

SHELXTL/PC (Sheldrick, 1990). Program(s) used to refine structure: *SHELXL93* (Sheldrick, 1993). Molecular graphics: *SHELXTL/PC*. Software used to prepare material for publication: *SHELXL93*.

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Lists of structure factors, anisotropic displacement parameters, H-atom coordinates and bond distances and angles involving non-H atoms have been deposited with the IUCr (Reference: FG1035). Copies may be obtained through The Managing Editor, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

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3-(5-Oxo-L-prolyl)-L-thiazolidine-4-carboxylic Acid

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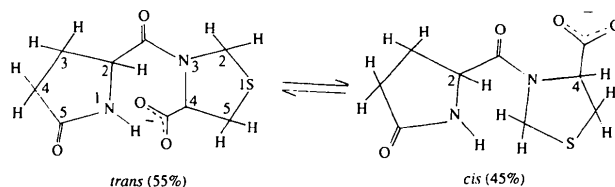
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Abstract

The molecular structure of the title compound, $C_9H_{12}N_2O_4S$, with (2*S*,4*S*) absolute configuration, is characterized by the *cisoid* geometry of the carboxylic acid residue and by the presence of two different disordered conformations of the thiazolidine moiety.

Comment

The title compound is an immunomodulant drug active on CD4 + T-lymphocyte functions (Pugliese, Biglino, Uslenghi, Marinelli, Forno & Girardello, 1992). It induces maturation and activation of T-lymphocytes and stimulates polymorphonuclear granulocytes, macrophages and natural killer-cell activity. NMR studies in solution and conformational calculations on its conjugate base (probably the bioactive form of the molecule) indicate the existence of *trans* and *cis* conformers around the peptide bond with a very close conformational population (55 and 45%, respectively) (Villani, Pucciariello, Crimella & Stradi, 1993).



This study proves that the conformation of the acidic form of the molecule in the solid state is *cis*. Although only the relative stereochemistry of the molecule is shown in Fig. 1, its absolute (2*S*,4*S*) configuration is assigned on the basis of the chemical pathway followed during the preparation of the compound [the chirality of the molecule originates from the absolute configuration of (*S*)-pyroglutamic acid and (*S*)-thiazolidine-4-carboxylic acid employed in its preparation].

The molecular structure with the atom-numbering scheme is illustrated as an *ORTEP* (Johnson, 1976) plot in Fig. 1.

The thiazolidine and prolyl rings are rotated by 98.95°, and the thiazolidine moiety is present in two conformations (envelope and quasipolar) due

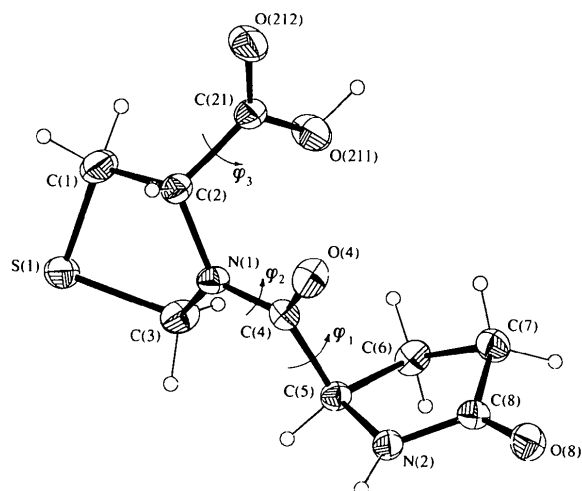


Fig. 1. *ORTEP*II (Johnson, 1976) drawing of the title compound illustrating the stereochemistry and the atomic labelling (displacement ellipsoids are drawn at the 40% probability level). The H atoms are drawn as spheres with fixed radii.

to two alternative disordered positions of the S atom (population factors 0.8 and 0.2, respectively). The conformational flexibility is confirmed by the different conformations found in various thiazolidine derivatives; for example, the twist conformation in *N*-acetyl-2-(*p*-tolyl)thiazolidine-4-carboxylic acid (Parthasarathy, Paul & Korytnyk, 1976) and 2-oxo-4-thiazolidinecarboxylic acid (Keszler, Johnson & White, 1991), and the envelope conformation in 3-(4-nitrobenzoyl)-4-thiazolidinecarboxylic acid ethyl ester (Averbuch-Pouchot, Durif, Pera & Hamri, 1990).

