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1,5-Dibromo-2,4-dimethoxybenzene

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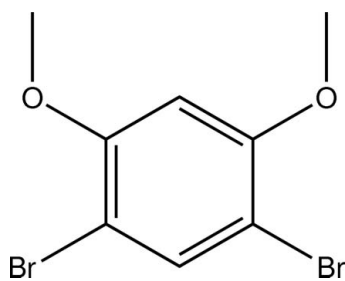
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 Key indicators: single-crystal X-ray study; $T = 200$ K; mean $\sigma(\text{C}-\text{C}) = 0.002$ Å; R factor = 0.021; wR factor = 0.049; data-to-parameter ratio = 21.2.

In the title compound, $\text{C}_8\text{H}_8\text{Br}_2\text{O}_2$, all non-H atoms lie essentially in a common plane (r.m.s deviation of all fitted non-H atoms = 0.0330 Å). In the crystal, weak $\text{C}-\text{H}\cdots\text{O}$ hydrogen bonds connect the molecules, forming chains which extend along the b -axis direction.

Related literature

For background to the pharmacological importance of the title compound, see: Pahari & Rohr (2009). For the synthesis of the title compound, see: Yang *et al.* (2009). For a report listing the crystal structure of 1-bromo-5-chloro-2,4-dimethoxybenzene but entered incorrectly as the title compound in the CSD (TASBAR), see: Yang *et al.* (2005). For graph-set analysis of hydrogen bonds, see: Bernstein *et al.* (1995).



Experimental

Crystal data

 $\text{C}_8\text{H}_8\text{Br}_2\text{O}_2$
 $M_r = 295.96$

Monoclinic, $P2_1/c$
 $a = 7.7944$ (2) Å
 $b = 8.5884$ (4) Å
 $c = 14.7877$ (4) Å
 $\beta = 107.838$ (1)°
 $V = 942.32$ (6) Å³

$Z = 4$
 Mo $K\alpha$ radiation
 $\mu = 8.56$ mm⁻¹
 $T = 200$ K
 $0.47 \times 0.46 \times 0.34$ mm

Data collection

Bruker APEXII CCD diffractometer
 Absorption correction: multi-scan (SADABS; Bruker, 2008)
 $T_{\min} = 0.674$, $T_{\max} = 1.000$

15097 measured reflections
 2350 independent reflections
 2094 reflections with $I > 2\sigma(I)$
 $R_{\text{int}} = 0.032$

Refinement

$R[F^2 > 2\sigma(F^2)] = 0.021$
 $wR(F^2) = 0.049$
 $S = 1.08$
 2350 reflections

111 parameters
 H-atom parameters constrained
 $\Delta\rho_{\text{max}} = 0.55$ e Å⁻³
 $\Delta\rho_{\text{min}} = -0.52$ e Å⁻³

Table 1

Hydrogen-bond geometry (Å, °).

$D-H\cdots A$	$D-H$	$H\cdots A$	$D\cdots A$	$D-H\cdots A$
$\text{C7}-\text{H7C}\cdots\text{O1}^i$	0.98	2.70	3.632 (3)	160

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

Data collection: APEX2 (Bruker, 2010); cell refinement: SAINT (Bruker, 2010); data reduction: SAINT; program(s) used to solve structure: SHELXS97 (Sheldrick, 2008); program(s) used to refine structure: SHELXL97 (Sheldrick, 2008); molecular graphics: ORTEP-3 (Farrugia, 2012) and Mercury (Macrae *et al.*, 2008); software used to prepare material for publication: SHELXL97 and PLATON (Spek, 2009).

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Supplementary data and figures for this paper are available from the IUCr electronic archives (Reference: ZS2243).

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supporting information

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1,5-Dibromo-2,4-dimethoxybenzene

A. M. Vijesh, Arun M. Isloor, Thomas Gerber, Benjamin van Brecht and Richard Betz

S1. Comment

The title compound 1,5-dibromo-2,4-dimethoxybenzene is an important intermediate for the synthesis of the anti-HIV drug Elvitegravir and the anticancer drug Psoralidin (Pahari *et al.*, 2009). The crystal structure of 1-bromo-5-chloro-2,4-dimethoxybenzene has been determined (Yang *et al.*, 2005), but the compound was in fact reported erroneously as 1,5-dibromo-2,4-dimethoxybenzene in the CSD (CCDC 271922, ref-code: TASBAR). The error is the result of 50% rotational disorder between the two halogen atoms in the molecule and this fact is also mentioned among the deposited experimental details in the CSD entry. Furthermore, the cell constants reported in this entry [$a = 7.722$ (4) Å, $b = 7.949$ (3) Å, $c = 7.405$ (3) Å, $\beta = 91.78$ (1)°, $V = 454.315$ Å³, $Z = 2$, space group $P 2/c$] differed significantly from those of the title compound. In view of the importance of the title compound in synthetic as well as medicinal chemistry, and to rectify the anomaly in the deposited crystallographic data, it was resynthesized and the crystal structure is reported herein.

