

thiopeptide groups in two thiopeptide containing tripeptides (Jensen, Lawesson, Bardi, Piazzesi & Toniolo, 1985) shows a significantly longer C—S bond length, 1.663 Å, as compared with 1.635 Å in this study and a correspondingly shorter amide bond length. This indicates a redistribution of electrons in the peptide unit, probably caused by the delocalization of electrons on the S atom since this atom acts as acceptor in a weak hydrogen-bond system.

The influence of the hydrogen bonds on the packing of the molecules in the unit cell is shown in Fig. 2. Molecules *A* and *B* are alternately arranged to form ribbons extended along *a* and *b* axes; obviously the β -like sheets give the crystals a stability in these directions. Along the *c* axis, the ribbons are separated by regions that are very rich in phenyl groups. Together these features explain the macroscopic appearance of the crystals as thin plates, with the *c* axis perpendicular to the plates.

Both in the oxopeptide and the thiopeptide units, there are only minor deviations from the planar *trans* form ($\omega = 180^\circ$), the angles being $\omega_1 = -176$ (180°) and $\omega_2 = -172$ (172°). The S atom is not involved in any hydrogen bonding, the distance to the nearest non-covalently bonded atom, which is an H atom, is 3.01 Å, in agreement with the sum of the van der Waals radii of the atoms involved.

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Structure of the Dithiopeptide (Z)-Glyt-Glyt-Gly-OBzl

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Abstract. *N*-(Benzyloxycarbonyl)thioglycylthioglycylglycine benzyl ester, $C_{21}H_{23}N_3O_4S_2$, $M_r = 445.6$, triclinic, $P\bar{1}$, $a = 10.291$ (4), $b = 14.880$ (6), $c = 8.033$ (3) Å, $\alpha = 97.72$ (3), $\beta = 110.13$ (3), $\gamma = 73.46$ (3)°, $V = 1106.3$ (9) Å³, $Z = 2$, $D_m = 1.30$, $D_x = 1.34$ Mg m⁻³, $\lambda(\text{Cu } K\alpha) = 1.5418$ Å, $\mu = 2.41$ mm⁻¹, $F(000) = 468$, $T = 293$ K, $R = 0.044$ for 1479 unique reflections with $F_o > \sigma(F_o)$. The peptide molecules are in a bent form, owing to the unusual torsion angle $\psi_1 = -8^\circ$ at the first α -C atom and contain an extremely short thiopeptide bond, 1.301 Å. The packing of the molecules follows a well known scheme with ribbons of hydrogen bonds alternating

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with regions rich in phenyl groups. The S atoms are not involved in hydrogen bonding; the distance to the nearest amide H atom is more than 3.5 Å.

Introduction. The structural study of (Z)-Glyt-Glyt-Gly-OBzl is part of an investigation of the influence of thiopeptide units on the conformation and hydrogen-bonding pattern in a range of endothiopeptides synthesized and described by Clausen (1982). These types of compounds are of interest in the search for new drugs of potential use in neuropharmacology.

Experimental. The compound was synthesized as reported previously, m.p. 389–391 K (Clausen, 1982). Crystals shaped as parallelepipeds were obtained from an MeOH/H₂O vapour diffusion system. D_m measured

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by gradient method in chlorobenzene–bromobenzene solution. A crystal with the approximate dimensions $0.5 \times 0.5 \times 0.12$ mm was used for data collection. Hilger & Watts FC diffractometer with an Ni filter. Cell constants from a least-squares fit of 25 reflections in the 2θ range $13\text{--}48^\circ$. Intensity data collection using $\theta\text{--}2\theta$ scan; max. $2\theta = 80^\circ$, $h\text{--}8$ to 8 , $k\text{--}12$ to 12 and $l\text{--}6$ to 6 . Lp correction, but absorption and extinction ignored. Three standard reflections monitored every 50 reflections showed some random variation in intensity, max. 4%. 3274 reflections were collected and reduced to 1479 unique reflections with $F_o > \sigma(F_o)$ which were used in structure determination and refinement. $R_{\text{int}} = 0.013$. The structure was solved by direct methods, *MULTAN80* (Main, Fiske, Hull, Lessinger, Germain, Declercq & Woolfson, 1980) in space group *P1*. The best set of phases revealed 30 of 60 non-H atoms in this space group. The remainder of the non-H atoms were found by subsequent Fourier syntheses using *JIMDAP* (State Univ. of New York at Buffalo).

