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2-*C*-Methyl-3,4-*O*-methylidene-D-arabinono-1,5-lactone

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Key indicators

Single-crystal X-ray study
T = 150 K
Mean σ(C–C) = 0.003 Å
R factor = 0.038
wR factor = 0.079
Data-to-parameter ratio = 9.4

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

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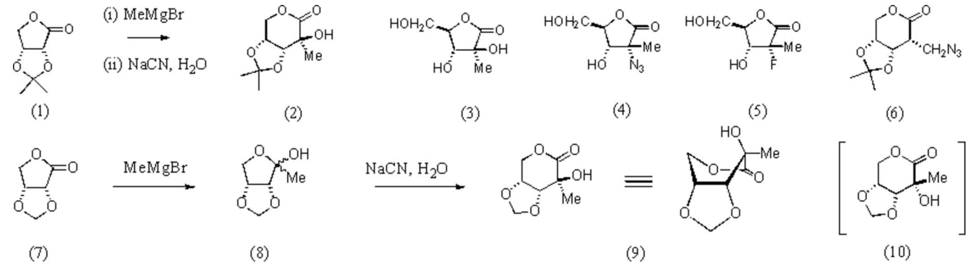
The relative stereochemistry at C-2 of the title compound, $C_7H_{10}O_5$, was determined by X-ray crystallographic analysis of the arabinonolactone, which adopts a boat conformation with a flagpole hydroxyl group. Its absolute configuration was determined by the use of D-erythronolactone as the starting material.

Comment

Until recently, only linear carbohydrate chirons have been available as scaffolds for the synthesis of complex synthetic targets (Lichtenthaler & Peters, 2004). However, the Kiliani cyanide reaction on ketohexoses (Hotchkiss *et al.*, 2004; Soengas *et al.*, 2005) affords versatile intermediates with carbon branches at C-2 of the sugar for the synthesis of imino sugars and complex sugar amino acids with non-linear carbon chains (Simone *et al.*, 2005). The Kiliani reaction on hamamelose provides access to carbohydrates with a branch at C-3 (Parker, Watkin, Simone & Fleet, 2006).



Carbohydrate building blocks with a C-2 methyl group can be formed by the reaction of cyanide on 1-deoxyketoses, themselves prepared by the addition of organometallic reagents to sugar lactones (Hotchkiss *et al.*, 2006). Thus, reaction of the isopropylidene-protected D-erythronolactone, (1), with methyl magnesium bromide followed by sodium cyanide gave the *arabino*-protected derivative, (2), as the only 1,5-lactone isolated (Punzo *et al.*, 2005*a*). The potential of (2) as a route to sugar derivatives with a C-2 methyl group bearing a functional group at the tertiary centre is shown by its easy conversion to the branched arabinose, (3) (Punzo *et al.*, 2005*b*), the quaternary *ribo*-azide, (4) (Punzo, Watkin, Jenkinson, Cruz & Fleet, 2005), and the quaternary *ribo*-fluoride, (5) (Parker, Watkin, Mayes *et al.*, 2006). The branched azidomethyl lactone, (6), has also been prepared from (2) and is a precursor to complex piperidine amino acids and iminosugars (Punzo *et al.*, 2006).

In order to optimize the protecting group strategy for the synthesis of complex targets (and to investigate the diastereoselectivity of the Kiliani cyanide extension), the

