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Isopropyl 2,5-anhydro-6-azido-3,6-dideoxy-D-*xylo*-hexonate

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Key indicators

Single-crystal X-ray study
T = 190 K
Mean σ(C–C) = 0.003 Å
R factor = 0.040
wR factor = 0.104
Data-to-parameter ratio = 9.1

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

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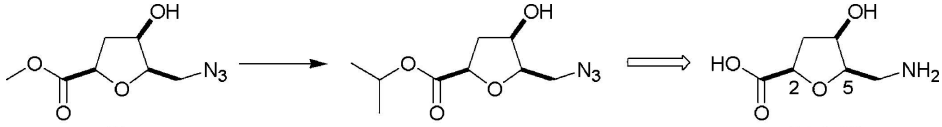
Determination of the crystal structure of the title isopropyl azido ester, $C_9H_{15}N_3O_4$, confirmed its relative stereochemistry and validated further work on the use of a derived sugar amino acid (SAA) as a peptidomimetic.

Comment

Sugar amino acids (SAAs) are carbohydrates which contain amine and acid groups; SAAs have been the focus of much interest as dipeptide isosteres, foldamers and library scaffolds (Hill *et al.*, 2001; Gruner *et al.*, 2002; Schweizer, 2002; Chakraborty, Srinivasu, Tapadar & Mohan, 2004; Trabocchi *et al.*, 2005). The preference for SAA oligomers (carbopeptoids) to adopt compact conformations as relatively short homo-oligomers will provide insight into the paradigm of protein folding. SAAs (2,5-O-*cis* configuration) structurally related to SAA (3) have a high propensity to adopt repeating β-turn conformations (Hungerford *et al.*, 2000; Smith *et al.*, 2003; Chakraborty, Srinivasu, Sakunthala *et al.*, 2004). In contrast, some 2,5-O-*trans* SAAs have been shown to adopt helical conformations (Claridge *et al.*, 1999; Claridge *et al.*, 2005). The conformational complexity of these dipeptide isosteres is being further explored by preparation of structurally related analogues of the original SAA systems *i.e.* SAA (3) and corresponding diastereoisomers (Watterson *et al.*, 2003).



(1) (2) SAA (3)

The X-ray crystal structure (Fig. 1) firmly established the relative stereochemistry of the stereogenic centres in the title compound, (2). The absolute configuration of (2) (see scheme) is determined by the use of D-gulono-1,4-lactone as starting material.

The crystal packing consists of chains of molecules linked by hydrogen bonds and lying parallel to the *a* axis (Fig. 2). There are no unusual intermolecular contacts.

Experimental

The title compound, (2), was prepared from the methyl azido ester (1) in good yield by transesterficiation in acidic propan-2-ol, as described by Watterson *et al.* (2003); subsequent deprotection by hydrolysis and hydrogenation afforded SAA (3). The sample of (2) was crystallized from diethyl ether–hexane.

Crystal data

$C_9H_{15}N_3O_4$
M_r = 229.24
Orthorhombic, $P2_12_12_1$
a = 5.4778 (7) Å
b = 11.0701 (13) Å
c = 18.2529 (15) Å
V = 1106.9 (2) Å^3
Z = 4
D_x = 1.376 Mg m^{-3}
Cu $K\alpha$ radiation
Cell parameters from 22 reflections
θ = 21–44°
μ = 0.92 mm^{-1}
T = 190 K
Block, colourless
0.60 × 0.40 × 0.40 mm

Data collection

Enraf–Nonius Mach3 diffractometer
$\omega/2\theta$ scans
Absorption correction: ψ scan (North *et al.*, 1968)
T_{min} = 0.58, T_{max} = 0.69
1335 measured reflections
1335 independent reflections
1329 reflections with $I > 2\sigma(I)$
θ_{max} = 73.9°
$h = 0 \rightarrow 6$
$k = 0 \rightarrow 13$
$l = 0 \rightarrow 22$
3 standard reflections
frequency: 60 min
intensity decay: 2.2%

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.040
$wR(F^2)$ = 0.104
S = 0.94
1335 reflections
146 parameters
H-atom parameters constrained
$w = 1/[\sigma^2(F^2) + (0.07P)^2 + 0.57P]$, where $P = [\max(F_o^2,0) + 2F_c^2]/3$
$(\Delta/\sigma)_{max}$ = 0.001
$\Delta\rho_{max}$ = 0.25 e Å^{-3}
$\Delta\rho_{min}$ = −0.17 e Å^{-3}
Extinction correction: Larson (1970), Equation 22
Extinction coefficient: 159 (14)

Table 1
Selected geometric parameters (Å, °).