The title compound is essentially planar (r.m.s. of all fitted non-hydrogen atoms = 0.0330 Å), with one of the methyl carbon atoms deviating most from this common plane by -0.073 (2) Å (Fig. 1). Intracyclic C–C–C angles cover a range from 118.96 (16)° to 120.73 (17)° with the smallest angle found at one of the carbon atoms bearing a methoxy substituent (C4) and the largest angle at the bromo-substituted carbon atom (C1) in the *para* position to C4.

In the crystal, a weak intermolecular methyl C—H \cdots O contact (Table 1) whose value falls slightly below the sum of van-der-Waals radii of the atoms participating, is observed, connecting the molecules into chains which extend along b (Fig. 2). A C1—Br1 \cdots Cgⁱⁱ contact is also present. According to a graph-set analysis (Bernstein *et al.*, 1995), the descriptor for the C—H \cdots O contacts is $C(7)$. The shortest intercentroid distance between two aromatic ring systems is 4.0267 (10) Å (Fig. 3).

S2. Experimental

1,5-Dibromo-2,4-dimethoxybenzene was synthesized according to a published procedure (Yang *et al.*, 2009). The crude product was recrystallized from hot ethanol.

S3. Refinement

Carbon-bound H atoms were placed in calculated positions [C—H(aromatic) = 0.95 Å and C—H(methyl) = 0.98 Å] and with $U_{\text{iso}}(\text{H}) = 1.2U_{\text{eq}}(\text{C})$ (aromatic) and allowed to ride in the refinement. The H atoms of the methyl groups were allowed to rotate with a fixed angle around the C—C bond to best fit the experimental electron density, with $U_{\text{iso}}(\text{H}) = 1.5U_{\text{eq}}(\text{C})$.

