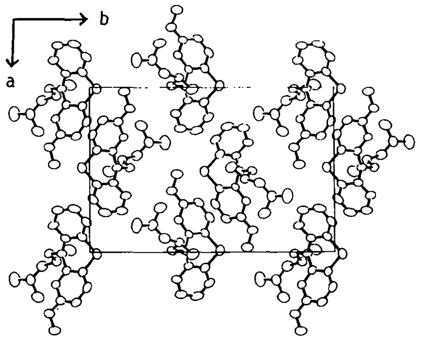

Fig. 2. Crystal structure projected down the *c* axis.

Helm, 1976). The other interatomic distances and bond angles in the phenothiazine ring are also normal (McDowell, 1976). The phenothiazine ring is folded about the axis passing through the S and N(*A*) atoms with a dihedral angle of 135·4°, which agrees well with that of the thiazinamium ion (135·6°) (Marsau & Cam, 1973). However, the geometry around the N(*A*) atom is approximately planar. N(*A*) deviates from the plane defined by C(1), C(13) and C(14) by 0·140 (2) Å.

The crystal structure viewed along the *c* axis is given in Fig. 2. All the intermolecular atomic contacts are usual van der Waals distances.

References

Ashida, T. (1973). *The Universal Crystallographic Computing System – Osaka*, pp. 55–61. The Computation Center, Osaka Univ., Japan.

Chu, S. S. C. & van der Helm, D. (1976). *Acta Cryst.* **B32**, 1012–1016.

International Tables for X-ray Crystallography (1974). Vol. IV, pp. 71–98, 148–150. Birmingham: Kynoch Press.

Johnson, C. K. (1976). *ORTEP* II. Report ORNL-5138. Oak Ridge National Laboratory, Tennessee.

McDowell, J. J. H. (1976). *Acta Cryst.* **B32**, 5–10.

Main, P., Woolfson, M. M., Lessinger, L., Germain, G. & Declercq, J. P. (1974). *MULTAN 74. A System of Computer Programs for the Automatic Solution of Crystal Structures from X-ray Diffraction Data.* Univs. of York, England, and Louvain, Belgium.

Marsau, P. & Busetta, B. (1973). *Acta Cryst.* **B29**, 986–991.

Marsau, P. & Cam, Y. (1973). *Acta Cryst.* **B29**, 980–986.

Stewart, R. F., Davidson, E. R. & Simpson, W. T. (1965). *J. Chem. Phys.* **42**, 3175–3187.

Acta Cryst. (1980). **B36**, 2178–2181

Trifluoperazine Hydrochloride, a Phenothiazine Derivative

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Abstract. $C_{21}H_{26}F_3N_3S^{2+}.2Cl^-$, 10-[3-(4-methyl-1-piperazinyl)propyl]-2-trifluoromethylphenothiazine dihydrochloride (trade name Stelazine), monoclinic, $C2/c$, $a = 35{\cdot}290\ (2)$, $b = 5{\cdot}665\ (2)$, $c = 23{\cdot}595\ (2)$ Å, $\beta = 101{\cdot}24\ (8)°$, $D_m = 1{\cdot}36$, $D_c = 1{\cdot}38$ Mg m^{-3}, $Z = 8$, final $R_w = 0{\cdot}097$. In the tricyclic group, C—S—C is 97·7 (7)°, C—S (mean) = 1·758 (15), C—N (mean) = 1·415 (16), C—F (mean) = 1·285 (16) Å. The angle between the planes of the benzene rings is 141·1°.

