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Methyl 3,6-anhydro-4-azido-5,7-*O*-(*S*)-benzylidene-2,4-dideoxy-D-*talo*-heptonate

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Key indicators

Single-crystal X-ray study
T = 293 K
Mean σ(C–C) = 0.004 Å
R factor = 0.035
wR factor = 0.092
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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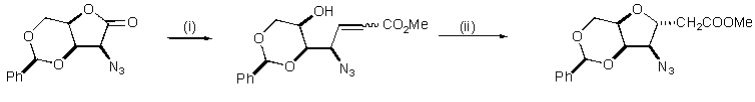
The title compound, $C_{15}H_{17}N_3O_5$, was formed by carrying out a Wittig reaction, under basic conditions, on 2-azido-3,5–*O*-benzylidene-2-deoxy-D-lyxose.

Comment

Sugar amino acids (SAA) (Schweizer, 2002) have been utilized in peptidomimetics (Gruner *et al.*, 2002), as carbopeptoid foldamers (Gellman, 1998) and, to a lesser extent, as molecular scaffolds (Sofia, 1998). Although the generation of well defined libraries from SAA is rare (Chakraborty *et al.*, 2003; Edwards *et al.*, 2004), SAA peptidomimetics have been employed as chiral scaffolds in the parallel production of ligands for the melanocortin and somastatin GPCR receptors (Le *et al.*, 2003). The recognition of templated SAA in forming different but predictable secondary structure is likely to lead to further exploitation of this structural motif (Smith *et al.*, 2003). A wide range of tetrahydrofuran (THF) amino acid scaffolds are readily available (Watterson *et al.*, 1996) and a series of γ-THF amino acids have recently been reported (Sanjayan *et al.*, 2003). The title compound, (3), is an example of a γ-THF amino acid with a different structural motif. A novel THF scaffold (3) with an azide directly attached to the THF was prepared in good yield by the three-step one-pot procedure outlined below. Reduction of azido lactone (1) with 1.5 equivalents of diisobutylaluminium hydride, DIBAL-H, provided a lactol that was immediately subjected to Wittig olefination to afford the enoate (2). Upon prolonged stirring, (2) underwent a conjugate addition of the unprotected OH group to the enoate (2) to give the highly functionalized scaffold (3) in good yield; optimization of the conditions for the overall sequence are currently being investigated. Two structural ambiguities arose in the formation of (3): one based on the easy epimerization of azides in azidolactones (Krulle *et al.*, 1996) and the other on the new stereogenic centre generated by the intramolecular Michael addition. These uncertainties were firmly resolved by single-crystal X-ray crystallography of the title compound (3).



(1) (2) (3)

Reagents: (i) DIBAL-H then $Ph_3PCH{=}CHCO_2Me$ (ii) see text

Experimental

The title material was obtained by solvent evaporation (EtOAc–cyclohexane), appearing as orange–yellow block-shaped crystals.

These were recrystallized from methanol to give colourless plate-like crystals.

Crystal data

$C_{15}H_{17}N_3O_5$	D_x = 1.339 Mg m^{-3}
M_r = 319.32	Mo Kα radiation
Monoclinic, $P2_1$	Cell parameters from 1851 reflections
a = 8.2135 (3) Å	θ = 5–27°
b = 9.2262 (3) Å	μ = 0.10 mm^{-1}
c = 10.9944 (3) Å	T = 293 K
β = 108.0414 (15)°	Plate, colourless
V = 792.19 (4) Å^3	0.40 × 0.40 × 0.10 mm
Z = 2	

Data collection

Nonius KappaCCD diffractometer	1906 independent reflections
ω scans	1464 reflections with $I > 2.00\,\sigma(I)$
Absorption correction: multi-scan (*DENZO/SCALEPACK*; Otwinowski & Minor, 1997)	R_{int} = 0.011
	θ_{max} = 27.5°
T_{min} = 0.96, T_{max} = 0.99	$h = -10 \rightarrow 10$
3420 measured reflections	$k = -11 \rightarrow 11$
	$l = -14 \rightarrow 14$

Refinement

Refinement on F^2	$w = 1/[\sigma^2(F^*) + (0.0434p)^2 + 0.113p]$ where $p = 0.333\max(F_o^2,0) + 0.667F_c^2$
$R[F^2 > 2\sigma(F^2)]$ = 0.035	$(\Delta/\sigma)_{max}$ = 0.002
$wR(F^2)$ = 0.092	$\Delta\rho_{max}$ = 0.17 e Å^{-3}
S = 0.89	$\Delta\rho_{min}$ = −0.15 e Å^{-3}
1906 reflections	Extinction correction: Larson (1970)
209 parameters	Extinction coefficient: 4.3 (6) × 10^2
H-atom parameters constrained	

Table 1
Selected geometric parameters (Å, °).

