

## 3-C-Methyl-D-allono-1,5-lactone

Nigel A. Jones,<sup>a\*</sup> David J. Watkin,<sup>b</sup> Louise A. Curran,<sup>a</sup> Sarah F. Jenkinson<sup>a</sup> and George W. J. Fleet<sup>a</sup>

<sup>a</sup>Department of Organic Chemistry, Chemistry Research Laboratory, University of Oxford, 12 Mansfield Road, Oxford OX1 3TA, England, and <sup>b</sup>Department of Chemical Crystallography, Chemistry Research Laboratory, University of Oxford, 12 Mansfield Road, Oxford OX1 3TA, England

Correspondence e-mail: nigel.jones@chem.ox.ac.uk

## Key indicators

Single-crystal X-ray study  
 T = 150 K  
 Mean  $\sigma(\text{C}-\text{C}) = 0.003 \text{ \AA}$   
 R factor = 0.031  
 wR factor = 0.075  
 Data-to-parameter ratio = 8.5

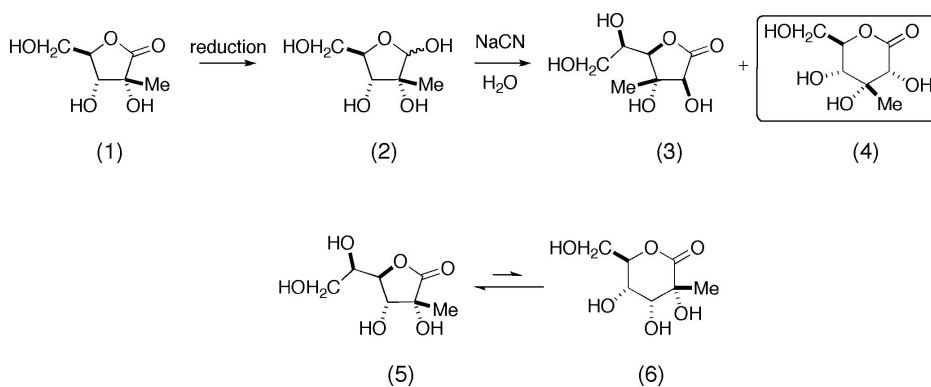
For details of how these key indicators were automatically derived from the article, see <http://journals.iucr.org/e>.

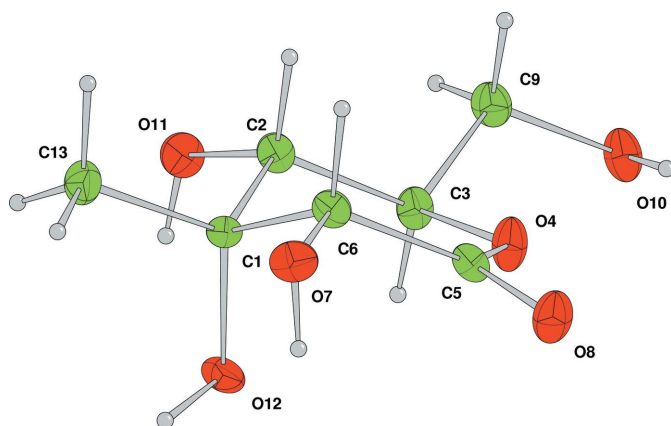
The relative configuration and ring size of the title compound,  $\text{C}_7\text{H}_{12}\text{O}_6$ , were established by X-ray crystallographic analysis. The absolute configuration was determined by the use of 2-C-methyl-D-ribonolactone as a starting material. Almost all unprotected carbohydrate lactones are five-membered ring 1,4-lactones; the title compound provides a very rare example of a stable six-membered ring lactone.

