

## 6-[[[(Benzyloxy)carbonyl]oxy]-2-methylhexahydropyrano[3,2-*d*][1,3]dioxin-7,8-diyl bis(chloroacetate)

Jerry P. Jasinski,<sup>a\*</sup> Ray J. Butcher,<sup>b</sup> M. T. Swamy,<sup>c</sup> H. S. Yathirajan<sup>d</sup> and B. Narayana<sup>e</sup>

<sup>a</sup>Department of Chemistry, Keene State College, 229 Main Street, Keene, NH 03435-2001, USA, <sup>b</sup>Department of Chemistry, Howard University, 525 College Street NW, Washington DC 20059, USA, <sup>c</sup>Department of Studies in Chemistry, University of Mysore, Manasagangotri, Mysore 570006, India, <sup>d</sup>Department of Studies in Chemistry, University of Mysore, Manasagangotri, Mysore 570 006, India, and <sup>e</sup>Department of Studies in Chemistry, Mangalore University, Mangalagangotri 574 199, India

Correspondence e-mail: jjasinski@keene.edu

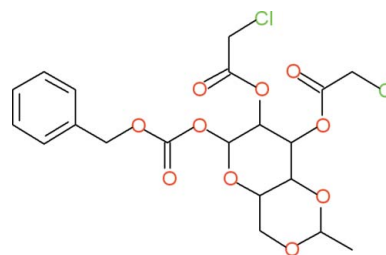
Received 30 December 2009; accepted 3 February 2010

Key indicators: single-crystal X-ray study;  $T = 200$  K; mean  $\sigma(\text{C}-\text{C}) = 0.004$  Å;  $R$  factor = 0.040;  $wR$  factor = 0.084; data-to-parameter ratio = 20.1.

The asymmetric unit of the title compound,  $\text{C}_{20}\text{H}_{22}\text{O}_{10}\text{Cl}_2$ , consists of a 6-[[[(benzyloxy)carbonyl]oxy]group and two chloroacetate groups bonded to a 2-methylhexahydropyrano[3,2-*d*][1,3]dioxin group at the carbon 1,2 and 3 positions, respectively, of a pyrano ring fused to a dioxin ring. The dihedral angle between the mean planes of the dioxin and benzyl rings is  $42.2(2)^\circ$ . An extensive array of weak intermolecular  $\text{C}-\text{H}\cdots\text{O}$  hydrogen bonds links the molecules into chains along [011]. Additional weak intermolecular  $\text{C}-\text{H}\cdots\pi$  interactions occur between  $\text{C}-\text{H}$  atoms of the dioxin and benzyl rings and a nearby benzene ring. A MOPAC geometry optimization calculation *in vacuo* revealed that the dihedral angle between the mean planes of the dioxin and benzyl rings increased by  $24.42$  to  $66.64^\circ$ , suggesting that the weak intermolecular hydrogen-bonding interactions, in coordination with weak  $\text{C}-\text{H}\cdots\pi$  interactions, influence the geometry of the resultant crystalline species and help to stabilize the crystal packing.

### Related literature

For background to the title compound, see: Ernst & Derendorf, (1995); Ji *et al.* (1997); Sanford *et al.* (1990); Budavari (1989); Wrasidlo *et al.* (2002). For related structures, see: Shi & Wang, (2003); Wu *et al.* (2005); Zhou *et al.* (2005). For bond-length data, see: Allen *et al.* (1987). For puckering parameters, see: Cremer & Pople (1975). For MOPAC PM3 calculations, see: Schmidt & Polik, (2007).



### Experimental

#### Crystal data

$\text{C}_{20}\text{H}_{22}\text{Cl}_2\text{O}_{10}$   
 $M_r = 493.28$   
 Orthorhombic,  $P2_12_12_1$   
 $a = 8.1780(1)$  Å  
 $b = 14.9165(3)$  Å  
 $c = 19.3555(4)$  Å

$V = 2361.12(7)$  Å<sup>3</sup>  
 $Z = 4$   
 Mo  $K\alpha$  radiation  
 $\mu = 0.33$  mm<sup>-1</sup>  
 $T = 200$  K  
 $0.44 \times 0.34 \times 0.27$  mm

#### Data collection

Oxford Diffraction Gemini diffractometer  
 Absorption correction: multi-scan (*CrysAlis RED*; Oxford Diffraction, 2007)  
 $T_{\min} = 0.821$ ,  $T_{\max} = 1.000$

30676 measured reflections  
 5818 independent reflections  
 3677 reflections with  $I > 2\sigma(I)$   
 $R_{\text{int}} = 0.049$

#### Refinement

$R[F^2 > 2\sigma(F^2)] = 0.040$   
 $wR(F^2) = 0.084$   
 $S = 0.92$   
 5818 reflections  
 290 parameters  
 H-atom parameters constrained

$\Delta\rho_{\max} = 0.34$  e Å<sup>-3</sup>  
 $\Delta\rho_{\min} = -0.23$  e Å<sup>-3</sup>  
 Absolute structure: Flack (1983),  
 2513 Friedel pairs  
 Flack parameter: 0.05 (5)

**Table 1**

Hydrogen-bond geometry (Å, °).

*Cg*3 is the centroid of the C10–C15 ring.

| <i>D</i> – <i>H</i> ⋯ <i>A</i>      | <i>D</i> – <i>H</i> | <i>H</i> ⋯ <i>A</i> | <i>D</i> ⋯ <i>A</i> | <i>D</i> – <i>H</i> ⋯ <i>A</i> |
|-------------------------------------|---------------------|---------------------|---------------------|--------------------------------|
| C6–H6B⋯O8 <sup>i</sup>              | 0.99                | 2.57                | 3.235 (3)           | 125                            |
| C13–H13A⋯O10 <sup>ii</sup>          | 0.95                | 2.54                | 3.452 (4)           | 162                            |
| C17–H17B⋯O5 <sup>iii</sup>          | 0.99                | 2.42                | 3.310 (3)           | 149                            |
| C19–H19A⋯O3 <sup>iv</sup>           | 0.99                | 2.52                | 3.460 (3)           | 158                            |
| C19–H19B⋯O2 <sup>v</sup>            | 0.99                | 2.38                | 3.364 (3)           | 170                            |
| C20–H20B⋯O4 <sup>iv</sup>           | 0.98                | 2.59                | 3.494 (3)           | 154                            |
| C4–H4A⋯ <i>Cg</i> 3 <sup>iv</sup>   | 1.00                | 2.89                | 3.879 (2)           | 171                            |
| C14–H14A⋯ <i>Cg</i> 3 <sup>vi</sup> | 0.95                | 2.87                | 3.818 (4)           | 173                            |

