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Key indicators

Single-crystal X-ray study
 $T = 150$ K
Mean $\sigma(C-C) = 0.003$ Å
 R factor = 0.029
 wR factor = 0.070
Data-to-parameter ratio = 8.2For details of how these key indicators were automatically derived from the article, see <http://journals.iucr.org/e>.3,4:5,6-Di-*O*-isopropylidene-3-*C*-hydroxymethyl-*D*-altrono-1,3'-lactone

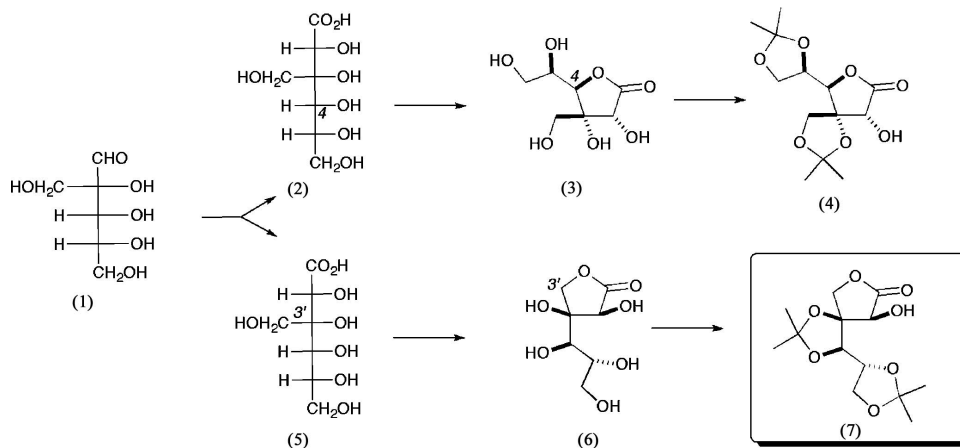
The title compound, $C_{13}H_{20}O_7$, a rare example of a sugar with a carbon branch at C-3, is one of the major products isolated from the treatment of *D*-hamamelose with cyanide (the Kiliani reaction), followed by protection as a diacetone. The material crystallizes with two molecules in the asymmetric unit, related to each other by a non-crystallographic twofold axis.

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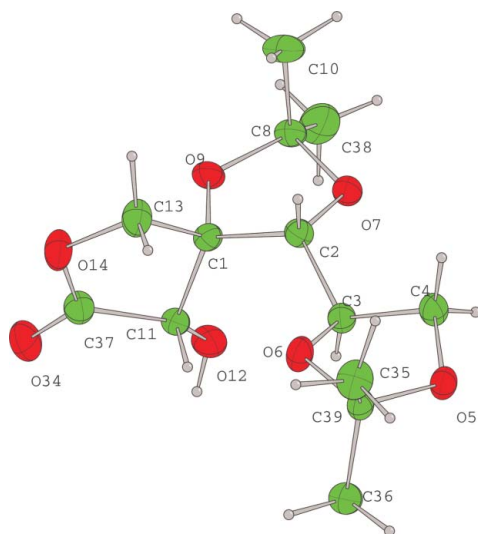
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Comment

The value of the Kiliani reaction of cyanide with ketoses (Hotchkiss *et al.*, 2004; Soengas *et al.*, 2005) and 1-deoxyketoses (Hotchkiss *et al.*, 2006) has been recognized for the easy synthesis of carbohydrate scaffolds with branched carbon chains at C-2 of the sugar. Such branched sugars are powerful intermediates for the synthesis of enantiomerically pure bioactive compounds (Simone *et al.*, 2005).



Examples of carbohydrates with a carbon branch at C-3 are very rare, although the synthesis of a crystalline derivative of 3-*C*-methyl-*D*-lyxono-1,4-lactone from the Kiliani reaction on 2-*C*-methyl-*D*-threose has been reported (Bream *et al.*, 2006). This paper reports a short synthesis of two carbohydrates with a branch at C-3 of a hexose from the Kiliani reaction of *D*-hamamelose, (1), which may be prepared in two steps from *D*-ribose (Ho, 1978; Hricoviniova-Bilikovaa *et al.*, 1999; Hricoviniova *et al.*, 2005). Thus, treatment of (1) with sodium cyanide in water gives a mixture of the diastereomeric 3-*C*-hydroxymethylhexonic acids, (2) and (5). Treatment of the crude reaction mixture of (2) and (5) with acid in dimethoxypropane induces cyclization to the respective lactones, (3) and (6), together with subsequent formation of the diacetone, (4) and (7); experimental details for the procedure are given below.

