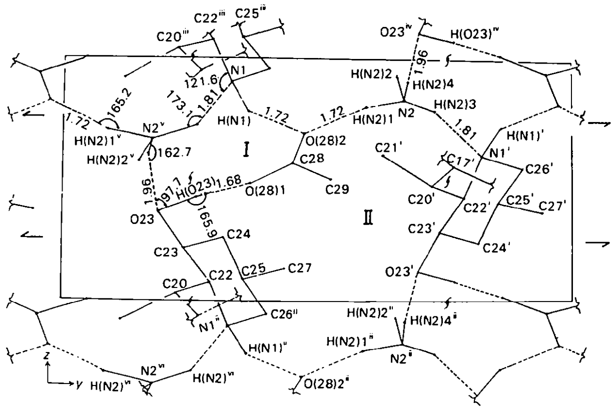


Fig. 1. (100) projection of the layer content of one unit cell at $x = 0$, showing the symmetry elements that are on the plane yz and the H-bond distances (Å) and angles (°). The numbered atoms are those which belong to the 10- and 20-membered rings, shown as I and II, respectively. Superscripts refer to the following symmetry operations: (i) $-x, 0{\cdot}5+y, 0{\cdot}5-z$; (ii) $x, y, z-1$; (iii) $x, y, 1+z$; (iv) $-x, 0{\cdot}5+y, 1{\cdot}5-z$; (v) $-x, y-0{\cdot}5, 1{\cdot}5-z$; (vi) $-x, y-0{\cdot}5, 0{\cdot}5-z$. E.s.d.'s for distances 0·5 Å, for angles 8·0°.

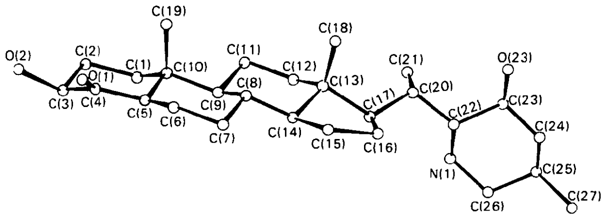


Fig. 2. A perspective view of the molecule showing the labeling of the atoms.

respectively, *vs* the expected 1·479 (5) Å. The observed lengthening of these C—N bonds could be a consequence of the H bonds present in the crystalline structure involving N(1) and the H attached to it, H(N1).

A comparison between the structure reported here and that of solamalidine, an alkaloid with a similar substituted androstane skeleton (Usubillaga, Zabel & Watson, 1982), shows that the bond distances and angles of the androstane moieties are similar within standard deviations.

The authors are grateful to the CDCH–ULA (Grants C–81–77 and FA–07) and the CEDEC–ULA for the allocated time.

References

International Tables for X-ray Crystallography (1968). Vol. III, 2nd ed. Birmingham: Kynoch Press. (Present distributor D. Reidel, Dordrecht.)

Main, P., Lessinger, L., Woolfson, M. M., Germain, G. & Declercq, J.-P. (1977). *MULTAN77. A System of Computer Programs for the Automatic Solution of Crystal Structures from X-ray Diffraction Data.* Univs. of York, England, and Louvain, Belgium.

Sheldrick, G. M. (1977). Program for crystal structure determination. Univ. of Cambridge, England.

Usubillaga, A. (1973). *Rev. Latinoam. Quím.* **4**(1), 32–34.

Usubillaga, A. (1984). *J. Nat. Prod.* **47**(1), 52–54.

Usubillaga, A., Paredes, A., Martinod, P. & Hidalgo, J. (1973). *Planta Med.* **23**(3), 286–289.

Usubillaga, A., Seelkopf, C., Karle, J. L., Daly, J. W. & Witkop, B. (1970). *J. Am. Chem. Soc.* **92**, 700–701.

Usubillaga, A., Zabel, V. & Watson, W. (1982). *Acta Cryst.* B**38**, 966–969.

Waser, J. (1963). *Acta Cryst.* **16**, 1091–1094.

