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

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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.

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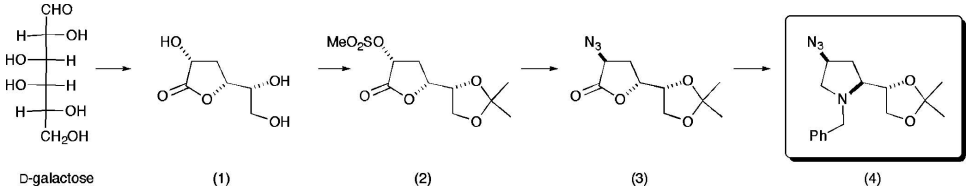
The relative stereochemistry of the title compound, $C_{16}H_{22}N_4O_2$, a key intermediate in the synthesis of 3-deoxy imino sugars, was firmly established by X-ray crystallographic analysis. The absolute configuration was inferred from the starting material, D-galactose. There are no unusual crystal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

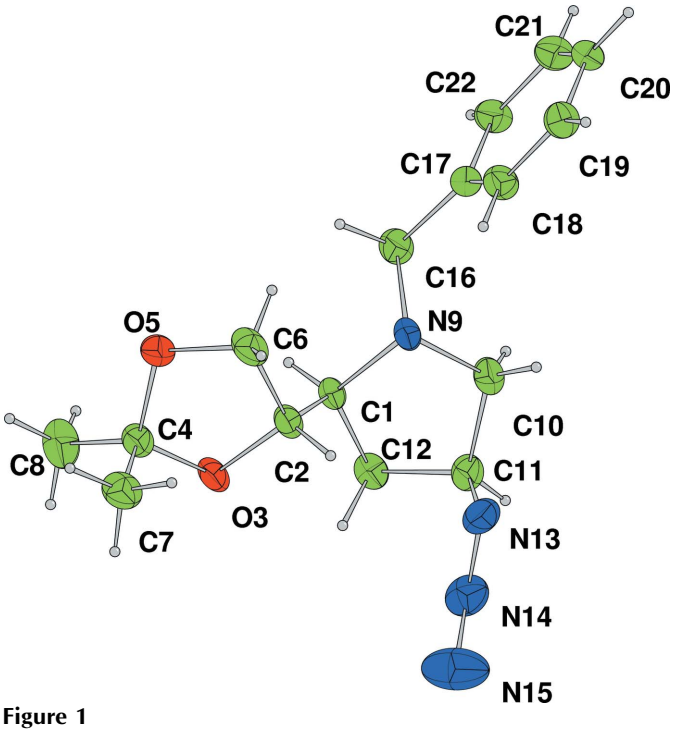


Figure 1
The title compound with displacement ellipsoids drawn at the 50% probability level. H atoms are shown as spheres of arbitary radius.

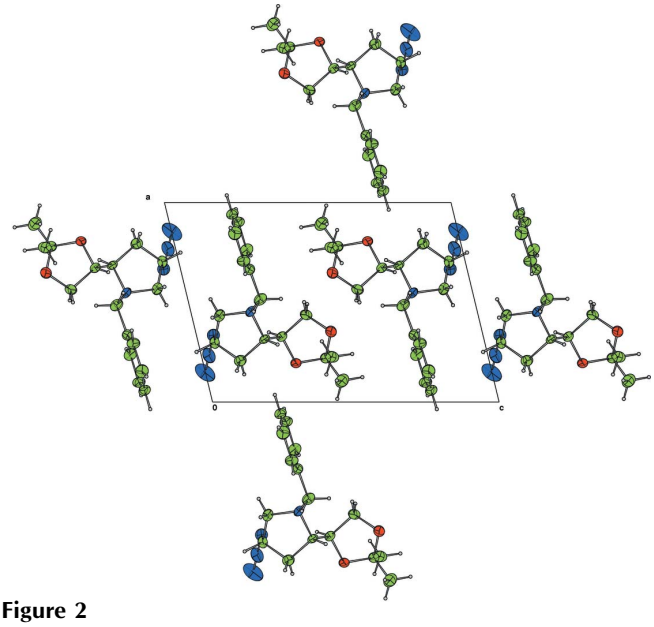


Figure 2
A projection down the *b* axis of the title structure. There are no unusually short intermolecular contacts. Curiously, there are no π–π interactions between the phenyl groups.

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*.

