Synthesis, Crystal Structure and Chemical Reactivity of Dichloro(thiosemicarbazide)copper(II) †

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The structure of dichloro(thiosemicarbazide)copper(II), [Cu(tsc)Cl_2], has been determined by X-ray crystallography. Contrary to earlier proposals the compound is found to be monomeric. Electron spin resonance studies of the compound both as a polycrystalline solid and in dimethylformamide solution are also in accordance with a monomeric structure. The reactivity of [Cu(tsc)Cl_2] towards some Lewis bases such as imidazole, 2,2′-bipyridyl *etc.* has also been studied.

The chemistry of copper ligated to a variety of N,S donors has been studied extensively[1–14] because of its relevance to different enzymes, many of which contain copper co-ordinated to nitrogen and sulphur donor points as their prosthetic group.[15–17] Among the different N,S donors studied, thiosemicarbazides and thiosemicarbazones are of special interest as both of these free ligands and their copper complexes exhibit a variety of biological activities including antitumour activity.[8–13] It has also been indicated[18–20] that in some cases the *in vivo* activity of the free ligand is due to its complexation with copper ions present within the test system and that it is the copper complex which is the actual active species. Campbell and Grzeskowiak[21] studied the copper complexes of thiosemicarbazide (tsc) and on the basis of IR and electronic spectra proposed a polymeric structure for [Cu(tsc)Cl_2] with a square-planar arrangement of halide ions bridging adjacent Cu^{II} ions and with the hydrazinic N and S atoms of the thiosemicarbazide molecule occupying axial positions of adjacent Cu^{II} octahedra. However, as the proposed polymeric structure is inconsistent with the chemical and magnetic properties of the compound and because the proposed bridging mode for thiosemicarbazide has not been observed in any of the numerous complexes of tsc so far studied, we decided to reinvestigate this problem. In this paper we therefore report the single-crystal X-ray structure determination of [Cu(tsc)Cl_2] together with EPR results, all of which indicate a simple monomeric structure. Some interesting and new chemical properties of the compound are also reported, which are also consistent with its monomeric structure.

Experimental

The room-temperature magnetic moment was measured using a PAR vibrating sample magnetometer with Hg[Co(SCN)$_4$] as the calibrant. Infrared spectra were recorded on a Perkin-Elmer 783 infrared spectrophotometer and electronic spectra on a Pye-Unicam SP8-150 UV–visible spectrophotometer. X-Band EPR spectra were recorded on a Varian E-4 X-band (9.5 GHz) spectrometer with 100 kHz field modulation and phase-sensitive detection, using diphenylpicrylhydrazyl (dpph) as an internal field marker.

Preparation of Crystals.—A cold solution of thiosemicarbazide (0.91 g, 0.01 mol) in 2 mol dm^{-3} hydrochloric acid (10 cm^3) was added dropwise to a stirred ice-cold solution of $CuCl_2 \cdot 2H_2O$ (1.7 g, 0.01 mol) also in 2 mol dm^{-3} hydrochloric acid (10 cm^3) in an ice-bath. Together with a green precipitate a few plate-shaped green crystals were obtained by slow evaporation of the reaction medium at room temperature. The crystals were dried over fused calcium chloride (Found: C, 5.5; H, 2.3; Cl, 31.6; Cu, 28.2; N, 18.7. Calc. for $CH_5Cl_2CuN_3S$: C, 5.3; H, 2.2; Cl, 31.4; Cu, 28.1; N, 18.6%), $\mu = 1.90$ at room temperature.

Crystallography.—*Crystal data.* $CH_5Cl_2CuN_3S$, $M = 225.58$, monoclinic, space group $P2_1/n$, $a = 9.161(3)$, $b = 6.980(3)$, $c = 10.437(4)$ Å, $\beta = 99.50(4)°$, $U = 658.2(4)$ Å^3 [by least-squares refinement of diffractometer angles for 25 automatically centred reflections, λ(Mo-Kα) = 0.7107 Å], $D_m = 2.28$ g cm^{-3} (by flotation in benzene–bromoform), $Z = 4$, $D_c = 2.276$ g cm^{-3}, green, plate-shaped crystal $0.5 \times 0.35 \times 0.13$ mm, μ(Mo-Kα) = 43.499 cm^{-1}.

