

# Synthesis, crystal structure and absolute configuration of (3*S*,4*R*,5*S*,7*aR*)-7-(but-3-en-1-yn-1-yl)-2,2-dimethyl-3*a*,4,5,7*a*-tetrahydro-2*H*-1,3-benzodioxole-4,5-diol

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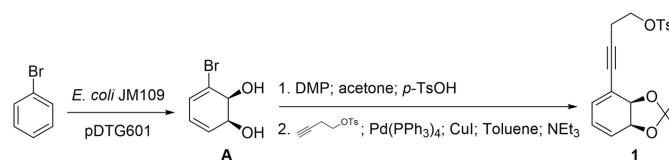
**Supporting information:** this article has supporting information at journals.iucr.org/e

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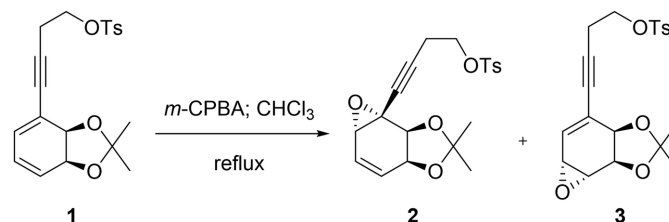
The absolute configuration of the title compound, C<sub>13</sub>H<sub>16</sub>O<sub>4</sub>, determined as 1*S*,2*R*,3*S*,4*R* based on the synthetic pathway, was confirmed by single-crystal X-ray diffraction. The molecule is a relevant intermediary for the synthesis of speciosins, epoxyquinoids or their analogues. The molecule contains fused five- and six-membered rings with two free hydroxyl groups and two protected as an isopropylidenedioxo ring. The packing is directed by hydrogen bonds that define double planes of molecules laying along the *ab* plane and van der Waals interactions between aliphatic chains that point outwards of the planes.

## 1. Chemical context

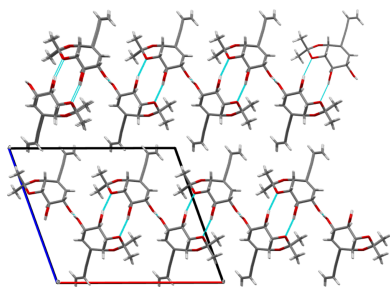
Speciosins are a group of epoxyquinoids isolated from fungal origins that exhibit diverse biological activities (Jiang *et al.*, 2009, 2011; Kim *et al.*, 2006). So far, only one racemic synthesis has been reported (Hookins *et al.*, 2011). We proposed the first synthetic enantioselective approach towards speciosins starting from halodiolols obtained from halobenzene (Vila *et al.*, 2013). In our reported enantioselective route for the synthesis of speciosin A, we obtained molecule **1** in two steps in 65% yield from the diol **A** (Fig. 1). Compound **1** had to be epoxidized in order to functionalize the most substituted double bond (Peixoto de Abreu Lima *et al.*, 2019). That reaction yielded epoxides **2** and **3**, a pair of regioisomers. Despite our

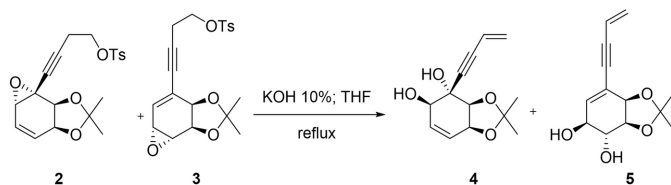


**Figure 1**  
Biotransformation of bromobenzene and alkyne side chain introduction via Sonogashira coupling.



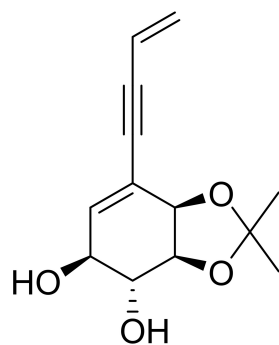
**Figure 2**  
Epoxidation of molecule **1**.





**Figure 3**  
Epoxide opening in basic aqueous conditions.

efforts, we could not obtain the desired regioselectivity towards **2**, and we obtained a mixture of **2** and **3** using a wide variety of solvents, temperature, and concentration (Fig. 2). Another problem we faced was the separation of **2** and **3**, which obliged us to continue our synthetic route using the mixture of both epoxides. Treating **2** and **3** under basic conditions we obtained the products of tosylate elimination and epoxide basic opening for each regioisomer (Fig. 3). Diols **4** and **5** could be successfully separated by column chromatography. Compound **4** is a valuable intermediate for the synthesis of speciosin A. On the other hand, **5** may be useful as an intermediate for the synthesis of other epoxyquinoides like harveynone or its analogues (Pandolfi *et al.*, 2013; Nagata *et al.*, 1992), especially given that it could easily be obtained in higher proportions (Peixoto de Abreu Lima *et al.*, 2019). The epoxide opening in basic aqueous conditions can yield two diastereomers depending on which carbon is attacked by the hydroxyl, though it is expected that the allylic position is more reactive. Thus, it is important to confirm the stereochemistry of the formed diol before continuing with further synthetic steps by means of crystallization and crystal structure determination.



