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(±)-2,2-Dimethyl-5-oxotetrahydrofuran-3-carboxylic acid (terebic acid): a racemic layered structure

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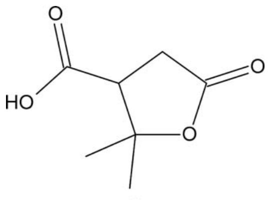
A racemic crystalline form of terebic acid, $C_7H_{10}O_4$, which is an important industrial chemical compound, is reported for the first time. The crystal structure is stabilized by O—H···O and C—H···O hydrogen bonds which form racemic double layers parallel to (001).

Comment

Terebic acid, (I), belongs to the γ-lactone family (five-membered cyclic esters). Lactones are generally formed by an intramolecular dehydration reaction (cyclocondensation) of hydroxy acid or by an intermolecular dehydration followed by a cyclization involving an alcohol and a carboxylic acid (Yoshida *et al.*, 2011; Eckert *et al.*, 2011).



(I)

Terebic acid and its derivatives have been reported as having anti-inflammatory, antibiotic (Fisnerova *et al.*, 1982), antithrombotic (Franciskovich *et al.*, 2006) and antitumor (Gielen *et al.*, 1998) properties. Derivatives of (I) are also present in pharmaceutical formulations with dermatological (Malle, 2009) and capillary (Kang & Lim, 2004) applications, and have been shown to be useful as a prophylactic agent for physiological disorders (Ikeura *et al.*, 2009). Although the first synthesis of terebic acid dates from the end of the 19th century and the compound is industrially important, its crystal structure remains unknown. In the present study, the first racemic crystalline form of (I) (Fig. 1) is reported.

The intramolecular geometry of (I) was analyzed using *Mogul* (Bruno *et al.*, 2004), a knowledge base of molecular geometry derived from the Cambridge Structural Database (CSD; Version 5.33 of November 2011, with January 2012 and May 2012 updates; Allen, 2002). This study shows that all bond lengths and bond angles are in agreement with the values expected for a good X-ray diffraction structure refinement. As expected in the case of γ-lactones, differences in the two C—O3 bond distances are observed; the O3—C4 bond [1.4718 (16) Å; *Mogul* average = 1.48 (2) Å] is longer than the O3—C3 bond [1.3262 (17) Å; *Mogul* average = 1.35 (2) Å].

In (I), the lactone ring adopts an envelope conformation with atom C1 at the flap position. The puckering parameters of Cremer & Pople (1975) [q_2 = 0.282 (2) Å and φ_2 = 114.0 (3)°] confirm the envelope on C1 for the five-membered ring. Atoms O1 and C1 deviate by −0.076 (6) and 0.446 (2) Å, respectively, from the least-squares plane through the C2—C3—O3—C4 moiety [r.m.s. deviation = 0.0153 Å and largest deviation = 0.019 (1) Å for atom O3]. This plane forms an angle of 28.1 (1)° with that through the C2—C1—C4 moiety. An intramolecular nonclassical hydrogen bond is observed, in which C2 acts as hydrogen-bond donor to the carboxyl O4 atom. The hydrogen-bond geometry is given in Table 1.

The supramolecular analysis of (I) shows that there are O—H···O and C—H···O hydrogen bonds involving the ketone and carboxyl groups and the lactone ring, contributing to the stabilization of the crystal packing (Figs. 2 and 3, Table 1). In the solid state, carboxylic acids generally form supramolecular dimers with $R_2^2(8)$ assemblies [see Bernstein *et al.* (1995) for the nomenclature of hydrogen-bond motifs], as observed, for example, for the three polymorphs of 4-(dimethylamino)-benzoic acid (Aakeröy *et al.*, 2005). However, when there are other hydrogen-bond donating or accepting functional group(s) in the same molecule, the occurrence of the carboxylic dimer motif is less frequent (Beyer & Price, 2000), as observed for (I). The strongest intermolecular force is a

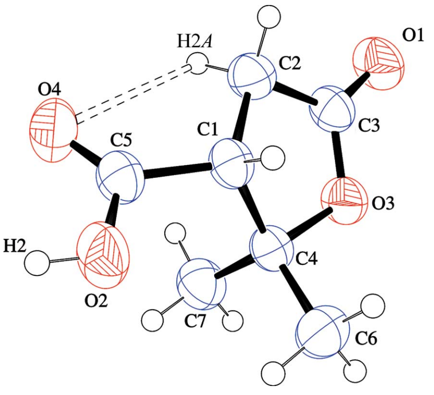


Figure 1
The molecular structure of (I) (*R* enantiomer), showing the atom-numbering scheme. Displacement ellipsoids are drawn at the 50% probability level and H atoms are shown as small spheres of arbitrary radii. The intramolecular interaction is shown as a dashed line.

