Acta Crystallographica Section C
Crystal Structure Communications
ISSN 0108-2701

Cinerin C: a macrophyllin-type bicyclo[3.2.1]octane neolignan from *Pleurothyrium cinereum* (Lauraceae)

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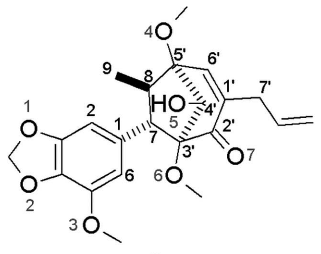
Received 7 May 2012
Accepted 6 July 2012
Online 19 July 2012

The structure of naturally-occurring cinerin C [systematic name: (7*S*,8*R*,3′*R*,4′*S*,5′*R*)-$\Delta^{8'}$-4′-hydroxy-5,5′,3′-trimethoxy-3,4-methylenedioxy-2′,3′,4′,5′-tetrahydro-2′-oxo-7.3′,8.5′-neolignan], isolated from the ethanol extract of leaves of *Pleurothyrium cinereum* (Lauraceae), has previously been established by NMR and HRMS spectroscopy, and its absolute configuration established by circular dichroism measurements. For the first time, its crystal strucure has now been established by single-crystal X-ray analysis, as the monohydrate, $C_{22}H_{26}O_7\cdot H_2O$. The bicyclooctane moiety comprises fused cyclopentane and cyclohexenone rings which are almost coplanar. An intermolecular O—H···O hydrogen bond links the 4′-OH and 5′-OCH$_3$ groups along the *c* axis.

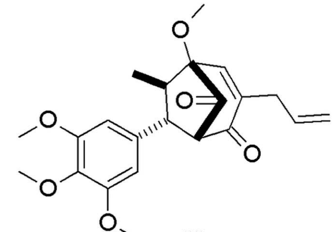
Comment

The title compound, (I), is a 7.3′,8.5′-connected bicyclo[3.2.1]octane neolignan related to the macrophyllin type (Sefkow, 2003). This fascinating class of neolignans has attracted significant attention because of its chemistry, configuration and biological activities, and its occurrence is limited to certain plants belonging to the Magnoliaceae, Piperaceae and Lauraceae families (Coy-Barrera *et al.*, 2009). Although the macrophyllin-type neolignans are less common than the guianin-type, the macrophyllin-type bicyclooctanes have exhibited better platelet-activating factor antagonism (anti-PAF activity) (Wang *et al.*, 2002; Coy-Barrera *et al.*, 2009). Indeed, the title compound, cinerin C, was found to be the most potent PAF antagonist (IC$_{50}$ = 1.1 μ*M*) among 26 evaluated neolignans (Coy *et al.*, 2009*a*).

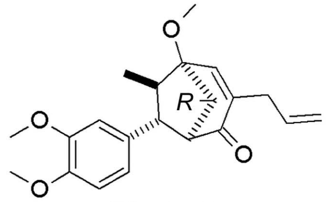
As part of our research on Lauraceaous neolignans, cinerin C was first isolated from the chloroform-soluble fraction obtained from an ethanol extract of leaves of *Pleurothyrium cinereum* (Lauraceae family; Coy *et al.*, 2009*b*), a tree important to the Awá tribe in Colombia (Coy & Cuca, 2008). The structure was previously determined by NMR spectroscopy and high-resolution mass spectrometry (HRMS), establishing the bicyclo[3.2.1]octane group as well as the 7*S*,8*R*,3′*R*,4′*S*,5′*R* absolute configuration [by circular dichroism (CD) measurements; Coy *et al.*, 2009*b*]. In order to grow suitable crystals of (I), different crystallization methods were investigated, including: (*a*) recrystallization from various solvents and solvent mixtures by heating and subsequent slow cooling; (*b*) overlaying a solution of the compound with an antisolvent; and (*c*) diffusion of an antisolvent into a solution of the compound *via* the gas phase, in a closed chamber. Procedures (*a*) and (*b*) failed to afford any suitable crystals, and only procedure (*c*), using *n*-hexane as antisolvent, was successful. Because there are no heavy atoms in the structure with a sufficiently strong anomalous scattering effect, a reliable crystallographic determination of the absolute configuration cannot be assured. Therefore, the enantiomer shown, (I), was chosen to be compatible with the configuration established by the CD measurements.



(I)



(II)



(III) *R* = OAc
(IV) *R* = OH

So far, only three crystal structures of macrophyllin-type neolignans have been reported: the oxidation product from macrophyllin B, (II) (*Nectandra* spp. Lauraceae; Rodrigues *et al.*, 1984), piperulin A, (III) [*Piper puberulum* (Piperaceae); Zhang *et al.*, 1995, 1996], and kadsurenin C, (IV) [*Piper kadsura* (Piperaceae); Jiang *et al.*, 2003]. The first two neolignans [which differ structurally from (I) by a methoxy group at C3′ and a veratryl group instead of a 5-methoxypiperonyl group, as well as by an acetyl group at C4′ in (III)] have similar relative configurations to that of (I), since both molecules have an aryl—C7/methyl—C8 *trans* relationship, an *endo*-methyl group at C8 (which is easily determined from a ^{13}C NMR chemical shift at *ca* 13 p.p.m.), and the 4′-OAc or 4′-OH group, respectively, oriented towards the aryl group. In addition, (I) and (IV) showed negative Cotton effects at 246 and 330 nm by CD measurements (Han *et al.*, 1992), which

