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Crystal structure of (1*R*,3a*R*,7a*R*)-1-{(*S*)-1-[(2*R*,5*S*)-5-(3-hydroxypentan-3-yl)tetrahydrofuran-2-yl]-ethyl}-7a-methyl-2,3,3a,4,5,6,7,7a-octahydro-1*H*-inden-4-one

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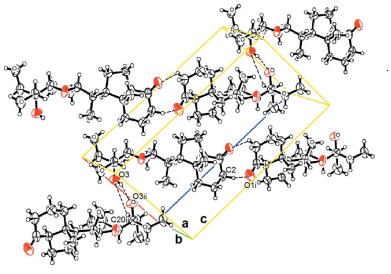
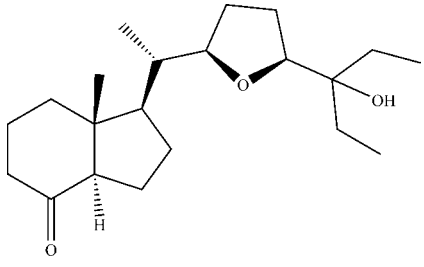
The title compound, $C_{21}H_{36}O_3$, contains an oxolane ring, and six defined stereocentres and may serve as a useful synthon for the synthesis of calcitriol analogues. The configurations of the chiral C atoms of the side chain were unambiguously established in the refinement. In the crystal, C—H···O and extremely weak O—H···O hydrogen bonds arising from the sterically hindered alcohol group link the molecules into a three-dimensional network.

1. Chemical context

The discovery of vitamin D3 (calcitriol) and its biological activity had a very important impact in the search for analogues of Vitamin D. In the structure of vitamin D, it is recognized that the side chain is the main site of metabolic degradation. Synthetic chemists have devoted considerable efforts to varying this chain in order to prepare analogues of vitamin D (Dai & Posner, 1994; Zhu *et al.*, 1995; Posner & Kahraman, 2003) and study the degradation metabolisms of these new molecules. Our ongoing interest in the chemistry of heterocyclic compounds, and particularly in the synthesis of vitamin D analogues, has led us to develop several methods for the synthesis of these compounds (Fernández *et al.*, 2016; Gándara *et al.*, 2009). We have also looked at their biological activities which are reported in the literature (Maehr *et al.*, 2004). Recently, we reported the synthesis of a new vitamin D2 analogue and the evaluation of its biological activity on colon cancer (Gándara *et al.*, 2012). In a continuation of our work on the analogues of vitamin D, we synthesized two new molecules of cacitriol from an oxolane ring and its side chains (Martínez *et al.*, 2013). In this study we present the structure of a new analog of calcitriol with six stereo centres.





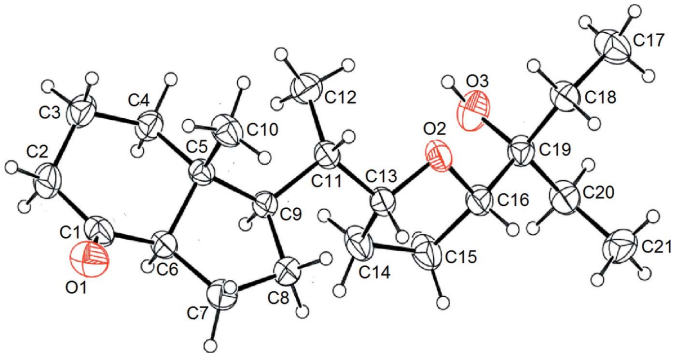


Figure 1
An *ORTEP* view of the title compound with displacement ellipsoids plotted at the 50% probability level.

