Crystal structure of (+)-(1S,5S,6S,7S,10S,11S,16S)-16-hydroxy-7-(methoxymethoxy)-11,15,18,18-tetramethyl-3,13-dioxo-2,4-dioxatetracyclo-[12.3.1.0\textsuperscript{1,5}.0\textsuperscript{6,11}]octadec-14-en-10-yl benzoate

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In the fused tetracyclic system of the title compound, C\textsubscript{29}H\textsubscript{36}O\textsubscript{9}, the five-membered dioxolane ring adopts a twist conformation; the two adjacent C atoms deviate alternately from the mean plane of the other three atoms by 0.252 (6) and 0.340 (6) Å. The cyclohexane, cyclohexene and central cyclooctane rings show chair, half-chair and boat-chair forms, respectively. There are three intramolecular C—H\cdots O interactions supporting the molecular conformation, with one S(6) and two S(7) graph-set motifs. In the crystal, intermolecular O—H\cdots O hydrogen bonds connect the molecules into a helical chain running along the c-axis direction, generating a C(7) graph-set motif. The chains are further linked by intermolecular C—H\cdots O interactions to construct a three-dimensional network. There is no valid C—H\cdots \pi interaction.

1. Chemical context

Paclitaxel (systematic name: (1S,2S,3R,4S,7R,9S,10S,12R,-15S)-4,12-diacetoxy-1,9-dihydroxy-15-[(2R,3S)-3-benzyloxy-propanoyl]oxy-10,14,17,17-tetramethyl-11-oxo-6-oxatetracyclo[11.3.1.0\textsuperscript{3,10}.0\textsuperscript{4,7}]heptadec-13-en-2-yl benzoate) is a well-known natural diterpenoid containing a taxane framework (tricyclo[9.3.1.0\textsuperscript{3,8}]pentadecane; Fig. 1), with potent antitumor activity (Wall & Wani, 1995). Its highly complicated structure and significant bioactivity have attracted wide chemical and medicinal interest.

Figure 1
Left: Structure of tricyclo[9.3.1.0\textsuperscript{3,8}]pentadecane (taxane) skeleton. Right: Core structure of the title compound. Red lines indicate the taxane skeleton. $R^1 = \text{OC(\text{==O})Ph}$, $R^2 = \text{OCH}_3\text{OCH}_3$. 

https://doi.org/10.1107/S2056989021011518
The title compound, which has a fused tetracyclic core composed of a taxane skeleton with an external cyclic carbonate, was afforded as a chiral form in an improved synthesis of paclitaxel (Iiyama et al., 2021). Several closely related structures (Oishi, Yamaguchi et al., 2015; Oishi, Fukaya et al., 2015a,b) obtained in another synthetic pathway (Fukaya, Tanaka et al., 2015; Fukaya, Kodama et al., 2015) have been reported previously as racemic crystals.

2. Structural commentary

The molecular structure of the title compound is shown in Fig. 2. The dioxolane ring (C1/C2/O22/C21/O20) adopts a twisted form with puckering parameters of $Q(2) = 0.351 (2)$ Å and $\varphi(2) = 56.6 (4)^\circ$. Atoms C1 and C2 deviate from the mean plane of the other three atoms by $0.250 (6)$ and $0.342 (6)$ Å, respectively. The cyclohexane ring (C3–C8) adopts a chair form with puckering parameters of $Q = 0.580 (2)$ Å and $\varphi (2) = 296.5 (17)^\circ$, $Q(2) = 0.083 (2)$ Å and $Q(3) = 0.574 (2)$ Å. The large substituents at C3, C4, C7 and C8 are in equatorial positions. The cyclohexene ring (C1/C14/C13/C12/C11) adopts a half-chair form with puckering parameters of $Q = 1.200 (2)$ Å, $Q(2) = 0.948 (2)$ Å, $Q(3) = 183.33 (15)^\circ$, $Q(4) = 0.588 (2)$ Å, $\varphi(3) = 3.3 (2)^\circ$ and $Q(4) = 0.444 (2)$ Å.

There are three intramolecular C–H⋯O interactions (C35–H35⋯O22, C18–H18A⋯O33 and C14–H14B⋯O34; Table 1), generating $S(7)$, $S(6)$ and $S(7)$ graph-set motifs, respectively (Fig. 3). The absolute structure was confirmed by the Flack parameter of 0.01 (7) with 1649 quotients $[(I^+) - (I^-)]/[[(I^+) + (I^-)]$ (Parsons et al., 2013).

![Figure 2](image1.png)

**Figure 2**
The molecular structure of the title compound with the atom labels. Displacement ellipsoids are drawn at the 30% probability levels. Only H atoms connected to O and chiral C atoms are shown for clarity.