## Comment

Although carbohydrates are the most varied of cheap chiral building blocks (Lichtenthaler & Peters, 2004), only recently have the first examples of branched 2-C-methylpentoses become readily available by treatment of an Amadori ketose with aqueous calcium hydroxide (Hotchkiss *et al.*, 2007). The recognition of the value of a family of 2-C-methylnucleosides in the treatment of hepatitis C has led to current interest in the synthesis of 2-C-carbon-substituted sugars (Sorbera *et al.*, 2006). The Kiliani reaction of ketoses and deoxyketoses with cyanide has provided an environmentally friendly procedure for the generation of a set of carbohydrate scaffolds with a branched carbon substituent at C-2 (Hotchkiss *et al.*, 2004; Soengas *et al.*, 2005). X-ray crystallographic analysis was vital in determining the structures of the products in these reactions (Punzo *et al.*, 2006; Watkin *et al.*, 2005). At present, free sugars and their lactones with a carbon branch at C-3 are essentially unknown. A 3-C-methylpentonolactone of unknown stereochemistry has been isolated from cigarette smoke (Schumacher *et al.*, 1977), 3-C-methyl-D-mannose (Kwon *et al.*, 2004) is one of the components of the trisaccharide repeating unit of the polysaccharide from *Helicobacter pylori* (Kocharova *et al.*, 2000) and 3-C-methyl-L-mannose is one of the sugars in a pentasaccharide hapten of the GPL of *Mycobacterium avium* serovar (Fekete *et al.*, 2006).

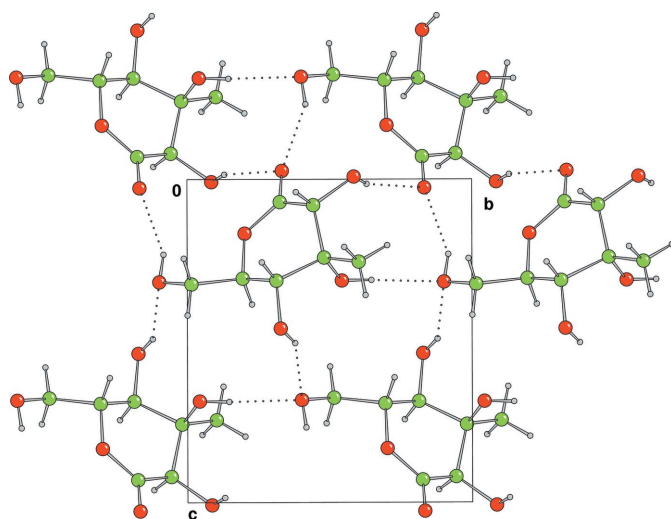
Received 11 January 2007  
 Accepted 18 January 2007





**Figure 1**

The molecular structure of (4), with displacement ellipsoids drawn at the 50% probability level. H atoms are shown as spheres of arbitrary radii.



**Figure 2**

A projection along the *a* axis of part of a hydrogen-bonded sheet of (I). There are no strong interactions between the sheets. Hydrogen bonds are shown as dotted lines.

The value of the Kiliani reaction on 2-*C*-carbon-substituted carbohydrates in the synthesis of 3-*C*-hydroxymethyl branched sugars (Parker *et al.*, 2006; Simone *et al.*, 2007) and 3-*C*-methyl branched sugars (Bream *et al.*, 2006) has been established. Under completely environmentally friendly aqueous conditions, the reaction of cyanide in water with 2-*C*-methyl-*D*-ribose, (2), derived from 2-*C*-methyl-*D*-ribonolactone, (1) (Hotchkiss *et al.*, 2006), gave a major product which crystallized from the reaction mixture. X-ray crystallographic analysis shows (Fig. 1) that the structure is the title compound, (4), removing ambiguities as to the stereochemistry at the new *C*-2 chiral centre and the ring size of the lactone. The minor product is most likely the five-membered ring altrono-lactone, (3). The strain in five-membered ring lactones is generally considerably less than in six-membered ring lactones (Luisa *et al.*, 1990; Brown *et al.*, 1989). Compound (4) is thus a very rare example of the preferential formation of a six-membered ring lactone. Its *C*-2 isomer crystallizes as the 2-*C*-methyl-*D*-allono-

1,4-lactone, (5), rather than the six-membered ring isomer, (6) (Harding *et al.*, 2005). The absolute configuration of compound (4) was determined by the use of the *D*-sugar (1) as the starting material.

