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Key indicators

Single-crystal X-ray study
 $T = 120\text{ K}$
 Mean $\sigma(\text{C}-\text{C}) = 0.003\text{ \AA}$
 R factor = 0.034
 wR factor = 0.077
 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>.

(3*R*,4*R*,5*S*)-5-(Acetamidomethyl)-*N*-benzyl-3,4-dihydroxytetrahydrofuran-3-carboxamide

The title compound, $\text{C}_{15}\text{H}_{20}\text{N}_2\text{O}_5$, is the first example of a branched tetrahydrofuran sugar amino acid dipeptide isostere incorporated into a peptidomimetic. The crystal structure contains intermolecular $\text{N}-\text{H}\cdots\text{O}$ and $\text{O}-\text{H}\cdots\text{O}$ hydrogen bonds.

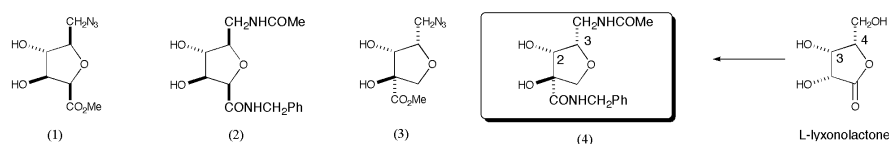
Comment

δ -Tetrahydrofuran (THF) sugar amino acids (SAA) have been extensively investigated as dipeptide isosteres (Baron *et al.*, 2004; Grotenberg *et al.*, 2004; Raunkjær *et al.*, 2004). Introduction of δ -THF SAA building blocks has been shown to induce secondary structural features such as β -turn-like structures (Chakraborty *et al.*, 2004; Smith *et al.*, 2003; Hungerford *et al.*, 2000) and helices (Claridge *et al.*, 1999; Osterkamp *et al.*, 2000) in small peptidomimetics. All the previously reported δ -THF SAA scaffolds have linear carbon chains, as in (1), which has been incorporated into peptidomimetics such as (2). The synthesis of branched sugar lactones (Hotchkiss *et al.*, 2004) has allowed ready access to a new class of δ -THF SAA building blocks, such as (3), which contain a branched carbon chain. The monomer (3) was prepared as an oil from *L*-lyxonolactone in a sequence in which the branched carbon chain was introduced by the Ho (1978, 1985*a,b*) crossed aldol procedure, and the δ -THF ring was subsequently formed by an intramolecular alkylation. The branched scaffold (3) was transformed into the crystalline branched peptidomimetic (4).

Received 10 December 2004

Accepted 14 January 2005

Online 29 January 2005



The structure of (4) has been determined in order to remove any ambiguity in the stereochemical outcomes of either the aldol or the ring closure reactions. Additionally, the crystal structure of (4) may give some indication of the

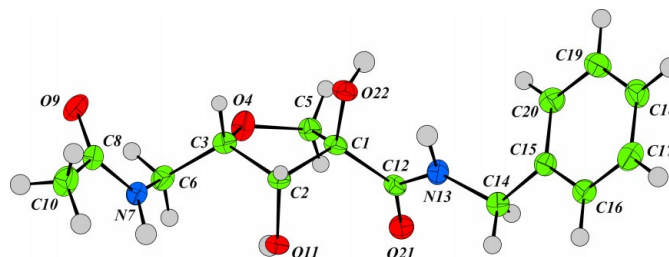


Figure 1
 The molecular structure of (4), with displacement ellipsoids drawn at the 50% probability level.

secondary structural motif likely to be induced by the incorporation of the monomer (3) into peptidomimetics. The molecular structure of (4) is shown in Fig. 1. As usually expected for sugar derivatives, there are intermolecular hydrogen bonds (Table 2 and Fig. 2).

Experimental

Compound (4) was dissolved in acetone in a small glass cylinder and then crystallized as the solvent evaporated slowly to give colourless needle-like crystals.