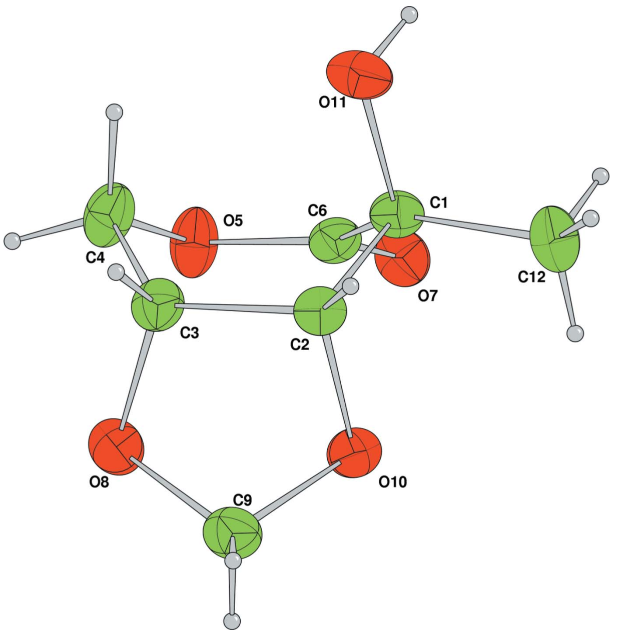


Figure 1
The molecular structure of the title compound, with displacement ellipsoids drawn at the 50% probability level. H atoms are shown as spheres of arbitrary radii.

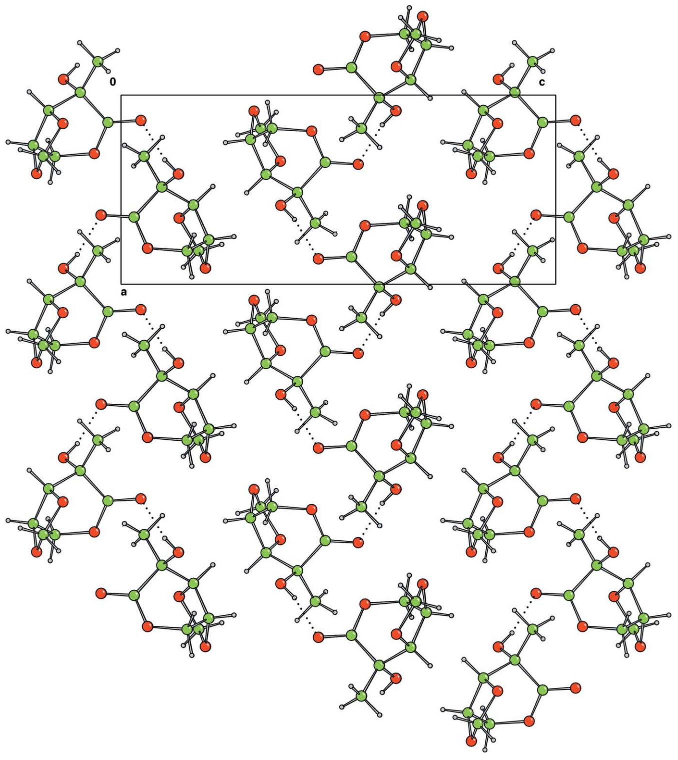


Figure 2
The crystal packing, viewed down the *a* axis. Hydrogen bonds are shown as dashed lines.

formaldehyde acetal of D-erythronolactone, (7), was treated with methyl magnesium bromide to give the 1-deoxy-D-ribulose, (8). The Kiliani reaction of (8) with sodium cyanide gave a single diastereomeric product, (9), as the only 1,5-lactone isolated (Jenkinson *et al.*, 2006). This paper shows, by X-ray crystallography, that the arabinonolactone, (9), was formed in this reaction with none of the epimeric ribono diastereomer, (10), isolated.

The X-ray crystal structure determination shows that (9) is in a boat conformation (Fig. 1). The formation of (9) with the smaller hydroxyl group in the flagpole position may be due to the alternative product, (10), having the larger methyl group in the more hindered flagpole environment. The potential of (9) as a chiron is under investigation.

In the crystal structure, intermolecular O—H···O hydrogen bonds (Table 1) link the molecules into zigzag chains extending along the *a* axis (Fig. 2).