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

Data collection: *CrysAlis PRO* (Oxford Diffraction, 2007); cell refinement: *CrysAlis PRO*; data reduction: *CrysAlis PRO*; program(s) used to solve structure: *SHELXS97* (Sheldrick, 2008); program(s) used to refine structure: *SHELXL97* (Sheldrick, 2008); molecular graphics: *SHELXTL* (Sheldrick, 2008); software used to prepare material for publication: *SHELXTL*.

MTS thanks the University of Mysore for use of their research facilities. RJB acknowledges the NSF MRI program (grant No. CHE-0619278) for funds to purchase an X-ray diffractometer.

---

Supplementary data and figures for this paper are available from the IUCr electronic archives (Reference: HG2627).

---

## References

- Allen, F. H., Kennard, O., Watson, D. G., Brammer, L., Orpen, A. G. & Taylor, R. (1987). *J. Chem. Soc. Perkin Trans. 2*, pp. S1–19.
- Budavari, S. (1989). Editor. *The Merck Index: An Encyclopedia of Chemicals, Drugs and Biologicals*, Rahway, NJ: Merck & Co.
- Cremer, D. & Pople, J. A. (1975). *J. Am. Chem. Soc.* **97** 1354–1355.
- Ernst, M. & Derendorf, H. (1995). *Drug Actions: Basic Principles and Therapeutic Aspects*. Stuttgart: Medpharm Scientific Publishers.
- Flack, H. D. (1983). *Acta Cryst.* **A39**, 876–881.
- Ji, Z., Wang, H.-K., Bastow, K. F., Zhu, X.-K., Cho, S. J., Cheng, Y.-C. & Lee, K.-H. (1997). *Bioorg. Med. Chem. Lett.* **7**, 607–612.
- Oxford Diffraction (2007). *CrysAlis PRO* and *CrysAlis RED*. Oxford Diffraction Ltd, Abingdon, England.
- Sanford, G. L., Gilman, A. & Gilman, A. G. (1990). *The Pharmacological Basis of Therapeutics*, 8th Edition. Elmsford, NY, Pergamon Press.
- Schmidt, J. R. & Polik, W. F. (2007). *WebMO Pro*. WebMO, LLC: Holland, MI, USA, available from <http://www.webmo.net>.
- Sheldrick, G. M. (2008). *Acta Cryst.* **A64**, 112–122.
- Shi, J.-F. & Wang, Y.-G. (2003). *Acta Cryst.* **E59**, o756–o758.
- Wrasidlo, W., Schröder, U., Bernt, K., Hübener, N., Shabat, D., Gaedicke, G. & Lode, H. (2002). *Bioorg. Med. Chem. Lett.* **12**, 557–560.
- Wu, Q.-X., Shi, Y.-P. & Shi, Y.-P. (2005). *Acta Cryst.* **E61**, o3502–o3504.
- Zhou, F.-Y., Jian, S.-Z., He, X.-Y. & Wang, Y.-G. (2005). *Acta Cryst.* **E61**, o1374–o1376.

## supporting information

*Acta Cryst.* (2010). E66, o572–o573 [doi:10.1107/S1600536810004356]

## 6-[[**(Benzyloxy)carbonyl**]oxy]-2-methylhexahydropyrano[3,2-*d*][1,3]dioxin-7,8-diyl bis(chloroacetate)

**Jerry P. Jasinski, Ray J. Butcher, M. T. Swamy, H. S. Yathirajan and B. Narayana**

### S1. Comment

The title compound is an intermediate in the preparation of etoposide phosphate (Budavari, 1989), an inhibitor of the enzyme topoisomerase II. It is used as a form of chemotherapy for malignancies such as Ewing's sarcoma, lung cancer, testicular cancer, lymphoma, non-lymphocytic leukemia, and glioblastoma multiforme. It is often given in combination with other drugs. Chemically it derives from podophyllotoxin, a toxin found in the American Mayapple (Sanford *et al.*, 1990; Ernst & Derendorf, 1995). Design, synthesis, and biological evaluation of novel etoposide analogs bearing pyrrole-carboxamidino group as DNA topoisomerase II inhibitors have been reported (Ji *et al.*, 1997). Two 4'-propylcarboxy derivatives of etoposide were synthesized and evaluated as potential prodrugs for anticancer therapy (Wrasidlo *et al.*, 2002). Structures of few derivatives of etoposide are published, viz, 10-hydroxy-1-oxoeremophila-7(11),8(9)-dien-12,8-olide (Wu *et al.*, 2005), (5*R*,5*aR*,8*aR*,9*S*)-5-(3,4-dihydroxy-5-methoxyphenyl)-9-fluoro-5,8,8*a*,9-tetrahydro-furo[3',4':6,7]naphtho[2,3-*d*]-1,3-dioxol-6(5*aH*)-one acetone solvate (Zhou *et al.*, 2005), (5*aR*,8*aR*,9*R*)-9-(3,4,5-trimethoxyphenyl)-5*a*,6,8*a*,9-tetrahydrofuro[3',4':6,7]naphtho[2,3-*d*][1,3]dioxole-5,8-dione (Shi & Wang, 2003). In view of the importance of the title compound, C<sub>20</sub>H<sub>22</sub>Cl<sub>2</sub>O<sub>10</sub>, (I), a crystal structure is reported here.

