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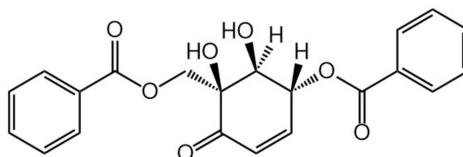
Crystal structure of 5-[(benzoyloxy)methyl]-5,6-dihydroxy-4-oxocyclohex-2-en-1-yl benzoate

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The crystal structure of the natural product zeylenone, C₂₁H₁₈O₇, was confirmed by single-crystal X-ray diffraction. The crystal structure has three chiral centers at positions C1, C5 and C6 of the cyclohexanone ring, but the absolute configuration could not be determined reliably. The methyl benzoate and benzoyloxy substituents at positions C1 and C5 of the cyclohexenone ring are on the same side of the ring with the dihedral angle between their mean planes being 16.25 (10)°. These rings are almost perpendicular to the cyclohexenone ring. The benzoate groups and two hydroxyl groups on the cyclohexenone ring form strong hydrogen bonds to consolidate the crystal structure. In addition, weak C—H···O hydrogen bonds also contribute to the packing of the structure.

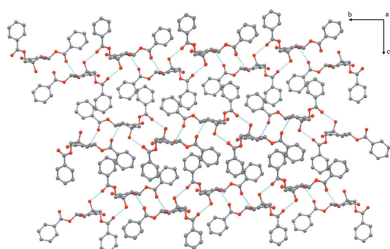
1. Chemical context

Zeylenone is a naturally occurring polyoxygenated cyclohexene derived from the shikimate pathway. It has been found in a few plant families such as *Piperaceae* and *Annonaceae*. The biological activity of zeylenone was reported as inducing apoptosis in the mitochondria of gastric cancer cells (Yang *et al.*, 2018) and cervical carcinoma cells (Zhang *et al.*, 2017). The absolute configuration of natural zeylenone was determined by CD spectroscopy to be (–)-zeylenone (Takeuchi *et al.*, 2001).



2. Structural commentary

The molecular structure of the title compound (I) is shown in Fig. 1. It has three chiral centers at positions C1, C5 and C6 of the cyclohexanone ring. However, the absolute configuration (probably 1*S*, 5*R* and 6*S*) could not be deduced from the X-ray data because of the large standard deviation of the Flack parameter [0.0 (3)]. The two main substituents are methyl benzoate and benzoyloxy at positions C1 and C5, and positioned at the same side of the cyclohexenone ring. The dihedral angle between the methyl benzoate and benzoyloxy mean planes is 16.24 (10)°, indicating that the rings are almost



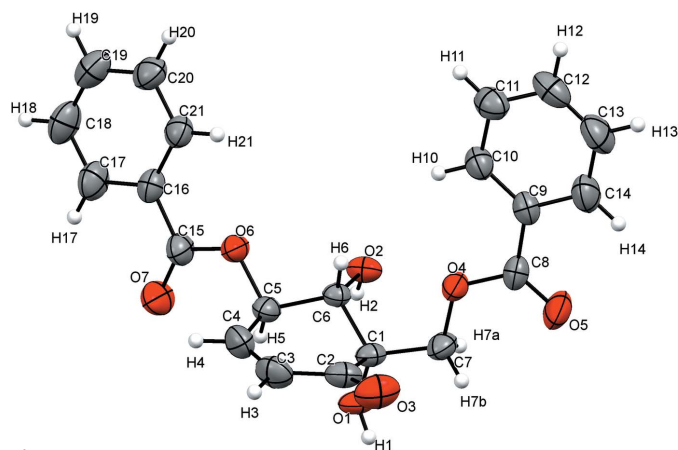


Figure 1
The molecular structure of compound (I) with the atom labelling and 50% probability displacement ellipsoids.

coplanar. The dihedral angle between the cyclohexenone ring and the methyl benzoate and benzoyloxy rings are $74.92(9)$ and $69.23(10)^\circ$, respectively, indicating that the aromatic and cyclohexenone rings are almost perpendicular. The conformation of the cyclohexenone ring, the core structure of (–)-zeylenone, is described as a half-chair based on the torsion angles $\text{H4}–\text{C4}–\text{C3}–\text{C2}$ [$-178.7(3)^\circ$, almost planar] and $\text{C5}–\text{C6}–\text{C1}–\text{C2}$ [$-60.65(16)^\circ$, perfectly staggered] and the puckering parameters [$Q = 0.4989(17)$ Å, $\theta = 130.8(2)^\circ$ and $\Phi = 143.9(3)^\circ$].

