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An N-protected depsipeptide free acid prepared by direct synthesis without using a terminal-C protecting group: *tert*-butoxycarbonyl-L-alanyl-L-leucyl-L-lactic acid (Boc-L-Ala-L-Leu-L-Lac-OH)

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Crystals of the title compound, $C_{17}H_{30}N_2O_7$, were successfully grown from ethyl acetate at room temperature. In the crystal structure, a free carboxylic acid group is found at the terminal C atom. The free acid —OH group contributes to a hydrogen-bond network, together with two N—H···O interactions, forming tight packing.

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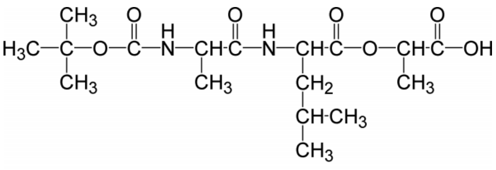
Key indicators

Single-crystal X-ray study
T = 173 K
Mean σ(C–C) = 0.009 Å
R factor = 0.068
wR factor = 0.156
Data-to-parameter ratio = 8.9

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

Comment

The title compound, (I), is an important example of our new approach for the direct synthesis of N-protected depsipeptide free acids (Katakai *et al.*, 2004). In this method, we can obtain a polydepsipeptide, such as poly(L-Ala-L-Leu-L-Lac), without using any protecting group at the C-terminus during the synthesis.



Boc-L-Ala-L-Leu-L-Lac-OH

(I)

The molecular structure of (I) is shown in Fig. 1. The molecule has a free carboxylic acid group at the end of the main chain. Fig. 2 shows a view of the packing; there is one molecule of (I) in the asymmetric unit. The molecules are tightly linked together by three hydrogen bonds to two O atoms, forming an

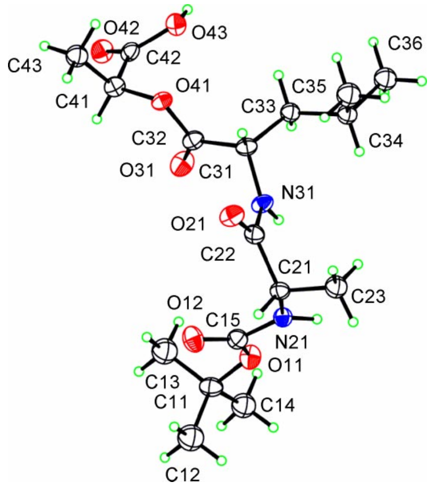


Figure 1
A view of (I), with the atomic numbering scheme. Displacement ellipsoids are drawn at the 20% probability level.

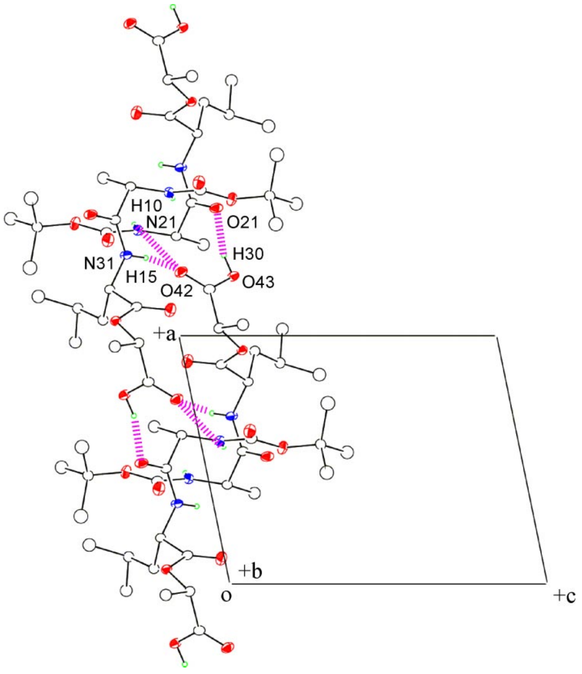


Figure 2
A packing diagram of (I), projected down the *b* axis. Hydrogen bonds are shown as dashed lines.

infinite column along the *a* axis. For O21, the —OH moiety of the carboxylic acid acts as a donor to form an O43—H30$\cdots$O21$^{\rm ii}$ interaction. For O42, there are two donors, forming N21—H10$\cdots$O42$^{\rm i}$ and N31—H1$\cdots$O42$^{\rm i}$ interactions (symmetry codes as in Table 2).