Data collection and processing. 3205 Reflections were measured (of which 1508 were independent), on an Enraf-Nonius CAD-4 diffractometer using graphite monochromated Mo-Kα radiation in the range $2 < \theta < 25°$. Scan mode ω–2θ, scan angle $(1 + 0.35 \tan \theta)°$. The intensity was checked every 2 h of X-ray exposure time and the orientation checked after every 200 reflections. The intensities were corrected for Lorentz and polarization effects but not for absorption.

Structure analysis and refinement. The structure was solved by Patterson and Fourier syntheses. Full-matrix least-squares refinement of the non-H atoms was carried out first with isotropic and then with anisotropic thermal parameters. The hydrogen atoms, located from difference electron density maps, were refined isotropically. The final R value was 0.041 using 1361 observed reflections [$I > 2.5\sigma(I)$]; $R' = 0.038$, $w = 22.5/(\sigma^2|F_o| + 0.0001|F_o|^2)$. The value of R' using all unique reflections is 0.052. Refinement was carried out using[22] SHELX 76 and atomic scattering factors were taken from ref. 23.

Additional material available from the Cambridge Crystallographic Data Centre comprises H-atom coordinates, thermal parameters and remaining bond lengths and angles.

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† *Supplementary data available:* see Instructions for Authors, *J. Chem. Soc., Dalton Trans.*, 1991, Issue 1, pp. xviii–xxii.

Non-SI unit employed: G = 10^{-4} T.

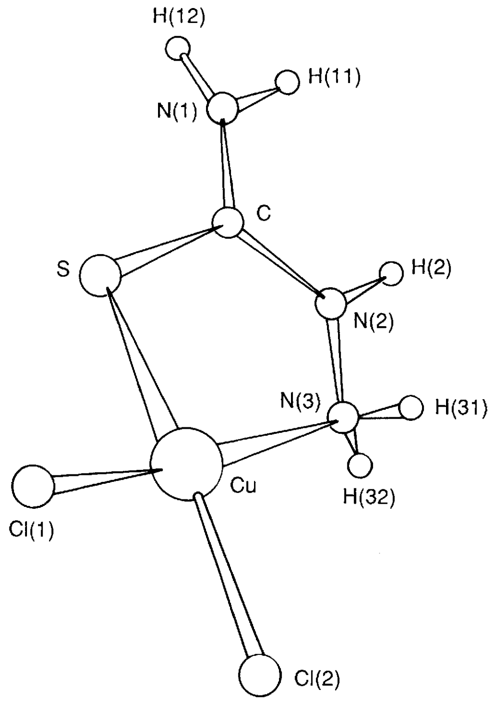

Fig. 1 Atom labelling scheme for [Cu(tsc)Cl_2]

Table 1 Fractional atomic coordinates for [Cu(tsc)Cl_2] with estimated standard deviations (e.s.d.s) in parentheses

Atom	*x*	*y*	*z*
Cu	0.080 56(5)	−0.172 45(6)	0.168 23(4)
Cl(1)	−0.018 6(1)	−0.030 6(1)	0.326 4(1)
Cl(2)	−0.035 0(1)	−0.457 2(1)	0.185 2(1)
S	0.166 3(1)	0.110 3(1)	0.104 1(1)
N(1)	0.346 9(4)	0.131 1(6)	−0.068 2(4)
N(2)	0.279 9(4)	−0.169 5(4)	−0.020 7(3)
N(3)	0.206 7(4)	−0.296 2(4)	0.052 2(3)
C	0.272 0(4)	0.018 0(5)	−0.002 6(3)

Table 2 Bond distances (Å) and angles (°) for [Cu(tsc)Cl_2] with e.s.d.s in parentheses *

