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L-Seryl-L-leucine

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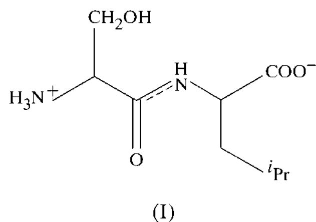
The structure of L-seryl-L-leucine, $C_9H_{18}N_2O_4$, has been determined and analysed in relation to the geometries of its amino acid constituents. The most important feature is the different conformational behaviour of the side chains at the C^β atoms; a less pronounced discrepancy concerns the orientation of the C=O bond with respect to the C^α—N bond. The conformational preferences of these torsion angles are also established for related structures stored in the Cambridge Structural Database [Allen & Kennard (1993). *Chem. Des. Autom. News*, **8**, 1, 31–37]; the title structure compares well with these data. The molecules are organized in double layers, with the hydrophilic faces linked by an extensive hydrogen-bonding network, as in L-leucine.

Comment

The α-amino acids constitute one of the most extensively studied classes of organic compounds crucial for all living organisms. Yet the relationship between the sequence of amino acids in the polypeptide chain and the resulting spatial architecture still remains a challenging issue for both theoreticians and bio-organic chemists. For certain structural fragments, non-bonded interaction patterns in small molecules resemble those in macromolecular systems. Therefore, it is important to study structural relationships in small polypeptide systems such as L-seryl-L-leucine, (I).



(I)

The title molecule is zwitterionic with a *trans* configuration of the peptide linkage [$\Delta\omega$ = −17.7 (2)°] (Fig. 1). A comparison of its geometrical parameters (Table 1) with the most accurate structure determinations of its amino acid components in the literature (LSERIN01, Kistenmacher *et al.*, 1974; LSERIN10, Benedetti *et al.*, 1973; LEUCIN02, Görbitz & Dalhus, 1996) does not reveal any systematic differences, although a few deviations exist depending on the data source and may be attributed, at least partially, to the underestimation of the standard deviations in the given papers. The discrepancy in the isopropyl side-chain geometry is clearly due to the large displacement parameters of the terminal C atoms. The only noticeable shortening, obviously resulting from the peptide linkage formation, is observed for N2—C4 (0.04 Å).

The most striking differences occur at the C^β atoms, the side chains adopting *gauche*$^-$ conformations towards the C^α—N bonds [N1—C1—C2—O1 −53.90 (15)° and N2—C4—C5—C6 −60.8 (2)°] compared to *gauche*$^+$ (61.5°) in L-serine (Kistenmacher *et al.*, 1974) and *trans* (−176.81 and −170.01°) in L-leucine (Görbitz & Dalhus, 1996) (Fig. 2). The conformational preferences of seryl and leucyl fragments were further studied based on the data retrieved from the Cambridge Structural Database (Allen & Kennard, 1993).

The conformational analysis of the available data (164 serine/seryl fragments and 121 leucine/leucyl fragments) demonstrates the apparent tendency of the torsion angles to cluster around selected values, *i.e.* ±60° for N—C^α—C^β—OH

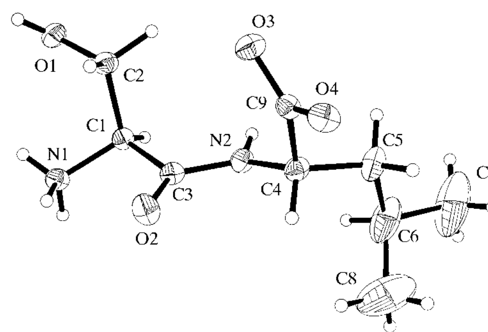


Figure 1
The structure of (I) showing 50% probability displacement ellipsoids.

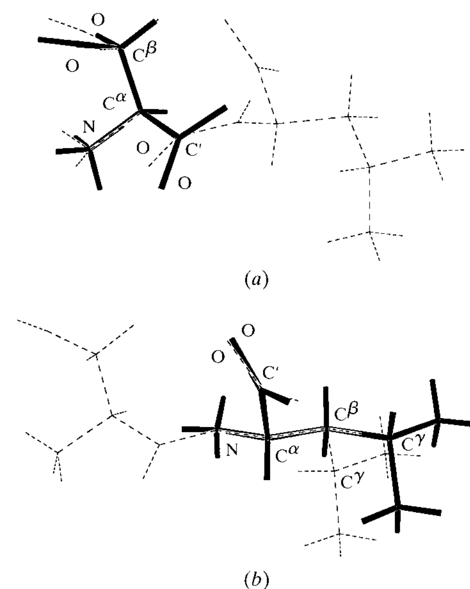


Figure 2
Superposition of L-seryl-L-leucine (dashed line) and (*a*) L-serine (full line) (LSERIN01; Kistenmacher *et al.*, 1974) and (*b*) L-leucine (full line) (LEUCIN02, molecule *A*; Görbitz & Dalhus, 1996). Fitting was performed on C^α and its three neighbouring non-H atoms (C^β, C′ and N).

