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3,3′:5,6-Di-*O*-isopropylidene-3-*C*-hydroxymethyl-D-*allono*-1,4-lactone: an organic structure containing large unoccupied voids

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The Kiliani reaction of D-hamamelose with sodium cyanide, followed by acetonation, affords crystalline 3,3′:5,6-di-*O*-isopropylidene-3-*C*-hydroxymethyl-D-allono-1,4-lactone, $C_{13}H_{20}O_7$, a carbon-branched sugar with potential as an enantiomerically pure carbohydrate scaffold. The lactone has one single free hydroxyl group unprotected, with six other functional groups protected in a single step as ketals or esters. The resulting crystal structure is unusual in that it contains large voids (544 Å^3) within which there is no evidence of included solvent.

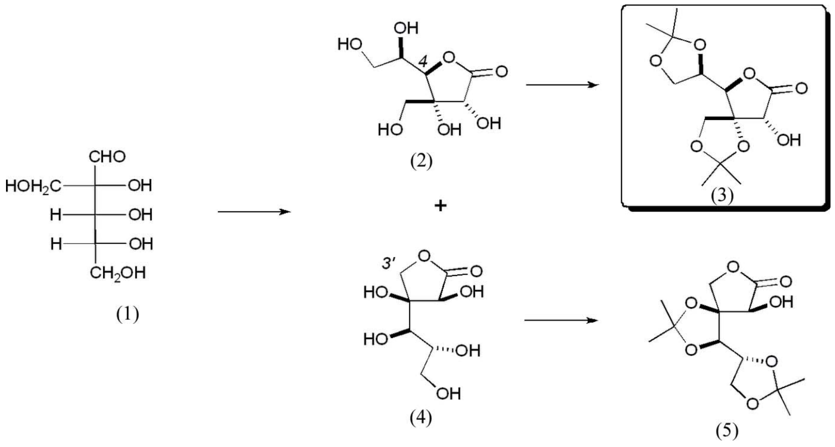
Key indicators

Single-crystal X-ray study
T = 150 K
Mean σ(C–C) = 0.004 Å
R factor = 0.046
wR factor = 0.044
Data-to-parameter ratio = 10.0

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

Comment

At present, there are very few accessible branched carbohydrate scaffolds (Lichtenthaler & Peters, 2004; Bols, 1996) for use in the synthesis of complex enantiomerically pure targets (Simone *et al.*, 2005). The reactions of calcium oxide on Amadori 1-deoxyamino-ketoses (Hotchkiss *et al.*, 2006) and the Kiliani reaction of cyanide with ketoses (Hotchkiss *et al.*, 2004; Soengas *et al.*, 2005) allow the preparation of 2-*C*-methyl and 2-*C*-hydroxymethyl lactones in relatively short sequences. However, syntheses of carbohydrates bearing a carbon branch at C-3 are very rare (Bream *et al.*, 2006). One approach to such chirons is the Kiliani cyanide reaction on 2-*C*-hydroxymethyl sugars [such as hamamelose (1)] to produce 3-*C*-hydroxymethyl lactones [such as (2) and (4)]. The experimental details for the Kiliani reaction of D-hamamelose (1) with cyanide to give a mixture of the two branched sugar lactones (2) and (4), followed by treatment with dimethoxypropane to afford a separable mixture of the two diacetonides (3) and (5), have been reported in a previous paper (Parker *et al.*, 2006).



A significant number of ambiguities arise from the formation of possible lactones, the sites for the formation of cyclic

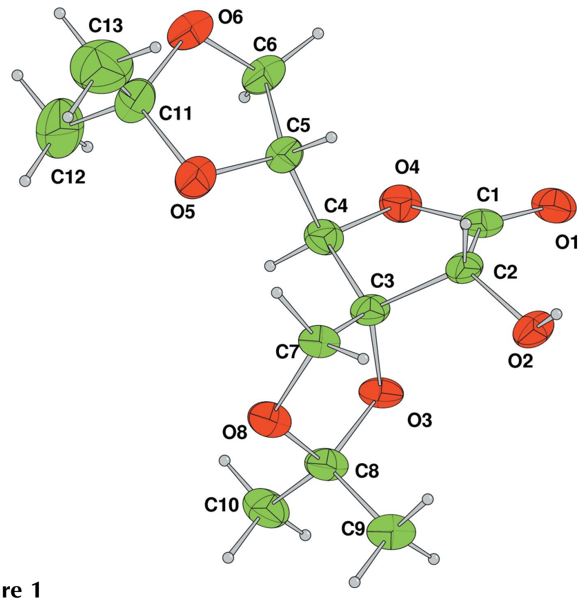


Figure 1
The molecular structure of the title compound with displacement ellipsoids drawn at the 50% probability level. H atoms are shown as spheres of arbitary radius.