C1—O9	1.437 (2)	C10—C15	1.368 (4)
C1—C5	1.517 (3)	C10—C11	1.396 (4)
C1—C2	1.513 (4)	C11—C12	1.375 (4)
C2—N21	1.464 (3)	C12—C13	1.361 (6)
C2—C3	1.537 (3)	C13—C14	1.365 (6)
C3—C16	1.523 (3)	C14—C15	1.392 (4)
C3—O4	1.419 (3)	C16—C17	1.502 (4)
O4—C5	1.444 (3)	C17—O20	1.186 (3)
C5—C6	1.491 (4)	C17—O18	1.320 (3)
C6—O7	1.432 (3)	O18—C19	1.453 (3)
O7—C8	1.408 (3)	N21—N22	1.232 (4)
C8—C10	1.499 (3)	N22—N23	1.133 (4)
C8—O9	1.421 (3)		
O9—C1—C5	111.79 (19)	O9—C8—O7	109.96 (18)
O9—C1—C2	105.98 (19)	C8—O9—C1	113.72 (16)
C5—C1—C2	101.85 (19)	C15—C10—C11	119.8 (2)
N21—C2—C3	115.4 (2)	C15—C10—C8	121.2 (2)
N21—C2—C1	116.74 (19)	C11—C10—C8	119.0 (2)
C3—C2—C1	102.4 (2)	C12—C11—C10	119.7 (3)
C16—C3—O4	110.4 (2)	C13—C12—C11	120.2 (3)
C16—C3—C2	112.3 (2)	C14—C13—C12	120.7 (3)
O4—C3—C2	105.1 (2)	C15—C14—C13	120.1 (4)
C5—O4—C3	110.88 (18)	C10—C15—C14	119.6 (3)
C6—C5—O4	110.1 (2)	C17—C16—C3	114.7 (2)
C6—C5—C1	113.1 (2)	O20—C17—O18	123.5 (3)
O4—C5—C1	105.3 (2)	O20—C17—C16	124.4 (3)
O7—C6—C5	112.12 (19)	O18—C17—C16	112.1 (2)
C8—O7—C6	110.38 (18)	C19—O18—C17	116.2 (2)
C10—C8—O9	106.41 (17)	N22—N21—C2	115.7 (2)
C10—C8—O7	109.96 (19)	N23—N22—N21	171.7 (3)

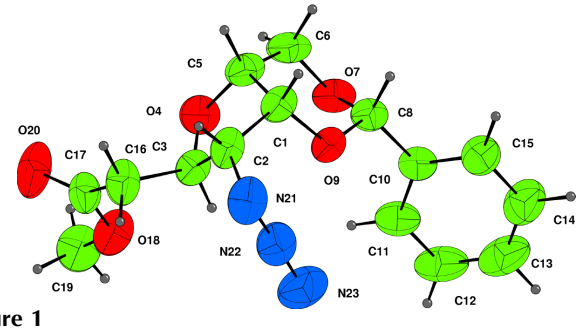


Figure 1
The molecular structure of (3), with 50% probability displacement ellipsoids.

H atoms were placed geometrically after each cycle, at a distance of 1.0 Å; U_{iso} values were set to 1.2 times the U_{eq} value of the parent atom. The absolute configuration was assumed to be the same as that of the sugar and the Friedel pairs were merged in the final refinement.

Data collection: *COLLECT* (Nonius, 1997–2001); cell refinement: *DENZO/SCALEPACK* (Otwinowski & Minor, 1997); data reduction: *DENZO/SCALEPACK*; program(s) used to solve structure: *SIR*92 (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*.

