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2-(L-Alanylamino)-L-butyric acid

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Key indicators

Single-crystal X-ray study
T = 105 K
Mean σ(C–C) = 0.007 Å
Disorder in main residue
R factor = 0.066
wR factor = 0.145
Data-to-parameter ratio = 8.1

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

The title dipeptide, $C_7H_{14}N_2O_3$, with the common name L-alanyl-L-2-aminobutyric acid, has previously been crystallized as the 0.33-hydrate [Görbitz (2002). *Acta Cryst.* C**58**, o533–o536]. By using 1,1,1,3,3,3-hexafluoropropan-2-ol as the solvent, water-free crystals were obtained. The two crystal structures are related ($P2_1$, Z' = 3 for both), but the molecular conformations and details of the hydrogen-bonding network are different.

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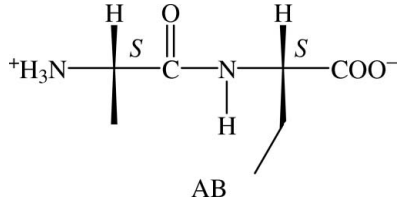
Comment

In a series of investigations, we have focused on the crystal structures of dipeptides with two hydrophobic residues (Görbitz *et al.*, 2005, and references therein). One of the most important results is that compounds constructed using the three amino acids L-alanine (A), L-valine (V) and L-isoleucine (I) as building blocks form nanotubular packing patterns with hydrophobic pores [with the exception of AA (Fletterick *et al.*, 1971) and II (Görbitz, 2004)]. The size of these pores is inversely related to the bulk of the two side chains, and ranges from 3.3 Å for IV and VI (Görbitz, 2003) to 5.2 Å for VA (Görbitz & Gundersen, 1996) and AV (Görbitz, 2002*a*). An attempt to build still larger pores was made by replacing the isopropyl side chains of valine in VA and AV by ethyl groups in BA and AB, where B is the non-natural amino acid L-2-aminobutyric acid. However, nanoporous structures were obtained for neither AB nor BA (Görbitz, 2002*b*); BA proved to have a tetragonal crystal packing arrangment, just like AA, while AB crystallized as a close-packed 0.33-hydrate, AB-w, in the monoclinic space group $P2_1$ with Z' = 3.



AB

The water molecule in the AB-w crystal structure plays a crucial role in completing the three-dimensional hydrogen-bond network. We thus wanted to find out if elimination of water during the crystallization process would force the formation of an alternative, nanoporous, structure related to VA and AV. The solubility of AB is very low in most organic solvents, but is adequate in 1,1,1,3,3,3-hexafluoro-2-propanol. Crystallization experiments with acetonitrile as the precipitant yielded extremely thin needles, as observed for most hydrophobic dipeptides with hexagonal symmetry, but the structure determination of the title compound did not reveal the

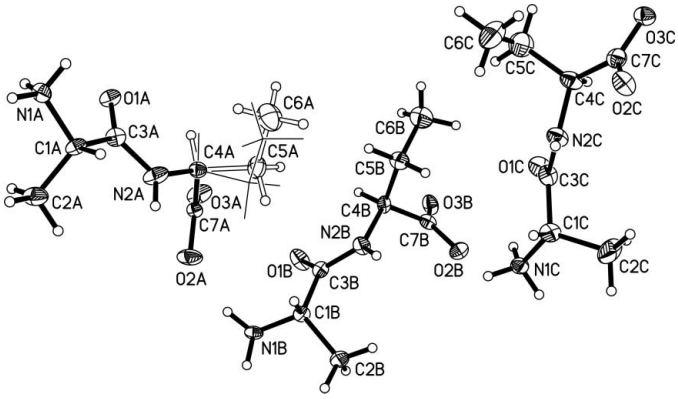


Figure 1
The structure of AB, with the atom-numbering scheme. Displacement ellipsoids are drawn at the 50% probability level and H atoms are shown as small spheres of arbitrary size. Two alternative side-chain orientations, with occupancy 0.67 (2) (open bonds) and 0.33 (2) (stick drawing), are shown for peptide molecule *A*.

