

Nanotubes of L-isoleucyl-L-leucine 0.91-hydrate

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Key indicators

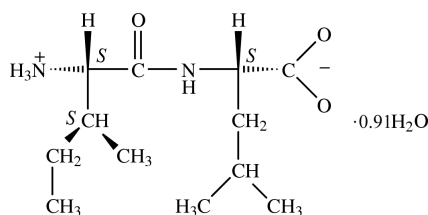
Single-crystal X-ray study
 $T = 105\text{ K}$
Mean $\sigma(\text{C}-\text{C}) = 0.004\text{ \AA}$
Disorder in solvent or counterion
 R factor = 0.038
 wR factor = 0.095
Data-to-parameter ratio = 8.1For details of how these key indicators were
automatically derived from the article, see
<http://journals.iucr.org/e>.

As the only dipeptide containing an L-Ile residue, the title compound, $\text{C}_{12}\text{H}_{24}\text{N}_2\text{O}_3 \cdot 0.91\text{H}_2\text{O}$, forms nanotubes with hydrophilic inner surfaces. There are two dipeptide molecules in the asymmetric unit, together with disordered water molecules.

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Comment

A systematic survey of the crystal structures of dipeptides constructed from the five hydrophobic amino acid residues L-Ala, L-Val, L-Ile, L-Leu and L-Phe has revealed that compounds with two small side chains tend to form structures with hexagonally symmetric hydrophobic pores (Görbitz, 2003, and references therein). Two large side chains may also give porous structures, but with hydrophilic rather than hydrophobic inner surfaces. This structural family has been referred to as the FF-class after L-Phe-L-Phe (FF), and includes L-Leu-L-Leu (LL), L-Leu-L-Phe (LF) and L-Phe-L-Leu (FL) (Görbitz, 2001) as well as L-Trp-Gly (WG) (Emge *et al.*, 2000; Birkedal *et al.*, 2002).



(I)

The asymmetric unit of the title hydrate of L-Ile-L-Leu (IL) is shown in Fig. 1. It contains two dipeptide molecules and disordered water molecules. All bond lengths and bond angles are normal. There is considerable anisotropy for atoms C3B and O2A, but the structure is generally well behaved. The two peptide molecules are very similar, as can be seen from the torsion angles in Table 1.

The crystal packing diagram in Fig. 2 and a comparison with details of the structures of LL and FL in Fig. 3 (Görbitz, 2001) immediately identify IL as a new member of the FF-class, characterized by the water-filled hydrophilic channels and the unique one-dimensional hydrogen-bond pattern along the shortest axis (three-dimensional pattern for WG through side-chain hydrogen bonding). It follows that peptide molecules *A* and *B*, like other compounds in the FF-class, have both side chains located on the same side of the peptide plane. This property can be described in short as giving absolute values for the torsion angle $\theta = \text{C}_1^\beta - \text{C}_1^\alpha \cdots \text{C}_2^\alpha - \text{C}_2^\beta < 90^\circ$. IL has $\theta = 10.6(2)^\circ$ for molecule *A* and $15.5(3)^\circ$ for molecule *B*.

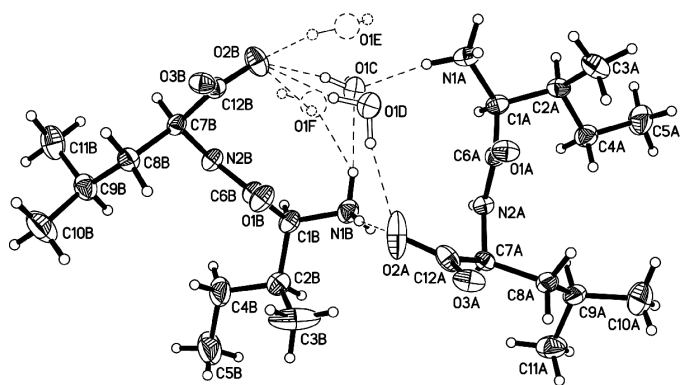


Figure 1

The molecular structure of IL. Displacement ellipsoids are shown at the 50% probability level, and H atoms are shown as spheres of arbitrary size. Dashed lines indicate hydrogen bonds. Water molecules *E* and *F* have low occupancy (0.173) and are shown with dotted circles.

