Acta Crystallographica Section C
Crystal Structure Communications
ISSN 0108-2701

meso-*N*,*N*′-Oxalyldivaline

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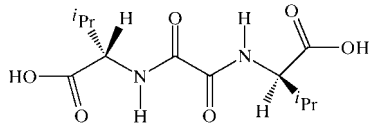
Received 18 January 2001
Accepted 14 March 2001

The title compound, 2,2′-(oxalyldiimino)bis(3-methylbutanoic acid), $C_{12}H_{20}N_2O_6$, possesses a centre of symmetry. In the crystal, molecules are connected by hydrogen bonds between oxamide and carboxyl groups, similar to the pattern of the monoclinic forms of HO–Gly–CO–CO–Gly–OH and HO–Aib–CO–CO–Aib–OH (Gly is glycine and Aib is 2-amino-isobutyric acid). The characteristic torsion angles in the title compound are close to those in peptide α-helices.

Comment

The molecule of the title compound, (I), belongs to the specific class of retrobipeptides having an oxamide (–NH–CO–CO–NH–) unit (Karle *et al.*, 1994). It is reported that compounds of this class are good gelators of water and organic solvents, their gelling properties depend on the stereochemistry of substituents at the oxamide unit (Jokić *et al.*, 1995). On the other hand, the oxamide moiety was chosen as a good structural unit in the design of molecular solids (Coe *et al.*, 1997; Nguyen *et al.*, 1998). Coe *et al.* (1997) investigated centrosymmetric oxamides with terminal-substituted carboxyl groups. The authors found two modes of connection of molecules into infinite two-dimensional hydrogen-bonding patterns. The first mode involves intermolecular N—H···O hydrogen bonds between the oxamide units and simultaneous intermolecular O—H···O hydrogen bonds between carboxyl groups. The second mode includes intermolecular hydrogen bonds between the oxamide unit and carboxyl group. Coe *et al.* (1997) also reported a polymorphism of the retrobipeptide of glycine with the oxamide unit (HO–Gly–CO–CO–Gly–OH). These two polymorphs represent two described modes of hydrogen-bonding patterns: the first mode appears in the triclinic polymorph whereas the second is characteristic of the monoclinic $P2_1/c$ form. The second mode is also observed in the crystal packing of the retrobipeptide of isobutyric amino acid with the oxamide unit, HO–Aib–CO–CO–Aib–OH (Karle & Ranganathan, 1995). Coe *et al.* (1997) argued that the second mode is favoured for retrobipeptides containing amino acids with larger substituents attached at the oxamide unit. Hydrogen bonds between oxamide and carboxyl groups are not disturbed by the steric hindrances of side chains, which are significant in the interactions of two oxamide groups. This argument is also valid for the structure reported in this paper.



(I)

The molecular structure of (I) is given in Fig. 1. The crystal structure with the hydrogen-bond pattern is shown in Fig. 2. The structural parameters of (I) are compared with those of HO–Gly–CO–CO–Gly–OH and HO–Aib–CO–CO–Aib–OH. The conformations of these retropeptides are defined by the set of torsion angles ω, φ, ψ and χ, as proposed in the literature (Karle *et al.*, 1994). The ψ angle in (I) defines (−)-synperiplanar conformation (Klyne & Prelog, 1960; Table 1), whereas in Gly and Aib analogues, (±)-antiperiplanar was observed. The only retrobipeptide of this kind with a synperiplanar conformation found in the Cambridge Structural Database (CSD, Version of October 2000; Allen & Kennard, 1993) was the methyl ester of the Aib analogue (YIDGEX; Karle *et al.*, 1994). However, the characteristics of the crystal packing of

