'average' oxirane ring, although the C—O bonds appear to have been shortened by about 0·013 Å. It may be fortuitous that this is the value that would have been expected on the basis of the cyclopropane work. A similar effect has been observed in two related compounds (Kerr, to be published).

The molecules are linked in pairs by intermolecular hydrogen bonds in which O(7) acts as both donor and acceptor with O···O 2·655 (4) Å, H···O 1·88 (4) Å and $\angle$O—H···O 157 (2)°. However, the NMR spectrum in deutero-acetone (Sekiguchi & Gaucher, 1978) shows coupling between the protons on C(7) and C(3). This has been interpreted as strong evidence for an intramolecular hydrogen bond to O(1) in solution. There are four additional intermolecular O···H contacts between 2·56 (3) and 2·64 (3) Å.

The most significant intramolecular interactions involve the hydroxymethyl side chain: C(7)···O(1) 2·844, O(7)···C(3) 2·788 (3) Å. The epoxy oxygen makes short contacts of 2·911 (3) and 2·915 (3) Å with atoms C(2) and C(3), respectively.

Examination of Fig. 1 yields the impression that phyllostine may be librating about an axis corresponding to the smallest moment of inertia. This is borne out by rigid-body analysis (Table 3). The mean-square amplitudes of libration are 20·0, 10·4 and 3·5 deg^2 in the three principal directions while the translational component is more nearly isotropic with eigenvalues of 0·0302, 0·0235 and 0·0178 Å^2 (after symmetrizing S). The corrected bond lengths for the oxirane ring are close to the gas-phase values of 1·470 Å (C—C) and 1·434 Å (C—O) observed by Hirose (1974).

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Methoxypromazine at 120 K*

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Abstract. $C_{18}H_{22}N_2OS$, $M_r = 314\cdot5$, monoclinic, $P2_1/n$, $a = 7\cdot462(2)$, $b = 17\cdot223(6)$, $c = 12\cdot745(3)$ Å, $\beta = 96\cdot18(2)°$, $V = 1628\cdot3(8)$ Å^3, $Z = 4$, $D_m = 1\cdot29$ (1), $D_x = 1\cdot28$ (1) Mg m^{-3}, $\lambda(Cu K\alpha) = 1\cdot5418$ Å, $\mu = 0\cdot173$ mm^{-1}, $F(000) = 672$, $T = 120$ K, $R = 0\cdot067$, 2484 contributing reflections. The 3-(dimethylamino)-propyl side chain is located with respect to the

* The Structures of (Dimethylaminopropyl)phenothiazine Drugs and Their Metabolites. IV. Part III: Hough, Wold & Dahl (1985).

phenothiazine system in a conformation similar to that in chlorpromazine, but different to that in methoxypromazine maleate. The bond lengths and angles of the ring system are similar to those in methoxypromazine maleate, but the dihedral angle between the phenyl rings is smaller in the title compound.

Introduction. The molecular and crystal structures of two metabolites of chlorpromazine (CPZ), chlorpromazine sulfoxide (CPZSO) and monode-N-methylchlorpromazine sulfoxide (DCPZSO), were recently reported from our laboratories (Hough, Hjorth & Dahl, 1985; Hough, Wold & Dahl, 1985). The structures of CPZSO and DCPZSO had an N(10) side-chain conformation which was different to that in CPZ (McDowell, 1969), and more similar to that in methoxypromazine maleate (Marsau & Gauthier, 1973). This paper reports the molecular and crystal structure of the free base of methoxypromazine at 120 K.

