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6-Deoxy-3,4-*O*-isopropylidene-2-*C*-methyl-L-galactono-1,5-lactone

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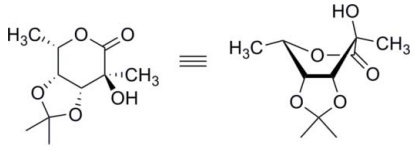
Key indicators: single-crystal X-ray study; T = 150 K; mean σ(C–C) = 0.003 Å; R factor = 0.038; wR factor = 0.090; data-to-parameter ratio = 10.7.

X-ray crystallography unequivocally confirmed the stereochemistry of the 2-*C*-methyl group in the title molecule, $C_{10}H_{16}O_5$, in which the 1,5-lactone ring exists in a boat conformation. The absolute stereochemistry was determined by the use of D-ribose in the synthesis. The crystal exists as O—H···O hydrogen bonded chains of molecules running parallel to the *a* axis with each molecule acting as a donor and acceptor for one hydrogen bond.

Related literature

For branched iminosugars, see: Håkansson *et al.* (2007, 2008); Asano *et al.* (2000); da Cruz *et al.* (2011); Best *et al.* (2010) and for branched sugars, see: Booth *et al.* (2008, 2009); da Cruz *et al.* (2008); Hotchkiss *et al.* (2006, 2007); Jenkinson *et al.* (2007); Jones *et al.* (2007, 2008); Rao *et al.* (2008). For conformations of related 1,5-lactones, see: Baird *et al.* (1987); Booth *et al.* (2007*a*,*b*); Bruce *et al.* (1990); Punzo *et al.* (2005, 2006); Dai *et al.* (2010).



Experimental

Crystal data

$C_{10}H_{16}O_5$
M_r = 216.23
Orthorhombic, $P2_12_12_1$
a = 6.1132 (2) Å
b = 12.2963 (4) Å
c = 14.6367 (5) Å
V = 1100.24 (6) Å^3
Z = 4
Mo $K\alpha$ radiation
μ = 0.11 mm^{-1}
T = 150 K
0.20 × 0.20 × 0.04 mm

Data collection

Nonius KappaCCD diffractometer
Absorption correction: multi-scan (*DENZO*/*SCALEPACK*; Otwinowski & Minor, 1997)
T_{min} = 0.95, T_{max} = 1.00
8628 measured reflections
1454 independent reflections
1131 reflections with $I > 2\sigma(I)$
R_{int} = 0.067

Refinement

$R[F^2 > 2\sigma(F^2)]$ = 0.038
$wR(F^2)$ = 0.090
S = 0.89
1454 reflections
136 parameters
H-atom parameters constrained
$\Delta\rho_{max}$ = 0.40 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
O11—H111···O1^{i}	0.86	1.93	2.793 (3)	172

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

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*.

Supplementary data and figures for this paper are available from the IUCr electronic archives (Reference: LH5321).

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supporting information

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6-Deoxy-3,4-*O*-isopropylidene-2-*C*-methyl-L-galactono-1,5-lactone

Sarah F. Jenkinson, Loren L. Parry, Francis X. Wilson, George W. J. Fleet and David J. Watkin

S1. Comment

2-*C*-Methyl branched sugars, as well as being chirons for the enantiospecific synthesis of complex targets (Hotchkiss *et al.*, 2006; Hotchkiss *et al.*, 2007; da Cruz *et al.*, 2008; Booth *et al.*, 2009) including 2′-*C*-methyl nucleosides (Jenkinson *et al.*, 2007), are a class of rare sugars with chemotherapeutic potential (Rao *et al.*, 2008; Jones *et al.*, 2008; Booth *et al.*, 2008). Branched iminosugars have also been shown to exhibit interesting biological activity. For example: 6-*C*-methyl-swainsonine is a more potent inhibitor of *L*-rhamnosidase than *L*-swainsonine (Håkansson *et al.*, 2007; Håkansson *et al.*, 2008; Asano *et al.*, 2000); 4-*C*-methylDAB and 4-*C*-methylLAB are both potent and specific *α*-glucosidase inhibitors (da Cruz *et al.* 2011) and isoLAB has been shown to partially rescue the defective F508del-CFTR function and therefore may have a role in the study of cyctic fibrosis (Best *et al.*, 2010).