Refinement by full-matrix least squares on *F* using *LINUS* (Coppens & Hamilton, 1970), $w(F) = 1/\sigma^2(F_o)$. The calculated *E* statistics and the refinement suggested the choice of space group *P1*, which was consequently used in the refinement. Positions of all 23 H atoms found from difference Fourier map. Anisotropic temperature factors for non-H atoms and isotropic for H atoms. Temperature factors non-positive definite for two H atoms. Final $R = 0.044$, $wR = 0.047$. Max. and min. peak heights in final difference Fourier synthesis 0.21 and -0.19 e \AA^{-3} . Max. Δ/σ in final cycle 0.18 , $S = 1.20$. Atomic scattering factors: C, N and O from Cromer & Mann (1968), H from Stewart, Davidson & Simpson (1965) and S from *International Tables for X-ray Crystallography* (1968). Data reduction programs used: *DIFRED* and *RADCOR* (Thirup, 1984).*

Discussion. A listing of the final positional and thermal parameters is seen in Table 1, and the atomic numbering scheme, together with the principal torsion angles of the molecule, is shown in Fig. 1. Bond lengths and bond angles are given in Table 2. There are only few deviations from values normally found in peptides. Most marked is the thioamide bond distance C(10)–N(2) (1.30 \AA), which is 0.03 \AA shorter than the corresponding distance in the second thioamide bond and the value found in (*Z*)-Glyt-Gly-OBzl (Hansen, Clausen & la Cour, 1987). On the other hand, the distance C(10)–S(1) is slightly longer than C(12)–S(2), indicating a minor difference in the π -electron distribution, comparing the two thiopeptide units.

* 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 43432 (9 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

Another unusual feature is the torsion angle $\psi_1 = -8^\circ$ defined by N(1)–C(9)–C(10)–N(2), resulting in a correspondingly long C $^\alpha$ –C distance of 1.54 \AA between C(9) and C(10) owing to the prohibitive contact between N(1) and HN(2) [the nomenclature of the torsion angles is in accordance with the IUPAC–IUB Commission on Biochemical Nomenclature (1970)]. These anomalies also cause changes in the bond angles around C(10) compared to C(12). However, the planarity of the thiopeptide units is not affected, the largest deviation from the least-squares plane being 0.08 \AA found for HN(3).

Table 1. Atomic coordinates ($\times 10^4$) for non-H atoms and equivalent isotropic thermal parameters (\AA^2) with e.s.d.'s in parentheses

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

	x	y	z	B_{eq}
C(8)	−3572 (7)	4320 (6)	2263 (12)	2.750 (6)
O(2)	−3471 (5)	4903 (3)	3471 (7)	3.760 (3)
O(1)	−3983 (5)	3543 (4)	2153 (6)	3.430 (3)
C(7)	−4260 (10)	3354 (6)	3714 (11)	4.332 (7)
C(6)	−4599 (12)	2405 (6)	3295 (12)	2.974 (7)
C(5)	−3682 (10)	1598 (9)	4121 (12)	3.673 (7)
C(4)	−3979 (12)	748 (7)	3723 (14)	4.580 (8)
C(3)	−5244 (14)	669 (8)	2402 (15)	5.010 (8)
C(2)	−6186 (10)	1450 (10)	1547 (12)	4.732 (7)
C(1)	−5867 (11)	2294 (8)	1973 (13)	3.943 (8)
N(1)	−3194 (6)	4365 (5)	819 (11)	3.110 (5)
C(9)	−2758 (9)	5145 (6)	550 (13)	3.331 (7)
C(10)	−1187 (8)	5129 (5)	1580 (9)	2.418 (5)
S(1)	−630 (2)	6068 (1)	1575 (2)	3.558 (1)
N(2)	−430 (7)	4362 (5)	2411 (7)	2.386 (4)
C(11)	1061 (8)	4218 (5)	3470 (11)	2.946 (6)
C(12)	1617 (9)	3279 (4)	4324 (10)	2.467 (5)
S(2)	745 (2)	2453 (1)	3724 (2)	4.168 (1)
N(3)	2895 (7)	3180 (5)	5561 (9)	2.485 (5)
C(13)	3625 (9)	2327 (6)	6497 (12)	3.276 (6)
C(14)	5091 (8)	2395 (6)	7709 (9)	2.816 (6)
O(3)	5569 (5)	3064 (3)	7896 (6)	3.541 (3)
O(4)	5771 (5)	1591 (4)	8522 (7)	3.569 (4)
C(15)	7238 (9)	1518 (6)	9781 (11)	4.038 (6)
C(16)	8337 (7)	1244 (7)	8863 (8)	2.711 (5)
C(17)	9021 (10)	1881 (6)	8750 (10)	3.809 (6)
C(18)	10037 (11)	1603 (9)	7902 (13)	4.876 (8)
C(19)	10387 (8)	711 (10)	7191 (10)	4.289 (7)
C(20)	9660 (11)	95 (7)	7335 (11)	4.260 (7)
C(21)	8635 (9)	336 (7)	8180 (10)	3.317 (6)

