Crystal Structure Determination of 10-Trifluoroacetylphenothiazine
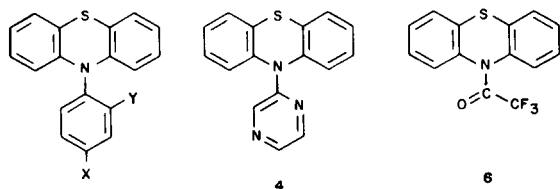
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The structure of the title compound has been determined by single crystal X-ray methods. The crystals are monoclinic, space group $P2_1/n$ with four molecules in a cell of dimensions a = 14.365(4), b = 5.942 (2), c = 17.359(3) Å, β = 119.88(2)° and V = 1298.0(6) Å. The structure has been refined by full-matrix least-squares to R = 0.043 using 1650 observed reflections. This study shows that the folding angle between the two benzo planes is 131.8(1)°, one of the smallest values observed in phenothiazine derivatives. Also, the trifluoroacetyl group is perpendicular to the plane bisecting the tricyclic ring, in contrast to most 10-aryl-substituted phenothiazines where the substituent is approximately parallel to the plane bisecting the tricyclic ring.

Structural studies of 10-phenylphenothiazine, 1 [1] and of many other 10-arylphenothiazines e.g. 2'-methoxy-10-phenylphenothiazine, 2 [2] and 4'-bromo-phenylphenothiazine, 3 [3] have shown that the plane of the 10 aryl substituent is approximately parallel to the plane defined by S, N and C(1') which bisects the tricyclic ring. However, when the substituent exerts a strong electron withdrawing effect of phenothiazine, the geometry of the molecule undergoes important changes as it has been recently found in 10(2'-pyrazyl)phenothiazine 4 [4] and in 4'-nitro-10-phenylphenothiazine, 5 [5]. In 4 and 5, the folding angle between the two benzo rings is much smaller than that observed for 1-3, the plane of the substituent is almost perpendicular to the plane bisecting the tricyclic ring and the N-C' bond is shorter. The structure of 10-trifluoroacetylphenothiazine 6, which is reported here, provides a further example of the influence of an electron withdrawing substituent on the geometry of the phenothiazine tricyclic ring.
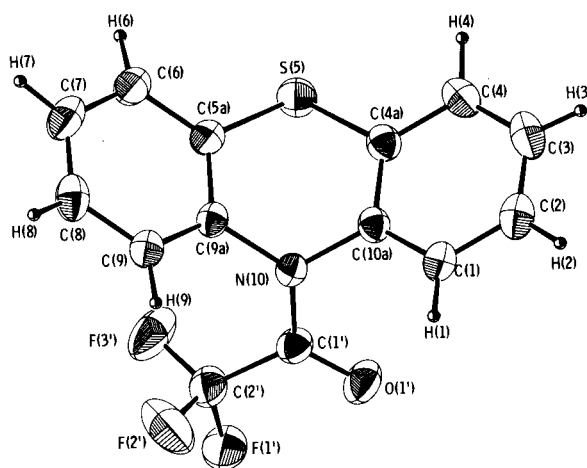

Figure 1. ORTEP drawing of the molecule. Thermal ellipsoids are scaled at the 50% probability level. Hydrogen atoms are represented as spheres of arbitrary radii.

1   X = H,   Y = H
2   X = H,   Y = OCH₃
3   X = Br,   Y = H
5   X = NO₂,   Y = H
7   X = CH₃,   Y = H
8   X = H,   Y = NO₂

(a)

(b)
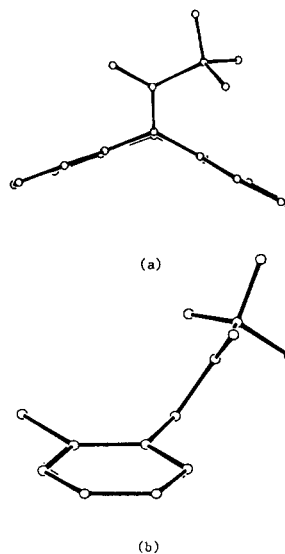
Figure 2. (a) Front view of the molecule showing the folding angle between the two benzo planes. (b) Side view of the molecule sharing the orientation of the trifluoroacetyl group relative to the tricyclic ring. Atoms are represented as circles of arbitrary size and H atoms are omitted for clarity.

