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# L-Phenylalanyl-L-tryptophan 0.75-hydrate

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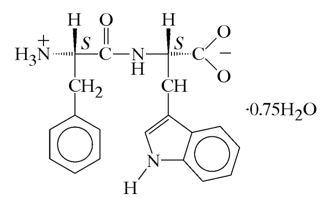
The title compound, $C_{20}H_{21}N_3O_3 \cdot 0.75H_2O$, crystallizes as exceedingly thin fibers. The crystal packing arrangement is related to those of other hydrophobic dipeptides with phenylalanine residues, but the structure has pseudo-tetragonal symmetry in an orthorhombic space group with four peptide molecules and three water molecules in the asymmetric unit.

## Comment

In a series of papers, it has been shown that dipeptides with two hydrophobic residues can form two different classes of nanoporous crystal structures (Görbitz, 2005, and references therein). The FF class, named after L-phenylalanyl-L-phenylalanine, includes also L-phenylalanyl-L-leucine (FL), L-leucyl-L-phenylalanine (LF), L-leucyl-L-leucine (LL) (Görbitz, 2001), L-isoleucyl-L-leucine (Görbitz, 2004) and L-tryptophylglycine (WG) (Emge *et al.*, 2000; Birkedal *et al.*, 2002). The common characteristic of this group is aggregation of peptide molecules into hydrophobic tubes with a hydrophilic core that incorporates a central channel filled with solvent molecules.

As part of an investigation focused on the self-assembly of FF, Reches & Gazit (2003) reported that very thin hollow fibers with a diameter of less than 300 nm could be formed by



FW

dilution of a concentrated solution of the dipeptide in 1,1,1,3,3,3-hexafluoropropan-2-ol with water. Furthermore, it