![Figure 3](image2.png)

**Figure 3**
The molecular conformation with the intramolecular C–H⋯O interactions (black dashed lines). Only H atoms involved in these interactions and the hydroxy H atom are shown for clarity.

| $D$–H⋯$A$ | $D$–H | H⋯$A$ | $D$⋯$A$ | $D$–H⋯$A$ |
|-----------|-------|-------|--------|-----------|
| O38⋯H38⋯O33 | 0.84 | 2.49 | 3.251 (2) | 151 |
| C14⋯H14B⋯O34 | 0.99 | 2.57 | 3.423 (3) | 145 |
| C18⋯H18A⋯O33 | 0.98 | 2.53 | 3.244 (3) | 130 |
| C35⋯H35A⋯O22 | 0.99 | 2.36 | 2.990 (3) | 121 |
| C16⋯H16C⋯O26 | 0.98 | 2.43 | 3.331 (3) | 153 |
| C19⋯H19B⋯O26 | 0.98 | 2.59 | 3.534 (3) | 162 |
| C37⋯H37A⋯O23 | 0.98 | 2.52 | 3.445 (3) | 158 |

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

Table 1

Hydrogen-bond geometry (Å, °).
3. Supramolecular features

The crystal packing is stabilized by an O—H⋯O hydrogen bond (O38—H38⋯O33; symmetry code as given in Table 1), connecting the molecules into a helical chain running along the c-axis direction, with a C(7) graph-set motif (Fig. 4). The chains are linked by an intermolecular C—H⋯O hydrogen bond (C16—H16⋯O26; Table 1) to build a three-dimensional architecture. Furthermore, two weak C—H⋯O interactions (C37—H37⋯O23 and C19—H19⋯O26; Table 1) support to form the network densely (Figs. 5 and 6). There is no valid C—H⋯π interaction.

4. Database survey

In the Cambridge Structural Database (CSD Version 5.42, last update September 2021; Groom et al., 2016), 113 structures containing a tricyclo[9.3.1.03,8]pentadec-11-ene skeleton, (a), are registered (Fig. 7). These include two chiral compounds (CSD refcodes NEGBOQ; Poujol et al., 1997 and SUBQAJ; Hirai et al., 2015) possessing a 2,4-dioxatetracyclo[12.3.1.01,5.06,11]octadec-14-ene skeleton, (b), composed...
of syn-AB, anti-BC and anti-BD fused-ring systems similar to the title compound. Their ring conformations of the fused tetracycles (dioxolane, cyclohexane, cyclohexene and central cyclooctane) in the former structure are envelope, chair, half-chair and boat-chair forms, respectively, while those in the latter one are similar to the title compound as twist, chair, half-chair and boat-chair, respectively.

Four racemic structures closely related to the title compound, afforded by our previous synthesis, were also documented (XULNAV, XULMOI and XULMUO; Oishi, Fukaya et al., 2015a and GUHWUD; Oishi, Fukaya et al., 2015b). For the former three structures, possessing a 2,4-dioxatetracyclo[12.3.1.01,5.06,11]octadec-15-ene core, (c), their ring conformations of the tetracycles (dioxolane, cyclohexane, cyclohexene and central cyclooctane) are similar to one another as essentially planar, chair, half-chair and boat-chair forms, respectively. For the latter structure with a 2,4-dioxatetracyclo[12.3.1.01,5.06,11]octadeca-14,16-diene skeleton, (d), the ring conformations of dioxolane, cyclohexane, cyclohexene and central cyclooctane are twist, chair, half-boad and boat-chair forms, respectively. Although two crystalline compounds with a 2,4-dioxatetracyclo[12.3.1.01,5.06,11]octadeca-8,14-diene skeleton, (e), have been reported (Nicolaou, Ueno et al., 1995; Nicolaou, Yang et al., 1995), they are not registered in the CSD.

5. Synthesis and crystallization

The title compound was provided in an improved chiral synthesis of paclitaxel (Iiyama et al., 2021). The cyclohexene unit (C1/C14/C13/C12/C11/C15) was prepared according to the reported procedure (Nicolaou, Liu et al., 1995) from cyclohexene-1,3-dione, while the tetrasubstituted chiral cyclohexane unit (C3–C8) was derived from 3-methoxy-cyclohexane-1,3-dione, while the tetrasubstituted chiral deca-8,14-diene skeleton, (f), was registered in the CSD.

6. Refinement

Crystal data, data collection and structure refinement details are summarized in Table 2. C-bound H atoms were positioned geometrically with C–H = 0.95–1.00 Å, and constrained to ride on their parent atoms with Uiso(H) = 1.2Ueq(C) or 1.5Ueq(C/methyl C). The hydroxy H atom was located in a difference map and was allowed to refine as riding, with O–H = 0.84 Å, and with Uiso(H) = 1.5Ueq(O).

