final cycle of refinement included 235 variable parameters and converged with $R = 0{\cdot}058$. $wR = 0{\cdot}069$; $S = 1{\cdot}07$; the highest peak in the final ΔF map had a height of 0·21 (6) e Å^{-3}, $(\Delta/\sigma)_{\max} = 0{\cdot}282$. All calculations were performed on a PDP-11 minicomputer using *SDP* (Frenz, 1978) and local programs.

Discussion. The final atomic positions and equivalent isotropic temperature factors for non-H atoms are given with their e.s.d.'s in Table 1.* Bond lengths, bond angles and relevant torsion angles are listed in Table 2. A perspective view of the molecule with the atom-labelling system is shown in Fig. 1. Distances and angles in the five-membered triazole ring are in excellent agreement with those reported earlier (Ribár, Stanković, Argay, Kálmán & Koczó, 1987), except the N(3)—N(1) distance which is significantly shorter. The triazole ring is fairly planar. The dihedral angles formed by the least-squares planes of the triazole and the two benzene rings are 84·4 (2) for C(4)—C(9) and 86·7 (2)° for C(10)—C(15). Between the best planes of two benzene rings the dihedral angle is 9·0 (2)°. Torsion angles indicate that C(7), N(6), O(1), O(2) and C(13), N(7), C(16), C(17) lie in the planes of the corresponding benzene rings.

The symmetry-related molecules are linked together by a pair of N···N hydrogen bonds with N(5)···N(2)′ = 3·028 (6), H(N5)···N(2)′ = 2·080 (6) Å and N(5)—H(N5)···N(2)′ = 149·0 (4)°, forming dimers (Fig. 1). Fig. 2 shows the molecular packing in a stereoview down *a* axis.

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* Lists of structure factors, anisotropic thermal parameters and H-atom parameters have been deposited with the British Library Document Supply Centre as Supplementary Publication No. SUP 53483 (13 pp.). Copies may be obtained through The Technical Editor, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

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4,5-Dimethoxy-2-[3-(1,4-oxazinan-4-yl)-3-oxopropyl]-*N*-(2-pyridyl)-benzenesulfonamide Methanol Solvate

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Abstract. $C_{20}H_{25}N_3O_6S.CH_4O$, $M_r = 467{\cdot}54$, triclinic, $P\bar{1}$, $a = 8{\cdot}429\,(6)$, $b = 11{\cdot}271\,(3)$, $c = 12{\cdot}606\,(3)$ Å, $\alpha = 76{\cdot}302\,(8)$, $\beta = 78{\cdot}320\,(4)$, $\gamma = 78{\cdot}227\,(8)°$, $V = 1124{\cdot}02\,(90)$ Å^3, $Z = 2$, $D_m = 1{\cdot}34$, $D_x = 1{\cdot}38$ Mg m^{-3}, $\lambda(\text{Cu } K\alpha) = 1{\cdot}5418$ Å, $\mu = 1{\cdot}54$ mm^{-1}, $F(000) = 496$, $T = 293$ K, final $R = 0{\cdot}051$ for 2940 observed reflections. There are two molecules of methanol per unit cell, each with two alternative orientations. C(*A*1) is common to both orientations whereas the methanol O atom occupies sites O(*A*1) and O(*A*2) with equal probability.

Introduction. Derivatives of benzothiazinone have anti-inflammatory activity (Lombardino & Wiseman, 1971) and are known to affect the central nervous system (Sianesi, Redaelli, Magistretti & Massarani, 1973). Sulfonamides, similar in structure to benzothiazinone, have been synthesized (Camoutsis & Catsoulakos, 1976, 1980; Catsoulakos & Camoutsis, 1980) and are being tested for pharmacological properties.

