Acta Crystallographica Section E
Structure Reports Online
ISSN 1600-5368

Pentafluorophenyl (3*R*,4*R*,5*R*)-5-{[(3*R*,4*R*,5*R*)-5-azidomethyl-3,4-dimethoxy-2,3,4,5-tetrahydrofuran-3-carbonylamino]methyl}-3,4-dimethoxy-2,3,4,5-tetrahydrofuran-3-carboxylate

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Key indicators

Single-crystal X-ray study
T = 120 K
Mean σ(C–C) = 0.004 Å
R factor = 0.036
wR factor = 0.081
Data-to-parameter ratio = 11.8

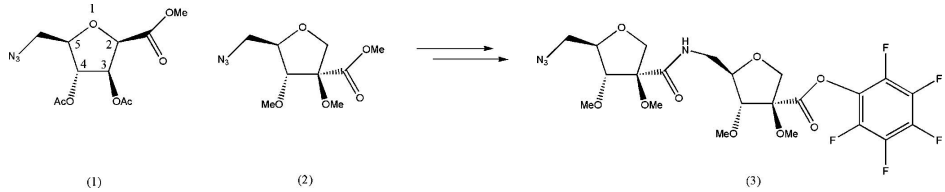
For details of how these key indicators were automatically derived from the article, see http://journals.iucr.org/e.

Received 12 December 2005
Accepted 25 December 2005
Online 7 January 2006

The crystal structure of the title compound, $C_{22}H_{25}F_5N_4O_9$, an important intermediate in the synthesis of novel biopolymers containing branched carbon chains, establishes the relative stereochemistry at all six chiral centres of the dipeptide. The structure may indicate a predisposition to the organization of secondary structure by novel dipeptide isosteres. An intermolecular hydrogen bond between the NH group and one of the N atoms of the azide group contributes to the stabilization of the packing.

Comment

Sugar amino acids (SAAs) have been extensively studied as peptidomimetics (Chakraborty *et al.*, 2005). δ-Tetrahydrofuran (THF) SAAs such as (1) (Smith *et al.*, 2003; Chakraborty *et al.*, 2004) have become well established as dipeptide isosteres (Grotenberg *et al.*, 2004). Such systems continue to provide an increased understanding of the factors inducing secondary structure and insight into the complex nature of protein folding (Billing & Nilsson, 2005; Claridge *et al.*, 2005; Long *et al.*, 1999) with potential chemotherapeutic activities as integrin antagonists (van Well *et al.*, 2004), enkephalin analogues (Montero *et al.*, 2004) and somatastatin mimics (Gruner *et al.*, 2002). In the past, almost all THF SAAs have contained linear carbon chains, since the only carbohydrate building blocks from which they can be derived have unbranched chains (Bols, 1996). Knowledge of the predisposition of monomers to adopt particular secondary structural motif may allow the design of bioactive peptidomimetic libraries.



(1) (2) (3)

However, new classes of branched carbohydrates suitable for short syntheses of branched carbon chain SAAs have recently become available by Kiliani or other procedures (Soengas *et al.*, 2005; Hotchkiss *et al.*, 2004,2006). The Ho crossed aldol (Ho, 1979, 1985) was the crucial step in the synthesis of branched SAAs such as (2) (Simone *et al.*, 2005). The azidoester (2) was converted by standard peptide procedures into the dimeric pentafluorophenyl ester (3) as a key intermediate for the generation of homooligomers having the branched *trans*-δ-SAA scaffold (2) as a component.

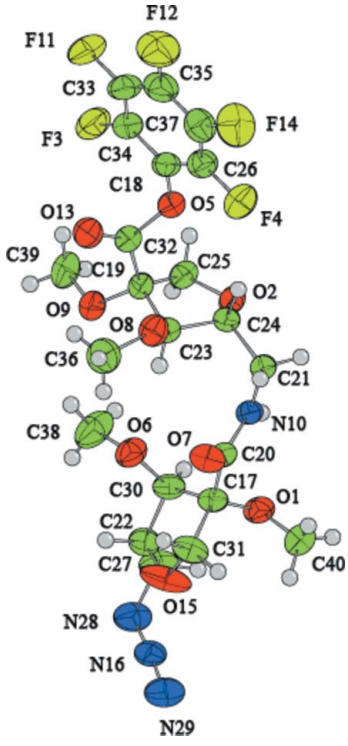


Figure 1
The structure of (3), with displacement ellipsoids drawn at the 50% probability level. H-atom radii are arbitrary.