| Table 2 | Experimental details. |
|-----------------|-----------------------|
| Chemical formula | C29H36O9Na+ |
| Crystal system, space group | Orthorhombic, P212121 |
| Temperature (K) | 90 |
| a, b, c (Å) | 13.2073 (2), 13.2580 (2), 14.8563 (2) |
| V (Å³) | 2601.37 (7) |
| Z | 4 |
| Radiation type | Cu Kα |
| µ (mm⁻¹) | 0.83 |
| Crystal size (mm) | 0.27 × 0.14 × 0.09 |
| Data collection | Bruker D8 Venture |
| Diffractometer | Multi-scan (SADABS; Bruker, 2016) |
| Absorption correction | 0.041 |
| Tmin, Tmax | 0.595 |
| No. of measured, independent and observed | 17552, 4488, 4049 |
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Crystal structure of (+)-(1S,5S,6S,7S,10S,11S,16S)-16-hydroxy-7-(methoxymethoxy)-11,15,18,18-tetramethyl-3,13-dioxo-2,4-dioxatetracyclo[12.3.1.0^1,5.0^6,11]octadec-14-en-10-yl benzoate

Takeshi Oishi, Keisuke Fukaya, Takaaki Sato and Noritaka Chida

Computing details

Data collection: APEX3 (Bruker, 2016); cell refinement: SAINT (Bruker, 2016); data reduction: SAINT (Bruker, 2016); program(s) used to solve structure: SHELXT2014 (Sheldrick, 2015a); program(s) used to refine structure: SHELXL2014 (Sheldrick, 2015b); molecular graphics: Mercury (Macrae et al., 2020); software used to prepare material for publication: publCIF (Westrip, 2010) and PLATON (Spek, 2020).

(+)-(1S,5S,6S,7S,10S,11S,16S)-16-Hydroxy-7-(methoxymethoxy)-11,15,18,18-tetramethyl-3,13-dioxo-2,4-dioxatetracyclo[12.3.1.0^1,5.0^6,11]octadec-14-en-10-yl benzoate

Crystal data

\[C_{29}H_{36}O_9\]

\[M_r = 528.58\]

Orthorhombic, \(P2_12_12_1\)

\(a = 13.2073 (2) \text{ Å}\)

\(b = 13.2580 (2) \text{ Å}\)

\(c = 14.8563 (2) \text{ Å}\)

\(V = 2601.37 (7) \text{ Å}^3\)

\(Z = 4\)

\(F(000) = 1128\)

\(D_x = 1.350 \text{ Mg m}^{-3}\)

Melting point = 508–505 K

\(\theta = 4.5–66.6^\circ\)

\(\mu = 0.83 \text{ mm}^{-1}\)

\(T = 90 \text{ K}\)

Needle, colorless

0.27 \times 0.14 \times 0.09 \text{ mm}

Data collection

Bruker D8 Venture diffractometer

Radiation source: fine-focus sealed tube

Multilayered confocal mirror monochromator

Detector resolution: 10.4167 pixels mm\(^{-1}\)

\(\varphi\) and \(\omega\) scans

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

\(T_{\text{min}} = 0.84, T_{\text{max}} = 0.93\)

17552 measured reflections

4488 independent reflections

4049 reflections with \(I > 2\sigma(I)\)

\(R_{\text{int}} = 0.041\)

\(\theta_{\text{max}} = 66.6^\circ, \theta_{\text{min}} = 4.5^\circ\)

\(h = -15\rightarrow15\)

\(k = -13\rightarrow15\)

\(l = -17\rightarrow17\)

Refinement

Refinement on \(F^2\)

Least-squares matrix: full

\(R(F^2 > 2\sigma(F^2)) = 0.028\)

\(wR(F^2) = 0.058\)

\(S = 1.00\)

4488 reflections

349 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-atom parameters constrained
\[ w = \frac{1}{\sigma^2(F_o^2) + 0.9512P} \]
where \( P = (F_o^2 + 2F_c^2)/3 \)
\( (\Delta/\sigma)_{\text{max}} < 0.001 \)
\( \Delta \rho_{\text{max}} = 0.19 \text{ e} \text{Å}^{-3} \)
\( \Delta \rho_{\text{min}} = -0.17 \text{ e} \text{Å}^{-3} \)
Absolute structure: Flack \( \times \) determined using 1649 quotients \([ (I^+)-(I^-)]/[(I^+)+(I^-)]\) (Parsons et al., 2013).
Absolute structure parameter: 0.01 (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.

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 \( F^2 > 2 \sigma(F^2) \) 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.
Problematic ten reflections (1 7 0, 0 9 1, 5 1 5, 0 0 8, 1 1 1 1, 2 7 0, –2 13 2, 2 1 7, 1 1 2 2, 2 1 3 2) with \( |I(\text{obs})-I(\text{calc})|/\sigma W(I) \) greater than 10 have been omitted in the final refinement.