Crystallographic studies of a series of these compounds have been carried out (Hamodrakas &

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

$$U_{eq} = (1/3)\sum_i \sum_j U_{ij} a_i^* a_j^* \mathbf{a}_i . \mathbf{a}_j .$$

	x	y	z	U_{eq}
S(1)	3506 (1)	− 846 (1)	− 1581 (1)	449
O(1)	4472 (3)	− 2062 (2)	− 1342 (2)	520
O(2)	4163 (3)	163 (2)	− 1411 (2)	584
O(3)	124 (3)	3621 (2)	− 2111 (2)	764
O(4)	− 5588 (3)	4373 (3)	− 1801 (3)	877
O(5)	2713 (3)	− 338 (2)	− 6235 (2)	590
O(6)	4366 (3)	− 2333 (2)	− 5245 (2)	561
N(1)	1696 (3)	− 773 (3)	− 865 (2)	460
N(2)	− 836 (3)	− 1318 (2)	− 232 (2)	469
N(3)	− 2389 (3)	3097 (2)	− 1663 (2)	546
C(1)	3230 (3)	− 583 (3)	− 2985 (2)	422
C(2)	2391 (3)	518 (3)	− 3521 (2)	437
C(3)	2200 (4)	595 (3)	4617 (3)	466
C(4)	2848 (4)	− 357 (3)	− 5171 (3)	466
C(5)	3726 (4)	− 1449 (3)	− 4630 (2)	437
C(6)	3904 (4)	− 1553 (3)	− 3550 (2)	426
C(7)	703 (4)	- 1612 (3)	− 786 (2)	402
C(8)	1063 (4)	− 2709 (3)	− 1201 (3)	478
C(9)	− 100 (5)	− 3434 (3)	− 1037 (3)	605
C(10)	− 1675 (5)	− 3107 (3)	− 471 (3)	702
C(11)	− 1984 (5)	− 2053 (4)	− 86 (3)	640
C(12)	1676 (4)	1638 (3)	− 3004 (3)	495
C(13)	− 162 (4)	1789 (3)	− 2646 (3)	520
C(14)	− 797 (4)	2919 (3)	− 2136 (3)	488
C(15)	− 3661 (5)	2448 (4)	− 1766 (4)	662
C(16)	− 4942 (6)	3356 (4)	− 2335 (4)	806
C(17)	− 4325 (6)	4990 (4)	− 1735 (4)	704
C(18)	− 3065 (5)	4152 (3)	− 1131 (3)	599
C(19)	1937 (6)	781 (4)	− 6851 (3)	680
C(20)	5351 (6)	− 3415 (3)	− 4720 (3)	650
C(*A*1)	− 868 (10)	3829 (8)	4131 (8)	1542
O(*A*1)*	− 1781 (11)	4775 (8)	3692 (10)	1569
O(*A*2)*	604 (11)	3907 (8)	3694 (10)	1633

* Site occupancy 0·5.