2. Structural commentary

The molecular structure of the title compound is shown in Fig. 1: the compound crystallizes in the non-centrosymmetric space group $P2_1$ and the absolute structure was unambiguously established. The molecule contains a cyclopentane ring *trans*-fused to a cyclohexanone ring. The lateral chain contains an oxolane ring. The cyclohexanone ring adopts a chair conformation, the cyclopentane ring is an envelope (flap atom = C5) and the heterocyclic ring is twisted about C13—O2. The configurations of the stereogenic centres are C5(*R*), C6(*R*), C9(*R*), C11(*S*), C13(*R*) and C16(*S*). All bond distances and angles are within their expected ranges. The Csp^3—Csp^2 bonds involving C1 [1.499 (3) and 1.500 (3) Å] are naturally slightly shorter than the Csp^3—Csp^3 bonds [1.514 (3)–1.549 (5) Å]. The C1═O1 bond length [1.208 (3) Å] is typical of a C═O double bond, confirming oxidation of the starting alcohol.

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

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
O3—H3*O*···O3^{i}	0.82	2.67	3.4495 (9)	161
C2—H2*B*···O1^{ii}	0.97	2.57	3.273 (3)	130

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

3. Supramolecular features

In the crystal, C2—H2*B*···O1═C hydrogen bonds (Table 1, Fig. 2) link the molecules into *C*(4) chains, which propagate parallel to [101]. The chains are linked through very weak *C*(2) O3—H3*O*···O3 hydrogen bonds, giving rise to a three-dimensional supramolecular architecture. The O—H···O hydrogen bond is very long, presumably due to steric hindrance of the –OH group.

4. Database survey

A survey of the Cambridge Structural Database (Version 5.38, last update Nov 2016; Groom *et al.*, 2016) for the bicyclic moiety fragment (1*S*,3a*R*,7a*R*)-1-ethyl-7a-methyl-octahydro-inden-4-one) of the title compound revealed just three matches, *viz*. EFEHEE (Pietraszek *et al.*, 2013), LESNEE (Rivadulla *et al.*, 2013) and ZEBZIP (Schwarz *et al.*, 1995). In each case, the shared C—C bond of the [4.3.0]-bicyclic moiety presents a *trans* configuration, as does the structure reported here.

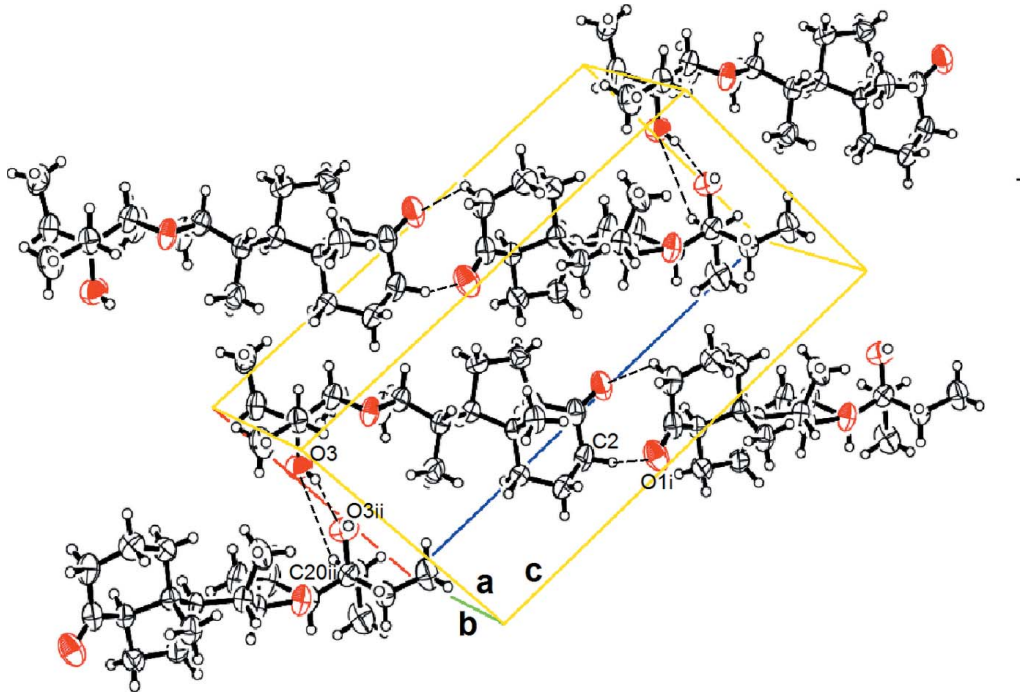
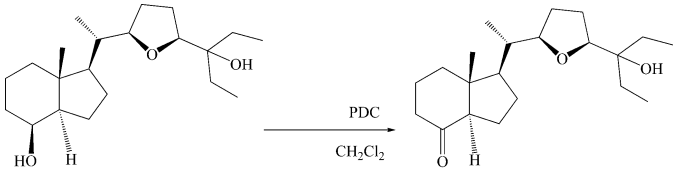


