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# 2,3:5,6-Di-*O*-isopropylidene-3,5-di-*C*-methyl-L-mannono-1,4-lactone

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**Key indicators**

Single-crystal X-ray study
*T* = 150 K
Mean σ(C–C) = 0.004 Å
*R* factor = 0.038
*wR* factor = 0.106
Data-to-parameter ratio = 11.5

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

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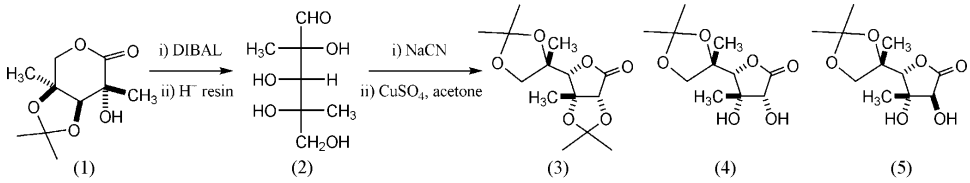
The relative configuration at C-2 of the title lactone, $C_{14}H_{22}O_6$, which exists in the five-membered ring form, was unequivocally established by X-ray crystallographic analysis. The absolute configuration was determined by the use of 2,4-di-*C*-methyl-L-arabinose as the starting material.

## Comment

Rare and new monosaccharides have potential as healthy dietary alternatives (Sun *et al.*, 2007; Skytte, 2002); L-glucose has been shown to be a low-calorie sugar alternative (Levin *et al.*, 1995). Rare sugars may also be therapeutically useful; branched triglyceride analogues have shown inhibition of glycogen phosphorylase (Sher & Ellsworth, 2004) which may help in the treatment of type 2 diabetes (Oikonomakos *et al.*, 2006). Branched 3-*C*-methyl sugars are rarely found in nature, and, to date, no examples of the free sugars have been reported in the literature. 3-*C*-Methyl-D-mannose was found to be a component of a lipopolysaccharide of the *Helicobacter pylori* pathogen (Kocharova *et al.*, 2000). There have been no biological studies on unprotected monosaccharides with more than one carbon branch.

2,4-Di-*C*-methyl-L-arabinose, (1) (Booth, Watkin *et al.*, 2007), was the starting material in the synthesis of 3,5-dimethyl sugar lactones (Booth, Best *et al.*, 2007). Treatment of (2) with aqueous cyanide gave a mixture of four inseparable sugar lactones – both the five- and six-membered ring lactones of the *gluco* and *manno* configured sugars; these two lactones are epimeric at C-2. Isopropylidene protection with acetone and copper(II) sulfate gave three easily separable crystalline sugars, (3), (4) and (5). The crystal structure determination has resolved the ambiguity at C-2 and unequivocally established the relative stereochemistry of the title compound as the diisopropylidene-protected mannono-1,4-lactone (3), as the mono-protected mannono-1,4-lactone (4) and as the mono-protected glucono-1,4-lactone (5). The absolute configuration of these sugars is determined by the use of 2,4-di-*C*-methyl-L-arabinose, (1), as the starting material.




The crystal structure is layered, with no short-range intermolecular contacts. The structure has a channel running along

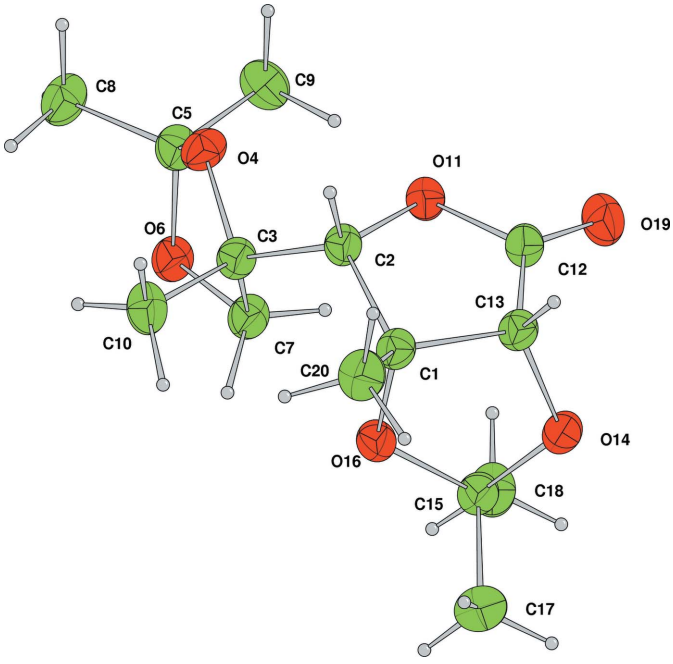



**Figure 1**
The molecular structure of (3) with displacement ellipsoids drawn at the 50% probability level. H atoms are shown as spheres of arbitary radius.