Acta Cryst. (1985). C**41**, 1199–1202

Structure of 6-Azidotetrazolo[5,1-*a*]phthalazine, $C_8H_4N_8$, Isolated from the Toxic Dinoflaggelate *Gymnodinium breve*

By M. Bilayet Hossain and Dick van der Helm

Department of Chemistry, Oklahoma University, Norman, Oklahoma 73019, *USA*

and Radhika Sanduja and Maktoob Alam

Department of Medicinal Chemistry, College of Pharmacy, University of Houston, Houston, TX 77004, *USA*

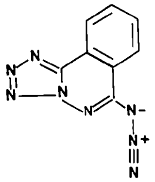
(*Received* 14 *December* 1984; *accepted* 26 *March* 1985)

Abstract. $M_r = 212$, orthorhombic, $P2_12_12_1$, $a = 12{\cdot}458$ (3), $b = 14{\cdot}669$ (4), $c = 4{\cdot}980$ (1) Å, $V = 910{\cdot}1$ Å^3, $Z = 4$, $D_x = 1{\cdot}547$ g cm^{-3}, Mo $K\alpha$, $\lambda = 0{\cdot}71069$ Å, $\mu = 0{\cdot}7$ cm^{-1}, $F(000) = 432$, $T = 293$ K, final $R = 0{\cdot}035$ for 892 observed reflections. The three-fused-ring system is perfectly planar; the r.m.s. deviation of individual atoms from the mean plane is 0·020 Å, with the azido group slightly bent (9·1°) out

0108-2701/85/081199-04$01.50

of the plane. The bond lengths and bond angles of the tetrazole ring and the azido group compare well with those observed in other related structures.

Introduction. The dinoflagellate *Gymnodinium breve* (*Ptychodiscus brevis*) has been implicated in the production of toxic red tides along the Gulf Coast of Florida (Shimizu, 1978). Recent investigations of the secondary metabolites of this microorganism have resulted in the identification of a number of cyclic polyethers and phosphorus compounds (Lin, Rish, Ray, van Engen, Clardy, Golik, James & Naskanishi, 1981; Golik, James & Nakanishi, 1982; Chou & Shimizu, 1982; Alam, Sanduja, Hossain & van der Helm, 1982; Dinovi, Trainor, Nakanishi, Sanduja & Alam, 1983). In this communication we report the isolation and X-ray structure of 6-azidotetrazolo[5,1-*a*]phthalazine, (I), a new toxic metabolite of the dinoflagellate *G. breve*.



(I)

Experimental. Unialgal cultures of *G. breve* were grown, harvested and processed according to a previously described method (Alam *et al.*, 1982); high-pressure liquid chromatography (silica-gel column) of the residue from the chloroform extract resulted in the elution of PB-1, Gb-4 followed by a group of fractions containing (I); rechromatography of the combined fractions [combined on the basis of their TLC pattern, solvent system EtOAc:benzene (20:80 v/v), silica gel 60] gave crystalline (I), which was recrystallized from benzene to give yellow well-formed prismatic crystals, m.p. 413 K; D_m not determined; all X-ray measurements on an Enraf–Nonius CAD-4 automatic diffractometer; cell constants from 48 reflections (2θ range 20–27°) using Mo $K\alpha_1$ ($\lambda = 0{\cdot}70926$ Å); 1127 unique reflections, Mo $K\bar{\alpha}$, graphite monochromator, $2\theta_{\max} = 53°$, h 0 to 15, k 0 to 18, l 0 to 6, θ–2θ scan with variable scan width $(0{\cdot}80 + 0{\cdot}20\tan\theta)°$; three standard reflections monitored every 2 h showed no significant variation; 892 observed reflections [$I > 2\sigma(I)$]; Lorentz and polarization corrections but no correction for absorption or extinction. Structure solved by direct methods; all non-hydrogen atoms from an E map using 125 reflections ($E > 1{\cdot}8$); phases by using *MULTAN*78 (Main, Hull, Lessinger, Germain, Declercq & Woolfson, 1978); final atom identification by refining several models and from a comparison of molecular geometry; H atoms from a difference Fourier map; final refinements by full-matrix least-squares routine in *SHELX*76 (Sheldrick, 1976) with all non-hydrogen atoms anisotropic and H atoms isotropic. Refinement on F converged at $R = 0{\cdot}035$, $wR = 0{\cdot}034$ for 892 observed reflections, $w = 1/\sigma^2(F)$, $S = 1{\cdot}6$, $\Delta/\sigma = 0{\cdot}03$ (max.), $= 0{\cdot}02$ (ave.), no peak greater than $0{\cdot}2$ e Å^{-3} in final difference map. The high-resolution mass spectrum of (I) established the molecular formula $C_8H_4N_8$ {calc. M_r 212·03744, found 212·03790 [N found 52·68, calc. 52·82% (determined by elemental analysis)]}. The 400 MHz ^{1}H NMR spectrum showed the presence of a disubstituted aromatic ring only [CDCl$_3$, $\delta = 8{\cdot}682$ (1*H*, *d*, $J = 7{\cdot}9$ Hz), 8·233 (1*H*, *d*, $J = 7{\cdot}9$ Hz), 8·089 (1*H*, *dd*, $J = 8{\cdot}5$, 7·9 Hz), 7·948 (1*H*, *dd*, $J = 8{\cdot}5$, 7·9 Hz)]. The ^{13}C NMR spectrum (100 MHz, CDCl$_3$; 135·52, 135·31, 132·82, 132·61, 125·93, 125·75, 124·99 and 124·81 p.p.m.) was consistent with the structure. The ichthyotoxicity of (I) (LD$_{100}$ 0·4 µg ml^{-1}) was determined as described by Martin & Chatterjee (1970).

