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L-Seryl-L-phenylalanine

Ina Høydal Helle,[a] Camilla Victoria Løkken,[a] Carl Henrik Görbitz[b]* and Bjørn Dalhus[b]

[a]Department of Molecular Biosciences, University of Oslo, PO Box 1041 Blindern, N-0316 Oslo, Norway, and [b]Department of Chemistry, University of Oslo, PO Box 1033 Blindern, N-0315 Oslo, Norway
Correspondence e-mail: c.h.gorbitz@kjemi.uio.no

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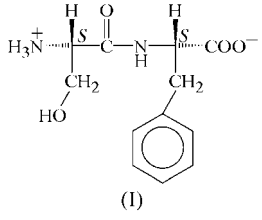
The peptide bond in the crystal structure of the title compound, $C_8H_{16}N_2O_4$, deviates substantially from planarity in the same manner as in other L-Ser-L-Xaa dipeptides, where Xaa is a hydrophobic residue.

Comment

The structure of L-Ser-L-Phe, (I), has been investigated as part of a systematic survey of dipeptides with one hydrophobic and one small polar residue (Netland *et al.*, 2004, and references therein). The molecular structure of (I) is shown in Fig. 1. Bond lengths and bond angles are normal, except in the Phe phenyl ring, where the bond lengths, in particular C8—C9 and C9—C10, are shortened significantly (Table 1) as a result of strong librational motion, reflected by the very elongated displacement ellipsoids in Fig. 1.



(I)

The peptide bond of (I) is unusually non-planar for a small linear peptide. The associated C1—C3—N2—C4 torsion angle (ω) is 157.51 (17)° (Table 1). Equivalent deviations from 180° occur also for L-Ser-L-Leu, (II) [157.99 (12)°; Słowikowska & Lipkowski, 2001], and L-Ser-L-Val, (III) [157.37 (15)°; Moen *et al.*, 2004], which, despite the shift in space group from $P2_1$ for (II) and (III) to $P2_12_12_1$ for (I), share the same hydrogen-bonding network and general crystal packing arrangement as (I). The conversion to an orthorhombic system, which involves an increase in the length of the *c* axis from 18.1263 (9) Å for (II) and 15.588 (10) Å for (III) to 36.741 (9) Å for (I), is a prerequisite for the formation of the classical herring-bone stacking pattern of aromatic groups seen in Fig. 2, with C9—H91···C9($\frac{1}{2}+x$, $-\frac{1}{2}-y$, $1-z$) as the most prominent intermolecular C—H···π interaction (H···C = 3.00 Å). Retention of the monoclinic space group would have given a less favourable, almost coplanar, arrangement of the phenyl rings.

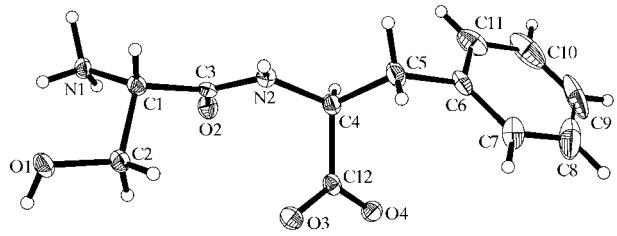


Figure 1
The molecular structure of L-Ser-L-Phe. Displacement ellipsoids are shown at the 50% probability level and H atoms are shown as spheres of arbitrary size.

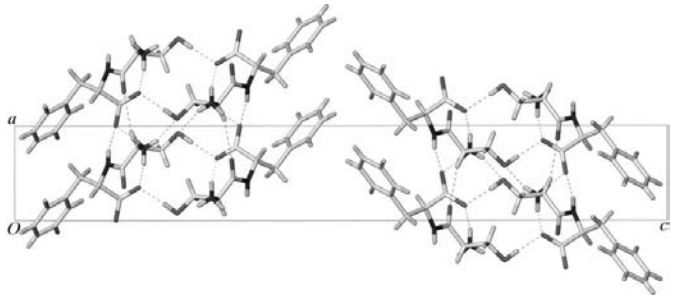


Figure 2
The molecular packing and unit cell of L-Ser-L-Phe, viewed along the *b* axis.

The low ω values for these structures result, as discussed for (III) (Moen *et al.*, 2004), from the need to fix the side-chain Ser–OH group as well as the C-terminal carboxylate group in favourable positions for the formation of hydrogen bonds (Table 2). Notably, the hydroxy H atom points in the direction of its carboxylate acceptor thanks to a conformation [C1—C2—O1—H5 = 127.4 (17)°] that causes an eclipse with one of the H atoms bonded to atom C2 (H21—C2—O1—H5 = 6.5°). The overall molecular geometry of (I) corresponds closely to that observed for (II) and (III). The Phe side chain is in a common *trans* orientation, as defined by the N2—C4—C5—C6 torsion angle.

