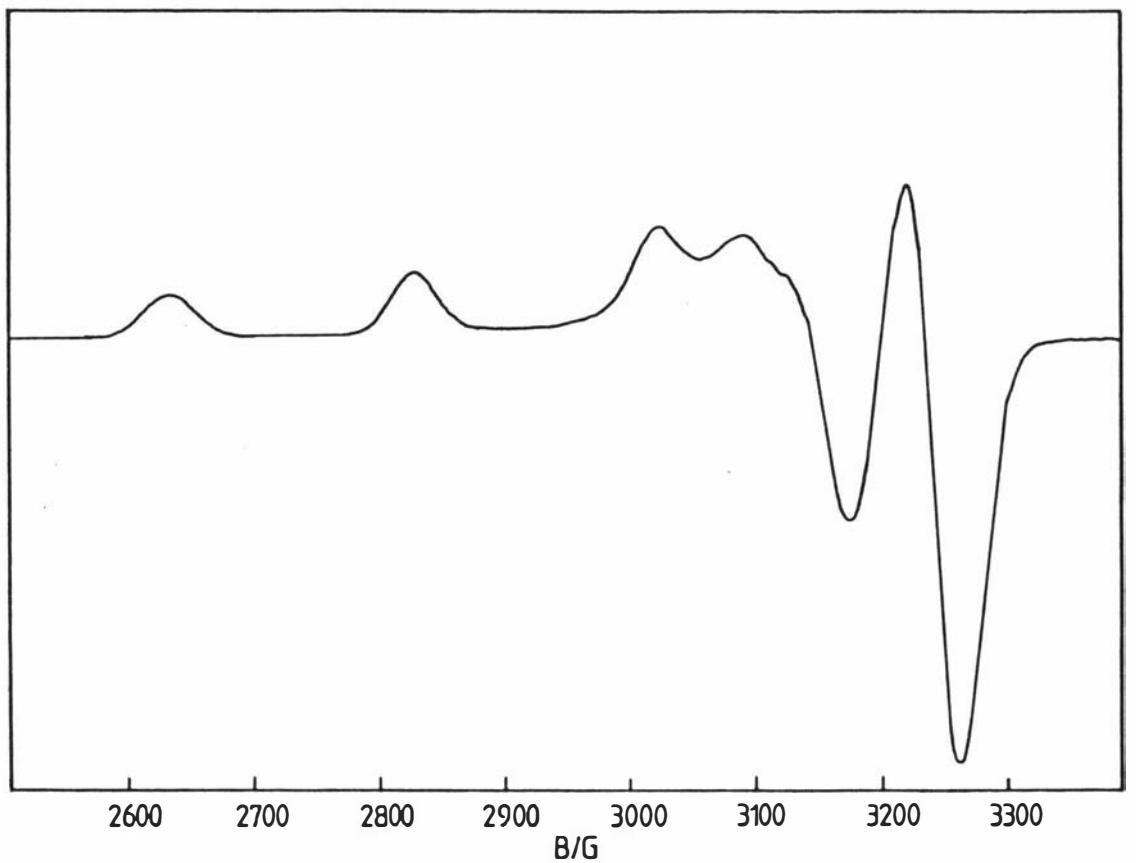


Figure 3.8 Esr spectrum of $[Cu(en)_2(mbt)_2].H_2O$ in N,N'-dimethylformamide.

pyridine, given the differences in behaviour between it and pyridine in the copper interaction. However refluxing $[Co(mbt)_2]$ in 3-methylpyridine produced brown crystals on cooling, for which the analytical figures obtained agreed again with the bis adduct formulation $[Co(mbt)_2(3\text{-Mepy})_2]$.

From these results it would appear that the reactions seen for the copper compounds are related more to the characteristics of the metal itself in such solvents rather than the nature of the ligand. The accessibility of a lower oxidation state to copper may be a factor in rationalising such differences.

Conclusion

Although there appears little relationship between the nature of the product and the particular base used as solvent, nonetheless it can be shown that a number of common threads exist in the synthesis of the compounds which greatly simplifies the apparently diverse reactivity.

Firstly where the compound is of the type $[Cu(LH)_xCl]$ (where LH is a thioamide ligand and x = 1 or 2), on dissolution in pyridine or a picoline the immediate production of the compound $[Cu(base)_3Cl]$ may be proposed. The final product obtained depends on the stability of this compound to oxidation; or if oxidised, on the reactive nature of the oxidised product. Thus for 3-methylpyridine as solvent, $[Cu(3\text{-Mepy})_3Cl]$ is isolated because of this compound's inherent stability to oxidation(3). When the base, however is 2-chloropyridine, 3-chloropyridine or 4-methylpyridine the initial complex is susceptible to oxidation and stable cupric products $[Cu(2\text{-Clpy})_2Cl_2]$, $[Cu(3\text{-Clpy})_2Cl_2]$

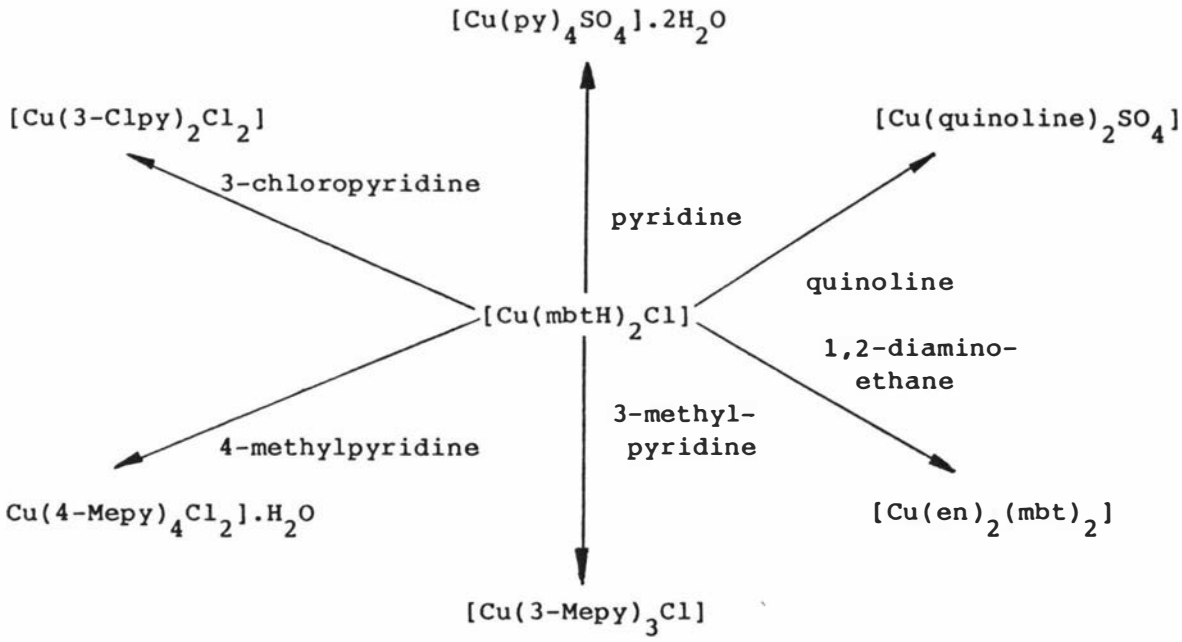
and $[Cu(4\text{-Mepy})_2Cl_2].H_2O$ are isolated which do not undergo further reaction. With solvents pyridine and 3-ethylpyridine the $[Cu(base)_3Cl]$ compound is presumably oxidised to a new reactive species capable of attacking the dislodged thiol ligand to produce sulphate anion. Details of the nature of this species will be presented in Chapter 4.

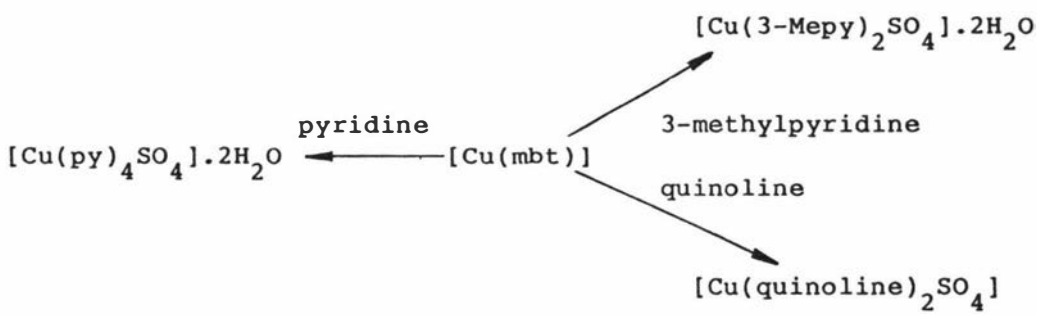
Quinoline proved an exception to this general pattern, however the difference may be rationalised on the basis that [Cu(mbt)] is the initial stable product on reaction rather than $[Cu(base)_3Cl]$. Similarly, 1,2-diaminoethane for which the $[Cu(base)_3Cl]$ compound is also not formed may react immediately to deprotonate the thioamide ligand and with oxidation produce $[Cu(en)_2(mbt)_2]$.

A further common feature is provided by the connection existing between the reactivity of cuprous thiolate compounds of the type [CuL]. When dissolved in pyridne, or produced <u>in situ</u> as in the reactions of quinoline, these react to produce $[Cu(py)_4SO_4].2H_2O$ or [Cu(quinoline) SO_4]. Again a common reactive species capable of attacking a thiol substrate may be postulated (see Chapter 4).

Summary

1. Cuprous thioamide and thiolate complexes undergo a variety of reactions in organic nitrogen bases involving solvent substitution and in some cases alteration of the original ligands. A reactivity scheme for $[Cu(mbtH)_2Cl]$ and [Cu(mbt)] is shown.





2. X-ray diffraction studies of $[Cu(3\text{-}Mepy)_3Cl]$ show that copper(I) is tetrahedrally coordinated. Preliminary studies of $[Cu(4\text{-}Mepy)_4Cl_2].H_2O$ indicate that a square pyramidal stoichiometry of ligands is adopted.

3. Cobalt and nickel complexes of 2-mercaptobenzothiazole do not react similarly to their copper counterpart. This difference may result from the ease of accessibility of a lower oxidation state to copper, and its ability to form reactive species in aprotic solvents.

3.2 EXPERIMENTAL

3.2.1 Instrumentation

This was as described in Chapter 1.7.1

3.2.2 Preparation of the complexes

$[Cu(py)_4SO_4].2H_2O$

(1) from complexes of the type $[Cu(LH)_xCl]$.

$[Cu(mbtH)_2Cl].\frac{1}{2}$(mbt-mbt) or $[Cu(mbtH)_2Cl]$ (0.70 g), $[Cu(etmbtH)_2Cl]$ (0.31 g), [Cu(phmtzH)Cl].½(RSSR) (0.4 g), [Cu(etuH)Cl] (0.20 g), $[Cu(mbimH)Cl].\frac{1}{2}H_2O$ (0.50 g) and $[Cu(Ph_2PS_2H)Cl]$ (0.41 g) were dissolved in 17,20,30,6,15 and 30 cm^3 of pyridine respectively and if necessary gently heated to dissolve the solid. A transient yellow fluorescent precipitate quickly dissappeared to yield green coloured solutions. Within a period of 12 hours to two days crystals of $[Cu(py)_4SO_4].2H_2O$ would appear which were collected and washed with pyridine. Yields were normally ≈40%.

(2) from complexes of the type [CuL]

[Cu(mbt)] (0.50 g) and [Cu(pftp)] (prepared according to the method of Peach(20)) (0.40 g) were dissolved in cold pyridine (40 cm^3 and 30 cm^3 respectively) giving green coloured solutions. Within five days crystals of $[Cu(py)_4SO_4).2H_2O$ had precipitated which were collected and washed with pyridine. Yield : [Cu(pftp)] - 30%, [Cu(mbt)] - 40%.

(3) from $CuSO_4.5H_2O$ and pyridine

To $CuSO_4.5H_2O$ (3.0 g) dissolved in water (8 cm^3) was added dropwise

pyridine (15 cm^3). $[Cu(py)_4SO_4].2H_2O$ commenced to precipitate after addition of 12 cm^3 pyridine, and was collected.

$[Cu(quinoline)_2SO_4]$

$[Cu(mbtH)_2Cl].\frac{1}{2}$(mbt-mbt) (0.70 g) was heated gently to dissolve in quinoline (20 cm^3). After five days, during which time the solution was filtered to remove dibenzothiazol-2-yl disulphide, a low yield of blue crystals of ($Cu(quinoline)_2SO_4$) was observed. These were collected and washed with ether and acetone. The compound readily forms a more amorphous hydrated form $[Cu(quinoline)_2SO_4].3\ H_2O$.
$[Cu(quinoline)_2SO_4]$ was similarly prepared by heating crushed $CuSO_4.5H_2O$ (3.0 g) to reflux temperature in quinoline (30 cm^3). The compound was collected and washed with quinoline.

$[Cu(3\text{-}Etpy)_2SO_4].2H_2O$

$[Cu(mbimH)Cl].\frac{1}{2}H_2O$(0.40 g) was dissolved in 3-ethylpyridine (4 cm^3) and the solution left to stand. Large blue green crystals of $[Cu(3\text{-}Etpy)_2SO_4].2H_2O$ appeared within four weeks. These were collected and washed with 3-ethylpyridine.

$[Cu(3\text{-}Mepy)_2SO_4].2H_2O$

[Cu(mbt)] (0.70 g) was refluxed in 3-methylpyridine for six hours, after which any undissolved material was filtered off. On standing the solution yielded pale blue crystals of $[Cu(3\text{-}Mepy)_2SO_4].2H_2O$ overnight. These were collected and washed with ether.

$[Cu(2\text{-}Clpy)_2Cl_2]$ and $[Cu(3\text{-}Clpy)_2Cl_2]$

0.70 g $[Cu(mbtH)_2Cl].\frac{1}{2}(mbt\text{-}mbt)$ was refluxed in 2- or 3- chloropyridine for 10-15 minutes. On cooling blue green crystals of $[Cu(2\text{-}Clpy)_2Cl_2]$ or $[Cu(3\text{-}Clpy)_2Cl_2]$ appeared which were collected and washed with ether.

$[Cu(4\text{-}Mepy)_4Cl_2].H_2O$

$CuCl_2.2H_2O$ (1.70 g, 0.01 mol) was added to ethanethiol (1.55 g, 0.025 mol) to produce a creamy white precipitate. 4-Methylpyridine (10 cm^3) was added to the slurry, and the mixture left to stand. Over a period of one week dark blue lustrous plates of $[Cu(4\text{-}Mepy)_4Cl_2].H_2O$ appeared, which were collected and washed with 4-methylpyridine. On standing in moist air the crystals readily lost 2 molecules of 4-methylpyridine to form $[Cu(4\text{-}Mepy)_2Cl_2]$, a pale blue amorphous powder.

$[Cu(3\text{-}Mepy)_3Cl]$

$[Cu(3\text{-}Mepy)_3Cl]$ could be prepared from any of the $[Cu(LH)_xCl]$ compounds mentioned in Chapter 2. The appropriate complex (0.70 g) was added to 3-methylpyridine (17 cm^3) which was gently heated, if necessary, to dissolve the solid. Almost immediately on dissolution yellow green microcrystals of $[Cu(3\text{-}Mepy)_3Cl]$ appeared which were filtered off and washed with ether. Yields were typically 60-100%.

$[Co(3\text{-}Mepy)_2(mbt)_2]$

$[Co(mbt)_2]$ (0.70 g) (a gift of Dr E. Ainscough) was refluxed for two hours in 3-methylpyridine (17 cm^3) during which time the original green colour of the complex changed to brown. The brown solid, $[Co(3\text{-}Mepy)_2(mbt)_2]$ was collected and washed with ether. (Yield 40%).

$[Cu(en)_2(mbt)_2]$

$[Cu(mbtH)_2Cl]$ (0.70 g) was dissolved in 1,2-diaminoethane (10 cm^3) with stirring and the solution filtered. Ethanol (10 cm^3) was added to the solution cooled in an ice bath, then diethyl ether (7 cm^3) was added dropwise ensuring that a milkiness in the solution was just persisting. Over two days needles of product would appear which were collected and washed with ethanol.

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CHAPTER 4

FURTHER ASPECTS OF THE OXIDATION OF THIOLATES IN THE PRESENCE OF COPPER

Introduction

The previous chapter dealt with the reactivity of cuprous thiolate or thioamide complexes in various nitrogen bases. Here a study is made in greater depth of one of the more intriguing examples; that involving oxidation of the sulphhydryl group to sulphate anion in the presence of copper(II) and neat pyridine. Although sulphate is produced in other nitrogen base solvents, pyridine was chosen because of the comparatively reactive nature of the system and the fact that comparisons can be made with an extensive body of literature relating to copper/pyridine promoted oxidation of other organic compounds.

Aliphatic and aromatic thiols are oxidised by a variety of reagents to disulphides and to higher oxidation products depending on the specific reaction conditions(1). Figure 4.1 shows the compounds obtainable through oxidation, which normally proceeds in a stepwise fashion as illustrated(2). Although sulphonic acids are usually the assumed end products of oxidation of sulphhydryl compounds(2), +4 being the highest oxidation state achieved without C-S bond cleavage(3), an early report of oxidation by hydrogen peroxide suggests the formation of sulphuric acid(4).

Cupric and ferric salts and oxides are observed to oxidise thiols only as far as disulphides(5,6). Mercury(I) and silver(I) can oxidatively cleave disulphides to form sulphinates, RSO_2^- (7), whereas

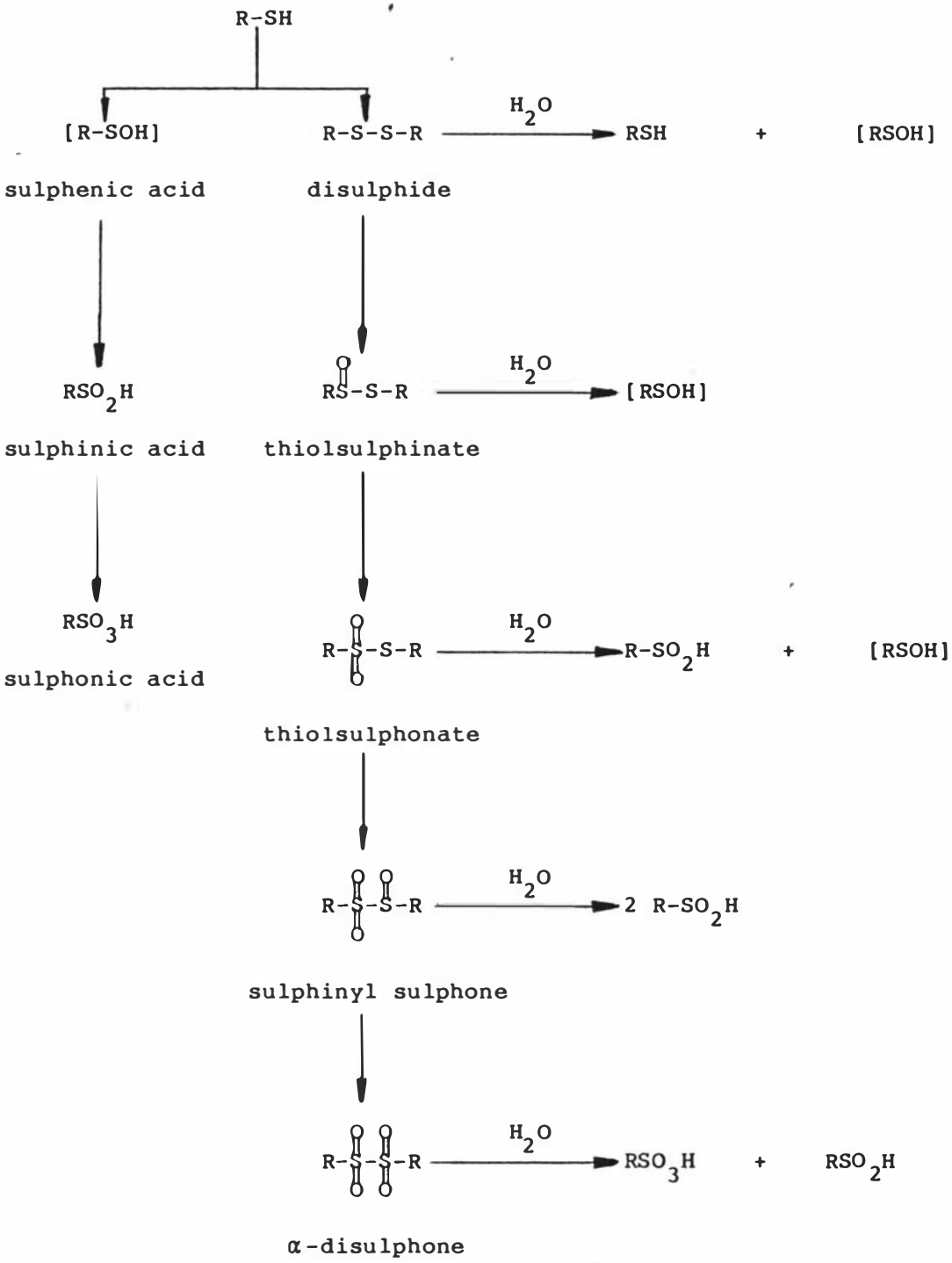


Figure 4.1 Products of thiol oxidation.

gold(III) reacts with disulphides giving sulphonates, RSO_3^- (3) and metallic gold. There are, however, no reports to date of a metal promoted oxidation of a thiol group as far as the sulphate ion, as has occurred for the Cu(II) - pyridine system.

The approach to defining and characterising the system has been divided into the following areas.

1. Thé nature and extent of substrates capable of being oxidised.

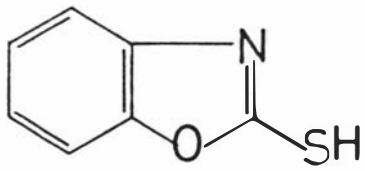
2. The identification of proposed reactive species responsible for attacking and oxidising sulphur.

3. Possible routes for the production of these reactive species and their relationship to other components of copper pyridine chemistry.

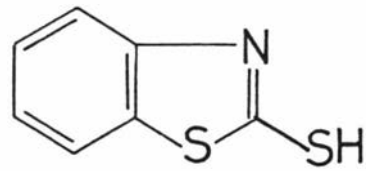
This research has revealed that the reaction is quite extensive, allowing oxidation of not only sulphhydryl containing ligands but also reactants as diverse as elemental sulphur. It appears that there are two possible reactive species. A cupric-pyridine-oxo reagent is predicted where halogens are present in solution otherwise a cupric-pyridine-hydroxo compound is hypothesised. Esr evidence is presented in proof of these postulations, and the reason for the existence of two active agents related to intermediate compounds possible in the presence of halogens.

Finally an account is made of sulphate producing systems involving ethanol rather than pyridine as solvent. Mention is also made of the

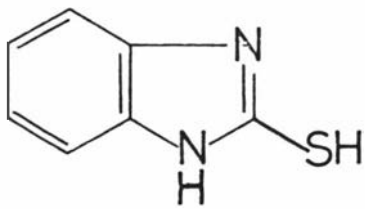
Figure 4.2 Ligands discussed in this chapter and their abbreviations



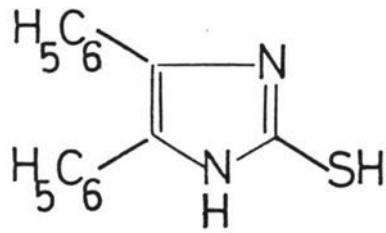
2-mercaptobenzoxazole
(mboH)



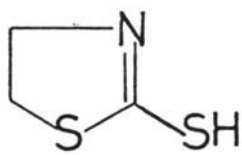
2-mercaptobenzothiazole
(mbtH)



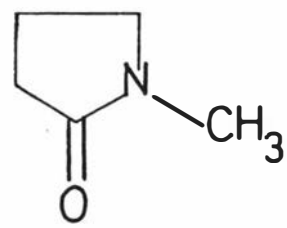
2-mercaptobenzimidazole
(mbimH)



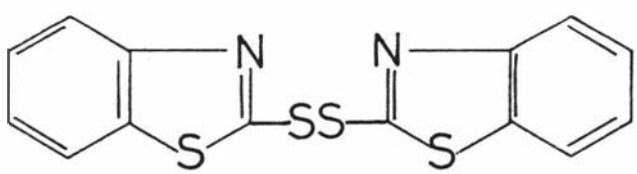
4,5-diphenyl-2-mercaptoimidazole
(dipmimH)



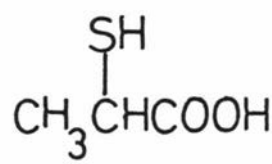
2-mercaptothiazoline
(ttzH)



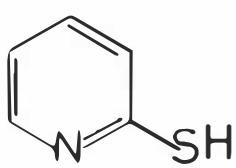
N-methylpyrrolidin-2-one



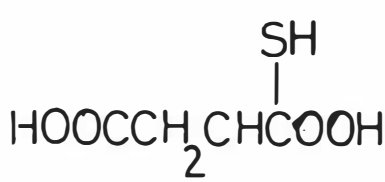
dibenzothiazol-2-yl disulphide



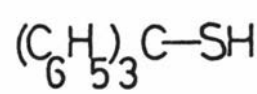
thiolactic acid
(tla)



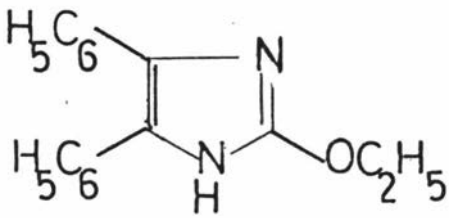
2-mercaptopyridine
(mpyH)



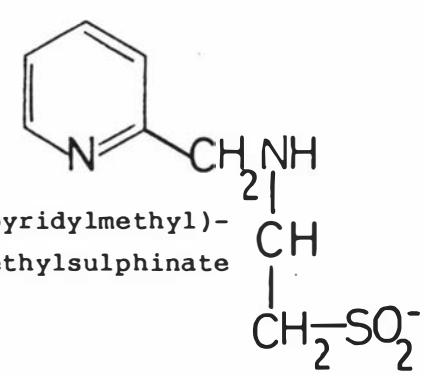
thiomalic acid



tritylthiol



4,5-diphenyl-2-imidazolyl
ethyl ether



2-[(2-pyridylmethyl)-
amino]ethylsulphinate

similarity of these reactions to the chemolithotrophic processes occurring in sulphur oxidising bacteria such as Thiobacillus thiooxidans.

4.1 RESULTS AND DISCUSSION

4.1.1 Substrates capable of being oxidised

The previous chapter mentioned isolation of $[Cu(py)_4SO_4].2H_2O$ from reaction of a variety of cuprous thiolate and thioamide complexes in pyridine. The reaction occurs also for a number of representative cupric species which were investigated, that is $[Cu(mboH)_2Cl_2]$, [Cu(dipmim)Cl], $[Cu(ttzH)_3Cl_2]$and [Cu(tla)].

The knowledge that the complex $[Cu(py)_3Cl]$ was produced as an intermediate on contact of cuprous thioamide chloride compounds with neat pyridine (see Chapter 3) suggested that a probing approach would involve the reaction of independently prepared $[Cu(py)_3Cl]$ with neutral ligand in pyridine. Accordingly by adding CuCl to pyridine, $[Cu(py)_3Cl]$ was generated in situ(8) and dissolved. To such a solution was added various thioamide ligands under conditions where atmospheric oxygen and water were not removed. In all cases $[Cu(py)_4SO_4].2H_2O$ was produced on standing (see Figure 4.3). Similarly when dibenzothiazol-2-yl disulphide was substituted for a thioamide, the sulphate compound was again obtained. Even elemental sulphur resulted in production of $[Cu(py)_4SO_4].2H_2O$. In all the above cases $[Cu(py)_2Cl_2]$ was obtained as a co-precipitant.

$[Cu(py)_4SO_4].2H_2O$ was also obtained when other sources of copper such as cupric oxide, cupric sulphide, and $[Cu(py)_2Cl_2]$ were dissolved or used as a slurry (depending on their solubility in pyridine) and

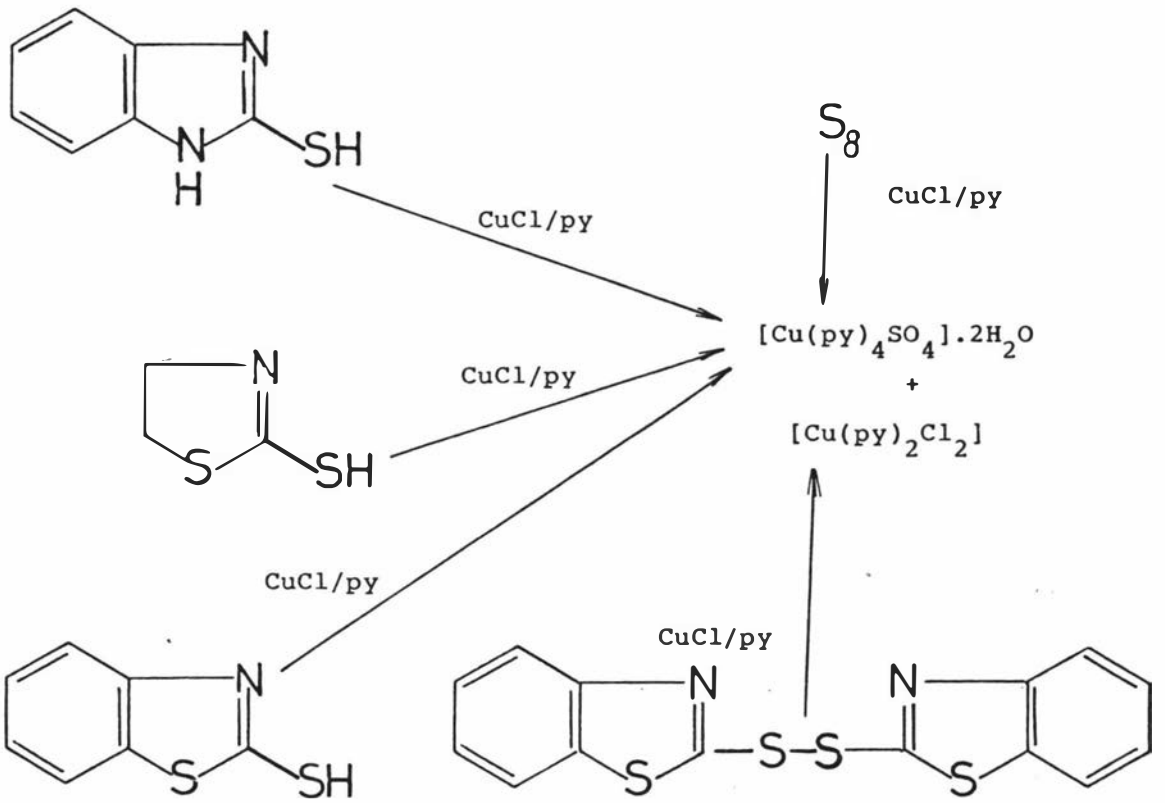


Figure 4.3 Reaction of CuCl dissolved in pyridine with a variety of compounds.

reacted with neutral 2-mercaptobenzimidazole (see Figure 4.4).

