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L-Asparaginyl-L-valine 1.33-hydrate

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Key indicators

Single-crystal X-ray study
T = 105 K
Mean σ(C–C) = 0.001 Å
R factor = 0.032
wR factor = 0.086
Data-to-parameter ratio = 18.7

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

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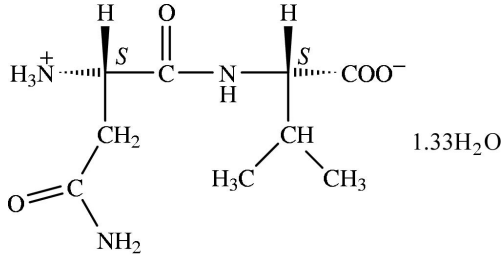
The title compound, $C_9H_{17}N_3O_4\cdot1.33H_2O$, crystallizes with three peptide molecules and four water molecules in the asymmetric unit. Two of the peptide molecules contain an intramolecular hydrogen bond between the N-terminal amino group and the asparagine side chain. Valine side chains aggregate into large hydrophobic columns.

Comment

As part of a systematic survey of dipeptides with one hydrophobic and one hydrophilic residue (Netland *et al.*, 2004), the structure of L-asparaginyl-L-valine, (I), has been determined. This is the first dipeptide after glycyl-L-asparagine (Pasternak *et al.*, 1954) to contain an L-asparagine residue. In the Cambridge Structural Database (Version 5.25 of November 2003; Allen, 2002), there is a total of 25 organic and seven organometallic structures with asparagine.



(I)

The asymmetric unit of (I), shown in Fig. 1, is unusual in containing three peptide molecules, observed among short linear peptides only for L-alanyl-L-2-aminobutyric acid (Görbitz, 2002) and for one of the forms of the commercial sweetener aspartame (L-aspartyl-L-phenylalanine methyl ester; Meguro *et al.*, 2000). The peptide main chains of (I) are semi-extended, with significantly different torsion angles (Table 1).

The absolute values for the $\chi^{2,1}$ torsion angle of asparagine side chains in peptides [C1—C2—C3—O2 in (I)] are almost without exception <70°. The carbonyl group thus bends back on the peptide main chain, and when χ^1 [N1—C1—C2—C3 in (I)] is *gauche*+ or *gauche*−, conformations that occur with about the same frequency as *trans*, it may accept an H atom from a main-chain donor. Such intramolecular interactions are present for peptide molecules *A* and *C* (Fig. 1). Geometric parameters for hydrogen bonds are given in Table 2. There are no previous peptide structures with a N-terminal asparagine residue, but the structure of L-asparagine itself has been extensively studied (Verbist *et al.*, 1972; Wang *et al.*, 1985; Weisinger-Lewin *et al.*, 1989; Arnold *et al.*, 2000; Flaig *et al.*, 2002), and there is also a structure of a complex with squaric

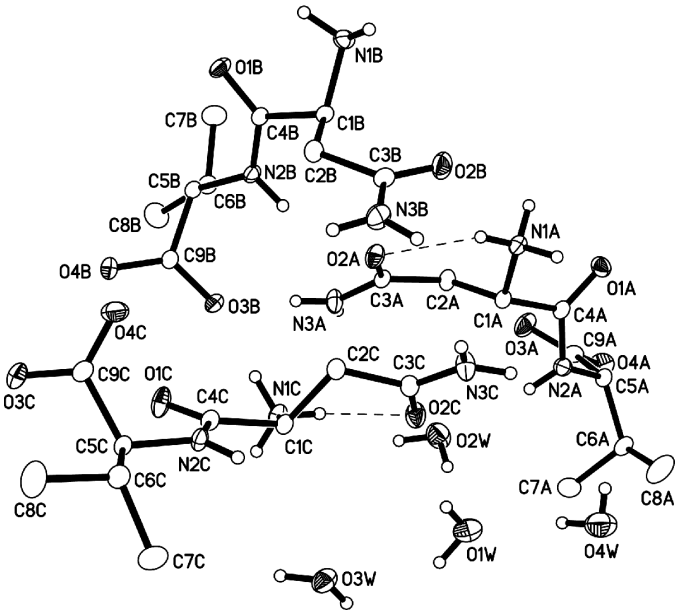


Figure 1
The structure of the asymmetric unit of (I). Displacement ellipsoids are drawn at the 50% probability level and H atoms are shown as spheres of arbitrary size. H atoms bonded to C atoms have been omitted for clarity. Displacement ellipsoids are shown with shaded segments for O atoms, with principal ellipses for N atoms and with boundary ellipse only for C atoms. Dashed lines indicate intramolecular hydrogen bonds for peptide molecules *A* and *C*.