The isolated molecule of (4) (Fig. 1) shows no unusual bond lengths or angles, in spite of the strain mentioned above. The largest differences from the *MOGUL* norms (Bruno *et al.*, 2004) are *C*6—*O*7 (00.01 Å; *MOGUL* s.u. 0.02 Å) and *C*3—*C*5—*O*4 (5.0°; *MOGUL* s.u. 2.2°).

The crystal structure of (4) is composed of hydrogen-bonded sheets of molecules lying parallel to the *bc* plane. Both the ketonic atom *O*8 and the hydroxyl atom *O*10 act as acceptors for two hydrogen bonds (Table 1 and Fig. 2).

## Experimental

3-*C*-Methyl-*D*-allono-1,5-lactone, (4), was crystallized from a 3:1:1 mixture of ethyl acetate, methanol and cyclohexane. Analysis: m.p. 421–423 K;  $[\alpha]_{\text{D}}^{23}$  63.5 (*c*, 0.795 in MeOH).

### Crystal data

$\text{C}_7\text{H}_{12}\text{O}_6$	$Z = 2$
$M_r = 192.17$	$D_x = 1.551 \text{ Mg m}^{-3}$
Monoclinic, $P2_1$	Mo $K\alpha$ radiation
$a = 5.6603(2) \text{ \AA}$	$\mu = 0.14 \text{ mm}^{-1}$
$b = 8.0045(2) \text{ \AA}$	$T = 150 \text{ K}$
$c = 9.3242(3) \text{ \AA}$	Needle, colourless
$\beta = 103.1470(13)^\circ$	$0.20 \times 0.05 \times 0.05 \text{ mm}$
$V = 411.39(2) \text{ \AA}^3$	

### Data collection

Nonius KappaCCD area-detector diffractometer	5511 measured reflections
$\omega$ scans	1000 independent reflections
Absorption correction: multi-scan ( <i>DENZO</i> and <i>SCALEPACK</i> ; Otwinowski & Minor, 1997)	930 reflections with $I > 2\sigma(I)$
$T_{\text{min}} = 0.75$ , $T_{\text{max}} = 1.0$	$R_{\text{int}} = 0.050$
	$\theta_{\text{max}} = 27.4^\circ$

### Refinement

Refinement on $F^2$	$w = 1/[\sigma^2(F^2) + (0.02P)^2 + 0.12P]$
$R[F^2 > 2\sigma(F^2)] = 0.031$	where $P = [\max(F_o^2, 0) + 2F_c^2]/3$
$wR(F^2) = 0.076$	$(\Delta/\sigma)_{\text{max}} < 0.001$
$S = 1.16$	$\Delta\rho_{\text{max}} = 0.29 \text{ e \AA}^{-3}$
1000 reflections	$\Delta\rho_{\text{min}} = -0.26 \text{ e \AA}^{-3}$
118 parameters	
H-atom parameters constrained	

**Table 1**

Hydrogen-bond geometry (Å, °).

<i>D</i> — <i>H</i> ... <i>A</i>	<i>D</i> — <i>H</i>	<i>H</i> ... <i>A</i>	<i>D</i> ... <i>A</i>	<i>D</i> — <i>H</i> ... <i>A</i>
<i>O</i> 10— <i>H</i> 7... <i>O</i> 8 <sup>i</sup>	0.84	2.08	2.856 (2)	153
<i>O</i> 7— <i>H</i> 8... <i>O</i> 8 <sup>ii</sup>	0.85	2.06	2.832 (2)	152
<i>O</i> 11— <i>H</i> 12... <i>O</i> 10 <sup>iii</sup>	0.82	2.09	2.836 (2)	152
<i>O</i> 12— <i>H</i> 3... <i>O</i> 10 <sup>iv</sup>	0.83	2.07	2.901 (2)	173

Symmetry codes: (i)  $-x + 2, y - \frac{1}{2}, -z$ ; (ii)  $-x + 2, y + \frac{1}{2}, -z$ ; (iii)  $-x + 2, y + \frac{1}{2}, -z + 1$ ; (iv)  $x, y + 1, z$ .