## 2. Structural commentary

Fig. 4 shows the structure of **5** (the title compound) as determined by single-crystal X-ray diffraction. All bond distances and angles fall within the expected values for this kind of organic molecule. The absolute configuration, determined as *1S,2R,3S,4R* based on the synthetic pathway, was confirmed by X-ray diffraction on the basis of anomalous dispersion of light atoms only. The cyclohexene core of the molecule shows puckering angles (Cremer & Pople, 1975) of  $\Theta = 61.0$  (7) $^\circ$  and  $\Phi = 51.7$  (8) $^\circ$ , indicating a conformation between envelope ( $\Theta = 54.7^\circ$ ,  $\Phi = 60^\circ$ ) and screw-boat ( $\Theta = 67.5^\circ$ ,  $\Phi = 30^\circ$ ) with C2 forming the flap. The planar part of the C1–C6–C5–C4–C3

**Table 1**  
Hydrogen-bond geometry ( $\text{\AA}$ ,  $^\circ$ ).

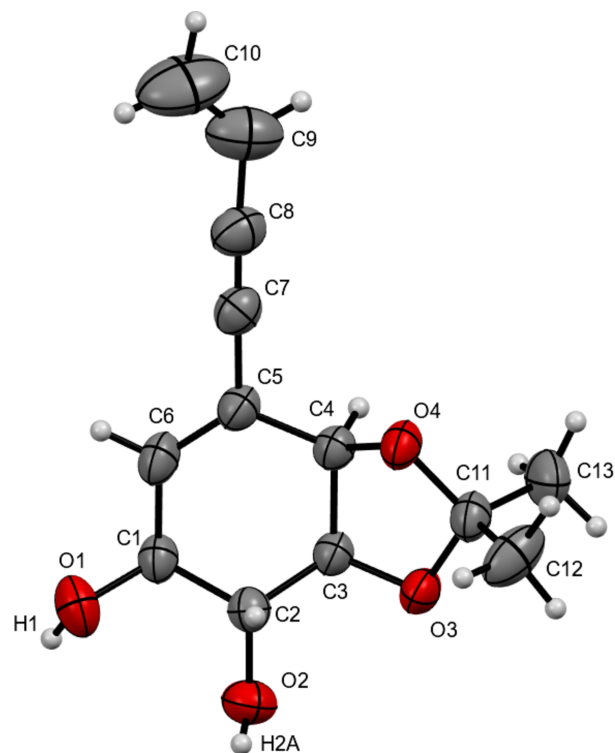
| $D-H\cdots A$          | $D-H$ | $H\cdots A$ | $D\cdots A$ | $D-H\cdots A$ |
|------------------------|-------|-------------|-------------|---------------|
| $O1-H1\cdots O1^i$     | 0.82  | 2.00        | 2.803 (3)   | 167           |
| $O2-H2A\cdots O3^{ii}$ | 0.82  | 2.19        | 2.995 (6)   | 168           |

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

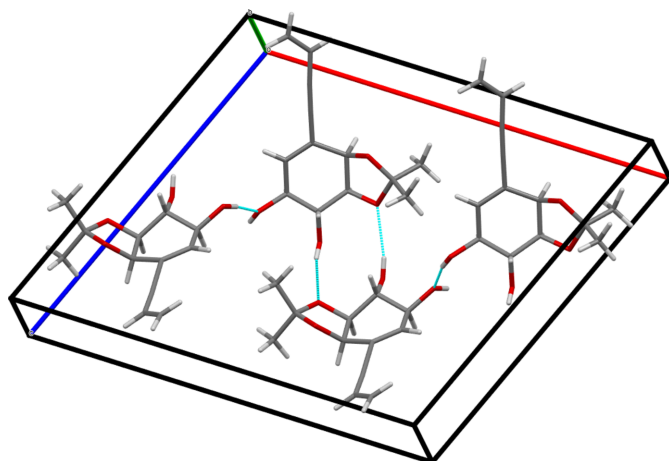
ring (fit of the plane with an r.m.s. deviation of 0.0405  $\text{\AA}$ ) forms a dihedral angle of 52.5 (3) $^\circ$  with the flap (C1–C2–C3). The linear buten-3-en-1-ynyl chain is coplanar with the main part of the ring with a maximum deviation from the plane of 0.21  $\text{\AA}$  for C10 (see supporting information). The five-membered isopropylidenedioxo ring (O3–C3–C4–O4–C11) is also envelope-shaped with  $\Phi_2 = 289.1$  (10) $^\circ$  (idealized  $\Phi_2 = 288^\circ$ ) with O4 forming the flap. The absolute configuration of the four chiral centers and the double bond allows for the five substituents of the cyclohexene ring to be equatorial (O1, O2, C7) or bisectinal (O3, O4) with three of the five H atoms being in axial positions.