doi:10.1107/S0108270112030946

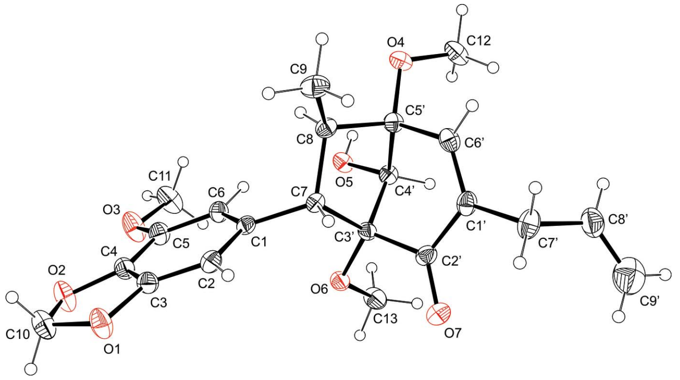


Figure 1
The molecular structure of (I), showing the atom-labelling scheme. One component of the disordered vinyl group has been omitted for clarity. Displacement ellipsoids are drawn at the 30% probability level for the non-H atoms.

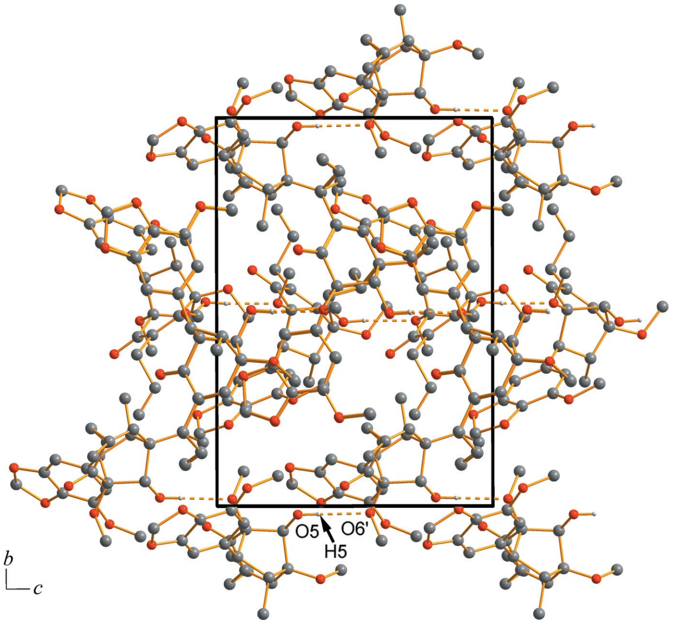


Figure 2
The intermolecular hydrogen bonds (dashed lines) in the crystal structure of (I), running along the crystallographic *c* axis. With the exception of atom H5, all H atoms have been omitted for clarity. [Symmetry code: (i) $-x + 1, -y, z + \frac{1}{2}$.]

means that both molecules have identical absolute configurations. On the other hand, although (II) exhibits a mutually *trans* arrangement of the aryl–C7 and methyl–C8 bonds, there are two significant differences: the OH group is located at C2′ and the methyl group at C8 has an *exo* orientation (^{13}C NMR chemical shift at *ca* 16 p.p.m.; Guilhon *et al.*, 1992). However, the space group for the closely related molecules (III) and (IV) is $P2_12_12_1$ (orthorhombic), while (I) crystallizes in the hexagonal space group $P6_1$. This suggests that the 3′-methoxy group significantly affects the symmetry of the crystal structure, possibly through the presence of an intermolecular O—H⋯O hydrogen bond between the 4′-OH and 3′-OCH_3 groups [$O5—H5\cdots O6^{i}$ = 2.947 (3) Å; symmetry code: (i) $-x + 1, -y, z + \frac{1}{2}$]. These hydrogen bonds link the molecules into chains which run parallel to the crystallographic *c* axis (Fig. 2).

A view of the solid-state conformation of (I), with the atom-numbering scheme, is provided in Fig. 1. The bond lengths agree in general with expected values (Zhang *et al.*, 1995; Jiang *et al.*, 2003), except for the elongated C7—C3′ bond of 1.585 (3) Å, which is due to repulsion between the aromatic ring at atom C7 and atoms O5 and O6. The molecule of (I) can be subdivided into three parts, namely a 5-methoxypiperonyl group, a bicyclooctane group and an allyl group. The 5-methoxypiperonyl group has a methoxy group at C5 nearly coplanar with the benzene ring, with a C11—O3—C5—C6 torsion angle of 3.5 (5)°, and, as expected, the methylenedioxy group is twisted slightly out of the plane of the benzene ring, having torsion angles of C10—O2—C4—C3 = 6.6 (3)° and C10—O1—C3—C4 = −6.9 (3)°. In addition, the benzene ring is oriented through the C1—C7 bond by a *gauche* conformation with respect to atoms C7 and C8 of the bicyclooctane group, with torsion angles of C8—C7—C1—C6 = 60.4 (3)° and C3′—C7—C1—C2 = 118.1 (3)°.