O1—C2	1.331 (3)	C6—C11	1.543 (3)
O1—C14	1.462 (3)	C7—N8	1.494 (3)
C2—O3	1.218 (3)	N8—N9	1.227 (3)
C2—C4	1.525 (3)	N9—N10	1.133 (3)
C4—O5	1.421 (3)	C11—C12	1.519 (3)
C4—C12	1.539 (3)	C11—O13	1.424 (3)
O5—C6	1.439 (3)	C14—C15	1.509 (3)
C6—C7	1.505 (3)	C14—C16	1.510 (4)
C2—O1—C14	116.44 (17)	C6—C7—N8	109.04 (19)
O1—C2—O3	124.2 (2)	C7—N8—N9	113.4 (2)
O1—C2—C4	111.63 (18)	N8—N9—N10	173.7 (3)
O3—C2—C4	124.07 (19)	C6—C11—C12	102.52 (17)
C2—C4—O5	109.68 (17)	C6—C11—O13	108.97 (17)
C2—C4—C12	113.67 (18)	C12—C11—O13	110.87 (18)
O5—C4—C12	104.84 (17)	C4—C12—C11	101.61 (18)
C4—O5—C6	109.60 (16)	O1—C14—C15	106.30 (18)
O5—C6—C7	111.26 (19)	O1—C14—C16	108.05 (19)
O5—C6—C11	106.93 (16)	C15—C14—C16	113.3 (2)
C7—C6—C11	112.91 (18)		

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

D—H···A	D—H	H···A	D···A	D—H···A
O13—H13···O3^{i}	0.82	2.08	2.897 (2)	175

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

Attempted refinement of the Flack (1983) parameter gave an inconclusive result, in the absence of Friedel pairs and the presence of only weak anomalous scattering effects. The absolute configuration was assigned from the known configuration of the starting material. The H atoms were all located in a difference map, but 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 = 0.93–0.98 Å and O—H = 0.82 Å) and U_{iso}(H) values (in the range 1.2–1.5 times U_{eq} of the parent atom), after which they were refined with riding constraints.

Data collection: *CAD-4 EXPRESS*, (Straver, 1992); cell refinement: *CAD-4 EXPRESS*; data reduction: *RC93* (Watkin *et al.*, 1994); 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 from the EPSRC to AAE and MPW is gratefully acknowledged.

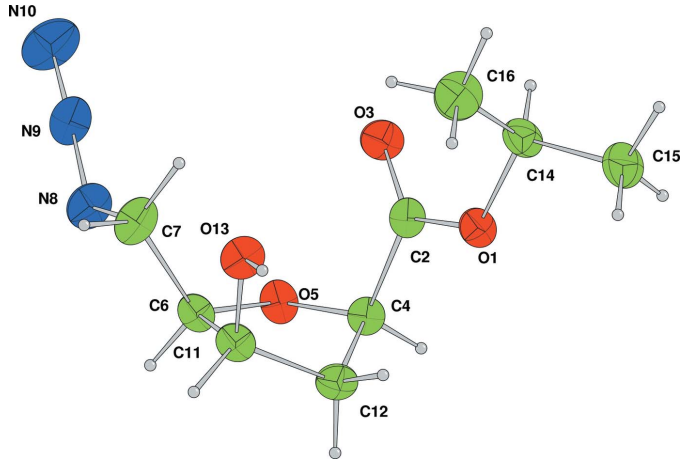


Figure 1
The title compound, with displacement ellipsoids drawn at the 50% probability level. H atoms are shown as spheres of arbitrary radius.

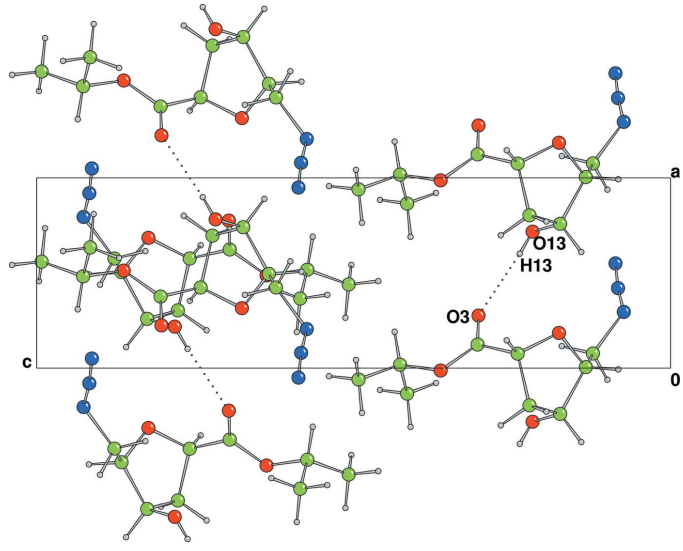


Figure 2
Projection of the title compound down the *b* axis, showing the hydrogen bonds (dashed lines) which link the molecules into columns.