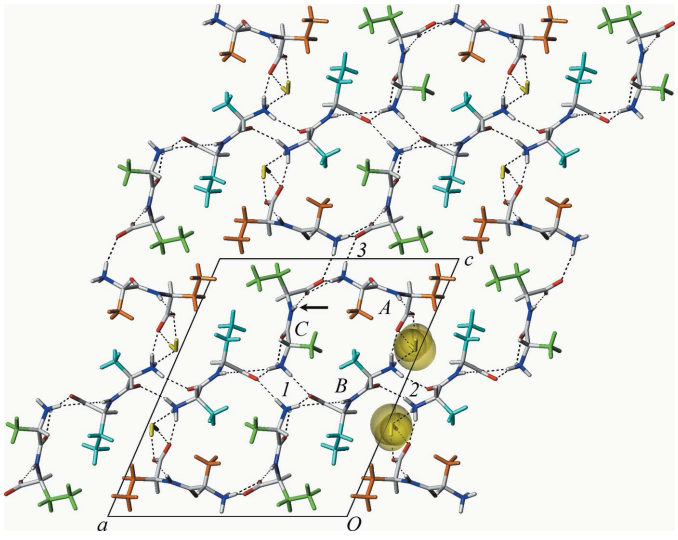


Figure 2
The unit cell and crystal packing of AB-w (Görbitz, 2002*b*). The letters *A*, *B* and *C* identify the three independent peptide molecules in the asymmetric unit, while the numbers 1, 2 and 3 designate three regions of hydrogen bonding (see *Comment*). The side chains of peptide *A* molecules have been coloured in orange, those of *B* molecules in cyan and those of *C* molecules in green. Water molecules have been shown in yellow, and two have been highlighted by van der Waals spheres. The arrow points to atom H4*C*, which is involved in a short hydrogen bond.

anticipated porous structure. Instead, a second monoclinic form with $Z' = 3$ was obtained (Fig. 1).

The unit cells of AB and AB-w shown in Figs. 3 and 2, respectively, have roughly the same cell dimensions (for AB-w, a = 15.43 Å, b = 5.46 Å, c = 18.13 Å, β = 113.5° and V = 1400.8 Å^3; Görbitz, 2002*b*). In both structures, hydrogen bonds are concentrated in three different regions, each involving four peptide molecules (and their translational relatives). As defined in Fig. 2, molecules *B* and *C* interact in region 1, *A* and *B* in region 2, and *A* and *C* in region 3.

Region 1 is almost identical in the two structures, but major differences are evident in region 2, which is where the co-

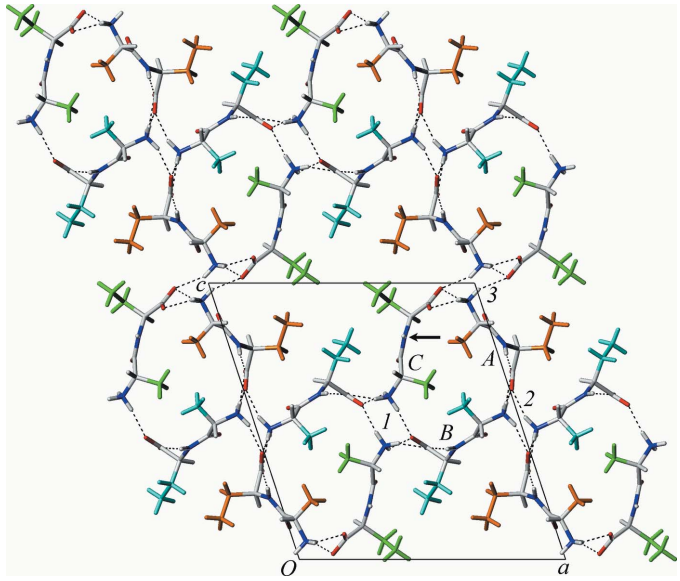


Figure 3
The unit cell and crystal packing of AB. The letters *A*, *B* and *C* identify the three independent peptide molecules in the asymmetric unit, while the numbers 1, 2 and 3 designate three regions of hydrogen bonding (see *Comment*). The side chains of peptide *A* molecules have been coloured in orange, those of *B* molecules in cyan and those of *C* molecules in green. The arrow points to atom H4*C*, which is not involved in a short hydrogen bond as in AB-w.