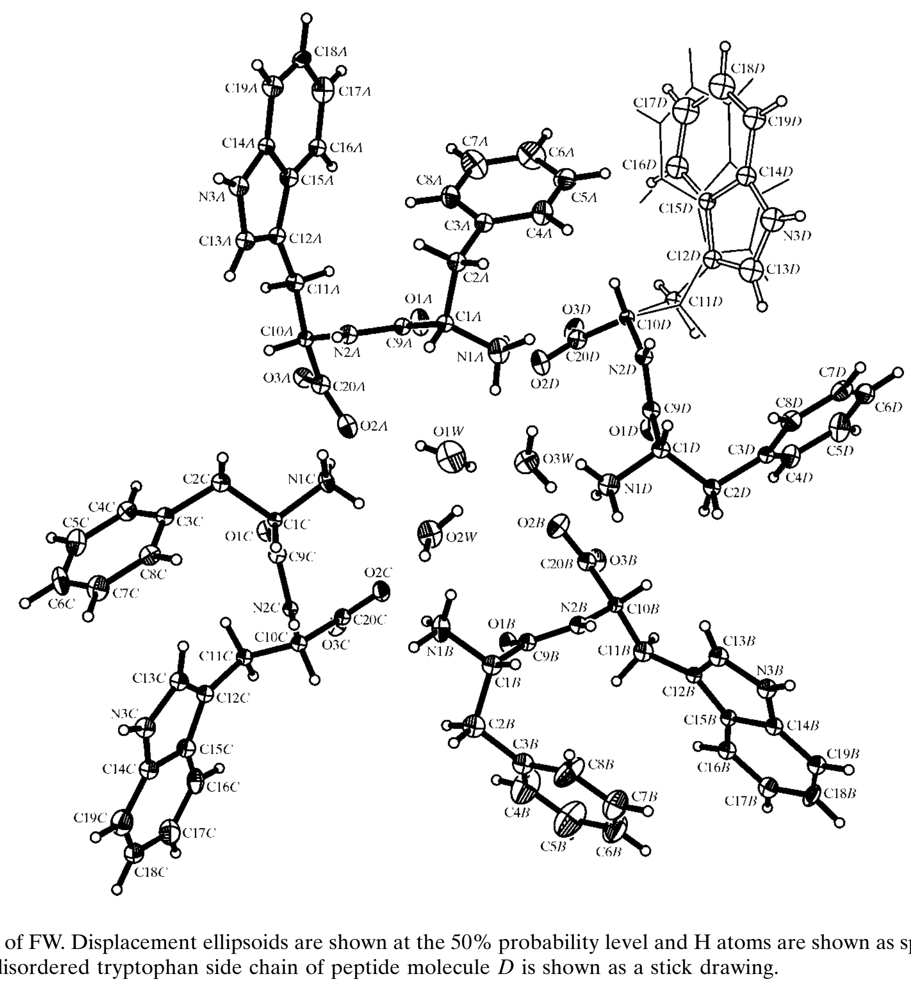


**Figure 1**
The molecular structure of FW. Displacement ellipsoids are shown at the 50% probability level and H atoms are shown as spheres of arbitrary size. The minor position for the disordered tryptophan side chain of peptide molecule *D* is shown as a stick drawing.