Table 1. *Atomic coordinates and equivalent isotropic temperature factors*

For non-H atoms $U_{\rm eq} = \frac{1}{3}\sum_i\sum_j U_{ij}a_i^*a_j^*\mathbf{a}_i.\mathbf{a}_j$.

	x	y	z	$U_{\rm eq}$ or U(Å^2)
N(1)	0·9617 (2)	0·7343 (1)	0·6094 (5)	0·0617 (8)
N(2)	0·8893 (2)	0·7256 (2)	0·8121 (5)	0·0691 (9)
N(3)	0·8471 (2)	0·8035 (2)	0·8790 (5)	0·0617 (8)
N(4)	0·8944 (1)	0·8648 (1)	0·7154 (4)	0·0490 (6)
N(5)	0·8671 (1)	0·9550 (1)	0·7245 (4)	0·0499 (7)
C(6)	0·9196 (2)	1·0033 (2)	0·5473 (5)	0·0456 (7)
C(7)	0·9999 (2)	0·9694 (1)	0·3602 (5)	0·0438 (7)
C(8)	1·0232 (2)	0·8760 (1)	0·3624 (5)	0·0442 (7)
C(9)	0·9638 (2)	0·8220 (1)	0·5515 (5)	0·0480 (8)
C(10)	1·0552 (2)	1·0270 (2)	0·1849 (6)	0·0516 (8)
C(11)	1·1314 (2)	0·9911 (2)	0·0159 (5)	0·0570 (9)
C(12)	1·1547 (2)	0·8984 (2)	0·0193 (6)	0·059 (1)
C(13)	1·1018 (2)	0·8406 (2)	0·1900 (6)	0·0538 (8)
N(14)	0·8998 (2)	1·0968 (1)	0·5329 (5)	0·0560 (7)
N(15)	0·8423 (2)	1·1276 (1)	0·7209 (5)	0·0560 (8)
N(16)	0·7946 (2)	1·1652 (2)	0·8739 (5)	0·0741 (9)
H(1)	1·120 (2)	0·775 (2)	0·197 (5)	0·061 (7)
H(2)	1·209 (2)	0·872 (1)	−0·099 (6)	0·062 (7)
H(3)	1·170 (2)	1·030 (2)	−0·096 (6)	0·059 (8)
H(4)	1·042 (2)	1·091 (1)	0·186 (5)	0·058 (7)

Discussion. The final atomic parameters are given in Table 1.* Bond distances and bond angles are listed in Table 2. Fig. 1 shows a perspective view of (I) and also the atom-numbering scheme. The overall molecule is planar; the r.m.s. deviation of individual ring atoms from the least-squares plane through all 13 ring atoms is 0·020 Å. The azido group is bent slightly out of the plane of the ring system, the deviations of the atoms N(15) and N(16) from the plane of the molecule are 0·165 and 0·349 Å respectively.

---

* Lists of structure factors and anisotropic thermal parameters have been deposited with the British Library Lending Division as Supplementary Publication No. SUP 42152 (6 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

The tetrazole-ring dimensions (bond distances and angles) in general compare very well with those observed in other related structures (Table 2), such as tetrazolo[1,5-*b*]pyridazine (Golič, Leban, Stanovnik & Tišler, 1978), tetrazolo[1,5-*b*]benzothiazole (Domiani & Musatti, 1974*a*) and azidopurine (Glusker, van der Helm, Love, Minkin & Patterson, 1968). However, in the present structure the two single bonds, N(1)—N(2) = 1·360 (3) and N(3)—N(4) = 1·349 (3) Å, are about 4–5σ longer than that observed in tetrazolo[1,5-*b*]pyridazine, and about 10σ longer than that observed in the tetrazole molecule itself (van der Putten, Heijdenrijk & Schenk, 1974), while the double-bond N(2)—N(3) distance of 1·301 (3) Å in the present structure is about 4σ shorter than that in tetrazolopyridazine. This would indicate that π delocalization is relatively less extensive in (I) than in tetrazolopyridazine and the tetrazole molecule itself.