The asymmetric unit of title compound, C<sub>20</sub>H<sub>22</sub>Cl<sub>2</sub>O<sub>10</sub>, (I), consists of a 6-[[**(benzyloxy)carbonyl**]oxy] group and two chloroacetate groups bonded to a 2-methylhexahydropyrano[3,2-*d*][1,3]dioxin group at the carbon 1,2 and 3 positions of the pyrano ring fused to a dioxin ring, respectively (Fig. 1). The fused [1,3]dioxin and 2-methylhexahydropyrano six-membered rings each adopt a slightly distorted normal chair configuration (Cremer & Pople, 1975) with puckering parameters  $Q$ ,  $\theta$  and  $\varphi$  of 0.598 (2) & 0.6025 (19) Å, 2.95 (19)° & 2.81 (18)°, and 33 (5)° & 357 (4)%, respectively (Fig. 2). For an ideal chair,  $\theta$  has a value of 0 or 180°. The keto groups in each chloroacetate group are arranged in an antiparallel fashion (Torsion angles C2/O7/C16/C8 = 2.2 (3)°; C3/O9/C18/O10 = 4.4 (3)°) and nearly perpendicular to the benzene ring, while the keto group in the 6-[[**(benzyloxy)carbonyl**]oxy] group is somewhat diagonal to and bisecting the benzyl ring (torsion angle C1/O4/C8/O5 = -3.1 (3)°). The dihedral angle between the mean planes of the dioxin and benzene rings is 42.2 (2)°. An extensive array of intermolecular C—H...O hydrogen bonds exists which involves acceptor oxygen atoms from the three carbonyl groups, two oxygen atoms from the pyrano-dioxin rings, a keto oxygen atom in the 6-[[**(benzyloxy)carbonyl**]oxy] group, donor C—H atoms from an sp<sup>2</sup> hybridized carbon in the benzene ring and sp<sup>3</sup> hybridized carbon atoms from the dioxin ring, a methyl group and each chloroacetate group (Table 1). In addition, intermolecular C—H...Cg  $\pi$ -ring interactions also occur between C4—H4A and C14—H14A atoms of the dioxin and benzene rings and a nearby benzene ring (C4—H4A...Cg3 = 3.879 (2) Å (2-*x*, 1/2+*y*, 1/2-*z*) and C14—H14A...Cg3 = 3.818 (4) Å (-1/2+*x*, -1/2-*y*, -*z*), where Cg3 = ring centroid for C10—C15), respectively. Bond lengths and angles are all within expected ranges (Allen *et al.* 1987).

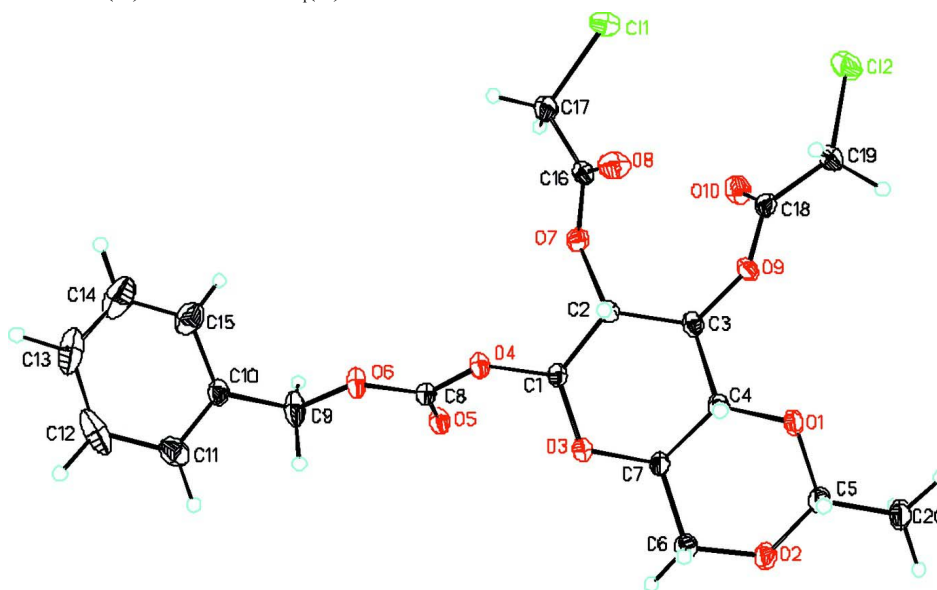
After a geometry optimized MOPAC PM3 computational calculation (Schmidt & Polik 2007) on (I), in vacuo, the dihedral angle between the mean planes of the dioxin and benzene rings became  $66.64^\circ$ , an increase of  $24.42^\circ$ . These observations support a suggestion that a collection of weak intermolecular forces influence the molecular conformation in the crystal and contribute to the packing of these molecules into chains propagating along the [011].

## S2. Experimental

The title compound was obtained as a gift sample from CAD Pharma, Bangalore, India. Suitable crystals were grown from methanol by slow evaporation (m.p.: 385-388 K).