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supporting information

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$c = 13.4942$ (7) Å
$\beta = 103.577$ (2)°
$V = 801.44$ (7) Å^3
$Z = 2$
$F(000) = 324$
$D_x = 1.253$ Mg m^{-3}
Mo $K\alpha$ radiation, $\lambda = 0.71073$ Å
Cell parameters from 1995 reflections
$\theta = 5$–30°
$\mu = 0.09$ mm^{-1}
$T = 150$ K
Plate, colourless
0.80 × 0.20 × 0.10 mm

Data collection

Nonius KappaCCD diffractometer
Graphite monochromator
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Absorption correction: multi-scan (DENZO/SCALEPACK, Otwinowski & Minor, 1997)
$T_{min} = 0.71$, $T_{max} = 0.99$
7271 measured reflections
2489 independent reflections
1254 reflections with $I > 2\sigma(I)$
$R_{int} = 0.064$
$\theta_{max} = 30.1°$, $\theta_{min} = 5.3°$
$h = -13 \rightarrow 13$
$k = -8 \rightarrow 8$
$l = -18 \rightarrow 18$

Refinement

Refinement on F^2
Least-squares matrix: full
$R[F^2 > 2\sigma(F^2)] = 0.044$
$wR(F^2) = 0.100$
$S = 0.86$
1833 reflections
199 parameters
1 restraint
Primary atom site location: structure-invariant direct methods
Hydrogen site location: inferred from neighbouring sites
H-atom parameters constrained
Method = Modified Sheldrick $w = 1/[\sigma^2(F^2) + (0.05P)^2 + 0.1P]$, where $P = [\max(F_o^2,0) + 2F_c^2]/3$
$(\Delta/\sigma)_{max} = 0.000154$
$\Delta\rho_{max} = 0.41$ e Å^{-3}
$\Delta\rho_{min} = -0.36$ e Å^{-3}

Fractional atomic coordinates and isotropic or equivalent isotropic displacement parameters (Å^2)

	x	*y*	*z*	U_{iso}*/U_{eq}
C1	0.6851 (3)	0.6747 (5)	0.76546 (19)	0.0238
C2	0.6720 (3)	0.4736 (5)	0.70332 (19)	0.0276
O3	0.80551 (18)	0.4369 (4)	0.67623 (13)	0.0336
C4	0.7797 (3)	0.4069 (5)	0.5685 (2)	0.0294

O5	0.6470 (2)	0.5082 (4)	0.52745 (14)	0.0367
C6	0.5632 (3)	0.4806 (6)	0.6004 (2)	0.0399
C7	0.7737 (3)	0.1746 (5)	0.5447 (2)	0.0376
C8	0.8935 (3)	0.5214 (6)	0.5299 (2)	0.0467
N9	0.5465 (2)	0.7252 (4)	0.79036 (16)	0.0255
C10	0.5668 (3)	0.7219 (5)	0.9024 (2)	0.0344
C11	0.7025 (3)	0.5979 (5)	0.9430 (2)	0.0328
C12	0.7931 (3)	0.6543 (5)	0.8683 (2)	0.0305
N13	0.6655 (3)	0.3690 (5)	0.94096 (19)	0.0387
N14	0.7675 (3)	0.2518 (5)	0.97347 (19)	0.0425
N15	0.8531 (4)	0.1274 (5)	1.0014 (3)	0.0697
C16	0.4857 (3)	0.9242 (5)	0.7467 (2)	0.0327
C17	0.3358 (3)	0.9657 (5)	0.7593 (2)	0.0265
C18	0.2372 (3)	0.8035 (5)	0.7527 (2)	0.0313
C19	0.0989 (3)	0.8455 (5)	0.7596 (2)	0.0318
C20	0.0578 (3)	1.0514 (5)	0.7727 (2)	0.0324
C21	0.1543 (3)	1.2138 (5)	0.7796 (2)	0.0368
C22	0.2932 (3)	1.1712 (5)	0.7730 (2)	0.0315
H11	0.7118	0.7893	0.7249	0.0294*
H21	0.6511	0.3568	0.7451	0.0325*
H61	0.4993	0.6005	0.5966	0.0480*
H62	0.5096	0.3487	0.5873	0.0477*
H71	0.7592	0.1557	0.4722	0.0539*
H72	0.8620	0.1103	0.5796	0.0542*
H73	0.6959	0.1128	0.5676	0.0539*
H81	0.8755	0.5077	0.4564	0.0718*
H82	0.9844	0.4598	0.5621	0.0717*
H83	0.8921	0.6690	0.5482	0.0717*
H101	0.5772	0.8658	0.9293	0.0421*
H102	0.4850	0.6537	0.9204	0.0423*
H111	0.7489	0.6418	1.0138	0.0388*
H121	0.8433	0.7879	0.8886	0.0336*
H122	0.8610	0.5430	0.8661	0.0339*
H161	0.5465	1.0401	0.7806	0.0430*
H162	0.4829	0.9236	0.6747	0.0430*
H181	0.2654	0.6646	0.7440	0.0374*
H191	0.0335	0.7340	0.7563	0.0371*
H201	−0.0360	1.0805	0.7765	0.0373*
H211	0.1275	1.3523	0.7907	0.0440*
H221	0.3584	1.2813	0.7781	0.0392*