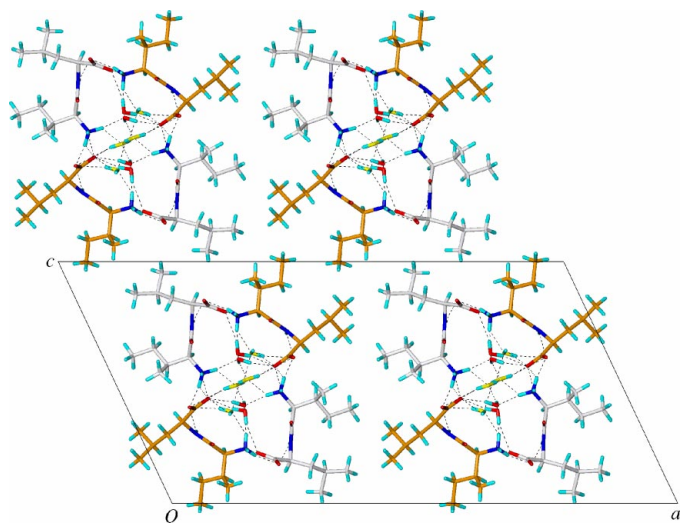


Figure 2

The molecular packing and unit cell viewed along the *b* axis. The C atoms in molecule *B* are colored orange; O atoms in the low-occupancy water molecules *E* and *F* are yellow.

Within the FF-class, IL (space group *C2*) is first of all remarkably similar to the structures of LL (*P2₁2₁2₁*; Fig. 3) and LF (*P2₁*; not shown), which have θ values in the narrow range -1.5 – 3.0° . FL and FF have higher θ values, 33.9 – 40.2° . Furthermore, the 123.4° relative rotation between the two molecules in the asymmetric unit of IL (Fig. 1) is about the same as for LL (122.1°) and LF (121.1°), while a relative rotation of only 102.0° was observed for FL (Fig. 3) (WG and FF have tetragonal and hexagonal symmetry, respectively, with only one peptide molecule in the asymmetric unit). The IL central cavity is of rectangular shape, with van der Waals dimensions $2.5 \times 6.0 \text{ \AA}$, as found also for LL and LF. A small difference between the three structures is, however, found in the arrangement of water molecules inside the channels. In LL (Fig. 3) and LF, two independent water molecules with full occupancy form bridges between amino groups and carboxylate groups across the channels. The same water positions, called *C* and *D*, are found for IL, as well as two

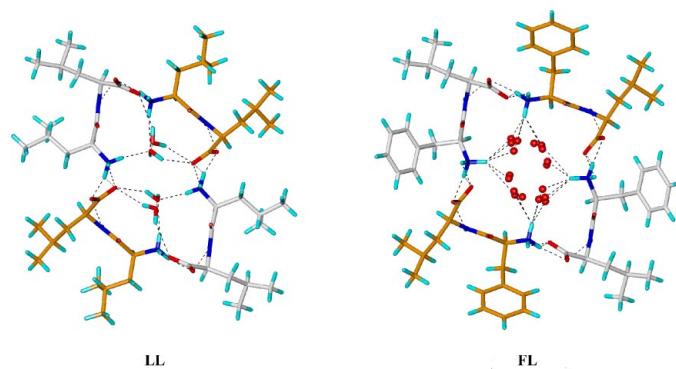


Figure 3

Individual nanotubes in the structures of LL and FL (Görbitz, 2001). Color coding as in Fig. 2.

minor water positions *E* and *F* with occupancy 0.173 (3). Introduction of an *E*–*F* pair blocks one *C* site and two *D* sites, so that water molecule *C* has occupancy 0.827 (3), while molecule *D* has occupancy 0.653 (3).

As is evident from Fig. 3, FL represents an expansion of the central channel compared with LL, LF and IL, to $4.0 \times 6.0 \text{ \AA}$, with nine refined water positions.

Hydrogen bonds between the IL peptide molecules, listed in Table 2, are equivalent to those observed in other FF-class crystal structures (Görbitz, 2001).

