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A second polymorph of β-arteether

Jerry P. Jasinski,[a]* Ray J. Butcher,[b] H. S. Yathirajan,[c] B. Narayana[d] and T. V. Sreevidya[d]

[a]Department of Chemistry, Keene State College, 229 Main Street, Keene, NH 03435-2001, USA, [b]Department of Chemistry, Howard University, 525 College Street NW, Washington, DC 20059, USA, [c]Department of Studies in Chemistry, University of Mysore, Manasagangotri, Mysore 570 006, India, and [d]Department of Studies in Chemistry, Mangalore University, Mangalagangotri 574 199, India
Correspondence e-mail: jjasinski@keene.edu

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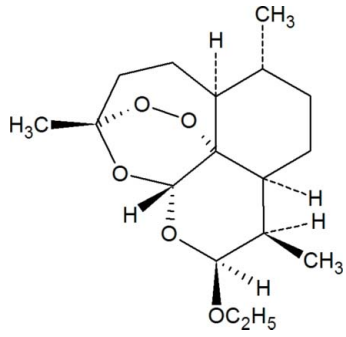
Key indicators: single-crystal X-ray study; T = 103 K; mean σ(C–C) = 0.002 Å; R factor = 0.041; wR factor = 0.101; data-to-parameter ratio = 24.3.

The crystal structure of the title compound, $C_{17}H_{28}O_5$, reported here is a polymorph of the structure first reported by El-Feraly, Al-Yahya, Orabi, McPhail & McPhail [*J. Nat. Prod.* (1992). **55**, 878–883]. It is a derivative of the antimalaria compound artemisinin and consists primarily of three substituted ring systems fused together. A cyclohexane ring (distorted chair conformation) fused to a tetrahydropyran group (distorted chair) is adjacent to an oxacycloheptane unit containing an *endo*-peroxide bridge, giving the molecule its particular three-dimensional arrangement. The crystal packing is stabilized by intermolecular C—H···O interactions between an O atom from the *endo*-peroxide bridge and H atoms from both the cyclohexane and seven-membered oxacycloheptane fused rings, as well as between an O atom and H atom from adjacent tetrahydropyran rings. The two polymorphs have the same space group and similar cell parameters for the *a* and *b* axes, but significantly different values for the *c* axis.

Related literature

For the first polymorph of this compound, see: El-Feraly *et al.* (1992). For crystal structures of similar compounds, see: Brossi *et al.* (1988); Flippen-Anderson *et al.* (1989); Karle & Lin (1995); Li *et al.* (2006); Luo *et al.* (1984); Yue *et al.* (2006); Butcher *et al.* (2007); Jasinski *et al.* (2008). For biological activity of artemisinin derivatives *in vitro* and *in vivo*, see: Grace *et al.* (1998); Li *et al.* (2001); Maggs *et al.* (2000); Yang *et al.* (1997). For *endo*-peroxide sesquiterpene lactone derivatives, see: Saxena *et al.* (2003); Venugopalan *et al.* (1995); Wu *et al.* (2001). For the synthesis of artemisinin and its derivatives, see: Lui *et al.* (1979); Liu (1980); Robert *et al.* (2001). For related literature, see: Cremer & Pople (1975); Lisgarten *et al.* (1998); Qinghaosu Research Group (1980); Shen & Zhuang (1984); Wu & Li (1995).



Experimental

Crystal data

$C_{17}H_{28}O_5$
M_r = 312.39
Trigonal, $P3_221$
a = 10.0253 (6) Å
c = 28.628 (3) Å
V = 2491.8 (3) Å^3
Z = 6
Mo $K\alpha$ radiation
μ = 0.09 mm^{-1}
T = 103 (2) K
0.42 × 0.22 × 0.18 mm

Data collection

Bruker APEXII CCD area-detector diffractometer
Absorption correction: multi-scan (*SADABS*; Sheldrick, 1996)
T_{min} = 0.963, T_{max} = 0.984
27842 measured reflections
4935 independent reflections
4517 reflections with $I > 2\sigma(I)$
R_{int} = 0.034

Refinement

$R[F^2 > 2\sigma(F^2)]$ = 0.040
$wR(F^2)$ = 0.101
S = 1.04
4935 reflections
203 parameters
H-atom parameters constrained
$\Delta\rho_{max}$ = 0.38 e Å^{-3}
$\Delta\rho_{min}$ = −0.17 e Å^{-3}

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

D—H···A	D—H	H···A	D···A	D—H···A
C5—H5A···O4^{i}	1.00	2.45	3.3150 (15)	144
C7—H7A···O4^{i}	0.99	2.55	3.4704 (16)	155

Symmetry code: (i) $y+1, x, -z$.