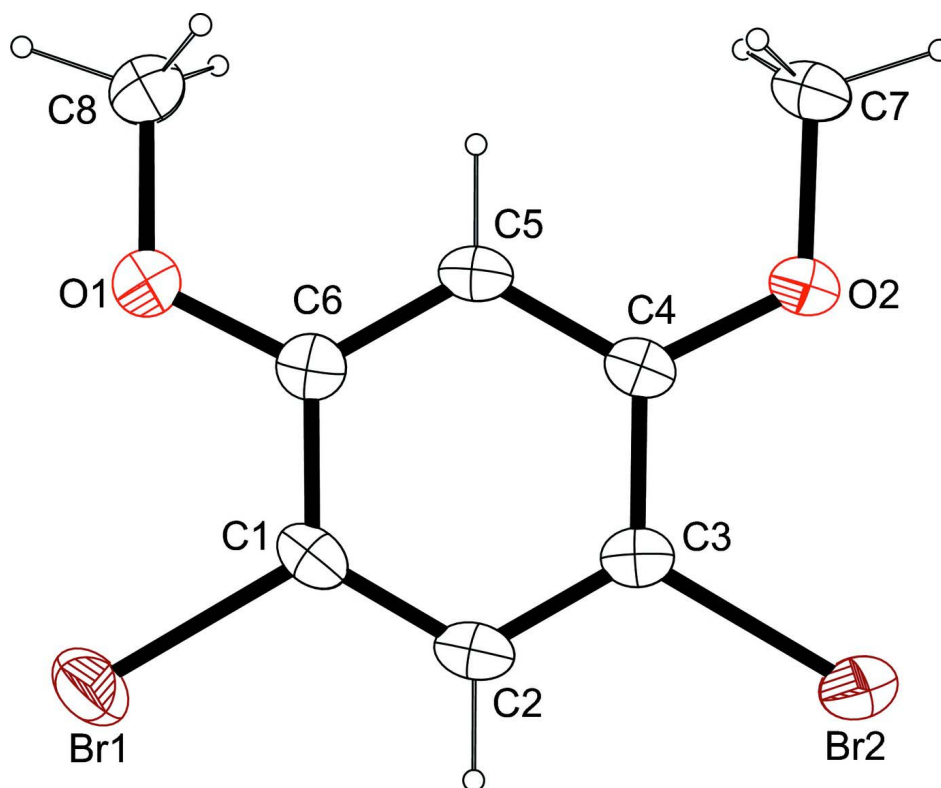
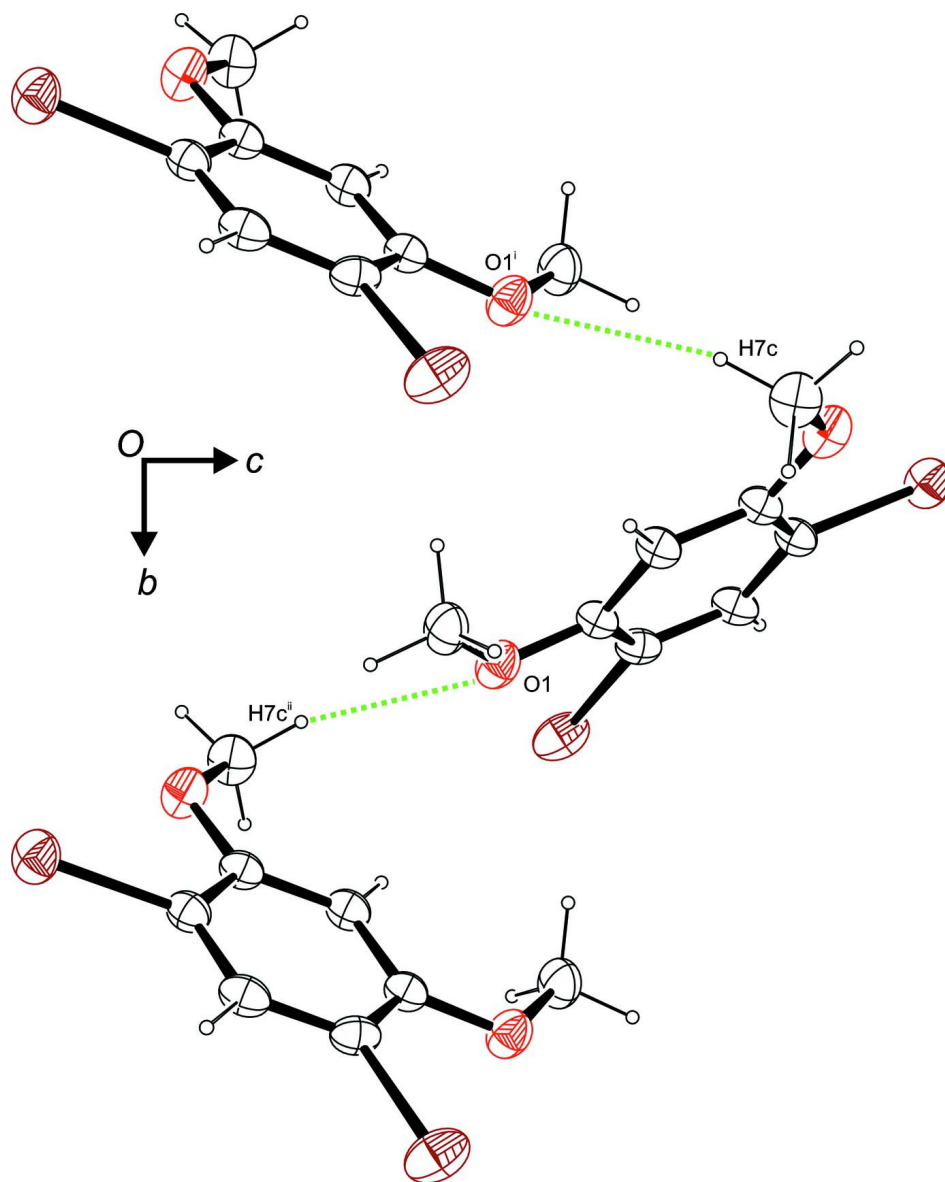