Introduction. A sample of trifluoperazine, kindly supplied by Smith, Kline & French Laboratories, was recrystallized from 333–353 K petroleum spirit with a small volume of ethyl alcohol to give colourless transparent needles. The systematic absences were *hkl*, $h + k \neq 2n$ and $h0l$, $l \neq 2n$, indicating space groups *Cc* or *C*2/*c*. Faint layer lines between the normal lines were observed in all oscillation films taken about **b**, but the corresponding Weissenberg photographs did not exhibit discrete reflexions. A Philips PW 1100 four-circle diffractometer with graphite-monochromated Mo $K\alpha$ ($\lambda = 0{\cdot}7107$ Å) radiation at 293 K was used to collect 2446 intensities, including 286 systematically extinct and 1112 unobserved [$I < 2\sigma(I)$], within a sphere $\theta_{\max} = 20°$. The ω-scan mode was used with a scan rate of 0·03° s^{-1} and a scan width of 0·9° in θ. Background counts of 15 s on each side of the reflexion were taken. The cell parameters were obtained by least squares from 25 reflexions. No absorption corrections were applied as μr for the crystal (0·4 × 0·3 × 0·05 mm) was <0·1.

The space group *C*2/*c* was indicated by the analysis of the $|E|$ statistics and distribution. With *SHELX* 76 (Sheldrick, 1976), the correct phasing of eight reflexions, which were hand-selected out of 388 with $E_{\min} \geq 1{\cdot}2$, produced an *E* map which located all 28 non-H atoms of the main molecule. In addition, the two Cl atoms were represented by the three strongest peaks, and it was found that the subsequent refinement of the structure could not be continued without the inclusion of all three. Full-matrix least-squares refinement of coordinates and individual isotropic *B*'s of non-H

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atoms brought R to 0·23. The calculations were performed on a Univac 1106 computer; the programs used were *SHELX* 76 and those of the XRAY system (1976); R is defined as $\sum ||F_o| - |F_c||/\sum |F_o|$; the function minimized, $R_w = \sum w(hkl)[|F_o(hkl) - F_c(hkl)|]^2$. Scattering factors of Cromer & Mann (1968) were used for Cl^-, S, F, N and C, and those of Stewart, Davidson & Simpson (1965) for H.

Most of the H atoms were located on a difference map but, in view of the limited number of observed reflexions (1048) compared with the number of variables, the H atoms were placed in calculated positions, and constrained to ride at 1·08 Å from their corresponding parent atoms. Isotropic thermal parameters derived from those of the carrier atoms were assigned to them. The Cl atoms were given site-occupation factors of 0·5 and six cycles with anisotropic β's of non-H atoms converged to a final R for 2160 reflexions of 0·103 [$R_w = 0{\cdot}097$ with $w(hkl) = k/(\sigma^2|F_o| + |g|F_o^2)$; $k = 0{\cdot}52$ and $g = 0{\cdot}0002$]. The site-occupancy factors of Cl(1), Cl(2) and Cl(3) refined to 1·01, 0·49 and 0·71 respectively. The final positional parameters are given in Table 1.*

Discussion. The actions and uses of the powerful tranquillizer trifluoperazine are similar to those of chlorpromazine, but its onset of action is more rapid and its effects more long-lasting. When trifluoperazine is given in conjunction with chlorpromazine to patients suffering from acute psychoses, the response is generally more rapid and more effective than if either drug is used alone (Martindale, 1977).

Table 2 lists bond lengths and angles ·(uncorrected for thermal motion); Fig. 1 illustrates the molecular configuration and atomic numbering (Johnson, 1970). Within the tricyclic group, the mean C—C lengths, which are 1·386 Å for both benzene rings, the mean C—S, 1·758 (15), mean C—N, 1·415 (16) Å, C—S—C, 97·7 (7), and C—N—C, 118·4 (10)°, are in excellent agreement with those found in related compounds (McDowell, 1976). The mean C—F, 1·285 (16) Å, is shorter than the normal C—F single bond. However, in a study of fluorohalomethanes and -ethanes, it was found that within the range of C—F lengths, shorter C—F distances were associated with multiple F substitution on a single C atom (Gallaher, Yokozeki & Bauer, 1974). Short C—F bonds were also observed in other compounds containing the trifluoromethyl or -ethyl group, such as triflupromazine, 1·285 (25) Å (Phelps & Cordes, 1974), *N*,2,4,6-tetranitro-*N*-trifluoroethylaniline, 1·29–1·36 Å (Holden & Dickinson, 1969), and 9-(3-dimethylaminopropyl)-10-meth-

