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2,5-Anhydro-*N*-benzyl-2-*C*-methyl-D-arabinonamide [(2*S*,3*R*,4*R*)-*N*-benzyl-3,4-dihydroxy-2-methyltetrahydrofuran-2-carboxamide]

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Key indicators

Single-crystal X-ray study
T = 190 K
Mean σ(C–C) = 0.003 Å
R factor = 0.038
wR factor = 0.087
Data-to-parameter ratio = 9.7

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

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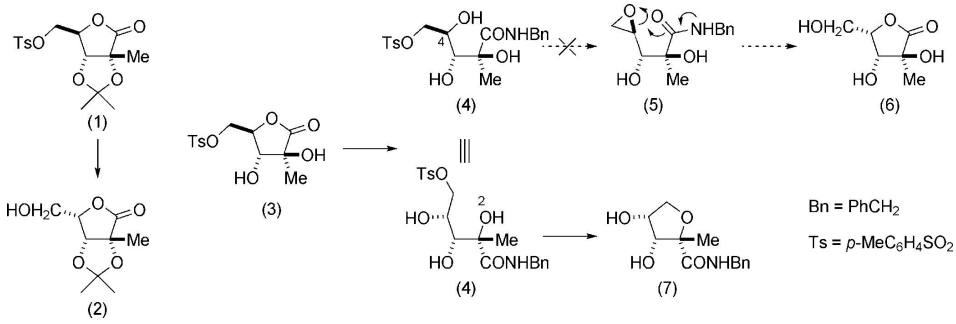
The size of the ring and relative configuration of the chiral centres in the title compound, $C_{13}H_{17}NO_4$, formed by the preferential formation of the hindered five-membered ring tetrahydrofuran rather than the expected three-membered ring epoxide, was established by X-ray crystallographic analysis; the absolute configuration was determined by the use of 2-*C*-methyl-D-*arabinono*-lactone as the starting material. The crystal structure consists of hydrogen-bonded layers lying with their hydrophobic surfaces in contact.

Comment

Carbohydrate lactones are among the most powerful chirons (Lundt & Madsen, 2001), being ideal scaffolds for the synthesis of optically pure complex natural products (Lichtenthaler & Peters, 2004; Bols, 1996). Epimerization at C4 of the lactone is usually a very efficient reaction, which effectively doubles the number of lactones that are readily available (Kold *et al.*, 1994; Frank & Lundt, 1995); the transformation can be conducted on a multikilogram scale (Batra *et al.*, 2006). Among other recent examples (Håkansson *et al.*, 2006; Van Ameijde *et al.*, 2004; Simone *et al.*, 2005), the treatment of the 2-*C*-methyl-D-ribonolactone tosylate (1) with base allows access to the L-lyxono-epimer (2) in very high yield (Hotchkiss *et al.*, 2007).



It was thus expected that treatment of the tosylate (3) of 2-*C*-methyl-D-arabinonolactone (Hotchkiss *et al.*, 2006) would give the L-xylono epimer (6); however, a complex mixture of products was obtained. Accordingly the reaction sequence treatment of (3) with benzylamine was expected to give ring opening of the lactone unit to (4) which would be followed by formation of the epoxide (5) from attack of the C4 hydroxyl group; (5) could be subsequently closed to the target (6). A product was isolated from the reaction of benzylamine with (3) in 61% yield. X-ray crystallographic analysis showed that the much hindered tertiary alcohol at C2 of (4) had closed to form the tetrahydrofuran (7). The connectivity of the C and H

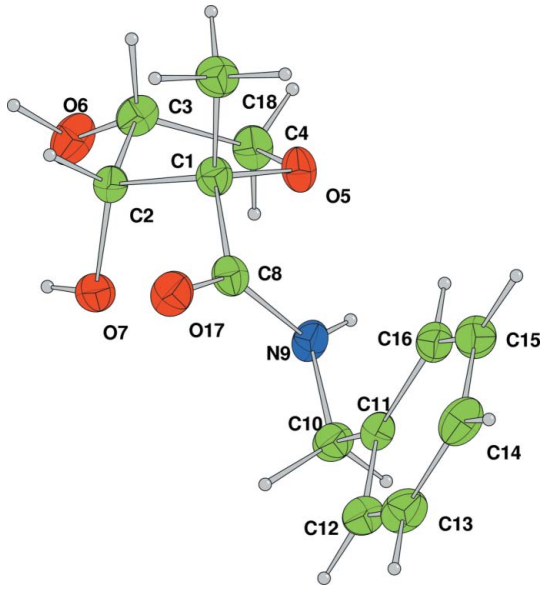


Figure 1
The molecular structure of the title compound, with displacement ellipsoids drawn at the 50% probability level. H atoms are shown as spheres of arbitary radius.