Cu–Cl(1)	2.242(1)	N(1)–C	1.311(6)
Cu–Cl(2)	2.272(1)	N(2)–N(3)	1.407(5)
Cu–S	2.266(1)	N(2)–C	1.326(4)
Cu–N(3)	2.002(4)	Cu–S^I	3.355(2)
S–C	1.717(4)	Cu–S^{II}	3.392(2)
S–Cu–N(3)	86.2(1)	N(3)–Cu–S^I	85.3
Cl(2)–Cu–N(3)	89.58(9)	N(3)–Cu–S^{II}	80.5
Cl(2)–Cu–S	166.79(5)	S–Cu–S^{II}	111.5
Cl(1)–Cu–N(3)	168.6(1)	S^I–Cu–S^{II}	159.8
Cl(1)–Cu–S	92.02(4)	Cu–S–C	97.2(1)
Cl(1)–Cu–Cl(2)	94.49(5)	N(3)–N(2)–C	120.1(3)
Cl(1)–Cu–S^I	105.6	Cu–N(3)–N(2)	115.5(2)
Cl(2)–Cu–S^I	85.5	N(1)–C–N(2)	118.3(3)
S–Cu–S^I	81.7	S–C–N(2)	120.8(3)
Cl(1)–Cu–S^{II}	89.7	S–C–N(1)	120.8(3)
Cl(2)–Cu–S^{II}	80.1		

* Symmetry code: I $-x, -y, -z$; II $-x + \frac{1}{2}, y - \frac{1}{2}, -z + \frac{1}{2}$.

Results and Discussion

Crystal and Molecular Structure of [Cu(tsc)Cl_2].—In [Cu(tsc)Cl_2] (Fig. 1) the thiosemicarbazide molecule acts as a bidentate ligand co-ordinating through the thione S atom and the terminal hydrazinic N atom to the same Cu^{II} acceptor centre. The two Cl ions are also co-ordinated. The four co-ordinating atoms are markedly non-planar while the five-membered chelate ring deviates from planarity with the N(3) atom having the maximum deviation [0.049(3) Å] from the mean plane. Each copper centre is also very weakly bonded to two further S atoms (S^I and S^{II}), one (S^I) from a centrosymmetric molecule and the other (S^{II}) from a 2_1 related molecule translated along *b*. Thus the copper lies in a distorted-octahedral co-ordination environment, in which the S atoms bridge the chelate units and each co-ordinates to three Cu^{II} ions. Such long-range co-ordination of sulphur to Cu^{II} is not that unusual.[24] There is, however, no evidence of bridging by the chloride ions. Atomic coordinates are listed in Table 1 and bond distances in Table 2.

In the unprotonated and uncomplexed thiosemicarbazide and thiosemicarbazone derivatives, the S and hydrazinic N atoms assume a *trans* configuration and in metal complexes where the ligand acts as a monodentate S donor this conformation is retained. However when the ligand behaves as a bidentate N,S donor chelating ligand, as in the present structure, these atoms lie *cis* to each other. The S–C–N(2)–N(3) torsion angle in [Cu(tsc)Cl_2] is −2.9(5)° with the N(1) atom deviating considerably from the plane of these atoms.

The Cu–S bond length in [Cu(tsc)Cl_2] is comparable to those in $[Cu(tsc)_2]SO_4$[25] but is slightly shorter than those in $[Cu(tsc)_2][NO_3]_2$.[26] The Cu–N bond, on the other hand, is slightly shorter than those in the sulphate complex but similar to those in the nitrate. The Cu–S^I and Cu–S^{II} distal co-ordination bonds are, however, very long.

The C–N(1), C–N(2) and N(2)–N(3) bond lengths in [Cu(tsc)Cl_2] are similar to those in the uncomplexed ligand. The C–S bond is only slightly longer than that in the uncomplexed ligand.[27]

The molecules are extensively hydrogen bonded as indicated in Fig. 2 which also shows the crystal packing arrangement. The hydrogen bonding interactions are summarised in Table 3.