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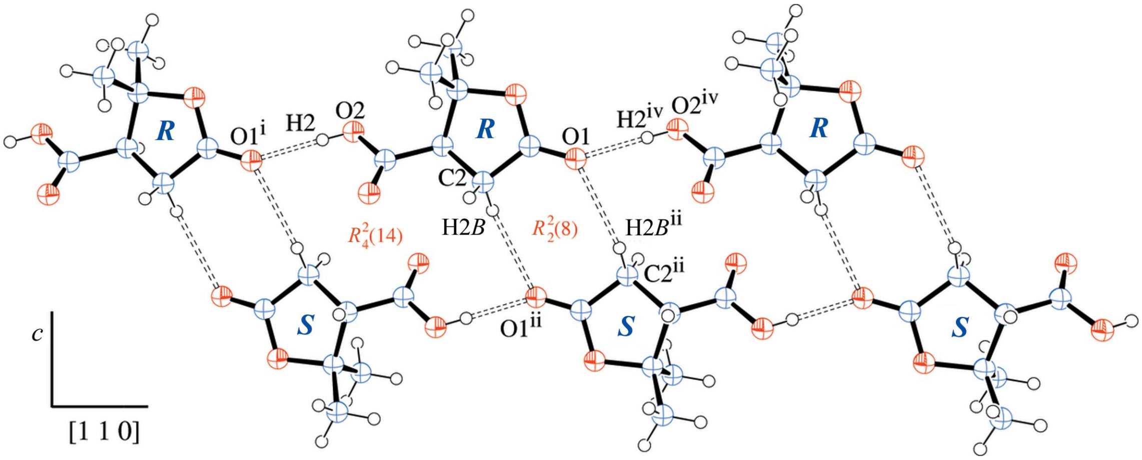

Figure 2
A partial packing diagram for (I), showing the racemic double chain formed along [110]. The *R* and *S* enantiomers are identified. Hydrogen bonds are shown as dashed lines. [Symmetry codes: (i) $x - 1, y - 1, z$; (ii) $-x + 1, -y + 2, -z$; (iv) $x + 1, y + 1, z$.]

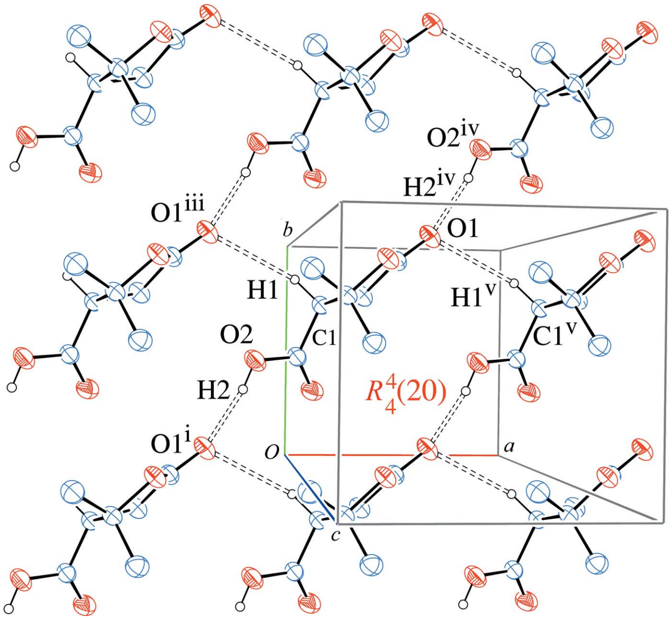

Figure 3
A section of the supramolecular two-dimensional assembly of (I) (*R* enantiomer), projected onto (201). The chain propagation along [$\bar{1}$10] is evident. Hydrogen bonds are shown as dashed lines. Displacement ellipsoids are drawn at the 30% probability level. [Symmetry codes: (i) $x - 1, y - 1, z$; (iii) $x - 1, y, z$; (iv) $x + 1, y + 1, z$; (v) $x + 1, y, z$.]