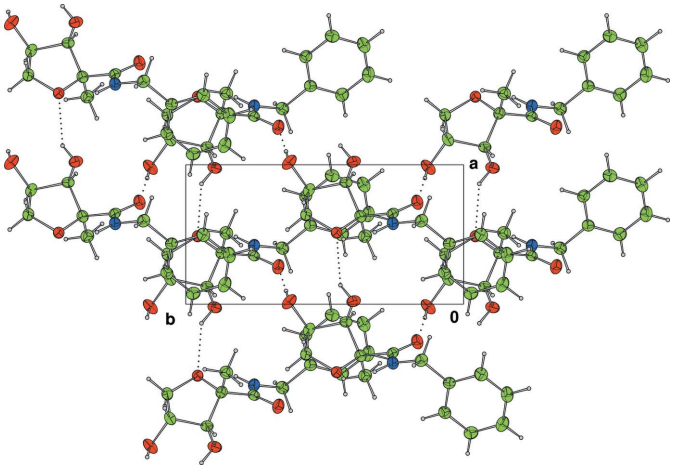


Figure 2
Partial packing diagram of the title compound showing a single hydrogen-bonded (dotted lines) layer lying perpendicular to the *c* axis. Each molecule is involved in only two hydrogen bonds.

atoms is the same in both (5) and (7), and the X-ray experiment unequivocally established that the five-membered ring THF (7) was formed in preference to the three-membered ring epoxide (5); the absolute configuration of (7) is determined by the use of 2-*C*-methyl-D-arabinonolactone as the starting material.

The molecular structure (Fig. 1) shows no abnormal features, even a short internal N—H···O contact (Table 1) having no visible influence [largest distance deviation from the *MOGUL* norms (Bruno *et al.*, 2004) is C1—O5 (1.46 *vs* 1.43 Å), largest angle deviation is C11—C16—C10 (122.8 *vs* 120.8°)]. The crystal structure consists of hydrogen-bonded sheets (Fig. 2). Both faces of the sheets are composed largely

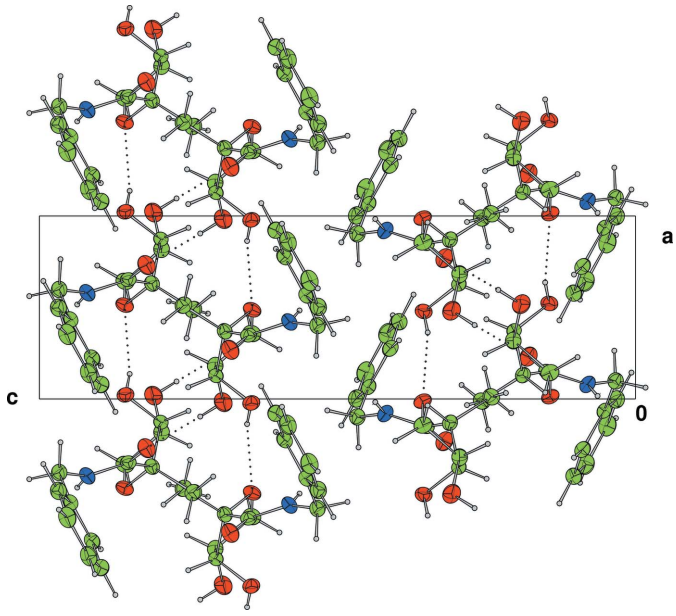


Figure 3
Partial packing diagram viewed perpendicular to the plane of the molecular sheets showing hydrophobic (largely aromatic) plane-to-plane contacts at $(x, y, \frac{1}{2})$. Hydrogen bonds are shown as dotted lines.

of phenyl groups which lie in contact in the crystal structure (Fig. 3).

Experimental

The synthesis of (3) is described in the *Comment* and shown in the scheme; full details will be reported elsewhere. The sample for analysis was crystallized from a 2:1 mixture of ethanol and methanol to yield colourless needles with m.p. 402–404 K and $[\alpha]_D^{19} = -18.5$ (c =1.00, CH_3OH).