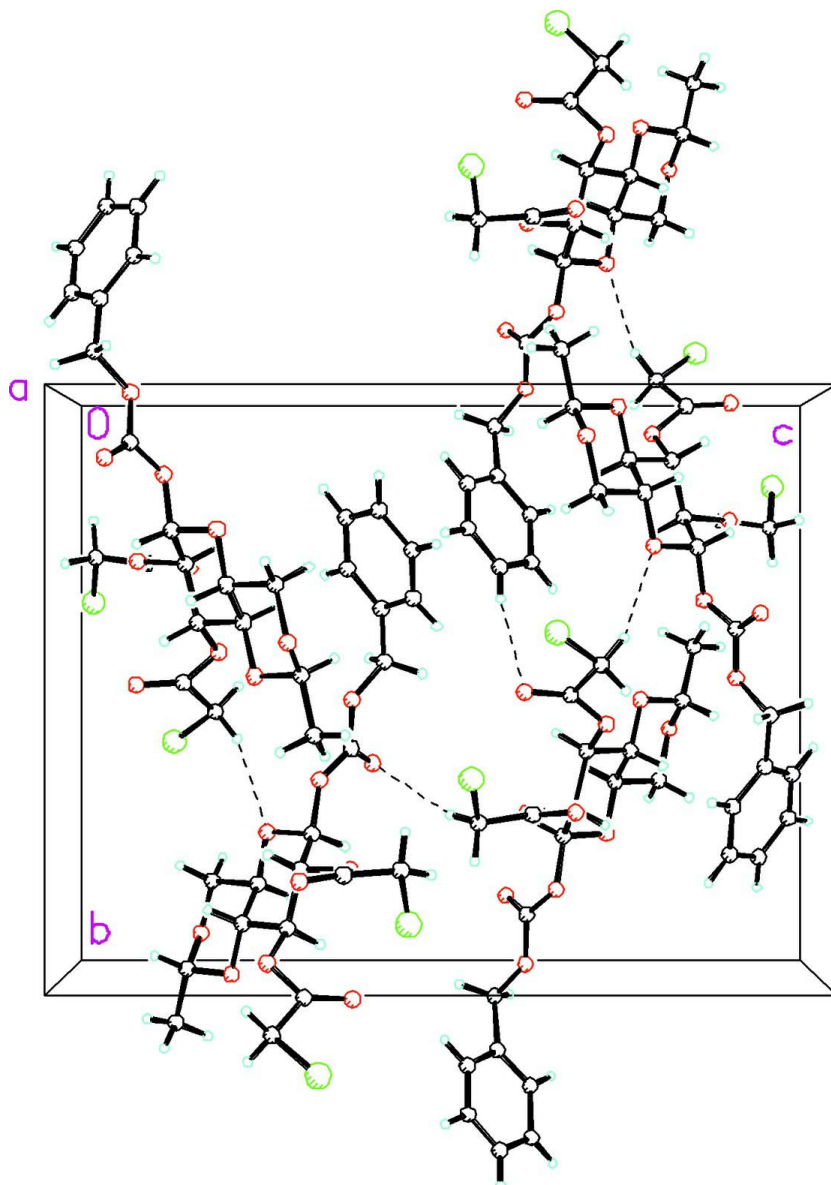
## S3. Refinement

All of the H atoms were placed in their calculated positions and then refined using the riding model with C—H = 0.95-1.00 Å, and with  $U_{\text{iso}}(\text{H}) = 1.18\text{-}1.49U_{\text{eq}}(\text{C})$ .



**Figure 1**

Molecular structure of (I),  $\text{C}_{20}\text{H}_{22}\text{O}_{10}\text{Cl}_2$ , showing the atom labeling scheme and 50% probability displacement ellipsoids.



**Figure 2**

The molecular packing for (I) viewed down the *a* axis. Dashed lines indicate weak C—H···O intermolecular hydrogen bond interactions which link the molecule into chains propagating along the [011].

**6-[[[(Benzyloxy)carbonyl]oxy]-2-methylhexahydropyrano[3,2-*d*][1,3]dioxin-7,8-diyl bis(chloroacetate)]**

*Crystal data*

$C_{20}H_{22}Cl_2O_{10}$

$M_r = 493.28$

Orthorhombic,  $P2_12_12_1$

Hall symbol: P 2ac 2ab

$a = 8.1780$  (1) Å

$b = 14.9165$  (3) Å

$c = 19.3555$  (4) Å

$V = 2361.12$  (7) Å<sup>3</sup>

$Z = 4$

$F(000) = 1024$

$D_x = 1.388$  Mg m<sup>-3</sup>

Mo  $K\alpha$  radiation,  $\lambda = 0.71073$  Å

Cell parameters from 8966 reflections

$\theta = 4.8$ – $32.5^\circ$

$\mu = 0.33$  mm<sup>-1</sup>

$T = 200$  K

Prism, colorless

$0.44 \times 0.34 \times 0.27$  mm

*Data collection*

|  |  |
|--|--|
| Oxford Diffraction Gemini diffractometer   | 30676 measured reflections   |
| Radiation source: Enhance (Mo) X-ray Source  | 5818 independent reflections   |
| Graphite monochromator   | 3677 reflections with $I > 2\sigma(I)$                                 |
| Detector resolution: 10.5081 pixels mm <sup>-1</sup>                                   | $R_{\text{int}} = 0.049$   |
| $\omega$ scans   | $\theta_{\text{max}} = 28.3^\circ$ , $\theta_{\text{min}} = 4.9^\circ$ |
| Absorption correction: multi-scan<br>( <i>CrysAlis RED</i> ; Oxford Diffraction, 2007) | $h = -10 \rightarrow 10$   |
| $T_{\text{min}} = 0.821$ , $T_{\text{max}} = 1.000$                                    | $k = -19 \rightarrow 19$   |
|  | $l = -25 \rightarrow 25$   |

*Refinement*

|  |  |
|--|--|
| Refinement on $F^2$  | Hydrogen site location: inferred from neighbouring sites     |
| Least-squares matrix: full                                     | H-atom parameters constrained                                |
| $R[F^2 > 2\sigma(F^2)] = 0.040$                                | $w = 1/[\sigma^2(F_o^2) + (0.0439P)^2]$                      |
| $wR(F^2) = 0.084$  | where $P = (F_o^2 + 2F_c^2)/3$                               |
| $S = 0.92$   | $(\Delta/\sigma)_{\text{max}} < 0.001$                       |
| 5818 reflections   | $\Delta\rho_{\text{max}} = 0.34 \text{ e } \text{\AA}^{-3}$  |
| 290 parameters   | $\Delta\rho_{\text{min}} = -0.23 \text{ e } \text{\AA}^{-3}$ |
| 0 restraints   | Absolute structure: Flack (1983), 2513 Friedel pairs         |
| Primary atom site location: structure-invariant direct methods | Absolute structure parameter: 0.05 (5)                       |
| Secondary atom site location: difference Fourier map           |  |

