The Crystal and Molecular Structure of 1,3-Bis(thiocarbamoyl)-2-*NN*-dimethylaminopropane Hydrochloride (Cartap)[1]

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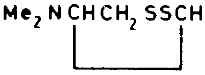
The crystal and molecular structure of 1,2-bis(thiocarbamoyl)-2-*NN*-dimethylaminopropane hydrochloride (II) was determined from three-dimensional diffractometer data with 1 910 observed reflections. The compound crystallizes in the orthorhombic space group $P2_12_12_1$ with a = 9.861(1), b = 9.987(1), c = 13.006(2) Å, Z = 4. The structure was solved by the heavy atom method and refined by least squares to R 0.075 and R_w 0.082.

THE importance of molecular structure in the activity of insecticides has been well established for cyclodiene[2] and DDT related[3] insecticides. Other classes of insecticidal compounds have remained relatively unexplored. Nereistoxin (I), a compound isolated from the marine annelid *Lumbrineris heteropoda*, has been reported to have pharmacological properties.[4,5] Further studies on a number of derivatives of nereistoxin[6] indicate that the 2-dimethylaminopropane-1,3-dithiols are the active compounds. In order to provide accurate structural information about this class of insecticide, we have undertaken the crystal structure determination of 1,3-bis(thiocarbamoyl)-2-*NN*-dimethylaminopropane hydrochloride, also called cartap hydrochloride (II), and marketed under the trade name Padan^R by Takeda Chemical Industries, Ltd.

TABLE 1

Fractional co-ordinates (× 10^4) and anisotropic temperature factor coefficients (× 10^3)

Atom	x	y	z	U_{11}	U_{22}	U_{33}	U_{12}	U_{13}	U_{23}
C(1)	2 986(7)	9 414(6)	1 874(6)	42(3)	32(3)	41(4)	1(2)	0(3)	4(2)
C(2)	3 628(6)	8 795(6)	2 812(5)	24(2)	29(2)	39(4)	2(2)	6(2)	−6(2)
C(3)	4 565(6)	9 798(7)	3 382(6)	30(3)	43(3)	55(5)	−9(2)	4(3)	−15(3)
C(4)	3 277(15)	7 450(12)	456(8)	121(10)	69(6)	39(5)	37(7)	5(6)	6(5)
C(5)	6 978(7)	8 467(7)	3 062(6)	38(3)	38(3)	46(4)	0(3)	−7(3)	0(3)
C(6)	3 212(9)	7 447(10)	4 444(6)	51(4)	76(6)	34(4)	−23(4)	1(3)	8(4)
C(7)	1 628(8)	9 264(10)	4 005(8)	43(4)	80(6)	77(7)	−13(4)	20(4)	−40(5)
N(1)	3 580(5)	8 242(6)	3 577(4)	29(2)	44(3)	34(3)	−9(2)	0(2)	−11(2)
N(2)	2 763(14)	6 497(10)	−198(7)	183(12)	90(7)	58(6)	32(8)	−10(7)	−43(5)
N(3)	8 278(6)	8 455(7)	2 778(6)	32(3)	59(4)	77(5)	3(3)	−1(3)	22(4)
O(1)	4 445(9)	7 702(9)	578(6)	90(5)	116(7)	61(5)	52(5)	16(4)	−6(5)
O(2)	6 370(5)	7 584(5)	3 500(5)	38(2)	40(2)	73(4)	−4(2)	−0(2)	16(2)
S(1)	1 950(2)	8 308(2)	1 117(1)	61(1)	51(1)	39(1)	3(1)	−10(1)	−5(1)
S(2)	6 144(1)	10 002(1)	2 684(1)	30(1)	32(1)	73(1)	−2(1)	6(1)	9(1)
Cl⁻	389(1)	5 990(1)	3 778(2)	29(1)	38(1)	83(1)	−2(1)	1(1)	−4(1)



(I)

$Me_2N\cdot CH(CH_2SCONH_2)_2HCl$

(II)