D-ribose **1** was converted by a number of steps to the lactols **2** (Fig. 1). The reaction of **2** with sodium cyanide in water gave a chain extension to afford a single isolated crystalline product **3** (Fig. 2).

3,4-*O*-Isopropylidene-1,5-lactones, such as **3**, invariably crystallize in boat conformations (Baird *et al.*, 1987; Bruce *et al.*, 1990; Punzo *et al.*, 2005). The diastereoselectivity of the reaction may be rationalized by the formation of the lactone **3** with less steric congestion (Punzo *et al.*, 2006; Booth *et al.*, 2007*a*; Booth *et al.*, 2007*b*; Dai *et al.* 2010) with the smaller hydroxy group rather than the methyl group in the flagpole position (Fig. 2). The structure of **3** was confirmed by the X-ray crystallographic analysis. The absolute configuration was assigned from the use of D-ribose as the starting material. The title compound exists as O—H···O hydrogen bonded chains of molecules running parallel to the *a*-axis (Fig. 3). Each molecule acts as a donor and acceptor for 1 hydrogen bond. Only classical hydrogen bonding has been considered.

S2. Experimental

The title compound was recrystallized by diffusion from a mixture of ethyl acetate and cyclohexane: m.p. 369–371 K; $[\alpha]_D^{25}$ -84.6 (*c*, 1.03 in $CHCl_3$).

S3. Refinement

In the absence of significant anomalous scattering, Friedel pairs were merged and the absolute configuration was assigned from the use of D-ribose as the starting material.

The H atoms were all located in a difference map, but those attached to carbon 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, O—H = 0.82 Å) and U_{iso}(H) (in the range 1.2–1.5 timesU_{eq} of the parent atom), after which the positions were refined with riding constraints.

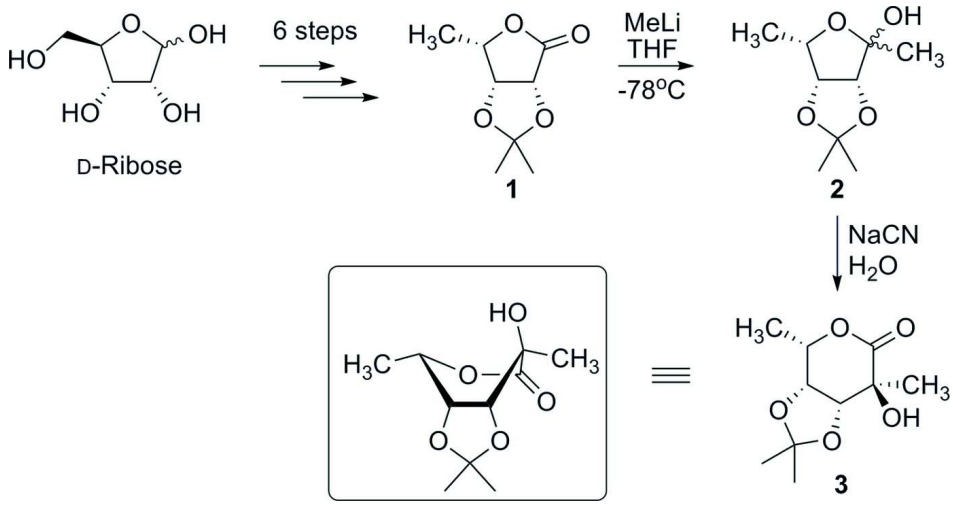

Figure 1

Synthetic Scheme.