Experimental. Methoxypromazine [10-(3-dimethylaminopropyl)-2-methoxyphenothiazine], kindly supplied by Rhône-Poulenc Industries, Paris, France. Single crystals by evaporation of m-xylene solution at room temperature, fragments of irregular shape. D_m by flotation in aqueous KI solutions; single crystal approximately $0.1 \times 0.1 \times 0.2$ mm. Data collection on Enraf–Nonius CAD-4 diffractometer, graphite-monochromated Cu$K\alpha$ radiation; $T = 120$ K. 25 reflections used ($\theta_{max} = 40°$) to measure lattice parameters. hkl ranges 0–8, 0–20, −14–14, respectively; 2θ up to 132°. Standard reflection $\bar{1}3\bar{1}$, no decline in intensity during data collection. 2779 unique reflections measured, 295 unobserved [$I < 3\sigma(I)$]. Lp correction, no correction for absorption. Solved by direct methods ($MULTAN80$; Main et al., 1980), refinement based on $|F|$ using $XRAY76$ (Stewart, Machin, Dickinson, Ammon, Heck & Flack, 1976), using 2484 reflections. Scattering factors from Cromer & Mann (1968) for C,O,N,S and Stewart, Davidson & Simpson (1965) for H. H atoms located by direct calculation of position except for methyl groups, where H's located in ΔF map. Final refinement, non-hydrogen atoms anisotropic, H's isotropic, $R = 0.067$ and $wR = 0.091$ using $w = 1/\sigma^2(F)$, $(\Delta/\sigma)_{av} = 0.06$, $(\Delta/\sigma)_{max} = 2.07$ (see below), residual electron density in final ΔF map ± 0.3 e Å^{-3}. Calculations on a Cyber 171MP computer.*

Discussion. The positional parameters of methoxypromazine are given in Table 1, bond lengths, bond

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* Lists of structure factors, anisotropic thermal parameters and H-atom parameters have been deposited with the British Library Lending Division as Supplementary Publication No. SUP 42741 (15 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

angles and torsion angles of the N(10)-substituted side chain are given in Table 2, and the molecular structure and atomic numbering system are shown in Fig. 1.

Table 1. *Positional parameters and equivalent isotropic thermal parameters*

$$B_{eq} = \tfrac{4}{3}[a^2B(1,1) + b^2B(2,2) + c^2B(3,3) + ab(\cos\gamma)B(1,2) + ac(\cos\beta)B(1,3) + bc(\cos\alpha)B(2,3)].$$

	x	y	z	$B_{eq}(\text{Å}^2)$
S(5)	0.3861 (2)	0.2123 (1)	0.4226 (1)	1.6
O(21)	0.4930 (5)	0.4061 (2)	0.0537 (3)	2.4
N(10)	0.6343 (5)	0.3434 (2)	0.4171 (3)	1.4
N(18)	0.9728 (5)	0.4696 (2)	0.2408 (3)	1.6
C(1)	0.5565 (6)	0.3742 (3)	0.2293 (4)	1.5
C(2)	0.4615 (6)	0.3571 (3)	0.1337 (4)	1.7
C(3)	0.3407 (6)	0.2953 (3)	0.1233 (4)	1.8
C(4)	0.3161 (6)	0.2522 (3)	0.2129 (4)	1.7
C(6)	0.2982 (7)	0.2892 (3)	0.5995 (4)	2.1
C(7)	0.3189 (7)	0.3472 (3)	0.6736 (4)	2.2
C(8)	0.4383 (7)	0.4078 (3)	0.6623 (4)	2.1
C(9)	0.5412 (7)	0.4086 (3)	0.5758 (4)	1.7
C(11)	0.5368 (6)	0.3293 (3)	0.3178 (4)	1.4
C(12)	0.4121 (6)	0.2680 (3)	0.3084 (4)	1.5
C(13)	0.4032 (6)	0.2883 (3)	0.5143 (4)	1.6
C(14)	0.5265 (6)	0.3482 (3)	0.5035 (4)	1.4
C(15)	0.7938 (6)	0.3941 (3)	0.4209 (4)	1.6
C(16)	0.9429 (6)	0.3580 (3)	0.3607 (4)	1.6
C(17)	1.0637 (6)	0.4229 (3)	0.3252 (4)	1.8
C(19)	1.0599 (7)	0.5444 (3)	0.2348 (5)	2.5
C(20)	0.9670 (7)	0.4317 (3)	0.1382 (4)	2.2
C(22)	0.4087 (9)	0.3902 (4)	−0.0484 (4)	2.9