This structural information is also valuable since its use on various crops to control many insects of both the Lepidoptera and Coleoptera orders is widespread in many European and Asian countries.[7] Cartap's larvicidal[8,9] and ovicidal activity[10] and use as a seed disinfectant[11] have also been demonstrated. The activity on sucking insects is observed even when it is added to the soil during transplantation of rice plants.[12] A number of analytical methods for cartap have been reported.[13] Cartap hydrochloride has been shown to have low residual levels[14] and extremely low toxicity to mammals[15] and fish.[16-18] It also has been demonstrated that cartap shows little or no toxicity among insect predators[19] or along the food chains of aquatic life.[16]

RESULTS AND DISCUSSION

An illustration of the molecular structure is shown in Figure 1. The positional and thermal parameters are listed in Table 1 and the interatomic distances and angles with standard deviations are listed in Table 2.

All bond lengths in the molecule are within experimental error of accepted literature values, with the exception of the C(4)–O(1) carbonyl bond [1.19(1)] which

TABLE 2

Fractional co-ordinates (× 10^4) and isotropic temperature factor coefficients (× 10^3) of hydrogen atoms

Atom	x	y	z	U
H(1)	2 361	10 231	2 123	351
H(2)	3 782	9 786	1 391	351
H(3)	4 218	7 943	2 582	338
H(4)	4 064	10 751	3 435	387
H(5)	4 777	9 432	4 139	387
H(6)	3 772	8 127	4 952	498
H(7)	2 405	6 939	4 881	498
H(8)	3 911	6 691	4 127	498
H(9)	825	8 756	4 440	562
H(10)	2 191	9 944	4 512	562
H(11)	1 171	9 842	3 370	562
H(12)	2 135	7 637	3 107	432
H(13)	3 399	5 935	−619	991
H(14)	1 765	6 359	−253	991
H(15)	8 859	7 760	2 944	456
H(16)	8 679	9 241	2 413	456

appears shortened. The cause of this apparent shortening is not presently known. The chloride ion resides almost equidistant between the quaternary nitrogen N(1) and the amide nitrogen N(3) of an adjacent molecule. The corresponding intermolecular contact distances are 3.13(2) and 3.22(1) Å, respectively. Interestingly, the N(3)–C(5) amide bond distance of 1.33(1) Å is slightly shorter than the corresponding N(2)–C(4) amide bond distance of 1.37(1) Å in the other carbamate group. It is conceivable that this bond shortening is a result of increased double bond character between N(3) and C(5) caused by the proximity of the chloride ion to N(3). Intermolecular packing diagrams in Figures 2 and 3 illustrate this proximity.

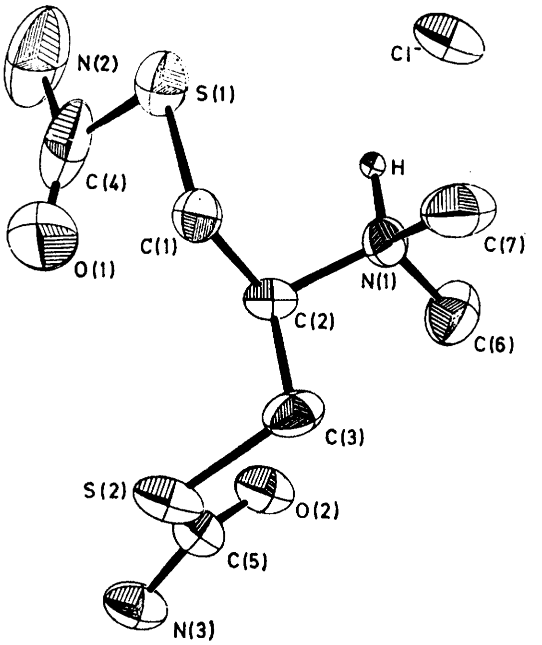


FIGURE 1 Perspective drawing of cartap (II). Hydrogen atoms have been omitted for clarity