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

	Present structure	Tetrazolo[1,5-*b*]pyridazine	Tetrazolo[1,5-*b*]benzothiazole	Azidopurine
N(1)–N(2)	1·360 (3)	1·346 (2)	1·372 (3)	1·37 (1)
N(2)–N(3)	1·301 (3)	1·312 (2)	1·309 (3)	1·28 (1)
N(3)–N(4)	1·349 (3)	1·338 (2)	1·352 (3)	1·38 (1)
N(4)–C(9)	1·345 (3)	1·359 (2)	1·344 (3)	1·36 (1)
N(1)–C(9)	1·319 (3)	1·324 (2)	1·322 (3)	1·33 (1)
N(4)–N(5)	1·366 (3)	1·353 (2)		
N(5)–C(6)	1·307 (3)	1·298 (2)		
C(6)–C(7)	1·455 (3)	1·426 (3)		
C(7)–C(8)	1·400 (3)	1·353 (3)		
C(8)–C(9)	1·436 (3)	1·406 (2)		
C(7)–C(10)	1·397 (3)			
C(10)–C(11)	1·374 (4)			
C(11)–C(12)	1·390 (4)			
C(12)–C(13)	1·370 (4)			
C(13)–C(8)	1·402 (3)			
C(6)–N(14)	1·396 (3)			
N(14)–N(15)	1·262 (3)			
N(15)–N(16)	1·113 (4)			
C(9)–N(1)–N(2)	105·5 (2)	105·7 (1)	104·2 (4)	104 (1)
N(1)–N(2)–N(3)	112·1 (2)	112·3 (2)	112·6 (4)	114 (1)
N(2)–N(3)–N(4)	104·8 (2)	104·9 (1)	104·5 (4)	105 (1)
N(3)–N(4)–C(9)	109·6 (1)	109·5 (1)	109·4 (4)	108 (1)
N(4)–C(9)–N(1)	108·1 (2)	107·7 (1)	109·3 (4)	109 (1)
N(3)–N(4)–N(5)	121·2 (2)	122·5 (1)		
N(5)–N(4)–C(9)	129·2 (2)	128·0 (1)		
N(4)–N(5)–C(6)	112·2 (2)	112·5 (1)		
N(5)–C(6)–C(7)	126·3 (2)	125·3 (2)		
C(6)–C(7)–C(8)	118·2 (2)	120·0 (2)		
C(7)–C(8)–C(9)	116·0 (2)	115·3 (1)		
N(4)–C(9)–C(8)	118·1 (2)	117·9 (1)		
N(1)–C(9)–C(8)	133·7 (2)	134·4 (1)		
C(6)–C(7)–C(10)	122·2 (2)			
C(8)–C(7)–C(10)	119·7 (2)			
C(7)–C(10)–C(11)	119·4 (2)			
C(10)–C(11)–C(12)	120·8 (3)			
C(11)–C(12)–C(13)	120·8 (3)			
C(12)–C(13)–C(8)	119·2 (2)			
C(7)–C(8)–C(13)	120·1 (2)			
C(9)–C(8)–C(13)	123·9 (2)			
N(5)–C(6)–N(14)	118·6 (2)			
C(7)–C(6)–N(14)	115·1 (2)			
C(6)–N(14)–N(15)	114·4 (2)			
N(14)–N(15)–N(16)	171·2 (3)			

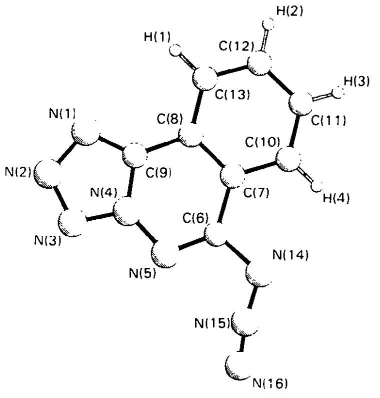


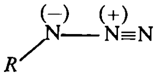
Fig. 1. A perspective view of 6-azidotetrazolo[5,1-*a*]phthalazine.

