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Crystal structure of olivetolic acid: a natural product from *Cetrelia sanguinea* (Schaer.)

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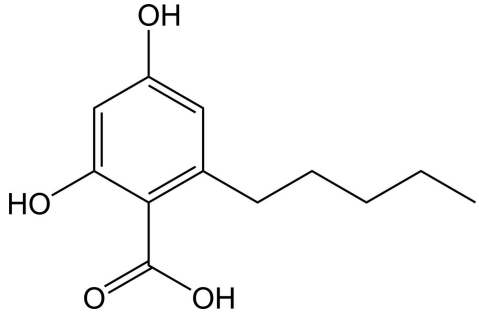
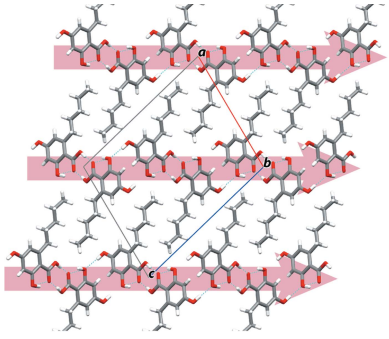
The title compound, $C_{12}H_{16}O_4$ (systematic name: 2,4-dihydroxy-6-pentylbenzoic acid) is a natural product isolated from *C. sanguinea* (Schaer.) and is reported to have various pharmacological activities. The molecule is approximately planar (r.m.s. deviation for the non-H atoms = 0.096 Å) and features an intramolecular O—H···O hydrogen bond. In the crystal, each olivetolic acid molecule is connected to three neighbours *via* O—H···O hydrogen bonds, generating $(10\bar{1})$ sheets. This crystal is essentially isostructural with a related resorcinolic acid with a longer alkyl chain.

1. Chemical context

Monoaromatic compounds from lichens have attracted a great interest in the pharmaceutical field due to their potential pharmacological activities such as antibacterial, antifungal, cytotoxic, and photoprotective activities (Gianini *et al.*,2008: Stocker-Wörgötter, 2008; Ismed *et al.*, 2012). The title compound, $C_{12}H_{16}O_4$, is a derivative of alkyl resorcinolic acid which is commonly found in certain species of lichens (Gomes *et al.*, 2006).





2. Structural commentary

The title compound (Fig. 1) crystallizes with monoclinic metric symmetry and adopts a roughly planar conformation (r.m.s. deviation = 0.093 Å). All bond distances, angles and dihedral angles appear to be usual except the bond angle of C6—C5—C12 [124.61 (13)°] compared to the mean value and their standard deviation of selected 24 similar structures reported in Cambridge Structural Database (CSD, Version 5.37, Update 2 Feb 2016; Groom *et al.*, 2016). In this case, the deviating bond angle may be a result of the strong intramolecular O2—H2···O3 interaction.

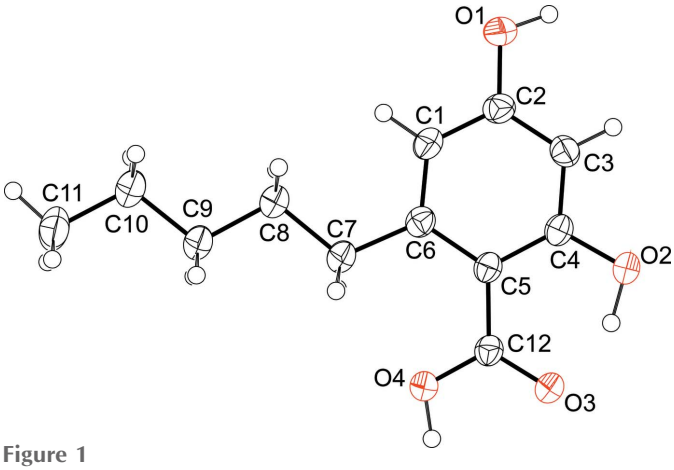


Figure 1
The molecular structure of the title compound, showing 50% probability displacement ellipsoids.

3. Supramolecular features

In the crystal, each molecule is connected with three others (Fig. 2): O1 acts as an O—H···O hydrogen bond donor while O2 is an O—H···O acceptor, forming a $C_1^1(6)$ infinite chain. In addition, an O4—H4···O3 carboxylic acid homodimer synthon is observed, generating an $R_2^2(8)$ loop. Together, these hydrogen bonds construct a layered architecture propagating in the $(10\bar{1})$ plane. Details of the hydrogen bonds are given in Table 1.

