Discussion. Fig. 1 is a stereoscopic projection of the molecule showing the system of nomenclature. Final atomic coordinates and equivalent isotropic temperature factors are given in Table 1.* Interatomic bond distances and angles are given in Table 2; all these values are within the expected range. Atoms O(2) and O(5) are involved in an intramolecular hydrogen bond as suggested by the O(2)···O(5) distance of 2·445 (5) Å. The shortest intermolecular contact between non-hydrogen atoms is O(2)···O(4^{i}) = 3·321 (5) Å [(i): $1+x, y, z$)].

The main result of the present study is that the three-dimensional structure of isomammeigin is now unambiguously determined.

* Lists of H-atom positions, anisotropic thermal parameters and structure factors have been deposited with the British Library Document Supply Centre as Supplementary Publication No. SUP 51125 (15 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

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Structure of Suriclone, a Benzodiazepine Receptor Agonist

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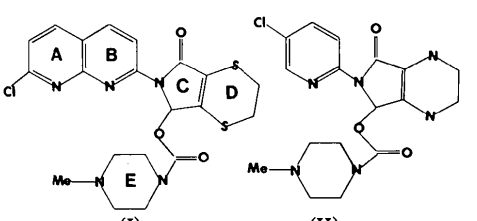
Abstract. 6-(7-Chloro-1,8-naphthyridin-2-yl)-2,3,6,7-tetrahydro-4-methyl-7-oxo-5*H*-1,4-dithiino[2,3-*c*]-pyrrol-5-yl-1-piperazinecarboxylic acid, $C_{20}H_{20}ClN_5O_3S_2$, $M_r = 477{\cdot}9$, triclinic, $P\bar{1}$, $a = 8{\cdot}7066$ (3), $b = 9{\cdot}7665$ (8), $c = 14{\cdot}2515$ (16) Å, $\alpha = 80{\cdot}986$ (9), $\beta = 75{\cdot}168$ (6), $\gamma = 65{\cdot}884$ (5)°, $V = 1067{\cdot}4$ (2) Å^3, $Z = 2$, $F(000) = 496$, room temperature, $D_m = 1{\cdot}482$, $D_x = 1{\cdot}487$ g cm^{-3}, λ(Cu $K\alpha$) = 1·54178 Å, Ni filter, $\mu = 36{\cdot}3$ cm^{-1}, $R = 0{\cdot}053$, $wR = 0{\cdot}070$ for the 3538 reflections included in the refinement. Comparisons of the structures of the two enantiomers of suriclone and the active conformer of the 1,4-benzodiazepine anxiolytics allow the identification of the active form of suriclone as the *R* isomer.

Introduction. The existence of specific benzodiazepine (BZD) receptors in various mammalian brain tissues is well documented. The receptors are linked to γ-aminobutyric acid (GABA) receptor sites which control chloride anion channels, and benzodiazepines elicit their biological actions *via* allosteric modulation of the GABA receptor. Other chemical classes of drugs different from the benzodiazepines bind tightly to the BZD receptor; examples include pyrazoloquinolinones, thiazolopyridazines, quinolines and the cyclopyrrolones, suriclone (I) and zopiclone (II). The cyclopyrrolones are the only non-1,4-benzodiazepine drugs that simultaneously exhibit high potency in displacing benzodiazepines from their binding sites and the diverse pharmacological properties of agonist benzodiazepine receptor ligands (Zundel, Blanchard & Julou, 1985).



(I) (II)

