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Structure of (3a*S*)-7-Chloro-4-(2-dimethylaminoethyl)-8-methyl-2,3,3a,4-tetrahydro-1*H*-pyrrolo[2,1-*c*][1,2,4]benzothiadiazine 5,5-Dioxide, C₁₅H₂₂ClN₃O₂S

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Abstract. $M_r = 343.9$, monoclinic, $P2_1/c$, $a = 10.226$ (1), $b = 13.155$ (1), $c = 12.722$ (1) Å, $\beta = 100.59$ (1)°, $V = 1682.3$ (3) Å³, $Z = 4$, $D_m = 1.35$ (3), $D_x = 1.358$ Mg m⁻³, graphite-monochromated Cu $K\alpha$, $\lambda = 1.5418$ Å, $\mu = 3.26$ mm⁻¹, $F(000) = 728$, room temperature, final $R = 0.064$ for 1341 observed reflections. As in the 7-chloro-4-ethyl-2,3,3a,4-tetrahydro-1*H*-pyrrolo[2,1-*c*][1,2,4]benzothiadiazine 5,5-dioxide [Oberti, Bernabei, Forni, Cameroni & Galli (1983). *Acta Cryst.* **C39**, 1278–1280] the thiadiazine and pyrrolidine rings exhibit sofa and twist conformations with some conjugation between N(2), which is sp^2 hybridized, and the benzene ring. Only minor differences have been found on comparison of the structure of the title compound with that of the above mentioned compound.

Introduction. A series of 4-dimethylaminoethyl and 4-diethylaminoethyl derivatives of 2,3,3a,4-tetrahydro-1*H*-pyrrolo[2,1-*c*][1,2,4]benzothiadiazine 5,5-dioxide substituted or unsubstituted in the benzene ring was prepared and subjected to preliminary investigation using the cardiovascular system of the anesthetized rat by Bernabei, Cameroni, Forni, Bellei & Baggio (1978). The introduction of a basic group in the alkyl chain gives compounds with a most pronounced hypotensive activity and a marked increase in differential pressure, sometimes accompanied by some bradycardiac activity. The X-ray crystal-structure determination of the title compound was undertaken in order to study the geometry of the tetrahydro-1*H*-pyrrolobenzo-

thiadiazine system, the results of which should be useful in the interpretation of its biological properties.

Experimental. Transparent lath-shaped crystals (from 2-propanol), $0.6 \times 0.3 \times 0.2$ mm; D_m by flotation; Philips PW 1100 four-circle diffractometer; accurate cell parameters from 25 high-angle reflections using the Philips *LAT* routine; ω - 2θ scan mode, scan width = 1.2° , scan speed = 0.04° s⁻¹, each background time 5 s; 3 standard reflections monitored at 4 h intervals with max. intensity variation 4.6% (correction applied); 1740 unique reflections ($h = -10$ to 10, $k = 0$ to 13, $l = 0$ to 13, $2 \leq \theta \leq 50^\circ$), 399 of which [$I \leq 3\sigma(I)$] were considered unobserved; corrections for L_p and absorption (spherical shape, $r = 0.025$ cm; max. and min. absorption corrections 1.440 and 0.751); direct methods (*MULTAN*; Main, Hull, Lessinger, Germain, Declercq & Woolfson, 1978), $C(14)$ from ΔF synthesis; full-matrix refinement on F (*ORFLS*; Busing, Martin & Levy, 1962); coordinates of H atoms calculated by geometrical considerations (*XANADU*; Roberts & Sheldrick, 1975) and confirmed by ΔF synthesis; refined parameters: coordinates and anisotropic thermal parameters for non-H atoms, and alternately scale factor and secondary anisotropic extinction coefficient [final value = $2.1(1) \times 10^{-4}$ following Coppens & Hamilton (1970)]; R (including zeros) = 0.064, R (omitting zeros) = 0.047, $R_w = 0.048$, each reflection given a weight based on counting statistics; max. and min. heights in final difference Fourier map 0.27 and -0.26 e Å⁻³; max. Δ/σ in the final refinement cycle

0.702; atomic scattering factors for neutral atoms from *International Tables for X-ray Crystallography* (1974); *PARST* program (Nardelli, 1983a) was used for calculating molecular parameters; figures drawn with *ORTEPII* (Johnson, 1976).

