



Crystal structure of 7-iodo-4-oxo-4*H*-chromene-3-carbaldehyde

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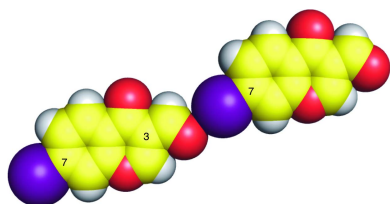
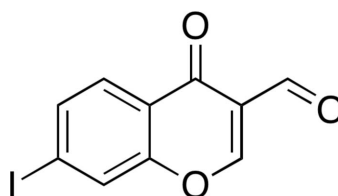
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Keywords: crystal structure; π - π stacking; hydrogen bond; halogen bond.**CCDC reference:** 1511202**Supporting information:** this article has supporting information at journals.iucr.org/e

In the title compound, C₁₀H₅IO₃, an iodinated 3-formylchromone derivative, the non-H atoms are essentially coplanar (r.m.s. deviation = 0.0344 Å), with the largest deviation from the least-squares plane [0.101 (3) Å] being found for the formyl O atom. In the crystal, molecules are linked through stacking interactions [centroid-centroid distance between the benzene rings = 3.700 (3) Å] and C—H...O hydrogen bonds. Halogen bonds between the I atoms at 7-position and the formyl O atoms [I1...O3 = 3.056 (2) Å, C6—I1...O3 = 173.18 (8)° and I1...O3—C10 = 111.12 (18)°] are also formed along [110], resulting in sheets perpendicular to the *c* axis, constructed by C—H...O hydrogen bonds and I...O halogen bonds.

1. Chemical context

3-Formylchromone and its derivatives show versatile biological activities such as anti-inflammatory activity (Khan *et al.*, 2010) and the inhibition of protein tyrosine phosphatase 1B (Shim *et al.*, 2005), thymidine phosphorylase (Khan *et al.*, 2009), carbonic anhydrase (Ekinici *et al.*, 2012), and metallo- β -lactamase (Christopeit *et al.*, 2016). Interestingly, 6,8-dichloro- and 6,8-dibromo-3-formylchromones possess potent urease inhibitory activity, whereas 6-fluoro-, 6-chloro- and 6-bromo-3-formylchromones exhibit no ability to inhibit urease (Kawase *et al.*, 2007). Thus, the position of halogen atoms on the chromone ring should be associated with the urease inhibitory activity.



We have previously reported the crystal structures of 6,8-dichloro-4-oxochromene-3-carbaldehyde (6,8-dichloro-3-formylchromone; Ishikawa & Motohashi, 2013) and 6,8-dibromo-4-oxo-4*H*-chromene-3-carbaldehyde (6,8-dibromo-3-formylchromone; Ishikawa, 2014*a*). In these crystals, halogen bonds are observed between the formyl oxygen atoms and the halogen atoms at the 8-position. Halogen bonding is defined as a net attractive interaction between an electrophilic region of a halogen atom in a molecule and a nucleophilic region of an atom in a molecule, and is characterized by a shorter contact between the two atoms. Halogen bonding has attracted much

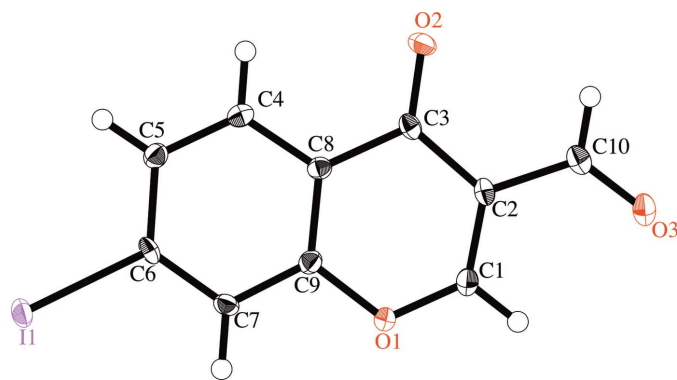


Figure 1
The molecular structure of the title compound, with displacement ellipsoids drawn at the 50% probability level. H atoms are shown as small spheres of arbitrary radius.

attention in medicinal chemistry, chemical biology, supramolecular chemistry and crystal engineering (Scholfield *et al.*, 2013; Wilcken *et al.*, 2013; Persch *et al.*, 2015; Cavallo *et al.*, 2016).