classical hydrogen bond having the carboxyl O2 atom as hydrogen-bond donor to the ketone $O1^i$ atom [symmetry code: (i) $x - 1, y - 1, z$], giving rise to a translation-related single-enantiomer chain running along the [110] direction, as shown in Fig. 2. An extended racemic double chain is formed in the same direction since a nonclassical hydrogen bond gives rise to a related centrosymmetric dimer with the $R_2^2(8)$ motif having C2 as the hydrogen-bond donor to the ketone $O1^{ii}$ atom [symmetry code: (ii) $-x + 1, -y + 2, -z$]. The aggregation in [110] includes $R_4^2(14)$ and $R_2^2(8)$ assemblies (Fig. 2). Each chain shown in Fig. 2 is itself connected along the [$\bar{1}$10] direction by weak intermolecular interactions involving the H atoms of the asymmetric C atom and the O atoms of an adjacent lactone carbonyl group, $C1—H1\cdots O1^{iii}$ [symmetry code: (iii) $x - 1, y, z$], which contribute to an $R_4^4(20)$ assembly (Fig. 3). The chains which form the layers are separated by 3.908 Å, considering a least-squares plane through the adjacent lactone rings. Fig. 3 shows the layer formed by the *R* enantiomers, which contains translation-related molecules along the *a* and *b* axes relative to the asymmetric unit. Finally, a racemic double layer parallel to (001) is completed by a layer consisting of the *S* enantiomer at ($-x, -y, -z$) and its translations along the *a* and *b* axes. Because of the space-group symmetry, another racemic double layer also occurs at the middle of the *c* axis defined by translation along the *a* and *b* axes of molecules generated by the 2_1 screw axis and the *c*-glide plane (Fig. 4). The difference is that chains grow along [$\bar{1}$10] and they are themselves stacked along [110]. Considering the three intermolecular hydrogen bonds, it is noted that atom O1 acts as a trifurcated hydrogen-bond acceptor (Figs. 2 and 3).

Experimental

Commercial racemic terebic acid (Sigma–Aldrich) was used. Colorless prismatic crystals of (I) were obtained from an isopropyl alcohol solution by slow evaporation at room temperature.

Crystal data

$C_7H_{10}O_4$
$M_r = 158.15$
Monoclinic, $P2_1/c$
$a = 5.989$ (1) Å
$b = 5.663$ (1) Å
$c = 22.282$ (1) Å
$\beta = 97.07$ (1)°
$V = 750.0$ (2) Å^3
$Z = 4$
Mo $K\alpha$ radiation
$\mu = 0.12$ mm^{-1}
$T = 293$ K
0.09 × 0.06 × 0.03 mm

Data collection

Nonius KappaCCD diffractometer
2864 measured reflections
1516 independent reflections
1130 reflections with $I > 2\sigma(I)$
$R_{\rm int} = 0.034$