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

|     | x          | y          | z          | \( U_{\text{eq}} \) |
|-----|------------|------------|------------|-------------------|
| C1  | 0.29313 (18)| 0.36157 (17)| 0.52288 (15)| 0.0185 (5)       |
| C2  | 0.40702 (17)| 0.34711 (17)| 0.54120 (14)| 0.0165 (5)       |
| H2  | 0.4148     | 0.2822     | 0.5748     | 0.02*            |
| C3  | 0.46542 (17)| 0.42818 (16)| 0.59392 (14)| 0.0154 (5)       |
| C4  | 0.6045     | 0.4258     | 0.524      | 0.02*            |
| C5  | 0.60464 (18)| 0.55792 (19)| 0.60195 (15)| 0.0222 (5)       |
| C6  | 0.6669     | 0.5815     | 0.5713     | 0.027*           |
| C7  | 0.6688     | 0.4729     | 0.6928     | 0.024*           |
| C8  | 0.49959 (17)| 0.38399 (17)| 0.68729 (14)| 0.0163 (5)       |
| C9  | 0.42449 (18)| 0.33002 (18)| 0.74281 (15)| 0.0190 (5)       |
| H9A | 0.405      | 0.2628     | 0.7151     | 0.023*           |
| H9B | 0.4427     | 0.3181     | 0.8036     | 0.023*           |
| C10 | 0.30917 (18)| 0.37388 (17)| 0.75641 (16)| 0.0192 (5)       |
| C11 | 0.25421 (17)| 0.40784 (17)| 0.67406 (15)| 0.0184 (5)       |
| C12 | 0.24790 (18)| 0.50668 (17)| 0.65522 (16)| 0.0194 (5)       |
| C13 | 0.22472 (18)| 0.54081 (18)| 0.55976 (15)| 0.0219 (5)       |
| H13 | 0.1498     | 0.5487     | 0.5533     | 0.026*           |
| C14 | 0.26259 (19)| 0.46571 (18)| 0.48757 (15)| 0.0206 (5)       |
| H14A| 0.2085     | 0.4568     | 0.4421     | 0.025*           |
| H14B| 0.3217     | 0.4959     | 0.4566     | 0.025*           |
| C15 | 0.22581 (18)| 0.32944 (18)| 0.60119 (15)| 0.0203 (5)       |
### Atomic displacement parameters (Å²)

