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2,4-Dimethyl-3,4-*O*-isopropylidene-L-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 = 0.102
Data-to-parameter ratio = 10.4

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

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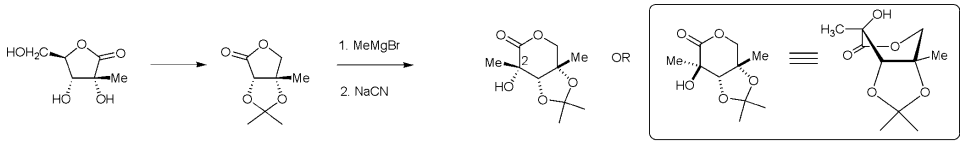
The relative configuration at C-2 of 2,4-dimethyl-3,4-*O*-isopropylidene-L-arabinono lactone, $C_{10}H_{16}O_5$, which exists in the boat form, was unequivocally established by X-ray crystallographic analysis. The absolute configuration was determined by the use of 2-*C*-methyl-D-ribonolactone as a starting material.

Comment

Rare and new monosaccharides have potential both as healthy dietary alternatives (Sun *et al.*, 2007; Skytte, 2002) and for specific chemotherapeutic uses (Nakajima *et al.*, 2004; Menavuvu *et al.*, 2006; Hossain *et al.*, 2006). Branched 2-*C*-methyl pentoses have become readily available by treatment of an Amadori ketose with aqueous calcium hydroxide (Hotchkiss *et al.*, 2007) and are key intermediates in the synthesis of 2-*C*-methyl nucleosides, a new class of drugs for the treatment of hepatitis C (Sorbera *et al.*, 2006). Carbohydrates with a branch at C-2 may also be accessed by the reaction of ketoses and deoxyketoses with cyanide (Hotchkiss *et al.*, 2004; Soengas *et al.*, 2005). In contrast, there have been no biological studies on unprotected monosaccharides with more than one carbon branch.



(1) (2) (3) (4)

The protected lactone (4) is a key intermediate in the synthesis of monosaccharides with two *C*-methyl branches (Booth *et al.*, 2007). 2-*C*-Methyl-D-ribonolactone, (1), prepared by the green environmentally friendly aqueous isomerization of D-glucose (Hotchkiss *et al.*, 2006), may be converted to the 3-*C*-methyl-L-erythronolactone (2) as previously described (Barrett & Dhanak, 1987; Barrett *et al.*, 1989). Sequential treatment of (2) with methyl magnesium bromide followed by aqueous cyanide leads to the isolation of a major crystalline product which has a new stereogenic centre, which could be either the epimeric *ribo*- (3) or *arabino*-lactone (4). X-ray crystallographic analysis resolved the ambiguity at C-2 and unequivocally established the relative stereochemistry as the arabinono-1,5-lactone (4), which exists in a boat form; the absolute configuration of (4) is determined by the use of 2-*C*-methyl-D-ribonolactone (1) as the starting material.

The molecular structure of (4) is shown in Fig. 1. The molecular geometry contains no unusual features. The largest