Figure 2
The packing of the title compound showing hydrogen bonds as dashed lines. [Symmetry codes: (i)-$x+2, y-\frac{1}{2}, -z+1$, (ii)-$x+1, y+\frac{1}{2}, -z+2$.]

5. Synthesis and crystallization

To a solution of diol **2** (0.18 mmol) in CH_2Cl_2 (5 ml), pyridinium dichromate (PDC) (0.37 mmol) was added, and the mixture stirred at room temperature for 12 h, then the solvent was evaporated and the residue was chromatographed on sílica gel using (10% EtOAc/hexane) to afford ketone **1**. The title compound was recrystallized as colourless blocks using a solvent mixture of hexane/ethyl ether (1:1).



2 **1**

Compound **1**: white solid; m.p. 382–384 K. yield: 83%; R_f: 0.54 (30% EtOAc/hexane). $[\alpha]_{20}^{D}$ = +31.39° (*c* 1.0, $CDCl_3$). ^{1}H NMR ($CDCl_3$, δ): 3.87 (1H, *m*, H-5′), 3.72 (1H, *m*, H-2′), 2.44 (1H, *dd*, *J* = 11.2, 7.4 Hz), 2.49–1.8 (6H, *m*), 1.79–1.65 (4H, *m*), 1.65–1.28 (8H, *m*), 1.27 (3H, *d*, *J* = 9.7 Hz), 0.95 (3H, *d*, *J* = 6.7 Hz, CH_3-21), 0.88 (6H,*q*, *J* = 7.6 Hz, CH_3-Et), 0.67 (3H, *S*, CH_3-18). ^{13}C NMR ($CDCl_3$, δ): 211.91 (C═O), 82.17 (CH-2′), 80.67 (CH-5′), 74.96 (C-3′′), 61.49 (CH-14), 54.50, 50.25 (CH-17, CH-13), 41.01 (CH_2), 38.97 (CH_2), 38.12 (CH-20), 28.65 (CH_2), 26.93 (CH_2), 26.23 (CH_2), 24.98 (CH_2), 24.52 (CH_2), 24.04 (CH_2), 19.21 (CH_2), 12.70 (CH_3-21), 12.55 (CH_3-18), 8.02 (CH_3-Et), 7.52 (CH_3-Et). IR (NaCl, cm^{-1}): 3532, 2964, 2939, 2881, 2347, 1714, 1460, 1381, 1246, 1136,1077, 958, 837. MS (ESI$^+$) [*m*/*z*, (%)]: 359.25 [(M + Na)$^+$, (54)]; 319.26 [(M − OH)$^+$,(100)]; 301.25 (15). HRMS (ESI$^+$): calculated for $C_{21}H_{36}NaO_3$, 359.25567 g mol^{-1}; found: 359.2556 g mol^{-1}.

6. Refinement

Crystal data, data collection and structure refinement details are summarized in Table 2. The hydroxy H atom was located from a difference Fourier map and relocated to an idealized (O—H = 0.82Å) location. The other H atoms (CH, CH_2 and CH_3 groups) were placed geometrically and refined as riding atoms with U_{iso}(H) = 1.2U_{eq}(C) (1.5 for CH_3 groups).

Table 2
Experimental details.