|     | U₁₁       | U₂₂       | U₃₃       | U₁₂     | U₁₃     | U₂₃    |
|-----|-----------|-----------|-----------|---------|---------|--------|
| C1  | 0.0221 (13)| 0.0182 (13)| 0.0153 (12)| −0.0001 (9)| −0.0062 (10)| −0.0049 (9) |
| C2  | 0.0206 (12)| 0.0169 (13)| 0.0121 (11)| 0.0014 (9)| 0.0000 (9)| 0.0006 (9) |
| C3  | 0.0181 (12)| 0.0143 (12)| 0.0139 (10)| 0.0033 (9)| −0.0001 (10)| −0.0004 (9) |
| C4  | 0.0198 (12)| 0.0166 (13)| 0.0146 (11)| 0.0021 (9)| −0.0008 (10)| 0.0015 (9) |
| C5  | 0.0231 (13)| 0.0230 (14)| 0.0204 (12)| −0.0060 (10)| 0.0013 (11)| 0.0029 (10) |
| C6  | 0.0221 (13)| 0.0172 (14)| 0.0204 (12)| −0.0046 (9)| −0.0034 (10)| −0.0015 (9) |
| C7  | 0.0237 (13)| 0.0151 (13)| 0.0124 (11)| 0.0021 (9)| −0.0030 (9)| 0.0005 (9) |
| C8  | 0.0187 (12)| 0.0156 (12)| 0.0148 (11)| −0.0003 (9)| −0.0017 (10)| 0.0007 (9) |
| C9  | 0.0251 (14)| 0.0174 (12)| 0.0144 (11)| −0.0032 (9)| −0.0033 (10)| 0.0012 (9) |
| C10 | 0.0255 (13)| 0.0129 (12)| 0.0193 (13)| −0.0056 (9)| 0.0010 (11)| −0.0023 (9) |
| C11 | 0.0141 (12)| 0.0226 (14)| 0.0184 (11)| 0.0001 (9)| 0.0031 (10)| −0.0020 (9) |
| C12 | 0.0162 (11)| 0.0219 (13)| 0.0202 (12)| 0.0033 (9)| 0.0029 (10)| −0.0032 (9) |
| C13 | 0.0218 (13)| 0.0201 (13)| 0.0238 (12)| 0.0048 (10)| 0.0001 (10)| 0.0005 (10) |
| C14 | 0.0207 (13)| 0.0241 (13)| 0.0169 (11)| 0.0034 (10)| −0.0029 (10)| −0.0004 (9) |
| C15 | 0.0196 (13)| 0.0208 (13)| 0.0204 (12)| −0.0012 (10)| −0.0026 (10)| −0.0003 (10) |
| C16 | 0.0246 (13)| 0.0214 (13)| 0.0258 (13)| −0.0052 (10)| −0.0020 (11)| −0.0016 (10) |
| C17 | 0.0220 (14)| 0.0322 (16)| 0.0308 (14)| −0.0043 (11)| −0.0020 (11)| −0.0027 (11) |
| C18 | 0.0402 (16)| 0.0227 (14)| 0.0206 (12)| 0.0036 (11)| 0.0015 (12)| −0.0039 (10) |
| C19 | 0.0241 (13)| 0.0185 (13)| 0.0166 (11)| 0.0019 (9)| −0.0047 (10)| 0.0001 (9) |
| O20 | 0.0252 (9) | 0.0228 (9) | 0.0182 (8) | 0.0006 (7) | −0.0064 (7) | −0.0071 (7) |
| C21 | 0.0291 (14)| 0.0180 (13)| 0.0190 (12)| 0.0069 (10)| −0.0067 (11)| −0.0015 (10) |
| O22 | 0.0238 (9) | 0.0204 (9) | 0.0138 (8) | 0.0029 (7) | −0.0007 (7) | −0.0039 (6) |
| O23 | 0.0308 (9) | 0.0314 (11)| 0.0189 (9) | 0.0117 (8) | −0.0075 (8) | −0.0098 (8) |
| O24 | 0.0239 (9) | 0.0150 (9) | 0.0134 (7) | 0.0014 (6) | −0.0047 (7) | −0.0004 (6) |
| C25 | 0.0161 (11)| 0.0186 (14)| 0.0183 (11)| −0.0016 (9)| −0.0003 (10)| −0.0035 (9) |
| O26 | 0.0350 (10)| 0.0170 (10)| 0.0221 (9) | 0.0007 (7) | 0.0006 (8) | −0.0025 (7) |
| C27 | 0.0149 (12)| 0.0245 (14)| 0.0159 (11)| 0.0008 (9)| −0.0006 (10)| 0.0000 (9) |
| C28 | 0.0253 (14)| 0.0276 (15)| 0.0193 (12)| −0.0007 (11)| −0.0033 (11)| 0.0005 (10) |
| C29 | 0.0337 (15)| 0.0334 (16)| 0.0287 (15)| −0.0021 (12)| −0.0025 (12)| 0.0114 (11) |
| C30 | 0.0332 (16)| 0.055 (2)  | 0.0186 (13)| 0.0010 (13)| −0.0009 (12)| 0.0112 (12) |
| C31 | 0.0275 (14)| 0.055 (2)  | 0.0150 (12)| 0.0018 (13)| −0.0016 (11)| −0.0082 (12) |
| C32 | 0.0218 (13)| 0.0300 (15)| 0.0224 (13)| 0.0014 (10)| −0.0001 (10)| −0.0056 (10) |
| O33 | 0.0354 (10)| 0.0296 (10)| 0.0188 (9) | 0.0012 (8) | 0.0062 (8) | 0.0013 (7) |
| O34 | 0.0247 (9) | 0.0197 (9) | 0.0124 (8) | 0.0025 (6) | 0.0011 (7) | 0.0023 (6) |
| C35 | 0.0290 (14)| 0.0253 (14)| 0.0163 (12)| 0.0019 (11)| 0.0031 (10)| 0.0004 (9) |
| O36 | 0.0272 (10)| 0.0276 (10)| 0.0236 (9) | 0.0022 (7) | 0.0067 (7) | 0.0051 (7) |
| C37 | 0.0298 (15)| 0.0291 (16)| 0.0307 (14)| −0.0024 (11)| 0.0034 (12)| 0.0113 (11) |
| O38 | 0.0482 (12)| 0.0182 (10)| 0.0269 (9) | 0.0012 (8) | 0.0030 (9) | 0.0029 (7) |

### Geometric parameters (Å, °)

|     | C1—O20  | C15—C17 | C1—C14 | C16—H16A | C16—H16B | C1—C2 |
|-----|---------|---------|--------|-----------|-----------|--------|
|     | 1.480 (3)| 1.539 (3)| 1.531 (3)| 0.98      | 0.98      | 1.541 (3) |

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| Bond            | Distance (Å) | Torsion (°) | Bond Angle (°) |
|-----------------|--------------|-------------|----------------|
| C2—O22          | 1.456 (3)    |             |                |
| C2—C3           | 1.537 (3)    |             |                |
| C2—H2           | 1.0          |             |                |
| C3—C4           | 1.540 (3)    |             |                |
| C3—C8           | 1.572 (3)    |             |                |
| C3—H3           | 1.0          |             |                |
| C4—O34          | 1.437 (3)    |             |                |
| C4—C5           | 1.528 (3)    |             |                |
| C4—H4           | 1.0          |             |                |
| C5—C6           | 1.528 (3)    |             |                |
| C5—H5A          | 0.99         |             |                |
| C5—H5B          | 0.99         |             |                |
| C6—C7           | 1.512 (3)    |             |                |
| C6—H6A          | 0.99         |             |                |
| C6—H6B          | 0.99         |             |                |
| C7—O24          | 1.452 (3)    |             |                |
| C7—C8           | 1.543 (3)    |             |                |
| C7—H7           | 1.0          |             |                |
| C8—C9           | 1.567 (3)    |             |                |
| C8—C10          | 1.521 (3)    |             |                |
| C9—H9A          | 0.99         |             |                |
| C9—H9B          | 0.99         |             |                |
| C10—O33         | 1.219 (3)    |             |                |
| C10—C11         | 1.492 (3)    |             |                |
| C11—C12         | 1.343 (3)    |             |                |
| C11—C15         | 1.547 (3)    |             |                |
| C12—C18         | 1.500 (3)    |             |                |
| C12—C13         | 1.520 (3)    |             |                |
| C13—O38         | 1.428 (3)    |             |                |
| C13—C14         | 1.547 (3)    |             |                |
| C13—H13         | 1.0          |             |                |
| C14—H14A        | 0.99         |             |                |
| C14—H14B        | 0.99         |             |                |
| C15—C16         | 1.538 (3)    |             |                |