Table 1. *Final atomic fractional coordinates* (×10^4) *with e.s.d.'s in parentheses*

	x	y	z		x	y	z
Cl(1)	4497(1)	-459(8)	4547(2)	H(2)	2602(5)	4586(30)	714(7)
Cl(2)	5196(2)	6771(12)	2703(3)	H(3)	2571(4)	6973(31)	1581(7)
Cl(3)	5899(2)	7201(12)	3331(3)	H(6)	3538(4)	618(25)	1694(5)
S	3018	7065(8)	2721	H(8)	2794(4)	6445(30)	3830(7)
C(1)	3063(4)	2529(29)	1164(6)	H(9)	3007(4)	3643(33)	4608(7)
C(2)	2796(5)	4276(30)	1122(7)	H(10)	3465(4)	536(22)	4511(6)
C(3)	2781(4)	5569(31)	1609(7)	H(11)	3700(4)	116(30)	3580(6)
C(4)	3030(4)	5221(25)	2130(6)				
C(5)	3305(4)	3385(28)	2154(5)	H(131)	3907(4)	97(29)	2844(5)
C(6)	3323(4)	1987(25)	1678(5)	H(132)	3997(4)	1884(29)	2272(5)
C(21)	3084(4)	1037(33)	646(6)				
F(1)	2777(3)	-193(22)	454(5)	H(141)	4170(4)	3412(27)	3533(5)
F(2)	3364(4)	-337(32)	680(5)	H(142)	4300(4)	4944(27)	2948(5)
F(3)	3086(5)	2321(24)	184(5)				
C(7)	3153(4)	4936(27)	3271(5)	H(151)	4701(4)	1734(26)	2785(6)
C(8)	3003(4)	5102(30)	3784(7)	H(152)	4571(4)	199(26)	3369(6)
C(9)	3114(4)	3495(33)	4211(7)				
C(10)	3376(4)	1763(32)	4160(6)	H(161)	4846(5)	6254(25)	3695(7)
C(11)	3517(4)	1576(30)	3645(6)	H(162)	4716(5)	4356(25)	4218(7)
C(12)	3416(4)	3207(27)	3202(6)				
N(1)	3563(3)	3070(25)	2681(4)	H(171)	5203(4)	5340(26)	4796(6)
				H(172)	5320(4)	7355(26)	4286(6)
C(13)	3928(4)	1892(29)	2699(5)				
C(14)	4257(4)	3220(27)	3121(5)	H(181)	5872(5)	2691(33)	3780(7)
C(15)	4625(4)	1920(26)	3205(6)	H(182)	5720(5)	908(33)	4307(7)
N(2)	4954(3)	2909(24)	3595(5)				
C(16)	4937(5)	4761(25)	3973(7)	H(191)	5248(4)	-232(25)	3705(6)
C(17)	5270(4)	5519(26)	4370(6)	H(192)	5376(4)	1758(25)	3199(6)
N(3)	5627(3)	4378(24)	4378(5)				
C(18)	5642(5)	2372(33)	4014(7)	H(201)	6206(4)	4049(28)	4739(6)
C(19)	5304(4)	1596(25)	3622(6)	H(202)	5915(4)	5003(28)	5222(6)
C(20)	5964(4)	5140(28)	4786(6)	H(203)	6024(4)	6954(28)	4694(6)

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* Lists of structure factors and thermal parameters have been deposited with the British Library Lending Division as Supplementary Publication No. SUP 35289 (15 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

Table 2. *Bond lengths* (Å) *and angles* (°)