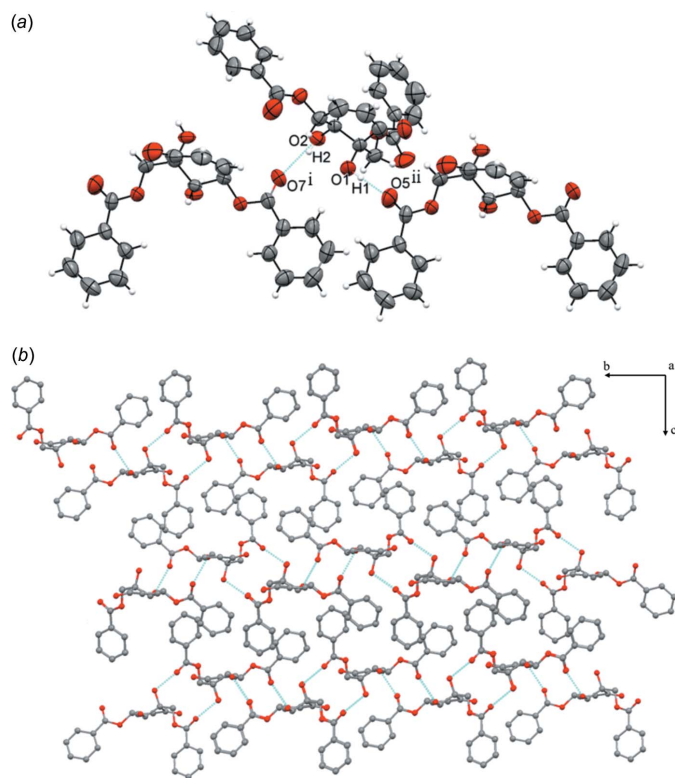


Figure 2
(a) $\text{O}–\text{H}\cdots\text{O}$ hydrogen bond formation in (I) and (b) the crystal packing viewed along the *a* axis. Hydrogen bonds are shown as dashed lines.

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

$D–\text{H}\cdots A$	$D–\text{H}$	$\text{H}\cdots A$	$D\cdots A$	$D–\text{H}\cdots A$
$\text{O2}–\text{H2}\cdots\text{O7}^{\text{i}}$	0.82	1.93 (1)	2.7029 (17)	157 (1)
$\text{O1}–\text{H1}\cdots\text{O5}^{\text{ii}}$	0.82	1.89 (1)	2.7112 (17)	177 (2)
$\text{C13}–\text{H13}\cdots\text{O2}^{\text{iii}}$	0.93 (1)	2.53 (1)	3.221 (3)	132 (1)

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

3. Supramolecular features

The crystal packing is characterized by both strong and weak hydrogen bonds and also by partial $\pi–\pi$ interactions. The strong hydrogen bonds are formed between hydroxyl groups on the cyclohexenone ring and the uncoordinated oxygen atom of methyl benzoate and benzoyloxy substituents ($\text{O2}–\text{H2}\cdots\text{O7}^{\text{i}}$ and $\text{O1}–\text{H1}\cdots\text{O5}^{\text{ii}}$, Fig. 2*a*, Table 1). These inter-

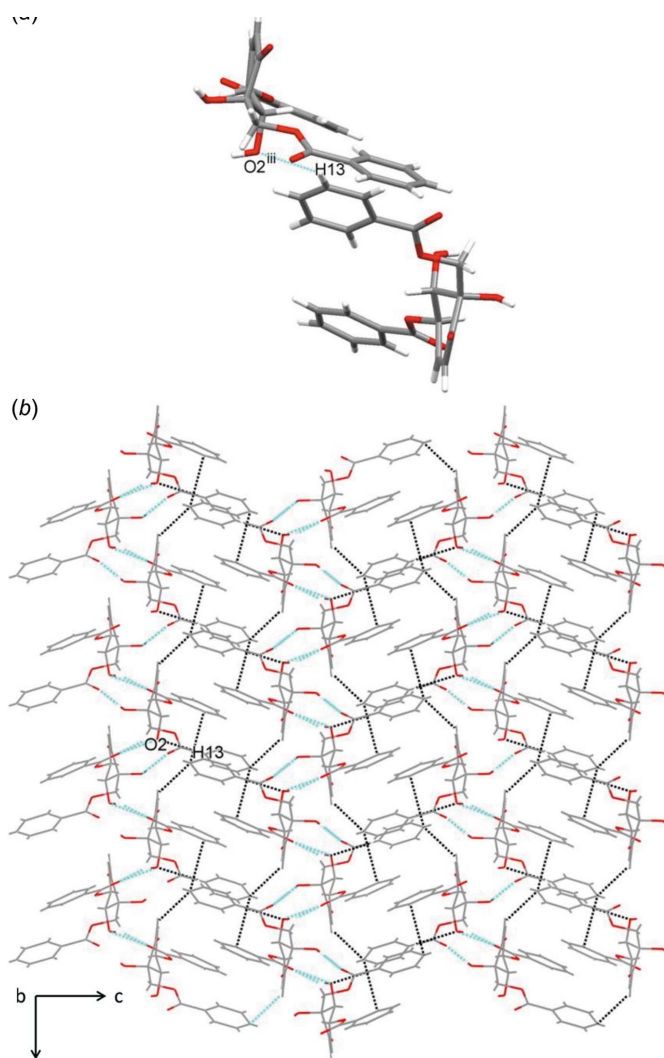


Figure 3
(a) $\text{C}–\text{H}\cdots\text{O}$ hydrogen bonds and (b) the crystal packing viewed along the *b* axis. Blue dashed lines represent $\text{O}–\text{H}\cdots\text{O}$ hydrogen bonds and black dashed lines represent the $\text{C}–\text{H}\cdots\text{O}$ and the weak $\pi–\pi$ interactions.