Data collection: *APEX2* (Bruker, 2006); cell refinement: *APEX2*; data reduction: *SAINT* (Bruker, 2006); program(s) used to solve structure: *SHELXS90* (Sheldrick, 2008); program(s) used to refine structure: *SHELXL97* (Sheldrick, 2008); molecular graphics: *SHELXTL* (Sheldrick, 2008); software used to prepare material for publication: *SHELXTL*.

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Supplementary data and figures for this paper are available from the IUCr electronic archives (Reference: AT2510).

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supporting information

Acta Cryst. (2008). E**64**, o585–o586 [doi:10.1107/S1600536807062812]

A second polymorph of *β*-arteether

Jerry P. Jasinski, Ray J. Butcher, H. S. Yathirajan, B. Narayana and T. V. Sreevidya

S1. Comment

Artemisinin and its derivatives, dihydroartemisinin, artemether, arteether and artesunate, are antimalarial drugs which possess bioactivity with reduced toxicity (Wu & Li, 1995). Artemisinin is isolated from the leaves of the plant *Artemisia annua* (Qinghao). It is a sesquiterpene lactone with an *endo*-peroxide linkage. Artemisinin derivatives are more potent than artemisinin and are active by virtue of the *endo*-peroxide. Because of their activity against strains of the parasite that had become resistant to conventional chloroquine therapy and the ability, due to the lipophilic structure, to cross the blood brain barrier, it was particularly effective for the deadly cerebral malaria (Shen & Zhuang, 1984). Because of their shorter lifetime and decreasing activity, they are used in combination with other antimalarial drugs. The notable activity of artemesinin derivatives *in vitro* and *in vivo* has been reported in the literature (Li *et al.* 2001 & Yang *et al.* 1997). However, some derivatives of artimisinine showed moderate cytotoxicity *in vitro*. The electronegativity and bulk of the substituents that are attached to the aryl group play an insignificant role in cytotoxicity. The antimalarial activity and cytotoxicity of some sesquiterpenoids has been reported in the literature (Venugopalan *et al.*, 1995; Wu *et al.*, 2001; Saxena *et al.*, 2003). The *endo*-peroxide group present in these compounds plays an important role in antimalarial activity. Its 1,2,4-trioxane ring is unique in nature. After being opened in the plasmodium it liberates singlet oxygen and forms free radicals, which in turn produce oxidative damage of the parasite's membrane. Artemisinin is hydrophobic in nature and is partitioned into the membrane of the plasmodium. The crystal structure of an ether dimer of deoxydihydro-qinghaosu, a potential metabolite of the antimalarial arteether, has been reported (Flippen-Anderson *et al.*, 1989). The correlation of the crystal structures of diastereomeric artemisinin derivatives with their proton NMR spectra in $CDCl_3$ has been reported (Karle & Lin, 1995). The crystal structure of artemisinin has been reported (Lisgarten *et al.*, 1998). The crystal structure of a dimer of *α*- and *β*-dihydroartemisinin (Yue *et al.*, 2006) and that of 9,10-dehydro-deoxyartemisin has recently been reported (Li *et al.*, 2006). The synthesis of artemisinin and its derivatives have been described (Lui *et al.*, 1979; Liu, 1980; Robert *et al.*, 2001). *β*-Arteether (AE) is an *endo*-peroxide sesquiterpene lactone derivative currently being developed for the treatment of severe, complicated malaria caused by multidrug-resistant Plasmodium falciparum (Grace *et al.*, 1998). *β*-Artemether (AM), the *O*-methyl ether prodrug of dihydroartemisinin (DHA), is an *endo*-peroxide antimalarial (Maggs *et al.*, 2000). In view of the importance of the title compound, $C_{17}H_{28}O_5$ (I), *β*-arteether, as an antimalarial drug, this paper describes a new polymorphic form of the crystal structure first reported by El-Feraly *et al.* (1992), from data measured at 103 (2) K.