As part of an investigation of halogenated 3-formylchromones relevant to urease inhibitory activity and halogen bonding, I herein report the crystal structure of 7-iodo-4-oxo-4*H*-chromene-3-carbaldehyde (7-iodo-3-formylchromone). The main objective of this study is to reveal the interaction mode of the iodine substituent at the 7-position of the chromone ring in the solid state.

2. Structure commentary

The mean deviation of the least-square planes for the non-hydrogen atoms is 0.0344 Å, and the largest deviation is 0.101 (3) Å for O3, indicating that these atoms are essentially coplanar (Fig. 1). All bond distances and angles are within their expected ranges.

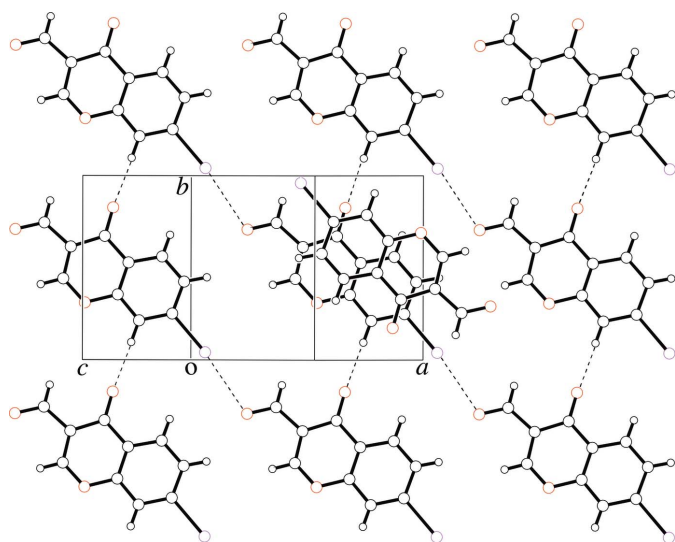


Figure 2
A packing view of the title compound. C—H...O hydrogen bonds and I...O halogen bonds are represented as dashed lines.

Table 1
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>
C7—H4...O2 ⁱ	0.95	2.35	3.208 (4)	150 (1)

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

3. Supramolecular features

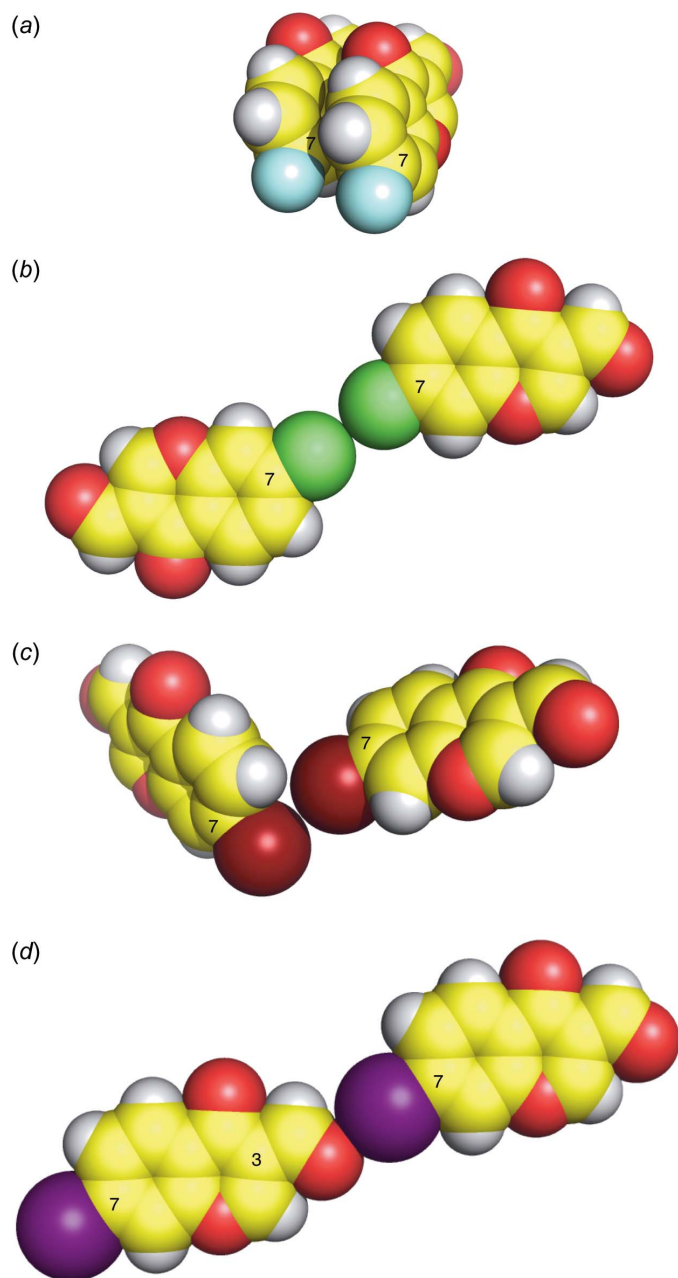
In the crystal, the molecules are linked through π – π stacking interactions between inversion-symmetry-equivalentⁱ molecules [centroid–centroid distance between the benzene rings of the 4*H*-chromene units = 3.700 (3) Å; symmetry code: (i) $-x, -y, -z$], and through C—H...O hydrogen bonds (Table 1) that involve the C7/O2 atoms. In particular, significant shorter contacts are observed between the iodine atoms and the formyl oxygen atoms of translation-symmetry equivalentⁱⁱ molecules [I1...O3 = 3.056 (2) Å, C6—I1...O3 = 173.18 (8)°, I1...O3—C10 = 111.12 (18)°; symmetry code: (ii) $x + 1, y - 1, z$] along [1 1 0], resulting in sheets perpendicular to the *c*-axis, constructed by C—H...O hydrogen bonds and I...O halogen bonds (Fig. 2).