Table 2

Comparison of geometric parameters (Å, °) between the experimental and optimized structures.

Parameter	Exp.	Calc.	Parameter	Exp.	Calc.
O1—C1	1.425 (2)	1.43	C5—C6	1.512 (2)	1.53
O2—C6	1.403 (2)	1.40	C8—C9	1.480 (2)	1.49
O3—C2	1.211 (2)	1.21	C9—C10	1.372 (3)	1.40
O4—C7	1.446 (2)	1.43	C9—C14	1.384 (2)	1.40
O4—C8	1.327 (2)	1.35	C10—C11	1.385 (3)	1.39
O5—C8	1.196 (2)	1.21	C11—C12	1.382 (3)	1.39
O6—C5	1.455 (2)	1.43	C12—C13	1.346 (3)	1.39
O6—C15	1.334 (2)	1.35	C13—C14	1.378 (3)	1.39
O7—C15	1.206 (2)	1.21	C15—C16	1.476 (2)	1.49
C1—C2	1.534 (2)	1.54	C16—C17	1.392 (2)	1.40
C1—C6	1.530 (2)	1.53	C16—C21	1.382 (3)	1.40
C1—C7	1.509 (2)	1.52	C17—C18	1.376 (3)	1.39
C2—C3	1.456 (3)	1.47	C18—C19	1.364 (3)	1.39
C3—C4	1.322 (3)	1.34	C19—C20	1.377 (3)	1.39
C4—C5	1.489 (3)	1.50	C20—C21	1.381 (3)	1.39
O1—C1—C7	108.46 (13)	108.9	C2—C1—C6	108.75 (13)	113.5
O4—C8—C9	113.45 (13)	113.1	C3—C4—C5	123.74 (19)	122.6
O6—C5—C6	106.27 (11)	106.4	C4—C5—C6	112.53 (15)	111.9
O6—C15—C16	113.40 (14)	112.5	C5—O6—C15	116.55 (12)	115.8
C1—O1—H1	109.5	108.0	C6—O2—H2	109.5	106.4
C1—C2—C3	115.64 (16)	118.1	C8—O4—C7	116.34 (13)	114.4
C1—C6—C5	108.92 (12)	110.1	C8—C9—C10	122.49 (14)	112.7
C1—C7—O4	108.20 (12)	107.2	C15—C16—C21	122.2 (2)	122.19 (15)
O6—C15—C16—C21	−0.4 (3)	3.5	C8—O4—C7—C1	175.99 (13)	179.9
C5—O6—C15—C16	−179.95 (15)	−175.2	C9—C8—O4—C7	173.83 (14)	179.6
C6—C1—C2—C3	43.70 (19)	19.5	C10—C9—C8—O4	−11.7 (2)	3.0
C6—C5—C4—C3	−19.8 (3)	−29.8			

actions form a layer parallel to the *bc* plane (Fig. 2*b*). In addition, the crystal packing features weak C—H...O hydrogen-bonding interactions (C13—H13...O2ⁱⁱⁱ, Table 1) and contacts between the aromatic rings [the shortest centroid-centroid distance between phenyl rings is 4.641 (2) Å], as shown in Fig. 3.

4. Computational calculations

The structure of the title compound was optimized using density functional theory (DFT) calculations at the M062X/6-31G(d) level using *GAUSSIAN 09* (Frisch *et al.*, 2016). The optimized structure was then used for the analysis of the highest occupied molecular orbital (HOMO) and the lowest unoccupied molecular orbital (LUMO) using the same level of theory in order to determine the reactivity of the compound *via* the energy gap.

The DFT-optimized geometry was compared with the geometry obtained from the crystal structure using the molecular overlay module based on 50% steric and 50% electrostatic similarities in the *Discovery Studio* visualizer (Dassault, 2018), as shown in Fig. 4. The overlay similarity, which is calculated based on the steric and electrostatic overlaps, is high with a value of 0.86 and the r.m.s.d. of the heavy atoms (non-H atoms) is 0.67 Å. Geometrical parameters (*i.e.* bond lengths, bond angles and torsion angles) of the experimental and optimized structures are given in Table 2.

Finally, the molecular orbitals of zeylenone were calculated. The HOMO and LUMO plots are shown in Fig. 5. At the

HOMO level, the orbitals are located on the phenyl ring of the methylene benzoate group and the orbitals are shifted to the cyclohexenone ring at the LUMO level. The energy gap ($E_{\text{HOMO}} - E_{\text{LUMO}}$) is 7.61 eV. The large energy gap indicates the stability of the title compound.