*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  $F^2 > \sigma(F^2)$  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 ( $\text{\AA}^2$ )*

|     | <i>x</i>     | <i>y</i>     | <i>z</i>     | $U_{\text{iso}}^*/U_{\text{eq}}$ |
|-----|--------------|--------------|--------------|----------------------------------|
| C11 | 0.46237 (7)  | 0.35551 (4)  | 0.03846 (3)  | 0.05778 (17)                     |
| C12 | 0.51793 (9)  | 0.59375 (5)  | 0.14719 (4)  | 0.0793 (2)                       |
| O1  | 1.17773 (16) | 0.47514 (9)  | 0.26910 (8)  | 0.0450 (4)                       |
| O2  | 1.42110 (16) | 0.41973 (10) | 0.31523 (8)  | 0.0520 (4)                       |
| O3  | 1.21358 (17) | 0.23957 (9)  | 0.22343 (7)  | 0.0377 (3)                       |
| O4  | 1.06875 (15) | 0.14810 (9)  | 0.15336 (7)  | 0.0371 (3)                       |
| O5  | 1.29642 (18) | 0.12683 (10) | 0.08848 (8)  | 0.0456 (4)                       |
| O6  | 1.11749 (18) | 0.01657 (9)  | 0.11327 (8)  | 0.0452 (4)                       |
| O7  | 0.86643 (16) | 0.28806 (9)  | 0.11292 (7)  | 0.0376 (3)                       |
| O8  | 0.63005 (18) | 0.29606 (12) | 0.17188 (8)  | 0.0542 (4)                       |
| O9  | 0.86234 (16) | 0.43867 (9)  | 0.21585 (7)  | 0.0366 (3)                       |
| O10 | 0.8181 (2)   | 0.49330 (10) | 0.10897 (8)  | 0.0553 (4)                       |
| C1  | 1.1148 (2)   | 0.23894 (13) | 0.16396 (11) | 0.0346 (5)                       |
| H1A | 1.1759       | 0.2628       | 0.1232       | 0.042*                           |

|      |            |               |              |             |
|------|------------|---------------|--------------|-------------|
| C2   | 0.9602 (2) | 0.29229 (13)  | 0.17650 (10) | 0.0340 (4)  |
| H2A  | 0.8964     | 0.2650        | 0.2152       | 0.041*      |
| C3   | 1.0049 (2) | 0.38910 (13)  | 0.19405 (10) | 0.0354 (5)  |
| H3A  | 1.0567     | 0.4189        | 0.1533       | 0.043*      |
| C4   | 1.1217 (2) | 0.38731 (13)  | 0.25368 (11) | 0.0349 (5)  |
| H4A  | 1.0646     | 0.3623        | 0.2951       | 0.042*      |
| C5   | 1.2792 (3) | 0.47197 (16)  | 0.32884 (14) | 0.0512 (6)  |
| H5A  | 1.2172     | 0.4459        | 0.3686       | 0.061*      |
| C6   | 1.3804 (3) | 0.32825 (15)  | 0.29908 (12) | 0.0458 (6)  |
| H6A  | 1.3251     | 0.2997        | 0.3389       | 0.055*      |
| H6B  | 1.4808     | 0.2938        | 0.2885       | 0.055*      |
| C7   | 1.2681 (2) | 0.32912 (13)  | 0.23705 (11) | 0.0358 (5)  |
| H7A  | 1.3271     | 0.3535        | 0.1959       | 0.043*      |
| C8   | 1.1749 (3) | 0.09907 (14)  | 0.11513 (11) | 0.0367 (5)  |
| C9   | 1.2170 (3) | -0.04574 (16) | 0.07276 (15) | 0.0623 (7)  |
| H9A  | 1.3284     | -0.0502       | 0.0924       | 0.075*      |
| H9B  | 1.2256     | -0.0250       | 0.0243       | 0.075*      |
| C10  | 1.1332 (3) | -0.13444 (14) | 0.07586 (11) | 0.0418 (5)  |
| C11  | 1.1874 (3) | -0.20073 (18) | 0.12047 (13) | 0.0600 (7)  |
| H11A | 1.2783     | -0.1907       | 0.1500       | 0.072*      |
| C12  | 1.1032 (5) | -0.2844 (2)   | 0.12081 (18) | 0.0876 (11) |
| H12A | 1.1381     | -0.3321       | 0.1497       | 0.105*      |
| C13  | 0.9681 (5) | -0.2943 (2)   | 0.0776 (2)   | 0.0910 (10) |
| H13A | 0.9089     | -0.3490       | 0.0780       | 0.109*      |
| C14  | 0.9205 (5) | -0.2287 (3)   | 0.03579 (19) | 0.0983 (11) |
| H14A | 0.8289     | -0.2372       | 0.0063       | 0.118*      |
| C15  | 1.0007 (3) | -0.1510 (2)   | 0.03498 (14) | 0.0686 (7)  |
| H15A | 0.9640     | -0.1052       | 0.0046       | 0.082*      |
| C16  | 0.7027 (3) | 0.28930 (13)  | 0.11876 (11) | 0.0383 (5)  |
| C17  | 0.6253 (3) | 0.27921 (16)  | 0.04854 (12) | 0.0501 (6)  |
| H17A | 0.5842     | 0.2172        | 0.0430       | 0.060*      |
| H17B | 0.7084     | 0.2901        | 0.0123       | 0.060*      |
| C18  | 0.7850 (3) | 0.48932 (14)  | 0.16859 (13) | 0.0395 (5)  |
| C19  | 0.6518 (3) | 0.54010 (16)  | 0.20523 (12) | 0.0494 (6)  |
| H19A | 0.7019     | 0.5856        | 0.2359       | 0.059*      |
| H19B | 0.5886     | 0.4981        | 0.2345       | 0.059*      |
| C20  | 1.3316 (3) | 0.56632 (18)  | 0.34550 (18) | 0.0757 (9)  |
| H20A | 1.4078     | 0.5654        | 0.3846       | 0.114*      |
| H20B | 1.2354     | 0.6022        | 0.3576       | 0.114*      |
| H20C | 1.3856     | 0.5927        | 0.3052       | 0.114*      |