A substantial increase in the length of the unit cell *c* axis from 25.720 to 28.628 Å in the new structure along with a redetermination of the cell constants and the cell volume for (I) at room temperature (296 K) [a = 10.1557 (14), c = 28.714 (4) Å and V = 2564.8 (8) Å^3] provides solid support for the recognition of this new polymorphic form for (I). The six-membered cyclohexane ring (C1–C6) is a slightly distorted chair, with Cremer & Pople (1975) puckering parameters Q, *θ* and *φ* of 0.563 (8) Å, 177.8 (2)° and 20.3 (1)°, respectively (Fig. 1). The tetrahydropyran group (C1/C2/C10–C12/O2) has also a slightly distorted chair conformation with puckering parameters Q, *θ* and *φ* of 0.518 (5) Å, 176.8 (9)°

and 16.9 (6)°, respectively. For an ideal chair θ has a value of 0 or 180°. Similar conformations were found in 9,10-dehydrodeoxyartemisinin (Shu-Hui Li *et al.*, 2006). The seven-membered ring (C1/C6–C9/O1–C10) contains the important peroxy linkage [O3—O4 = 1.4759 (13) Å]. The six-membered ring C (O1/O3/O4/C1/C9/C10) which contains both an oxygen bridge and a peroxy bridge is best described by a twist-boat conformation with puckering parameters Q, θ and φ of 0.749 (2) Å, 94.8 (5)° and 276.8 (8)°, respectively. For an ideal twist-boat conformation, θ and φ are 90° and (60n + 30)°, respectively. This conformation is consistent with 9,10-dehydrodeoxyartemisinin (Li *et al.*, 2006), dihydroartemisinin (Qinghaosu Research Group, 1980; Jasinski *et al.*, 2008) and artemether (Butcher *et al.*, 2007)

Crystal packing is stabilized by intermolecular C—H···O interactions between hydrogen atoms from the cyclohexane ring (H5A and H7A) and an oxygen atom (O4) from the *endo*-peroxide bridge (Fig. 2).

S2. Experimental

The title compound ($C_{17}H_{28}O_5$) was obtained in the pure form from Strides Arco Labs, Mangalore, India. X-ray diffraction quality crystals were grown from acetone [m.p.: 353 K]).

S3. Refinement

All H atoms were initially located in a difference Fourier map. The methyl H atoms were then constrained to an ideal geometry with C—H distances of 0.98Å and U_{iso}(H) = 1.5U_{eq}(C), but each group was allowed to rotate freely about its C—C bond. All other H atoms were placed in geometrically idealized positions and constrained to ride on their parent atoms with C—H distances in the range 0.90–1.00 Å and U_{iso}(H) = 1.17–1.22U_{eq}(C).