The polymeric structure of [Cu(tsc)Cl_2] with chloro bridging as posed by Campbell and Grzeskowiak[21] seemed untenable in the light of the rapid interconversion between [Cu(tsc)Cl_2] and monomeric $[Cu(tsc)_2Cl_2]$. On stirring with an excess of $CuCl_2$ in 2 mol dm^{-3} HCl $[Cu(tsc)_2Cl_2]$ is converted to [Cu(tsc)Cl_2] within a few minutes. Similarly [Cu(tsc)Cl_2] is converted rapidly to $[Cu(tsc)_2Cl_2]$ when treated with an excess of ligand in 2 mol dm^{-3} HCl. Moreover, washing [Cu(tsc)Cl_2] with water acidified with HCl converts it to $[Cu(tsc)_2Cl_2]$ and $CuCl_2$. A polymeric structure for [Cu(tsc)Cl_2] would not be expected to show facile interconversion since this would require disruption of the bridging ligand system. The solution behaviour thus points to a monomeric structure for [Cu(tsc)Cl_2] as found in the solid state. That [Cu(tsc)Cl_2], both in the crystal and powdered form (which constitutes the bulk of the product), does not adopt bridging co-ordination is clearly reflected in the following observations: (*a*) the compound strictly obeys the Curie–Weiss law. A plot of $1/\chi$ *vs.* T is linear with $\theta = -14$ K (the variable-temperature susceptibility data of Campbell *et al.*[28] were used after verifying that the room-temperature data of our compound were identical); (*b*) the powder EPR spectrum of [Cu(tsc)Cl_2] exhibits an axial spectrum ($g_{\parallel} = 2.19$, $g_{\perp} = 2.07$) characteristic of monomeric square-planar complexes. A freshly prepared dimethylformamide (dmf) solution of the compound chilled rapidly to 77 K also exhibits a similar axial spectrum ($g_{\parallel} = 2.23$, $g_{\perp} = 2.08$, $g_{iso} = 2.13$, $A_N = 15$ G) with $g_{\parallel}$ showing only a four-line hyperfine splitting ($A^{Cu} = 166$ G) due to the coupling of the unpaired electron with a single copper nucleus. Moreover, neither the powder nor the solution spectrum contains any transition corresponding to $\Delta M_S = \pm 2$. The small increase in the $g_{\parallel}$ value on going from the powder to the frozen dmf solution may be attributed to an increase in axial field strength[29] in the latter when two very long Cu–S axial interactions (> 3.3 Å) are replaced by relatively strong Cu–N axial bonds formed in dmf solution.