Crystal data	
Chemical formula	$C_{21}H_{36}O_3$
M_r	336.50
Crystal system, space group	Monoclinic, $P2_1$
Temperature (K)	296
a, *b*, *c* (Å)	9.4601 (3), 6.3779 (2), 16.7425 (4)
β (°)	104.196 (1)
V (Å^3)	979.32 (5)
Z	2
Radiation type	Cu $K\alpha$
μ (mm^{-1})	0.58
Crystal size (mm)	0.25 × 0.12 × 0.10
Data collection	
Diffractometer	Bruker *SMART APEX* CCD
Absorption correction	Multi-scan *SADABS* (Bruker, 2016)
T_{min}, T_{max}	0.662, 0.753
No. of measured, independent and observed [$I > 2\sigma(I)$] reflections	13069, 3679, 3594
R_{int}	0.036
(sin $\theta/\lambda)_{max}$ (Å^{-1})	0.613
Refinement	
$R[F^2 > 2\sigma(F^2)]$, $wR(F^2)$, S	0.033, 0.097, 1.05
No. of reflections	3679
No. of parameters	222
No. of restraints	1
H-atom treatment	H atoms treated by a mixture of independent and constrained refinement
$\Delta\rho_{max}$, $\Delta\rho_{min}$ (e Å^{-3})	0.14, −0.14
Absolute structure	Flack *x* determined using 1566 quotients [$(I^+)-(I^-)$]/[$(I^+)+(I^-)$] (Parsons et al., 2013)
Absolute structure parameter	−0.07 (7)

Computer programs: *APEX3* and *SAINT* (Bruker, 2016), *SHELXT* (Sheldrick, 2015*a*), *SHELXL-2014/7* (Sheldrick, 2015*b*) and *ORTEP-3 for Windows* (Farrugia, 2012).

Acknowledgements

The work of the MS and X-ray divisions of the research support service of the University of Vigo (CACTI) is also gratefully acknowledged. Andrea Martínez thanks the University of Vigo for a PhD fellowship.

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supporting information

Acta Cryst. (2017). E**73**, 115-117 [https://doi.org/10.1107/S2056989016020648]

Crystal structure of (1*R*,3a*R*,7a*R*)-1-{(*S*)-1-[(2*R*,5*S*)-5-(3-hydroxypentan-3-yl)tetrahydrofuran-2-yl]ethyl}-7a-methyl-2,3,3a,4,5,6,7,7a-octahydro-1*H*-inden-4-one

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Computing details

Data collection: *APEX3* (Bruker, 2016); cell refinement: *SAINT* (Bruker, 2016); data reduction: *SAINT* (Bruker, 2016); program(s) used to solve structure: *SHELXT* (Sheldrick, 2015a); program(s) used to refine structure: *SHELXL-2014/7* (Sheldrick, 2015b); molecular graphics: *ORTEP-3 for Windows* (Farrugia, 2012); software used to prepare material for publication: *SHELXL-2014/7* (Sheldrick, 2015b).

(1*R*,3a*R*,7a*R*)-1-{(*S*)-1-[(2*R*,5*S*)-5-(3-Hydroxypentan-3-yl)tetrahydrofuran-2-yl]ethyl}-7a-methyl-2,3,3a,4,5,6,7,7a-octahydro-1*H*-inden-4-one

Crystal data

$C_{21}H_{36}O_3$
M_r = 336.50
Monoclinic, $P2_1$
a = 9.4601 (3) Å
b = 6.3779 (2) Å
c = 16.7425 (4) Å
β = 104.196 (1)°
V = 979.32 (5) Å^3
Z = 2
$F(000)$ = 372
D_x = 1.141 Mg m^{-3}
Cu $K\alpha$ radiation, λ = 1.54178 Å
Cell parameters from 9988 reflections
θ = 2.4–28.6°
μ = 0.58 mm^{-1}
T = 296 K
Block, colourless
0.25 × 0.12 × 0.10 mm

Data collection

Bruker SMART APEX CCD diffractometer
Radiation source: fine-focus sealed tube
Detector resolution: 8.3333 pixels mm^{-1}
φ and ω scans
Absorption correction: multi-scan *SADABS* (Bruker, 2016)
T_{min} = 0.662, T_{max} = 0.753
13069 measured reflections
3679 independent reflections
3594 reflections with $I > 2\sigma(I)$
R_{int} = 0.036
θ_{max} = 71.0°, θ_{min} = 2.7°
h = −11→11
k = −7→7
l = −20→20

