symmetry-related sheet (through the operation of the screw axes contained in the *ab* plane), the water molecules being the 'cement' that holds together the resulting double layer. Such bilayers pack with each other through hydrophobic interaction in the **c** direction. The formation of these bilayers resembles that found in the crystal structure of amino acids.

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Dimethyl 3-(1-Pyrrolidinyl)benzo[*b*]thiocin-4,5-dicarboxylate

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Abstract. $C_{19}H_{21}NO_4S$, $M_r = 359\cdot1$, triclinic, $P\bar{1}$, $a = 9\cdot919$ (4), $b = 10\cdot518$ (5), $c = 10\cdot240$ (5) Å, $\alpha = 93\cdot32$ (4), $\beta = 95\cdot99$ (4), $\gamma = 58\cdot43$ (3)°, $V = 905\cdot2$ Å^3, $Z = 2$, $D_c = 1\cdot32$ Mg m^{-3}; $R = 0\cdot046$ for 1520 diffractometer data. The structure contains a new type of thiocin ring, which has a rigid boat conformation.

Introduction. The compound was prepared and crystallized by Lamm & Aurell (1980). It was obtained through a (2 + 2) cycloaddition of dimethyl acetylenedicarboxylate to the pyrrolidine enamine of thiochroman-3-one, followed by acid-catalysed ring opening. Yellow crystals were grown from an ether solution. The crystal used for data collection was a parallelepiped $0\cdot16 \times 0\cdot10 \times 0\cdot12$ mm. Cell parameters and intensities were obtained on a four-circle automatic Syntex $P2_1$ diffractometer with the θ–2θ scan method and graphite-monochromatized Mo $K\alpha$ radiation. 2016 reflections were collected up to $2\theta = 42°$. The 2θ scan speed was varied between 3 and 30° min^{-1} and a 96-step profile was recorded for each reflection. The profile analysis was made according to the Lehmann & Larsen (1974) method with *LELA* (Lindqvist & Ljungström, 1979). The intensities were corrected for Lorentz and polarization effects, but not for absorption.

The crystal structure was solved with *MULTAN* 77 (Main, Lessinger, Woolfson, Germain & Declercq, 1977). The complete non-hydrogen skeleton was found and the refinement of these atoms with isotropic temperature factors by the least-squares block-diagonal approximation gave R ($= \sum ||F_o| - |F_c||/\sum |F_o|$) = $0\cdot11$. H atoms were located from a difference map. The final refinement ($R = 0\cdot046$) was based on 1520 observed reflections having $I > 3\sigma(I)$, and included isotropic and anisotropic thermal parameters for the H and non-hydrogen atoms, respectively. The weights were calculated as $w = 1/(A + F_o + CF_o^2)$ with $A = 35\cdot0$ and $C = 0\cdot0025$ giving a good weight analysis.
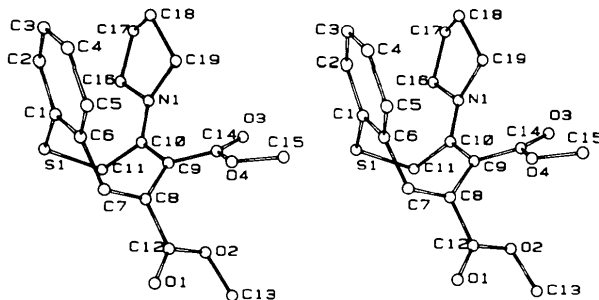

Fig. 1. Stereoscopic picture of the molecule (*ORTEP*; Johnson, 1965). The notation is in accordance with Tables 1–3.

Table 1. *Fractional atomic coordinates* (×10³ *for* H *and* ×10⁴ *for other atoms*)

The temperature factors are given as refined B_{iso} values for H atoms and as B_{eq} values for other atoms (e.s.d.'s $\simeq$ 0·15 Å²). The thermal isotropic equivalents of the anisotropic thermal parameters for non-hydrogen atoms are calculated according to Hamilton (1959) by $B_{eq} = \frac{4}{3}\Sigma_i \Sigma_j b_{ij}(\mathbf{a}_i \cdot \mathbf{a}_j)$.