The crystal structure reported in this paper firmly establishes the relative configuration of the six stereogenic centres in (3); the absolute configuration is consistent with the one determined by the use of D-ribose as the starting material for the synthesis. An intermolecular hydrogen bond between the H atom connected to N10 and N28, the first nitrogen of the azide chain, contributes to the stabilization of the packing.

Experimental

Compound (3) was crystallized by dissolving it in dichloromethane, adding a few drops of cyclohexane and allowing the slow competitive evaporation of the two solvents until clear colourless crystals formed.

Crystal data

$C_{22}H_{25}F_5N_4O_9$
M_r = 584.45
Orthorhombic, $P2_12_12_1$
a = 7.18471 (11) Å
b = 11.04142 (15) Å
c = 32.6727 (5) Å
V = 2591.91 (7) Å^3
Z = 4
D_x = 1.498 Mg m^{-3}
Cu $K\alpha$ radiation
Cell parameters from 11003 reflections
θ = 4.2–69.3°
μ = 1.22 mm^{-1}
T = 120 K
Lath, colourless
0.50 × 0.20 × 0.10 mm

Data collection

Oxford Diffraction Gemini R CCD diffractometer
$\omega/2\theta$ scans
Absorption correction: multi-scan (CrysAlis; Oxford Diffraction, 2005)
T_{min} = 0.783, T_{max} = 0.885
11003 measured reflections
4281 independent reflections
3387 reflections with $I > 2\sigma(I)$
R_{int} = 0.020
θ_{max} = 69.3°
$h = -6 \rightarrow 8$
$k = -9 \rightarrow 13$
$l = -39 \rightarrow 33$

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.036
$wR(F^2)$ = 0.081
S = 0.92
4281 reflections
362 parameters
H-atom parameters constrained
$w = 1/[\sigma^2(F^2) + (0.04P)^2 + 0.55P]$ where $P = [\max(F_o^2,0) + 2F_c^2]/3$
$(\Delta/\sigma)_{max}$ = 0.001
$\Delta\rho_{max}$ = 0.29 e Å^{-3}
$\Delta\rho_{min}$ = −0.14 e Å^{-3}
Absolute structure: Flack (1983), 1237 Friedel pairs
Flack parameter: 0.00 (16)

Table 1
Selected geometric parameters (Å, °).

O1—C17	1.425 (3)	O15—C22	1.422 (3)
O1—C40	1.418 (4)	O15—C31	1.403 (3)
O2—C24	1.431 (3)	N16—N28	1.183 (3)
O2—C25	1.424 (3)	N16—N29	1.146 (3)
F3—C34	1.334 (3)	C17—C20	1.537 (3)
F4—C26	1.342 (3)	C17—C30	1.532 (4)
O5—C18	1.390 (3)	C17—C31	1.515 (3)
O5—C32	1.387 (3)	C18—C26	1.383 (4)
O6—C30	1.411 (3)	C18—C34	1.376 (3)
O6—C38	1.421 (4)	C19—C23	1.540 (3)
O7—C20	1.222 (3)	C19—C25	1.532 (4)
O8—C23	1.404 (3)	C19—C32	1.522 (3)
O8—C36	1.434 (4)	C21—C24	1.514 (3)
O9—C19	1.409 (3)	C22—C27	1.502 (4)
O9—C39	1.437 (4)	C22—C30	1.546 (4)
N10—C20	1.336 (3)	C23—C24	1.517 (3)
N10—C21	1.450 (3)	C26—C37	1.355 (4)
F11—C33	1.338 (3)	C27—N28	1.495 (4)
F12—C35	1.333 (3)	C33—C34	1.382 (4)
O13—C32	1.180 (3)	C33—C35	1.364 (5)
F14—C37	1.342 (3)	C35—C37	1.369 (4)