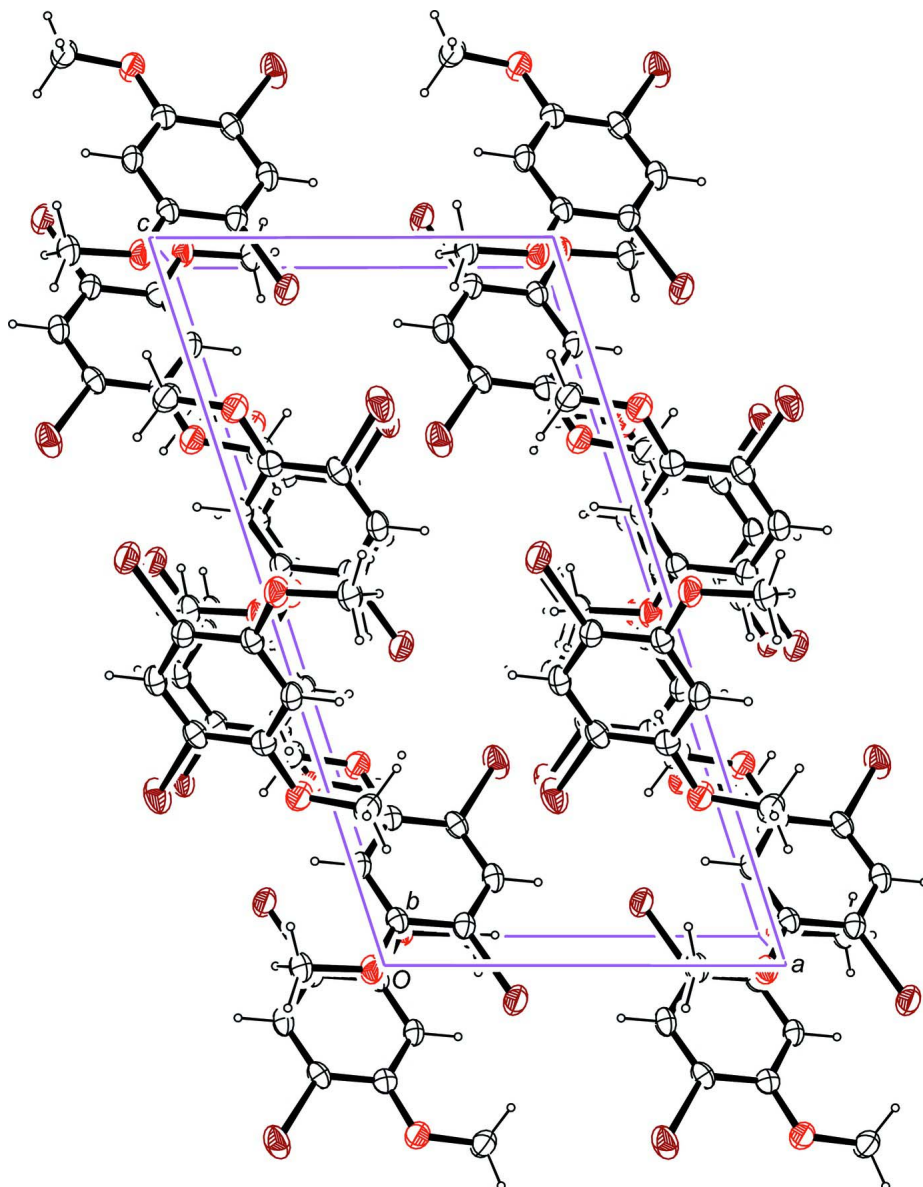