The prolyl ring has puckering parameters $\varphi = 25.5(4)^\circ$ and $Q = 0.296(2) \text{ \AA}$ (Cremer & Pople, 1975), indicative of a 'twisted' conformation.

The torsion angles $\varphi_1, \varphi_2, \varphi_3$ (see Fig. 1), which characterize the structure, are $88.2(2), 2.4(3)$ and $88.7(3)^\circ$, respectively [$\varphi_1 = \text{N}(1)\text{—C}(4)\text{—C}(5)\text{—C}(6)$, $\varphi_2 = \text{C}(3)\text{—N}(1)\text{—C}(4)\text{—C}(5)$, $\varphi_3 = \text{C}(1)\text{—C}(2)\text{—C}(21)\text{—O}(212)$], and confirm the results of the conformational analysis on the conjugate base (Villani *et al.*, 1993) for the most stable conformation.

The N(1)—C(4) bond distance [1.347(3) Å] has some double-bond character, confirmed by the planarity of the C(5)—C(4)—N(1)—C(3) fragment ($\varphi_2 = 2.4^\circ$), as found in 3-(4-nitrobenzoyl)-4-thiazolidinecarboxylic acid ethyl ester (Averbuch-Pouchot *et al.*, 1990), while the C(4)—O(4) bond distance of 1.230(3) Å maintains its double-bond character.

Intermolecular hydrogen-bond interactions are indicated by the distances between the hydroxyl proton of

the carboxylic group and the keto O atom of an adjacent molecule [O(211)H(211)···O(8ⁱ) 1.64(5) Å, O(211)—H(211)···O(8ⁱ) 166(5)°; symmetry code: (i) $-\frac{1}{2} + x, \frac{1}{2} - y, -z$], and between the amidic proton of the N atom and the next carboxylic O atom [N(2)H(2)···O(212ⁱⁱ) 1.99(3) Å, N(2)—H(2)···O(212ⁱⁱ) 170(3)°; symmetry code: (ii) $\frac{3}{2} - x, -y, -\frac{1}{2} + z$]. The hydrogen bonds create a sheet structure developing in the *bc* plane (Fig. 2). A similar polymeric structure has been found for the 2-oxo-4-thiazolidinecarboxylic acid derivative (Keszler *et al.*, 1991) where the interatomic distances N···O 2.961(3) and O···O 2.622(3) Å are comparable to the present values of 2.945(3) and 2.556(3) Å, respectively.

Experimental

Crystal data

C₉H₁₂N₂O₄S
M_r = 244.271
 Orthorhombic
*P*2₁2₁2₁
a = 5.593(1) Å
b = 12.227(2) Å
c = 15.705(7) Å
V = 1074.1(6) Å³
Z = 4
D_x = 1.51 Mg m⁻³

Mo K α radiation
 λ = 0.71069 Å
 Cell parameters from 25 reflections
 θ = 10–15°
 μ = 0.25 mm⁻¹
T = 298 K
 Irregular prism
 1.2 × 0.7 × 0.2 mm
 Colourless

Data collection

Enraf–Nonius CAD-4 diffractometer
 ω -2 θ scans
 Absorption correction: empirical (ψ scan)
T_{min} = 0.893, *T_{max}* = 0.995
 2424 measured reflections
 1852 independent reflections
 1706 observed reflections
 [*I* ≥ 2.5 σ (*I*)]

R_{int} = 0.012
 θ_{max} = 25°
h = -6 → 6
k = -1 → 14
l = -1 → 18
 3 standard reflections
 frequency: 60 min
 intensity decay: none

Refinement

Refinement on *F*
R = 0.0367
wR = 0.0409
S = 0.85
 1706 reflections
 193 parameters
 $w = 1/[\sigma^2(F_o) + 0.003739(F_o)^2]$