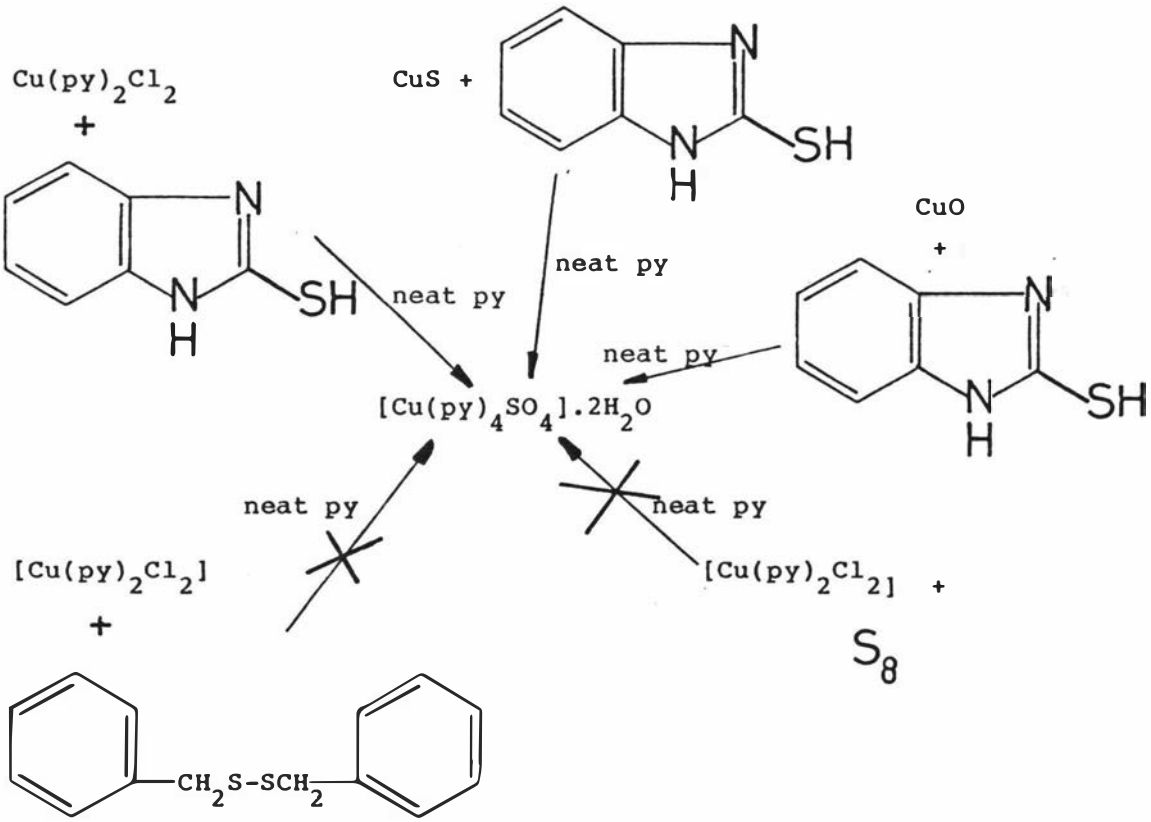


Figure 4.4 Reaction of cupric species with some sulphur sources.

$[Cu(py)_4SO_4].2H_2O$ was not however produced on reaction of $[Cu(py)_2Cl_2]$ with dibenzyl disulphide or elemental sulphur in neat pyridine, suggesting that a substrate capable of reducing $[Cu(py)_2Cl_2]$ is required.

Considering these results,the fact that sulphate could be obtained from such a variety of reactants, for which the only common factor was the presence of copper, suggested that the reaction may be due to a reactive copper-pyridine-oxy entity, rather than the oxidation of a specific copper-ligand complex. The key to the unravelling of the apparently ubiquitous production of sulphate was achieved through

spectroscopic analysis, particularly esr, of the early stages of reaction, in an attempt to identify and characterise these postulated reactive intermediates.

4.1.2 Identification of the proposed reactive species

On mixing of the reaction solutions depicted in Figures 4.3 and 4.4 or before deposition of the sulphate crystals, green or yellow-green solutions developed which were found to contain paramagnetic copper. Investigation of these solutions via esr spectroscopy showed remarkably, that despite the cosmopolitan nature of reactants, only two basic signals were generated, one of which was dependent on the presence of chloride or bromide.

Where halogens were absent (reactions coming under this category were those of [CuL] (L = a thiolate ligand) or CuO + LH, the spectrum of the intermediate obtained typically displayed a signal with parameters $g_{\perp}$ =2.065, $|A_{11}| \approx 175 \times 10^{-4} cm^{-1}$ and $g_{11} \approx 2.268$. In addition five nitrogen superhyperfine peaks were discernible in the 3100 G region suggesting the coordination of two pyridine ligands per copper. A spectrum similar in appearance was reported and simulated for the postulated N_2O_2 copper binding site of bacitracin A(9). The visible electronic spectrum of these solutions showed only a single weak absorbance at ca 700 nm attributable to a d-d transition. Extinction coefficients were typically ≈3 1 $mol^{-1} cm^{-1}$/Cu suggesting that not all of the copper has been oxidised to a reactive form.

In reaction solutions containing chloride and bromide (i.e. those involving $[Cu(LH)_nX]$ (LH = thioamide ligand, X = Cl,Br) or $[Cu(py)_2Cl_2]$+ LH, the esr spectrum showed an intermediate which had

parameters $g_{\perp} \approx 2.065$, $|A_{11}| \approx 183 \times 10^{-4} cm^{-1}$ $g_{11} \approx 2.270$. Nitrogen superhyperfine was again observed at ca 3100 G, this time seven lines being visible indicating the presence at least three pyridine ligands. The electronic spectra of $[Cu(mbtH)_2Cl]$ and $[Cu(py)_2Cl_2]$ + 2mercapto-benzimidazole in pyridine showed d-d transitions at 790 nm (ε= 113 1 $mol^{-1}cm^{-1}$ for the latter).

The solution compositions in which such intermediates appeared and the similarity of their esr parameters are displayed in Tables 4.1 and 4.2. Representative spectra for the two cases are shown in Figure 4.5 (a) and (b). Comparison of the spectra with those of $[Cu(py)_4](BF_4)_2$ (Figure 4.5(c)) run in neat pyridine and $[Cu(py)_4](SO_4)(10)$ run in aqueous solution eliminated the possibility that a $[Cu(py)_4]^{2+}$ entity was responsible for the signal of 4.5(a).

The fact that a basically similar spectrum is obtained in each group implies that both intermediates are independent of the original ligands. For the case where halides are absent strong support for such a hypothesis is provided by the obtention of an identical esr signal from refluxed pyridine solutions of CuO and CuS. Indeed this observation also dispels any notion that the ligand is acting even as a counterion, forcing us to consider less conventional anionic species such as oxo and hydroxo ligands to maintain charge neutrality.

4.1.3 Characterisation of the Reactive Species

The extensive investigations conducted into the nature of the catalytic agents resulting from oxidation of CuCl in pyridine(11-17) have been of great use in aiding the characterisation of what are

Table 4.1 Esr parameters for reaction solutions where Cl^- and Br^- were absent[a]

Solution composition: Reactants	Volume of pyridine (cm^3)	$g_\perp$[d]	g_{11}[e]	A_{11}[f] ($10^{-4}cm^{-1}$)
[Cu(dipmim)]	saturated solution	2.063	2.268	174
[Cu(mpy)]	saturated solution	2.062	2.267	172
[Cu(mbt)]	saturated solution	2.068	2.270	174
$[Cu^{II}_2Cu^{I}_{10}(mmim)_{12}(H_2O)_4]^{2+}$	saturated solution	2.060	2.264	178
$[Cu(ttzH)_3NO_3]$	saturated solution	2.065	2.267	180
CuS[b]	saturated solution	2.064	2.270	176
CuO[c]	saturated solution	2.062	2.267	178
CuO(0.55g)[b] + 2-mercaptobenzimidazole(0.6g)	30	2.058	2.272	169

Notes: a. $[Cu(py)_2(OH)_2]$ may be the common species; b. left in solution overnight; c. refluxed solution; d. ± 0.002; e. ± 0.005; f. $\pm 4 \times 10^{-4} cm^{-1}$

Table 4.2 Esr parameters for reaction solutions containing Cl^- and Br^- [a]

Solution composition: Reactants	Volume of pyridine (cm^3)	$g_\perp$ [c]	g_{11} [d]	A_{11} [e] ($10^{-4} cm^{-1}$)
$[Cu(py)_2Cl_2)]$ (10mg) + 2-mercaptopyridine (11mg)	20	2.067	2.272	184
$[Cu(py)_2Cl_2]$ (10mg) + 2-mercaptobenzimidazole (15mg)	20	2.066	2.271	182
[Cu(mpyH)Cl] (16mg)	5	2.059	2.270	180
[Cu(mpyH)Br] [b] (25mg)	20	2.061	ca 2.25	ca 183
$[Cu(mbtH)_2Cl]$ (10mg)	10	2.068	2.274	174
$[Cu(mbtH)_2Br]$ (16mg)	5	2.062	2.269	183

Notes: a. $[Cu(py)_xO]$ $(x \geq 3)$ may be the common species

b. signal weak

c. ± 0.002; d, ± 0.005; e, $\pm 4 \times 10^{-4} cm^{-1}$

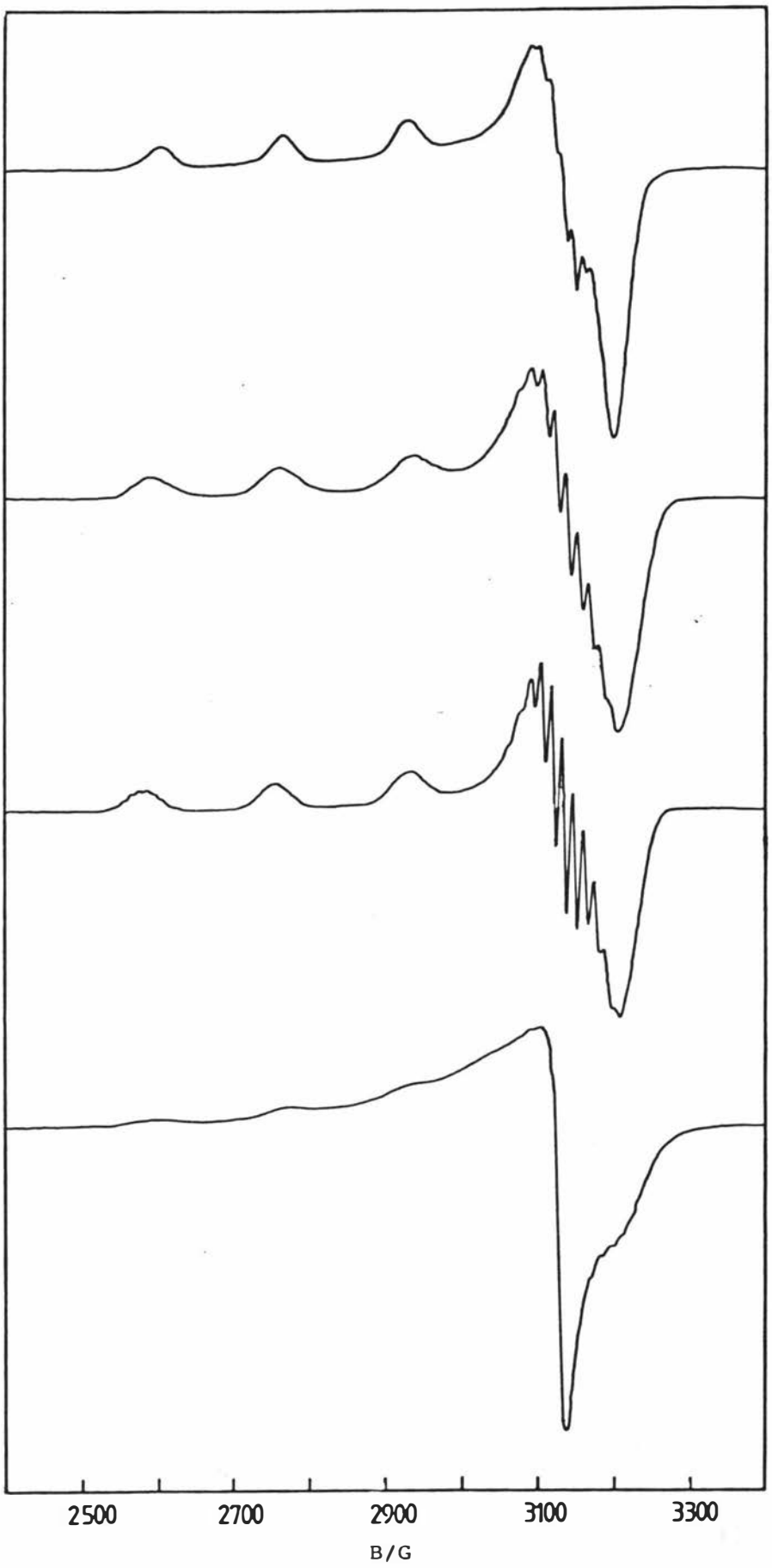
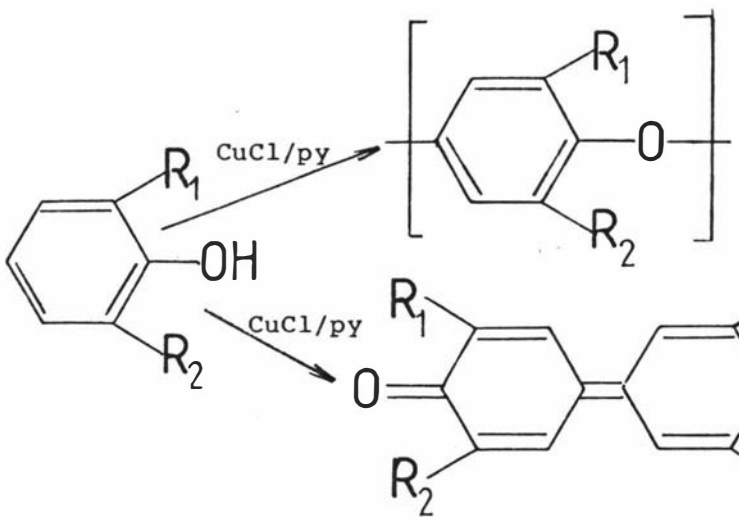


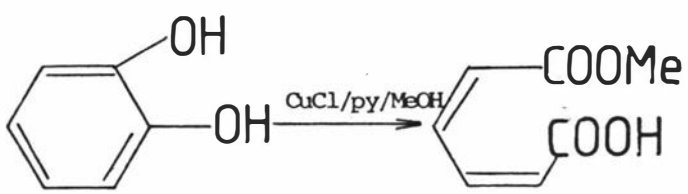
Figure 4.5 Esr spectra of (a) proposed $[Cu(py)_2(OH)_2]$, (b) proposed $[Cu(py)_xO]$, (c) $[Cu(py)_4(BF_4)_2]$, and (d) $[Cu(py)_2Cl_2]$, all in pyridine.

assumed to be reactive intermediates in our work. CuCl dissolved in pyridine in the presence of oxygen has been known since the 1950's(18) to be an active catalyst in the homogeneous oxidative coupling of phenols (Reaction I) and more recently the cleavage of σ-benzoquinones and catechols to muconic acid mono alkyl esters. (Reaction II)(16).

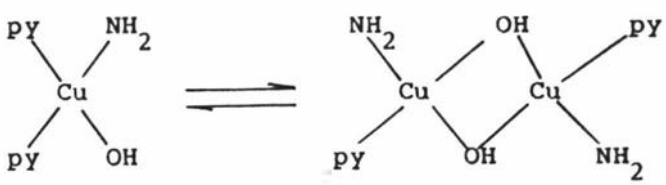
I



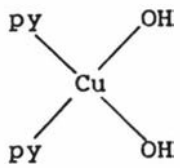
II



Demmin et al.(17) have investigated II and examined the CuCl/O_2/py catalyst in the presence of nucleophiles such as CH_3OH, or NH_3 New reactive species incorporating the nucleophile are believed to be formed. The postulated form for ammonia as nucleophile is shown:



Considering our reaction solutions where halides are absent; that the above hydroxy compounds have been attributed with reactivity by researchers may allow the hypothesis of the following structure for our intermediate:



Such a structure would prove consistent with the esr interpretation. Strong support comes also from the fact that $Cu(OH)_2$ dissolved in pyridine shows a similar esr spectrum. Conceivably the hydroxo ligands could arise from atmospheric water. Certainly when CuO/pyridine solutions were refluxed in conditions where water had been rigorously excluded, no esr signal was observed. The following equation represents the stoichiometry for the reaction of $[Cu(py)_2(OH)_2]$ with, for instance, a disulphide species:

$$[Cu(py)_2(OH)_2] + RSSR + \tfrac{1}{2}O_2 \xrightarrow{\text{pyridine}} [Cu(py)_4SO_4] + RSR + H_2O$$

When chloride or bromide are present the system becomes a little more complex to interpret. Bodek et al(15) have extensively investigated the $CuCl/O_2$/pyridine catalytic system used in the polymerisation of phenols. Through gel permeation chromatography they established the following stoichiometry:

$$2CuCl + \tfrac{1}{2}O_2 \xrightarrow{\text{pyridine}} [Cu(py)_2Cl_2] + [(py)_mCuO]_n \quad (1)$$

where the polymeric species $[(py)_mCuO]_n$ is believed to be the active initiator of polymerisation. The compound was found to be esr silent. Also $[Cu(py)_2Cl_2]$ was shown to be an inactive initiator.

The reaction conditions for our experiments are so similar to those of Bodek et al. that it is quite conceivable that the copper reagent responsible for sulphur oxidation is very similar to that isolated by them. All the processes are connected by production of the common intermediate $[Cu(py)_3Cl]$. (In the instances where $[Cu(py)_2Cl_2]$ was used as the source of copper, thiol reduction would allow in situ synthesis of $[Cu(py)_3Cl]$).

The postulation of equimolar production of $[Cu(py)_2Cl_2]$ and reactive species $[(py)_mCuO]_n$ and the observation that the latter had no detectable esr signal(14,15) appear at first in contention with the strong esr spectra obtained for our reactive solutions. That these species were not $[Cu(py)_2Cl_2]$ was confirmed by the differences in the esr spectrum of pure $[Cu(py)_2Cl_2]$ run in neat pyridine (see Figure 4.5(d)). The spectrum of $[Cu(py)_2Br_2]$ in pyridine is presented also for reference (Figure 4.6). A plausible fate for the $[Cu(py)_2Cl_2]$ constituent is reduction by thiolate ligand which is present in all cases in at least 2-fold excess. Furthermore the detection of an esr signal may be a consequence of the rapidity with which samples were run - normally within five minutes of mixing of reactants. The tendency of cupric-oxo intermediates to polymerise has been emphasised(11). It is quite likely that the compound observed is the monomeric form of $[(py)_mCuO]_n$, that is $[Cu(py)_xO]$ $(x \geq 3)$. Electron superexchange would not occur in a monomer to cause collapse of the esr signal. Such an assignment is consistent also with the spectral features, i.e. the presence of seven nitrogen superhyperfine indicating coordination of at least three pyridine ligands.

$[Cu(py)_xO]$ might be expected to react in the following way with

a disulphide substrate:

$$[Cu(py)_xO] + RSSR + 1\tfrac{1}{2}O_2 \xrightarrow{\text{pyridine}} [Cu(py)_4SO_4] + RSR$$

In support of such a mechanism dibenzothiazol-2-yl sulphide was isolated from the reaction of CuCl and dibenzothiazol-2-yl disulphide in pyridine.

4.1.4 Oxidation of Compounds of the Type CuL_3X - A Synthetic Route for Production of $[Cu(py)_xO]$

An understanding of the reactivity towards oxygen of cuprous compounds of the type $[CuL_3X]$ (where L= pyridine or a picoline and X= Cl or Br) may well prove advantageous as an aid in interpreting the production of the species $[Cu(py)_xO]$. $[CuL_3X]$ compounds are unexpectedly reactive towards oxidation in both solution and the solid state. For instance oxidation of $[Cu(3\text{-Mepy})_3Cl]$ in solution is rapid, the crystals dissolving in a variety of solvents (e.g., acetonitrile, nitromethane, acetone, dichloromethane and ethanol) to give orange-yellow solutions. The electronic spectra of these (430sh, 785 and 875 nm) pointed to the formation of the μ-oxo copper tetramer $[Cu_4Cl_6O(3\text{-Mepy})_4]$(19). Indeed refluxing $[Cu(3\text{-Mepy})_3Cl]$ in ethanol produces orange brown crystals of $[Cu_4Cl_6O(3\text{-Mepy})_4]$ verified by elemental analysis. Similarly $[Cu(3\text{-Mepy})_3Br]$, $[Cu(py)_3Cl]$ and $[Cu(2\text{-Mepy})_3Cl]$ gave complexes identified as $[Cu_4Br_6O(3\text{-Mepy})_4]$, $[Cu_4Cl_6O(py)_4]$ and $[Cu_4Cl_6O(2\text{-Mepy})_4]$ respectively.

$$[CuL_3X] \xrightarrow[\text{ethanol}]{\text{reflux in}} [Cu_4X_6OL_4] + \text{an unidentified cupric species}$$

$[Cu_4Cl_6O(py)_4]$ and $[Cu_4Cl_6O(2\text{-Mepy})_4]$ have been structurally characterised by X-ray crystallography(20,21). In each case the copper atoms are not entirely equivalent, but all are found in essentially a trigonal bipyramidal stereochemistry with varying degrees of distortion. The esr solution spectral profiles of these complexes, recorded for the first time, are all very similar (e.g., Figure 4.6(a)) showing nine nitrogen superhyperfine lines in the perpendicular region and are typical of compounds possessing structures intermediate between trigonal bipyramid and square pyramidal.

Signs that oxidation was possible in solid $[CuL_3X]$ was shown by the appearance of weak bands at 700 and 875 nm in the nujol mull spectrum of even freshly prepared $[Cu(3\text{-Mepy})_3Cl]$. That trace amounts of copper(II) were present was confirmed by the low magnetic moment of 0.6 B.M.. A rhombic type esr powder spectrum identical to that of $[Cu_4Cl_6O(3\text{-Mepy})_4]$ run in powder form indicated its presence in the copper(I) complex.

With regard to the problem of oxidation of CuCl in pyridine, the additional production of $[Cu_4Cl_6O(py)_4]$ where organic solvents were also present may well have caused some confusion in the literature, especially with respect to solution studies involving solvents of mixtures of pyridine and other organic compounds. Electronic spectral work by Ludwig and Gasser(22) conducted on compounds of the type $[CuL_2Cl_2]$ (L= pyridine or a picoline) allowed the authors to state that new five coordinate copper(II) complexes were being formed. It thus seems likely that $[Cu_4Cl_6O(py)_4]$ may be prepared by dissolution of $[Cu(py)_2Cl_2]$ in dichloromethane. Such a solution certainly has an identical esr spectrum to that of $[Cu_4Cl_6O(py)_4]$ in the same solvent. Hence if CuCl were to be dissolved in a mixed pyridine/dichoromethane, pyridine/chloroform or pyridine/alcohol solvent

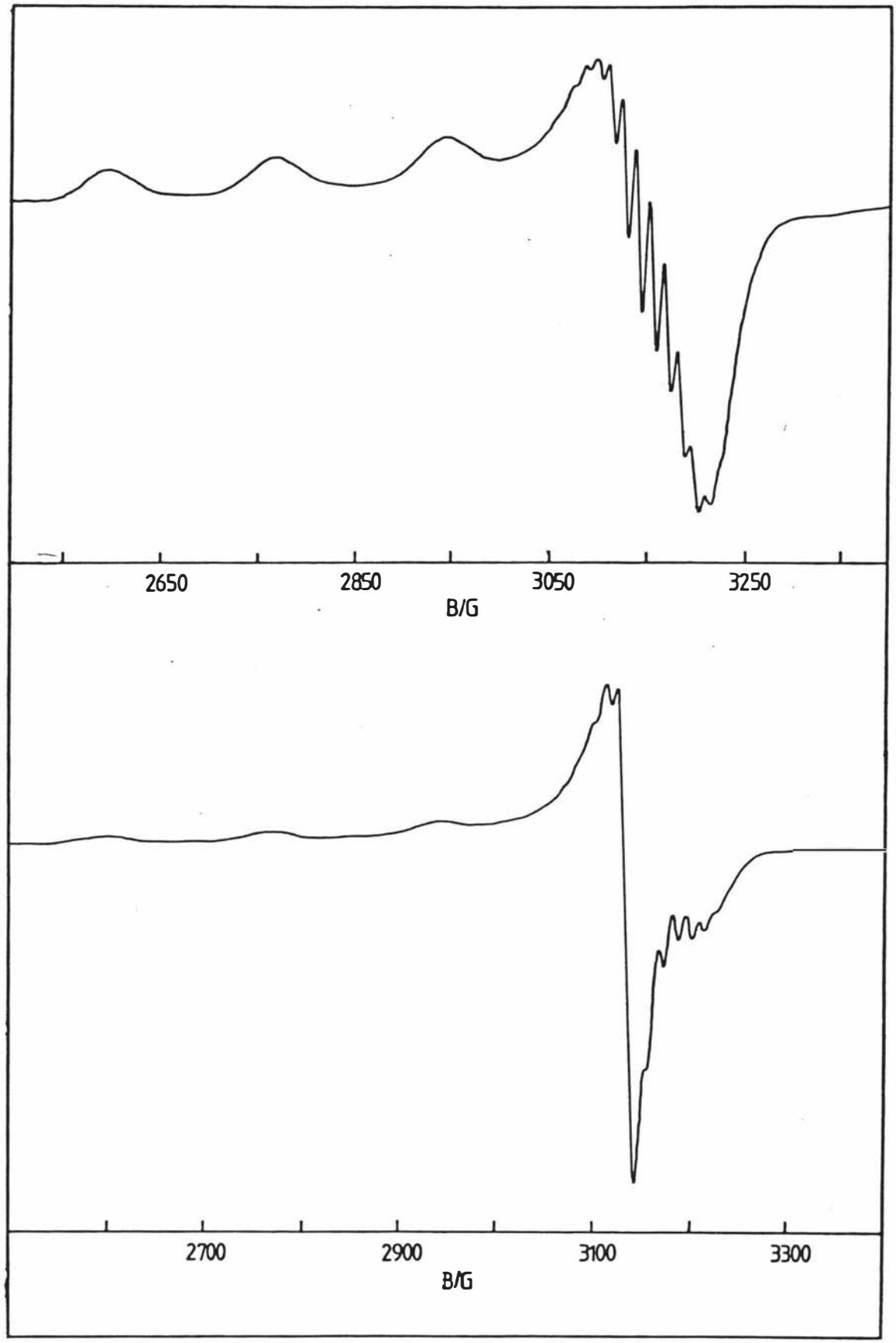


Figure 4.6 Esr spectrum of (a) $[Cu_4Br_6O(3\text{-Mepy})_4]$ in nitromethane and (b) $[Cu(py)_2Br_2]$ in pyridine.

the $[Cu(py)_2Cl_2]$ produced in the oxidation reaction (equation 1) may well be transformed into $[Cu_4Cl_6O(py)_4]$ with corresponding esr signal. Esr spectra of CuCl oxidation products were run under such conditions by Praliaud et al.(13) and Ochiai(12) and this may explain the characteristic $[Cu_4Cl_6O(py)_4]$ lineshape obtained but not so interpreted by them.

$[Cu_4Cl_6O(py)_4]$ may be used as an oxidising agent in reaction (I) (23) but is not catalytically active(24). However compounds based on a similar tetrameric copper core containing two oxygen atoms - one bridging all coppers and the other terminal - have been prepared and found to have much greater activity(24). For instance Davies and El-Sayed(25) synthesised the compounds $[Cu_4Cl_4O_2(py)_3]$ and $[Cu_4Cl_4O_2(py)_4]$ from reaction of $[Cu(py)Cl]_4$ with pyridine in nitromethane. Their structures are believed to be similar to that of the X-ray characterised compound $[Cu_4Cl_6OL_3H_2O.L]$ (where L = N-methylpyrrolidin-2-one)(26)

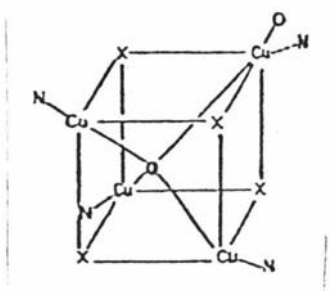
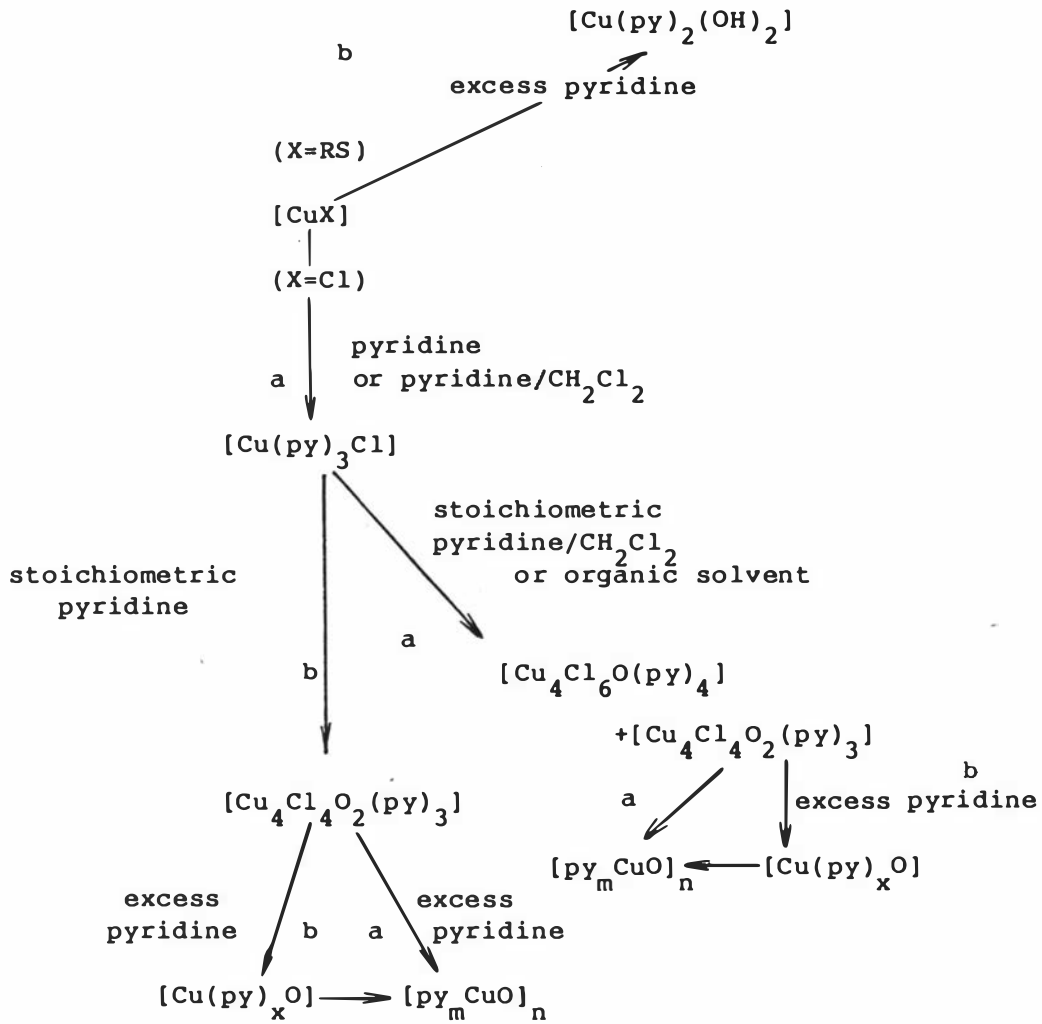


Figure 4.7, Proposed structure of $[Cu_4Cl_4O_2(py)_3]$ and $[Cu_4Cl_4O_2(py)_4]$

The terminal oxo group is attributed high basicity and nucleophilic character and is believed to be the site of catalytic activity. Treatment of $[Cu_4Cl_4O_2(py)_4]$ with excess pyridine leads to the formation of the original catalytic initiator(24):

$$[Cu_4Cl_4O_2(py)_4] + npy \xrightarrow{CH_2Cl_2} 2[Cu(py)_2Cl_2] + (py)_n(CuO)_2 \rightarrow [(py)_mCuO]_n$$

A reaction scheme may then be drawn for the oxidation of CuCl in neat pyridine showing the possible interrelationships of the various species encountered.



a: reaction confirmed b: reaction step proposed

This scheme may then account for the formation of <u>two</u> active complexes, $[Cu(py)_xO]$ and $(Cu(py)_2(OH)_2)$, in our work. $[Cu(py)_xO]$ is postulated to be formed via the tetrameric copper cluster $[Cu_4Cl_4O_2(py)_3]$ involving a framework of bridging halogens. Such a structure with the

ability to allow formation of a reactive copper-oxo entity cannot occur when chloride or bromide are not present in the reaction solution. Gampp and Zuberbuhler(11) have emphasised this prerequisite: supplied as $[Cu(CH_3CN)_4](BF_4)$, Cu(I) autooxidises only after addition of equimolar amounts of Cl^- in pyridine, supporting the above hypothesis. Consequently when the halogens are absent $[Cu(py)_2(OH)_2]$ is presumably formed via another route.

