

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 $\sigma(\text{C}-\text{C}) = 0.004 \text{ \AA}$
R factor = 0.035
wR factor = 0.092
Data-to-parameter ratio = 9.1For details of how these key indicators were automatically derived from the article, see <http://journals.iucr.org/e>.The title compound, $\text{C}_{15}\text{H}_{17}\text{N}_3\text{O}_5$, was formed by carrying out a Wittig reaction, under basic conditions, on 2-azido-3,5-O-benzylidene-2-deoxy-D-lyxose.

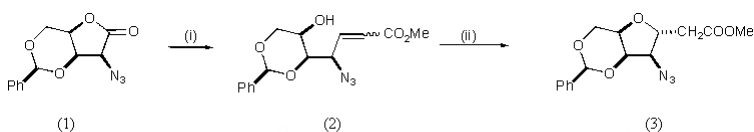
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Comment

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).

Reagents: (i) DIBAL-H then $\text{Ph}_3\text{PCH}=\text{CHCO}_2\text{Me}$ (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

C₁₅H₁₇N₃O₅
M_r = 319.32
 Monoclinic, *P*2₁
a = 8.2135 (3) Å
b = 9.2262 (3) Å
c = 10.9944 (3) Å
 β = 108.0414 (15)°
V = 792.19 (4) Å³
Z = 2

D_x = 1.339 Mg m⁻³
 Mo K α radiation
 Cell parameters from 1851 reflections
 θ = 5–27°
 μ = 0.10 mm⁻¹
T = 293 K
 Plate, colourless
 0.40 × 0.40 × 0.10 mm

Data collection

Nonius KappaCCD diffractometer
 ω scans
 Absorption correction: multi-scan
 (DENZO/SCALEPACK;
 Otwinowski & Minor, 1997)
T_{min} = 0.96, *T_{max}* = 0.99
 3420 measured reflections

1906 independent reflections
 1464 reflections with *I* > 2.00 $\sigma(I)$
R_{int} = 0.011
 θ_{max} = 27.5°
h = -10 → 10
k = -11 → 11
l = -14 → 14

Refinement

Refinement on *F*²
R[*F*² > 2 σ (*F*²)] = 0.035
wR(*F*²) = 0.092
S = 0.89
 1906 reflections
 209 parameters
 H-atom parameters constrained

$w = 1/[\sigma^2(F^*) + (0.0434p)^2 + 0.113p]$
 where $p = 0.333\max(F_o^2, 0) + 0.667F_c^2$
 $(\Delta/\sigma)_{max} = 0.002$
 $\Delta\rho_{max} = 0.17 \text{ e \AA}^{-3}$
 $\Delta\rho_{min} = -0.15 \text{ e \AA}^{-3}$
 Extinction correction: Larson (1970)
 Extinction coefficient: 4.3 (6) × 10²

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)

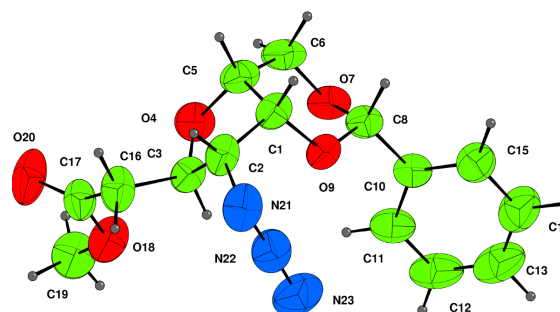


Figure 1
 The molecular structure of (3), with 50% probability displacement ellipsoids.

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: 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.

References

Altomare, A., Casciarano, G., Giacovazzo, C., Guagliardi, A., Burla, M. C., Polidori, G. & Camalli, M. (1994). *J. Appl. Cryst.* **27**, 435.
 Betteridge, P. W., Carruthers, J. R., Cooper, R. I., Prout, K. & Watkin, D. J. (2003). *J. Appl. Cryst.* **36**, 1487.
 Chakraborty, T. K., Jayaprakash, S. & Ghosh, S. (2003). *Comb. Chem. High Throughput Screening*, **5**, 373–387.
 Edwards, A. A., Ichihara, O., Murfin, S., Wilkes, R., Watkin, D. J. & Fleet, G. W. J. (2004). *J. Combinatorial Chem.* **6**, 230–238.
 Gellman, S. H. (1998). *Acc. Chem. Res.* **31**, 173–180.
 Gruner, S. A. W., Locardi, E., Lohof, E. & Kessler, H. (2002). *Chem. Rev.* **102**, 491–514.
 Krulle, T. M., Davis, B. G., Ardron, H., Long, D. D., Hindle, N. A., Smith, C., Brown, D., Lane, A. L., Watkin, D. J., Marquess, D. G. & Fleet, G. W. J. (1996). *J. Chem. Soc. Chem. Commun.* pp. 1271–1272.
 Larson, A. C. (1970). *Crystallographic Computing*, edited by F. R. Ahmed, S. R. Hall and C. P. Huber, pp. 291–294. Copenhagen: Munksgaard.
 Le, G. T., Abbenante, G., Becker, B., Gratwohl, M., Halliday, J., Tometzki, G., Zuegg, J. & Meuterms, W. (2003). *Drug Discovery Today*, **8**, 701–709.
 Nonius (1997–2001). COLLECT. Nonius BV, Delft, The Netherlands.
 Otwinowski, Z. & Minor, W. (1997). *Methods in Enzymology*, Vol. 276, *Macromolecular Crystallography*, Part A, edited by C. W. Carter Jr and R. M. Sweet, pp. 307–326. New York: Academic Press.
 Sanjayan, G., Stewart, A., Hachisu, S., Gonzalez, R., Watterson, M. P. & Fleet, G. W. J. (2003). *Tetrahedron Lett.* **44**, 5847–5852.
 Schweizer, F. (2002). *Angew. Chem. Int. Ed.* **41**, 231–253.
 Smith, M. D., Claridge, T. D. W., Sansom, M. P. & Fleet, G. W. J. (1996). *Org. Biomol. Chem.* **1**, 3647–3655.
 Sofia, M. J. (1998). *Med. Chem. Res.* **8**, 362–378.
 Watkin, D. J., Prout, C. K. & Pearce, L. J. (1996). CAMERON. Chemical Crystallography Laboratory, Oxford, England.
 Watterson, M. P., Edwards, A. A., Leach, J. A., Smith, M. D., Ichihara, O. & Fleet, G. W. J. (2003). *Tetrahedron Lett.* **44**, 5853–5857.