The Crystal Structure of *N*-Isopropylphenothiazine

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The crystal structure of *N*-isopropylphenothiazine, $C_{15}H_{15}NS$, has been determined by the heavy-atom method. The refinement was carried out by the least-squares method with anisotropic temperature factors based on three-dimensional data to give a final R value of 0·045 for 4826 reflections. The space group is $P2_1/c$ with $Z=8$, and the unit-cell dimensions are $a=11·011$ (4), $b=17·186$ (6), $c=13·598$ (5) Å and $\beta=90·653$ (3)°. There are two crystallographically independent molecules in one asymmetric unit of the crystal, and the two molecules have significantly different folding angles, and C–S–C and C–N–C bond angles within the central ring. The dihedral angles between the best planes of the benzene rings are 136·1 and 146·8°, the C–S–C bond angles are 97·3 and 98·9°, and the C–N–C bond angles within the central ring are 117·4 and 118·6°, respectively, for the two crystallographically independent molecules. The average sulfur–carbon bond length is 1·760 (1) Å, and the average carbon–nitrogen bond length within the ring is 1·412 (2) Å. The three carbon–nitrogen bonds around the nitrogen atom are approximately planar in configuration. The packing of the molecules in the crystal is determined by the van der Waals interaction.

Introduction

The determination of the crystal structure of *N*-isopropylphenothiazine (I) is a continuation of the studies on a series of phenothiazine derivatives. The objective of this study is to determine the effect of different substituents on the stereochemistry of phenothiazines and on the chemical reactivity of the different *N*-substituted phenothiazines (Biehl, 1975).

(I)
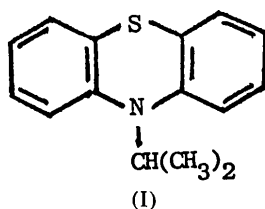
Experimental

Samples of *N*-isopropylphenothiazine were obtained through the courtesy of Dr Edward R. Biehl of the Chemistry Department of Southern Methodist University. Single crystals in the form of clear prisms were grown from ethyl alcohol solutions. The unit-cell parameters and the intensity data were measured on a Nonius-CAD 4 automatic diffractometer. The crystal data are summarized in Table 1. An $\omega/2\theta$ scanning mode with Ni-filtered Cu $K\alpha$ radiation was used to measure 5302 independent reflections with 2θ values

below 150°, of which 4836 reflections were considered as observed. A reflection was considered as observed if its intensity was greater than $2·0\sigma(I)$, where $\sigma(I)$ was determined from counting statistics. The intensity data were reduced to structure factors, and no absorption corrections were applied.

Table 1. *Crystal data of N-isopropylphenothiazine*

Chemical formula: $C_{15}H_{15}NS$, M.W. 241·36
Crystal system: monoclinic
Space group: $P2_1/c$ from the systematic extinctions $0k0$ absent with k odd and $h0l$ absent with l odd.
$a=11·011$ (1) Å
$b=17·186$ (1)   (obtained from + and −2θ values of 40
$c=13·598$ (1)   reflections)
$\beta=90·65$ (1)°
$V=2573·00$ Å³ $Z=8$
$F(000)=1024$
$D_x=1·246$ g cm^{-3}
$D_m=1·26$ g cm^{-3} (by flotation in a mixture of acetone and carbon tetrachloride)
λ(Cu $K\alpha$)=1·5418 Å μ(Cu $K\alpha$)=19·60 cm^{-1}
Crystal dimensions: 0·40 × 0·36 × 0·25 mm

Structure determination and refinement

The structure was determined by the heavy-atom method. There are two crystallographically independent molecules in one asymmetric unit of the crystal. The refinement was carried out by the full-matrix least-squares method with isotropic temperature factors and block-diagonal least-squares method with anisotropic temperature factors. All the H atoms were located on

two successive difference Fourier syntheses. Their positional parameters were refined; however, their thermal parameters were assigned the same values as those of the atoms to which they are bonded. Cruickshank's (1965) weighting scheme was used, and the weight of each reflection was calculated according to the formula $1/w = (0.58 - 0.065|F_o| + 0.0025|F_o|^2)$. The quantity $\sum w\{||F_o| - |F_c||\}^2$ was minimized. The final R value $(\sum ||F_o| - |F_c||/\sum|F_o|)$ was 0.045. The magnitude, $\{\sum w(F_o - F_c)^2/(m-n)\}^{1/2}$, where m is the number of reflections and n is the number of parameters refined, was 1.15. There were ten low-order strong reflections, whose calculated structure amplitudes were much higher than the observed values due to extinction. These were given zero weight in the least-squares refinement and were excluded in the calculation of the final R value.