Atomic displacement parameters (Å²)

	U^{11}	U^{22}	U^{33}	U^{12}	U^{13}	U^{23}
C1	0.0183 (14)	0.0288 (16)	0.0269 (14)	0.0004 (13)	0.0103 (11)	0.0020 (13)
C2	0.0222 (16)	0.0362 (17)	0.0263 (14)	0.0041 (14)	0.0095 (12)	−0.0022 (15)
O3	0.0201 (11)	0.0552 (14)	0.0252 (10)	0.0104 (10)	0.0048 (8)	−0.0065 (10)
C4	0.0233 (16)	0.0396 (18)	0.0250 (15)	0.0041 (15)	0.0053 (12)	−0.0030 (15)

O5	0.0286 (12)	0.0536 (15)	0.0272 (10)	0.0136 (11)	0.0051 (9)	0.0042 (11)
C6	0.0230 (17)	0.064 (2)	0.0302 (15)	0.0077 (17)	0.0021 (13)	−0.0097 (18)
C7	0.0276 (17)	0.046 (2)	0.0374 (18)	0.0021 (17)	0.0031 (14)	−0.0048 (16)
C8	0.043 (2)	0.057 (2)	0.0445 (19)	−0.0071 (19)	0.0189 (15)	−0.0064 (19)
N9	0.0248 (13)	0.0282 (14)	0.0272 (12)	0.0031 (11)	0.0132 (10)	0.0020 (12)
C10	0.0335 (17)	0.044 (2)	0.0278 (15)	0.0061 (16)	0.0122 (13)	−0.0021 (16)
C11	0.0321 (18)	0.045 (2)	0.0211 (16)	0.0035 (15)	0.0049 (14)	−0.0036 (14)
C12	0.0271 (16)	0.0321 (17)	0.0330 (15)	−0.0004 (14)	0.0087 (13)	−0.0034 (15)
N13	0.0337 (16)	0.0479 (18)	0.0344 (15)	0.0019 (15)	0.0081 (12)	0.0153 (14)
N14	0.0500 (19)	0.0412 (17)	0.0327 (15)	0.0001 (17)	0.0024 (14)	−0.0039 (14)
N15	0.070 (2)	0.049 (2)	0.073 (2)	0.0144 (19)	−0.0167 (19)	−0.0150 (19)
C16	0.0327 (18)	0.0283 (17)	0.0409 (17)	0.0017 (15)	0.0163 (14)	0.0069 (15)
C17	0.0253 (16)	0.0293 (17)	0.0253 (14)	0.0044 (14)	0.0069 (12)	0.0036 (14)
C18	0.0321 (18)	0.0260 (16)	0.0381 (18)	0.0029 (14)	0.0129 (15)	0.0035 (14)
C19	0.0239 (17)	0.0352 (18)	0.0371 (18)	−0.0049 (15)	0.0090 (13)	0.0054 (15)
C20	0.0250 (17)	0.0407 (19)	0.0333 (17)	0.0109 (15)	0.0106 (13)	0.0084 (15)
C21	0.041 (2)	0.0312 (18)	0.0392 (18)	0.0092 (17)	0.0106 (15)	0.0021 (16)
C22	0.0275 (17)	0.0278 (17)	0.0391 (17)	0.0012 (15)	0.0076 (14)	0.0033 (15)

Geometric parameters (Å, º)

