X-Ray Crystal Structure of the Thiamine Hydrochloride–Copper(II) Complex

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Summary In the molecular structure of the thiamine hydrochloride·$CuCl_2$ complex, the organic cation is closely surrounded by three copper tetrachloride anions whose configurations deviate significantly from ideal tetrahedral geometry.

Interactions of copper with thiamine are important because it has recently been shown[1] that copper specifically promotes reactions involving the thiazole ring either by breaking the ring to form thiamine disulphide or by linking with the amino-group to form thiochrome. We have commenced studies on the role of the Cu in particular to see if it might be associated with the thiazole fragment.

We report the first determination of the crystal and molecular structure of the thiamine hydrochloride·$CuCl_2$ complex. Marzotto, Nicolini, Signor, and Galzigna,[2] on the basis of u.v., fluorescence, i.r., and n.m.r. spectroscopy, have suggested that in solution, the thiamine molecule is bonded to the metal by a pyrimidine nitrogen atom.

The crystals were prepared according to the method of Marzotto *et al.*[2] The spherical, yellow-orange crystal selected for intensity measurements had a radius of 0·2 mm.

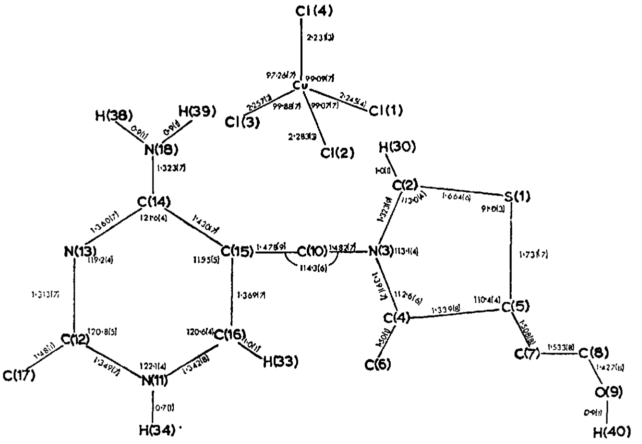

Figure 1. Relevant bond lengths and bond angles in the complex thiamine hydrochloride·$CuCl_2$. E.s.d.s. are given in parentheses: Cl(1)–Cu–Cl(3) = 136·2(1)°, Cl(2)–Cu–Cl(4) = 131·4(1)°

From systematic absences the space group is $P2_1/c$ (monoclinic, 2nd setting) with $a = 9{\cdot}488(5)$, $b = 16{\cdot}871(7)$, $c = 12{\cdot}940(5)$ Å, $\beta = 117{\cdot}2(2)°$, $D_m = 1{\cdot}723$ g cm^{-3} and $D_c = 1{\cdot}700$ g cm^{-3} for $Z = 4$. X-Ray intensity data (1607 independent reflections) were measured using Zr-filtered Mo-K_α radiation and a computer-controlled four-circle diffractometer. The copper atom was located from a three-dimensional Patterson synthesis prepared with LP-corrected data. A Fourier synthesis phased on Cu alone revealed the four chlorine atoms. A subsequent Fourier synthesis yielded the locations of all the non-hydrogen atoms. Atomic parameters, including anisotropic thermal parameters for non-hydrogen atoms were refined by full-matrix least-squares methods. The hydrogen atoms were located in difference Fourier syntheses and were assigned the anisotropic thermal parameters of the atoms to which they were bonded. Their positional parameters were refined. The final R factor was 0·029, unit weights being assigned to each reflection.

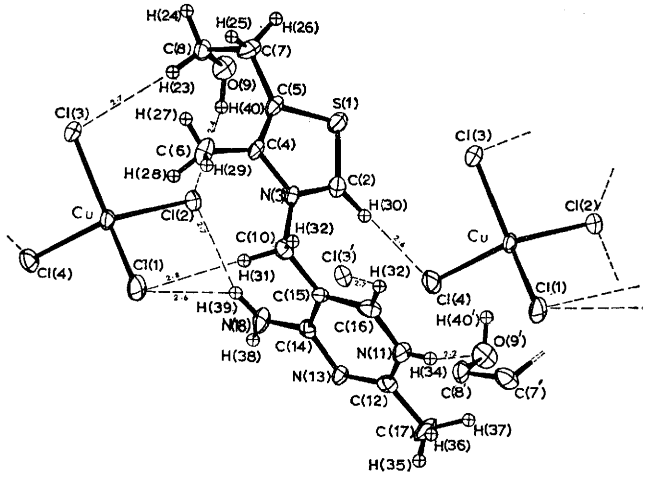

Figure 2. The molecular structure of the complex showing hydrogen bonding and C–H · · · Cl interactions.

The bond lengths and angles in the organic fraction are similar to those fouund in the structure of the parent hydrochloride.[3] The dihedral angle between the thiazolium ring and the pyrimidine ring planes is 89·3°. The unusual feature of the structure is the shape of the copper tetrachloride anion. The four chlorine atoms surrounding the copper atom have a distorted tetrahedral configuration. Although the four Cu–Cl bond lengths do not differ significantly (average Cu–Cl = 2·25 Å), the deviation of the Cl–Cu–Cl angles from ideal tetrahedral geometry bears out this distortion. Four of these angles are roughly equal, their average being about 99° (Figure 1). In addition, the angles Cl(1)–Cu–Cl(3) and Cl(2)–Cu–Cl(4) are 136·2(1)° and 131·4(1)°, respectively.

As in thiamine hydrochloride,[3] atom N(11) [and not N(13)] is protonated. The structure is extensively hydrogen bonded. For a hydrogen bond to exist between the two atoms H and B, we adopt the criterion $d(\mathrm{H} - \mathrm{B}) < W_\mathrm{H} + W_\mathrm{B} - 0{\cdot}2$ Å, where W_H and W_B are the van der Waals radii for the H atom and the acceptor atom B, respectively.[4] On this basis, each thiamine cation exhibits eight hydrogen bonds in this complex. These interactions are represented by dashed lines in Figure 2 in which the primed atoms are symmetry related to the unprimed atoms. The two $[\mathrm{CuCl_4}]^{2-}$ units drawn are equivalent by translation along the x-axis while the atom labelled Cl(3′) is a chlorine of the third $[\mathrm{CuCl_4}]^{2-}$ unit surrounding the thiamine cation. (The errors in the H · · · · Cl distances for C–H · · · · Cl interactions are *ca.* 0·1 Å). Whether these C–H · · · · Cl interactions may be regarded as true hydrogen bonds is questionable,[5] but we nevertheless report four such interactions for direct comparison with those found in the structure of the parent hydrochloride.

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