	x	y	z	B (Å²)
S(1)	1704 (2)	8592 (3)	7910 (2)	4·7
O(1)	3967 (7)	4119 (7)	4362 (6)	6·3
O(2)	5330 (6)	2833 (6)	6168 (5)	4·7
O(3)	4034 (6)	2487 (6)	9157 (5)	5·3
O(4)	2729 (6)	2692 (6)	7175 (5)	3·1
N(1)	2701 (6)	5775 (6)	6 (5)	3·0
C(1)	148 (8)	8212 (8)	7649 (7)	3·9
C(2)	8868 (9)	8976 (10)	8398 (8)	5·2
C(3)	7593 (10)	8806 (11)	8197 (9)	6·3
C(4)	7574 (11)	7850 (11)	7220 (9)	5·3
C(5)	8868 (9)	7032 (10)	6478 (8)	4·0
C(6)	168 (9)	7198 (9)	6674 (8)	3·9
C(7)	1563 (9)	6202 (9)	5917 (8)	3·5
C(8)	2856 (8)	5003 (8)	6428 (7)	2·6
C(9)	3111 (8)	4622 (8)	7846 (7)	3·1
C(10)	3082 (8)	5662 (8)	8764 (7)	2·9
C(11)	3471 (8)	6764 (9)	8325 (8)	2·8
C(12)	4090 (9)	3966 (9)	5553 (8)	3·1
C(13)	6517 (10)	1684 (10)	5367 (9)	6·2
C(14)	3328 (8)	3212 (9)	8172 (7)	3·9
C(15)	3052 (11)	1196 (11)	7313 (10)	5·6
C(16)	2641 (9)	6922 (9)	950 (8)	2·9
C(17)	1775 (10)	6877 (10)	2045 (9)	5·0
C(18)	767 (10)	6281 (10)	1441 (9)	6·1
C(19)	1802 (9)	5155 (9)	428 (7)	4·2
H(2)	100 (9)	46 (10)	90 (8)	6·8 (2·4)
H(3)	322 (11)	77 (11)	125 (10)	8·9 (2·9)
H(4)	326 (9)	230 (9)	300 (8)	6·4 (2·3)
H(5)	105 (7)	378 (8)	427 (7)	3·6 (1·7)
H(7)	845 (10)	349 (10)	489 (9)	7·5 (2·5)
H'(11)	592 (7)	305 (7)	91 (6)	3·3 (1·6)
H''(11)	596 (8)	352 (9)	246 (7)	5·4 (2·0)
H'(13)	725 (8)	95 (8)	594 (7)	4·6 (1·9)
H''(13)	682 (8)	221 (8)	491 (7)	4·6 (1·9)
H'''(13)	583 (9)	151 (10)	461 (8)	7·4 (2·4)
H'(15)	309 (6)	102 (6)	813 (5)	1·1 (1·2)
H''(15)	411 (10)	65 (10)	709 (8)	7·4 (2·5)
H'''(15)	248 (7)	129 (7)	652 (6)	3·7 (1·7)
H'(16)	365 (8)	672 (8)	118 (7)	5·1 (1·9)
H''(16)	202 (6)	788 (7)	56 (6)	2·2 (1·4)
H'(17)	267 (8)	603 (8)	266 (7)	4·6 (1·9)
H''(17)	902 (11)	205 (11)	770 (10)	9·3 (3·0)
H'(18)	−29 (7)	711 (7)	102 (6)	3·5 (1·6)
H''(18)	905 (8)	440 (8)	797 (7)	5·2 (1·9)
H'(19)	253 (6)	421 (6)	84 (6)	2·0 (1·3)
H''(19)	898 (7)	472 (7)	32 (6)	2·8 (1·5)

Scattering factors were obtained from *International Tables for X-ray Crystallography* (1974).

Discussion. Atomic coordinates are given in Table 1,* bond lengths and angles in Tables 2 and 3. All bond

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* Lists of structure factors and anisotropic thermal parameters have been deposited with the British Library Lending Division as Supplementary Publication No. SUP 35735 (18 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

Table 2. *Bond distances* (Å) *with e.s.d.'s in parentheses*

C(1)–C(2)	1·382 (11)	C(17)–C(18)	1·503 (12)
C(2)–C(3)	1·360 (12)	C(18)–C(19)	1·530 (12)
C(3)–C(4)	1·383 (14)	C(19)–N(1)	1·459 (9)
C(4)–C(5)	1·392 (12)	C(2)–H(2)	0·95 (9)
C(5)–C(6)	1·382 (11)	C(3)–H(3)	0·93 (10)
C(6)–C(1)	1·411 (11)	C(4)–H(4)	0·92 (8)
C(6)–C(7)	1·491 (11)	C(5)–H(5)	1·09 (7)
C(7)–C(8)	1·323 (11)	C(7)–H(7)	0·90 (9)
C(8)–C(9)	1·489 (10)	C(13)–H'(13)	0·92 (7)
C(9)–C(10)	1·390 (10)	C(13)–H''(13)	0·92 (7)
C(10)–C(11)	1·503 (11)	C(13)–H'''(13)	1·05 (8)
C(11)–S(1)	1·833 (8)	C(15)–H'(15)	0·86 (5)
C(1)–S(1)	1·779 (7)	C(15)–H''(15)	0·94 (8)
C(8)–C(12)	1·486 (10)	C(15)–H'''(15)	0·91 (7)
C(12)–O(1)	1·225 (10)	C(11)–H'(11)	1·01 (6)
C(12)–O(2)	1·312 (9)	C(11)–H''(11)	0·97 (7)
O(2)–C(13)	1·455 (10)	C(16)–H'(16)	0·91 (7)
C(9)–C(14)	1·437 (11)	C(16)–H''(16)	0·95 (6)
C(14)–O(3)	1·213 (9)	C(17)–H'(17)	1·05 (7)
C(14)–O(4)	1·358 (9)	C(17)–H''(17)	1·02 (10)
O(4)–C(15)	1·445 (12)	C(18)–H'(18)	1·02 (6)
C(10)–N(1)	1·345 (9)	C(18)–H''(18)	0·90 (8)
N(1)–C(16)	1·481 (10)	C(19)–H'(19)	0·95 (6)
C(16)–C(17)	1·499 (12)	C(19)–H''(19)	0·99 (6)