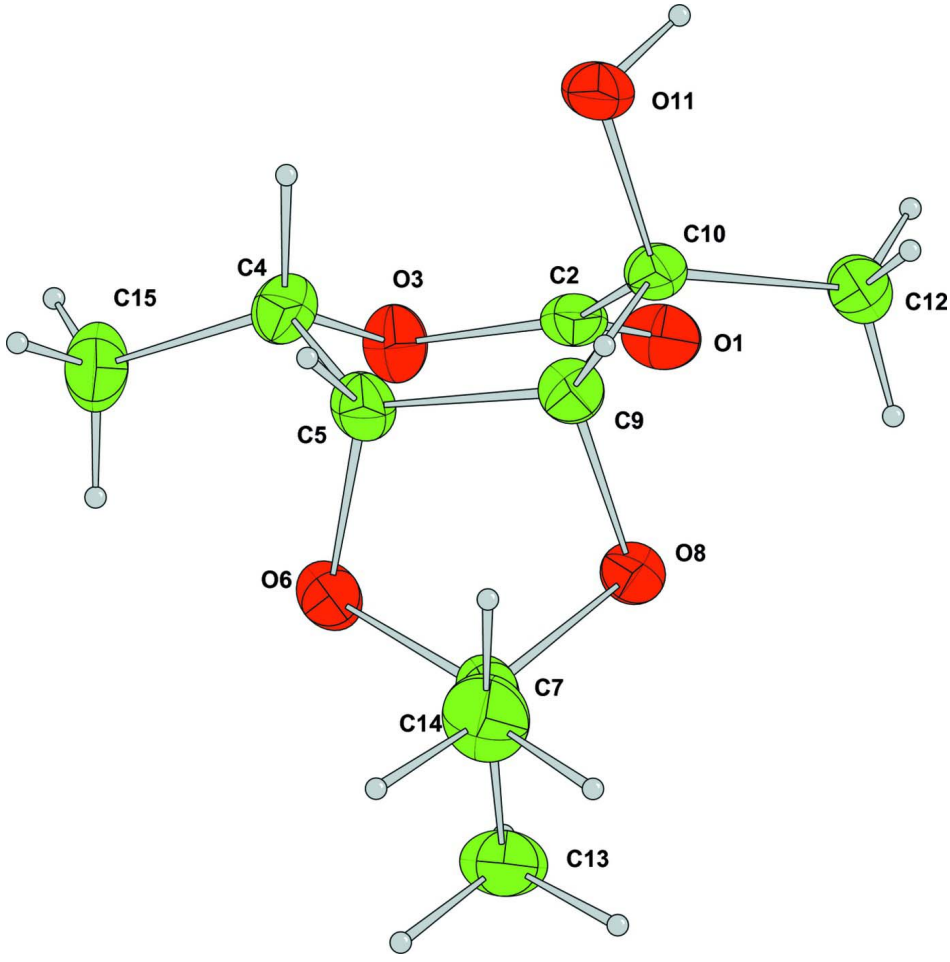

Figure 2

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

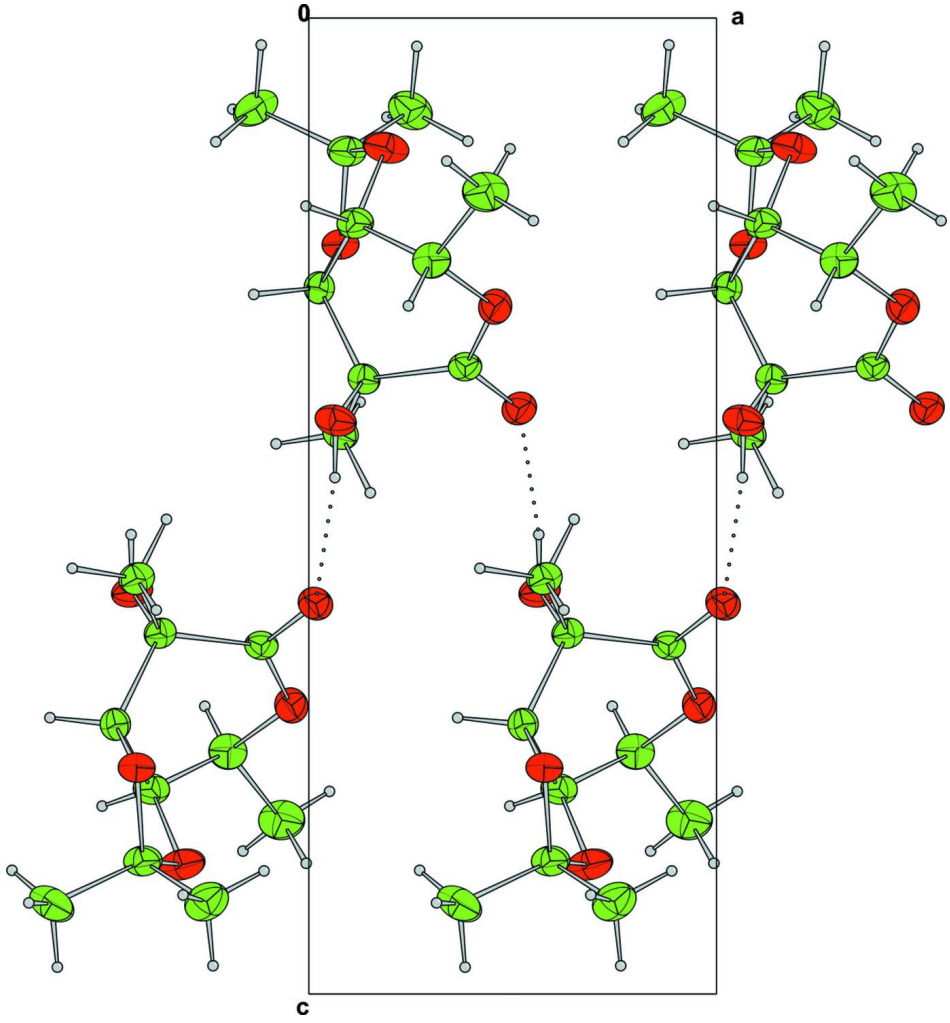

Figure 3

Packing diagram of the title compound projected along the *b*-axis. Hydrogen bonds are shown by dotted lines.

6-Deoxy-3,4-*O*-isopropylidene-2-*C*-methyl-L-galactono-1,5-lactone

Crystal data

$C_{10}H_{16}O_5$
$M_r = 216.23$
Orthorhombic, $P2_12_12_1$
Hall symbol: P 2ac 2ab
$a = 6.1132$ (2) Å
$b = 12.2963$ (4) Å
$c = 14.6367$ (5) Å
$V = 1100.24$ (6) Å^3
$Z = 4$
$F(000) = 464$
$D_x = 1.305$ Mg m^{-3}
Mo $K\alpha$ radiation, $\lambda = 0.71073$ Å
Cell parameters from 1433 reflections
$\theta = 5$–27°
$\mu = 0.11$ mm^{-1}
$T = 150$ K
Plate, colourless
0.20 × 0.20 × 0.04 mm

Data collection

Nonius KappaCCD diffractometer
Graphite monochromator
ω scans
Absorption correction: multi-scan (*DENZO*/*SCALEPACK*; Otwinowski & Minor, 1997)
$T_{min} = 0.95$, $T_{max} = 1.00$

8628 measured reflections
1454 independent reflections
1131 reflections with $I > 2\sigma(I)$
$R_{int} = 0.067$
$\theta_{max} = 27.5°$, $\theta_{min} = 5.2°$
$h = -7 \rightarrow 7$
$k = -15 \rightarrow 15$
$l = -18 \rightarrow 19$