EXPERIMENTAL

The crystals of 10-trifluoroacetylphenothiazine are transparent colorless prisms, stable in air but decomposing rapidly under X-rays when they are not coated. A crystal of approximate size 0.76 × 0.67 × 0.61 mm, coated in an epoxy resin, was used for the determination of the unit-cell parameters and the intensity measurements. Accurate unit-cell parameters were obtained by least-squares refinement of 15 reflections centered in the range 26 < 2θ < 36° on a Syntex P2₁ automatic diffracto-

Figure 3. Stereoscopic drawing showing the packing of the molecules in the cell. The H atoms have been excluded.

meter with graphite monochromated MoKα radiation. The crystal data are summarized in Table 1. The space group P2₁/n was determined from the systematic absences O k O, k odd; h O ℓ, h + ℓ od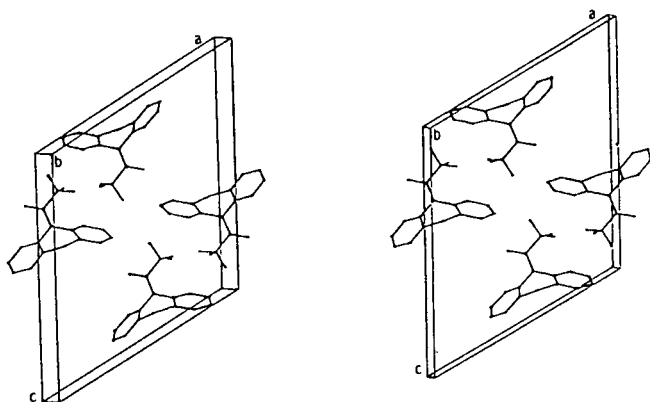d. No decay was observed during data collection as 3 standard reflections remeasured after every 100 reflections did not show any significant change in intensity.

Table 1

Crystal and Experimental Data

Chemical formula	$C_{14}H_8ONF_3S$
Formula weight	295.3
Crystal system	Monoclinic
Space group	P2₁/n
Unit-cell dimensions	a = 14.365(4) Å
	b = 5.942(2)
	c = 17.539(3)
	β = 119.88(2)°
	V = 1298.0(6) Å³
Number of molecules per cell	4
Density (calculated)	1.511 g/cm³
X-ray radiation used for data collection	λ(MoKα) = 0.71069 Å
Linear absorption coefficient	μ(MoKα) = 2.28 cm⁻¹
Total number of independent reflections with 2θ < 50°	2293
Number of reflections with I > 3σ(I)	1650
R-indexes for 1650 observed reflections R	0.043
R$_w$	0.049
Maximum residual electron density	0.25 e/Å³

Table 2

Fractional Atomic Coordinates and Anisotropic Temperature Factors for the Non Hydrogen Atoms and
Isotropic for the Hydrogen Atoms

