the *m*-hydroxybenzoyl ester group [O(6′)–H···O(1″), 2·75 (1) Å]; it contributes in the formation of a double spiral along **b** and also serves as a bridge between spirals running in perpendicular directions (**a**,**b**). The space left between these spirals is occupied by vinyl groups of the secoiridoid moieties and forms with the 'non-oxygen' part of the *m*-hydroxybenzoyl residue a hydrophobic region. Hydrophobic and hydrophilic regions alternate along **b**. The strongest interaction occurring between the double spiral chains [O(4′)–H···O(6′), 2·65 (1) Å] connects them into waved layers with an amplitude in the **a** direction. The short non-hydrogen-bonding interactions involving the C=O part of the lactone group of the secoiridoid moiety [O(11)···H(71), 2·35 (1); O(11)···H(O2′), 2·31 (1) Å] and O(4″) of the *m*-hydroxybenzoyl residue [O(4″)···H(1), 2·43 (1) Å] complete the three-dimensional packing. These interactions are permitted by the conformation of the molecule; the dihedral angles between the pyranose–secoiridoid and pyranose – *m*-hydroxybenzoyl moieties are 59·7 (4) and 89·7 (4)° respectively.

The investigations were supported in part (ALS and BK-P) by the Netherlands Foundation for Chemical Research (SON) with financial aid from the Netherlands Organization for the Advancement of Pure Research (ZWO).

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The Structures of (Dimethylaminopropyl)phenothiazine Drugs and Their Metabolites. II. Chlorpromazine Sulphoxide, $C_{17}H_{19}ClN_2OS$, at 120 K

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(*Received* 16 *December* 1982; *accepted* 10 *October* 1984)

Abstract. $M_r = 334·7$, orthorhombic, *Pbca*, $a = 10·357$ (1), $b = 14·090$ (2), $c = 23·585$ (4) Å, $V = 3442$ (1) Å^3, $Z = 8$, $D_m = 1·290$, $D_x = 1·292$ (1) g cm^{-3}, λ(Cu $K\alpha$) = 1·5418 Å, $\mu = 30·6$ cm^{-1}, $F(000) = 1408$, room temperature, $R = 0·067$ for 2144 contributing reflections; $a = 10·210$ (2), $b = 13·961$ (2), $c = 23·441$ (3) Å, $V = 3341$ (1) Å^3, $D_x = 1·331$ (1) g cm^{-3}, $\mu = 32·1$ cm^{-1}, $T = 120$ K, $R = 0·051$ for 2634 contributing reflections. Only the results at 120 K are reported. The sulphoxide O atom lies in a boat-axial conformation, and the solid-state conformation of the N(10) side chain is different from that of chlorpromazine.

Introduction. 2-Chloro-10-(3-dimethylaminopropyl)-phenothiazine 5-oxide (chlorpromazine sulphoxide, CPZSO) is one of the major metabolites of chlorpromazine (CPZ) in man (Salzman, Moran & Brodie, 1955). Pharmacokinetic studies in psychiatric patients have demonstrated that it may reach blood

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levels about half as high as that of the parent compound, after oral doses of CPZ (Dahl & Strandjord, 1977). As reviewed previously (Dahl, 1981), CPZSO has relatively low biological activity compared to CPZ. The crystal and molecular structure of the sulphoxide metabolite (LMSO) of another phenothiazine drug, levomepromazine, has previously been reported from our laboratories (Hough, Hjorth & Dahl, 1982). LMSO is biologically more active than CPZSO (Dahl & Refsum, 1976; Dahl & Hall, 1981). The structure of CPZSO was solved in order to compare its molecular conformation in the solid state with that of the parent drug CPZ (McDowell, 1969) and that of LMSO.

