Acta Crystallographica Section E
**Structure Reports Online**
ISSN 1600-5368

# 2-(2-Oxopyrrolidin-1-yl)butyramide

**Jian Song,[a] Ke-Xia Lou,[a]* Xiao-Jun Li,[b] Xiao-Ping Wu[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: loukexia@twtmail.tju.cn

**Key indicators**

Single-crystal X-ray study
*T* = 293 K
Mean σ(C–C) = 0.007 Å
*R* factor = 0.045
*wR* factor = 0.144
Data-to-parameter ratio = 8.7

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

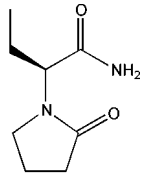


Received 29 September 2003
Accepted 8 October 2003
Online 23 October 2003

The title compound, $C_8H_{14}N_2O_2$, also known as levetiracetam and (−)-(*S*)-α-ethyl-2-oxo-1-pyrrolidineacetamide, was synthesized from L-methionine. The pyrrolidinone ring has a half-chair conformation. Screw-related molecules are linked by N—H···O hydrogen bonds to form layers parallel to the *bc* plane.

## Comment

Levetiracetam is an ethyl analog of the nootropic drug piracetam. It is a new antiepileptic drug (AED) (Bialer *et al.*, 1999), recently approved by the US Food and Drug Administration. It possesses a chiral center but only the *S* enantiomer has anticonvulsant activity, and therefore it is administered as a single enantiomer (Haria *et al.*, 1997). We report here the crystal structure of Levetiracetam, (I). The molecular structure of (I) is illustrated in Fig. 1. The structure reported and the scheme assume the *S* configuration for chiral C atom C6. The pyrrolidinone ring adopts a half-chair conformation. Weak N—H···N, C—H···O and C—H···N interactions are observed in the molecular structure. In the crystal structure, screw-related molecules are linked by N—H···O hydrogen bonds to form layers parallel to the *bc* plane (Fig. 2 and Table 2).




(I)

## Experimental

The title compound 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 obtain L-methionine amide. This amide (50 mmol) was treated with potassium hydroxide (14.0 g), tetrabutylammonium bromide (2.5 mmol) and 4-chlorobutyryl chloride (55 mmol) in dichloromethane to obtain (*S*)-α-[2-(methylthio)ethyl]-2-oxopyrrolidineacetamide. This compound was reacted with Raney Nickel (T-1) to yield (*S*)-α-ethyl-2-oxo-1-pyrrolidineacetamide. The reaction mixture was filtered and the filtrate was evaporated under reduced pressure. The residue was purified by column chromatography over silica (eluant: dichloromethane/methanol/ammonia, 94.5:4.3:0.2 *v*/*v*/*v*). The resulting powder was dissolved in 100 ml ethyl acetate. Single crystals of the title compound, suitable for X-ray analysis, were grown by slow evaporation of the solvent. $[\alpha]D_{25}$ −87.5° (*c* = 1 in acetone); $^1$H NMR

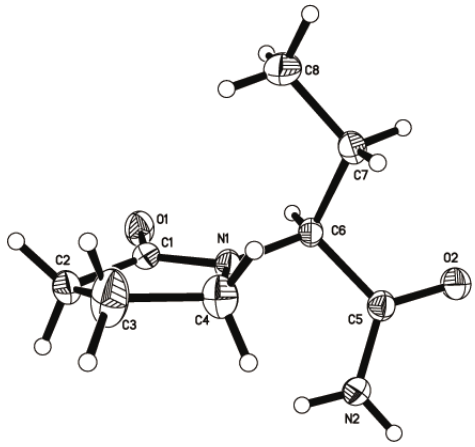



**Figure 1**
The molecular structure of (I), showing 30% probability displacement ellipsoids and the atom-numbering scheme.

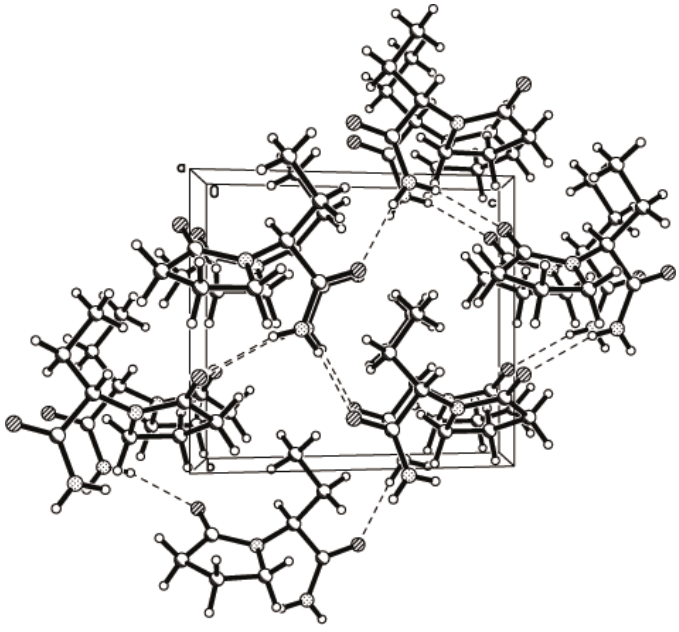


**Figure 2**
The crystal structure of (I), viewed along the *a* axis.

(CDCl$_3$, p.p.m.): 0.91 (2H, *t*), 1.66 (2H, *m*), 1.93 (2H, *m*), 2.36 (2H, *m*), 3.40 (2H, *m*), 4.45 (1H, *t*), 6.28 (2H, *d*); $^{13}$C NMR: 10.7 ($CH_3$), 18.3 ($CH_2$), 21.2 ($CH_2$), 31.3 ($CH_2$), 44.0 ($CH_2$), 56.3 (CH).