Table 2. *Bond lengths (Å), bond angles (°) and some relevant torsion angles (°)*

C(2)–C(3)	1.391 (7)	S(5)–C(12)	1.771 (5)
C(3)–C(4)	1.391 (7)	S(5)–C(13)	1.751 (5)
C(4)–C(12)	1.372 (6)	O(21)–C(2)	1.364 (6)
C(6)–C(7)	1.371 (7)	O(21)–C(22)	1.410 (6)
C(6)–C(13)	1.405 (7)	N(10)–C(11)	1.410 (6)
C(7)–C(8)	1.390 (8)	N(10)–C(14)	1.435 (6)
C(8)–C(9)	1.410 (7)	N(10)–C(15)	1.472 (6)
C(9)–C(14)	1.385 (7)	N(18)–C(17)	1.452 (6)
C(11)–C(12)	1.404 (6)	N(18)–C(19)	1.449 (7)
C(13)–C(14)	1.399 (7)	N(18)–C(20)	1.458 (7)
C(15)–C(16)	1.549 (7)	C(1)–C(2)	1.374 (6)
C(16)–C(17)	1.534 (7)	C(1)–C(11)	1.388 (7)

C(12)–S(5)–C(13)	97.9 (3)	C(17)–N(18)–C(20)	112.5 (4)
S(5)–C(12)–C(4)	121.9 (4)	N(18)–C(17)–C(16)	112.3 (4)
S(5)–C(12)–C(11)	117.9 (4)	C(19)–N(18)–C(20)	108.7 (5)
S(5)–C(13)–C(6)	121.2 (4)	C(2)–C(1)–C(11)	120.8 (5)
S(5)–C(13)–C(14)	119.1 (4)	C(1)–C(2)–C(3)	121.1 (5)
C(2)–O(21)–C(22)	118.3 (5)	C(1)–C(11)–C(12)	118.4 (5)
O(21)–C(2)–C(1)	114.6 (5)	C(2)–C(3)–C(4)	118.1 (5)
O(21)–C(2)–C(3)	124.3 (5)	C(3)–C(4)–C(12)	121.3 (5)
C(11)–N(10)–C(14)	114.9 (4)	C(4)–C(12)–C(11)	120.3 (5)
C(11)–N(10)–C(15)	118.0 (4)	C(7)–C(6)–C(13)	120.6 (5)
N(10)–C(11)–C(1)	122.9 (5)	C(6)–C(7)–C(8)	120.1 (5)
N(10)–C(11)–C(12)	118.7 (5)	C(6)–C(13)–C(14)	119.7 (5)
C(14)–N(10)–C(15)	117.3 (4)	C(7)–C(8)–C(9)	119.8 (5)
N(10)–C(14)–C(9)	122.9 (5)	C(8)–C(9)–C(14)	120.1 (5)
N(10)–C(14)–C(13)	117.5 (5)	C(9)–C(14)–C(13)	119.6 (5)
N(10)–C(15)–C(16)	111.5 (4)	C(15)–C(16)–C(17)	109.3 (4)
C(17)–N(18)–C(19)	110.8 (4)		

C(11)–N(10)–C(15)–C(16)	64.3 (5)
C(14)–N(10)–C(15)–C(16)	−151.7 (4)
N(10)–C(15)–C(16)–C(17)	−155.5 (4)
C(15)–C(16)–C(17)–N(18)	71.0 (5)
C(16)–C(17)–N(18)–C(19)	−159.4 (4)
C(16)–C(17)–N(18)–C(20)	78.6 (5)

The relatively high R factors obtained in this determination were apparently due to the poor quality of the crystal, although this was the best out of a number of crystallization experiments. Refinement of the temperature factors for H(7) and H(8) resulted in unrealistic values and high Δ/σ. $(\Delta/\sigma)_{max}$ for all other atoms was 0·42. Preliminary results from work on two other phenothiazine derivatives imply a small amount of disorder of the phenothiazine ring systems, apparent in the 2, 3, 7 and 8 substituent positions.