Experimental. CPZSO kindly supplied by Rhône–Poulenc Industries, Paris, France. Single crystals obtained by slow cooling of hexane solution in sealed glass ampoule, needle prisms with a axis parallel to needle axis, D_m by flotation in aqueous KI solutions. Data collection on Enraf–Nonius CAD-4 diffractometer, graphite-monochromated Cu $K\alpha$ radiation, ω–2θ scan up to $2\theta = 140°$, hkl ranges 0 to 12, 17, 28 respectively, unobserved reflections $I < 3\sigma(I)$, corrections for Lp and absorption, least-squares refinements based on F and $1/\sigma(I)$ weights, using *XRAY76* (Stewart, Machin, Dickinson, Ammon, Heck & Flack, 1976). Scattering factors from Cromer & Mann (1968) for C, N, O, S, Cl and from Stewart, Davidson & Simpson (1965) for H. Calculations on a Cyber 171MP computer.

Initial data collection at room temperature, crystal size 0·1 × 0·4 × 0·6 mm, cell parameters from setting angles of 25 reflections ($\theta < 50°$), 4% decline in intensity of standards $43\bar{4}$ and $\bar{2}\bar{2}9$ during data collection, 3264 unique reflections measured, 1120 unobserved. Structure solved by heavy-atom method, Cl and S atoms fixed by Patterson function, H atoms located by difference synthesis. Final refinement, H's isotropic, other atoms anisotropic, to $R = 0{\cdot}067$, $wR = 0{\cdot}072$.

Another data set collected at 120 K, otherwise same experimental conditions, to obtain more exact atom positions. Crystal size 0·1 × 0·3 × 0·5 mm, cell parameters from setting angles of 25 reflections ($\theta < 50°$), 7% decline in intensity of standards 800 and $44\bar{2}$, 3168 unique reflections measured, 534 unobserved, refinement to $R = 0{\cdot}051$, $wR = 0{\cdot}057$, $(\Delta/\sigma)_{av} = 0{\cdot}03$, $(\Delta/\sigma)_{max} = 0{\cdot}09$, residual electron density in final ΔF map $\pm 0{\cdot}5$ e Å^{-3}.*

* Lists of structure factors, anisotropic thermal parameters, H-atom coordinates and a stereoview of the molecular packing approximately down the c axis, all for the 120 K structure, have been deposited with the British Library Lending Division as Supplementary Publication No. SUP 39816 (14 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

Discussion. Positional and thermal parameters obtained from the low-temperature data are given in Table 1, and an *ORTEP* drawing (Johnson, 1971) of the molecular structure is shown in Fig. 1. Bond lengths, bond angles and torsion angles obtained from the structure determination at 120 K are given in Table 2. The low-temperature data resulted in approximately 50% smaller standard deviations of the bond lengths, compared with the structure at room temperature.

The mean bond lengths in the aromatic rings are normal, 1·399 (6) Å in the substituted aromatic ring and 1·402 (5) Å in the unsubstituted aromatic ring. The C–Cl distance of 1·734 (3) Å in CPZSO (Table 2) is

Table 1. *Positional parameters and equivalent isotropic thermal parameters* (Å^2 × 10^3)

$U_{eq} = (U_1U_2U_3)^{1/3}$.

	x	y	z	U_{eq}
C(1)	0·4241 (3)	0·7245 (3)	0·8636 (2)	21 (2)
C(2)	0·5201 (4)	0·7705 (3)	0·8951 (2)	24 (2)
C(3)	0·6106 (4)	0·8334 (3)	0·8715 (2)	25 (2)
C(4)	0·6010 (4)	0·8507 (3)	0·8133 (2)	23 (2)
S(5)	0·4969 (1)	0·8481 (1)	0·7092 (1)	17 (1)
C(6)	0·4296 (4)	0·7364 (3)	0·6212 (2)	25 (2)
C(7)	0·3586 (4)	0·6673 (3)	0·5925 (2)	28 (2)
C(8)	0·2736 (4)	0·6092 (3)	0·6237 (2)	26 (2)
C(9)	0·2594 (4)	0·6185 (3)	0·6828 (1)	21 (2)
N(10)	0·3207 (3)	0·6957 (2)	0·7716 (1)	17 (1)
C(11)	0·4147 (3)	0·7430 (3)	0·8042 (1)	18 (2)
C(12)	0·5049 (3)	0·8078 (2)	0·7798 (1)	18 (2)
C(13)	0·4162 (3)	0·7475 (3)	0·6812 (2)	20 (2)
C(14)	0·3326 (3)	0·6876 (3)	0·7125 (1)	18 (2)
O(15)	0·4032 (2)	0·9304 (2)	0·7074 (1)	25 (1)
Cl(16)	0·5314 (1)	0·7431 (1)	0·9671 (1)	31 (1)
C(17)	0·2246 (3)	0·6346 (3)	0·8007 (1)	19 (2)
C(18)	0·2747 (3)	0·5329 (3)	0·8128 (1)	22 (2)
C(19)	0·2048 (4)	0·4890 (3)	0·8638 (2)	25 (2)
N(20)	0·2470 (3)	0·5322 (2)	0·9180 (1)	26 (1)
C(21)	0·3725 (4)	0·4925 (3)	0·9369 (2)	41 (2)
C(22)	0·1491 (5)	0·5153 (4)	0·9624 (2)	38 (3)