Atom	x	y	z	U_{11}	U_{22}	U_{33}	U_{12}	U_{13}	U_{23}
C(1)	1.1202(2)	0.6720(6)	0.6805(2)	0.044(2)	0.061(2)	0.059(2)	0.000(2)	0.022(1)	0.005(2)
C(2)	1.1921(3)	0.6288(7)	0.6523(2)	0.050(2)	0.081(2)	0.070(2)	−0.001(2)	0.028(2)	0.015(2)
C(3)	1.1855(3)	0.4308(7)	0.6090(2)	0.059(2)	0.097(3)	0.073(2)	0.019(2)	0.041(2)	0.022(2)
C(4)	1.1070(3)	0.2759(7)	0.5920(2)	0.068(2)	0.071(2)	0.066(2)	0.012(2)	0.040(2)	0.003(2)
C(4A)	1.0346(2)	0.3174(5)	0.6207(2)	0.050(2)	0.059(2)	0.052(2)	0.006(1)	0.025(1)	0.005(1)
S(5)	0.9326(1)	0.1209(1)	0.6010(1)	0.067(1)	0.052(0)	0.078(1)	−0.001(0)	0.038(0)	−0.005(0)
C(5A)	0.8297(2)	0.3116(5)	0.5820(2)	0.049(2)	0.055(2)	0.046(2)	−0.004(1)	0.023(1)	0.004(1)
C(6)	0.7237(2)	0.2677(6)	0.5180(2)	0.055(2)	0.072(2)	0.054(2)	−0.010(2)	0.024(2)	−0.001(2)
C(7)	0.6466(3)	0.4239(7)	0.5025(2)	0.051(2)	0.097(3)	0.054(2)	−0.015(2)	0.016(2)	0.007(2)
C(8)	0.6721(3)	0.6249(7)	0.5469(2)	0.048(2)	0.083(3)	0.069(2)	0.011(2)	0.028(2)	0.021(2)
C(9)	0.7774(2)	0.6715(6)	0.6100(2)	0.048(2)	0.060(2)	0.056(2)	−0.001(2)	0.025(2)	0.003(2)
C(9A)	0.8546(2)	0.5122(6)	0.6291(2)	0.040(1)	0.052(2)	0.044(1)	−0.002(1)	0.020(1)	0.005(1)
N(10)	0.9657(2)	0.5479(4)	0.6952(1)	0.040(1)	0.053(1)	0.046(1)	0.000(1)	0.019(1)	−0.001(1)
C(10A)	1.0426(2)	0.5149(5)	0.6654(2)	0.042(1)	0.055(2)	0.046(1)	0.005(1)	0.021(1)	0.005(1)
C(1′)	1.0043(2)	0.5632(5)	0.7833(2)	0.052(2)	0.066(2)	0.046(2)	−0.004(2)	0.021(1)	0.001(2)
O(1′)	1.0984(2)	0.5750(5)	0.8370(1)	0.051(1)	0.139(2)	0.050(1)	−0.013(1)	0.015(1)	0.000(1)
C(2′)	0.9244(3)	0.5623(8)	0.8166(2)	0.055(2)	0.122(3)	0.049(2)	−0.001(2)	0.023(2)	0.000(2)
F(1′)	0.9757(1)	0.5258(4)	0.9029(1)	0.079(1)	0.155(2)	0.049(1)	−0.012(1)	0.031(1)	0.000(1)
F(2′)	0.8770(2)	0.7612(6)	0.8046(2)	0.127(2)	0.197(3)	0.099(2)	0.074(2)	0.071(2)	0.020(2)
F(3′)	0.8496(2)	0.4134(5)	0.7815(1)	0.093(1)	0.248(3)	0.066(1)	−0.088(2)	0.043(1)	−0.022(2)
H(1)	1.126(2)	0.808(4)	0.709(2)	0.042(7)					
H(2)	1.244(2)	0.736(5)	0.664(2)	0.073(10)					
H(3)	1.238(2)	0.402(5)	0.597(2)	0.076(10)					
H(4)	1.094(2)	0.136(5)	0.557(2)	0.072(9)					
H(6)	0.720(2)	0.121(6)	0.477(2)	0.100(11)					
H(7)	0.580(3)	0.393(6)	0.458(2)	0.084(10)					
H(8)	0.625(2)	0.731(5)	0.532(2)	0.068(10)					
H(9)	0.800(2)	0.805(4)	0.641(2)	0.046(8)					

