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Synthesis, structure and *in vitro* cytotoxicity testing of some 2-arylbenzofuran-3-ols

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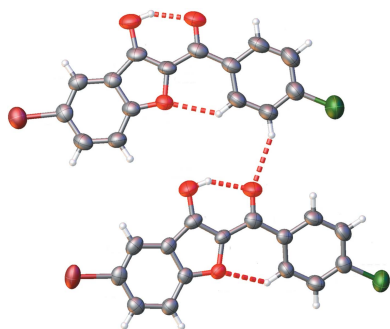
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Five 2-aryl-5-bromobenzo[*b*]furan-3-ol compounds (two of which are new) and four new 2-aryl-5-iodobenzo[*b*]furan-3-ol compounds were synthesized starting from salicylic acid. The compounds were characterized by mass spectrometry and ¹H NMR and ¹³C NMR spectroscopy. Single-crystal X-ray diffraction studies of four compounds, namely, (5-bromo-3-hydroxybenzofuran-2-yl)(4-fluorophenyl)methanone, C₁₅H₈BrFO₃, (5-bromo-3-hydroxybenzofuran-2-yl)(4-chlorophenyl)methanone, C₁₅H₈BrClO₃, (5-bromo-3-hydroxybenzofuran-2-yl)(4-bromophenyl)methanone, C₁₅H₈Br₂O₃, and (4-bromophenyl)(3-hydroxy-5-iodobenzofuran-2-yl)methanone, C₁₅H₈BrIO₃, were also carried out. The compounds were tested for their *in vitro* cytotoxicity on the four human cancer cell lines KB, Hep-G2, Lu-1 and MCF7. Six compounds show good inhibiting abilities on Hep-G2 cells, with IC₅₀ values of 1.39–8.03 μM.

1. Introduction

Benzofurans have been considered as fundamental units in numerous bioactive compounds and are present in a large number of bioactive natural compounds. The benzofuran nucleus is present in a huge number of bioactive natural compounds. For example, (+)-liphagal is a selective phosphoinositide-3-kinase α -inhibitor (Marion *et al.*, 2006), cyclopenta[*b*]benzofuran compounds possess antitumour and antiviral activities (Kim *et al.*, 2006), while derivatives of egonol have antioxidant and anti-inflammatory activities (Timmers *et al.*, 2015). Synthetic benzofuran derivatives are found to possess antitumour and anticancer (Shi *et al.*, 2016; Marquès *et al.*, 2016; Napiórkowska *et al.*, 2019; Asadi *et al.*, 2017), antimicrobial (Asadi *et al.*, 2017; He *et al.*, 2017; Xu *et al.*, 2019) and antitubercular (Xu *et al.*, 2019) activities. Some synthetic benzofuran derivatives have been investigated in the role of osteogenic (Marquès *et al.*, 2016; Kushwaha *et al.*, 2018; Modukuri *et al.*, 2017) or vasorelaxant (Hassan *et al.*, 2014) agents. 2-Arylbenzofuran-3-ols, being a class of typical benzofuran derivatives, not only possess antimicrobial (Kulkarni *et al.*, 2014), antitumour (Sargolzaei *et al.*, 2016) and α -glucosidase inhibition (Spasov *et al.*, 2017) properties, but are also useful intermediates for the synthesis of several compounds having various biological activities (Shi *et al.*, 2016; Dong *et al.*, 2013; Rashmi *et al.*, 2015). Although many 2-arylbenzofuran-3-ols have been synthesized and studied for



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their biological activities, the structural characteristics and cytotoxic activity of 2-aryl-5-bromobenzo[*b*]furan-3-ol and 2-aryl-5-iodobenzo[*b*]furan-3-ol compounds have not been studied much. We present here the synthesis of nine 2-aryl-5-bromo/iodobenzo[*b*]furan-3-ol compounds starting from salicylic acid. In addition to the synthesis and structure analysis of these compounds, the *in vitro* toxicity on the four human cancer cell lines KB, Hep-G2, Lu-1 and MCF7 has been tested.

2. Experimental

All chemicals were obtained from commercial sources and were used without further purification. The melting points were determined in open capillaries and are uncorrected. The IR spectra were recorded on an FT-IR Shimadzu 8400-S. NMR spectra were measured on a Bruker Avance 500 MHz in DMSO-*d*₆ using residual solvent DMSO-*d*₆ signals as the internal references. Mass spectra were recorded on a Sciex X500 QTOF mass spectrometer.

2.1. Synthesis and crystallization

Benzofuran derivatives **4a–4i** were synthesized as shown in Fig. 1. Methyl salicylate (**2**) (Cong *et al.*, 2012), methyl 5-bromo-2-hydroxybenzoate (**3a**) (Thin *et al.*, 2018) and methyl 2-hydroxy-5-iodobenzoate (**3b**) (Cong *et al.*, 2018) were synthesized according to previously reported methods.

Methyl salicylate (2): liquid; b.p. 494–495 K, yield 73%.

Methyl 5-bromo-2-hydroxybenzoate (methyl 5-bromosalicylate) (3a): white needles, m.p. 332–333 K, yield 92%; IR (ν , cm^{-1}): 3188, 2957, 1680, 1605, 625; ^1H NMR (δ , ppm): 10.50 (1H, *br*, OH), 7.82 (1H, *d*, $^4J = 2.5$ Hz, H6), 7.64 (1H, *dd*, $^3J = 8.0$ Hz, $^4J = 2.5$ Hz, H4), 6.96 (1H, *d*, $^3J = 8.0$ Hz, H3), 3.88 (3H, *s*, OCH₃).

Methyl 2-hydroxy-5-iodobenzoate (methyl 5-iodosalicylate) (3b): white needles, m.p. 347–348 K, yield 85%; IR (ν , cm^{-1}): 3156, 3080, 2949, 1676, 1604, 527; ^1H NMR (δ , ppm): 10.46 (1H, *s*, OH), 7.98 (1H, *d*, $^4J = 2.0$ Hz, H6), 7.75 (1H, *d*, $^3J =$

8.5 Hz, $^4J = 2.5$ Hz, H4), 6.82 (1H, *d*, $^3J = 9.0$ Hz, H3), 3.87 (3H, *s*, OCH₃).

2.1.1. General procedure for the synthesis of 2-aryl-5-halobenzo[*b*]furan-3-ol compounds 4a–4i. Anhydrous potassium carbonate (0.896 mg, 6.4 mmol) was added to a mixture of methyl 5-halosaliolate (2.1 mmol) and substituted phenacyl bromide (2.1 mmol) in dried dimethylformamide (DMF, 10 ml) at room temperature while stirring. After 1 h of stirring, the reaction mixture was poured into ice-cold water and acidified with 1 N HCl. The precipitate obtained was filtered off and crystallized from an appropriate solvent to give the corresponding products **4a–4i**.

The crystals of **4a**, **4b**, **4c** and **4h** were suitable for X-ray diffraction.

(5-Bromo-3-hydroxybenzofuran-2-yl)(4-fluorophenyl)methanone (4a): yellow crystals, recrystallized from a mixture of ethanol and water; m.p. 391–393 K [melting point according to Kulkarni *et al.* (2014): 393 K]; yield 84%. IR (ν , cm^{-1}): 3057 ($\text{Csp}^2\text{—H}$), 1614 (C=O), 1597, 1528 (C=C), 625 (C—Br); ^1H NMR: 8.06 (3H, *m*, Ar-H), 7.71 (1H, *m*, Ar-H), 7.64 (1H, *m*, Ar-H), 7.40 (2H, *m*, Ar-H); ^{13}C NMR: 181.8, 166.1, 164.1, 152.4, 148.3, 136.4, 134.2, 132.8, 132.4, 132.3, 124.4, 123.7, 115.9, 115.8, 115.6, 115.3; MS: m/z 332.9564 [$M - \text{H}$]⁺; calculation for C₁₅H₇BrFO₃: $M = 332.9568$ a.u.

(5-Bromo-3-hydroxybenzofuran-2-yl)(4-chlorophenyl)methanone (4b): yellow crystals, recrystallized from a mixture of ethanol and water; m.p. 436–437 K [melting point according to Kulkarni *et al.* (2014): 435–438 K]; yield 93%. IR (ν , cm^{-1}): 3254 (O—H), 3078 ($\text{Csp}^2\text{—H}$), 1599, 1566 (C=O , C=C), 660 (C—Br); ^1H NMR: 8.13 (1H, *d*, $^4J = 2.0$ Hz, Ar-H), 7.98 (2H, *d*, $^3J = 8.5$ Hz, Ar-H), 7.72 (1H, *dd*, $^3J = 8.5$, $^4J = 2.0$ Hz, Ar-H), 7.63 (3H, *m*, Ar-H); ^{13}C NMR: 181.9, 152.5, 148.4, 137.8, 136.4, 132.9, 131.3, 128.9, 124.5, 123.7, 115.6, 115.3; MS: m/z 350.9434 [$M + \text{H}$]⁺; calculation for C₁₅H₉BrClO₃: $M = 350.9424$ a.u.