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Suriclone is an anxiolytic and anticonvulsant drug that potently inhibits the binding of both the antagonist, Ro15–1788 [$IC_{50} = 0{\cdot}4$ n*M* (Trifiletti & Snyder, 1984)], and of an agonist, flunitrazepam [$IC_{50} = 2{\cdot}2$ n*M* (Blanchard & Julou, 1983)]. This activity profile indicates that suriclone binds strongly to the receptor, although some evidence suggests that it does not necessarily bind in the same manner as the 1,4-benzodiazepines (Trifiletti & Snyder, 1984). Nevertheless, suriclone exhibits the same pharmacological profile *in vivo* as do the benzodiazepines and is a more potent inhibitor of the binding of Ro15–1788 than zopiclone. As well, suriclone shows stereospecificity at the receptor similar to that shown by the chiral 3-methyl and anthramycin-analogue benzodiazepines: in both of these benzodiazepines, the *S* enantiomer is more active than the *R* enantiomer (Blount, Fryer, Gilman & Todaro, 1983). Recent experiments indicate that, like the 1,4-benzodiazepines, only one of the two enantiomers of suriclone is biologically active (Jacqmin, Delcour & Lesne, 1986); however, this enantiomer has not been identified. The crystal structure of suriclone has been determined as part of a study of the structure–function relationships of benzodiazepine receptor ligands and to compare the structures of the enantiomers of suriclone to the active conformation of benzodiazepine agonists. [Most high-affinity and clinically useful benzodiazepines are achiral; however, of the two mirror images, the active conformation can be identified by comparison to the structures of the active 3-methyl and anthramycin-analogue benzodiazepines (Blount *et al.*, 1983).]

Experimental. A colorless needle of dimensions 0·36 × 0·18 × 0·14 mm was used for data collection on an Enraf–Nonius CAD-4F diffractometer. The data were collected over a range of $+h, \pm k, \pm l$ and to a maximum θ of 70°. The θ range for the 25 reflections that were used to define the orientation matrix and cell constants was 18·3–42·8°. Data were collected at room temperature using an $\omega/2\theta$ scan of variable speed to achieve $I > 2{\cdot}5\sigma(I)$ within a maximum measurement time of 200 s. The scan width was defined as $\Delta\omega = 1{\cdot}5 \times (1{\cdot}0 + 1{\cdot}4 \tan\theta)°$; two-thirds of the scan time, at the center of the scan, was taken as peak (*P*) and one-sixth of the time, on each side of the scan, was taken as background (*B*1 and *B*2). Then $I = |P - 2(B1 + B2)|Q$, where Q is the scan rate. Three standard reflections, $0\bar{5}\bar{1}$, $0\bar{1}7$ and 410, were monitored every 2000 s of X-ray exposure; the variation in the intensities of these reflections was <2·0%. Of the 3909 reflections measured, 2813 had $I > 2{\cdot}5\sigma(I)$ and were taken as observed. The transformation of the reduced triclinic cell to a conventional setting (Kennard, Speakman & Donnay, 1967) is 0,−1,0/0,0,−1/1,0,0 which gives a cell with $a = 8{\cdot}7665$, $b = 14{\cdot}2515$, $c = 8{\cdot}7066$ Å, $\alpha = 104{\cdot}83$, $\beta = 114{\cdot}12$ and $\gamma = 80{\cdot}98°$.

The data were corrected for Lorentz and polarization effects and converted to normalized structure factors. The structure was solved with direct methods (*MULTAN*78, Main, Hull, Lessinger, Germain, Declercq & Woolfson, 1978). All of the hydrogen atoms were identified in a difference Fourier synthesis; the H atoms were included in the model at calculated positions with idealized geometry. The parameters for the hydrogen atoms attached to C(2) and C(3) were ill behaved during the refinement; therefore, the coordinates for these four atoms were held at calculated values and the isotropic vibration parameters for these atoms were set to 1·2 × the B_{eq} of the atoms to which they were attached. With this exception, the final cycles of least squares included the coordinates of all atoms, the anisotropic vibration parameters of the non-hydrogen atoms and the isotropic vibration parameters of the H atoms. The 3538 reflections used in the refinement were the observed reflections and those unobserved reflections with $|F_c| > 2{\cdot}5\sigma(F_o)$. The function minimized was $\sum w(|F_o| - |F_c|)^2$ where $w^{-1} = |\sigma^2(F_o) + 0{\cdot}0008F_o^2|$. The refinement converged with the maximum shift/e.s.d. = 0·01, $S = 1{\cdot}15$, $R = 0{\cdot}053$ and $wR = 0{\cdot}070$. The maximum and minimum peaks in the final difference Fourier synthesis were 0·3 and −0·1 e Å^{-3}, respectively, and represent the series termination error around the S atom.

