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A peptide sequence containing a hydroxy acid residue: (*S*)-2-hydroxy-3-methylbutanoyl-L-alanyl-L-proline benzyl ester (H–L-Hmb–L-Ala–L-Pro–OBzl)

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Key indicators

Single-crystal X-ray study
T = 173 K
Mean σ(C–C) = 0.007 Å
R factor = 0.079
wR factor = 0.067
Data-to-parameter ratio = 8.6

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

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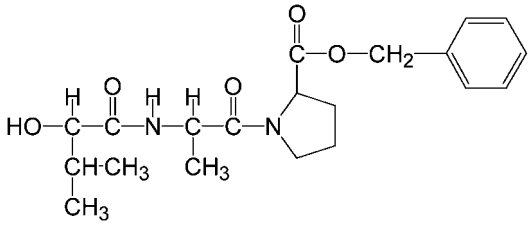
Crystals of the title compound, $C_{20}H_{28}N_2O_5$, have been successfully grown from dimethylformamide–water at room temperature. In the packing structure, no NH···O=C interactions were observed. Independent molecules are connected together *via* an –OH···O=C hydrogen bond.

Comment

The title compound, (I), is a derivative of the –Ala–Pro– sequence, which has been extensively studied in our laboratory (*e.g.* Oku *et al.*, 2003; Ishiguro *et al.*, 2001; Abe *et al.*, 2001) to make synthetic antigens and enzyme active sites. In this paper, (I) has been prepared as a hydroxy acid analogue of the –Val–Ala–Pro– sequence. Our ongoing studies of depsipetides have shown that those molecules containing hydroxy acid residues often form single crystals suitable for X-ray crystallography (Ohyama *et al.*, 2000, 2001), in contrast with the corresponding amino acid compounds. In this case, a sequence containing –Val–Ala–Pro–, such as Boc–Val–Ala–Pro–OBzl (Boc is *tert*-butyloxycarbonyl) gives an oily state at room temperature. To show an example of the excellent crystallinity of hydroxy acid compounds, the crystal structure of (I) has been determined.



H-L-Hmb-L-Ala-L-Pro-OBzl

(I)

The molecular structure of (I) is shown in Fig. 1. The molecule has an extended sheet-like conformation (see torsion angles in Table 1). Disordered atoms (C134 and C136) are observed in the side chain of Pro, due to the conformational isomerism of the five-membered ring in the Pro residue. This side-chain disorder leads to unusual geometrical parameters, such as the close contact between atoms C136 and O131.

No intermolecular NH···O=C hydrogen bonds are observed in the packing structure of (I). As shown in Fig. 2, the molecules are connected together *via* an —OH···O=C interaction along the *a* axis, to give an infinite arrangement.

Generally, intermolecular NH···O=C networks connect peptides together into an infinite antiparallel β-sheet aggre-

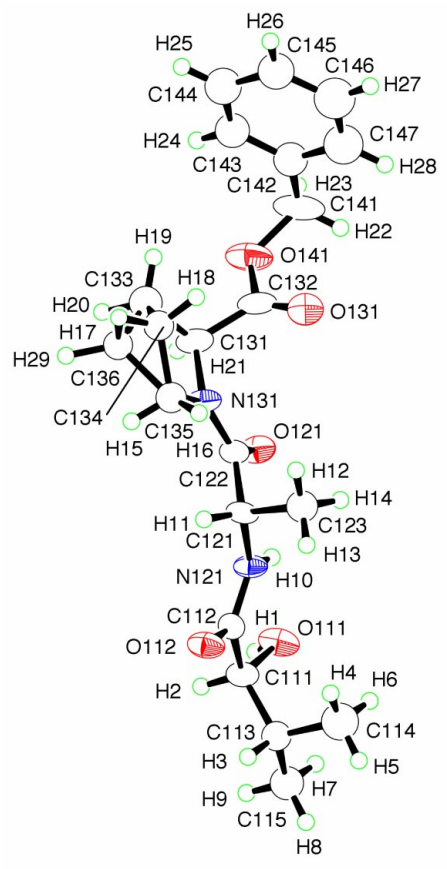


Figure 1
A view of (I) with the atomic numbering scheme. Displacement ellipsoids are drawn at the 50% probability level and H atoms are shown as small spheres of arbitrary radii.