Figure 1

The molecular structure of the title compound showing atom labels, with anisotropic displacement ellipsoids drawn at the 50% probability level.

**Figure 2**

Intermolecular contacts, viewed along $[-1\ 0\ 0]$, with hydrogen bonds shown as dashed lines. For symmetry codes, see Table 1.

**Figure 3**

Molecular packing of the title compound, viewed down [0 1 0] (anisotropic displacement ellipsoids drawn at 50% probability level).

1,5-Dibromo-2,4-dimethoxybenzene*Crystal data* $C_8H_8Br_2O_2$ $M_r = 295.96$ Monoclinic, $P2_1/c$ Hall symbol: $-P\ 2_1/c$ $a = 7.7944(2)\ \text{\AA}$ $b = 8.5884(4)\ \text{\AA}$ $c = 14.7877(4)\ \text{\AA}$ $\beta = 107.838(1)^\circ$ $V = 942.32(6)\ \text{\AA}^3$ $Z = 4$ $F(000) = 568$ $D_x = 2.086\ \text{Mg m}^{-3}$

Melting point = 414–413 K

Mo $K\alpha$ radiation, $\lambda = 0.71073\ \text{\AA}$

Cell parameters from 9980 reflections

 $\theta = 2.7\text{--}28.3^\circ$

$\mu = 8.56 \text{ mm}^{-1}$
 $T = 200 \text{ K}$

Block, white
 $0.47 \times 0.46 \times 0.34 \text{ mm}$

Data collection

Bruker APEXII CCD
 diffractometer
 Radiation source: fine-focus sealed tube
 Graphite monochromator
 φ and ω scans
 Absorption correction: multi-scan
 (SADABS; Bruker, 2008)
 $T_{\min} = 0.674$, $T_{\max} = 1.000$

15097 measured reflections
 2350 independent reflections
 2094 reflections with $I > 2\sigma(I)$
 $R_{\text{int}} = 0.032$
 $\theta_{\max} = 28.4^\circ$, $\theta_{\min} = 2.8^\circ$
 $h = -10 \rightarrow 10$
 $k = -11 \rightarrow 11$
 $l = -18 \rightarrow 19$

Refinement

Refinement on F^2
 Least-squares matrix: full
 $R[F^2 > 2\sigma(F^2)] = 0.021$
 $wR(F^2) = 0.049$
 $S = 1.08$
 2350 reflections
 111 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
 $w = 1/[\sigma^2(F_o^2) + (0.0199P)^2 + 0.5315P]$
 where $P = (F_o^2 + 2F_c^2)/3$
 $(\Delta/\sigma)_{\max} = 0.001$
 $\Delta\rho_{\max} = 0.55 \text{ e } \text{\AA}^{-3}$
 $\Delta\rho_{\min} = -0.52 \text{ e } \text{\AA}^{-3}$

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

	<i>x</i>	<i>y</i>	<i>z</i>	$U_{\text{iso}}^*/U_{\text{eq}}$
Br1	0.43964 (3)	0.63810 (3)	0.268745 (16)	0.04029 (7)
Br2	0.29505 (3)	0.26527 (3)	-0.060701 (15)	0.03453 (7)
O1	0.07656 (18)	0.52208 (17)	0.26640 (10)	0.0321 (3)
O2	-0.04398 (17)	0.19995 (17)	-0.01445 (10)	0.0323 (3)
C1	0.2839 (2)	0.5013 (2)	0.18080 (13)	0.0256 (4)
C2	0.3359 (2)	0.4436 (2)	0.10619 (13)	0.0265 (4)
H2	0.4487	0.4729	0.0992	0.032*
C3	0.2236 (2)	0.3432 (2)	0.04159 (13)	0.0243 (4)
C4	0.0576 (2)	0.2998 (2)	0.05093 (13)	0.0235 (4)
C5	0.0069 (2)	0.3587 (2)	0.12664 (13)	0.0250 (4)
H5	-0.1056	0.3292	0.1339	0.030*
C6	0.1190 (2)	0.4601 (2)	0.19174 (13)	0.0244 (4)
C7	-0.2196 (3)	0.1625 (3)	-0.00979 (15)	0.0338 (4)
H7A	-0.2815	0.0957	-0.0636	0.051*
H7B	-0.2888	0.2585	-0.0123	0.051*
H7C	-0.2089	0.1075	0.0498	0.051*
C8	-0.0860 (3)	0.4691 (3)	0.28213 (15)	0.0340 (4)
H8A	-0.0983	0.5179	0.3397	0.051*
H8B	-0.0816	0.3557	0.2898	0.051*
H8C	-0.1894	0.4976	0.2277	0.051*

Atomic displacement parameters (\AA^2)

