Acta Crystallographica Section E
Structure Reports Online
ISSN 1600-5368

(2*S*,4*S*)-4-Azido-1-benzyl-2-[(*S*)-2,2-dimethyl-1,3-dioxolan-4-yl]pyrrolidine

Amy K. S. Chesterton,[a] Sarah F. Jenkinson,[a]* Nigel A. Jones,[a] George W. J. Fleet[a] and David J. Watkin[b]

[a]Department of Organic Chemistry, Chemistry Research Laboratory, University of Oxford, Mansfield Road, Oxford OX1 3TA, England, and [b]Chemical Crystallography Laboratory, Chemistry Research Laboratory, University of Oxford, Mansfield Road, Oxford OX1 3TA, England

Correspondence e-mail: sarah.jenkinson@chem.ox.ac.uk

Key indicators

Single-crystal X-ray study
T = 150 K
Mean σ(C–C) = 0.004 Å
R factor = 0.044
wR factor = 0.100
Data-to-parameter ratio = 9.2

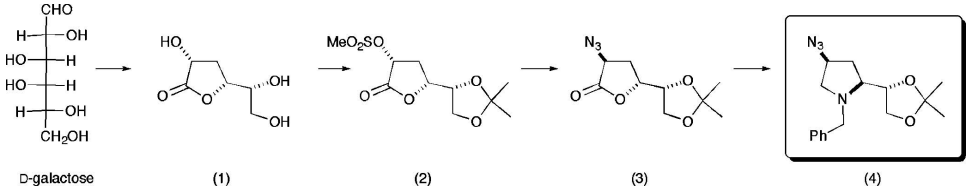
For details of how these key indicators were automatically derived from the article, see http://journals.iucr.org/e.

Received 8 June 2006
Accepted 16 June 2006

The relative stereochemistry of the title compound, $C_{16}H_{22}N_4O_2$, a key intermediate in the synthesis of 3-deoxy imino sugars, was firmly established by X-ray crystallographic analysis. The absolute configuration was inferred from the starting material, D-galactose. There are no unusual crystal packing features.

Comment

The reaction of calcium hydroxide with D-galactose has been shown to generate 3-deoxy-D-galactono-1,4-lactone, (1), directly (Whistler & BeMiller, 1963; Kiliani & Kleeman, 1884), the stereochemistry of which has been determined by X-ray crystallographic analysis (Punzo *et al.* 2006). The 3-deoxy sugar (1) has great potential as a building block for the synthesis of complex highly functionalized targets. It has been utilized in the synthesis of carnitine (Bols *et al.*, 1992) and hydroxylated azepanes (Anderson *et al.*, 2000) and could prove useful in the synthesis of bulgecinines (Bashyal *et al.*, 1987; Chavan *et al.*, 2005; Khalaf & Datta, 2004) and other highly substituted prolines and pyrrolidines. Polyhydroxylated nitrogen heterocycles, known as imino sugars, are an important class of glycosidase inhibitor (Watson *et al.*, 2001; Asano *et al.*, 2000). The title compound, (4), is a key intermediate in the synthesis of 2-acetamido-3-deoxy imino sugars.



The absolute stereochemistry of (4) was known from the use of D-galactose as the starting material. The conversion of (2) to (4) involved nucleophilic dispacement at both C2 and C4 of the sugar. The X-ray crystal structure (Fig. 1) showing the relative configuration of (4) thus establishes that both nucleophilic displacements occurred with inversion of configuration.

There are no unusual bond lengths or angles. As is common with these materials, the azide group is non-linear [N13—N14—N15 = 173.5 (3)°]. There are no short intermolecular contacts (Fig. 2), nor evidence of π–π interactions between the phenyl groups.