The conformation of the bicyclooctane group is characterized by two fragments: a cyclohexenone fragment (comprising atoms C1′, C2′, C3′, C4′, C5′ and C6′) and a cyclopentane fragment (comprising atoms C3′, C4′, C5′, C8 and C7), fused along C3′—C4′—C5′. The first fragment adopts an envelope conformation, where atoms C1′/C2′/C3′/C5′/C6′ lie in a plane [the maximum deviation from the least-squares plane is 0.046 (2) Å for atom C2′], and atom C4′ lies 0.885 (2) Å out of that plane. An approximate C_2 symmetry axis passing through atom C7 and the mid-point of the C5′—C4′ bond relates the cyclopentane ring torsion angles, indicating a half-chair form. Likewise, the cyclohexenone ring has an approximate mirror plane of symmetry passing through atoms C4′ and C1′, with two adjacent torsion angles [Cl′—C2′—C3′—C4′ = 45.0 (3)° and C1′—C6′—C5′—C4′ = −31.7 (3) °] indicating that the ring has a half-boat (1,2-diplanar) form. The dihedral angle between the C1′/C2′/C3′/C4′and C1′/C6′/C5′/C4′ planes is 43.6 (2)°. The olefin from the allyl fragment is disordered over two sites, which lie on the same side as the methyl group at C8, with a C1⋯C7′ distance of 5.817 (5) Å. Finally, the methoxy groups at C5′ and C3′ have a pseudo-1,3-diequatorial orientation, with an O4⋯O6 distance of 4.866 (3) Å.

Experimental

Plant material was collected from *P. cinereum* in the indigenous reservation Awá at Alto Albí, Tumaco County, Department of Narinho, Colombia, in November 2005 and identified by biologist Ayda Lucia Patino. A voucher specimen (No. COL518334) was deposited at the Herbario Nacional Colombiano of the Universidad Nacional de Colombia in Bogota. Detailed extraction and isolation processes and spectroscopic features for (I) have been reported previously (Coy *et al.*, 2009*b*). The isolated compound was crystallized by diffusion of *n*-hexane antisolvent vapour into a solution of the compound in ethyl acetate. Elemental analysis: C 65.7, H 6.3, O 27.9%; $C_{22}H_{26}O_7$ requires: C 65.7, H 6.5, O 27.8%.

Table 1
Selected geometric parameters (Å, °).

C1—C7	1.514 (3)	C1′—C2′	1.474 (4)
C7—C8	1.541 (4)	C1′—C7′	1.508 (4)
C8—C5′	1.534 (4)	C7′—C8′	1.551 (11)
C1—C7—C8	115.2 (2)	C3′—C4′—C5′	99.13 (19)
C6′—C1′—C2′	117.8 (2)	C1′—C7′—C8′	110.1 (4)
C2′—C3′—C7	107.0 (2)	C9′—C8′—C7′	119.6 (14)
C1—C7—C8—C9	88.1 (3)	C6′—C1′—C2′—C3′	−5.1 (3)
C3′—C7—C8—C5′	−17.5 (2)	C1′—C2′—C3′—C4′	45.0 (3)

Table 2
Hydrogen-bond geometry (Å, °).

D—H⋯*A*	*D*—H	H⋯*A*	*D*⋯*A*	*D*—H⋯*A*
O5—H5⋯O6^{i}	0.83 (4)	2.12 (4)	2.947 (3)	175 (3)

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

Crystal data

$C_{22}H_{26}O_7 \cdot H_2O$
$M_r = 420.46$
Hexagonal, $P6_1$
$a = 18.2223$ (12) Å
$c = 11.2387$ (6) Å
$V = 3231.9$ (3) Å^3
$Z = 6$
Mo $K\alpha$ radiation
$\mu = 0.10$ mm^{-1}
$T = 210$ K
1.0 × 0.35 × 0.34 mm

Data collection

Stoe IPDS 2 diffractometer
19695 measured reflections
1930 independent reflections
1816 reflections with $I > 2\sigma(I)$
$R_{\rm int} = 0.188$

Refinement

$R[F^2 > 2\sigma(F^2)] = 0.036$
$wR(F^2) = 0.092$
$S = 1.04$
1930 reflections
325 parameters
8 restraints
H atoms treated by a mixture of independent and constrained refinement
$\Delta\rho_{\rm max} = 0.20$ e Å^{-3}
$\Delta\rho_{\rm min} = -0.16$ e Å^{-3}

The $R_{\rm int}$ value is relatively high because of the overall poor quality of the data, which, in turn, is the result of limited crystal quality. Friedel opposites were merged because of the absence of significant anomalous scattering effects. The crystal structure displays channels (*ca* 3.7 Å in diameter) containing water molecules. In spite of several attempts, the electron density in this area could not be resolved satisfactorily. Therefore, the contribution of the disordered solvent species was subtracted from the structure-factor calculations using the SQUEEZE module of *PLATON* (Spek, 2009). The electron count of 71 per unit cell corresponds to approximately one water molecule per asymmetric unit. Although solvent atoms were not included in the refinement model, they are included in the calculation of the formula weight, density, μ and $F(000)$.