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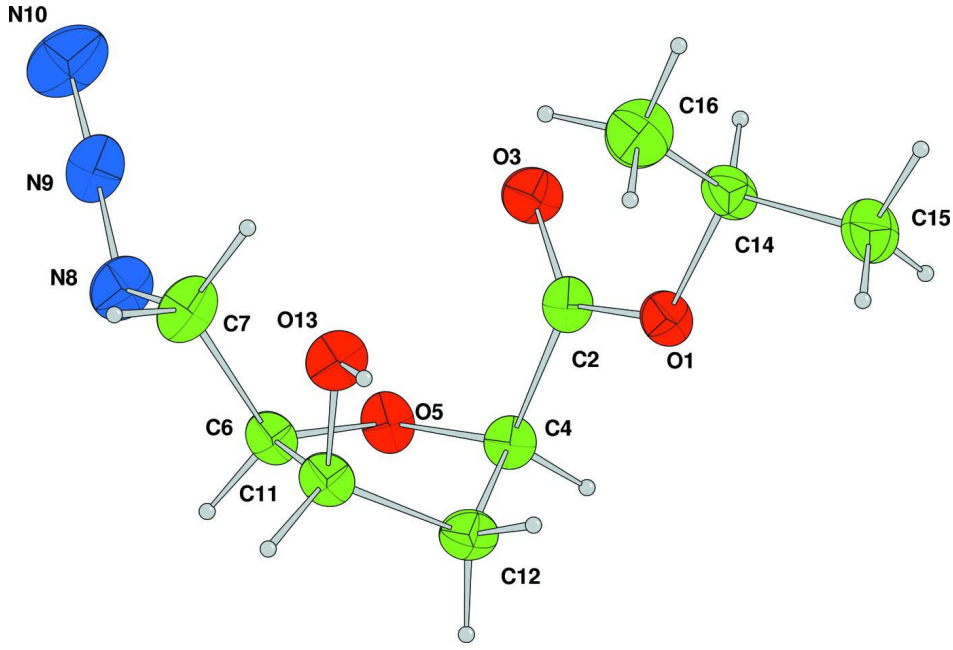

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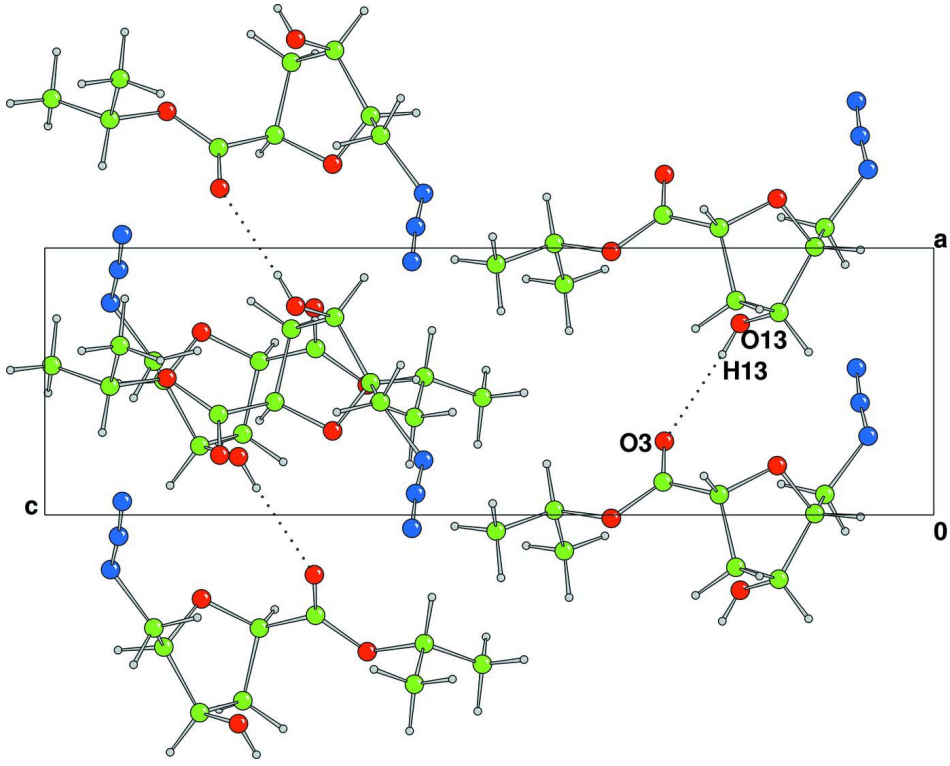