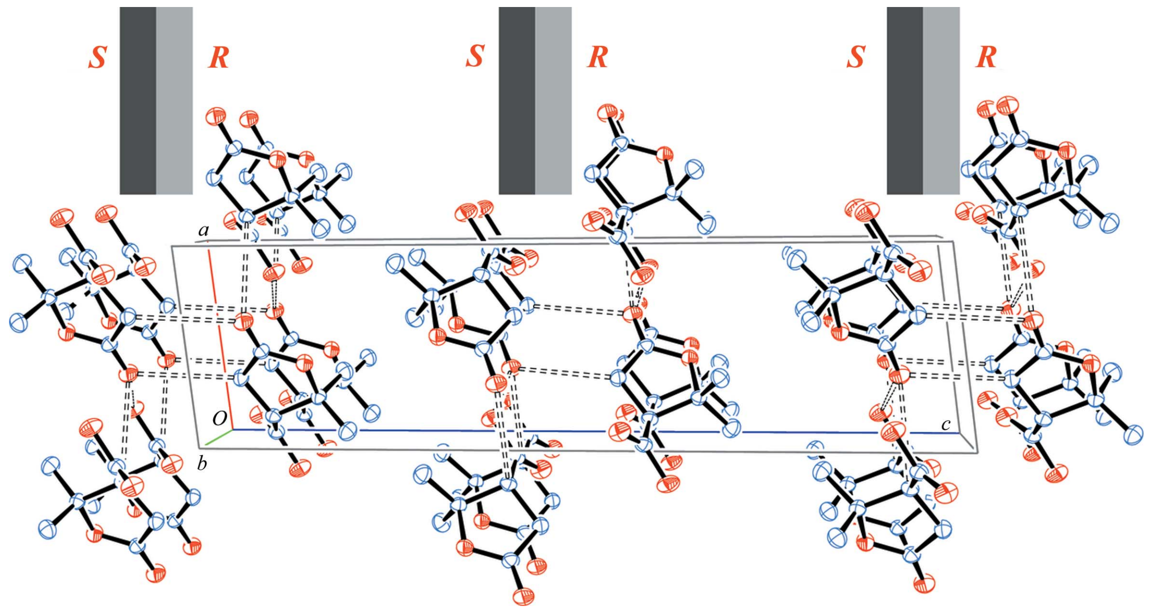

Figure 4
The packing of (I), projected onto (101). Ribbons in dark and light gray representing, respectively, the layers formed by the *S* and *R* enantiomers of (I) are included. Hydrogen bonds are shown as dashed lines. Displacement ellipsoids are drawn at the 30% probability level.

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

$D-H\cdots A$	$D-H$	$H\cdots A$	$D\cdots A$	$D-H\cdots A$
$C2-H2A\cdots O4$	0.97	2.51	2.863 (2)	101
$O2-H2\cdots O1^{i}$	0.91 (2)	1.77 (2)	2.673 (2)	174 (2)
$C2-H2B\cdots O1^{ii}$	0.97	2.51	3.373 (2)	149
$C1-H1\cdots O1^{iii}$	0.98	2.64	3.557 (2)	156

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

Refinement

$R[F^2 > 2\sigma(F^2)] = 0.042$
$wR(F^2) = 0.115$
$S = 1.04$
1516 reflections
105 parameters
H atoms treated by a mixture of independent and constrained refinement
$\Delta\rho_{max} = 0.17$ e Å^{-3}
$\Delta\rho_{min} = -0.13$ e Å^{-3}

H atoms on C atoms were positioned stereochemically and were refined with fixed individual displacement parameters [$U_{iso}(H) = 1.5U_{eq}(C)$ for methyl groups or $1.2U_{eq}(C)$ for methine and methylene groups], using a riding model and rotating group model (for methyl groups), with C—H bond lengths of 0.96, 0.97 and 0.98 Å for methyl, methine and methylene groups, respectively. The hydroxy H atom was located by difference Fourier synthesis and was refined with free coordinates and $U_{iso}(H) = 1.5U_{eq}(O)$.

Data collection: *COLLECT* (Nonius, 1999); cell refinement: *SCALEPACK* (Otwinowski & Minor, 1997); data reduction: *DENZO* (Otwinowski & Minor, 1997) and *SCALEPACK*; program(s) used to solve structure: *SHELXS97* (Sheldrick, 2008); program(s) used to refine structure: *SHELXL97* (Sheldrick, 2008); molecular graphics: *ORTEP-3 for Windows* (Farrugia, 1997) and *Mercury* (Macrae *et al.*, 2006); software used to prepare material for publication: *WinGX* (Farrugia, 1999) and *publCIF* (Westrip, 2010).

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Supplementary data for this paper are available from the IUCr electronic archives (Reference: UK3046). Services for accessing these data are described at the back of the journal.