C(1)-C(2)	1.358(20)	C(4)-S	1.749(15)
C(2)-C(3)	1.373(20)	C(7)-S	1.767(14)
C(3)-C(4)	1.379(19)	C(5)-N(1)	1.402(15)
C(4)-C(5)	1.416(19)	C(12)-N(1)	1.428(17)
C(5)-C(6)	1.385(18)		
C(6)-C(1)	1.406(18)	N(1)-C(13)	1.443(16)
		C(13)-C(14)	1.566(17)
C(1)-C(21)	1.498(21)	C(14)-C(15)	1.474(16)
C(21)-F(1)	1.292(16)	C(15)-N(2)	1.447(16)
C(21)-F(2)	1.249(18)		
C(21)-F(3)	1.313(16)	N(2)-C(16)	1.387(17)
		C(16)-C(17)	1.417(17)
C(7)-C(8)	1.415(18)	C(17)-N(3)	1.413(16)
C(8)-C(9)	1.358(20)	N(3)-C(18)	1.433(19)
C(9)-C(10)	1.369(20)	C(18)-C(19)	1.429(18)
C(10)-C(11)	1.403(18)	C(19)-N(2)	1.432(16)
C(11)-C(12)	1.388(19)	N(3)-C(20)	1.442(16)
C(12)-C(7)	1.382(18)		
C(6)-C(1)-C(2)	123.3(14)	C(2)-C(1)-C(21)	119.7(14)
C(1)-C(2)-C(3)	117.9(14)	C(6)-C(1)-C(21)	117.0(14)
C(2)-C(3)-C(4)	123.3(14)	C(1)-C(21)-F(1)	114.9(13)
C(3)-C(4)-C(5)	117.0(14)	C(1)-C(21)-F(2)	117.6(12)
C(4)-C(5)-C(6)	121.8(12)	C(1)-C(21)-F(3)	112.0(15)
C(5)-C(6)-C(1)	116.7(13)	F(1)-C(21)-F(2)	106.5(17)
		F(2)-C(21)-F(3)	105.4(15)
C(12)-C(7)-C(8)	121.3(13)	F(3)-C(21)-F(1)	98.4(12)
C(7)-C(8)-C(9)	119.2(14)		
C(8)-C(9)-C(10)	121.2(14)		
C(9)-C(10)-C(11)	119.3(15)	N(1)-C(13)-C(14)	110.1(11)
C(10)-C(11)-C(12)	121.3(15)	C(13)-C(14)-C(15)	111.8(11)
C(11)-C(12)-C(7)	117.5(13)	C(14)-C(15)-N(2)	118.0(12)
		C(15)-N(2)-C(16)	124.8(12)
C(4)-S-C(7)	97.7(7)	C(15)-N(2)-C(19)	113.9(11)
S-C(7)-C(12)	119.2(10)		
C(7)-C(12)-N(1)	120.4(13)		
C(12)-N(1)-C(5)	118.4(10)	C(19)-N(2)-C(16)	120.7(11)
N(1)-C(5)-C(4)	116.8(13)	N(2)-C(16)-C(17)	121.2(13)
C(5)-C(4)-S	122.0(11)	C(16)-C(17)-N(3)	119.5(11)
		C(17)-N(3)-C(18)	119.5(11)
C(3)-C(4)-S	121.0(12)	N(3)-C(18)-C(19)	120.5(14)
C(8)-C(7)-S	119.4(12)	C(18)-C(19)-N(2)	118.2(12)
C(6)-C(5)-N(1)	121.4(13)		
C(11)-C(12)-N(1)	122.0(13)		
C(5)-N(1)-C(13)	120.5(10)	C(17)-N(3)-C(20)	119.3(11)
C(12)-N(1)-C(13)	118.1(10)	C(18)-N(3)-C(20)	120.9(12)

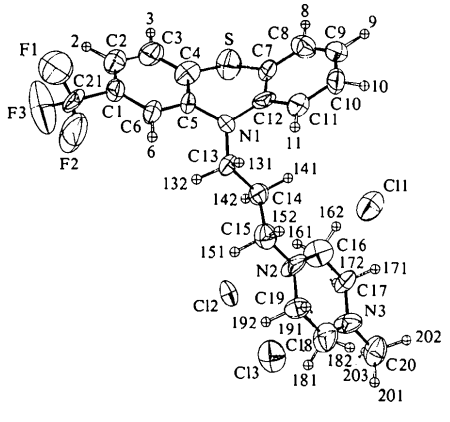

Fig. 1. Thermal-vibration ellipsoids and atomic numbering; ⊕ denotes H atoms.

yl-2-trifluoromethyl-9,10-dihydroanthracene, 1·26 (2) Å (Chu & Chung, 1976).