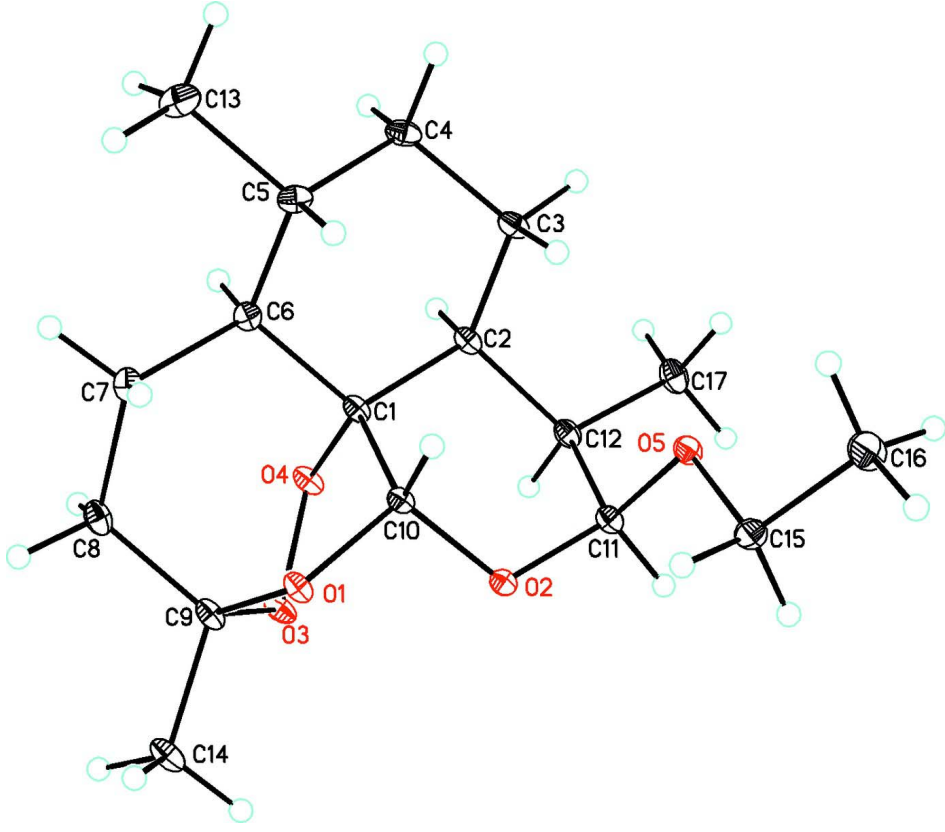

Figure 1

The molecular structure of (I), showing the atom numbering scheme and 50% probability displacement ellipsoids.

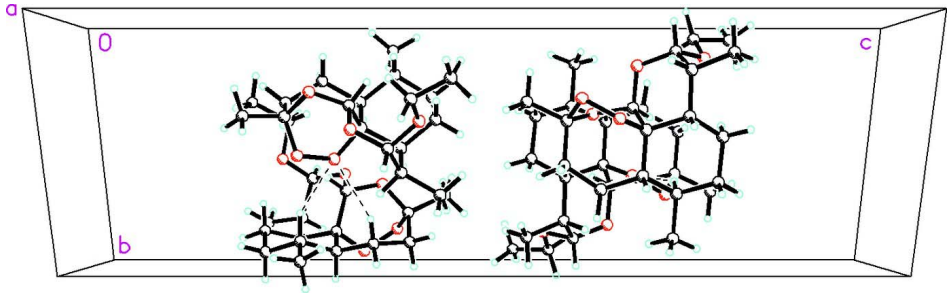

Figure 2

The molecular packing for (I) viewed down the *c* axis. Dashed lines indicate C–H···O intermolecular hydrogen bonds.

β-Arteether

Crystal data

$C_{17}H_{28}O_5$
$M_r = 312.39$
Trigonal, $P3_221$
Hall symbol: P 32 2"
$a = 10.0253\ (6)$ Å
$c = 28.628\ (3)$ Å
$V = 2491.8\ (3)$ Å^3
$Z = 6$
$F(000) = 1020$
$D_x = 1.249$ Mg m^{-3}
Mo $K\alpha$ radiation, $\lambda = 0.71073$ Å
Cell parameters from 5075 reflections
$\theta = 2.4–30.0°$
$\mu = 0.09$ mm^{-1}
$T = 103$ K
Chunk, colourless
0.42 × 0.22 × 0.18 mm

Data collection

Bruker APEXII CCD area-detector diffractometer
Radiation source: fine-focus sealed tube
Graphite monochromator
φ and ω scans
Absorption correction: multi-scan (*SADABS*; Sheldrick, 1996)
$T_{min} = 0.963$, $T_{max} = 0.984$
27842 measured reflections
4935 independent reflections
4517 reflections with $I > 2\sigma(I)$
$R_{int} = 0.034$
$\theta_{max} = 30.8°$, $\theta_{min} = 2.1°$
$h = -11\rightarrow14$
$k = -14\rightarrow14$
$l = -39\rightarrow39$

Refinement

Refinement on F^2
Least-squares matrix: full
$R[F^2 > 2\sigma(F^2)] = 0.040$
$wR(F^2) = 0.101$
$S = 1.05$
4935 reflections
203 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
$w = 1/[\sigma^2(F_o^2) + (0.0551P)^2 + 0.4841P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} = 0.005$
$\Delta\rho_{max} = 0.38$ e Å^{-3}
$\Delta\rho_{min} = -0.17$ e Å^{-3}
Absolute structure: Flack (1983), 2049 Friedel pairs