Refinement

Refinement on F^2
Least-squares matrix: full
$R[F^2 > 2\sigma(F^2)]$ = 0.033
$wR(F^2)$ = 0.097
S = 1.05
3679 reflections
222 parameters
1 restraint

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
$w = 1/[\sigma^2(F_o^2) + (0.0549P)^2 + 0.0933P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} < 0.001$
$\Delta\rho_{max} = 0.14$ e Å^{-3}
$\Delta\rho_{min} = -0.14$ e Å^{-3}
Extinction correction: SHELXL-2014/7 (Sheldrick 2015b), $Fc^* = kFc[1+0.001xFc^2\lambda^3/\sin(2\theta)]^{-1/4}$
Extinction coefficient: 0.0034 (10)
Absolute structure: Flack *x* determined using 1566 quotients $[(I^+)-(I^-)]/[(I^+)+(I^-)]$ (Parsons et al., 2013)
Absolute structure parameter: −0.07 (7)

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	0.9190 (2)	0.6570 (3)	0.46585 (10)	0.0761 (5)
O2	0.41676 (15)	0.5028 (2)	0.80627 (9)	0.0555 (4)
O3	0.44001 (17)	0.3383 (4)	0.97018 (11)	0.0768 (5)
H3O	0.480163	0.453143	0.975052	0.115*
C1	0.9416 (2)	0.6116 (3)	0.53792 (13)	0.0552 (5)
C2	1.0862 (2)	0.6426 (4)	0.59799 (15)	0.0651 (6)
H2A	1.147857	0.727399	0.572289	0.078*
H2B	1.133002	0.507331	0.611064	0.078*
C3	1.0739 (2)	0.7482 (4)	0.67748 (15)	0.0630 (6)
H3A	1.054571	0.896302	0.667028	0.076*
H3B	1.166385	0.735483	0.717955	0.076*
C4	0.9536 (2)	0.6548 (4)	0.71321 (12)	0.0523 (4)
H4A	0.981399	0.514090	0.732883	0.063*
H4B	0.943984	0.738532	0.759957	0.063*
C5	0.80678 (19)	0.6465 (3)	0.65022 (10)	0.0412 (4)
C6	0.82896 (19)	0.5162 (3)	0.57614 (11)	0.0456 (4)
H6	0.868329	0.380487	0.598623	0.055*
C7	0.6765 (2)	0.4733 (4)	0.52444 (13)	0.0626 (6)
H7A	0.673148	0.343325	0.493967	0.075*
H7B	0.642601	0.586840	0.485945	0.075*
C8	0.5838 (2)	0.4576 (4)	0.58867 (12)	0.0562 (5)
H8A	0.502692	0.554932	0.575205	0.067*
H8B	0.545476	0.316752	0.589496	0.067*
C9	0.68560 (18)	0.5124 (3)	0.67337 (10)	0.0422 (4)
H9	0.731850	0.380868	0.696278	0.051*
C10	0.7521 (3)	0.8691 (3)	0.62341 (14)	0.0589 (5)
H10A	0.653632	0.862000	0.590462	0.088*
H10B	0.813277	0.930699	0.591728	0.088*
H10C	0.755209	0.953355	0.671323	0.088*

