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A synthetic fragment of a cyclic depsipeptide, aureobasidine A: *tert*-butoxycarbonyl-L-*allo*-isoleucyl-*N*-methyl-L-valine (Boc-L-*allo*-Ile-L-MeVal-OH)

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Key indicators

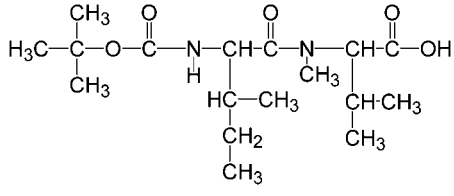
Single-crystal X-ray study
T = 173 K
Mean σ(C–C) = 0.010 Å
R factor = 0.058
wR factor = 0.116
Data-to-parameter ratio = 9.9

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

Crystals of the title compound, $C_{16}H_{30}N_2O_5$, were successfully grown from an ethyl acetate solution. There are two independent molecules in the asymmetric unit. One molecule has a *cis* and the other a *trans* conformation at the urethane linkage, –O—CO—NH–. Independent molecules are linked into chains by NH···O=C and OH···O=C hydrogen bonds along the *c* axis.

Comment

Aureobasidine A is a potent antifungal cyclic depsipeptide, which is composed of one hydroxy acid and eight hydrophobic amino acids and four *N*-methylated amino acids (Takesako *et al.*, 1991). The title compound, (I), is known as a key fragment for the total synthesis of aureobasidine A (Kurome *et al.*, 1996). In this paper, we report the structural data of (I) as one of our synthetic studies of antibacterial peptides containing unusual amino acids (Yamada *et al.*, 2004; Urakawa *et al.*, 2004) and *N*-methylated amino acids (Endo *et al.*, 2003).



(I)

The molecular structure of (I) is shown in Fig. 1. Two independent molecules, (I*a*) and (I*b*), were found in the asymmetric unit. The difference between these two fragments is found at the linkage between Boc (*tert*-butoxycarbonyl) and *allo*-Ile. Each has a *cis* or a *trans* conformation at the urethane linkage, —O—CO—NH—. The *cis* conformation is not common, but it is sometimes observed in short peptides (Oku *et al.*, 2003; Benedetti *et al.*, 1980).

Unprotected C-terminals are found as —COOH groups. There are two pairs of O—H···O and N—H···O hydrogen bonds, as shown in Fig. 2. These four intermolecular interactions link both fragments into chains along the *c* axis. In one pair, the *cis*-urethane in (I*a*) (C115=O112 and N121—H121) forms interactions with a carboxylic acid groups of (I*b*) (C232=O231 and O232—H232). In the other pair, the carboxylic acid group of (I*a*) (C132=O131 and O132—H132) forms interactions with (I*b*) at the NH group of *trans*-urethane (N221—H221) and the amide C=O (*C*222=O221). Shorter distances observed for OH···O=C hydrogen bonds suggest the stronger interaction forces of the carboxyl groups compared with N—H···O=C interactions. These differences