Atomic displacement parameters ( $\text{\AA}^2$ )

|     | $U^{11}$   | $U^{22}$    | $U^{33}$    | $U^{12}$   | $U^{13}$    | $U^{23}$    |
|-----|------------|-------------|-------------|------------|-------------|-------------|
| C11 | 0.0480 (3) | 0.0624 (4)  | 0.0629 (4)  | 0.0086 (3) | -0.0107 (3) | 0.0046 (3)  |
| C12 | 0.0861 (5) | 0.0687 (5)  | 0.0832 (5)  | 0.0365 (4) | -0.0317 (4) | -0.0064 (4) |
| O1  | 0.0382 (8) | 0.0321 (8)  | 0.0646 (10) | 0.0006 (7) | 0.0006 (7)  | -0.0154 (7) |
| O2  | 0.0352 (8) | 0.0465 (10) | 0.0741 (11) | 0.0012 (7) | -0.0012 (8) | -0.0234 (8) |

|     |             |             |             |              |              |              |
|-----|-------------|-------------|-------------|--------------|--------------|--------------|
| O3  | 0.0399 (7)  | 0.0291 (8)  | 0.0441 (8)  | 0.0021 (6)   | -0.0029 (7)  | -0.0041 (6)  |
| O4  | 0.0384 (7)  | 0.0287 (8)  | 0.0441 (8)  | 0.0000 (6)   | 0.0061 (6)   | -0.0039 (6)  |
| O5  | 0.0382 (8)  | 0.0352 (8)  | 0.0635 (10) | -0.0013 (7)  | 0.0091 (7)   | -0.0066 (7)  |
| O6  | 0.0512 (8)  | 0.0281 (8)  | 0.0564 (9)  | -0.0049 (7)  | 0.0165 (8)   | -0.0094 (7)  |
| O7  | 0.0386 (8)  | 0.0397 (9)  | 0.0344 (8)  | 0.0017 (6)   | 0.0018 (7)   | -0.0024 (7)  |
| O8  | 0.0422 (8)  | 0.0779 (12) | 0.0426 (10) | 0.0057 (8)   | 0.0049 (8)   | -0.0066 (8)  |
| O9  | 0.0376 (7)  | 0.0325 (8)  | 0.0398 (8)  | 0.0086 (6)   | 0.0007 (7)   | -0.0017 (6)  |
| O10 | 0.0732 (11) | 0.0471 (10) | 0.0457 (10) | 0.0091 (9)   | 0.0007 (9)   | 0.0060 (8)   |
| C1  | 0.0397 (11) | 0.0251 (11) | 0.0392 (12) | -0.0026 (9)  | 0.0019 (9)   | -0.0029 (9)  |
| C2  | 0.0346 (10) | 0.0354 (11) | 0.0321 (11) | 0.0014 (9)   | 0.0026 (9)   | 0.0019 (9)   |
| C3  | 0.0356 (11) | 0.0313 (11) | 0.0394 (12) | 0.0004 (9)   | 0.0088 (9)   | -0.0015 (9)  |
| C4  | 0.0332 (10) | 0.0308 (12) | 0.0406 (12) | -0.0038 (8)  | 0.0047 (9)   | -0.0039 (9)  |
| C5  | 0.0352 (11) | 0.0495 (14) | 0.0688 (16) | 0.0033 (10)  | -0.0041 (12) | -0.0253 (12) |
| C6  | 0.0400 (11) | 0.0456 (14) | 0.0519 (14) | 0.0027 (10)  | 0.0004 (11)  | -0.0110 (11) |
| C7  | 0.0355 (10) | 0.0285 (11) | 0.0434 (13) | -0.0010 (9)  | 0.0040 (9)   | -0.0079 (9)  |
| C8  | 0.0413 (12) | 0.0301 (12) | 0.0388 (12) | 0.0017 (10)  | -0.0051 (10) | -0.0039 (10) |
| C9  | 0.0675 (15) | 0.0362 (14) | 0.0832 (18) | -0.0035 (12) | 0.0294 (15)  | -0.0192 (13) |
| C10 | 0.0482 (12) | 0.0330 (12) | 0.0441 (12) | 0.0022 (10)  | 0.0056 (11)  | -0.0114 (11) |
| C11 | 0.0559 (14) | 0.0621 (19) | 0.0620 (16) | 0.0183 (14)  | 0.0053 (13)  | -0.0025 (14) |
| C12 | 0.119 (3)   | 0.0480 (19) | 0.096 (3)   | 0.0332 (19)  | 0.049 (2)    | 0.0267 (17)  |
| C13 | 0.109 (3)   | 0.051 (2)   | 0.113 (3)   | -0.030 (2)   | 0.028 (3)    | -0.024 (2)   |
| C14 | 0.119 (3)   | 0.087 (3)   | 0.089 (2)   | -0.035 (2)   | -0.008 (2)   | -0.025 (2)   |
| C15 | 0.0832 (19) | 0.0692 (19) | 0.0534 (16) | -0.0104 (16) | -0.0070 (15) | -0.0092 (14) |
| C16 | 0.0428 (12) | 0.0312 (12) | 0.0409 (13) | 0.0055 (10)  | -0.0012 (11) | -0.0014 (10) |
| C17 | 0.0548 (13) | 0.0468 (14) | 0.0489 (14) | 0.0091 (11)  | -0.0107 (12) | -0.0084 (11) |
| C18 | 0.0466 (12) | 0.0274 (11) | 0.0446 (14) | -0.0023 (10) | -0.0083 (11) | -0.0007 (10) |
| C19 | 0.0518 (13) | 0.0403 (13) | 0.0562 (14) | 0.0130 (11)  | -0.0099 (12) | -0.0024 (11) |
| C20 | 0.0435 (13) | 0.0595 (18) | 0.124 (3)   | 0.0071 (13)  | -0.0108 (15) | -0.0508 (17) |