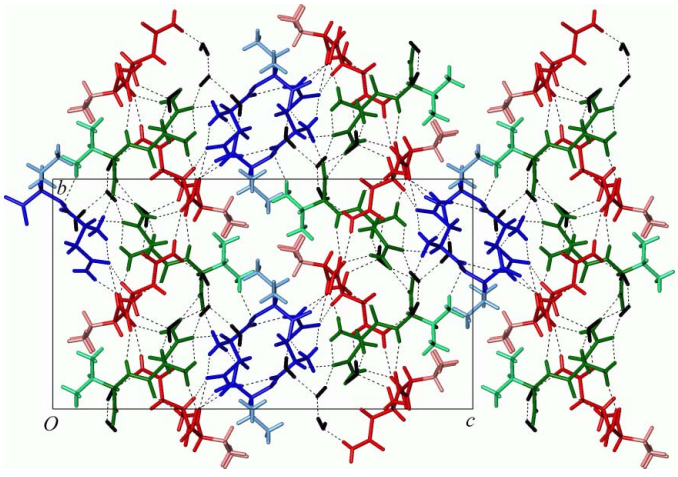


Figure 2
The molecular packing and unit-cell outline of (I), viewed along the *a* axis. Hydrogen bonds with H···O < 2.6 Å appear as dashed lines. Peptide molecule *A* is depicted in blue, molecule *B* in red, molecule *C* in green and water molecules in black. Valine side chains are shown in a lighter colour.

acid (Kolev *et al.*, 1998). Neither of these two structures has intramolecular hydrogen bonds as observed for (I); the pertinent H···O distances are about 2.56 Å, and all three amino H atoms are engaged in much shorter intermolecular hydrogen bonds. Intramolecular hydrogen bonds do, however, occur in three peptides with non-terminal asparagine residues (Mauguen *et al.*, 1976; Howes *et al.*, 1983; Sheldrick *et al.*, 1995), in each case associated with a χ^1 *gauche*+ orientation for the asparagine residue compared to *gauche*− for (I).

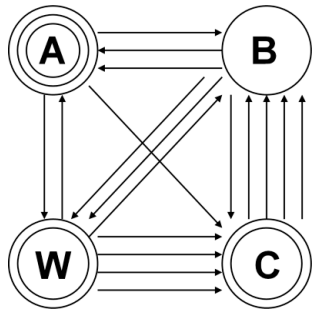


Figure 3
Schematic illustration of the N—H···O hydrogen bonds between the three peptide molecules *A*, *B* and *C* and the four water molecules W. A circle denotes a hydrogen bond to a molecule of the same type and arrows go from the donor to the acceptor.

The crystal packing, illustrated in Fig. 2, can conceptually be seen as being divided into three different types of regions: (i) hydrophobic regions or columns with valine side chains from all three peptide molecules; (ii) molecule *A* main chain columns; (iii) molecule *B* + molecule *C* layers. Water molecule 1 (W1) is in the *A* column, while other water molecules are in (W3) or on the surface (W2 and W4) of the *B*–*C* layers. Fig. 3 gives a schematic representation of the hydrogen-bonding connections in the structure, and demonstrates that *B* and *C* molecules interact heavily with each other, and not so much with molecule *A*. Molecule *C* is furthermore the main acceptor for water H atoms. This is seen in detail in Fig. 4, which also shows how W2 forms a bridge between peptide *A* molecules.

Experimental

The title compound was obtained from Sigma. Crystals were grown by slow evaporation of an aqueous solution of the peptide at room temperature.

Crystal data

$C_9H_{17}N_3O_4\cdot1.33H_2O$
$M_r = 255.28$
Orthorhombic, $P2_12_12_1$
$a = 9.0002\ (5)$ Å
$b = 15.0542\ (7)$ Å
$c = 27.4541\ (14)$ Å
$V = 3719.8\ (3)$ Å^3
$Z = 12$
$D_x = 1.367$ Mg m^{-3}
Mo $K\alpha$ radiation
Cell parameters from 7607 reflections
$\theta = 2.6$–37.1°
$\mu = 0.11$ mm^{-1}
$T = 105\ (2)$ K
Plate, colourless
0.60 × 0.45 × 0.10 mm