Experimental

The side-chain diol in (1) was protected as an acetonide and the remaining free hydroxyl group was esterified with methanesulfonyl

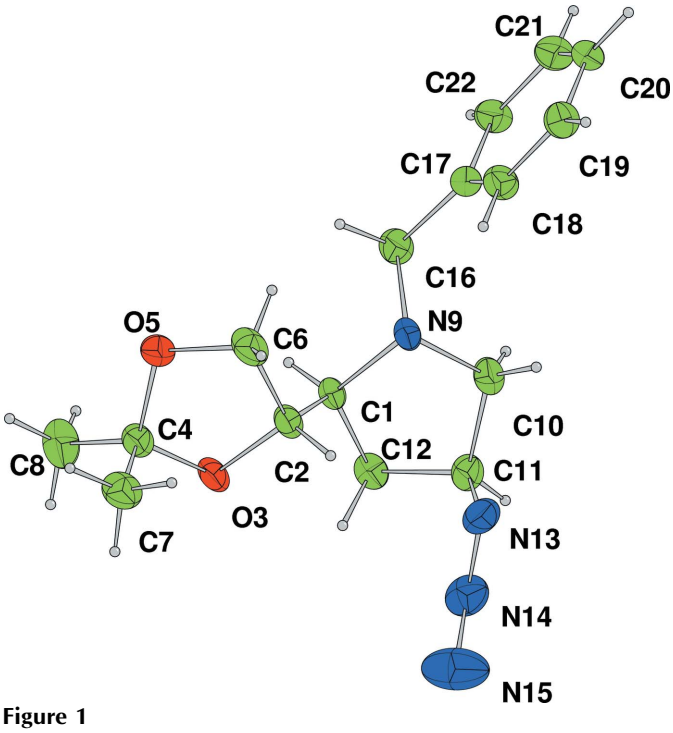


Figure 1
The title compound with displacement ellipsoids drawn at the 50% probability level. H atoms are shown as spheres of arbitary radius.

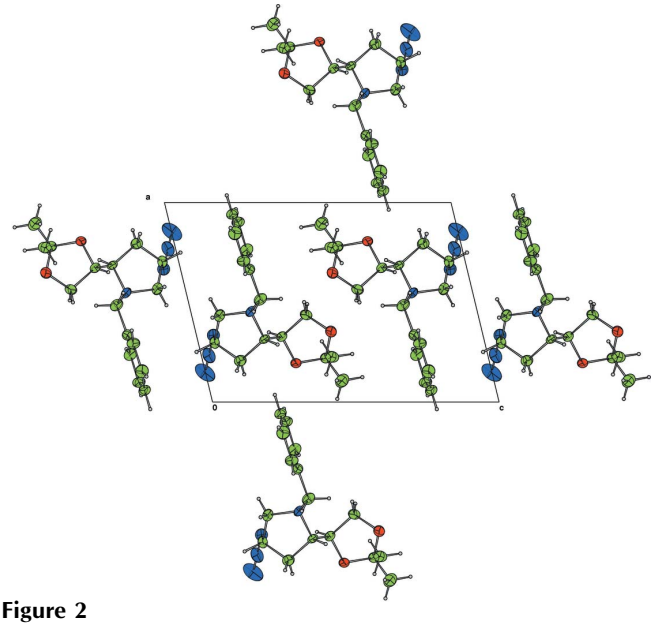


Figure 2
A projection down the *b* axis of the title structure. There are no unusually short intermolecular contacts. Curiously, there are no π–π interactions between the phenyl groups.

chloride. Nucleophilic displacement of the resulting methanesulfonate ester (2) with sodium azide generated the azide (3) in good yield. Reduction of the lactone to the diol with lithium borohydride and activation of both hydroxyl groups with methanesulfonyl chloride followed by a double nucleophilic displacement reaction with benzylamine generated the 3-deoxy imino sugar (4) (Chesterton *et al.*, 2006). The final product was recrystallized from dichloromethane to give colourless needles [m.p. 305–307 K; $[\alpha]_D^{18}$ −48.3 (*c* 0.76 in acetone)].