Special details

Geometry. All e.s.d.'s (except the e.s.d. in the dihedral angle between two l.s. planes) are estimated using the full covariance matrix. The cell e.s.d.'s are taken into account individually in the estimation of e.s.d.'s in distances, angles and torsion angles; correlations between e.s.d.'s in cell parameters are only used when they are defined by crystal symmetry. An approximate (isotropic) treatment of cell e.s.d.'s is used for estimating e.s.d.'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_{iso}*/U_{eq}
O1	0.71973 (10)	0.35233 (10)	−0.03898 (3)	0.01837 (18)
O2	0.57224 (11)	0.39122 (11)	0.01212 (3)	0.01993 (19)
O3	0.47049 (10)	0.15908 (12)	−0.05520 (3)	0.0219 (2)
O4	0.45576 (11)	0.06611 (11)	−0.01350 (3)	0.02042 (19)
O5	0.60247 (12)	0.45429 (11)	0.09195 (3)	0.02137 (19)
C1	0.58206 (14)	0.15089 (14)	0.01942 (4)	0.0169 (2)
C2	0.50124 (14)	0.12064 (15)	0.06716 (4)	0.0182 (2)
H2A	0.4266	0.0075	0.0686	0.022*
C3	0.61370 (16)	0.15728 (16)	0.10811 (4)	0.0222 (3)
H3A	0.6848	0.2699	0.1097	0.027*
H3B	0.5550	0.1246	0.1377	0.027*
C4	0.70709 (16)	0.07586 (16)	0.10279 (4)	0.0232 (3)
H4A	0.7788	0.1028	0.1295	0.028*
H4B	0.6367	−0.0370	0.1031	0.028*
C5	0.79822 (16)	0.12223 (15)	0.05735 (4)	0.0213 (2)
H5A	0.8658	0.2368	0.0574	0.026*
C6	0.68604 (15)	0.07809 (14)	0.01577 (4)	0.0185 (2)
H6A	0.6163	−0.0360	0.0174	0.022*
C7	0.77196 (15)	0.11190 (16)	−0.03110 (4)	0.0221 (3)
H7A	0.8677	0.2129	−0.0287	0.027*
H7B	0.8024	0.0330	−0.0361	0.027*
C8	0.68289 (16)	0.11487 (16)	−0.07417 (4)	0.0235 (3)
H8A	0.5935	0.0104	−0.0791	0.028*
H8B	0.7505	0.1408	−0.1019	0.028*
C9	0.62470 (15)	0.23007 (15)	−0.07075 (4)	0.0204 (2)
C10	0.66650 (14)	0.32307 (14)	0.00757 (4)	0.0162 (2)
H10A	0.7569	0.3776	0.0290	0.019*
C11	0.49721 (16)	0.37047 (16)	0.05576 (4)	0.0204 (3)
H11A	0.4239	0.4102	0.0527	0.024*
C12	0.40444 (15)	0.20099 (16)	0.06911 (4)	0.0204 (2)
H12A	0.3232	0.1506	0.0446	0.024*
C13	0.90173 (19)	0.05086 (19)	0.05316 (6)	0.0329 (3)
H13A	0.9584	0.0664	0.0824	0.049*
H13B	0.9748	0.1002	0.0275	0.049*
H13C	0.8382	−0.0597	0.0469	0.049*

C14	0.62461 (17)	0.30416 (18)	−0.11675 (4)	0.0270 (3)
H14A	0.5651	0.3570	−0.1135	0.040*
H14B	0.5779	0.2247	−0.1409	0.040*
H14C	0.7308	0.3788	−0.1256	0.040*
C15	0.68313 (17)	0.61729 (15)	0.08415 (5)	0.0241 (3)
H15A	0.6102	0.6513	0.0743	0.029*
H15B	0.7612	0.6446	0.0593	0.029*
C16	0.7603 (2)	0.69468 (18)	0.12949 (5)	0.0367 (4)
H16A	0.8216	0.8063	0.1247	0.055*
H16B	0.8277	0.6557	0.1398	0.055*
H16C	0.6817	0.6722	0.1533	0.055*
C17	0.31881 (17)	0.17746 (18)	0.11531 (5)	0.0279 (3)
H17A	0.2512	0.2216	0.1130	0.042*
H17B	0.3935	0.2286	0.1405	0.042*
H17C	0.2569	0.0670	0.1220	0.042*