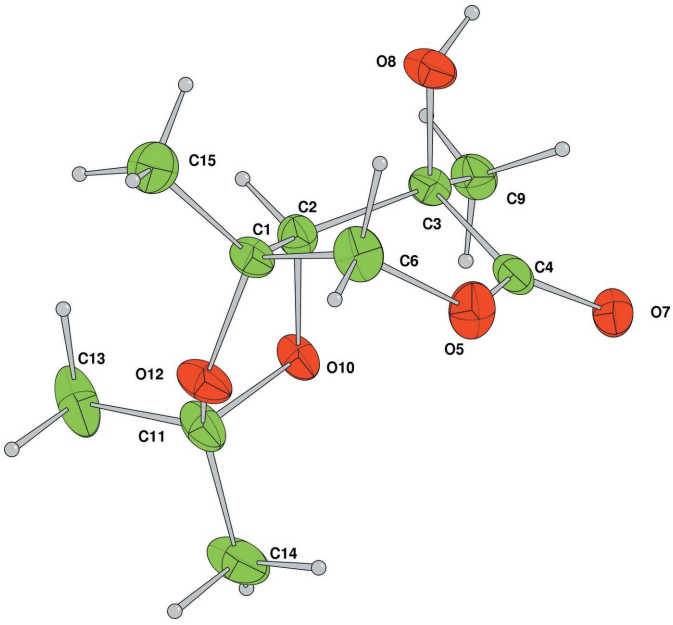


Figure 1
The molecular structure of the title compound with displacement ellipsoids drawn at the 50% probability level. H atoms are shown as spheres of arbitrary radius.

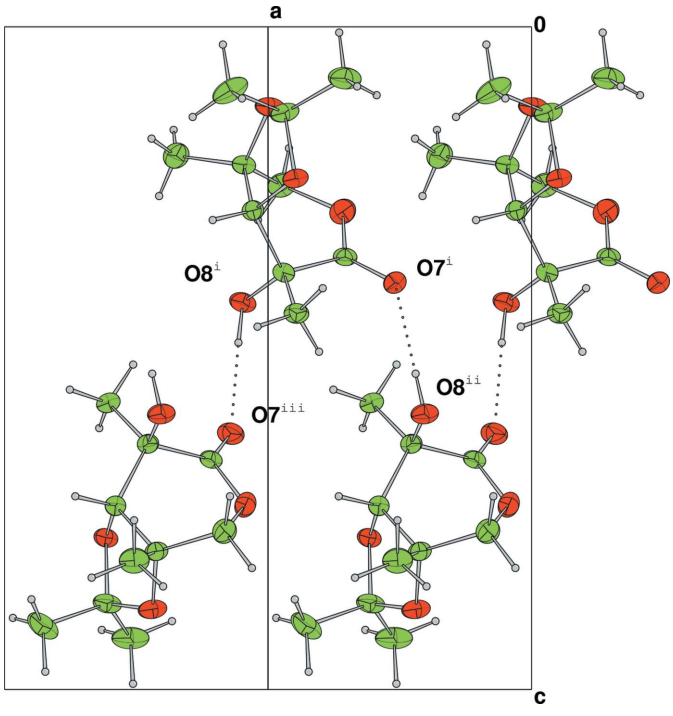


Figure 2
Part of the hydrogen-bonded (dotted lines) ribbon lying parallel to *a*. The image has been rotated about *c* (out of the plane of the ribbon) to clarify the hydrogen-bonding chain. The molecule corresponding to the published coordinates does not form any hydrogen bonds within the natural unit cell. [Symmetry codes: (i) $-x+1, y-\frac{1}{2}, -z+\frac{1}{2}$; (ii) $-x+\frac{1}{2}, -y+1, z+\frac{1}{2}$; (iii) $-x+\frac{3}{2}, -y+1, z+\frac{1}{2}$.]

differences from the *Mogul* norms (Bruno *et al.*, 2004) are C2—O3 (0.02 Å, *Mogul* s.u. 0.01 Å) and C3—C9—O8 (3.4 Å, *Mogul* s.u. 1.9°). The crystal structure consists of broad ribbons of hydrogen-bonded molecules lying with the plane of the ribbon perpendicular to *b*, and the length of the ribbon lying along *a* (Fig. 2). The hydrogen bonds form the backbone of the ribbon, with the individual molecules lying alternately on either side. The backbone of each ribbon lies above and parallel to the interface between two ribbons in the adjacent layers.

