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The peptide (*Z*)-Pro–Leuol

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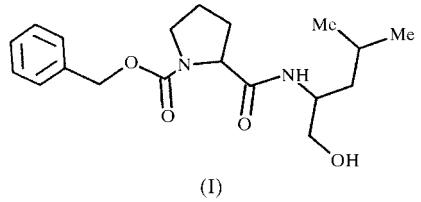
The structure of the synthetic protected dipeptide (*Z*)-Pro–Leuol [systematic name: benzyl 2-(1-hydroxymethyl-3-methylbutylaminocarbonyl)pyrrolidine-1-carboxylate], $C_{19}H_{28}N_2O_4$, was determined by X-ray crystallography. The peptide adopts a novel backbone conformation compared with other longer oligopeptides containing Pro–Leuol.

Comment

The sequence Pro–Leucinol is the C-terminal dipeptide of several naturally occurring peptaibols, *i.e.* peptides containing α-aminoisobutyric acid (Aib) and an alcoholic C-terminus (Brückner & Graf, 1983; Benedetti *et al.*, 1982), among them harzianin (Rebuffat *et al.*, 1994, 1995), hypomuricin (Becker, 1996; Becker *et al.*, 1997) and trichovirin (Kieß & Brückner, 1990; Brückner *et al.*, 1991). The crystal structures of the four, eight and twelve C-terminal residues comprising peptides of trichovirin were solved by our group (Geßmann *et al.*, 1994, 1999). Interestingly, while proline in the longer peptides adopts main-chain torsion angles φ and ψ which lie in the 3_{10}-helical region, proline in the dipeptide adopts a semi-extended conformation with φ and ψ values of −71.3 and 146.1°, respectively. The φ values of Leu in the longer peptides have



(I)

been observed as unusually small for the helical region, while the φ value (−77.8°) of Leu in the title compound, (I), lies inside the helical region. The pyrrolidine ring of Pro adopts the C_γ-*exo* (Ashida & Kakudo, 1974) conformation, with puckering parameters (Cremer & Pople, 1975) Q = 0.284 Å and Φ = 292.98°. In the crystal, the peptides are hydrogen bonded along the [$\bar{1}$00] direction *via* two hydrogen bonds (see Table 2). In the other directions, these columns of molecules are packed *via* apolar crystal contacts.

Experimental

(*Z*)-Pro–Leuol was synthezized from commercially available (*Z*)-L-Pro–OH (from Bachem, Bubendorf, Switzerland) and H–L-Leuol (from Fluka, Buchs, Switzerland) by using WSC (water-soluble carbodiimide) and HOBt (1-hydroxybezotrialole) as coupling reagents. This approach is known to prevent racemization. Further, it is known that C-terminal Pro in peptide coupling does not racemize as no azlactone can be formed on activation. Chiral purity was also confirmed by enantioselective gas chromatography of a total hydrolysate of the dipeptide on a Chirasil–L-Val capillary column according to procedures described previously (Brückner & Jung, 1982). For this reason, the Flack parameter was not refined. The protected dipeptide was crystallized from a hot ethanol–water mixture (60:40). Very few plate-like crystals were obtained and all reached a length of 1 mm. The crystals were fragile and easily damaged. An intact crystal was sealed in a glass capillary for data collection. The collimator used has a diameter of 1 mm.

Crystal data

$C_{19}H_{28}N_2O_4$
M_r = 348.44
Orthorhombic, $P2_12_12_1$
a = 6.371 (4) Å
b = 8.824 (8) Å
c = 34.303 (10) Å
V = 1928 (2) Å^3
Z = 4
D_x = 1.200 Mg m^{-3}
Cu $K\alpha$ radiation
Cell parameters from 25 reflections
θ = 10.02–21.41°
μ = 0.682 mm^{-1}
T = 293 K
Rod, colourless
1.0 × 0.4 × 0.2 mm

Data collection

CAD-4 diffractometer
ω–$\frac{4}{3}\theta$ scans
Absorption correction: analytical (*Xtal*3.7 *ABSORB*; Hall *et al.*, 2000)
T_{min} = 0.736, T_{max} = 0.875
4821 measured reflections
2111 independent reflections
1398 reflections with $I > 2.5\sigma(I)$
R_{int} = 0.069
θ_{max} = 70.02°
$h = -6 \rightarrow 7$
$k = -8 \rightarrow 10$
$l = -33 \rightarrow 41$
5 standard reflections
frequency: 3600 min
intensity decay: 11.2%

Refinement

Refinement on F^2
$R(F)$ = 0.067
$wR(F^2)$ = 0.093
S = 1.995
2049 reflections
227 parameters
H-atom parameters constrained
$w = 1/\sigma^2(F)$
$(\Delta/\sigma)_{max} < 0.001$
$\Delta\rho_{max}$ = 0.388 e Å^{-3}
$\Delta\rho_{min}$ = −0.489 e Å^{-3}
Extinction correction: Zachariasen (1967)
Extinction coefficient: 4647.9 (18)
Absolute structure: assumed from synthesis

Table 1
Selected torsion angles (°).

C06—C07—O01—C08	−164.0 (4)	C1*A*—C1*B*—C1*G*—C1*D*	28.3 (7)
C07—O01—C08—N1	−174.0 (4)	C1*B*—C1*G*—C1*D*—N1	−29.6 (6)
O01—C08—N1—C1*A*	0.5 (6)	C1*A*—N1—C1*D*—C1*G*	20.1 (5)
C08—N1—C1*A*—C1	−71.3 (6)	C1*D*—N1—C1*A*—C1*B*	−3.6 (5)
N1—C1*A*—C1—N2	146.1 (4)	N1—C1A—C1*B*—C1*G*	−15.1 (6)
C1*A*—C1—N2—C2*A*	171.2 (4)	N2—C2*A*—C2*B*—C2*G*	−177.2 (4)
C1—N2—C2*A*—C2	−77.8 (5)	C2*A*—C2*B*—C2*G*—C2*D*1	−179.2 (5)
N2—C2*A*—C2—O2	−53.9 (5)	C2*A*—C2*B*—C2*G*—C2*D*2	58.7 (7)

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

D—H···A	D—H	H···A	D···A	D—H···A
$N2^{i}$—$H2^{i}$···O2	0.92	2.13	3.044 (5)	176
$O2^{i}$—H^{i}···O1	0.893 (5)	2.053 (5)	2.733 (5)	132.14 (?)

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

Data were collected from θ = 1–70°. Subsequently, 1978 Friedel pairs were measured, from θ = 1–49°. All equivalent data were averaged, including the Friedel pairs. H atoms were calculated and a riding model was used during the refinement. The C-terminal H atom was located by difference Fourier syntheses and its displacement parameter was fixed during refinement.

Data collection: *CAD*-4 *Software* (Enraf–Nonius, 1989); cell refinement: *CAD*-4 *Software*; data reduction: *Xtal*3.7 *DIFDAT ABSORB ADDREF* (Hall *et al.*, 2000); program(s) used to solve structure: *Xtal*3.7 *CRISP*; program(s) used to refine structure: *Xtal*3.7 *CRILSQ*; software used to prepare material for publication: *Xtal*3.7 *BONDLA CIFIO*.

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