The H atoms of the methyl groups and of the allyl group were placed geometrically and refined as riding, with C—H = 0.96 (methyl) or 0.93 Å (allyl) and $U_{\rm iso}({\rm H}) = 1.2U_{\rm eq}({\rm C})$. All other H atoms were located from a difference Fourier map and their positions were refined, with displacement parameters constrained to $U_{\rm iso}({\rm H}) = 1.2U_{\rm eq}({\rm C})$. For atom H5, the isotropic displacement parameter was also allowed to refine. The H atoms attached to C7 were modelled as disordered over two orientations, with the four C7—H and two H⋯H distances restrained to common refined values with an s.u. of 0.02 Å.

Data collection: *X-AREA* (Stoe & Cie, 2004); cell refinement: *X-AREA*; data reduction: *X-RED* (Stoe & Cie, 2004); program(s) used to solve structure: *SHELXS97* (Sheldrick, 2008); program(s) used to refine structure: *SHELXL97* (Sheldrick, 2008); molecular graphics: *ORTEP-3 for Windows* (Farrugia, 1997), based on *ORTEPIII* (Burnett & Johnson, 1996), and *DIAMOND* (Brandenburg, 2007); software used to prepare material for publication: *SHELXL97*.

The authors thank the University of Potsdam and the Deutscher Akademischer Austauschdienst (DAAD) for a fellowship.

Supplementary data for this paper are available from the IUCr electronic archives (Reference: BM3119). Services for accessing these data are described at the back of the journal.

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supplementary materials

Acta Cryst. (2012). C**68**, o320–o322 [doi:10.1107/S0108270112030946]

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(7*S*,8*R*,3′*R*,4′*S*,5′*R*)-$\Delta^{8'}$-4′-hydroxy- 5,5′,3′-trimethoxy-3,4-methylenedioxy-2′,3′,4′,5′-tetrahydro-2′-oxo-7.3′,8.5′-neolignan monohydrate

Crystal data

$C_{22}H_{26}O_7{\cdot}H_2O$
$M_r = 420.46$
Hexagonal, $P6_1$
$a = 18.2223$ (12) Å
$c = 11.2387$ (6) Å
$V = 3231.9$ (3) Å^3
$Z = 6$
$F(000) = 1344$
$D_x = 1.296$ Mg m^{-3}
Melting point: 448 K
Mo *Kα* radiation, $\lambda = 0.71073$ Å
Cell parameters from 27502 reflections
$\theta = 2.6$–$50.3°$
$\mu = 0.10$ mm^{-1}
$T = 210$ K
Needle, colourless
1.0 × 0.35 × 0.34 mm

Data collection

Stoe IPDS 2 diffractometer
Radiation source: fine-focus sealed tube
Plane graphite monochromator
Detector resolution: 6.67 pixels mm^{-1}
ω scan, 0.5°
19695 measured reflections
1930 independent reflections
1816 reflections with $I > 2\sigma(I)$
$R_{\rm int} = 0.188$
$\theta_{\rm max} = 24.7°$, $\theta_{\rm min} = 1.3°$
$h = -20 \rightarrow 21$
$k = -21 \rightarrow 21$
$l = -12 \rightarrow 13$

Refinement

Refinement on F^2
Least-squares matrix: full
$R[F^2 > 2\sigma(F^2)] = 0.036$
$wR(F^2) = 0.092$
$S = 1.04$
1930 reflections
325 parameters
8 restraints
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
$w = 1/[\sigma^2(F_o^2) + (0.054P)^2]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{\rm max} < 0.001$
$\Delta\rho_{\rm max} = 0.20$ e Å^{-3}
$\Delta\rho_{\rm min} = -0.16$ e Å^{-3}
Extinction correction: *SHELXL97* (Sheldrick, 2008), $Fc^* = kFc[1+0.001xFc^2\lambda^3/\sin(2\theta)]^{-1/4}$
Extinction coefficient: 0.0038 (12)
Absolute structure: Friedel opposites were merged because of the absence of significant anomalous scattering effects

Special details

Experimental. Attempts to yield smaller crystals by cutting were not successful because of uncontrolled fragmentation.

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.