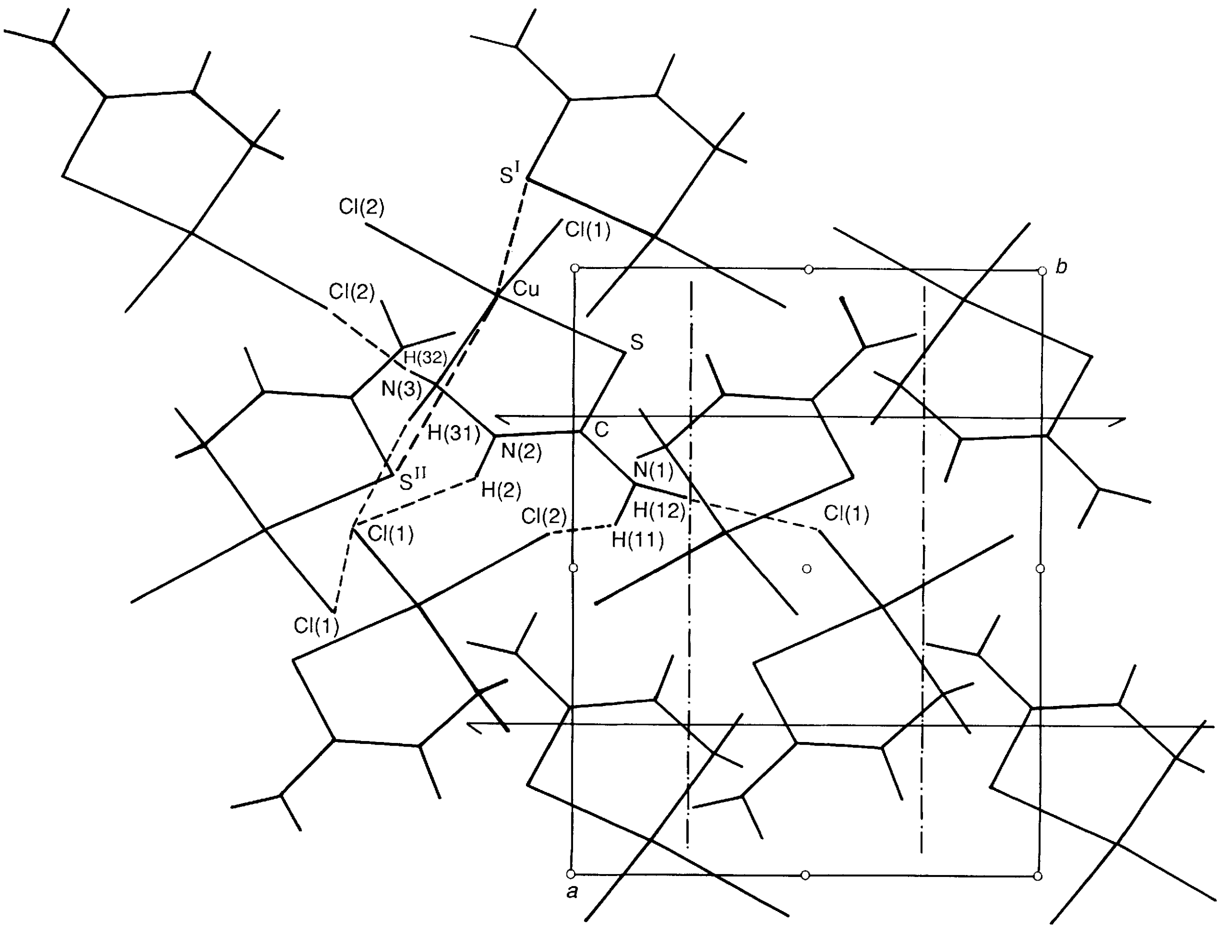

Fig. 2 View of the crystal packing in the *ab* plane

Table 3 Hydrogen bonding interactions; distances in Å, angles in °

	D–H	D···A	A···H	D–H···A	Symmetry
N(1)–H(1)···Cl(2^1)	0.94(5)	3.192(5)	2.27(6)	164(4)	1 $x + \frac{1}{2}, -y - \frac{1}{2}, z - \frac{1}{2}$
N(2)–H(2)···Cl(1^1)	0.83(5)	3.363(4)	2.60(5)	154(4)	
N(1)–H(12)···Cl(1^2)	0.81(8)	3.309(4)	2.57(7)	153(6)	2 $x + \frac{1}{2}, -y + \frac{1}{2}, z - \frac{1}{2}$
N(3)–H(31)···Cl(1^3)	0.90(4)	3.354(4)	2.52(4)	155(3)	3 $-x + \frac{1}{2}, -y + \frac{1}{2}, -z + \frac{1}{2}$
N(3)–H(32)···Cl(2^4)	0.76(5)	3.208(3)	2.46(5)	172(5)	4 $-x, -y - 1, -z$

The compound [Cu(tsc)Cl$_2$] is sparingly soluble in common organic solvents, but appreciably soluble in dimethyl sulphoxide or dmf giving green solutions. These are not stable however and a red compound identified as [Cu(tsc)$_2$Cl$_2$] gradually separates out from the green mother-liquor.