Crystal data

$C_{13}H_{17}NO_4$
$M_r = 251.28$
Orthorhombic, $P2_12_12_1$
$a = 5.6899\ (2)$ Å
$b = 11.3507\ (4)$ Å
$c = 18.5291\ (9)$ Å
$V = 1196.69\ (8)$ Å^3
$Z = 4$
$D_x = 1.395$ Mg m^{-3}
Mo $K\alpha$ radiation
$\mu = 0.10$ mm^{-1}
$T = 190$ K
Needle, colourless
0.40 × 0.06 × 0.06 mm

Data collection

Nonius KappaCCD diffractometer
ω scans
Absorption correction: multi-scan (*DENZO*/*SCALEPACK*; Otwinowski & Minor, 1997)
$T_{min} = 0.96$, $T_{max} = 0.99$
5880 measured reflections
1575 independent reflections
1249 reflections with $I > 2\sigma(I)$
$R_{int} = 0.049$
$\theta_{max} = 27.5°$

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)] = 0.038$
$wR(F^2) = 0.087$
$S = 0.93$
1575 reflections
163 parameters
H-atom parameters constrained
$w = 1/[\sigma^2(F^2) + (0.03P)^2 + 0.15P]$, where $P = [\max(F_o^2,0) + 2F_c^2]/3$
$(\Delta/\sigma)_{max} < 0.001$
$\Delta\rho_{max} = 0.26$ e Å^{-3}
$\Delta\rho_{min} = -0.29$ e Å^{-3}

Table 1
Hydrogen-bond geometry (Å, °).

D—H···A	D—H	H···A	D···A	D—H···A
N9—H1···O5	0.88	2.15	2.606 (2)	112
O7—H15···O5^{i}	0.86	2.15	2.878 (2)	142
O6—H19···O17^{ii}	0.85	1.96	2.816 (2)	179

Symmetry codes: (i) $x-1, y, z$; (ii) $-x, y+\frac{1}{2}, -z+\frac{3}{2}$.

In the absence of significant anomalous scattering, Friedel pairs were merged and the absolute configuration assigned on the basis of the starting material.

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 in the range 0.93–0.98, N—H to 0.86, O—H = 0.82 Å) and U_{iso}(H) (in the range 1.2–1.5 times U_{eq} of the 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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$a = 5.6899\ (2)$ Å
$b = 11.3507\ (4)$ Å
$c = 18.5291\ (9)$ Å
$V = 1196.69\ (8)$ Å^3
$Z = 4$
$F(000) = 536$
$D_x = 1.395$ Mg m^{-3}
Mo $K\alpha$ radiation, $\lambda = 0.71073$ Å
Cell parameters from 1482 reflections
$\theta = 5$–$27°$
$\mu = 0.10$ mm^{-1}
$T = 190$ K
Needle, colourless
0.40 × 0.06 × 0.06 mm

Data collection

Nonius KappaCCD diffractometer
Graphite monochromator
ω scans
Absorption correction: multi-scan (DENZO/SCALEPACK; Otwinowski & Minor, 1997)
$T_{min} = 0.96$, $T_{max} = 0.99$
5880 measured reflections
1575 independent reflections
1249 reflections with $I > 2\sigma(I)$
$R_{int} = 0.049$
$\theta_{max} = 27.5°$, $\theta_{min} = 5.2°$
$h = -7 \rightarrow 7$
$k = -14 \rightarrow 14$
$l = -23 \rightarrow 24$

Refinement

Refinement on F^2
Least-squares matrix: full
$R[F^2 > 2\sigma(F^2)] = 0.038$
$wR(F^2) = 0.087$
$S = 0.93$
1575 reflections
163 parameters
0 restraints
Primary atom site location: structure-invariant direct methods
Hydrogen site location: inferred from neighbouring sites
H-atom parameters constrained
$w = 1/[\sigma^2(F^2) + (0.03P)^2 + 0.15P]$, where $P = [\max(F_o^2,0) + 2F_c^2]/3$
$(\Delta/\sigma)_{max} = 0.000314$
$\Delta\rho_{max} = 0.26$ e Å^{-3}
$\Delta\rho_{min} = -0.29$ e Å^{-3}

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

	x	*y*	*z*	U_{iso}*/U_{eq}
C1	0.3695 (4)	0.87162 (16)	0.68888 (11)	0.0238
C2	0.1269 (4)	0.92388 (17)	0.70375 (12)	0.0232
C3	0.1815 (4)	1.05659 (17)	0.70497 (12)	0.0263