The atomic scattering factors used for S, N, and C atoms were those from *International Tables for X-ray Crystallography* (1962), and the values given by Stewart, Davidson & Simpson (1965) were used for H. The computer programs used in this analysis were *ORFLS* (Busing, Martin & Levy, 1962), the block-diagonal least-squares program (Shiono, 1971), the Zalkin Fourier synthesis program modified by Dr R. Shiono of the University of Pittsburgh, and a number of structure interpretation programs (Shiono, 1971; Chu, 1973). All calculations were carried out on a CDC CYBER 72 computer in the Bradfield Computing Laboratory at Southern Methodist University. The final positional and thermal parameters are given in Table 2.*

Discussion of structure

Stereoscopic views of the configurations of the two crystallographically independent molecules are shown

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* A table of calculated and observed structure factors has been deposited with the British Library Lending Division as Supplementary Publication No. SUP 31337 (29 pp., 1 microfiche). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 13 White Friars, Chester CH1 1NZ, England.

Table 2. *Fractional atomic coordinates ($\times 10^4$) and thermal parameters*

The estimated standard deviations are given in parentheses and refer to the last positions of respective values. The expression for the temperature factor exponent consistent with B values in Å^2 is:
$$-\tfrac{1}{4}(h^2a^{*2}B_{11} + k^2b^{*2}B_{22} + l^2c^{*2}B_{33} + 2hka^*b^*B_{12} + 2hla^*c^*B_{13} + 2klb^*c^*B_{23}).$$

Molecule A	x	y	z	B_{11}	B_{22}	B_{33}	B_{12}	B_{13}	B_{23}
S	1108 (0)	6464 (0)	1962 (0)	4·56 (1)	3·70 (1)	5·32 (2)	0·75 (1)	−0·50 (1)	−0·94 (1)
N	1180 (1)	4743 (1)	2069 (1)	3·16 (4)	3·89 (5)	4·53 (5)	−0·10 (3)	−0·27 (4)	0·91 (4)
C(1)	3445 (2)	6234 (1)	1371 (1)	4·34 (7)	4·26 (7)	5·11 (8)	−0·84 (6)	−0·63 (5)	0·34 (6)
C(2)	4459 (1)	5786 (1)	1205 (1)	3·58 (6)	5·79 (9)	6·10 (9)	−0·87 (6)	0·04 (6)	0·54 (7)
C(3)	4406 (1)	4990 (1)	1352 (1)	3·14 (6)	5·66 (8)	5·74 (8)	0·22 (6)	−0·11 (5)	−0·18 (7)
C(4)	3345 (1)	4641 (1)	1649 (1)	3·43 (6)	4·00 (7)	4·90 (7)	0·33 (5)	−0·48 (5)	0·01 (5)
C(5)	−797 (1)	4557 (1)	1225 (1)	3·40 (6)	5·06 (8)	4·61 (7)	−0·30 (6)	0·13 (5)	0·03 (6)
C(6)	−1817 (1)	4872 (1)	778 (1)	3·11 (6)	6·99 (10)	4·22 (7)	−0·22 (6)	−0·11 (5)	−0·16 (6)
C(7)	−1934 (1)	5667 (1)	663 (1)	3·73 (6)	6·98 (10)	4·16 (7)	1·51 (6)	−0·27 (5)	0·03 (6)
C(8)	−1021 (1)	6146 (1)	996 (1)	4·07 (7)	5·35 (8)	4·33 (7)	1·50 (5)	−0·05 (5)	−0·15 (6)
C(11)	2378 (1)	5884 (1)	1684 (1)	3·53 (5)	3·56 (5)	3·86 (6)	0·04 (4)	−0·61 (4)	−0·10 (4)
C(12)	2299 (1)	5079 (1)	1809 (1)	3·01 (5)	3·76 (5)	3·42 (5)	−0·04 (4)	−0·40 (4)	0·14 (4)
C(13)	125 (1)	5031 (1)	1599 (1)	2·92 (5)	4·45 (7)	3·37 (5)	0·24 (4)	0·21 (4)	0·19 (4)
C(14)	−11 (1)	5836 (1)	1473 (1)	3·39 (5)	4·49 (7)	3·55 (5)	0·75 (5)	0·25 (4)	−0·21 (5)
C(15)	1192 (1)	3997 (1)	2615 (1)	4·06 (6)	4·41 (7)	5·25 (8)	−0·31 (6)	−0·52 (5)	1·60 (6)
C(16)	200 (2)	3980 (1)	3370 (2)	5·66 (9)	7·99 (12)	5·88 (10)	−0·91 (9)	0·40 (7)	2·35 (9)
C(17)	1193 (2)	3262 (1)	1984 (2)	5·54 (9)	4·20 (8)	8·53 (13)	−0·45 (6)	−0·71 (8)	0·62 (8)