The programs used were those of the *XRAY*76 (Stewart, 1976) package. The scattering factors used were those of Cromer & Mann (1968) except for the H atom (from Stewart, Davidson & Simpson, 1965). The molecular conformation and atomic labeling scheme are shown in Fig. 1. The atomic coordinates for the non-hydrogen atoms are given in Table 1* and the bond

* Lists of structure factors, anisotropic vibration parameters, least-squares planes, hydrogen-atom parameters and all bond distances and angles have been deposited with the British Library Document Supply Centre as Supplementary Publication No. SUP 51195 (19 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

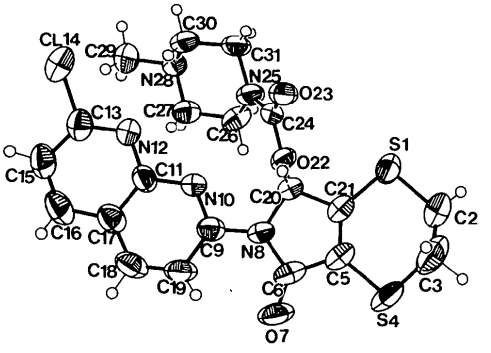

Fig. 1. The molecular conformation and atomic labeling scheme for suriclone. The figure was drawn with the program *ORTEP* (Johnson, 1976).

Table 1. *The fractional coordinates and B_{eq} values for the non-hydrogen atoms of suriclone*

$$B_{eq} = \tfrac{8}{3}\pi^2 \sum_i \sum_j U_{ij} a_i^* a_j^* \mathbf{a}_i . \mathbf{a}_j .$$

	x	y	z	B_{eq}(Å^2)
S(1)	0·7575 (1)	0·0298 (1)	0·5546 (1)	6·16 (5)
C(2)	0·8044 (6)	0·0196 (6)	0·6722 (3)	8·18 (26)
C(3)	0·7263 (8)	−0·0652 (6)	0·7496 (3)	9·45 (31)
S(4)	0·8146 (2)	−0·2690 (1)	0·7375 (1)	7·58 (6)
C(5)	0·7890 (4)	−0·2625 (4)	0·6195 (2)	5·04 (16)
C(6)	0·7841 (4)	−0·3924 (4)	0·5817 (2)	4·70 (15)
O(7)	0·8039 (4)	−0·5155 (3)	0·6228 (2)	6·45 (14)
N(8)	0·7501 (4)	−0·3468 (3)	0·4895 (2)	4·48 (12)
C(9)	0·7106 (4)	−0·4210 (3)	0·4284 (2)	4·36 (14)
N(10)	0·6584 (4)	−0·3399 (3)	0·3519 (2)	4·54 (12)
C(11)	0·6184 (4)	−0·4047 (3)	0·2892 (2)	4·46 (14)
N(12)	0·5686 (4)	−0·3163 (3)	0·2100 (2)	5·11 (13)
C(13)	0·5289 (5)	−0·3768 (4)	0·1486 (2)	5·30 (16)
Cl(14)	0·4749 (1)	−0·2647 (1)	0·0448 (1)	7·50 (6)
C(15)	0·5294 (5)	−0·5218 (4)	0·1578 (3)	6·28 (20)
C(16)	0·5775 (6)	−0·6084 (4)	0·2360 (3)	6·52 (21)
C(17)	0·6287 (5)	−0·5543 (4)	0·3050 (3)	5·07 (16)
C(18)	0·6848 (6)	−0·6368 (4)	0·3872 (3)	5·93 (19)
C(19)	0·7287 (5)	−0·5748 (4)	0·4492 (3)	5·49 (18)
C(20)	0·7275 (4)	−0·1894 (3)	0·4656 (2)	3·92 (13)
C(21)	0·7628 (4)	−0·1484 (4)	0·5532 (2)	4·54 (14)
O(22)	0·8489 (3)	−0·1778 (2)	0·3798 (1)	4·31 (9)
O(23)	0·6449 (3)	0·0318 (2)	0·3287 (2)	4·98 (11)
C(24)	0·7791 (4)	−0·0753 (3)	0·3097 (2)	4·22 (14)
N(25)	0·8813 (4)	−0·1062 (3)	0·2223 (2)	4·75 (13)
C(26)	1·0377 (5)	−0·2395 (4)	0·1994 (2)	5·17 (16)
C(27)	1·0270 (4)	−0·3215 (4)	0·1215 (2)	4·70 (15)
N(28)	0·9908 (4)	−0·2228 (3)	0·0361 (2)	4·78 (13)
C(29)	0·9859 (6)	−0·3030 (4)	−0·0411 (3)	6·90 (21)
C(30)	0·8267 (5)	−0·0979 (4)	0·0621 (2)	5·35 (17)
C(31)	0·8318 (5)	−0·0075 (4)	0·1373 (2)	5·39 (17)

