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3-Azido-3-deoxy-2,2′:5,6-di-*O*-isopropylidene-2-*C*-hydroxmethyl-D-gulono-1,4-lactone

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The title azidolactone, $C_{13}H_{19}O_6N_3$, formed by S_N2 displacement of the trifluoromethanesulfonate with sodium azide, is the first example of a branched β-sugar amino acid scaffold.

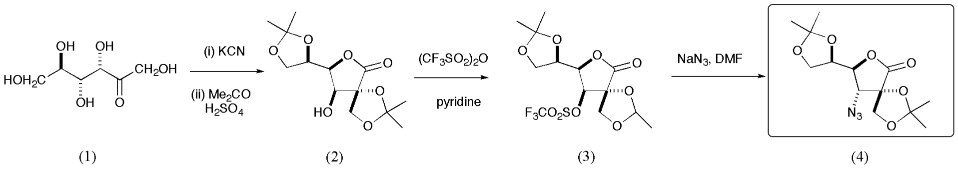
Key indicators

Single-crystal X-ray study
T = 120 K
Mean σ(C–C) = 0.005 Å
R factor = 0.045
wR factor = 0.108
Data-to-parameter ratio = 9.3

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

Comment

Gellman (Lai & Gellman, 2003; Hayen *et al.*, 2004) and Seebach (Lelais & Seebach, 2003; Rueping *et al.*, 2004) have pioneered studies on the exploitation of β-amino acids in their adoption of secondary structural features in short chains. Although sugar amino acids (SAA) have been extensively investigated as peptidomimetics and dipeptide isosteres (Schweizer, 2002; Chakraborty *et al.*, 2004), there have been very few studies of β-SAAs (Jenkinson & Fleet, 2004; Johnson *et al.*, 2004), even though some oxetane-derived β-SAAs exhibited novel helical structures (Barker *et al.*, 2001). This paper reports the structure of the β-azidolactone, (4), which is a novel β-SAA scaffold containing a branched carbon chain.



D-Fructose may be readily converted into the diacetonide (2) (Hotchkiss *et al.*, 2004); esterification of (2) with triflic anhydride gave the corresponding stable trifluoromethanesulfonate. Reaction of (3) with sodium azide in DMF gave an organic azide in good yield. The structure of this azide is fraught with uncertainties; the trifluoromethanesulfonate in (3) has two β-O atoms and the adjacent α-C atom is trisubstituted, so the efficiency of the S_N2 reaction is surprising. There is considerable ambiguity in the stereochemistry of the product, since there may well be neighbouring group participation by the O atom; it is also possible that some rearrangement that maintained the same connectivity of CH atoms may have occurred. However, X-ray crystallographic analysis of the product of the reaction showed that the anticipated inverted azide, (4), had indeed been produced.

Experimental

The full preparative method is not available for publication as yet. The sample was crystallized from diethyl ether by inward diffusion of *n*-hexane to give lath-shaped colourless crystals.

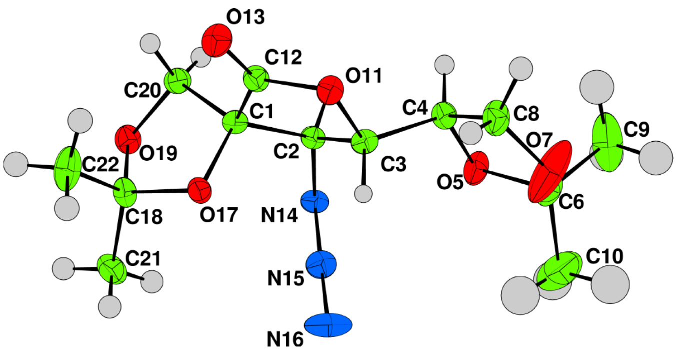


Figure 1
The title molecule at 120 K, with displacement ellipsoids drawn at the 50% probability level. The large ellipsoids at atoms 07, C9 and C10 are discussed in the text. H atoms are shown as spheres of arbitrary radii.

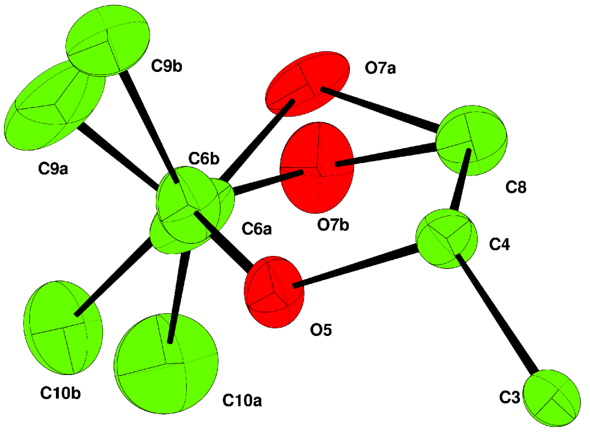


Figure 2
The disordered fragment of the title molecule at 120 K, displayed as a 'split atom' model. Even with firm anisotropic displacement parameter similarity restraints, the ellipsoids do not conform to any reasonable physical model.