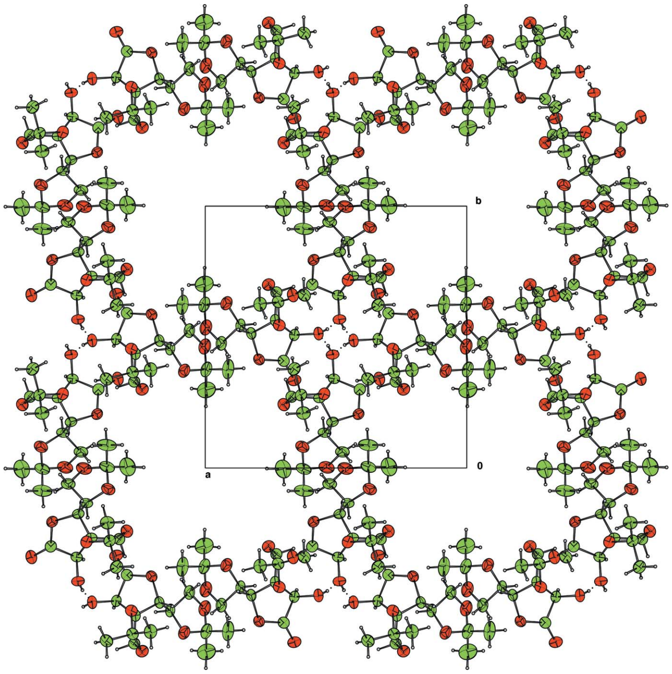


Figure 2
Packing diagam of the title compound viewed along *c*. The residual electron density in the void has a maximum value of 0.22 e Å^{-3}. Hydrogen bonds are drawn as dotted lines

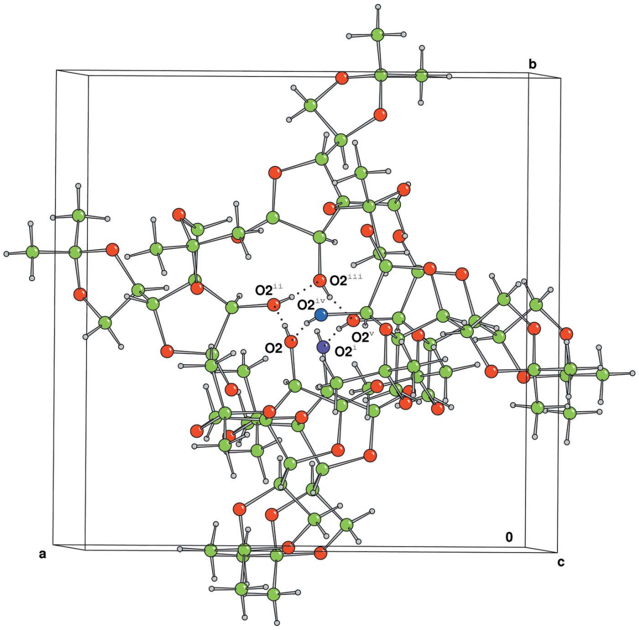


Figure 3
Oblique packing diagram of the title compound, showing the hydrogen-bonded helix which is the main structural feature. The ends of one turn of the helix are coloured blue and purple. Operators involved in forming the helix are: (i) $x, y, z + 1$; (ii) $-y + 1, x, z + \frac{1}{4}$; (iii) $-x + 1, -y + 1, z + \frac{1}{2}$; (iv) $y, -x + 1, z - \frac{1}{4}$; (v) $y, -x + 1, z + \frac{3}{4}$. Hydrogen bonds are drawn as dotted lines.

ketals and the sizes of both the lactone and ketal rings. This is an area in which X-ray crystallography is needed to have any confidence at all in the structures of diacetonides obtained by this short procedure. The crystal structure of the altrono-diacetonide (5), formed from the lactone (4) derived by cyclization of the branched C-3′ hydroxymethyl group on to the carboxylic acid, has been established by X-ray crystallography (Parker *et al.*, 2006). This paper firmly assigns the structure of the second crystalline product as the branched allono-lactone (3) formed from lactone formation from the C-4 hydroxyl group; the absolute configuration of (3) is determined by the use of D-ribose as the starting material for the synthesis. It is noteworthy that both lactones (3) and (5) have only the C-2 hydroxyl group unprotected; the sequence provides access to two sugars with seven functional groups but with six of the them protected in one simple step.

The component molecules have no unusual torsion angles, and show no evidence of internal strain. The relatively large anisotropic displacement parameters for the methyl groups and O atoms in the acetonide protecting group may indicate some ring fluxion (Fig. 1).

The crystal structure is unusual in that it contains substantial voids (544 Å^3) within which there is no evidence for included solvent (Fig. 2). The voids are big enough to have contained dichloromethane, but the maximum residual electron density is only 0.2 e Å^{-3}. We do not know if the voids in the dry crystals ever contained solvent, though generally solvent loss from organic crystals is associated with either a total loss of crystallinity, or at least a degradation of the crystal quality. In this case the crystals remained glass-clear.