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$k = 0 \rightarrow 13$
$l = 0 \rightarrow 22$
3 standard reflections every 60 min
intensity decay: 2.2%

Refinement

Refinement on F^2
Least-squares matrix: full
$R[F^2 > 2\sigma(F^2)] = 0.040$
$wR(F^2) = 0.104$
$S = 0.94$
1335 reflections
146 parameters
0 restraints
Primary atom site location: structure-invariant direct methods
Hydrogen site location: inferred from neighbouring sites
H-atom parameters constrained
$w = 1/[\sigma^2(F^2) + (0.07P)^2 + 0.57P]$, where $P = [\max(F_o^2,0) + 2F_c^2]/3$
$(\Delta/\sigma)_{max} = 0.001$
$\Delta\rho_{max} = 0.25$ e Å^{-3}
$\Delta\rho_{min} = -0.17$ e Å^{-3}
Extinction correction: Larson (1970), Equation 22
Extinction coefficient: 159 (14)

Fractional atomic coordinates and isotropic or equivalent isotropic displacement parameters (Å²)

	x	*y*	*z*	U_{iso}*/U_{eq}
O1	1.0131 (3)	0.04582 (14)	0.13732 (8)	0.0286
C2	0.8763 (4)	0.07207 (19)	0.19548 (12)	0.0265
O3	0.7238 (3)	0.15214 (14)	0.19695 (9)	0.0327
C4	0.9240 (4)	−0.0150 (2)	0.25865 (11)	0.0260
O5	0.8152 (3)	0.03051 (14)	0.32375 (8)	0.0283
C6	0.9954 (4)	0.0942 (2)	0.36612 (11)	0.0265
C7	0.9236 (5)	0.2241 (2)	0.37739 (14)	0.0347
N8	0.7043 (4)	0.22905 (18)	0.42600 (11)	0.0370
N9	0.5797 (4)	0.31992 (19)	0.41699 (12)	0.0358
N10	0.4495 (5)	0.3992 (2)	0.41294 (17)	0.0538
C11	1.2409 (4)	0.0802 (2)	0.32561 (12)	0.0273
C12	1.1963 (4)	−0.0296 (2)	0.27753 (13)	0.0291
O13	1.2826 (3)	0.18508 (14)	0.28216 (9)	0.0319

C14	0.9818 (5)	0.1232 (2)	0.07308 (11)	0.0319
C15	1.0604 (6)	0.0491 (2)	0.00784 (12)	0.0430
C16	1.1340 (6)	0.2355 (2)	0.08420 (15)	0.0458
H41	0.8578	−0.0940	0.2460	0.0306*
H61	1.0054	0.0554	0.4140	0.0318*
H71	1.0540	0.2685	0.3992	0.0425*
H72	0.8814	0.2605	0.3297	0.0418*
H111	1.3776	0.0681	0.3590	0.0315*
H121	1.2259	−0.1050	0.3045	0.0333*
H122	1.2955	−0.0277	0.2341	0.0346*
H141	0.8056	0.1442	0.0675	0.0368*
H151	1.0365	0.0977	−0.0357	0.0639*
H152	1.2331	0.0309	0.0141	0.0642*
H153	0.9649	−0.0252	0.0055	0.0642*
H161	1.1211	0.2894	0.0430	0.0688*
H162	1.3011	0.2149	0.0890	0.0694*
H163	1.0845	0.2801	0.1274	0.0683*
H13	1.4026	0.1766	0.2560	0.0476*

Atomic displacement parameters (Å²)

