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Montanastatin, cyclo[–(Val-D-Hyv-D-Val-Lac)$_2$–]

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Key indicators

Single-crystal X-ray study
T = 100 K
Mean σ(C–C) = 0.003 Å
R factor = 0.049
wR factor = 0.111
Data-to-parameter ratio = 19.5

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

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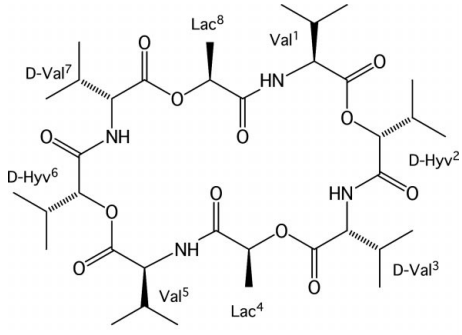
Crystals of montanastatin anhydride, $C_{36}H_{60}N_4O_{12}$, were grown from a hexylene glycol solution. A crystallographic twofold axis runs through the centre of the molecule. The aliphatic side chains located on one side of the peptide ring form a hydrophobic region. The shape of the whole molecule is rectangular and is similar to the structure of the valinomycin analogue, *viz.* cyclo[–(D-Val-L-Hyv-L-Val-D-Hyv)$_2$–].

Comment

Montanastatin has been isolated from a Montana soil actinomycete, *Streptomyces anulatus*, as a cancer-cell-growth inhibitory cyclooctadepsipeptide (Pettit *et al.*, 1999). This peptide contains α-hydroxyisovaleric acid (Hyv) and lactic acid (Lac), and is composed of two repeating units of tetrapeptide, Val-D-Hyv-D-Val-Lac. Such a repeated sequence is similar to that in valinomycin, which has three repeating units. Montanastatin gives some solvated crystals (refcode KAHMAH in the Cambridge Structural Database; Allen & Kennard, 1993). An anhydrous form, (I), was obtained from hexylene glycol solution, and its structure is reported here.



(I)

A crystallographic twofold axis is located in the montanastatin molecule; the asymmetric unit is thus one half molecule. The backbone shape is a rectangular ring (Fig. 1*a*). The Lac residues shift from the peptide ring (Fig. 1*b*) making a small loop with an intramolecular hydrogen bond between D-Val^3 and Lac^4: N_3···O_4 (Table 1). The aliphatic side chains of Val^1, D-Hyv^2 and D-Val^3 are located on one side of the peptide ring (Fig. 1*b*), forming a hydrophobic region. Only the methyl groups of Lac residues are located on the other side. In this structure, the chiral sequence of (L—D—D—L) is important for creating a hydrophobic region. However, the relative positions of the side chains are different from those of valinomycin (Duax *et al.*, 1972; Karle, 1975). The conformational characteristics of montanastatin are similar to those of a valinomycin analogue, *cyclo*[–D-Val-L-Hyv-L-Val-D-Hyv)$_2$–] (Grochulski *et al.*, 1992).

Experimental

Hyv was synthesized according to a previously reported method (Gisin *et al.*, 1969), and montanastatin was synthsized by a conventional liquid-phase method. Montanastatin (20 mg) was dissolved in 0.2–0.3 ml hexylene glycol, and crystals grew after about 30 d at room temperature. A crystal was mounted on a nylon loop (Hampton Research Inc., USA) with glycerol and was flash-frozen under a nitrogen stream at 100 K.

Crystal data

$C_{36}H_{60}N_4O_{12}$
M_r = 740.88
Orthorhombic, $C222_1$
a = 13.488 (6) Å
b = 17.868 (7) Å
c = 16.452 (7) Å
V = 3965 (3) Å^3
Z = 4
D_x = 1.241 Mg m^{-3}
Mo $K\alpha$ radiation
Cell parameters from 3994 reflections
θ = 2.3–28.0°
μ = 0.09 mm^{-1}
T = 100 (2) K
Block, colourless
0.32 × 0.24 × 0.20 mm

Data collection

Bruker SMART APEX CCD diffractometer
ω scans
Absorption correction: multi-scan (*SADABS*; Sheldrick, 1996)
T_{min} = 0.854, T_{max} = 0.982
13003 measured reflections
4717 independent reflections
4545 reflections with $I > 2\sigma(I)$
R_{int} = 0.031
θ_{max} = 28.6°
$h = -17 \rightarrow 17$
$k = -15 \rightarrow 23$
$l = -22 \rightarrow 22$