Table 2. *Bond lengths* (Å) *and angles* (°) *with e.s.d.'s in parentheses*

S(1)—O(1)	1·443 (3)	C(1)—C(2)	1·391 (6)
S(1)—O(2)	1·438 (3)	C(1)—C(6)	1·406 (5)
S(1)—C(1)	1·779 (4)	C(2)—C(3)	1·403 (6)
S(1)—N(1)	1·605 (3)	C(2)—C(12)	1·517 (6)
		C(3)—C(4)	1·378 (6)
N(1)—C(7)	1·360 (5)	C(4)—C(5)	1·402 (6)
N(2)—C(7)	1·360 (5)	C(5)—C(6)	1·375 (6)
N(2)—C(11)	1·357 (6)	C(7)—C(8)	1·409 (6)
N(3)—C(14)	1·349 (5)	C(8)—C(9)	1·355 (6)
N(3)—C(15)	1·458 (6)	C(9)—C(10)	1·397 (7)
N(3)—C(18)	1·461 (5)	C(10)—C(11)	1·345 (7)
		C(12)—C(13)	1·510 (7)
O(3)—C(14)	1·225 (5)	C(13)—C(14)	1·514 (6)
O(4)—C(16)	1·423 (7)	C(15)—C(16)	1·497 (8)
O(4)—C(17)	1·410 (7)	C(17)—C(18)	1·476 (8)
O(5)—C(19)	1·424 (6)		
O(5)—C(4)	1·364 (5)	O(*A*1)—C(*A*1)	1·262 (14)
O(6)—C(5)	1·364 (5)	O(*A*2)—C(*A*1)	1·263 (14)
O(6)—C(20)	1·428 (6)		
O(2)—S(1)—O(1)	116·6 (2)	O(5)—C(4)—C(3)	125·2 (4)
C(1)—S(1)—O(1)	106·4 (2)	O(5)—C(4)—C(5)	115·3 (4)
C(1)—S(1)—O(2)	109·7 (2)	C(6)—C(5)—C(4)	119·1 (4)
N(1)—S(1)—O(1)	112·2 (2)	O(6)—C(5)—C(4)	115·9 (4)
N(1)—S(1)—O(2)	105·6 (2)	O(6)—C(5)—C(6)	125·0 (4)
N(1)—S(1)—C(1)	105·9 (2)	C(5)—C(6)—C(1)	121·2 (4)
		C(8)—C(7)—N(1)	128·8 (4)
C(7)—N(1)—S(1)	122·9 (3)	N(2)—C(7)—N(1)	113·7 (3)
C(11)—N(2)—C(7)	121·2 (4)	N(2)—C(7)—C(8)	117·6 (4)
C(15)—N(3)—C(14)	126·4 (4)	C(9)—C(8)—C(7)	120·2 (4)
C(18)—N(3)—C(14)	120·6 (4)	C(10)—C(9)—C(8)	121·1 (4)
C(18)—N(3)—C(15)	112·2 (4)	C(11)—C(10)—C(9)	117·4 (5)
		N(2)—C(11)—C(10)	122·6 (5)
C(16)—O(4)—C(17)	110·9 (5)	C(13)—C(12)—C(2)	113·8 (4)
C(19)—O(5)—C(4)	117·7 (4)	C(14)—C(13)—C(12)	111·2 (4)
C(20)—O(6)—C(5)	116·1 (3)	O(3)—C(14)—C(13)	121·0 (4)
		N(3)—C(14)—C(13)	117·9 (4)
C(2)—C(1)—S(1)	122·9 (3)	N(3)—C(14)—O(3)	121·0 (4)
C(6)—C(1)—S(1)	116·8 (3)	C(16)—C(15)—N(3)	109·1 (5)
C(6)—C(1)—C(2)	120·2 (4)	O(4)—C(16)—C(15)	112·4 (5)
C(3)—C(2)—C(1)	117·5 (4)	C(18)—C(17)—O(4)	111·7 (5)
C(12)—C(2)—C(1)	124·5 (4)	C(17)—C(18)—N(3)	109·7 (4)
C(12)—C(2)—C(3)	118·0 (4)		
C(4)—C(3)—C(2)	122·4 (4)		
C(5)—C(4)—C(3)	119·5 (4)		

Filippakis, 1977; Hamodrakas, Filippakis & Sheldrick, 1977; Hamodrakas, Akrigg, Sheldrick & Camoutsis, 1978; Perdikatsis, Catsoulakos & Filippakis, 1979; Panagiotopoulos, Filippakis & Catsoulakos, 1980; Panagiotopoulos & Filippakis, 1980; Eliopoulos, Sheldrick & Hamodrakas, 1983*a*,*b*) in attempts to relate structure and activity. The title compound is a member of this series.

Experimental. Crystal 0·08 × 0·09 × 0·6 mm. Enraf–Nonius CAD-4 diffractometer, Ni-filtered Cu $K\alpha$, moving-crystal/moving-counter technique, $2 < 2\theta < 140°$. 64 reflections, with $8 < \theta < 62°$, used to measure lattice parameters. Index range − 10–10 (h), − 12–12 (k), − 14–14 (l), $\bar{2}\bar{2}1$ used as intensity standard, average count 5404 with $\sigma = 161$ (3·0%). 7737 reflections measured (all available), merging ($R_{\rm int}$ = 0·06) gave 3241 unique reflections with $F > 3\sigma(F)$; the analysis is based on 2940 reflections with $I > 3{\cdot}0\sigma(I)$. No absorption corrections applied. Structure solved in $P1$ by direct methods using *MULTAN* (Declercq, Germain, Main & Woolfson, 1973). All the H atoms except HN1 were located from difference Fourier maps. Refinement of 400 parameters by least squares on F, space group $P\bar{1}$; In final cycles anisotropic temperature factors for non-H atoms, overall scale factor refined anisotropically (Shakked & Rabinovich, 1977); solvent H-atom positions were not refined and $U_{\rm iso} = 0{\cdot}075$ Å^2 was assumed for these atoms, only $U_{\rm iso}$ of H(N1) was refined, other H atoms were refined isotropically; unit weights. Final R = 0·051. $(\Delta/\sigma)_{\rm max}$ = 0·06. $\Delta\rho$ = − 0·21–0·16 e Å^{-3}. Refinement calculations with *SHELX* (Sheldrick, 1976); atomic scattering factors as supplied by the program.