**Figure 1**

One of the two independent molecules of the title compound, with displacement ellipsoids drawn at the 50% probability level. H atoms are shown as spheres of arbitrary radii. The second molecule has a similar geometry and is numbered by adding 100 to equivalent atoms in the first molecule.

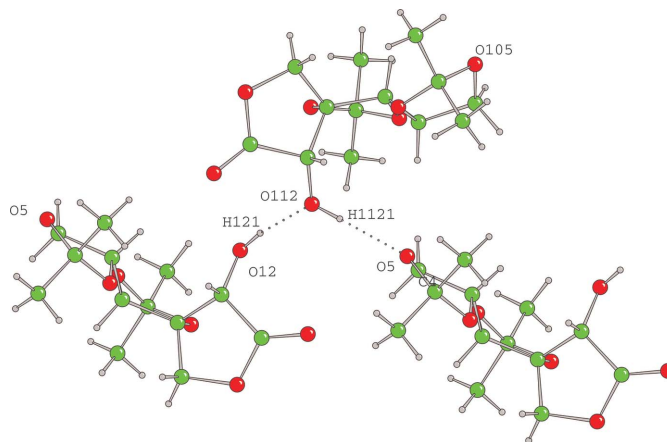
The possible combinations for the formation of different diacetonides from acids (2) and (5) are numerous. Thus, it is seen that 1,4-lactones can be formed from either the C-4 hydroxyl group of the sugar [to give (3)] or the C-3' hydroxyl group [to give (6)], and from each of these products several different diacetonides may arise. Only X-ray crystallographic analysis can resolve the structural ambiguities that arise in this reaction. This paper firmly identifies the relative configuration of the four stereocentres in the altrono-diacetonide, (7). The absolute configuration of (7) is determined by the use of D-ribose as the starting material for the synthesis. The crystal structure of the allono-lactone, (4), is reported in a subsequent paper (Cowley *et al.*, 2006).

Compound (7) crystallizes with two molecules in the asymmetric unit, related by a well-defined non-crystallographic twofold axis. After mapping the molecules together by least-squares, the r.m.s. positional deviation of the non-H atoms is 0.378 Å, and the r.m.s. deviation in equivalent bond lengths is 0.009 Å. The major difference between the two molecules is at O5 and O105, where the envelope flap is on opposite sides of the plane of the rest of the ring.

The crystal structure of (7) is built up of infinite columns, two molecules wide, connected by hydrogen bonds (Table 1). Note that atom O105 is not involved in the network, and is thus free to adopt a different conformation from O5.

Experimental

The synthesis of 3,4:5,6-di-*O*-isopropylidene-3-*C*-hydroxymethyl-*D*-altrono-1,3'-lactone, (7), and 3,3':5,6-di-*O*-isopropylidene-3-*C*-hydroxymethyl-*D*-allono-1,4-lactone, (4), was carried out as follows. Sodium cyanide (1.04 g, 21.184 mmol) was added to a solution of D-hamamelose, (1) (1.26 g, 7.007 mmol), in water (80 ml). The reaction mixture was stirred at room temperature for 24 h and then heated to reflux for a further 24 h. The solution was then passed through an ion-

**Figure 2**

Part of the hydrogen-bonding network, showing the formation of columns, two molecules wide, linking the two independent molecules. Hydrogen bonds are shown as dotted lines. The columns run parallel to the *b* axis and there are no interactions between columns. Note that atom O5 is involved in the hydrogen bonding but atom O105 is not.