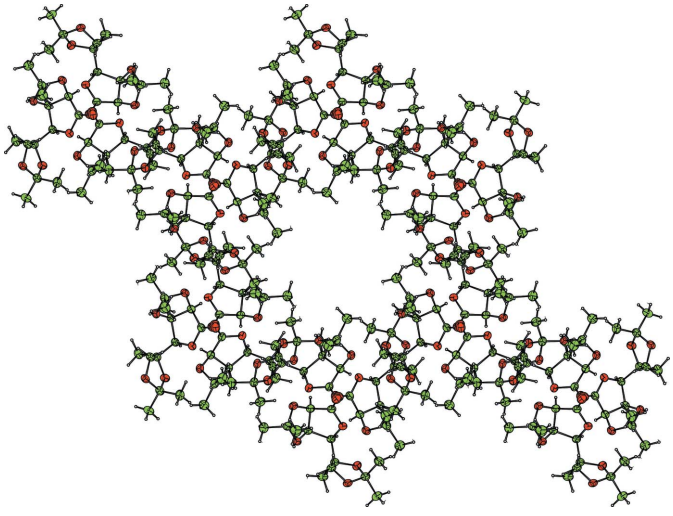


**Figure 2**
A packing diagram of the title compound projected along the *c* axis, showing the channel that runs parallel to *c*.

the threefold axis parallel to *c* (Fig. 2). Two isolated atoms have been identified in the cavity. The distance between them (1.88 Å), was too short to be a non-bonding interaction, but too long to be identified as a real chemical entity. For these reasons the electron density in the cavity was modelled using SQUEEZE (Spek, 2003) which replaces the contribution from individual atoms by the discrete Fourier transform of the residual electron density. In *CRYSTALS* (Betteridge *et al.*, 2003), this is achieved by adding contributions to the *A* and *B* parts of the structure factor expression rather than subtracting a contribution from the observed structure factors.

## Experimental

The title lactone (3) was recrystallized from chloroform, m.p. 465–469 K, $[\alpha]_D^{17}$-48.2 (*c*, 0.88 in $CHCl_3$).

*Crystal data*

$C_{14}H_{22}O_6$
$M_r$ = 286.33
Hexagonal, $P6_5$
*a* = 15.6104 (3) Å
*c* = 12.4340 (3) Å
*V* = 2624.03 (10) Å$^3$
*Z* = 6
Mo *K*α radiation
$\mu$ = 0.09 mm$^{-1}$
*T* = 150 K
0.60 × 0.10 × 0.05 mm

*Data collection*

Bruker–Nonius KappaCCD diffractometer
Absorption correction: multi-scan (*DENZO*/*SCALEPACK*; Otwinowski & Minor, 1997)
$T_{min}$ = 0.50, $T_{max}$ = 1.00
18890 measured reflections
2078 independent reflections
1777 reflections with $I > 2\sigma(I)$
$R_{int}$ = 0.054

*Refinement*

$R[F^2 > 2\sigma(F^2)]$ = 0.038
$wR(F^2)$ = 0.106
*S* = 0.97
2078 reflections
181 parameters
1 restraint
H-atom parameters constrained
$\Delta\rho_{max}$ = 0.26 e Å$^{-3}$
$\Delta\rho_{min}$ = −0.21 e Å$^{-3}$

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 multiscan process (1:2) reflects changes in the illuminated volume of the crystal. 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 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) 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*.

## References

Altomare, A., Cascarano, G., Giacovazzo, G., Guagliardi, A., Burla, M. C., Polidori, G. & Camalli, M. (1994). *J. Appl. Cryst.* **27**, 435.
Betteridge, P. W., Carruthers, J. R., Cooper, R. I., Prout, K. & Watkin, D. J. (2003). *J. Appl. Cryst.* **36**, 1487.
Booth, K. V., Best, D., Jenkinson, S. F. & Fleet, G. W. J. (2007). In preparation.
Booth, K. V., Watkin, D. J., Jenkinson, S. F. & Fleet, G. W. J. (2007). *Acta Cryst.* E**63**, o1128–o1130.
Görbitz, C. H. (1999). *Acta Cryst.* B**55**, 1090–1098.
Kocharova, N. A., Knirel, Y. A., Widmalm, G., Jansson, P. & Moran, A. P. (2000). *Biochemistry*, **39**, 4755–4760.
Levin, G. V., Zehner, L. R., Saunders, J. P. & Beadle, J. R. (1995). *Am. J. Clin. Nutr.* **62**, 1161–1168.

Nonius (2001). *COLLECT*. Nonius BV, Delft, The Netherlands.
Oikonomakos, N. G., Tiraidis, C., Leonidas, D. D., Zographos, S. E., Kristiansen, M., Jessen, C. U., Norskov-Lauritsen, L. & Agius, L. (2006). *J. Med. Chem.* **49**, 5687–5701.
Otwinowski, Z. & Minor, W. (1997). *Methods in Enzymology*, Vol. 276, *Macromolecular Crystallography*, Part A, edited by C. W. Carter Jr & R. M. Sweet, pp. 307–326. New York: Academic Press.
Sher, P. M. & Ellsworth, B. A. (2004). US Patent Application 20 040 142 938.
Skytte, U. P. (2002). *Cereal Foods World*, **47**, 224.
Spek, A. L. (2003). *J. Appl. Cryst.* **36**, 7–13.
Sun, Y. X., Hayakawa, S., Ogawa, M. & Izumori, K. (2007). *Food Contr.* **18**, 220–227.
Watkin, D. J., Prout, C. K. & Pearce, L. J. (1996). *CAMERON*. Chemical Crystallography Laboratory, Oxford, England.