

## Refinement

Refinement on *F**R* = 0.034*wR* = 0.032*S* = 1.950

1483 reflections

181 parameters

All H atoms refined

Weighting scheme based on measured e.s.d.'s

 $(\Delta/\sigma)_{\max} = 0.003$  $\Delta\rho_{\max} = 0.296 \text{ e } \text{Å}^{-3}$  $\Delta\rho_{\min} = -0.250 \text{ e } \text{Å}^{-3}$ 

Extinction correction:

Zachariasen (1968) type

2 Gaussian isotropic

Extinction coefficient:

 $1.09(2) \times 10^{-5}$ Scattering factors from *International Tables for X-ray Crystallography* (Vol. IV)

Table 1. Selected geometric parameters (Å, °)

S1—O1s	1.457(2)	O5—C4	1.322(3)
S1—O2s	1.469(2)	O6—C6	1.432(4)
S1—O3s	1.485(2)	N1—C2	1.480(4)
S1—O4s	1.477(2)	N2—C5	1.493(3)
O1—C1	1.207(3)	C1—C2	1.510(4)
O2—C1	1.324(3)	C2—C3	1.529(4)
O3—C3	1.414(4)	C4—C5	1.513(4)
O4—C4	1.194(4)	C5—C6	1.524(4)
O1s—S1—O2s	111.5(1)	N1—C2—C3	111.2(3)
O1s—S1—O3s	109.9(1)	C1—C2—C3	111.2(3)
O1s—S1—O4s	108.8(1)	O3—C3—C2	110.8(3)
O2s—S1—O3s	108.0(1)	O4—C4—O5	125.6(3)
O2s—S1—O4s	109.1(1)	O4—C4—C5	123.7(3)
O3s—S1—O4s	109.6(1)	O5—C4—C5	110.6(3)
O1—C1—O2	124.8(3)	N2—C5—C4	108.2(2)
O1—C1—C2	124.0(3)	N2—C5—C6	110.8(2)
O2—C1—C2	111.2(3)	C4—C5—C6	111.0(3)
N1—C2—C1	107.7(2)	O6—C6—C5	112.3(3)

Table 2. Hydrogen-bonding geometry (Å, °)

D—H...A	D—H	H...A	D...A	D—H...A
N1—H5...O1s	0.81	2.17	2.923(4)	155
N2—H11...O1s <sup>i</sup>	1.03	2.02	3.02(1)	163
N1—H3...O2s <sup>i</sup>	0.97	1.90	2.839(4)	161
N2—H12...O2s	0.89	1.95	2.822(3)	163
N1—H4...O3s <sup>ii</sup>	1.03	1.85	2.873(4)	172
N2—H13...O3s <sup>ii</sup>	1.10	1.73	2.831(4)	168
O1W—H18...O3s	1.04	1.84	2.82(1)	154
O6—H16...O4s <sup>i</sup>	0.78	1.90	2.683(3)	177
O1W—H17...O4s <sup>iii</sup>	0.87	1.98	2.76(1)	149
N2—H13...O1s <sup>ii</sup>	1.10	2.54	3.25(1)	121
N1—H4...O2s <sup>ii</sup>	1.03	2.64	3.23(1)	116
N2—H11...O4s <sup>i</sup>	1.03	2.38	3.110(4)	127
O2—H1...O6 <sup>iv</sup>	0.96	1.66	2.613(3)	171
O5—H9...O3 <sup>v</sup>	0.92	1.67	2.589(3)	176
O3—H8...O1W <sup>i</sup>	0.89	1.71	2.59(1)	167
O3—H8...O2W <sup>i</sup>	0.89	1.75	2.60(1)	159
O1W—H17...O2W <sup>iii</sup>	0.87	2.68	2.840(4)	134

Symmetry codes: (i)  $\frac{1}{2} - x, 1 - y, z - \frac{1}{2}$ ; (ii)  $\frac{1}{2} - x, 1 - y, \frac{1}{2} + z$ ; (iii)  $\frac{3}{2} - x, 1 - y, z - \frac{1}{2}$ ; (iv)  $-x, \frac{1}{2} + y, -\frac{1}{2} - z$ ; (v)  $-x, y - \frac{1}{2}, -\frac{1}{2} - z$ ; (vi)  $x - 1, y, z$ ; (vii)  $\frac{1}{2} - x, 1 - y, z - \frac{1}{2}$ .