(5-Bromo-3-hydroxybenzofuran-2-yl)(4-bromophenyl)methanone (4c): yellow crystals, recrystallized from a mixture of ethanol and water; m.p. 426–427 K [melting point according to Kulkarni *et al.* (2014): 425–426 K]; yield 91%. IR (ν , cm^{-1}):

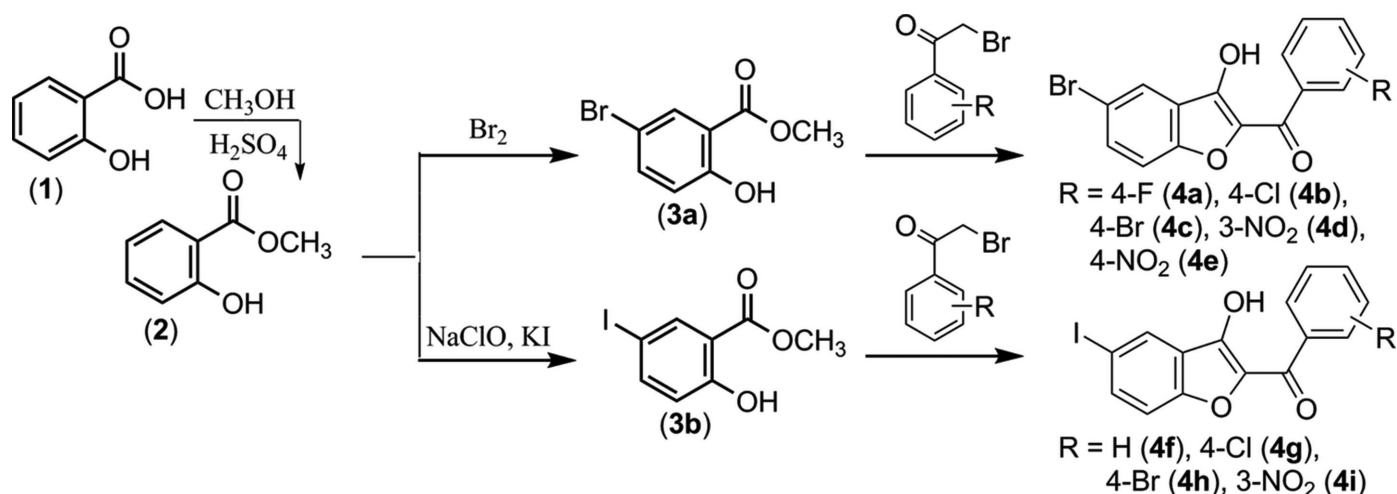


Figure 1
The synthetic route for the preparation of benzofuran derivatives **4a–4i**.

Table 1

Experimental details.

Experiments were carried out with Mo $K\alpha$ radiation using a Rigaku OD SuperNova Single source diffractometer with an Eos detector. H atoms were treated by a mixture of independent and constrained refinement.

	4a	4b	4c	4h
Crystal data				
Chemical formula	C ₁₅ H ₈ BrFO ₃	C ₁₅ H ₈ BrClO ₃	C ₁₅ H ₈ Br ₂ O ₃	C ₁₅ H ₈ BrIO ₃
M_r	335.12	351.57	396.03	443.02
Crystal system, space group	Monoclinic, $P2_1/c$	Monoclinic, $P2_1/c$	Triclinic, $P\bar{1}$	Monoclinic, $I2/a$
Temperature (K)	293	294	294	293
a, b, c (Å)	3.8598 (4), 11.7229 (10), 27.679 (2)	26.4034 (10), 3.9818 (1), 26.2773 (10)	7.0725 (4), 7.0884 (5), 14.6069 (8)	26.4214 (8), 4.76309 (13), 46.6213 (14)
α, β, γ (°)	90, 93.255 (9), 90	90, 104.605 (4), 90	92.230 (5), 103.091 (5), 101.219 (6)	90, 106.034 (3), 90
V (Å ³)	1250.38 (19)	2673.34 (17)	696.98 (8)	5638.9 (3)
Z	4	8	2	16
μ (mm ⁻¹)	3.30	3.28	5.82	5.11
Crystal size (mm)	0.5 × 0.15 × 0.05	0.4 × 0.15 × 0.05	0.35 × 0.15 × 0.05	0.35 × 0.15 × 0.05
Data collection				
Absorption correction	Multi-scan (CrysAlis PRO; Rigaku OD, 2018)	Multi-scan (CrysAlis PRO; Rigaku OD, 2018)	Multi-scan (CrysAlis PRO; Rigaku OD, 2018)	Gaussian (CrysAlis PRO; Rigaku OD, 2018)
$T_{\min}, T_{\max}$	0.447, 1.000	0.572, 1.000	0.523, 1.000	0.582, 1.000
No. of measured, independent and observed [$I > 2\sigma(I)$] reflections	7646, 2543, 1873	27661, 5419, 3168	14183, 2840, 1867	30966, 5733, 4448
R_{int}	0.040	0.064	0.046	0.036
$(\sin \theta/\lambda)_{\text{max}}$ (Å ⁻¹)	0.625	0.625	0.625	0.625
Refinement				
$R[F^2 > 2\sigma(F^2)], wR(F^2), S$	0.045, 0.097, 1.07	0.052, 0.102, 1.01	0.046, 0.109, 1.04	0.048, 0.123, 1.07
No. of reflections	2543	5419	2840	5733
No. of parameters	185	369	185	369
No. of restraints	0	0	0	2
$\Delta\rho_{\text{max}}, \Delta\rho_{\text{min}}$ (e Å ⁻³)	0.44, -0.45	0.56, -0.42	0.44, -0.40	1.78, -1.21

Computer programs: CrysAlis PRO (Rigaku OD, 2018), olex2.solve (Bourhis *et al.*, 2015), SHELXS (Sheldrick, 2008), SHELXT (Sheldrick, 2015a), SHELXL2016 (Sheldrick, 2015b) and OLEX2 (Dolomanov *et al.*, 2009).

3337 (O—H), 3076 (Csp²—H), 1601, 1562 (C=O, C=C), 658 (C—Br); ¹H NMR: 8.13 (1H, *d*, ⁴*J* = 2.0 Hz, Ar-H), 7.90 (2H, *d*, ³*J* = 8.5 Hz, Ar-H), 7.77 (1H, *dd*, ³*J* = 8.5, ⁴*J* = 2.0 Hz, Ar-H), 7.72 (2H, *d*, ⁴*J* = 2.0 Hz, Ar-H), 7.62 (1H, *d*, ³*J* = 8.5 Hz, Ar-H); ¹³C NMR: 182.0, 152.5, 148.4, 136.8, 136.4, 132.9, 131.5, 126.8, 124.5, 123.7, 115.6, 115.4; MS: *m/z* 394.8757 [*M* + H]⁺; calculation for C₁₅H₉Br₂O₃: *M* = 394.8918 a.u.

(5-Bromo-3-hydroxybenzofuran-2-yl)(3-nitrophenyl)methanone (4d): yellow crystals, recrystallized from a mixture of ethanol and water; m.p. 428–431 K; yield 76%. IR (ν , cm⁻¹): 3274 (O—H), 1631 (C=O), 1613, 1577, 1530 (C=C), 659 (C—Br); ¹H NMR: 8.62 (1H, *m*, Ar-H), 8.38 (1H, *s*, Ar-H), 8.24 (2H, *m*, Ar-H), 8.12 (1H, *d*, ³*J* = 8.5 Hz, Ar-H), 7.89 (1H, *m*, Ar-H), 7.75 (1H, *m*, Ar-H); ¹³C NMR: 180.5, 152.9, 148.0, 139.2, 136.2, 135.8, 133.2, 130.5, 127.1, 124.8, 124.1, 123.7, 115.5, 115.3; MS: *m/z* 361.9642 [*M* + H]⁺; calculation for C₁₅H₉BrNO₅: *M* = 361.9664 a.u.

(5-Bromo-3-hydroxybenzofuran-2-yl)(4-nitrophenyl)methanone (4e): yellow crystals, recrystallized from a mixture of acetone and water; m.p. 438–439 K; yield 83%. IR (ν , cm⁻¹): 3292 (O—H), 3098 (Csp²—H), 1624 (C=O), 1597, 1547 (C=C), 660 (C—Br); ¹H NMR: 8.37 (2H, *d*, ³*J* = 8.5 Hz, Ar-H), 8.23 (1H, *d*, ⁴*J* = 2.5 Hz, Ar-H), 8.12 (2H, *d*, ³*J* = 8.5 Hz, Ar-H), 7.74 (1H, *dd*, ³*J* = 8.5, ⁴*J* = 2.5 Hz, Ar-H), 7.63 (1H, ³*J* = 9.0 Hz, Ar-H); ¹³C NMR: 181.3, 152.9, 149.7, 143.5, 136.3, 133.3, 130.6,

125.4, 124.9, 123.8, 116.3, 115.6, 115.3; MS: *m/z* 359.9510 [*M* - H]⁺; calculation for C₁₅H₇BrNO₅: *M* = 359.9513 a.u.

(3-Hydroxy-5-iodobenzofuran-2-yl)(phenyl)methanone (4f): yellow crystals, recrystallized from a mixture of acetone and water; m.p. 411–412 K; yield 78%. IR (ν , cm⁻¹): 3084 (OH), 1609 (C=O), 1572, 1520 (C=C), 561 (C—I); ¹H NMR: 8.30 (1H, *d*, ⁴*J* = 1.5 Hz, Ar-H), 7.97 (2H, *d*, ³*J* = 7.0 Hz, Ar-H), 7.84 (1H, *m*, Ar-H), 7.65 (1H, *dd*, ³*J*₁ = ³*J*₂ = 7.0, Ar-H), 7.56 (2H, *d*, ³*J* = 7.0 Hz, Ar-H), 7.49 (1H, *dd*, ³*J*₁ = 9.0, ⁴*J*₂ = 5.0, Ar-H); ¹³C NMR: 183.2, 152.9, 148.0, 138.3, 138.7, 136.1, 132.9, 130.4, 129.4, 128.8, 124.4, 115.6, 87.3; MS: *m/z* 364.9652 [*M* + H]⁺; calculation for C₁₉H₁₆ClI₂NaO₄: *M* = 364.9675 a.u.