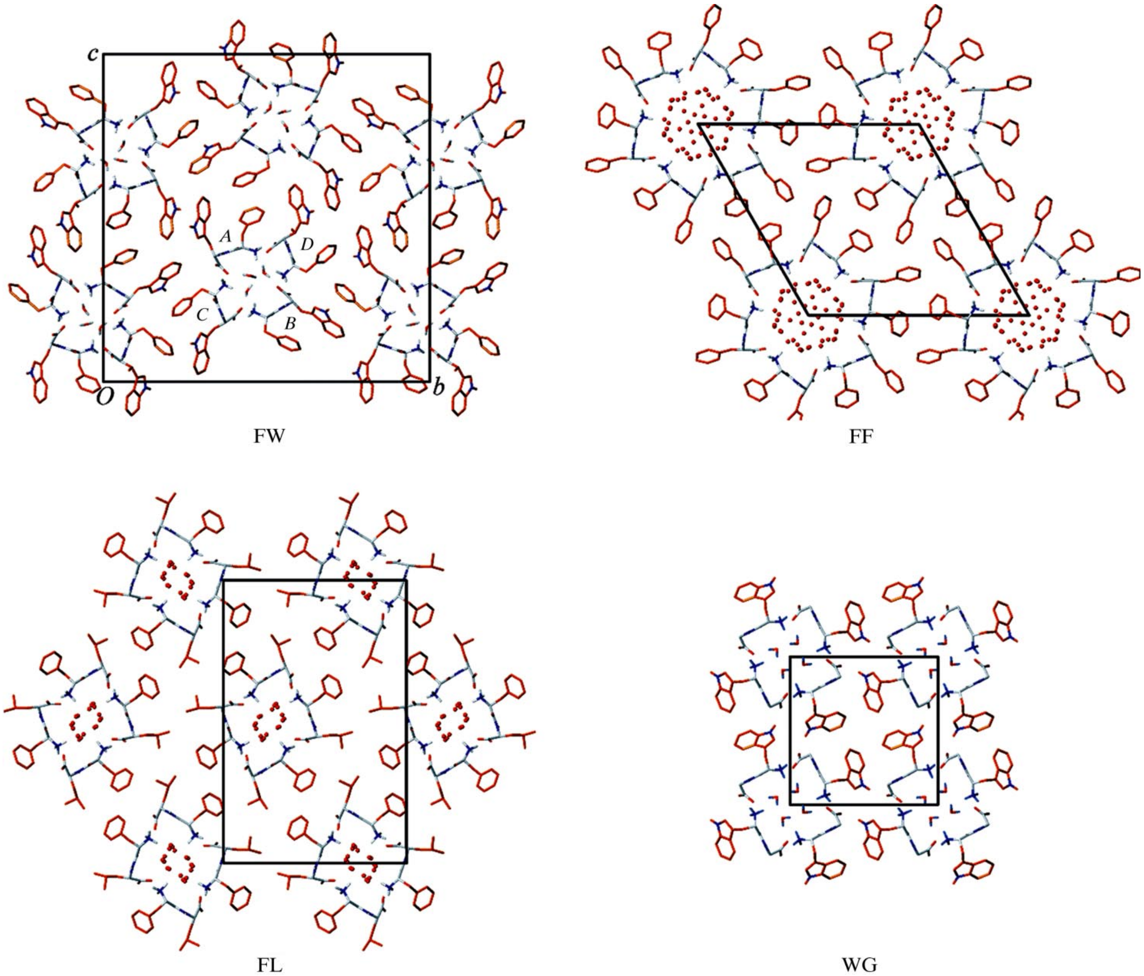



**Figure 2**
The molecular packing and unit cell of FW viewed along the *a* axis. The four independent peptide molecules in the asymmetric unit have been labeled *A*, *B*, *C* and *D*. For comparison, the structures of FF, FL (Görbitz, 2001) and WG (Emge *et al.*, 2000; Birkedal *et al.*, 2002) are shown on the same scale. Atoms in side chains are shown in a darker tone.

was reported that fibers of similar dimensions could be formed by L-phenylalanyl-L-tryptophan (FW). Following continued research efforts on the nature of the FF fibers (Görbitz, 2006), we wondered what the nature of the FW fibers could be and decided to test if it was possible to grow them large enough for single-crystal structure determination. This proved to be a challenging task, but eventually needles with diameters of up to 20 µm were grown by diffusion of acetonitrile into a saturated 1,1,1,3,3,3-hexafluoropropan-2-ol solution of FW (Görbitz, 2006). The structure of this peptide is presented in detail here.

The asymmetric unit of FW, shown in Fig. 1, contains four peptide molecules and three water molecules. The main chains of the peptide molecules have rather similar conformations, but the phenylalanine side chain of molecule *A* is in a *gauche*+ orientation, as opposed to the more common *trans* orientation adopted by molecules *B*, *C* and *D*. Furthermore, even if all tryptophan side chains have well defined *gauche*− $\chi^1$ torsion angles (N2—C10—C11—C12), the $\chi^{2,1}$ torsion angles (C10—C11—C12—C13) differ considerably (Table 1).

The crystal packing arrangement of FW is compared in Fig. 2 with the crystal structures of FF, FL (Görbitz, 2001) and WG (Emge *et al.*, 2000; Birkedal *et al.*, 2002). The hexagonal FF structure and the tetragonal WG structure both have one peptide molecule in the asymmetric unit, while $Z' = 2$ for the orthorhombic structure of FL as well as for the structures of LL, LF (Görbitz, 2001) and IL (Görbitz, 2004) (not shown). It follows that the water-filled channels of FW are the first to be devoid of crystallographic symmetry, and they also have a more irregular appearance than those of the other structures in the family.

In accordance with previous findings, each peptide amino group donates one of its H atoms to a water molecule located in the channel (Table 2). In WG, the side-chain $N^{\varepsilon}$—H donor manages to find a carboxylate acceptor. In the present structure, the equivalent four H atoms are accepted by aromatic groups, two by phenylalanyl side chains and two by the six-membered ring of the tryptophan side chains.

## Experimental

The title compound was obtained from Bachem. Extremely thin fibers were grown by diffusion of acetonitrile into a saturated 1,1,1,3,3,3-hexafluoropropan-2-ol solution (50 µl) of the peptide. A 20 × 18 µm cross-section specimen was used for data collection.

*Crystal data*

$C_{20}H_{21}N_3O_3 \cdot 0.75H_2O$
$M_r$ = 364.91
Orthorhombic, $P2_12_12_1$
$a$ = 5.6207 (6) Å
$b$ = 35.556 (4) Å
$c$ = 35.835 (4) Å
$V$ = 7161.5 (15) Å$^3$
$Z$ = 16
$D_x$ = 1.354 Mg m$^{-3}$
Mo $K\alpha$ radiation
$\mu$ = 0.10 mm$^{-1}$
$T$ = 105 (2) K
Needle, colorless
0.540 × 0.020 × 0.018 mm