## 3. Supramolecular features

In the crystal, molecules are connected through strong  $O-H\cdots O$  hydrogen bonds (see Table 1 and Fig. 5). Pairs of  $O2-H2A\cdots O3^i$  hydrogen bonds connect molecules related by a twofold rotation along [010].  $O1-H1$  groups pointing outwards from the axis form infinite  $O1-H1\cdots O1^{ii}$  chains along [010] between twofold-screw-rotated equivalent molecules [symmetry codes: (i)  $\frac{1}{2} - x, y - \frac{1}{2}, 1 - z$ ; (ii)  $1 - x, y,$



**Figure 4**  
ORTEP view of the title compound showing the numbering scheme. Ellipsoids are drawn at the 30% probability level.

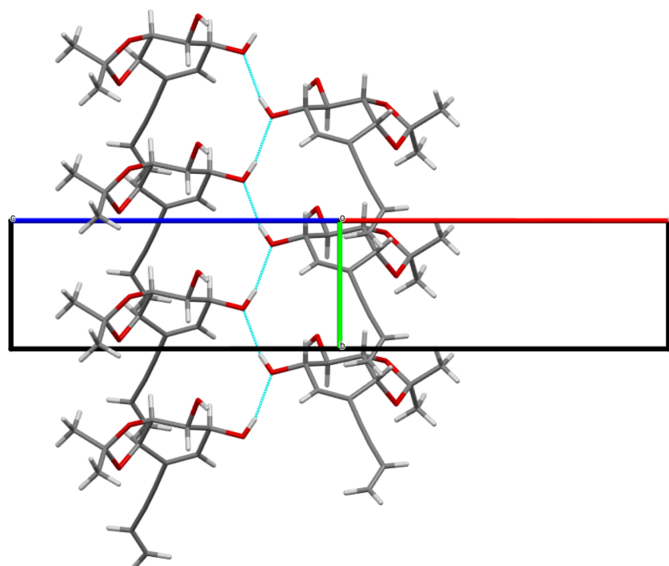


**Figure 5**  
Unit-cell contents of **5**. Note that two hydrogen bonds involving O2 and O3 connect twofold-rotation-related molecules, and a third one connects screw-rotation-related molecules.

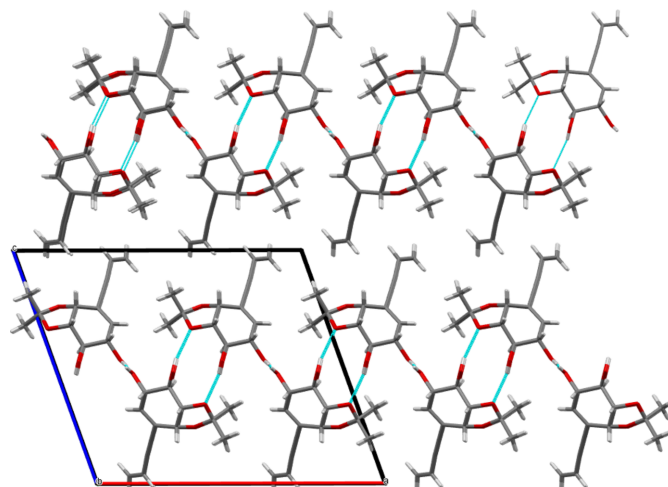
$1 - z]$  as shown in Fig. 6. The combination of both hydrogen bonds provides a strong set of intermolecular interactions that define planes parallel to the *ac* plane with the but-3-en-1-ynyl chains pointing outwards on both sides. Weak van der Waals interactions connect these planes along  $[001]$  as shown in Fig. 7.

#### 4. Database survey

One dozen entries in the 2024.1 version of the CSD (Groom *et al.*, 2016) are related to the title compound sharing a mono-substituted tetrahydroxy-cyclohexene core. The most interesting ones are discussed hereafter. The asymmetric unit of TEDZUA (Buckler *et al.*, 2017) contains two independent molecules that only differ from **5** in the substituent at C5 sharing the same absolute structure at all the chiral centers



**Figure 6**  
View of the unit cell along the  $[101]$  direction showing linear chains of molecules connected through  $O1-H1 \cdots O1$  hydrogen bonds.



**Figure 7**  
View of the unit cell along  $[010]$  direction showing the weak interactions between aliphatic chains in parallel hydrogen-bonded molecular planes of **5**.

and the isopropylidenedioxo ring containing O3 and O4. The cyclohexene cores show an almost perfect envelope conformation in both molecules, but the shape of the bulky vanillin substituent affects the conformation of the five-membered ring and the positions of O4 substituents of C4 in each molecule making them axial. The packing is directed by  $\pi$ -stacking between vanillin residues and a more complex hydrogen-bond network including one crystallization water molecule. RAQLED (Taher *et al.*, 2017) is a tetrahydroxy-cyclohexene with a  $-C_{sp}-C_{sp}-$  chain at C5 (ending in a substituted benzene ring) but the hydroxyl groups at C3 and C4 are free (not part of a five-membered ring) and C2 has an inverted absolute configuration making the cyclohexene ring fall between an envelope and a half-chair conformation with two of the OH substituents on C4 and C1 in axial positions. The packing is similar to that of **5** with a complex hydrogen-bond network defining planes of molecules with the non-polar substituents pointing outwards, interacting weakly with parallel planes. RURVEH (Macías *et al.*, 2015) and HOYFIN (Tibhe *et al.*, 2018) show a tetrahydroxy-cyclohexene core with inverted configurations at C1 and C2 with respect to **5**. The ring conformations fall between envelope and half-chair with the flap at the opposite side of the ring plane, keeping both OH substituents close to equatorial positions. RURVEH also shares the isopropylidenedioxo ring including O3 and O4 with **5**. The packing in HOYFIN is directed by a complex 3D hydrogen-bond network while two different intermolecular hydrogen bonds define the packing of RURVEH, but in this case linear chains of hydrogen-bonded molecules are observed with weak interactions between parallel chains.