Interestingly, the title compound showed isostructurality with alkyl resorsinolic acid derivatives with longer alkyl chain of 6-*n*-pentadecyl-2,4-dihydroxy-benzoic acid (Gadret *et al.*, 1975; refcode: PDCHBZ10). Both structures exhibited extremely similar hydrogen bond in resorsinolic acid shown in Fig. 3*a* and 3*b*. Both crystal structures consist of a hydrophilic layer of the resorcinol acid moiety with hydrogen-bonding interactions, and a hydrophobic layer of normal alkyl chains.

4. Crystallization

Crystallization of the title compound was conducted by dissolving 700 mg of the isolate in an ethyl acetate–hexane solvent mixture (1:1). The solution was kept for one week at room temperature yielding colourless needles of the title compound.

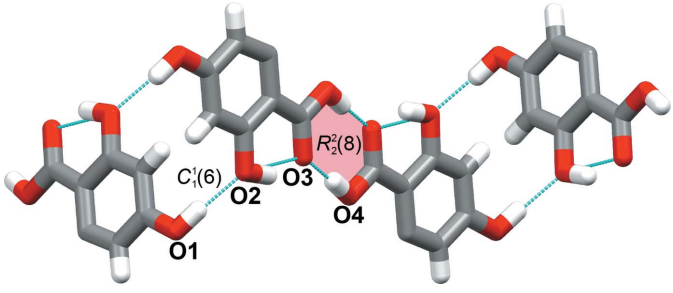


Figure 2
A partial view of the packing in the title compound, showing the hydrogen-bonded chain structure, formed through O—H···O hydrogen bonds. Blue dashed lines indicate hydrogen bonds.

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

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
O1—H1*A*···O2^{i}	0.93 (2)	1.90 (2)	2.8168 (16)	169.6 (19)
O2—H2···O3	1.00 (3)	1.58 (3)	2.5043 (14)	152 (2)
O4—H4···O3^{ii}	0.94 (3)	1.70 (3)	2.6368 (15)	177 (2)

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

5. Refinement

Crystal data, data collection and structure refinement details are summarized in Table 2. All non-hydrogen atoms were refined anistropically. The hydrogen atoms of O hydroxy and O carboxylic acid were located from a difference Fourier map and were refined isotropically. All other hydrogen atoms were located geometrically and refined as riding [U_{iso} = 1.5U_{iso}(C) for the terminal alkyl group and U_{iso} = 1.2U_{iso}(C) for other hydrogen atoms].

Acknowledgements

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Table 2
Experimental details.

Crystal data	
Chemical formula	$C_{12}H_{16}O_4$
M_r	224.25
Crystal system, space group	Monoclinic, $P2_1/n$
Temperature (K)	173
a, *b*, *c* (Å)	14.2527 (8), 4.7524 (3), 17.6489 (11)
β (°)	103.538 (4)
V (Å^3)	1162.22 (12)
Z	4
Radiation type	Cu $K\alpha$
μ (mm^{-1})	0.79
Crystal size (mm)	0.12 × 0.10 × 0.10
Data collection	
Diffractometer	RIGAKU R-AXIS RAPID II
Absorption correction	Multi-scan (*ABSCOR*; Higashi, 1995)
T_{min}, T_{max}	0.789, 0.924
No. of measured, independent and observed [$I > 2\sigma(I)$] reflections	12627, 2087, 1762
R_{int}	0.036
(sin $\theta/\lambda)_{max}$ (Å^{-1})	0.602
Refinement	
$R[F^2 > 2\sigma(F^2)]$, $wR(F^2)$, S	0.045, 0.136, 1.14
No. of reflections	2087
No. of parameters	158
H-atom treatment	H atoms treated by a mixture of independent and constrained refinement
$\Delta\rho_{max}$, $\Delta\rho_{min}$ (e Å^{-3})	0.29, −0.18

Computer programs: *PROCESS-AUTO* (Rigaku, 1998), *SHELXS2014* (Sheldrick, 2008) and *SHELXL2014* (Sheldrick, 2015).