*Data collection*

Siemens SMART CCD diffractometer
$\omega$ scans
Absorption correction: multi-scan (*SADABS*; Sheldrick, 1996)
$T_{min}$ = 0.876, $T_{max}$ = 0.998
33425 measured reflections
7087 independent reflections
3234 reflections with $I > 2\sigma(I)$
$R_{int}$ = 0.170
$\theta_{max}$ = 25.0°

*Refinement*

Refinement on $F^2$
$R[F^2 > 2\sigma(F^2)]$ = 0.079
$wR(F^2)$ = 0.182
$S$ = 1.04
7087 reflections
726 parameters
H atoms treated by a mixture of independent and constrained refinement
$w = 1/[\sigma^2(F_o^2) + (0.064P)^2]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max}$ = 0.004
$\Delta\rho_{max}$ = 0.45 e Å$^{-3}$
$\Delta\rho_{min}$ = −0.37 e Å$^{-3}$
Extinction correction: *SHELXL97*
Extinction coefficient: 0.0127 (6)

**Table 1**
Selected torsion angles (°) in molecules *A*–*D* of (I).

| | *A* | *B* | *C* | *D* |
|---|---|---|---|---|
| N1—C1—C9—N2 | 144.6 (7) | 117.9 (8) | 106.6 (8) | 108.5 (8) |
| C1—C9—N2—C10 | −179.0 (6) | 177.9 (6) | −174.2 (6) | −171.3 (6) |
| C9—N2—C10—C20 | 56.0 (10) | 51.2 (10) | 55.1 (9) | 51.2 (9) |
| N2—C10—C20—O2 | 29.6 (11) | 41.7 (11) | 33.3 (10) | 39.2 (11) |
| N1—C1—C2—C3 | 56.7 (8) | 172.8 (7) | −177.0 (6) | 179.3 (6) |
| C1—C2—C3—C4 | −97.2 (10) | −117.6 (10) | −116.5 (9) | −113.4 (9) |
| C1—C2—C3—C8 | 81.5 (10) | 57.7 (12) | 62.9 (11) | 64.3 (10) |
| N2—C10—C11—C12 | −55.5 (8) | −81.0 (8) | −64.7 (8) | −74.6 (10) |
| C10—C11—C12—C13 | −31.9 (11) | −4.1 (12) | 62.5 (11) | 72.9 (17) |
| C10—C11—C12—C15 | 148.0 (8) | −179.0 (8) | −118.0 (9) | −90.6 (14) |

Owing to the combination of a large unit cell and a small crystal, more than 80% of the reflections with $2\theta$ between 40 and 50° were unobserved, resulting in a high value for $R_{int}$. In order not to further impair the rather poor reflection-to-parameter ratio, only O atoms, N atoms and side-chain C atoms that had large $U_{iso}$ values in the initial isotropic refinement were refined anisotropically. Other C atoms were refined isotropically. Covalent bond lengths and angles in each peptide molecule were restrained, using *SHELXTL* (Bruker, 2000) SAME commands, to values fairly similar to those of corresponding geometric parameters in the other three peptide molecules. The tryptophan side chain of peptide molecule *D* is disordered over two nearby positions with occupancies of 0.620 (14) and 0.380 (14), respectively. C- and N-bound H atoms were positioned with idealized geometry and fixed N—H and C—H distances in the range 0.88–1.00 Å. Six water H atoms were positioned by consideration of the local atomic environment, but three of them could also be detected in electron-density maps. The intramolecular water geometries were restrained by tight DFIX commands and the s.u. values associated with these atoms are underestimated. $U_{iso}$(H) atoms were set at $1.2U_{eq}$ of the carrier atom or $1.5U_{eq}$ for amine groups and water molecules. In the absence of significant anomalous scattering effects, 5310 Friedel pairs were merged. The absolute configuration was known for the purchased material.

