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Structure of the 1:1 Complex of Histamine with Copper(II) Chloride*

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Abstract. [$Cu(C_5H_9N_3)Cl_2$], $M_r = 245{\cdot}6$, triclinic, $P\bar{1}$, $a = 8{\cdot}592$ (3), $b = 9{\cdot}045$ (3), $c = 5{\cdot}893$ (2) Å, $\alpha = 91{\cdot}2$ (1), $\beta = 98{\cdot}7$ (1), $\gamma = 79{\cdot}9$ (1)°, $Z = 2$, $D_m = 1{\cdot}81$ (flotation), $D_c = 1{\cdot}88$ Mg m^{-3}, $\mu r = 1{\cdot}07$. The structure was determined by the heavy-atom method and refined by least-squares calculations to $R = 0{\cdot}061$. Octahedral coordination of the Cu is observed with two histamine N atoms (at 1·98 and 2·01 Å) and two Cl atoms (at 2·34 and 2·28 Å) in a plane. Two symmetrically transformed Cl(1) atoms at 2·95 and 2·97 Å complete the coordination polyhedron.

Introduction. Histamine is a small-molecule hormone commonly present in the tissues of living organisms. The contribution of histamine in many physiological and pathological processes, *e.g.* regulation of microcirculation and blood pressure, stimulation of gastric secretion, mediation of symptoms of allergy and inflammation or nervous transmission, renders it a highly attractive research subject for many specialists in various fields of biological sciences. The action of histamine on its tissue receptors in various organs has been investigated extensively and some observations concerning structure–activity relationships have been made.

The physiological action of histamine, as well as of most biologically active compounds, strongly depends on the form and route of administration. Since histamine can form salts and complexes of biological interest with a number of heavy metals we have studied some complexes to look for a correlation between the chemical structure of the complex and its histaminic action. So far the crystal structures of $[Cu(hm)_2](ClO_4)_2$ (Bonnet & Jeannin, 1970*a*), $[Cu(hm)_2](BF_4)_2$ (Bonnet & Jeannin, 1970*b*), $[Ni(hm)_2](ClO_4)_2.H_2O$ (Bonnet & Jeannin, 1970*c*) and $[Co(hm)]Cl_2.2HCl$ (Bonnet & Jeannin, 1972) have been solved by the X-ray method and their stereochemical features are well known. Since there are suggestions that in the body histamine might form complexes with copper (Walker, Reeves & Kay, 1975) and these complexes can be of physiological importance the present study was undertaken.

Dark-green prismatic crystals of the compound were kindly furnished by Professor A. Łodzińska, N. Copernicus University. Intensity data were collected with a Syntex diffractometer using monochromatized Cu radiation. Measurements were made for 1196 independent reflections to $2\theta_{\max} = 128{\cdot}3°$. The structure was solved by the heavy-atom method and refined by full-matrix least-squares calculations. Five cycles of refinement with isotropic and four successive cycles with anisotropic thermal parameters resulted in an R of 0·067 and enabled all the H atoms to be located from a difference synthesis. A final refinement with H atoms included with isotropic temperature factors decreased R to 0·061 after four cycles.† The weighting scheme applied was $w = [\sigma(F)]^{-2}$. The scattering factors used in the calculations were those given by Doyle & Turner (1968) for neutral Cu, Cl, N and C atoms, and for H the values from *International Tables for X-ray Crystallography* (1962) were taken. Calculations were carried out on a Riad 32 computer using the XRAY 70 system (Stewart, Kundell & Baldwin, 1970).

Discussion. Positional parameters are in Table 1, and bond lengths and angles in Table 2. A general view of the structure is shown in Fig. 1, which also shows the specific positions of the heavy atoms as well as those of the imidazole ring. The α angle is close to 90°, the x and z coordinates of the heavy atoms correspond to special-position values, and pseudo systematic

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* Structure and Action of Histamine Complexes with Metals. I.

† Lists of structure factors and anisotropic thermal parameters have been deposited with the British Library Lending Division as Supplementary Publication No. SUP 35279 (8 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

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Table 1. *Positional parameters* ($\times 10^4$, *for* H $\times$ 10^3) *and isotropic thermal parameters*