(4-Chlorophenyl)(3-hydroxy-5-iodobenzofuran-2-yl)methanone (4g): yellow crystals, recrystallized from a mixture of ethanol and water; m.p. 443–444 K; yield 88%. IR (ν , cm⁻¹): 3231 (OH), 1616 (C=O), 1591, 1567, 1531 (C=C), 565 (C—I); ¹H NMR: 8.29 (1H, *d*, ⁴*J* = 1.5 Hz, Ar-H), 7.97 (2H, *d*, ³*J* = 9.0 Hz, Ar-H), 7.84 (1H, *dd*, ³*J* = 9.0, ⁴*J* = 2.0 Hz, Ar-H), 7.62 (2H, *d*, ³*J* = 9.0 Hz, Ar-H), 7.48 (1H, *d*, ³*J* = 9.0 Hz, Ar-H); ¹³C NMR: 181.4, 152.5, 147.6, 137.9, 137.2, 135.9, 135.4, 130.8, 130.0, 128.3, 123.8, 115.0, 86.7; MS: *m/z* 396.9119 [*M* - H]⁺; calculation for C₁₅H₇ClIO₃: *M* = 396.9134 a.u.

(4-Bromophenyl)(3-hydroxy-5-iodobenzofuran-2-yl)methanone (4h): yellow crystals, recrystallized from a mixture of acetone and water; m.p. 441–442 K; yield 91%. IR (ν , cm⁻¹):

Table 2
Hydrogen-bond geometry (Å, °) for **4a**.

$D-H\cdots A$	$D-H$	$H\cdots A$	$D\cdots A$	$D-H\cdots A$
O19—H19 $\cdots$ O11	0.77 (5)	2.03 (4)	2.692 (4)	144 (4)
C17—H17 $\cdots$ O1	0.93	2.32	2.942 (4)	124
C16—H16 $\cdots$ O11 ⁱ	0.93	2.51	3.428 (4)	170
C5—H5 $\cdots$ O19 ⁱⁱ	0.93	2.61	3.454 (5)	150

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

3447 (O—H), 1614 (C=O), 1584, 1561, 1522 (C=C), 561 (C—I); ¹H NMR: 8.31 (1H, *d*, ⁴*J* = 1.5 Hz, Ar-H), 7.87 (3H, *m*, Ar-H), 7.78 (2H, *d*, ³*J* = 8.5 Hz, Ar-H), 7.50 (1H, *d*, ³*J* = 9.0 Hz, Ar-H); ¹³C NMR: 181.8, 152.9, 148.0, 138.3, 136.9, 135.9, 131.8, 131.5, 130.6, 128.1, 126.7, 124.4, 115.6, 87.3; MS: *m/z* 442.8761 [*M* + *H*]⁺; calculation for C₁₅H₉BrIO₃: *M* = 442.8780 a.u.

(3-Hydroxy-5-iodobenzofuran-2-yl)(3-nitrophenyl)methanone (4i): yellow crystals, recrystallized from a mixture of ethanol and water; m.p. 435–436 K; yield 80%. IR (*v*, cm^{−1}): 3245 (O—H), 3072 (Csp²—H), 1614 (C=O), 1577, 1527 (C=C), 560 (C—I); ¹H NMR: 8.59 (1H, *s*, Ar-H), 8.39 (1H, *dd*, ³*J* = 8.0, ⁴*J* = 2.0 Hz, Ar-H), 8.26 (1H, *d*, ⁴*J* = 8.0 Hz, Ar-H), 8.08 (1H, *s*, Ar-H), 7.76 (1H, *dd*, ³*J*₁ = ³*J*₂ = 8.0 Hz, Ar-H), 7.66 (1H, *dd*, ³*J* = 8.0, ⁴*J* = 1.5 Hz, Ar-H), 7.56 (1H, *d*, ³*J* = 8.0 Hz, Ar-H); ¹³C NMR: 180.4, 153.6, 148.4, 147.8, 138.8, 137.3, 136.4, 135.6, 130.3, 129.7, 127.4, 124.2, 118.1, 115.4, 87.1; MS: *m/z* 407.9374 [*M* − *H*][−]; calculation for C₁₅H₇INO₅: *M* = 407.9374 a.u.

2.2. Refinement

Crystal data, data collection and structure refinement details for **4a**, **4b**, **4c** and **4h** are summarized in Table 1. The O-bound H atoms (H19 and also H39 for **4b** and **4h**) were located from a difference Fourier map and refined freely for **4a–4c** or with O—H = 0.78 ± 0.01 Å for **4h**. The C-bound H atoms were placed in calculated positions (C—H = 0.93 Å) and were refined using a riding model, with *U*_{iso}(H) values set at 1.2*U*_{eq}(C).

2.3. In vitro cell tests

Compounds **4a**, **4b** and **4d–4i** were evaluated for their cytotoxicity against four human cancer cell lines, namely, KB (epidermoid carcinoma cancer), Hep-G2 (hepatoma carcinoma cancer), Lu (human lung adenocarcinoma cells) and MCF7 (human breast cancer cells). The cell lines were obtained from the American Type Culture Collection (USA) ATCC. The cells were grown in RPMI 1640 medium supplemented with 10% fetal bovine serum, 100 U ml^{−1} penicillin and 100 µg ml^{−1} streptomycin at 310 K in a humidified atmosphere (95% air and 5% CO₂). The exponentially growing cells were used throughout the experiments. The inhibitory effects of the compounds on the growth of the human cancer cell lines were determined by measuring the metabolic activity using a 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) assay, as reported previously (Cong *et al.*, 2018).

All the experiments were performed four or five times and the mean absorbance values were calculated. The results are expressed as the percentage of inhibition that produced a reduction in the absorbance by the treatment of the compounds compared to the untreated controls. A dose–response curve was generated and the inhibitory concentration of 50% (IC₅₀) was determined for each compound, as well as each cell line.

3. Results and discussion

3.1. Synthesis of 2-aryl-5-halobenzo[*b*]furan-3-ol compounds **4a–4i**

Nine 2-aryl-5-halobenzofuran-3-ol derivatives, **4a–4i**, were synthesized with yields between 76 and 93% starting from salicylic acid **1** (Fig. 1). Methyl salicylate (**2**), methyl 5-bromo-2-hydroxybenzoate (**3a**) and methyl 2-hydroxy-5-iodobenzoate (**3a**) were synthesized previously by our research group (Cong *et al.*, 2012, 2018; Thin *et al.*, 2018). The IR spectra of **3a–3b** show a strong band at 1680 cm^{−1} corresponding to a C=O stretching vibration of the ester group. The ¹H NMR spectra of **3a** and **3b** show the presence of the methoxy group as a singlet signal (3H) at δ 3.88 and 3.87, respectively. The three signals in the aromatic area, including a doublet signal (1H, ⁴*J* = 2.0 Hz), a doublet of doublet signals (1H, ³*J* = 8.0, ⁴*J* = 2.0 Hz) and a doublet signal (1H, ³*J* = 8.0 Hz), are typical for a benzene ring with three substituents at positions 1, 2 and 5.

To obtain the desired (5-halo-3-hydroxybenzo[*b*]furan-2-yl)(substituted phenyl)methanones (**4a–4i**), methyl 5-bromosalicylate (**3a**) or methyl 5-iodosalicylate (**3b**) were reacted with a substituted phenacyl bromide compound in DMF in the presence of potassium carbonate. This is considered an effective synthesis method for the preparation of 2-arylbenzofuran-3-ol compounds (Kulkarni *et al.*, 2014). The physical and spectral properties of **4a–4c** were available in the literature (Kulkarni *et al.*, 2014).

In the IR spectra of **4a–4i**, the OH group often shows only a weak absorption. The reason is that these compounds may exist in the 2-arylbenzofuran-3(2*H*)-one form (Kulkarni *et al.*, 2014). The C=O bond in the aryl group absorbs at low

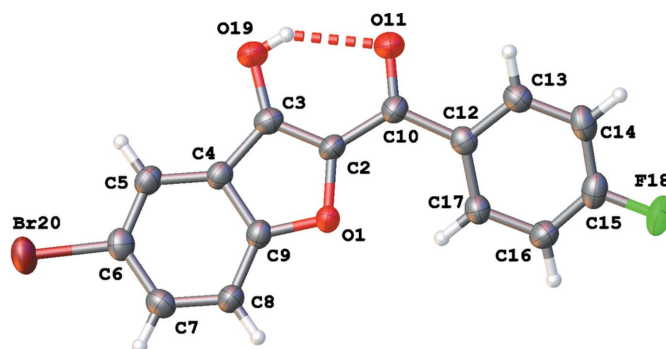


Figure 2
The molecular structure of **4a**, showing the atom-labelling scheme. Displacement ellipsoids are drawn at the 50% probability level.

Table 3
Hydrogen-bond geometry (Å, °) for **4b**.