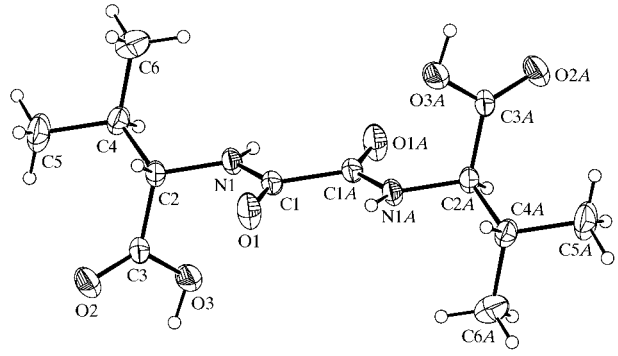


Figure 1
*ORTEP*II (Johnson, 1976) drawing of (I) showing 30% probability displacement ellipsoids.

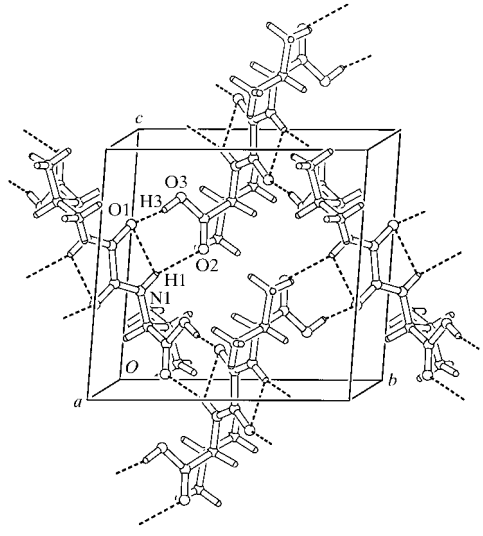


Figure 2
The crystal packing of (I). Intermolecular N1—H1···O2 and O3—H3···O1 hydrogen bonds generate the characteristic $R_2^2(9)$ pattern. Intramolecular N1—H1···O1 hydrogen bonds occur in the structure.

HO–Gly–CO–CO–Gly–OH, HO–Aib–CO–CO–Aib–OH and (I) are similar. They all crystallize in the $P2_1/c$ space group. Molecules are connected by hydrogen bonds between the oxamide and carboxyl groups (second mode described above), with a characteristic $R_2^2(9)$ graph-set descriptor (Bernstein *et al.*, 1995). According to arguments given by Coe *et al.* (1997), we can conclude that retrobipeptides with the oxamide unit having achiral amino acids larger than glycine, or those having amino acids of opposite chirality substituted at the oxamide unit, tend to crystallize in the $P2_1/c$ space group with the $R_2^2(9)$ hydrogen-bonding pattern including oxamide and carboxyl groups.

Experimental

A solution of *meso-N,N′*-oxalylbis(valine methyl ester), (II) (221 mg, 0.698 mmol), in MeOH (5 ml) and LiOH (1 *M*, 4.3 ml) was stirred for 2 d at room temperature. Most of the solvent was evaporated under reduced pressure, H_2O (5 ml) was added and the solution was acidified with HCl (1 *M*) to pH 2. The resulting aqueous solution was partitioned with EtOAc (2 × 15 ml) and the organic phase was dried (Na_2SO_4) and evaporated to give the title compound, (I) (191 mg, 89.9%); m.p. 512–514 K (from MeOH–EtOAc–light petroleum). Single crystals suitable for X-ray analysis were obtained by vapour diffusion of pentane into a solution of (I) in MeOH/EtOAc (1:7 *v*/*v*). ^{1}H NMR (DMSO-d_6, 300 MHz, δ, p.p.m.): 12.99 (*m*, 2H, COOH), 8.42 (*d*, J = 8.6, 2H, NH), 4.14 (*dd*, J = 8.6, J' = 6.0 Hz, 2H, CH_α), 2.23–2.16 (*m*, 2H, CH_β), 0.90 and 0.88 (2*d*, J = 6.6 and 6.5 Hz, 12H, $CH_{3(\gamma)}$);^{13}C NMR (DMSO-d_6, 75 MHz, δ, p.p.m.): 172.1 (COOH), 159.5 (CONH), 58.0 (CH_α), 29.8 (CH_β), 19.2 and 18.3 ($CH_{3(\gamma)}$); IR (KBr, ν_{max}, cm^{-1}): 3280 and 3130 (*br*, NH), 1715 (COOH), 1652 (amide I), 1508 (amide II). Analysis calculated for $C_{12}H_{20}N_2O_6$: C 49.99, H 6.99, N 9.72%; found: C 50.07, H 7.20, N 9.84%. Compound (II) was prepared from L,D-valine methyl ester hydrochloride according to the procedure described by Talma *et al.* (1985) and was separated from the reaction mixture by crystallization from CH_2Cl_2–light petroleum.