C11	0.6037 (2)	0.5963 (3)	0.73561 (12)	0.0474 (4)
H11	0.553105	0.724547	0.712223	0.057*
C12	0.7015 (3)	0.6528 (5)	0.81908 (14)	0.0695 (6)
H12A	0.766322	0.538155	0.839097	0.104*
H12B	0.642665	0.680515	0.857150	0.104*
H12C	0.757405	0.775343	0.813787	0.104*
C13	0.4871 (2)	0.4371 (3)	0.74389 (13)	0.0500 (4)
H13	0.413816	0.429521	0.691234	0.060*
C14	0.5382 (3)	0.2155 (4)	0.77004 (18)	0.0672 (6)
H14A	0.633369	0.217278	0.808473	0.081*
H14B	0.543273	0.130859	0.722683	0.081*
C15	0.4227 (3)	0.1314 (4)	0.81102 (19)	0.0726 (7)
H15A	0.467379	0.066789	0.863599	0.087*
H15B	0.361078	0.028941	0.776109	0.087*
C16	0.3342 (2)	0.3267 (3)	0.82279 (13)	0.0532 (5)
H16	0.240605	0.323844	0.781623	0.064*
C17	0.0673 (3)	0.1360 (5)	0.86855 (17)	0.0792 (8)
H17A	0.077247	0.115555	0.813379	0.119*
H17B	0.009832	0.259036	0.870492	0.119*
H17C	0.020167	0.016174	0.885197	0.119*
C18	0.2170 (3)	0.1631 (4)	0.92637 (15)	0.0613 (5)
H18A	0.272883	0.036389	0.924591	0.074*
H18B	0.205358	0.177567	0.982067	0.074*
C19	0.3051 (2)	0.3499 (3)	0.90802 (13)	0.0506 (4)
C20	0.2324 (2)	0.5598 (3)	0.91465 (13)	0.0543 (5)
H20A	0.298507	0.670669	0.907616	0.065*
H20B	0.145850	0.570583	0.869632	0.065*
C21	0.1888 (3)	0.5971 (5)	0.99509 (15)	0.0750 (7)
H21A	0.153005	0.737676	0.995988	0.113*
H21B	0.272144	0.577529	1.040541	0.113*
H21C	0.113814	0.499588	0.999528	0.113*

Atomic displacement parameters (Å²)

	U^{11}	U^{22}	U^{33}	U^{12}	U^{13}	U^{23}
O1	0.1052 (13)	0.0728 (11)	0.0592 (9)	−0.0108 (10)	0.0371 (9)	0.0039 (8)
O2	0.0597 (8)	0.0400 (7)	0.0789 (9)	0.0002 (6)	0.0399 (7)	−0.0013 (6)
O3	0.0565 (8)	0.0872 (12)	0.0808 (11)	0.0013 (9)	0.0058 (8)	0.0121 (10)
C1	0.0704 (12)	0.0458 (10)	0.0583 (11)	0.0007 (9)	0.0326 (10)	−0.0009 (9)
C2	0.0582 (11)	0.0691 (14)	0.0773 (14)	−0.0098 (11)	0.0346 (11)	0.0008 (12)
C3	0.0544 (11)	0.0678 (14)	0.0690 (13)	−0.0168 (10)	0.0191 (10)	−0.0012 (10)
C4	0.0473 (9)	0.0599 (11)	0.0501 (9)	−0.0094 (9)	0.0129 (8)	−0.0010 (9)
C5	0.0460 (8)	0.0364 (9)	0.0433 (8)	0.0003 (7)	0.0150 (7)	0.0002 (7)
C6	0.0499 (9)	0.0429 (9)	0.0469 (9)	0.0016 (8)	0.0177 (7)	−0.0020 (8)
C7	0.0580 (11)	0.0794 (16)	0.0504 (10)	−0.0021 (11)	0.0133 (9)	−0.0143 (10)
C8	0.0446 (9)	0.0656 (13)	0.0573 (11)	−0.0028 (9)	0.0106 (8)	−0.0132 (10)
C9	0.0417 (8)	0.0392 (9)	0.0475 (9)	−0.0008 (7)	0.0142 (7)	−0.0020 (7)
C10	0.0729 (13)	0.0402 (10)	0.0700 (13)	0.0075 (9)	0.0299 (11)	0.0051 (9)