Table 3. *Bond angles* (°) *with e.s.d.'s in parentheses*

C(1)–C(2)–C(3)	121·5 (8)	C(5)–C(4)–H(4)	115 (5)
C(2)–C(3)–C(4)	119·3 (8)	C(4)–C(5)–H(5)	124 (3)
C(3)–C(4)–C(5)	120·3 (8)	C(6)–C(5)–H(5)	115 (3)
C(4)–C(5)–C(6)	120·8 (8)	C(6)–C(7)–H(7)	117 (6)
C(5)–C(6)–C(1)	118·2 (7)	C(8)–C(7)–H(7)	120 (5)
C(6)–C(1)–C(2)	119·9 (7)	S(1)–C(11)–H'(11)	106 (4)
C(1)–C(6)–C(7)	123·8 (7)	S(1)–C(11)–H''(11)	104 (5)
C(6)–C(7)–C(8)	123·0 (7)	C(10)–C(11)–H'(11)	108 (4)
C(7)–C(8)–C(9)	122·7 (7)	C(10)–C(11)–H''(11)	115 (5)
C(8)–C(9)–C(10)	118·3 (6)	H'(11)–C(11)–H''(11)	111 (5)
C(9)–C(10)–C(11)	117·5 (6)	O(2)–C(13)–H'(13)	106 (4)
C(10)–C(11)–S(1)	113·1 (5)	O(2)–C(13)–H''(13)	103 (5)
C(11)–S(1)–C(1)	103·6 (4)	O(2)–C(13)–H'''(13)	103 (5)
S(1)–C(1)–C(6)	121·7 (6)	H'(13)–C(13)–H''(13)	120 (6)
S(1)–C(1)–C(2)	118·4 (6)	H'(13)–C(13)–H'''(13)	100 (6)
C(5)–C(6)–C(7)	117·8 (7)	H''(13)–C(13)–H'''(13)	123 (7)
C(7)–C(8)–C(12)	119·1 (7)	O(4)–C(15)–H'(15)	109 (4)
C(9)–C(8)–C(12)	118·3 (6)	O(4)–C(15)–H''(15)	99 (5)
C(8)–C(12)–O(2)	113·8 (6)	O(4)–C(15)–H'''(15)	89 (4)
C(8)–C(12)–O(1)	124·0 (7)	H'(15)–C(15)–H''(15)	106 (6)
O(1)–C(12)–O(2)	122·2 (7)	H''(15)–C(15)–H'''(15)	103 (6)
C(12)–O(2)–C(13)	117·3 (6)	H'(15)–C(15)–H'''(15)	142 (5)
C(8)–C(9)–C(14)	117·3 (6)	N(1)–C(16)–H'(16)	109 (5)
C(10)–C(9)–C(14)	124·4 (7)	N(1)–C(16)–H''(16)	110 (4)
C(9)–C(14)–O(3)	126·8 (7)	C(17)–C(16)–H'(16)	116 (5)
C(9)–C(14)–O(4)	111·3 (6)	C(17)–C(16)–H''(16)	108 (3)
O(3)–C(14)–O(4)	121·8 (7)	H'(16)–C(16)–H''(16)	110 (6)
C(14)–O(4)–C(15)	116·6 (6)	C(16)–C(17)–H'(17)	104 (4)
C(9)–C(10)–N(1)	125·0 (7)	C(16)–C(17)–H''(17)	108 (6)
C(11)–C(10)–N(1)	117·6 (6)	C(18)–C(17)–H'(17)	106 (4)
C(10)–N(1)–C(16)	123·6 (6)	C(18)–C(17)–H''(17)	105 (5)
C(10)–N(1)–C(19)	122·8 (6)	H'(17)–C(17)–H''(17)	127 (7)
C(16)–N(1)–C(19)	110·6 (6)	C(17)–C(18)–H'(18)	112 (4)
N(1)–C(16)–C(17)	104·5 (6)	C(17)–C(18)–H''(18)	102 (5)
C(16)–C(17)–C(18)	105·5 (7)	C(19)–C(18)–H'(18)	112 (4)
C(17)–C(18)–C(19)	103·0 (7)	C(19)–C(18)–H''(18)	96 (5)
C(18)–C(19)–N(1)	104·0 (6)	H'(18)–C(18)–H''(18)	128 (6)
C(1)–C(2)–H(2)	115 (5)	C(18)–C(19)–H'(19)	110 (3)
C(3)–C(2)–H(2)	123 (5)	C(18)–C(19)–H''(19)	103 (3)
C(2)–C(3)–H(3)	122 (6)	N(1)–C(19)–H'(19)	109 (3)
C(4)–C(3)–H(3)	118 (6)	N(1)–C(19)–H''(19)	106 (4)
C(3)–C(4)–H(4)	125 (5)	H'(19)–C(19)–H''(19)	123 (5)