4.2 OXIDATION OF THE SULPHHYDRYL GROUP IN SOLVENTS OTHER THAN PYRIDINE

The production of sulphate from a thiol ligand in the presence of copper is not restricted to nitrogen base solvents. Sulphato compounds have also been isolated here from systems reacting in ethanol. For instance $CuSO_4.5H_2O$ has been produced from ethanolic solutions of tritylthiol and $CuCl_2.2H_2O$ or $CuBr_2$. On addition of $CuCl_2.2H_2O$ to ligand a brownish red precipitate attributed to CuS appears. The filtered mother liquor retains a blue green tinge, which after one day has the esr and electronic features of $[Cu(EtOH)_6]^{2+}$. After 3-4 days a white compound starts to precipitate, identified as di-triphenyl methyltrisulphide $((C_6H_5)_3C)_2S_3$ from its elemental analysis. Within five weeks of standing at room temperature light blue cystals of $CuSO_4.5H_2O$ precipitated from solution accompanied by another white crystalline product identified as triphenylcarbinol, $(C_6H_5)_3COH$. A similar reaction is observed for $CuBr_2$ with the exception that triphenylmethylethyl ether, $(C_6H_5)_3COCH_2CH_3$, is obtained instead of triphenylcarbinol.

$CuSO_4.5H_2O$ may also be obtained when thiomalic acid is added to an

ethanolic solution of $CuCl_2.2H_2O$ in equimolar ratio. The product appears after five weeks. Attempts to accelerate the reaction by refluxing the solution or reducing the volume of solvent were unsuccessful.

On slow evaporation over a period of a year of a solution containing $Cu(ClO_4)_2.6H_2O$, and the sodium salt of 4,5-diphenyl-2-mercaptoimidazole, $CuSO_4.5H_2O$ and the organic compounds 4,5-diphenyl-2-imidazolylethyl ether, (see Figure 4.2) and benzoic acid were produced (see Appendix for mass spectra).

A product in which the sulphato group is coordinated to copper was obtained when [Cu(mpyH)Cl] produced <u>in situ</u> from reaction of $CuCl_2.2H_2O$ was further oxidised by addition of nine-fold equivalent $CuCl_2.2H_2O$. A green solid was obtained from slow evaporation of the ethanol. Elemental analysis was consistent with a formulation of $[Cu(mpyH)_2SO_4]$. The infrared spectrum shows new strong bands due to sulphate ligand at 1270, 1180 and 1150 $cm^{-1}(\nu_3)$, 940 cm^{-1} (ν_1) and 640 cm^{-1} (ν_4) which is suggestive of bridging or chelating sulphate(27). The mercaptopyridine ligand, present in neutral thione form, shows movement of the thioamide moiety vibrations (ν(NH) 3095(sh), I - 1470 cm^{-1} and IV - 740 cm^{-1}) indicative of nitrogen coordination. A band at 275 cm^{-1} may be due to ν(CuN)(28), and a shoulder at 380 nm in the nujol mull electronic spectrum may be tentatively assigned to a N$\rightarrow$Cu LMCT band. The compound's magnetic moment was normal at 1.93 B.M.

Little can be said about the nature of the reactions leading to the production of sulphate in these systems because the time taken for the product to appear, and the interference of $[Cu(EtOH)_6]^{2+}$ to the

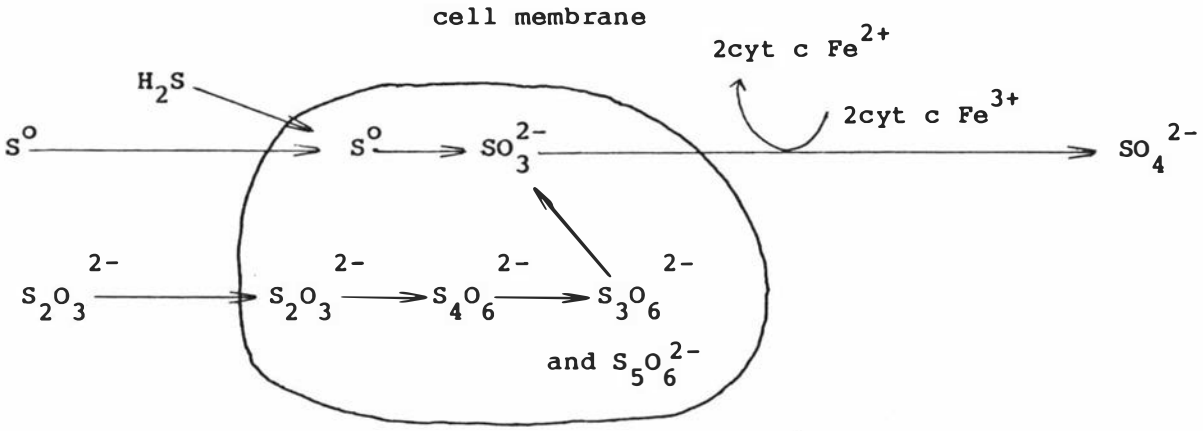
spectroscopic probes, made them less amenable to study. A comparison can be made however with the oxidation of disulphide species to sulphinates as observed by Higashi et al.(29) in the reaction of bis(2-pyridyl)disulphide with $Cu(ClO_4)_2$ in methanol. As well as a copper(I)-disulphide complex a low yield of the complex [Cu(2-pyridinesulphinate)$_2$] (2-pyridinesulphinate = $C_5H_4NSO_2$) was also obtained. Similarly [Cu(2-(2-pyridylmethyl)amino))ethyl sulphinate Cl] (see Figure 4.2) has been formed(30) by cleavage of the disulphide bond for the corresponding disulphide complex in water. In the former case a copper promoted heterolytic cleavage of disulphide to give RS^- and RS^+ was envisaged. RS^+ may then react with water to give RSO_3^- and the thiol RSH by subsequent disproportionation. Such a mechanism combined with further oxidation of sulphonate written as: $Cu^{2+} + RSO_3^- + H_2O \longrightarrow SO_4^{2-} + 2H^+ + \frac{1}{2}(R\text{-}R) + Cu^+$, may well be in operation in our systems. A balanced equation incorporating such intermediates can be written thus:

$$2RSSR + 10\ Cu^{2+} + 8H_2O \longrightarrow 2SO_4^{2-} + 10\ Cu^+ + 14H^+ + 2RSH + R\text{-}R$$

4.3 BACTERIAL OXIDATION OF SULPHUR

A biological reaction related to the studies of this chapter occurs in certain chemolithotrophic bacteria, chiefly those of the genus Thiobacillus which utilise the oxidation of reduced inorganic sulphur compounds such as hydrogen sulphide, sulphur, and thiosulphate as an energy source. The mechanism of sulphur oxidation still remains obscure(31) the great reactivity and chemical instability of many of the proposed intermediates making biochemical investigations difficult. Nonetheless it is thought that some of the processes are enzymic and

that the electrons are transferred via cytochrome 'c' finally to oxygen(32). A hypothetical pathway of oxidation is shown below.



In relation to the bacterial mechanism our findings show that copper may promote sulphide, sulphur and disulphide oxidation as far as the sulphate form. This leads to the tentative suggestion that a copper or perhaps iron containing enzyme may well be active in the bacterial metabolism of sulphur and may provide a stimulus for biological researchers to locate such an entity.

Summary

Sulphur in a variety of substrates has been oxidised to sulphate in the presence of Cu(II) in pyridine. Two reactive species are believed responsible for the oxidative process. Where chloride or bromide ions are present in the initial reaction mixture the reactive entity $[Cu(py)_xO]$ is proposed. However when no chloride or bromide is present the species $[Cu(py)_2(OH)_2]$ is postulated. The interrelationship of precursors to $[Cu(py)_xO]$ has provided a rationalisation for the existence of two reactive compounds.

Oxidation of sulphur has been seen to occur also in ethanolic solvents in the presence of copper but the process occurs more slowly

and appears to involve a different mechanism from that of the pyridine reaction.

Oxidation of sulphhydryl and sulphur substrates is reminiscent of the chemolithotrophic process of sulphur oxidising bacteria. Any underlying similarity in the two areas remains to be proven.

4.4 EXPERIMENTAL

4.4.1 Instrumentation was as described in 1.7.1.

4.4.2 Synthesis of the complexes

Production of $[Cu(py)_4SO_4].2H_2O$

In each case below $[Cu(py)_4SO_4].2H_2O$ was confirmed after collection, washing with pyridine and drying in vacuo from comparison of its infrared spectrum with an authentic sample and the precipitate formed with $BaCl_2$ in water. This was possible in mixtures where $[Cu(py)_2Cl_2]$ appeared as a co-precipitant. The latter compound could be identified by the appearance of a band at 280 cm^{-1} in the mixture infrared spectra attributed to ν(CuCl). Yields were not calculated in such instances.

Reactants cupric thiolate or thioamide complexes

$[Cu(ttzH)_3Cl_2]$, $[Cu(mboH)_2Cl_2]$, [Cu(tla)] or [Cu(dipmim)Cl] (0.40 g) were added to pyridine (30 cm^3) and stirred. Any insoluble material remaining after thirty five minutes was filtered off. $[Cu(py)_4SO_4].2H_2O$ appeared overnight. Yields were typically 40-60%.

Reactants CuCl + thioamide compounds

CuCl (1.0 g, 10 mmol) was added to pyridine (30 cm^3) under dinitrogen. To this was added LH (10 mmol) (LH = 2-mercaptothiazoline (1.19 g); 2-mercaptobenzothiazole (1.67 g) and 2-mercaptobenzimidazole (1.50 g)), the yellow green solution agitated and left open to the atmosphere. Undissolved solid was filtered after thirty minutes. $[Cu(py)_4SO_4].2H_2O$ and $[Cu(py)_2Cl_2]$ were produced overnight or within 1-2 days.

Reactants CuCl + benzothiazol-2-yl-disulphide

Benzothiazol-2-yl-disulphide (0.3 g, 0.9 mmol) was dissolved in hot pyridine (20 cm^3). To this was added with agitation CuCl (0.36 g, 3.7 mmol) under dinitrogen. Insoluble material remaining after thirty minutes was filtered from the yellow green solution $[Cu(py)_4SO_4].2H_2O$ and $[Cu(py)_2Cl_2]$ appeared within two days.

Reactants CuCl + S_8.

CuCl (1.0 g, 10 mmol) was dissolved with heating in pyridine (30 cm^3) under dinitrogen. Separately sulphur (0.60 g, 9 mmol) was dissolved in pyridine (30 cm^3) and this solution added to the former. After 2 days an amorphous green precipitate containing some $[Cu(py)_2Cl_2]$ was filtered off, the filtrate yielding $[Cu(py)_4SO_4).2H_2O$, the same day.

Reactants $[Cu(py)_2Cl_2]$ + 2-mercaptobenzimidazole

$[Cu(py)_2Cl_2]$ (1.0 g, 3.4 mmol) was dissolved in pyridine (70 cm^3) with heating. To this solution was added 2-mercaptobenzimida-

zole (0.55 g, 3.7 mmol) with stirring and the yellow green solution filtered. Crystals of $[Cu(py)_2Cl_2]$ appeared within hours followed by $[Cu(py)_4SO_4].2H_2O$.

Reactants CuS, CuO and thioamide compounds

CuS and CuO (0.5 g) were added to pyridine solutions (40 cm^3) containing 2-mercaptobenzothiazole (0.50 g) and 2-mercaptobenzimidazole (0.50 g) respectively the pyridine solution developing a yellow colour. Only a small amount of the CuS and CuO dissolved, the remaining solid being filtered off after 2 hours $[Cu(py)_4SO_4].2H_2O$ appeared within 1-2 days. Yields 0.025 g (1%). A similar reaction was observed for CuS (0.3 g) and 2-mercaptobenzimidazole (0.5 g).

Reaction of $CuCl_2.2H_2O$ and $CuBr_2$ with trityl thiol

$CuCl_2.2H_2O$ (0.43 g, 2.5 mmol) in ethanol (50 cm^3) or $CuBr_2$(0.56 g, 2.5 mmol) in ethanol (100 cm^3) was added to tritylthiol (1.38 g, 5 mmol) in ethanol (130 cm^3). On stoichiometric addition of copper(II) CuS precipitated which was filtered off. The filtrate yielded white crystals (Mpt 142-146^oC), analysing as di-triphenylmethyl trisulphide, within 3-4 days (yield: 0.3 g) (Found: C, 78.5; H, 5.5; S, 16.4; Calc. for $C_{38}H_{30}S_3$: C, 78.3; H, 5.2; S, 16.5) Within five weeks $CuSO_4.5H_2O$ precipitated as blue crystals (yield from $CuCl_2.2H_2O$: 0.055 g; from $CuBr_2$ 0.105 g) identified by infrared spectroscopy. A second organic species was obtained simultaneous to deposition of sulphate. For the reaction involving $CuCl_2.2H_2O$ triphenyl carbinol was obtained (Mpt 162-163^oC Literature - 164^oC) (Found C, 87.2, H, 6.1 Calc. for $C_{19}H_{16}O$: C, 87.7; H, 6.2). (Yield: 0.17 g) whereas for $CuBr_2$, tri-

phenylmethylethyl ether was isolated. (Found C, 87.2; H, 7.1. Calc. for $C_{21}H_{20}O$: C, 87.5; H, 7.0)

Reaction of thiomalic acid and $CuCl_2.2H_2O$.

Thiomalic acid (3.0 g, 20 mmol) in ethanol (100 cm^3) was added to $CuCl_2.2H_2O$ (3.4 g, 20 mmol) in ethanol (60 cm^3). Within five weeks $CuSO_4.5H_2O$ precipitated which was collected, washed with ethanol and identified by its infrared spectrum.

Preparation of $[Cu(mpyH)_2SO_4]$

$CuCl_2.2H_2O$ (13.6 g, 80 mmol) in ethanol (200 cm^3) was added to 2-mercaptopyridine (1.11 g, 10 mmol) in ethanol (50 cm^3) and the solution stirred overnight. The precipitate of [Cu(mpyH)Cl] initially produced dissappeared within three or four days. On slow evaporation over a period of weeks $CuCl_2.2H_2O$ and a green product precipitated. This was collected and the $CuCl_2.2H_2O$ contaminant removed with copious washing with water, and the product dried <u>in vacuo</u>. (Found: C, 31.6; H, 2.4; N, 7.2. Calc. for $C_{10}H_{10}CuN_2O_4S_3$: C, 31.5; H, 2.6; N, 7.3).

[Cu(dipmim)Cl] and $[Cu(ttzH)_3Cl_2]$ were prepared as shown in Chapters 2 and 4 respectively. $[Cu(mbo)_2Cl_2]$ was prepared according to the method of Preti and Tosi(33) [Cu(tla)] was a gift of Dr E. Ainscough.

$[CuL_3X]$ (L = py, 2-Mepy, or 3-Mepy, X = Cl; L = 3-Mepy, X = Br)

These compounds were prepared by adding CuX to an excess of the appropriate pyridine under dinitrogen following a method similar to that described by de Ahna and Hardt(8).

$[Cu_4X_6OL_4]$ (L = py, 2-Mepy, or 3-Mepy, X = Cl;

L = 3-Mepy, X = Br).

These were obtained by refluxing the appropriate $[CuL_3X]$ complex (1.0 g) in anhydrous ethanol (50 cm^3) for 15 min, followed by immediate fltration of the hot solution. On cooling crystals of the product appeared which were then collected and washed with anhydrous ethanol. Yield: 0.20 g (35%) $[Cu_4Cl_6O(3\text{-Mepy})_4]$: (Found: C, 33.7; H, 3.6; N, 6.2%. Calc. for $C_{24}H_{28}Cl_6Cu_4N_4O$: C, 33.7; H, 3.3; N, 6.55%). The other compounds were verified by comparison of their melting ponts with literature values (given in parentheses). $[Cu_4Cl_6O(py)_4]$ m.p. 251-3°C (251 °C) $[Cu_4Cl_6O(2\text{-Mepy})_4]$ m.p. 208 °C (223 °C) $[Cu_4Br_6O\ (3\text{-Mepy})_4]$ m.p. 243-4 °C (241 °C).

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CHAPTER 5

CUPRIC COMPLEXES FROM THIOAMIDE LIGANDS

Introduction

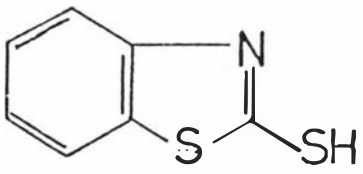
This chapter is concerned with the synthesis and characterisation using spectroscopic techniques, of cupric and mixed-valence complexes of copper, containing thioamide ligands or their deprotonated thiolato forms. Although reduction to copper(I) is most commonly observed on interaction of such compounds with copper(II), occasionally the ligands may stabilise the cupric state sufficiently to allow isolation of non-labile solid complexes. Previously some success has been achieved by the utilisation of certain experimental techniques or by ligand modification. For instance, a route employed by Devillanova et al. (1) to ensure cupric species, involved the adoption of N-alkylated imidazolethiones which effectively prevent thiol-thioketo tautomerism by arresting the ligand in the thione form. In this way complexes of the form $[CuL_2X_2]$ were prepared (where L = N,N'-dimethyl-1,3-imidazolidine-2-thione and N,N'-diethyl-1,3-imidazolidine-2-thione and X = Cl or Br) (see Figure 5.1 for structures). Preti and Tosi(2,3) have isolated the cupric complexes of 2-mercaptobenzoxazole, $[Cu(mboH)_3SO_4]$ and $[Cu(mboH)_2Cl_2].2H_2O$, by combining the appropriate copper salt with molten ligand.

Nonetheless, application of such techniques has not proved universally necessary. Indeed one of the first documented cupric thiolate species involved the reaction of the thioamide 2-mercaptobenzimidazole with copper sulphate at high pH to produce [Cu(mbim)OH](4). Similarly stable cupric complexes have been reported for the ligand

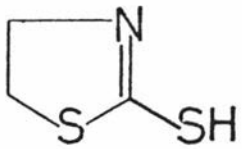
2-mercaptothiazoline. Geetharani and Sathanyanaryana(5) prepared the green compound $[Cu(ttzH)_2Cl_2]$ and Devillanova and Verani(7) have commented on the appearance of coloured products in the synthesis of cuprous halide complexes of the ligand. With the exception of [Cu(mbim)(OH)] and the mixed valence compounds $[Cu^{II}_2Cu^{I}_{10}(mmim)_{12}(X)_4]^+$ (8) derived from 2-mercapto-1-methylimidazole, there are few accounts of species involving Cu(II) and a deprotonated thioamide ligand. In some instances compounds so envisaged have on further investigation proved to have been misformulated. "$[Cu(mmim)_2]$" and "$[Cu(mbt)_2]$" have been reformulated already as $[Cu^{II}_2Cu^{I}_{10}(mmim)_{12}(H_2O)_4](CH_3COO)_2$ and $[Cu(mbtH)_2Cl]$ in Chapters 1 and 2 respectively. Similarly, as will be shown here, the compound "$[Cu(ttz)_2]$" proposed by Basson and du Preez(9) is more probably $[Cu(ttzH)_3NO_3]$.

Accordingly the moving impetus for this research has been to study in a more exhaustive fashion than before the interaction between copper(II) and ligands of cyclic thioamide origin particularly, where possible, those involving a thiolate interaction. The pursuit of thiolato species has not however, been at the expense of a complete account of any cupric-thioamide aspects encountered. The compounds have been characterised by infrared, visible and esr spectroscopy. Also some aspects of the reactivity of selected compounds have been investigated with the subsequent production of new complexes encompassing some interesting ligand modifications. The crystal structure of one of these, [Cu(tztdz)Br] has been established, allowing an insight into the nature of products obtained by a similar route.

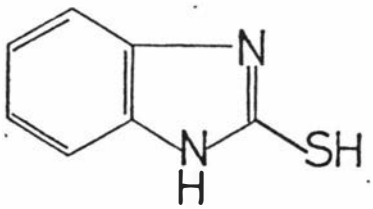
Figure 5.1 Ligands encountered in this chapter and their abbreviations



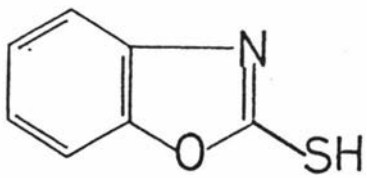
2-mercaptobenzothiazole (mbtH)



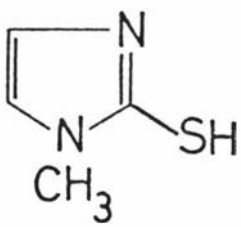
2-mercaptothiazoline (ttzH)



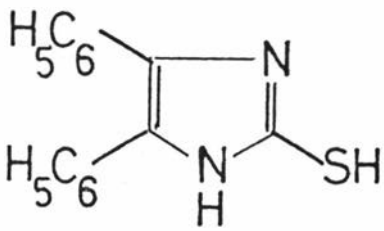
2-mercaptobenzimidazole (mbimH)



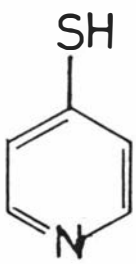
2-mercaptobenzoxazole (mboH)



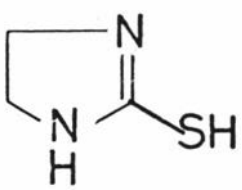
2-mercapto-1-methylimidazole (mmimH)



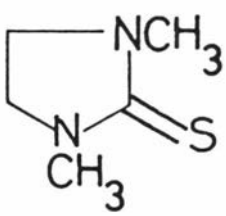
4,5-diphenyl-2-mercaptoimidazole (dipmimH)



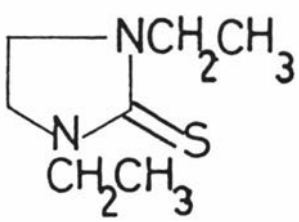
4-mercaptopyridine (mpyH)



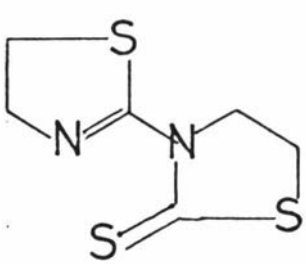
2-mercaptoimidazoline (etuH)



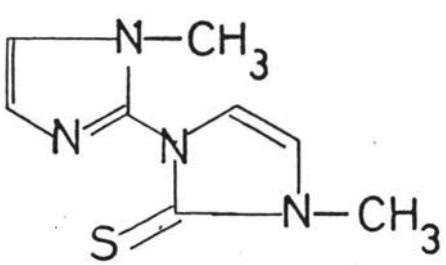
N,N'-dimethyl-1,3-imidazolidine-2-thione



N,N'-diethyl-1,3-imidazolidine-2-thione



3-(4,5-dihydro-2-thiazolyl)-2-thiazolidinethione (tztdz)



3-(2,1-methylimidazolyl)-2,1-methylimidazolinethione (mimmimz)

5.1 SYNTHESIS OF THE COMPOUNDS

Structures and abbreviations for the ligands used in Chapter 5 are presented in Figure 5.1.

A detailed account of the preparation of the complexes is presented in the experimental section. For the ligand system 2-mercaptothiazoline the compounds $[Cu(ttzH)_3Cl_2]$, $[Cu(ttzH)_3Br_2]$ $[Cu(ttzH)_2Br_2]$, and $[Cu^{II}Cu^{I}_3(ttz)_5]$ have been prepared. Where the ligand was 2-mercapto-1-methylimidazole the complexes $[Cu^{II}Cu^{I}(mmim)(mmimH)_2Cl]$ and $[Cu^{II}Cu^{I}(mmimH)_2Cl_3]$ were synthesised. [Cu(etu)OH] and [Cu(dipmim)Cl] were obtained from the ligands 2-mercaptoimidazoline and 4,5-diphenyl-2-mercaptoimidazole respectively. For the system 2-mercaptobenzimidazole the complexes $[Cu(mbim)_2(NH_3)(H_2O]$ and $[Cu(mbim)_2(H_2O)]$ were obtained. Also <u>in situ</u> cupric species are reported for the interaction of the appropriate copper salt with the ligands 2-mercaptobenzimidazole and 4-mercaptopyridine.

Reactivity studies in nitromethane, in which a gross modification of the 2-mercaptothiazoline ligand occurred in forming 3-(4,5 dihydro-2-thiazolyl)-2-thiazolidinethione, allowed the isolation of the new complex [Cu(tztdz)Br] from reaction of $[Cu(ttzH)_3Br_2]$, and the postulated products [Cu(tztdz)Cl], $[Cu(tztdz)Cl_2]$ and $[Cu(mimmimz)Cl_2]$ from $[Cu(ttzH)_3Cl_2]$ and $[Cu^{II}Cu^{I}(mmimH)_2Cl_3]$ starting materials.

5.2 RESULTS AND DISCUSSION

Elemental analyses and magnetic results for the complexes can be found in Table 5.1, selected infrared data in Table 5.2, electronic band

maxima in Table 5.3 and esr parameters in Table 5.4. To facilitate discussion and in an attempt to achieve a degree of homogeneity a ligand by ligand account for the complexes has been undertaken.

5.2.1 Complexes of 2-mercaptothiazoline

A flow diagram indicating the products formed and their interrelationship is shown in Figure 5.2.

The interaction of cupric halides with 2-mercaptothiazoline has been investigated by Devillanova and Verani(7) who observed that when a methanolic solution of CuX_2 (where X = Cl or Br) was added to the ligand in methanol at a metal:ligand ratio of 1:4 the cuprous species $[Cu(ttzH)_3X]$ were obtained. However if these complexes were not removed, and a further amount of CuX_2 added to bring the ratio to 1:3, coloured species appeared, which on standing yielded pale yellow cuprous complexes of the form $[Cu(ttzH)_2X]$. No attempt was made by the authors to characterise the coloured intermediates. Nevertheless if the ratio of metal:ligand is brought down to 1:1.54 immediately, green and brown complexes, corresponding to the formulations $[Cu(ttzH)_3Cl_2]$ and $[Cu(ttzH)_3Br_2]$ can be isolated.

It is possible to write a coherent scheme for the reaction processes supporting the formulation of the new cupric complexes. At a metal to ligand ratio of 1:4, copper is reduced and a cuprous complex and disulphide are produced according to the equation

$$CuX_2 + 4ttzH \longrightarrow [Cu^{I}(ttzH)_3X] + \tfrac{1}{2}(ttz\text{-}ttz) + HX.$$

Adding excess CuX_2 at this stage until the ratio is 1:3

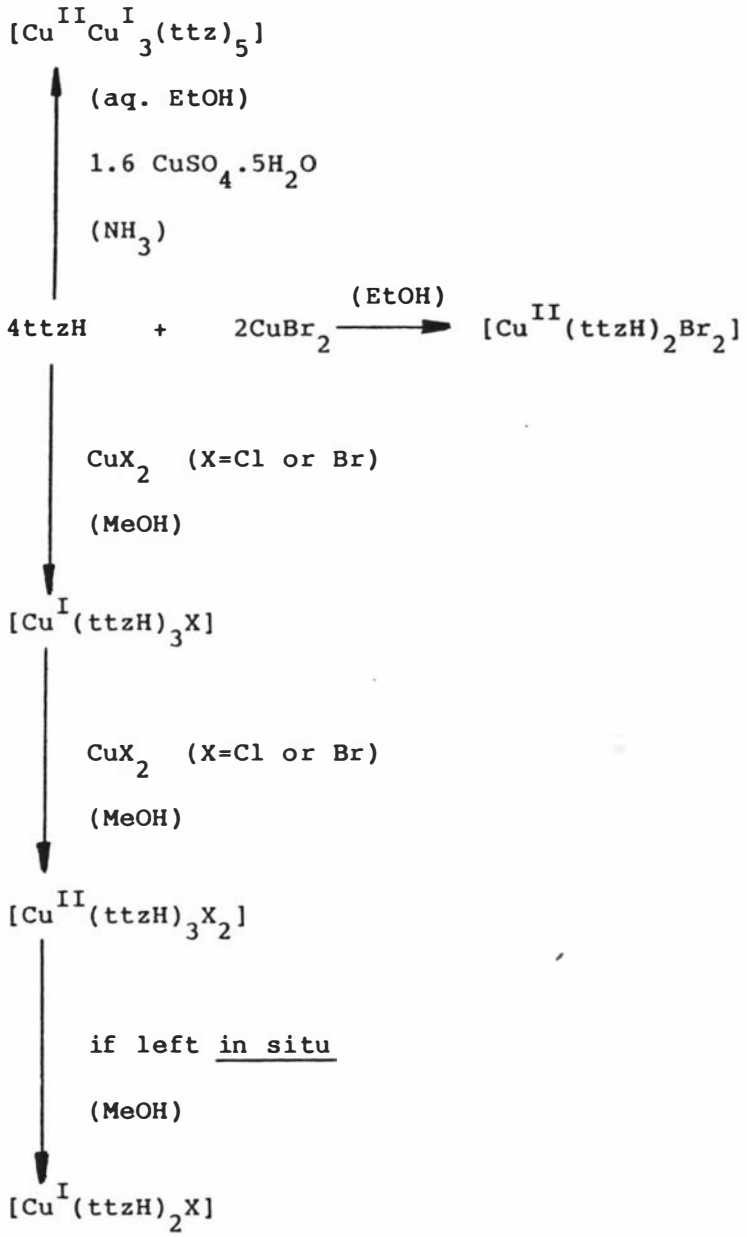


Figure 5.2 Flow diagram for the products derived from 2-mercaptothiazoline.

Table 5.1 Elemental analyses and magnetic data for the complexes

Compound	Colour	%C	%H	%N	Other	μeff/B.M.
$[Cu(ttzH)_3Cl_2$	green	21.0 (22.0)	3.1 (3.1)	8.1 (8.5)		1.16
$[Cu(ttzH)_3Br_2]$	brown	17.6 (18.6)	2.55 (2.6)	6.9 (7.2)	27.1[a] (27.5)	1.16
$[Cu(ttzH)_2Br_2]$	brown	16.3 (15.6)	2.85 (2.2)	5.95 (6.1)		1.28
$[Cu^{II}Cu^{I}_3(ttz)_5]$	grey	21.9 (21.3)	2.7 (2.4)	8.3 (8.3)		
$[Cu^{II}Cu^{I}(mmim)(mmimH)_2Cl_2]$	green	26.7 (26.7)	3.6 (3.3)	15.6 (15.95)	12.8[b] (13.1)	1.39
$[Cu^{II}Cu^{I}(mmimH)_2Cl_3]$	dark green	21.45 (20.8)	2.7 (2.6)	12.1 (12.2)	23.0[b] (23.0)	1.85
$[Cu(mbim)_2(H_2O)(NH_3)]$	grey blue	41.7 (42.4)	2.9 (3.8)	18.3 (17.7)		0.94
$[Cu(mbim)_2(H_2O)]$	grey	44.0 (44.25)	2.8 (3.2)	14.2 (14.75)		0.56
[Cu(etu)OH]	purple	20.0 (19.8)	3.2 (3.3)	15.7 (15.4)		0.70
[Cu(dipmim)Cl]	dark blue	51.4 (51.35)	4.1 (3.3)	7.5 (8.0)	10.2[b] (10.1)	1.10
[Cu(tztdz)Cl]	brown	23.7 (23.8)	2.9 (2.7)	9.3 (9.2)		
$[Cu(tztdz)Cl_2]$	green	21.5 (21.3)	2.5 (2.4)	8.3 (8.3)	20.2[b] (20.9)	
[Cu(tztdz)Br]	brown	20.5 (20.7)	2.5 (2.3)	8.0 (8.1)		
$[Cu(mimmimz)Cl_2]$	green	28.7 (29.2)	3.1 (3.1)	16.8 (17.05)	22.2[b] (21.6)	

Notes: a. %Br, b. %Cl.