<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>
O19—H19...O11	0.86 (5)	1.87 (5)	2.631 (5)	147 (5)
C17—H17...O1	0.93	2.29	2.951 (5)	128
O39—H39...O31	0.91 (6)	1.80 (6)	2.627 (6)	150 (7)
C37—H37...O21	0.93	2.25	2.926 (6)	129
C36—H36...O11	0.93	2.40	3.235 (6)	149
C8—H8...O39 ⁱ	0.93	2.67	3.434 (6)	140

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

Table 4
Hydrogen-bond geometry (Å, °) for **4c**.

<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>
O19—H19...O11	0.84 (6)	1.93 (6)	2.669 (5)	146 (5)
C17—H17...O1	0.93	2.28	2.948 (5)	129
O19—H19...O11 ⁱ	0.84 (6)	2.60 (6)	3.174 (5)	127
C14—H14...Br20 ⁱⁱ	0.93	3.05	3.959 (5)	165
C16—H16...O11 ⁱⁱⁱ	0.93	2.61	3.287 (6)	130

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

frequency (around 1610 cm⁻¹) due to conjugation with both the benzene and the benzofuran rings. In the ¹H NMR spectra of **4a–4i**, the signal of the OH proton is also rarely observed, which can be explained by the exchangeable character of the proton and/or hydrogen-bond formation. Apart from the Csp² signals in the aromatic area, the C=O carbon signal of the aroyl group usually appears at δ 180–182 in the ¹³C NMR spectra of **4a–4i**. In the mass spectra, the pseudo-molecular peaks [*M* + H]⁺ or [*M* − H][−] of **4a–4i** are in agreement with their molecular formulae.

3.2. Crystal structures of 2-aroyle-5-halobenzofuran-3-ol derivatives **4a–4c** and **4h**

For compounds **4a–4c** and **4h**, crystals suitable for X-ray diffraction were obtained during crystallization experiments using ethanol–water and acetone–water mixtures.

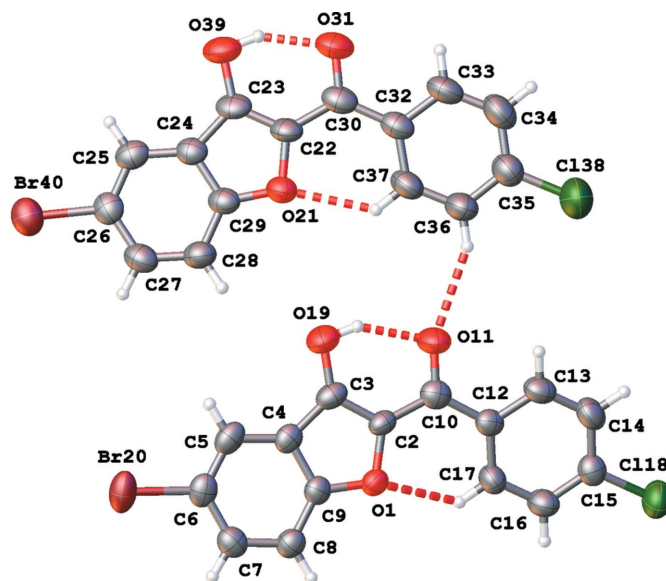


Figure 4
The molecular structure of **4b**, showing the atom-labelling scheme for both crystallographically unique molecules. Displacement ellipsoids are drawn at the 50% probability level.

Compound **4a** crystallizes in the space group *P*2₁/*c* with one molecule in the asymmetric unit (Fig. 2). The dihedral angle between the best planes through the benzofuran (atoms O1–C9) and phenyl (C12–C17) rings is 23.00 (16)°. The intramolecular O19—H19...O11 hydrogen bond (Table 2) keeps the last atom close to the benzofuran plane [deviation = 0.123 (3) Å]. The small value for the O11—C10—C12—C13 torsion angle [17.1 (5)°] causes a second intramolecular C17—H17...O1 interaction (Table 2).

The crystal packing of **4a** is characterized by F...Br contacts [3.136 (2) Å], resulting in chain formation in the *c* direction (Fig. 3). Parallel chains interact through two types of C—H...O interactions (Table 2), of which one involves the formation of an inversion dimer generating an R₂²(10) loop. The resulting layers are almost parallel to the (102) plane and

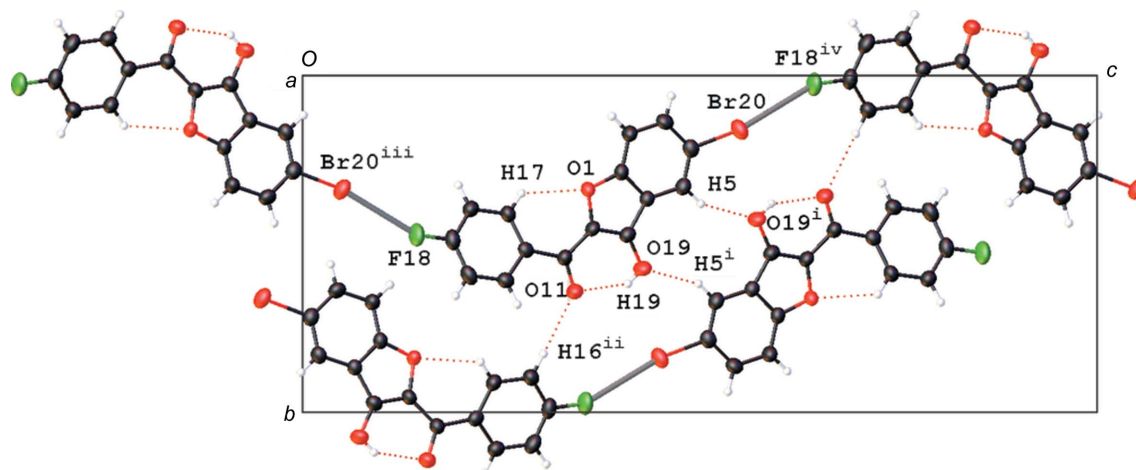


Figure 3
Packing diagram for **4a**, viewed along the *a* axis, showing the F...Br (green), O—H...O (red) and C—H...O (red) interactions. [Symmetry codes: (i) $-x + 1, -y + 1, -z + 1$; (ii) $-x + 2, y + \frac{1}{2}, -z + \frac{1}{2}$; (iii) $x + 1, -y + \frac{1}{2}, z - \frac{1}{2}$; (iv) $x - 1, -y + \frac{1}{2}, z + \frac{1}{2}$.]

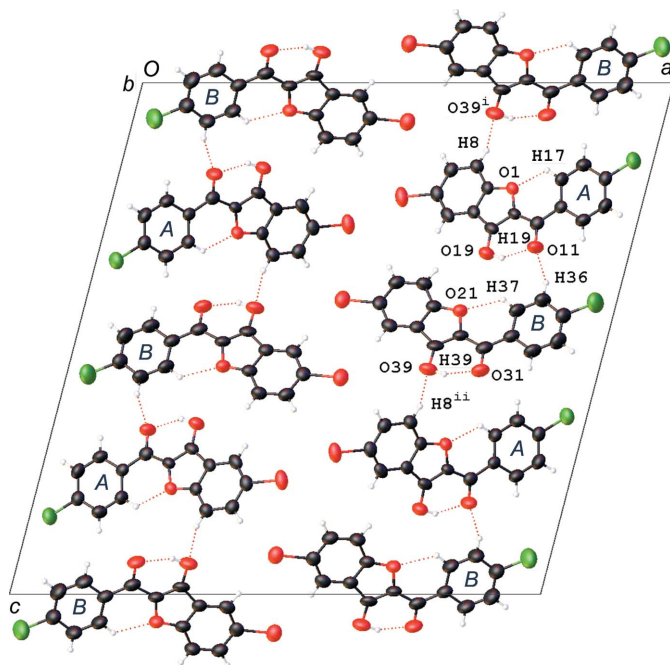


Figure 5

Packing diagram for **4b**, viewed along the *b* axis, showing the O—H...O (red) and C—H...O (red) interactions. Letters *A* and *B* indicate molecules *A* (atoms O1–Br20) and *B* (atoms O21–Br40). [Symmetry codes: (i) $x, -y + \frac{1}{2}, z - \frac{1}{2}$; (ii) $x, -y + \frac{1}{2}, z + \frac{1}{2}$.]

stack further along the *a* axis with centroid-to-centroid distances between stacking rings of 3.860 (2) Å.

Compound **4b** also crystallizes in the space group $P2_1/c$, but with two molecules (denoted *A* for that containing atoms O1–

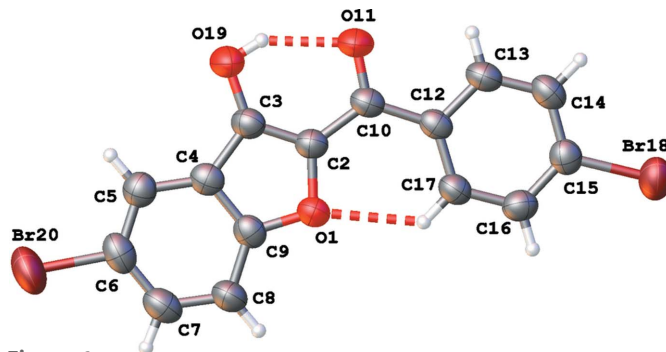


Figure 6

The molecular structure of **4c**, showing the atom-labelling scheme. Displacement ellipsoids are drawn at the 50% probability level.