5. Database survey

In the first reported total synthesis of zeylenone from shikimic acid, the absolute configuration was assigned as 1*R*, 5*S*, 6*R*. A circular dichroism study of the synthesized product gave (+)-

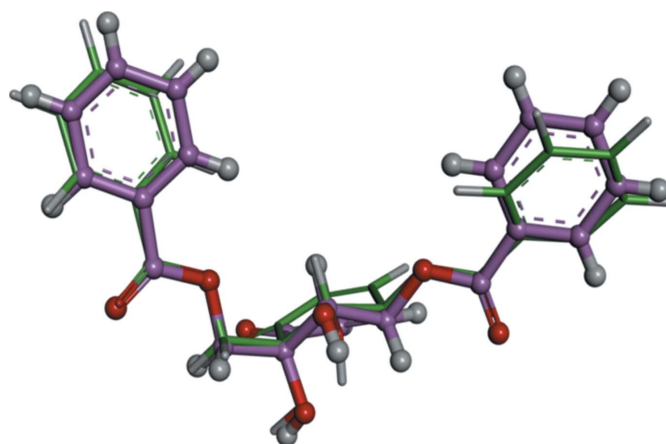


Figure 4
Superposition of the experimental (ball-and-stick model) and optimized (stick model) structures.

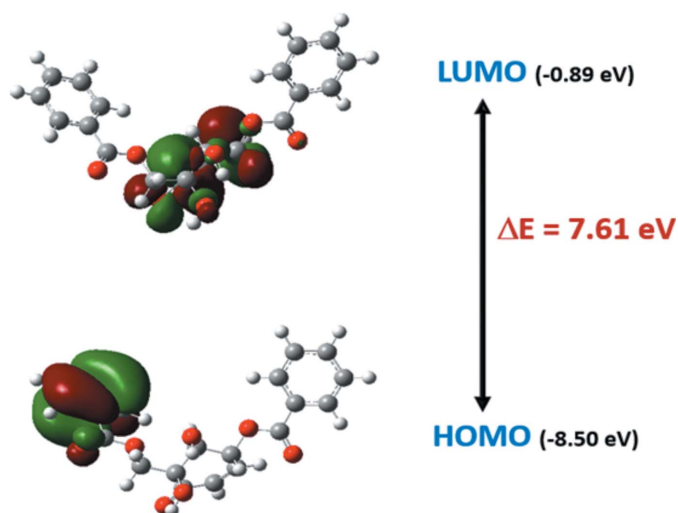


Figure 5
The HOMO–LUMO plot for the title compound (1).

zeylenone (Liu *et al.*, 2004). The first total synthesis of (–)-zeylenone was also achieved from shikimic acid (Zhang *et al.*, 2006). Similar structures to (–)-zeylenone are (–)-zeylenol and an alcohol form, (–)-zeylenone, from *Piper cubeba* (Taneja *et al.*, 1991).

The closest related structure is that of Cherrevenone, a polyoxygenated cyclohexene derivative from *Uvaria cherre-venensis*. Here, the absolute configuration could again not be determined from the X-ray data, but was confirmed by an electronic circular dichroism analysis (CCDC refcode WOJLIT; Jaipetch *et al.*, 2019).

Other reported crystal structures containing a cyclohexenone ring as a core structure include URIPUH (Mayekar *et al.*, 2010), KADROW (Lynch *et al.*, 1989), WINTUI (Sondossi *et al.*, 1995) and CEZXUD (Atioğlu *et al.*, 2018). In all of these, the cyclohexenone ring adopts a half-chair conformation, as observed in the title compound.

6. Synthesis and crystallization

Pipers griffithii leaves, collected from Kanchanaburi province in Eastern Thailand, were dried in air and then powdered with a grinder. Piper powder (400 g) was macerated at room temperature in hexane for a week and then filtered. This was repeated with the remaining *Piper* powder using ethyl acetate. The filtrate was evaporated to yield about 2.60 g crude extract from ethyl acetate, which was dissolved again in ethyl acetate and mixed with silica gel. The mixture was evaporated by rotary evaporator, loaded on the column and eluted by gradient elution using 20–50% EtOAc in hexane. The fractions were collected and combined, monitoring with thin layer chromatography, to provide eleven fractions. The sixth fraction was separated by column chromatography using MeOH:EtOAc:Hexane (1:4:5) as eluents, yielding a pale-yellow solid (0.60 g), which was recrystallized from dichloromethane and hexane (1:1), giving colourless in CIF crystals, m.p. 423–424 K.

Table 3
Experimental details.

Crystal data	
Chemical formula	C ₂₁ H ₁₈ O ₇
<i>M_r</i>	382.37
Crystal system, space group	Orthorhombic, <i>P</i> 2 ₁ 2 ₁ 2 ₁
Temperature (K)	296
<i>a</i> , <i>b</i> , <i>c</i> (Å)	7.4958 (11), 12.422 (2), 20.325 (4)
<i>V</i> (Å ³)	1892.4 (6)
<i>Z</i>	4
Radiation type	Mo <i>K</i> α
μ (mm ⁻¹)	0.10
Crystal size (mm)	0.24 × 0.08 × 0.04
Data collection	
Diffractometer	Bruker APEXII D8 QUEST CMOS
Absorption correction	Multi-scan (<i>SADABS</i> ; Bruker, 2016)
<i>T_{min}</i> , <i>T_{max}</i>	0.708, 0.745
No. of measured, independent and observed [<i>I</i> ≥ 2 σ (<i>I</i>)] reflections	36963, 3587, 3199
<i>R_{int}</i>	0.045
(<i>sin</i> θ / λ) _{max} (Å ⁻¹)	0.611
Refinement	
$R[F^2 > 2\sigma(F^2)]$, $wR(F^2)$, <i>S</i>	0.032, 0.082, 1.10
No. of reflections	3587
No. of parameters	255
H-atom treatment	H-atom parameters constrained
$\Delta\rho_{\max}$, $\Delta\rho_{\min}$ (e Å ⁻³)	0.12, -0.10
Absolute structure	Flack <i>x</i> determined using 1259 quotients [(<i>I</i> ⁺) – (<i>I</i> ⁻)] / [(<i>I</i> ⁺) + (<i>I</i> ⁻)] (Parsons <i>et al.</i> , 2013)
Absolute structure parameter	0.0 (3)