Experimental

2,4-Dimethyl-3,4-*O*-isopropylidene-L-arabinono lactone (4) was crystallized from a mix of ethyl acetate and cyclohexane by vapour diffusion: m.p. 385–391 K; $[\alpha]_D^{23}$ +131 (*c*, 1.5 in chloroform)

Crystal data

$C_{10}H_{16}O_5$
M_r = 216.23
Orthorhombic, $P2_12_12_1$
a = 6.3457 (2) Å
b = 12.0530 (4) Å
c = 14.1034 (5) Å
V = 1078.69 (6) Å^3
Z = 4
D_x = 1.331 Mg m^{-3}
Mo *K*α radiation
μ = 0.11 mm^{-1}
T = 150 K
Plate, colourless
0.40 × 0.40 × 0.20 mm

Data collection

Nonius KappaCCD diffractometer
ω scans
Absorption correction: multi-scan (*DENZO*/*SCALEPACK*; Otwinowski & Minor, 1997)
T_{min} = 0.82, T_{max} = 0.98
6458 measured reflections
1421 independent reflections
1301 reflections with $I > 2\sigma(I)$
R_{int} = 0.051
θ_{max} = 27.5°

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.038
$wR(F^2)$ = 0.102
S = 0.86
1421 reflections
136 parameters
H-atom parameters constrained
$w = 1/[\sigma^2(F^2) + (0.07P)^2 + 0.5P]$, where $P = [\max(F_o^2,0) + 2F_c^2]/3$
$(\Delta/\sigma)_{max} < 0.001$
$\Delta\rho_{max}$ = 0.26 e Å^{-3}
$\Delta\rho_{min}$ = −0.18 e Å^{-3}

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

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
O8—H1···O7^{iv}	0.88	1.99	2.870 (2)	178

Symmetry code: (iv) $x-\frac{1}{2}, -y+\frac{3}{2}, -z$.

In the absence of significant anomalous scattering, Friedel pairs were merged and the absolute configuration was assigned from the starting material. The relatively large ratio of minimum to maximum corrections applied in the multi-scan process (1:1.2) reflects effects in addition to absorption, possibly connected with the flake-like aspect of the sample. Changes in illuminated volume 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 in the range 0.93–0.98 Å, 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*.

A generous gift of 2-*C*-methyl-D-ribonolactone from Novartis Pharma AG Basel is gratefully acknowledged.

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Crystal data

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Orthorhombic, $P2_12_12_1$
Hall symbol: P 2ac 2ab
$a = 6.3457$ (2) Å
$b = 12.0530$ (4) Å
$c = 14.1034$ (5) Å
$V = 1078.69$ (6) Å^3
$Z = 4$
$F(000) = 464$
$D_x = 1.331$ Mg m^{-3}
Mo $K\alpha$ radiation, $\lambda = 0.71073$ Å
Cell parameters from 1339 reflections
$\theta = 5$–27°
$\mu = 0.11$ mm^{-1}
$T = 150$ K
Plate, colourless
0.40 × 0.40 × 0.20 mm

Data collection

Nonius KappaCCD diffractometer
Graphite monochromator
ω scans
Absorption correction: multi-scan (DENZO/SCALEPACK; Otwinowski & Minor, 1997)
$T_{min} = 0.82$, $T_{max} = 0.98$
6458 measured reflections
1421 independent reflections
1301 reflections with $I > 2\sigma(I)$
$R_{int} = 0.051$
$\theta_{max} = 27.5°$, $\theta_{min} = 5.3°$
$h = -8 \rightarrow 8$
$k = -15 \rightarrow 15$
$l = -18 \rightarrow 18$

Refinement

Refinement on F^2
Least-squares matrix: full
$R[F^2 > 2\sigma(F^2)] = 0.038$
$wR(F^2) = 0.102$
$S = 0.86$
1421 reflections
136 parameters
0 restraints
Primary atom site location: structure-invariant direct methods
Hydrogen site location: inferred from neighbouring sites
H-atom parameters constrained
$w = 1/[\sigma^2(F^2) + (0.07P)^2 + 0.5P]$, where $P = [\max(F_o^2,0) + 2F_c^2]/3$
$(\Delta/\sigma)_{max} = 0.000299$
$\Delta\rho_{max} = 0.26$ e Å^{-3}
$\Delta\rho_{min} = -0.18$ e Å^{-3}