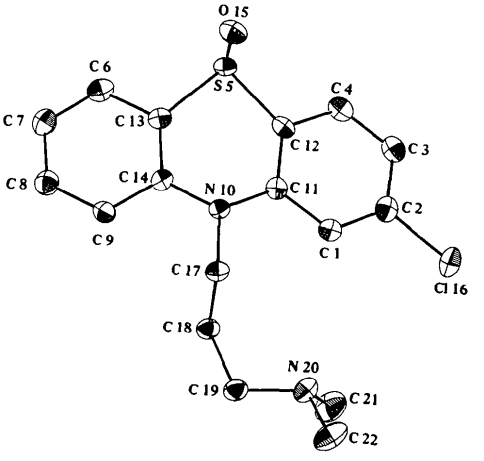

Fig. 1. Molecular structure and atom-numbering system of chlorpromazine sulphoxide.

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

C(1)–C(2)	1·385 (4)	C(8)–C(9)	1·399 (4)
C(1)–C(11)	1·419 (4)	C(9)–C(14)	1·405 (4)
C(2)–C(3)	1·390 (4)	N(10)–C(11)	1·393 (4)
C(2)–Cl(16)	1·734 (3)	N(10)–C(14)	1·395 (4)
C(3)–C(4)	1·389 (4)	N(10)–C(17)	1·468 (4)
C(4)–C(12)	1·392 (4)	C(11)–C(12)	1·412 (4)
S(5)–C(12)	1·750 (3)	C(13)–C(14)	1·402 (4)
S(5)–C(13)	1·756 (3)	C(17)–C(18)	1·536 (4)
S(5)–O(15)	1·496 (3)	C(18)–C(19)	1·521 (5)
C(6)–C(7)	1·382 (4)	C(19)–N(20)	1·471 (5)
C(6)–C(13)	1·422 (4)	N(20)–C(21)	1·465 (5)
C(7)–C(8)	1·395 (4)	N(20)–C(22)	1·462 (5)
C(2)–C(1)–C(11)	119·1 (3)	C(6)–C(7)–C(8)	118·5 (3)
C(1)–C(2)–C(3)	123·5 (3)	C(6)–C(13)–C(14)	120·7 (3)
C(1)–C(2)–Cl(16)	117·6 (2)	C(7)–C(8)–C(9)	122·0 (3)
C(1)–C(11)–N(10)	119·9 (3)	C(8)–C(9)–C(14)	120·0 (3)
C(1)–C(11)–C(12)	118·0 (3)	C(9)–C(14)–N(10)	120·1 (3)
C(3)–C(2)–Cl(16)	118·9 (2)	C(9)–C(14)–C(13)	118·3 (3)
C(2)–C(3)–C(4)	117·0 (3)	C(11)–N(10)–C(14)	121·5 (3)
C(3)–C(4)–C(12)	121·9 (3)	C(11)–N(10)–C(17)	118·7 (3)
C(4)–C(12)–S(5)	115·3 (3)	N(10)–C(11)–C(12)	122·1 (3)
C(4)–C(12)–C(11)	120·5 (3)	C(14)–N(10)–C(17)	118·2 (3)
C(12)–S(5)–C(13)	96·8 (2)	N(10)–C(14)–C(13)	121·6 (3)
C(12)–S(5)–O(15)	107·7 (2)	N(10)–C(17)–C(18)	113·6 (3)
S(5)–C(12)–C(11)	124·0 (3)	C(17)–C(18)–C(19)	111·2 (3)
C(13)–S(5)–O(15)	107·7 (2)	C(18)–C(19)–N(20)	112·1 (3)
S(5)–C(13)–C(6)	114·3 (3)	C(19)–N(20)–C(21)	111·2 (3)
S(5)–C(13)–C(14)	124·6 (3)	C(19)–N(20)–C(22)	110·4 (3)
C(7)–C(6)–C(13)	120·5 (3)	C(21)–N(20)–C(22)	108·8 (3)