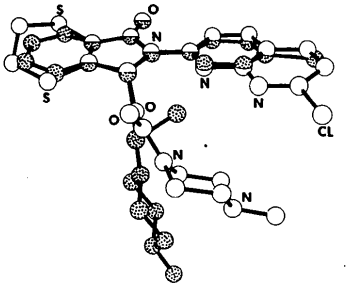

Fig. 2. The superposition of the molecular conformation of suriclone and zopiclone (Borea *et al.*, 1987). Zopiclone is shown with stippled atoms. The superposition was calculated using the program *PROFIT* (Smith, 1983) and plotted with the program *PLUTO* (Motherwell, 1979).

distances and bond angles for the non-hydrogen atoms are in Table 2.

Table 2. *The bond distances* (Å) *and angles* (°) *for the non-hydrogen atoms of suriclone*

S(1)–C(2)	1·803 (6)	C(2)–S(1)–C(21)	100·6 (2)
S(1)–C(21)	1·725 (4)	S(1)–C(2)–C(3)	115·2 (5)
C(2)–C(3)	1·468 (9)	C(2)–C(3)–S(4)	115·4 (3)
C(3)–S(4)	1·835 (9)	C(3)–S(4)–C(5)	97·1 (2)
S(4)–C(5)	1·740 (4)	S(4)–C(5)–C(6)	121·2 (2)
C(5)–C(6)	1·474 (7)	S(4)–C(5)–C(21)	129·0 (3)
C(5)–C(21)	1·326 (6)	C(6)–C(5)–C(21)	109·7 (3)
C(6)–O(7)	1·216 (5)	C(5)–C(6)–O(7)	127·4 (3)
C(6)–N(8)	1·386 (5)	C(5)–C(6)–N(8)	106·5 (3)
N(8)–C(9)	1·398 (6)	O(7)–C(6)–N(8)	126·1 (4)
N(8)–C(20)	1·463 (5)	C(6)–N(8)–C(9)	129·0 (3)
C(9)–N(10)	1·308 (6)	C(6)–N(8)–C(20)	110·8 (3)
C(9)–C(19)	1·436 (6)	C(9)–N(8)–C(20)	119·4 (2)
N(10)–C(11)	1·355 (6)	N(8)–C(9)–N(10)	114·8 (3)
C(11)–N(12)	1·359 (6)	N(8)–C(9)–C(19)	121·5 (3)
C(11)–C(17)	1·412 (5)	N(10)–C(9)–C(19)	123·6 (4)
N(12)–C(13)	1·311 (6)	C(9)–C(10)–C(11)	118·1 (3)
C(13)–Cl(14)	1·743 (7)	N(10)–C(11)–N(12)	115·5 (3)
C(13)–C(15)	1·399 (6)	N(10)–C(11)–C(17)	122·2 (3)
C(15)–C(16)	1·337 (7)	N(12)–C(11)–C(17)	122·3 (4)
C(16)–C(17)	1·422 (8)	C(11)–N(12)–C(13)	116·4 (3)
C(17)–C(18)	1·391 (7)	N(12)–C(13)–Cl(14)	115·7 (3)
C(18)–C(19)	1·350 (8)	N(12)–C(13)–C(15)	126·4 (3)
C(20)–C(21)	1·505 (6)	Cl(14)–C(13)–C(15)	117·9 (3)
C(20)–O(22)	1·421 (6)	C(13)–C(15)–C(16)	117·1 (5)
O(22)–C(24)	1·367 (7)	C(15)–C(16)–C(17)	120·5 (4)
O(23)–C(24)	1·208 (9)	C(11)–C(17)–C(16)	117·1 (3)
C(24)–N(25)	1·329 (6)	C(11)–C(17)–C(18)	118·0 (4)
N(25)–C(26)	1·453 (11)	C(16)–C(17)–C(18)	124·9 (4)
N(25)–C(31)	1·464 (6)	C(17)–C(18)–C(19)	120·5 (4)
C(26)–C(27)	1·507 (7)	C(9)–C(19)–C(18)	117·6 (3)
C(27)–N(28)	1·447 (6)	N(8)–C(20)–C(21)	102·6 (2)
N(28)–C(29)	1·465 (6)	N(8)–C(20)–O(22)	109·8 (2)
