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(2*S*)-4-(Methylsulfanyl)-2-(pyrrolidin-1-yl)-butanamide

Jian Song,[a] Xiao-Jun Li,[b]* Xiao-Ping Wu,[a] Ke-Xia Lou[a] and Rong-Xiu Feng[a]

[a]College of Pharmaceuticals and Biotechnology, Tianjin University, Tianjin 300072, People's Republic of China, and [b]College of Chemical Engineering, Hebei University of Technology, Tianjin 300130, People's Republic of China

Correspondence e-mail: xjlee@hebut.edu.cn

Key indicators

Single-crystal X-ray study
T = 273 K
Mean σ(C–C) = 0.006 Å
R factor = 0.062
wR factor = 0.120
Data-to-parameter ratio = 16.0

For details of how these key indicators were automatically derived from the article, see http://journals.iucr.org/e.

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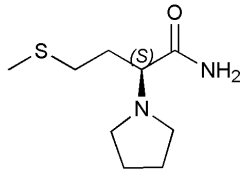
The title compound, $C_9H_{16}N_2O_2S$, was synthesized from L-methionine. The pyrrolidinone ring has an envelope conformation. Molecules are connected into two-dimensional layers by two independent intermolecular N—H···O hydrogen bonds, with N···O distances of 2.939 (5) and 2.914 (5) Å.

Comment

Levetiracetam [(*S*)-α-ethyl-2-oxopyrrolidine acetamide, LEV] is an ethyl analog of the nootropic drug piracetam. LEV is a new antiepileptic drug (AED) (Bialer *et al.*, 1999), recently approved by the US Food and Drug Administration. LEV possesses a chiral center but only the (*S*) enantiomer of α-ethyl-2-oxo-pyrrolidine acetylamide has anticonvulsant activity, and therefore it is administered as a single enantiomer (Haria & Balfour, 1997). The title compound, (I), is an intermediate in the synthesis of LEV, and the molecular structure is illustrated in Fig. 1.



(I)

Atom C6 is chiral, and it has an *S* configuration. The molecule consists of a pyrrolidinone ring (N1/C1/C2/C3/C4), which has an envelope conformation. Atoms N1/C4/C2/C1 are nearly coplanar and the mean deviation from this plane is

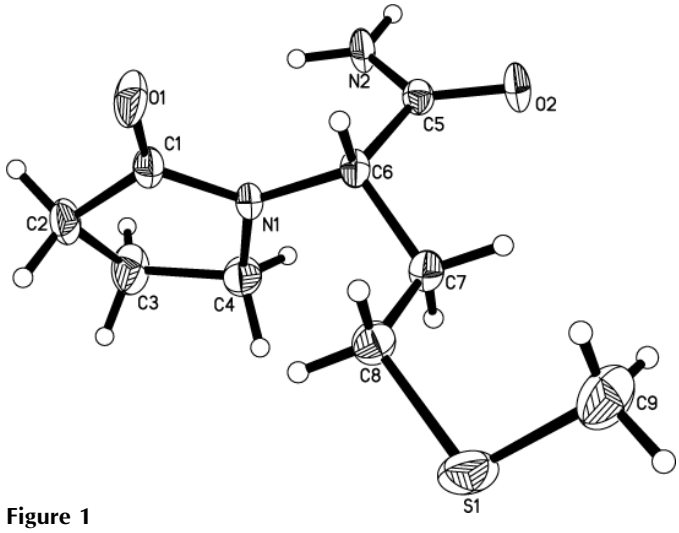


Figure 1
The molecular structure of (I), drawn with 30% probability ellipsoids.

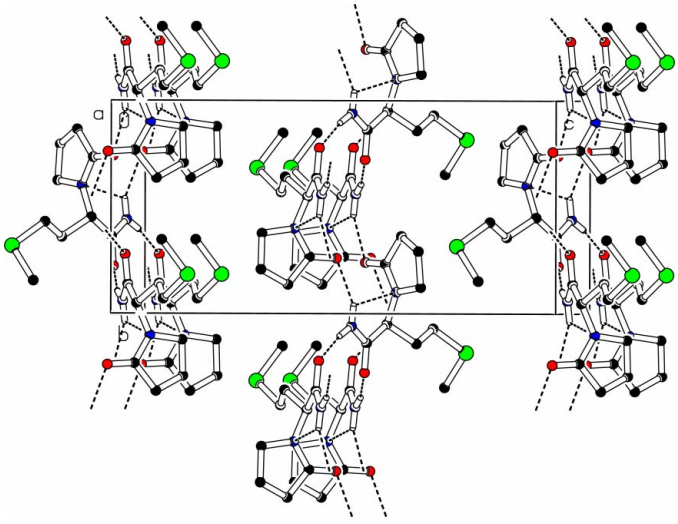


Figure 2
A packing diagram of (I), viewed along the *a* axis. Hydrogen bonding is indicated by dashed lines and the following are the atom colour codes: green S, red O, blue N, black C and white H.

0.008 (3) Å. Atom C3 is 0.306 (2) Å from this plane and forms the flap of the envelope. The dihedral angle between the N1/C4/C2/C1 mean plane and the C2/C3/C4 plane is 160.7 (2)°. The conformation of the rest of the molecule can be described by a series of dihedral angles. Atoms S1/C8/C7/C6 are nearly coplanar and the mean deviation from this plane is 0.025 (3) Å. The dihedral angle between the N1/C4/C2/C1 and S1/C8/C7/C6 planes is 91.3 (3)°. The dihedral angle between the N1/C4/C2/C1 and N2/C5/C6 planes is 100.1 (2)° and the dihedral angle between the S1/C8/C7/C6 and N2/C5/C6 planes is 34.7 (3)°.