C17—O1—C40	114.6 (2)	C19—C23—O8	115.53 (19)
C24—O2—C25	110.12 (19)	C19—C23—C24	103.4 (2)
C18—O5—C32	115.64 (19)	O8—C23—C24	109.2 (2)
C30—O6—C38	113.3 (2)	C23—C24—C21	115.6 (2)
C23—O8—C36	113.0 (2)	C23—C24—O2	104.3 (2)
C19—O9—C39	114.5 (2)	C21—C24—O2	108.6 (2)
C20—N10—C21	121.8 (2)	C19—C25—O2	107.9 (2)
C22—O15—C31	109.17 (19)	C18—C26—F4	118.9 (2)
N28—N16—N29	172.9 (3)	C18—C26—C37	121.6 (3)
O1—C17—C20	111.3 (2)	F4—C26—C37	119.5 (3)
O1—C17—C30	104.20 (19)	C22—C27—N28	112.0 (3)
C20—C17—C30	113.26 (19)	C27—N28—N16	115.4 (2)
O1—C17—C31	113.9 (2)	C22—C30—C17	103.0 (2)
C20—C17—C31	112.2 (2)	C22—C30—O6	111.7 (2)
C30—C17—C31	101.3 (2)	C17—C30—O6	108.6 (2)
O5—C18—C26	118.8 (2)	C17—C31—O15	105.3 (2)
O5—C18—C34	123.2 (3)	C19—C32—O5	111.3 (2)
C26—C18—C34	118.0 (2)	C19—C32—O13	126.2 (3)
O9—C19—C23	108.06 (19)	O5—C32—O13	122.4 (2)
O9—C19—C25	113.9 (2)	F11—C33—C34	119.2 (3)
C23—C19—C25	102.24 (19)	F11—C33—C35	120.1 (3)
O9—C19—C32	107.94 (19)	C34—C33—C35	120.6 (3)
C23—C19—C32	108.4 (2)	C33—C34—C18	120.2 (3)
C25—C19—C32	115.9 (2)	C33—C34—F3	119.6 (3)
C17—C20—N10	115.5 (2)	C18—C34—F3	120.2 (3)
C17—C20—O7	121.0 (2)	F12—C35—C33	119.9 (3)
N10—C20—O7	123.4 (2)	F12—C35—C37	120.7 (3)
N10—C21—C24	114.3 (2)	C33—C35—C37	119.4 (3)
O15—C22—C27	106.1 (2)	F14—C37—C35	119.6 (3)
O15—C22—C30	106.8 (2)	F14—C37—C26	120.2 (3)
C27—C22—C30	114.9 (2)	C35—C37—C26	120.2 (3)

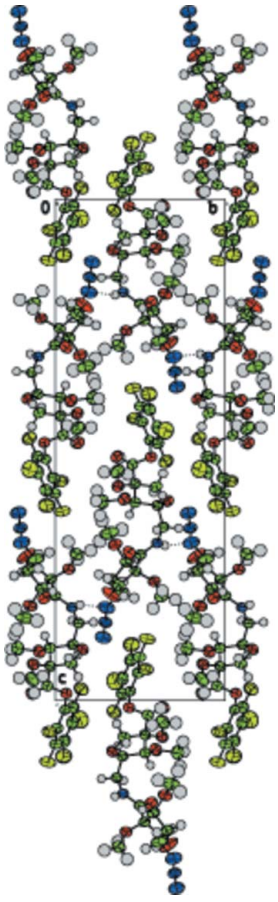


Figure 2
Packing diagram of (3), viewed down the *a* axis. Dashed lines indicate intermolecular hydrogen bonds.

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

D—H···A	D—H	H···A	D···A	D—H···A
N10—H1···N28^{i}	0.94	2.23	3.120 (3)	158

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

The H atoms were located in a difference map, but those attached to C atoms were repositioned geometrically. They were initially refined with soft restraints on the bond lengths and angles to regularize their geometry (C—H in the range 0.93–98 Å, N—H in the range 0.86–0.89 Å and U_{iso}(H) in the range 1.2–1.5 times U_{eq} of the parent atom), after which their positions were refined with riding constraints.

Data collection: *CrysAlis* (Oxford Diffraction, 2005); cell refinement: *CrysAlis*; data reduction: *CrysAlis*; 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 AAE) from the EPSRC (grant No. GR/S44105/01) and (to MIS) from the European Community's Human Potential Programme under contract HPRN-CT-2002-00173 is gratefully acknowledged. The authors thank Oxford Diffraction for use of the Gemini R X-ray system.

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