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Structure of 10-[Di(*n*-propyl)aminoethyl]phenothiazine Hydrochloride

BY LISA C. SOUTHALL, MARY CARL MALMSTROM AND CHERYL L. KLEIN

Department of Chemistry, Xavier University of Louisiana, New Orleans, Louisiana 70125, *USA*

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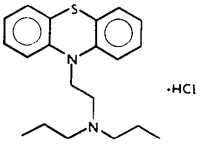
Abstract. $C_{20}H_{27}N_2S^+.Cl^-$, $M_r = 363{\cdot}0$, monoclinic, $P2_1/c$, $a = 14{\cdot}430$ (4), $b = 7{\cdot}565$ (2), $c = 17{\cdot}516$ (6) Å, $\beta = 91{\cdot}49$ (2)°, $V = 1911{\cdot}5$ Å^3, $Z = 4$, $D_x = 1{\cdot}26$ g cm^{-3}, Mo $K\alpha_1$, $\lambda = 0{\cdot}70930$ Å, $\mu = 3{\cdot}1$ cm^{-1}, $F(000) = 776$, $T = 100$ (2) K, final $R = 0{\cdot}040$ for 2540 observed reflections [$I > 3\sigma(I)$]. The title compound crystallizes with a 'butterfly' fold angle of 139·1° between the two benzo rings. The N atom in the side chain is protonated and there is a hydrogen bond between it and the chloride ion. There are no unusual intramolecular distances or angles.

Introduction. Phenothiazine derivatives form a class of drugs which can be used as neuroleptics, sedatives, analgesics, antiemetics and antihistamines. Although the pharmacological activity of the title compound (I) has not been fully tested, the substituent bound to the phenothiazine skeleton causes this compound to be structurally similar to compounds that are known to possess antihistiminic activity (promethazine and thiazinamium methyl sulfate) and anti-parkinsonian activity (diethazine and isothiazine) (Tollenaere, Moereels & Raymaekers, 1979). In order to understand better the varied pharmacological activity of these compounds, we have been studying the structural characteristics of a series of phenothiazine derivatives (Klein, Conrad & Morris, 1985; Klein & Conrad, 1986; Malmstrom & Cordes, 1972, 1973).



(I)

Experimental. Colorless crystal, approximate dimensions 0·40 × 0·15 × 0·15 mm recrystallized from a dichloromethane, hexane, 2-propanol (5:3:1) solution. Enraf–Nonius CAD-4 diffractometer with graphite-crystal-monochromatized Mo $K\alpha$ radiation. All measurements were made at 100 (2) K with a locally modified Enraf–Nonius nitrogen flow system. Unit-cell dimensions and systematic absences $h0l$, $l = 2n + 1$ and $0k0$, $k = 2n + 1$ uniquely determined the space group as $P2_1/c$ with $Z = 4$. Lattice constants determined by least-squares fit of 25 reflections with $26{\cdot}5 \le 2\theta \le 46{\cdot}5°$ measured on diffractometer. Three-dimensional intensity data collected in ω:2θ scan mode; total of 3750 independent reflections, 2540 observed with $I > 3\sigma(I)$; $0 \le 2\theta \le 50°$; $-17 \le h \le 17$, $0 \le k \le 9$, $0 \le l \le 20$. Data corrected for Lorentz and polarization effects. Three standard reflections measured every 2 h during data collection, 400, 020 and 002, showed no significant change in intensity. Absorption as a function of ψ was observed to be minimal and therefore no absorption correction was applied to the data. Structure solved by direct methods using the *MULTAN*11/82 series of programs (Main, Fiske, Hull, Lessinger, Germain, Declercq & Woolfson, 1982). Initial E map contained 23 peaks corresponding to all except one non-H atom which was located on a subsequent difference Fourier map. All H-atom positions were calculated on the basis of sp^2 or sp^3 geometry and a C—H bond length of 0·95 Å. Full-matrix least-squares refinement on F of 24 anisotropic non-H atoms (217 variables) with the fractional coordinates and isotropic thermal parameters of 27 H atoms ($B = 3{\cdot}0$ Å^2) fixed. Final $R = 0{\cdot}040$, $wR = 0{\cdot}059$ where $w = 1/\sigma(F)^2$ and $\sigma(F^2) = [\sigma(I)^2_{cs} + (0{\cdot}04)^2(F^2)^2]^{1/2}$, $S = 1{\cdot}86$ for 2540 observed reflections. In final least-squares cycle $(\Delta/\sigma)_{max} = 0{\cdot}00$. Maximum and minimum peaks in difference Fourier map were 0·33 and −0·27 e Å^{-3}, respectively. Scattering factors taken from *International Tables for X-ray Crystallography* (1974) are corrected for anomalous-scattering contributions, CAD-4 *SDP* programs used (Frenz, 1978).