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

	x	*y*	*z*	$U_{\rm iso}$*/$U_{\rm eq}$	Occ. (<1)
C1	0.35526 (15)	−0.09747 (15)	0.0278 (2)	0.0267 (5)	
C2	0.32171 (16)	−0.12066 (17)	−0.0858 (2)	0.0307 (6)	
H2	0.333 (2)	−0.150 (2)	−0.133 (3)	0.037*	
C3	0.27196 (16)	−0.08865 (17)	−0.1265 (2)	0.0327 (6)	
C4	0.25688 (17)	−0.03499 (17)	−0.0600 (3)	0.0339 (6)	
C5	0.28924 (18)	−0.01127 (17)	0.0528 (3)	0.0356 (6)	
C6	0.33845 (16)	−0.04412 (16)	0.0972 (2)	0.0310 (6)	
H6	0.3637 (19)	−0.027 (2)	0.183 (3)	0.037*	
C7	0.41150 (15)	−0.13042 (15)	0.0737 (2)	0.0256 (5)	
H7	0.4149 (18)	−0.1670 (19)	0.003 (3)	0.031*	
C8	0.38012 (16)	−0.18409 (16)	0.1880 (2)	0.0293 (6)	
H8	0.3560 (19)	−0.1593 (19)	0.241 (3)	0.035*	
C9	0.3202 (2)	−0.27837 (18)	0.1671 (3)	0.0440 (7)	
H9A	0.2714	−0.2862	0.1239	0.053*	
H9B	0.3027	−0.3070	0.2423	0.053*	
H9C	0.3488	−0.3013	0.1219	0.053*	
C10	0.1862 (2)	−0.0580 (2)	−0.2287 (3)	0.0464 (7)	
H10A	0.199 (2)	−0.023 (3)	−0.294 (4)	0.056*	
H10B	0.133 (3)	−0.099 (3)	−0.219 (4)	0.056*	
C11	0.3140 (3)	0.0772 (2)	0.2215 (3)	0.0540 (9)	
H11A	0.3009	0.0307	0.2741	0.065*	
H11B	0.2944	0.1126	0.2559	0.065*	
H11C	0.3742	0.1098	0.2099	0.065*	
C12	0.5135 (2)	−0.1646 (2)	0.4494 (3)	0.0447 (7)	
H12A	0.4952	−0.1945	0.5236	0.054*	
H12B	0.5417	−0.1047	0.4640	0.054*	
H12C	0.5518	−0.1787	0.4108	0.054*	
C13	0.59942 (18)	0.08963 (18)	0.0967 (3)	0.0432 (7)	
H13A	0.5921	0.1017	0.1776	0.052*	
H13B	0.6131	0.1380	0.0479	0.052*	
H13C	0.6446	0.0770	0.0926	0.052*	
C1′	0.55934 (17)	−0.16483 (17)	0.1008 (2)	0.0330 (6)	
C2′	0.56420 (16)	−0.08848 (17)	0.0479 (2)	0.0312 (6)	
C3′	0.50582 (15)	−0.05989 (15)	0.1038 (2)	0.0263 (5)	
C4′	0.51291 (16)	−0.06382 (15)	0.2390 (2)	0.0271 (6)	
H4′	0.575 (2)	−0.0386 (19)	0.262 (3)	0.032*	
C5′	0.46184 (16)	−0.16115 (16)	0.2559 (2)	0.0280 (5)	
C6′	0.51047 (17)	−0.19813 (17)	0.1973 (2)	0.0328 (6)	
H6′	0.505 (2)	−0.244 (2)	0.236 (3)	0.039*	

C7′	0.6102 (2)	−0.2003 (2)	0.0447 (3)	0.0430 (7)	
H7A′	0.603 (9)	−0.206 (5)	−0.040 (3)	0.052*	0.50
H7B′	0.577 (9)	−0.258 (2)	0.071 (8)	0.052*	0.50
H7C′	0.612 (9)	−0.191 (5)	−0.040 (3)	0.052*	0.50
H7D′	0.580 (9)	−0.261 (2)	0.053 (8)	0.052*	0.50
O1	0.23470 (14)	−0.10028 (14)	−0.23660 (19)	0.0473 (5)	
O2	0.20904 (15)	−0.00975 (15)	−0.1233 (2)	0.0503 (6)	
O3	0.27330 (16)	0.04545 (16)	0.1098 (2)	0.0532 (6)	
O4	0.44152 (12)	−0.18833 (12)	0.37456 (17)	0.0348 (5)	
O5	0.47394 (12)	−0.02205 (11)	0.29278 (18)	0.0314 (4)	
H5	0.478 (2)	−0.021 (2)	0.367 (4)	0.035 (9)*	
O6	0.52241 (11)	0.01819 (10)	0.05493 (16)	0.0308 (4)	
O7	0.60851 (14)	−0.05200 (15)	−0.03744 (19)	0.0495 (6)	
C8′	0.6960 (6)	−0.1665 (6)	0.1105 (11)	0.053 (2)	0.50
H8′	0.6971	−0.1746	0.1920	0.063*	0.50
C9′	0.7654 (9)	−0.1273 (7)	0.0517 (14)	0.079 (3)	0.50
H9A′	0.7641	−0.1192	−0.0298	0.094*	0.50
H9B′	0.8171	−0.1068	0.0906	0.094*	0.50
C81′	0.7041 (5)	−0.1394 (6)	0.0533 (9)	0.0378 (15)	0.50
H81′	0.7274	−0.0866	0.0169	0.045*	0.50
C91′	0.7536 (9)	−0.1604 (8)	0.1118 (11)	0.072 (3)	0.50
H91C	0.7306	−0.2131	0.1483	0.086*	0.50
H91D	0.8115	−0.1224	0.1167	0.086*	0.50

Atomic displacement parameters (Å^2)