C(11)–N(10)–C(17)–C(18)	−83·9 (3)
C(14)–N(10)–C(17)–C(18)	83·3 (3)
N(10)–C(17)–C(18)–C(19)	154·0 (3)
C(17)–C(18)–C(19)–N(20)	−72·6 (4)
C(18)–C(19)–N(20)–C(21)	−79·6 (4)
C(18)–C(19)–N(20)–C(22)	159·6 (3)

near the mean C–Cl distance [1·737 (16) Å] of 26 different Cl-substituted aromatic compounds, which were tabulated by Palenik, Donohue & Trueblood (1968).

The largest angle between C atoms in the aromatic system, 123·5 (3)°, is the C(1)–C(2)–C(3) angle at the substituted C atom (Table 2). It has previously been shown that CPZ (McDowell, 1969) and two other Cl-substituted aromatic compounds, 1,5-dichloroanthraquinone (Bailey, 1958) and 9,10-dichloroanthracene (Trotter, 1959), also have aromatic C–C–C angles in the range 122·0–124·1° at the Cl-substituted C atom. Comparison with the structure of CPZ at room temperature (McDowell, 1969) indicates that sulphoxidation has slightly decreased (by 0·5°) the endocylic C–S–C angle, and increased the endocylic C–N–C angle by about 3° from 118° in CPZ to 121° in CPZSO.

The deviations of the atoms of the rings from least-squares planes, calculated by equal weighting, range from 0·001 (4) to 0·010 (3) Å [average 0·005 (4) Å] for the unsubstituted aromatic ring, from 0·001 (4) to 0·007 (3) Å [average 0·005 (4) Å] for the substituted aromatic ring, and are 0·001 (3) Å for all the four C atoms of the central thiazine ring.

The angle between the planes of the two phenyl rings is 159·5 (3)°, which is larger than in any other phenothiazine derivative for which the structure has been reported. The corresponding angle is 139·4 (6)° in CPZ (McDowell, 1969) and 144·7 (3)° in LMSO (Hough, Hjorth & Dahl, 1982).

As in LMSO, the central thiazine ring of CPZSO has a boat conformation, with the sulphoxide oxygen atom O(15) in an axial position. The thiazine ring in CPZSO is, however, more flat than in CPZ and LMSO. Thus, the displacement of N(10) from the least-squares plane of the four C atoms of the thiazine ring is 0·18 (4) Å in CPZSO, 0·29 (4) Å in LMSO, and was calculated to 0·40 (7) Å for CPZ from the data published by McDowell (1969). Furthermore, the distance of S(5) from the plane of the C atoms of the thiazine ring is 0·63 (7) Å in CPZ, 0·63 (4) Å in LMSO, and 0·44 (4) Å in CPZSO.

The N(10)–C(17) bond in CPZSO lies in a position equatorial to the central thiazine ring, as in CPZ and LMSO. The C(11)–N(10)–C(17)–C(18) torsion angle is −83·9 (3)° in CPZSO (Table 2), placing C(19) and the rest of the 3-dimethylaminopropyl side chain on the opposite side of the plane of the C atoms of the thiazine ring, compared to the sulphoxide O(15).

Fig. 2 shows the crystal structure of CPZSO. The molecules are packed in two layers approximately perpendicular to each other and parallel to the *c* axis. The shortest intermolecular contact distance involving the 3-dimethylaminopropyl side chain [3·384 (4) Å] is between C(18) and O(15) of the neighbouring molecule. The sum of the corresponding van der Waals radii is 3·22 Å (Bondi, 1964).