Discussion. Final fractional coordinates for the non-hydrogen atoms are given in Table 1.* The numbering system for the molecule can be found in Fig. 1. Bond lengths and angles are in Table 2. The title compound crystallizes as the HCl salt with one molecule in the

* Lists of structure factors, anisotropic thermal parameters and H-atom coordinates have been deposited with the British Library Document Supply Centre as Supplementary Publication No. SUP 43286 (22 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

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asymmetric unit and the di(*n*-propyl)aminoethyl nitrogen atom [N(2)] protonated. There is a hydrogen bond between N(2) and the chloride ion [N(2)···Cl(1) 3·024 (2) Å; N(2)–H(N2)···Cl(1) 161·2 (1)°]. There are no unusual intramolecular distances or angles. A stereoscopic packing diagram can be found in Fig. 2. Torsion angles that describe the conformation of the di(*n*-propyl)aminoethyl side chain can also be found in Table 2.

The hybridization of N(2) appears from its bond lengths and angles to be characteristically sp^3. However, N(1) (the N atom in the phenothiazine skeleton) appears to be hybridized between sp^2 and sp^3, resulting in a flattened synperiplanar conformation. The average N(1)–C bond length, 1·435 (3) Å, is shorter than the average N(2)–C bond length, 1·502 (3) Å,

Table 1. *Positional parameters and their estimated standard deviations*

Anisotropically refined atoms are given in the form of the isotropic equivalent thermal parameter defined as: $B_{eq} = \frac{4}{3}[a^2B_{1,1} + b^2B_{2,2} + c^2B_{3,3} + ab(\cos\gamma)B_{1,2} + ac(\cos\beta)B_{1,3} + bc(\cos\alpha)B_{2,3}]$.

	x	*y*	*z*	B_{eq}(Å²)
Cl(1)	0·41669 (5)	−0·25881 (9)	0·59695 (4)	1·85 (1)
S(1)	0·05948 (5)	0·2127 (1)	0·39378 (5)	2·44 (1)
N(1)	0·2525 (2)	0·3056 (3)	0·4347 (1)	1·48 (4)
N(2)	0·3628 (2)	0·1272 (3)	0·5887 (1)	1·34 (4)
C(1)	0·1561 (2)	0·1395 (4)	0·3436 (2)	1·90 (6)
C(2)	0·1446 (2)	0·0277 (4)	0·2812 (2)	2·44 (6)
C(3)	0·2224 (2)	−0·0425 (4)	0·2472 (2)	2·52 (6)
C(4)	0·3098 (2)	0·0025 (4)	0·2745 (2)	2·32 (6)
C(5)	0·3214 (2)	0·1207 (4)	0·3343 (2)	1·80 (5)
C(6)	0·2448 (2)	0·1907 (3)	0·3706 (2)	1·50 (5)
C(7)	0·0988 (2)	0·4280 (4)	0·4145 (2)	1·87 (5)
C(8)	0·0365 (2)	0·5676 (4)	0·4135 (2)	2·26 (6)
C(9)	0·0659 (2)	0·7351 (4)	0·4345 (2)	2·31 (6)
C(10)	0·1580 (2)	0·7606 (4)	0·4544 (2)	2·19 (6)
C(11)	0·2212 (2)	0·6229 (4)	0·4539 (2)	1·91 (5)
C(12)	0·1922 (2)	0·4539 (3)	0·4349 (2)	1·46 (5)
C(13)	0·3443 (2)	0·3241 (4)	0·4716 (2)	1·65 (5)
C(14)	0·3789 (2)	0·1496 (4)	0·5048 (2)	1·58 (5)
C(15)	0·2616 (2)	0·1249 (4)	0·6061 (2)	1·78 (5)
C(16)	0·2425 (2)	0·0556 (4)	0·6853 (2)	1·93 (5)
C(17)	0·1396 (2)	0·0235 (5)	0·6943 (2)	2·74 (6)
C(18)	0·4153 (2)	0·2562 (4)	0·6391 (2)	1·62 (5)
C(19)	0·5177 (2)	0·2675 (4)	0·6236 (2)	1·85 (5)
C(20)	0·5651 (2)	0·3813 (4)	0·6840 (2)	2·08 (6)