Refinement

Refinement on F^2
Least-squares matrix: full
$R[F^2 > 2\sigma(F^2)] = 0.038$
$wR(F^2) = 0.090$
$S = 0.89$
1454 reflections
136 parameters
0 restraints
Primary atom site location: structure-invariant direct methods
Hydrogen site location: inferred from neighbouring sites
H-atom parameters constrained
Method = Modified Sheldrick $w = 1/[\sigma^2(F^2) + (0.06P)^2 + 0.14P]$, where $P = [\max(F_o^2,0) + 2F_c^2]/3$
$(\Delta/\sigma)_{max} = 0.000259$
$\Delta\rho_{max} = 0.40$ 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}
O1	−0.0165 (3)	0.80556 (12)	0.89995 (10)	0.0290
C2	0.1164 (4)	0.75275 (16)	0.85712 (12)	0.0226
O3	0.0426 (3)	0.68163 (11)	0.79561 (10)	0.0287
C4	0.1986 (4)	0.60986 (16)	0.74843 (14)	0.0289
C5	0.3861 (4)	0.67578 (16)	0.71001 (14)	0.0271
O6	0.3108 (3)	0.73556 (12)	0.63264 (9)	0.0355
C7	0.4068 (4)	0.84132 (17)	0.63637 (13)	0.0292
O8	0.4222 (3)	0.86365 (10)	0.73198 (9)	0.0261
C9	0.4744 (4)	0.76299 (15)	0.77626 (13)	0.0240
C10	0.3643 (4)	0.76166 (16)	0.86972 (13)	0.0221
O11	0.4337 (3)	0.66259 (11)	0.91228 (10)	0.0301
C12	0.4222 (4)	0.86099 (16)	0.92581 (13)	0.0277
C13	0.2506 (5)	0.92177 (19)	0.59465 (16)	0.0401
C14	0.6306 (5)	0.8415 (2)	0.59246 (16)	0.0422
C15	0.0664 (5)	0.55020 (19)	0.67809 (16)	0.0402
H41	0.2554	0.5572	0.7948	0.0338*
H51	0.5068	0.6260	0.6926	0.0337*
H91	0.6348	0.7543	0.7832	0.0290*
H121	0.5803	0.8627	0.9363	0.0432*
H122	0.3490	0.8570	0.9864	0.0426*
H123	0.3742	0.9272	0.8933	0.0431*
H131	0.3082	0.9961	0.6014	0.0583*
H132	0.2349	0.9048	0.5289	0.0582*
H133	0.1099	0.9171	0.6262	0.0586*
H141	0.6868	0.9161	0.5934	0.0627*
H142	0.7280	0.7929	0.6268	0.0622*
H143	0.6166	0.8179	0.5275	0.0623*
H153	0.1616	0.4999	0.6465	0.0610*
H152	−0.0508	0.5092	0.7077	0.0613*
H151	0.0062	0.6022	0.6340	0.0612*

H111	0.4361	0.6716	0.9708	0.0460*

Atomic displacement parameters (Å²)

	U^{11}	U^{22}	U^{33}	U^{12}	U^{13}	U^{23}
O1	0.0284 (9)	0.0329 (8)	0.0257 (7)	0.0061 (7)	0.0025 (7)	0.0035 (7)
C2	0.0264 (11)	0.0224 (10)	0.0191 (8)	0.0006 (10)	0.0006 (9)	0.0049 (9)
O3	0.0263 (8)	0.0302 (8)	0.0295 (8)	−0.0029 (7)	0.0011 (6)	−0.0051 (6)
C4	0.0344 (13)	0.0224 (10)	0.0299 (11)	0.0027 (9)	0.0008 (10)	−0.0023 (9)
C5	0.0315 (12)	0.0276 (10)	0.0222 (9)	0.0034 (10)	0.0012 (10)	−0.0035 (9)
O6	0.0500 (11)	0.0332 (8)	0.0234 (7)	−0.0145 (8)	−0.0068 (7)	0.0026 (7)
C7	0.0354 (13)	0.0305 (12)	0.0216 (10)	−0.0092 (11)	−0.0011 (10)	−0.0005 (9)
O8	0.0326 (8)	0.0250 (7)	0.0208 (7)	−0.0002 (7)	0.0006 (6)	0.0007 (6)
C9	0.0220 (11)	0.0253 (10)	0.0248 (9)	0.0032 (9)	0.0000 (9)	−0.0009 (9)
C10	0.0246 (11)	0.0198 (10)	0.0220 (9)	0.0042 (9)	−0.0017 (9)	0.0009 (8)
O11	0.0405 (9)	0.0267 (7)	0.0233 (7)	0.0089 (7)	−0.0047 (7)	0.0023 (6)
C12	0.0300 (12)	0.0288 (11)	0.0243 (10)	0.0005 (10)	−0.0028 (10)	−0.0022 (9)
C13	0.0453 (16)	0.0394 (13)	0.0355 (12)	−0.0026 (13)	−0.0080 (13)	0.0110 (12)
C14	0.0470 (16)	0.0480 (14)	0.0316 (11)	−0.0057 (14)	0.0137 (12)	−0.0004 (12)
C15	0.0509 (17)	0.0330 (12)	0.0368 (12)	−0.0104 (12)	−0.0011 (13)	−0.0088 (10)