**Bond Angle (°)**

| Bond Angle      | Value       |
|-----------------|-------------|
| O20—C1—C14     | 106.57 (17) |
| O20—C1—C15     | 110.51 (18) |
| C14—C1—C15     | 111.1 (2)   |
| O20—C1—C2      | 98.67 (17)  |
| C14—C1—C2      | 115.5 (2)   |
| C15—C1—C2      | 113.56 (18) |
| O22—C2—C1      | 101.31 (16) |
| O22—C2—C3      | 113.62 (18) |
| C1—C2—C3       | 119.53 (18) |
| O22—C2—H2      | 107.2       |
| C1—C2—H2       | 107.2       |
| C3—C2—H2       | 107.2       |

**Bond Torsion (°)**

| Torsion         | Value       |
|-----------------|-------------|
| H14A—C14—C14—C14| 107.5      |
| C16—C15—C1      | 113.3 (2)   |
| C16—C15—C11     | 115.70 (19) |
| C1—C15—C11      | 101.82 (18) |
| C16—C15—C17     | 105.1 (2)   |
| C1—C15—C17      | 111.90 (19) |
| C11—C15—C17     | 109.2 (2)   |
| C15—C16—H16A    | 109.5       |
| C15—C16—H16B    | 109.5       |
| H16A—C16—H16C   | 109.5       |