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supplementary materials

Acta Cryst. (2012). C**68**, o294–o297   [doi:10.1107/S0108270112029563]

(±)-2,2-Dimethyl-5-oxotetrahydrofuran-3-carboxylic acid (terebic acid): a racemic layered structure

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Crystal data

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$b = 5.663$ (1) Å
$c = 22.282$ (1) Å
$\beta = 97.07$ (1)°
$V = 750.0$ (2) Å^3
$Z = 4$
$F(000) = 336$
$D_x = 1.401$ Mg m^{-3}
Mo $K\alpha$ radiation, $\lambda = 0.71073$ Å
Cell parameters from 2814 reflections
$\theta = 2.9$–25.7°
$\mu = 0.12$ mm^{-1}
$T = 293$ K
Prism, colourless
0.09 × 0.06 × 0.03 mm

Data collection

KappaCCD diffractometer
Graphite monochromator
Detector resolution: 9 pixels mm^{-1}
CCD scans
2864 measured reflections
1516 independent reflections
1130 reflections with $I > 2\sigma(I)$
$R_{\rm int} = 0.034$
$\theta_{\rm max} = 26.4°$, $\theta_{\rm min} = 3.4°$
$h = -7\rightarrow7$
$k = -7\rightarrow6$
$l = -27\rightarrow27$

Refinement

Refinement on F^2
Least-squares matrix: full
$R[F^2 > 2\sigma(F^2)] = 0.042$
$wR(F^2) = 0.115$
$S = 1.04$
1516 reflections
105 parameters
0 restraints
Primary atom site location: structure-invariant direct methods
Secondary atom site location: difference Fourier map
Hydrogen site location: inferred from neighbouring sites
H atoms treated by a mixture of independent and constrained refinement
$w = 1/[\sigma^2(F_o^2) + (0.061P)^2 + 0.0594P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{\rm max} < 0.001$
$\Delta\rho_{\rm max} = 0.17$ e Å^{-3}
$\Delta\rho_{\rm min} = -0.13$ e Å^{-3}

Special details

Geometry. All s.u.'s (except the s.u. in the dihedral angle between two l.s. planes) are estimated using the full covariance matrix. The cell s.u.'s are taken into account individually in the estimation of s.u.'s in distances, angles and torsion angles; correlations between s.u.'s in cell parameters are only used when they are defined by crystal symmetry. An approximate (isotropic) treatment of cell s.u.'s is used for estimating s.u.'s involving l.s. planes.

Refinement. Refinement of F^2 against ALL reflections. The weighted R-factor wR and goodness of fit S are based on F^2, conventional R-factors R are based on F, with F set to zero for negative F^2. The threshold expression of $F^2 > \sigma(F^2)$ is used only for calculating R-factors(gt) *etc*. and is not relevant to the choice of reflections for refinement. R-factors based on F^2 are statistically about twice as large as those based on F, and R- factors based on ALL data will be even larger.

Fractional atomic coordinates and isotropic or equivalent isotropic displacement parameters (Å²)

	x	y	z	$U_{\rm iso}$*/$U_{\rm eq}$
C1	0.1384 (2)	0.7159 (2)	0.09276 (6)	0.0421 (4)
H1	0.0216	0.8344	0.0813	0.051*
C2	0.3341 (2)	0.7630 (3)	0.05786 (6)	0.0497 (4)
H2A	0.4144	0.6183	0.0514	0.06*
H2B	0.2838	0.8347	0.019	0.06*
C3	0.4780 (2)	0.9284 (3)	0.09742 (7)	0.0461 (4)
C4	0.2389 (2)	0.7599 (2)	0.15913 (6)	0.0435 (4)
C5	0.0359 (2)	0.4746 (3)	0.08306 (7)	0.0459 (4)
C6	0.0779 (3)	0.8764 (3)	0.19646 (7)	0.0587 (5)
H6A	0.0288	1.0241	0.1782	0.088*
H6B	0.1519	0.9041	0.2366	0.088*
H6C	−0.0498	0.7755	0.1984	0.088*
C7	0.3506 (3)	0.5455 (3)	0.19020 (7)	0.0566 (4)
H7A	0.4523	0.477	0.165	0.085*
H7B	0.2379	0.4317	0.1972	0.085*
H7C	0.4325	0.5918	0.2281	0.085*
O1	0.63122 (18)	1.0478 (2)	0.08425 (5)	0.0612 (4)
O2	−0.15315 (18)	0.4562 (2)	0.10829 (6)	0.0639 (4)
H2	−0.219 (3)	0.308 (4)	0.0998 (9)	0.096*
O3	0.41873 (16)	0.93195 (19)	0.15283 (4)	0.0507 (3)
O4	0.11153 (18)	0.3154 (2)	0.05664 (5)	0.0626 (4)

Atomic displacement parameters (Å²)