C4	0.3572 (4)	1.06701 (17)	0.64355 (12)	0.0276
O5	0.4874 (3)	0.95765 (11)	0.64303 (8)	0.0252
O6	−0.0177 (3)	1.12786 (12)	0.69160 (8)	0.0350
O7	−0.0220 (3)	0.89610 (12)	0.64455 (8)	0.0285
C8	0.3483 (4)	0.75530 (17)	0.64905 (11)	0.0234
N9	0.4204 (4)	0.75485 (14)	0.58042 (9)	0.0251
C10	0.4019 (4)	0.65227 (17)	0.53332 (11)	0.0270
C11	0.5649 (4)	0.55154 (18)	0.55273 (11)	0.0237
C12	0.5025 (5)	0.43760 (18)	0.53198 (11)	0.0298
C13	0.6467 (5)	0.34319 (19)	0.54704 (13)	0.0336
C14	0.8585 (5)	0.36011 (19)	0.58300 (12)	0.0325
C15	0.9219 (5)	0.47346 (18)	0.60362 (12)	0.0294
C16	0.7760 (4)	0.56814 (18)	0.58866 (11)	0.0265
O17	0.2690 (3)	0.66711 (11)	0.67971 (8)	0.0310
C18	0.5116 (5)	0.85472 (17)	0.75818 (12)	0.0291
H21	0.0645	0.8960	0.7502	0.0298*
H31	0.2547	1.0760	0.7522	0.0332*
H41	0.4648	1.1341	0.6513	0.0358*
H42	0.2711	1.0756	0.5971	0.0353*
H101	0.2363	0.6224	0.5355	0.0336*
H102	0.4378	0.6791	0.4831	0.0332*
H121	0.3554	0.4257	0.5067	0.0376*
H131	0.6045	0.2649	0.5329	0.0439*
H141	0.9573	0.2931	0.5930	0.0413*
H151	1.0701	0.4855	0.6277	0.0365*
H161	0.8204	0.6463	0.6032	0.0324*
H181	0.6674	0.8204	0.7470	0.0452*
H182	0.5332	0.9322	0.7826	0.0449*
H183	0.4234	0.8015	0.7916	0.0450*
H1	0.4836	0.8202	0.5635	0.0321*
H15	−0.1367	0.9437	0.6516	0.0451*
H19	−0.0960	1.1394	0.7302	0.0551*

Atomic displacement parameters (Å²)

	U^{11}	U^{22}	U^{33}	U^{12}	U^{13}	U^{23}
C1	0.0249 (12)	0.0234 (9)	0.0231 (11)	−0.0022 (10)	0.0022 (10)	0.0027 (9)
C2	0.0201 (12)	0.0275 (10)	0.0220 (10)	0.0004 (10)	0.0014 (10)	−0.0018 (9)
C3	0.0299 (14)	0.0234 (9)	0.0255 (11)	0.0064 (11)	−0.0004 (10)	−0.0002 (9)
C4	0.0276 (13)	0.0217 (9)	0.0334 (12)	0.0015 (11)	0.0030 (11)	0.0003 (9)
O5	0.0226 (8)	0.0209 (6)	0.0319 (8)	−0.0002 (8)	0.0055 (8)	0.0037 (6)
O6	0.0369 (10)	0.0352 (7)	0.0328 (8)	0.0166 (9)	0.0048 (9)	0.0012 (7)
O7	0.0221 (9)	0.0337 (7)	0.0297 (8)	0.0038 (8)	−0.0020 (8)	−0.0065 (7)
C8	0.0197 (11)	0.0243 (9)	0.0262 (10)	0.0032 (10)	−0.0011 (10)	0.0026 (9)
N9	0.0283 (10)	0.0223 (7)	0.0248 (9)	−0.0013 (9)	0.0066 (9)	−0.0005 (7)
C10	0.0279 (13)	0.0282 (10)	0.0248 (11)	0.0020 (11)	0.0003 (10)	−0.0030 (9)
C11	0.0235 (13)	0.0264 (9)	0.0210 (10)	0.0008 (10)	0.0039 (10)	−0.0012 (9)
C12	0.0315 (14)	0.0310 (10)	0.0268 (11)	−0.0017 (13)	0.0014 (12)	−0.0046 (9)