#### 5. Synthesis and crystallization

The synthesis of the title compound was carried out through a mixture of epoxides **2** and **3**. The epoxides (400 mg; 1.00 mmol, ratio **2:3** 5:1) were dissolved in tetrahydrofuran

(40 mL) at room temperature and a solution of potassium hydroxide 10% mV (40 mL) was added (Fig. 3). The mixture was refluxed for 4 h. After completion of the reaction, the mixture was diluted with 50 mL of ethyl acetate. The aqueous fraction was neutralized with 10% HCl and extracted with ethyl acetate (portions of 20 mL) until no further products were seen on the aqueous phase on TLC. The combined ethereal fractions were dried with Na<sub>2</sub>SO<sub>4</sub> and filtered. Concentration of the filtrate, followed by column chromatography (hexanes:ethyl acetate 7:3) yielded **4** (177 mg; 81%) and **5** (33 mg; 15%). Small, plate-shaped crystals suitable for X-ray structure analysis were obtained by dissolving **5** in MeOH and slowly evaporating the solvent at room temperature, (m.p.) dec. 435 K. HRMS: C<sub>13</sub>H<sub>16</sub>O<sub>4</sub>+Na calc:259.0946; exp: 259.0953.  $[\alpha]_D^{25.5}$ <sub>589nm</sub> = -13.10° (0.32 g/100 mL of MeOH). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ (ppm): 6.18 (*d*, *J* = 2.1 Hz, 1H), 5.94 (*dd*, *J* = 17.6, 11.2 Hz, 1H), 5.71 (*dd*, *J* = 17.6, 2.0 Hz, 1H), 5.54 (*dd*, *J* = 11.2, 2.1 Hz, 1H), 4.61 (*d*, *J* = 6.4 Hz, 1H), 4.18 (*d*, *J* = 8.5 Hz, 1H), 4.12 (*dd*, *J* = 8.7, 6.3 Hz, 1H), 3.66 (*t*, *J* = 8.5 Hz, 1H), 2.90 (*br s*, 2H), 1.54 (*s*, 3H), 1.43 (*s*, 3H). <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ (ppm): 138.6, 128.0, 119.2, 117.0, 111.1, 89.3, 87.3, 77.4, 74.6, 74.2, 70.4, 28.3, 26.1.

## 6. Refinement

Crystal data, data collection and structure refinement details are summarized in Table 2. All C and O atoms in the structure were refined anisotropically with restraints applied to the thermal ellipsoids of C9 and C10 and their bond distance that appeared shorter than expected due to significant librational disorder of the final atoms of the chain. Neither C9 nor C10 were split due to the lack of clear alternative positions. All H atoms were located in difference  $\Delta F$  maps and refined freely in the initial model to confirm the absolute structure of the chiral centers. In the final model they were modeled in geometrically suitable positions and refined as riding with  $U_{\text{iso}}=1.2/1.5U_{\text{eq}}$  of the core/terminal parent atom.

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**Table 2**

Experimental details.

|   |  |
|---|--|
| Crystal data  |  |
| Chemical formula  | C <sub>13</sub> H <sub>16</sub> O <sub>4</sub>   |
| <i>M<sub>r</sub></i>  | 236.26   |
| Crystal system, space group   | Monoclinic, C2   |
| Temperature (K)   | 296  |
| <i>a</i> , <i>b</i> , <i>c</i> (Å)  | 17.4126 (13), 5.0996 (4),<br>14.9856 (11)  |
| $\beta$ (°)   | 109.652 (2)  |
| <i>V</i> (Å <sup>3</sup> )  | 1253.17 (16)   |
| <i>Z</i>  | 4  |
| Radiation type  | Cu <i>K</i> $\alpha$   |
| $\mu$ (mm <sup>-1</sup> )   | 0.77   |
| Crystal size (mm)   | 0.38 × 0.26 × 0.12   |
| Data collection   |  |
| Diffractometer  | Bruker D8 Venture/Photon 100<br>CMOS   |
| Absorption correction   | Multi-scan (SADABS; Krause <i>et al.</i> , 2015)   |
| <i>T<sub>min</sub></i> , <i>T<sub>max</sub></i>   | 0.646, 0.754   |
| No. of measured, independent and observed [ <i>I</i> > 2 $\sigma$ ( <i>I</i> )] reflections | 10420, 2628, 2138  |
| <i>R<sub>int</sub></i>  | 0.049  |
| ( <i>sin</i> $\theta$ / $\lambda$ ) <sub>max</sub> (Å <sup>-1</sup> )                       | 0.642  |
| Refinement  |  |
| $R[F^2 > 2\sigma(F^2)]$ , $wR(F^2)$ , <i>S</i>  | 0.080, 0.248, 1.13   |
| No. of reflections  | 2628   |
| No. of parameters   | 157  |
| No. of restraints   | 3  |
| H-atom treatment  | H-atom parameters constrained  |
| $\Delta\rho_{\text{max}}$ , $\Delta\rho_{\text{min}}$ (e Å <sup>-3</sup> )                  | 0.41, -0.21  |
| Absolute structure  | Flack <i>x</i> determined using 752<br>quotients $[(I^+) - (I^-)] / [(I^+) + (I^-)]$<br>(Parsons <i>et al.</i> , 2013) |
| Absolute structure parameter  | 0.1 (4)  |