Table 3. *Geometry of azide groups attached to ring carbons:* C—N′—N″—N‴

Compound*	(*a*)	(*b*)	(*c*)	(*d*)	(*e*)
C–N′ (Å)	1·396 (3)	1·407	1·444	1·417	1·426
N′–N″ (Å)	1·262 (3)	1·244	1·245	1·270	1·248
N″–N‴ (Å)	1·113 (4)	1·140	1·115	1·127	1·122
C–N′–N″ (°)	114·4 (2)	114·2	114·9	115·0	116
N′–N″–N‴ (°)	171·2 (3)	171·9	174·2	173·4	172

* (*a*) Present work, (*b*) 4-phenyl-3-azidopyrazole (Domiano & Musatti, 1974*b*), (*c*) Δ^6-6-azidobetamethason-21-yl acetate (Nassimbeni, Sheldrick & Kennard, 1974), (*d*) *p*-nitrophenyl azide (Mugnoli, Mariani & Simonetta, 1965), (*e*) 3-azidotropolone (Cruickshank, Filippini & Mills, 1972).

The bond angles in the tetrazole ring range from 104·8 (2) at N(3) to 112·1 (2)° at N(2). These angles are significantly different from those in the tetrazole structure itself (van der Putten *et al.*, 1974) in which the angles at N(1), N(2) and N(3) are all approximately 108°. The nature of the angular distortion indicates that N(2) is displaced towards the N(4)—C(9) bond thereby increasing the bond angle at N(2) and decreasing the bond angles at N(1) [105·5 (2)°] and at N(3) from the average value of 108°. Bond distances and angles in the azido group are in good agreement with those quoted by Müller (1973) for molecular azides. The geometry of the azide group is compared in Table 3. The bond lengths of 1·262 (3) Å for N(14)—N(15) and 1·113 (4) Å for N(15)—N(16) indicate the resonance formula:



$$R-\overset{(-)}{N}-\overset{(+)}{N}\equiv N$$

Müller (1973) cited many examples to show that in azides of carbon having π-bond systems next to the azido group, the N_3 group is bent and inclined against the plane of the π system by angles up to 20°. In the present structure the azido group is inclined by about 9°.

In the pyridazine ring, bonds C(6)—C(7) 1·455 (3), C(7)—C(8) 1·400 (3) and C(8)—C(9) 1·436 (3) Å are all significantly longer than those found in tetrazolo[1,5-*b*]pyridazine. Such lengthening may be attributed to the effect of fusion of a benzene ring at C(7) and C(8). While C(7)—C(8) is a pure double bond in tetrazolopyridazine, it has a resonance form in the present structure.

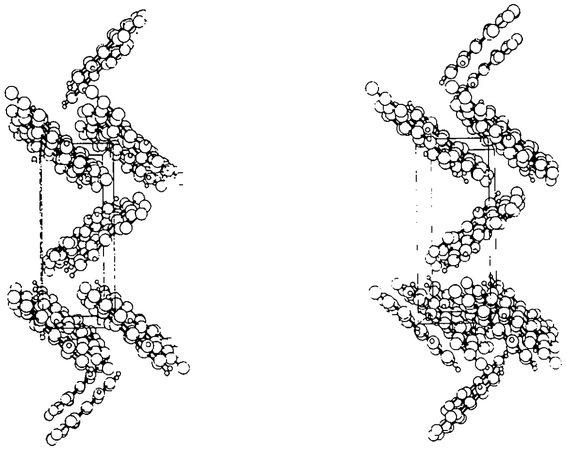


Fig. 2. A stereoview of the packing, viewed down the *b* axis; the long axis is *a*.

A stereoview of the packing of (I) is shown in Fig. 2. Planar molecules are arranged in such a way that they approximately lie on two mutually perpendicular lattice planes forming a see-saw pattern. An examination of intermolecular distances [shortest, N(3)···C(8)-($x,y,z+1$) = 3·426 (3) Å] shows that the crystal structure is stabilized by van der Waals interactions only.

This work was supported by a grant (CA 17562) to DvdH from the National Cancer Institute, Department of Health and Human Services, and by grant E-745 to MA from the Robert A. Welch Foundation, Houston, Texas.

References

ALAM, M., SANDUJA, R., HOSSAIN, M. B. & VAN DER HELM, D. (1982). *J. Am. Chem. Soc.* **104**, 5232–5234.