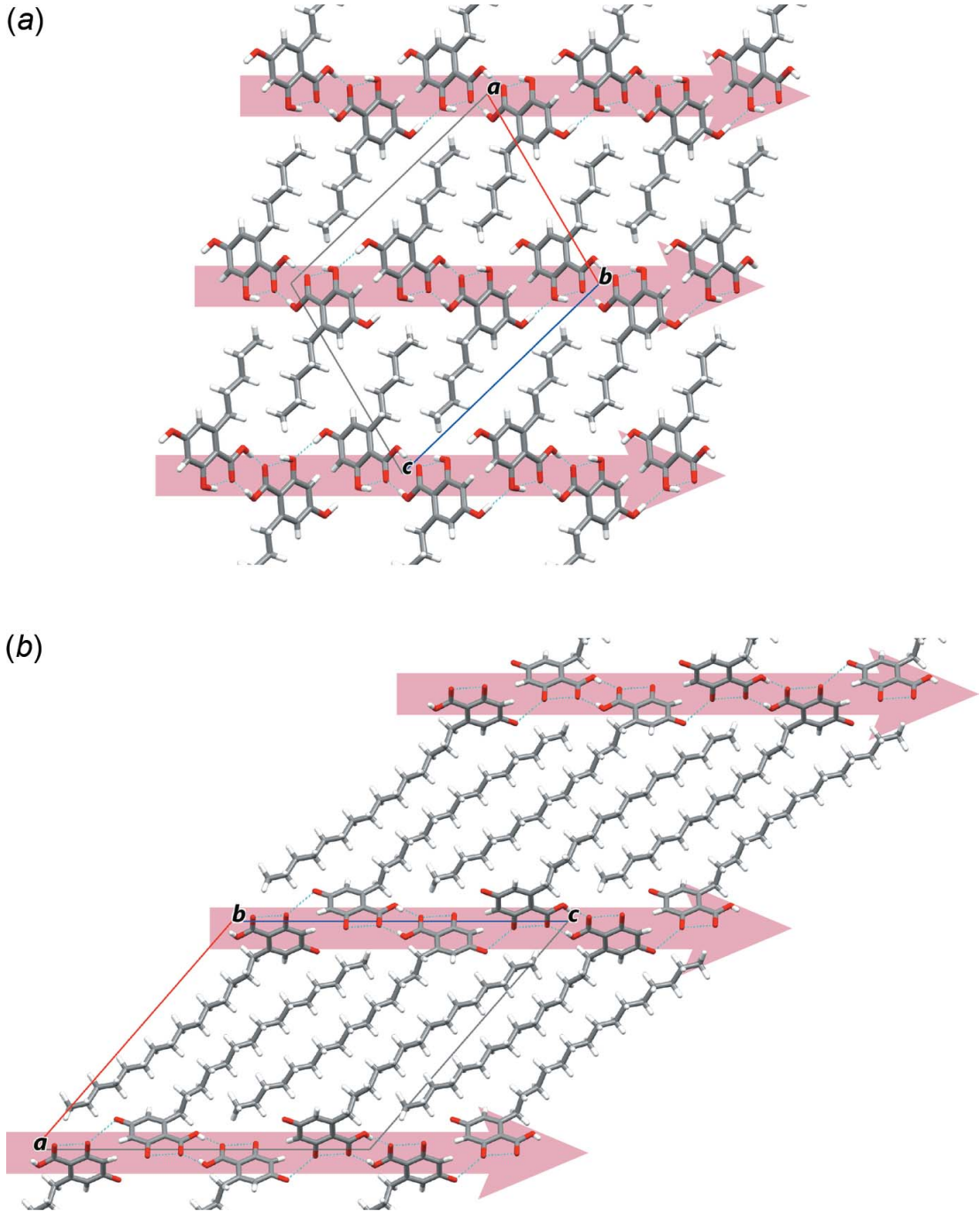

Figure 3
Crystal-packing views along *b* axis of (*a*) the title compound and (*b*) 6-*n*-pentadecyl-2,4-dihydroxybenzoic acid. Both structures possess isostructurality. The arrows indicate the one-dimensional hydrogen-bond chains involving resorsinolic acid.