4. Database survey

A search of WebCSD (Version 1.1.2, last update Oct 2016; Groom *et al.*, 2014) for 7-halogeno-3-formylchromones gave the following three hits: 7-fluoro- (Asad *et al.*, 2011), 7-chloro- (Ishikawa, 2014*b*), and 7-bromo-3-formylchromone (Ishikawa, 2014*c*). In 7-fluoro-3-formylchromone, no contact around the fluorine atom is seen (Fig. 3*a*). In the crystals of 7-chloro- and 7-bromo-3-formylchromones, type I and type II halogen...halogen contacts are found, respectively (Fig. 3*b* and 3*c*), and these halogen...halogen contacts are commonly found for Cl and Br atoms (Mukherjee *et al.*, 2014). It should be noted that shorter contacts between oxygen atoms and halogen atoms are observed in 7-iodo-3-formylchromone (this work, Fig. 3*d*), but not in 7-fluoro-, 7-chloro-, and 7-bromo-3-formylchromones. This is in agreement with an assumption that the iodine atom should have the largest σ -hole (Clark *et al.*, 2007) among the halogen atoms in 7-halogeno-3-formylchromones. These findings should be helpful in understanding the interaction of halogenated 3-formylchromones with urease, and is thus valuable for rational drug design.

5. Synthesis and crystallization

2'-Hydroxy-4'-iodoacetophenone was prepared from 3-acetoxyiodobenzene by a Fries rearrangement reaction. To a solution of 2'-hydroxy-4'-iodoacetophenone (4.4 mmol) in *N,N*-dimethylformamide (10 ml) was added dropwise POCl₃ (13.2 mmol) at 273 K. After the mixture was stirred for 14 h at room temperature, water (100 ml) was added. The precipitates were collected, washed with water, and dried *in vacuo* at 333 K (yield 86%). ¹H NMR (400 MHz, CDCl₃): δ 7.84 (dd, 1H, *J* = 8.8 and 1.5 Hz), 7.96 (d, 1H, *J* = 1.5 Hz), 7.99 (d, 1H, *J* =


Figure 3

Sphere models of the crystal structures of (a) 7-fluoro-4-oxo-4H-chromene-3-carbaldehyde (Asad *et al.*, 2011), (b) 7-chloro-4-oxo-4H-chromene-3-carbaldehyde (Ishikawa, 2014b), (c) 7-bromo-4-oxo-4H-chromene-3-carbaldehyde (Ishikawa, 2014c) and (d) the title compound (this work).