Table 5.2 Selected principal infrared vibrations[a] for the complexes

Compound	ν(OH)	ν(NH)	Thioamide I	Thioamide II	Thioamide III	Thioamide IV
(ttzH)	-	3130[b]	1510[b]	1345	-	1085[b]
$[Cu(ttzH)_3Cl_2]$	-	3080	1515	1348	-	1092
$[Cu(ttzH)_3Br_2]$	-	3100	1518	1348	-	1092
$[Cu(ttzH)_2Br_2]$	-	3090	1525	1345(sh)	-	1100
mmimH	-	3115	-	1277[c]	1080[c]	770[c]
$[Cu^{II}Cu^{I}(mmim)(mmimH)_2Cl_2]$	-	3150	-	1280	1073	770
$[Cu^{II}Cu^{I}(mmimH)_2Cl_3]$	-	3100	-	1279	1080	762
$[Cu(mbim)_2(NH_3)(H_2O)]$	3350	3160	-	-	-	-
$[Cu(mbim)_2(H_2O)]$	3350	3160	-	-	-	-
[Cu(etu)OH]	3160					

Note: a. vibrations in cm^{-1} recorded as nujol mulls

b. from Ref. 7

c. assigned from Ref. 10

Table 5.3 Electronic spectra for the complexes

Compound	Solvent (state)	Band maxima (nm)	Assignment
$[Cu(ttzH)_3Cl_2]$	nujol mull	430(sh)	Cl→Cu
		732	d→d
	acetonitrile[a]	445(sh)	Cl→Cu
$[Cu(ttzH)_3Br_2]$	nujol mull	520	Br→Cu
		770	d→d
	acetonitrile[a]	535(sh)	Br→Cu
$[Cu(ttzH)_2Br_2]$	nujol mull	555(sh)	Br→Cu
		727	d→d
	acetonitrile[a]	540	Br→Cu
$[Cu^{II}Cu^{I}_3(ttz)_5]$	reflectance	ca 710	d→d
$[Cu^{II}Cu^{I}(mmim)(mmimH)_2Cl_2]$	nujol mull	430(sh)	Cl→Cu
		838	d→d
$[Cu^{II}Cu^{I}(mmimH)_2Cl_3]$	nujol null	425(sh)	Cl→Cu
		837	d→d
$[Cu(bimt)_2(H_2O)(NH_3)]$	reflectance	685	d→d
[Cu(etu)OH]	nujol mull	570(sh)	S→Cu
[Cu(dipmim)Cl]	nujol mull	620(br)	S→Cu
$[Cu(tztdz)Cl_2]$	nitromethane	420	Cl→Cu
		815	d→d
$[Cu(mimmimz)Cl_2]$	nujol mull	384	Cl→Cu
		770	d→d

Notes: a. freshly prepared solution, sh. shoulder

Table 5.4 Electronic spin resonance parameters for the complexes

compound	solvent (state)	g_{11}	$g_{\perp}$	$\lvert A_{11}\rvert$	$\lvert A_N\rvert$
$[Cu(ttzH)_3Cl_2]$	acetonitrile[c]	2.296	2.072	178	
$[Cu(ttzH)_3Br_2]$	acetonitrile[c]	2.292	2.066	178	15
$[Cu(ttzH)_2Br_2]$	acetonitrile[c]	2.306	2.081	167	
$[Cu^{II}Cu^{I}_3(ttz)_5]$	solid	2.196	2.082	166	
$[Cu^{II}Cu^{I}(mmim)(mmimH)_2Cl_2]$	powder		2.117[d]		
[Cu(etu)OH]	water/acetone	2.244	2.097	157	
[Cu(dipmim)Cl]	solid		2.063[d]		
$[Cu(mbim)_2(H_2O)(NH_3)]$	solid	2.263	2.078[e] 2.015[f]	156	
$[Cu(mbim)_2H_2O]$	solid	2.265	2.073[e] 2.019[f]	164	
$[Cu(tttdz)Cl_2]$	nitromethane	2.229	2.050	151	16
$[Cu(mimmimz)Cl_2]$	nitromethane	2.258	2.062	172	
Cu(II)-4(mmimH)	ethanol[g]	2.126	2.023	126	
Cu(II)-4(mpyH)	water[g]	2.092	2.015	158	
Cu(II)-4(mbimH)	water/ethanol[g]	2.129	2.027	132	

Notes: a. in units of $cm^{-1}x10^{-4}$ b. in units of Gauss

c. freshly prepared solution d. isotropic value e. g_1

f. g_2 g. compound prepared in situ

effectively causes oxidation of the cuprous complex to the corresponding cupric form $[Cu(ttzH)_3Cl_2]$:

$$[Cu^{I}(ttzH)_3X] + Cu^{II}X_2 \rightarrow [Cu^{II}(ttzH)_3X_2] + Cu^{I}X$$

Bringing the ratio down to 1:1.54 as was done in the preparation of the complexes ensures rapid and complete oxidation of $[Cu(ttzH)_3X]$. When the reaction was repeated, using ethanol as solvent, $[Cu(ttzH)_3Cl_2]$ was again the observed product for $CuCl_2$, however a new compound, $[Cu(ttzH)_2Br_2]$, resulted for the $CuBr_2$ reaction. If $[Cu(ttzH)_3X_2]$ is left in solution, it may then self-reduce to give $[Cu(ttzH)_2X]$ according to the equation:

$$[Cu^{II}(ttzH)_3X_2] \rightarrow [Cu^{I}(ttzH)_2X] + \tfrac{1}{2}(ttz\text{-}ttz) + HCl$$

One other cupric containing thiolato complex of 2-mercaptothiazoline was formed when copper(II) sulphate was added to an aqueous ethanolic solution of the ligand in a copper to ligand ratio of 1:2.5 the pH of which had been raised by adding ammonia. The grey compound produced had elemental analysis figures indicating the empirical formulation $[Cu_4(ttz)_5]$ for which a likely mixed valence formulation is $[Cu^{II}Cu^{I}_3(ttz)_5]$.

Basson and du Preez(9) have prepared a compound formulated as $[Cu(ttz)_2]$ from the reaction of 2-mercaptothiazoline and cupric nitrate in an ethanol/dimethyl sulphoxide solvent. On repeating the preparation, orange crystals of a compound with analytical figures and infrared spectrum more consistent with $[Cu(ttzH)_3NO_3]$ were obtained. This compound has been prepared previously(11). Similar doubts as to the compound's authenticity have been expressed by Preti and Tosi(6).

$[Cu(ttzH)_3Cl_2]$, $[Cu(ttzH)_3Br_2]$ and $[Cu(ttzH)_2Br_2]$ displayed some slight solubility in acetonitrile and nitromethane but were found to react in the latter producing new species involving modification of the ligand (see later). $[Cu^{II}Cu^{I}_3(ttz)_5]$ proved insoluble in most organic solvents and was susceptible to reduction. The lack of solubility and the depressed magnetic moments observed for the compounds are indicative of polymeric structures.

Infrared spectra

Considering infrared spectral evidence (see Table 5.2) the appearance of bands attributable to the thioamide moiety in $[Cu(ttzH)_3Cl_2]$ $[Cu(ttzH)_3Br_2]$ and $[Cu(ttzH)_2Br_2]$ confirmed that the ligand was present in the neutral thione form in these compounds. Conversely their absence or diminuition in intensity in $[Cu^{II}Cu^{I}_3(ttz)_5]$ is supportive of the ligand binding as a thiolate (see Chapter 2). The spectrum of $[Cu^{II}Cu^{I}_3(ttz)_5]$ is similar to that reported for [Cu(ttz)](6) which involves the ligand bound as a thiolate. The infrared spectra of $[Cu(ttzH)_3Cl_2]$ and $[Cu^{II}Cu^{I}_3(ttz)_5]$ are shown in Figure 5.3 and are illustrative of the differences observed when the ligand binds in the thioamide (former case) and thiolate (latter case) form.

The ν(NH) vibration occurring at 3130 cm^{-1} in the free ligand is shifted to 3080, 3100 and 3090 cm^{-1} for $[Cu(ttzH)_3Cl_2]$ $[Cu(ttzH)_3Br_2]$ and $[Cu(ttzH)_2Br_2]$ respectively, suggesting that the ligand coordination occurs through nitrogen(12). Conversely the behaviour of the band assigned to primarily ν(CS) (Thioamide IV) in blue shifting implicates a non-participatory role for thione sulphur(13). Nitrogen only coordination has been proposed also for cupric complexes

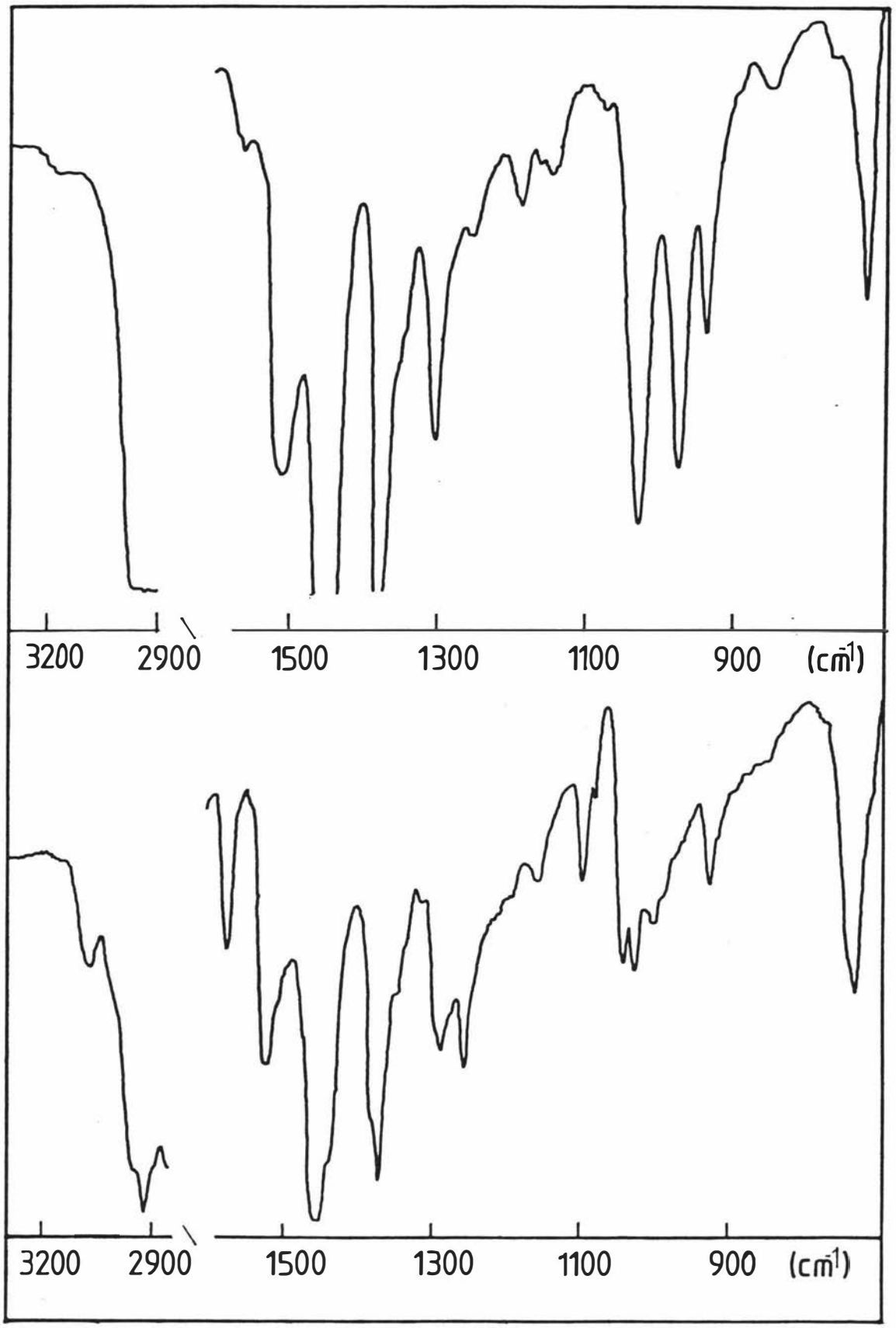


Figure 5.3 Infrared spectra of (a) $[Cu^{II}Cu^{I}_{3}(ttz)_{5}]$ and (b) $[Cu(ttzH)_{3}Cl_{2}]$ in nujol.

of the thioamide ligand, 2-meraptobenzoxazole(2). The close similarity of the spectrum of $[Cu^{II}Cu^{I}_{3}(ttz)_5]$ to that of the compound $[H(Os)_3(CO)_9(ttz)]$(14) for which X-ray crystallographic studies have confirmed chelation of the ligand through thiolate sulphur and endocyclic nitrogen, allows the assignment of a similar ligand coordination for it.

Electronic spectra

Electronic band maxima and postulated assignments are given in Table 5.3.

The visible spectra of the three thioamide complexes $[Cu(ttzH)_3Cl_2]$ $[Cu(ttzH)_3Br_2]$ and $[Cu(ttzH)_2Br_2]$ run as nujol mulls are dominated by absorbances at relatively high energy, which can be attributed to charge transfer transition of a ligand to metal variety (LMCT).

A shoulder at 430 nm for $[Cu(ttzH)_3Cl_2]$ is most likely a Cl $\longrightarrow$ Cu(LMCT) although a N$\rightarrow$Cu(LMCT) cannot be excluded since such bands can occur near 400 nm for tetrahedral imidazole type Cu(II) complexes(15). A distinct band at 520 nm for $[Cu(ttzH)_3Br_2]$ and a shoulder at 540 nm for $[Cu(ttzH)_2Br_2]$ may be assigned as analogous Br$\rightarrow$Cu(LMCT). The spectra of $[Cu(ttzH)_3Cl_2]$ and $[Cu(ttzH)_3Br_2]$ are shown in Figure 5-4. Only comparatively small changes are observed when the spectra are run in acetonitrile suggesting that the integrity of the complexes has been maintained. The reflectance spectrum of $[Cu^{II}Cu^{I}_{3}(ttz)_5]$ shows only a broad band at ca 710 nm which is probably of d-d character. The near u.v. region proved broad and featureless also.

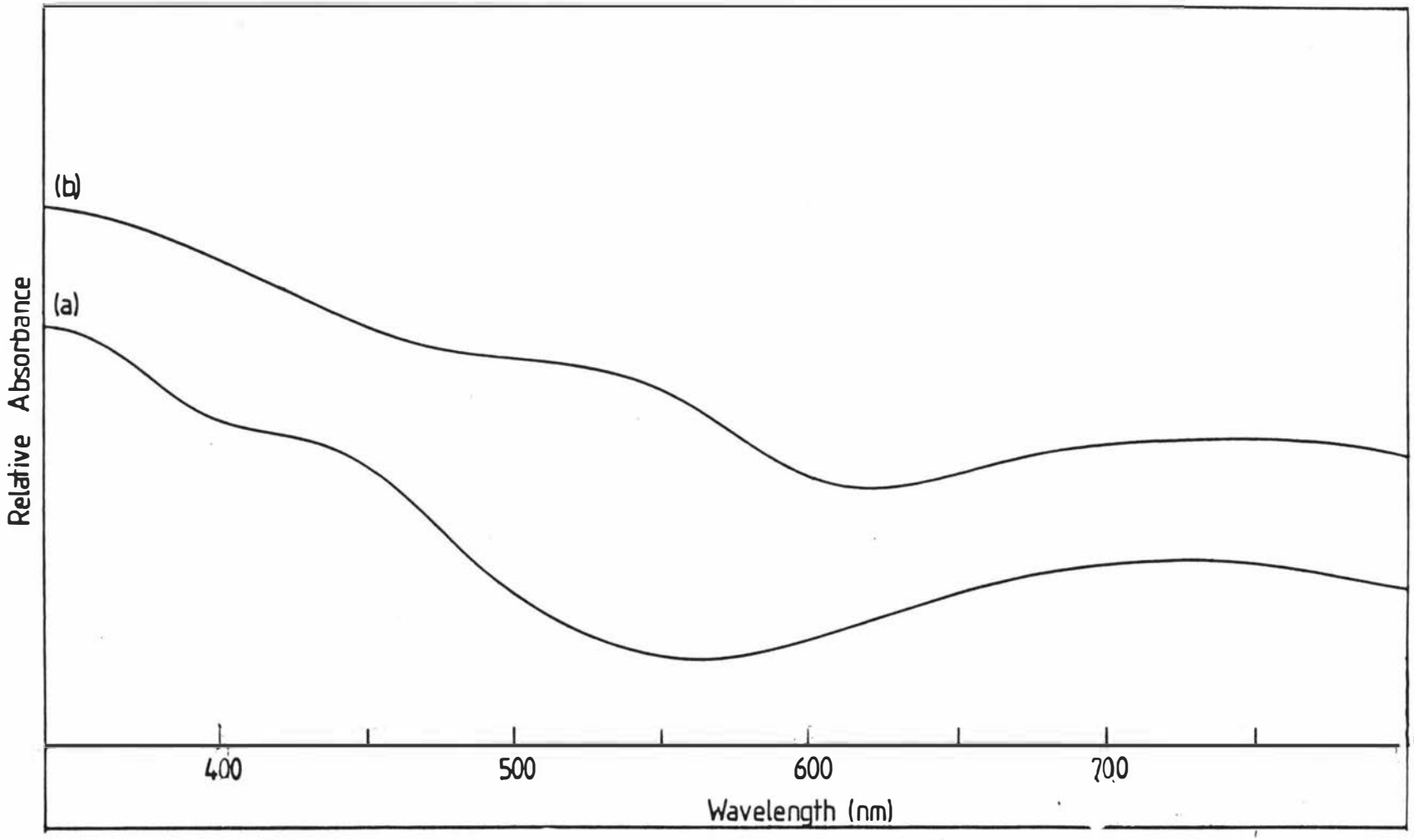


Figure 5.4 Electronic spectra of (a) $[Cu(ttzH)_3Cl_2]$ and (b) $[Cu(ttzH)_3Br_2]$ as nujol mulls.

Esr spectra

The esr parameters of the complexes $[Cu(ttzH)_3Cl_2]$ and $[Cu(ttzH)_3Br_2]$ in acetonitrile (see Figure 5.5) are very similar suggesting that their structures may be closely related. Seven lines due to nitrogen superhyperfine may be resolved in the $g_\perp$ region for both compounds although in $[Cu(ttzH)_3Cl_2]$ they are poorly resolved. This is the number predicted by selection rules for the interaction of three nitrogen donor nuclei and provides support for the contention that the ligand is coordinating via nitrogen.

The spectrum of $[Cu^{II}Cu^{I}_3(ttz)_5]$ run as a solid (see Figure 5.5) fortunately resolved the copper hyperfine components. When g_{11} is plotted versus $|A_{11}|$ the parameters fall in the region associated with an N_2S_2 donor set as defined by Peisach and Blumberg(16). The spectral lineshape is also consistent with this assignment.

The spectrum of $[Cu(ttzH)_2Br_2]$ in acetonitrile displays axial character and is not inconsistent with a square planar or tetragonal ligation.

Assignment of structures

Taking all available spectroscopic and magnetic evidence into consideration, it is likely therefore that both $[Cu(ttzH)_3Cl_2]$ and $[Cu(ttzH)_3Br_2]$ involve polymeric tetragonal structures in which the 2-mercaptothiazoline ligand, in thioketo configuration, binds through imino-type nitrogen. Bridging of copper atoms by halide ligands may occur. In the case of $[Cu^{II}Cu^{I}_3(ttz)_5]$ it appears that the cupric atom

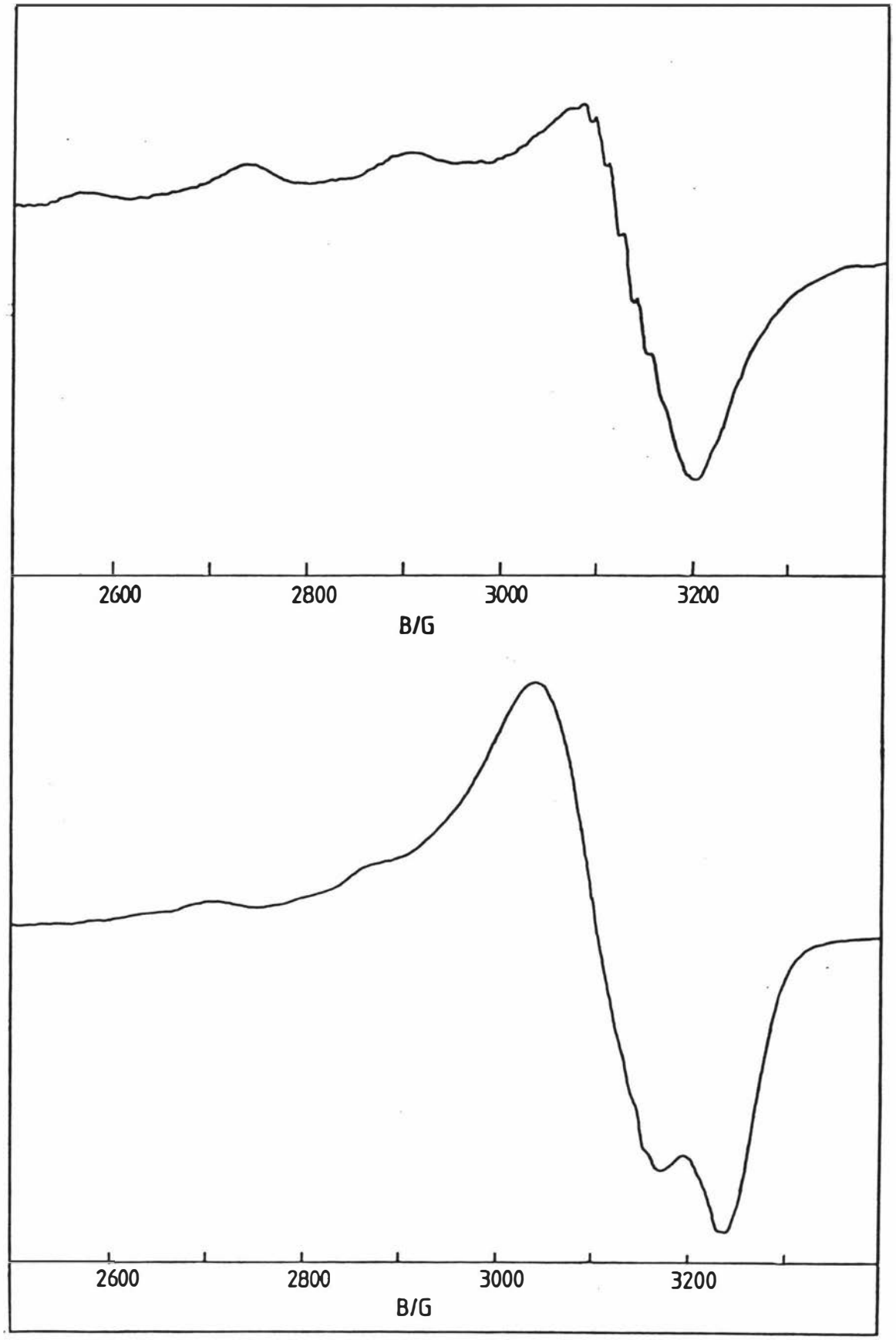


Figure 5.5 Esr spectra of (a) $[Cu(ttzH)_3Br_2]$ in acetonitrile and (b) $[Cu^{II}Cu^{I}_3(ttz)_5]$ as a solid.

is coordinated by a square planar N_2S_2 donor set, with the ligand in chelating form binding through thiolato-type sulphur, and nitrogen. The cuprous atoms of the cluster probably have a similar ligation, however their geometry is much more likely to be tetrahedral as in the cluster complex $[Cu^{II}_2Cu^{I}_{10}(mmim)_{12}(CH_3CN)_4]^{2+}$(8). Evidence for $[Cu(ttzH)_2Br_2]$ also suggests a tetragonal polymeric structure with possibly an N_2Br_2 in plane donor set.

Summary

The complexes $[Cu(ttzH)_3Cl_2]$, $[Cu(ttzH)_3Br_2]$ $[Cu(ttzH)_2Br_2]$ and $[Cu^{II}Cu^{I}_3(ttz)_5]$ have been prepared and characterised by infrared, electronic and esr spectroscopy and their magnetic chemistry. Tetragonal or square planar stereochemistries are postulated from experimental evidence. When in neutral form the 2-mercaptothiazoline ligand is envisaged as binding through nitrogen only, however sulphur nitrogen chelation is proposed when the molecule is deprotonated.

5.2.2 Complexes of 2-mercapto-1-methylimidazole

Reaction between cupric salts and the ligand 2-mercapto-1-methylimidazole provides a wealth of cupric, cuprous and mixed valence compounds depending very much on the nature of the salt anion, and, in some instances, the order in which the reactants are mixed. The extensive series of mixed valence compounds of the form $[Cu^{II}_2Cu^{I}_{10}(mmim)_{12}(H_2O)_4]^{2+}$ formed from the interaction of perchlorate and acetate salts have already been described (p.31) and will not be further considered. New products, however, are encountered when copper(II)chloride is used as the source of copper.

When an ethanolic solution of $CuCl_2.2H_2O$ is added to a solution of 2-mercapto-1-methylimidazole, also in ethanol, a number of colour changes and precipitates are observed as the mole ratio of copper to ligand increases. At a copper to ligand ratio of 1:10 an intense green colour is observed which gradually develops into a red solution only to disappear as the ratio approaches 1:3 and the cuprous thioamide compound $[Cu(mmimH)_2Cl]$ (see Chapter 2) precipitates. If the complex is left in the mother liquor and a further amount of $CuCl_2$ solution added to bring the copper to ligand ratio to 1:1.54 the flocculent white precipitate redissolves and a new fine green precipitate appears for which elemental analytical figures were consistent with a formulation of $[Cu^{II}Cu^{I}(mmim)(mmimH)_2Cl_2]$.

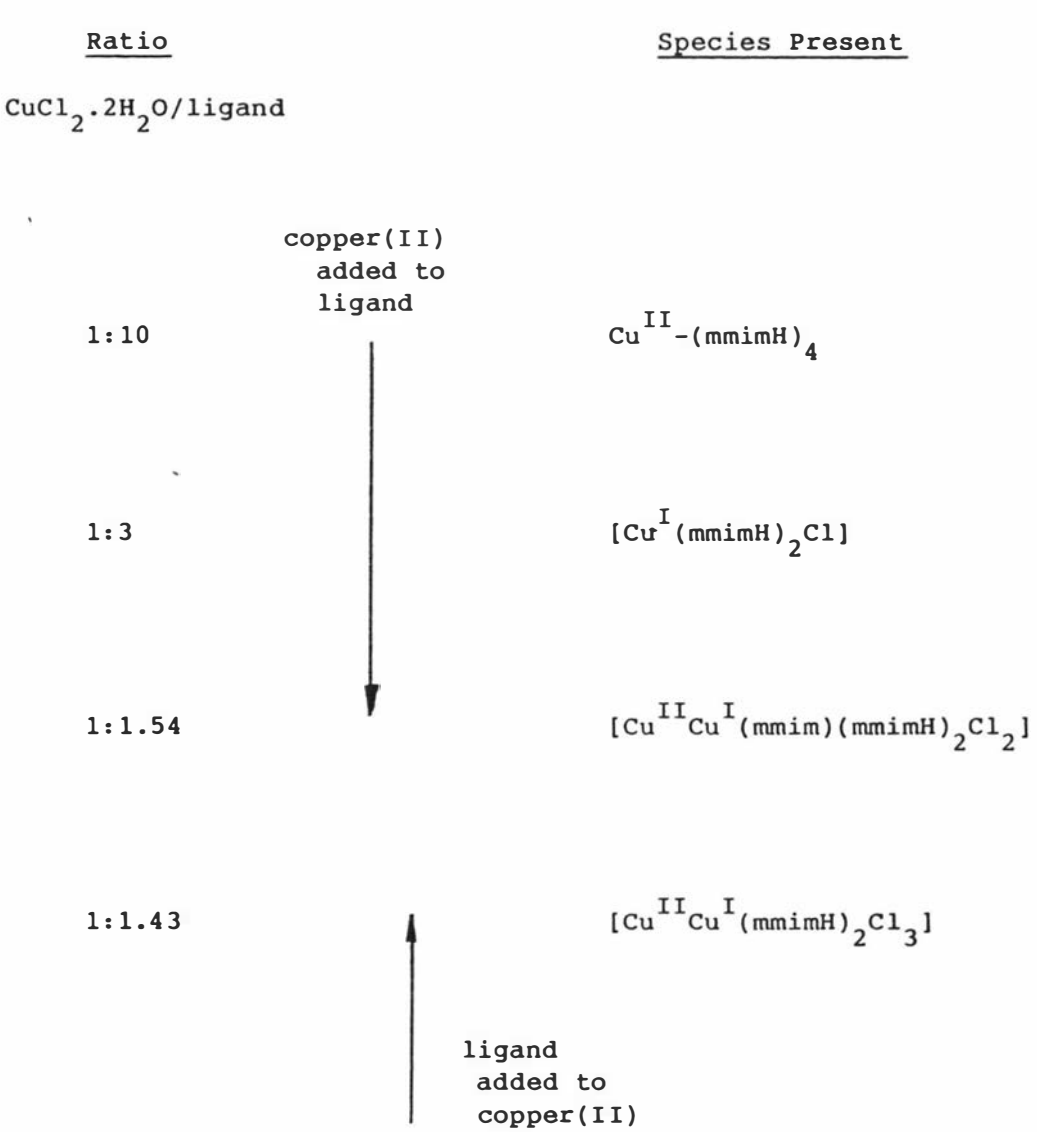
Alternatively if the process is reversed and ligand is added to copper, another green precipitate may be obtained at a copper to ligand ratio of 1:1.43. Elemental analysis indicated that a plausible formulation for this compound was $[Cu^{II}Cu^{I}(mmimH)_2Cl_3]$.

A flow chart for the compounds prepared from the 2-mercapto-1-methyl imidazole ligand is shown in Figure 5.6.

Infrared spectra

The appearance of the thioamide quartet and ν(NH) in the infrared spectra of $[Cu^{II}Cu^{I}(mmim)(mmimH)_2Cl_2]$ and $[Cu^{II}Cu^{I}(mmimH)_2Cl_3]$ confirmed the presence of the ligand in the thione form. Because both copper(I) and copper(II) are thought to be present, it is therefore possible that the ligand may adopt two modes of binding. Consequently analysis of the shifts of thioamide bands to denote atom coordination may not prove

Figure 5.6 Complexes obtained for various ratios of $CuCl_2.2H_2O$ and 2-mercapto-1-methylimidazole mixtures.



meaningful. Nonetheless the appearance of additional bands at 1270 cm^{-1} and 670 cm^{-1} in the spectrum of $[Cu^{II}Cu^{I}(mmim)(mmimH)_2Cl_2]$ indicates the presence of ligand in the thiolato form as well as the thione. Strong bands appearing at 270 cm^{-1} for $[Cu^{II}Cu^{I}(mmim)(mmimH)_2Cl_2]$ and at 290 cm^{-1} for $[Cu^{II}Cu^{I}(mmimH)_2Cl_3]$ may be tentatively assigned to Cu-Cl stretches. For instance Lever and Ramaswamy(17) have assigned ν(Cu-Cl) to a band at 305 cm^{-1} in $[Cu(2\text{-methylpyridine})_2Cl_2]$.

Electronic spectra

Although partially soluble in solvents such as chloroform, acetonitrile and nitromethane, significant changes from those of the solid state spectra indicated breakdown of the complexes was occurring. The nujol mull spectra of $[Cu^{II}Cu^{I}(mmim)(mmimH)_2Cl_2]$ and $[Cu^{II}Cu^{I}(mmimH)_2Cl_3]$ show great similarity suggesting that the environment of the cupric atom for both compounds may be quite similar. Both show a shoulder at *ca* 430 nm assigned to a chlorine to copper charge transfer transition, on the tail of an intense ligand band. Ligand field absorbance appear for both compounds at about 840 nm.