In the absence of significant anomalous scattering, Friedel pairs were merged and the absolute configuration assigned from the starting material.

The relatively large ratio of minimum to maximum corrections applied in the multiscan process (1:1.33) reflects changes in the illuminated volume of the very thin needle-like crystal. These changes were kept to a minimum and were taken into account (Görbitz, 1999) by multiscan interframe scaling (*DENZO* and *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, with C–H in the range 0.93–0.98 Å and O–H = 0.82 Å, and with  $U_{\text{iso}}(\text{H}) = 1.2\text{--}1.5U_{\text{eq}}(\text{parent atom})$ , after which the positions were refined with riding constraints.

Data collection: *COLLECT* (Nonius, 1997–2001); cell refinement: *DENZO* and *SCALEPACK* (Otwinowski & Minor, 1997); data reduction: *DENZO* and *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*.

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

## References

- Altomare, A., Casciarano, G., Giacovazzo, C., 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.
- Bream, R., Watkin, D., Soengas, R., Eastwick-Field, V. & Fleet, G. W. J. (2006). *Acta Cryst.* **E62**, o977–o979.
- Brown, J. M., Conn, A. D., Pilcher, G., Leitao, M. L. P. & Yang, M. Y. (1989). *J. Chem. Soc. Chem. Commun.* pp. 1817–1819.
- Bruno, I. J., Cole, J. C., Kessler, M., Luo, J., Motherwell, W. D. S., Purkis, L. H., Smith, B. R., Taylor, R., Cooper, R. I., Harris, S. E. & Orpen, A. G. (2004). *J. Chem. Inf. Comput. Sci.* **44**, 2133–2144.
- Fekete, A., Gyergyoi, K., Kover, K. E., Bajza, I. & Liptak, A. (2006). *Carbohydr. Res.* **341**, 1312–1321.
- Görbitz, C. H. (1999). *Acta Cryst.* **B55**, 1090–1098.
- Harding, C. C., Watkin, D. J., Sawyer, N. K., Jenkinson, S. F. & Fleet, G. W. J. (2005). *Acta Cryst.* **E61**, o1472–o1474.
- Hotchkiss, D. J., Jenkinson, S. F., Storer, R., Heinz, T. & Fleet, G. W. J. (2006). *Tetrahedron Lett.* **47**, 315–318.
- Hotchkiss, D. J., Soengas, R., Booth, K. V., Weymouth-Wilson, A. C., Eastwick-Field, V. & Fleet, G. W. J. (2007). *Tetrahedron Lett.* **48**, 517–520.
- Hotchkiss, D. J., Soengas, R., Simone, M. I., van Ameijde, J., Hunter, S., Cowley, A. R. & Fleet, G. W. J. (2004). *Tetrahedron Lett.* **45**, 9461–9464.
- Kocharova, N. A., Knirel, Y. A., Widmalm, G., Jansson, P. E. & Moran, A. P. (2000). *Biochemistry*, **39**, 4755–4760.
- Kwon, Y. T., Lee, Y. J., Lee, K. & Kim, K. S. (2004). *Org. Lett.* **6**, 3901–3904.
- Lichtenthaler, F. W. & Peters, S. (2004). *C. R. Chim.* **7**, 65–90.
- Luisa, M., Pilcher, G., Yang, M. Y., Brown, J. M. & Conn, A. D. (1990). *J. Chem. Thermodyn.* **22**, 885–891.
- Nonius (1997–2001). *COLLECT*. Nonius BV, Delft, The Netherlands.
- 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.
- Parker, S. G., Watkin, D. J., Simone, M. I. & Fleet, G. W. J. (2006). *Acta Cryst.* **E62**, o3961–o3963.
- Punzo, F., Watkin, D. J., Hotchkiss, D. & Fleet, G. W. J. (2006). *Acta Cryst.* **E62**, o98–o100.
- Schumacher, J. N., Green, C. R., Best, F. W. & Newell, M. P. (1977). *J. Agric. Food Chem.* **25**, 310–320.
- Simone, M. I., Fleet, G. W. J. & Watkin, D. J. (2007). *Acta Cryst.* **E63**, o799–o801.
- Soengas, R., Izumori, K., Simone, M. I., Watkin, D. J., Skytte, U. P., Soetaert, W. & Fleet, G. W. J. (2005). *Tetrahedron Lett.* **46**, 5755–5759.
- Sorbera, L. A., Castaner, J. & Leeson, P. A. (2006). *Drugs Future* **31**, 320–324.
- Watkin, D. J., Parry, L. L., Hotchkiss, D. J., Eastwick-Field, V. & Fleet, G. W. J. (2005). *Acta Cryst.* **E61**, o3302–o3303.
- Watkin, D. J., Prout, C. K. & Pearce, L. J. (1996). *CAMERON*. Chemical Crystallography Laboratory, University of Oxford, England.