The conformation of the molecule is staggered about both the C(1)–C(2) and C(2)–N(1) bonds. The C(1) carbon atom is *anti* to C(6). The C(7) carbon atom is *gauche* (*synclinal*) [20] to both C(1) and C(3) and bisects the angle between them. The sulphur atom S(1), which is bonded to the propane carbon C(1), is *gauche* to the quaternary nitrogen N(1) with the S(1)–C(1) bond coplanar with the H–N(1) bond. The torsion angle S(1)–C(1)–C(2)–N(1) is −60°. The sulphur atom S(2), which is bonded to the propane carbon C(3), is directed away from the quaternary nitrogen N(1). The S(2)–C(3)–C(2)–N(1) torsion angle is 159°. Both of the thiocarbamate functional groups are planar. The carboxy-oxygen atoms, O(1) and O(2), are synplanar to the propane carbons, C(1) and C(3), respectively. The torsion angle of the thiocarbamate and the propane moiety, C(5)–S(2)–C(3)–C(2), is −77°. The torsion angle C(4)–S(1)–C(1)–C(2) is −78°. The dihedral angle between the plane of the S(1) thiocarbamate group and the plane C(1)–C(2)–N(1) is 112°. The corresponding dihedral angle of the plane of the S(2) thiocarbamate group and the plane defined by C(3)–C(2)–N(1) is 83°.

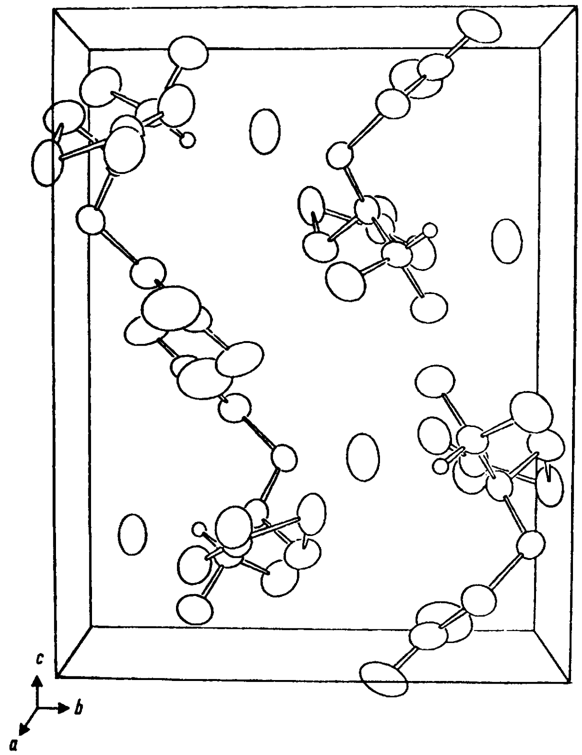


FIGURE 2 Perspective drawing of the unit cell of cartap (I), viewed along the *a* axis

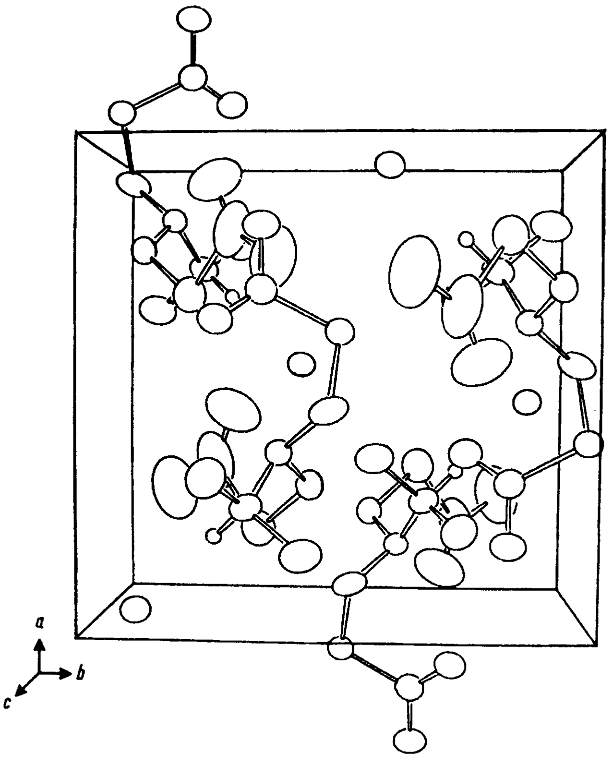


FIGURE 3 Perspective drawing of the unit cell of cartap (II) viewed along the *c* axis

