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(2*R*,5*S*,11*S*,12*S*)-Cyclol of α-Mercaptopropionyl-(*S*)-Phe-(*S*)-Pro-lactam,* $C_{17}H_{20}N_2O_3S$

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Abstract. $M_r = 332{\cdot}42$, monoclinic, $P2_1$, $a = 9{\cdot}331$ (2), $b = 10{\cdot}597$ (3), $c = 8{\cdot}922$ (5) Å, $\beta = 108{\cdot}99$ (3)°, $V = 834{\cdot}2$ (6) Å^3, $Z = 2$, $D_x = 1{\cdot}323$ g cm^{-3}, λ(Mo $K\alpha$) $= 0{\cdot}71069$ Å, $\mu = 1{\cdot}67$ cm^{-1}, $F(000) = 354$, $T = 295$ K, $R = 0{\cdot}068$ for 1290 observed reflexions. The title compound is the 1-thio analogue of the peptide part of ergotamine. The thiazolidine ring has an envelope conformation while the pyrrolidine and piperazine rings adopt half-chair and boat conformations respectively. There is a possible intermolecular hydrogen bond of 2·63 (1) Å between the hydroxy group and the piperazine-ring keto group.

Introduction. The title compound was synthesized (Rothe, Schoen & Debaerdemaeker, 1985) as part of our work on mercaptoacyl incorporation (Rothe & Steinberger, 1968, 1970*a*,*b*). It is the 1-thio analogue of the peptide part of ergotamine having the same configuration as the peptide part of the alkaloid at all chiral centres.

The synthesis was performed from an S-protected α-mercaptopropionyl-(*S*)-phenylalanyl-(*S*)-prolyl-lactam, using racemic thiolactic acid. As expected, both the diastereomeric thiacyclols *A* (2*R*,5*S*,11*S*,12*S*) and *B* (2*S*,5*S*,11*S*,12*S*), respectively, could be obtained in optically pure form. A crystal-structure determination of cyclol *A*, melting point 462 K, $[\alpha]_D^{20{\cdot}0\,°\mathrm{C}} = +44{\cdot}8°$[MeOH, 0·5 g dm^{-3}], afforded the assignment of the configuration at C(2). So far, only the structures of a racemic (Lucente, Pinnen, Zanotti, Cerrini, Fedeli & Mazza, 1980) and the all-*S* cyclol (Zanotti, Pinnen, Lucente, Cerrini, Fedeli & Mazza, 1983) have been reported.

Experimental. Crystals of title compound crystallize as colourless needles with well shaped faces (~0·2 × 0·2 × 0·6 mm). D_m measured by flotation. 1393 unique reflexions with $\theta \leq 24°$, Philips PW-1100 four-circle diffractometer, Mo $K\alpha$ radiation, graphite monochromator, θ–2θ scan, 1290 observed reflexions [$F > 1{\cdot}5\sigma(F)$, $-10 \leq h \leq 10$, $0 \leq k \leq 12$, $0 \leq l \leq 10$]. Intensity of three standard reflexions did not vary during period of measurement. Cell parameters obtained from refinement of 25 reflexions ($9{\cdot}0 \leq \theta \leq 18°$). No absorption correction ($\mu = 1{\cdot}67$ cm^{-1}). Structure solved by direct methods using random-phase approach of Debaerdemaeker & Woolfson (1983). Structure refined by full-matrix least squares on F, first with isotropic then with anisotropic temperature parameters, using unit weights (Sheldrick, 1977), until parameter shifts less than corresponding standard deviation. A difference map showed only a part of the H atoms and they were therefore ignored. Final $R = 0{\cdot}068$ for all 1290 observed reflexions. $\Delta/\sigma < 0{\cdot}01$. Max. peak in final difference Fourier map 0·42 e Å^{-3}. Scattering factors those of Cromer & Mann (1968) and Doyle & Turner (1968), corrections for anomalous dispersion from Cromer & Liberman (1970).

Discussion. Final atomic coordinates and equivalent isotropic thermal parameters are given in Table 1,† main interatomic distances and angles in Table 2.

Fig. 1 shows the conformation of a single molecule with the atomic numbering, Fig. 2 shows a stereoscopic drawing of the contents of a unit cell. As one can see from Fig. 1, the structure has indeed the 2*R* configuration of the oxygen analogue (Ott, Frey & Hofmann, 1963). The retention of both configurations at C(5) and C(11) with thiacyclols and mercaptoacyldiketopiperazines of this type was proven by chemical degradation to the original (*S*)-Pro-(*S*)-Phe-lactam (Rothe *et al.*, 1985).

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* Systematic name: (1*S*,2*S*,8*S*,11*R*)-8-benzyl-1-hydroxy-11-methyl-12-thia-6,9-diazatricyclo[7.3.0.0^{2,6}]dodecane-7,10-dione.

† Lists of structure factors, anisotropic thermal parameters and a complete list of interatomic distances and angles have been deposited with the British Library Lending Division as Supplementary Publication No. SUP 39827 (10 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