	U^{11}	U^{22}	U^{33}	U^{12}	U^{13}	U^{23}
C1	0.0209 (11)	0.0229 (12)	0.0307 (13)	0.0068 (10)	0.0003 (10)	0.0011 (10)
C2	0.0274 (12)	0.0305 (13)	0.0326 (14)	0.0133 (11)	0.0001 (11)	−0.0048 (11)
C3	0.0296 (13)	0.0335 (13)	0.0284 (13)	0.0109 (11)	−0.0052 (11)	−0.0006 (11)
C4	0.0323 (13)	0.0324 (13)	0.0354 (15)	0.0150 (11)	−0.0054 (12)	0.0014 (12)
C5	0.0384 (14)	0.0356 (14)	0.0374 (15)	0.0219 (12)	−0.0023 (12)	−0.0029 (12)
C6	0.0295 (12)	0.0314 (13)	0.0316 (14)	0.0148 (11)	−0.0037 (11)	−0.0031 (11)
C7	0.0222 (11)	0.0245 (11)	0.0284 (12)	0.0104 (10)	0.0016 (10)	−0.0013 (10)
C8	0.0280 (13)	0.0251 (12)	0.0317 (14)	0.0110 (11)	0.0037 (11)	−0.0012 (11)
C9	0.0431 (16)	0.0280 (14)	0.0452 (16)	0.0059 (13)	0.0024 (14)	0.0020 (13)
C10	0.0512 (18)	0.0415 (17)	0.0488 (18)	0.0248 (15)	−0.0181 (16)	−0.0038 (16)
C11	0.085 (2)	0.0552 (19)	0.0421 (17)	0.0503 (19)	−0.0151 (17)	−0.0143 (16)
C12	0.066 (2)	0.0477 (17)	0.0342 (15)	0.0383 (16)	−0.0069 (15)	0.0019 (13)
C13	0.0348 (15)	0.0306 (14)	0.0487 (16)	0.0048 (12)	−0.0108 (14)	0.0058 (13)
C1′	0.0330 (13)	0.0384 (14)	0.0329 (14)	0.0219 (11)	−0.0020 (12)	−0.0076 (12)
C2′	0.0267 (12)	0.0388 (14)	0.0241 (12)	0.0134 (11)	0.0010 (11)	−0.0013 (12)
C3′	0.0259 (12)	0.0228 (11)	0.0277 (12)	0.0104 (10)	−0.0006 (10)	0.0040 (10)
C4′	0.0304 (13)	0.0229 (12)	0.0285 (13)	0.0138 (10)	0.0005 (10)	−0.0016 (10)
C5′	0.0317 (13)	0.0260 (12)	0.0275 (12)	0.0154 (10)	0.0019 (11)	0.0003 (10)
C6′	0.0381 (14)	0.0256 (13)	0.0390 (16)	0.0193 (12)	−0.0046 (13)	−0.0031 (12)
C7′	0.0376 (16)	0.0461 (16)	0.0512 (18)	0.0253 (14)	−0.0001 (15)	−0.0107 (15)
O1	0.0516 (12)	0.0590 (13)	0.0398 (11)	0.0339 (11)	−0.0198 (10)	−0.0128 (11)
O2	0.0612 (14)	0.0574 (13)	0.0495 (12)	0.0425 (12)	−0.0218 (12)	−0.0114 (11)

O3	0.0777 (16)	0.0636 (14)	0.0456 (12)	0.0559 (14)	−0.0199 (12)	−0.0196 (11)
O4	0.0441 (11)	0.0335 (10)	0.0285 (9)	0.0207 (9)	0.0024 (9)	0.0063 (8)
O5	0.0432 (11)	0.0307 (9)	0.0267 (10)	0.0234 (8)	−0.0020 (8)	−0.0029 (8)
O6	0.0260 (9)	0.0243 (9)	0.0350 (9)	0.0072 (7)	−0.0040 (8)	0.0052 (8)
O7	0.0466 (12)	0.0663 (15)	0.0442 (12)	0.0347 (12)	0.0164 (10)	0.0148 (11)
C8′	0.062 (6)	0.061 (5)	0.053 (5)	0.044 (4)	−0.003 (5)	0.000 (4)
C9′	0.070 (8)	0.062 (6)	0.106 (9)	0.035 (5)	−0.001 (7)	−0.006 (6)
C81′	0.035 (4)	0.048 (4)	0.041 (4)	0.028 (3)	−0.002 (3)	−0.004 (4)
C91′	0.056 (6)	0.084 (8)	0.093 (8)	0.049 (6)	−0.011 (6)	−0.001 (6)

Geometric parameters (Å, º)

C1—C2	1.387 (4)	C13—O6	1.434 (3)
C1—C6	1.395 (4)	C13—H13A	0.9600
C1—C7	1.514 (3)	C13—H13B	0.9600
C2—C3	1.379 (4)	C13—H13C	0.9600
C2—H2	0.86 (4)	C1′—C6′	1.340 (4)
C3—C4	1.363 (4)	C1′—C2′	1.474 (4)
C3—O1	1.376 (3)	C1′—C7′	1.508 (4)
C4—O2	1.371 (3)	C2′—O7	1.215 (3)
C4—C5	1.374 (4)	C2′—C3′	1.534 (4)
C5—O3	1.365 (3)	C3′—O6	1.410 (3)
C5—C6	1.396 (4)	C3′—C4′	1.530 (3)
C6—H6	1.05 (3)	C4′—O5	1.410 (3)
C7—C8	1.541 (4)	C4′—C5′	1.548 (3)
C7—C3′	1.585 (3)	C4′—H4′	1.01 (3)
C7—H7	1.06 (3)	C5′—O4	1.406 (3)
C8—C9	1.524 (4)	C5′—C6′	1.507 (4)
C8—C5′	1.534 (4)	C6′—H6′	0.90 (3)
C8—H8	0.98 (3)	C7′—C81′	1.506 (9)
C9—H9A	0.9600	C7′—C8′	1.551 (11)
C9—H9B	0.9600	C7′—H7A′	0.96 (3)
C9—H9C	0.9600	C7′—H7B′	0.96 (3)
C10—O2	1.408 (4)	C7′—H7C′	0.96 (3)
C10—O1	1.438 (4)	C7′—H7D′	0.96 (3)
C10—H10A	0.91 (4)	O5—H5	0.83 (4)
C10—H10B	0.89 (4)	C8′—C9′	1.280 (17)
C11—O3	1.426 (4)	C8′—H8′	0.9300
C11—H11A	0.9600	C9′—H9A′	0.9300
C11—H11B	0.9600	C9′—H9B′	0.9300
C11—H11C	0.9600	C81′—C91′	1.317 (13)
C12—O4	1.431 (4)	C81′—H81′	0.9300
C12—H12A	0.9600	C91′—H91C	0.9300
C12—H12B	0.9600	C91′—H91D	0.9300
C12—H12C	0.9600		
C2—C1—C6	120.7 (2)	H13B—C13—H13C	109.5
C2—C1—C7	118.4 (2)	C6′—C1′—C2′	117.8 (2)
C6—C1—C7	120.9 (2)	C6′—C1′—C7′	123.8 (3)
C3—C2—C1	117.4 (3)	C2′—C1′—C7′	118.4 (2)