distances and angles have normal values. The thiocin ring has a boat conformation (Fig. 1). The length of the $C(sp^3)$—S bond, 1·833 (8) Å, is in agreement with corresponding values [1·836 (10), 1·819 (14), 1·803 (10) and 1·785 (10) Å] reported for N-methyl-1,4-dithiane-2,3-dicarboximide (Dobrowolska & Bukowska-Strzyżewska, 1980). The $C(sp^2)$—S bond, 1·779 (7) Å, is a typical single bond [$C(sp^2)$—S = 1·77 Å (Argay, Kálmán, Nahlovski & Ribár, 1975)]. The angle $C(sp^2)$—S—$C(sp^3)$, 103·6 (4)°, agrees well with the corresponding value of 103·0 (6)° reported by Argay, Kálmán, Kapor & Ribár (1980).

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X-ray Structure and Absolute Configuration of (−)-(2S,4R)-4-Methylcyclophosphamide {2-[Bis(2-chloroethyl)amino]-4-methyltetrahydro-2H-1,3,2-oxazaphosphorine 2-Oxide}

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Abstract. $C_8H_{17}Cl_2N_2O_2P$, $M_r = 275·2$, orthorhombic, $P2_12_12_1$, $a = 8·084$ (3), $b = 9·021$ (3), $c = 18·024$ (6) Å, $V = 1314·4$ Å^3, $Z = 4$, $d_o = 1·40$, $d_c = 1·390$ Mg m^{-3}, $[a]_D^{25°C} = -8·3$ (concentration = 3·0 g dm^{-3}, methanol), m.p. = 329–330 K. The structure has been solved by direct methods and refined by full-matrix least squares to $R = 0·068$ for 899 of the 1123 reflections collected. The 1,3,2-oxazaphosphorinane ring is in a conformation intermediate between sofa and half-chair with the P end flattened and with the 4-methyl and N,N-bis(2-chloroethyl) groups in equatorial positions. The molecules form chains along the [100] direction by means of $\geq$P=O$\cdots$HN hydrogen bonds with an O$\cdots$N distance of 2·860 (6) Å.

Introduction. Cyclophosphamide (CPA) is a widely used antitumour drug. The compound has virtually no cytotoxic activity against mammalian cell cultures (Arnold, Bourseaux & Brock, 1958) and only the products of its oxidation at C(4) are presumed to be responsible for the activation of CPA (Hill, Laster & Struck, 1972). 4-Methylcyclophosphamide is of interest since the methyl group prevents further oxidation, so the substitution must affect the biological activity. Besides, since biological systems normally exhibit a marked enantiomeric selectivity, it was expected, and found, that the optical isomers of CPA (Cox, Farmer, Jarman, Jones, Stec & Kinas, 1976) and 4-methyl-CPA (Kinas, Pankiewicz, Stec, Farmer, Foster & Jarman, 1977) have different therapeutic effects.

Up to the present time the crystal structures of racemic CPA monohydrate (Garcia-Blanco & Perales, 1972; Clardy, Mosbo & Verkade, 1974), 4-hydroperoxy-CPA (Camerman, Smith & Camerman, 1977), 4-peroxy-CPA (Sternglanz, Einspahr & Bugg, 1974), 4-keto-CPA (Camerman & Camerman, 1973) and enantiomeric CPA (Karle, Karle, Egan, Zon & Brandt, 1977; Adamiak, Saenger, Kinas & Stec, 1977) have been determined. Preliminary communications concerning the crystal data for two (Gałdecki & Główka, 1979) and configurations proposed on the basis of chemical data for all four enantiomeric 4-methyl-cyclophosphamides (Kinas et al., 1977) have been published. This study was undertaken to widen the experimental basis for discussing the relationship between structure (especially configuration) and biological activity of enantiomeric 4-methyl-CPA.