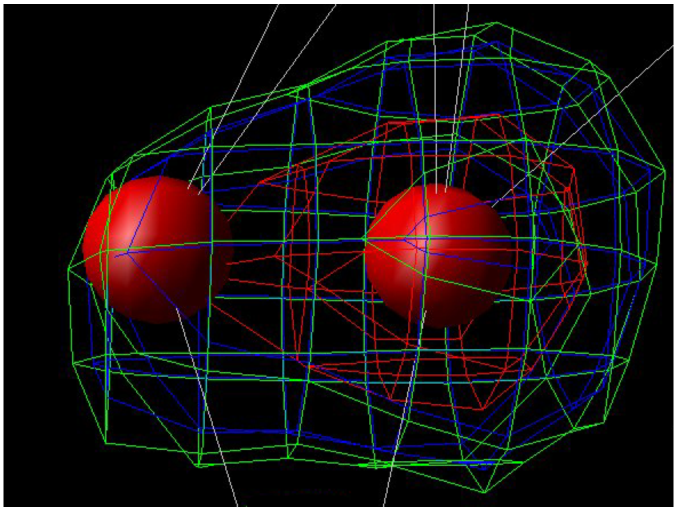


Figure 3
F_o electron density map viewed perpendicular to the line through atoms O7*a* and O7*b*, computed excluding phasing information derived from these two partial atoms. There are no distinct lobes near the two atom positions proposed by the 'split atom' refinement, suggesting that there still remains substantial dynamic disorder.

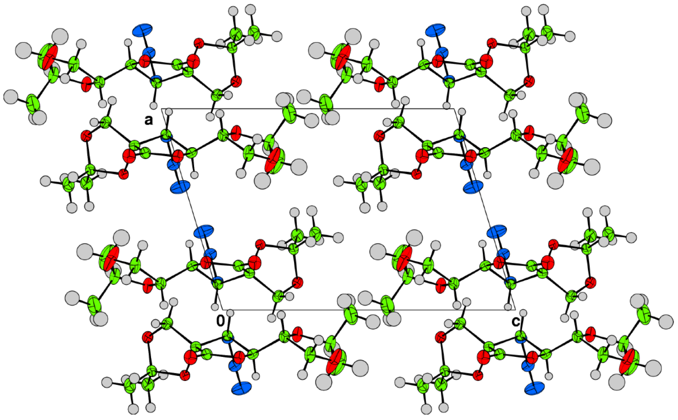


Figure 4
Packing diagram of the title compound, viewed along the *b* axis.

Crystal data

$C_{13}H_{19}N_3O_6$
$M_r = 313.31$
Monoclinic, $P2_1$
$a = 8.7755$ (2) Å
$b = 7.6452$ (2) Å
$c = 12.2232$ (3) Å
$\beta = 106.9659$ (11)°
$V = 784.37$ (3) Å^3
$Z = 2$
$D_x = 1.326$ Mg m^{-3}
Mo $K\alpha$ radiation
Cell parameters from 1734 reflections
$\theta = 5$–27°
$\mu = 0.11$ mm^{-1}
$T = 120$ K
Lath, colourless
0.30 × 0.20 × 0.10 mm

Data collection

Nonius KappaCCD diffractometer
ω scans
Absorption correction: multi-scan (*DENZO*/*SCALEPACK*; Otwinowski & Minor, 1997)
$T_{\min} = 0.98$, $T_{\max} = 0.99$
3320 measured reflections
1869 independent reflections
1655 reflections with $I > 2\sigma(I)$
$R_{\rm int} = 0.015$
$\theta_{\max} = 27.5°$
$h = -11 \rightarrow 11$
$k = -9 \rightarrow 9$
$l = -15 \rightarrow 15$

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)] = 0.045$
$wR(F^2) = 0.109$
$S = 0.93$
1866 reflections
200 parameters
H-atom parameters constrained
$w = 1/[\sigma^2(F) + (0.0522p)^2 + 0.571p]$, where $p = [\max(F_o^2,0) + 2F_c^2]/3$
$(\Delta/\sigma)_{\max} < 0.001$
$\Delta\rho_{\max} = 0.65$ e Å^{-3}
$\Delta\rho_{\min} = -0.42$ e Å^{-3}
Extinction correction: Larson (1970)
Extinction coefficient: 3.0 (5) × 10^2

Table 1
Selected interatomic distances (Å).

O5—C6	1.433 (3)	C6—C10	1.486 (7)
C6—O7	1.370 (5)	O7—C8	1.384 (4)
C6—C9	1.503 (6)		

An initial data set was collected at 190 K. This gave reasonable refinement [$N_{\rm measured} = 2766$, $R_{\rm int} = 0.02$, $N_{\rm ref} = 1748$, $R_w(2\sigma) = 0.081$, $R(2\sigma) = 0.034$], though atoms O7, C9 and C10 had very elongated displacement ellipsoids. It was unclear whether the C6/O7/C9/C10 fragment should be modelled with large anisotropic displacement parameters (ADPs) or with 'split atoms'. Refinement was continued with this fragment represented by 'split atoms'. However, the ADPs could not be explained by a rational physical model. As with the unsplit model, the bond lengths deviated unacceptably from averages drawn by *MOGUL* (Bruno *et al.*, 2004) from the Cambridge Structural Database (CSD; Version 5.25; Allen, 2002), even with the application of firm bond length similarity restraints.