Atomic displacement parameters (Å²)

	U^{11}	U^{22}	U^{33}	U^{12}	U^{13}	U^{23}
O1	0.0161 (4)	0.0163 (4)	0.0141 (4)	0.0017 (3)	0.0008 (3)	−0.0006 (3)
O2	0.0224 (5)	0.0212 (4)	0.0165 (4)	0.0111 (4)	0.0022 (3)	0.0025 (3)
O3	0.0158 (4)	0.0247 (5)	0.0149 (4)	0.0025 (4)	−0.0014 (3)	0.0020 (3)
O4	0.0157 (4)	0.0187 (4)	0.0149 (4)	−0.0004 (3)	−0.0015 (3)	0.0003 (3)
O5	0.0256 (5)	0.0165 (4)	0.0181 (4)	0.0076 (4)	−0.0010 (4)	−0.0004 (3)
C1	0.0143 (5)	0.0152 (5)	0.0134 (5)	0.0015 (4)	−0.0007 (4)	−0.0012 (4)
C2	0.0159 (5)	0.0161 (5)	0.0150 (5)	0.0024 (5)	0.0003 (4)	0.0006 (4)
C3	0.0255 (6)	0.0191 (6)	0.0163 (5)	0.0068 (5)	−0.0032 (5)	0.0007 (4)
C4	0.0220 (6)	0.0184 (6)	0.0217 (6)	0.0046 (5)	−0.0041 (5)	0.0046 (5)
C5	0.0181 (6)	0.0150 (5)	0.0260 (6)	0.0045 (5)	−0.0020 (5)	0.0039 (5)
C6	0.0168 (6)	0.0124 (5)	0.0208 (5)	0.0031 (4)	0.0015 (4)	0.0007 (4)
C7	0.0187 (6)	0.0177 (6)	0.0246 (6)	0.0052 (5)	0.0040 (5)	−0.0009 (5)
C8	0.0209 (6)	0.0209 (6)	0.0200 (6)	0.0040 (5)	0.0019 (5)	−0.0044 (5)
C9	0.0167 (6)	0.0201 (6)	0.0145 (5)	0.0019 (5)	0.0004 (4)	−0.0014 (4)
C10	0.0158 (5)	0.0142 (5)	0.0142 (5)	0.0041 (4)	−0.0009 (4)	0.0001 (4)
C11	0.0202 (6)	0.0210 (6)	0.0171 (5)	0.0083 (5)	−0.0007 (4)	−0.0009 (4)
C12	0.0175 (5)	0.0218 (6)	0.0164 (5)	0.0058 (5)	0.0007 (4)	−0.0004 (5)
C13	0.0279 (8)	0.0321 (8)	0.0408 (8)	0.0166 (7)	0.0010 (6)	0.0085 (6)
C14	0.0254 (7)	0.0309 (7)	0.0147 (5)	0.0066 (6)	−0.0010 (5)	0.0006 (5)
C15	0.0282 (7)	0.0160 (6)	0.0243 (6)	0.0082 (5)	0.0009 (5)	0.0022 (5)
C16	0.0504 (10)	0.0186 (7)	0.0300 (7)	0.0090 (7)	−0.0053 (7)	−0.0018 (6)
C17	0.0240 (7)	0.0294 (7)	0.0229 (6)	0.0079 (6)	0.0055 (5)	−0.0007 (5)

Geometric parameters (Å, º)

O1—C10	1.4105 (14)	C7—H7A	0.990
O1—C9	1.4386 (15)	C7—H7B	0.990
O2—C11	1.4192 (15)	C8—C9	1.536 (2)
O2—C10	1.4221 (15)	C8—H8A	0.990