Computer programs: *APEX3* and *SAINT* (Bruker, 2016), *olex2.solve* (Bourhis *et al.*, 2015), *SHELXL* (Sheldrick, 2015) and *OLEX2* (Dolomanov *et al.*, 2009).

¹H NMR (400 MHz, CDCl₃): δ 3.22 (1H, *s*, *br*), 4.11 (1H, *s*, *br*), 4.38 (1H, *d*, *J* = 4 Hz), 4.60 (1H, *d*, *J* = 12 Hz), 4.85 (1H, *d*, *J* = 8 Hz), 5.96 (1H, *d*, *J* = 4 Hz), 6.34 (1H, *dd*, *J* = 8, 8 Hz), 6.96 (1H, *dd*, *J* = 4, 8 Hz), 7.38–7.44 (4H, *m*), 7.56 (2H, *dd*, *J* = 8, 16 Hz), 7.94 (2H, *dd*, *J* = 4, 8 Hz), 8.02 (2H, *dd*, *J* = 4, 8 Hz). ¹³C NMR (CDCl₃): δ 65.4, 69.2, 71.6, 77.2, 128.4, 128.5, 128.6, 128.7, 129.1, 129.7, 129.78, 133.4, 133.7, 142.6, 165.3, 166.1, 196.2. Mass spectroscopy *m/z* 383.1125 (*M* + 1)⁺. IR (KBr, cm⁻¹): 712 cm⁻¹ (*s*, C–H bending); 1103 cm⁻¹ (*s*, C–O stretching); 1277 cm⁻¹ (*s*, C–O stretching); 1593 cm⁻¹ (*w*, C=C aromatic ring); 1705 cm⁻¹ (*s*, C=O); 2933 cm⁻¹ (*w*, C=C–H stretching aromatic ring); 3423 cm⁻¹ (*s*, O–H stretching).

7. Refinement

Crystal data, data collection and structure refinement details are summarized in Table 3. All H atoms, ternary C(H), secondary C(H,H), aromatic H and tetrahedral OH, were placed in calculated positions (C–H = 0.98, 0.97, 0.93 and 0.82 Å, respectively). They are refined using a riding model with $U_{\text{iso}}(\text{H}) = 1.5U_{\text{eq}}(\text{C})$ or $1.5U_{\text{eq}}(\text{O})$.

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supporting information

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Crystal structure of 5-[(benzoyloxy)methyl]-5,6-dihydroxy-4-oxocyclohex-2-en-1-yl benzoate

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Computing details

Data collection: *APEX3* (Bruker, 2016); cell refinement: *S SAINT* (Bruker, 2016); data reduction: *S SAINT* (Bruker, 2016); program(s) used to solve structure: *olex2.solve* (Bourhis *et al.*, 2015); program(s) used to refine structure: *SHELXL* (Sheldrick, 2015); molecular graphics: *OLEX2* (Dolomanov *et al.*, 2009); software used to prepare material for publication: *OLEX2* (Dolomanov *et al.*, 2009).

5-[(Benzoyloxy)methyl]-5,6-dihydroxy-4-oxocyclohex-2-en-1-yl benzoate

Crystal data

$C_{21}H_{18}O_7$

$M_r = 382.37$

Orthorhombic, $P2_12_12_1$

$a = 7.4958$ (11) Å

$b = 12.422$ (2) Å

$c = 20.325$ (4) Å

$V = 1892.4$ (6) Å³

$Z = 4$

$F(000) = 800.5281$

$D_x = 1.342$ Mg m⁻³

Mo $K\alpha$ radiation, $\lambda = 0.71073$ Å

Cell parameters from 9916 reflections

$\theta = 2.6$ – 24.7°

$\mu = 0.10$ mm⁻¹

$T = 296$ K

Plate, colourless

$0.24 \times 0.08 \times 0.04$ mm

Data collection

Bruker APEX2 D8 QUEST CMOS diffractometer

ω and φ scans

Absorption correction: multi-scan (SADABS; Bruker, 2016)