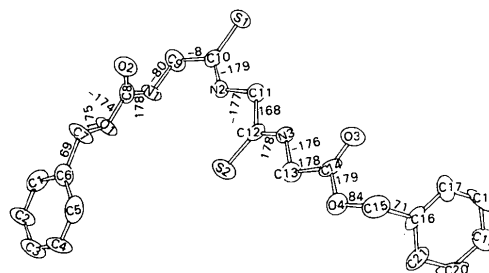


Fig. 1. Atomic numbering and the torsion angles, shown on an ORTEP (Johnson, 1965) perspective drawing. [Nomenclature of torsion angles is in agreement with the recommendation of IUPAC–IUB Commission of Biochemical Nomenclature (1970).] The thermal ellipsoids are drawn at 50% probability. Only non-H atoms are shown.

The molecule forms four hydrogen bonds. The bonds are pairwise related to each other by the centre of symmetry, resulting in two different types of hydrogen bonds. The geometry of both is shown in Table 3. One type binds the molecule to the centrosymmetrically related molecule, the other type binds to the same molecule in a neighbouring cell. The hydrogen bonds are extended along the *a* and *c* axes, resulting in the packing pattern shown in Fig. 2. This pattern consists of bands of regions of hydrophobic phenyl groups, alternating with similar regions of hydrogen bonds

Table 2. Bond lengths (Å) and angles (°) with *e.s.d.*'s from ORFFE (Busing, Martin & Levy, 1964)

Only non-H atoms are included. Bond lengths involving H atoms are in the range 0.7–1.3 Å.