Discussion. Atomic parameters are given in Table 1,* bond distances and angles in Table 2. Fig. 1 is a view of the molecule showing the atom numbering and Fig. 2 shows the molecular packing.

The results of this study are in close agreement with those of related compounds (Hamodrakas *et al.*, 1978; Hamodrakas, Filippakis & Sheldrick, 1977; Hamodrakas & Filippakis, 1977; Eliopoulos *et al.*, 1983*a*,*b*). Thus, the peptide group, C(13), C(14),

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* Lists of structure factors, anisotropic thermal parameters, torsion angles and H-atom parameters have been deposited with the British Library Document Supply Centre as Supplementary Publication No. SUP 53558 (29 pp.). Copies may be obtained through The Technical Editor, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

O(3), N(3), C(15), C(18) is almost planar [maximum deviation from the plane 0·105 (3) Å] and the C(14)—N(3) bond [1·349 (5) Å] displays partial double-bond character.

In the propionyl(1,4-oxazine) side chain, the plane containing C(12), C(13), C(14) and O(3) [maximum deviation from least-squares plane 0·020 (3) Å], is arranged at an angle of 68·7 (1)° to the phenyl ring; torsion angles C(1)—C(2)—C(12)—C(13) = − 103·1 (4) and C(2)—C(12)—C(13)—C(14) = 179·9 (3)°, similar to those of related structures (Hamodrakas *et al.*, 1978; Eliopoulos *et al.*, 1983*a*,*b*). The oxazine ring is in the chair conformation. The methoxy groups O(5)—C(19) and O(6)—C(20) are almost coplanar with the phenyl ring [torsion angles 4·4 (5) and 2·9 (5)° respectively] with C(19) and C(20) being 0·07 (1) and 0·14 (1) Å from the plane of the ring. This planar arrangement has been observed in more than 70 structures while the O(5)—C(4) and O(6)—C(5) bond lengths, 1·364 (5) and 1·364 (5) Å respectively, indicate partial double-bond character and compare well with the average calculated value of 1·36 Å for similar bonds (Hamodrakas, 1974). The tendency of the methoxy groups to be coplanar with the phenyl ring has resulted in some close contacts between C(19) and C(3), and C(20) and C(6) and the H atoms attached to them, which have been relieved by an increase of the angles C(3)—C(4)—O(5) and C(6)—C(5)—O(6) from 120 to 125·2 (4) and 125·0 (4)° respectively.

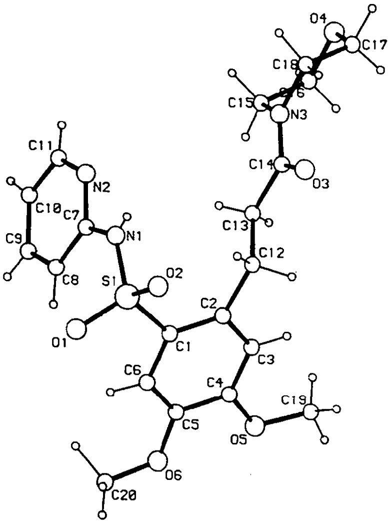

Fig. 1. *PLUTO78* (Motherwell & Clegg, 1978) drawing of the molecule showing numbering of the atoms.

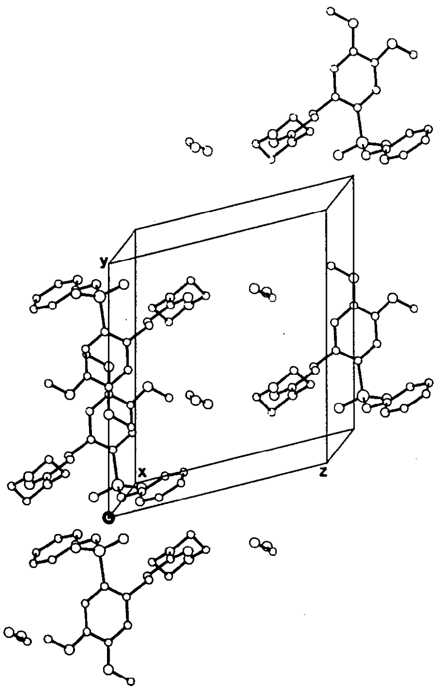

Fig. 2. *x*-axis projection packing diagram drawn by the program *PLUTO78*.