Experimental

Crystals in the shape of needles, suitable for X-ray analysis, were grown by fast evaporation of an aqueous solution at elevated temperature (333 K), the same technique used for crystallizing other compounds in the FF-class (Görbitz, 2001).

Crystal data

$C_{12}H_{24}N_2O_3 \cdot 0.91H_2O$
 $M_r = 260.82$
 Monoclinic, *C2*
 $a = 34.243 (2) \text{ \AA}$
 $b = 5.3251 (4) \text{ \AA}$
 $c = 18.1469 (12) \text{ \AA}$
 $\beta = 114.830 (2)^\circ$
 $V = 3003.1 (4) \text{ \AA}^3$
 $Z = 8$

$D_x = 1.155 \text{ Mg m}^{-3}$
 Mo $K\alpha$ radiation
 Cell parameters from 4227 reflections
 $\theta = 2.3$ – 26.4°
 $\mu = 0.09 \text{ mm}^{-1}$
 $T = 105 (2) \text{ K}$
 Flat needle, colorless
 $1.350 \times 0.070 \times 0.020 \text{ mm}$

Data collection

Bruker SMART CCD diffractometer
 ω scans
 Absorption correction: multi-scan (SADABS; Sheldrick, 1996)
 $T_{\min} = 0.857$, $T_{\max} = 1.000$
 8896 measured reflections

3390 independent reflections
 2948 reflections with $I > 2\sigma(I)$
 $R_{\text{int}} = 0.025$
 $\theta_{\text{max}} = 26.4^\circ$
 $h = -42 \rightarrow 42$
 $k = -6 \rightarrow 6$
 $l = -22 \rightarrow 15$

Refinement

Refinement on F^2
 $R[F^2 > 2\sigma(F^2)] = 0.038$
 $wR(F^2) = 0.095$
 $S = 1.04$
 3390 reflections
 416 parameters
 H atoms treated by a mixture of independent and constrained refinement

$w = 1/[\sigma^2(F_o^2) + (0.0448P)^2 + 1.7788P]$
 where $P = (F_o^2 + 2F_c^2)/3$
 $(\Delta/\sigma)_{\text{max}} = 0.004$
 $\Delta\rho_{\text{max}} = 0.36 \text{ e \AA}^{-3}$
 $\Delta\rho_{\text{min}} = -0.37 \text{ e \AA}^{-3}$

Table 1

Selected torsion angles (°).

N1A—C1A—C6A—N2A	136.8 (2)	N1B—C1B—C6B—N2B	130.9 (2)
C1A—C6A—N2A—C7A	174.61 (19)	C1B—C6B—N2B—C7B	−174.5 (2)
C6A—N2A—C7A—C12A	49.9 (3)	C6B—N2B—C7B—C12B	50.4 (3)
N2A—C7A—C12A—O2A	47.9 (3)	N2B—C7B—C12B—O2B	49.3 (3)
N1A—C1A—C2A—C3A	55.6 (3)	N1B—C1B—C2B—C3B	54.2 (4)
N1A—C1A—C2A—C4A	−179.0 (2)	N1B—C1B—C2B—C4B	−178.7 (3)
C1A—C2A—C4A—C5A	170.1 (3)	C1B—C2B—C4B—C5B	166.9 (4)
N2A—C7A—C8A—C9A	−66.9 (3)	N2B—C7B—C8B—C9B	−63.6 (3)
C7A—C8A—C9A—C10A	163.1 (2)	C7B—C8B—C9B—C10B	174.5 (2)
C7A—C8A—C9A—C11A	−73.1 (3)	C7B—C8B—C9B—C11B	−63.3 (3)

Table 2

Hydrogen-bonding geometry (Å, °).