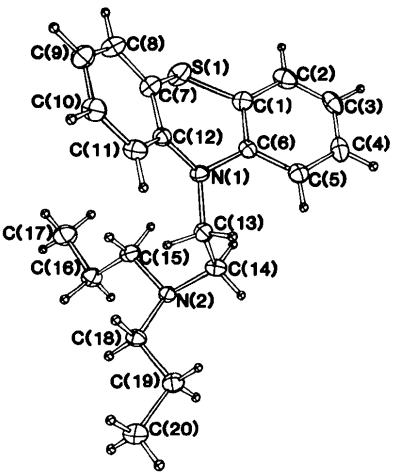

Fig. 1. Molecular structure and numbering system for one molecule of the title compound. The thermal ellipsoids are drawn at 50% probability levels.

Table 2. *Bond distances* (Å), *bond angles* (°) *and selected torsion angles* (°) *for the side chain*

S(1)–C(1)	1·755 (2)	C(5)–C(6)	1·392 (3)
S(1)–C(7)	1·759 (2)	C(7)–C(8)	1·386 (3)
N(1)–C(6)	1·421 (3)	C(7)–C(12)	1·399 (3)
N(1)–C(12)	1·420 (3)	C(8)–C(9)	1·383 (3)
N(1)–C(13)	1·464 (3)	C(9)–C(10)	1·379 (3)
N(2)–C(14)	1·501 (3)	C(10)–C(11)	1·384 (3)
N(2)–C(15)	1·499 (3)	C(11)–C(12)	1·383 (3)
N(2)–C(18)	1·507 (3)	C(13)–C(14)	1·522 (3)
C(1)–C(2)	1·388 (3)	C(15)–C(16)	1·513 (3)
C(1)–C(6)	1·407 (3)	C(16)–C(17)	1·515 (3)
C(2)–C(3)	1·389 (3)	C(18)–C(19)	1·511 (3)
C(3)–C(4)	1·379 (3)	C(19)–C(20)	1·514 (3)
C(4)–C(5)	1·383 (3)		

C(1)–S(1)–C(7)	98·0 (1)	S(1)–C(7)–C(8)	119·8 (2)
C(6)–N(1)–C(12)	116·7 (2)	S(1)–C(7)–C(12)	119·0 (2)
C(6)–N(1)–C(13)	117·2 (2)	C(8)–C(7)–C(12)	121·1 (2)
C(12)–N(1)–C(13)	118·1 (2)	C(7)–C(8)–C(9)	120·1 (2)
C(14)–N(2)–C(15)	112·0 (2)	C(8)–C(9)–C(10)	118·8 (2)
C(14)–N(2)–C(18)	114·3 (2)	C(9)–C(10)–C(11)	121·6 (2)
C(15)–N(2)–C(18)	111·4 (2)	C(10)–C(11)–C(12)	120·1 (2)
S(1)–C(1)–C(2)	120·3 (2)	N(1)–C(12)–C(7)	118·4 (2)
S(1)–C(1)–C(6)	118·2 (2)	N(1)–C(12)–C(11)	123·3 (2)
C(2)–C(1)–C(6)	121·5 (2)	C(7)–C(12)–C(11)	118·3 (2)
C(1)–C(2)–C(3)	119·2 (2)	N(1)–C(13)–C(14)	111·7 (2)
C(2)–C(3)–C(4)	119·9 (2)	N(2)–C(14)–C(13)	114·4 (2)
C(3)–C(4)–C(5)	121·0 (2)	N(2)–C(15)–C(16)	113·0 (2)
C(4)–C(5)–C(6)	120·6 (2)	C(15)–C(16)–C(17)	110·6 (2)
N(1)–C(6)–C(1)	119·0 (2)	N(2)–C(18)–C(19)	114·2 (2)
N(1)–C(6)–C(5)	123·1 (2)	C(18)–C(19)–C(20)	109·5 (2)
C(1)–C(6)–C(5)	117·8 (2)		