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$c = 10.9944$ (3) Å
$\beta = 108.0414$ (15)°
$V = 792.19$ (4) Å^3
$Z = 2$
$F(000) = 336$
$D_x = 1.339$ Mg m^{-3}
Mo $K\alpha$ radiation, $\lambda = 0.71073$ Å
Cell parameters from 1851 reflections
$\theta = 5$–27°
$\mu = 0.10$ mm^{-1}
$T = 293$ K
Plate, colourless
0.40 × 0.40 × 0.10 mm

Data collection

Nonius KappaCCD diffractometer
Graphite monochromator
ω scans
Absorption correction: multi-scan (DENZO/SCALEPACK; Otwinowski & Minor, 1996)
$T_{min} = 0.96$, $T_{max} = 0.99$
3420 measured reflections
1906 independent reflections
1464 reflections with $I > 2.00u(I)$
$R_{int} = 0.01$
$\theta_{max} = 27.5°$, $\theta_{min} = 5.1°$
$h = -10 \rightarrow 10$
$k = -11 \rightarrow 11$
$l = -14 \rightarrow 14$

Refinement

Refinement on F^2
Least-squares matrix: full
$R[F^2 > 2\sigma(F^2)] = 0.035$
$wR(F^2) = 0.092$
$S = 0.89$
1906 reflections
209 parameters
1 restraint
Primary atom site location: structure-invariant direct methods
Hydrogen site location: inferred from neighbouring sites
H-atom parameters constrained
$w = 1/[\sigma^2(F^*) + (0.0434p)^2 + 0.113p]$ where $p = 0.333\max(F_o^2,0) + 0.667F_c^2$
$(\Delta/\sigma)_{max} = 0.002$
$\Delta\rho_{max} = 0.17$ e Å^{-3}
$\Delta\rho_{min} = -0.15$ e Å^{-3}
Extinction correction: Larson 1970 Crystallographic Computing eq 22
Extinction coefficient: 430 (60)

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

	x	*y*	*z*	U_{iso}*/U_{eq}
C1	0.6257 (3)	0.3880 (2)	0.6894 (2)	0.0578

C2	0.7296 (3)	0.3406 (3)	0.8225 (2)	0.0602
C3	0.6887 (3)	0.1780 (3)	0.8208 (2)	0.0544
O4	0.5199 (2)	0.1644 (2)	0.73553 (18)	0.0720
C5	0.4647 (3)	0.2976 (3)	0.6661 (3)	0.0652
C6	0.3786 (3)	0.2660 (3)	0.5281 (3)	0.0711
O7	0.4980 (2)	0.22373 (19)	0.46346 (16)	0.0629
C8	0.6232 (3)	0.3318 (3)	0.4764 (2)	0.0539
O9	0.72305 (18)	0.34582 (17)	0.60683 (13)	0.0523
C10	0.7445 (3)	0.2885 (3)	0.4051 (2)	0.0552
C11	0.8300 (3)	0.1560 (3)	0.4336 (3)	0.0705
C12	0.9423 (4)	0.1152 (4)	0.3696 (3)	0.0915
C13	0.9725 (4)	0.2047 (5)	0.2805 (3)	0.0993
C14	0.8901 (5)	0.3346 (5)	0.2521 (3)	0.0952
C15	0.7747 (4)	0.3775 (3)	0.3149 (2)	0.0712
C16	0.6979 (4)	0.1208 (3)	0.9527 (2)	0.0706
C17	0.6358 (4)	−0.0321 (3)	0.9541 (2)	0.0622
O18	0.7011 (3)	−0.1205 (2)	0.8869 (2)	0.0799
C19	0.6553 (5)	−0.2725 (3)	0.8879 (3)	0.0857
O20	0.5424 (4)	−0.0707 (3)	1.0110 (3)	0.1000
N21	0.9120 (3)	0.3774 (3)	0.8639 (2)	0.0763
N22	1.0011 (3)	0.3082 (3)	0.8126 (2)	0.0764
N23	1.0993 (3)	0.2529 (4)	0.7754 (3)	0.1079
H11	0.5991	0.4937	0.6762	0.0727*
H21	0.6969	0.3953	0.8900	0.0752*
H31	0.7743	0.1200	0.7934	0.0668*
H51	0.3777	0.3516	0.6951	0.0802*
H61	0.3168	0.3551	0.4860	0.0829*
H62	0.2943	0.1858	0.5210	0.0829*
H81	0.5631	0.4245	0.4424	0.0635*
H111	0.8095	0.0910	0.5004	0.0817*
H121	1.0024	0.0196	0.3886	0.1060*
H131	1.0558	0.1749	0.2353	0.1192*
H141	0.9128	0.3993	0.1860	0.1164*
H151	0.7143	0.4728	0.2942	0.0857*
H161	0.8202	0.1251	1.0083	0.0886*
H162	0.6269	0.1852	0.9892	0.0886*
H191	0.7111	−0.3293	0.8344	0.1061*
H192	0.6948	−0.3097	0.9778	0.1061*
H193	0.5280	−0.2831	0.8524	0.1061*