All H atoms were found *via* difference Fourier syntheses and refined. The correct enantiomorph under the non-centrosymmetric space group was determined by inverting the coordinates during the final cycles of least-square refinement. In the final cycles of refinement, non-H atoms were refined anisotropically, while H atoms were fixed. The water molecule was treated as a disordered model with an occupancy factor of 0.5 for both O1W and O2W, and was refined isotropically.

Data collection: *MSCIAFC Diffractometer Control Software* (Molecular Structure Corporation, 1992). Data reduction: *MSCIAFC Diffractometer Control Software*. Program(s) used to solve structure: *TEXSAN* (Molecular Structure Corporation, 1992). Program(s) used to refine structure: *TEXSAN*.

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Supplementary data for this paper are available from the IUCr electronic archives (Reference: TA1155). Services for accessing these data are described at the back of the journal.

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**(11*R*,11*aS*-*trans*)-11-Ethylthio-2,3,5,10,11,11*a*-hexahydro-1*H*-pyrrolo-[2,1-*c*][1,4]benzodiazepin-5-one**

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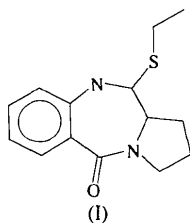
## Abstract

The pyrrolo ring in the title compound, C<sub>14</sub>H<sub>18</sub>N<sub>2</sub>OS, exhibits a flattened envelope conformation, while the benzodiazepine ring exists as a twisted boat. The

intermolecular N—H...O hydrogen bonds form helical chains of molecules connected by a  $4_3$  screw axis. The structure is disordered: both the pyrrolo and the ethylthio fragments occupy two alternative positions, with site-occupancy factors of 0.55 (1) and 0.45 (1).

### Comment

Pyrrolo[2,1-*c*][1,4]benzodiazepine derivatives exhibit antitumor activity, with two well known examples being anthramycin (Kohn, 1975) and tomaymycin (Arima, Kohsaka, Tamura, Imanaka & Sakai, 1972). Several tricyclic analogues have been synthesized and screened against P388 lymphocytic leukemia (Kaneko, Wong, Doyle, Rose & Bradner, 1985). These compounds are believed to act through covalent DNA–drug linkages (Hurley, 1977). The title compound, (I), is one of the simplest members of the family, because it has no substituents in either the aromatic or pyrrolo rings; however, the methoxy group of the antitumor compounds is replaced by an ethylthio group. Therefore, it could serve as the basic model for further structure–activity correlation studies.



The crystal structure is significantly disordered; the disorder involves both the pyrrolo and ethylthio moieties. Nevertheless, the refinement with weak restraints applied to the geometric parameters of the pyrrolo moiety was successful and the quality of the results justifies a reasonable discussion. The title compound consists of three fused rings: the aromatic ring is almost strictly planar, with a maximum deviation from the least-squares plane of 0.013 (6) Å; the conformation of the seven-membered benzodiazepine ring is close to a twisted boat; and the pyrrolo ring is a flattened envelope, with C1, C11a, N4 and C3 almost coplanar, and C2 significantly out of plane, by 0.49 (2) and 0.29 (4) Å for C2 and C2', respectively. The relevant torsion angles are listed in Table 2. A similar conformation pattern is observed in related compounds, for example, anthramycin methyl ester (Mostad, Rømming & Storm, 1978; Arora, 1979) and tomaymycin (Arora, 1981). The overall twist, defined as the dihedral angle between the least-squares plane of the aromatic ring and the planar part of the pyrrolo ring, is 17.0 (6)° for the more occupied and 33.7 (6)° for the less occupied alternatives, and is intermediate between the values for tomaymycin, 9.0 (1)°, and anthramycin methyl ester, 45.0 (1)°.

For compounds with a carbonyl group at C11 (see, for example, Neidle, Webster, Jones & Thurston, 1991), the overall conformation pattern is similar. The presence of an  $sp^2$ -hybridized C atom (C11) causes the approximate planarity of the C9a—N10—C11—C11a fragment, as compared with the torsion angle of  $-48.7(6)^\circ$  in (I). The similar overall shape of the compounds results from the associated change in the C5a—C9a—N10—C11 fragment: it is almost planar in (I) [torsion angle  $2.7(8)^\circ$ ] and significantly folded in the above-mentioned compounds (torsion angles of *ca*  $-44^\circ$ ). It is noteworthy that these angles within the pyrrolo ring have similar absolute values but different signs.

In the crystal structure, the intermolecular N10—H10...O5 hydrogen bonds make infinite helical chains of the molecules connected by a  $4_3$  screw axis along the [001] direction.