	x	y	z	B_{iso} (Å^2)
Cu	4710 (2)	1234 (1)	2463 (2)	2·22 (5)
Cl(1)	5608 (3)	−1360 (3)	2586 (4)	1·65 (6)
Cl(2)	7306 (3)	1581 (3)	3055 (5)	2·21 (7)
N(1)	3660 (12)	5851 (10)	2512 (15)	2·7 (2)
N(2)	2514 (9)	682 (9)	1906 (15)	1·8 (2)
N(3)	3833 (9)	3410 (8)	2488 (13)	1·4 (2)
C(2)	4628 (13)	4542 (12)	2428 (16)	2·0 (3)
C(4)	2246 (11)	4062 (12)	2684 (18)	2·2 (3)
C(41)	1029 (13)	3114 (13)	2879 (22)	3·1 (3)
C(42)	1086 (12)	1842 (12)	1119 (20)	2·7 (3)
C(5)	2133 (14)	5572 (13)	2655 (20)	3·1 (3)
H(N1)	354 (23)	658 (23)	183 (32)	8 (4)
H′(N2)	254 (17)	33 (15)	125 (23)	4 (2)
H″(N2)	234 (18)	24 (18)	399 (28)	3 (2)
H(C2)	570 (17)	454 (16)	216 (22)	6 (3)
H′(C41)	133 (13)	251 (13)	455 (20)	2 (3)
H″(C41)	19 (13)	357 (12)	243 (19)	2 (3)
H′(C42)	2 (14)	141 (13)	139 (19)	3 (3)
H″(C42)	92 (14)	229 (14)	−16 (21)	3 (3)
H(C5)	88 (18)	656 (17)	273 (24)	9 (5)

Table 2. *Significant interatomic distances* (Å) *and angles* (°)

Cl(1) transforms to Cl(1′) and Cl(1″) by centres of symmetry at $\frac{1}{2}$,0,$\frac{1}{2}$ and $\frac{1}{2}$,0,0 respectively.

Cu–Cl(1)	2·337 (3)	N(1)–C(2)	1·327 (13)
Cu–Cl(2)	2·281 (3)	N(1)–C(5)	1·394 (17)
Cu–Cl(1′)	2·970 (3)	N(2)–C(42)	1·490 (12)
Cu–Cl(1″)	2·949 (3)	N(3)–C(2)	1·330 (14)
Cu–N(2)	2·014 (9)	N(3)–C(4)	1·408 (13)
Cu–N(3)	1·981 (8)	C(4)–C(41)	1·482 (17)
N(2)···N(3)	2·884 (12)	C(4)–C(5)	1·352 (16)
		C(41)–C(42)	1·532 (17)

Cl(1)–Cu–Cl(2)	89·1 (1)	Cu–N(2)–C(42)	120·3 (7)
Cl(1)–Cu–Cl(1′)	92·7 (1)	Cu–N(3)–C(2)	127·3 (7)
Cl(1)–Cu–Cl(1″)	93·0 (1)	Cu–N(3)–C(4)	126·4 (7)
Cl(1)–Cu–N(2)	84·6 (2)	N(1)–C(2)–N(3)	110·7 (10)
Cl(1)–Cu–N(3)	176·0 (4)	N(1)–C(5)–C(4)	106·4 (9)
Cl(1′)–Cu–Cl(1″)	169·4 (1)	N(2)–C(42)–C(41)	108·1 (8)
Cl(1′)–Cu–N(2)	86·8 (3)	N(3)–C(4)–C(41)	120·9 (9)
Cl(1′)–Cu–N(3)	84·4 (2)	N(3)–C(4)–C(5)	108·2 (10)
Cl(1′)–Cu–Cl(2)	94·4 (1)	C(2)–N(1)–C(5)	108·2 (9)
Cl(1″)–Cu–Cl(2)	94·7 (1)	C(2)–N(3)–C(4)	106·3 (8)
Cl(1″)–Cu–N(2)	84·9 (3)	C(4)–C(41)–C(42)	111·7 (10)
Cl(1″)–Cu–N(3)	89·4 (2)	C(5)–C(4)–C(41)	130·9 (10)
Cl(2)–Cu–N(2)	173·6 (3)		
Cl(2)–Cu–N(3)	93·9 (3)		
N(2)–Cu–N(3)	92·5 (3)		

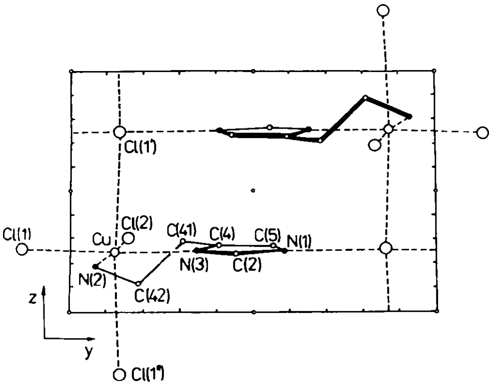

Fig. 1. Projection of the unit cell on the yz plane. H atoms are omitted for clarity.