**Table 2**
Hydrogen-bond geometry (Å, °).

| $D$—H···$A$ | $D$—H | H···$A$ | $D$···$A$ | $D$—H···$A$ |
|---|---|---|---|---|
| N1*A*—H1*A*···O1*W* | 0.91 | 2.17 | 2.917 (11) | 139 |
| N1*A*—H1*A*···O3*W* | 0.91 | 2.45 | 3.135 (10) | 132 |
| N1*A*—H2*A*···O3*D*$^{i}$ | 0.91 | 1.87 | 2.752 (9) | 162 |
| N1*A*—H3*A*···O2*D* | 0.91 | 1.96 | 2.740 (9) | 143 |
| N2*A*—H4*A*···O3*A*$^{i}$ | 0.88 | 1.99 | 2.791 (8) | 151 |
| N3*A*—H5*A*···C19*A*$^{ii}$ | 0.88 | 2.55 | 3.365 (10) | 155 |
| C1*A*—H11*A*···O1*A*$^{i}$ | 1.00 | 2.59 | 3.302 (8) | 128 |
| N1*B*—H1*B*···O2*W*$^{i}$ | 0.91 | 1.92 | 2.731 (10) | 147 |
| N1*B*—H2*B*···O2*C* | 0.91 | 1.88 | 2.751 (9) | 159 |
| N1*B*—H3*B*···O3*C*$^{i}$ | 0.91 | 1.95 | 2.811 (8) | 158 |
| N2*B*—H4*B*···O3*B*$^{i}$ | 0.88 | 2.01 | 2.807 (8) | 150 |
| N3*B*—H5*B*···C5*C*$^{iii}$ | 0.88 | 2.66 | 3.458 (11) | 151 |
| C1*B*—H11*B*···O1*B*$^{i}$ | 1.00 | 2.45 | 3.383 (9) | 155 |
| N1*C*—H1*C*···O2*W* | 0.91 | 1.97 | 2.842 (9) | 160 |
| N1*C*—H2*C*···O3*A*$^{i}$ | 0.91 | 1.91 | 2.800 (9) | 166 |
| N1*C*—H3*C*···O2*A* | 0.91 | 1.89 | 2.788 (9) | 171 |
| N2*C*—H4*C*···O3*C*$^{i}$ | 0.88 | 1.99 | 2.784 (8) | 150 |
| N3*C*—H5*C*···C6*D*$^{iv}$ | 0.88 | 2.77 | 3.542 (10) | 147 |
| C1*C*—H11*C*···O1*C*$^{i}$ | 1.00 | 2.47 | 3.333 (8) | 144 |
| N1*D*—H1*D*···O3*W* | 0.91 | 2.02 | 2.809 (9) | 144 |
| N1*D*—H2*D*···O3*B*$^{i}$ | 0.91 | 1.85 | 2.763 (9) | 175 |
| N1*D*—H3*D*···O2*B* | 0.91 | 1.92 | 2.815 (9) | 166 |
| N2*D*—H4*D*···O3*D*$^{i}$ | 0.88 | 2.00 | 2.730 (8) | 139 |
| N3*D*—H5*D*···C17*C*$^{v}$ | 0.88 | 2.39 | 3.257 (13) | 167 |
| C1*D*—H11*D*···O1*D*$^{i}$ | 1.00 | 2.47 | 3.278 (8) | 138 |
| O1*W*—H11*W*···O2*A* | 0.85 (1) | 1.95 (2) | 2.793 (9) | 172 (9) |
| O1*W*—H12*W*···O3*W*$^{vi}$ | 0.86 (1) | 2.37 (4) | 3.138 (9) | 148 (6) |
| O2*W*—H21*W*···O2*C*$^{i}$ | 0.85 (1) | 1.93 (2) | 2.750 (9) | 159 (7) |
| O2*W*—H22*W*···O3*W* | 0.85 (1) | 1.93 (2) | 2.774 (9) | 170 (9) |
| O3*W*—H31*W*···O2*B*$^{i}$ | 0.86 (1) | 1.84 (2) | 2.684 (8) | 167 (9) |
| O3*W*—H32*W*···O2*D*$^{i}$ | 0.86 (1) | 1.84 (3) | 2.664 (9) | 161 (7) |

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

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: FG3015). Services for accessing these data are described at the back of the journal.

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