Br20 and *B* for that containing atoms O21–Br40) in the asymmetric unit (Fig. 4). An overlay of both structures gives an r.m.s. deviation of 0.0899 Å. Compared to **4a**, both molecules are more planar, as indicated by the smaller dihedral angle between the two ring systems of 6.58 (19)° in molecule *A* and 15.98 (18)° in molecule *B*. Atoms O11 and O31 deviate by only −0.033 (3) and 0.030 (4) Å, respectively, from the benzofuran plane. Also, the O11—C10—C12—C13 [11.6 (6)°] and O31—C30—C32—C33 [3.5 (7)°] torsion angles are reduced. The intramolecular O—H...O hydrogen bonds are shorter compared to those in **4a** (Table 3).

Molecules *A* and *B* are linked via C36—H36...O11 hydrogen-bond interactions. These *A*–*B* dimers form chains running in the *c* direction through C8—H8...O39ⁱ hydrogen bonds (Table 3 and Fig. 5). The planes of neighbouring *A*–*B* dimers in this chain make an angle of 113.0 (2)°. Parallel

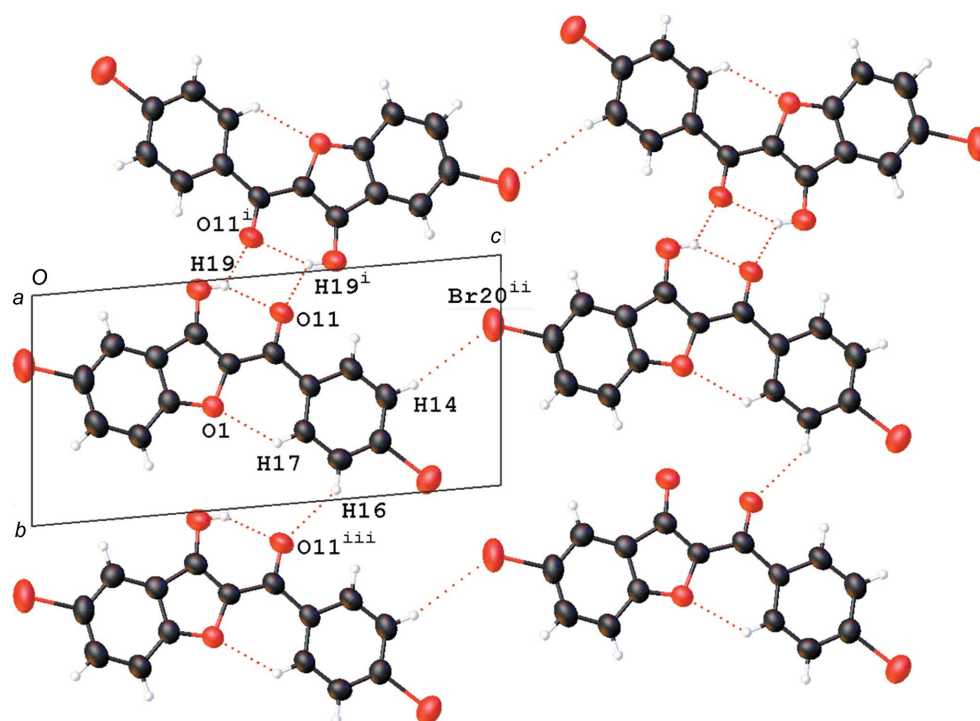


Figure 7

Packing diagram for **4c**, viewed along the *a* axis, showing the O—H...O (red), C—H...O (red) and C—H...Br (brown) interactions. [Symmetry codes: (i) $-x, -y, -z + 1$; (ii) $x, y, z + 1$; (iii) $x, y + 1, z$.]

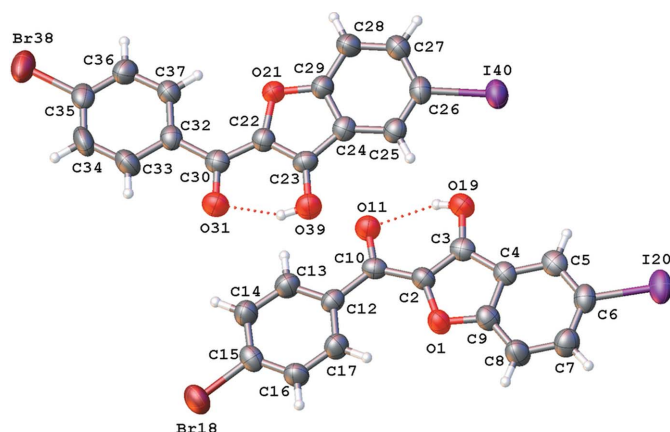


Figure 8

The molecular structure of **4h**, showing the atom-labelling scheme for both crystallographically unique molecules. Displacement ellipsoids are drawn at the 50% probability level.

chains show close Br20...Br20 [3.5934 (7) Å] and Cl18...Cl38 [3.452 (2) Å] contacts, and form a corrugated board-like layer extending in the *ac* plane.

Compound **4c** crystallizes in the space group $P\bar{1}$ and is quasi-planar (Fig. 6). The r.m.s. deviation of the best plane through all the non-H atoms is 0.024 Å, with atom O1 deviating most (0.049 Å). The ring systems are inclined to each other by only 1.74 (18)° and the O11—C10—C12—C13 torsion angle is 0.0 (6)°. The quasi-planarity of the molecule does not further shorten the intramolecular hydrogen bonds (Table 4).

The crystal packing of **4c** is built up by C14—H14...Br20ⁱⁱ interactions, resulting in chains of molecules running in the *c* direction. At one side of the chain, inversion dimers are

Table 5

Hydrogen-bond geometry (Å, °) for **4h**.

<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>
O19—H19...O11 ⁱ	0.76 (10)	2.05 (9)	2.680 (7)	140 (9)
C17—H17...O1	0.93	2.24	2.919 (8)	129
O39—H39...O31	0.79 (7)	1.90 (9)	2.617 (7)	151
C37—H37...O21	0.93	2.28	2.950 (8)	128
C13—H13...O39 ⁱ	0.93	2.50	3.231 (9)	135

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

formed by O19—H19...O11ⁱ interactions. At the other side of the chain, C16—H16...O11ⁱⁱⁱ interactions extend further the layer of molecules parallel to the (720) plane (Table 4 and Fig. 7). The rings in the layers stack on top of each other. The shortest centroid-to-centroid distance is observed for the stacking of the benzofuran and phenyl rings [*Cg*...*Cg* = 3.483 (2) Å and slippage = 0.399 Å].

Compound **4h** crystallizes in the space group $I2/a$ and comprises two equivalents of the molecule (denoted *A* for that containing atoms O1—I20 and *B* for that containing atoms O21—I40) in the asymmetric unit, as shown in Fig. 8. An overlay of both structures gives an r.m.s. deviation of 0.1233 Å. The dihedral angle between the two ring systems is 1.6 (3)° in *A* and 7.1 (3)° in *B*. Atoms O11 and O31 deviate by 0.113 (5) and −0.037 (5) Å, respectively, from the benzofuran plane. The O11—C10—C12—C13 [0.4 (9)°] and O31—C30—C32—C33 [7.0 (9)°] torsion angles are small. The intramolecular O—H...O hydrogen bonds are comparable to those in **4a** and **4c** (Table 5).

Molecules of **4h** are held together in the solid state by *X*... π interactions (with *X* = I, Br and O): I40...*Cg*6ⁱ [3.992 (3) Å], Br38...*Cg*7ⁱⁱ [3.684 (3) Å], O11...*Cg*1ⁱⁱ [3.411 (5) Å] and

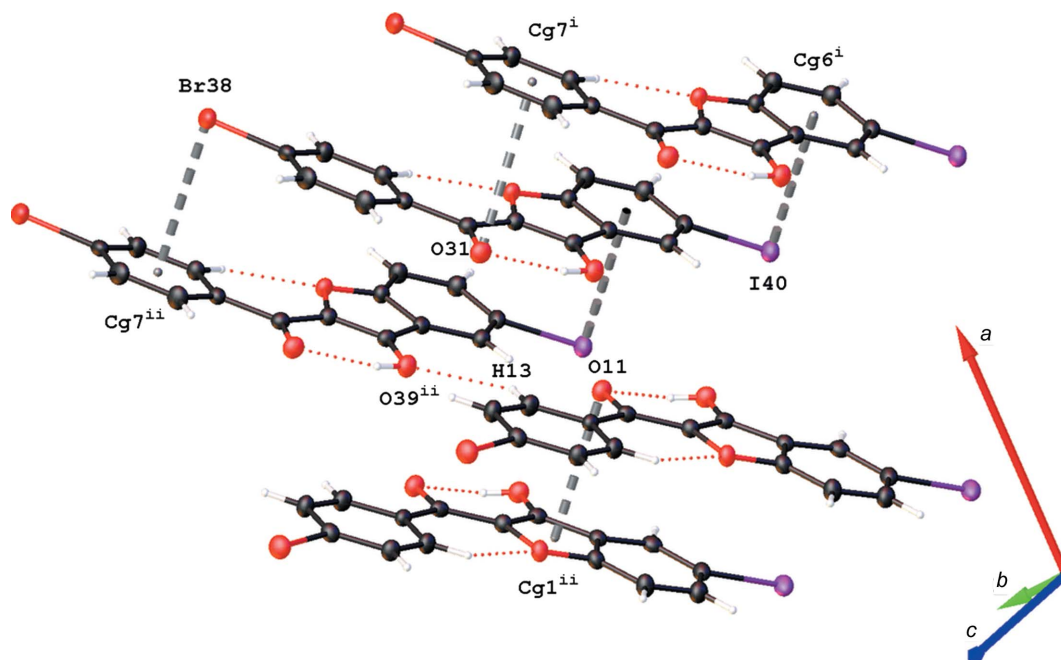


Figure 9

Partial packing diagram for **4h**, showing the *X*... π interactions, with *X* = I, Br and O (grey), and O—H...O (red) interactions. *Cg*1, *Cg*6 and *Cg*7 are the centroids of the O1/C2—C4/C9, C24—C29 and C32—C37 rings, respectively. [Symmetry codes: (i) *x*, *y* − 1, *z*; (ii) *x*, *y* + 1, *z*.]