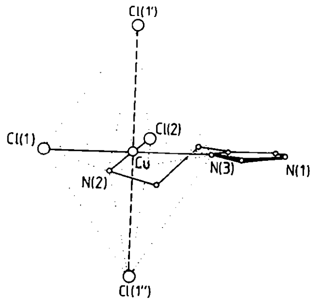

Fig. 2. The Cu coordination polyhedron.

absences for $h0l$ reflections are clearly visible. Coordination of the Cu is octahedral (Fig. 2) (distorted tetragonal bipyramid) with two histamine N atoms with Cu···N distances of 1·98 and 2·01 Å and two Cl atoms (2·28 and 2·34 Å for Cu···Cl) in a plane. Two symmetrically transformed Cl(1) atoms at 2·95 and 2·97 Å complete the coordination polyhedron. Similar coordination occurs in two other histamine–copper complexes, namely in bis(histamino)copper(II) perchlorate and the isomorphic tetrafluoroborate (Bonnet & Jeannin, 1970*a*,*b*). In these compounds, two histamine molecules are chelated to one Cu atom, and perchlorate (or tetrafluoroborate) ions form chains and are 'semi-coordinated' to the Cu. When considering the question of metal coordination by histamine a decisive factor which cannot be neglected is the degree of histamine protonation. It is to be expected that lone pairs of amine and pyridine N atoms of non-protonated histamine will form bonds with the metal cation, where both N atoms act as donors of lone pairs of electrons. As a consequence, pyridine and pyrrole N atoms become alike; this is manifested by the equalization of bond lengths N(1)–C(2) and C(2)–N(3) in the histamine molecule. Lengths of these bonds in the present work are 1·32 and 1·33 Å, while 1·35 and 1·34 Å were found in $[\mathrm{Cu(hm)_2}](\mathrm{ClO_4})_2$ (Bonnet & Jeannin, 1970*a*), as compared with 1·35 and 1·30 Å in histamine free base.

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Benzylammonium Bis[dichloromercury(II)] Chloride

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Abstract. $C_7H_{10}N^+.2HgCl_2.Cl^-$, M_r = 686·6, monoclinic, $C2/c$, $Z = 8$, a = 17·370 (5), b = 6·891 (2), c = 24·735 (7) Å, β = 104·06 (2)°, V = 2872 (1) Å^3, D_c = 3·18, D_m = 3·1 (1) Mg m^{-3}, μ(Mo $K\alpha$) = 22·69 mm^{-1}, single-crystal diffractometer data up to $\sin\theta/\lambda$ = 0·65 Å^{-1}, $R_w(F)$ = 0·056. The structure consists of $C_6H_5CH_2NH_3^+$, $HgCl_2$ and Cl^- groups. The distorted $HgCl_2$ groups have average Hg—Cl = 2·282 (4) and 2·300 (4) Å. The Cl—Hg—Cl angles are 166·6 (2) and 169·9 (1)°. Long Hg—Cl bonds [2·917 (6)–3·094 (7) Å] form a chain structure along b.

Introduction. Colorless crystals of the title compound were obtained from a solution of $C_6H_5CH_2NH_3^+.Cl^-$ and $HgCl_2$ in ethanol. A crystal 0·12 × 0·16 × 0·37 mm was selected. Precession photographs showed the space group to be either Cc or $C2/c$; the latter was accepted during the refinement. Data were collected in two quadrants of reciprocal space, up to $\sin\theta/\lambda$ = 0·65 and 0·60 Å^{-1}, on a Syntex $P2_1$ diffractometer with Nb-filtered Mo $K\alpha$ radiation. 5873 reflections were obtained of which 3229 were independent. Background corrections were made (Blessing, Coppens & Becker, 1974). Three standard reflections observed after every 60 reflections showed small long-term fluctuations up to about 5%. The data were rescaled with respect to the standards.

An absorption correction was applied (transmission range 0·030 to 0·125). A weight was assigned to the reflections according to $w(I) = [\sigma^2(I)_{\text{counting}} + (0{\cdot}03I)^2]^{-1}$. The equivalent reflections were averaged. The internal consistency was $R = \sum |I - \langle I\rangle|/\sum I$ = 0·043. 587 reflections with $\langle I\rangle < 0$ were not used in the analysis. The structure was determined by the Patterson method. A complication arose as the structure contains a pseudo-mirror plane about $y = 0$ and 0·5. The deviation from the mirror symmetry is given by the reflections with l odd, all of which are weak. An inspection of a Patterson synthesis with l odd data only, however, resulted in the directions of the shifts of the atoms from the pseudo-symmetry plane. No H atoms could be located. For those attached to C, positions were calculated and included in the structure factor calculation.

An isotropic extinction correction was made. The structure refined to $R(F)$ = 0·103, $R_w(F)$ = 0·056 and $S = [\sum(|F_o| - |F_c|)^2/(\text{NO} - \text{NV})]^{1/2}$ = 2·23. A final difference synthesis showed features between −3·3 and +3·7 e Å^{-3} at a distance of 1·05 Å from the Hg atoms. Otherwise no features >1·0 e Å^{-3} were found. Scattering factors were taken from *International Tables for X-ray Crystallography* (1974), anomalous scattering factors for Hg and Cl from Cromer & Liberman (1970). The calculations were performed with the XRAY system (Stewart, Kruger, Ammon, Dickinson & Hall, 1972) on the Univac 1108 computer of the University of Frankfurt. Positional parameters are given in Table 1,* bond lengths and angles in Table

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