Discussion. The stereochemistry of the molecule is illustrated in Fig. 1, which also gives the atom numbering; the molecular packing is shown in Fig. 2. Table 1 contains the final atomic coordinates together with the equivalent isotropic temperature factors for non-H atoms. The intramolecular bond distances and angles are listed in Table 2.*

* Lists of structure factors, anisotropic thermal parameters of non-H atoms, coordinates of H atoms, torsion angles, equations of least-squares planes with the deviations of the atoms from the planes, and the ring-puckering coordinates with the asymmetry parameters have been deposited with the British Library Lending Division as Supplementary Publication No. SUP 39160 (18 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

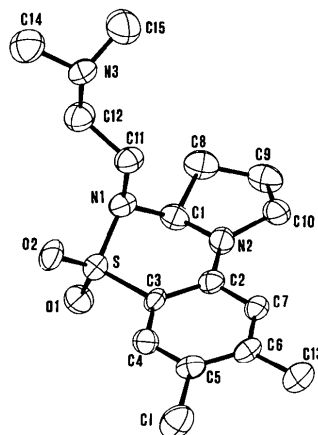


Fig. 1. Perspective view of the molecule.

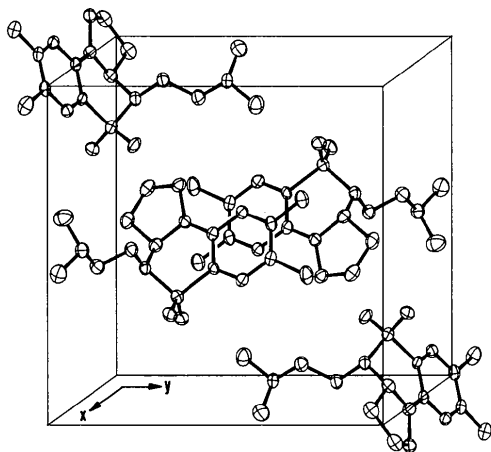


Fig. 2. Packing of the molecules.

Table 1. *Fractional atomic coordinates* ($\times 10^4$) and *equivalent isotropic temperature factors* (\AA^2) for non-hydrogen atoms, with e.s.d.'s in parentheses

$$B_{eq} = \frac{1}{3} \sum_i \sum_j \beta_{ij} a_i^* a_j^* a_i \cdot a_j$$

	x	y	z	B_{eq}
Cl	4976 (1)	-1683 (1)	8687 (1)	6.1 (1)
S	8179 (1)	1522 (1)	8524 (1)	4.1 (0)
O(1)	9270 (3)	1177 (3)	8047 (3)	5.1 (1)
O(2)	7062 (3)	1969 (2)	7833 (3)	5.3 (1)
N(1)	8781 (4)	2355 (2)	9455 (3)	3.9 (1)
N(2)	9151 (4)	1090 (3)	10878 (3)	4.0 (1)
N(3)	6687 (4)	4658 (3)	9668 (3)	5.0 (1)
C(1)	9771 (5)	1831 (4)	10274 (4)	4.1 (2)
C(2)	8165 (4)	462 (3)	10377 (4)	3.5 (1)
C(3)	7643 (4)	547 (3)	9279 (4)	3.4 (1)
C(4)	6653 (5)	-104 (4)	8787 (4)	4.0 (2)
C(5)	6187 (4)	-858 (4)	9356 (4)	4.0 (2)
C(6)	6656 (5)	-964 (3)	10451 (4)	3.9 (2)
C(7)	7629 (5)	-306 (4)	10937 (4)	3.8 (1)
C(8)	10563 (5)	2511 (4)	11123 (5)	5.5 (2)
C(9)	10829 (5)	1856 (4)	12118 (5)	5.3 (2)
C(10)	9613 (5)	1176 (4)	12023 (4)	4.5 (2)
C(11)	7757 (5)	2977 (4)	9853 (4)	4.3 (2)
C(12)	7661 (5)	4005 (4)	9326 (4)	5.1 (2)
C(13)	6140 (5)	-1782 (4)	11104 (5)	5.4 (2)
C(14)	6259 (6)	5448 (5)	8905 (5)	6.8 (2)
C(15)	7164 (7)	5102 (5)	10696 (5)	8.1 (3)