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| Bond          | Value (°)   | Bond          | Value (°)   |
|---------------|-------------|---------------|-------------|
| C4—C3—C2     | 115.54 (18) | C16B—C16—H16C| 109.5       |
| C4—C3—C8     | 111.83 (18) | C15—C17—H17A | 109.5       |
| C2—C3—C8     | 109.45 (17) | C15—C17—H17B | 109.5       |
| C4—C3—H3     | 106.5       | H17A—C17—H17B| 109.5       |
| C2—C3—H3     | 106.5       | C15—C17—H17C | 109.5       |
| C8—C3—H3     | 106.5       | H17A—C17—H17C| 109.5       |
| O34—C4—C5    | 106.83 (17) | H17B—C17—H17C| 109.5       |
| O34—C4—C3    | 107.50 (18) | C12—C18—H18A | 109.5       |
| C5—C4—C3     | 110.50 (18) | C12—C18—H18B | 109.5       |
| O34—C4—H4    | 110.6       | C18A—C18—H18B| 109.5       |
| C5—C4—H4     | 110.6       | C12—C18—H18C | 109.5       |
| C3—C4—H4     | 110.6       | H18A—C18—H18C| 109.5       |
| C6—C5—C4     | 114.42 (19) | C18B—C18—H18C| 109.5       |
| C6—C5—H5A    | 108.7       | C8—C19—H19A  | 109.5       |
| C4—C5—H5A    | 108.7       | C8—C19—H19B  | 109.5       |
| C6—C5—H5B    | 108.7       | H19A—C19—H19B| 109.5       |
| C4—C5—H5B    | 108.7       | C8—C19—H19C  | 109.5       |
| H5A—C5—H5B   | 107.6       | H19A—C19—H19C| 109.5       |
| C7—C6—C5     | 110.63 (19) | H19B—C19—H19C| 109.5       |
| C7—C6—H6A    | 109.5       | C21—O20—C1   | 108.42 (17) |
| C5—C6—H6A    | 109.5       | O23—C21—O22  | 124.0 (2)   |
| C7—C6—H6B    | 109.5       | O23—C21—O20  | 124.7 (2)   |
| C5—C6—H6B    | 109.5       | O22—C21—O20  | 111.32 (19) |
| H6A—C6—H6B   | 108.1       | C21—O22—C2   | 107.14 (17) |
| O24—C7—C6    | 110.20 (18) | C21—O24—C7   | 117.86 (17) |
| O24—C7—C8    | 106.39 (17) | O26—C25—O24  | 123.7 (2)   |
| C6—C7—C8     | 112.53 (18) | O26—C25—C27  | 124.6 (2)   |
| O24—C7—H7    | 109.2       | O24—C25—C27  | 111.59 (19) |
| C6—C7—H7     | 109.2       | C28—C27—C32  | 119.6 (2)   |
| C8—C7—H7     | 109.2       | C28—C27—C25  | 121.9 (2)   |
| C19—C8—C7    | 109.88 (18) | C32—C27—C25  | 118.3 (2)   |
| C19—C8—C9    | 104.65 (18) | C27—C28—C29  | 120.8 (2)   |
| C7—C8—C9     | 109.74 (17) | C27—C28—H28  | 119.6       |
| C19—C8—C3    | 110.79 (17) | C29—C28—H28  | 119.6       |
| C7—C8—C3     | 106.39 (17) | C28—C29—C30  | 119.1 (3)   |
| C9—C8—C3     | 115.39 (18) | C28—C29—H29  | 120.5       |
| C10—C9—C8    | 123.5 (2)   | C30—C29—H29  | 120.5       |
| C10—C9—H9A   | 106.5       | C31—C30—C29  | 120.5 (2)   |
| C8—C9—H9A    | 106.5       | C31—C30—H30  | 119.7       |
| C10—C9—H9B   | 106.5       | C29—C30—H30  | 119.7       |
| C8—C9—H9B    | 106.5       | C30—C31—C32  | 120.2 (2)   |
| H9A—C9—H9B   | 106.5       | C30—C31—H31  | 119.9       |
| O33—C10—C11  | 123.3 (2)   | C32—C31—H31  | 119.9       |
| O33—C10—C9   | 119.9 (2)   | C31—C32—C27  | 119.7 (3)   |
| C11—C10—C9   | 116.8 (2)   | C31—C32—H32  | 120.2       |
| C12—C11—C10  | 119.7 (2)   | C27—C32—H32  | 120.2       |
| C12—C11—C15  | 119.7 (2)   | C35—O34—C4   | 115.45 (17) |
| C10—C11—C15  | 119.28 (19) | O36—C35—O34  | 114.06 (19) |
C1—C12—C18 124.2 (2)  O36—C35—H35A 108.7
C11—C12—C13 119.8 (2)  O34—C35—H35A 108.7
C18—C12—C13 115.7 (2)  O36—C35—H35B 108.7
O38—C13—C14 107.78 (19)  O34—C35—H35B 108.7
C12—C13—C14 112.97 (19)  O35A—C35—H35B 107.6
C13—C14—H13 108.7  O36—C37—H37A 109.5
C12—C13—H13 108.7  O36—C37—H37B 109.5
C14—C13—H13 108.7  H37A—C37—H37B 107.6
C1—C14—C13 115.35 (19)  C35—O36—C37 113.11 (19)
O38—C13—C14 109.87 (19)  C15—C1—C14—C13 13.7 (3)
H35A—C35—H35B 107.6  O20—C1—C15—C16 169.37 (19)
C12—C13—C14—C1 13.7 (3)  C14—C1—C15—C16 −65.7 (2)
O38—C13—C14—C1 107.78 (19)  C12—C13—C14—C1 13.7 (3)
O34—C35—H35A 108.7  C12—C13—C14—C1 13.7 (3)