Data collection

Bruker SMART CCD diffractometer
ω scans
Absorption correction: multi-scan (*SADABS*; Sheldrick, 1996)
$T_{min} = 0.848$, $T_{max} = 0.989$
56666 measured reflections
10215 independent reflections
9027 reflections with $I > 2\sigma(I)$
$R_{int} = 0.031$
$\theta_{max} = 37.4^\circ$
$h = -14 \rightarrow 15$
$k = -25 \rightarrow 22$
$l = -45 \rightarrow 46$

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)] = 0.032$
$wR(F^2) = 0.086$
$S = 1.05$
10215 reflections
547 parameters
H atoms treated by a mixture of independent and constrained refinement
$w = 1/[\sigma^2(F_o^2) + (0.0518P)^2 + 0.1965P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} = 0.004$
$\Delta\rho_{max} = 0.33$ e Å^{-3}
$\Delta\rho_{min} = -0.23$ e Å^{-3}

Table 1
Selected torsion angles (°).

N1*A*—C1*A*—C4*A*—N2*A*	157.91 (8)	C1*B*—C2*B*—C3*B*—O2*B*	2.05 (14)
C1*A*—C4*A*—N2*A*—C5*A*	165.88 (8)	C1*B*—C2*B*—C3*B*—N3*B*	−176.72 (9)
C4*A*—N2*A*—C5*A*—C9*A*	−83.12 (11)	N2*B*—C5*B*—C6*B*—C7*B*	−72.40 (10)
N2*A*—C5*A*—C9*A*—O3*A*	6.45 (13)	N2*B*—C5*B*—C6*B*—C8*B*	165.61 (9)
N1*A*—C1*A*—C2*A*—C3*A*	−70.21 (10)	N1*C*—C1*C*—C4*C*—N2*C*	168.50 (8)
C1*A*—C2*A*—C3*A*—O2*A*	40.23 (13)	C1*C*—C4*C*—N2*C*—C5*C*	−172.04 (8)
C1*A*—C2*A*—C3*A*—N3*A*	−140.72 (9)	C4*C*—N2*C*—C5*C*—C9*C*	−59.81 (11)
N2*A*—C5*A*—C6*A*—C7*A*	66.87 (12)	N2*C*—C5*C*—C9*C*—O3*C*	140.32 (8)
N2*A*—C5*A*—C6*A*—C8*A*	−59.32 (12)	N1*C*—C1*C*—C2*C*—C3*C*	−69.38 (10)
N1*B*—C1*B*—C4*B*—N2*B*	156.04 (8)	C1*C*—C2*C*—C3*C*—O2*C*	31.02 (13)
C1*B*—C4*B*—N2*B*—C5*B*	171.65 (8)	C1*C*—C2*C*—C3*C*—N3*C*	−150.60 (9)
C4*B*—N2*B*—C5*B*—C9*B*	−129.34 (9)	N2*C*—C5*C*—C6*C*—C7*C*	−62.23 (11)
N2*B*—C5*B*—C9*B*—O3*B*	−48.87 (11)	N2*C*—C5*C*—C6*C*—C8*C*	176.15 (9)
N1*B*—C1*B*—C2*B*—C3*B*	−83.00 (10)		