Computer programs: APEX3 and SAINT (Bruker, 2018), OLEX2.solve (Bourhis *et al.*, 2015, Dolomanov *et al.*, 2009), SHELXL2019/2 (Sheldrick, 2015) and ShelXle (Hübschle *et al.*, 2011).

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## supporting information

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## Synthesis, crystal structure and absolute configuration of (3a*S*,4*R*,5*S*,7*aR*)-7-(but-3-en-1-yn-1-yl)-2,2-dimethyl-3a,4,5,7a-tetra- hydro-2*H*-1,3-benzodioxole-4,5-diol

Alejandro Peixoto de Abreu Lima, Enrique Pandolfi, Valeria Schapiro and Leopoldo Suescun

### Computing details

(3a*S*,4*R*,5*S*,7*aR*)-7-(But-3-en-1-yn-1-yl)-2,2-dimethyl-3a,4,5,7a-tetrahydro-2*H*-1,3-benzodioxole-4,5-diol

#### Crystal data

C<sub>13</sub>H<sub>16</sub>O<sub>4</sub>

$M_r = 236.26$

Monoclinic, *C*2

$a = 17.4126$  (13) Å

$b = 5.0996$  (4) Å

$c = 14.9856$  (11) Å

$\beta = 109.652$  (2)°

$V = 1253.17$  (16) Å<sup>3</sup>

$Z = 4$

$F(000) = 504$

$D_x = 1.252$  Mg m<sup>-3</sup>

Cu *K* $\alpha$  radiation,  $\lambda = 1.54178$  Å

Cell parameters from 7392 reflections

$\theta = 5.2$ – $77.8$ °

$\mu = 0.77$  mm<sup>-1</sup>

$T = 296$  K

Plate, colourless

$0.38 \times 0.26 \times 0.12$  mm

#### Data collection

Bruker D8 Venture/Photon 100 CMOS  
diffractometer

Radiation source: Cu Incoatec microsource

Detector resolution: 10.4167 pixels mm<sup>-1</sup>

$\omega$  and  $\phi$  scans

Absorption correction: multi-scan  
(SADABS; Krause *et al.*, 2015)

$T_{\min} = 0.646$ ,  $T_{\max} = 0.754$

10420 measured reflections

2628 independent reflections

2138 reflections with  $I > 2\sigma(I)$

$R_{\text{int}} = 0.049$

$\theta_{\max} = 81.6$ °,  $\theta_{\min} = 5.3$ °

$h = -22 \rightarrow 22$

$k = -6 \rightarrow 6$

$l = -18 \rightarrow 19$

#### Refinement

Refinement on  $F^2$

Least-squares matrix: full

$R[F^2 > 2\sigma(F^2)] = 0.080$

$wR(F^2) = 0.248$

$S = 1.13$

2628 reflections

157 parameters

3 restraints

Hydrogen site location: inferred from  
neighbouring sites

H-atom parameters constrained

$w = 1/[\sigma^2(F_o^2) + (0.1316P)^2 + 0.6357P]$

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

$(\Delta/\sigma)_{\max} < 0.001$

$\Delta\rho_{\max} = 0.41$  e Å<sup>-3</sup>

$\Delta\rho_{\min} = -0.21$  e Å<sup>-3</sup>

Absolute structure: Flack  $x$  determined using

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

Absolute structure parameter: 0.1 (4)



*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.

