Table 4. *Hydrogen bonds (Å, °) in β-DL-norleucine*

D—H···A	H···A[a]	D—H[a]	D—H···A[a]	D···A	H···A[b]
N1—H1···O1^{i}	1.83 (2)	0.95 (2)	171 (2)	2.769 (1)	1.746
N1—H2···O2^{ii}	1.89 (2)	0.94 (2)	165 (1)	2.799 (1)	1.795
N1—H3···O2^{iii}	1.90 (2)	0.93 (2)	169 (1)	2.814 (1)	1.797

Symmetry codes: (i) $\frac{3}{2}-x, y+\frac{1}{2}, \frac{3}{2}-z$; (ii) $x, 1-y, z-\frac{1}{2}$; (iii) $x, -y, z-\frac{1}{2}$.

Notes: (*a*) experimental H-atom positions; (*b*) N—H bonds normalized to 1.030 Å (Taylor & Kennard, 1983).

Diffraction intensities, measured at 120 K, were corrected for Lorentz and polarizing effects. The structure was solved by direct methods using *SIR*92 (Altomare *et al.*, 1994) and refined with *SHELXL*93 (Sheldrick, 1993). All heavy atoms were refined anisotropically. Amino H atoms were refined isotropically. Remaining H atoms were kept in idealized positions, refining a single C—H distance for all H atoms connected to the same C atom. A common isotropic displacement parameter for the methyl H atoms was refined. U_{iso} values for tertiary and secondary H atoms were fixed at 1.2 × U_{eq} of the bonded C atom.

Lists of structure factors, anisotropic displacement parameters, H-atom coordinates and complete geometry have been deposited with the IUCr (Reference: PA1228). Copies may be obtained through The Managing Editor, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

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Acta Cryst. (1996). C**52**, 1764–1767

L-Valyl-L-alanine

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(*Received 6 December 1995; accepted 14 February 1996*)

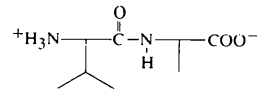
Abstract

L-Valyl-L-alanine, $C_8H_{16}N_2O_3$, crystallizes in space group $P6_1$. The side chains aggregate into large hydrophobic columns parallel to the hexagonal axis, with conspicuous empty central channels. The three-dimensional hydrogen-bond pattern is unique among dipeptide structures.

Comment

Dipeptide crystals are often divided into distinct hydrophilic and hydrophobic layers (Görbitz & Etter, 1992). In a hydrophilic layer, two of the three amino H atoms usually form hydrogen bonds to the C-terminal carboxylate group, generating two separate head-to-tail chains in two-dimensional hydrogen-bonded sheets (Suresh & Vijayan, 1985). Alternatively, one of the two chains may be interrupted by a solvent water molecule. In the case of glycine residues, the important third amino H atom can be accepted by a main-chain carboxylate or carbonyl group in a molecule of an adjacent sheet, but more generally, when the inter-sheet distances are larger, the H atom is accepted by a group in one of the two peptide side chains (Görbitz & Backe, 1996). Dipeptides with two hydrophobic residues represent a problem in this respect since there are no hydrogen-bond acceptors (or donors) in the side chains. In the crystal structure of L-Met-L-Met (Stenkamp & Jensen, 1975), the last amino H atom is not used for hydrogen bonding. Such a failure to use all active H atoms may clearly be regarded as an exception (Görbitz & Etter, 1992). In L-Leu-L-Leu.DMSO (Mitra & Subramanian, 1994) and L-Leu-L-Val.2-propanol (Görbitz & Gundersen, 1996*b*), the cocrystallized solvent molecule accepts the third amino H atom, preserving a layered structural build-up. L-Leu-L-Val can also be crystallized as a hydrate in the hexagonal space group $P6_2$, with four dipeptide molecules in the asymmetric unit (Görbitz & Gundersen, 1996*a*) and the water molecules acting as both hydrogen-bond acceptors and hydrogen-bond donors. In L-Ala-L-Ala (Fletterick, Tsai & Hughes, 1971), however, the demand for maximum hydrogen bonding has been satisfied through the formation of a chessboard-like pattern with fourfold symmetry (tetragonal, $I4$). The crystal structure of the title compound, L-Val-L-Ala,

also devoid of solvent, is unsensational as far as molecular geometry and conformation are concerned, but represents yet another interesting solution to the molecular packing problem of hydrophobic dipeptides.