The donation of chlorpromazine sulphoxide by Rhône–Poulenc Industries, Paris, France, is gratefully acknowledged. We would also like to thank Drs L. Hansen and K. Jynge for valuable discussions during the preparation of this manuscript.

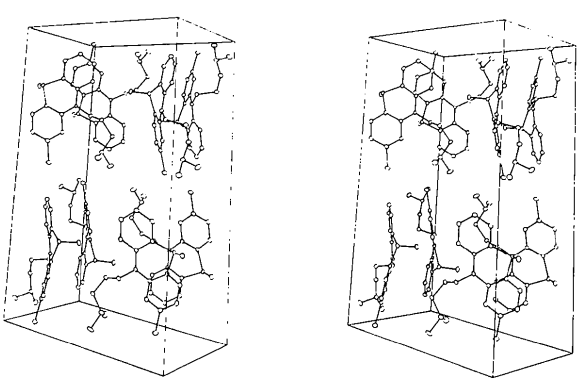

Fig. 2. Stereoscopic illustration of the molecular packing, viewed perpendicular to the *c* axis.

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The Structures of (Dimethylaminopropyl)phenothiazine Drugs and Their Metabolites. III. Monode-*N*-methylchlorpromazine Sulphoxide, $C_{16}H_{17}ClN_2OS$, at 120 K

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(*Received* 17 *January* 1983; *accepted* 10 *October* 1984)

Abstract. $M_r = 320{\cdot}7$, orthorhombic, *Pbca*, $a = 8{\cdot}088\ (2)$, $b = 19{\cdot}051\ (5)$, $c = 19{\cdot}604\ (5)$ Å, $V = 3021\ (1)$ Å^3, $Z = 8$, $D_m = 1{\cdot}35$, $D_x = 1{\cdot}410\ (1)$ g cm^{-3}, λ(Mo $K\alpha$) $= 0{\cdot}71069$ Å, $\mu = 3{\cdot}77$ cm^{-1}, $F(000) = 1408$, $R = 0{\cdot}039$ for 2140 contributing reflections. The central thiazine ring has a boat conformation with the sulphoxide O atom in an axial position. The 3-methylaminopropyl side chain has a conformation more similar to that of chlorpromazine sulphoxide than to that of chlorpromazine.

Introduction. The molecular and crystal structure of chlorpromazine sulphoxide (CPZSO), which is a metabolite of chlorpromazine (CPZ), has been reported from our laboratories (Hough, Hjorth & Dahl, 1985). CPZSO is less folded along the central S–N axis, and has a different conformation for the N(10)-substituted 3-dimethylaminopropyl side chain than CPZ (McDowell, 1969). (The structure of CPZSO was examined both at room temperature and at 120 K. Standard deviations in bond lengths and angles obtained from the low-temperature data were about half those obtained from the room-temperature data.)

CPZ is metabolized in man and other species by both sulphoxidation and oxidative *N*-demethylation, and a metabolite formed by a combination of these two pathways, 2-chloro-10-(3-methylaminopropyl)phenothiazine 5-oxide (monode-*N*-methylchlorpromazine sulphoxide, DCPZSO), has also been identified in man (Fishman & Goldenberg, 1960). This paper reports the molecular and crystal structure of DCPZSO at 120 K.

Experimental. DCPZSO kindly supplied by Rhône–Poulenc Industries, Paris, France. Single crystals by slow cooling of *m*-xylene solution in sealed glass ampoule, flat orthogonal prisms, with longest edge parallel to *a* axis. D_m by flotation in aqueous KI solution, single crystal $0{\cdot}1 \times 0{\cdot}2 \times 0{\cdot}4$ mm. Cell parameters from setting angles of 25 reflections ($\theta < 20°$). Data collection on Enraf–Nonius CAD-4 diffractometer, graphite-monochromated Mo $K\alpha$ radiation, *hkl* ranges 0–10, 0–25, 0–25 respectively, 2θ range 4–56°. No decline in intensity of standards 173, 406 and 048 during data collection. 3727 unique reflections measured, 1587 unobserved [$I < 3\sigma(I)$]. Lp correction,

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