C11	0.0493 (9)	0.0417 (9)	0.0565 (10)	−0.0005 (7)	0.0228 (8)	−0.0038 (8)
C12	0.0716 (13)	0.0848 (17)	0.0594 (12)	−0.0226 (13)	0.0300 (10)	−0.0189 (12)
C13	0.0483 (9)	0.0452 (10)	0.0623 (11)	−0.0007 (8)	0.0244 (8)	−0.0052 (8)
C14	0.0746 (14)	0.0435 (11)	0.0989 (18)	0.0047 (10)	0.0503 (14)	0.0000 (11)
C15	0.0794 (15)	0.0432 (11)	0.1116 (19)	−0.0006 (11)	0.0550 (15)	−0.0024 (12)
C16	0.0538 (10)	0.0430 (10)	0.0695 (12)	−0.0031 (9)	0.0277 (9)	−0.0007 (9)
C17	0.0825 (16)	0.0829 (18)	0.0812 (15)	−0.0360 (14)	0.0372 (13)	−0.0116 (14)
C18	0.0705 (13)	0.0470 (11)	0.0751 (13)	−0.0012 (10)	0.0345 (11)	0.0064 (10)
C19	0.0470 (9)	0.0462 (10)	0.0603 (11)	0.0007 (8)	0.0165 (8)	0.0039 (8)
C20	0.0638 (11)	0.0476 (10)	0.0560 (11)	0.0007 (9)	0.0233 (9)	0.0001 (8)
C21	0.1001 (18)	0.0679 (15)	0.0673 (14)	0.0002 (13)	0.0401 (14)	−0.0036 (12)

Geometric parameters (Å, º)

O1—C1	1.208 (3)	C10—H10C	0.9600
O2—C13	1.432 (2)	C11—C12	1.518 (3)
O2—C16	1.433 (2)	C11—C13	1.531 (3)
O3—C19	1.437 (2)	C11—H11	0.9800
O3—H3O	0.8200	C12—H12A	0.9600
C1—C2	1.499 (3)	C12—H12B	0.9600
C1—C6	1.500 (3)	C12—H12C	0.9600
C2—C3	1.521 (3)	C13—C14	1.523 (3)
C2—H2A	0.9700	C13—H13	0.9800
C2—H2B	0.9700	C14—C15	1.523 (3)
C3—C4	1.530 (3)	C14—H14A	0.9700
C3—H3A	0.9700	C14—H14B	0.9700
C3—H3B	0.9700	C15—C16	1.540 (3)
C4—C5	1.525 (2)	C15—H15A	0.9700
C4—H4A	0.9700	C15—H15B	0.9700
C4—H4B	0.9700	C16—C19	1.525 (3)
C5—C10	1.540 (3)	C16—H16	0.9800
C5—C6	1.549 (2)	C17—C18	1.517 (4)
C5—C9	1.553 (2)	C17—H17A	0.9600
C6—C7	1.514 (3)	C17—H17B	0.9600
C6—H6	0.9800	C17—H17C	0.9600
C7—C8	1.548 (3)	C18—C19	1.527 (3)
C7—H7A	0.9700	C18—H18A	0.9700
C7—H7B	0.9700	C18—H18B	0.9700
C8—C9	1.546 (3)	C19—C20	1.521 (3)
C8—H8A	0.9700	C20—C21	1.521 (3)
C8—H8B	0.9700	C20—H20A	0.9700
C9—C11	1.539 (2)	C20—H20B	0.9700
C9—H9	0.9800	C21—H21A	0.9600
C10—H10A	0.9600	C21—H21B	0.9600
C10—H10B	0.9600	C21—H21C	0.9600
C13—O2—C16	106.49 (15)	C13—C11—H11	107.3
C19—O3—H3O	109.5	C9—C11—H11	107.3