Experimental

The title arabinono-1,5-lactone, (9), was obtained (Jenkinson *et al.*, 2006) by vapour diffusion of cyclohexane into a solution in ethyl acetate until crystals of a suitable size were formed (m.p. 373–375 K). $[\alpha]_D$ −126.0 (*c* 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$, δ, p.p.m.): 1.67 (3H, *s*, Me), 3.04 (1H, *s*, OH), 4.25 (1H, *d*, $J_{3,4}$ = 7.9 Hz, H3), 4.46–4.50 (2H, *m*, H4, H5a), 4.82 (1H, *s*, OCH_2O), 4.97 (1H, *dd*, $J_{4,5\,b}$ = 1.9 Hz, $J_{5a,5\,b}$ = 12.0 Hz, H5b), 5.17 (1H, *s*, OCH_2O); ^{13}C NMR (100 MHz, $CDCl_3$, δ, p.p.m.): 22.1 (Me), 68.7 (C5), 71.5 (C4), 72.2 (C3), 78.8 (C2), 94.9 (OCH_2O), 171.4 (CO).

Crystal data

$C_7H_{10}O_5$
$M_r = 174.15$
Orthorhombic, $P2_12_12_1$
$a = 6.8693$ (3) Å
$b = 7.0382$ (3) Å
$c = 15.7909$ (7) Å
$V = 763.45$ (6) Å^3
$Z = 4$
$D_x = 1.515$ Mg m^{-3}
Mo $K\alpha$ radiation
$\mu = 0.13$ mm^{-1}
$T = 150$ K
Needle, colourless
0.50 × 0.20 × 0.20 mm

Data collection

Nonius KappaCCD area-detector diffractometer
ω scans
Absorption correction: multi-scan (*DENZO*/*SCALEPACK*; Otwinowski & Minor, 1997)
$T_{min} = 0.882$, $T_{max} = 0.974$
1726 measured reflections
1032 independent reflections
784 reflections with $I > 2\sigma(I)$
$R_{int} = 0.032$
$\theta_{max} = 27.5°$

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)] = 0.038$
$wR(F^2) = 0.080$
$S = 1.00$
1027 reflections
109 parameters
H-atom parameters constrained
$w = 1/[\sigma^2(F^2) + (0.04P)^2 + 0.03P]$
where $P = (\max(F_o^2,0) + 2F_c^2)/3$
$(\Delta/\sigma)_{max} < 0.001$
$\Delta\rho_{max} = 0.36$ e Å^{-3}
$\Delta\rho_{min} = -0.34$ e Å^{-3}

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

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
O11—H1···O7^{i}	0.83	2.10	2.911 (2)	167

Symmetry code: (i) $x+\frac{1}{2}, -y+\frac{1}{2}, -z+1$.

A $[\sin(\theta)/\lambda]^2$ threshold of 0.01 was used to guard against the risk of including low angle reflections partially occluded by the beam stop. In the absence of significant anomalous scattering, 873 Friedel pairs

Acta Cryst. (2006). E**62**, o4356–o4358 Bream *et al.* • $C_7H_{10}O_5$ **o4357**

were merged and the absolute configuration was assigned from the known starting material. All H atoms were 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 0.93–98 Å, and O—H = 0.825 Å) and isotropic displacement parameters [U_{iso}(H) in the range 1.2–1.5U_{eq} of the parent atom], after which they 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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o4358 Bream *et al.* • $C_7H_{10}O_5$ *Acta Cryst.* (2006). E**62**, o4356–o4358

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$V = 763.45$ (6) Å^3
$Z = 4$
$F(000) = 368$
$D_x = 1.515$ Mg m^{-3}
Mo $K\alpha$ radiation, $\lambda = 0.71073$ Å
Cell parameters from 981 reflections
$\theta = 1$–27°
$\mu = 0.13$ mm^{-1}
$T = 150$ K
Needle, colourless
0.50 × 0.20 × 0.20 mm

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Nonius KappaCCD area-detector diffractometer
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1032 independent reflections
784 reflections with $I > 2\sigma(I)$
$R_{\text{int}} = 0.032$
$\theta_{\max} = 27.5°$, $\theta_{\min} = 2.6°$
$h = -8 \rightarrow 8$
$k = -9 \rightarrow 9$
$l = -20 \rightarrow 20$