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supporting information

Acta Cryst. (2016). E**72**, 1587-1589 [https://doi.org/10.1107/S2056989016016273]

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Computing details

Data collection: *PROCESS-AUTO* (Rigaku, 1998); cell refinement: *PROCESS-AUTO* (Rigaku, 1998); data reduction: *PROCESS-AUTO* (Rigaku, 1998); program(s) used to solve structure: *SHELXS2014* (Sheldrick, 2008); program(s) used to refine structure: *SHELXL2014* (Sheldrick, 2015); software used to prepare material for publication: *SHELXL2014* (Sheldrick, 2015).

2,4-Dihydroxy-6-pentylbenzoic acid

Crystal data

$C_{12}H_{16}O_4$
$M_r = 224.25$
Monoclinic, $P2_1/n$
$a = 14.2527$ (8) Å
$b = 4.7524$ (3) Å
$c = 17.6489$ (11) Å
$\beta = 103.538$ (4)°
$V = 1162.22$ (12) Å^3
$Z = 4$
$F(000) = 480$
$D_x = 1.282$ Mg m^{-3}
Cu $K\alpha$ radiation, $\lambda = 1.54186$ Å
Cell parameters from 12628 reflections
$\theta = 3.6$–$68.2°$
$\mu = 0.79$ mm^{-1}
$T = 173$ K
Block, colorless
0.12 × 0.10 × 0.10 mm

Data collection

RIGAKU R-AXIS RAPID II diffractometer
Radiation source: rotating anode X-ray
Detector resolution: 10.0 pixels mm^{-1}
ω–scan
Absorption correction: multi-scan (ABSCOR; Higashi, 1995)
$T_{min} = 0.789$, $T_{max} = 0.924$
12627 measured reflections
2087 independent reflections
1762 reflections with $I > 2\sigma(I)$
$R_{int} = 0.036$
$\theta_{max} = 68.2°$, $\theta_{min} = 3.6°$
$h = -17\rightarrow17$
$k = -5\rightarrow5$
$l = -20\rightarrow21$

Refinement

Refinement on F^2
Least-squares matrix: full
$R[F^2 > 2\sigma(F^2)] = 0.045$
$wR(F^2) = 0.136$
$S = 1.14$
2087 reflections
158 parameters
0 restraints
Primary atom site location: structure-invariant direct methods
Secondary atom site location: none
Hydrogen site location: mixed
H atoms treated by a mixture of independent and constrained refinement
$w = 1/[\sigma^2(F_o^2) + (0.0808P)^2 + 0.1676P]$ where $P = (F_o^2 + 2F_c^2)/3$

$(\Delta/\sigma)_{max} < 0.001$
$\Delta\rho_{max} = 0.29$ e Å^{-3}
$\Delta\rho_{min} = -0.18$ e Å^{-3}

Special details

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

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

	x	*y*	*z*	U_{iso}*/U_{eq}
O1	0.38939 (8)	0.5564 (2)	0.16723 (7)	0.0419 (3)
C1	0.32068 (11)	0.2528 (3)	0.06446 (9)	0.0333 (4)
H1	0.3726	0.2983	0.0413	0.040*
H1A	0.3901 (15)	0.588 (4)	0.2194 (14)	0.060 (6)*
O2	0.09864 (8)	0.0870 (2)	0.17140 (6)	0.0348 (3)
H2	0.0574 (18)	−0.059 (5)	0.1389 (14)	0.079 (7)*
C2	0.31656 (11)	0.3787 (3)	0.13488 (9)	0.0321 (4)
C3	0.24081 (11)	0.3235 (3)	0.16913 (9)	0.0317 (4)
H3	0.2370	0.4140	0.2163	0.038*
O3	0.03156 (7)	−0.2603 (2)	0.06590 (6)	0.0345 (3)
C4	0.17037 (10)	0.1334 (3)	0.13338 (8)	0.0286 (4)
O4	0.10317 (8)	−0.3497 (2)	−0.03022 (6)	0.0378 (3)
H4	0.0556 (18)	−0.491 (6)	−0.0410 (14)	0.080 (7)*
C5	0.17377 (10)	−0.0040 (3)	0.06311 (8)	0.0275 (3)
C6	0.25149 (10)	0.0639 (3)	0.02743 (8)	0.0287 (4)
C7	0.25914 (11)	−0.0625 (3)	−0.04994 (9)	0.0336 (4)
H7A	0.1981	−0.0241	−0.0887	0.040*
H7B	0.2648	−0.2692	−0.0435	0.040*
C8	0.34233 (11)	0.0400 (3)	−0.08352 (9)	0.0368 (4)
H8A	0.3396	0.2476	−0.0879	0.044*
H8B	0.4042	−0.0109	−0.0474	0.044*
C9	0.33918 (12)	−0.0863 (3)	−0.16340 (9)	0.0374 (4)
H9A	0.3426	−0.2939	−0.1587	0.045*
H9B	0.2768	−0.0377	−0.1992	0.045*
C10	0.42080 (13)	0.0161 (4)	−0.19841 (10)	0.0454 (5)
H10A	0.4185	0.2240	−0.2015	0.054*
H10B	0.4831	−0.0373	−0.1632	0.054*
C11	0.41710 (14)	−0.1014 (4)	−0.27894 (11)	0.0516 (5)
H11A	0.4215	−0.3071	−0.2762	0.077*
H11B	0.4713	−0.0265	−0.2982	0.077*
H11C	0.3562	−0.0466	−0.3145	0.077*
C12	0.09866 (10)	−0.2112 (3)	0.03296 (8)	0.0283 (3)