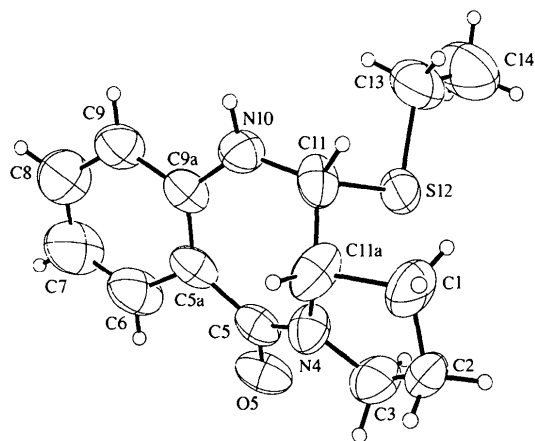


Fig. 1. Displacement ellipsoid (50% probability) representation of the title compound with the numbering scheme; the H atoms are drawn as spheres of arbitrary radii. Only the part of the molecule with the larger occupancy factor is shown.

### Experimental

The preparation of the title compound has been described elsewhere (Kaneko, Wong & Doyle, 1983). The sample was provided by Bristol-Myers Co., Syracuse, NY, USA.

#### Crystal data

C<sub>14</sub>H<sub>18</sub>N<sub>2</sub>O<sub>5</sub>  
*M<sub>r</sub>* = 262.36  
 Tetragonal  
*P*4<sub>3</sub>  
*a* = 8.9850 (8) Å  
*c* = 17.1652 (10) Å  
*V* = 1385.8 (2) Å<sup>3</sup>  
*Z* = 4  
*D<sub>x</sub>* = 1.258 Mg m<sup>-3</sup>  
*D<sub>m</sub>* not measured

Cu Kα radiation  
 $\lambda$  = 1.54178 Å  
 Cell parameters from 25 reflections  
 $\theta$  = 14–39°  
 $\mu$  = 1.989 mm<sup>-1</sup>  
*T* = 293 (2) K  
 Block  
 0.3 × 0.2 × 0.2 mm  
 Colorless

## Data collection

Enraf–Nonius CAD-4F diffractometer  
 $\omega/2\theta$  scans  
 Absorption correction: none  
 3162 measured reflections  
 1472 independent reflections  
 1347 reflections with  $I > 2\sigma(I)$   
 $R_{\text{int}} = 0.044$

$\theta_{\text{max}} = 74.73^\circ$   
 $h = -11 \rightarrow 11$   
 $k = 0 \rightarrow 11$   
 $l = 0 \rightarrow 21$

3 standard reflections  
 frequency: 33 min  
 intensity decay: 4%

## Refinement

Refinement on  $F^2$   
 $R[F^2 > 2\sigma(F^2)] = 0.053$   
 $wR(F^2) = 0.148$   
 $S = 1.083$   
 1472 reflections  
 223 parameters  
 $w = 1/[\sigma^2(F_o^2) + (0.078P)^2 + 0.3355P]$   
 where  $P = (F_o^2 + 2F_c^2)/3$   
 $(\Delta/\sigma)_{\text{max}} = -0.002$   
 $\Delta\rho_{\text{max}} = 0.230 \text{ e } \text{\AA}^{-3}$   
 $\Delta\rho_{\text{min}} = -0.236 \text{ e } \text{\AA}^{-3}$

Extinction correction: *SHELXL93* (Sheldrick, 1993)  
 Extinction coefficient: 0.0041 (16)  
 Scattering factors from *International Tables for Crystallography* (Vol. C)  
 Absolute configuration: Flack (1983)  
 Flack parameter = 0.06 (5)

Table 1. Fractional atomic coordinates and equivalent isotropic displacement parameters ( $\text{\AA}^2$ )
$$U_{\text{eq}} = (1/3)\sum_i\sum_j U^{ij} a_i^* a_j^* \mathbf{a}_i \cdot \mathbf{a}_j$$