*Crystal data*

| | |
|---|---|
| $C_8H_{14}N_2O_2$ | $D_x$ = 1.294 Mg m$^{-3}$ |
| $M_r$ = 170.21 | Mo $K\alpha$ radiation |
| Monoclinic, $P2_1$ | Cell parameters from 789 reflections |
| $a$ = 6.272 (5) Å | $\theta$ = 3.4–23.1° |
| $b$ = 7.993 (5) Å | $\mu$ = 0.09 mm$^{-1}$ |
| $c$ = 9.199 (7) Å | $T$ = 293 (2) K |
| $\beta$ = 108.645 (9)° | Plate, colorless |
| $V$ = 437.0 (6) Å$^3$ | 0.20 × 0.18 × 0.16 mm |
| $Z$ = 2 | |

*Data collection*

| | |
|---|---|
| Bruker SMART CCD area-detector diffractometer | 731 reflections with $I > 2\sigma(I)$ |
| | $R_{int}$ = 0.048 |
| $\omega$ scans | $\theta_{max}$ = 26.5° |
| Absorption correction: none | $h = -7 \rightarrow 7$ |
| 2515 measured reflections | $k = -9 \rightarrow 9$ |
| 960 independent reflections | $l = -4 \rightarrow 11$ |

*Refinement*

| | |
|---|---|
| Refinement on $F^2$ | $w = 1/[\sigma^2(F_o^2) + (0.0884P)^2]$ where $P = (F_o^2 + 2F_c^2)/3$ |
| $R[F^2 > 2\sigma(F^2)]$ = 0.045 | $(\Delta/\sigma)_{max}$ = 0.001 |
| $wR(F^2)$ = 0.144 | $\Delta\rho_{max}$ = 0.23 e Å$^{-3}$ |
| $S$ = 1.08 | $\Delta\rho_{min}$ = −0.22 e Å$^{-3}$ |
| 960 reflections | Extinction correction: *SHELXL*97 |
| 110 parameters | Extinction coefficient: 0.24 (4) |
| H-atom parameters constrained | |

**Table 1**
Selected geometric parameters (Å, °).

| | | | |
|---|---|---|---|
| O1—C1 | 1.231 (5) | C1—C2 | 1.507 (6) |
| O2—C5 | 1.231 (5) | C2—C3 | 1.500 (7) |
| N1—C1 | 1.352 (5) | C3—C4 | 1.484 (6) |
| N1—C6 | 1.451 (4) | C5—C6 | 1.538 (5) |
| N1—C4 | 1.473 (5) | C6—C7 | 1.521 (6) |
| N2—C5 | 1.325 (5) | C7—C8 | 1.508 (6) |
| | | | |
| C1—N1—C6 | 122.9 (3) | C6—N1—C4 | 123.5 (3) |
| C1—N1—C4 | 112.7 (3) | | |

**Table 2**
Hydrogen-bonding geometry (Å, °).

| $D$—H···$A$ | $D$—H | H···$A$ | $D$···$A$ | $D$—H···$A$ |
|---|---|---|---|---|
| N2—H2$A$···O2$^{i}$ | 0.86 | 2.15 | 2.995 (5) | 168 |
| N2—H2$B$···O1$^{ii}$ | 0.86 | 2.23 | 3.038 (5) | 156 |
| N2—H2$B$···N1 | 0.86 | 2.39 | 2.771 (5) | 107 |
| C6—H6···O1 | 0.98 | 2.39 | 2.840 (5) | 107 |
| C8—H8$C$···N1 | 0.96 | 2.59 | 2.919 (6) | 100 |

Symmetry codes: (i) $2-x, \frac{1}{2}+y, 1-z$; (ii) $2-x, \frac{1}{2}+y, 2-z$.

H atoms were positioned geometrically (N—H = 0.86 Å and C—H = 0.96–0.98 Å) and refined using a riding model, with $U_{iso}$ values constrained to be $1.5U_{eq}$ of the carrier atom for methyl H atoms and $1.2U_{eq}$ for the remaining H atoms. The Flack (1983) parameter could not be determined reliably because of insufficient anomalous scattering effects. During the final cycles of refinement, the Friedel pairs in the data set were merged.

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*.

## References


Bialer, M., Johannessen, S. I., Kupferberg, H. J., Levy, R. H., Loiseau, P. & Perucca, E. (1999). *Epilepsy Res.* **34**, 1–41.
Bruker (1997). *SMART, SAINT* and *SHELXTL*. Versions 5.10. Bruker AXS Inc., Madison, Wisconsin, USA.
Cossement, E., Motte, G., Geerts, J. P. & Gobert. J. (1990). GB Patent No. 2 225 322.
Flack, H. D. (1983). *Acta Cryst.* A**39**, 876–881.
Haria, M. & Balfour, J. A. (1997). *CNS Drugs*, **7**, 159–164.
Sheldrick, G. M. (1997). *SHELXL*97 and *SHELXS*97. University of Göttingen, Germany.