Both [Cu(tsc)Cl$_2$] and [Cu(tsc)$_2$Cl$_2$] are unstable with respect to deprotonation of the ligand, which ultimately leads to decomposition of the ligand and reduction of Cu^{II} to give a Cu^{I} species. Thus aqueous solutions, of both [Cu(tsc)Cl$_2$] and [Cu(tsc)$_2$Cl$_2$] are initially blue, but on standing the blue colour gradually fades and a white solid is deposited. When the reaction is complete {24 h for [Cu(tsc)$_2$Cl$_2$], ≈ 2 weeks for [Cu(tsc)Cl$_2$]} the supernatant liquid becomes colourless (pH 1–2) and contains no copper. The white precipitate was identified as Cu(SCN). The above decomposition can be prevented to a large extent if the aqueous solution is acidified with HCl or if 2,2′-bipyridyl is added to the solution.

Treatment of [Cu(tsc)Cl$_2$] in dmf with equimolar 2,2′-bipyridyl (bipy) results in the precipitation of a grass-green compound of formula Cu(tsc)(bipy)Cl$_2$·dmf. However, treatment of an aqueous solution of CuCl$_2$ with an equimolar amount of bipy followed by the addition of a cold solution of an equimolar amount of tsc in 2 mol dm^{-3} produces a grey precipitate of formula Cu(tsc)(bipy)Cl$_2$. This latter compound when suspended in dmf gradually dissolves yielding a grass-green solution.

When the green solution of [Cu(tsc)Cl$_2$] in dmf is treated with a five-fold excess of imidazole (Him) the solution quickly becomes colourless with evolution of a gas and simultaneous deposition of a red precipitate. On standing, this redissolves and the solution ultimately becomes blue from which a blue compound, Cu(Him)$_4$Cl$_2$, separates. Similar observations were made with [Cu(tsc)$_2$Cl$_2$] and Cu(tsc)(bipy)Cl$_2$, although in the latter case a brown solution was formed initially on the addition of Him and the development of the blue colour together with the appearance of a blue precipitate required 24 h. If the reaction of [Cu(tsc)Cl$_2$] with Him is carried out under an N$_2$ atmosphere, then again a red precipitate of [Cu(tsc)$_2$Cl$_2$] appears initially and the mother-liquor becomes colourless. On standing overnight under nitrogen the precipitate redissolves completely, but the solution remains almost colourless, even after weeks of standing. Thus in the presence of an excess of Him, which acts as a base, the thiosemicarbazide moiety of the complex undergoes enolisation and deprotonation, and the deprotonated thiosemicarbazide moiety, being a stronger reducing agent, reduces the Cu^{II} to Cu^{I} which goes to solution while the oxidised organic moiety itself undergoes decomposition as evidenced by the evolution of a gas. That the colourless solution formed after the addition of Him contains a Cu^I species is suggested by the fact that it is EPR silent and its electronic spectra contains no band in the visible region. On exposure to air this Cu^I species reacts with oxygen and is reoxidized to Cu^{II} which then combines with Him to produce $Cu(Him)_2Cl_2$ (green) and $Cu(Him)_4Cl_2$ (blue). Similar reactions take place in the presence of other bases such as histidine, pyridine, NH_3, Et_3N or OH^- indicating that enolisation of the thiosemicarbazide and subsequent deprotonation is responsible for the reduction of Cu^{II} to Cu^I. This observation is in accord with a similar observation made by Jensen and Rancke Madsen.[30]

Details of the chemical, spectroscopic, magnetic and structural studies of the various products derived from $[Cu(tsc)Cl_2]$ will be reported elsewhere.