C(1)–C(2)	1.359 (10)	C(2)–C(3)	1.369 (10)
C(3)–C(4)	1.392 (11)	C(4)–C(5)	1.355 (10)
C(5)–C(6)	1.383 (9)	C(6)–C(1)	1.407 (8)
C(6)–C(7)	1.516 (9)	C(7)–O(1)	1.456 (8)
O(1)–C(8)	1.323 (8)	C(8)–O(2)	1.209 (8)
C(8)–N(1)	1.360 (9)	N(1)–C(9)	1.423 (10)
C(9)–C(10)	1.537 (9)	C(10)–S(1)	1.656 (7)
C(10)–N(2)	1.302 (7)	N(2)–C(11)	1.445 (8)
C(11)–C(12)	1.510 (8)	C(12)–S(2)	1.648 (7)
C(12)–N(3)	1.330 (7)	N(3)–C(13)	1.437 (8)
C(13)–C(14)	1.511 (9)	C(14)–O(3)	1.203 (7)
C(14)–O(4)	1.329 (7)	O(4)–C(15)	1.482 (8)
C(15)–C(16)	1.490 (9)	C(16)–C(17)	1.360 (9)
C(16)–C(21)	1.380 (9)	C(17)–C(18)	1.378 (11)
C(18)–C(19)	1.372 (11)	C(19)–C(20)	1.377 (11)
C(20)–C(21)	1.383 (10)		
C(1)–C(2)–C(3)	119.7 (9)	C(2)–C(3)–C(4)	119.9 (9)
C(3)–C(4)–C(5)	119.3 (9)	C(4)–C(5)–C(6)	122.2 (9)
C(5)–C(6)–C(7)	123.1 (10)	C(2)–C(1)–C(6)	122.3 (9)
C(1)–C(6)–C(7)	121.0 (9)	C(5)–C(6)–C(1)	115.9 (10)
C(6)–C(7)–O(1)	104.7 (9)	O(1)–C(8)–O(2)	127.2 (9)
O(1)–C(8)–N(1)	109.9 (7)	O(2)–C(8)–N(1)	122.8 (8)
C(8)–N(1)–C(9)	122.2 (7)	N(1)–C(9)–C(10)	114.6 (6)
C(9)–C(10)–S(1)	118.5 (6)	C(9)–C(10)–N(2)	115.0 (6)
S(1)–C(10)–N(2)	126.5 (5)	C(10)–N(2)–C(11)	123.2 (6)
N(2)–C(11)–C(12)	110.5 (6)	C(11)–C(12)–S(2)	123.1 (6)
C(11)–C(12)–N(3)	113.0 (6)	S(2)–C(12)–N(3)	123.9 (6)
C(12)–N(3)–C(13)	121.6 (6)	N(3)–C(13)–C(14)	109.6 (7)
C(13)–C(14)–O(3)	125.5 (7)	C(13)–C(14)–O(4)	109.0 (7)
O(3)–C(14)–O(4)	125.5 (7)	C(14)–O(4)–C(15)	117.2 (6)
O(4)–C(15)–C(16)	112.1 (6)	C(15)–C(16)–C(17)	119.7 (9)
C(15)–C(16)–C(21)	117.8 (7)	C(17)–C(16)–C(21)	122.5 (7)
C(16)–C(17)–C(18)	118.1 (8)	C(17)–C(18)–C(19)	122.5 (8)
C(18)–C(19)–C(20)	117.0 (8)	C(19)–C(20)–C(21)	122.9 (8)
C(20)–C(21)–C(16)	117.0 (8)		

Table 3. Hydrogen-bond lengths (Å) and angles (°) with *e.s.d.*'s in parentheses

Donor Symmetry	Acceptor Symmetry	H–D	H...A	A...D	∠AHD	
N(3)	O(2)	–x, –y, –z	0.944 (6)	2.112 (6)	2.980 (5)	161 (1)
N(1)	O(3)	1+x, y, 1+z	0.728 (4)	2.298 (5)	2.999 (6)	161 (1)

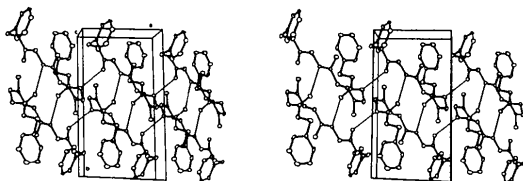


Fig. 2. Stereoscopic packing diagram of the crystal structure.

traversing the crystal along the diagonal in the *ac* plane. The packing forces along the *b* axis are predominantly hydrophobic interactions between phenyl groups.

The non-covalent distance from the two S atoms to their nearest neighbours, which in both cases are phenyl-group H atoms, is 2.89 Å for S(1) and 3.13 Å for S(2), in agreement with van der Waals contacts. However, their environments are slightly different. The S atom of peptide unit 1 is located in the hydrophilic band of hydrogen bonds. These bands have a higher dielectric constant locally than the bands consisting of the phenyl groups. This may exert a neutralizing effect on the electron distribution around the S atom in thiopeptide unit 1, resulting in a longer C–S and concomitantly a shorter C–N bond length, as compared to thiopeptide unit 2 where the S atom is situated in the hydrophobic band of phenyl groups.

With the exception of ψ_1 and ϕ_1 of the first thiopeptide unit, all the torsion angles in the peptide backbone are within 12° of 180°, which characterizes a fully extended chain. These exceptions give the molecule a characteristic bend. The packing of the phenyl groups in the hydrophobic regions is edge on plane (Burley & Petsko, 1985), and the thermal parameters of the atoms in these areas indicate some minor disorder. The crystal structures of both (Z)-Glyt-Gly-OBzl (Hansen *et al.*, 1987) and (Z)-Glyt-Gly-Gly-OBzl suggest that the driving force in the molecular packing is strongly influenced by the capability of the non-polar phenyl groups to pack together in hydrophobic regions, as well as the formation of the optimal number of hydrogen bonds. It also suggests a high degree of flexibility of the molecules in solution.

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