The expression for the thermal parameters with U values is

$$T = \exp\{-2\pi^2(U_{11}h^2a^{*2} + U_{22}k^2b^{*2} + U_{33}\ell^2c^{*2} + 2U_{12}hka^*b^* + 2U_{13}h\ell a^*c^* + 2U_{23}k\ell b^*c^*)\}$$

Table 3

Selected Dihedral Angles (°) with e.s.d.'s in Parentheses

C(4a)	-	S(5)	-	C(5a)	-	C(9a)	− 35.6(4)
S(5)	-	C(5a)	-	C(9a)	-	N(10)	− 2.7(5)
C(5a)	-	C(9a)	-	N(10)	-	C(10a)	51.0(5)
C(9a)	-	N(10)	-	C(10a)	-	C(4a)	− 49.9(5)
N(10)	-	C(10a)	-	C(4a)	-	S(5)	0.9(5)
C(10a)	-	C(4a)	-	S(5)	-	C(5a)	36.6(4)
C(9a)	-	N(10)	-	C(1')	-	C(2')	− 5.3(5)
C(9a)	-	N(10)	-	C(1')	-	O(1')	173.8(4)
C(10a)	-	N(10)	-	C(1')	-	C(2')	− 170.9(4)
C(10a)	-	N(10)	-	C(1')	-	O(1')	8.2(6)

Table 4

Least-squares Planes
Equation of Planes: Ax + By + Cz = D
(x,y, and z in fractional coordianates)

Plane	A	B	C	D
(a)	2.95(2)	−2.645(9)	11.40(2)	9.29(2)
(b)	−8.46(2)	−2.468(8)	15.65(1)	1.33(2)
(c)	−0.33(3)	5.916(1)	−0.82(4)	2.35(3)

Atomic Displacements (Å) from the Least-squares Planes

(a)		(b)		(c)	
N(1)	− 0.006(4)	C(5a)	− 0.010(4)	N(10)	− 0.001(4)
C(2)	− 0.001(5)	C(6)	− 0.007(4)	C(1')	0.004(4)
C(3)	0.009(5)	C(7)	0.017(5)	O(1')	− 0.001(4)
C(4)	− 0.007(5)	C(8)	0.000(5)	C(2')	− 0.002(7)
C(4a)	− 0.003(4)	C(9)	− 0.018(4)		
C(10a)	0.008(4)	C(9a)	0.022(4)		
S(5)*	− 0.009(5)	S(5)*	− 0.112(5)		
N(10)*	0.033(5)	N(10)*	− 0.009(5)		

* Atoms excluded from the calculation of the least-squares planes.

The data were collected in the $\theta/2\theta$ scanning mode with a variable scan rate of 2.93-14.65°/min using a scan width of 1.0° below $K\alpha_1$, to 1.2° above $K\alpha_2$. A total of 2293 independent reflections was collected to $2\theta = 50°$, of which 1650 were judged as being observed with $I > 3\ \sigma(I)$, where $\sigma(I)$ was determined from counting statistics. The intensity data were reduced to structure amplitudes by application of the Lorentz and polarization corrections. No correction for absorption was applied.

The structure was solved by direct methods, using MULTAN78 [6] which showed the positions of all non-hydrogen atoms. Refinement was carried out using the SHELX76 [7] system of programs. Non-hydrogen atoms were refined with anisotropic temperature factors. A subsequent difference Fourier map allowed to locate the hydrogen atoms which were then refined with isotropic temperature factors. The quantity minimized in the least-squares refinement was $\Sigma w(|F_o|-|F_c|)^2$. In the final stages of refinement, a weight $w = 1/(\sigma^2(F) + 2.47 \times 10^{-4}F^2)$ was used. The final R indexes are R = 0.043 and wR = 0.048 for the 1650 observed reflections. During the last cycle, no parameter underwent a shift of more than 0.06 times its standard deviation. The atomic scattering factors for C, H, O, N, F and S and the effects of the anomalous dispersion for S used were those stored in SHELX76. The final atomic parameters are given in Table 2.