L-Val-L-Ala

The hexagonal structure of L-Val-L-Ala is shown in Fig. 2. As in the case of L-Leu-L-Val.$\frac{3}{4}H_2O$ (Görbitz & Gundersen, 1996*a*), the side chains have segregated into a large hydrophobic column around the hexagonal axis. The two structures are, however, not as closely related as one would imagine, since there are no solvent molecules and only one dipeptide molecule in the asymmetric unit of L-Val-L-Ala. It can be readily appreciated from Fig. 2 that symmetry elements in the $P6_1$ space group include secondary threefold and twofold screw axes. Details of the complex three-dimensional hydrogen-bond network are given in Table 3 and illustrated in Fig. 3. The amino H3 atom (C5—C1—N1—H3 is *trans*) is donated to a carboxylate *anti* lone pair. The resulting head-to-tail chains occur in parallel pairs running around the threefold screw axes, as seen on the left in Fig. 3 (one chain is shown in a grey tone). The two chains in this left-handed double helix are interconnected by an amino–peptide carbonyl interaction (C5—C1—N1—H2 is *gauche*$^-$). The most important part of the hydrogen-bond network is the head-to-tail chain formed by the third amino H atom (C5—C1—N1—H1 is *gauche*$^+$), also to a carboxylate *anti* lone pair. The large right-handed helix surrounding the hydrophobic column is shown in the centre of Fig. 3. The right-hand side of Fig. 3 shows how the peptide N—H is donated to a carboxylate *syn* lone pair. There is also a peculiar three-centre *syn* C$^\alpha$—H···carboxylate interaction, shown in a grey tone. Although C—H donors are quite common in peptide crystals, the peptide carbonyl group is invariably the preferred acceptor. Carboxylate acceptors, on the other hand, are very rare.

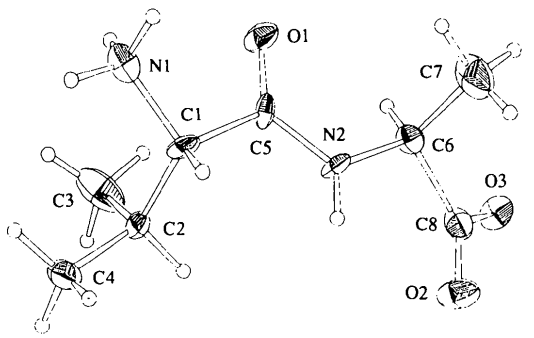


Fig. 1. The asymmetric unit of L-Val-L-Ala with the atomic numbering scheme (*ORTEP*II; Johnson, 1976). Displacement ellipsoids are shown at the 50% probability level and H atoms are shown as spheres of arbitrary size.

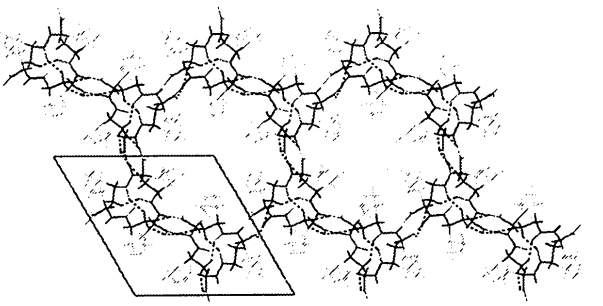


Fig. 2. The crystal packing viewed along the *c* axis with hydrogen bonds indicated. Side chains are shown in a grey tone. In one hydrophobic column, the van der Waals' surface is indicated for selected H atoms lining the interior of the empty central channel.

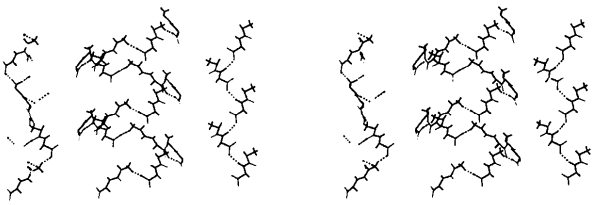


Fig. 3. Stereodiagram with excerpts of the crystal structure showing the various hydrogen-bonded chains. The peptide side chains have been omitted for clarity; hydrogen-bonding details are given in Table 3.