Crystal data

$C_{15}H_{20}N_2O_5$	Mo $K\alpha$ radiation
$M_r = 308.33$	Cell parameters from 3224 reflections
Orthorhombic, $P2_12_12_1$	$\theta = 5-27^\circ$
$a = 15.3802$ (6) Å	$\mu = 0.10$ mm $^{-1}$
$b = 5.4473$ (2) Å	$T = 120$ K
$c = 18.0635$ (8) Å	Needle, colourless
$V = 1513.37$ (10) Å 3	$0.40 \times 0.04 \times 0.02$ mm
$Z = 4$	
$D_x = 1.353$ Mg m $^{-3}$	

Data collection

Nonius KappaCCD diffractometer ω scans	1973 independent reflections 1594 reflections with $I > 2\sigma(I)$
Absorption correction: multi-scan (<i>DENZO/SCALEPACK</i> ; Otwinowski & Minor, 1997)	$R_{int} = 0.048$ $\theta_{max} = 27.4^\circ$ $h = -19 \rightarrow 19$ $k = -7 \rightarrow 5$ $l = -23 \rightarrow 23$
$T_{min} = 0.820$, $T_{max} = 0.998$	
5747 measured reflections	

Refinement

Refinement on F^2	$w = 1/[\sigma^2(F^2) + 0.02 + 0.04P]$,
$R[F^2 > 2\sigma(F^2)] = 0.034$	where $P = [\max(F_o^2, 0) + 2F_c^2]/3$
$wR(F^2) = 0.077$	$(\Delta/\sigma)_{max} = 0.001$
$S = 0.93$	$\Delta\rho_{max} = 0.27$ e Å $^{-3}$
1973 reflections	$\Delta\rho_{min} = -0.23$ e Å $^{-3}$
200 parameters	Extinction correction: Larson (1970)
H-atom parameters constrained	Extinction coefficient: 16 (5)

Table 1

Selected bond lengths (Å).

C1—C2	1.551 (2)	C6—N7	1.453 (2)
C1—C5	1.525 (3)	N7—C8	1.334 (2)
C1—C12	1.531 (3)	C8—O9	1.236 (2)
C1—O22	1.421 (2)	C8—C10	1.501 (3)
C2—C3	1.518 (3)	C12—N13	1.333 (2)
C2—O11	1.421 (2)	C12—O21	1.235 (2)
C3—O4	1.438 (2)	N13—C14	1.454 (2)
C3—C6	1.522 (3)	C14—C15	1.515 (3)
O4—C5	1.436 (2)		

Table 2

Hydrogen-bond geometry (Å, °).

$D-H \cdots A$	$D-H$	$H \cdots A$	$D \cdots A$	$D-H \cdots A$
O22—H6 \cdots O9 ⁱ	0.95	1.75	2.649 (2)	158
N7—H12 \cdots O21 ⁱⁱ	1.00	1.95	2.953 (2)	177
O11—H1 \cdots O11 ⁱⁱⁱ	0.95	1.95	2.886 (2)	166

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

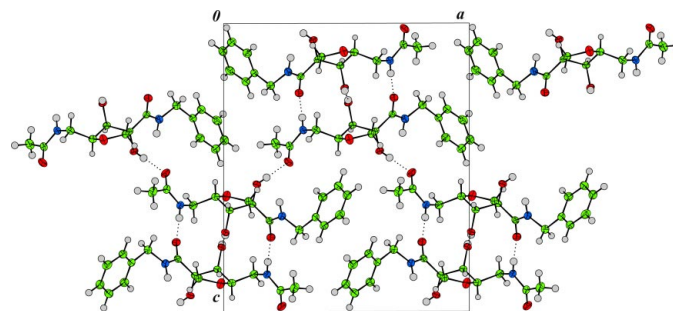


Figure 2

A packing diagram of (4), viewed down the b axis. Hydrogen bonds are indicated by dashed lines.

In the absence of significant anomalous scattering, Friedel pairs were merged. The absolute configuration of (4) was assigned since the starting material was L-lyxonolactone with known absolute configuration and two of the chiral centres are retained (see scheme). H atoms were located in difference density maps. Those attached to C atoms were repositioned geometrically. The H atoms were initially refined with soft restraints on the bond lengths and angles to regularize their geometry (C—H = 0.98–1.01 Å, O—H = 0.95 Å and N—H = 0.95–1.00 Å), after which they were refined as riding, with $U_{iso}(H) = 1.2U_{eq}(C)$, and $U_{iso}(H) = 0.05$ Å 2 for those bonded to N and O atoms.

Data collection: *COLLECT* (Nonius, 2001); cell refinement: *DENZO/SCALEPACK* (Otwinowski & Minor, 1997); data reduction: *DENZO/SCALEPACK*; program(s) used to solve structure: *SIR92* (Altomare *et al.*, 1994); program(s) used to refine structure: *CRYSTALS* (Betteridge *et al.*, 2003); molecular graphics: *CAMERON* (Watkin *et al.*, 1996); software used to prepare material for publication: *CRYSTALS*.

Financial support (to MIS) provided through the European Community's Human Potential Programme under contract HPRN-CT-2002-00173 is gratefully acknowledged.

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