CHOU, H.-N. & SHIMIZU, Y. (1982). *Tetrahedron Lett.* **23**, 5521–5524.

CRUICKSHANK, D. W. J., FILIPPINI, G. & MILLS, O. S. (1972). *Chem. Commun.* pp. 101–102.

DINOVI, M., TRAINOR, D. A., NAKANISHI, K., SANDUJA, R. & ALAM, M. (1983). *Tetrahedron Lett.* **24**, 855–858.

DOMIANO, P. & MUSATTI, A. (1974*a*). *Cryst. Struct. Commun.* **3**, 335–338.

DOMIANO, P. & MUSATTI, A. (1974*b*). *Cryst. Struct. Commun.* **3**, 713–715.

GLUSKER, J. P., VAN DER HELM, D., LOVE, W. E., MINKIN, J. A. & PATTERSON, A. L. (1968). *Acta Cryst.* B**24**, 359–366.

GOLIČ, L., LEBAN, I., STANOVNIK, B. & TIŠLER, M. (1978). *Acta Cryst.* B**34**, 1136–1140.

GOLIK, J., JAMES, J. C. & NAKANISHI, K. (1982). *Tetrahedron Lett.* **23**, 2535–2538.

LIN, Y., RISH, M., RAY, S. M., VAN ENGEN, D., CLARDY, J., GOLIK, J., JAMES, J. C. & NAKANISHI, K. (1981). *J. Am. Chem. Soc.* **103**, 6773–6774.

MAIN, P., HULL, S. E., LESSINGER, L., GERMAIN, G., DECLERCQ, J.-P. & WOOLFSON, M. M. (1978). *MULTAN78. A System of Computer Programs for the Automatic Solution of Crystal Structures from X-ray Diffraction Data.* Univs. of York, England, and Louvain, Belgium.

MARTIN, D. F. & CHATTERJEE, A. A. (1970). *Fish. Bull.* **68**, 433–443.

MUGNOLI, A., MARIANI, C. & SIMONETTA, M. (1965). *Acta Cryst.* **19**, 367–372.

MÜLLER, U. (1973). *Struct. Bonding (Berlin)*, **14**, 141–172.

NASSIMBENI, L. R., SHELDRICK, G. M. & KENNARD, O. (1974). *Acta Cryst.* B**30**, 2401–2406.

PUTTEN, N. VAN DER, HEIJDENRIJK, D. K. & SCHENK, H. (1974). *Cryst. Struct. Commun.* **3**, 321–322.

SHELDRICK, G. M. (1976). *SHELX76*. Program for crystal structure determination. Univ. of Cambridge, England.

SHIMIZU, Y. (1978). *Marine Natural Products*, Vol. I, edited by P. J. SCHEUER, ch. 1. New York: Academic Press.

Acta Cryst. (1985). C**41**, 1202–1204

Structure of *N*-Phenylphenothiazine, $C_{18}H_{13}NS$

BY CHERYL L. KLEIN, JOSEPH M. CONRAD III AND STEVEN A. MORRIS

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

(*Received* 20 *November* 1984; *accepted* 12 *April* 1985)

Abstract. $M_r = 275·0$, triclinic, $P\bar{1}$, $a = 10·369$ (5), $b = 10·596$ (6), $c = 15·468$ (6) Å, $\alpha = 68·26$ (4), $\beta = 65·49$ (5), $\gamma = 68·04$ (5)°, $V = 1383·3$ Å^3, $Z = 4$, $D_x = 1·32$ g cm^{-3}, Mo $K\alpha_1$, $\lambda = 0·70930$ Å, $\mu = 2·1$ cm^{-1}, $F(000) = 576$, $T = 110$ K, final $R = 0·055$ for 2921 observed reflections. The title compound is a phenothiazine derivative with two unique molecules in the asymmetric unit. The folding angles between the least-squares planes of the two benzo rings are 162·6 and 150·7°. There are no unusual intramolecular bond lengths or angles.

Introduction. Phenothiazine is the parent molecule of a class of compounds known to possess tranquilizing properties. However, phenothiazine itself and the title compound (I) are not effective drugs. It is well known that an electronegative substituent on the 3-position of the phenothiazine benzo ring and an *N*-substituted propylamine group are necessary for enhanced psychopharmacological activity. There has also been some speculation on the effect of the butterfly folding angle on the tranquilizing activity (Phelps & Cordes, 1974, 1976). The structure determination of *N*-phenylpheno-

0108-2701/85/081202-03$01.50