References

1 M. Downs, J. Whelan and B. Bosnich, *Inorg. Chem.*, 1981, **20**, 1081.

2 L. Birker, J. Helder, G. Henkel, B. Krebs and J. Reedijk, *Inorg. Chem.*, 1982, **21**, 357.

3 F. J. Reitmeijer, P. J. M. W. L. Birker, S. Gorter and J. Reedijk, *J. Chem. Soc., Dalton Trans.*, 1982, 1191.

4 A. R. Amundsen, J. Whelan and B. Bosnich, *J. Am. Chem. Soc.*, 1977, **99**, 6730.

5 J. V. Davdigian and C. A. Reed, *Inorg. Chem.*, 1979, **18**, 2623.

6 E. W. Ainscough, A. M. Bordic and N. G. Larsen, *Inorg. Chim. Acta*, 1982, **60**, 25.

7 E. W. Ainscough, E. N. Baker, A. M. Bordic, N. G. Larsen and K. L. Brown, *J. Chem. Soc., Dalton Trans.*, 1981, 1746.

8 D. H. Petering and H. G. Petering, *Handbook of Experimental Pharmacology*, eds. C. Sartorelli and D. G. Johns, Springer, Berlin, 1975, p. 841.

9 D. H. Petering, W. E. Antholine and L. A. Saryan, *Anticancer and Interferon agents, Synthesis and Properties*, eds. L. A. Saryan and G. B. Butler, Marcel Dekker, New York, 1984, p. 203.

10 F. A. French and E. J. Blanz, jun., *Cancer Res.*, 1965, **25**, 45.

11 D. H. Petering, *Adv. Exp. Med. Biol.*, 1978, **91**, 179.

12 D. H. Petering in *Metal Ions in Biological Systems*, ed. H. Sigel, Marcel Dekker, New York, 1980, vol. 11, p. 197.

13 D. L. Klayman, J. P. Scovill, C. J. Mason, J. F. Bartosevich, J. Bruce and A. J. Lin, *Arzneim.-Forsch.*, 1983, **33**, 909.

14 C. F. Bell, K. A. K. Lott and N. Hearn, *Polyhedron*, 1987, **6**, 39.

15 *Metal Ions in Proteins, Vol. 3. Copper Proteins*, ed. T. G. Spiro, Wiley, New York, 1981.

16 *Invertebrate Oxygen Binding Proteins*, eds. J. Lamy and J. Lamy, Marcel Dekker, New York, 1981.

17 *The Biochemistry of Copper*, eds. J. Peisach, W. E. Blumberg and P. Aisen, Academic Press, New York, 1966.

18 W. E. Antholine, P. Gunn and L. E. Hopwood, *Int. J. Radiat. Oncology Biol. Phys.*, 1981, **7**, 491.

19 H. G. Petering, H. H. Buskirk, J. A. Crim and G. J. Van Giessen, *Pharmacologist*, 1963, **5**, 271.

20 G. J. Van Giessen and H. G. Petering, 149th National Meeting of the American Chemical Society, Detroit, MI, April 1965, Abstracts, Paper P-13N.

21 M. J. Campbell and R. Grzeskowiak, *J. Chem. Soc. A*, 1967, 396.

22 G. M. Sheldrick, SHELX 76, a Program for Crystal Structure Determination, Cambridge University, 1976.

23 *International Tables for X-Ray Crystallography*, Kynoch Press, Birmingham, 1974, vol. 4.

24 J. Willemse, J. A. Cras, J. J. Steggerda and C. P. Keijzers, *Struct. Bonding (Berlin)*, 1976, p. 83.

25 A. Chiesi Villa, A. G. Manfredotti and C. Gustani, *Cryst. Struct. Commun.*, 1972, **1**, 125.

26 A. Chiesi Villa, A. G. Manfredotti and C. Gustani, *Cryst. Struct. Commun.*, 1972, **1**, 207.

27 G. P. Andreetti, P. Domiano, G. F. Gasparri, M. Nardelli and P. Sgarabotto, *Acta Crystallogr., Sect. B*, 1970, **26**, 1005.

28 M. J. M. Campbell, R. Grezeskowiak and F. B. Tayler, *J. Chem. Soc. A*, 1970, 19.

29 D. W. Smith, *J. Chem. Soc. A*, 1970, 3108.

30 K. A. Jensen and E. Rancke Madsen, *Z. Anorg. Allg. Chem.*, 1934, **219**, 243; K. A. Jensen, *Z. Anorg. Chem.*, 1934, **221**, 6.

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