N(28)–C(30)	1·453 (11)	C(21)–C(20)–O(22)	111·5 (3)
C(30)–C(31)	1·510 (7)	S(1)–C(21)–C(5)	131·1 (3)
		S(1)–C(21)–C(20)	118·7 (2)
		C(5)–C(21)–C(20)	110·2 (3)
		C(20)–O(22)–C(24)	114·6 (2)
		O(22)–C(24)–O(23)	122·4 (2)
		O(22)–C(24)–N(25)	111·3 (2)
		O(23)–C(24)–N(25)	126·2 (3)
		C(24)–N(25)–C(26)	125·8 (2)
		C(24)–N(25)–C(31)	119·9 (2)
		C(26)–N(25)–C(31)	114·1 (2)
		N(25)–C(26)–C(27)	110·6 (3)
		C(26)–C(27)–N(28)	110·9 (3)
		C(27)–N(28)–C(29)	111·2 (3)
		C(27)–N(28)–C(30)	109·2 (2)
		C(29)–N(28)–C(30)	109·9 (3)
		N(28)–C(30)–C(31)	111·0 (3)
		N(25)–C(31)–C(30)	109·6 (3)

Discussion. As shown in Fig. 1, suriclone has an extended planar conformation with a piperazine amide side chain that is twisted out of the basic molecular plane. The four unsaturated heterocyclic rings (*A*, *B*, *C* and *D*) form a slightly curved backbone: the plane of the diazanaphthalene ring (*A* and *B*) is tipped 7·5° out of the plane of the pyrrolidone ring (*C*). The five-membered pyrrolidone ring (*C*) is planar [the estimated standard deviation of the plane calculated for all five atoms plus O(7) is 0·02 Å]; the dithiacyclohexene ring (*D*) adopts a sofa conformation with C(3) 0·72 (4) Å from the mean plane of the other five atoms; and the piperazine ring (*E*) has a chair conformation with N(25) and N(28) −0·586 (4) and 0·685 (4) Å, respectively, out of the plane of the four C atoms. The plane of the amide, defined by O(22), C(24), O(23) and N(25), is rotated 62·6 (2)° from the plane of the pyrrolidone ring; however, the piperazine ring (*E*) that completes this side chain is more nearly coplanar with the basic molecular plane: the angle between ring (*C*) and the plane containing the four C atoms of the piperazine is 31·7 (2)°.

No hydrogen bonds are present in the crystal lattice owing to the lack of hydrogen donor atoms. The closest intermolecular contacts are between centrosymmetrically related molecules: O(7)···O(22) (at $2-x$, $-1-y$, $1-z$) 3·27 (2) Å and O(7)···C(16) (at $1-x$, $-1-y$, $1-z$) 3·26 (2) Å.