The hydrophobic layers in the structure of (I) are composed of the benzyl side chains of the Phe residues. Similarly, the isobutyl and isopropyl side chains of Leu and Val residues can form hydrophobic layers on their own, as in the structures of (II) and (III). In contrast, no examples, to our knowledge, have been found of peptide structures with hydrophobic layers composed exclusively of Ala methyl groups, which are apparently too small to fill a layer without leaving large unfavourable voids. Hence, L-Ser-L-Ala (Görbitz, 2000), the third peptide in the Cambridge Structural Database (Version 5.25 of November 2003; Allen, 2002) in which an N-terminal Ser residue is coupled with a hydrophobic residue, forms a structure with a three-dimensional hydrogen-bonding pattern that is completely different from that of (I), (II) and (III).

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Experimental

The title compound was obtained from Bachem. Crystals were prepared by slow diffusion of ethanol into an aqueous solution of the peptide at ambient temperature.

Crystal data

$C_{12}H_{16}N_2O_4$
$M_r = 252.27$
Orthorhombic, $P2_12_12_1$
$a = 5.3382\ (13)$ Å
$b = 6.3827\ (16)$ Å
$c = 36.741\ (9)$ Å
$V = 1251.8\ (5)$ Å^3
$Z = 4$
$D_x = 1.339$ Mg m^{-3}
Mo $K\alpha$ radiation
Cell parameters from 3760 reflections
$\theta = 2.2$–26.7°
$\mu = 0.10$ mm^{-1}
$T = 105\ (2)$ K
Needle, colourless
$0.75 \times 0.15 \times 0.10$ mm

Data collection

Bruker SMART CCD diffractometer
ω scans
Absorption correction: multi-scan (*SADABS*; Sheldrick, 1996)
$T_{min} = 0.894$, $T_{max} = 0.990$
6723 measured reflections
1592 independent reflections
1428 reflections with $I > 2\sigma(I)$
$R_{int} = 0.054$
$\theta_{max} = 26.7^\circ$
$h = -6 \rightarrow 6$
$k = -7 \rightarrow 7$
$l = -45 \rightarrow 46$

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)] = 0.038$
$wR(F^2) = 0.098$
$S = 1.07$
1592 reflections
190 parameters
H atoms treated by a mixture of independent and constrained refinement
$w = 1/[\sigma^2(F_o^2) + (0.0645P)^2 + 0.0136P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} = 0.002$
$\Delta\rho_{max} = 0.28$ e Å^{-3}
$\Delta\rho_{min} = -0.23$ e Å^{-3}

Table 1
Selected geometric parameters (Å, °).

O1—C2	1.420 (2)	C4—C12	1.544 (3)
O2—C3	1.226 (2)	C4—C5	1.547 (3)
O3—C12	1.264 (2)	C5—C6	1.515 (3)
O4—C12	1.255 (3)	C6—C11	1.389 (3)
N1—C1	1.490 (3)	C6—C7	1.391 (3)
N2—C3	1.345 (3)	C7—C8	1.381 (4)
N2—C4	1.458 (3)	C8—C9	1.377 (5)
C1—C3	1.526 (3)	C9—C10	1.372 (5)
C1—C2	1.540 (3)	C10—C11	1.390 (4)
N1—C1—C3—N2	154.21 (16)	C1—C2—O1—H5	127.4 (17)
C4—N2—C3—C1	157.51 (17)	N2—C4—C5—C6	−163.69 (17)
C3—N2—C4—C12	−66.2 (2)	C4—C5—C6—C7	−105.0 (2)
N2—C4—C12—O3	−21.2 (3)	C4—C5—C6—C11	74.7 (3)
N1—C1—C2—O1	−53.3 (2)		

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

D—H···A	D—H	H···A	D···A	D—H···A
N1—H1···O3^{i}	0.90 (3)	2.14 (3)	2.930 (2)	146 (2)
N1—H2···O1^{ii}	0.84 (3)	2.13 (3)	2.876 (2)	149 (2)
N1—H3···O4^{iii}	1.01 (2)	1.71 (3)	2.718 (2)	168 (2)
N2—H4···O4^{iv}	0.87 (3)	1.97 (3)	2.819 (2)	165 (2)
O1—H5···O3^{v}	0.87 (3)	1.77 (3)	2.638 (2)	176 (2)
C1—H11···O2^{iv}	0.94 (2)	2.36 (2)	3.225 (3)	153 (2)

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

Positional parameters were refined for H atoms involved in hydrogen bonds; other H atoms were positioned geometrically and refined with constraints to keep all C—H distances and C—C—H angles on one C atom the same (C—H = 0.84–1.00 Å). U_{iso}(H) values were set at $1.2U_{eq}$ of the carrier atom, or $1.5U_{eq}$ for amino and methyl groups. In the absence of significant anomalous scattering effects, 1012 Friedel pairs were merged. The absolute configuration of the purchased material was known.

Data collection: *SMART* (Bruker, 1998); cell refinement: *SAINT-Plus* (Bruker, 2001); data reduction: *SAINT-Plus*; program(s) used to solve structure: *SHELXTL* (Bruker, 2000); program(s) used to refine structure: *SHELXTL*; molecular graphics: *SHELXTL*; software used to prepare material for publication: *SHELXTL*.

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Supplementary data for this paper are available from the IUCr electronic archives (Reference: SX1147). Services for accessing these data are described at the back of the journal.

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