*Geometric parameters (Å, °)*

|         |           |          |           |
|---------|-----------|----------|-----------|
| C11—C17 | 1.763 (2) | C5—H5A   | 1.0000    |
| C12—C19 | 1.761 (2) | C6—C7    | 1.512 (3) |
| O1—C4   | 1.420 (2) | C6—H6A   | 0.9900    |
| O1—C5   | 1.424 (3) | C6—H6B   | 0.9900    |
| O2—C5   | 1.423 (2) | C7—H7A   | 1.0000    |
| O2—C6   | 1.439 (3) | C9—C10   | 1.491 (3) |
| O3—C1   | 1.406 (2) | C9—H9A   | 0.9900    |
| O3—C7   | 1.433 (2) | C9—H9B   | 0.9900    |
| O4—C8   | 1.355 (2) | C10—C15  | 1.365 (3) |
| O4—C1   | 1.421 (2) | C10—C11  | 1.386 (3) |
| O5—C8   | 1.194 (2) | C11—C12  | 1.426 (4) |
| O6—C8   | 1.318 (2) | C11—H11A | 0.9500    |
| O6—C9   | 1.463 (3) | C12—C13  | 1.393 (5) |
| O7—C16  | 1.343 (2) | C12—H12A | 0.9500    |
| O7—C2   | 1.452 (2) | C13—C14  | 1.328 (5) |
| O8—C16  | 1.192 (2) | C13—H13A | 0.9500    |
| O9—C18  | 1.345 (3) | C14—C15  | 1.331 (4) |



|           |             |               |             |
|-----------|-------------|---------------|-------------|
| O9—C3     | 1.444 (2)   | C14—H14A      | 0.9500      |
| O10—C18   | 1.187 (3)   | C15—H15A      | 0.9500      |
| C1—C2     | 1.513 (3)   | C16—C17       | 1.507 (3)   |
| C1—H1A    | 1.0000      | C17—H17A      | 0.9900      |
| C2—C3     | 1.528 (3)   | C17—H17B      | 0.9900      |
| C2—H2A    | 1.0000      | C18—C19       | 1.504 (3)   |
| C3—C4     | 1.499 (3)   | C19—H19A      | 0.9900      |
| C3—H3A    | 1.0000      | C19—H19B      | 0.9900      |
| C4—C7     | 1.513 (3)   | C20—H20A      | 0.9800      |
| C4—H4A    | 1.0000      | C20—H20B      | 0.9800      |
| C5—C20    | 1.506 (3)   | C20—H20C      | 0.9800      |
|           |             |               |             |
| C4—O1—C5  | 109.16 (16) | O5—C8—O4      | 125.60 (19) |
| C5—O2—C6  | 111.76 (15) | O6—C8—O4      | 106.92 (17) |
| C1—O3—C7  | 109.60 (15) | O6—C9—C10     | 106.67 (18) |
| C8—O4—C1  | 115.07 (15) | O6—C9—H9A     | 110.4       |
| C8—O6—C9  | 114.21 (17) | C10—C9—H9A    | 110.4       |
| C16—O7—C2 | 117.04 (15) | O6—C9—H9B     | 110.4       |
| C18—O9—C3 | 117.98 (16) | C10—C9—H9B    | 110.4       |
| O3—C1—O4  | 106.07 (15) | H9A—C9—H9B    | 108.6       |
| O3—C1—C2  | 110.18 (15) | C15—C10—C11   | 119.1 (2)   |
| O4—C1—C2  | 107.64 (14) | C15—C10—C9    | 120.2 (2)   |
| O3—C1—H1A | 110.9       | C11—C10—C9    | 120.8 (2)   |
| O4—C1—H1A | 110.9       | C10—C11—C12   | 118.2 (3)   |
| C2—C1—H1A | 110.9       | C10—C11—H11A  | 120.9       |
| O7—C2—C1  | 106.42 (15) | C12—C11—H11A  | 120.9       |
| O7—C2—C3  | 110.85 (15) | C13—C12—C11   | 118.2 (3)   |
| C1—C2—C3  | 109.45 (15) | C13—C12—H12A  | 120.9       |
| O7—C2—H2A | 110.0       | C11—C12—H12A  | 120.9       |
| C1—C2—H2A | 110.0       | C14—C13—C12   | 121.4 (3)   |
| C3—C2—H2A | 110.0       | C14—C13—H13A  | 119.3       |
| O9—C3—C4  | 107.40 (14) | C12—C13—H13A  | 119.3       |
| O9—C3—C2  | 110.87 (15) | C13—C14—C15   | 120.3 (4)   |
| C4—C3—C2  | 107.87 (15) | C13—C14—H14A  | 119.9       |
| O9—C3—H3A | 110.2       | C15—C14—H14A  | 119.9       |
| C4—C3—H3A | 110.2       | C14—C15—C10   | 122.8 (3)   |
| C2—C3—H3A | 110.2       | C14—C15—H15A  | 118.6       |
| O1—C4—C3  | 110.57 (16) | C10—C15—H15A  | 118.6       |
| O1—C4—C7  | 108.61 (15) | O8—C16—O7     | 124.80 (19) |
| C3—C4—C7  | 110.53 (16) | O8—C16—C17    | 125.23 (19) |
| O1—C4—H4A | 109.0       | O7—C16—C17    | 109.96 (19) |
| C3—C4—H4A | 109.0       | C16—C17—C11   | 110.66 (16) |
| C7—C4—H4A | 109.0       | C16—C17—H17A  | 109.5       |
| O2—C5—O1  | 110.07 (17) | C11—C17—H17A  | 109.5       |
| O2—C5—C20 | 108.63 (18) | C16—C17—H17B  | 109.5       |
| O1—C5—C20 | 108.0 (2)   | C11—C17—H17B  | 109.5       |
| O2—C5—H5A | 110.0       | H17A—C17—H17B | 108.1       |
| O1—C5—H5A | 110.0       | O10—C18—O9    | 125.6 (2)   |