Comparison of the methoxypromazine structure with that of its maleate salt at room temperature (Marsau & Gauthier, 1973) shows that bond lengths in the two structures are similar, the average and maximum differences being 0·02 and 0·04 Å, respectively. As expected, the largest differences are found in the bonds to N(18) which are 0·4 Å shorter in the free base whereas the C(16)–C(17) bond is 0·4 Å longer.

Bond angles of the two phenyl rings are also very similar in the two structures. The C–S–C angle of the central thiazine ring in the free base [97·9 (2)°] is, however, 2° smaller than in the maleate [99·8 (3)°], but still within the range found in similar compounds. The endocyclic C–N–C angle of the thiazine ring is 7° smaller in methoxypromazine [114·9 (4)°] than in the maleate structure [122·3 (5)°] and appears to be the smallest value yet reported. The sum of the three angles around N(10) is 350·2 (7)°, whereas the equivalent values for methoxypromazine maleate, levome-promazine and levomepromazine sulfoxide are 357·3 (8), 357·2 (5) and 359·8 (3)°, respectively. Furthermore, N(10) lies further out of the plane through C(11), C(14) and C(15) [0·26 (2) Å] than in the case for methoxypromazine maleate [0·14 (3) Å], levomepromazine [0·16 (3) Å] and levomepromazine sulfoxide [0·03 (2) Å], all of which indicate a larger extent of sp^2 hybridization of the˙ N(10) atom in methoxypromazine.
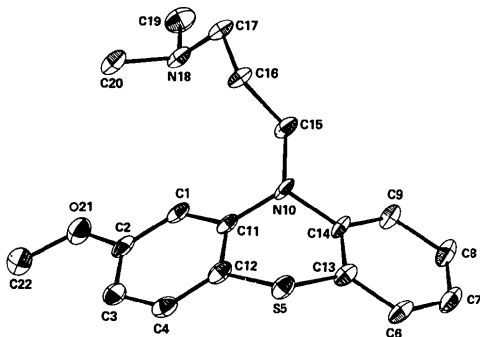
The C(3)–C(2)–O angle of the methoxy group is 124·3 (4)° in the free base and 125·9 (6)° in the maleate salt, and the O–CH_3 group is almost coplanar with the substituted benzene ring in both compounds. The N(10)–C(15)–C(16) angle of the side chain is 3° smaller in the free base [111·5 (4)°] than in the maleate salt [114·5 (5)°], while the C(15)–C(16)–C(17), C(16)–C(17)–N(18), C(17)–N(18)–C(19) and C(17)–N(18)–C(20) angles differ by 1·4° or less (average difference 1·0°) between the two structures.

The most striking differerences between the structures of methoxypromazine as the free base and as its maleate salt are that the phenothiazine nucleus is more folded along the central S–N axis in the free base, and that the N(10) side chains have different conformations. The dihedral angle between the least-squares planes of the two phenyl rings is 134·3 (2)° in the free base. This is is at the lower end of the range 134–146° which has been found for most psychoactive phenothiazines (Tollenaere, Moereels & Koch, 1977). The corresponding angle in the maleate salt is 157·7 (3)° (Marsau & Gauthier, 1973). The distances of the terminal N atom of the side chain to the centroids of the substituted and unsubstituted aromatic rings are 4·79 (2) and 6·70 (2) Å, respectively, in methoxypromazine base, compared to 6·36 (2) and 6·64 (2) Å in the maleate salt.