D—H...A	D—H	H...A	D...A	D—H...A
N1A—H1A...O1C	0.96 (2)	2.00 (3)	2.927 (4)	161 (3)
N1A—H1A...O1E ⁱ	0.96 (2)	1.96 (3)	2.655 (11)	128 (2)
N1A—H2A...O3B ⁱ	0.99 (3)	1.73 (3)	2.717 (3)	171 (3)
N1A—H3A...O2B ⁱⁱ	0.92 (3)	2.38 (3)	3.117 (3)	136 (2)
N2A—H4A...O3A ⁱⁱⁱ	0.84 (3)	2.15 (3)	2.838 (3)	138 (2)
C1A—H11A...O1A ⁱⁱⁱ	0.93 (3)	2.45 (3)	3.343 (3)	160 (2)
C7A—H71A...O3A ⁱⁱⁱ	1.01 (3)	2.50 (3)	3.167 (3)	123 (2)
N1B—H1B...O1C	0.95 (3)	1.98 (3)	2.930 (4)	171 (3)
N1B—H1B...O1F	0.95 (3)	2.13 (3)	2.914 (13)	139 (3)
N1B—H2B...O3A ⁱⁱⁱ	0.95 (3)	1.88 (3)	2.800 (3)	163 (3)
N1B—H2B...O2A ⁱⁱⁱ	0.95 (3)	2.24 (3)	2.902 (3)	126 (3)
N1B—H3B...O2A	0.96 (3)	1.77 (3)	2.714 (3)	167 (3)
N2B—H4B...O3B ⁱⁱⁱ	0.82 (3)	2.30 (3)	2.992 (3)	142 (3)
C1B—H11B...O1B ⁱⁱⁱ	0.96 (3)	2.43 (3)	3.355 (3)	162 (3)
O1C—H11C...O2B	0.853 (10)	1.933 (12)	2.779 (3)	169 (4)
O1C—H12C...O1D ⁱⁱⁱ	0.848 (10)	1.87 (3)	2.638 (7)	149 (5)
O1D—H11D...O2A	0.848 (10)	2.19 (3)	2.993 (4)	159 (7)
O1D—H12D...O2B	0.849 (10)	2.195 (17)	3.024 (4)	164 (6)
O1E—H11E...O2B	0.851 (11)	1.739 (17)	2.589 (10)	176 (9)
O1E—H12E...O1F ⁱⁱ	0.850 (11)	2.13 (6)	2.733 (16)	127 (9)
O1F—H11F...O2B	0.852 (11)	2.09 (4)	2.896 (13)	156 (8)
O1F—H12F...O3B ⁱⁱⁱ	0.853 (11)	2.42 (6)	3.155 (13)	145 (8)

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

O atoms in water molecules with occupancy less than 0.5 were refined isotropically. Positional parameters were refined for peptide H atoms involved in hydrogen bonds; other peptide H atoms were positioned geometrically and refined as riding, with C—H = 0.95–1.04 Å. Water H atoms were introduced from a consideration of the hydrogen-bond network in the related LL and LF compounds (Görbitz, 2001) and refined with restraints of 0.85 (1) Å for O—H distances and 1.35 (1) Å for H...H distances, together with some weak restraints on hydrogen-bond O...H distances. U_{iso} values for H atoms were set at $1.2U_{\text{eq}}$ of the carrier atom, or $1.5U_{\text{eq}}$ for water, methyl and amine groups. In the absence of significant anomalous scattering effects, Friedel pairs were merged; the absolute configuration is known for naturally occurring amino acids.

Data collection: *SMART* (Bruker, 1998); cell refinement: *SAINTE-Plus* (Bruker, 2001); data reduction: *SAINTE-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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References

- Birkedal, H., Schwarzenbach, D. & Pattison, P. (2002). *Angew. Chem. Int. Ed.* **41**, 754–756.
- Bruker (1998). *SMART*. Version 5.054. Bruker AXS Inc., Madison, Wisconsin, USA.
- Bruker (2000). *SHELXTL*. Version 6.10. Bruker AXS Inc., Madison, Wisconsin, USA.
- Bruker (2001). *SAINTE-Plus*. Version 6.22. Bruker AXS Inc., Madison, Wisconsin, USA.
- Emge, T. J., Agrawal, A., Dalessio, J. P., Dukovic, G., Inghrim, J. A., Janjua, K., Macaluso, M., Robertson, L. L., Stiglic, T. J., Volovik, Y. & Georgiadis, M. (2000). *Acta Cryst.* **C56**, e469–e471.
- Görbitz, C. H. (2001). *Chem. Eur. J.* **7**, 5153–5159.
- Görbitz, C. H. (2003). *New J. Chem.* **27**, 1789–1793.
- Sheldrick, G. M. (1996). *SADABS*. University of Göttingen, Germany.