There is an empty channel running parallel to the hexagonal axis (Fig. 2). Hence, the calculated density of the crystal is only 1.041 Mg m^{-3}, by far the lowest value recorded among linear dipeptides: L-Leu-L-Val.$\frac{3}{4}H_2O$ = 1.121 (Görbitz & Gundersen, 1996*a*) and Gly-L-Leu = 1.178 Mg m^{-3} (Pattabhi, Venkatesan & Hall, 1974). The apparent diameter of the channel in Fig. 2 is roughly 3 Å, but since this is a projection of the unit-cell contents, the actual size of the irregularly shaped channel at any point along the *c* axis is much larger, about 5 Å. If the observed volume occupied by the asymmetric unit (300 Å^3) is divided by the mean van der Waals' volume of 18 Å^3 (Kempster & Lipson, 1972), one finds 16.7 atomic sites. With 13 heavy atoms in L-Val-L-Ala, this means that a space is left which can be occupied by three to four atoms, *i.e.* one propanol molecule or four water molecules. These can fit and glide inside the channels. The crystal used for data collection was first left to dry for a few days after being removed from the mother solvent. In this period it apparently lost solvent. There is no sign of remnant electron density in the channel. Although the crystal survived this process, it did turn slightly opaque and the quality was clearly not first class with relatively poor diffraction. A new batch of crystals were even more unstable in air and decayed within a few seconds. A new set of data, thought to be of good quality, was collected from one specimen. The cell dimensions [$a = b = 14.15(1)$, $c = 10.06(1)$ Å], intensity symmetry and systematic absences indicated the space group to be $P6_3$, but the structure of this

second polymorph has yet to be solved. There is no indication that the initial drying of the first batch of crystals involved a phase transition.

Crystallization experiments have been carried out for a number of hydrophobic dipeptides other than L-Leu-L-Val and L-Val-L-Ala. All of them share a common crystal habit in forming exceedingly thin needles. The empty central channel of the current crystal structure means that larger side chains could be fitted in the hydrophobic column with only minor adjustments to the hydrogen-bond network. We therefore hypothesize that other hydrophobic dipeptides may also have hexagonal unit cells with crystal structures similar to L-Val-L-Ala. The cell dimensions of L-Ala-L-Ile, which indeed appears to crystallize in a hexagonal space group [$a = b = 14.19(3)$ and $c = 10.19(4)$ Å], were measured and were very close to the values obtained for L-Val-L-Ala. The crystal was too small for collection of even a limited data set. The much larger unit cell observed for L-Leu-L-Val.$\frac{3}{4}H_2O$, with four dipeptide molecules in the asymmetric unit, is a less likely template for crystallization of other compounds.

Experimental

Crystals of L-Val-L-Ala were grown by diffusion of 2-propanol into 30 µl of an aqueous solution containing about 3 mg of the peptide.

Crystal data

$C_8H_{16}N_2O_3$
$M_r = 188.23$
Hexagonal
$P6_1$
$a = 14.424(4)$ Å
$c = 9.996(6)$ Å
$V = 1801.1(13)$ Å^3
$Z = 6$
$D_x = 1.041$ Mg m^{-3}
D_m not measured

Mo $K\alpha$ radiation
$\lambda = 0.71069$ Å
Cell parameters from 25 reflections
$\theta = 12.5$–$17.5°$
$\mu = 0.080$ mm^{-1}
$T = 120(2)$ K
Needle
1.20 × 0.45 × 0.20 mm
Colourless

Data collection

Nicolet $P3$ diffractometer
2θ scans
Absorption correction: none
1453 measured reflections
1453 independent reflections
627 observed reflections [$I > 2\sigma(I)$]

$\theta_{max} = 27.50°$
$h = 0 \rightarrow 16$
$k = 0 \rightarrow 15$
$l = 0 \rightarrow 12$
3 standard reflections monitored every 96 reflections
intensity decay: 1.2%

Refinement

Refinement on F^2
$R(F) = 0.0854$
$wR(F^2) = 0.1685$
$S = 0.954$
1452 reflections
122 parameters
H-atom parameters not refined
$w = 1/[\sigma^2(F_o^2) + (0.0462P)^2]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} < 0.001$
$\Delta\rho_{max} = 0.322$ e Å^{-3}
$\Delta\rho_{min} = -0.285$ e Å^{-3}
Extinction correction: none
Atomic scattering factors from *International Tables for Crystallography* (1992, Vol. C, Tables 4.2.6.8 and 6.1.1.4)