Atomic displacement parameters (Å²)

	U^{11}	U^{22}	U^{33}	U^{12}	U^{13}	U^{23}
O1	0.0439 (6)	0.0464 (7)	0.0368 (7)	−0.0190 (5)	0.0123 (5)	−0.0070 (5)

C1	0.0333 (8)	0.0361 (8)	0.0328 (8)	−0.0048 (6)	0.0128 (6)	0.0029 (6)
O2	0.0348 (6)	0.0417 (6)	0.0319 (6)	−0.0064 (5)	0.0160 (5)	−0.0050 (5)
C2	0.0332 (7)	0.0317 (7)	0.0307 (8)	−0.0051 (6)	0.0061 (6)	0.0033 (6)
C3	0.0372 (8)	0.0312 (8)	0.0270 (8)	−0.0014 (6)	0.0081 (7)	−0.0017 (6)
O3	0.0350 (6)	0.0378 (6)	0.0342 (6)	−0.0084 (4)	0.0151 (5)	−0.0036 (5)
C4	0.0300 (7)	0.0292 (7)	0.0278 (8)	0.0010 (6)	0.0094 (6)	0.0048 (6)
O4	0.0409 (6)	0.0421 (6)	0.0350 (6)	−0.0140 (5)	0.0182 (5)	−0.0108 (5)
C5	0.0297 (7)	0.0273 (7)	0.0267 (8)	−0.0001 (6)	0.0089 (6)	0.0041 (6)
C6	0.0309 (7)	0.0285 (7)	0.0271 (8)	−0.0006 (6)	0.0076 (6)	0.0054 (6)
C7	0.0363 (8)	0.0352 (8)	0.0327 (9)	−0.0053 (6)	0.0148 (7)	0.0004 (6)
C8	0.0381 (8)	0.0414 (9)	0.0348 (9)	−0.0073 (7)	0.0161 (7)	−0.0018 (7)
C9	0.0399 (8)	0.0406 (9)	0.0362 (9)	−0.0048 (7)	0.0179 (7)	−0.0009 (7)
C10	0.0467 (9)	0.0509 (10)	0.0457 (10)	−0.0076 (8)	0.0253 (8)	−0.0038 (8)
C11	0.0581 (11)	0.0594 (11)	0.0462 (11)	−0.0007 (9)	0.0299 (9)	0.0023 (9)
C12	0.0310 (7)	0.0279 (7)	0.0271 (7)	−0.0004 (6)	0.0090 (6)	0.0034 (6)

Geometric parameters (Å, º)