Atomic displacement parameters (Å²)

	U^{11}	U^{22}	U^{33}	U^{12}	U^{13}	U^{23}
C1	0.0694 (14)	0.0348 (11)	0.0799 (14)	−0.0026 (11)	0.0387 (12)	−0.0072 (11)
C2	0.0787 (16)	0.0408 (12)	0.0713 (13)	−0.0136 (12)	0.0380 (12)	−0.0090 (11)
C3	0.0600 (13)	0.0399 (11)	0.0697 (13)	−0.0068 (11)	0.0294 (11)	−0.0063 (10)
O4	0.0648 (10)	0.0493 (9)	0.1030 (13)	−0.0126 (9)	0.0276 (9)	0.0109 (10)
C5	0.0563 (13)	0.0499 (13)	0.0971 (17)	0.0039 (11)	0.0349 (13)	0.0052 (13)

C6	0.0451 (12)	0.0570 (15)	0.108 (2)	0.0039 (12)	0.0188 (13)	0.0069 (15)
O7	0.0491 (8)	0.0478 (9)	0.0862 (11)	−0.0051 (8)	0.0125 (8)	−0.0093 (8)
C8	0.0542 (12)	0.0384 (11)	0.0683 (12)	0.0007 (11)	0.0178 (10)	−0.0024 (10)
O9	0.0536 (8)	0.0445 (9)	0.0629 (8)	−0.0091 (7)	0.0238 (7)	−0.0084 (7)
C10	0.0547 (12)	0.0485 (13)	0.0588 (11)	−0.0002 (11)	0.0124 (10)	−0.0119 (11)
C11	0.0645 (15)	0.0583 (15)	0.0834 (16)	0.0093 (13)	0.0151 (13)	−0.0107 (14)
C12	0.0766 (18)	0.090 (2)	0.101 (2)	0.0251 (18)	0.0171 (17)	−0.0306 (19)
C13	0.076 (2)	0.134 (4)	0.091 (2)	0.012 (2)	0.0308 (17)	−0.039 (2)
C14	0.094 (2)	0.126 (3)	0.0740 (16)	0.000 (2)	0.0378 (16)	−0.013 (2)
C15	0.0795 (17)	0.0705 (18)	0.0670 (13)	0.0040 (15)	0.0277 (13)	−0.0079 (14)
C16	0.107 (2)	0.0459 (14)	0.0704 (14)	−0.0090 (14)	0.0446 (15)	−0.0049 (12)
C17	0.0870 (17)	0.0486 (13)	0.0581 (13)	−0.0026 (13)	0.0327 (13)	0.0009 (11)
O18	0.1059 (15)	0.0488 (11)	0.1039 (14)	−0.0088 (10)	0.0601 (12)	−0.0129 (10)
C19	0.113 (3)	0.0477 (15)	0.106 (2)	−0.0046 (17)	0.047 (2)	−0.0117 (14)
O20	0.162 (2)	0.0595 (12)	0.1151 (15)	−0.0126 (14)	0.0962 (17)	0.0001 (11)
N21	0.0880 (16)	0.0674 (15)	0.0744 (13)	−0.0312 (13)	0.0263 (12)	−0.0161 (12)
N22	0.0641 (14)	0.0817 (18)	0.0783 (14)	−0.0264 (14)	0.0147 (11)	0.0003 (14)
N23	0.0623 (15)	0.133 (3)	0.130 (2)	−0.0115 (19)	0.0331 (17)	−0.001 (2)