$T_{\min} = 0.708$, $T_{\max} = 0.745$

36963 measured reflections

3587 independent reflections

3199 reflections with $I \geq 2\sigma(I)$

$R_{\text{int}} = 0.045$

$\theta_{\max} = 25.7^\circ$, $\theta_{\min} = 2.9^\circ$

$h = -9 \rightarrow 9$

$k = -15 \rightarrow 15$

$l = -24 \rightarrow 24$

Refinement

Refinement on F^2

Least-squares matrix: full

$R[F^2 > 2\sigma(F^2)] = 0.032$

$wR(F^2) = 0.082$

$S = 1.10$

3587 reflections

255 parameters

0 restraints

35 constraints

Primary atom site location: iterative

H-atom parameters constrained

$w = 1/[\sigma^2(F_o^2) + (0.0343P)^2 + 0.1967P]$

where $P = (F_o^2 + 2F_c^2)/3$

$(\Delta/\sigma)_{\max} = 0.0003$

$\Delta\rho_{\max} = 0.12$ e Å⁻³

$\Delta\rho_{\min} = -0.10$ e Å⁻³

Absolute structure: Flack x determined using

1259 quotients $[(I^+) - (I^-)] / [(I^+) + (I^-)]$ (Parsons *et al.*, 2013)

Absolute structure parameter: 0.0 (3)

Fractional atomic coordinates and isotropic or equivalent isotropic displacement parameters (\AA^2)

	<i>x</i>	<i>y</i>	<i>z</i>	$U_{\text{iso}}^*/U_{\text{eq}}$
O6	0.48269 (18)	0.70917 (9)	0.38884 (5)	0.0630 (3)
O2	0.20328 (14)	0.56656 (10)	0.43093 (5)	0.0586 (3)
H2	0.1932 (6)	0.5895 (17)	0.4686 (4)	0.0879 (4)*
O1	0.43371 (18)	0.46452 (9)	0.52550 (5)	0.0637 (3)
H1	0.477 (3)	0.4158 (8)	0.54749 (17)	0.0956 (5)*
O4	0.25100 (18)	0.33708 (9)	0.38037 (5)	0.0649 (3)
O5	0.0902 (2)	0.19256 (12)	0.40208 (7)	0.0929 (5)
O7	0.5956 (3)	0.82489 (11)	0.46087 (7)	0.1010 (6)
O3	0.6515 (2)	0.30383 (12)	0.42569 (8)	0.0923 (5)
C8	0.1399 (2)	0.25864 (12)	0.36344 (9)	0.0586 (4)
C6	0.3807 (2)	0.53548 (12)	0.41980 (7)	0.0452 (3)
H6	0.3924 (2)	0.51900 (12)	0.37285 (7)	0.0542 (4)*
C15	0.5290 (3)	0.80813 (13)	0.40783 (9)	0.0655 (5)
C1	0.4302 (2)	0.43358 (12)	0.45798 (7)	0.0511 (4)
C2	0.6172 (3)	0.39738 (15)	0.43677 (8)	0.0639 (5)
C16	0.4927 (2)	0.89129 (13)	0.35772 (9)	0.0605 (4)
C10	0.1230 (2)	0.34822 (16)	0.25339 (9)	0.0660 (5)
H10	0.1836 (2)	0.40757 (16)	0.27012 (9)	0.0793 (5)*
C7	0.2932 (3)	0.34568 (14)	0.44959 (8)	0.0637 (4)
H7a	0.1864 (3)	0.36290 (14)	0.47445 (8)	0.0764 (5)*
H7b	0.3402 (3)	0.27786 (14)	0.46567 (8)	0.0764 (5)*
C5	0.5144 (2)	0.62285 (13)	0.43577 (8)	0.0567 (4)
H5	0.4933 (2)	0.64941 (13)	0.48050 (8)	0.0681 (5)*
C9	0.0875 (2)	0.26165 (13)	0.29324 (8)	0.0560 (4)
C21	0.4190 (3)	0.86669 (15)	0.29726 (9)	0.0651 (4)
H21	0.3903 (3)	0.79577 (15)	0.28711 (9)	0.0781 (5)*
C12	-0.0180 (3)	0.2577 (2)	0.16356 (11)	0.0823 (6)
H12	-0.0545 (3)	0.2567 (2)	0.11984 (11)	0.0988 (7)*
C11	0.0688 (3)	0.3472 (2)	0.18828 (10)	0.0775 (5)
H11	0.0905 (3)	0.4063 (2)	0.16137 (10)	0.0930 (6)*
C3	0.7495 (3)	0.4826 (2)	0.43087 (11)	0.0824 (6)
H3	0.8696 (3)	0.4646 (2)	0.42780 (11)	0.0989 (7)*
C4	0.7022 (3)	0.58513 (18)	0.42980 (11)	0.0776 (6)
H4	0.7913 (3)	0.63662 (18)	0.42504 (11)	0.0931 (7)*
C13	-0.0499 (3)	0.1720 (2)	0.20235 (13)	0.0959 (7)
H13	-0.1063 (3)	0.1117 (2)	0.18499 (13)	0.1150 (9)*
C19	0.4324 (3)	1.05213 (18)	0.26647 (13)	0.0881 (7)
H19	0.4110 (3)	1.10627 (18)	0.23586 (13)	0.1057 (8)*
C20	0.3877 (3)	0.94726 (18)	0.25191 (11)	0.0797 (6)
H20	0.3365 (3)	0.93070 (18)	0.21149 (11)	0.0957 (7)*
C14	0.0004 (3)	0.17290 (16)	0.26754 (11)	0.0831 (6)
H14	-0.0243 (3)	0.11396 (16)	0.29425 (11)	0.0997 (7)*
C18	0.5079 (4)	1.07685 (15)	0.32565 (14)	0.0927 (7)
H18	0.5396 (4)	1.14762 (15)	0.33491 (14)	0.1112 (9)*
C17	0.5372 (3)	0.99762 (15)	0.37173 (11)	0.0815 (6)