A majority of choline esters whose crystal structure has been determined,[21] as well as other substances possessing the $O{-}C{-}C{-}\overset{+}{N}$ system, have been shown to adopt a *gauche*-conformation in the solid state[22] as well as in solution.[23] This preference is apparently controlled by the intramolecular energetics of the system. By contrast, substances with $S{-}C{-}C{-}\overset{+}{N}$ or $Se{-}C{-}C{-}\overset{+}{N}$ systems preferentially adopt the ***anti*** (antiperiplanar[20]) conformation both in the solid state[24] and in solution.[25] Given the presence of two thiocarbamate groups in cartap, one of these must necessarily assume a conformation *gauche* to the amino nitrogen, and the presence of this conformation in cartap, suggests that its mode of action in insects is cholinergic. Other studies[26] have indicated that the active form of nereistoxin analogues may be dihydronereistoxin and cartap hydrochloride is readily hydrolysed to this form.[27]

TABLE 3

Bond distances (Å) and internuclear and torsion angles (°)

C(4)–N(2)	1.37(1)	C(6)–N(1)–C(7)	109.8(6)
C(5)–N(3)	1.33(1)	C(6)–N(1)–C(2)	113.1(5)
C(4)–O(1)	1.19(1)	C(7)–N(1)–C(2)	114.6(6)
C(5)–O(2)	1.214(9)	N(1)–C(2)–C(3)	108.8(5)
S(1)–C(4)	1.78(1)	N(1)–C(2)–C(1)	112.8(5)
S(2)–C(5)	1.804(8)	C(1)–C(2)–C(3)	111.8(5)
S(1)–C(1)	1.797(7)	C(2)–C(1)–S(1)	115.4(4)
S(2)–C(3)	1.814(7)	C(2)–C(3)–S(2)	110.1(5)
C(2)–C(1)	1.50(1)	C(1)–S(1)–C(4)	98.1(5)
C(2)–C(3)	1.551(9)	C(3)–S(2)–C(5)	99.3(3)
N(1)–C(2)	1.537(8)	S(1)–C(4)–N(2)	111.0(1)
N(1)–C(6)	1.51(1)	S(1)–C(4)–O(1)	122.9(9)
N(1)–C(7)	1.49(1)	N(2)–C(4)–O(1)	125.0(1)
N(1)–Cl$^-$	3.129(6)	S(2)–C(5)–N(3)	112.0(5)
H(1)–C(1)	1.073(7)	S(2)–C(5)–O(2)	121.2(5)
H(2)–C(1)	1.071(8)	N(3)–C(5)–O(2)	126.6(7)
H(3)–C(2)	1.073(6)	C(4)–S(1)–C(1)–C(2)	−78.6(6)
H(4)–C(3)	1.074(7)	S(1)–C(1)–C(2)–N(1)	−60.0(7)
H(5)–C(3)	1.070(9)	N(3)–C(5)–S(2)–C(3)	−169.4(6)
H(6)–C(6)	1.096(9)	S(2)–C(3)–C(2)–C(1)	−75.4(6)
H(7)–C(6)	1.102(9)	S(2)–C(3)–C(2)–N(1)	159.1(4)
H(8)–C(6)	1.103(10)	N(2)–C(4)–S(1)–C(1)	179.5(8)
H(9)–C(7)	1.098(10)	C(3)–C(2)–N(1)–C(6)	−63.4(7)
H(10)–C(7)	1.096(10)	C(3)–C(2)–N(1)–C(7)	63.7(7)
H(11)–C(7)	1.104(10)	C(1)–C(2)–N(1)–C(6)	171.8(6)
H(12)–N(1)	0.966(6)	C(1)–C(2)–N(1)–C(7)	−61.0(7)
H(13)–N(2)	1.004(12)	C(2)–C(3)–S(2)–C(5)	−77.0(5)
H(14)–N(2)	0.997(14)		
H(15)–N(3)	0.925(7)		
H(16)–N(3)	0.999(8)		

EXPERIMENTAL

1,3-Bis(thiocarbamoyl)-2-NN-dimethylaminopropane Hydrochloride (II).—*Crystal data*. $C_7H_{16}ClO_2N_3S_2$, M = 273.8. Orthorhombic, a = 9.861(1), b = 9.987(1), c = 13.006(2) Å, U = 1 280.95 Å^3, D_m = 1.39 (flotation), D_c = 1.419, Z = 4, F(000) = 576. Space group, $P2_12_12_1$ (D_2^4, No. 19).