Refinement

Refinement on F^2
Least-squares matrix: full
$R[F^2 > 2\sigma(F^2)] = 0.038$
$wR(F^2) = 0.080$
$S = 1.01$
1027 reflections
109 parameters
0 restraints
Primary atom site location: structure-invariant direct methods
Hydrogen site location: inferred from neighbouring sites
H-atom parameters constrained
$w = 1/[\sigma^2(F^2) + (0.04P)^2 + 0.03P]$
where $P = (\max(F_o^2,0) + 2F_c^2)/3$
$(\Delta/\sigma)_{\max} = 0.000146$
$\Delta\rho_{\max} = 0.36$ e Å^{-3}
$\Delta\rho_{\min} = -0.34$ e Å^{-3}

Special details

Experimental. [α]D -126.0 (c 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$, δ, p.p.m.): 1.67 (3*H*, s, Me), 3.04 (1*H*, s, OH), 4.25 (1*H*, d, $J_{3,4} = 7.9$ Hz, H3), 4.46–4.50 (2*H*, m, H4, H5a), 4.82 (1*H*, s, OCH_2O), 4.97 (1*H*, dd, $J_{4,5\text{ b}} = 1.9$ Hz, $J_{5\text{a},5\text{ b}} = 12.0$ Hz, H5b), 5.17 (1*H*, s, OCH_2O); ^{13}C NMR (100 MHz, $CDCl_3$, δ, p.p.m.): 22.1 (Me), 68.7 (C5), 71.5 (C4), 72.2 (C3), 78.8 (C2), 94.9 (OCH_2O), 171.4 (CO).

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

	x	y	z	U_{iso}*/U_{eq}
C1	0.5144 (3)	0.4702 (3)	0.40608 (13)	0.0239
C2	0.4191 (3)	0.5797 (3)	0.33348 (13)	0.0229
C3	0.2346 (3)	0.4823 (4)	0.29802 (14)	0.0265
C4	0.1759 (4)	0.3085 (4)	0.34774 (14)	0.0315
O5	0.1906 (2)	0.3444 (3)	0.43863 (9)	0.0308
C6	0.3551 (3)	0.4201 (3)	0.46975 (13)	0.0230
O7	0.3657 (2)	0.4406 (2)	0.54569 (9)	0.0280
O8	0.0852 (2)	0.6217 (2)	0.30591 (10)	0.0338
C9	0.1773 (4)	0.7974 (4)	0.32128 (16)	0.0299
O10	0.3496 (2)	0.7553 (2)	0.36642 (10)	0.0315
O11	0.5831 (2)	0.2984 (2)	0.36767 (10)	0.0312
C12	0.6764 (3)	0.5837 (4)	0.44681 (15)	0.0324
H21	0.5170	0.5978	0.2888	0.0257*
H31	0.2515	0.4494	0.2401	0.0317*
H41	0.0385	0.2805	0.3369	0.0378*
H42	0.2600	0.1971	0.3317	0.0373*
H91	0.2107	0.8636	0.2684	0.0341*
H92	0.0908	0.8822	0.3566	0.0339*
H121	0.7348	0.5108	0.4921	0.0481*
H122	0.7769	0.6091	0.4049	0.0476*
H123	0.6253	0.6978	0.4707	0.0472*
H1	0.6575	0.2398	0.3993	0.0572*

Atomic displacement parameters (Å²)