Geometric parameters (Å, º)

O1—C2	1.214 (2)	C9—H91	0.992
C2—O3	1.334 (2)	C10—O11	1.433 (2)
C2—C10	1.530 (3)	C10—C12	1.514 (3)
O3—C4	1.472 (3)	O11—H111	0.864
C4—C5	1.512 (3)	C12—H121	0.979
C4—C15	1.501 (3)	C12—H122	0.995
C4—H41	1.000	C12—H123	0.987
C5—O6	1.426 (2)	C13—H131	0.985
C5—C9	1.543 (3)	C13—H132	0.989
C5—H51	0.992	C13—H133	0.978
O6—C7	1.428 (3)	C14—H141	0.979
C7—O8	1.429 (2)	C14—H142	0.982
C7—C13	1.505 (3)	C14—H143	0.997
C7—C14	1.512 (3)	C15—H153	0.967
O8—C9	1.433 (2)	C15—H152	0.977
C9—C10	1.525 (3)	C15—H151	0.980
O1—C2—O3	118.2 (2)	C2—C10—O11	106.55 (17)
O1—C2—C10	124.18 (18)	C9—C10—O11	105.58 (16)
O3—C2—C10	117.60 (18)	C2—C10—C12	110.78 (18)
C2—O3—C4	119.38 (17)	C9—C10—C12	112.01 (17)
O3—C4—C5	110.13 (15)	O11—C10—C12	112.40 (15)
O3—C4—C15	105.41 (19)	C10—O11—H111	109.1
C5—C4—C15	114.54 (18)	C10—C12—H121	109.5
O3—C4—H41	107.1	C10—C12—H122	109.8

C5—C4—H41	109.7	H121—C12—H122	107.8
C15—C4—H41	109.6	C10—C12—H123	109.5
C4—C5—O6	109.09 (18)	H121—C12—H123	110.5
C4—C5—C9	113.83 (17)	H122—C12—H123	109.7
O6—C5—C9	104.69 (15)	C7—C13—H131	110.0
C4—C5—H51	109.2	C7—C13—H132	108.5
O6—C5—H51	110.7	H131—C13—H132	109.2
C9—C5—H51	109.3	C7—C13—H133	109.2
C5—O6—C7	107.85 (16)	H131—C13—H133	108.7
O6—C7—O8	103.85 (15)	H132—C13—H133	111.2
O6—C7—C13	108.81 (18)	C7—C14—H141	108.2
O8—C7—C13	108.23 (18)	C7—C14—H142	109.3
O6—C7—C14	110.92 (18)	H141—C14—H142	110.5
O8—C7—C14	110.89 (19)	C7—C14—H143	109.1
C13—C7—C14	113.65 (18)	H141—C14—H143	108.4
C7—O8—C9	106.95 (14)	H142—C14—H143	111.3
C5—C9—O8	103.77 (15)	C4—C15—H153	108.4
C5—C9—C10	113.70 (17)	C4—C15—H152	110.1
O8—C9—C10	108.47 (15)	H153—C15—H152	108.9
C5—C9—H91	109.6	C4—C15—H151	109.6
O8—C9—H91	111.1	H153—C15—H151	109.1
C10—C9—H91	110.1	H152—C15—H151	110.7
C2—C10—C9	109.25 (16)		

Hydrogen-bond geometry (Å, º)

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
C13—H131···O11^{i}	0.99	2.59	3.536 (3)	161
O11—H111···O1^{ii}	0.86	1.93	2.793 (3)	172

Symmetry codes: (i) −*x*+1, *y*+1/2, −*z*+3/2; (ii) *x*+1/2, −*y*+3/2, −*z*+2.