(Δ/σ)_{max} = 0.03
 $\Delta\rho_{\text{max}}$ = 0.34 e Å⁻³
 $\Delta\rho_{\text{min}}$ = -0.60 e Å⁻³
 Atomic scattering factors from *International Tables for X-ray Crystallography* (1974, Vol. IV)

Table 1. Fractional atomic coordinates and equivalent isotropic displacement parameters (Å²)

$$U_{\text{eq}} = (1/3)\sum_i\sum_j U_{ij}a_i^*a_j^*a_i\cdot a_j$$

	<i>x</i>	<i>y</i>	<i>z</i>	<i>U_{eq}</i>
S(1)†	0.1915(2)	-0.25356(6)	0.09969(5)	0.0409(3)
S(2)‡	0.104(1)	-0.2091(5)	0.1212(3)	0.067(1)
O(4)	0.7023(3)	0.0378(1)	0.0147(1)	0.0408(5)

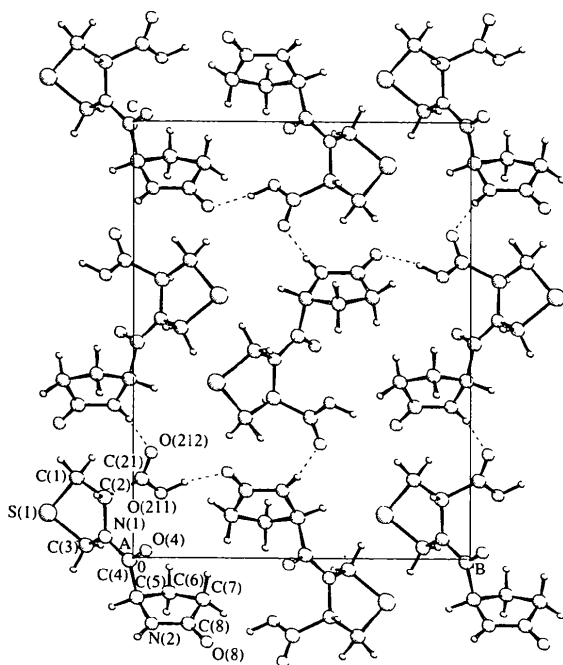


Fig. 2. Packing diagram (dotted lines indicate hydrogen-bond interactions).

O(8)	0.7277 (3)	0.2193 (1)	-0.1951 (1)	0.0436 (5)
O(211)	0.2768 (4)	0.0828 (2)	0.1458 (1)	0.0501 (6)
O(212)	0.5668 (4)	0.0541 (1)	0.2392 (1)	0.0564 (6)
N(1)	0.4093 (3)	-0.0817 (1)	0.0454 (1)	0.0282 (5)
N(2)	0.5754 (3)	0.0567 (1)	-0.1536 (1)	0.0302 (5)
C(1)	0.3175 (6)	-0.1675 (2)	0.1798 (2)	0.0503 (9)
C(2)	0.4817 (4)	-0.0846 (2)	0.1356 (1)	0.0299 (6)
C(3)	0.1880 (5)	-0.1398 (2)	0.0260 (2)	0.0389 (7)
C(4)	0.5214 (4)	-0.0117 (2)	-0.0075 (1)	0.0270 (6)
C(5)	0.4026 (4)	0.0116 (2)	-0.0933 (1)	0.0282 (6)
C(6)	0.2270 (4)	0.1084 (2)	-0.0818 (2)	0.0362 (6)
C(7)	0.3859 (5)	0.2081 (2)	-0.0970 (2)	0.0375 (7)
C(8)	0.5825 (4)	0.1651 (2)	-0.1535 (1)	0.0310 (6)
C(21)	0.4505 (4)	0.0260 (2)	0.1786 (1)	0.0329 (6)

† Occupation factor: 0.8.

‡ Occupation factor: 0.2.