	U^{11}	U^{22}	U^{33}	U^{12}	U^{13}	U^{23}
O1	0.0233 (8)	0.0367 (8)	0.0259 (7)	0.0027 (7)	0.0025 (7)	0.0002 (6)
C2	0.0200 (10)	0.0311 (10)	0.0285 (10)	−0.0031 (9)	0.0022 (9)	−0.0033 (8)
O3	0.0252 (8)	0.0400 (8)	0.0330 (8)	0.0063 (7)	0.0068 (7)	0.0024 (6)
C4	0.0210 (10)	0.0289 (10)	0.0279 (10)	−0.0023 (9)	0.0029 (8)	−0.0010 (8)
O5	0.0174 (7)	0.0401 (8)	0.0274 (7)	−0.0041 (7)	0.0043 (6)	−0.0021 (6)
C6	0.0200 (11)	0.0351 (11)	0.0242 (10)	−0.0004 (9)	0.0003 (9)	0.0020 (8)
C7	0.0251 (12)	0.0370 (11)	0.0421 (12)	−0.0031 (10)	0.0117 (11)	−0.0067 (10)
N8	0.0306 (10)	0.0408 (10)	0.0396 (10)	0.0029 (10)	0.0132 (9)	−0.0015 (9)
N9	0.0243 (10)	0.0402 (10)	0.0430 (10)	−0.0049 (10)	0.0035 (9)	−0.0087 (9)
N10	0.0306 (12)	0.0486 (13)	0.0823 (18)	0.0056 (12)	0.0026 (13)	−0.0082 (13)
C11	0.0155 (10)	0.0370 (11)	0.0295 (10)	0.0030 (9)	0.0008 (9)	0.0015 (9)
C12	0.0222 (11)	0.0335 (11)	0.0317 (10)	0.0053 (9)	0.0048 (9)	0.0039 (9)
O13	0.0225 (8)	0.0357 (8)	0.0375 (8)	−0.0018 (7)	0.0091 (7)	0.0008 (7)
C14	0.0299 (12)	0.0424 (12)	0.0235 (10)	0.0058 (11)	0.0024 (10)	0.0027 (9)
C15	0.0497 (16)	0.0508 (13)	0.0284 (11)	0.0106 (14)	0.0050 (12)	−0.0012 (10)
C16	0.0517 (17)	0.0447 (13)	0.0410 (12)	−0.0036 (14)	0.0114 (13)	0.0049 (11)

Geometric parameters (Å, º)

O1—C2	1.331 (3)	C11—C12	1.519 (3)
O1—C14	1.462 (3)	C11—O13	1.424 (3)
C2—O3	1.218 (3)	C11—H111	0.974
C2—C4	1.525 (3)	C12—H121	0.983
C4—O5	1.421 (3)	C12—H122	0.962
C4—C12	1.539 (3)	O13—H13	0.817
C4—H41	0.975	C14—C15	1.509 (3)

O5—C6	1.439 (3)	C14—C16	1.510 (4)
C6—C7	1.505 (3)	C14—H141	0.998
C6—C11	1.543 (3)	C15—H151	0.969
C6—H61	0.976	C15—H152	0.974
C7—N8	1.494 (3)	C15—H153	0.976
C7—H71	0.954	C16—H161	0.962
C7—H72	0.986	C16—H162	0.947
N8—N9	1.227 (3)	C16—H163	0.968
N9—N10	1.133 (3)		

C2—O1—C14	116.44 (17)	C6—C11—H111	112.6
O1—C2—O3	124.2 (2)	C12—C11—H111	112.0
O1—C2—C4	111.63 (18)	O13—C11—H111	109.7
O3—C2—C4	124.07 (19)	C4—C12—C11	101.61 (18)
C2—C4—O5	109.68 (17)	C4—C12—H121	111.2
C2—C4—C12	113.67 (18)	C11—C12—H121	111.4
O5—C4—C12	104.84 (17)	C4—C12—H122	111.1
C2—C4—H41	108.9	C11—C12—H122	111.6
O5—C4—H41	111.1	H121—C12—H122	109.7
C12—C4—H41	108.6	C11—O13—H13	111.1
C4—O5—C6	109.60 (16)	O1—C14—C15	106.30 (18)
O5—C6—C7	111.26 (19)	O1—C14—C16	108.05 (19)
O5—C6—C11	106.93 (16)	C15—C14—C16	113.3 (2)
C7—C6—C11	112.91 (18)	O1—C14—H141	109.4
O5—C6—H61	107.7	C15—C14—H141	108.8
C7—C6—H61	108.2	C16—C14—H141	110.9
C11—C6—H61	109.7	C14—C15—H151	107.9
C6—C7—N8	109.04 (19)	C14—C15—H152	107.3
C6—C7—H71	110.7	H151—C15—H152	110.1
N8—C7—H71	109.6	C14—C15—H153	109.9
C6—C7—H72	109.3	H151—C15—H153	111.1
N8—C7—H72	108.7	H152—C15—H153	110.5
H71—C7—H72	109.5	C14—C16—H161	111.4
C7—N8—N9	113.4 (2)	C14—C16—H162	110.4
N8—N9—N10	173.7 (3)	H161—C16—H162	107.0
C6—C11—C12	102.52 (17)	C14—C16—H163	112.0
C6—C11—O13	108.97 (17)	H161—C16—H163	107.4
C12—C11—O13	110.87 (18)	H162—C16—H163	108.5

Hydrogen-bond geometry (Å, º)

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
O13—H13···O3^{i}	0.82	2.08	2.897 (2)	175

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