	U^{11}	U^{22}	U^{33}	U^{12}	U^{13}	U^{23}
C1	0.0389 (7)	0.0393 (8)	0.0478 (8)	−0.0059 (6)	0.0032 (6)	0.0004 (6)
C2	0.0526 (9)	0.0519 (10)	0.0453 (8)	−0.0129 (7)	0.0087 (6)	−0.0011 (7)
C3	0.0426 (8)	0.0454 (9)	0.0503 (9)	−0.0076 (7)	0.0063 (6)	0.0033 (7)
C4	0.0445 (8)	0.0411 (9)	0.0455 (8)	−0.0082 (6)	0.0082 (6)	0.0000 (6)
C5	0.0423 (8)	0.0443 (9)	0.0505 (8)	−0.0057 (7)	0.0029 (6)	0.0007 (7)
C6	0.0634 (10)	0.0574 (10)	0.0574 (9)	−0.0036 (8)	0.0162 (8)	−0.0086 (8)
C7	0.0612 (10)	0.0534 (10)	0.0538 (9)	−0.0022 (8)	0.0013 (7)	0.0054 (8)
O1	0.0539 (6)	0.0612 (8)	0.0691 (8)	−0.0224 (6)	0.0104 (5)	0.0028 (6)
O2	0.0529 (7)	0.0536 (7)	0.0888 (9)	−0.0180 (6)	0.0231 (6)	−0.0115 (6)
O3	0.0526 (6)	0.0502 (7)	0.0488 (6)	−0.0173 (5)	0.0043 (4)	−0.0033 (5)
O4	0.0618 (7)	0.0473 (7)	0.0804 (8)	−0.0077 (6)	0.0154 (6)	−0.0135 (6)

Geometric parameters (Å, º)

C1—C5	1.503 (2)	C4—C7	1.512 (2)
C1—C2	1.5080 (19)	C5—O4	1.1958 (18)
C1—C4	1.5468 (19)	C5—O2	1.3285 (18)
C1—H1	0.98	C6—H6A	0.96
C2—C3	1.487 (2)	C6—H6B	0.96
C2—H2A	0.97	C6—H6C	0.96
C2—H2B	0.97	C7—H7A	0.96
C3—O1	1.2049 (17)	C7—H7B	0.96
C3—O3	1.3262 (17)	C7—H7C	0.96
C4—O3	1.4718 (16)	O2—H2	0.94 (2)
C4—C6	1.501 (2)		

C5—C1—C2	114.61 (12)	C6—C4—C1	113.54 (12)
C5—C1—C4	112.84 (11)	C7—C4—C1	114.00 (12)
C2—C1—C4	103.22 (11)	O4—C5—O2	122.91 (14)
C5—C1—H1	108.6	O4—C5—C1	125.68 (14)
C2—C1—H1	108.6	O2—C5—C1	111.40 (13)
C4—C1—H1	108.6	C4—C6—H6A	109.5
C3—C2—C1	103.68 (12)	C4—C6—H6B	109.5
C3—C2—H2A	111	H6A—C6—H6B	109.5
C1—C2—H2A	111	C4—C6—H6C	109.5
C3—C2—H2B	111	H6A—C6—H6C	109.5
C1—C2—H2B	111	H6B—C6—H6C	109.5
H2A—C2—H2B	109	C4—C7—H7A	109.5
O1—C3—O3	121.16 (13)	C4—C7—H7B	109.5
O1—C3—C2	127.77 (13)	H7A—C7—H7B	109.5
O3—C3—C2	111.07 (12)	C4—C7—H7C	109.5
O3—C4—C6	106.80 (12)	H7A—C7—H7C	109.5
O3—C4—C7	106.71 (11)	H7B—C7—H7C	109.5
C6—C4—C7	112.17 (13)	C5—O2—H2	110.1 (12)
O3—C4—C1	102.64 (10)	C3—O3—C4	111.19 (11)

Hydrogen-bond geometry (Å, º)

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
C2—H2*A*···O4	0.97	2.51	2.863 (2)	101
O2—H2···O1^{i}	0.91 (2)	1.77 (2)	2.673 (2)	174 (2)
C2—H2*B*···O1^{ii}	0.97	2.51	3.373 (2)	149
C1—H1···O1^{iii}	0.98	2.64	3.557 (2)	156

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