Least-squares planes (x,y,z in crystal coordinates) and deviations from them (\* indicates atom used to define plane)  
 7.1271 (0.0500) x + 3.5828 (0.0094) y + 6.1525 (0.0364) z = 4.8815 (0.0081)

\* -0.0395 (0.0049) C1 \* 0.0862 (0.0063) C2 \* -0.0383 (0.0049) C4 \* -0.0247 (0.0051) C5 \* 0.0316 (0.0054) C6 \*  
 0.0183 (0.0075) C7 \* -0.0331 (0.0100) C8 \* -0.1482 (0.0159) C9 \* 0.1478 (0.0145) C10 0.7181 (0.0077) C3 1.0769  
 (0.0080) O1 0.9312 (0.0104) O2 0.6098 (0.0104) O3 0.5627 (0.0104) O4

Rms deviation of fitted atoms = 0.0798

6.7576 (0.0357) x + 3.6373 (0.0092) y + 6.2811 (0.0338) z = 4.8211 (0.0091)

Angle to previous plane (with approximate esd) = 1.364 ( 0.435 )

\* -0.0646 (0.0036) C1 \* 0.0457 (0.0028) C2 \* -0.0264 (0.0029) C4 \* 0.0026 (0.0042) C5 \* 0.0427 (0.0038) C6 0.6990  
 (0.0071) C3 0.0448 (0.0094) C7 0.0054 (0.0126) C8 -0.0921 (0.0258) C9 0.2316 (0.0289) C10 1.0394 (0.0069) O1  
 0.8638 (0.0074) O2 0.5755 (0.0096) O3 0.5959 (0.0094) O4

Rms deviation of fitted atoms = 0.0419

- 1.1053 (0.0796) x - 4.9917 (0.0065) y + 3.0656 (0.0891) z = 0.2849 (0.0528)

Angle to previous plane (with approximate esd) = 52.465 ( 0.318 )

\* 0.0000 (0.0000) C2 \* 0.0000 (0.0000) C3 \* 0.0000 (0.0000) C4

Rms deviation of fitted atoms = 0.0000

*Fractional atomic coordinates and isotropic or equivalent isotropic displacement parameters ( $\text{\AA}^2$ )*

|      | x            | y            | z           | $U_{\text{iso}}^*/U_{\text{eq}}$ |
|------|--------------|--------------|-------------|----------------------------------|
| C2   | 0.3746 (3)   | 0.1116 (12)  | 0.4110 (3)  | 0.0683 (11)                      |
| H2   | 0.398970     | 0.279483     | 0.437829    | 0.082*                           |
| C1   | 0.2844 (3)   | 0.1188 (12)  | 0.3889 (4)  | 0.0709 (12)                      |
| H1A  | 0.261212     | -0.053188    | 0.365494    | 0.085*                           |
| O1   | 0.2645 (3)   | 0.1853 (10)  | 0.4702 (3)  | 0.0957 (14)                      |
| H1   | 0.252857     | 0.051859     | 0.493396    | 0.144*                           |
| O3   | 0.47692 (19) | 0.0935 (9)   | 0.3375 (3)  | 0.0779 (11)                      |
| O4   | 0.4120 (2)   | 0.4298 (8)   | 0.2405 (3)  | 0.0750 (10)                      |
| C3   | 0.3927 (3)   | 0.0527 (10)  | 0.3215 (3)  | 0.0635 (11)                      |
| H3   | 0.377713     | -0.128755    | 0.301629    | 0.076*                           |
| C4   | 0.3504 (3)   | 0.2420 (11)  | 0.2399 (3)  | 0.0661 (11)                      |
| H4   | 0.333731     | 0.145670     | 0.179805    | 0.079*                           |
| C5   | 0.2776 (3)   | 0.3908 (12)  | 0.2485 (4)  | 0.0714 (12)                      |
| O2   | 0.4080 (3)   | -0.0979 (11) | 0.4766 (3)  | 0.0939 (13)                      |
| H2A  | 0.433176     | -0.036444    | 0.528898    | 0.141*                           |
| C6   | 0.2469 (3)   | 0.3234 (12)  | 0.3150 (5)  | 0.0791 (15)                      |
| H6   | 0.199730     | 0.407119     | 0.315916    | 0.095*                           |
| C7   | 0.2395 (3)   | 0.5872 (13)  | 0.1767 (4)  | 0.0790 (14)                      |
| C8   | 0.2085 (4)   | 0.7380 (16)  | 0.1167 (5)  | 0.0968 (19)                      |
| C9   | 0.1732 (7)   | 0.918 (2)    | 0.0403 (7)  | 0.139 (4)                        |
| H9   | 0.190917     | 0.900463     | -0.011464   | 0.167*                           |
| C10  | 0.1213 (9)   | 1.096 (3)    | 0.0339 (11) | 0.197 (7)                        |
| H10A | 0.101128     | 1.123418     | 0.083313    | 0.295*                           |
| H10B | 0.103243     | 1.200024     | -0.020116   | 0.295*                           |
| C11  | 0.4859 (3)   | 0.2806 (12)  | 0.2714 (4)  | 0.0750 (14)                      |

|      |            |             |            |           |
|------|------------|-------------|------------|-----------|
| C12  | 0.5552 (4) | 0.4617 (17) | 0.3208 (8) | 0.119 (3) |
| H12A | 0.562490   | 0.585508    | 0.276005   | 0.179*    |
| H12B | 0.604292   | 0.361554    | 0.347503   | 0.179*    |
| H12C | 0.543123   | 0.553832    | 0.370311   | 0.179*    |
| C13  | 0.5005 (5) | 0.131 (2)   | 0.1907 (5) | 0.113 (3) |
| H13A | 0.459372   | -0.001682   | 0.167864   | 0.170*    |
| H13B | 0.553287   | 0.049946    | 0.213143   | 0.170*    |
| H13C | 0.497907   | 0.250061    | 0.140183   | 0.170*    |