Table 3 shows that the benzene rings are planar, while S and N(1) lie asymmetrically outside the planes. The angle between the planes is 141·1°, well within the range found in other phenothiazine derivatives (Chu & van der Helm, 1975). The torsion angles of the tail, τ_1 to τ_8 (Table 4), have values comparable with those of prochlorperazine (McDowell, 1979), except for the interchange of τ_3 and τ_4, indicating that in both cases the tail is fairly extended, but in trifluoperazine the tail swings away from the CF_3 group. The piperazine-ring values, τ_9 to τ_{18}, show that the ring is considerably flatter than is usual. From Table 3 it can be seen that the largest deviation from the least-squares plane (III) is only 0·033 Å.

Table 3. *Mean-plane parameters and deviations* (Å) *of atoms from the planes*

E.s.d.'s of deviations range from 0·02 to 0·03 Å.

	Deviations of atoms defining the plane		Distances of atoms not defining the plane	
(I)	C(1)-C(6)			
	$25.3369x + 3.6564y - 9.3343z = 7.5928$			
	C(1)	0.0066	S	0.0992
	C(2)	0.0067	N(1)	0.0552
	C(3)	-0.0129	C(13)	0.5317
	C(4)	0.0052	C(21)	-0.0042
	C(5)	0.0080		
	C(6)	-0.0135		
(II)	C(7)-C(12)			
	$24.4618x + 3.3824y + 6.1562z = 11.3994$			
	C(7)	-0.0041	S	0.0498
	C(8)	0.0008	N(1)	0.0051
	C(9)	-0.0071	C(13)	0.5101
	C(10)	0.0166		
	C(11)	-0.0199		
	C(12)	0.0137		
(III)	N(2)-C(16)-C(17)-N(3)-C(18)-C(19)			
	$12.9587x + 3.5072y - 17.7535z = 1.0253$			
	N(2)	0.0326	C(15)	-0.0475
	C(16)	-0.0121	C(20)	0.0096
	C(17)	-0.0190		
	N(3)	0.0285		
	C(18)	-0.0079		
	C(19)	-0.0221		

Table 4. *Selected torsion angles* (°)

E.s.d.'s are about 1·5°.

τ_1	C(4)–C(5)–N(1)–C(13)	−157·8
τ_2	C(7)–C(12)–N(1)–C(13)	157·5
τ_3	C(5)–N(1)–C(13)–C(14)	138·0
τ_4	C(12)–N(1)–C(13)–C(14)	−62·2
τ_5	N(1)–C(13)–C(14)–C(15)	173·3
τ_6	C(13)–C(14)–C(15)–N(2)	−178·6
τ_7	C(14)–C(15)–N(2)–C(16)	11·8
τ_8	C(14)–C(15)–N(2)–C(19)	−176·5
τ_9	C(15)–N(2)–C(16)–C(17)	175·6
τ_{10}	C(15)–N(2)–C(19)–C(18)	−177·4
τ_{11}	C(19)–N(2)–C(16)–C(17)	4·4
τ_{12}	C(16)–N(2)–C(19)–C(18)	−5·3
τ_{13}	N(2)–C(16)–C(17)–N(3)	0·0
τ_{14}	N(2)–C(19)–C(18)–N(3)	1·4
τ_{15}	C(16)–C(17)–N(3)–C(20)	180·0
τ_{16}	C(19)–C(18)–N(3)–C(20)	178·5
τ_{17}	C(16)–C(17)–N(3)–C(18)	−4·2
τ_{18}	C(19)–C(18)–N(3)–C(17)	3·2

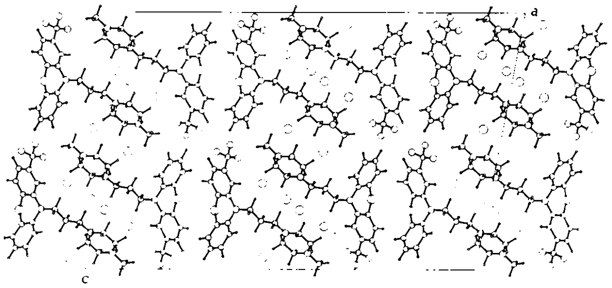

Fig. 2. The structure viewed down **b**.