The melting point of (I) is 414–415 K. Interestingly, a lower melting point of 336–337 K has been reported for an isomeric compound, Boc-L-Leu-L-Ala-L-Lac-OH, (II) (Katakai *et al.*, 2004), which has a different order of Ala and Leu residues compared with (I). As found in our previous study (Oku, Shichiri *et al.*, 2003; Oku *et al.*, 2004, 2003*a*,*b*), a smaller number of hydrogen bonds is expected in the crystal packing of (II) and this probably contributes to the lower melting point.

Experimental

The title compound, (I), was isolated from the reaction mixture of a liquid-phase peptide synthesis (Katakai *et al.*, 2004; Ohyama *et al.*, 2000, 2001). Crystals of the title compound were successfully grown from ethyl acetate solution. Analytical data (melting point, ^{1}H NMR, ESI–MS, and $[\alpha]_D^{20}$) are in accordance with the expected structure; m.p. = 414–415 K, $[\alpha]_D^{20} = -29.9^\circ$ (1 mg ml^{-1} in chloroform).

Crystal data

$C_{17}H_{30}N_2O_7$
$M_r = 374.43$
Monoclinic, $P2_1$
$a = 8.826\ (2)$ Å
$b = 10.951\ (2)$ Å
$c = 11.043\ (2)$ Å
$\beta = 101.57\ (2)^\circ$
$V = 1045.7\ (4)$ Å^3
$Z = 2$

$D_x = 1.189$ Mg m^{-3}
Cu $K\alpha$ radiation
Cell parameters from 8126 reflections
$\theta = 4.0$–67.9°
$\mu = 0.77$ mm^{-1}
$T = 173.1$ K
Needle, colorless
$0.40 \times 0.05 \times 0.05$ mm

Data collection

Rigaku R-AXIS RAPID diffractometer
ω scans
Absorption correction: refined from ΔF (*DIFABS*; Walker & Stuart, 1983)
$T_{\rm min} = 0.672$, $T_{\rm max} = 0.962$
16 364 measured reflections

1963 independent reflections
1437 reflections with $F^2 > 2\sigma(F^2)$
$R_{\rm int} = 0.051$
$\theta_{\rm max} = 68.1^\circ$
$h = -10 \rightarrow 10$
$k = -12 \rightarrow 12$
$l = -13 \rightarrow 12$

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)] = 0.068$
$wR(F^2) = 0.156$
$S = 1.26$
1963 reflections
220 parameters

H atoms treated by a mixture of independent and constrained refinement
$w = 1/[0.001F_o^2 + 3\sigma(F_o^2) + 0.5]/(4F_o^2)$
$(\Delta/\sigma)_{\rm max} = 0.009$
$\Delta\rho_{\rm max} = 0.36$ e Å^{-3}
$\Delta\rho_{\rm min} = -0.38$ e Å^{-3}

Table 1
Selected torsion angles (°).

O11—C15—N21—C21	176.1 (4)	N31—C31—C32—O41	142.0 (5)
C15—N21—C21—C22	−75.7 (6)	C31—C32—O41—C41	171.1 (4)
N21—C21—C22—N31	−32.6 (8)	C32—O41—C41—C42	−75.1 (5)
C21—C22—N31—C31	−171.8 (5)	O41—C41—C42—O43	−23.8 (7)
C22—N31—C31—C32	−101.6 (6)		

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

D—H$\cdots A$	D—H	H$\cdots A$	$D\cdots A$	D—H$\cdots A$
N21—H10$\cdots$O42$^{\rm i}$	0.95	2.60	3.015 (6)	107
N31—H15$\cdots$O42$^{\rm i}$	0.95	1.96	2.896 (7)	170
O43—H30$\cdots$O21$^{\rm ii}$	0.90	1.72	2.590 (6)	161

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

For non-H atoms, refinement was performed with anisotropic displacement parameters mostly for main-chain atoms and isotropic refinements for the side chains (Ala, Leu and Lac), owing to the limited number of observed reflections. H atoms were positioned geometrically, except for H30, which was found in a difference Fourier map. They were refined using a riding model, with $U_{\rm iso} = 1.2U_{\rm eq}$ of the carrier atom. The absolute stereochemistry was not established from the diffraction experiment. Friedel pairs were averaged. The absolute configuration was confirmed from the analytical data, α_D, of the compound.

Data collection: *RAPID-AUTO* (Rigaku/MSC and Rigaku, 2003); cell refinement: *RAPID-AUTO*; data reduction: *CrystalStructure* (Rigaku/MSC and Rigaku, 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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