crystallized water molecule resides in the AB-w structure. In AB, this water molecule is missing, and molecule *A* is displaced to create a new region 2 that is qualitatively identical to region 1 as far as the types of interactions are concerned (Table 2), a major rearrangement compared with AB-w, as detailed in Fig. 4. Region 3 survives the structural modifications largely intact, except that the short >N2*C*—H4*C*···O3*C* hydrogen bond in AB-w (H4*C*···O3*C* 1.995 Å) is broken; atom H4*C* in AB is involved only in a very weak intramolecular interaction. The shortest intermolecular H4*C*···O distance is 3.18 Å (to O1*C*). This failure to utilize the full hydrogen-bonding potential in AB obviously favours the formation of the 0.33 hydrate (AB-w) in the presence of water. In AB-w, all (N–)H atoms participate in short hydrogen bonds.

The overall layout of the crystal packing patterns in Fig. 2 is quite similar, with a large hydrophobic column encompassing six aminobutyric acid side chains, surrounded in a pseudohexagonal manner by six smaller hydrophobic columns, each with three alanine side chains. Nevertheless, subtle changes to the shape and orientation of the aminobutyric columns are evident, resulting not only from the structural rearrangements of region 2, but also from the change of conformation for the aminobutyric acid residue of molecule *C* from *gauche*− for AB-w to *gauche*+ for AB (Table 1).

Experimental

The title compound was obtained from Bachem. Crystals were grown by diffusion of acetonitrile into 50 µl of a 1,1,1,3,3,3-hexafluoro-2-propanol solution containing about 1 mg of the peptide.

Crystal data

$C_7H_{14}N_2O_3$
M_r = 174.20
Monoclinic, $P2_1$
a = 15.665 (5) Å
b = 5.470 (2) Å
c = 17.147 (7) Å
β = 108.233 (9)°
V = 1395.6 (9) Å^3
Z = 6
D_x = 1.244 Mg m^{-3}
Mo $K\alpha$ radiation
Cell parameters from 1396 reflections
θ = 1.3–25.0°
μ = 0.10 mm^{-1}
T = 105 (2) K
Needle, colourless
0.900 × 0.025 × 0.015 mm

Data collection

Siemens SMART CCD area-detector diffractometer
ω scans
Absorption correction: multi-scan (*SADABS*; Sheldrick, 1996)
T_{min} = 0.776, T_{max} = 0.999
7493 measured reflections
2752 independent reflections
1596 reflections with $I > 2\sigma(I)$
R_{int} = 0.094
θ_{max} = 25.0°
$h = -18 \rightarrow 15$
$k = -6 \rightarrow 6$
$l = -15 \rightarrow 20$

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.066
$wR(F^2)$ = 0.145
S = 1.09
2752 reflections
340 parameters
H-atom parameters constrained
$w = 1/[\sigma^2(F_o^2) + (0.0533P)^2]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} < 0.001$
$\Delta\rho_{max}$ = 0.35 e Å^{-3}
$\Delta\rho_{min}$ = −0.33 e Å^{-3}
Extinction correction: *SHELXTL* (Bruker, 2000)
Extinction coefficient: 0.090 (6)

Table 1
Selected torsion angles (°).