## supporting information

*Acta Cryst.* (2007). E63, o992–o994 [https://doi.org/10.1107/S1600536807002899]

## 3-C-Methyl-D-allono-1,5-lactone

Nigel A. Jones, David J. Watkin, Louise A. Curran, Sarah F. Jenkinson and George W. J. Fleet

## 3-C-Methyl-D-allono-1,5-lactone

*Crystal data*

$C_7H_{12}O_6$   
 $M_r = 192.17$   
 Monoclinic,  $P2_1$   
 Hall symbol: P 2y b  
 $a = 5.6603$  (2) Å  
 $b = 8.0045$  (2) Å  
 $c = 9.3242$  (3) Å  
 $\beta = 103.1470$  (13)°  
 $V = 411.39$  (2) Å<sup>3</sup>  
 $Z = 2$

$F(000) = 204$   
 $D_x = 1.551$  Mg m<sup>-3</sup>  
 Mo  $K\alpha$  radiation,  $\lambda = 0.71073$  Å  
 Cell parameters from 976 reflections  
 $\theta = 5$ – $27^\circ$   
 $\mu = 0.14$  mm<sup>-1</sup>  
 $T = 150$  K  
 Plate, colourless  
 $0.20 \times 0.05 \times 0.05$  mm

*Data collection*

Nonius KappaCCD area-detector  
 diffractometer  
 Graphite monochromator  
 $\omega$  scans  
 Absorption correction: multi-scan  
 (DENZO and SCALEPACK; Otwinowski &  
 Minor, 1997)  
 $T_{\min} = 0.75$ ,  $T_{\max} = 1.0$

5511 measured reflections  
 1000 independent reflections  
 930 reflections with  $I > 2\sigma(I)$   
 $R_{\text{int}} = 0.050$   
 $\theta_{\max} = 27.4^\circ$ ,  $\theta_{\min} = 5.1^\circ$   
 $h = -7 \rightarrow 7$   
 $k = -10 \rightarrow 10$   
 $l = -12 \rightarrow 12$

*Refinement*

Refinement on  $F^2$   
 Least-squares matrix: full  
 $R[F^2 > 2\sigma(F^2)] = 0.031$   
 $wR(F^2) = 0.076$   
 $S = 1.16$   
 1000 reflections  
 118 parameters  
 1 restraint

Primary atom site location: structure-invariant  
 direct methods  
 Hydrogen site location: inferred from  
 neighbouring sites  
 H-atom parameters constrained  
 $w = 1/[\sigma^2(F^2) + (0.02P)^2 + 0.12P]$   
 where  $P = [\max(F_o^2, 0) + 2F_c^2]/3$   
 $(\Delta/\sigma)_{\max} = 0.000084$   
 $\Delta\rho_{\max} = 0.29$  e Å<sup>-3</sup>  
 $\Delta\rho_{\min} = -0.26$  e Å<sup>-3</sup>