Table 2. *Bond distances* (\AA) and *angles* ($^\circ$) for non-H atoms, with e.s.d.'s in parentheses

Cl-C(5)	1.746 (5)	N(3)-C(15)	1.434 (8)
S-O(1)	1.438 (4)	C(1)-C(8)	1.516 (7)
S-O(2)	1.434 (3)	C(2)-C(3)	1.405 (6)
S-N(1)	1.647 (4)	C(2)-C(7)	1.404 (7)
S-C(3)	1.750 (5)	C(3)-C(4)	1.384 (6)
N(1)-C(1)	1.483 (6)	C(4)-C(5)	1.365 (7)
N(1)-C(11)	1.489 (6)	C(5)-C(6)	1.394 (7)
N(2)-C(1)	1.456 (6)	C(6)-C(7)	1.377 (6)
N(2)-C(2)	1.367 (6)	C(6)-C(13)	1.513 (7)
N(2)-C(10)	1.451 (6)	C(8)-C(9)	1.515 (8)
N(3)-C(12)	1.442 (7)	C(9)-C(10)	1.519 (7)
N(3)-C(14)	1.436 (7)	C(11)-C(12)	1.505 (7)
O(1)-S-O(2)	117.6 (2)	N(2)-C(2)-C(7)	121.4 (4)
O(1)-S-N(1)	107.3 (2)	C(3)-C(2)-C(7)	116.7 (4)
O(1)-S-C(3)	110.2 (2)	S-C(3)-C(2)	120.2 (3)
O(2)-S-N(1)	108.6 (2)	S-C(3)-C(4)	118.8 (4)
O(2)-S-C(3)	110.0 (2)	C(2)-C(3)-C(4)	120.9 (4)
N(1)-S-C(3)	101.9 (2)	C(3)-C(4)-C(5)	120.5 (5)
S-N(1)-C(1)	108.2 (3)	Cl-C(5)-C(4)	118.6 (4)
S-N(1)-C(11)	114.7 (3)	Cl-C(5)-C(6)	120.5 (4)
C(1)-N(1)-C(11)	116.7 (4)	C(4)-C(5)-C(6)	120.9 (4)
C(1)-N(2)-C(2)	121.0 (4)	C(5)-C(6)-C(7)	118.2 (4)
C(1)-N(2)-C(10)	112.6 (4)	C(5)-C(6)-C(13)	122.0 (4)
C(2)-N(2)-C(10)	126.2 (4)	C(7)-C(6)-C(13)	119.8 (5)
C(12)-N(3)-C(14)	111.7 (4)	C(2)-C(7)-C(6)	122.8 (4)
C(12)-N(3)-C(15)	112.4 (5)	C(1)-C(8)-C(9)	104.5 (4)
C(14)-N(3)-C(15)	109.4 (5)	C(8)-C(9)-C(10)	104.4 (4)
N(1)-C(1)-N(2)	112.0 (4)	N(2)-C(10)-C(9)	103.7 (4)
N(1)-C(1)-C(8)	115.6 (4)	N(1)-C(11)-C(12)	109.5 (4)
N(2)-C(1)-C(8)	104.3 (4)	N(3)-C(12)-C(11)	113.1 (4)
N(2)-C(2)-C(3)	121.9 (4)		

The benzene ring is almost planar [maximum deviation 0.013 (5) \AA], with the chlorine and the methyl substituents displaced 0.049 (2) and 0.0001 (53) \AA respectively from the mean plane.