Table 6

Inhibition capacity of compounds **4a**, **4b** and **4d–4i** against four human cancer cell lines at a concentration of 128 $\mu\text{g ml}^{-1}$.

Compound	Inhibition percentage (%)			
	KB	Hep-G2	Lu-1	MCF-7
4a	88	88	90	96
4b	93	96	100	100
4d	96	90	97	74
4e	95	88	87	85
4f	85	92	96	100
4g	82	92	92	100
4h	76	85	95	94
4i	90	92	97	98

O31...Cg7ⁱ [3.890 (6) Å] [Fig. 9; Cg1, Cg6 and Cg7 are the centroids of the O1/C2–C4/C9, C24–C29 and C32–C37 rings, respectively; symmetry codes: (i) $x, y - 1, z$; (ii) $x, y + 1, z$]. This is complemented by an intermolecular C13–H13...O39ⁱ hydrogen bond between molecules *A* and *B* (Fig. 9 and Table 5).

No voids are observed in the crystal packings of these compounds.

3.3. *In vitro* cytotoxicity of compounds **4a**, **4b** and **4d–4i**

Compounds **4a**, **4b** and **4d–4i** were evaluated for their cytotoxicity against the four cancer cell lines KB (mouth epidermal carcinoma cells), Hep-G2 (human liver hepatocellular carcinoma cells), Lu-1 (human lung adenocarcinoma cells) and MCF7 (human breast cancer cells). The cytotoxic effects of these compounds were estimated in terms of growth inhibition percentage and expressed as IC_{50} , which is the concentration of a compound which reduces the absorbance of treated cells by 50% with reference to the control (untreated cells). The inhibition capacities against the four human cancer cell lines are listed in Table 6. All of compounds **4a**, **4b** and **4d–4i** displayed significant growth inhibition in the range 74–100% at 128 $\mu\text{g ml}^{-1}$ on the four cancer cell lines. In particular, compound **4b** expressed an inhibition ability in the range 93–100% at the same concentration.

The IC_{50} values in Table 7 indicate that most of the examined compounds possess at least moderate cytotoxic activity, and some compounds even display a promising activity profile. It is important to note that the separate pharmacophores display considerably less potent cytotoxic activities compared to the most promising compounds, *i.e.* **4a**, **4b**, **4e** and **4g–4i** (IC_{50} values between 1.39 and 8.03 μM), which show a reasonable activity against the two human cancer cell lines Hep-G2 and MCF7. In particular, compound **4e** exhibits a strong anticancer effect against Hep-G2 cells, with an IC_{50} value (1.39 μM) similar to ellipticine (1.34 μM).

4. Conclusions

Starting from salicylic acid, we have synthesized nine 2-aroil-5-halobenzofuran-3-ol derivatives, **4a–4i**, with yields between 76 and 93%. The compounds were characterized by

Table 7

Cytotoxicity of compounds **4a**, **4b** and **4d–4i** (IC_{50}^a , μM).

Compound	KB	Hep-G2	Lu-1	MCF-7
4a	15.72 $\pm$ 0.36	5.69 $\pm$ 0.12	60.61 $\pm$ 1.20	23.95 $\pm$ 0.45
4b	13.72 $\pm$ 0.31	8.03 $\pm$ 0.23	34.06 $\pm$ 0.60	14.86 $\pm$ 0.23
4d	17.56 $\pm$ 0.33	13.16 $\pm$ 0.28	210.91 $\pm$ 5.01	88.65 $\pm$ 1.58
4e	12.27 $\pm$ 0.22	1.39 $\pm$ 0.02	62.86 $\pm$ 1.33	5.54 $\pm$ 0.08
4f	21.98 $\pm$ 0.38	11.14 $\pm$ 0.26	48.55 $\pm$ 0.71	21.98 $\pm$ 0.44
4g	20.07 $\pm$ 0.48	3.2 $\pm$ 0.09	49.60 $\pm$ 0.98	10.54 $\pm$ 0.20
4h	42.93 $\pm$ 0.93	5.50 $\pm$ 0.11	115.08 $\pm$ 2.31	18.10 $\pm$ 0.32
4i	43.72 $\pm$ 0.86	3.25 $\pm$ 0.07	56.44 $\pm$ 1.30	42.67 $\pm$ 0.81
Ellipticine	1.22 $\pm$ 0.08	1.34 $\pm$ 0.08	1.83 $\pm$ 0.20	2.15 $\pm$ 0.20

Note: (a) IC_{50} is the concentration of the compound required to inhibit cell growth by 50%. Values < 10 μM are indicated in **bold**.

MS and NMR spectroscopy. Crystals suitable for X-ray diffraction were obtained for compounds **4a**, **4b**, **4c** and **4h**. An intramolecular O–H...O hydrogen bond keeps the molecules close to being planar, with dihedral angles between the planes of the benzofuran and phenyl rings ranging from 1.6 (3) to 23.00 (16)°. In the solid state, molecules are held together by halogen–halogen and C–H...O/Br interactions, complemented by π – π interactions for **4c** and X ... π interactions in the case of **4h** (with X = I, Br and O). Compounds **4a**, **4b** and **4d–4i** were evaluated for their cytotoxicity against four human cancer cell lines. Six compounds showed significant inhibiting abilities on Hep-G2 cells, with IC_{50} values of 1.39–8.03 μM . With a shape similar to DAPI (4',6-diamidino-2-phenylindole), these compounds can bind to DNA as a minor-groove binder (Vlieghe *et al.*, 1999), which could explain the cytotoxicity. However, it cannot be excluded that the compounds intercalate between DNA base pairs in a way similar to ellipticine (Canals *et al.*, 2005).

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supporting information

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Synthesis, structure and *in vitro* cytotoxicity testing of some 2-aryloxybenzofuran-3-ols

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Computing details

For all structures, data collection: *CrysAlis PRO* (Rigaku OD, 2018); cell refinement: *CrysAlis PRO* (Rigaku OD, 2018); data reduction: *CrysAlis PRO* (Rigaku OD, 2018). Program(s) used to solve structure: olex2.solve (Bourhis *et al.*, 2015) for (4a); *SHELXS* (Sheldrick, 2008) for (4b); *SHELXT* (Sheldrick, 2015a) for (4c), (4h). For all structures, program(s) used to refine structure: *SHELXL2016* (Sheldrick, 2015b); molecular graphics: *OLEX2* (Dolomanov *et al.*, 2009); software used to prepare material for publication: *OLEX2* (Dolomanov *et al.*, 2009).

(5-Bromo-3-hydroxybenzofuran-2-yl)(4-fluorophenyl)methanone (4a)

Crystal data

$C_{15}H_8BrFO_3$	$F(000) = 664$
$M_r = 335.12$	$D_x = 1.780 \text{ Mg m}^{-3}$
Monoclinic, $P2_1/c$	Mo $K\alpha$ radiation, $\lambda = 0.71073 \text{ \AA}$
$a = 3.8598 (4) \text{ \AA}$	Cell parameters from 2736 reflections
$b = 11.7229 (10) \text{ \AA}$	$\theta = 2.9\text{--}25.3^\circ$
$c = 27.679 (2) \text{ \AA}$	$\mu = 3.30 \text{ mm}^{-1}$
$\beta = 93.255 (9)^\circ$	$T = 293 \text{ K}$
$V = 1250.38 (19) \text{ \AA}^3$	Needle, yellow
$Z = 4$	$0.5 \times 0.15 \times 0.05 \text{ mm}$

Data collection

Rigaku OD SuperNova Single source diffractometer with an Eos detector	$T_{\min} = 0.447, T_{\max} = 1.000$
Radiation source: micro-focus sealed X-ray tube, SuperNova (Mo) X-ray Source	7646 measured reflections
Mirror monochromator	2543 independent reflections
Detector resolution: $15.9631 \text{ pixels mm}^{-1}$	1873 reflections with $I > 2\sigma(I)$
ω scans	$R_{\text{int}} = 0.040$
Absorption correction: multi-scan (CrysAlis PRO; Rigaku OD, 2018)	$\theta_{\max} = 26.4^\circ, \theta_{\min} = 2.8^\circ$
	$h = -4 \rightarrow 4$
	$k = -14 \rightarrow 14$
	$l = -34 \rightarrow 33$

Refinement

Refinement on F^2	185 parameters
Least-squares matrix: full	0 restraints
$R[F^2 > 2\sigma(F^2)] = 0.045$	Primary atom site location: iterative
$wR(F^2) = 0.097$	Hydrogen site location: mixed
$S = 1.07$	H atoms treated by a mixture of independent and constrained refinement
2543 reflections	

$$w = 1/[\sigma^2(F_o^2) + (0.0352P)^2 + 0.4417P]$$

where $P = (F_o^2 + 2F_c^2)/3$
 $(\Delta/\sigma)_{\max} = 0.001$

$$\Delta\rho_{\max} = 0.44 \text{ e } \text{\AA}^{-3}$$

$$\Delta\rho_{\min} = -0.45 \text{ e } \text{\AA}^{-3}$$

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.