Results and Discussion.

The identification of the atoms and the configuration of the molecule are shown in the ORTEP [8] drawing of Figure 1. The central ring is in a boat conformation as shown in Figure 2(b) and also by the torsion angles around the central ring which are given in Table 3 and the puckering parameters [9] $q_2 = 0.647(3)$, $q_3 = −0.022(3)$, $Q = 0.647(3)$ Å, $\phi_2 = 119.0(3)$ and $\theta = 91.9(3)°$. For ideal boat conformation, these parameters are $q_2 = Q$, $q_3 = 0$ Å, $\phi_2 = 120$ and $\theta = 90°$. The substituent is in equiatorial position relative to the central ring. The plane C(1'), O(1'), C(2') of the trifluoroacetyl group is virtually perpendicular to the plane S(5) N(10), C(1') bisecting the tricyclic ring with an angle of 89.2(2)° between these two planes. The deviations of the atoms from the least-squares planes calculated for the two benzo rings are presented in Table 4. The benzo rings are folded along the S(5)...N(10) line as can be seen from Figure 2(a), with a folding of 131.8(1)°. In Table 5, the angle between the substituent and the plane bisecting the tricyclic ring as well as the folding angle of several phenothiazine derivatives are compared to those of the title compound. From this table, it can be seen that when the substituent is approximately parallel to the plane bisecting the tricyclic ring as observed for compounds 1-3, 7, and 8, the folding angle is substantially higher than when the substituent is perpendicular as found in compounds 4, 5 and 6. In these three last com-

Table 5

Geometric Data of some N(10) Substituted Phenothiazines
(a) Angle (°) between the substituents and the plane S,N,C'. (b) Folding angle (°) between the two benzo planes.
(c) N(10)-C'(substituent) bond length (Å). (d) C(9a)-N(10)-C(10a) angle (°).

Compound	Substituent	(a)	(b)	(c)	(d)	Reference
1*	phenyl	2.3,5.4	150.7,162.6	1.452,1.458	123.0,120.7	1
7	4'-methylphenyl	6.0	151.9	1.445	120.8	11
2	2'-methoxyphenyl	2.9	157.5	1.436	122.5	2
3*	4'-bromophenyl	4.6,2.5	144.9,150.8	1.430,1.436	120.0,120.8	3
8	2'-nitrophenyl	6.6	154.8	1.437	122.1	10
5*	4'-nitrophenyl	80.8,80.2	120.8,124.4	1.383,1.389	113.4,114.4	5
4	2'-pyrazyl	88.2	132.2	1.388	115.3	4
6	trifluoroacetyl	89.2	131.8	1.356	115.1	this work

* Two crystallographically independent molecules.

Table 6

Bond Lengths (Å) and Bond Angles (°) with e.s.d.'s in Parenthese

Bond lengths

C(1)	-	C(2)	1.371(5)
C(1)	-	C(10A)	1.371(5)
C(2)	-	C(3)	1.375(6)
C(3)	-	C(4)	1.365(6)
C(4)	-	C(4A)	1.382(5)
C(4A)	-	S(5)	1.763(3)
C(4A)	-	C(10A)	1.381(4)
S(5)	-	C(5A)	1.753(3)
C(5A)	-	C(6)	1.389(5)
C(5A)	-	C(9A)	1.389(4)
C(6)	-	C(7)	1.361(5)
C(7)	-	C(8)	1.369(6)
C(8)	-	C(9)	1.381(5)
C(9)	-	C(9A)	1.363(5)
C(9A)	-	N(10)	1.441(4)
N(10)	-	C(10A)	1.449(4)
N(10)	-	C(1')	1.356(4)
C(1')	-	O(1')	1.200(4)
C(1')	-	C(2')	1.522(5)
C(2')	-	F(1')	1.326(5)
C(2')	-	F(2')	1.324(5)
C(2')	-	F(3')	1.284(5)