Esr spectra

The solid state spectrum of $[Cu^{II}Cu^{I}(mmim)(mmimH)_2Cl_2]$ displayed only a broad isotropism allowing few structural deductions. The yellow green compound prepared *in situ* appearing at a copper to ligand ratio of 1:10 (see p.) proved more amenable to study by this method. The esr spectrum of such a solution showed an exceptionally sharp lineshape allowing resolution of not only the A_{11} but also the $A_{\perp}$ component of the copper hyperfine. The spectrum is shown in Figure 5.7(a). The parameters are similar to those of many compounds

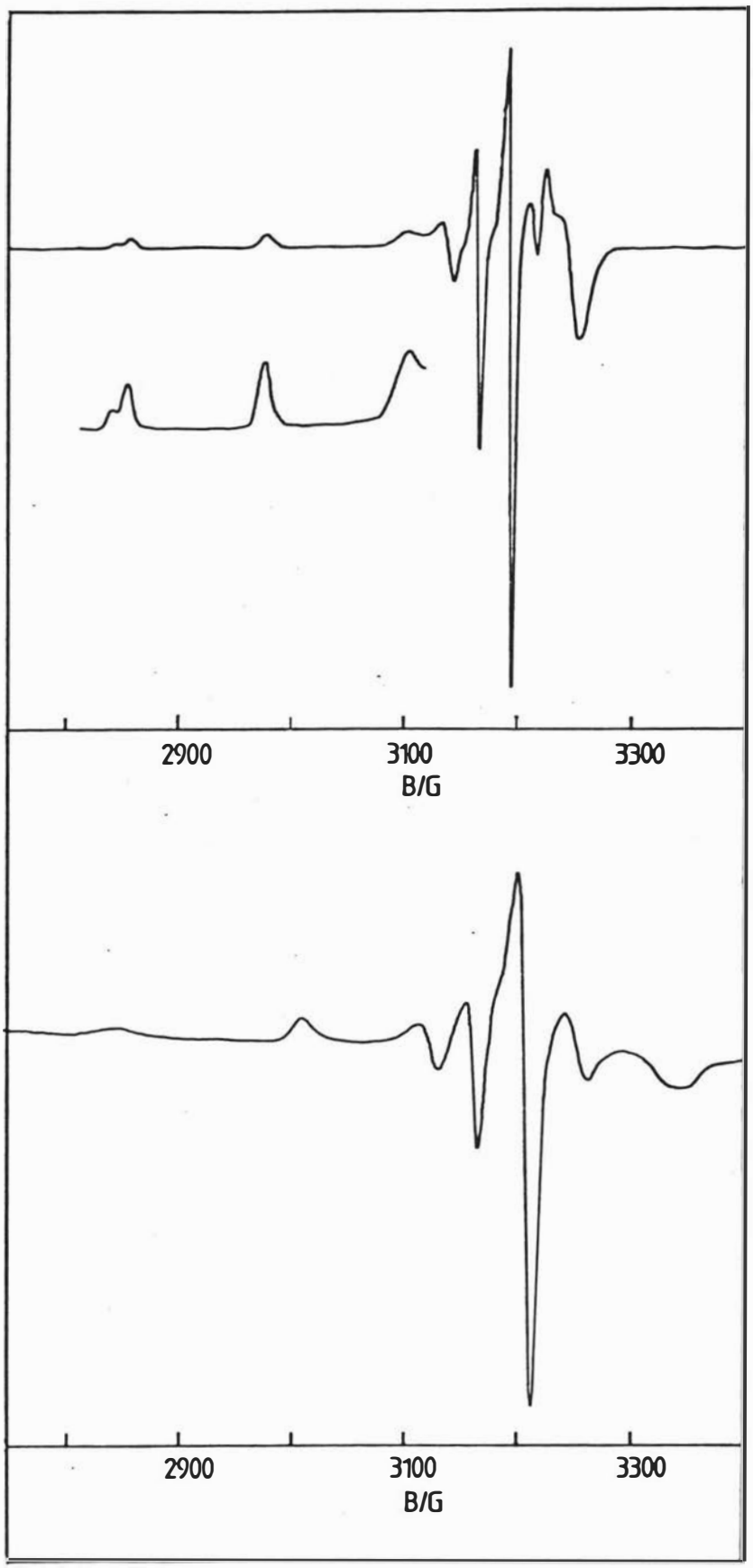


Figure 5.7 Esr spectra of

(a) Cu(II)-4(mmimH) in ethanol and

(b) Cu(II)-4(mpyH) in water.

containing an S_4 donor set(18). $^{63}Cu/^{65}Cu$ isotopic splitting resolvable on the lowest field copper hyperfine does not normally appear when nitrogen is bound(19). Further support for an S_4 coordination sphere comes from the similarity of the spectral lineshape to that of the well-characterised diethyldithiocarbamate system(20). As will be elaborated in Chapter 6 this lineshape is a general feature of S_4 ligated copper complexes.

2-mercapto-1-methyl imidazole is not the only thioamide ligand to produce such species. On interaction of $Cu(ClO_4)_2.6H_2O$ with an aqueous solution of 4-mercaptopyridine, and $CuCl_2.2H_2O$ with an aqueous ethanolic solution of 2-mercaptobenzimidazole, orange and yellow coloured solutions were obtained respectively with identical esr lineshapes to the 2-mercapto-1-methylimidazole compound, indicating that here also S_4 type compounds are being produced. The spectrum of the 4-mercapto-pyridine reaction is shown in Figure 5.7(b).

A point of importance is that the nature of the sulphur donor cannot be distinguished from the esr spectrum. Both thioether, thioketo and thiolate sulphurs interact to give similar parameters and lineshapes (see Chapter 6 p.198). However, the appearance of cuprous thioamide complexes from the reaction solutions when the ratio of copper to ligand is raised suggests that in the above cases the ligand may be binding in the thione form.

Summary

The complexes $[Cu^{II}Cu^{I}(mmim)(mmimH)_2Cl_2]$ and $[Cu^{II}Cu^{I}(mmimH)_2Cl_3]$ have been prepared. Infrared and esr spectroscopy has provided little

information, consequently few inferences have been drawn with regard to their structure. An *in situ* complex obtained when $CuCl_2.2H_2O$ is present in an excess of ligand has been assigned a $[Cu(mmimH)_4]^{2+}/S_4$ structure on the basis of its characteristic esr signal. Similar complexes are proposed for the ligands 4-mercaptopyridine and 2-mercaptobenzimidazole.

5.2.3 Complexes of 2-mercaptobenzimidazole 4,5-diphenyl-2-mercaptoimidazole and 2-mercaptoimidazoline

Adoption of a method employed by Kuras(4) involving the addition of an aqueous ammoniacal solution of ligand to copper sulphate allowed the new species $[Cu(mbim)_2(H_2O)(NH_3)]$ (from which $[Cu(mbim)_2(H_2O)]$ can be obtained by washing with ethanol) and [Cu(etu)OH] to be isolated. The complex [Cu(dipmim)Cl] however, precipitated from ethanolic solutions of $CuCl_2.2H_2O$ and ligand in the ratio 1:2.

Infrared spectra

Absence, or loss of intensity, of the thioamide bands again provides confirmation that the ligands are in the thiolate form as postulated for the various formulations. The spectra of $[Cu(mbim)_2(H_2O)(NH_3)]$ and $[Cu(mbim)_2(H_2O)]$ are very similar, with the exception of bands attributable to $\delta(NH_3)$ at *ca* 1600 cm^{-1} and $\rho(NH_3)$ at 806 cm^{-1} (21(a)) in the former. Further support for a thiolato ligand comes from the close resemblance of the spectra to that of the compound [Cu(2-thiamethylbenzimidazole)Cl_2](22). Here the ligand sulphhydryl group has been replaced by -SMe for which there are no thioamide vibrational modes. $\nu(OH)$ is discernible as a broad band in both compounds at 3350 cm^{-1}, and water, rather than hydroxo ligand is assigned by virtue of the $\delta(HOH)$ vibration at 1615 cm^{-1} (21(b)). On the other hand the

absence of such a band in the spectrum of [Cu(etu)OH] has been used to implicate the presence of hydroxide. Here ν(OH) appears at 3345 cm^{-1}. Ferraro et al (23) investigated a series of hydroxo bridged Cu(II) complexes and observed ν(OH) in the range 3600-3340 cm^{-1}. A band appearing at 1075 cm^{-1} has been assigned as ∂(OH). Finally a broad band centred at 545 cm^{-1} can probably be assigned as a ν(CuO) stretching vibration. McWhinnie(24) observed this mode at 515 cm^{-1} in $[Cu(bipyridyl)OH]_2(NO_3)_2$. The similarity in spectra between [Cu(etu)OH] and that of $[H(Os)_3(CO)_9etu]$(14) which has been shown to have a chelating ligand similarly allows tentative prediction of simultaneous coordination of thiolate sulphur and ring nitrogen in this case.

Electronic spectra

The intriguing blue and purple colours of some of these complexes are caused by thiolate-to-copper charge transfer transitions which are indicative of the binding of sulphur to copper. For the nujol mull spectra the bands appear at 570 nm (as a shoulder) for [Cu(etu)OH] and at 620 nm for [Cu(dipmim)Cl]. Only d-d bands could be resolved from the reflectance spectrum of $[Cu(mbim)_2(H_2O)(NH_3)]$, and the spectrum of $[Cu(mbim)_2(H_2O)]$ tailed into the visible region. Insolubility prevented the investigation and quantitation of these bands in solution.

Esr spectra

Well resolved spectra were obtained for all compounds except that of [Cu(dipmim)Cl] which did not show any copper hyperfine splittings. The spectrum of [Cu(etu)OH] shown in Figure 5.8 shows faint resolution of nitrogen superhyperfine suggesting that a nitrogen from the 2-mercaptoimidazoline ligand is bound. A similar spectrum was observed by Sugiura et al.(25) for Na[Cu(N-mercaptopropionylglycine)] to

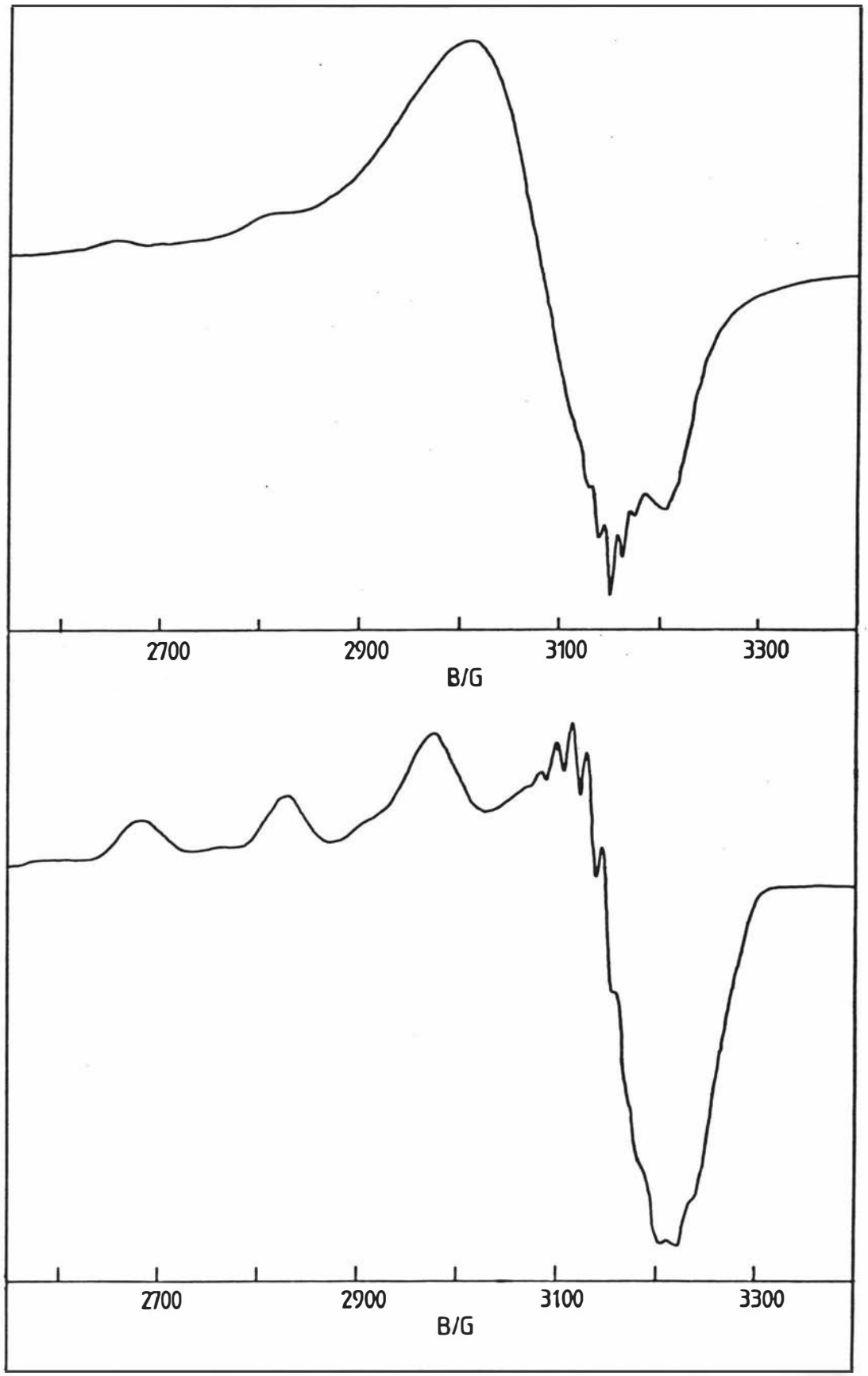


Figure 5.8 Esr spectra of (a) [Cu(etu)OH] in acetone/water and (b) [Cu(tztdz)Cl_2] in nitromethane

which was assigned an SNO_2 coordination sphere. As discussed in Chapter 6 an S_2O_2 ligation, possible for [Cu(etu)OH] if thiolato and hydroxo ligands were both bridging, shows particularly tight conformity to a linear region of g_{11} versus $|A_{11}|$. In this case the parameters fall outside the S_2O_2 line disfavouring such a structure.

The powder spectra of $[Cu(mbim)_2(H_2O)(NH_3)]$ and $[Cu(mbim)_2(H_2O)]$ are very similar intimating that the ammonia in the former may not coordinate strongly to copper. An interesting feature of the spectra is the appearance of rhombic character - two absorbances are particularly prominent in the $g_\perp$ region of $[Cu(mbim)_2(H_2O)(NH_3)]$ run at room temperature. Bencini et al.(26) have observed similar behaviour in the spectrum of five coordinate complexes intermediate in geometry between trigonal bipyramidal and square pyramidal.

Structural proposals

Unfortunately suitable crystals could not be obtained for any of the compounds so structural deductions are necessarily tentative.

The insoluble character and depressed magnetic moments are indicative of polymeric structures for the compounds. Evidence for [Cu(etu)OH] favours an SNO_2 donor set with a bridging hydroxo ligand suggested by the infrared spectrum. A structure consistent with these observations is shown in Figure 5.9. It is likely that a similar structure involving chlorine bridges may be present for [Cu(dipmim)Cl].

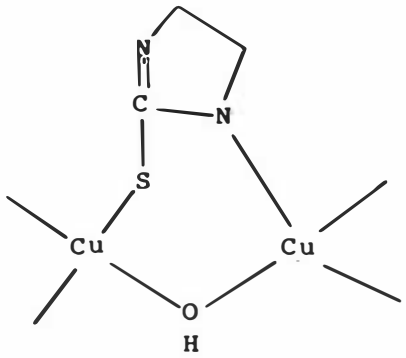


Figure 5.9 A possible structure for [Cu(etu)OH]

Polymeric structures with bridging 2-mercaptobenzimidazole ligands are suggested for $[Cu(mbim)_2(H_2O)(NH_3)]$ and $[Cu(mbim)_2(H_2O)]$ from data to hand, and a coordination sphere consisting of a planar S_2N_2 donor set from the two mbim molecules with an axial aquo ligand may be envisaged. It is apparent that the NH_3 ligand in $[Cu(mbim)_2(H_2O)(NH_3)]$ plays little part in coordination.

Summary

The complexes [Cu(etu)OH], [Cu(dipmim)Cl], $[Cu(mbim)_2(H_2O)(NH_3)]$ and $[Cu(mbim)_2(H_2O)]$ have been prepared and characterised by infrared, electronic and esr spectroscopy. Polymeric structures in which the ligands are bound through thiolato sulphur and imino nitrogen are likely.

5.3 REACTIVITY STUDIES IN NITROMETHANE

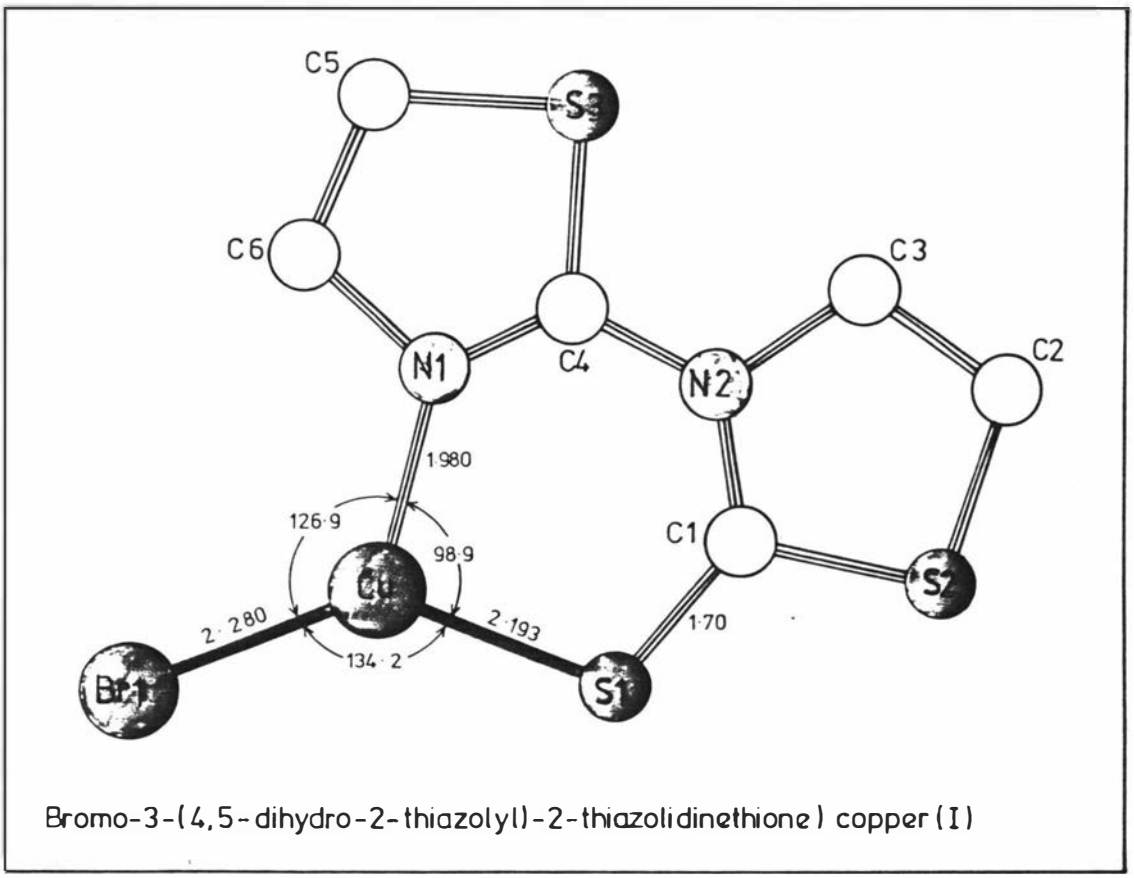
The compounds $[Cu(ttzH)_3Cl_2]$ and $[Cu(ttzH)_3Br_2]$ are partially soluble in nitromethane. Attempts to grow crystals of these compounds for X-ray diffraction studies from this solvent appeared successful - suitable green and brown needles were obtained respectively. However

the infrared spectrum of the crystallised product was markedly different to that of the starting material, with evidence suggesting that the thioamide chromophore was no longer present in the ligands, by token of the absence of ν(NH) and other principal thioamide absorptions. However it was not until the structure of the brown crystals was determined through X-ray crystallography by Dr G. Gainsford, DSIR, Wellington, that the true nature of the considerable rearrangement that had occurred for the ligand was resolved.

The structure of the complex is shown in Figure 5.10. Two 2-mercaptothiazoline ligands have reacted in such a way that one sulphur has been lost with the formation of a new C-N bond between the ligands in place of the original C-S bond. A new ligand 3-(4,5-dihydro-2-thiazolyl)-2-thiazolidinethione) (tztdz) has thus been formed.

Tztdz effectively chelates through imimo nitrogen and thione sulphur atoms. A bromine atom is the third ligand in a trigonal planar arrangement of atoms around Cu(I). Bond lengths and angles for the complex [Cu(tztdz)Br] can be found in Table 5.5. A diagram indicating the non-planarity of the ligand rings and the flattened boat character of the six-membered ring containing copper (the prows being Cu and N(2)) is shown in Figure 5.11.

A feature of the complex is the length of the Cu-Br bond which at 2.280 Å is short compared to other Cu(I) complexes of similar geometry. For instance [Cu(triphenylphosphine)Br](27) and $[Cu_2Br_4]^{2-}$(28), both trigonal planar complexes, have terminal Cu-Br bonds of 2.345Å and 2.328 Å respectively.



Bromo-3-(4,5-dihydro-2-thiazolyl)-2-thiazolidinethione) copper (I)

Figure 5.10 Ligand geometry about copper in [Cu(tztdz)Br]

Table 5.5 Bond lengths (Å) and angles (°)

for [Cu(tztdz)Br]

(a) Bond lengths

Cu -Br	2.280	N(1)-C(4)	1.271
Cu -S(1)	2.193	N(1)-C(6)	1.472
Cu -N(1)	1.980	N(2)-C(1)	1.365
S(1)-C(1)	1.664	N(2)-C(3)	1.496
S(2)-C(1)	1.734	N(2)-C(4)	1.399
S(2)-C(2)	1.805	C(2)-C(3)	1.511
S(3)-C(4)	1.768	C(5)-C(6)	1.522
S(3)-C(5)	1.803		

(b) Bond angles

Br -Cu -S(1)	134.2
Br -Cu -N(1)	126.9
S(1)-Cu -N(1)	98.9
Cu -S(1)-C(1)	106.4
Cu -N(1)-C(4)	128.8
Cu -N(1)-C(6)	118.8

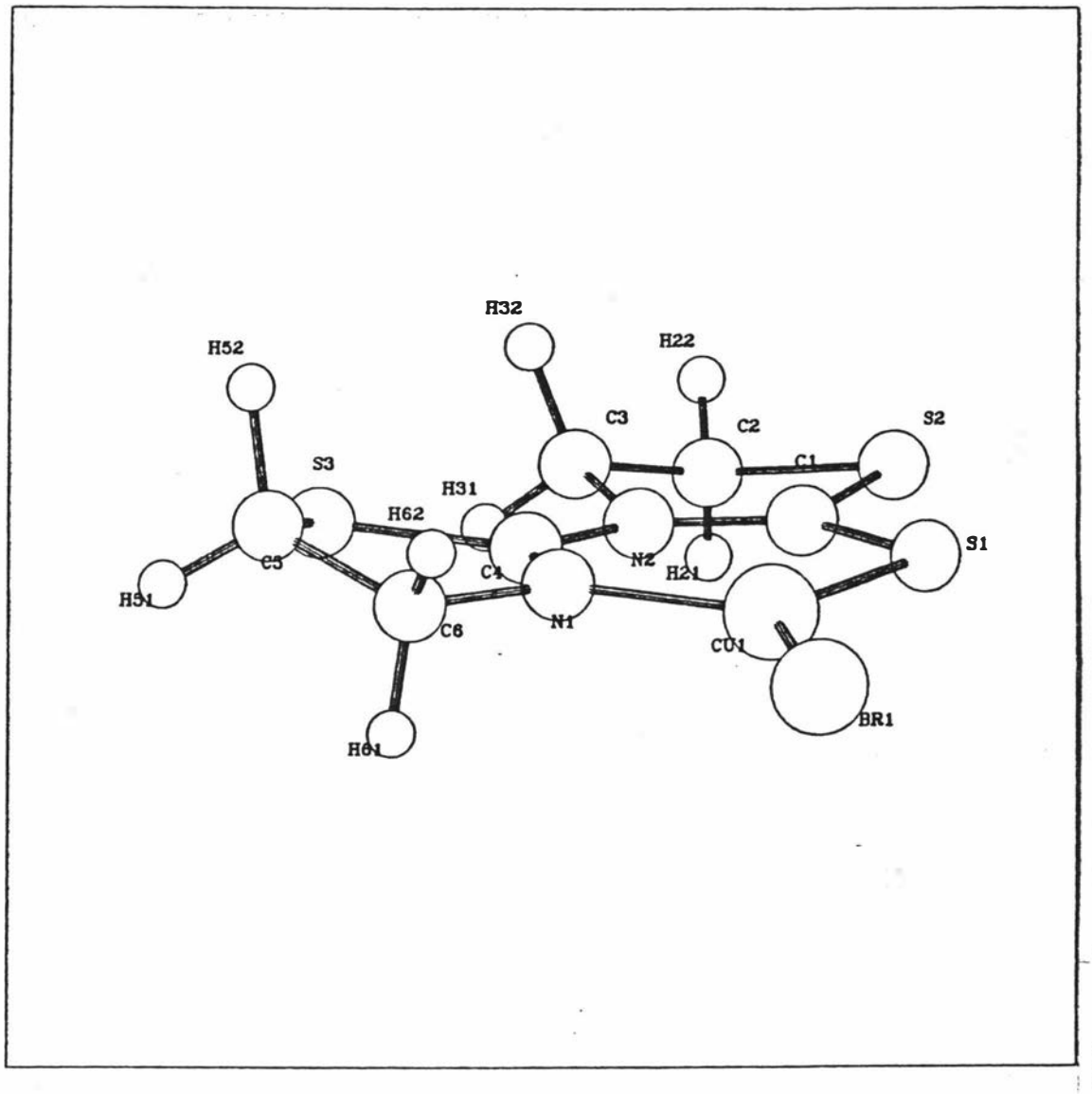


Figure 5.11 Flattened boat character and non-planar rings in [Cu(tztdz)Br].

The reaction of 2-mercaptothiazoline or its derivatives to produce tztdz is not unknown in organic chemistry. For instance Clark and Sykes(29) reported its preparation from treatment of 2-mercaptothiazoline with hydrogen peroxide. Barrett, Barton and Colle(30) obtained tztdz from the reaction of bis-1,3-thiazolin-2-yl-disulphide with trifluoroacetic acid in chloroform. Tztdz was also a product in the reaction of [Tl(ttz)] with thiophosgene(31).

A plausible mechanism involving the formation of disulphide and subsequent intramolecular loss of sulphur based on the postulation of Barret et al.(30) may be proposed and is shown in Figure 5.12. The reaction may be interpreted as being promoted by copper via the oxidation of 2-mercaptothiazoline to the disulphide.

Having established by crystallography that ligand modification for 2-mercaptothiazoline can occur, it is possible to formulate products from reaction of $[Cu(ttzH)_3Cl_2]$ in nitromethane taking this into account. Thus the green crystals obtained from fresh samples of $[Cu(ttzH)_3Cl_2]$ have been assigned as the cupric complex $[Cu(tztdz)Cl_2]$. On ageing, samples of the normally green $[Cu(ttzH)_3Cl_2]$ are seen to adopt a brown coloured coating, and on dissolution in nitromethane an additional brown crystalline complex analysing as [Cu(tztdz)Cl] can be obtained.

A dark-green crystalline product obtained from reaction of $[Cu^{II}Cu^{I}(mmim)(mmimH)_2Cl_2]$ or $[Cu^{II}Cu^{I}(mmimH)_2Cl_3]$ in nitromethane may conceivably have involved an analogous modification of the 2-mercapto-1-methylimidazole system to produce a compound involving the new ligand 3-(2,1-methylimidazolyl)-2,1-methylimidazolinethione (mimmimz) i.e.

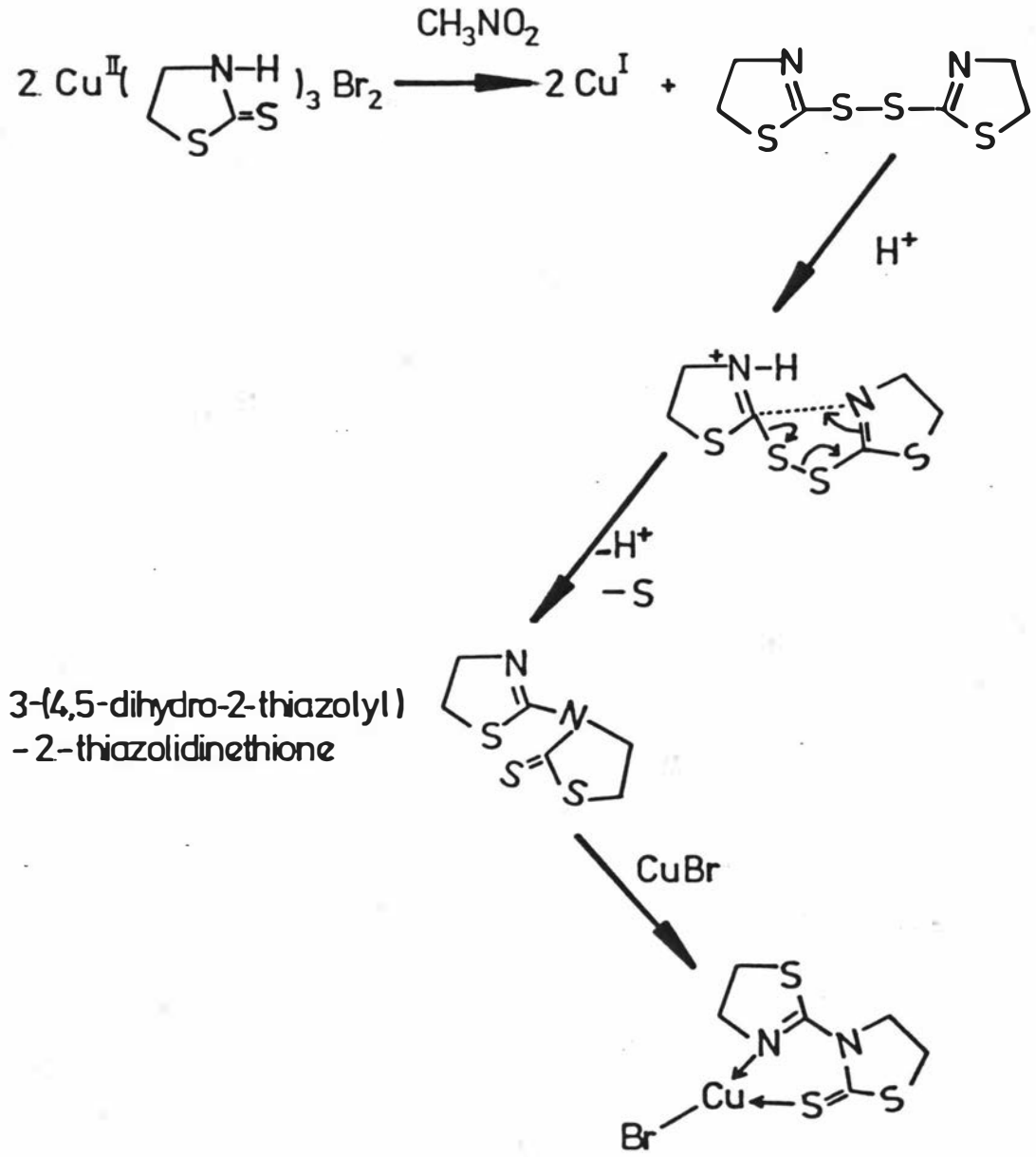


Figure 5.12 A mechanism for the formation of [Cu(tztdz)Br] from $[Cu(ttzH)_3Br_2]$

$[Cu(mimmimz)Cl_2]$.

A flow diagram showing proposed reaction products for the reaction of cupric thioamide starting materials in nitromethane is shown in Figure 5.13.

Spectroscopic evidence for the cupric compounds $[Cu(tztdz)Cl_2]$ and $[Cu(mimmimz)Cl_2]$ is consistent with such formulations. The esr spectra of both (Table 5.4) have parameters indicating a square planar or tetragonal environment about copper. In $[Cu(tztdz)Cl_2]$ (Figure 5.8(b)) nitrogen superhyperfine can be distinctly resolved confirming ligation of a nitrogen atom. Cl→Cu (LMCT) transitions are prominent also in the electronic spectra of both complexes (see Table 5.3).

Further investigation is required to establish the exact role of copper in promoting sulphur extrusion from 2-mercaptothiazoline and to verify that mimmimz is indeed the new ligand formed from reactions involving 2-mercapto-1-methylimidazole.

Summary

$[Cu(ttzH)_3Br_2]$ reacts in nitromethane to produce [Cu(tztdz)Br] which has been definitively characterised by X-ray crystallography. In the reaction two 2-mercaptothiazoline ligands have combined with loss of sulphur to form a new ligand - 3-(4,5-dihydro-2-thiazolyl)-2-thiazolidinethione. Similar reactions are envisaged to occur in the production of [Cu(tztdz)Cl] and $[Cu(tztdz)Cl_2]$ from $[Cu(ttzH)_3Cl_2]$ and $[Cu(mimmimz)Cl_2]$ from $[Cu^{II}Cu^{I}(mmimH)_2Cl_3]$.