Geometric parameters (Å, º)

C1—H11	1.000	C10—C11	1.396 (4)
C1—O9	1.437 (2)	C11—H111	1.002
C1—C5	1.517 (3)	C11—C12	1.375 (4)
C1—C2	1.513 (4)	C12—H121	1.001
C2—H21	1.000	C12—C13	1.361 (6)
C2—N21	1.464 (3)	C13—H131	1.001
C2—C3	1.537 (3)	C13—C14	1.365 (6)
C3—H31	1.001	C14—H141	1.001
C3—C16	1.523 (3)	C14—C15	1.392 (4)
C3—O4	1.419 (3)	C15—H151	1.001
O4—C5	1.444 (3)	C16—H162	0.999
C5—H51	1.001	C16—H161	1.002
C5—C6	1.491 (4)	C16—C17	1.502 (4)
C6—H62	1.000	C17—O20	1.186 (3)
C6—H61	1.001	C17—O18	1.320 (3)
C6—O7	1.432 (3)	O18—C19	1.453 (3)
O7—C8	1.408 (3)	C19—H193	1.001
C8—H81	1.001	C19—H192	1.001
C8—C10	1.499 (3)	C19—H191	0.998
C8—O9	1.421 (3)	N21—N22	1.232 (4)
C10—C15	1.368 (4)	N22—N23	1.133 (4)
H11—C1—O9	108.170	C8—O9—C1	113.72 (16)
H11—C1—C5	111.834	C15—C10—C11	119.8 (2)
O9—C1—C5	111.79 (19)	C15—C10—C8	121.2 (2)
H11—C1—C2	117.051	C11—C10—C8	119.0 (2)
O9—C1—C2	105.98 (19)	H111—C11—C12	120.184

C5—C1—C2	101.85 (19)	H111—C11—C10	120.109
H21—C2—N21	97.832	C12—C11—C10	119.7 (3)
H21—C2—C3	113.240	H121—C12—C13	119.784
N21—C2—C3	115.4 (2)	H121—C12—C11	120.033
H21—C2—C1	111.780	C13—C12—C11	120.2 (3)
N21—C2—C1	116.74 (19)	H131—C13—C14	119.623
C3—C2—C1	102.4 (2)	H131—C13—C12	119.722
H31—C3—C16	105.628	C14—C13—C12	120.7 (3)
H31—C3—O4	112.780	H141—C14—C15	119.950
C16—C3—O4	110.4 (2)	H141—C14—C13	119.942
H31—C3—C2	110.792	C15—C14—C13	120.1 (4)
C16—C3—C2	112.3 (2)	H151—C15—C10	120.260
O4—C3—C2	105.1 (2)	H151—C15—C14	120.169
C5—O4—C3	110.88 (18)	C10—C15—C14	119.6 (3)
H51—C5—C6	105.154	H162—C16—H161	109.357
H51—C5—O4	113.166	H162—C16—C17	108.240
C6—C5—O4	110.1 (2)	H161—C16—C17	108.084
H51—C5—C1	110.120	H162—C16—C3	108.243
C6—C5—C1	113.1 (2)	H161—C16—C3	108.149
O4—C5—C1	105.3 (2)	C17—C16—C3	114.7 (2)
H62—C6—H61	109.403	O20—C17—O18	123.5 (3)
H62—C6—O7	108.873	O20—C17—C16	124.4 (3)
H61—C6—O7	108.792	O18—C17—C16	112.1 (2)
H62—C6—C5	108.829	C19—O18—C17	116.2 (2)
H61—C6—C5	108.793	H193—C19—H192	109.351
O7—C6—C5	112.12 (19)	H193—C19—H191	109.535
C8—O7—C6	110.38 (18)	H192—C19—H191	109.543
H81—C8—C10	111.363	H193—C19—O18	109.420
H81—C8—O9	111.259	H192—C19—O18	109.412
C10—C8—O9	106.41 (17)	H191—C19—O18	109.566
H81—C8—O7	107.889	N22—N21—C2	115.7 (2)
C10—C8—O7	109.96 (19)	N23—N22—N21	171.7 (3)
O9—C8—O7	109.96 (18)		