C3—C2—H2	119 (2)	O7—C2′—C1′	123.0 (3)
C1—C2—H2	124 (2)	O7—C2′—C3′	121.4 (3)
C4—C3—O1	110.0 (2)	C1′—C2′—C3′	115.5 (2)
C4—C3—C2	122.2 (2)	O6—C3′—C4′	117.0 (2)
O1—C3—C2	127.7 (3)	O6—C3′—C2′	110.4 (2)
C3—C4—O2	110.3 (2)	C4′—C3′—C2′	107.6 (2)
C3—C4—C5	121.5 (2)	O6—C3′—C7	109.50 (19)
O2—C4—C5	128.2 (3)	C4′—C3′—C7	104.9 (2)
O3—C5—C4	116.8 (3)	C2′—C3′—C7	107.0 (2)
O3—C5—C6	125.7 (3)	O5—C4′—C3′	108.8 (2)
C4—C5—C6	117.5 (3)	O5—C4′—C5′	112.9 (2)
C1—C6—C5	120.8 (3)	C3′—C4′—C5′	99.13 (19)
C1—C6—H6	120.4 (17)	O5—C4′—H4′	112.8 (17)
C5—C6—H6	118.8 (17)	C3′—C4′—H4′	109.7 (16)
C1—C7—C8	115.2 (2)	C5′—C4′—H4′	112.5 (17)
C1—C7—C3′	115.20 (19)	O4—C5′—C6′	111.6 (2)
C8—C7—C3′	104.2 (2)	O4—C5′—C8	109.1 (2)
C1—C7—H7	105.1 (16)	C6′—C5′—C8	111.6 (2)
C8—C7—H7	110.1 (16)	O4—C5′—C4′	114.9 (2)
C3′—C7—H7	106.9 (15)	C6′—C5′—C4′	107.9 (2)
C9—C8—C5′	115.8 (2)	C8—C5′—C4′	101.4 (2)
C9—C8—C7	114.6 (2)	C1′—C6′—C5′	123.9 (3)
C5′—C8—C7	103.89 (19)	C1′—C6′—H6′	123 (2)
C9—C8—H8	112.4 (18)	C5′—C6′—H6′	113 (2)
C5′—C8—H8	99.8 (17)	C81′—C7′—C1′	111.9 (3)
C7—C8—H8	109.1 (18)	C1′—C7′—C8′	110.1 (4)
C8—C9—H9A	109.5	C1′—C7′—H7A′	112 (10)
C8—C9—H9B	109.5	C8′—C7′—H7A′	125 (9)
H9A—C9—H9B	109.5	C81′—C7′—H7B′	130 (2)
C8—C9—H9C	109.5	C1′—C7′—H7B′	99 (8)
H9A—C9—H9C	109.5	C8′—C7′—H7B′	104 (10)
H9B—C9—H9C	109.5	H7A′—C7′—H7B′	102 (6)
O2—C10—O1	108.5 (2)	C1′—C7′—H7C′	108 (9)
O2—C10—H10A	110 (2)	C1′—C7′—H7D′	110 (7)
O1—C10—H10A	108 (2)	C8′—C7′—H7D′	107 (10)
O2—C10—H10B	106 (3)	H7C′—C7′—H7D′	104 (6)
O1—C10—H10B	105 (3)	C3—O1—C10	104.5 (2)
H10A—C10—H10B	119 (4)	C4—O2—C10	105.5 (2)
O3—C11—H11A	109.5	C5—O3—C11	117.1 (2)
O3—C11—H11B	109.5	C5′—O4—C12	114.3 (2)
H11A—C11—H11B	109.5	C4′—O5—H5	112 (2)
O3—C11—H11C	109.5	C3′—O6—C13	114.0 (2)
H11A—C11—H11C	109.5	C9′—C8′—C7′	119.6 (14)
H11B—C11—H11C	109.5	C9′—C8′—H8′	120.2
O4—C12—H12A	109.5	C7′—C8′—H8′	120.2
O4—C12—H12B	109.5	C8′—C9′—H9A′	120.0
H12A—C12—H12B	109.5	C8′—C9′—H9B′	120.0
O4—C12—H12C	109.5	H9A′—C9′—H9B′	120.0
H12A—C12—H12C	109.5	C91′—C81′—C7′	120.6 (11)