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

	x	*y*	*z*	U_{iso}*/U_{eq}
C1	0.2418 (3)	0.83400 (16)	0.29155 (13)	0.0226
C2	0.1810 (3)	0.73928 (16)	0.22279 (13)	0.0215
C3	0.3015 (3)	0.74232 (16)	0.12915 (13)	0.0209
C4	0.5380 (3)	0.74540 (17)	0.15287 (14)	0.0234

O5	0.5983 (2)	0.81516 (14)	0.22116 (11)	0.0313
C6	0.4429 (4)	0.89114 (18)	0.26103 (16)	0.0299
O7	0.6698 (2)	0.68862 (15)	0.11399 (10)	0.0312
O8	0.2491 (3)	0.84518 (11)	0.08425 (10)	0.0283
C9	0.2504 (4)	0.64316 (17)	0.06758 (14)	0.0253
O10	0.2439 (2)	0.64042 (11)	0.27115 (9)	0.0235
C11	0.2262 (4)	0.66333 (16)	0.37041 (14)	0.0279
O12	0.2837 (3)	0.77729 (11)	0.37897 (9)	0.0289
C13	0.0003 (5)	0.6445 (2)	0.40394 (18)	0.0429
C14	0.3840 (5)	0.5936 (2)	0.42241 (15)	0.0407
C15	0.0713 (4)	0.92003 (18)	0.30548 (17)	0.0333
H21	0.0287	0.7394	0.2085	0.0263*
H61	0.5088	0.9295	0.3166	0.0383*
H62	0.4079	0.9467	0.2084	0.0377*
H91	0.3402	0.6474	0.0096	0.0402*
H92	0.1033	0.6442	0.0475	0.0414*
H93	0.2831	0.5762	0.1055	0.0416*
H131	−0.0088	0.6629	0.4733	0.0662*
H132	−0.0928	0.6940	0.3641	0.0656*
H133	−0.0343	0.5655	0.3920	0.0667*
H141	0.3784	0.6088	0.4914	0.0584*
H142	0.5234	0.6119	0.3969	0.0597*
H143	0.3535	0.5157	0.4100	0.0591*
H151	0.1210	0.9798	0.3445	0.0480*
H152	0.0386	0.9522	0.2446	0.0501*
H153	−0.0564	0.8859	0.3313	0.0484*
H1	0.2235	0.8363	0.0234	0.0405*

Atomic displacement parameters (Å²)

	U^{11}	U^{22}	U^{33}	U^{12}	U^{13}	U^{23}
C1	0.0272 (10)	0.0237 (9)	0.0169 (8)	−0.0009 (9)	−0.0020 (8)	−0.0002 (7)
C2	0.0211 (9)	0.0243 (9)	0.0189 (9)	−0.0011 (8)	0.0007 (7)	−0.0011 (7)
C3	0.0226 (9)	0.0223 (9)	0.0176 (8)	−0.0006 (8)	−0.0016 (7)	0.0009 (7)
C4	0.0242 (9)	0.0309 (10)	0.0152 (8)	−0.0017 (9)	0.0010 (8)	0.0048 (8)
O5	0.0234 (7)	0.0404 (8)	0.0301 (8)	−0.0062 (7)	−0.0002 (7)	−0.0081 (7)
C6	0.0332 (12)	0.0278 (10)	0.0287 (11)	−0.0059 (9)	0.0009 (10)	−0.0062 (9)
O7	0.0249 (7)	0.0461 (9)	0.0226 (7)	0.0056 (7)	0.0034 (6)	0.0007 (7)
O8	0.0378 (9)	0.0276 (7)	0.0195 (7)	0.0021 (7)	−0.0042 (6)	0.0031 (5)
C9	0.0280 (10)	0.0290 (9)	0.0190 (8)	−0.0017 (10)	−0.0025 (8)	−0.0035 (7)
O10	0.0317 (8)	0.0217 (6)	0.0171 (6)	−0.0023 (7)	0.0037 (6)	−0.0005 (5)
C11	0.0430 (12)	0.0232 (9)	0.0176 (9)	−0.0003 (10)	0.0063 (9)	−0.0023 (7)
O12	0.0458 (9)	0.0237 (7)	0.0172 (7)	−0.0011 (7)	−0.0037 (7)	−0.0004 (5)
C13	0.0550 (16)	0.0391 (13)	0.0345 (13)	−0.0082 (12)	0.0226 (12)	−0.0031 (11)
C14	0.0671 (18)	0.0324 (11)	0.0226 (10)	0.0087 (12)	−0.0016 (11)	0.0031 (9)
C15	0.0399 (13)	0.0294 (10)	0.0307 (11)	0.0070 (10)	0.0012 (10)	−0.0042 (9)