Crystal data

$C_{16}H_{22}N_4O_2$
M_r = 302.38
Monoclinic, $P2_1$
a = 9.6539 (4) Å
b = 6.3289 (3) Å
c = 13.4942 (7) Å
β = 103.577 (2)°
V = 801.44 (7) Å^3
Z = 2
D_x = 1.253 Mg m^{-3}
Mo $K\alpha$ radiation
μ = 0.09 mm^{-1}
T = 150 K
Needle, colourless
0.80 × 0.20 × 0.10 mm

Data collection

Nonius KappaCCD diffractometer
ω scans
Absorption correction: multi-scan (*DENZO*/*SCALEPACK*, Otwinowski & Minor, 1997)
T_{min} = 0.71, T_{max} = 0.99
7271 measured reflections
1833 independent reflections
1254 reflections with $I > 2\sigma(I)$
R_{int} = 0.064
θ_{max} = 30.1°

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.044
$wR(F^2)$ = 0.100
S = 0.86
1833 reflections
199 parameters
H-atom parameters constrained
$w = 1/[\sigma^2(F^2) + (0.05P)^2 + 0.1P]$, where $P = [\max(F_o^2,0) + 2F_c^2]/3$
$(\Delta/\sigma)_{max} < 0.001$
$\Delta\rho_{max}$ = 0.41 e Å^{-3}
$\Delta\rho_{min}$ = −0.36 e Å^{-3}

In the absence of significant anomalous scattering, Friedel pairs were merged and the absolute configuration assigned from the starting material. The relatively large ratio of minimum to maximum corrections applied in the multi-scan process (1:1.45) reflect changes in the illuminated volume of the crystal. These were kept to a minimum and were taken into account (Görbitz, 1999) by the multi-scan inter-frame scaling (*DENZO*/*SCALEPACK*; Otwinowski & Minor, 1997). 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 U_{iso}(H) = 1.2–1.5U_{eq}(parent atom)], after which the positions were refined with riding constraints.

Data collection: *COLLECT* (Nonius, 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., Cascarano, G., Giacovazzo, C., Guagliardi, A., Burla, M. C., Polidori, G. & Camalli, M. (1994). *J. Appl. Cryst.* **27**, 435–436.
Anderson, S. M., Ekhart, C., Lundt, I. & Stutz, A. E. (2000). *Carbohydr. Res.* **326**, 22–33.
Asano, N., Nash, R. J., Molyneux, R. J. & Fleet, G. W. J. (2000). *Tetrahedron Asymmetry*, **11**, 1645–1680.
Bashyal, B. P., Chow, H.-F. & Fleet, G. W. J. (1987). *Tetrahedron*, **43**, 423–430.
Betteridge, P. W., Carruthers, J. R., Cooper, R. I., Prout, K. & Watkin, D. J. (2003). *J. Appl. Cryst.* **36**, 1487.
Bols, M., Lundt, I. & Pedersen, C. (1992). *Tetrahedron*, **48**, 319–324.
Chavan, S. P., Praveen, C., Sharma, P. & Kalkote, U. (2005). *Tetrahedron Lett.* **46**, 439–441.
Chesterton, A. K. S., Jenkinson, S. F., Jones, N. A., Watkin, D. J. & Fleet, G. W. J. (2006). In preparation.
Görbitz, C. H. (1999). *Acta Cryst.* B**55**, 1090–1098.
Khalaf, J. K. & Datta, A. (2004). *J. Org. Chem.* **69**, 387–390.
Kiliani, H. & Kleeman, S. (1884). *Berichte*, **17**, 1296-1310.

Nonius (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.
Punzo, F., Watkin, D. J., Hotchkiss, D. & Fleet, G. W. J. (2006). *Acta Cryst.* E**62**, o1344–o1346.
Watkin, D. J., Prout, C. K. & Pearce, L. J. (1996). *CAMERON*. Chemical Crystallography Laboratory, Oxford, England.
Watson, A. A., Fleet, G. W. J., Asano, N., Molyneux, R. J. & Nash, R. J. (2001). *Phytochemistry*, **56**, 265–295.
Whistler, R. L. & BeMiller, J. N. (1963). *Method Carbohydr. Chem.* **2**, 483–484.