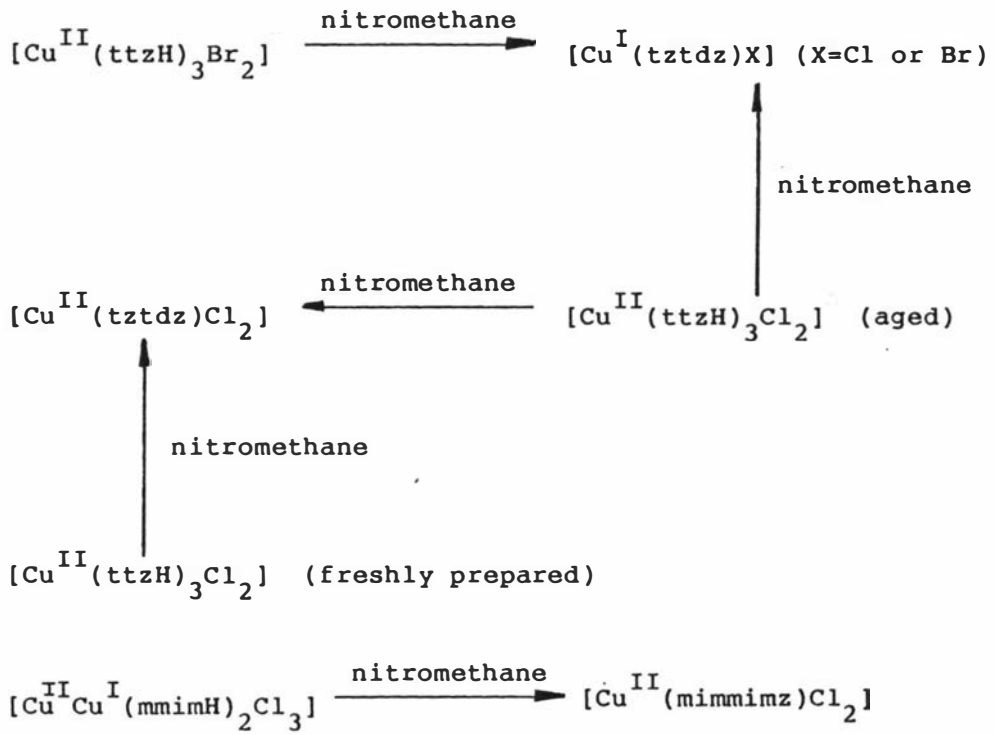


Figure 5.13 Flow diagram for the reactivity studies in nitromethane

5.4 EXPERIMENTAL

5.4.1 Instrumentation

This was as described in 1.7.1.

5.4.2 Preparation of the complexes

$[Cu(ttzH)_3Cl_2]$

$CuCl_2.2H_2O$ (1.11g, 6.5 mmol) in methanol (70 cm^3) was added to the ligand (1.19 g, 10 mmol) in methanol (150 cm^3). The green product was collected and washed with methanol and chloroform. Yield 1.17 g (95%).

$[Cu(ttzH)_3Br_2]$

$CuBr_2$ (1.50 g, 6.7 mmol) in methanol (100 cm^3) was added to ligand (1.19 g, 10 mmol) in methanol (250 cm^3). The dark brown product was washed with methanol and chloroform. Yield: 1.20 g (83%).

$[Cu(ttzH)_2Br_2]$

$CuBr_2$ (0.91, 4.1 mmol) in ethanol (75 cm^3) was added to ligand (0.75 g, 6.3 mmol). The dark brown product was collected and washed with ethanol and chloroform.

$[Cu^{II}Cu_3{}^{I}(ttz)_5]$, $[Cu(mbim)_2(H_2O)(NH_3)]$ and $[Cu(mbim)_2(H_2O)]$

12 cm^3 of a 1% solution (in 50% ethanol) of the appropriate ligand containing 7 drops of concentrated NH_4OH was added to 0.1 g $CuSO_4.5H_2O$

in water (20 cm^3). The resulting products - $[Cu^{II}Cu_3^{i}(ttz)_5]$(I) and $[Cu(bimt)_2(H_2O)(NH_3)]$(II) were carefully washed with 50% ethanol solution.

Yield of (I): 0.10 g (90%), Yield of (II): 0.15 g (90%). $[Cu(mbim)_2(H_2O)]$ was obtained by washing $[Cu(mbim)_2(H_2O)(NH_3)]$ with absolute ethanol after synthesis.

[Cu(etu)OH]

A solution of 2-mercaptoimidazoline (0.41 g, 4.0 mmol) in water (50 cm^3) containing 28 drops concentrated NH_4OH was added slowly to $CuSO_4.5H_2O$ (0.50 g, 2.0 mmol) in water (30 cm^3). The very fine purple precipitate produced was collected and washed with water. Yield: 0.1 g (30%).

[Cu(dipmim)Cl]

$CuCl_2.2H_2O$ (0.68, 2.0 mmol) in ethanol was added dropwise to the ligand (1.0 g, 4.0 mmol) in ethanol (350 cm^3). An intense yellow solution resulted which on standing for 2 hours produced a flocculent blue precipitate which was collected and washed with ethanol.

$[Cu^{II}Cu^{I}(mmim)(mmimH)_2Cl_2]$

$CuCl_2.2H_2O$ (1.11 g, 6.6 mmol) in ethanol (70 cm^3) was added dropwise to 2-mercapto-1-methylimidazole (1.14 g, 10.0 mmol) in ethanol (100 cm^3). The fine bright green precipitate produced was collected and washed with chloroform and ethanol.

$[Cu^{II}Cu^{I}(mmimH)_2Cl_3]$

2-mercapto-1-methylimidazole (1.67 g, 14.6 mmol) in ethanol (150 cm^3) was added to $CuCl_2.2H_2O$ (1.729 g, 1.0 mmol) in ethanol (100 cm^3). The yellow green precipitate obtained was washed with chloroform and ethanol prior to vacuum drying. Over a period of four days the yellow green colour became progressively more dark. Yield: 1.25 g (55%).

$[Cu^{II}(tztdz)Cl_2]$, $[Cu^{I}(tztdz)Br]$ and $[Cu^{I}(tztdz)Cl]$

0.80 g of $[Cu(ttzH)_3Cl_2]$ or $[Cu(ttzH)_3Br_2]$ were dissolved with heating in nitromethane (care should be taken as nitromethane is potentially explosive on heating) and the solutions filtered to remove undissolved starting material. The green and brown respective solutions were then filtered four times within the next three hours to remove co-precipitates of cuprous compounds. When aged $[Cu(ttzH)_3Cl_2]$ was used, the compound $[Cu^{I}(tztdz)Cl]$ could be isolated within one hour of preparation as brown needle-like crystals and separated from the remaining mother liquor. The compounds $[Cu^{II}(tztdz)Cl_2]$ and $[Cu^{I}(tztdz)Br]$ appeared from the appropriate solution on standing overnight and were collected and vacuum dried.

$[Cu^{II}(mimmimz)Cl_2]$

A similar procedure to the above preparations was used except 0.6 g of $[Cu^{II}Cu^{I}(mmimH)_2Cl_3]$ and 30 cm^3 of nitromethane were used. Crystals of product appeared within one week, which were collected and vacuum dried.

Preparation of *in situ* species.

Cu(II)-4(mmimH): $CuCl_2.2H_2O$ (0.018 g) in ethanol (2 cm^3) was added to mmimH (0.2 g) in ethanol (20 cm^3) to give a bright green solution.

. Cu(II)-4(mpyH): $Cu(ClO_4)_2.6H_2O$ (0.171 g) in water (10 cm^3) was added to mpyH (0.222 g) in water (50 cm^3) to give an orange solution.

Cu(II)-4(mbimH): $CuCl_2.2H_2O$ (0.085 g) in water (20 cm^3) was added to ligand (0.300 g) in 50% ethanol (50 cm^3). A yellow solution was obtained with much co-precipitation of [Cu(mbimH)Cl].

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CHAPTER 6

A SPECTROSCOPIC INVESTIGATION OF SOME CUPRIC AND MIXED VALENCE THIOLATE COMPLEXES

Introduction

One of the greatest problems confronting investigators of the cupric-thiolate interaction is that of characterising the nature and the stoichiometry of their compounds. This condition arises because in most cases the species are either metastable solutions, or, if isolatible as solids, are too amorphous for crystallographic analysis(1). Consequently it is of importance that the investigative techniques available be developed to their full potential for providing structural information.

In this chapter a number of different cupric thiolate species involving a variety of co-ligating atoms have been synthesised with the intention of studying the changes in spectral features, particularly esr, as the coordinating atoms around copper are changed. With respect to the esr technique emphasis has been placed here on the spectral lineshapes associated with various sets of bonding atoms. In this way primary coordination spheres of S_4, S_2O_2, S_2N_2, SO_3 and O_4(where the term S_4 implies the ligation of four sulphur donor atoms; likewise S_2O_2 refers to a donor quartet consisting of two sulphurs and two oxygens and so on) are shown to give spectra which are characteristic and differentiable. Such information is valuable not only for its aid in interpretation of the more classic inorganic thiolate complexes, but also for the use of esr as a probe in bioinorganic chemistry. For

instance recently Antholine and Taneka(2) were able to implicate preferential binding of a thiolato cysteine in cat haemoglobin (as opposed to an N histidyl donor in human haemoglobin) to the anti-tumour agent [Cu(2-formylpyridinemonothiosemi- carbazone)]$^{+}$ on the basis of the characteristic S_2N_2 type esr spectrum obtained.

In copper esr studies it is from the g_{11} and $|A_{11}|$ parameters that most structural inferences are made(3). Thompson et al.(4) have considered the factors which determine the magnitude of g_{11} and $|A_{11}|$ in four coordinate cupric complexes. The most important factor for determining g_{11} is the nature of the ligands. Atoms which are capable of delocalising the unpaired spin density away from the copper nucleus via a more covalent interaction (sulphur and to a lesser extent nitrogen and chlorine are exponents of this) promote low g_{11} values, whereas those which form less covalent bonds with copper, and are more electronegative, give rise to high values of g_{11}. Thus the parameter increases in the series $S_4, N_2S_2, N_4, N_3O, N_2O_2, O_4$. In addition it has been shown that g_{11} increases as the coordination geometry is distorted from square planar to tetrahedral for a number of CuN_4, CuN_2O_2 and CuS_4 derivatives(5,6). Also the overall charge on the complex has a small effect, g_{11} increasing as the charge becomes more positive(3).

Geometry is probably the single most important factor in determining the size of $|A_{11}|$, and this has been discussed fully in Chapter 1. To a lesser extent the nature of the donor atoms affect $|A_{11}|$. Thus substitution of an oxygen donor ligand for a sulphur ligand may decrease $|A_{11}|$(7). Trends are however less clear.

A graphic plot of g_{11} versus $|A_{11}|$ for a particular ligation may

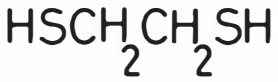
thus give a set of points in an approximate straight line(3) the coordinates depending on the degree of distortion towards tetrahedral geometry and the charge on the complex. By virtue of the dependency of g_{11} on the coordination sphere, the straight lines for different donor sets will be separated. Where plausible coordinating atoms are present in an unknown compound the fitting of the point to a particular ligation line can be a good indication of that donor set being present(3).

In this chapter, then, the strength of the esr technique in providing details regarding the nature of the ligands surrounding copper(II) in cupric thiolate compounds is illustrated. For some of the compounds prepared here the method is indeed the only one available to give such information, in instances where the complex is amorphous and insoluble. A systematic discussion of the various coordination spheres represented by the new complexes, with special emphasis on their distinctive esr spectra has therefore been conducted. This study was not intended to be rigorous, rather the moving impetus was to reveal trends and patterns which have not been emphasised fully in the literature. Coinciding with the study of S_2N_2 species, a more detailed analysis of the esr spectrum of the anti-tumour agent [Cu(KTS)] has been performed in an attempt to clarify some interestng literature deductions(8) with regard to ligand hinderance to the complex's susceptibility to axial coordination.

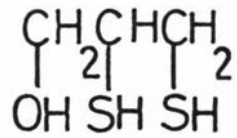
6.1 SYNTHESIS OF THE COMPOUNDS

Cupric containing thiolate complexes for a number of different thiol ligands have been isolated as solids, or where this was not possible, prepared <u>in situ</u> in solution. For the solid species,

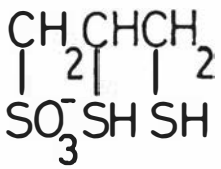
Figure 6.1 Ligands discussed in this chapter and their abbreviations.



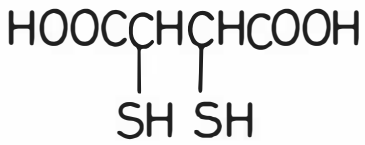
1,2-dimercaptoethane (dimetH_2)



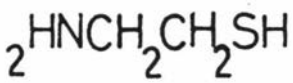
2,3-dimercaptopropanol (dimprolH_2)



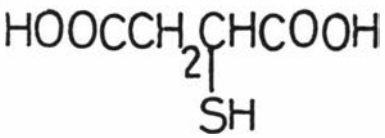
2,3 -dimercaptopropanesulphonate



2,3-dimercaptosuccinic acid

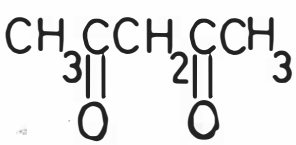


cysteamine

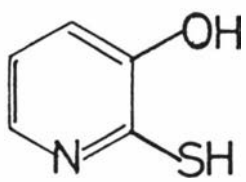


thiomalic acid

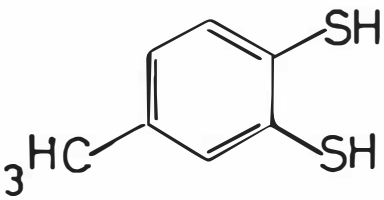
sodium thioglycolate



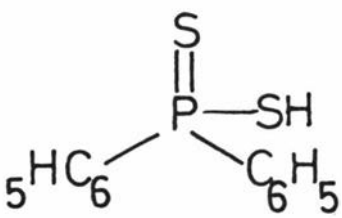
acetylacetone



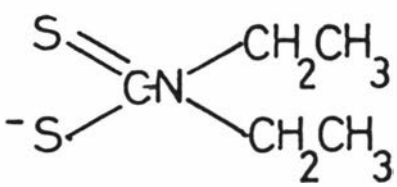
2-mercapto-3-pyridinol (mpoH_2)



3,4-dimercaptotoluene (dimtolH_2)

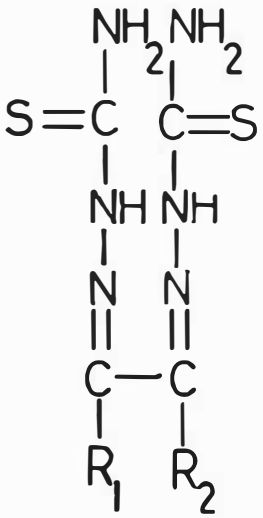


diphenyldithiophosphinic acid



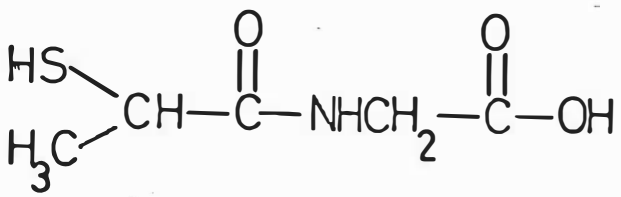
N,N-diethyldithiocarbamate (edtc)

Figure 6.1 Contd.

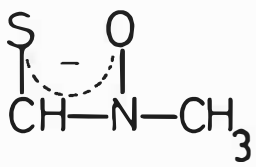


R_1	R_2	Name
C_6H_5	H	phenylglyoxaldtscH_2
C_6H_5	C_6H_5	benzildtscH_2
CH_3	CH_3	diacetyldtscH_2
$CH_3CHOC_2H_5$	H	3-ethoxy-2-oxo-butyraldehydedtscH_2
$CH_3CHOC_7H_{15}$	H	3-n-heptoxy-2-oxo-butyraldehydedtscH_2

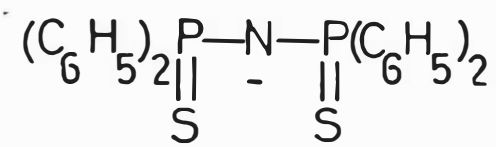
(dtscH_2 = bis thiosemicarbazide)



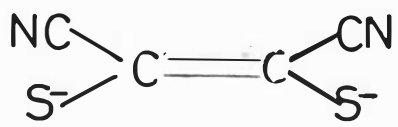
N-2-mercaptopropionylglycine



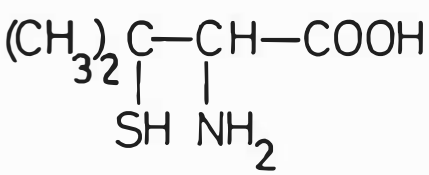
N-methylformothiohydroxamate (HC(=S)N(Me)O)



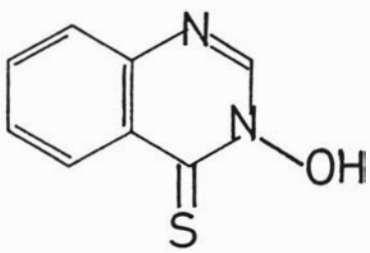
tetraphenyldithioimidodiphosphinate



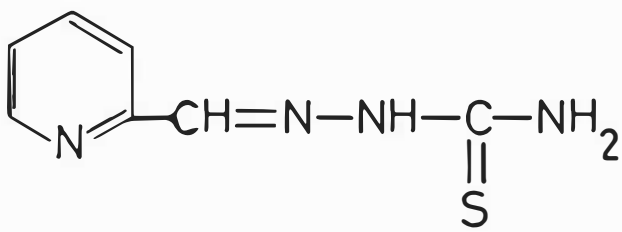
maleonitriledithiolate



penicillamine



3-hydroxyquinazoline-4-thione



2-formylpyridinemonothiosemicarbazone

formulations based largely on elemental analysis results (see Table 6.1) have been proposed. Complexes synthesised include $[Cu^{II}Cu^{I}_{2}(dimetH_{2})\ (dimetH)_{3}Cl]$, $[Cu^{II}Cu^{I}_{3}(dimetH_{2})_{3}(dimetH)(ClO_{4})_{4}].\frac{1}{2}H_{2}O$, $[Cu^{II}Cu^{I}_{3}(dimtolH)_{5}]$, $[Cu^{II}Cu^{I}_{3}(dimprolH)_{5}]$, $[Cu^{II}(mpoH_{2})(mpoH)(ClO_{4})]$, $[Cu^{II}$(phenylglyoxaldtsc)], $[Cu^{II}$(3-n-heptoxy-2-oxobutyraldehydedtsc)] and $[Cu^{II}$(benzildtsc)].$H_{2}O$. For those compounds not isolated, an intrinsic relationship between the mole ratio of cupric salt to ligand has in most cases been assumed in assigning the stoichiometry of the complexes. Full details for the preparation of the compounds are provided in the experimental section.

An analysis of the isolated species reveals the postulation of a number of unusual formulations, particularly for those compounds prepared from dithiol ligands. Partially ionised ligands are proposed, that is, only one sulphhydryl group per ligand has been formally deprotonated. There are no precedents for such behaviour in copper-sulphur chemistry, although the oxy-analogue catechol ligand system has been observed to show similar preferential oxygen deprotonation(9). pKa evidence(10) provides a rationale for this phenomenon, as in most cases there is a difference in acidity between the two sulphhydryl groups. For instance the first and second dissociation constants for 2,3-dimercaptopropanol have pKa values of 8.6 and 10.6 while those for 2,3-dimercaptopropanesulphonate are 8.93 and 12.3. Nonetheless cupric compounds have been reported for dithiol ligands in which they have been fully deprotonated, e.g., $[Cu(dimtol)_{2}]^{2-}$ (11) and $[Cu(maleonitriledithiolate)_{2}]^{2-}$ (12), however complete ionisation required the addition of potassium metal to the former ethanolic ligand system.

Table 6.1 Elemental analysis and magnetic data for the complexes

Compound	Colour	%C	%H	%N	Other	μeff/B.M.
$[Cu^{II}Cu^{I}_2(dimetH_2)(dimetH)_3Cl]$	grey blue	14.4 (14.6)	2.4 (2.6)		6.1[a] (5.4)	1.05
$[Cu^{II}Cu^{I}_3(dimetH_2)_3(dimetH)(ClO_4)_4].1/2H_2O$	khaki	8.2 (9.1)	1.9 (2.3)		13.9[a] (13.4)	0.90
$[Cu^{II}Cu^{I}_3(dimtolH)_5]$	blue black	40.7 (40.8)	2.9 (3.4)		24.0[b] (24.7)	1.46
$[Cu^{II}Cu^{I}_3(dimprolH)_5]$	grey green	20.5 (20.6)	3.6 (4.0)			0.83
$[Cu^{II}(mpoH_2)(mpoH)(ClO_4)]$	brown	28.7 (28.7)	2.5 (1.9)	6.5 (6.5)	6.0 [a] (8.5)	1.09
[Cu(phenylglyoxaldtsc)]	dark red	34.9 (35.1)	2.95 (2.95)	23.9 (24.6)		
[Cu(3-n-heptoxy-2-oxobutyraldehydedtsc]	dark red	39.2 (38.3)	6.0 (5.9)	16.6 (20.6)		
$[Cu(benzildtsc)].H_2O$	yellow brown	43.7 (44.1)	3.6 (3.7)	18.9 (19.3)		

Notes: a. %Cl, b. %Cu

The mixed valence ratios of copper species to ligand are, on the other hand, not entirely novel. Siiman et al.(13) have observed similar stoichiometries in the complex [$Cu^{II}Cu^{I}_2$(tetraphenyldithioimidodi phosphinate)$_4$].

6.2 CHARACTERISATION OF THE COMPLEXES

As was mentioned in the Introduction the techique of esr spectroscopy is especially suitable for the differentiation of the coordination sphere of thiolate containing Cu(II) complexes. In the following sections the characteristic esr features corresponding to equatorial ligation spheres of S_4, S_2O_2, S_2N_2, SO_3 and O_4 are presented, where possible on the basis of spectral details from well defined examples in the literature (representative spectra of each stoichiometry are shown in Figure 6.2). Such features have been correlated with the complexes prepared in this chapter in an attempt to establish their equatorial atoms, assuming at all times an approximately axial coordination for copper.

Principal esr parameters for the new complexes are shown in Table 6.2.

6.2.1. Cupric complexes with proposed S_4 donor sites

There are a number of complexes containing an S_4 donor atom ligation which have been studied by esr spectroscopy(5,11,14-22). A particularly well-characterised system is that of [Cu(edtc)$_2$], where edtc is N,N-diethyldithiocarbamate, which has been shown crystallographically to involve copper bound in a plane containing four sulphur atoms(23). With reference to the esr spectra of [Cu(edtc)$_2$]

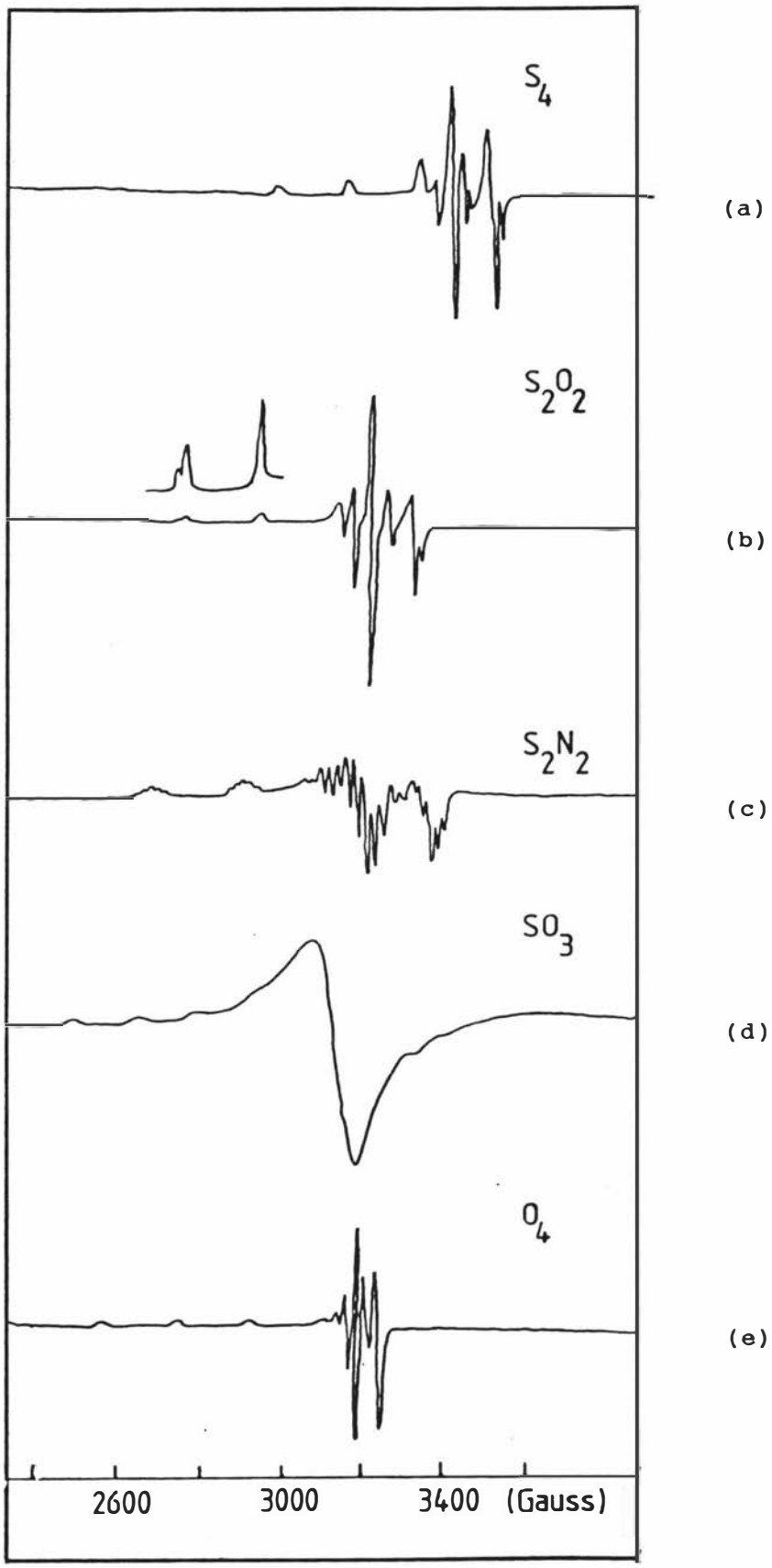


Figure 6.2 Representative esr spectral line shapes for various equatorial donor atom sets.

Table 6.2 Electronic and esr spectral data for the complexes

Compound	Solvent	λ max* (nm)	$g_{\perp}$	g_{11}	$\lvert A_{11} \rvert$ ($10^{-4}cm^{-1}$)	$\lvert A_{\perp} \rvert$ (G)	Proposed Donor Atoms
$[Cu^{II}Cu^{I}_2(dimetH_2)_2(dimetH)_3Cl]$	solid	a	2.031	2.090	143		S_4
$[Cu^{II}Cu^{I}_3(dimetH_2)_3(dimetH)(ClO_4)_3].1/2H_2O$	solid	a	2.026	2.090	143		S_4
$[Cu^{II}Cu^{I}_3(dimtolH)_5]$	solid	a	2.024	2.087	148		S_4
$[Cu^{II}Cu^{I}_3(dimprolH)_5]$	solid	a	2.024	2.092	143		S_4
Cu(II)-2(2,3-dimercaptopropanesulphonate)	water	335(sh)[b]	2.024	2.093	143		S_4
Cu(II)-2(2,3-dimercaptosuccinic acid)	methanol	320(sh)[b] 690[c]	2.031	2.097	151		S_4
Cu(II)-2(diphenyldithiophosphinic acid)	acetone	445(≈1200)[b] 730(≈60)[c]	2.020	2.110	151 164	36	S_4
Cu(II)-2(1,2-dimercaptoethane disodium salt)	ethanol	-	2.015	2.094	157[d] 173[e]	43	S_4
$[Cu(mpoH_2)(mpoH)(ClO_4)]$	ethanol	378(24,608) 440 (1148)sh[b]	2.035	2.175 2.278[f]	185[d] 206[e] 162[f]	37	S_2O_2
Cu(II)-2(2-mercapto-3-pyridinol)	ethanol	-	2.035	2.175	185[d] 206[e]	37	S_2O_2

Table 6.2 contd

Compound	Solvent	λmax* (nm)	$g_{\perp}$	g_{11}	$\|A_{11}\|$ ($10^{-4}cm^{-1}$)	$\|A_{\perp}\|$ (G)	Proposed Donor Atoms
Cu(II)-2(thiomalic acid)	water	365(sh)[b] 540(sh)[c]	2.047	2.177	169		S_2O_2
Cu(II)-2(N-2-mercaptopropionylglycine)	water	350(1010)sh[b]	2.049	2.194	161		S_2O_2
Cu(II)-(2,3-dimercaptosuccinic acid)	methanol	555(125)[b] ≈900sh	2.031	2.202	153		S_2O_2
[Cu(phenylglyoxaldtsc)]	DMF	510(7375)[b] 560(5580)[b]	2.042	2.123	189		S_2N_2
	pyridine	-	2.044	2.141	175		S_2N_2
[Cu(benzildtsc)].H_2O	$CHCl_3$	-	2.042	2.120	186		
[Cu(3-n-heptoxy-2-oxo-butyraldehydedtsc)]	DMF	497(2853)[b] 550(1680)[b]	2.033	2.125	188		S_2N_2
Cu(II)-2(penicillamine)	water	-	2.026	2.139	184		S_2N_2
Cu(II)-2(cysteamine)	water	-	2.044	2.151	179		S_2N_2
Cu(II)-(2,3-dimercaptopropanesulphonate)	water	642[b]	2.075	2.357	155		SO_3
Cu(II)-(cysteamineHCl)	water	517[b]					SO_3

Table 6.2 contd

Compound	Solvent	λ max* (nm)	$g_{\perp}$	g_{11}	$\lvert A_{11} \rvert$ ($10^{-4}cm^{-1}$)	$\lvert A_{\perp} \rvert$ (G)	Proposed Donor Atoms
Cu(II)-(thiomalic acid)	methanol		2.144	2.331	163		SO_3
Cu(II)-(2-mercaptoimidazole)	water	625[b] 750(sh)[c]	2.110	2.334	160		SO_3
Cu(II)-2(thioglycolate)	water	420(sh)	2.072	2.315	165[d] 183[e]	11	O_4
Cu(II)-2(thiomalic acid) (pH 11)	water		2.049	2.260	184[d] 202[e]		O_4

Notes: a. band tails into the visible region b. S→Cu charge transfer transition c. d-d band

d. ^{63}Cu e. ^{65}Cu f. second species g. ±0.002 h. ±0.005 i. $\pm 4 \times 10^{-4} cm^{-1}$

*. extinction coefficient bracketed - units, 1 $mol^{-1} cm^{-1}$ sh. shoulder

(15) (see Figure 6.2(a)) and other S_4 systems it would appear that an S_4 ligation may be readily identified by its characteristic esr spectral lineshape. Three features of the spectrum are particularly striking. Firstly the g_{11} parameter is low compared to other planar complexes of copper(5). Indeed g_{11} is so low that often only two of the parallel copper hyperfine peaks can be seen prior to the perpendicular resonances. Secondly the $g_{\perp}$ transition linewidths in the spectra are narrow (often as small as 1-2 G)(18), giving it a characteristically sharp appearance. Similar sharpness in the m_I=3/2 parallel hyperfine component often allows resolution of a splitting, due to ^{63}Cu and ^{65}Cu having slightly different magnetic moments. Thirdly the spectrum appears quite complex in the $g_{\perp}$ region because of the resolution of perpendicular copper hyperfine and the presence of the fourth parallel hyperfine peak which may also be isotopically split.