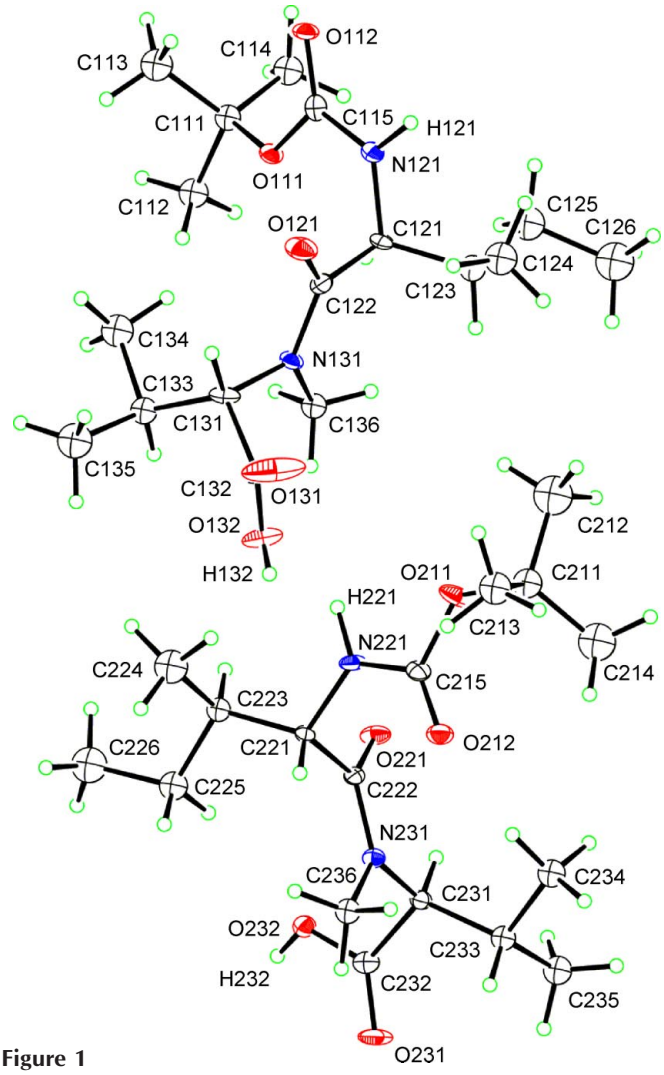


Figure 1
A view of the asymmetric unit of (I), with the atomic numbering scheme. Displacement ellipsoids are drawn at the 20% probability level.

clearly originate from the acidity of the hydrogen-bond-donating groups (OH and NH).

Experimental

The title peptide, (I), was prepared by an improved method, as described in a previous paper (Naito *et al.*, 2005). Crystals of the title compound were successfully grown from ethyl acetate–hexane. Analytical data (melting point, ^{1}H NMR and $[\alpha]_D^{20}$) are in accordance with the expected structure; m.p. 408–409 K, $[\alpha]_D^{20} = -110^\circ$ (*c* 0.1, methanol).

Crystal data

$C_{17}H_{32}N_2O_5$
$M_r = 344.45$
Monoclinic, $P2_1$
$a = 6.359$ (2) Å
$b = 21.158$ (5) Å
$c = 15.374$ (5) Å
$\beta = 95.43$ (2)°
$V = 2059.2$ (11) Å^3
$Z = 4$
$D_x = 1.111$ Mg m^{-3}
Cu $K\alpha$ radiation
Cell parameters from 2607 reflections
$\theta = 3.6$–67.6°
$\mu = 0.67$ mm^{-1}
$T = 173.1$ K
Needle, colorless
0.40 × 0.05 × 0.05 mm

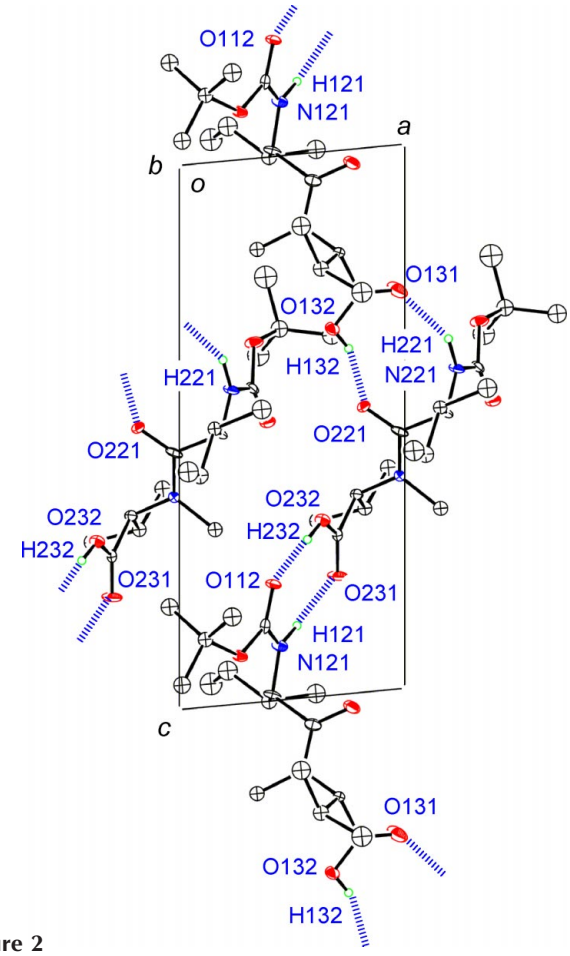


Figure 2
A packing diagram of (I), projected down the *b* axis. Hydrogen bonds are shown as dashed lines. H atoms have been omitted for clarity, except for those on N and O atoms.