The crystal selected for data collection was mounted along the b axis and aligned from the angular settings of twelve reflections from different regions of reciprocal space. These reflections were automatically centred on a Picker FACS-I auto-diffractometer using Mo-K_α radiation (λ = 0.710 7 Å) with a graphite monochromater by a least-squares refinement from which the lattice parameters were determined.

Intensity data were collected using θ—2θ scans with a take-off angle of 3.0°, and a scan rate of 1° min^{-1} over a range of 1.55°. A background reading of 10 s was recorded at the two extremities of the scan. The intensities of three standard reflections were monitored every 100 reflections and the deviation of these were $< 7.2\%$ during the data collection.

Lorentz and polarization factors were applied to the data after correction for background intensities, yielding a set of F_o^2 values, where F_o is the observed structure factor amplitude [equation (1) where C is the total integrated

$$F_o = \{1/Lp[C - t_c/2t_b(B_1 + B_2)]\}^{\frac{1}{2}} \qquad (1)$$

count taken over time t_c, B_1 and B_2 are the background counts each taken over time t_b, and Lp represents the combined Lorentz and polarization correction factors]. Intensities of 1947 reflections (with $h,k,l < 12$) were recorded in the range 2θ 5—65°. The values of 1904 reflections which were greater than $\sigma(F_o^2)$ were considered observed, where equation (2) applies. The linear absorption coefficient was calculated (μ 5.988 cm^{-1}) and no absorption corrections were applied.

$$\sigma(F_o) = [C - (t_c/2t_b)^2(B_1 + B_2)]^{\frac{1}{2}}/Lp2F_o \qquad (2)$$

Solution and refinement. The structure was solved using the heavy atom method. The locations of the three heavy atoms were determined from a sharpened, origin-removed Patterson synthesis. No distinction between the sulphur atoms and chloride ion could be made at this point. Successive difference Fourier maps revealed the remaining carbon, nitrogen, and oxygen atoms and distinguished the sulphur atoms from the chloride ion. Full-matrix, least-squares refinement of a scale factor and positional and isotropic thermal parameters for all atoms reduced the unweighted and weighted residuals R and R_w to 0.161 and 0.100 respectively {where $R_w = [\Sigma w|F_o - F_c|^2/\Sigma|F_o|^2]^{\frac{1}{2}}$, and $w = 1/(\sigma)^{\frac{1}{2}}$}. The function minimized was the difference $(|F_o| - |F_c|)^2$.

The hydrogen atoms were located on a difference Fourier map. The hydrogen atoms were assigned the isotropic thermal parameters of the atoms to which they were attached, and entered into the structure. The position of the proton related to the ammonium nitrogen was calculated assuming a nearly tetrahedral geometry and a distance of 1.05 Å from the nitrogen.

The structure was then refined allowing a scale factor and the positional and anisotropic thermal parameters of all non-hydrogen atoms to vary. Hydrogen atom positions were readjusted to normal bound distances and not refined. This reduced the residuals R and R_w to 0.075 and 0.082.

Crystallization of cartap in the form of either enantiomer is possible since the compound is not chiral but the space group is accentric. No conclusion as to appropriate enantiomer could be made since no Friedel pairs were collected, and Hamilton's test[28] was not conclusive. No difference in the residuals was observed when the positional and thermal parameters of either enantiomer were refined. Therefore, the enantiomer was arbitrarily chosen to correspond to the structure of acetylcholine discussed by Pauling.[29]

Bond distances and internuclear and torsion angles are given in Table 3. Observed and calculated structure factors are given in Supplementary Publication No. SUP 22894 (6 pp.).*

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* For details of Supplementary Publications see Notice to Authors No. 7, in *J.C.S. Perkin II*, 1979, Index issue.

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