O3—C9	1.4122 (16)	C8—H8B	0.990
O3—O4	1.4759 (13)	C9—C14	1.5122 (17)
O4—C1	1.4619 (14)	C10—H10A	1.000
O5—C11	1.4163 (15)	C11—C12	1.5224 (18)
O5—C15	1.4327 (16)	C11—H11A	1.000
C1—C10	1.5330 (16)	C12—C17	1.5295 (17)
C1—C2	1.5399 (16)	C12—H12A	1.000
C1—C6	1.5462 (18)	C13—H13A	0.980
C2—C3	1.5382 (17)	C13—H13B	0.980
C2—C12	1.5412 (19)	C13—H13C	0.980
C2—H2A	1.000	C14—H14A	0.980
C3—C4	1.526 (2)	C14—H14B	0.980
C3—H3A	0.990	C14—H14C	0.980
C3—H3B	0.990	C15—C16	1.512 (2)
C4—C5	1.5225 (18)	C15—H15A	0.990
C4—H4A	0.990	C15—H15B	0.990
C4—H4B	0.990	C16—H16A	0.980
C5—C13	1.532 (2)	C16—H16B	0.980
C5—C6	1.5427 (18)	C16—H16C	0.980
C5—H5A	1.000	C17—H17A	0.980
C6—C7	1.5380 (17)	C17—H17B	0.980
C6—H6A	1.000	C17—H17C	0.980
C7—C8	1.5315 (19)		

C10—O1—C9	113.55 (9)	O3—C9—C14	104.63 (11)
C11—O2—C10	116.17 (9)	O1—C9—C14	107.15 (11)
C9—O3—O4	108.17 (9)	O3—C9—C8	111.90 (11)
C1—O4—O3	111.72 (8)	O1—C9—C8	110.02 (10)
C11—O5—C15	113.02 (10)	C14—C9—C8	114.05 (11)
O4—C1—C10	110.01 (10)	O1—C10—O2	105.06 (9)
O4—C1—C2	103.89 (9)	O1—C10—C1	112.44 (9)
C10—C1—C2	110.98 (10)	O2—C10—C1	113.28 (10)
O4—C1—C6	105.93 (9)	O1—C10—H10A	108.6
C10—C1—C6	113.17 (10)	O2—C10—H10A	108.6
C2—C1—C6	112.30 (10)	C1—C10—H10A	108.6
C3—C2—C1	112.25 (10)	O5—C11—O2	111.96 (11)
C3—C2—C12	115.18 (10)	O5—C11—C12	109.68 (10)
C1—C2—C12	109.64 (10)	O2—C11—C12	111.59 (11)
C3—C2—H2A	106.4	O5—C11—H11A	107.8
C1—C2—H2A	106.4	O2—C11—H11A	107.8
C12—C2—H2A	106.4	C12—C11—H11A	107.8
C4—C3—C2	111.63 (11)	C11—C12—C17	111.82 (12)
C4—C3—H3A	109.3	C11—C12—C2	112.41 (10)
C2—C3—H3A	109.3	C17—C12—C2	113.72 (11)
C4—C3—H3B	109.3	C11—C12—H12A	106.1
C2—C3—H3B	109.3	C17—C12—H12A	106.1
H3A—C3—H3B	108.0	C2—C12—H12A	106.1
C5—C4—C3	110.91 (11)	C5—C13—H13A	109.5

C5—C4—H4A	109.5	C5—C13—H13B	109.5
C3—C4—H4A	109.5	H13A—C13—H13B	109.5
C5—C4—H4B	109.5	C5—C13—H13C	109.5
C3—C4—H4B	109.5	H13A—C13—H13C	109.5
H4A—C4—H4B	108.0	H13B—C13—H13C	109.5
C4—C5—C13	111.57 (11)	C9—C14—H14A	109.5
C4—C5—C6	109.36 (11)	C9—C14—H14B	109.5
C13—C5—C6	111.87 (12)	H14A—C14—H14B	109.5
C4—C5—H5A	108.0	C9—C14—H14C	109.5
C13—C5—H5A	108.0	H14A—C14—H14C	109.5
C6—C5—H5A	108.0	H14B—C14—H14C	109.5
C7—C6—C5	111.24 (11)	O5—C15—C16	107.69 (11)
C7—C6—C1	112.97 (10)	O5—C15—H15A	110.2
C5—C6—C1	112.30 (10)	C16—C15—H15A	110.2
C7—C6—H6A	106.6	O5—C15—H15B	110.2
C5—C6—H6A	106.6	C16—C15—H15B	110.2
C1—C6—H6A	106.6	H15A—C15—H15B	108.5
C8—C7—C6	116.04 (11)	C15—C16—H16A	109.5
C8—C7—H7A	108.3	C15—C16—H16B	109.5
C6—C7—H7A	108.3	H16A—C16—H16B	109.5
C8—C7—H7B	108.3	C15—C16—H16C	109.5
C6—C7—H7B	108.3	H16A—C16—H16C	109.5
H7A—C7—H7B	107.4	H16B—C16—H16C	109.5
C7—C8—C9	114.06 (11)	C12—C17—H17A	109.5
C7—C8—H8A	108.7	C12—C17—H17B	109.5
C9—C8—H8A	108.7	H17A—C17—H17B	109.5
C7—C8—H8B	108.7	C12—C17—H17C	109.5
C9—C8—H8B	108.7	H17A—C17—H17C	109.5
H8A—C8—H8B	107.6	H17B—C17—H17C	109.5
O3—C9—O1	108.78 (10)		