Molecule B									
S′	3458 (0)	2561 (0)	4401 (0)	3·90 (1)	3·91 (1)	5·51 (2)	−1·00 (1)	0·41 (1)	−0·62 (1)
N′	5609 (1)	3490 (1)	5062 (1)	4·10 (5)	4·37 (5)	3·06 (5)	−0·66 (4)	−0·14 (4)	−0·25 (4)
C′(1)	2350 (2)	3503 (1)	5727 (1)	4·66 (8)	5·81 (9)	5·28 (8)	0·68 (6)	0·94 (6)	1·05 (7)
C′(2)	2341 (2)	4024 (1)	6497 (1)	6·77 (10)	6·62 (10)	4·78 (8)	2·22 (9)	2·03 (7)	0·96 (7)
C′(3)	3407 (2)	4368 (1)	6793 (1)	8·35 (12)	5·45 (9)	4·27 (8)	1·47 (9)	1·01 (8)	−0·24 (6)
C′(4)	4473 (2)	4218 (1)	6312 (1)	6·79 (10)	4·56 (8)	3·80 (7)	−0·03 (7)	0·38 (6)	−0·38 (5)
C′(5)	6475 (1)	3580 (1)	3405 (1)	4·72 (7)	4·26 (7)	3·69 (6)	−1·05 (6)	−0·11 (5)	−0·03 (5)
C′(6)	6435 (2)	3389 (1)	2414 (1)	5·56 (8)	4·90 (8)	3·65 (6)	−0·24 (6)	0·63 (5)	0·21 (5)
C′(7)	5474 (2)	2977 (1)	2021 (1)	5·42 (8)	4·61 (7)	3·22 (5)	0·81 (6)	−0·32 (5)	−0·65 (5)
C′(8)	4542 (1)	2753 (1)	2632 (1)	4·13 (6)	3·81 (7)	4·31 (7)	0·72 (5)	−0·97 (5)	−1·06 (5)
C′(11)	3432 (1)	3321 (1)	5267 (1)	4·38 (6)	3·73 (7)	3·91 (6)	0·21 (5)	0·45 (5)	0·48 (5)
C′(12)	4518 (1)	3686 (1)	5542 (1)	4·96 (7)	3·45 (5)	3·26 (5)	0·02 (5)	0·27 (5)	0·31 (4)
C′(13)	5567 (1)	3343 (1)	4039 (1)	3·91 (6)	3·08 (5)	3·11 (5)	−0·13 (4)	−0·24 (4)	−0·13 (4)
C′(14)	4593 (1)	2924 (1)	3628 (1)	3·43 (5)	3·06 (5)	3·79 (5)	0·14 (4)	−0·30 (4)	−0·39 (4)
C′(15)	6774 (2)	3614 (1)	5595 (1)	4·85 (7)	5·02 (8)	3·22 (5)	−1·29 (6)	−0·62 (5)	0·10 (5)
C′(16)	7690 (2)	2979 (1)	5377 (1)	4·49 (7)	6·97 (10)	4·70 (8)	−0·31 (7)	−0·52 (6)	0·30 (7)
C′(17)	7340 (2)	4424 (1)	5489 (1)	7·29 (11)	6·00 (10)	4·65 (8)	−2·76 (9)	−0·92 (7)	−0·08 (7)

