Copper Complexes of Biologically Active Molecules: The Preparation and Structure of Chlorobis-(2-thiouracil)copper(I) Dimethylformamide Solvate

By GARY W. HUNT and ELMER L. AMMA*
(*Department of Chemistry, University of South Carolina, Columbia, South Carolina* 29208)

Summary Chlorobis-(2-thiouracil)copper(I) dimethylformamide solvate was prepared from cupric chloride and thiouracil and its structure determined and shown to be an almost trigonal planar Cu^{I} bound to sulphur and chlorine.

2-THIOURACIL is one of the uracil analogues that has chemotherapeutic activity because of its ready incorporation into the nucleic acids.[1,2] In addition, the interaction of ions, *e.g.*, Cu^{2+}, with the nucleic acid bases and their derivatives has in recent years attracted substantial attention.[3,4] Therefore, the reaction of Cu^{2+} with 2-thiouracil is of considerable importance as well as the stereochemistry of the product formed.

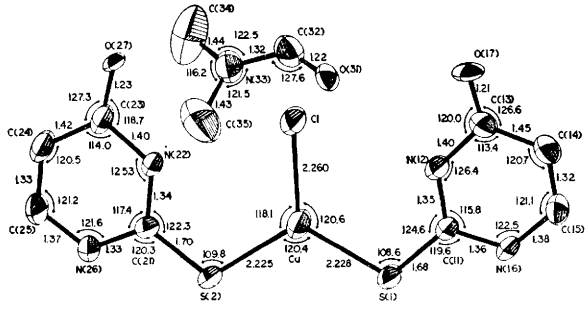

FIGURE. An ORTEP[13] drawing of the chlorobis-(2-thiouracil)-copper(I) molecule and its dimethylformamide molecule of solvation. E.s.d.'s are: distances: Cu–S, Cu–Cl ± 0·001 Å; C–C, C–N, S–C ± 0·01 Å; angles: C–C–C, N–C–N, N–C–C, O–C–C, N–C–O, S–C–N ± 0·5°; Cl–Cu–S, S–Cu–S ± 0·06° or less. Dihedral angles between normals to planes defined by sets of three atoms are: C(21)S(2)Cl–Cl**S(2)**S(1) = 176·0 ± 0·5°; S(1)-C(11)Cl–ClS(2)S(1) = 176·8 ± 0·5°; N(26)S(2)C(21)–C(2)ClC(21) = 177·3 ± 0·5°; N(6)C(11)S(1)–S(1)C(11)Cl = 166·0 ± 0·5°. (The rings are twisted slightly in opposite directions). Hydrogen atoms are omitted for clarity.

2-Thiouracil is also of physiological importance as a well known antithyroid agent.[5] It seems to perform two functions as an antigoitrogenic agent: (1) to reduce iodine to iodide and thus increase production of thyroxine, (2) to decrease the observed elevated copper levels by complexation.[6]

Chlorobis-(2-thiouracil)copper(I) dimethylformamide was prepared by the addition of solid thiouracil to 0·2M $CuCl_2$ at 70 °C. The insoluble product was recrystallized from DMF to give yellow octahedral crystals of diffraction quality. *Crystal data:* Monoclinic $P2_1/c$, $a = 12{\cdot}165(2)$, $b = 11{\cdot}362(2)$, $c = 14{\cdot}565(2)$ Å, $\beta = 122{\cdot}98(2)°$, $Z = 4$, $D_c = 1{\cdot}68$ g/cm^3, $D_m = 1{\cdot}64(2)$ g/cm^3. Mo-K_α $\lambda = 0{\cdot}71068$, $\mu = 18{\cdot}0$ cm^{-1}. A crystal 0·40 × 0·27 × 0·53 mm was mounted on an automated diffractometer and intensity data collected by standard θ—2θ scan techniques[7] to $2\theta = 60°$ with Mo-K_α. Of the 5000 *hkl* reflections measured 2873 were found to be statistically above background and these were used to solve and refine the structure. Absorption corrections[8] were made and maximum and minimum values of the transmission factor were found to be 0·962 and 0·939, respectively. The structure was solved by standard heavy-atom methods[9] and refined by full-matrix (including hydrogen atoms) least-squares[10] with anisotropic temperature factors for non-hydrogen atoms and anomalous dispersion corrections for Cu, Cl, and S to a final conventional R of 0·054. Hydrogen atom parameters in the DMF molecule were not allowed to vary.

The structure may be described as an almost planar $ClCu(SN_2C_4O)_2$ unit in a *cis* configuration with the dimethylformamide molecule simply filling a void (Figure). The environment of Cu^{I} is an almost trigonal plane with the Cu^{I} out of the plane of the sulphur and chlorine atoms by ~ 0·1 Å. The C–S–Cu angle is such that sulphur uses an in-plane sp^2 orbital to bind the copper. The Cu–Cl and Cu–S distances are both at least 0·1 Å shorter than those found in analogous Cu^{I} tetrahedral[11] species and consistent with those of other Cu^{I} trigonal planar systems.[12] The

carbon–sulphur distance clearly indicates a double bond as does the carbon–oxygen distance. Hence, the complexed pyrimidine ring is in the complete keto-form.

The reaction between the cupric chloride and thiouracil is therefore a redox reaction with reduction of the copper and then complexation of Cu^{I} by the free ligand.

G.W.H. thanks the University of South Carolina for a research fellowship.

(*Received*, 21*st September* 1973; *Com.* 1326.)

[1] M.-Y. W. Yu, J. Sedlak, and R. H. Lindsay, *Arch. Biochem. Biophys.*, 1973, **155**(1), 111.
[2] M.-Y. W. Yu, J. Sedlak, and R. H. Lindsay, *Proc. Soc. Exp. Biol. Med.*, 1972, **139**, 1292.
[3] G. L. Eichhorn, N. A. Berger, J. J. Butzow, P. Clark, J. M. Rifkind, Y. A. Shin, and E. Tarien, *Adv. Chem.*, 1971, **100**, 135.
[4] 'Metal Ions and the Transfer of Genetic Information,' G. L. Eichhorn, 166th Amer. Chem. Soc. Nat'l. Meeting, Chicago, Aug. 27—31, 1973, paper INOR 93.
[5] E. R. Garrett and D. J. Weber, *J. Pharm. Sci.*, 1970, **59**, 1383.
[6] D. Libermann, *Nature*, 1949, **164**, 142; D. Libermann, *Bull. Soc. Chim. biol.*, 1949, **31**, 1325.
[7] For data collection techniques see: P. F. Rodesiler and E. L. Amma, *Inorg. Chem.*, 1972, **11**, 388.
[8] Absorption corrections made with GONO9, originally written by W. C. Hamilton at Brookhaven National Laboratory but with local modifications for the IBM 360/65.
[9] Patterson and electron density calculations made with JIMDAP (1968 Brookhaven modification of Zalkin's program of FORDAP) on the IBM 360/65.
[10] ORFLS, 'A Fortran Crystallographic Least Squares Program,' W. R. Busing, K. O. Martin, and H. Levy, Oak Ridge Natl. Lab. ORNL-TM-305 1962.
[11] R. L. Girling and E. L. Amma, *Inorg. Chem.*, 1971, **10**, 335.
[12] M. S. Weininger, G. W. Hunt, and E. L. Amma, *J.C.S. Chem. Comm.*, 1972, 1140; W. A. Spofford III and E. L. Amma, *Acta Cryst.*, 1970, **B26**, 1474.
[13] C. K. Johnson, ORTEP, 'A Fortran Thermal-Ellipsoid Plot Program for Crystal Structure Illustrations,' ORNL-3794, 1970.