8.3 Hz), 8.49 (s, 1H), 10.36 (s, 1H). Single crystals suitable for X-ray diffraction were obtained by slow evaporation of a 1,2-dichloroethane solution of the title compound at room temperature.

6. Refinement

Crystal data, data collection and structure refinement details are summarized in Table 2. The C-bound hydrogen atoms

Table 2

Experimental details.

Crystal data	
Chemical formula	C ₁₀ H ₅ IO ₃
<i>M_r</i>	300.05
Crystal system, space group	Monoclinic, <i>P</i> 2 ₁ / <i>n</i>
Temperature (K)	100
<i>a</i> , <i>b</i> , <i>c</i> (Å)	9.572 (4), 7.533 (4), 13.095 (9)
β (°)	103.06 (4)
<i>V</i> (Å ³)	919.8 (9)
<i>Z</i>	4
Radiation type	Mo <i>K</i> α
μ (mm ⁻¹)	3.46
Crystal size (mm)	0.25 × 0.18 × 0.15
Data collection	
Diffractometer	Rigaku AFC7R
Absorption correction	ψ scan (North <i>et al.</i> , 1968)
<i>T_{min}</i> , <i>T_{max}</i>	0.528, 0.595
No. of measured, independent and observed [<i>F</i> ² > 2.0 σ (<i>F</i> ²)] reflections	2538, 2119, 1916
<i>R_{int}</i>	0.017
(<i>sin</i> θ / λ) _{max} (Å ⁻¹)	0.650
Refinement	
<i>R</i> [<i>F</i> ² > 2 σ (<i>F</i> ²)], <i>wR</i> (<i>F</i> ²), <i>S</i>	0.021, 0.053, 1.06
No. of reflections	2119
No. of parameters	128
H-atom treatment	H-atom parameters constrained
$\Delta\rho_{\max}$, $\Delta\rho_{\min}$ (e Å ⁻³)	0.56, -0.60

Computer programs: *WinAFC* (Rigaku, 1999), *SIR2011* (Burla *et al.*, 2012), *SHELXL2014* (Sheldrick, 2015) and *CrystalStructure* (Rigaku, 2015).

were placed in geometrical positions and refined using a riding model [C–H = 0.95 Å and *U*_{iso}(H) = 1.2*U*_{eq}(C)].

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Crystal structure of 7-iodo-4-oxo-4*H*-chromene-3-carbaldehyde

Yoshinobu Ishikawa

Computing details

Data collection: *WinAFC* (Rigaku, 1999); cell refinement: *WinAFC* (Rigaku, 1999); data reduction: *WinAFC* (Rigaku, 1999); program(s) used to solve structure: *SIR2011* (Burla *et al.*, 2012); program(s) used to refine structure: *SHELXL2014* (Sheldrick, 2015); molecular graphics: *CrystalStructure* (Rigaku, 2015); software used to prepare material for publication: *CrystalStructure* (Rigaku, 2015).

7-Iodo-4-oxo-4*H*-chromene-3-carbaldehyde

Crystal data

$C_{10}H_5IO_3$

$M_r = 300.05$

Monoclinic, $P2_1/n$

$a = 9.572$ (4) Å

$b = 7.533$ (4) Å

$c = 13.095$ (9) Å

$\beta = 103.06$ (4)°

$V = 919.8$ (9) Å³

$Z = 4$

$F(000) = 568.00$

$D_x = 2.167$ Mg m⁻³

Mo $K\alpha$ radiation, $\lambda = 0.71069$ Å

Cell parameters from 25 reflections

$\theta = 15.1$ – 17.1 °

$\mu = 3.46$ mm⁻¹

$T = 100$ K

Prismatic, yellow

$0.25 \times 0.18 \times 0.15$ mm

Data collection

Rigaku AFC7R

diffractometer

ω - 2θ scans

Absorption correction: ψ scan

(North *et al.*, 1968)