Table 2. Selected geometric parameters (Å, °)

S(1)—C(1)	1.785 (3)	S(1)—C(3)	1.810 (3)
O(4)—C(4)	1.230 (3)	O(8)—C(8)	1.235 (3)
O(211)—C(21)	1.301 (3)	O(212)—C(21)	1.203 (3)
N(1)—C(2)	1.474 (3)	N(1)—C(3)	1.460 (3)
N(1)—C(4)	1.347 (3)	N(2)—C(5)	1.462 (3)
N(2)—C(8)	1.326 (3)	C(1)—C(2)	1.533 (4)
C(2)—C(21)	1.521 (3)	C(4)—C(5)	1.529 (3)
C(5)—C(6)	1.548 (3)	C(6)—C(7)	1.528 (3)
C(7)—C(8)	1.508 (3)		
C(1)—S(1)—C(3)	90.1 (1)	C(2)—N(1)—C(4)	118.7 (2)
C(3)—N(1)—C(4)	125.1 (2)	C(5)—N(2)—C(8)	113.3 (2)
C(2)—N(1)—C(3)	115.0 (2)	N(1)—C(2)—C(1)	106.6 (2)
S(1)—C(1)—C(2)	107.9 (2)	N(1)—C(2)—C(21)	111.9 (2)
C(1)—C(2)—C(21)	108.6 (2)	S(1)—C(3)—N(1)	103.4 (2)
N(1)—C(4)—C(5)	117.4 (2)	O(4)—C(4)—N(1)	121.3 (2)
N(2)—C(5)—C(4)	110.7 (2)	O(4)—C(4)—C(5)	121.1 (2)
N(2)—C(5)—C(6)	101.9 (2)	C(4)—C(5)—C(6)	108.4 (2)
C(6)—C(7)—C(8)	103.7 (2)	C(5)—C(6)—C(7)	102.9 (2)
O(8)—C(8)—C(7)	127.1 (2)	N(2)—C(8)—C(7)	109.1 (2)
O(212)—C(21)—C(2)	122.9 (2)	O(8)—C(8)—N(2)	123.7 (2)
O(211)—C(21)—O(212)	124.4 (2)	O(211)—C(21)—C(2)	112.6 (2)

Program used to solve structure: *SHELXS86* (Sheldrick, 1985). The structure was refined by full-matrix least squares with anisotropic displacement parameters for all non-H atoms. H atoms were located on a difference Fourier map, except for H(11) [bonded to C(1)] which was introduced at a calculated position (C—H = 1.080 Å, $U_{150} = 0.07 \text{ \AA}^2$) and not refined; all other H atoms were refined isotropically. Program used to refine structure: *SHELX76* (Sheldrick, 1976).

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Lists of structure factors, anisotropic displacement parameters, H-atom coordinates and complete geometry have been deposited with the IUCr (Reference: NA1093). Copies may be obtained through The Managing Editor, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

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2-(*p*-Ethoxyphenyl)-5-hexyl-1,3-dithiane, $C_{18}H_{28}OS_2$

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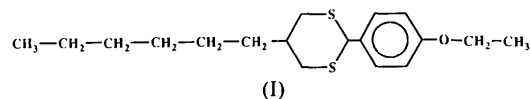
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Abstract

The molecules, which are *trans* isomers, are almost linearly extended and are stacked with their axes alternately oriented. The dithiane rings of the molecules are in chair conformations and are situated close together; the S··S interatomic distance is 3.006 (1) Å.

Comment

2,5-Disubstituted 1,3-dithianes, ($R-C_4H_6S_2-C_6H_4-R'$), have been reported as a new type of liquid-crystal compound (Haramoto & Kamogawa, 1983, 1985*a,b*; Haramoto, Nobe & Kamogawa, 1984; Haramoto, Akazawa & Kamogawa, 1984). The title compound, (I), with $R = n-C_6H_{13}$ and $R' = OC_2H_5$, exhibits monotropic behaviour and the nematic liquid-crystal phase appears in the temperature range 316–305 K.



The molecule of compound (I) is shown in Fig. 1. The molecule, which is the *trans* isomer, is almost linearly extended. The S··S interatomic distance, the mean S—C bond length and the mean C—C bond length in the dithiane ring are 3.006 (1), 1.808 (4) and 1.516 (5) Å, re-