C1—C2	1.513 (4)	C10—H101	0.977
C1—N9	1.488 (3)	C10—H102	0.979
C1—C12	1.533 (4)	C11—C12	1.524 (4)
C1—H11	0.980	C11—N13	1.491 (4)
C2—O3	1.439 (3)	C11—H111	0.995
C2—C6	1.533 (3)	C12—H121	0.981
C2—H21	0.979	C12—H122	0.968
O3—C4	1.429 (3)	N13—N14	1.228 (4)
C4—O5	1.423 (3)	N14—N15	1.140 (4)
C4—C7	1.502 (5)	C16—C17	1.519 (4)
C4—C8	1.507 (4)	C16—H161	0.982
O5—C6	1.424 (3)	C16—H162	0.965
C6—H61	0.971	C17—C18	1.389 (4)
C6—H62	0.976	C17—C22	1.389 (4)
C7—H71	0.964	C18—C19	1.385 (4)
C7—H72	0.962	C18—H181	0.936
C7—H73	0.960	C19—C20	1.386 (5)
C8—H81	0.970	C19—H191	0.941
C8—H82	0.965	C20—C21	1.376 (4)
C8—H83	0.967	C20—H201	0.938
N9—C10	1.479 (3)	C21—C22	1.391 (4)
N9—C16	1.455 (4)	C21—H211	0.936
C10—C11	1.514 (4)	C22—H221	0.931
C2—C1—N9	110.1 (2)	C11—C10—H101	110.1
C2—C1—C12	112.4 (2)	N9—C10—H102	109.8
N9—C1—C12	105.7 (2)	C11—C10—H102	111.2

C2—C1—H11	108.2	H101—C10—H102	109.7
N9—C1—H11	109.6	C10—C11—C12	102.8 (2)
C12—C1—H11	110.8	C10—C11—N13	108.3 (3)
C1—C2—O3	108.3 (2)	C12—C11—N13	112.8 (3)
C1—C2—C6	115.3 (3)	C10—C11—H111	111.1
O3—C2—C6	103.8 (2)	C12—C11—H111	111.7
C1—C2—H21	108.5	N13—C11—H111	109.9
O3—C2—H21	110.0	C1—C12—C11	104.1 (2)
C6—C2—H21	110.7	C1—C12—H121	111.5
C2—O3—C4	109.12 (18)	C11—C12—H121	109.8
O3—C4—O5	105.2 (2)	C1—C12—H122	110.8
O3—C4—C7	109.6 (3)	C11—C12—H122	110.4
O5—C4—C7	111.8 (3)	H121—C12—H122	110.0
O3—C4—C8	108.7 (2)	C11—N13—N14	114.4 (3)
O5—C4—C8	108.1 (3)	N13—N14—N15	173.5 (3)
C7—C4—C8	113.0 (3)	N9—C16—C17	114.1 (2)
C4—O5—C6	106.4 (2)	N9—C16—H161	108.5
C2—C6—O5	104.5 (2)	C17—C16—H161	107.5
C2—C6—H61	111.2	N9—C16—H162	108.5
O5—C6—H61	108.9	C17—C16—H162	108.1
C2—C6—H62	111.2	H161—C16—H162	110.1
O5—C6—H62	110.0	C16—C17—C18	121.5 (3)
H61—C6—H62	110.8	C16—C17—C22	119.7 (3)
C4—C7—H71	109.1	C18—C17—C22	118.7 (3)
C4—C7—H72	109.0	C17—C18—C19	120.7 (3)
H71—C7—H72	110.2	C17—C18—H181	119.2
C4—C7—H73	108.9	C19—C18—H181	120.1
H71—C7—H73	109.8	C18—C19—C20	119.9 (3)
H72—C7—H73	109.9	C18—C19—H191	120.0
C4—C8—H81	109.9	C20—C19—H191	120.1
C4—C8—H82	108.0	C19—C20—C21	120.1 (3)
H81—C8—H82	110.5	C19—C20—H201	120.1
C4—C8—H83	108.8	C21—C20—H201	119.8
H81—C8—H83	109.7	C20—C21—C22	119.9 (3)
H82—C8—H83	109.9	C20—C21—H211	120.2
C1—N9—C10	108.5 (2)	C22—C21—H211	119.9
C1—N9—C16	113.2 (2)	C21—C22—C17	120.7 (3)
C10—N9—C16	111.8 (2)	C21—C22—H221	119.7
N9—C10—C11	105.8 (2)	C17—C22—H221	119.6
N9—C10—H101	110.1		