$T_{\min} = 0.528$, $T_{\max} = 0.595$

2538 measured reflections

2119 independent reflections

1916 reflections with $F^2 > 2.0\sigma(F^2)$

$R_{\text{int}} = 0.017$

$\theta_{\max} = 27.5$ °, $\theta_{\min} = 3.0$ °

$h = -12$ → 12

$k = -9$ → 0

$l = -9$ → 17

3 standard reflections every 150 reflections

intensity decay: -0.3%

Refinement

Refinement on F^2

$R[F^2 > 2\sigma(F^2)] = 0.021$

$wR(F^2) = 0.053$

$S = 1.06$

2119 reflections

128 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

$w = 1/[\sigma^2(F_o^2) + (0.0244P)^2 + 1.8229P]$

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

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

$\Delta\rho_{\max} = 0.56$ e Å⁻³

$\Delta\rho_{\min} = -0.60$ e Å⁻³

Extinction correction: SHELXL2014

(Sheldrick, 2015)

Extinction coefficient: 0.0024 (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.

Refinement. Refinement was performed using all reflections. The weighted R -factor (wR) and goodness of fit (S) are based on F^2 . R -factor (gt) are based on F . The threshold expression of $F^2 > 2.0 \sigma(F^2)$ is used only for calculating R -factor (gt).

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

	x	y	z	$U_{\text{iso}}^*/U_{\text{eq}}$
I1	0.24361 (2)	0.04012 (2)	0.39087 (2)	0.01629 (8)
O1	-0.2715 (2)	0.3092 (3)	0.39728 (15)	0.0152 (4)
O2	-0.1775 (2)	0.8253 (3)	0.33965 (16)	0.0172 (4)
O3	-0.5743 (2)	0.7067 (3)	0.39144 (17)	0.0209 (4)
C1	-0.3676 (3)	0.4391 (4)	0.3915 (2)	0.0160 (5)
H1	-0.4603	0.4076	0.4004	0.019*
C2	-0.3435 (3)	0.6125 (4)	0.3740 (2)	0.0135 (5)
C3	-0.2044 (3)	0.6703 (4)	0.3577 (2)	0.0128 (5)
C4	0.0421 (3)	0.5595 (4)	0.3565 (2)	0.0143 (5)
H2	0.0697	0.6769	0.3434	0.017*
C5	0.1408 (3)	0.4232 (4)	0.3655 (2)	0.0144 (5)
H3	0.2365	0.4468	0.3604	0.017*
C6	0.0979 (3)	0.2499 (4)	0.3822 (2)	0.0133 (5)
C7	-0.0402 (3)	0.2124 (4)	0.3922 (2)	0.0135 (5)
H4	-0.0685	0.0945	0.4039	0.016*
C8	-0.0982 (3)	0.5267 (4)	0.3665 (2)	0.0123 (5)
C9	-0.1358 (3)	0.3530 (4)	0.3847 (2)	0.0132 (5)
C10	-0.4587 (3)	0.7427 (4)	0.3717 (2)	0.0162 (5)
H5	-0.4422	0.8619	0.3538	0.019*

Atomic displacement parameters (\AA^2)

	U^{11}	U^{22}	U^{33}	U^{12}	U^{13}	U^{23}
I1	0.01410 (10)	0.01533 (11)	0.01997 (11)	0.00472 (7)	0.00501 (7)	-0.00105 (7)
O1	0.0119 (9)	0.0131 (9)	0.0217 (10)	0.0010 (7)	0.0064 (8)	0.0019 (8)
O2	0.0186 (10)	0.0101 (9)	0.0221 (10)	-0.0001 (8)	0.0029 (8)	0.0011 (8)
O3	0.0155 (10)	0.0215 (11)	0.0263 (11)	0.0054 (8)	0.0064 (8)	0.0012 (9)
C1	0.0120 (12)	0.0173 (14)	0.0190 (13)	0.0022 (10)	0.0042 (10)	0.0010 (11)
C2	0.0119 (12)	0.0149 (13)	0.0135 (12)	0.0041 (10)	0.0020 (10)	0.0009 (11)
C3	0.0132 (12)	0.0126 (12)	0.0115 (12)	0.0031 (10)	0.0001 (9)	-0.0006 (10)
C4	0.0139 (12)	0.0140 (13)	0.0149 (12)	-0.0029 (10)	0.0029 (10)	-0.0004 (10)
C5	0.0125 (12)	0.0151 (14)	0.0156 (13)	-0.0014 (10)	0.0033 (10)	-0.0017 (10)
C6	0.0154 (12)	0.0111 (12)	0.0137 (12)	0.0051 (10)	0.0035 (10)	-0.0025 (10)
C7	0.0154 (12)	0.0093 (12)	0.0154 (12)	-0.0005 (10)	0.0027 (10)	-0.0014 (10)
C8	0.0129 (12)	0.0119 (12)	0.0121 (12)	-0.0013 (10)	0.0026 (9)	-0.0010 (10)
C9	0.0121 (12)	0.0142 (13)	0.0140 (12)	-0.0008 (10)	0.0044 (10)	0.0001 (10)