O1—C2	1.3563 (18)	C6—C7	1.519 (2)
O1—H1A	0.93 (2)	C7—C8	1.5243 (19)
C1—C6	1.380 (2)	C7—H7A	0.9900
C1—C2	1.393 (2)	C7—H7B	0.9900
C1—H1	0.9500	C8—C9	1.523 (2)
O2—C4	1.3657 (16)	C8—H8A	0.9900
O2—H2	1.00 (3)	C8—H8B	0.9900
C2—C3	1.380 (2)	C9—C10	1.519 (2)
C3—C4	1.388 (2)	C9—H9A	0.9900
C3—H3	0.9500	C9—H9B	0.9900
O3—C12	1.2520 (16)	C10—C11	1.516 (2)
C4—C5	1.412 (2)	C10—H10A	0.9900
O4—C12	1.3094 (17)	C10—H10B	0.9900
O4—H4	0.94 (3)	C11—H11A	0.9800
C5—C6	1.4333 (19)	C11—H11B	0.9800
C5—C12	1.460 (2)	C11—H11C	0.9800
C2—O1—H1A	110.4 (13)	C9—C8—C7	112.14 (13)
C6—C1—C2	121.82 (13)	C9—C8—H8A	109.2
C6—C1—H1	119.1	C7—C8—H8A	109.2
C2—C1—H1	119.1	C9—C8—H8B	109.2
C4—O2—H2	103.8 (14)	C7—C8—H8B	109.2
O1—C2—C3	122.28 (14)	H8A—C8—H8B	107.9
O1—C2—C1	117.06 (13)	C10—C9—C8	113.00 (13)
C3—C2—C1	120.66 (14)	C10—C9—H9A	109.0
C2—C3—C4	118.78 (14)	C8—C9—H9A	109.0
C2—C3—H3	120.6	C10—C9—H9B	109.0
C4—C3—H3	120.6	C8—C9—H9B	109.0
O2—C4—C3	115.27 (13)	H9A—C9—H9B	107.8
O2—C4—C5	122.70 (13)	C11—C10—C9	113.66 (15)

C3—C4—C5	122.02 (13)	C11—C10—H10A	108.8
C12—O4—H4	110.8 (15)	C9—C10—H10A	108.8
C4—C5—C6	118.06 (13)	C11—C10—H10B	108.8
C4—C5—C12	117.30 (12)	C9—C10—H10B	108.8
C6—C5—C12	124.61 (13)	H10A—C10—H10B	107.7
C1—C6—C5	118.60 (13)	C10—C11—H11A	109.5
C1—C6—C7	119.31 (13)	C10—C11—H11B	109.5
C5—C6—C7	122.09 (13)	H11A—C11—H11B	109.5
C6—C7—C8	116.69 (13)	C10—C11—H11C	109.5
C6—C7—H7A	108.1	H11A—C11—H11C	109.5
C8—C7—H7A	108.1	H11B—C11—H11C	109.5
C6—C7—H7B	108.1	O3—C12—O4	119.78 (13)
C8—C7—H7B	108.1	O3—C12—C5	122.09 (13)
H7A—C7—H7B	107.3	O4—C12—C5	118.12 (12)

C6—C1—C2—O1	178.54 (13)	C12—C5—C6—C1	−176.44 (13)
C6—C1—C2—C3	−1.8 (2)	C4—C5—C6—C7	−177.26 (12)
O1—C2—C3—C4	−178.34 (14)	C12—C5—C6—C7	4.3 (2)
C1—C2—C3—C4	2.0 (2)	C1—C6—C7—C8	−2.5 (2)
C2—C3—C4—O2	179.08 (12)	C5—C6—C7—C8	176.74 (13)
C2—C3—C4—C5	−0.2 (2)	C6—C7—C8—C9	−176.33 (13)
O2—C4—C5—C6	178.97 (12)	C7—C8—C9—C10	179.26 (14)
C3—C4—C5—C6	−1.8 (2)	C8—C9—C10—C11	−178.38 (15)
O2—C4—C5—C12	−2.5 (2)	C4—C5—C12—O3	2.4 (2)
C3—C4—C5—C12	176.76 (13)	C6—C5—C12—O3	−179.11 (13)
C2—C1—C6—C5	−0.3 (2)	C4—C5—C12—O4	−176.99 (12)
C2—C1—C6—C7	179.01 (13)	C6—C5—C12—O4	1.5 (2)
C4—C5—C6—C1	2.0 (2)		

Hydrogen-bond geometry (Å, º)

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
O1—H1*A*···O2^{i}	0.93 (2)	1.90 (2)	2.8168 (16)	169.6 (19)
O2—H2···O3	1.00 (3)	1.58 (3)	2.5043 (14)	152 (2)
O4—H4···O3^{ii}	0.94 (3)	1.70 (3)	2.6368 (15)	177 (2)

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