Table 1. *Fractional atomic coordinates and equivalent isotropic displacement parameters (Å^2)*

$U_{eq} = (1/3)\sum_i\sum_j U_{ij}a_i^*a_j^*\mathbf{a}_i.\mathbf{a}_j$.

	x	y	z	U_{eq}
O1	0.6258 (4)	0.3108 (4)	0.7320 (5)	0.0248 (13)
O2	0.5077 (4)	0.5619 (4)	0.8330 (5)	0.0338 (15)
O3	0.5936 (4)	0.5663 (4)	1.0216 (5)	0.0248 (13)
N1	0.5297 (5)	0.1985 (5)	0.5215 (6)	0.0229 (15)
N2	0.5583 (5)	0.4217 (4)	0.7169 (6)	0.0169 (13)
C1	0.4870 (5)	0.2664 (6)	0.5715 (7)	0.019 (2)
C2	0.3721 (5)	0.2003 (6)	0.6205 (8)	0.023 (2)
C3	0.3587 (6)	0.1154 (7)	0.7253 (9)	0.046 (3)
C4	0.2926 (6)	0.1473 (7)	0.5048 (8)	0.032 (2)
C5	0.5637 (6)	0.3362 (5)	0.6817 (6)	0.017 (2)
C6	0.6240 (5)	0.4882 (6)	0.8274 (7)	0.020 (2)
C7	0.7344 (6)	0.5733 (7)	0.7808 (9)	0.044 (2)
C8	0.5693 (6)	0.5427 (6)	0.8986 (7)	0.024 (2)

Table 2. *Selected geometric parameters (Å, °)*

O1—C5	1.231 (8)	C1—C2	1.522 (9)
O2—C8	1.241 (8)	C1—C5	1.528 (9)
O3—C8	1.277 (8)	C2—C4	1.536 (10)
N1—C1	1.481 (8)	C2—C3	1.549 (11)
N2—C5	1.322 (8)	C6—C7	1.518 (10)
N2—C6	1.459 (8)	C6—C8	1.539 (10)
C5—N2—C6	119.6 (6)	O1—C5—C1	119.5 (6)
N1—C1—C2	112.1 (6)	N2—C5—C1	116.4 (6)
N1—C1—C5	106.0 (5)	N2—C6—C7	111.9 (6)
C2—C1—C5	112.6 (6)	N2—C6—C8	110.8 (5)
C1—C2—C4	112.2 (6)	C7—C6—C8	109.1 (6)
C1—C2—C3	112.3 (6)	O2—C8—O3	125.5 (7)
C4—C2—C3	110.4 (6)	O2—C8—C6	118.5 (6)
O1—C5—N2	124.0 (6)	O3—C8—C6	116.0 (7)
N1—C1—C2—C4	−71.5 (8)	N1—C1—C5—N2	162.9 (6)
N1—C1—C2—C3	53.6 (8)	C5—N2—C6—C8	−150.6 (6)
C6—N2—C5—C1	176.0 (6)	N2—C6—C8—O2	−28.2 (9)

Table 3. *Hydrogen-bonding geometry (Å, °)*

D—H···A	D—H	H···A	D···A	D—H···A
N1—H1···O2^i	0.91	1.91	2.758 (8)	154
N1—H2···O1^{ii}	0.91	1.92	2.697 (8)	142
N1—H3···O3^{iii}	0.91	1.89	2.715 (7)	149
N2—H4···O3^{iv}	0.88	2.17	3.004 (7)	159
C1—H5···O2^{iv}	1.00	2.41	3.410 (8)	175
C1—H5···O3^{iv}	1.00	2.56	3.195 (8)	122

Symmetry codes: (i) $y, -x+y, z-\frac{1}{6}$; (ii) $1-x+y, 1-x, z-\frac{1}{3}$; (iii) $1-y, x-y, z-\frac{2}{3}$; (iv) $1-x, 1-y, z-\frac{1}{2}$.

The structure was solved using *SIR*92 (Altomare *et al.*, 1994) and refined with *SHELXL*93 (Sheldrick, 1993). H atoms were kept in theoretical positions with U_{iso} fixed at $1.2U_{eq}$ of the bonded atom or $1.5U_{eq}$ for amino and methyl groups, for which rigid rotation was permitted.