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

	<i>x</i>	<i>y</i>	<i>z</i>	$U_{\text{iso}}^*/U_{\text{eq}}$
O1	1.0511 (7)	0.33866 (19)	0.35954 (8)	0.0346 (6)
C2	0.9792 (10)	0.4552 (3)	0.36548 (12)	0.0331 (9)
C3	0.8510 (10)	0.4728 (3)	0.40944 (12)	0.0356 (9)
C4	0.8335 (9)	0.3665 (3)	0.43395 (12)	0.0307 (8)
C5	0.7327 (10)	0.3302 (3)	0.47925 (13)	0.0356 (9)
H5	0.648929	0.381124	0.501555	0.043*
C6	0.7633 (10)	0.2170 (3)	0.48907 (12)	0.0363 (9)
C7	0.8901 (10)	0.1380 (3)	0.45616 (13)	0.0394 (10)
H7	0.905416	0.061294	0.464530	0.047*
C8	0.9913 (11)	0.1730 (3)	0.41188 (13)	0.0383 (9)
H8	1.076432	0.121809	0.389793	0.046*
C9	0.9610 (9)	0.2874 (3)	0.40168 (12)	0.0319 (8)
C10	1.0400 (10)	0.5412 (3)	0.33035 (12)	0.0350 (9)
O11	0.9820 (8)	0.6415 (2)	0.34270 (9)	0.0525 (8)
C12	1.1635 (9)	0.5177 (3)	0.28145 (12)	0.0318 (8)
C13	1.2995 (10)	0.6084 (3)	0.25606 (13)	0.0375 (9)
H13	1.319832	0.679808	0.270563	0.045*
C14	1.4041 (10)	0.5935 (4)	0.20979 (13)	0.0433 (10)
H14	1.497366	0.653718	0.192927	0.052*
C15	1.3676 (11)	0.4884 (4)	0.18939 (13)	0.0420 (10)
C16	1.2279 (10)	0.3965 (3)	0.21210 (13)	0.0401 (10)
H16	1.200229	0.326544	0.196515	0.048*
C17	1.1296 (10)	0.4116 (3)	0.25904 (12)	0.0372 (9)
H17	1.040261	0.350361	0.275726	0.045*
F18	1.4709 (7)	0.4732 (2)	0.14395 (7)	0.0633 (8)
O19	0.7528 (9)	0.5730 (2)	0.42805 (11)	0.0509 (8)
Br20	0.63812 (11)	0.16145 (4)	0.55017 (2)	0.04886 (17)
H19	0.805 (12)	0.618 (4)	0.4097 (15)	0.053 (15)*

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

	U^{11}	U^{22}	U^{33}	U^{12}	U^{13}	U^{23}
O1	0.0478 (16)	0.0302 (12)	0.0266 (13)	0.0059 (13)	0.0097 (11)	0.0023 (10)
C2	0.041 (2)	0.0301 (19)	0.0289 (19)	0.0024 (18)	0.0076 (17)	−0.0044 (15)
C3	0.041 (2)	0.032 (2)	0.035 (2)	0.0031 (19)	0.0037 (18)	−0.0042 (16)
C4	0.031 (2)	0.0329 (19)	0.0286 (18)	0.0021 (17)	0.0047 (16)	−0.0016 (15)

C5	0.037 (2)	0.038 (2)	0.0318 (19)	0.003 (2)	0.0079 (17)	−0.0037 (17)
C6	0.033 (2)	0.042 (2)	0.034 (2)	−0.002 (2)	0.0049 (17)	0.0035 (17)
C7	0.047 (3)	0.032 (2)	0.039 (2)	0.0041 (19)	0.0029 (19)	0.0052 (16)
C8	0.052 (3)	0.033 (2)	0.030 (2)	0.006 (2)	0.0091 (18)	−0.0004 (16)
C9	0.034 (2)	0.036 (2)	0.0262 (18)	0.0014 (18)	0.0038 (16)	−0.0002 (16)
C10	0.044 (2)	0.032 (2)	0.0295 (19)	−0.0017 (19)	0.0060 (17)	−0.0022 (16)
O11	0.088 (2)	0.0311 (15)	0.0398 (16)	0.0041 (15)	0.0131 (15)	−0.0022 (12)
C12	0.031 (2)	0.0325 (19)	0.0317 (19)	0.0009 (17)	0.0004 (16)	0.0037 (15)
C13	0.044 (2)	0.032 (2)	0.037 (2)	0.0002 (19)	0.0028 (18)	0.0031 (16)
C14	0.045 (3)	0.049 (3)	0.037 (2)	−0.002 (2)	0.009 (2)	0.0125 (19)
C15	0.041 (2)	0.056 (3)	0.029 (2)	0.005 (2)	0.0053 (18)	0.0043 (18)
C16	0.053 (3)	0.034 (2)	0.033 (2)	0.003 (2)	0.0037 (19)	−0.0029 (17)
C17	0.047 (2)	0.035 (2)	0.030 (2)	−0.001 (2)	0.0053 (18)	0.0041 (16)
F18	0.090 (2)	0.0692 (16)	0.0332 (13)	0.0089 (16)	0.0262 (13)	0.0011 (12)
O19	0.080 (2)	0.0301 (15)	0.0444 (17)	0.0080 (16)	0.0208 (16)	−0.0018 (14)
Br20	0.0552 (3)	0.0534 (3)	0.0396 (3)	0.0052 (2)	0.0172 (2)	0.01369 (19)

Geometric parameters (Å, °)

O1—C2	1.406 (4)	C8—C9	1.374 (5)
O1—C9	1.374 (4)	C10—O11	1.249 (4)
C2—C3	1.355 (5)	C10—C12	1.486 (5)
C2—C10	1.429 (5)	C12—C13	1.393 (5)
C3—C4	1.422 (5)	C12—C17	1.393 (5)
C3—O19	1.345 (4)	C13—H13	0.9300
C4—C5	1.400 (5)	C13—C14	1.376 (5)
C4—C9	1.397 (5)	C14—H14	0.9300
C5—H5	0.9300	C14—C15	1.360 (6)
C5—C6	1.358 (5)	C15—C16	1.373 (5)
C6—C7	1.406 (5)	C15—F18	1.353 (4)
C6—Br20	1.900 (3)	C16—H16	0.9300
C7—H7	0.9300	C16—C17	1.385 (5)
C7—C8	1.370 (5)	C17—H17	0.9300
C8—H8	0.9300	O19—H19	0.77 (4)
C9—O1—C2	105.3 (2)	C8—C9—C4	123.1 (3)
O1—C2—C10	124.4 (3)	C2—C10—C12	124.3 (3)
C3—C2—O1	109.7 (3)	O11—C10—C2	116.1 (3)
C3—C2—C10	125.9 (3)	O11—C10—C12	119.7 (3)
C2—C3—C4	108.9 (3)	C13—C12—C10	117.9 (3)
O19—C3—C2	127.0 (3)	C13—C12—C17	119.0 (3)
O19—C3—C4	124.1 (3)	C17—C12—C10	122.9 (3)
C5—C4—C3	135.8 (3)	C12—C13—H13	119.6
C9—C4—C3	104.4 (3)	C14—C13—C12	120.8 (4)
C9—C4—C5	119.8 (3)	C14—C13—H13	119.6
C4—C5—H5	121.6	C13—C14—H14	120.9
C6—C5—C4	116.8 (3)	C15—C14—C13	118.2 (4)
C6—C5—H5	121.6	C15—C14—H14	120.9