Crystal data

$C_{12}H_{20}N_2O_6$
M_r = 288.30
Monoclinic, $P2_1/c$
a = 7.6058 (8) Å
b = 10.3780 (2) Å
c = 10.6950 (10) Å
β = 119.635 (7)°
V = 733.76 (10) Å^3
Z = 2
D_x = 1.305 Mg m^{-3}
Cu $K\alpha$ radiation
Cell parameters from 25 reflections
θ = 40.0–46.0°
μ = 0.89 mm^{-1}
T = 293 (2) K
Prism, colourless
0.27 × 0.20 × 0.07 mm

Data collection

Enraf–Nonius CAD-4 diffractometer
$\omega/2\theta$ scans
Absorption correction: analytical (*PLATON*; Spek, 1999)
T_{min} = 0.819, T_{max} = 0.941
1597 measured reflections
1485 independent reflections
1132 reflections with $I > 2\sigma(I)$
R_{int} = 0.025
θ_{max} = 74.0°
$h = 0 \rightarrow 9$
$k = -12 \rightarrow 0$
$l = -13 \rightarrow 11$
3 standard reflections
frequency: 120 min
intensity decay: none

Table 1
Selected torsion angles (°).

C1^i—C1—N1—C2 (ω)	175.99 (18)	N1—C2—C3—O3 (ψ)	−28.4 (3)
C1—N1—C2—C3 (φ)	−77.8 (2)	N1—C2—C4—C5 (χ)	178.0 (2)

Symmetry code: (i) $1-x, -y, 1-z$.

Refinement

Refinement on F^2
$R(F)$ = 0.063
$wR(F^2)$ = 0.194
S = 1.06
1485 reflections
101 parameters
H atoms treated by a mixture of independent and constrained refinement
$w = 1/[\sigma^2(F_o^2) + (0.1404P)^2 + 0.0375P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} < 0.001$
$\Delta\rho_{max}$ = 0.36 e Å^{-3}
$\Delta\rho_{min}$ = −0.34 e Å^{-3}

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

D—H···A	D—H	H···A	D···A	D—H···A
N1—H1···O1^i	0.90 (3)	2.37 (3)	2.727 (2)	104 (2)
N1—H1···O2^{ii}	0.90 (3)	2.25 (3)	3.112 (3)	161 (3)
O3—H3···O1^{iii}	0.91 (4)	1.73 (4)	2.627 (3)	167 (3)

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

H atoms were placed in calculated positions and restrained to ride on the atom to which they were bonded. Exceptions were the H atoms involved in hydrogen bonds (H1 and H3), which were refined without restraints.

Data collection: *CAD*-4 *EXPRESS* (Enraf–Nonius, 1992); cell refinement: *CAD*-4 *EXPRESS*; data reduction: *HELENA* (Spek, 1997); program(s) used to solve structure: *SIR*97 (Altomare *et al.*, 1997); program(s) used to refine structure: *SHELXL*97 (Sheldrick, 1997); molecular graphics: *PLATON* (Spek, 1999); software used to prepare material for publication: *PLATON*.

Supplementary data for this paper are available from the IUCr electronic archives (Reference: AV1074). Services for accessing these data are described at the back of the journal.

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