Lists of structure factors, anisotropic displacement parameters, H-atom coordinates, complete geometry and torsion angles have been deposited with the IUCr (Reference: PA1220). Copies may be obtained through The Managing Editor, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

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Acta Cryst. (1996). C**52**, 1767–1770

Intermediates in the Synthesis of (+)-Grandisol. I

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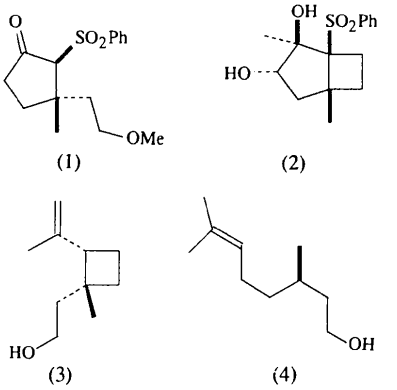
(Received 31 January 1996; accepted 26 March 1996)

Abstract

In both (2*R*,3*S*)-3-(2-methoxyethyl)-3-methyl-2-(phenylsulfonyl)cyclopentanone, $C_{15}H_{20}O_4S$ (1), and (1*S*,2*R*,3*S*,5*R*)-2,5-dimethyl-1-(phenylsulfonyl)bicyclo[3.2.0]heptane-2,3-diol, $C_{15}H_{20}O_4S$ (2), the five-membered ring is in an envelope conformation. In compound (1), the phenylsulfonyl and the methyl groups are *cis* to each other and the cyclization to the bicycloheptane, (2), occurs with retention of this stereochemistry. The hydroxyl groups in (2) are *trans* to each other.

Comment

The terpene, (+)-*cis*-2-isopropenyl-1-methylcyclobutaneethanol (3), named (+)-grandisol (Tumlinson *et al.*, 1971) is the principal component in the aggregation pheromone produced by the male of the cotton boll weevil, *Anthonomus grandis Boheman* (Franke *et al.*, 1989), which is a serious pest in Brazilian cotton fields. Its potential use in traps for monitoring crop infestation in integrated pest management makes this terpene, especially the more active (+)-enantiomer (Dickens & Mori, 1989), a target for the synthetic organic chemist. As the success of a synthetic route aiming at the synthesis of (+)-grandisol, starting with the easily available (+)-citronellol (4), depends on the generation of intermediates with the correct functionality and stereochemistry, the unambiguous stereostructure determination of them is required. We report here the crystal structure determination of two of them, (2*R*,3*S*)-3-(2-methoxyethyl)-3-methyl-2-(phenylsulfonyl)cyclopentanone, (1), and (1*S*,2*R*,3*S*,5*R*)-2,5-dimethyl-1-(phenylsulfonyl)bicyclo[3.2.0]heptan-2,3-diol, (2).



(1) (2) (3) (4)

In both compounds, the S atom is tetrahedrally bonded to two C and two O atoms with tetrahedral angles ranging from 108.1 (2) to 109.5 (3)° in (1) and from 106.59 (10) to 110.88 (10)° in (2), with the exception of the O—S—O angle which is 117.9 (3)° and 116.82 (10)° in (1) and (2), respectively. In compound (1), the phenylsulfonyl and the methyl groups are *cis* to each other and cyclization to bicycloheptane, (2), occurs with retention of this configuration, the rings being, therefore, *cis*-fused. Cremer & Pople's (1975) puckering parameters show that, in both compounds, the five-membered ring is in an envelope conformation, q_2 = 0.390 (6) Å, φ_2 = 75.1 (9)° (E_{C3}) for (1) and q_2 = 0.361 (3) Å, φ_2 = 65.3 (5)° (E_{C3}) for (2). The four-membered ring in compound (2) is planar within experimental accuracy, making a dihedral angle of 106.1 (1)° with the best least-squares plane through the five-membered ring. The phenyl ring makes a dihedral angle of 58.7 (3)° with the cyclopentanone ring in (1) and dihedral angles of 117.7 (1) and 15.2 (2)° with the five- and four-membered rings, respectively, in (2).

The molecules in (1) are joined through a C—H···O interaction: C4···O3^{i} = 3.334 (8), HC4···O3^{i} = 2.47 (8) Å, C4—HC4···O3^{i} = 142 (5)° [symmetry op-