exchange resin [Amberlite IR-120 (H⁺)]. The water was removed *in vacuo* to give a dark-yellow oily residue (1.32 g), which was then treated with dimethoxypropane (18 ml) and *para*-toluenesulfonic acid monohydrate (119 mg, catalyst). The reaction mixture was stirred at room temperature for 36 h, quenched with solid sodium bicarbonate and concentrated *in vacuo*. The residue was partitioned between dichloromethane (200 ml) and water (40 ml). The aqueous phase was washed twice with dichloromethane (2 × 160 ml). The organic layers were combined, dried (magnesium sulfate) and concentrated *in vacuo* to give a residue which was purified by flash chromatography (ethyl acetate-hexane, 1:3 to 1:2 to 1:1) to give 3,4:5,6-di-*O*-isopropylidene-3-*C*-hydroxymethyl-*D*-altrono-1,3'-lactone, (7) (*R*_f 0.56) (254 mg), and 3-*C*-hydroxymethyl-3,3':5,6-di-*O*-isopropylidene-*D*-allono-1,4-lactone, (4) (*R*_f 0.44) (251 mg) (25% combined yield, 1.75 mmol). Data for (7): m.p. 321–323 K (dichloromethane–cyclohexane as colourless chunky crystals); *m/z* (MS ES⁻): 287.2 [*M*–H]⁻, 100%; HRMS (MS ES⁺), found: 311.1101 [*M*+Na]⁺; C₁₃H₂₀NaO₇ requires 311.1101; [α]_D²³: 5.8 (*c*, 0.23 in acetone); IR (ν_{max}, thin film, cm⁻¹): 3439 (*br*, OH), 2989 (CH), 1797 (*sh*, C=O); ¹H NMR (CDCl₃, 400 MHz, δ, p.p.m.): 1.35, 1.43, 1.44, 1.50 [12H, 4s, 2 C(CH₃)₂], 2.60–2.70 (1H, *br s*, OH2), 3.87 (1H, *d*, *J*_{H4,H5} = 9.3 Hz, H4), 4.00 (1H, *dd*, *J*_{H6,H6'} = 9.0 Hz, *J*_{H6,H5} = 4.4 Hz, H6), 4.21 (1H, *dd*, *J*_{H6',H6} = 9.0 Hz, *J*_{H6',H5} = 6.1 Hz, H6'), 4.32 (2H, 2s, H3' and H3''), 4.31–4.39 (1H, *m*, H5), 4.75–4.80 (1H, *br s*, H2); ¹³C NMR (CDCl₃, 100 MHz, δ, p.p.m.): 25.0, 25.4, 26.8, 26.9 [2 C(CH₃)₂], 67.9 (C6), 68.5 (C2), 73.1 (C5), 74.3 (C3'), 77.7 (C4), 85.8 (C3), 110.3, 111.1 [2 C(CH₃)₂], 174.7 (C=O).

The sample for X-ray crystallographic analysis of (7) was grown by vapour diffusion of cyclohexane into a saturated solution of the material in dichloromethane until crystals formed. Data for the allono-lactone, (4), are given in Bream *et al.* (2006).

Crystal data

C₁₃H₂₀O₇
*M*_r = 288.30
 Monoclinic, *P*2₁
a = 11.5720 (2) Å
b = 9.2793 (2) Å
c = 13.1937 (3) Å
 β = 90.5971 (8)°
V = 1416.66 (5) Å³

Z = 4
*D*_x = 1.352 Mg m⁻³
 Mo Kα radiation
 μ = 0.11 mm⁻¹
T = 150 K
 Block, colourless
 0.55 × 0.50 × 0.45 mm

Data collection

Nonius KappaCCD area-detector diffractometer	17056 measured reflections
ω scans	3374 independent reflections
Absorption correction: multi-scan (DENZO/SCALEPACK; Otwinowski & Minor, 1997)	2956 reflections with $I > 3\sigma(I)$
$T_{\min} = 0.73$, $T_{\max} = 0.95$	$R_{\text{int}} = 0.028$
	$\theta_{\text{max}} = 27.5^\circ$

Refinement

Refinement on F^2	H-atom parameters constrained
$R[F^2 > 2\sigma(F^2)] = 0.029$	$w = 1/[\sigma^2(F^2) + (0.03P)^2 + 0.33P]$
$wR(F^2) = 0.070$	where $P = [\max(F_o^2, 0) + 2F_c^2]/3$
$S = 0.97$	$(\Delta/\sigma)_{\text{max}} < 0.001$
2956 reflections	$\Delta\rho_{\text{max}} = 0.19 \text{ e } \text{\AA}^{-3}$
361 parameters	$\Delta\rho_{\text{min}} = -0.16 \text{ e } \text{\AA}^{-3}$

Table 1

Hydrogen-bond geometry (\AA , $^\circ$).

$D-H\cdots A$	$D-H$	$H\cdots A$	$D\cdots A$	$D-H\cdots A$
O12—H121 \cdots O112 ¹	0.84	1.98	2.813 (2)	170
O112—H1121 \cdots O5 ¹	0.83	1.98	2.806 (2)	169

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

In the absence of significant anomalous scattering, Friedel pairs were merged and the absolute configuration was assigned from the known configuration of the starting materials. The values of T_{\min} and T_{\max} were computed by the multi-scan inter-frame scaling, and take into account factors other than simple absorption (Görbitz, 1999). 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 \AA and O—H = 0.82 \AA) and $U_{\text{iso}}(\text{H})$ (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; data reduction: DENZO/SCALEPACK (Otwinowski & Minor, 1997); 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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