The central thiazine ring of methoxypromazine has a boat conformation, with the four C atoms in relatively planar positions, the deviation of each of the four C atoms from their least-squares plane being 0·005 (1) Å. The distance of the S atom from the plane of the central C atoms is 0·39 (2) Å for the free base and 0·48 (2) Å for the maleate salt. The distance of the N(10) atom from the same plane is 0·63 (2) Å in the free base and 0·27 (2) Å in the maleate salt.

The N(10)–C(15) bond of methoxypromazine is equatorial to the ring system, as in the maleate salt and in chlorpromazine (McDowell, 1969). The dihedral angle [64·3 (3)°] about this bond viewed from C(11) (Table 2) has a similar value to that in chlorpromazine [68·7 (4)°], but different to that in methoxypromazine maleate [−80·3 (3)°]. This places the rest of the dimethylaminopropyl side chain in a *cis* position to the ring system in methoxypromazine and chlorpromazine and in a *trans* position in methoxypromazine maleate. The values of the other dihedral angles of the N(10) side chain of methoxypromazine (Table 2) are also close to the values observed in chlorpromazine, levome-promazine (Sato, Miki, Tanaka, Kasai, Ishimaru & Munakata, 1980) and levomepromazine sulfoxide (Hough, Hjorth & Dahl, 1982).

The crystal packing of methoxypromazine, viewed along the a axis, is shown in Fig. 2. The N(10) side chains lie in a relatively free environment; none of the intermolecular contact distances are shorter than the sum of the corresponding van der Waals radii. The N
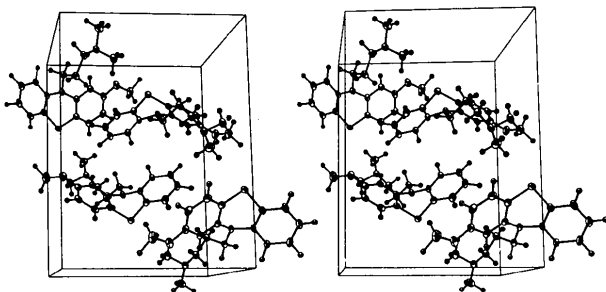

Fig. 1. Molecular structure and atom-numbering system of methoxypromazine (*ORTEP*; Johnson, 1971).

Fig. 2. Stereoscopic illustration of the molecular packing, viewed approximately down the *a* axis.

atom of the dimethylamino group of methoxypromazine maleate is connected to the maleate ion *via* a hydrogen bond (Marsau & Gauthier, 1973), which may be the reason for the difference between the conformations of the side chain in the maleate salt and the free base.

Methoxypromazine was generously donated by Rhône-Poulenc Industries, Paris, France.

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Structure de l'Amino-5 2*H*,4*H*-Thiadiazine-1,2,6 One-3 Dioxyde-1,1

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Abstract. $C_3H_5N_3O_3S$, $M_r = 163 \cdot 16$, monoclinic, $P2_1/c$, $a = 8 \cdot 780$ (2), $b = 7 \cdot 411$ (1), $c = 9 \cdot 750$ (2) Å, $\beta = 102 \cdot 76$ (2)°, $V = 618 \cdot 8$ (3) Å^3, $Z = 4$, $D_m = 1 \cdot 75$ (2), $D_x = 1 \cdot 751$ g cm^{-3}, Mo $K\alpha$, $\lambda = 0 \cdot 7107$ Å, $\mu = 4 \cdot 64$ cm^{-1}, $F(000) = 336$, $T = 295$ K, final $R = 0 \cdot 035$ for 1072 independent reflections with $I > 3\sigma(I)$. The 4*H*-thiadiazine ring shows a flattened boat conformation. The bond lengths and angles are in agreement with those of other 2*H*,4*H*-thiadiazines. There are two short intermolecular contacts between the NH_2 group and the oxide oxygens but neither are within the normal H-bond angular range.