	U^{11}	U^{22}	U^{33}	U^{12}	U^{13}	U^{23}
Br1	0.02623 (10)	0.04018 (13)	0.05077 (14)	-0.00833 (8)	0.00632 (9)	-0.01578 (9)
Br2	0.02932 (11)	0.04093 (12)	0.03863 (12)	-0.00448 (8)	0.01823 (9)	-0.00465 (8)
O1	0.0301 (7)	0.0358 (8)	0.0333 (7)	-0.0062 (6)	0.0138 (6)	-0.0083 (6)
O2	0.0238 (7)	0.0400 (8)	0.0353 (7)	-0.0105 (6)	0.0123 (6)	-0.0101 (6)
C1	0.0209 (8)	0.0209 (8)	0.0314 (9)	-0.0031 (6)	0.0026 (7)	-0.0002 (7)
C2	0.0195 (8)	0.0241 (9)	0.0356 (10)	-0.0015 (7)	0.0082 (7)	0.0049 (7)
C3	0.0215 (8)	0.0235 (9)	0.0288 (9)	0.0008 (6)	0.0093 (7)	0.0039 (7)
C4	0.0197 (8)	0.0222 (8)	0.0272 (9)	-0.0012 (7)	0.0053 (7)	0.0030 (7)
C5	0.0195 (8)	0.0257 (9)	0.0309 (9)	-0.0025 (7)	0.0094 (7)	0.0026 (7)
C6	0.0248 (8)	0.0218 (8)	0.0263 (9)	0.0015 (7)	0.0071 (7)	0.0034 (7)
C7	0.0227 (9)	0.0418 (11)	0.0371 (11)	-0.0098 (8)	0.0093 (8)	-0.0034 (9)
C8	0.0336 (10)	0.0397 (11)	0.0328 (10)	-0.0050 (8)	0.0165 (8)	-0.0030 (9)

Geometric parameters (\AA , $^\circ$)

Br1—C1	1.8918 (18)	C3—C4	1.393 (2)
Br2—C3	1.8873 (19)	C4—C5	1.392 (3)
O1—C6	1.355 (2)	C5—C6	1.391 (3)
O1—C8	1.431 (2)	C5—H5	0.9500
O2—C4	1.352 (2)	C7—H7A	0.9800
O2—C7	1.428 (2)	C7—H7B	0.9800
C1—C2	1.379 (3)	C7—H7C	0.9800
C1—C6	1.389 (2)	C8—H8A	0.9800
C2—C3	1.382 (3)	C8—H8B	0.9800
C2—H2	0.9500	C8—H8C	0.9800
C6—O1—C8	117.21 (15)	C4—C5—H5	119.6
C4—O2—C7	117.93 (15)	O1—C6—C1	117.41 (16)
C2—C1—C6	120.73 (17)	O1—C6—C5	123.47 (16)
C2—C1—Br1	119.28 (13)	C1—C6—C5	119.12 (17)
C6—C1—Br1	119.99 (14)	O2—C7—H7A	109.5
C1—C2—C3	119.87 (17)	O2—C7—H7B	109.5
C1—C2—H2	120.1	H7A—C7—H7B	109.5
C3—C2—H2	120.1	O2—C7—H7C	109.5
C2—C3—C4	120.59 (17)	H7A—C7—H7C	109.5
C2—C3—Br2	119.71 (13)	H7B—C7—H7C	109.5
C4—C3—Br2	119.70 (14)	O1—C8—H8A	109.5
O2—C4—C5	123.84 (16)	O1—C8—H8B	109.5
O2—C4—C3	117.20 (16)	H8A—C8—H8B	109.5
C5—C4—C3	118.96 (16)	O1—C8—H8C	109.5
C6—C5—C4	120.72 (16)	H8A—C8—H8C	109.5
C6—C5—H5	119.6	H8B—C8—H8C	109.5
C6—C1—C2—C3	-0.3 (3)	O2—C4—C5—C6	179.44 (17)
Br1—C1—C2—C3	179.81 (14)	C3—C4—C5—C6	0.5 (3)

C1—C2—C3—C4	0.2 (3)	C8—O1—C6—C1	-174.78 (17)
C1—C2—C3—Br2	179.77 (14)	C8—O1—C6—C5	5.2 (3)
C7—O2—C4—C5	5.2 (3)	C2—C1—C6—O1	-179.57 (17)
C7—O2—C4—C3	-175.84 (17)	Br1—C1—C6—O1	0.3 (2)
C2—C3—C4—O2	-179.34 (16)	C2—C1—C6—C5	0.5 (3)
Br2—C3—C4—O2	1.1 (2)	Br1—C1—C6—C5	-179.65 (13)
C2—C3—C4—C5	-0.3 (3)	C4—C5—C6—O1	179.48 (17)
Br2—C3—C4—C5	-179.86 (13)	C4—C5—C6—C1	-0.5 (3)

Hydrogen-bond geometry (\AA , $^\circ$)

$D-H\cdots A$	$D-H$	$H\cdots A$	$D\cdots A$	$D-H\cdots A$
C7—H7C \cdots O1 ⁱ	0.98	2.70	3.632 (3)	160
C1—Br1 \cdots C _g ⁱⁱ	1.89 (1)	3.75 (1)	5.5701 (19)	161 (1)

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