Table 2 (*cont.*)

Hydrogen atomic coordinates ($\times 10^3$)

Molecule *A*	*x*	*y*	*z*
H(1)	349 (1)	682 (1)	131 (1)
H(2)	524 (1)	602 (1)	105 (1)
H(3)	516 (1)	466 (1)	117 (1)
H(4)	334 (1)	409 (1)	178 (1)
H(5)	−73 (1)	398 (1)	127 (1)
H(6)	−238 (1)	453 (1)	53 (1)
H(7)	−267 (1)	586 (1)	30 (1)
H(8)	−106 (1)	678 (1)	89 (1)
H(15)	198 (1)	404 (1)	299 (1)
H(16)1	29 (2)	440 (1)	381 (1)
H(16)2	−62 (2)	399 (1)	308 (1)
H(16)3	27 (2)	345 (1)	374 (1)
H(17)1	174 (2)	328 (1)	145 (2)
H(17)2	43 (2)	306 (1)	181 (2)
H(17)3	152 (2)	280 (1)	237 (2)

Molecule *B*			
H′(1)	160 (2)	328 (1)	547 (1)
H′(2)	156 (2)	408 (1)	679 (1)
H′(3)	330 (2)	471 (1)	737 (1)
H′(4)	516 (2)	443 (1)	653 (1)
H′(5)	714 (1)	386 (1)	366 (1)
H′(6)	704 (2)	359 (1)	201 (1)
H′(7)	545 (2)	286 (1)	135 (1)
H′(8)	382 (1)	244 (1)	235 (1)
H′(15)	655 (1)	355 (1)	630 (1)
H′(16)1	732 (2)	246 (1)	543 (1)
H′(16)2	801 (2)	302 (1)	477 (1)
H′(16)3	840 (3)	299 (1)	583 (1)
H′(17)1	795 (2)	449 (1)	606 (1)
H′(17)2	772 (2)	451 (1)	486 (1)
H′(17)3	673 (2)	481 (1)	558 (1)

in Fig. 1 (Johnson, 1965). The identification of the atoms and the bond lengths and bond angles with their standard deviations are shown in Fig. 2. Since the crystal belongs to a centrosymmetric space group, both enantiomorphs are present in the crystal. The presence of both enamers is also verified by the fact that two different products are formed by bromination (Biehl, 1975).

The mean value of the four C–S bond lengths is $1\cdot760 \pm 0\cdot001$ Å, and that of the four C–N bond lengths within the central ring is $1\cdot412 \pm 0\cdot002$ Å. The C–S and C–N bond lengths are in good agreement with those in *N*-ethylphenothiazine (Chu & van der Helm, 1975) and in *N*-methylphenothiazine (Chu & van der Helm, 1974). However, the C–S–C and C–N–C bond angles within the central ring, as well as the dihedral angle between the best planes of the two benzene rings, are significantly different in the two crystallographically independent molecules [Fig. 2(*b*)]. The dihedral angles between the best planes of the two benzene rings are 136·1 and 146·8° for molecule *A* and molecule *B*, respectively, as compared with 134·4 and 141·0° for the two crystallographically independent molecules in triflupromazine (Phelps & Cordes, 1974). The crystal structure of *N*-isopropylphenothiazine shows the largest difference in dihedral angles observed between two crystallographically independent molecules in tricyclic compounds. Beside the differences in C–S–C and C–N–C bond angles and the dihedral angle, the two crystallographically independent molecules have the same configuration. It can be shown from the known
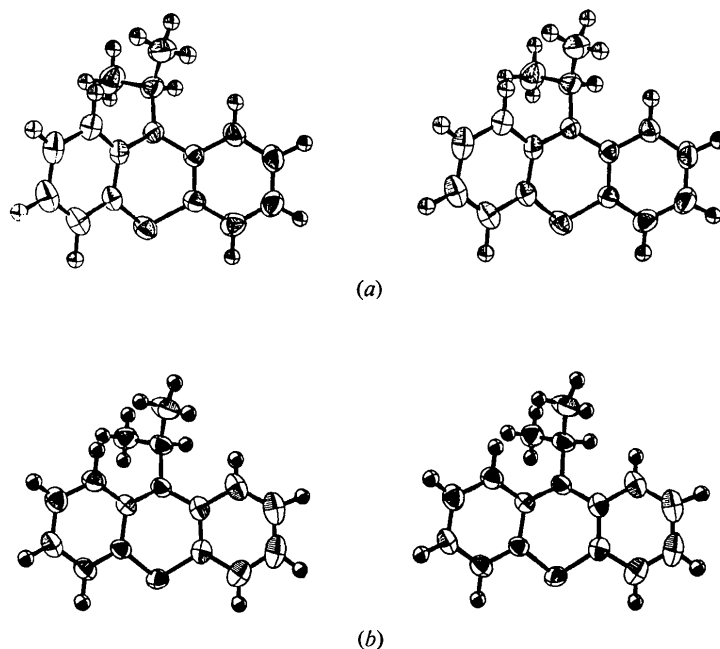