	U^{11}	U^{22}	U^{33}	U^{12}	U^{13}	U^{23}
C1	0.0250 (11)	0.0228 (14)	0.0239 (11)	0.0022 (11)	0.0032 (10)	0.0000 (10)
C2	0.0247 (10)	0.0235 (13)	0.0206 (11)	0.0009 (11)	0.0028 (10)	0.0011 (10)
C3	0.0299 (11)	0.0269 (14)	0.0227 (11)	0.0002 (12)	−0.0011 (10)	−0.0025 (11)
C4	0.0386 (13)	0.0316 (14)	0.0244 (12)	−0.0077 (13)	−0.0068 (12)	−0.0011 (11)
O5	0.0309 (8)	0.0378 (11)	0.0237 (8)	−0.0133 (8)	−0.0024 (7)	0.0046 (8)
C6	0.0265 (12)	0.0176 (12)	0.0250 (12)	−0.0003 (11)	0.0001 (10)	0.0041 (10)
O7	0.0286 (8)	0.0341 (11)	0.0215 (8)	0.0014 (8)	−0.0001 (7)	0.0006 (8)
O8	0.0281 (8)	0.0301 (10)	0.0432 (10)	−0.0002 (8)	−0.0045 (8)	0.0033 (9)
C9	0.0328 (12)	0.0281 (14)	0.0289 (12)	0.0040 (12)	−0.0023 (12)	0.0024 (11)
O10	0.0344 (9)	0.0251 (9)	0.0350 (9)	0.0041 (8)	−0.0080 (8)	−0.0047 (8)
O11	0.0373 (9)	0.0314 (10)	0.0248 (8)	0.0122 (8)	−0.0004 (8)	0.0007 (8)
C12	0.0245 (11)	0.0404 (16)	0.0324 (13)	−0.0055 (12)	−0.0027 (11)	0.0021 (12)

Geometric parameters (Å, º)

C1—C2	1.529 (3)	C4—H42	1.006
C1—C6	1.528 (3)	O5—C6	1.342 (3)
C1—O11	1.432 (3)	C6—O7	1.210 (3)
C1—C12	1.514 (3)	O8—C9	1.410 (3)

C2—C3	1.545 (3)	C9—O10	1.414 (3)
C2—O10	1.423 (3)	C9—H91	0.983
C2—H21	0.984	C9—H92	1.010
C3—C4	1.508 (3)	O11—H1	0.825
C3—O8	1.426 (3)	C12—H121	0.966
C3—H31	0.951	C12—H122	0.972
C4—O5	1.461 (3)	C12—H123	0.954
C4—H41	0.979		

C2—C1—C6	107.64 (17)	O5—C4—H42	110.0
C2—C1—O11	104.41 (17)	H41—C4—H42	110.6
C6—C1—O11	108.66 (18)	C4—O5—C6	119.11 (18)
C2—C1—C12	111.57 (19)	C1—C6—O5	116.98 (18)
C6—C1—C12	111.67 (18)	C1—C6—O7	125.5 (2)
O11—C1—C12	112.52 (18)	O5—C6—O7	117.47 (19)
C1—C2—C3	113.54 (19)	C3—O8—C9	107.19 (16)
C1—C2—O10	107.89 (17)	O8—C9—O10	106.18 (18)
C3—C2—O10	104.06 (17)	O8—C9—H91	112.0
C1—C2—H21	108.1	O10—C9—H91	109.4
C3—C2—H21	111.0	O8—C9—H92	110.4
O10—C2—H21	112.3	O10—C9—H92	109.7
C2—C3—C4	113.0 (2)	H91—C9—H92	109.1
C2—C3—O8	104.69 (17)	C2—O10—C9	106.17 (17)
C4—C3—O8	108.65 (18)	C1—O11—H1	111.7
C2—C3—H31	110.9	C1—C12—H121	109.8
C4—C3—H31	109.6	C1—C12—H122	109.3
O8—C3—H31	109.8	H121—C12—H122	107.8
C3—C4—O5	110.7 (2)	C1—C12—H123	110.0
C3—C4—H41	109.3	H121—C12—H123	107.9
O5—C4—H41	105.8	H122—C12—H123	112.1
C3—C4—H42	110.3		

Hydrogen-bond geometry (Å, º)

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
O11—H1···O7^{i}	0.83	2.10	2.911 (2)	167

Symmetry code: (i) *x*+1/2, −*y*+1/2, −*z*+1.