N1*A*—C1*A*—C3*A*—N2*A*	166.5 (5)	N2*B*—C4*B*—C7*B*—O2*B*	−42.4 (7)
C1*A*—C3*A*—N2*A*—C4*A*	−170.9 (5)	N2*B*—C4*B*—C5*B*—C6*B*	−179.0 (5)
C3*A*—N2*A*—C4*A*—C7*A*	−115.3 (6)	N1*C*—C1*C*—C3*C*—N2*C*	158.0 (5)
N2*A*—C4*A*—C7*A*—O2*A*	−48.7 (7)	C1*C*—C3*C*—N2*C*—C4*C*	162.8 (5)
N2*A*—C4*A*—C5*A*—C6*A*	−67.1 (12)	C3*C*—N2*C*—C4*C*—C7*C*	−141.8 (6)
N1*B*—C1*B*—C3*B*—N2*B*	174.9 (5)	N2*C*—C4*C*—C7*C*—O2*C*	−17.8 (7)
C1*B*—C3*B*—N2*B*—C4*B*	179.6 (5)	N2*C*—C4*C*—C5*C*—C6*C*	64.1 (7)
C3*B*—N2*B*—C4*B*—C7*B*	−100.2 (6)		

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

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
N1*A*—H1*A*···O3*C*^{i}	0.91	2.00	2.850 (6)	154
N1*A*—H2*A*···O3*C*^{ii}	0.91	1.92	2.808 (7)	164
N1*A*—H3*A*···O2*C*^{iii}	0.91	1.89	2.720 (7)	150
N2*A*—H4*A*···O3*A*^{iv}	0.88	2.02	2.897 (7)	174
C1*A*—H11*A*···O1*A*^{iv}	1.00	2.54	3.172 (7)	121
N1*B*—H1*B*···O2*A*^{v}	0.91	1.93	2.796 (7)	158
N1*B*—H2*B*···O3*A*^{vi}	0.91	1.96	2.808 (6)	154
N1*B*—H3*B*···O2*A*^{vii}	0.91	1.86	2.744 (7)	163
N2*B*—H4*B*···O3*B*^{iv}	0.88	2.03	2.906 (7)	172
C1*B*—H11*B*···O1*B*^{iv}	1.00	2.44	3.220 (7)	134
N1*C*—H1*C*···O3*B*^{iv}	0.91	1.83	2.722 (7)	167
N1*C*—H2*C*···O2*B*^{viii}	0.91	1.91	2.818 (6)	172
N1*C*—H3*C*···O2*B*^{v}	0.91	2.10	2.811 (7)	134
N2*C*—H4*C*···O2*C*^{v}	0.88	2.31	2.612 (6)	100
C1*C*—H11*C*···O1*C*^{iv}	1.00	2.55	3.442 (8)	149

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

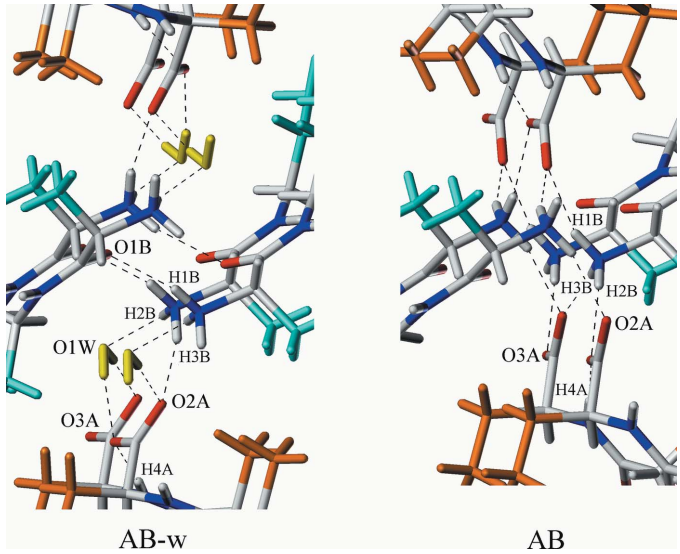


Figure 4
Detail of the interactions in region 2 of the AB-w (left) and AB (right) structures.

H atoms were positioned with idealized geometry and fixed X—H distances (X = C or N) in the range 0.88–1.00 Å. U_{iso}(H) values were $1.2U_{eq}$ of the carrier atom, or $1.5U_{eq}$ for amino and methyl groups. In the absence of significant anomalous scattering effects, 1948 Friedel pairs were merged. The absolute configuration was known for the purchased material.

Data collection: *SMART* (Bruker, 1998); cell refinement: *SAINT* (Bruker, 2001); data reduction: *SAINT*; 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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