Fig. 2 shows a superposition of the molecular conformation of suriclone and that of zopiclone, a less

potent cyclopyrrolone benzodiazepine receptor ligand (Borea, Gilli, Bertolasi & Ferretti, 1987). The only difference between the molecular conformations is in the relative orientation of the piperazine amide side chain to the aromatic portions of the molecule. The orientation of the side chain in the two structures differs in both the torsion angle C(20)–O(22)–C(24)–O(23) which is 26·0 (2) in suriclone and −72·1 (2)° in zopiclone and the angle O(22)–C(24)–N(25)–C(26), 7·0 (2) and −19·4 (2)° in suriclone and zopiclone, respectively.

Suriclone has a similar pharmacological profile to the benzodiazepines and is a competitive inhibitor to both agonist and antagonist ligands for the receptor. These pharmacological properties have been the basis for assuming that suriclone binds to the benzodiazepine receptor. Two recently published models (Borea *et al.*, 1987; Tebib, Bourguignon & Wermuth, 1987) include either suriclone or the related molecule, zopiclone, in their proposal for the agonist recognition site. Both of these models propose that an aromatic binding site recognizes the pyrrolidone and dithiacyclohexene rings (*C* and *D*) and that two agonist-determining regions bind the chloro-diazanaphthalene ring (*A* and *B*) and the saturated piperazine ring (*E*). A crucial hydrogen bond is proposed from the receptor to O(7) of the ligand. Features of these models are similar to our earlier benzodiazepine receptor model (Codding & Muir, 1985) which was based on the structures of inverse agonist ligands. In particular, Tebib *et al.* (1987) find a hydrophobic binding site that discriminates between agonist/antagonist/inverse-agonist activity depending upon the substitution pattern of the group that binds in that pocket; this was identified as site three in our earlier model. The model proposed by Tebib and co-workers would place the (*A*) and (*B*) rings of suriclone in this pocket; such placement suggests that the greater activity of suriclone over zopiclone may be due to the greater ability of suriclone to fill this hydrophobic pocket.

Since the models for the benzodiazepine receptor site have been constructed to accommodate only the known, active conformation (Blount *et al.*, 1983) of the seven-membered benzodiazepine ring, and since only one enantiomer of suriclone has activity (Jacqmin *et al.*, 1986), a comparison between each of the two enantiomers of suriclone and the active conformation of an achiral benzodiazepine will identify the enantiomer that most closely matches the active form of the benzodiazepine. Fig. 3 shows the two superpositions of suriclone and the active conformation of the potent benzodiazepine agonist, clonazepam (Chananont, Hamor & Martin, 1979); the left panel compares *R* suriclone to clonazepam and the right panel compares *S* suriclone. This figure was prepared by using two models for the receptor site (Codding & Muir, 1985; Tebib *et al.*, 1987) to identify the ligand features that should superimpose. The superposition was calculated by a least-squares fit of the positions of five atoms from each structure to produce an overlay of rings (*C*) and (*D*) of suriclone with the benzodiazepine portion of clonazepam; the average distance between pairs of matched atoms was 0·22 Å for the *S* enantiomer and 0·24 Å for the *R* enantiomer. The discrimination between the two enantiomers lies in the region of the out-of-plane rings in the two structures (Fig. 3): the separation between O(22) of the suriclone structure and the lead atom of the out-of-plane phenyl ring [C(51)] of clonazepam is 2·04 Å for the *S* enantiomer and 0·59 Å for the *R* enantiomer. Thus the *R* enantiomer has the best superposition with clonazepam and would, therefore, be the isomer that is predicted to demonstrate biological activity. Fig. 4 shows a stereoview of the superposition of *R* suriclone and the active con-

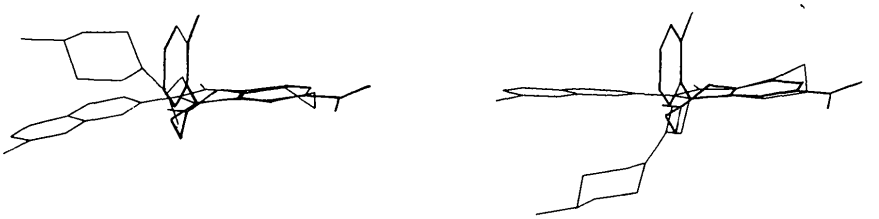

Fig. 3. The superposition of *R* suriclone (left panel) and *S* suriclone (right panel) with the active conformation of the agonist benzodiazepine, clonazepam (Chananont *et al.*, 1979). Clonazepam is drawn with darker bonds. The figure was prepared as described for Fig. 2.