C9—O3—O4—C1	45.64 (12)	O4—O3—C9—C8	48.52 (12)
O3—O4—C1—C10	15.48 (13)	C10—O1—C9—O3	31.99 (14)
O3—O4—C1—C2	134.33 (10)	C10—O1—C9—C14	144.59 (11)
O3—O4—C1—C6	−107.17 (10)	C10—O1—C9—C8	−90.91 (12)
O4—C1—C2—C3	162.62 (10)	C7—C8—C9—O3	−95.86 (13)
C10—C1—C2—C3	−79.19 (13)	C7—C8—C9—O1	25.20 (14)
C6—C1—C2—C3	48.60 (14)	C7—C8—C9—C14	145.62 (12)
O4—C1—C2—C12	−68.02 (12)	C9—O1—C10—O2	−93.06 (11)
C10—C1—C2—C12	50.16 (12)	C9—O1—C10—C1	30.57 (14)
C6—C1—C2—C12	177.96 (10)	C11—O2—C10—O1	176.80 (9)
C1—C2—C3—C4	−52.31 (14)	C11—O2—C10—C1	53.70 (13)
C12—C2—C3—C4	−178.73 (10)	O4—C1—C10—O1	−55.59 (13)
C2—C3—C4—C5	58.53 (14)	C2—C1—C10—O1	−170.00 (10)
C3—C4—C5—C13	175.80 (11)	C6—C1—C10—O1	62.68 (12)
C3—C4—C5—C6	−59.90 (14)	O4—C1—C10—O2	63.33 (12)
C4—C5—C6—C7	−175.83 (11)	C2—C1—C10—O2	−51.08 (12)
C13—C5—C6—C7	−51.70 (14)	C6—C1—C10—O2	−178.40 (9)

C4—C5—C6—C1	56.44 (13)	C15—O5—C11—O2	61.59 (14)
C13—C5—C6—C1	−179.43 (10)	C15—O5—C11—C12	−173.97 (11)
O4—C1—C6—C7	69.20 (12)	C10—O2—C11—O5	69.63 (13)
C10—C1—C6—C7	−51.41 (13)	C10—O2—C11—C12	−53.74 (14)
C2—C1—C6—C7	−178.04 (10)	O5—C11—C12—C17	57.32 (15)
O4—C1—C6—C5	−163.99 (9)	O2—C11—C12—C17	−178.03 (11)
C10—C1—C6—C5	75.39 (12)	O5—C11—C12—C2	−72.01 (13)
C2—C1—C6—C5	−51.23 (13)	O2—C11—C12—C2	52.64 (14)
C5—C6—C7—C8	−164.04 (11)	C3—C2—C12—C11	75.94 (13)
C1—C6—C7—C8	−36.68 (15)	C1—C2—C12—C11	−51.80 (13)
C6—C7—C8—C9	56.69 (15)	C3—C2—C12—C17	−52.41 (15)
O4—O3—C9—O1	−73.25 (12)	C1—C2—C12—C17	179.85 (10)
O4—O3—C9—C14	172.50 (10)	C11—O5—C15—C16	166.33 (13)

Hydrogen-bond geometry (Å, º)

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
C5—H5*A*···O4^{i}	1.00	2.45	3.3150 (15)	144
C7—H7*A*···O4^{i}	0.99	2.55	3.4704 (16)	155

Symmetry code: (i) *y*+1, *x*, −*z*.