Data collection

Rigaku R-AXIS RAPID diffractometer
ω scans
Absorption correction: refined from ΔF (*DIFABS*; Walker & Stuart, 1983)
$T_{min} = 0.810$, $T_{max} = 0.967$
18 832 measured reflections
3748 independent reflections
1729 reflections with $F^2 > 2\sigma(F^2)$
$R_{int} = 0.053$
$\theta_{max} = 68.1°$
$h = -7 \rightarrow 7$
$k = -25 \rightarrow 24$
$l = -18 \rightarrow 17$

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)] = 0.058$
$wR(F^2) = 0.116$
$S = 1.02$
3748 reflections
377 parameters
All H-atom parameters refined
$w = 1/[0.0003F_o^2 + 1.5\sigma(F_o^2)]/(4F_o^2)$
$(\Delta/\sigma)_{max} < 0.001$
$\Delta\rho_{max} = 0.59$ e Å^{-3}
$\Delta\rho_{min} = -0.39$ e Å^{-3}

Table 1
Selected torsion angles (°).

C121—N121—C115—O111	−4.0 (8)	C222—N231—C231—C232	−112.0 (6)
C115—N121—C121—C122	−85.7 (7)	N121—C121—C122—N131	150.6 (6)
C131—N131—C122—C121	−171.1 (5)	N131—C131—C132—O132	−76.3 (8)
C136—N131—C131—C132	73.1 (7)	N221—C221—C222—N231	125.6 (6)
C231—N231—C222—C221	−179.1 (5)	N231—C231—C232—O232	65.6 (6)

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

D—H···A	D—H	H···A	D···A	D—H···A
N221—H221···O131^{i}	0.98	2.03	2.897 (7)	147
O132—H132···O221^{ii}	0.78	1.91	2.650 (6)	157
N121—H121···O231^{iii}	0.98	1.99	2.946 (7)	164
O232—H232···O112^{iv}	0.82	1.84	2.656 (6)	177

Symmetry codes: (i) $x-1, y, z$; (ii) $1+x, y, z$; (iii) $1+x, y, z-1$; (iv) $x-1, y, 1+z$.

Even at low temperature (173 K), with Cu $K\alpha$ radiation, and an area detector, diffraction from the crystal was very weak and insufficient data were available for full anisotropic refinement. For non-H atoms, refinement was performed with anisotropic displacement parameters for main chain atoms (*allo*-Ile and MeVal), and the non-methyl atoms of the Boc group; isotropic refinement was used for the side-chains (*allo*-Ile and MeVal), and for the methyl atoms of the Boc group. H atoms except two OH H atoms of carboxylic acid groups were positioned geometrically, with C—H = 0.98 Å. The OH H atoms were located in a difference Fourier map. They were refined using a riding model, with U_{iso} values constrained to be $1.2U_{eq}$ of the carrier atom. In the absence of significant anomalous scattering effects, Friedel pairs were averaged and the absolute configuration could not be determined from the diffraction experiment. The absolute configuration of the compound was, however, confirmed from the spectroscopic data.

Data collection: *RAPID-AUTO* (Rigaku/MSC, 2003); cell refinement: *RAPID-AUTO*; data reduction: *CrystalStructure* (Rigaku/MSC, 2003); program(s) used to solve structure: *SIR*2002 (Burla *et al.*, 2003); program(s) used to refine structure: *CRYSTALS* (Watkin *et al.*, 1996); molecular graphics: *ORTEP* (Johnson, 1965); software used to prepare material for publication: *CrystalStructure*.

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