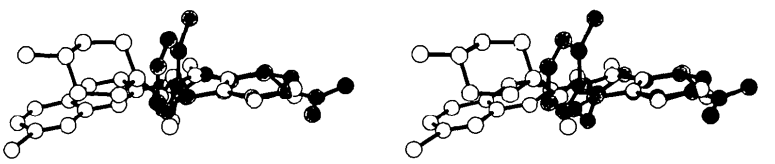

Fig. 4. A stereodrawing of the superposition of the *R* isomer of suriclone and clonazepam (Chananont *et al.*, 1979). Clonazepam is shown with blackened atoms. The figure was prepared as described for Fig. 2.

formation of clonazepam. Accordingly, the coordinates reported herein are those of the *R* isomer.

In conclusion, the molecular conformation of suriclone is found to be similar to that of its congener, zopiclone, and the *R* isomer of suriclone matches the active conformation of the agonist 1,4-benzodiazepines. The greater potency of suriclone over zopiclone is attributed to a larger hydrophobic group, formed by the coplanar rings (*A*) and (*B*), which can bind to a site on the benzodiazepine receptor that distinguishes ligands by the size of the group bound to the receptor at this point.

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Jacoline and Ethanol Solvate of Jaconine Hydrochloride. Pyrrolizidine Alkaloids

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Abstract. $T = 288$ (1) K, Cu $K\alpha$, $\lambda = 1{\cdot}5418$ Å. Jacoline (II): $C_{18}H_{27}NO_7$, $M_r = 369{\cdot}4$, monoclinic, $P2_1$, $a = 16{\cdot}585$ (2), $b = 12{\cdot}124$ (1), $c = 9{\cdot}430$ (1) Å, $\beta = 90{\cdot}72$ (2)°, $U = 1896{\cdot}0$ (5) Å^3, D_m (flotation) = 1·29 (1), $D_x = 1{\cdot}294$ Mg m^{-3}, $Z = 4$, $F(000) = 792$, μ(Cu $K\alpha$) = 0·74 mm^{-1}. Final $R = 0{\cdot}030$ for 3403 observed data. Ethanol solvate of jaconine hydrochloride (IV): $C_{18}H_{27}ClNO_6^+.Cl^-.C_2H_6O$, $M_r = 470{\cdot}4$, orthorhombic, $P2_12_12_1$, $a = 11{\cdot}330$ (1), $b = 14{\cdot}746$ (1), $c = 14{\cdot}021$ (1) Å, $U = 2342{\cdot}5$ (5) Å^3, D_m (flotation) = 1·33 (1), $D_x = 1{\cdot}334$ Mg m^{-3}, $Z = 4$, $F(000) = 1000$, μ(Cu $K\alpha$) = 2·71 mm^{-1}. Final $R = 0{\cdot}055$ for 1853 observed data. Jacoline and jaconine are closely related to jacobine as glycol–chlorohydrin–epoxide. The two independent molecules of (II) have very similar conformations. The conformations adopted by the 12-membered macrocyclic rings in these three alkaloids are very similar.

Introduction. The hepatotoxic alkaloids jacoline and jaconine have been isolated from the plant *Senecio jacobaea* L. (commonly known as ragwort) along with the closely related retronecine alkaloid jacobine (Bradbury & Culvenor, 1954). The molecular structures of jacobine, jaconine and jacoline were deduced by Geissman (1959) and Bradbury & Masamune (1959) from the chemical and spectral evidence, the three alkaloids being shown to be related as epoxide–chlorohydrin–glycol. An X-ray analysis of jacobine bromohydrin by Fridrichsons, Mathieson & Sutor

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