*Fractional atomic coordinates and isotropic or equivalent isotropic displacement parameters (Å<sup>2</sup>)*

	<i>x</i>	<i>y</i>	<i>z</i>	$U_{\text{iso}}^*/U_{\text{eq}}$
C1	0.6617 (4)	0.4808 (3)	0.2422 (2)	0.0134
C2	0.6307 (4)	0.3130 (3)	0.3137 (2)	0.0144
C3	0.8396 (4)	0.1948 (3)	0.3069 (2)	0.0144
O4	0.9188 (3)	0.2017 (2)	0.16759 (17)	0.0190

C5	0.8645 (4)	0.3256 (3)	0.0704 (2)	0.0144
C6	0.6588 (4)	0.4432 (3)	0.0802 (2)	0.0139
O7	0.6577 (3)	0.5857 (2)	−0.00803 (17)	0.0179
O8	0.9762 (3)	0.3333 (2)	−0.02633 (17)	0.0206
C9	0.7731 (4)	0.0148 (3)	0.3243 (3)	0.0177
O10	0.9679 (3)	−0.0981 (2)	0.31742 (18)	0.0192
O11	0.6110 (3)	0.3279 (2)	0.46166 (17)	0.0194
O12	0.8962 (3)	0.5429 (2)	0.31334 (18)	0.0169
C13	0.4618 (4)	0.6024 (3)	0.2552 (3)	0.0182
H21	0.4822	0.2623	0.2567	0.0171*
H31	0.9819	0.2273	0.3868	0.0172*
H61	0.5078	0.3822	0.0397	0.0173*
H91	0.7331	0.0010	0.4205	0.0226*
H92	0.6307	−0.0120	0.2449	0.0220*
H131	0.4845	0.7025	0.2044	0.0266*
H132	0.4745	0.6262	0.3588	0.0270*
H133	0.3052	0.5519	0.2097	0.0273*
H7	0.9904	−0.0831	0.2322	0.0289*
H8	0.7965	0.6309	0.0147	0.0280*
H12	0.7302	0.3786	0.5065	0.0306*
H3	0.9046	0.6468	0.3116	0.0251*

*Atomic displacement parameters (Å<sup>2</sup>)*

	$U^{11}$	$U^{22}$	$U^{33}$	$U^{12}$	$U^{13}$	$U^{23}$
C1	0.0109 (10)	0.0127 (12)	0.0165 (10)	−0.0016 (9)	0.0027 (8)	−0.0021 (9)
C2	0.0183 (11)	0.0133 (12)	0.0128 (10)	−0.0013 (10)	0.0060 (8)	0.0008 (11)
C3	0.0192 (11)	0.0143 (13)	0.0113 (10)	0.0001 (10)	0.0071 (8)	0.0015 (10)
O4	0.0272 (9)	0.0143 (9)	0.0187 (8)	0.0060 (8)	0.0120 (6)	0.0038 (8)
C5	0.0178 (11)	0.0119 (12)	0.0134 (10)	−0.0017 (10)	0.0031 (8)	−0.0016 (10)
C6	0.0161 (10)	0.0110 (12)	0.0145 (10)	−0.0006 (9)	0.0037 (8)	0.0023 (10)
O7	0.0180 (8)	0.0153 (9)	0.0201 (8)	−0.0007 (7)	0.0034 (6)	0.0066 (7)
O8	0.0257 (9)	0.0199 (10)	0.0199 (9)	0.0030 (8)	0.0127 (7)	0.0022 (8)
C9	0.0210 (12)	0.0134 (13)	0.0190 (11)	0.0010 (10)	0.0054 (10)	0.0014 (10)
O10	0.0285 (10)	0.0130 (9)	0.0170 (8)	0.0045 (8)	0.0068 (7)	0.0022 (7)
O11	0.0235 (9)	0.0215 (10)	0.0154 (7)	−0.0034 (8)	0.0092 (6)	−0.0007 (8)
O12	0.0170 (8)	0.0113 (9)	0.0208 (9)	−0.0030 (7)	0.0012 (7)	−0.0006 (7)
C13	0.0188 (12)	0.0145 (12)	0.0224 (11)	0.0021 (10)	0.0070 (9)	−0.0007 (11)