Some of the complexes prepared in this chapter have been assigned as containing an S_4 coordinated cupric atom on the basis of their esr lineshapes and parameters. These include the solids $[Cu^{II}Cu^{I}_2(dimetH_2)(dimetH)_3Cl]$, $[Cu^{II}Cu^{I}_3(dimetH_2)_3(dimetH)(ClO_4)_4].\frac{1}{2}H_2O$, $[Cu^{II}Cu^{I}_3(dimtolH)_5]$ and $[Cu^{II}Cu^{I}_3(dimprolH)_5]$ and the <u>in situ</u> species Cu(II)-2(2,3-dimercaptopropanesulphonate), Cu(II)-2(2,3-dimercaptosuccinic acid), Cu(II)-2(diphenyldithiophosphinic acid) and Cu(II)-2(1,2-dimercaptoethanedisodium salt). It is noticeable that all the complexes contain dimercapto ligands in which the sulphhydryl groups are vicinal. The insolubility of the solid compounds isolated suggests, furthermore, that polymeric structures are present.

The esr spectra of $[Cu^{II}Cu^{I}_3(dimprolH)_5]$ and Cu(II)-2(1,2-dimercaptoethane disodium salt) are shown in Figure 6.3.

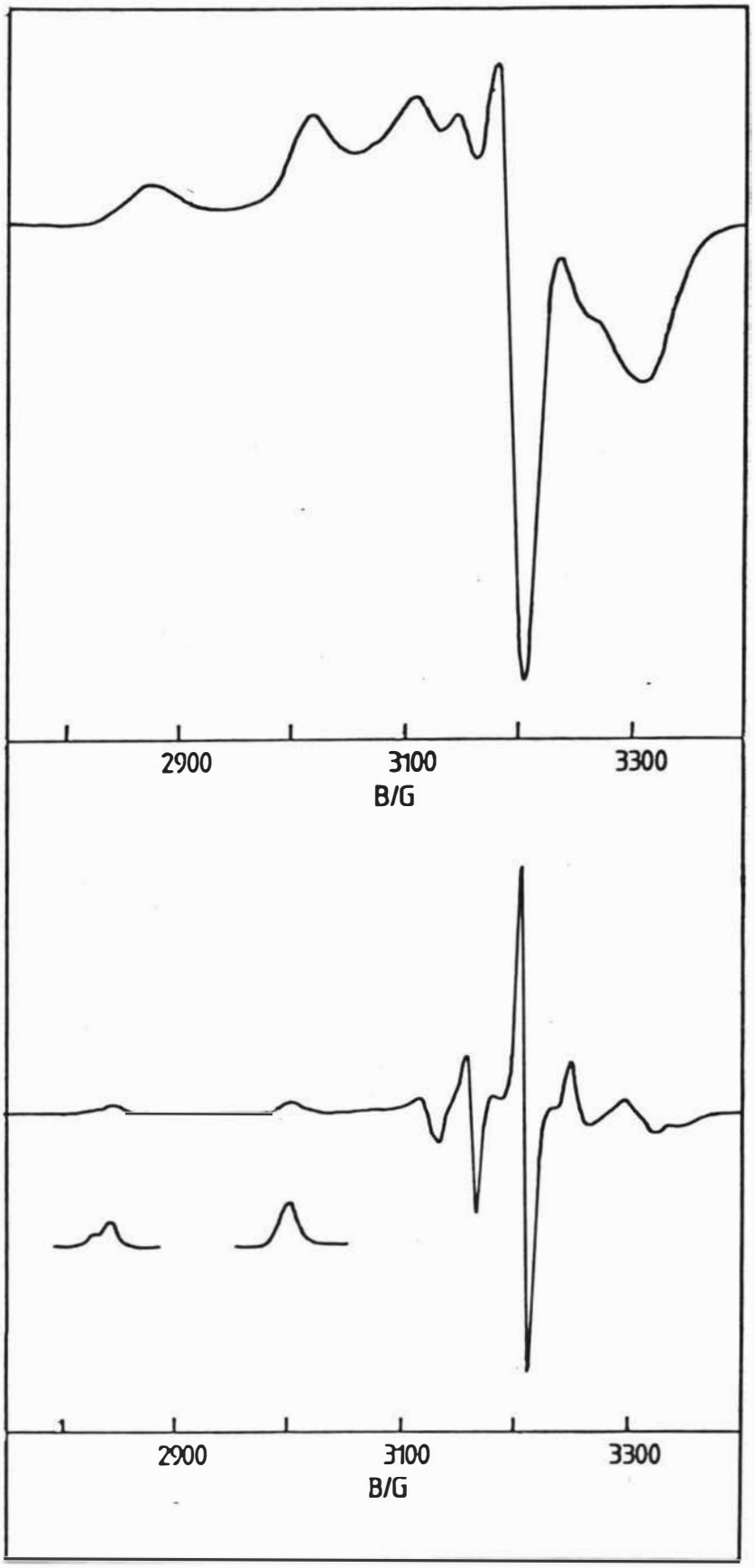


Figure 6.3 The esr spectra of S_4 types:
(a) $[Cu^{II}Cu^{I}_3(dimprolH)_5]$ as a solid and
(b) Cu(II)-2(1,2-dimercaptoethanedisodium salt) in ethanol.

From our studies and those of others it seems that the environment of sulphur has little bearing on the nature of the spectrum. Disulphide (21) thioether(18), thione (Chapter 4) and thiolate sulphur (this chapter) are equally capable of producing the characteristic S_4 spectrum.

6.2.2 Cupric complexes with proposed S_2O_2 donor sites

Copper(II) thiolate compounds with an S_2O_2 coordination sphere are rare. A few complexes have been prepared from monothio-β-diketones (R-C(SH)=CH-CO-R)(24), thiohydroxamates (R-CS-N(OH)-R)(25) and 3-hydroxyquinazoline-4-thione(26). A characteristic esr spectral lineshape is similarly observed for these donor atoms(25, 26, 27). A typical example is shown in Figure 6.2(b) for [Cu(N-methylformothio-hydroxamate)$_2$](25) which has been shown by X-ray diffraction to have a square planar configuration with the sulphurs and oxygens in trans arrangement(28). As with S_4 types the spectrum is typically sharp, $A_\perp$ hyperfine coupling is resolved and isotopic splitting may appear on the m_I=3/2 line. It should be noted that only the position of the g_{11} parameter can distinguish between an S_4 spectrum and that of a well resolved S_2O_2. For the latter, g_{11} is normally in the range 2.17-2.20 whereas for the former it is consistently less than 2.12.

The spectrum of [Cu(mpoH$_2$)(mpoH)(ClO$_4$)] (Figure 6.4(a)) allows us to designate the equatorial coordination sphere of the compound as S_2O_2. Investigation of the spectrum under high gain produced some unusual results. Firstly three additional lines at ca 2600, 2760 and 2910 G are resolved. These are not present when the complex is generated in situ (Figure 6.4(b)) by adding Cu(ClO$_4$)$_2$.6H$_2$O to the ligand in ethanol. Thus it appears that they are a phenomenon of the solid

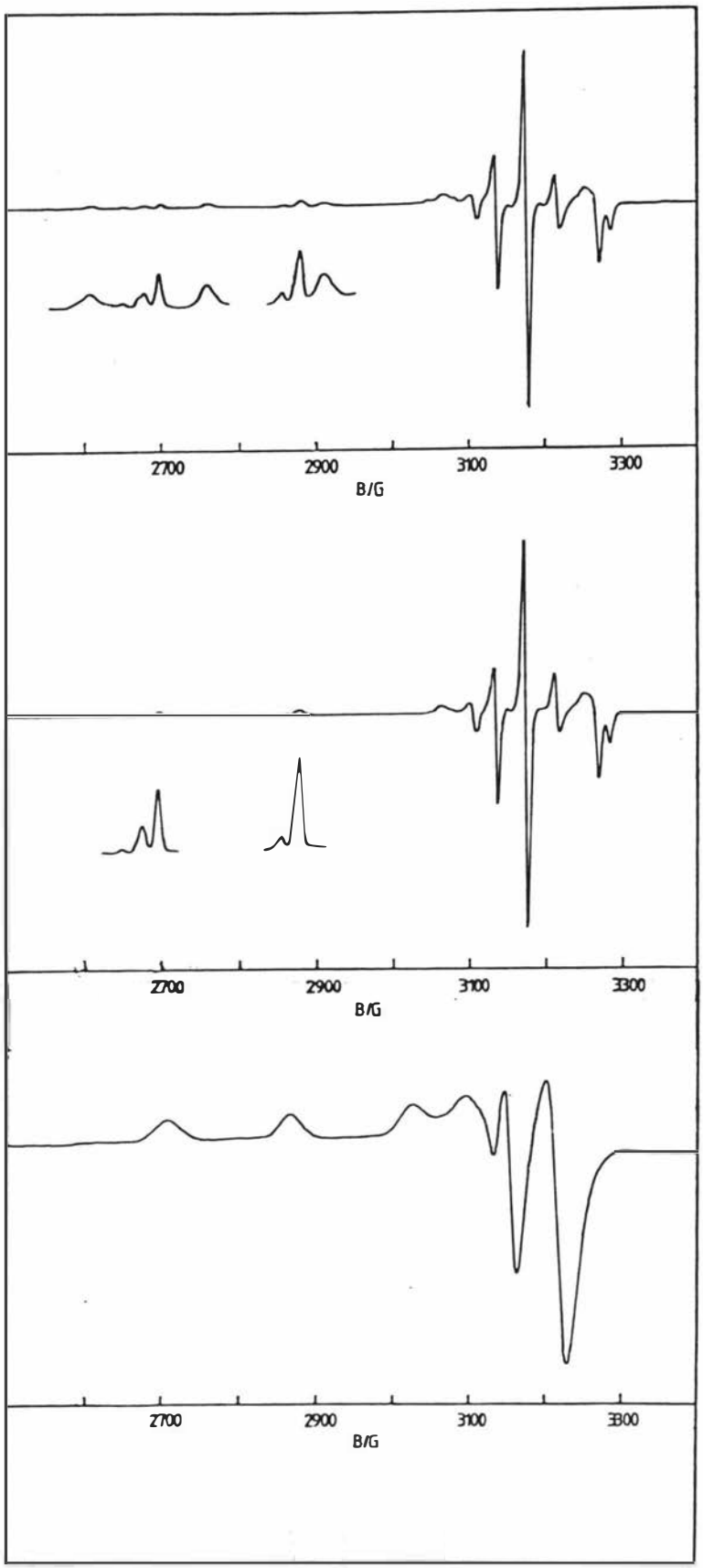


Figure 6.4 Esr spectra of S_2O_2 types

(a) [Cu(mpoH)(mpoH$_2$)ClO$_4$] and

(b) Cu(II)-2(2-mercapto-3-pyridinol), both in ethanol and

(c) Cu(II)-2(thiomalic acid) in water.

compound and may well arise from inhomogeneities in the copper coordination sphere. Such differences could result from an oxygen being deprotonated instead of sulphur. Secondly a small satellite line appears beside the principal m_I=3/2 and 1/2 parallel absorbances. This has been seen also in the spectrum of [Cu(HC(=S)N(Me)O)$_2$](25) where the extra line was attributed to solvation of some of the molecules, thus allowing their differentiation.

The esr spectrum of the complex Cu(II)-2(thiomalic acid) prepared in situ is shown in Figure 6.4(c). A similar spectrum for Cu(II)-2(mercaptopropionylglycine) was observed. The parameters for these are suggestive of an S_2O_2 configuration, which, considering potential donor atoms in the ligands, is a plausible stoichiometry. It may be inferred that the differences between the spectra of Cu(II)-2(thiomalic acid) and the representative S_2O_2 spectra arise from line broadening. This phenomenon has also been seen for monothio-β - diketone complexes in certain solvents(27). Judicious choice of solvent by the authors resulted in a sharpening of the spectra.

6.2.3 Cupric complexes with proposed S_2N_2 donor sites

An S_2N_2 arrangement of atoms around Cu(II) has been of considerable biological interest for some time as this is one of the proposed ligations for the type(I) blue copper proteins(29). Similarly the copper catalysed oxidation of cysteine(30) has prompted investigation into the bis-cysteinato compounds of copper and its S_2N_2 analogues (31-33). A lot of success in the isolation of cupric thiolate compounds with S_2N_2 donor sites has been achieved through the use of bi- and tetradentate ligands(33-37) in which the formal negative charge of the deprotonated sulphhydryl group is distributed over flanking

nitrogen atoms.

S_2N_2 esr spectra are well documented in the literature(26,30-36). The spectrum of [Cu(KTS)] (Figure 6.2(c)) proves typical. Characteristically two copper hyperfine peaks are visible with a strong fourth peak downfield of the major perpendicular absorption, although the number of upfield hyperfine peaks seen may be greater if there is considerable tetrahedral distortion of the ligand plane(36). The spectra are also characterised by the broadness of the absorptions compared with other thiolate stereochemistries - a consequence of nitrogen hyperfine interaction(18).

On the basis of their esr spectra Cu(II)-2(penicillamine), Cu(II)-2(cysteamine), [Cu(3-n-heptoxy-2-oxobutyraldehydedtsc)], [Cu(phenylglyoxaldtsc)] and [Cu(benzildtsc)].H_2O have been adjudged as having S_2N_2 donor sets. For the latter complexes which contain the dithiosemicarbazone moiety, this result is not surprising since the structurally similar complex [Cu(KTS)], which also contains a dithiosemicarbazone unit has been shown crystallographically to involve an S_2N_2 stoichiometry(38). Furthermore the spectra of Cu(II)-2(penicillamine)(32,33) and Cu(II)-2(cysteamine)(31) have been previously recorded and so assigned by the authors. For Cu(II)-2(cysteamine), however, this is the first instance where the compound has been prepared using the free ligand in stoichiometic ratio, the previous preparation having involved the hydrochloride salt in tenfold excess. Also there is confusion concerning the correct parameters for Cu(II)-2(penicillamine) . Laurie et al.(32) have reported an esr signal with $|A_{11}| = 0.0140$ cm^{-1} whereas Peisach and Blumberg(33) obtained a value of 0.0184 cm^{-1} which agrees well with our spectrum.

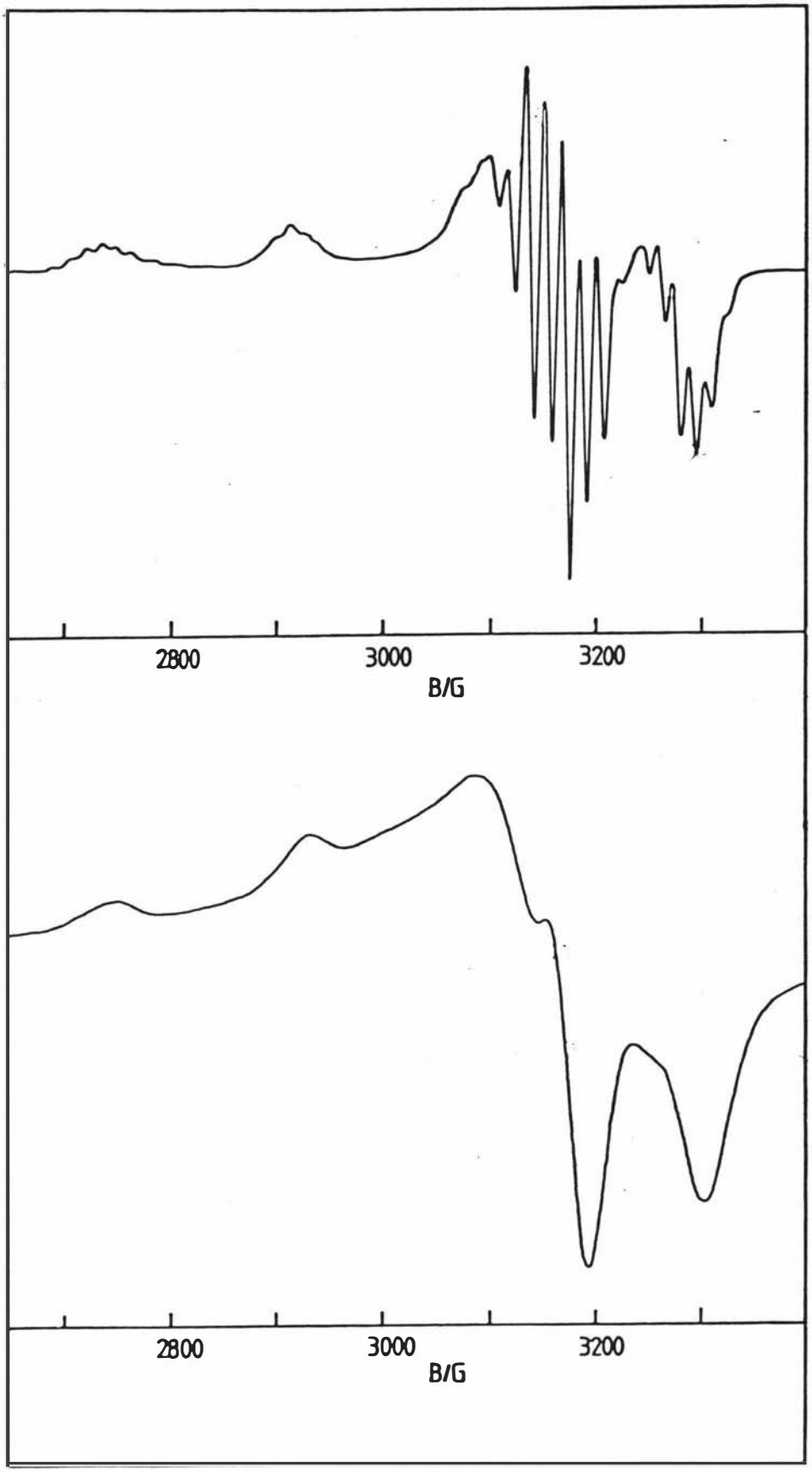


Figure 6.5 Esr spectra of S_2N_2 types

(a) [Cu(phenylglyoxaldtsc)] in ethanol and

(b) Cu(II)-2(penicillamine) in water.

The esr spectra shown in Figure 6.5 illustrate that superhyperfine splitting may or may not be present in the spectrum. The nine-line structure shown for [Cu(phenylglyoxaldtsc)] (Figure 6.5(a)) has been seen also in [Cu(KTS)](33). Initially this was interpreted as showing that the unpaired electron spin interacted with four approximately equivalent nitrogen nuclei. However a spectrum obtained from a complex containing isotopically pure ^{63}Cu showed only five superhyperfine splittings(39) - consistent with a two nitrogen interaction as suggested from crystallographic evidence(38). It has been rationalised that superimposition of the two isotopic five line structures would give rise to the nine-line spectrum observed.

A comparison of the g_{11} values in Table 6.2 shows that an S_2N_2 configuration is easily differentiated from that of S_2O_2 on the basis of the value of g_{11} ($S_2N_2 < 2.15$; $S_2O_2 > 2.17$).

6.2.4 Cupric complexes with proposed SO_3 donor sites

Tentative coordination spheres of SO_3 have been assigned to the *in situ* species Cu(II)-(cysteamine hydrochloride), Cu(II)-(dimercatopropanesulphonate), Cu(II)-(thiomalic acid) and Cu(II)-(2-mercaptoimidazole). That thiolato sulphur coordinates in each is intimated by the presence of bands attributable to S$\rightarrow$Cu charge transfer transitions. Three oxygen equatorial donor atoms are considered likely by virtue of the magnitude of g_{11}, the values of which approach those of known O_4 ligation. Unfortunately there are no esr precedents for SO_3 type complexes, so no valid comparisons with literature examples can be made.

The esr spectra of Cu(II)-(cysteamine hydrochloride) and

Cu(II)-(dimercaptopropanesulphonate) are shown in Figures 6.2(d) and 6.6(a) respectively. The SO_3 spectrum is characterised by the appearance of all four copper hyperfine peaks prior to the perpendicular resonances, and moderately low values of $|A_{11}|$. A few additional peaks due to a small amount of bis-ligand contaminant are apparent in the spectrum of Cu(II)-(dimercaptopropanesulphonate). The spectra of Cu(II)-(2-mercaptoimidazole) and Cu(II)-(thiomalic acid) were very broad, perhaps suggesting binuclear or greater structures.

6.2.5 Cupric complexes with proposed O_4 donor sites

Although containing no thiolate entity a discussion of this type of coordination is pertinent for its contribution to the overall consideration of parameter shifts. [Cu(acetylacetonate)$_2$] provides a well characterised example of copper bound by a plane of four oxygen donor atoms. The esr spectrum(40) of the complex is shown in Figure 6.2(e). Comparison with other O_4 literature examples(40-42) shows that the spectral lineshape shown is characteristic for an O_4 ligation. The attributes of spectral sharpness, i.e. isotopic splitting and resolution of the $A_\perp$ components, occur also for these complexes.

The O_4 spectrum differs from that of the S_4 and S_2O_2 types, in the position of g_{11} which occurs in the range 2.25-2.47 (5) allowing often the resolution of all four copper hyperfine prior to $g_\perp$; and in the presence of forbidden peaks in the 3100-3400 G region. Rollmann and Chan (43) have attributed these absorptions to large anisotropies in the nuclear hyperfine interactions, and developed a theory for the lineshape computation that accommodates second order terms containing quadrupole interaction and $\Delta m_I \neq 0$ transitions.

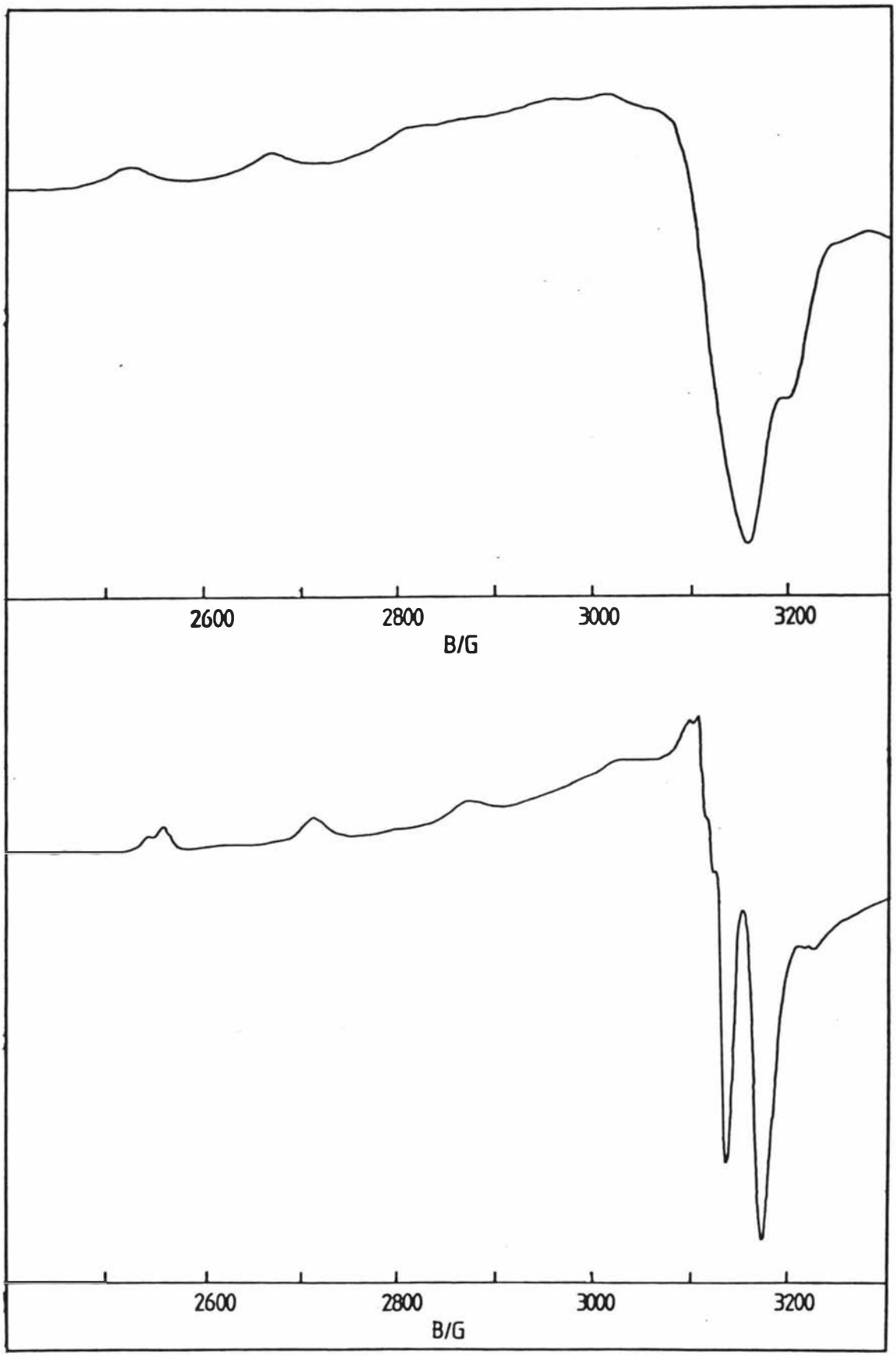


Figure 6.6 Esr spectra of (a) Cu(II)-(dimercaptopropanesulphonate) and (b) Cu(II)-4(thioglycolate)

Two solutions in our work have been designated as containing O_4 species. The spectrum of an aqueous solution of Cu(II)-2(thiomalic acid) raised to pH 11 shows $[Cu(OH)_4]^{2-}$ (42) as the major species. Figure 6.6(b) shows the spectrum of an aqueous solution of cupric acetate containing a large excess of sodium thioglycolate. $A_\perp$ for the complex is very small (ca 11 G) and weak making the spectrum appear more simple.

6.2.6 Graphic plots of g_{11} verses $|A_{11}|$

A Peisach-Blumberg type plot(3) of g_{11} verses $|A_{11}|$ has been drawn (Figure 6.7) with points obtained from Table 6.2. Where necessary literature examples have been included to clarify trends. Although by no means giving truly linear relationships the points do scatter into well defined regions depending on the type of donor atoms. Notably g_{11} is paramount in causing this differentiation. The effect of replacing sulphur donor ligands with those of oxygen in increasing g_{11} is well developed, the plot confirming Ibers' observation(4) that a decrease in covalent interaction promotes higher values of the parameter.

6.2.7 Electronic spectra

Absorbance spectra in the visible region have been recorded for some of the complexes prepared in this chapter and maxima with possible assignments are included in Table 6.2.

Though by no means clear cut, a few trends have emerged which may aid in discriminating the various ligations proposed. For those complexes with a postulated S_2O_2 donor set, a characteristic feature is the appearance of a S→Cu charge transfer transition as a band or shoulder in the 350-400 nm region. The proposed SO_3 complexes similarly

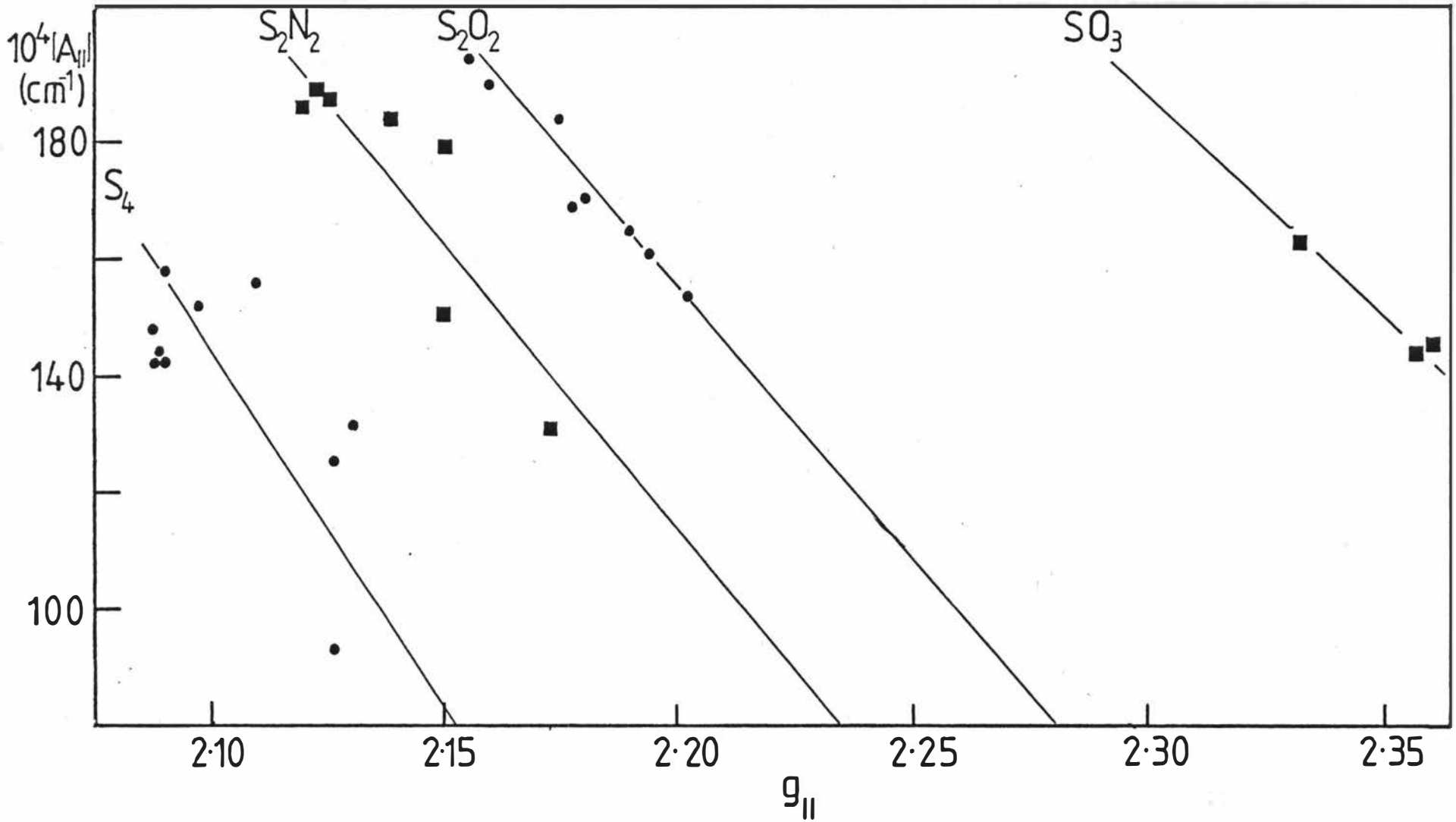
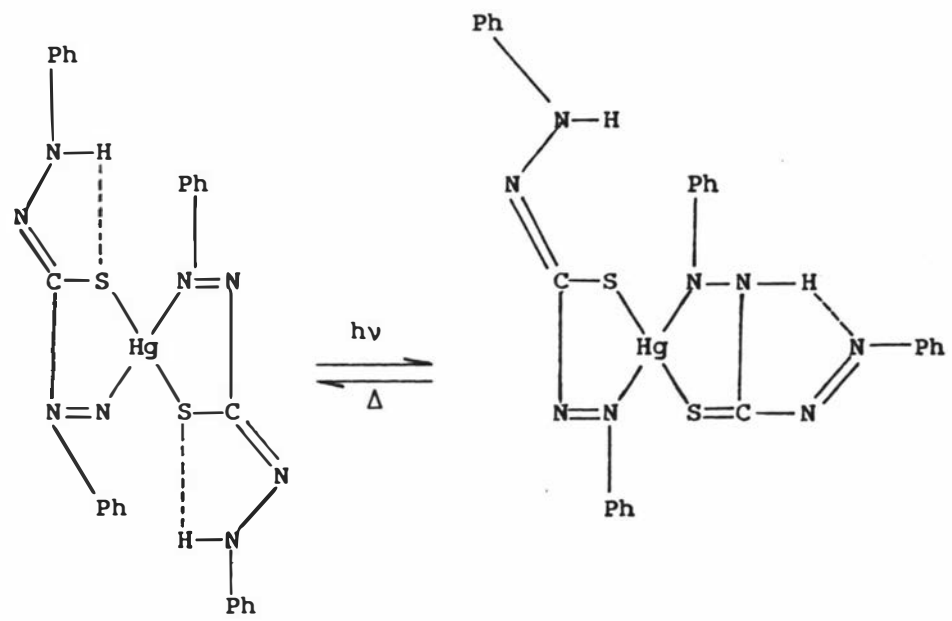


Figure 6.7 A plot of g_{11} versus A_{11} for various donor atom sets

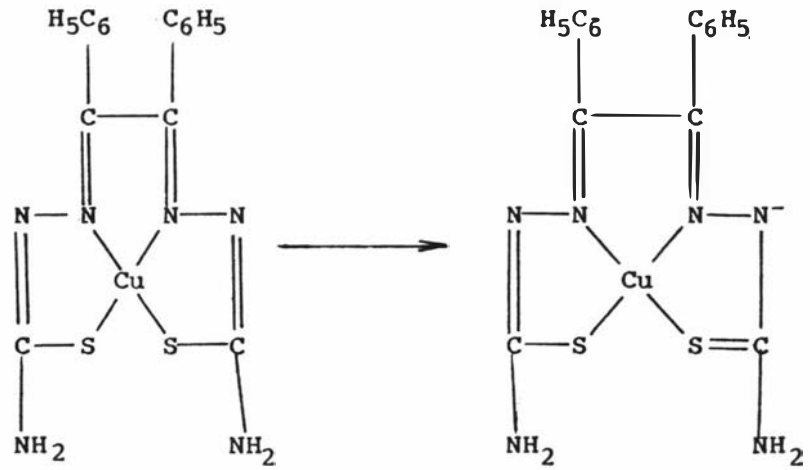
show this absorbance, but at lower energy in the region 550-650 nm. Those complexes with an S_2N_2 donor set and which contain the dithiosemicarbazone moiety normally show two S→Cu charge transfer bands at 500-600 nm.