The tetrahedral coordination around the S atom is distorted, with the O(1)—S(1)—O(2) angle being 116·6 (2)°, larger then the normal tetrahedral value, possibly due to repulsions between the sulfonamide O atoms (Kálmán, Duffin & Kucsman, 1971). The S(1)—O(1) and S(1)—O(2) bond lengths of 1·443 (3) and 1·438 (3) Å indicate π-bond character of over 60% (Cruickshank, 1961), while the S(1)—C(1) and S(1)—N(1) bond lengths of 1·779 (4) and 1·605 (3) Å are very close to values obtained for similar structures (Hamodrakas *et al.*, 1978; Eliopoulos *et al.*, 1983*a*,*b*).

This sample was crystallized from methanol. In the unit cell there are two molecules of methanol present each with two alternative orientations. C(*A*1) is common to both orientations whereas the methanol oxygen occupies sites O(*A*1) and O(*A*2) with equal probability.

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Structure of a Potent Oxytocin-Receptor Ligand

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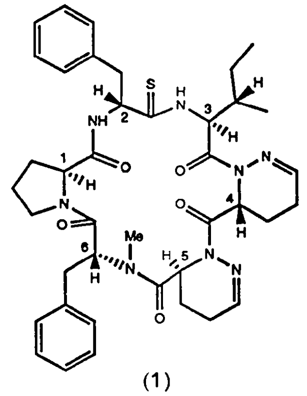
Abstract. *cyclo*[-Pro-D-Phe-ψ(CS—NH)-Ile-D-Thp-Thp-D-MePhe-] [where D-Thp is the residue formed from the cyclic imino acid (*R*)-2,3,4,5-tetrahydropyridazine-3-carboxylic acid], $C_{40}H_{50}N_8O_5S$, M_r = 754·96, monoclinic, $P2_1$, a = 10·413 (7), b = 17·225 (8), c = 11·200 (4) Å, β = 97·77 (4)°, V = 1990 Å^3, $Z = 2$, D_x = 1·260 Mg m^{-3}, λ(Cu $K\alpha$) = 1·54184 Å, μ = 1·12 mm^{-1}, $F(000) = 804$, T = 296 K, $R(F)$ = 0·067 for 2343 observed [$I \geq 3\sigma(I)$] reflections. A macrocycle containing six amino acids, all with peptide linkages, adopts a conformation in which the backbone is relatively flat except at Phe-ψ(CS) which is well out of the plane of the rest of the molecule. The presence of an S instead of an O atom in an amide unit may contribute to conformational changes as a result of the larger steric requirements of sulfur. Changing an amide to a thioamide does not result in changes to the bond distances or angles within an amino-acid residue.

Introduction. The compound *cyclo*[-Pro-D-Phe-ψ(CS—NH)-Ile-D-Thp-Thp-D-MePhe-]* (1) has been prepared (Bock, DiPardo, Williams, Pettibone, Clineschmidt, Ball, Veber & Freidinger, 1990) and found to be a highly potent and selective oxytocin-receptor ligand. The crystal structure analysis was undertaken to determine the conformation of the cyclic ring, the relative positioning of the ring substituents and what, if any, steric requirements can be ascribed to the presence of the isoteric group C═S in a modified phenylalanine.



(1)

Experimental. Crystals grown by slow evaporation of an ethanol solution. Crystal 0·15 × 0·07 × 0·24 mm. Enraf–Nonius CAD-4 diffractometer. Lattice parameters determined using 11 reflections with $18 < 2\theta < 34°$. Lorentz–polarization correction applied; absorption correction using empirical method (absorption surface) (Walker & Stuart, 1983). Maximum and minimum correction coefficients applied to F_o were 1·6394 and 0·6809. Intensity measurements in range $0 < 2\theta < 120°$ (index limits: h, 11; k, 19; l, ±

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* The nomenclature used is in accordance with IUPAC–IUB Joint Commission on Biochemical Nomenclature (1984).

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