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

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
N1*A*—H1*A*···O3*C*^{i}	0.997 (17)	1.750 (17)	2.7454 (11)	176.4 (16)
N1*A*—H2*A*···O2*A*	0.873 (18)	2.202 (18)	2.8782 (11)	134.1 (15)
N1*A*—H3*A*···O3*A*^{ii}	0.916 (18)	1.886 (18)	2.7909 (12)	168.9 (16)
N2*A*—H4*A*···O2*W*	0.841 (17)	2.168 (17)	3.0056 (13)	173.5 (16)
N3*A*—H5*A*···O3*B*	0.865 (18)	1.989 (18)	2.8381 (12)	166.7 (16)
N3*A*—H6*A*···O1*A*^{iii}	0.863 (17)	2.068 (17)	2.9085 (12)	164.4 (16)
C1*A*—H11*A*···O2*C*	1.00	2.51	3.4344 (12)	153
N1*B*—H1*B*···O1*C*^{iv}	0.842 (18)	1.906 (18)	2.7377 (11)	169.3 (17)
N1*B*—H2*B*···O3*W*^{v}	0.927 (18)	2.262 (18)	2.9573 (13)	131.3 (14)
N1*B*—H3*B*···O4*A*^{ii}	0.839 (18)	2.100 (18)	2.7441 (13)	133.3 (17)
N2*B*—H4*B*···O2*A*	0.887 (17)	2.112 (17)	2.9721 (11)	163.0 (16)
N3*B*—H5*B*···O4*B*^{i}	0.842 (18)	2.100 (18)	2.9199 (12)	164.7 (18)
N3*B*—H6*B*···O4*W*^{v}	0.905 (19)	1.889 (19)	2.7874 (15)	172.2 (17)
C1*B*—H11*B*···O4*A*^{ii}	1.00	2.43	3.0333 (12)	119
N1*C*—H1*C*···O2*B*^{vi}	0.896 (19)	2.112 (19)	2.9270 (13)	150.8 (15)
N1*C*—H2*C*···O2*C*	0.909 (18)	2.060 (18)	2.7522 (12)	131.9 (15)
N1*C*—H3*C*···O3*B*	0.936 (18)	1.858 (18)	2.7879 (12)	171.9 (16)
N2*C*—H4*C*···O1*B*^{i}	0.873 (16)	2.106 (16)	2.9317 (11)	157.5 (15)
N3*C*—H5*C*···O4*C*^{i}	0.923 (19)	2.056 (19)	2.9786 (13)	177.9 (17)
N3*C*—H6*C*···O4*B*^{i}	0.873 (19)	2.198 (19)	3.0205 (13)	156.9 (16)
C1*C*—H11*C*···O3*W*	1.00	2.25	3.1572 (13)	150
C8*C*—H83*C*···O1*A*^{v}	0.98	2.52	3.4126 (16)	152
O1*W*—H11*W*···O2*C*	0.82 (2)	2.04 (3)	2.7936 (13)	153 (2)
O1*W*—H12*W*···O3*C*^{vii}	0.88 (3)	1.90 (3)	2.7778 (14)	176 (2)
O2*W*—H21*W*···O3*A*^{iii}	0.87 (2)	2.03 (3)	2.8957 (14)	171 (2)
O2*W*—H22*W*···O1*W*	0.86 (2)	2.00 (2)	2.8512 (15)	170 (2)
O3*W*—H31*W*···O2*B*^{vi}	0.94 (2)	1.92 (2)	2.8390 (12)	164.0 (19)
O3*W*—H32*W*···O3*C*^{vii}	0.90 (2)	1.90 (2)	2.7896 (12)	168 (2)
O4*W*—H41*W*···O4*C*^{i}	0.77 (3)	2.00 (3)	2.7558 (15)	170 (3)
O4*W*—H42*W*···O1*W*	0.91 (3)	1.98 (3)	2.8508 (17)	160 (2)

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

Positional parameters were refined for H atoms bonded to N and O atoms. Other H atoms were positioned with idealized geometry and fixed C—H distances. U_{iso} values were set at $1.2U_{eq}$(carrier atom) or at $1.5U_{eq}$(carrier atom) for amino and methyl groups as well as water molecules. In the absence of significant anomalous scattering effects, 7949 Friedel pairs were merged. The absolute configuration was known for the purchased material.

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*.

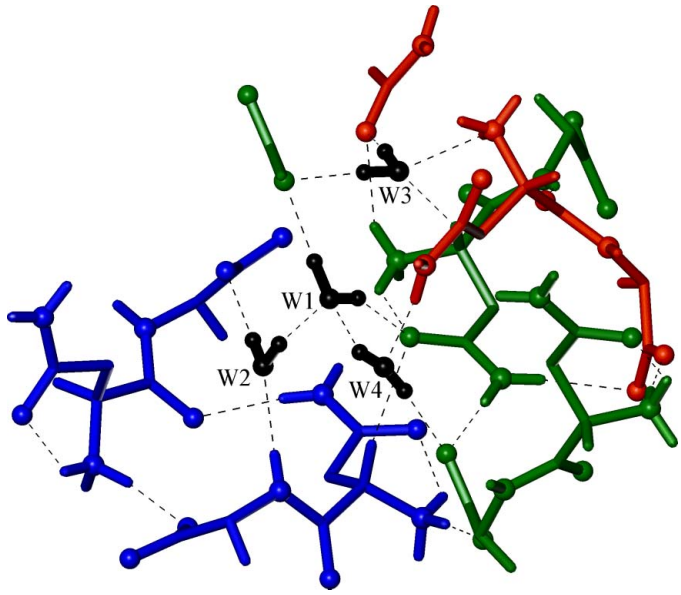


Figure 4
Detail of the hydrogen-bonding pattern, focusing on the interactions involving the four water molecules. The colour coding is as in Fig. 2, and O atoms, N atoms and water H atoms are highlighted as small spheres. In addition to five peptide molecules, shown without valine side chains and asparagine methylene H atoms, a molecule *B* asparagine side chain and a molecule *C* carboxylate group are included at the top.

The purchase of the Bruker SMART CCD diffractometer was made possible through support from the Research Council of Norway (NFR).

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