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.049
$wR(F^2)$ = 0.111
S = 1.18
4717 reflections
242 parameters
H-atom parameters constrained
$w = 1/[\sigma^2(F_o^2) + (0.0472P)^2 + 1.956P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} < 0.001$
$\Delta\rho_{max}$ = 0.32 e Å^{-3}
$\Delta\rho_{min}$ = −0.22 e Å^{-3}
Absolute structure: (Flack, 1983), 1912 Friedel pairs
Flack parameter = 0.1 (9)

Table 1
Hydrogen-bonding geometry (Å, °).

D—H···A	D—H	H···A	D···A	D—H···A
N_1—H5_1···O_2^{i}	0.880	2.037	2.901 (2)	167.1
N_3—H22_3···O_4^{ii}	0.880	2.363	3.037 (2)	133.6

Symmetry codes: (i) $\frac{1}{2}+x, \frac{3}{2}-y, 2-z$; (ii) $1-x, y, \frac{3}{2}-z$.

The structure of montanastatin is consistent with the absolute configurations of the amino acids and carboxylic acids, Val, D-Val, D-Hyv and Lac, although the Flack test results are meaningless.

Data collection: *SMART* (Bruker, 1998); cell refinement: *SMART*; data reduction: *SAINT-Plus* (Bruker, 1998); program(s) used to solve structure: *SHELXS*97 (Sheldrick, 1997); program(s) used to refine structure: *SHELXL*97 (Sheldrick, 1997); molecular graphics: *PLATON* (Spek, 2001); software used to prepare material for publication: *PARST* (Nardelli, 1995).

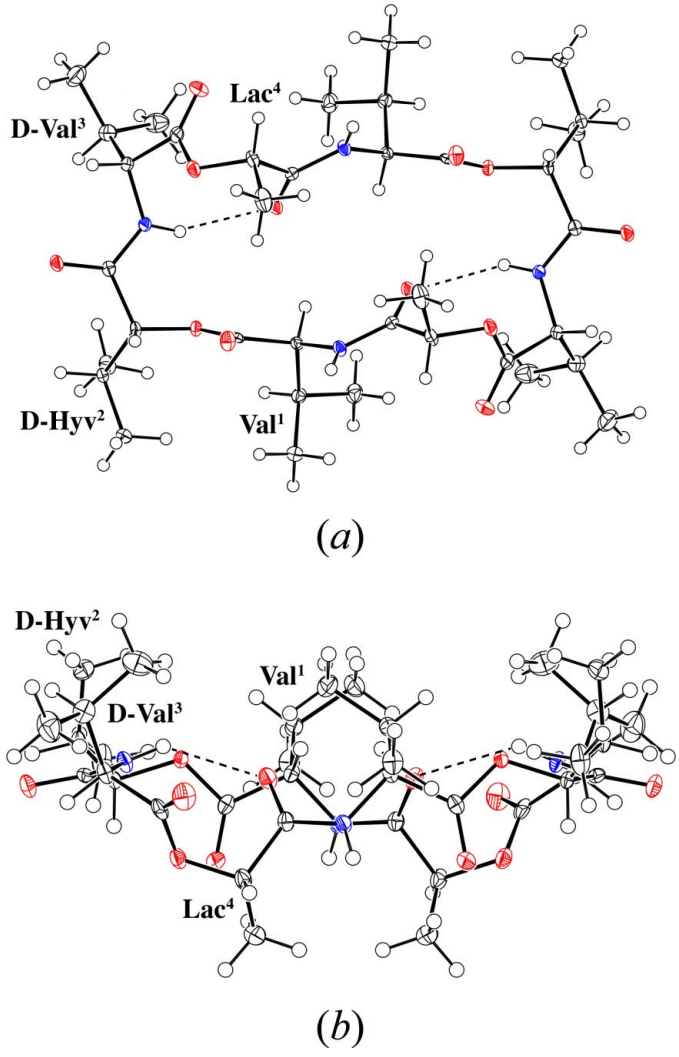


Figure 1
The structure of montanastatin (*PLATON*; Spek, 2001). Top (*a*) and side (*b*) views for the depsipeptide ring are shown. Dashed lines represent hydrogen bonds.

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