Bond Angles

C(2)	-	C(1)	-	C(10A)	119.1(3)
C(1)	-	C(2)	-	C(3)	120.1(4)
C(2)	-	C(3)	-	C(4)	121.1(4)
C(3)	-	C(4)	-	C(4A)	119.2(4)
C(4)	-	C(4A)	-	S(5)	120.7(3)
C(4)	-	C(4A)	-	C(10A)	119.5(3)
S(5)	-	C(4A)	-	C(10A)	119.8(2)
C(4A)	-	S(5)	-	C(5A)	98.4(2)
S(5)	-	C(5A)	-	C(6)	120.6(2)
S(5)	-	C(5A)	-	C(9A)	119.9(2)
C(6)	-	C(5A)	-	C(9A)	119.5(3)
C(5A)	-	C(6)	-	C(7)	119.0(3)
C(6)	-	C(7)	-	C(8)	121.3(4)
C(7)	-	C(8)	-	C(9)	120.2(4)
C(8)	-	C(9)	-	C(9A)	119.0(3)
C(5A)	-	C(9A)	-	C(9)	120.8(3)
C(5A)	-	C(9A)	-	N(10)	117.1(3)
C(9)	-	C(9A)	-	N(10)	122.0(3)
C(9A)	-	N(10)	-	C(10A)	115.1(2)
C(9A)	-	N(10)	-	C(1')	125.6(3)
C(10A)	-	N(10)	-	C(1')	117.9(2)
C(1)	-	C(10A)	-	C(4A)	121.0(3)
C(1)	-	C(10A)	-	N(10)	121.9(3)
C(4A)	-	C(10A)	-	N(10)	117.1(3)
N(10)	-	C(1')	-	O(1')	123.7(3)
N(10)	-	C(1')	-	C(2')	118.5(3)
O(1')	-	C(1')	-	C(2')	117.8(3)
C(1')	-	C(2')	-	F(1')	110.0(3)
C(1')	-	C(2')	-	F(2')	111.1(3)
C(1')	-	C(2')	-	F(3')	115.3(3)
F(1')	-	C(2')	-	F(2')	105.9(3)
F(1')	-	C(2')	-	F(3')	106.7(3)
F(2')	-	C(2')	-	F(3')	107.3(4)

tion between the central ring and the 10-substituent. The bond lengths and bond angles of **6** are listed in Table 6. The major differences in bond lengths and angles between the title compound and the phenothiazines mentioned earlier are centered on the N(10) atom. In Table 5, the N-C'(substituent) distances and the C-N-C angles within the central ring of these phenothiazines are compared to those of **6**. While the five first compounds tabulated present a N-C' distance ranging from 1.43 to 1.46 Å, there is a significant shortening of this distance in compounds **4-6**, with the lowest value of 1.356 Å in **6**. The C-N-C angles are also about 5° smaller in **4-6** than in the other phenothiazine listed. In compounds **4-6**, the resonance interaction favored by the perpendicular orientation of the substituent is evidenced by the shorter N-C' bond which presents a more pronounced double bond character than that found in **1-3, 7** and **8**. In 2'-nitro-10-phenylphenothiazine, **8**, the same effects are not observed because the presence of a nitro group in ortho position prevents the nitrophenyl group to be perpendicular to the plane bisecting the central ring as in 4'-nitro-10-phenylphenothiazine, **5**. In **8**, the substituent is approximately parallel, the folding angle is 154.8° and the longer N-C' distance of 1.437 Å indicates little interaction between the substituent and the central ring.

The packing of the molecules in the unit-cell is shown in the stereoscopic drawing of Figure 3. The shortest intermolecular contact between non H atoms is F(2')...F(3') of 2.966(4) Å.

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pounds, the electron withdrawing substituent adopts the perpendicular orientation necessary for resonance interac-