(*a*)

(*b*)

Fig. 1. The stereoscopic drawing of the two crystallographically independent molecules, (*a*) molecule *A* and (*b*) molecule *B*, of *N*-isopropylphenothiazine.

structures of phenothiazines that the magnitude of the folding angle is correlated with the C–N–C bond angle within the central ring (Chu & van der Helm, 1975).

The C–H bond lengths range from 0·89 to 1·10 Å with a mean value of 0·98 Å and a r.m.s. standard deviation of 0·02 Å. The C–C–H bond angles involving benzene rings range from 117 to 127° with a mean value of 120°, and the C–C–H and H–C–H bond angles involving tetrahedral C atoms range from 99 to 116° with a mean value of 109°. The r.m.s. standard deviation of these bond angles is 1°.

(a) N–C(15)

(b) N′–C′(15)

(c) C(9)–C(15)

(d) C′(9)–C′(15)

Fig. 3. The torsion angles (°) about the (a) N–C(15) and (b) N′–C′(15) bonds in N-isopropylphenothiazine and about the (c) C(9)–C(15) and (d) C′(9)–C′(15) bonds in 9-isopropyl-thioxanthene 10-oxide.

All C–N–C angles are close to 120°, indicating that the three N–C bonds around the N atom are approximately planar in configuration. However, unlike N-ethylphenothiazine the two C–N–C bond angles outside the ring are significantly different in N-isopropylphenothiazine. The difference can be attributed to the nonbonded interactions between H(5) and H(16)2 and between H(5) and H(17)2, which are 2·46 and 2·17 Å, respectively, for molecule A, and 2·29 and 2·07 Å, respectively, for molecule B. The torsion angles about the N–C(15) bond in N-isopropylphenothiazine (Fig. 3) are similar to those in N-ethylphenothiazine. (The torsion angles for N-isopropylphenothiazine are calculated from the coordinates for the enantiomorph given in Table 2.) The isopropyl substituent in N-isopropylphenothiazine, however, has a different conformation from that in 9-isopropylthioxanthene 10-oxide (II) (Chu, 1975). In 9-isopropylthioxanthene 10-oxide, the isopropyl substituent is in a 'boat axial' conformation and is almost symmetrical with respect to a plane passing through meso-atoms S, O, C(9), and C(15). For comparison, the torsion angles about the C(9)–C(15) bond in 9-isopropylthioxanthene 10-oxide are also shown in Fig. 3.

(II)

The packing of the molecules in the crystal is shown in the stereoscopic drawing, Fig. 4. There are no inter-molecular contacts less than van der Waals distances.

(a)

(b)

Fig. 2. (a) The bond lengths (Å) and (b) the bond angles (°) of the two independent molecules. Upper numbers refer to molecule A, lower numbers refer to molecule B; e.s.d.'s in parentheses.
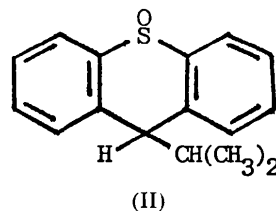
The closest intermolecular distances are 3·53 and 3·54Å between C(4) and C(7) and between C'(3) and C'(5), respectively.