C13	0.0436 (16)	0.0259 (10)	0.0313 (12)	−0.0021 (12)	0.0050 (12)	−0.0026 (10)
C14	0.0400 (16)	0.0290 (10)	0.0285 (12)	0.0078 (12)	0.0057 (12)	0.0023 (10)
C15	0.0278 (14)	0.0347 (11)	0.0257 (12)	0.0019 (11)	−0.0007 (11)	0.0025 (9)
C16	0.0268 (13)	0.0266 (10)	0.0260 (11)	−0.0028 (11)	0.0049 (11)	−0.0017 (10)
O17	0.0375 (10)	0.0241 (6)	0.0314 (8)	−0.0043 (8)	0.0063 (8)	0.0010 (6)
C18	0.0283 (12)	0.0299 (10)	0.0292 (11)	0.0018 (12)	−0.0026 (11)	0.0002 (9)

Geometric parameters (Å, º)

C1—C2	1.528 (3)	N9—H1	0.882
C1—O5	1.458 (2)	C10—C11	1.515 (3)
C1—C8	1.517 (3)	C10—H101	1.002
C1—C18	1.529 (3)	C10—H102	1.001
C2—C3	1.538 (3)	C11—C12	1.395 (3)
C2—O7	1.422 (2)	C11—C16	1.386 (3)
C2—H21	0.983	C12—C13	1.378 (3)
C3—C4	1.520 (3)	C12—H121	0.968
C3—O6	1.414 (3)	C13—C14	1.391 (4)
C3—H31	0.995	C13—H131	0.957
C4—O5	1.445 (2)	C14—C15	1.390 (3)
C4—H41	0.987	C14—H141	0.964
C4—H42	0.995	C15—C16	1.386 (3)
O6—H19	0.852	C15—H151	0.963
O7—H15	0.857	C16—H161	0.961
C8—N9	1.336 (3)	C18—H181	0.990
C8—O17	1.236 (2)	C18—H182	0.997
N9—C10	1.459 (2)	C18—H183	1.001
C2—C1—O5	105.11 (15)	C10—N9—H1	119.3
C2—C1—C8	110.72 (18)	N9—C10—C11	114.59 (17)
O5—C1—C8	109.64 (16)	N9—C10—H101	108.3
C2—C1—C18	112.01 (18)	C11—C10—H101	108.1
O5—C1—C18	109.28 (18)	N9—C10—H102	107.4
C8—C1—C18	109.96 (16)	C11—C10—H102	109.0
C1—C2—C3	101.57 (17)	H101—C10—H102	109.4
C1—C2—O7	108.26 (16)	C10—C11—C12	118.6 (2)
C3—C2—O7	110.41 (17)	C10—C11—C16	122.80 (19)
C1—C2—H21	111.1	C12—C11—C16	118.6 (2)
C3—C2—H21	112.0	C11—C12—C13	120.9 (2)
O7—C2—H21	112.9	C11—C12—H121	118.8
C2—C3—C4	101.42 (17)	C13—C12—H121	120.3
C2—C3—O6	113.31 (19)	C12—C13—C14	120.4 (2)
C4—C3—O6	110.59 (17)	C12—C13—H131	121.1
C2—C3—H31	108.4	C14—C13—H131	118.5
C4—C3—H31	111.5	C13—C14—C15	119.0 (2)
O6—C3—H31	111.3	C13—C14—H141	119.2
C3—C4—O5	105.97 (16)	C15—C14—H141	121.8
C3—C4—H41	111.0	C14—C15—C16	120.5 (2)

O5—C4—H41	110.2	C14—C15—H151	119.0
C3—C4—H42	109.3	C16—C15—H151	120.5
O5—C4—H42	109.3	C11—C16—C15	120.6 (2)
H41—C4—H42	110.9	C11—C16—H161	119.2
C1—O5—C4	109.63 (15)	C15—C16—H161	120.1
C3—O6—H19	111.1	C1—C18—H181	110.3
C2—O7—H15	101.4	C1—C18—H182	109.6
C1—C8—N9	116.22 (17)	H181—C18—H182	109.4
C1—C8—O17	120.67 (18)	C1—C18—H183	109.3
N9—C8—O17	123.11 (18)	H181—C18—H183	109.9
C8—N9—C10	123.38 (17)	H182—C18—H183	108.3
C8—N9—H1	117.3		

Hydrogen-bond geometry (Å, º)

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
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O7—H15···O5^{i}	0.86	2.15	2.878 (2)	142
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