The bond angles of the benzene ring agree well with the predicted sensitivity to the electronic properties of

substituents (Domenicano, Mazzeo & Vaciano, 1976), with an increase of the internal angle at the Cl substituent [C(4)–C(5)–C(6): 120.9 (4)°] and a decrease at the methyl group [C(5)–C(6)–C(7): 118.2 (4)°].

The thiadiazine ring is close to a sofa conformation with a local pseudo-mirror passing through N(1) and C(2) [$\Delta C_s(N1) = 0.062(2)$ according to Nardelli, 1983b]; the values of the ring-puckering coordinates calculated following Cremer & Pople (1975) are $Q = 0.560(4)$ Å, $\varphi = 9.1(5)^\circ$, $\theta = 53.8(5)^\circ$ [using the atomic sequence N(1), C(1), N(2), C(2), C(3), S], with the last five atoms almost coplanar. N(1) is displaced 0.710 (4) Å from the mean plane passing through C(1), N(2), C(2), C(3) and S. The C(11) atom is in an axial position, as the N(1)–C(11) bond forms a 7.5 (2)° angle with the normal to this mean plane; the asymmetric C(1) atom shows an *S* conformation.

The atoms around sulfur are arranged in a distorted tetrahedral configuration, with deviations from tetrahedral angles ranging from $-7.6(2)$ to $8.1(2)^\circ$.

The value of the bond angles at N(2) and the planarity of the system, *i.e.* the distance of this atom from the plane defined by C(1), C(2) and C(10) atoms [0.040 (4) Å], shows that N(2) is *sp*² hybridized. The C(2)–N(2) bond length [1.367 (6) Å] is shorter than the ideal value of 1.470 (5) Å (Camerman, 1970) for a C(*sp*²)–N(*sp*²) single-bond distance and indicates some conjugation between N(2) and the benzene ring. This is also confirmed by the values of the adjacent C–C bond lengths [C(2)–C(7): 1.404 (7) and C(2)–C(3): 1.405 (6) Å] and of the angle at the *ipso* carbon [C(3)–C(2)–C(7): 116.7 (4)°] in the benzene ring, which are longer and narrower than expected, respectively.

The pyrrolidine ring shows a twist conformation [$Q = 0.316(5)$ Å, $\varphi = 95.5(9)^\circ$ following the sequence N(2), C(1), C(8), C(9), C(10)], with a pseudo-twofold axis passing through N(2) and the center of C(8)–C(9), and a pseudo-mirror along C(9) and the middle of C(1)–N(2) [$\Delta C_2(N2) = 0.074(1)$ and $\Delta C_s(C9) = 0.054(3)$, after Nardelli (1983b)].

The dihedral angles between the mean plane of the thiadiazine ring and those of the pyrrolidine and benzene rings are 9.6 (1) and 9.0 (1)°, respectively.

The introduction of a basic group in the alkyl chain and of a methyl group in the benzene ring has not significantly modified the tetrahydro-1*H*-pyrrolobenzothiadiazine moiety, as found for another product of this series (Oberti, Bernabei, Forni, Camerani & Galli, 1983).

The presence of internal strain in the thiadiazine ring has been confirmed by the value of the angle C(3)–S–N(1) [101.9 (2)°].

The only structural modifications are the increasing of the angle between the thiadiazine and pyrrolidine mean planes [from 6.9 (2) to 9.6 (1)°], the lack of the pseudo-mirror along C(8) and the center of N(2)–C(10), not emphasized by Oberti *et al.* (1983), and the presence of the pseudo-mirror passing through the middle of the C(1)–N(2) bond and the C(9) atom, absent in the last mentioned compound.

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