C10	0.0164 (13)	0.0156 (13)	0.0153 (13)	0.0040 (11)	0.0008 (10)	-0.0012 (11)
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Geometric parameters (Å, °)

I1—C6	2.094 (3)	C4—C5	1.383 (4)
O1—C1	1.334 (3)	C4—C8	1.400 (4)
O1—C9	1.386 (3)	C4—H2	0.9500
O2—C3	1.230 (3)	C5—C6	1.401 (4)
O3—C10	1.222 (4)	C5—H3	0.9500
C1—C2	1.355 (4)	C6—C7	1.387 (4)
C1—H1	0.9500	C7—C9	1.389 (4)
C2—C3	1.462 (4)	C7—H4	0.9500
C2—C10	1.471 (4)	C8—C9	1.392 (4)
C3—C8	1.471 (4)	C10—H5	0.9500
C1—O1—C9	118.2 (2)	C7—C6—C5	121.6 (2)
O1—C1—C2	125.1 (3)	C7—C6—I1	118.6 (2)
O1—C1—H1	117.4	C5—C6—I1	119.8 (2)
C2—C1—H1	117.4	C6—C7—C9	117.7 (3)
C1—C2—C3	120.5 (2)	C6—C7—H4	121.2
C1—C2—C10	119.4 (3)	C9—C7—H4	121.2
C3—C2—C10	120.1 (3)	C9—C8—C4	118.2 (2)
O2—C3—C2	123.2 (3)	C9—C8—C3	120.2 (2)
O2—C3—C8	122.8 (2)	C4—C8—C3	121.5 (3)
C2—C3—C8	113.9 (2)	O1—C9—C7	115.5 (2)
C5—C4—C8	120.8 (3)	O1—C9—C8	122.0 (2)
C5—C4—H2	119.6	C7—C9—C8	122.5 (2)
C8—C4—H2	119.6	O3—C10—C2	123.9 (3)
C4—C5—C6	119.1 (3)	O3—C10—H5	118.0
C4—C5—H3	120.5	C2—C10—H5	118.0
C6—C5—H3	120.5		
C9—O1—C1—C2	0.1 (4)	O2—C3—C8—C9	-178.5 (3)
O1—C1—C2—C3	1.1 (4)	C2—C3—C8—C9	2.4 (4)
O1—C1—C2—C10	-178.8 (2)	O2—C3—C8—C4	1.2 (4)
C1—C2—C3—O2	178.6 (3)	C2—C3—C8—C4	-177.9 (2)
C10—C2—C3—O2	-1.5 (4)	C1—O1—C9—C7	179.6 (2)
C1—C2—C3—C8	-2.3 (4)	C1—O1—C9—C8	0.0 (4)
C10—C2—C3—C8	177.6 (2)	C6—C7—C9—O1	-178.8 (2)
C8—C4—C5—C6	1.6 (4)	C6—C7—C9—C8	0.7 (4)
C4—C5—C6—C7	-1.5 (4)	C4—C8—C9—O1	179.0 (2)
C4—C5—C6—I1	177.9 (2)	C3—C8—C9—O1	-1.4 (4)
C5—C6—C7—C9	0.3 (4)	C4—C8—C9—C7	-0.6 (4)
I1—C6—C7—C9	-179.1 (2)	C3—C8—C9—C7	179.1 (2)
C5—C4—C8—C9	-0.6 (4)	C1—C2—C10—O3	4.9 (4)
C5—C4—C8—C3	179.7 (2)	C3—C2—C10—O3	-175.0 (3)

Hydrogen-bond geometry (Å, °)

<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>
C7—H4 \cdots O2 ⁱ	0.95	2.35	3.208 (4)	150 (1)

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