O36—C35—H35B 108.7  C15—C1—C14—C13 13.7 (3)
O36—C35—H35B 108.7  C12—C13—C14—C1 13.7 (3)
C1—C14—C13 115.35 (19)  O36—C35—H35B 108.7
C1—C14—C13 115.35 (19)  O36—C37—H37A 109.5
C1—C14—C13 115.35 (19)  O36—C37—H37B 109.5
C1—C14—H14A 108.4  H37A—C37—H37B 107.6
C1—C14—H14B 108.4  C35—O36—C37 113.11 (19)
C13—C14—H14B 108.4  C15—C1—C14—C13 13.7 (3)
C13—C14—H14B 108.4  O20—C1—C15—C16 169.37 (19)
C13—C14—H14B 108.4  C14—C1—C15—C16 −65.7 (2)
C13—C14—H14B 108.4  O20—C1—C15—C11 176.24 (17)
O20—C1—C15—C11 34.9 (3)  C15—C1—C14—C13 −96.3 (2)
O20—C1—C15—C11 34.9 (3)  C2—C1—C14—C13 13.7 (3)
C14—C1—C2—O22 34.44 (19)  O20—C1—C15—C17 50.8 (3)
C14—C1—C2—O22 34.44 (19)  C14—C1—C15—C17 50.8 (3)
C15—C1—C2—O22 −78.6 (2)  C15—C1—C15—C17 −67.3 (3)
C15—C1—C2—O22 −78.6 (2)  C14—C1—C15—C17 −177.11 (19)
C14—C1—C2—C3 151.38 (18)  C2—C1—C15—C17 −177.11 (19)
C14—C1—C2—C3 151.38 (18)  C15—C1—C15—C17 −67.3 (3)
O20—C1—C2—C3 47.0 (3)  C14—C1—C15—C17 50.8 (3)
O20—C1—C2—C3 −83.0 (3)  O20—C1—C15—C11 64.4 (2)
O22—C2—C3—C4 −0.3 (3)  O20—C1—C15—C11 64.4 (2)
O22—C2—C3—C4 −0.3 (3)  C2—C1—C15—C11 −112.5 (2)
C1—C2—C3—C4 −119.9 (2)  C2—C1—C15—C11 −66.4 (2)
C2—C3—C4—C5 179.00 (18)  C2—C1—C15—C11 −112.5 (2)
C2—C3—C4—C5 179.00 (18)  C2—C1—C15—C11 64.4 (2)
C8—C3—C4—C5 −54.9 (2)  C2—C1—C15—C11 64.4 (2)
C8—C3—C4—C5 −54.9 (2)  C2—C1—C15—C11 64.4 (2)
O34—C4—C5—C6 160.10 (18)  C10—C11—C15—C16 177.5 (2)
C3—C4—C5—C6 50.4 (3)  C10—C11—C15—C16 10.9 (3)
C4—C5—C6—C7 −51.3 (3)  C12—C11—C15—C16 54.3 (3)
C5—C6—C7—O24 175.86 (18)  C12—C11—C15—C1 112.5 (2)
C5—C6—C7—O24 175.86 (18)  C12—C11—C15—C1 −64.2 (3)
C6—C7—C8—C9 −178.56 (18)  C14—C1—O20—C21 91.8 (2)
C6—C7—C8—C9 −178.56 (18)  C15—C1—O20—C21 −147.45 (19)
C6—C7—C8—C9 57.3 (3)  C2—C1—O20—C21 −28.2 (2)
C6—C7—C8—C9 57.3 (3)  C1—O20—C21—O23 −170.0 (2)
O24—C7—C8—C19 −61.5 (2)  C1—O20—C21—O23 10.3 (2)
C6—C7—C8—C9 −60.1 (2)  O23—C21—O22—C2 −165.5 (2)
C6—C7—C8—C9 −60.1 (2)  O20—C21—O22—C2 14.2 (2)
C2—C3—C4—C5 −51.3 (3)  C1—O20—C21—O23 −31.1 (2)
C2—C3—C4—C5 −51.3 (3)  C3—C2—O22—C21 160.57 (18)
C2—C3—C4—C5 −51.3 (3)  C6—C7—O24—C25 88.2 (2)
C2—C3—C4—C5 −51.3 (3)  C8—C7—O24—C25 −149.56 (18)
O24—C7—C8—C19 −61.5 (2)  C7—O24—C25—O26 −8.0 (3)
C6—C7—C8—C9 53.1 (2)  C7—O24—C25—O26 169.16 (18)
C6—C7—C8—C9 53.1 (2)  O26—C25—C27—C28 160.2 (2)
C6—C7—C8—C9 53.1 (2)  O26—C25—C27—C28 160.2 (2)
C3—C8—C9—C10  −45.9 (3) O24—C25—C27—C28  −17.0 (3)
C8—C9—C10—O33  −130.2 (2) O26—C25—C27—C32  −15.8 (4)
C8—C9—C10—C11  50.9 (3)  O24—C25—C27—C32  167.0 (2)
O33—C10—C11—C12  77.9 (3) C32—C27—C28—C29  2.4 (4)
C9—C10—C11—C12  −103.3 (3) C25—C27—C28—C29  −173.5 (2)
O33—C10—C11—C15  −115.4 (3) C27—C28—C29—C30  −0.2 (4)
C9—C10—C11—C15  63.4 (3)  C28—C29—C30—C31  −2.5 (4)
C10—C11—C12—C18  −14.1 (4) C29—C30—C31—C32  3.0 (4)
C15—C11—C12—C18  179.3 (2) C30—C31—C32—C27  −0.7 (4)
C10—C11—C12—C13  159.6 (2) C28—C27—C32—C31  −2.0 (4)
C15—C11—C12—C13  −7.0 (3)  C25—C27—C32—C31  174.1 (2)
C11—C12—C13—O38  −150.6 (2) C5—C4—O34—C35  110.5 (2)
C18—C12—C13—O38  23.6 (3)  C3—C4—O34—C35  −130.85 (19)
C11—C12—C13—C14  −29.0 (3) C4—O34—C35—O36  −63.4 (3)
C18—C12—C13—C14  145.2 (2) O34—C35—O36—C37  −71.5 (3)
O20—C1—C14—O38  155.30 (19)

Hydrogen-bond geometry (Å, °)

| D—H···A     | D—H | H···A | D···A  | D—H···A |
|-------------|------|-------|--------|---------|
| O38—H38···O33i | 0.84 | 2.49  | 3.251 (2) | 151     |
| C14—H14B···O34  | 0.99 | 2.57  | 3.423 (3) | 145     |
| C18—H18A···O33  | 0.98 | 2.53  | 3.244 (3) | 130     |
| C35—H35A···O22  | 0.99 | 2.36  | 2.990 (3) | 121     |
| C16—H16C···O26a  | 0.98 | 2.43  | 3.331 (3) | 153     |
| C19—H19B···O26a  | 0.98 | 2.59  | 3.534 (3) | 162     |
| C37—H37B···O23ii | 0.98 | 2.52  | 3.445 (3) | 158     |

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