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In order to resolve this issue, data were recollected at 120 K. It is the result of this refinement that is reported in the CIF. Even at this temperature, the ADPs of the problematic group remained large, though not as large as in the 190 K data set. Both the large ADP and the 'split atom' refinements continued to give unacceptable bond lengths and ellipsoids (see Fig. 2). Fig. 3, plotted with *MCE* (Hušák & Kratochvíl, 2003), shows the observed electron density perpendicular to the line connecting atoms O7*a* and O7*b*. The map is phased by all of the structure except these two atoms, which are included for illustrative purposes at the positions they refine to in the 'split atom' model. There is a smooth transition in electron density between the two sites, with no evident build-up of density at either site.

One interpretation of these observations is that neither the split atom model nor the large ADP model really represents what is occurring in this structure. It is clearly something more complicated than simply having the envelope flap (O7/O7*a*) distributed over two sites on opposite sides of a plane through the other ring atoms. Of 29 structures in the CSD containing this moiety some clearly have the atom corresponding to O7 as the 'flap', some have C6 as the flap, but there are also a number in which no four atoms form a convincing plane. It seems that, even in the solid state, there is a continuum between an O-flap and a C-flap geometry. The amount of material available was insufficient to enable low-temperature solid-state NMR measurements to be carried out.

For the large ADP model, all H atoms were seen in the difference electron density map (even those on the highly anisotropic C9 and C10). Their positions and $U_{\rm iso}$(H) values were regularized by several cycles of refinement using slack restraints, after which the refinement was completed using 'riding' constraints and all reflections with $I > -3\sigma(I)$. Fig. 4 is a packing diagram showing an alternation of highly mobile and highly ordered groups lying in a plane at approximately $c/2$.

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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References

Allen, F. H. (2002). *Acta Cryst.* B**58**, 380–388.

Altomare, A., Cascarano, G., Giacovazzo, C., Guagliardi, A., Burla, M. C., Polidori, G. & Camalli, M. (1994). *J. Appl. Cryst.* **27**, 435.

Barker, S. F., Angus, D., Taillefumier, C., Probert, M. R., Watkin, D. J., Watterson, M. P., Claridge, T. D. W., Hungerford, N. L. & Fleet, G. W. J. (2001). *Tetrahedron Lett.* **42**, 4247–4250.

Betteridge, P. W., Carruthers, J. R., Cooper, R. I., Prout, K. & Watkin, D. J. (2003). *J. Appl. Cryst.* **36**, 1487.

Bruno, I. J., Cole, J. C., Kessler, M., Luo, J., Motherwell, W. D. S., Purkis, L. H., Smith, B. R., Taylor, R., Cooper, R. I., Harris, S. E. & Orpen, A. G. (2004). *J. Chem. Inf. Comput. Sci.* In the press.

Chakraborty, T. K., Srinivasi, P., Tapadar, S. & Mohan, B. K. (2004). *J. Chem. Sci.* **116**, 187–207.

Hayen, A., Schmitt, M. A., Ngassa, F. N., Thomasson, K. A. & Gellman, S. H. (2004). *Angew. Chem. Int. Ed.* **43**, 505–510.

Hotchkiss, D., Soengas, R., Simone, M. I., van Ameijde, J., Hunter, S., Cowley, A. R. & Fleet, G. W. J. (2004). *Tetrahedron Lett.* **45**. In the press.

Hušák, M. & Kratochvíl, B. (2003). *J. Appl. Cryst.* **36**, 1104.

Jenkinson, S. F. & Fleet, G. W. J. (2004). *Tetrahedron Asymmetry*, **15**, 2667–2679.

Johnson, S. W., Jenkinson, S. F., Angus, D., Taillefumier, C., Jones, J. H. & Fleet, G. W. J. (2004). *Tetrahedron Asymmetry*, **15**, 2681–2686.

Lai, J. R. & Gellman, S. H. (2003). *Protein Sci.* **12**, 560–566.

Larson, A. C. (1970). *Crystallographic Computing*, edited by F. R. Ahmed, S. R. Hall & C. P. Huber, pp. 291–294. Copenhagen: Munksgaard.

Lelais, G. & Seebach, D. (2003). *Helv. Chim. Acta*, **86**, 4152–4168.

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 & R. M. Sweet, pp. 307–326. New York: Academic Press.

Rueping, M., Mahajan, Y. R., Jaun, B. & Seebach, D. (2004). *Chem. Eur. J.* **10**, 1607–1615.

Schweizer, F. (2002). *Angew. Chem. Int. Ed.* **41**, 230–253.

Watkin, D. J., Prout, C. K. & Pearce, L. J. (1996). *CAMERON*. Chemical Crystallography Laboratory, Oxford, England.

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