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in serine/seryl and −60° as well as ±180° for N—C$^{\alpha}$—C$^{\beta}$—C$^{\gamma}$ in leucine/leucyl fragments, indicating that in the latter, *trans* and *gauche*$^{-}$ conformations are strongly favoured, while in the former, both *gauche* locations are preferred. The C═O and the N—C$^{\alpha}$ bonds are not strictly coplanar in leucine/leucyl fragments (preferred ∼±30°). This departure is less pronounced in seryl subunits, where the dihedral N—C$^{\alpha}$—C′═O angle is close to 0° with an additional maximum at about 30°. The structure of (I) conforms closely to the above distribution [N1—C1—C3═O2 −29.01 (18)° and N2—C4—C9═O3 −19.08 (19)°]. The flexibility of the molecular shape is presumably associated with both the prospective intermolecular hydrogen-bonding pattern in the crystal and the compulsion for most efficient close packing (Harding & Howieson, 1976).

The wafer-like molecular packing with typical double layers formed alternatively by hydrophilic and hydrophobic sheets (Fig. 3) resembles that of the parent L-leucine, and also other amino acids containing non-polar groups as reported by Harding & Howieson (1976). On the hydrophilic side, the molecules are held together by an extensive hydrogen-bonding network, the two shortest H···O contacts are 1.76 (3) and 1.79 (3) Å. The hydrogen bonds in Table 2 were selected based on the hydrogen-bonding criteria developed by Pedireddi & Desiraju (1992).

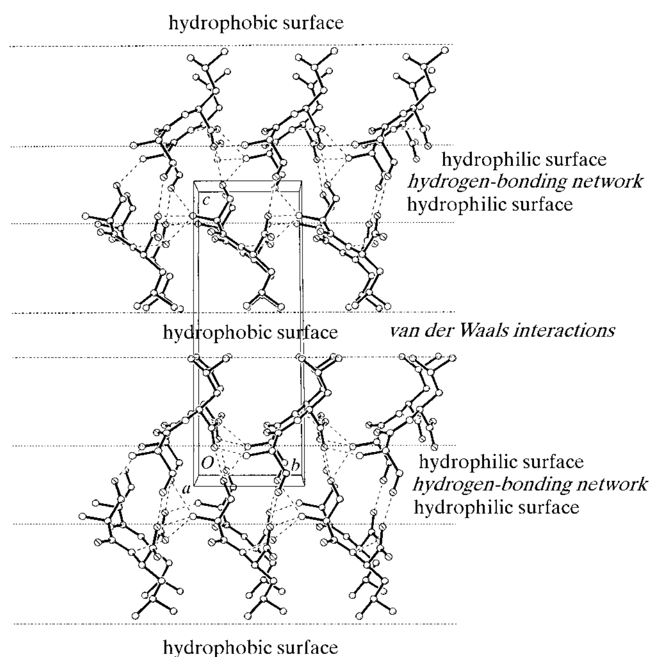

Figure 3
View of the crystal packing along the *a* axis showing the layered molecular architecture. H atoms have been omitted for clarity.

Experimental

A sample of L-seryl-L-leucine was purchased from Sigma and crystallized from an aqueous solution at room temperature. Single crystals were obtained after 24 d and like L-leucine, the crystals grew as filmy, slightly bent, transparent flakes (Görbitz & Dalhus, 1996), the shape corresponding closely to their internal layered structure.