O1—C1—C2	123.2 (2)	C11—C12—H12A	109.5
O1—C1—C6	123.6 (2)	C11—C12—H12B	109.5
C2—C1—C6	113.21 (17)	H12A—C12—H12B	109.5
C1—C2—C3	113.09 (18)	C11—C12—H12C	109.5
C1—C2—H2A	109.0	H12A—C12—H12C	109.5
C3—C2—H2A	109.0	H12B—C12—H12C	109.5
C1—C2—H2B	109.0	O2—C13—C14	103.51 (17)
C3—C2—H2B	109.0	O2—C13—C11	110.25 (15)
H2A—C2—H2B	107.8	C14—C13—C11	117.17 (17)
C2—C3—C4	113.19 (18)	O2—C13—H13	108.5
C2—C3—H3A	108.9	C14—C13—H13	108.5
C4—C3—H3A	108.9	C11—C13—H13	108.5
C2—C3—H3B	108.9	C13—C14—C15	104.13 (17)
C4—C3—H3B	108.9	C13—C14—H14A	110.9
H3A—C3—H3B	107.8	C15—C14—H14A	110.9
C5—C4—C3	112.45 (16)	C13—C14—H14B	110.9
C5—C4—H4A	109.1	C15—C14—H14B	110.9
C3—C4—H4A	109.1	H14A—C14—H14B	108.9
C5—C4—H4B	109.1	C14—C15—C16	104.18 (18)
C3—C4—H4B	109.1	C14—C15—H15A	110.9
H4A—C4—H4B	107.8	C16—C15—H15A	110.9
C4—C5—C10	110.68 (17)	C14—C15—H15B	110.9
C4—C5—C6	107.05 (14)	C16—C15—H15B	110.9
C10—C5—C6	111.29 (15)	H15A—C15—H15B	108.9
C4—C5—C9	116.71 (14)	O2—C16—C19	109.67 (16)
C10—C5—C9	111.36 (15)	O2—C16—C15	105.70 (15)
C6—C5—C9	99.07 (14)	C19—C16—C15	115.24 (19)
C1—C6—C7	120.41 (17)	O2—C16—H16	108.7
C1—C6—C5	111.94 (16)	C19—C16—H16	108.7
C7—C6—C5	104.92 (15)	C15—C16—H16	108.7
C1—C6—H6	106.2	C18—C17—H17A	109.5
C7—C6—H6	106.2	C18—C17—H17B	109.5
C5—C6—H6	106.2	H17A—C17—H17B	109.5
C6—C7—C8	103.70 (16)	C18—C17—H17C	109.5
C6—C7—H7A	111.0	H17A—C17—H17C	109.5
C8—C7—H7A	111.0	H17B—C17—H17C	109.5
C6—C7—H7B	111.0	C17—C18—C19	115.5 (2)
C8—C7—H7B	111.0	C17—C18—H18A	108.4
H7A—C7—H7B	109.0	C19—C18—H18A	108.4
C9—C8—C7	106.92 (16)	C17—C18—H18B	108.4
C9—C8—H8A	110.3	C19—C18—H18B	108.4
C7—C8—H8A	110.3	H18A—C18—H18B	107.5
C9—C8—H8B	110.3	O3—C19—C20	109.23 (18)
C7—C8—H8B	110.3	O3—C19—C16	109.91 (16)
H8A—C8—H8B	108.6	C20—C19—C16	110.00 (16)
C11—C9—C8	113.34 (14)	O3—C19—C18	104.20 (17)
C11—C9—C5	120.18 (15)	C20—C19—C18	113.14 (16)
C8—C9—C5	103.14 (14)	C16—C19—C18	110.19 (17)

C11—C9—H9	106.4	C21—C20—C19	115.33 (19)
C8—C9—H9	106.4	C21—C20—H20A	108.4
C5—C9—H9	106.4	C19—C20—H20A	108.4
C5—C10—H10A	109.5	C21—C20—H20B	108.4
C5—C10—H10B	109.5	C19—C20—H20B	108.4
H10A—C10—H10B	109.5	H20A—C20—H20B	107.5
C5—C10—H10C	109.5	C20—C21—H21A	109.5
H10A—C10—H10C	109.5	C20—C21—H21B	109.5
H10B—C10—H10C	109.5	H21A—C21—H21B	109.5
C12—C11—C13	111.35 (17)	C20—C21—H21C	109.5
C12—C11—C9	114.32 (16)	H21A—C21—H21C	109.5
C13—C11—C9	108.95 (15)	H21B—C21—H21C	109.5
C12—C11—H11	107.3		

Hydrogen-bond geometry (Å, º)

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
O3—H3*O*···O3^{i}	0.82	2.67	3.4495 (9)	161
C2—H2*B*···O1^{ii}	0.97	2.57	3.273 (3)	130

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