C(12)–N(1)–C(13)–C(14)	149·4
N(1)–C(13)–C(14)–N(2)	−97·3
C(13)–C(14)–N(2)–C(15)	−63·2
C(13)–C(14)–N(2)–C(18)	64·7

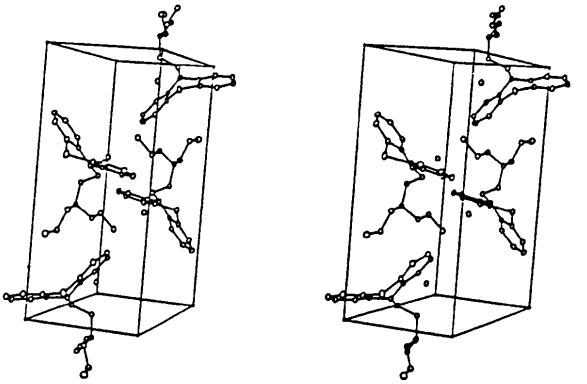

Fig. 2. Stereoscopic packing diagram of the contents of the unit cell.

and the average C—N(1)—C angle, 117·3 (2)°, is larger than the average C—N(2)—C angle, 112·6 (2)°. Although participation of the N(1) lone pair in the aromatic π system would stabilize the N atom, the long S—C bonds force the ring to exist in a boat conformation. This phenomenon has been observed in many neuroleptic drug molecules (Martin, Svensson, Bates & Ortega, 1985).

The angle between the benzo ring planes is 139·1° which compares favorably to the fold angle in other structurally similar compounds [*e.g.* promethazine, 141° (Marsau & Busetta, 1973); thiazinamium methyl sulfate, 136° (Marsau & Cam, 1973); diethazine, 138° (Marsau, 1971); and isothiazine, 138° (Marsau & Calas, 1971)] although wider fold angles are not uncommon [*N*-phenylphenothiazine, 162·6° and 150·7° (Klein *et al.*, 1985); 1-ethylphenothiazine, 154·8° (Chu, Napoleone, Ternay & Chang, 1982); methoxypromazine, 157·7° (Marsau & Gauthier, 1973); *etc.*].

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Structure of *N*,*N*-Dimethyl-2,4-dinitro-3-toluidine*

BY JAN K. MAURIN AND TADEUSZ M. KRYGOWSKI

Department of Chemistry, Warsaw University, Pasteura 1, 02-093 *Warszawa, Poland*

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Abstract. $C_9H_{11}N_3O_4$, $M_r = 225·20$, monoclinic, $P2_1/c$, $a = 7·645$ (2), $b = 10·147$ (3), $c = 14·416$ (5) Å, $\beta = 112·15$ (2)°, $V = 1035·70$ Å^3, $Z = 4$, $D_m = 1·434$ (5), $D_x = 1·444$ (10) g cm^{-3}, λ(Mo $K\alpha$) = 0·7107 Å, $\mu = 1·25$ cm^{-1}, $F(000) = 472$, $T = 297 \pm 1$ K, final $R = 0·0408$ for 1365 observed intensities. Twist angles for NO_2 groups are 18·6 (3) and 66·0 (3)°. Non-additivity of angles was studied using the models of Domenicano & Murray-Rust [*Tetrahedron Lett.* (1979), **24**, 2283–2286] and Norrestam & Schepper [*Acta Chem. Scand. Ser. A* (1981), **35**, 91–103] models. Bond-length variation was analyzed using the *HOSE* model [Krygowski, Anulewicz & Kruszewski (1983). *Acta Cryst.* B**39**, 732–739].

Experimental. Compound obtained by methylation of *m*-toluidine with dimethylsulfate and further nitration with dilute nitric acid. Purified by column chromatography and recrystallization. Crystals were grown from benzene solution. D_m measured at 293 K by flotation in an aqueous solution of KI. Monoclinic symmetry from oscillation and Weissenberg photographs. Systematic absences $h0l$, l odd, $0k0$, k odd; space group $P2_1/c$. Crystal, *ca* 0·5 × 0·4 × 0·4 mm, mounted on Syntex $P2_1$ single-crystal diffractometer. Cell constants determined by least-squares

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