*Geometric parameters (Å, °)*

C1—C2	1.527 (3)	C6—O7	1.405 (3)
C1—C6	1.536 (3)	C6—H61	0.982
C1—O12	1.431 (3)	O7—H8	0.847
C1—C13	1.518 (3)	C9—O10	1.439 (3)
C2—C3	1.527 (3)	C9—H91	0.980
C2—O11	1.415 (3)	C9—H92	0.987
C2—H21	0.975	O10—H7	0.842

C3—O4	1.469 (3)	O11—H12	0.816
C3—C9	1.507 (3)	O12—H3	0.833
C3—H31	0.999	C13—H131	0.954
O4—C5	1.332 (3)	C13—H132	0.972
C5—C6	1.516 (3)	C13—H133	0.979
C5—O8	1.215 (3)		
C2—C1—C6	106.28 (19)	C1—C6—C5	110.15 (18)
C2—C1—O12	106.85 (19)	C1—C6—O7	114.48 (19)
C6—C1—O12	108.97 (17)	C5—C6—O7	111.67 (17)
C2—C1—C13	111.55 (18)	C1—C6—H61	106.8
C6—C1—C13	111.25 (18)	C5—C6—H61	106.3
O12—C1—C13	111.7 (2)	O7—C6—H61	106.9
C1—C2—C3	111.12 (18)	C6—O7—H8	108.7
C1—C2—O11	113.2 (2)	C3—C9—O10	112.54 (19)
C3—C2—O11	109.01 (18)	C3—C9—H91	108.8
C1—C2—H21	107.4	O10—C9—H91	108.0
C3—C2—H21	107.4	C3—C9—H92	108.0
O11—C2—H21	108.5	O10—C9—H92	109.5
C2—C3—O4	114.06 (18)	H91—C9—H92	110.1
C2—C3—C9	111.93 (18)	C9—O10—H7	103.6
O4—C3—C9	105.38 (18)	C2—O11—H12	107.6
C2—C3—H31	108.0	C1—O12—H3	112.9
O4—C3—H31	107.0	C1—C13—H131	108.2
C9—C3—H31	110.3	C1—C13—H132	108.5
C3—O4—C5	124.10 (18)	H131—C13—H132	109.9
O4—C5—C6	118.87 (18)	C1—C13—H133	108.6
O4—C5—O8	117.6 (2)	H131—C13—H133	110.0
C6—C5—O8	123.4 (2)	H132—C13—H133	111.5

*Hydrogen-bond geometry (Å, °)*

<i>D</i> —H $\cdots$ <i>A</i>	<i>D</i> —H	H $\cdots$ <i>A</i>	<i>D</i> $\cdots$ <i>A</i>	<i>D</i> —H $\cdots$ <i>A</i>
O10—H7 $\cdots$ O8 <sup>i</sup>	0.84	2.08	2.856 (2)	153
O7—H8 $\cdots$ O8 <sup>ii</sup>	0.85	2.06	2.832 (2)	152
O11—H12 $\cdots$ O10 <sup>iii</sup>	0.82	2.09	2.836 (2)	152
O12—H3 $\cdots$ O10 <sup>iv</sup>	0.83	2.07	2.901 (2)	173

Symmetry codes: (i)  $-x+2, y-1/2, -z$ ; (ii)  $-x+2, y+1/2, -z$ ; (iii)  $-x+2, y+1/2, -z+1$ ; (iv)  $x, y+1, z$ .