*Atomic displacement parameters (Å<sup>2</sup>)*

|     | $U^{11}$    | $U^{22}$  | $U^{33}$   | $U^{12}$    | $U^{13}$    | $U^{23}$    |
|-----|-------------|-----------|------------|-------------|-------------|-------------|
| C2  | 0.064 (2)   | 0.073 (3) | 0.070 (2)  | -0.002 (2)  | 0.024 (2)   | 0.004 (2)   |
| C1  | 0.064 (3)   | 0.072 (3) | 0.085 (3)  | -0.001 (2)  | 0.037 (2)   | 0.002 (3)   |
| O1  | 0.113 (3)   | 0.091 (3) | 0.109 (3)  | -0.006 (3)  | 0.071 (3)   | -0.009 (2)  |
| O3  | 0.0525 (16) | 0.093 (3) | 0.090 (2)  | 0.0072 (17) | 0.0260 (15) | 0.016 (2)   |
| O4  | 0.0591 (17) | 0.073 (2) | 0.100 (2)  | 0.0048 (16) | 0.0359 (16) | 0.0134 (19) |
| C3  | 0.054 (2)   | 0.064 (3) | 0.074 (3)  | 0.0032 (19) | 0.0240 (19) | 0.001 (2)   |
| C4  | 0.058 (2)   | 0.069 (3) | 0.071 (2)  | -0.001 (2)  | 0.0226 (19) | 0.000 (2)   |
| C5  | 0.057 (2)   | 0.072 (3) | 0.084 (3)  | 0.005 (2)   | 0.023 (2)   | 0.004 (3)   |
| O2  | 0.102 (3)   | 0.099 (3) | 0.076 (2)  | 0.009 (3)   | 0.0231 (19) | 0.018 (2)   |
| C6  | 0.058 (2)   | 0.077 (3) | 0.109 (4)  | -0.001 (2)  | 0.037 (3)   | 0.003 (3)   |
| C7  | 0.068 (3)   | 0.079 (3) | 0.087 (3)  | -0.005 (3)  | 0.021 (2)   | -0.004 (3)  |
| C8  | 0.078 (4)   | 0.098 (4) | 0.103 (4)  | -0.003 (4)  | 0.015 (3)   | 0.010 (4)   |
| C9  | 0.158 (9)   | 0.114 (7) | 0.116 (6)  | -0.019 (6)  | 0.008 (6)   | 0.016 (6)   |
| C10 | 0.196 (13)  | 0.124 (9) | 0.219 (14) | 0.009 (9)   | 0.002 (10)  | 0.057 (11)  |
| C11 | 0.063 (3)   | 0.075 (3) | 0.096 (3)  | 0.002 (2)   | 0.038 (2)   | 0.008 (3)   |
| C12 | 0.069 (3)   | 0.086 (5) | 0.183 (8)  | -0.008 (3)  | 0.016 (4)   | 0.008 (5)   |
| C13 | 0.111 (5)   | 0.138 (6) | 0.111 (5)  | 0.035 (5)   | 0.064 (4)   | 0.007 (5)   |

*Geometric parameters (Å, °)*

|        |           |          |            |
|--------|-----------|----------|------------|
| C2—O2  | 1.437 (7) | C5—C7    | 1.457 (8)  |
| C2—C1  | 1.492 (6) | O2—H2A   | 0.8200     |
| C2—C3  | 1.508 (7) | C6—H6    | 0.9300     |
| C2—H2  | 0.9800    | C7—C8    | 1.168 (9)  |
| C1—O1  | 1.414 (7) | C8—C9    | 1.433 (12) |
| C1—C6  | 1.502 (8) | C9—C10   | 1.264 (16) |
| C1—H1A | 0.9800    | C9—H9    | 0.9300     |
| O1—H1  | 0.8200    | C10—H10A | 0.9300     |
| O3—C3  | 1.420 (5) | C10—H10B | 0.9300     |
| O3—C11 | 1.422 (7) | C11—C12  | 1.502 (9)  |
| O4—C11 | 1.431 (6) | C11—C13  | 1.521 (10) |
| O4—C4  | 1.436 (6) | C12—H12A | 0.9600     |
| C3—C4  | 1.538 (7) | C12—H12B | 0.9600     |
| C3—H3  | 0.9800    | C12—H12C | 0.9600     |
| C4—C5  | 1.520 (7) | C13—H13A | 0.9600     |
| C4—H4  | 0.9800    | C13—H13B | 0.9600     |