In the crystal structure of (I), molecules are connected into two-dimensional layers, which are approximately perpendicular to the *c* axis, by two independent intermolecular N—H···O hydrogen bonds, namely N2—H2*C*···O2^{i} [symmetry code: (i) $\frac{1}{2}+x, \frac{5}{2}-y, 1-z$], with N···O = 2.939 (5) Å, H···O = 2.09 Å and N—H···O = 170°, and also N2—H2*D*···O1^{ii} [symmetry code: (ii) $\frac{1}{2}-x, \frac{3}{2}-y, 1-z$], with N···O = 2.914 (5) Å, H···O = 2.12 Å and N—H···O = 153 Å (see Fig. 2). There is also a questionable intramolecular N—H···N hydrogen bond [N2···N1 = 2.748 (5) Å, H2*D*···N1 = 2.38 Å and N2—H2*D*···N1 = 107°].

Experimental

The title compoud was prepared, according to a previously published method (Cossement *et al.*, 1990), from L-methionine. L-Methionine was esterified to its methyl ester using absolute methanol and thionyl chloride. The resulting L-methionine methyl ester hydrochloride was amidated using gaseous ammonia to give L-methionine amide. This amide (50.0 mmol) was treated with potassium hydroxide (14.0 g), tetrabutylammonium bromide (2.5 mmol) and 4-chlorobutyryl chloride (55.0 mmol) in dichloromethane to yield (*S*)-α-[2-(methylthio)ethyl]-2-oxo-pyrrolidine acetylamide. The reaction mixture was filtered and the filtrate evaporated under reduced pressure. The residue was purified by column chromatography over silica (eluent: mixture of dichloromethane/methanol/ammonia 95.5:4.5:0.2, *v*/*v*/*v*). The resulting white power was dissolved in 60 ml dichloromethane/methanol (13:1, *v*/*v*). A single crystal of the title compound, suitable for X-ray analysis, was grown by slow evaporation of the solvent. $[\alpha]_D^{25}$ +36.5° (*c* = 1 in methanol); ^{1}H NMR ($CDCl_3$, p.p.m.): 1.85 (2H, *m*), 2.03 (3H, *m*), 2.12 (2H, *m*), 2.24 (2H, *m*), 2.69 (2H, *m*), 3.44 (2H, *m*); ^{13}C NMR ($CDCl_3$): 15.50 (CH_2), 18.10 (CH_3), 27.40 (CH_2), 30.45 (CH_2), 31.03 (CH_2).

Crystal data

$C_9H_{16}N_2O_2S$
M_r = 216.30
Orthorhombic, $P2_12_12_1$
a = 7.018 (6) Å
b = 8.818 (7) Å
c = 18.760 (16) Å
V = 1161.0 (17) Å^3
Z = 4
D_x = 1.237 Mg m^{-3}
Mo *Kα* radiation
Cell parameters from 687 reflections
θ = 2.6–22.4°
μ = 0.26 mm^{-1}
T = 273 (2) K
Plate, colorless
0.30 × 0.25 × 0.20 mm

Data collection

Bruker SMART CCD area-detector diffractometer
φ and ω scans
Absorption correction: multi-scan (*SADABS*; Sheldrick, 1996)
T_{min} = 0.927, T_{max} = 0.950
4477 measured reflections
2047 independent reflections
1574 reflections with $I > 2\sigma(I)$
R_{int} = 0.047
θ_{max} = 25.0°
h = −8 → 7
k = −10 → 10
l = −22 → 17

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.062
$wR(F^2)$ = 0.120
S = 1.08
2047 reflections
128 parameters
H-atom parameters constrained
$w = 1/[\sigma^2(F_o^2) + (0.084P)^2]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max}$ = 0.002
$\Delta\rho_{max}$ = 0.25 e Å^{-3}
$\Delta\rho_{min}$ = −0.20 e Å^{-3}
Absolute structure: (Flack, 1983), 830 Friedel pairs
Flack parameter = −0.02 (17)

Table 1
Selected geometric parameters (Å, °).

C1—N1	1.362 (5)	C6—N1	1.462 (4)
C4—N1	1.455 (5)	C8—S1	1.810 (4)
C5—N2	1.325 (5)	C9—S1	1.806 (5)
O1—C1—N1	124.4 (3)	O2—C5—N2	122.5 (4)
O1—C1—C2	127.3 (3)	C9—S1—C8	101.4 (2)
N2—C5—C6—C7	148.5 (3)	C7—C6—N1—C1	120.2 (4)
N1—C6—C7—C8	−64.2 (4)	C5—C6—N1—C1	−113.4 (4)
C5—C6—C7—C8	168.9 (3)	C7—C8—S1—C9	67.0 (4)

H atoms were placed in idealized calculated positions with C—H distances ranging from 0.96 to 0.98 Å and N—H distances of 0.86 Å. They were included in the refinement as riding atoms, with U_{iso} = 1.2U_{eq} (1.5U_{eq} for methyl) of the carrier atom.

Data collection: *SMART* (Bruker, 1997); cell refinement: *SMART*; data reduction: *SAINT* (Bruker, 1997); program(s) used to solve structure: *SHELXS*97 (Sheldrick, 1997); program(s) used to refine structure: *SHELXL*97 (Sheldrick, 1997); molecular graphics: *SHELXTL* (Bruker, 1997); software used to prepare material for publication: *SHELXTL*.

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