	<i>x</i>	<i>y</i>	<i>z</i>	$U_{\text{eq}}$
C11a	0.8622 (8)	0.5068 (6)	0.0558 (3)	0.072 (2)
C1'†	0.923 (2)	0.6125 (15)	0.1232 (7)	0.071 (4)
C2'†	1.010 (4)	0.736 (3)	0.0919 (11)	0.136 (8)
C3'†	0.969 (2)	0.747 (2)	0.0069 (8)	0.071 (5)
N4	0.9004 (5)	0.5900 (4)	-0.0146 (2)	0.0596 (10)
C1‡	0.8217 (19)	0.6383 (13)	0.1147 (7)	0.083 (4)
C2‡	0.9030 (15)	0.7650 (10)	0.0832 (7)	0.072 (3)
C3‡	0.9033 (18)	0.7444 (18)	-0.0041 (9)	0.082 (5)
C5	0.9054 (4)	0.5374 (6)	-0.0869 (3)	0.0536 (10)
O5	0.9357 (4)	0.6250 (5)	-0.1410 (2)	0.0715 (11)
C5a	0.8824 (5)	0.3762 (6)	-0.1028 (3)	0.0573 (11)
C6	0.9484 (8)	0.3293 (9)	-0.1731 (4)	0.089 (2)
C7	0.9381 (10)	0.1857 (11)	-0.1999 (5)	0.113 (3)
C8	0.8646 (8)	0.0808 (9)	-0.1566 (4)	0.097 (2)
C9	0.7959 (6)	0.1216 (7)	-0.0878 (3)	0.0705 (14)
C9a	0.8034 (5)	0.2672 (6)	-0.0594 (3)	0.0539 (11)
N10	0.7297 (5)	0.2914 (5)	0.0094 (2)	0.0579 (10)
C11	0.7132 (6)	0.4247 (5)	0.0479 (3)	0.0625 (12)
S12‡	0.5940 (4)	0.5820 (4)	0.0213 (2)	0.0659 (13)
C13‡	0.4168 (10)	0.4902 (17)	0.0413 (11)	0.107 (5)
C14‡	0.2918 (13)	0.575 (2)	0.0176 (14)	0.132 (6)
S12'†	0.5589 (3)	0.5194 (5)	-0.0093 (2)	0.0475 (12)
C13'†	0.4125 (11)	0.3852 (17)	0.0036 (9)	0.074 (4)
C14'†	0.2811 (13)	0.422 (2)	-0.0398 (12)	0.109 (7)

† Site occupancy = 0.446 (9). ‡ Site occupancy = 0.554 (9).

Table 2. Selected torsion angles ( $^\circ$ )

C5—C5a—C9a—N10	-0.3 (7)
C5a—C9a—N10—C11	2.7 (8)
C9a—N10—C11—C11a	-48.7 (6)
N10—C11—C11a—N4	82.3 (5)
C11—C11a—N4—C5	-52.7 (7)
C11a—N4—C5—C5a	-5.0 (8)
N4—C5—C5a—C9a	25.7 (7)
C11a—C1—C2—C3	33.4 (15)

C11a—C1'—C2'—C3'	18 (3)
C1—C2—C3—N4	-30.2 (16)
C2—C3—N4—C11a	14.0 (13)
C3—N4—C11a—C1	6.1 (11)
N4—C11a—C1—C2	-24.3 (12)
C1'—C2'—C3'—N4	-20 (3)
C2'—C3'—N4—C11a	15.7 (19)
C3'—N4—C11a—C1'	-5.0 (12)
N4—C11a—C1'—C2'	-8 (2)
C9a—N10—C11—S12	73.2 (7)
C1—C11a—C11—S12	53.0 (7)
N10—C11—S12—C13	69.1 (8)
C11—S12—C13—C14	-172.5 (16)
C9a—N10—C11—S12'	78.5 (5)
C1'—C11a—C11—S12	75.9 (9)
N10—C11—S12'—C13'	59.9 (7)
C11—S12'—C13'—C14'	-175.2 (13)

Table 3. Hydrogen-bonding geometry ( $\text{\AA}$ ,  $^\circ$ )

D—H...A	D—H	H...A	D...A	D—H...A
N10—H10...O5'	0.87 (5)	1.97 (5)	2.823 (6)	165 (4)

Symmetry code: (i)  $y, 1 - x, \frac{1}{2} + z$ .

The relatively low data-to-parameter ratio (6.6) for this study is related to the disorder and associated additional number of refined parameters. For H10, both positional and isotropic displacement parameters were refined. All other H atoms were refined as a riding model with an ideal geometry.

Data collection: *CAD-4 Software* (Enraf–Nonius, 1989). Cell refinement: *CAD-4 Software*. Data reduction: *ENPROC* (Rettig, 1978). Program(s) used to solve structure: *SHELXS86* (Sheldrick, 1990). Program(s) used to refine structure: *SHELXL93* (Sheldrick, 1993). Molecular graphics: *Stereochemical Workstation* (Siemens, 1989). Software used to prepare material for publication: *SHELXL93*.

Supplementary data for this paper are available from the IUCr electronic archives (Reference: SK1103). Services for accessing these data are described at the back of the journal.

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