H12B—C12—H12C	109.5	C91′—C81′—H81′	119.7
O6—C13—H13A	109.5	C7′—C81′—H81′	119.7
O6—C13—H13B	109.5	C81′—C91′—H91C	120.0
H13A—C13—H13B	109.5	C81′—C91′—H91D	120.0
O6—C13—H13C	109.5	H91C—C91′—H91D	120.0
H13A—C13—H13C	109.5		

C6—C1—C2—C3	0.3 (4)	O6—C3′—C4′—C5′	161.5 (2)
C7—C1—C2—C3	−178.8 (2)	C2′—C3′—C4′—C5′	−73.6 (2)
C1—C2—C3—C4	1.2 (4)	C7—C3′—C4′—C5′	40.0 (2)
C1—C2—C3—O1	177.5 (3)	C9—C8—C5′—O4	−68.9 (3)
O1—C3—C4—O2	0.3 (3)	C7—C8—C5′—O4	164.60 (19)
C2—C3—C4—O2	177.2 (3)	C9—C8—C5′—C6′	54.9 (3)
O1—C3—C4—C5	−178.3 (3)	C7—C8—C5′—C6′	−71.7 (3)
C2—C3—C4—C5	−1.4 (4)	C9—C8—C5′—C4′	169.5 (2)
C3—C4—C5—O3	177.3 (3)	C7—C8—C5′—C4′	43.0 (2)
O2—C4—C5—O3	−1.0 (5)	O5—C4′—C5′—O4	−53.7 (3)
C3—C4—C5—C6	0.1 (4)	C3′—C4′—C5′—O4	−168.7 (2)
O2—C4—C5—C6	−178.2 (3)	O5—C4′—C5′—C6′	−178.8 (2)
C2—C1—C6—C5	−1.5 (4)	C3′—C4′—C5′—C6′	66.1 (2)
C7—C1—C6—C5	177.5 (2)	O5—C4′—C5′—C8	63.8 (3)
O3—C5—C6—C1	−175.6 (3)	C3′—C4′—C5′—C8	−51.2 (2)
C4—C5—C6—C1	1.4 (4)	C2′—C1′—C6′—C5′	−1.3 (4)
C2—C1—C7—C8	−120.6 (3)	C7′—C1′—C6′—C5′	177.9 (3)
C6—C1—C7—C8	60.4 (3)	O4—C5′—C6′—C1′	−158.8 (2)
C2—C1—C7—C3′	118.1 (3)	C8—C5′—C6′—C1′	78.8 (3)
C6—C1—C7—C3′	−61.0 (3)	C4′—C5′—C6′—C1′	−31.7 (3)
C1—C7—C8—C9	88.1 (3)	C6′—C1′—C7′—C81′	−115.2 (5)
C3′—C7—C8—C9	−144.8 (2)	C2′—C1′—C7′—C81′	64.1 (5)
C1—C7—C8—C5′	−144.7 (2)	C6′—C1′—C7′—C8′	−83.6 (6)
C3′—C7—C8—C5′	−17.5 (2)	C2′—C1′—C7′—C8′	95.5 (6)
C6′—C1′—C2′—O7	177.8 (3)	C4—C3—O1—C10	−6.9 (3)
C7′—C1′—C2′—O7	−1.4 (4)	C2—C3—O1—C10	176.4 (3)
C6′—C1′—C2′—C3′	−5.1 (3)	O2—C10—O1—C3	11.0 (4)
C7′—C1′—C2′—C3′	175.7 (2)	C3—C4—O2—C10	6.6 (3)
O7—C2′—C3′—O6	−9.2 (3)	C5—C4—O2—C10	−174.9 (3)
C1′—C2′—C3′—O6	173.7 (2)	O1—C10—O2—C4	−10.8 (4)
O7—C2′—C3′—C4′	−137.9 (3)	C4—C5—O3—C11	−173.5 (3)
C1′—C2′—C3′—C4′	45.0 (3)	C6—C5—O3—C11	3.5 (5)
O7—C2′—C3′—C7	109.9 (3)	C6′—C5′—O4—C12	60.8 (3)
C1′—C2′—C3′—C7	−67.2 (3)	C8—C5′—O4—C12	−175.5 (2)
C1—C7—C3′—O6	−13.6 (3)	C4′—C5′—O4—C12	−62.5 (3)
C8—C7—C3′—O6	−140.8 (2)	C4′—C3′—O6—C13	48.9 (3)
C1—C7—C3′—C4′	112.7 (2)	C2′—C3′—O6—C13	−74.5 (3)
C8—C7—C3′—C4′	−14.4 (2)	C7—C3′—O6—C13	168.0 (2)
C1—C7—C3′—C2′	−133.3 (2)	C81′—C7′—C8′—C9′	−24.6 (9)
C8—C7—C3′—C2′	99.6 (2)	C1′—C7′—C8′—C9′	−123.7 (9)
O6—C3′—C4′—O5	43.4 (3)	C1′—C7′—C81′—C91′	118.5 (8)
C2′—C3′—C4′—O5	168.23 (19)	C8′—C7′—C81′—C91′	26.1 (10)

C7—C3′—C4′—O5	−78.1 (2)

Hydrogen-bond geometry (Å, º)

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
O5—H5···O6^{i}	0.83 (4)	2.12 (4)	2.947 (3)	175 (3)

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