The elucidation of the latter trend has allowed the postulation of a solution to an interesting problem which developed when cupric acetate was substituted for cupric chloride in the synthesis of [Cu(benzildtsc).H_2O. On quantitative addition of copper a brown compound rather than the usual red complex(44) precipitated. Elemental analysis figures consistent with the formulation [Cu(benzildtsc).H_2O were found but the compound displayed significant differences in spectroscopic properties from that reported for [Cu(benzildtsc)]. For instance the electronic spectrum showed a band at 325 nm instead of 510 nm and g_{11} decreased from 2.151 to 2.120. Such behaviour has been seen in a structurally similar system - that of the mercury(II) complex of dithizone in a reaction which was photomediated(45). Irradiation ($>$ 400nm) caused the orange square planar complex I to rearrange to a blue complex II:



I II

A similar proton shift could be envisaged to occur in [Cu(benzildtsc)].H_2O giving rise to an S_2N_2 coordination sphere, now with one thione sulphur and a negatively charged nitrogen. The hypsochromic shift observed in the electronic spectrum may be associated with the presence of a thione sulphur and a decrease in the extent of the conjugation in the system



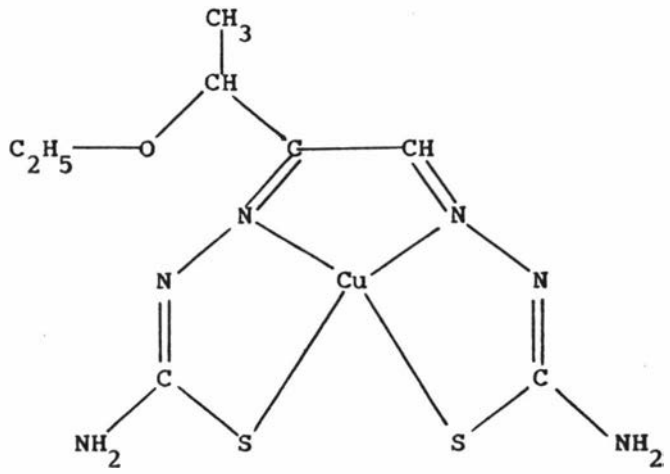
Summary

Copper complexes with S_4, S_2N_2, S_2O_2 and SO_3 coordination spheres derived from sulphhydryl containing ligands have been shown to give rise to characteristic esr spectra. Decreasing the number of sulphurs ligating leads to a systematic increase in the g_{11} parameter. In conjunction with electronic spectral details these criteria may allow cupric thiolate compounds to be distinguished from themselves and other complexes of copper.

6.3 USE OF THE ESR TECHNIQUE IN PROBING DIMERIC CUPRIC INTERACTIONS

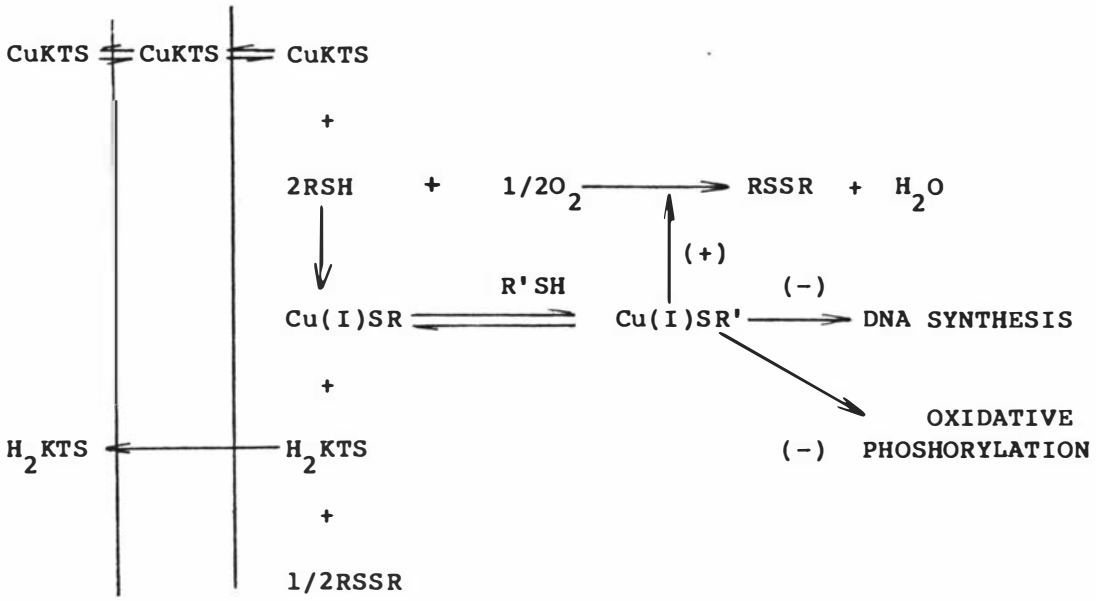
3-ethoxy-2-oxobutyraldehyde bis(thiosemicarbazone) (KTS) is a potent antitumour agent in animals able to cause regressions in a variety of

established tumours(46). Experiments <u>in vivo</u> show a dependence on the presence of copper ions for effectiveness and there is much evidence to suggest that the therapeutic agent is the complex [Cu(KTS)](47). Crystallographic studies(38) show that the compound has a planar structure:



Long axial contacts (3.101 Å and 3.312 Å) occur between copper and sulphurs of other molecules lying above and below the plane of the complex. The ethoxyethyl group was considered sufficiently large and in an appropriate position to partially block one of the axial positions leading to the larger Cu-S bond distance.

Investigative work has allowed the proposal of the following mechanism for the cytotoxicity of [Cu(KTS)](48).



Reaction of [Cu(KTS)] with Ehrlich cells; (+)= reaction stimulated by Cu(I)SR'; (-)= processes inhibited by Cu(I)SR'.

Petering and Petering(49) have suggested that the relatively sluggish nature of the initial reduction occuring with cellular sulphhydryl compounds such as cysteine, glutathione or coenzyme A may be important in that it allows [Cu(KTS)] to be transported to target cells before being dissociated by reaction with thiols en route. Furthermore it has been shown that when the β side chain is reduced in size from $CH(OEt)CH_3$ to CH_3 the rate of reduction increases(8) presumably due to a decrease in the axial steric interaction hindering association of thiols.

It was thought that a valuable contribution to enable testing of these ideas would be the synthesis and spectroscopic investigation of complexes in which the $CH(OCH_2CH_3)CH_3$ side chain of [Cu(KTS)] was replaced by sterically larger groups such as phenyl or $CH(OC_7H_{15})CH_3$. Primarily we were interested in the ability of the esr technique to elucidate the presence or absence of intermolecular axial interactions

in [Cu(KTS)] and analogues and to relate this to the effects of increasing the size of the side group, or the solvating power of the solvent in which the spectrum was run. Dimeric cupric species are conveniently detected by the presence of a low field signal in the esr spectrum at ca 1500 G(50). The results show that a dimeric axial interaction is indeed present in DMF solutions of [Cu(KTS)] and related compounds, regardless of the size of the side chain, but that the interaction disappears when the compounds are dissolved in the more strongly coordinating solvent pyridine.

Results and Discussion

Although the esr spectrum of [Cu(KTS)] has been investigated(33,39) the 1500 G region where copper-copper dimeric interactions give rise to additional absorbances has been ignored. A signal was however observed in this region for [Cu(diacetylbisthiosemicarbazone)] doped at 5% concentration in a nickel host(34).

Figure 6.8 shows the spectrum of a very concentrated solution (ca 10^{-2}mol l^{-1}) of [Cu(KTS)] in DMF. The inset shows the 1100-1800 G region at higher gain. According to theory, where the exchange parameter J is strong (J for [Cu(diacetylbisthiosemicarbazone)] was estimated to be -14 cm^{-1}) the predicted 16 line hyperfine interaction (from the product $[(2I_1+1)(2I_2+1)]$ where $I_1=I_2=3/2$ for the copper nucleus) is simplified to a seven-line pattern with a hyperfine spacing one half that of the spectrum due to the individual copper(II) components(51). As can seen from Figure 6.8, seven hyperfine lines are discernible in the spectrum with a splitting of 90 G i.e., roughly half the $g\approx2$ coupling constant of 189 G. A nearly identical set of signals

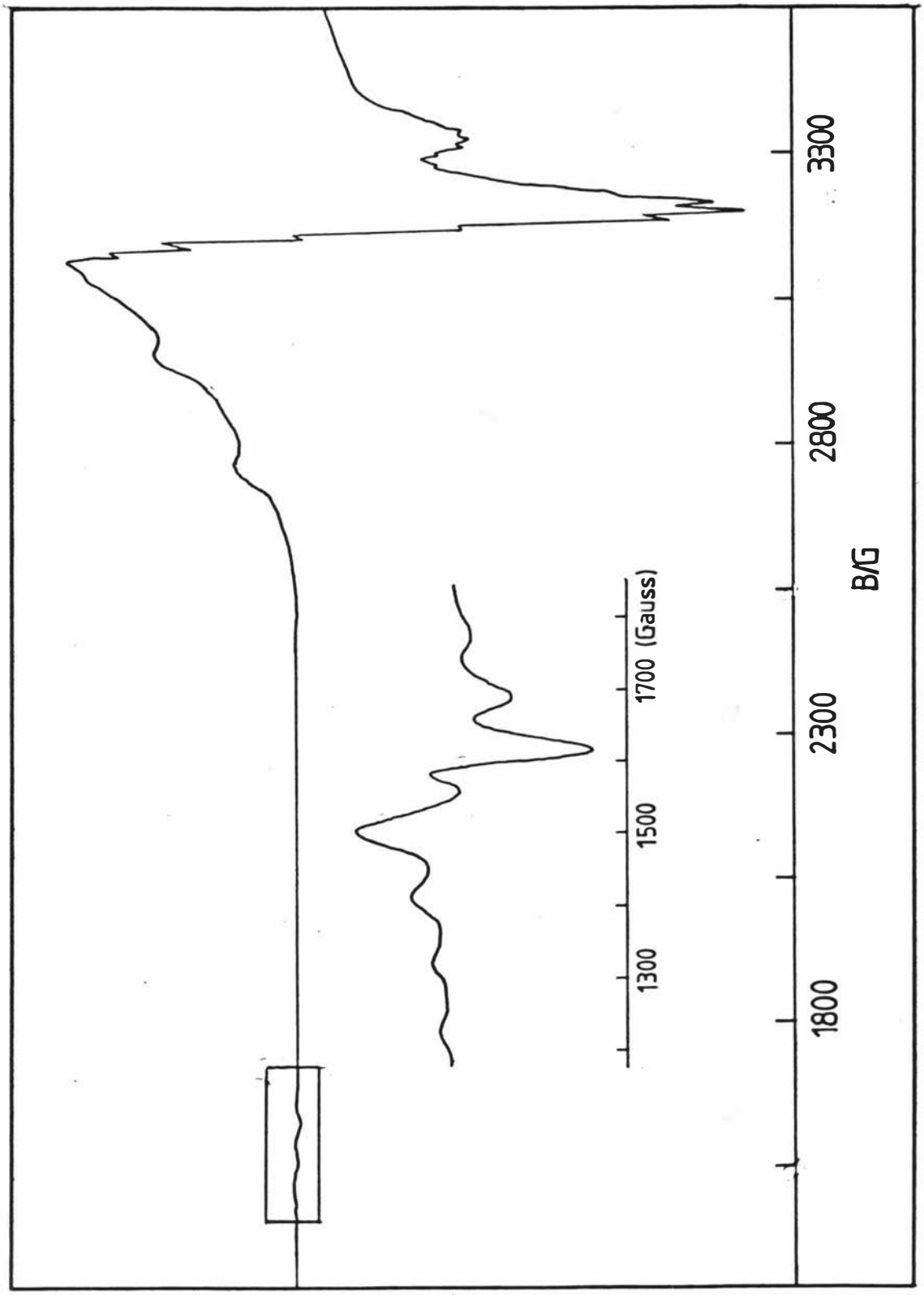
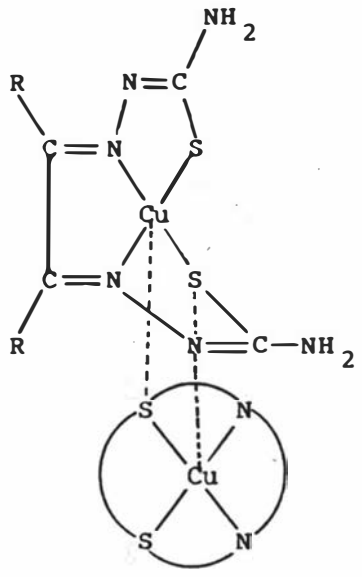


Figure 6.8 Low and high field esr spectrum of [Cu(KTS)].

are observed for concentrated DMF solutions of [Cu(phenylglyoxaldtsc)], [Cu(3-n-heptoxy-2-oxobutyraldehydedtsc)] and [Cu(benzildtsc)] suggesting that significant dimer formation occurs also for these compounds. As has been mentioned the crystallographic intermolecular Cu-S contacts for [Cu(KTS)] (see below) were 3.101 and 3.312 Å with alternating Cu-Cu internuclear distances of 3.833 and 3.896 Å(34).



Intermolecular contacts in [Cu(KTS)]

[Cu(benzildtsc)] has a similar coordination geometry, as determined by X-ray crystallography(44), however the phenyl side groups restrict intermolecular contacts to one Cu-S "bond" at a distance of 3.45 Å. As is evidenced by the low field esr signal such an interaction may be still sufficiently strong to allow the development of significant dimeric character in solution. It is unlikely that the monophenyl group in [Cu(phenylglyoxaldtsc)] or $-CH(OC_7H_{15})CH_3$ in [Cu(3-n-heptoxy-2-oxobutyraldehydedtsc)]) would further increase the Cu-S bond length allowing similar rationalisation of their low field signals.

When it is considered that these esr species are being observed in solution rather than the solid state, alternatives to superexchange as the means of production of the low field signal, were solvent molecules to increase intermolecular contacts, may be required. A plausible alternative explanation is to consider the dimers as arising from a $\pi - \pi$ face-to-face interaction in which the π electron clouds from the delocalised ligand systems approach one another, so as to form, as far as copper(II) is concerned, magnetically isolated pairs. This behaviour has been hypothesised for the similar copper(II) protoporphyrin IX system(52). Here the interaction between the copper ions was interpreted in terms of dipole-dipole coupling, the so-called "through space" interaction. A dipolar mechanism may thus be similarly likely for [Cu(KTS)] and related compounds in solution. That hyperfine broadening was not observed for the $g \approx 2$ signal in [Cu(KTS)] may indicate that the copper-copper distance is in the range 4.0-5.0 Å(52).

Axial coordination of solvent was seen when the esr spectra of [Cu(KTS)] and [Cu(phenylglyoxaldtsc)] were run in pyridine. At similar concentrations to the solutions in DMF no signal was detectable in the 1500 G region suggesting a breakup of the intermolecular interactions. Furthermore the hyperfine coupling constant was reduced from 0.0189 to 0.0175 cm^{-1} consistent with pyridine binding in the fifth and sixth positions. Petering has postulated similar solvent interaction from the shifts of visible absorbance bands run in pyridine(46).

Summary

[Cu(KTS)] and similar dithiosemicarbazide complexes have shown

signals at 1500 G. Increasing the size of the side chain from $-CH(OCH_2CH_3)CH_3$ to phenyl and $-CH(OC_7H_{15})CH_3$ has little effect in disrupting dimer formation. The interaction may be broken by dissolving the complexes in pyridine, where there is evidence for axial coordination of solvent. It is concluded that the side chains do not play a significant role in providing steric hindrance for axial coordination.

6.4 EXPERIMENTAL

6.4.1 Instrumentation

This was as for 1.7.1.

6.4.2 Preparation of the complexes

$[Cu^{II}Cu^{I}_2(dimetH_2)(dimetH)_3Cl]$

$CuCl_2.2H_2O$ (1.70 g, 10 mmol) in ethanol (30 cm^3) was added to 1,2-dimercaptoethane (2.35 g, 25 mmol) in ethanol (15 cm^3) immediately producing a grey blue precipitate. This was washed with ethanol. Yield: 1.16 g (58%).

$[Cu^{II}Cu^{I}_3(dimetH_2)_3(dimetH)(ClO_4)_4].\frac{1}{2}H_2O$

1,2-dimercaptoethane (0.471 g, 5 mmol) in ethanol (15 cm^3) containing potassium metal (0.40 g, 10 mmol) (extreme care necessary) was added dropwise to $Cu(ClO_4)_2.6H_2O$ (1.85 g, 5 mmol) in ethanol (15 cm^3) to give a grey-green precipitate. This was washed with ethanol, water, acetone and chloroform. Yield: 0.80 g (56%).

$[Cu^{II}Cu^{I}_3(dimtolH)_5]$

$Cu(ClO_4)_2.6H_2O$ (1.27 g, 3.4 mmol) in ethanol (20 cm^3) was added slowly to 3,4-dimercaptotoluene (1.0 g, 6.4 mmol) to give an immediate precipitation of a blue black compound. This was washed with ethanol. Yield: 0.753 g (86%).

$[Cu^{II}Cu^{I}_3(dimprolH)_5]$

$Cu(CH_3COO)_2.3H_2O$ (0.2 g, 1 mmol) in water (20 cm^3) was added dropwise to 2,3-dimercapto-1-propanol (0.124 g, 1 mmol) in water (15 cm^3). The resulting green solid was washed with water.

$[Cu(mpoH_2)(mpoH)ClO_4]$

$Cu(ClO_4)_2.6H_2O$ (1.85 g, 5 mmol) in ethanol (30 cm^3) was added dropwise to 2-mercapto-3-pyridinol (0.635 g, 5 mmol) in ethanol (100 cm^3). The brown coloured solution was left to stand for two days during which a brown crystalline product deposited which was collected and washed with ethanol.

[Cu(phenylglyoxaldtsc)], [Cu(benzildtsc)].H_2O,
[Cu(3-n-heptoxy-2-oxobutyraldehydedtsc)] and [Cu(KTS)]

$Cu(CH_3COO)_2.3H_2O$ (4 mmol) in water (100 cm^3) was added to the appropriate ligand (4 mmol) in N,N-dimethylformamide (80 cm^3). The respective red and brown products were collected and washed with water and ethanol.

Synthetic details for the <u>in situ</u> species are presented below.

Compound	Solvent used	Weight of Cupric salt(g)	Volume of Solvent(cm^3)	Weight of ligand(g)	Volume of solvent(cm^3)	Order of mixing
Cu(II)-2(2,3-dimercatopropanesuphonate)	water	0.024 $Cu(CH_3COO)_2.3H_2O$	15	0.050	4	ligand to copper
Cu(II)-2(2,3-dimercatosuccinic acid)	methanol	0.0864 $CuCl_2.2H_2O$	20	0.1828	30	copper to ligand
Cu(II)-2(diphenyldithiophosphinic acid)	acetone	0.0145 $CuCl_2.2H_2O$	10	1.00	50	copper to ligand
Cu(II)-2(1,2-dimercaptoethane disodium salt)	ethanol	0.0304 $CuCl_2.2H_2O$	20	0.337 (+0.162 Na)	20	copper to ligand
Cu(II)-2(thiomalic acid)	water	0.100 $Cu(CH_3COO)_2.3H_2O$	20	0.135	30	copper to ligand
Cu(II)-2(N-mercaptopropionylglycine)	water	0.085 $CuCl_2.2H_2O$	20	0.163	20	copper to ligand
Cu(II)-(2,3-dimercaptosuccinic acid)	methanol	0.0862 $CuCl_2.2H_2O$	30	0.0913	50	ligand to copper

Cu(II)-(cysteamine hydrochloride)[a]	water	0.100 $Cu(CH_3COO)_2.3H_2O$	20	0.060	10	ligand to copper
Cu(II)-(2,3-dimercaptopropanesulphonate)	water	0.047 $Cu(CH_3COO)_2.3H_2O$	15	0.050	7	ligand to copper
Cu(II)-(thiomalic acid)	water	0.0865 $CuCl_2.2H_2O$	40	0.0753	70	ligand to copper
Cu(II)-2(cysteamine)	water	0.185 $Cu(ClO_4)_2.6H_2O$	5	0.077	5	copper to ligand
Cu(II)-2(penicillamine)[a,b]	water	0.050 $Cu(CH_3COO)_2.3H_2O$	25	0.074	25	copper to ligand
Cu(II)-4(thioglycolate)	water	0.012 $Cu(CH_3COO)_2.3H_2O$	5	0.400	5	copper to ligand

Notes: a, process performed under dinitrogen

b, pH raised to 9 with NH_3

An *in situ* solution of [Cu(benzildtsc)] was obtained from the method of Bushnell and Tsang(44), with the exception that water was not added to precipitate the product.

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A summary of the possible factors leading to stabilisation of cupric thiolate or thioamide complexes

As expressed in the General Introduction one of the aims of this study was to evaluate the ability of ligands containing the thiol or thioamide group to produce complexes involving cupric rather than cuprous ions. As a consequence of our studies an attempt is made here to outline briefly a few of the effects which we now consider important to achieve such species, either in solid form or *in situ* in solution.

One of the strongest factors which may stabilise the cupric-thiolate entity is the ability of an adjacent ligating atom to chelate with the sulphur. Examples of such systems are thiomalic acid (S and O donors), penicillamine (S and N donors), the thiosemicarbazide derivatives (tetradentate S_2N_2) and the 1,2-dithiol ligands all of which give rise to cupric or mixed-valence thiolate complexes.

Where chelation is not possible or less likely, there is evidence to suggest that the acidity of the sulphhydryl group may be important. Thus thiol ligands with pKa values from 7-8.5 appear to give rise to cupric compounds, whereas those with values above 9 seem more susceptible to reduction of copper(II). For instance cysteamine hydrochloride with pKa = 8.35 may form cupric species, however, ethanethiol with pKa = 10.6 reduces copper(II) completely. This trend may be rationalised on the basis of the stronger conjugate base strength of the less acidic thiols having greater nucleophilic character and thus greater reducing power.

The nature of the solvent for the reaction may also play a part. More polar solvents such as water or aqueous ethanol seem to stabilise

the cupric state better than ethanol, methanol or acetone, especially when the pH has been raised with the addition of ammonia. As an example, thiomalic acid forms a 1:1 violet cupric complex in water but reduces copper(II) in ethanol.

Substituent or electronic effects may alter the reducing power of the ligand or its ability to stabilise the cupric state. For example 2-mercaptothiazoline gives rise to cupric thioamide halide complexes on interaction with excess $CuCl_2.2H_2O$, yet fusing a benzene ring to the thiazoline moiety to give 2-mercaptobenzothiazole or inserting a double bond and phenyl group as in 2-mercapto-4-phenylthiazole results only in cuprous compounds being formed. Unfortunately pKa values are seldom available for the sulphhydryl group in thioamide complexes so objective comparisons and rationalisation are difficult. For non-thioamide thiol ligands addition of electron-withdrawing groups may certainly aid in producing a cupric-binding thiolate ligand, presumably by increasing the acidity of the -SH group. Thus p-nitrothiophenol(LH) forms a compound $[CuLClO_4]$ with $Cu(ClO_4)_2.6H_2O$, however, thiophenol will quantitatively reduce copper(II).

Finally mention must be made of the at-times bewildering potential of certain ligand systems, particularly those of 2-mercaptothiazoline or 2-mercapto-1-methylimidazole to give rise to three or perhaps four different cupric species depending on the ratio of copper to ligand and the order of mixing of reactants. If a pattern were to be espoused it is more likely that cupric complexes will be obtained from situations where copper is in 1:1 ratio or in excess of the ligand, and the ligand added to copper to avoid a heavily reducing medium - although paradoxically at times a high excess of ligand may stabilise the cupric state via an S_4 type compound.

APPENDIX

1. Sources and preparation of ligands

The following ligands were used as supplied by the respective manufacturers:

Aldrich Chemical Company

- 2,5-dimercapto-1,3,4-thiadiazole
- 4,5-diphenyl-2-mercaptoimidazole
- 1,2-dimercaptoethane
- 3,4-dimercaptotoluene
- 2,3-dimercaptopropanol
- 3,4-dimercaptotoluene
- 2,3-dimercaptosuccinic acid
- 2-mercaptobenzimidazole
- 2-mercaptobenzoxazole
- 2-mercaptobenzothiazole
- 2-mercapto-1-methylimidazole
- 2-mercaptopyridine
- 2-mercaptothiazoline
- thiomalic acid

Alfa Products

- 6-ethoxy-2-mercaptobenzothiazole

Frinton Laboratories

- 2-mercapto-4-phenylthiazole
- tritylthiol

Koch

- 2-mercaptoimidazoline

K and K Laboratories Inc

- diphenylphosphinodithioic acid

Sigma

N-2-mercaptopropionyl glycine

Aliphatic and aromatic nitrogen bases were obtained from either Aldrich or B.D.H.

The remaining ligands were synthesised as follows:

phenylglyoxal

This was prepared according to the method of H.A. Riley and A.R. Gray (Organic Syntheses Collective Volume 1943 p.509).

phenylglyoxal bisthiosemicarbazide

Phenylglyoxal (5.6 g) was refluxed with thiosemicarbazide (5.6 g) in 95% ethanol for 3 hours. On cooling crystals precipitated which were collected and re-crystallised from 100% ethanol. Found(%): C, 43.2; H, 4.5; N, 28.9. $C_{10}H_{11}N_6S_2$ requires: C, 43.0; H, 4.0; N, 30.1.

benzil bisthiosemicarbazide

The compound was prepared according to the method of B.A. Gingras et al. (Can.J.Chem, 1962, 40, 1053).
Mpt = 213-216°C (Lit. = 217°C).

3-ethoxy-2-oxobutyraldehyde (I)

3-n-heptoxy-2-oxobutyraldehyde (II)

The glyoxals were prepared according to the method of R. Moffet et al. (J.Am.Chem.Soc., 1957, 79, 1687).

The new compound (II) was vacuum distilled at 96-98°C (0.15mm Hg).

The bisthiosemicarbazides of I and II were prepared according to the method of H.G. Petering et al (Cancer Res., 1964, 24, 367). That of (II) was identified by the mass spectrum of its copper and nickel derivatives obtained in situ (M^+(Cu) = 407, M^+(Ni) = 404.

2-benzimidazoleethanethiol

This compound was a generous gift of Dr E. Ainscough.

2. Preparation of Solvents

For synthetic work solvents were of laboratory reagent grade or better and were used as supplied. In spectroscopy, where available, "Analar" or spectroscopic grade solvents were used after the appropriate treatment:

acetone - distilled and dried over anhydrous K_2CO_3.

acetonitrile - a four-step purifying procedure was used entailing refluxing and distilling off anhydrous $AlCl_3$, $KMnO_4$, $KHSO_4$ and CaH_2 in that order. (Alternatively the solvent may be dried in one step by refluxing and storing over P_2O_{10}).

N,N'-dimethylformamide - refluxed and stored over CaH_2 (vacuum distillation required).

chloroform - dried over molecular sieves type 4A.

pyridine, 3-methylpyridine - refluxed over CaH_2, distilled on to molecular sieves type 4A.

nitromethane - dried over molecular sieves type 4A.

3. Mass spectral data

Parent ions and significant fragmentation peaks with intensities relative to the most abundant ion (100) are presented here for the following organic species:

compound	mass of parent ion(M^+)	mass of fragment peaks
dibenzothiazol-2-yl sulphide	300(100)	256(5), 242(29) 16(8), 108(22)
di-6-ethoxybenzothiazol-2-yl sulphide	388(100)	359(31), 331(17)
dibenzothiazol-2-yl disulphide	332(30)	268(6), 167(100)
di-6-ethoxybenzothiazol-2-yl disulphide	420(27)	211(100), 183(87)
di-4-phenylthiazol-2-yl disulphide	384(28)	193(78), 134(100)
4,5-diphenylimidazol-2-yl ethyl ether	312(90)	267(100,219(23) 193(28)

Note: relative intensity in brackets.

4. Miscellaneous Reactions

Recorded here are experimental details for a variety of compounds which warranted further investigation, but for reasons of their suitability to the thesis prescription were left at the stage indicated.

A. Phenolato-hydroxo complexes of copper(II)

Cupric acetate (0.01 mol) in water (50 cm^3) was added slowly to

the appropriate phenol (0.02 mol) in water containing 0.02 mol NaOH. In every case except ortho-aminophenol where a grey precipitate appeared ([Cu(ortho-aminophenol)$_2$]), a green solid precipitated with analysis figures corresponding to the formulation $Cu_2L(OH)_3.xH_2O$ (where LH was the phenol used):

Compound	Analysis (%)		
	C	H	Other
$[Cu_2(phenol)^d(OH)_3.H_2O]$	24.3(24.8)	3.3(3.8)	
$[Cu_2(p\text{-methoxyphenol})^d(OH)_3]$	28.5(27.8)	3.5(2.7)	11.4(10.3)[a]
$[Cu_2(p\text{-chlorophenol})^d(OH)_3]$	25.2(23.5)	2.4(2.6)	12.3(11.6)[b]
$[Cu_2(p\text{-nitrophenol})^d(OH)_3]$	22.7(21.7)	2.3(2.4)	4.2(4.2)[c]
$[Cu_2(3,4\text{-dimethylphenol})(OH)_3]$	31.8(31.9)	3.9(4.35)	
$[Cu(ortho\text{-aminophenol})^d_2].H_2O$	48.1(48.4)	4.6(4.7)	9.2(9.4)[c]

Note: theoretical figures bracketed.

a. % OMe b. %Cl

c. % N d. Anion bound

B. Compounds of 2-aminothiophenol (LH)

Addition of LH (0.01 mole) in ethanol (50 cm^3) to $Cu(ClO_4)_2.6H_2O$ or $Cu(NO_3)_2.3H_2O$ in ethanol (50 cm^3) produces a beige-brown-red precipitate which was immediately filtered and washed with ethanol twice. Compounds of formula $Cu^{II}_4Cu^{I}L_6X_3$ were postulated from analysis figures (theoretical bracketed):

$Cu^{II}_4Cu^{I}L_6(NO_3)_3$ C, 34.7(34.45) H, 3.05(3.4) N, 9.2(10.0);

$Cu^{II}_4Cu^{I}L_6(ClO_4)_3$ C, 31.9(31.7) H, 3.0(2.8) N, 5.8(6.2) Cl, 7.5(7.8).

C. Reaction of 2-mecaptobenzimidazole with excess $CuCl_2.2H_2O$

To $CuCl_2.2H_2O$ (13.6g, 0.080 mol) in ethanol (200 cm^3) was added dropwise 2-mercaptobenzimidazole (1.50g, 0.010 mol). After two weeks the remaining undissolved slurry was filtered. On evaporation of the ethanol the excess $CuCl_2.2H_2O$ was removed by washing with water. The remaining solid was dissolved in ethanol yielding a green unidentified compound (presumably cupric) and large white needles of a compound identified by mass spectroscopy as chlorobenzimidazole.