The structure consists of a tight helix (Fig. 3), involving O—H$\cdots$O^{i} hydrogen bonds (Table 1), which runs parallel to the *c* axis at ($\frac{1}{2}$, $\frac{1}{2}$, *z*). The main parts of the molecule hang off this backbone like leaves from a tree. The tips of the ‘leaves’ of four separate helices meet to form a second helix at (0, 0, *z*). The ‘leaves’ of each pair of adjacent hydrogen-bonded helices (separated by $\frac{z}{2}$ because of the 4_1 axis) interleave along (0, 0, *z*), but there is no evidence for particularly strong interactions at these points.

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Experimental

The title compound, (3), was crystallized by dissolving it in dichloromethane, adding a few drops of cyclohexane and allowing the slow competitive evaporation of the two solvents until needle-like colourless crystals formed [m.p. 353 K (dichloromethane/cyclohexane)]. MS–ES$^-$ (*m*/*z*): 287.2 ($[M - \text{H}]^-$, 15%); HRMS (MS ES$^+$): found 311.1101 $[M + \text{Na}]^+$ $C_{13}H_{20}NaO_7$ requires 311.1101; $[\alpha]_D^{23}$: +5.5 (*c* 1.25 in chloroform); $\nu_{\max}$ (thin film): 3445 (*br*, OH), 2989 (CH_2, CH_3), 1800 (C=O) cm^{-1}; δ_H (C_6D_6, 400 MHz): 1.20, 1.31, 1.36, 1.38 [12H, 4 × *s*, 2 × $C(CH_3)_2$], 3.30–3.40 (1H, *br s*, OH-2), 3.51 (1H, *ddd*, $J_{\text{H-5,H-4}}$ = 8.5 Hz, $J_{\text{H-5,H-6}}$ = 6.7 Hz, $J_{\text{H-5,H-6}'}$ = 5.3 Hz, H-5), 3.75 (1H, *dd*, $J_{\text{H-6,H-6}'}$ = 9.5 Hz, $J_{\text{H-6,H-5}}$ = 6.6 Hz, H-6), 3.82 (1H, *dd*, $J_{\text{H-6}',\text{H-6}}$ = 9.5 Hz, $J_{\text{H-6}',\text{H-5}}$ = 5.3 Hz, H-6′), 3.97 (1H, *d*, $J_{\text{H-3,H-3}'}$ = 10.0 Hz H-3), 4.20 (1H, *s*, H-2), 4.26 (1H, *d*, $J_{\text{H-4,H-5}}$ = 8.6 Hz, H-4), 4.55 (1H, *d*, $J_{\text{H-3}',\text{H-3}}$ = 10.0 Hz, H-3′); δ_C (C_6D_6, 100 MHz): 24.8, 25.5, 26.5, 26.9 [2 × $C(CH_3)_2$], 65.3 (C-3′), 65.8 (C-6), 67.0 (C-2), 73.7 (C-5), 84.9 (C-3), 85.0 (C-4), 110.7, 111.2 [2 × $C(CH_3)_2$], 173.2 (C=O).

Crystal data

$C_{13}H_{20}O_7$
M_r = 288.30
Tetragonal, $P4_1$
a = 14.1641 (4) Å
c = 9.2045 (3) Å
V = 1846.62 (10) Å^3
Z = 4
D_x = 1.037 Mg m^{-3}
Mo $K\alpha$ radiation
μ = 0.08 mm^{-1}
T = 150 K
Needle, colourless
0.44 × 0.12 × 0.10 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
21907 measured reflections
2229 independent reflections
1802 reflections with $I > 3\sigma(I)$
R_{int} = 0.068
$\theta_{\max}$ = 27.6°

Refinement

Refinement on F
$R[F^2 > 2\sigma(F^2)]$ = 0.046
$wR(F^2)$ = 0.044
S = 1.04
1802 reflections
181 parameters
H-atom parameters constrained
$w = [1 - (F_o - F_c)^2/36\sigma^2(F)]^2/[1.09T_0(x) + 0.255T_1(x) + 0.726T_2(x)]$ where T_i are Chebychev polynomials and $x = F_c/F_{\max}$ (Prince, 1982; Watkin, 1994) Modified Chebychev polynomial (Watkin, 1994; Prince, 1982)
$(\Delta/\sigma)_{\max}$ = 0.010
$\Delta\rho_{\max}$ = 0.22 e Å^{-3}
$\Delta\rho_{\min}$ = −0.21 e Å^{-3}

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

D—H···A	D—H	H···A	D···A	D—H···A
O2—H1···O2$^{\text{i}}$	0.80	1.91	2.679 (2)	160

Symmetry code: (i) $-y + 1, x, z + \frac{1}{4}$.

In the absence of significant anomalous scattering, Friedel pairs were merged and the absolute configuration assigned from the starting materials 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, O—H = 0.82 Å and U_{iso}(H) = 1.2 or 1.5 times U_{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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