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Table 1. *Atomic coordinates* ($\times 10^4$) *and equivalent isotropic thermal parameters* ($Å^2 \times 10^3$) *with e.s.d.'s in parentheses*

	x	*y*	*z*	$\langle U\rangle$*
S(1)	5222 (3)	5728	5932 (3)	67 (2)
C(2)	6727 (10)	4737 (10)	5697 (10)	56 (8)
C(3)	6929 (9)	3634 (10)	6877 (9)	46 (4)
O(3)	7864 (7)	2818 (8)	7031 (8)	67 (4)
N(4)	5922 (7)	3684 (8)	7690 (7)	43 (4)
C(5)	5802 (9)	2623 (9)	8717 (9)	42 (4)
C(6)	4131 (10)	2252 (10)	8443 (10)	47 (5)
O(6)	3840 (7)	1495 (8)	9326 (8)	65 (4)
N(7)	3072 (8)	2729 (9)	7175 (8)	54 (4)
C(8)	1431 (10)	2412 (15)	6897 (11)	82 (4)
C(9)	639 (10)	3363 (16)	5488 (12)	89 (8)
C(10)	1719 (11)	4494 (13)	5707 (12)	73 (7)
C(11)	3274 (10)	3786 (9)	6172 (10)	47 (5)
C(12)	4638 (10)	4564 (9)	7131 (10)	49 (5)
O(12)	4309 (7)	5111 (7)	8414 (8)	62 (5)
C(20)	6353 (12)	4186 (12)	3986 (11)	68 (8)
C(50)	6583 (9)	2975 (10)	10502 (9)	48 (5)
C(51)	8295 (9)	3078 (10)	10860 (9)	45 (4)
C(52)	9182 (12)	1993 (10)	10994 (11)	60 (6)
C(53)	10762 (14)	2093 (15)	11293 (13)	80 (8)
C(54)	11445 (11)	3291 (17)	11503 (12)	80 (8)
C(55)	10573 (13)	4376 (13)	11403 (12)	72 (7)
C(56)	8978 (10)	4261 (10)	11091 (10)	54 (8)

* $\langle U\rangle = \frac{1}{3}\sum_i\sum_j U_{ij}a_i^*a_j^*\mathbf{a}_i.\mathbf{a}_j$.

Table 2. *Main interatomic distances* (Å) *and angles* (°) *with e.s.d.'s in parentheses*

S(1)–C(2)	1·82 (1)	N(4)–C(12)	1·47 (1)
S(1)–C(12)	1·83 (1)	C(6)–O(6)	1·22 (1)
C(3)–N(4)	1·36 (1)	C(6)–N(7)	1·34 (1)
C(3)–O(3)	1·20 (1)	N(7)–C(8)	1·51 (1)
N(4)–C(5)	1·48 (1)	N(7)–C(11)	1·48 (1)

C(2)–S(1)–C(12)	93·8 (4)	O(6)–C(6)–N(7)	122·6 (8)
S(1)–C(2)–C(3)	106·6 (6)	C(6)–N(7)–C(8)	119·1 (8)
S(1)–C(2)–C(20)	113·1 (7)	C(6)–N(7)–C(11)	126·3 (8)
C(2)–C(3)–O(3)	123·0 (7)	C(8)–N(7)–C(11)	113·0 (8)
C(2)–C(3)–N(4)	112·4 (8)	N(7)–C(8)–C(9)	100·1 (8)
O(3)–C(3)–N(4)	124·5 (8)	N(7)–C(11)–C(10)	103·5 (7)
C(3)–N(4)–C(5)	120·4 (7)	N(7)–C(11)–C(12)	108·5 (7)
C(3)–N(4)–C(12)	118·1 (7)	S(1)–C(12)–N(4)	105·1 (6)
C(5)–N(4)–C(12)	118·4 (6)	S(1)–C(12)–C(11)	112·9 (6)
N(4)–C(5)–C(6)	111·8 (6)	S(1)–C(12)–O(12)	112·7 (7)
N(4)–C(5)–C(50)	110·2 (7)	N(4)–C(12)–C(11)	106·6 (7)
C(5)–C(6)–O(6)	119·4 (8)	N(4)–C(12)–O(12)	110·8 (6)
C(5)–C(6)–N(7)	117·8 (8)		

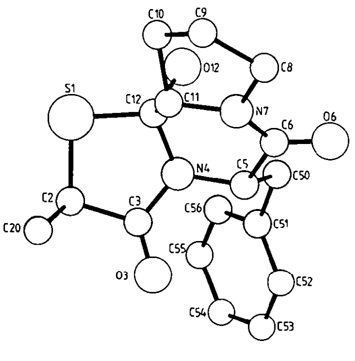

Fig. 1. Projection of the title compound on the S(1)–C(3)–N(4) plane.

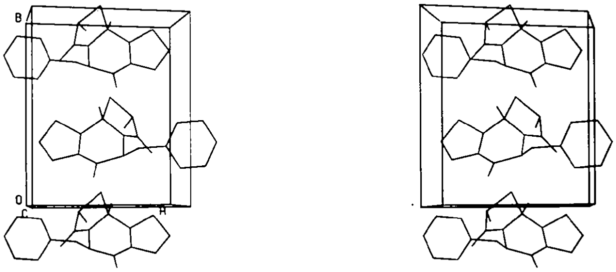

Fig. 2. Stereoscopic view of the packing of the molecules in a unit cell (along the *c* axis).

In the S(1)–C(2)–C(3)–N(4)–C(12) thiazolidinone ring the C(12) atom is out of the plane [−0·33 (2) Å]. The N(7)–C(8)–C(9)–C(10)–C(11) pyrrolidine ring has a half-chair conformation with C(10) and C(9) out of the plane [−0·56 (1), 0·10 (1) Å]. The two conformations agree with the observations of Lucente *et al.* (1980).

The six-membered N(4)–C(5)–C(6)–N(7)–C(11)–C(12) piperazine ring has the boat conformation with C(12) strongly [0·69 (1) Å] and C(6) slightly [0·15 (2) Å] out of the plane.

The molecules in the unit cell are separated by the only short distance of 2·63 (1) Å between O(12) and O(6), which would correspond to the distance of an expected hydrogen bond O(12)–H···O(6).

The interatomic distances and angles agree, within experimental error, with those found in similar compounds.

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