References

BIEHL, E. (1975). *J. Heterocycl. Chem.* Submitted for publication.
BUSING, W. R., MARTIN, K. O. & LEVY, H. A. (1962). *ORFLS.* Oak Ridge National Laboratory Report ORNL-TM-305.
CHU, S. S. C. (1973). *Structural Interpretation Programs,* Institute of Technology, Southern Methodist Univ.
CHU, S. S. C. (1975). *Acta Cryst.* B31, 1082–1087.
CHU, S. S. C. & VAN DER HELM, D. (1974). *Acta Cryst.* B30, 2489–2490.
CHU, S. S. C. & VAN DER HELM, D. (1975). *Acta Cryst.* B31, 1179–1183.
CRUICKSHANK, D. W. J. (1965). *Computing Methods in Crystallography,* edited by J. S. ROLLETT, pp. 112–116. Oxford: Pergamon Press.
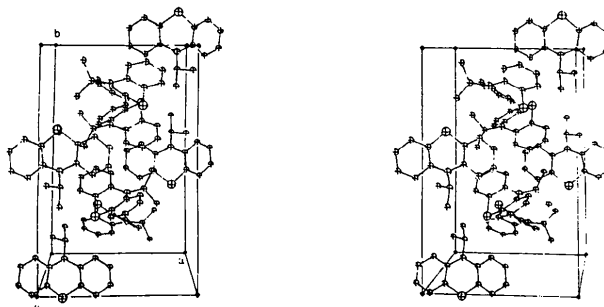

Fig. 4. The stereoscopic drawing of molecular packing of *N*-isopropylphenothiazine, excluding H atoms, in the unit cell.

International Tables for X-ray Crystallography (1962). Vol. III, pp. 201–207. Birmingham: Kynoch Press.
JOHNSON, C. K. (1965). *ORTEP.* Oak Ridge National Laboratory Report ORNL-3794.
PHELPS, D. W. & CORDES, A. W. (1974). *Acta Cryst.* B30, 2812–2816.
SHIONO, R. (1971). Technical Report 49, Crystallography Dept., Univ. of Pittsburgh.
STEWART, R. F., DAVIDSON, E. R. & SIMPSON, W. T. (1965). *J. Chem. Phys.* 42, 3175–3187.

The Crystal Structures of the α- and β-Anomers of D-Galactose

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The structures of α- and β-D-galactose have been determined by direct methods. Refinement was by least squares with anisotropic temperature factors for the C and O atoms to produce a final R of 0·0820 for 572 reflexions (α) and 0·0318 for 821 reflexions (β). The space groups are $P2_12_12_1$ with $Z=4$ and the cell parameters are (α) $a=15·7806$ (38), $b=7·8783$ (15), $c=5·9436$ (20) Å and (β) $a=7·6992$ (8), $b= 7·7726$ (8), $c=12·6408$ (17) Å. The molecules have the configurations 1*a*2*e*3*e*4*a* and 1*e*2*e*3*e*4*a* respectively with hydrogen-bonding systems which involve the five hydroxyl groups of each molecule.

Crystals of the α- and β-anomers of D-galactose were originally prepared to resolve the question of the unit-cell dimensions (Sheldrick, 1961). The crystal structures of both forms are now reported.

Experimental

α-D-*Galactose*

Confirmation of the cell dimensions was obtained by least-squares refinement of 41 measurements of 2θ taken at room temperature with Cu $K\alpha_1$ monochromatic radiation.

Crystal data

$C_6H_{12}O_6$, F.W. 180·15, space group $P2_12_12_1$, $a= 15·7806$ (38), $b=7·8783$ (15), $c=5·9436$ (20) Å, $V= 738·4$ Å^3, $D_m=1·60$ (in a mixture of $C_2H_2Cl_4$ and C_2Cl_4), $D_x=1·62$ g cm^{-3} for $Z=4$, Cu $K\alpha_1$ monochromatic, $\lambda=1·54051$ Å, crystal size$=0·2 \times 0·2 \times 0·002$ mm, crystal shape: flat plate.

Intensities were collected on an Enraf–Nonius CAD-4 diffractometer with a graphite crystal monochromator. Measurements were made in the range $3° < \theta \le 70°$, scanned in the ω–2θ mode. 572 independent reflexions were measured and 163 more were