---

|              |              |                 |              |
|--------------|--------------|-----------------|--------------|
| C20—C5—H5A   | 110.0        | O10—C18—C19     | 126.8 (2)    |
| O2—C6—C7     | 107.76 (18)  | O9—C18—C19      | 107.63 (19)  |
| O2—C6—H6A    | 110.2        | C18—C19—C12     | 112.21 (17)  |
| C7—C6—H6A    | 110.2        | C18—C19—H19A    | 109.2        |
| O2—C6—H6B    | 110.2        | C12—C19—H19A    | 109.2        |
| C7—C6—H6B    | 110.2        | C18—C19—H19B    | 109.2        |
| H6A—C6—H6B   | 108.5        | C12—C19—H19B    | 109.2        |
| O3—C7—C6     | 109.09 (17)  | H19A—C19—H19B   | 107.9        |
| O3—C7—C4     | 109.16 (15)  | C5—C20—H20A     | 109.5        |
| C6—C7—C4     | 108.45 (17)  | C5—C20—H20B     | 109.5        |
| O3—C7—H7A    | 110.0        | H20A—C20—H20B   | 109.5        |
| C6—C7—H7A    | 110.0        | C5—C20—H20C     | 109.5        |
| C4—C7—H7A    | 110.0        | H20A—C20—H20C   | 109.5        |
| O5—C8—O6     | 127.48 (19)  | H20B—C20—H20C   | 109.5        |
| <br>         |              |                 |              |
| C7—O3—C1—O4  | 178.93 (14)  | O2—C6—C7—O3     | -174.90 (16) |
| C7—O3—C1—C2  | -64.85 (19)  | O2—C6—C7—C4     | -56.1 (2)    |
| C8—O4—C1—O3  | -87.73 (18)  | O1—C4—C7—O3     | 178.26 (15)  |
| C8—O4—C1—C2  | 154.34 (16)  | C3—C4—C7—O3     | -60.3 (2)    |
| C16—O7—C2—C1 | 148.00 (16)  | O1—C4—C7—C6     | 59.5 (2)     |
| C16—O7—C2—C3 | -93.07 (19)  | C3—C4—C7—C6     | -179.03 (16) |
| O3—C1—C2—O7  | 179.99 (14)  | C9—O6—C8—O5     | -0.7 (3)     |
| O4—C1—C2—O7  | -64.77 (19)  | C9—O6—C8—O4     | 179.11 (18)  |
| O3—C1—C2—C3  | 60.1 (2)     | C1—O4—C8—O5     | -3.1 (3)     |
| O4—C1—C2—C3  | 175.39 (14)  | C1—O4—C8—O6     | 177.14 (15)  |
| C18—O9—C3—C4 | 145.41 (17)  | C8—O6—C9—C10    | -179.41 (19) |
| C18—O9—C3—C2 | -96.97 (19)  | O6—C9—C10—C15   | 78.9 (3)     |
| O7—C2—C3—O9  | 71.06 (18)   | O6—C9—C10—C11   | -100.5 (2)   |
| C1—C2—C3—O9  | -171.86 (16) | C15—C10—C11—C12 | 1.0 (3)      |
| O7—C2—C3—C4  | -171.62 (14) | C9—C10—C11—C12  | -179.6 (2)   |
| C1—C2—C3—C4  | -54.5 (2)    | C10—C11—C12—C13 | -1.7 (4)     |
| C5—O1—C4—C3  | 175.95 (16)  | C11—C12—C13—C14 | 1.6 (5)      |
| C5—O1—C4—C7  | -62.6 (2)    | C12—C13—C14—C15 | -0.8 (6)     |
| O9—C3—C4—O1  | -64.92 (19)  | C13—C14—C15—C10 | 0.1 (5)      |
| C2—C3—C4—O1  | 175.53 (15)  | C11—C10—C15—C14 | -0.2 (4)     |
| O9—C3—C4—C7  | 174.79 (15)  | C9—C10—C15—C14  | -179.6 (3)   |
| C2—C3—C4—C7  | 55.2 (2)     | C2—O7—C16—O8    | 2.2 (3)      |
| C6—O2—C5—O1  | -62.2 (2)    | C2—O7—C16—C17   | -176.82 (16) |
| C6—O2—C5—C20 | 179.8 (2)    | O8—C16—C17—C11  | 45.1 (3)     |
| C4—O1—C5—O2  | 63.6 (2)     | O7—C16—C17—C11  | -135.95 (16) |
| C4—O1—C5—C20 | -177.92 (18) | C3—O9—C18—O10   | 4.4 (3)      |
| C5—O2—C6—C7  | 58.2 (2)     | C3—O9—C18—C19   | -174.89 (16) |
| C1—O3—C7—C6  | -177.39 (16) | O10—C18—C19—C12 | 11.2 (3)     |
| C1—O3—C7—C4  | 64.27 (19)   | O9—C18—C19—C12  | -169.47 (15) |

---

*Hydrogen-bond geometry (Å, °)*

Cg3 is the centroid of the C10—C15 ring.

| <i>D</i> —H $\cdots$ <i>A</i>               | <i>D</i> —H | H $\cdots$ <i>A</i> | <i>D</i> $\cdots$ <i>A</i> | <i>D</i> —H $\cdots$ <i>A</i> |
|---|-------------|---------------------|----------------------------|-------------------------------|
| C6—H6 <i>B</i> $\cdots$ O8 <sup>i</sup>     | 0.99        | 2.57                | 3.235 (3)                  | 125                           |
| C13—H13 <i>A</i> $\cdots$ O10 <sup>ii</sup> | 0.95        | 2.54                | 3.452 (4)                  | 162                           |
| C17—H17 <i>B</i> $\cdots$ O5 <sup>iii</sup> | 0.99        | 2.42                | 3.310 (3)                  | 149                           |
| C19—H19 <i>A</i> $\cdots$ O3 <sup>iv</sup>  | 0.99        | 2.52                | 3.460 (3)                  | 158                           |
| C19—H19 <i>B</i> $\cdots$ O2 <sup>v</sup>   | 0.99        | 2.38                | 3.364 (3)                  | 170                           |
| C20—H20 <i>B</i> $\cdots$ O4 <sup>iv</sup>  | 0.98        | 2.59                | 3.494 (3)                  | 154                           |
| C4—H4 <i>A</i> $\cdots$ Cg3 <sup>iv</sup>   | 1.00        | 2.89                | 3.879 (2)                  | 171                           |
| C14—H14 <i>A</i> $\cdots$ Cg3 <sup>vi</sup> | 0.95        | 2.87                | 3.818 (4)                  | 173                           |

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