|              |            |               |            |
|--------------|------------|---------------|------------|
| C5—C6        | 1.324 (8)  | C13—H13C      | 0.9600     |
| O2—C2—C1     | 108.9 (4)  | C2—O2—H2A     | 109.5      |
| O2—C2—C3     | 107.6 (5)  | C5—C6—C1      | 123.4 (5)  |
| C1—C2—C3     | 109.1 (4)  | C5—C6—H6      | 118.3      |
| O2—C2—H2     | 110.4      | C1—C6—H6      | 118.3      |
| C1—C2—H2     | 110.4      | C8—C7—C5      | 177.7 (7)  |
| C3—C2—H2     | 110.4      | C7—C8—C9      | 176.9 (10) |
| O1—C1—C2     | 111.0 (4)  | C10—C9—C8     | 128.6 (13) |
| O1—C1—C6     | 107.3 (5)  | C10—C9—H9     | 115.7      |
| C2—C1—C6     | 110.1 (4)  | C8—C9—H9      | 115.7      |
| O1—C1—H1A    | 109.4      | C9—C10—H10A   | 120.0      |
| C2—C1—H1A    | 109.4      | C9—C10—H10B   | 120.0      |
| C6—C1—H1A    | 109.4      | H10A—C10—H10B | 120.0      |
| C1—O1—H1     | 109.5      | O3—C11—O4     | 106.5 (4)  |
| C3—O3—C11    | 109.3 (4)  | O3—C11—C12    | 109.1 (5)  |
| C11—O4—C4    | 103.6 (4)  | O4—C11—C12    | 108.5 (5)  |
| O3—C3—C2     | 109.5 (4)  | O3—C11—C13    | 107.7 (6)  |
| O3—C3—C4     | 103.5 (4)  | O4—C11—C13    | 112.4 (5)  |
| C2—C3—C4     | 113.2 (4)  | C12—C11—C13   | 112.3 (6)  |
| O3—C3—H3     | 110.1      | C11—C12—H12A  | 109.5      |
| C2—C3—H3     | 110.1      | C11—C12—H12B  | 109.5      |
| C4—C3—H3     | 110.1      | H12A—C12—H12B | 109.5      |
| O4—C4—C5     | 108.0 (4)  | C11—C12—H12C  | 109.5      |
| O4—C4—C3     | 104.9 (4)  | H12A—C12—H12C | 109.5      |
| C5—C4—C3     | 115.8 (4)  | H12B—C12—H12C | 109.5      |
| O4—C4—H4     | 109.3      | C11—C13—H13A  | 109.5      |
| C5—C4—H4     | 109.3      | C11—C13—H13B  | 109.5      |
| C3—C4—H4     | 109.3      | H13A—C13—H13B | 109.5      |
| C6—C5—C7     | 122.4 (5)  | C11—C13—H13C  | 109.5      |
| C6—C5—C4     | 119.6 (5)  | H13A—C13—H13C | 109.5      |
| C7—C5—C4     | 117.7 (5)  | H13B—C13—H13C | 109.5      |
| O2—C2—C1—O1  | 65.4 (6)   | C2—C3—C4—C5   | -19.9 (6)  |
| C3—C2—C1—O1  | -177.4 (5) | O4—C4—C5—C6   | -127.6 (5) |
| O2—C2—C1—C6  | -175.9 (5) | C3—C4—C5—C6   | -10.4 (7)  |
| C3—C2—C1—C6  | -58.7 (6)  | O4—C4—C5—C7   | 58.1 (6)   |
| C11—O3—C3—C2 | -122.7 (5) | C3—C4—C5—C7   | 175.4 (5)  |
| C11—O3—C3—C4 | -1.7 (5)   | C7—C5—C6—C1   | 179.1 (5)  |
| O2—C2—C3—O3  | -72.8 (5)  | C4—C5—C6—C1   | 5.1 (9)    |
| C1—C2—C3—O3  | 169.2 (4)  | O1—C1—C6—C5   | 151.3 (6)  |
| O2—C2—C3—C4  | 172.3 (4)  | C2—C1—C6—C5   | 30.3 (8)   |
| C1—C2—C3—C4  | 54.2 (6)   | C3—O3—C11—O4  | 22.5 (6)   |
| C11—O4—C4—C5 | 156.9 (4)  | C3—O3—C11—C12 | 139.5 (5)  |
| C11—O4—C4—C3 | 32.8 (5)   | C3—O3—C11—C13 | -98.3 (5)  |
| O3—C3—C4—O4  | -19.4 (5)  | C4—O4—C11—O3  | -34.5 (5)  |
| C2—C3—C4—O4  | 99.0 (5)   | C4—O4—C11—C12 | -151.9 (6) |
| O3—C3—C4—C5  | -138.4 (4) | C4—O4—C11—C13 | 83.2 (6)   |

*Hydrogen-bond geometry (Å, °)*

| <i>D</i> —H··· <i>A</i>   | <i>D</i> —H | H··· <i>A</i> | <i>D</i> ··· <i>A</i> | <i>D</i> —H··· <i>A</i> |
|---------------------------|-------------|---------------|-----------------------|-------------------------|
| O1—H1···O1 <sup>i</sup>   | 0.82        | 2.00          | 2.803 (3)             | 167                     |
| O2—H2A···O3 <sup>ii</sup> | 0.82        | 2.19          | 2.995 (6)             | 168                     |

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