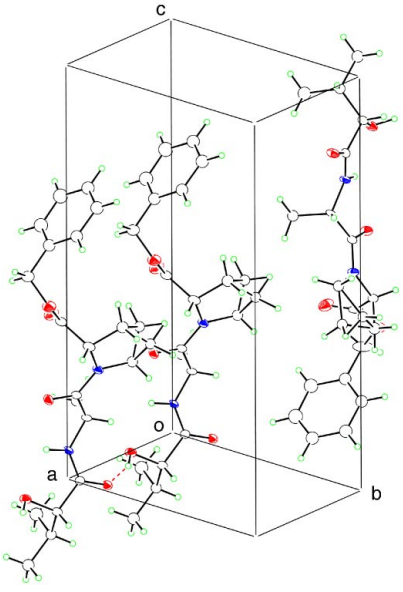


Figure 2
A packing view of (I). Hydrogen bonds are indicated by dotted lines.

gation in crystals (*e.g.* Antolić *et al.*, 1999; Ashida *et al.*, 1981; Cruse *et al.*, 1982). This is an important crystallizing force for short peptide compounds, although no such interactions were observed in the packing of (I).

Experimental

The title peptide, (I), was prepared by conventional liquid-phase peptide synthesis. Crystals of (I) were successfully grown from dimethylformamide-water. Analytical data (^{1}H NMR, ESI–MS and $[\alpha]_D^{20}$) were in accordance with the expected structure; $[\alpha]_D^{20}$ = −163.5° (*c* 0.1, methanol).

Crystal data

$C_{20}H_{28}N_2O_5$
M_r = 376.45
Monoclinic, $P2_1$
a = 5.8977 (7) Å
b = 10.1767 (16) Å
c = 16.941 (2) Å
β = 94.394 (10)°
V = 1013.8 (2) Å^3
Z = 2
D_x = 1.233 Mg m^{-3}
Cu $K\alpha$ radiation
Cell parameters from 9297 reflections
θ = 4.3–68.3°
μ = 0.73 mm^{-1}
T = 173.1 K
Platelet, colourless
0.50 × 0.50 × 0.05 mm

Data collection

Rigaku RAXIS-RAPID area-detector diffractometer
ω scans
Absorption correction: refined on ΔF (*DIFABS*; Walker & Stuart, 1983)
T_{min} = 0.730, T_{max} = 0.964
16 496 measured reflections
1844 independent reflections
1799 reflections with $F^2 > 2.0\sigma(F^2)$
R_{int} = 0.055
θ_{max} = 65.5°
$h = -7 \rightarrow 7$
$k = -11 \rightarrow 11$
$l = -20 \rightarrow 20$

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.079
$wR(F^2)$ = 0.067
S = 1.01
1844 reflections
215 parameters
H-atom parameters constrained
Weighting scheme: Chebychev polynomial with 3 parameters (Carruthers & Watkin, 1979); 25758.000, 31369.700, 698.529
$(\Delta/\sigma)_{max} < 0.001$
$\Delta\rho_{max}$ = 0.59 e Å^{-3}
$\Delta\rho_{min}$ = −0.41 e Å^{-3}

Table 1
Selected torsion angles(°).

O111—C111—C112—N121	6.4 (6)	C122—N131—C131—C132	−73.6 (5)
C111—C112—N121—C121	177.5 (4)	N131—C131—C132—O141	167.0 (3)
C112—N121—C121—C122	−148.9 (4)	C131—C132—O141—C141	166.4 (4)
N121—C121—C122—N131	156.4 (4)	C132—O141—C141—C142	−76.5 (5)
C121—C122—N131—C131	179.7 (4)		

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

D—H···A	D—H	H···A	D···A	D—H···A
O111—H1···O112^{i}	0.93	1.93	2.814 (4)	159
N121—H10···O111	0.95	2.08	2.562 (3)	110
N121—H10···O121	0.95	2.25	2.628 (4)	103

Symmetry code: (i) $1 + x, y, z$.

For non-H atoms, the refinement was performed with anisotropic displacement parameters for main-chain atoms, and with isotropic refinements for side-chains (Hmb, Ala and Pro) and protecting groups (benzene ring). This was due to the limited numbers of observed reflections. Even with the techniques available, such as low temperature (173 K), Cu $K\alpha$ radiation and an area detector, reflections from the crystal were too weak to collect enough data for anisotropic refinement. H atoms were placed geometrically, except for atoms H1, H17, H18 and H29 which were located in a difference

Fourier map. They were refined with a riding model, with U_{iso}(H) = 1.2U_{iso} of the parent atom. The absolute stereochemistry of (I) was not established from the diffraction experiment and Friedel pairs were averaged. The absolute configuration was confirmed from the spectroscopic data, α_D, of the compound.

Data collection: *RAPID-AUTO* (Molecular Structure Corporation & Rigaku Corporation, 2003); cell refinement: *RAPID-AUTO*; data reduction: *CrystalStructure* (Molecular Structure Corporation & Rigaku Corporation, 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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