Crystal data

$C_9H_{18}N_2O_4$
M_r = 218.25
Monoclinic, $P2_1$
a = 5.3288 (3) Å
b = 6.3696 (6) Å
c = 18.1263 (9) Å
β = 95.811 (4)°
V = 612.09 (7) Å^3
Z = 2
D_x = 1.184 Mg m^{-3}
Cu $K\alpha$ radiation
Cell parameters from 72 reflections
θ = 8.4–43.1°
μ = 0.779 mm^{-1}
T = 293 (2) K
Plate, colourless
0.70 × 0.70 × 0.05 mm

Data collection

Kuma KM-4 diffractometer
ω–2θ scans
Absorption correction: numerical (*SHELXTL*; Sheldrick, 1990*b*)
T_{min} = 0.625, T_{max} = 0.962
2765 measured reflections
1405 independent reflections
1325 reflections with $I > 2\sigma(I)$
R_{int} = 0.023
θ_{max} = 77.18°
$h = -6 \rightarrow 6$
$k = 0 \rightarrow 7$
$l = -22 \rightarrow 22$
3 standard reflections every 100 reflections intensity decay: none

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.029
$wR(F^2)$ = 0.077
S = 1.02
1405 reflections
166 parameters
H atoms treated by a mixture of independent and constrained refinement
$w = 1/[\sigma^2(F_o^2) + (0.0569P)^2 + 0.0176P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max}$ < 0.001
$\Delta\rho_{max}$ = 0.16 e Å^{-3}
$\Delta\rho_{min}$ = −0.14 e Å^{-3}
Extinction correction: *SHELXL*97 (Sheldrick, 1997)
Extinction coefficient: 0.027 (2)

Table 1
Selected geometric parameters (Å, °).

N1—C1	1.479 (2)	O4—C9	1.2558 (17)
N2—C3	1.3305 (19)	C1—C2	1.5282 (18)
N2—C4	1.4559 (17)	C1—C3	1.5290 (17)
O1—C2	1.4155 (17)	C4—C5	1.527 (2)
O2—C3	1.2254 (18)	C4—C9	1.5353 (18)
O3—C9	1.2572 (15)		
C3—N2—C4	119.88 (11)	N2—C3—C1	115.61 (12)
N1—C1—C2	109.08 (11)	N2—C4—C5	110.58 (11)
N1—C1—C3	108.67 (12)	N2—C4—C9	110.53 (11)
C3—C1—C2	107.28 (11)	C5—C4—C9	109.54 (13)
O1—C2—C1	109.24 (12)	O4—C9—O3	125.31 (13)
O2—C3—N2	124.74 (12)	O4—C9—C4	116.16 (11)
O2—C3—C1	119.51 (13)	O3—C9—C4	118.53 (11)
C4—N2—C3—O2	−17.7 (2)	C3—N2—C4—C9	−68.23 (16)
C4—N2—C3—C1	157.99 (12)	C4—C5—C6—C7	174.0 (2)
N1—C1—C3—N2	155.04 (11)	C4—C5—C6—C8	−63.4 (4)

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

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
N1—H1N*A*···O2	0.90 (2)	2.22 (2)	2.6978 (16)	113 (2)
N1—H1N*A*···O3^{i}	0.90 (2)	2.16 (2)	2.9509 (17)	146 (2)
N1—H1N*B*···O1^{ii}	0.90 (2)	2.08 (3)	2.8951 (16)	149 (2)
N1—H1N*C*···O4^{iii}	0.92 (2)	1.79 (3)	2.7066 (17)	168 (2)
N2—H2N···O4^{iv}	0.88 (2)	1.99 (2)	2.8449 (16)	164 (2)
O1—H1O···O3^{v}	0.86 (3)	1.76 (3)	2.6250 (15)	177 (3)
C1—H1···O2^{iv}	0.98	2.37	3.2575 (16)	150
C2—H2*B*···O1^{vi}	0.97	2.64	3.369 (2)	133
C5—H5*B*···O4^{iv}	0.97	2.82	3.474 (2)	125

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

Only H atoms involved in hydrogen bonding and bonded to N or O atoms were refined as isotropic. Those bonded to C atoms were treated by the riding model refinement (C—H = 0.96–0.98 Å) and H atoms in the CH_3 groups had their isotropic displacement parameters set equal to $1.5U_{eq}$ of their parent C atom.

Data collection: *KM4B8* (Gałdecki, Kowalski, Kucharczyk & Uszyński, 1997); cell refinement: *KM4B8*; data reduction: *DATAPROC* (Gałdecki, Kowalski & Uszyński, 1997); program(s) used to solve structure: *SHELXS86* (Sheldrick, 1990*a*); program(s) used to refine structure: *SHELXL97* (Sheldrick, 1997); molecular graphics: *SHELXTL/PC* (Sheldrick, 1990*b*); software used to prepare material for publication: *SHELXL97*.

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Supplementary data for this paper are available from the IUCr electronic archives (Reference: GG1024). Services for accessing these data are described at the back of the journal.

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