Geometric parameters (Å, º)

C1—C2	1.547 (3)	C9—H91	0.998
C1—C6	1.513 (3)	C9—H92	0.975
C1—O12	1.435 (2)	C9—H93	0.990
C1—C15	1.511 (3)	O10—C11	1.431 (2)
C2—C3	1.526 (3)	C11—O12	1.426 (2)
C2—O10	1.430 (2)	C11—C13	1.526 (3)
C2—H21	0.987	C11—C14	1.499 (3)
C3—C4	1.538 (3)	C13—H131	1.005
C3—O8	1.431 (2)	C13—H132	1.010
C3—C9	1.512 (3)	C13—H133	0.992
C4—O5	1.335 (3)	C14—H141	0.991
C4—O7	1.212 (3)	C14—H142	0.980
O5—C6	1.459 (3)	C14—H143	0.974
C6—H61	1.002	C15—H151	0.960
C6—H62	1.025	C15—H152	0.965
O8—H1	0.880	C15—H153	0.979
C2—C1—C6	111.59 (16)	H91—C9—H92	107.9
C2—C1—O12	103.50 (14)	C3—C9—H93	106.8
C6—C1—O12	107.74 (17)	H91—C9—H93	111.4
C2—C1—C15	114.17 (18)	H92—C9—H93	111.6
C6—C1—C15	109.17 (17)	C2—O10—C11	106.50 (14)
O12—C1—C15	110.37 (16)	O10—C11—O12	104.39 (15)
C1—C2—C3	113.57 (16)	O10—C11—C13	110.36 (19)
C1—C2—O10	104.26 (14)	O12—C11—C13	110.94 (19)
C3—C2—O10	107.03 (15)	O10—C11—C14	108.53 (17)
C1—C2—H21	111.8	O12—C11—C14	109.1 (2)
C3—C2—H21	108.3	C13—C11—C14	113.12 (19)
O10—C2—H21	111.9	C1—O12—C11	109.79 (15)
C2—C3—C4	107.53 (16)	C11—C13—H131	108.8
C2—C3—O8	106.69 (15)	C11—C13—H132	106.8
C4—C3—O8	107.58 (16)	H131—C13—H132	112.2
C2—C3—C9	111.74 (16)	C11—C13—H133	107.3
C4—C3—C9	110.67 (17)	H131—C13—H133	111.4
O8—C3—C9	112.38 (15)	H132—C13—H133	110.1
C3—C4—O5	116.88 (18)	C11—C14—H141	110.7
C3—C4—O7	124.15 (19)	C11—C14—H142	107.3
O5—C4—O7	118.97 (19)	H141—C14—H142	110.6
C4—O5—C6	118.67 (16)	C11—C14—H143	108.6
C1—C6—O5	113.22 (16)	H141—C14—H143	110.3
C1—C6—H61	109.9	H142—C14—H143	109.3
O5—C6—H61	108.0	C1—C15—H151	110.7
C1—C6—H62	108.7	C1—C15—H152	108.3
O5—C6—H62	106.1	H151—C15—H152	106.3
H61—C6—H62	110.9	C1—C15—H153	110.7
C3—O8—H1	111.6	H151—C15—H153	111.9

C3—C9—H91	107.9	H152—C15—H153	108.8
C3—C9—H92	111.2		

Hydrogen-bond geometry (Å, º)

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
O8—H1···O7^{i}	0.88	1.99	2.870 (2)	178

Symmetry code: (i) $x-1/2, -y+3/2, -z$.