H17 0.5869 (3) 1.01515 (15) 0.41227 (11) 0.0978 (7)*

Atomic displacement parameters (Å²)

	U^{11}	U^{22}	U^{33}	U^{12}	U^{13}	U^{23}
O6	0.0899 (8)	0.0477 (6)	0.0515 (6)	-0.0112 (6)	-0.0152 (6)	0.0009 (5)
O2	0.0561 (6)	0.0730 (7)	0.0468 (6)	0.0150 (6)	-0.0037 (5)	0.0023 (5)
O1	0.0901 (9)	0.0632 (7)	0.0378 (5)	0.0172 (6)	-0.0117 (5)	0.0021 (5)
O4	0.0891 (8)	0.0562 (6)	0.0493 (6)	-0.0231 (6)	-0.0050 (6)	0.0057 (5)
O5	0.1161 (12)	0.0786 (9)	0.0841 (10)	-0.0411 (9)	0.0108 (9)	0.0159 (8)
O7	0.1583 (16)	0.0694 (9)	0.0753 (9)	-0.0311 (10)	-0.0384 (10)	-0.0099 (7)
O3	0.1188 (12)	0.0758 (9)	0.0822 (9)	0.0425 (9)	0.0007 (8)	-0.0066 (8)
C8	0.0596 (9)	0.0467 (8)	0.0694 (10)	-0.0101 (7)	0.0105 (8)	-0.0016 (8)
C6	0.0513 (8)	0.0480 (7)	0.0362 (7)	0.0027 (6)	-0.0048 (6)	-0.0007 (6)
C15	0.0818 (12)	0.0530 (9)	0.0616 (10)	-0.0123 (9)	-0.0062 (9)	-0.0082 (8)
C1	0.0647 (9)	0.0509 (8)	0.0377 (7)	0.0075 (7)	-0.0067 (7)	0.0028 (6)
C2	0.0741 (11)	0.0695 (11)	0.0479 (9)	0.0199 (9)	-0.0099 (8)	0.0000 (8)
C16	0.0651 (10)	0.0499 (8)	0.0665 (10)	-0.0060 (8)	0.0097 (8)	-0.0026 (7)
C10	0.0619 (10)	0.0719 (11)	0.0643 (10)	-0.0136 (9)	0.0003 (8)	-0.0089 (9)
C7	0.0871 (12)	0.0570 (9)	0.0470 (8)	-0.0092 (9)	-0.0014 (8)	0.0097 (8)
C5	0.0712 (10)	0.0528 (8)	0.0461 (8)	-0.0060 (8)	-0.0139 (8)	0.0019 (7)
C9	0.0475 (8)	0.0561 (9)	0.0645 (10)	-0.0053 (7)	0.0034 (7)	-0.0114 (8)
C21	0.0688 (11)	0.0619 (10)	0.0646 (10)	-0.0105 (9)	0.0071 (9)	0.0044 (8)
C12	0.0619 (11)	0.1141 (17)	0.0710 (13)	0.0022 (12)	-0.0114 (9)	-0.0289 (12)
C11	0.0674 (11)	0.0993 (15)	0.0658 (11)	-0.0051 (11)	0.0001 (9)	-0.0011 (11)
C3	0.0533 (10)	0.1045 (16)	0.0894 (14)	0.0110 (11)	-0.0122 (10)	0.0037 (12)
C4	0.0609 (11)	0.0900 (15)	0.0819 (13)	-0.0174 (10)	-0.0138 (10)	0.0071 (11)
C13	0.0948 (16)	0.0893 (16)	0.1035 (17)	-0.0167 (14)	-0.0265 (14)	-0.0284 (14)
C19	0.0926 (15)	0.0704 (13)	0.1013 (17)	0.0091 (12)	0.0195 (14)	0.0237 (12)
C20	0.0843 (13)	0.0831 (14)	0.0718 (12)	-0.0052 (11)	0.0082 (10)	0.0185 (11)
C14	0.0847 (13)	0.0656 (12)	0.0991 (16)	-0.0195 (11)	-0.0116 (12)	-0.0095 (11)
C18	0.1104 (17)	0.0476 (10)	0.120 (2)	0.0003 (12)	0.0186 (16)	0.0019 (11)
C17	0.1022 (16)	0.0524 (10)	0.0900 (14)	-0.0077 (10)	0.0053 (12)	-0.0104 (9)

Geometric parameters (Å, °)