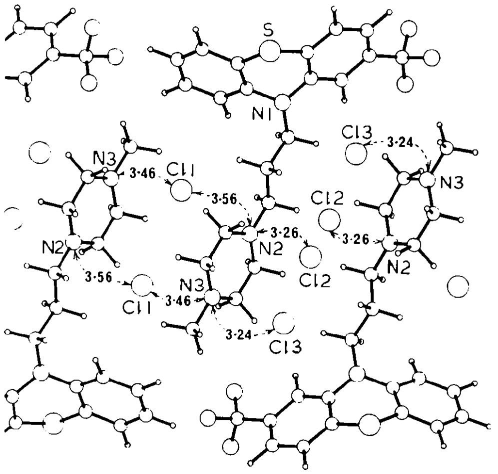

Fig. 3. Cl–N distances (Å).

Fig. 2 shows that the molecules are packed in layers along **b**. The details illustrated in Fig. 3 indicate a possible explanation of the disorder apparent in the Cl(2), Cl(3) half-atoms. The space to the left of the central molecule is occupied by the two Cl(1) ions, which are situated approximately half-way between the N atoms of the two molecules [N(2)–Cl(1) = 3·56, N(3)–Cl(1) = 3·46 Å]. However, the larger space on the right of the central molecule evidently cannot be satisfactorily filled by the two Cl^- ions, which therefore take up either of the alternative positions, *i.e.* Cl(2), at 3·26 Å from N(2), or Cl(3), at 3·24 Å from N(3). Both these distances are less than the sum of the van der Waals radii (3·3 Å). Thus we may regard the crystal as composed of a mixture of the two arrangements. This type of disorder is not unusual; a similar situation was found in prochlorperazine (McDowell, 1979) and in a trichlorodimolybdenum compound (Couldwell, Meunier & Prout, 1979).

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References

Chu, S. S. S. & Chung, B. (1976). *Acta Cryst.* **B32**, 836–842.

Chu, S. S. C. & van der Helm, D. (1975). *Acta Cryst.* **B31**, 1179–1183.

Couldwell, C., Meunier, B. & Prout, C. K. (1979). *Acta Cryst.* **B35**, 603–608.

Cromer, D. T. & Mann, J. B. (1968). *Acta Cryst.* **A24**, 321–324.

Gallaher, K. L., Yokozeki, A. & Bauer, S. H. (1974). *J. Phys. Chem.* **78**, 2389–2395.

Holden, J. R. & Dickinson, C. (1969). *J. Phys. Chem.* **73**, 1199–1204.

Johnson, C. K. (1970). *ORTEP*. Report ORNL-3794. Oak Ridge National Laboratory, Tennessee.

McDowell, J. J. H. (1976). *Acta Cryst.* **B32**, 5–10.

McDowell, J. J. H. (1979). *Acta Cryst.* **B35**, 2433–2436.

Martindale, W. (1977). *The Extra Pharmacopoeia*, edited by A. Wade, pp. 1567–1569. London: The Pharmaceutical Press.

Phelps, D. W. & Cordes, A. W. (1974). *Acta Cryst.* **B30**, 2812–2816.

Sheldrick, G. M. (1976). *SHELX* 76. A program for crystal structure determination. Univ. of Cambridge, England.

Stewart, R. F., Davidson, E. R. & Simpson, W. T. (1965). *J. Chem. Phys.* **42**, 3175–3187.

XRAY system (1976). Tech. Rep. TR-192, revised. Computer Science Center, Univ. of Maryland, College Park, Maryland.