O6—C15	1.3344 (19)	C7—H7a	0.9700
O6—C5	1.4545 (19)	C7—H7b	0.9700
O2—H2	0.8200	C5—H5	0.9800
O2—C6	1.4033 (18)	C5—C4	1.489 (3)
O1—H1	0.8200	C9—C14	1.384 (2)
O1—C1	1.4253 (17)	C21—H21	0.9300
O4—C8	1.3270 (19)	C21—C20	1.381 (3)
O4—C7	1.4460 (19)	C12—H12	0.9300
O5—C8	1.196 (2)	C12—C11	1.382 (3)
O7—C15	1.206 (2)	C12—C13	1.346 (3)
O3—C2	1.211 (2)	C11—H11	0.9300
C8—C9	1.480 (2)	C3—H3	0.9300

C6—H6	0.9800	C3—C4	1.322 (3)
C6—C1	1.530 (2)	C4—H4	0.9300
C6—C5	1.512 (2)	C13—H13	0.9300
C15—C16	1.476 (2)	C13—C14	1.378 (3)
C1—C2	1.534 (2)	C19—H19	0.9300
C1—C7	1.509 (2)	C19—C20	1.377 (3)
C2—C3	1.456 (3)	C19—C18	1.364 (3)
C16—C21	1.382 (3)	C20—H20	0.9300
C16—C17	1.392 (2)	C14—H14	0.9300
C10—H10	0.9300	C18—H18	0.9300
C10—C9	1.372 (3)	C18—C17	1.376 (3)
C10—C11	1.385 (3)	C17—H17	0.9300
C5—O6—C15	116.55 (12)	C4—C5—O6	109.45 (15)
C6—O2—H2	109.5	C4—C5—C6	112.53 (15)
C1—O1—H1	109.5	C4—C5—H5	109.51 (11)
C7—O4—C8	116.34 (13)	C10—C9—C8	122.49 (14)
O5—C8—O4	121.95 (17)	C14—C9—C8	117.97 (17)
C9—C8—O4	113.45 (13)	C14—C9—C10	119.54 (18)
C9—C8—O5	124.59 (16)	H21—C21—C16	119.96 (10)
H6—C6—O2	107.42 (7)	C20—C21—C16	120.09 (18)
C1—C6—O2	112.06 (13)	C20—C21—H21	119.96 (13)
C1—C6—H6	107.42 (8)	C11—C12—H12	119.78 (14)
C5—C6—O2	113.32 (13)	C13—C12—H12	119.78 (13)
C5—C6—H6	107.42 (8)	C13—C12—C11	120.4 (2)
C5—C6—C1	108.92 (12)	C12—C11—C10	119.5 (2)
O7—C15—O6	121.68 (16)	H11—C11—C10	120.23 (13)
C16—C15—O6	113.40 (14)	H11—C11—C12	120.23 (14)
C16—C15—O7	124.92 (16)	H3—C3—C2	119.37 (11)
C6—C1—O1	105.64 (12)	C4—C3—C2	121.27 (19)
C2—C1—O1	109.44 (13)	C4—C3—H3	119.37 (13)
C2—C1—C6	108.75 (13)	C3—C4—C5	123.74 (19)
C7—C1—O1	108.46 (13)	H4—C4—C5	118.13 (10)
C7—C1—C6	112.11 (13)	H4—C4—C3	118.13 (13)
C7—C1—C2	112.22 (14)	H13—C13—C12	119.73 (13)
C1—C2—O3	121.86 (19)	C14—C13—C12	120.5 (2)
C3—C2—O3	122.50 (19)	C14—C13—H13	119.73 (14)
C3—C2—C1	115.64 (16)	C20—C19—H19	119.90 (14)
C21—C16—C15	122.19 (15)	C18—C19—H19	119.90 (12)
C17—C16—C15	118.61 (18)	C18—C19—C20	120.2 (2)
C17—C16—C21	119.19 (18)	C19—C20—C21	120.1 (2)
C9—C10—H10	120.00 (10)	H20—C20—C21	119.96 (13)
C11—C10—H10	120.00 (13)	H20—C20—C19	119.96 (14)
C11—C10—C9	120.00 (18)	C13—C14—C9	119.9 (2)
C1—C7—O4	108.20 (12)	H14—C14—C9	120.04 (13)
H7a—C7—O4	110.06 (10)	H14—C14—C13	120.04 (14)
H7a—C7—C1	110.06 (10)	H18—C18—C19	119.82 (13)
H7b—C7—O4	110.06 (9)	C17—C18—C19	120.4 (2)

H7b—C7—C1	110.06 (9)	C17—C18—H18	119.82 (14)
H7b—C7—H7a	108.4	C18—C17—C16	120.1 (2)
C6—C5—O6	106.27 (11)	H17—C17—C16	119.96 (13)
H5—C5—O6	109.51 (8)	H17—C17—C18	119.96 (14)
H5—C5—C6	109.51 (8)		

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>
O2—H2 \cdots O7 ⁱ	0.82	1.93 (1)	2.7029 (17)	157 (1)
O1—H1 \cdots O5 ⁱⁱ	0.82	1.89 (1)	2.7112 (17)	177 (2)
C13—H13 \cdots O2 ⁱⁱⁱ	0.93 (1)	2.53 (1)	3.221 (3)	132 (1)

Symmetry codes: (i) $x-1/2, -y+3/2, -z+1$; (ii) $x+1/2, -y+1/2, -z+1$; (iii) $-x, y-1/2, -z+1/2$.