C5—C6—C7	122.9 (3)	C14—C15—C16	123.7 (3)
C5—C6—Br20	119.3 (3)	F18—C15—C14	118.5 (3)
C7—C6—Br20	117.8 (3)	F18—C15—C16	117.8 (4)
C6—C7—H7	119.7	C15—C16—H16	121.1
C8—C7—C6	120.7 (3)	C15—C16—C17	117.7 (3)
C8—C7—H7	119.7	C17—C16—H16	121.1
C7—C8—H8	121.6	C12—C17—H17	119.8
C7—C8—C9	116.8 (3)	C16—C17—C12	120.5 (3)
C9—C8—H8	121.6	C16—C17—H17	119.8
O1—C9—C4	111.6 (3)	C3—O19—H19	105 (3)
C8—C9—O1	125.3 (3)		
O1—C2—C3—C4	−0.2 (5)	C7—C8—C9—C4	−0.2 (6)
O1—C2—C3—O19	179.9 (4)	C9—O1—C2—C3	0.0 (4)
O1—C2—C10—O11	−175.6 (4)	C9—O1—C2—C10	178.9 (4)
O1—C2—C10—C12	4.6 (6)	C9—C4—C5—C6	−0.6 (6)
C2—O1—C9—C4	0.3 (4)	C10—C2—C3—C4	−179.2 (4)
C2—O1—C9—C8	−179.4 (4)	C10—C2—C3—O19	1.0 (7)
C2—C3—C4—C5	178.8 (4)	C10—C12—C13—C14	−177.1 (4)
C2—C3—C4—C9	0.4 (4)	C10—C12—C17—C16	175.6 (4)
C2—C10—C12—C13	−163.1 (4)	O11—C10—C12—C13	17.1 (6)
C2—C10—C12—C17	20.9 (6)	O11—C10—C12—C17	−158.9 (4)
C3—C2—C10—O11	3.2 (6)	C12—C13—C14—C15	0.7 (6)
C3—C2—C10—C12	−176.6 (4)	C13—C12—C17—C16	−0.4 (6)
C3—C4—C5—C6	−178.8 (4)	C13—C14—C15—C16	0.9 (7)
C3—C4—C9—O1	−0.4 (4)	C13—C14—C15—F18	−179.8 (3)
C3—C4—C9—C8	179.3 (4)	C14—C15—C16—C17	−2.1 (6)
C4—C5—C6—C7	0.2 (6)	C15—C16—C17—C12	1.8 (6)
C4—C5—C6—Br20	179.1 (3)	C17—C12—C13—C14	−1.0 (6)
C5—C4—C9—O1	−179.1 (3)	F18—C15—C16—C17	178.6 (3)
C5—C4—C9—C8	0.6 (6)	O19—C3—C4—C5	−1.4 (8)
C5—C6—C7—C8	0.2 (6)	O19—C3—C4—C9	−179.8 (4)
C6—C7—C8—C9	−0.2 (6)	Br20—C6—C7—C8	−178.7 (3)
C7—C8—C9—O1	179.5 (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>
O19—H19 $\cdots$ O11	0.77 (5)	2.03 (4)	2.692 (4)	144 (4)
C17—H17 $\cdots$ O1	0.93	2.32	2.942 (4)	124
C16—H16 $\cdots$ O11 ⁱ	0.93	2.51	3.428 (4)	170
C5—H5 $\cdots$ O19 ⁱⁱ	0.93	2.61	3.454 (5)	150

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

(5-Bromo-3-hydroxybenzofuran-2-yl)(4-chlorophenyl)methanone (4b)

Crystal data

 $C_{15}H_8BrClO_3$ $M_r = 351.57$ Monoclinic, $P2_1/c$ $a = 26.4034$ (10) Å $b = 3.9818$ (1) Å $c = 26.2773$ (10) Å $\beta = 104.605$ (4)° $V = 2673.34$ (17) Å³ $Z = 8$ $F(000) = 1392$ $D_x = 1.747$ Mg m⁻³Mo $K\alpha$ radiation, $\lambda = 0.71073$ Å

Cell parameters from 6124 reflections

 $\theta = 3.1$ – 24.1 ° $\mu = 3.28$ mm⁻¹ $T = 294$ K

Plate, yellow

 $0.4 \times 0.15 \times 0.05$ mm

Data collection

Rigaku OD SuperNova Single source

diffractometer with an Eos detector

Radiation source: micro-focus sealed X-ray

tube, SuperNova (Mo) X-ray Source

Mirror monochromator

Detector resolution: 15.9631 pixels mm⁻¹ ω scans

Absorption correction: multi-scan

(CrysAlis PRO; Rigaku OD, 2018)

 $T_{\min} = 0.572$, $T_{\max} = 1.000$

27661 measured reflections

5419 independent reflections

3168 reflections with $I > 2\sigma(I)$ $R_{\text{int}} = 0.064$ $\theta_{\max} = 26.4$ °, $\theta_{\min} = 2.4$ ° $h = -33 \rightarrow 33$ $k = -4 \rightarrow 4$ $l = -32 \rightarrow 32$

Refinement

Refinement on F^2

Least-squares matrix: full

 $R[F^2 > 2\sigma(F^2)] = 0.052$ $wR(F^2) = 0.102$ $S = 1.01$

5419 reflections

369 parameters

0 restraints

Primary atom site location: structure-invariant

direct methods

Hydrogen site location: mixed

H atoms treated by a mixture of independent

and constrained refinement

 $w = 1/[\sigma^2(F_o^2) + (0.029P)^2 + 2.0591P]$ where $P = (F_o^2 + 2F_c^2)/3$ $(\Delta/\sigma)_{\max} = 0.001$ $\Delta\rho_{\max} = 0.56$ e Å⁻³ $\Delta\rho_{\min} = -0.42$ e Å⁻³

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.

Fractional atomic coordinates and isotropic or equivalent isotropic displacement parameters (Å²)

	<i>x</i>	<i>y</i>	<i>z</i>	$U_{\text{iso}}^*/U_{\text{eq}}$
O1	0.74798 (10)	0.1478 (6)	0.20663 (11)	0.0451 (7)
C2	0.76425 (16)	0.2959 (10)	0.25631 (16)	0.0414 (10)
C3	0.72831 (17)	0.2377 (11)	0.28464 (18)	0.0474 (11)
C4	0.68645 (16)	0.0499 (10)	0.25260 (17)	0.0435 (10)
C5	0.63911 (17)	−0.0788 (11)	0.25851 (19)	0.0520 (12)
H5	0.628733	−0.049134	0.289505	0.062*
C6	0.60870 (16)	−0.2499 (10)	0.2169 (2)	0.0506 (12)
C7	0.62345 (17)	−0.3027 (11)	0.17041 (18)	0.0522 (12)

H7	0.601560	−0.424167	0.143395	0.063*
C8	0.67037 (16)	−0.1771 (10)	0.16363 (18)	0.0488 (11)
H8	0.680793	−0.210610	0.132745	0.059*
C9	0.70068 (16)	0.0011 (9)	0.20560 (17)	0.0422 (11)
C10	0.81144 (17)	0.4852 (10)	0.27453 (19)	0.0504 (12)
O11	0.82009 (13)	0.5813 (8)	0.32146 (13)	0.0703 (9)
C12	0.84822 (16)	0.5771 (10)	0.24301 (17)	0.0438 (10)
C13	0.89643 (17)	0.7151 (11)	0.26866 (18)	0.0563 (12)
H13	0.905122	0.738409	0.305052	0.068*
C14	0.93111 (17)	0.8166 (12)	0.2408 (2)	0.0614 (13)
H14	0.963255	0.907700	0.258215	0.074*
C15	0.91812 (16)	0.7830 (11)	0.18708 (19)	0.0515 (12)
C16	0.87094 (18)	0.6494 (11)	0.16089 (18)	0.0575 (12)
H16	0.862349	0.630215	0.124446	0.069*
C17	0.83643 (17)	0.5441 (11)	0.18891 (18)	0.0520 (12)
H17	0.804676	0.449286	0.171240	0.062*
Cl18	0.96251 (5)	0.9144 (4)	0.15236 (6)	0.0778 (4)
O19	0.73115 (15)	0.3394 (9)	0.33357 (14)	0.0678 (10)
Br20	0.54377 (2)	−0.42670 (12)	0.22329 (2)	0.06821 (19)
O21	0.70963 (11)	0.8529 (7)	0.44584 (11)	0.0543 (8)
C22	0.72238 (19)	1.0222 (11)	0.49411 (17)	0.0510 (12)
C23	0.6799 (2)	1.0408 (11)	0.51387 (17)	0.0540 (12)
C24	0.63657 (18)	0.8860 (10)	0.47749 (17)	0.0481 (11)
C25	0.58370 (18)	0.8345 (10)	0.47435 (18)	0.0537 (12)
H25	0.568715	0.905525	0.500961	0.064*
C26	0.55481 (17)	0.6758 (11)	0.43063 (19)	0.0527 (12)
C27	0.57635 (19)	0.5631 (11)	0.39031 (18)	0.0589 (13)
H27	0.555187	0.455037	0.361263	0.071*
C28	0.62855 (18)	0.6108 (11)	0.39319 (18)	0.0571 (12)
H28	0.643551	0.534760	0.366871	0.069*
C29	0.65764 (18)	0.7764 (11)	0.43690 (17)	0.0499 (11)
C30	0.77303 (19)	1.1543 (11)	0.51808 (19)	0.0567 (13)
O31	0.77683 (13)	1.2897 (9)	0.56258 (13)	0.0736 (10)
C32	0.81848 (18)	1.1521 (11)	0.49538 (18)	0.0541 (12)
C33	0.8658 (2)	1.2824 (12)	0.52436 (19)	0.0662 (14)
H33	0.867985	1.366531	0.557867	0.079*
C34	0.9090 (2)	1.2900 (14)	0.5049 (2)	0.0784 (16)
H34	0.940408	1.375615	0.525226	0.094*
C35	0.90609 (19)	1.1710 (13)	0.4553 (2)	0.0669 (14)
C36	0.8598 (2)	1.0437 (13)	0.4251 (2)	0.0691 (14)
H36	0.857813	0.964976	0.391294	0.083*
C37	0.81681 (19)	1.0340 (11)	0.44501 (19)	0.0631 (14)
H37	0.785654	0.946543	0.424512	0.076*
Cl38	0.96020 (6)	1.1822 (5)	0.42988 (7)	0.1069 (6)
O39	0.67804 (16)	1.1817 (9)	0.55988 (14)	0.0726 (11)
Br40	0.48242 (2)	0.59410 (13)	0.42371 (2)	0.07029 (19)
H19	0.7620 (18)	0.424 (12)	0.343 (2)	0.08 (2)*
H39	0.711 (2)	1.268 (17)	0.570 (3)	0.14 (3)*

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

	U^{11}	U^{22}	U^{33}	U^{12}	U^{13}	U^{23}
O1	0.0443 (16)	0.0494 (18)	0.0441 (19)	0.0027 (14)	0.0158 (14)	−0.0022 (14)
C2	0.045 (2)	0.047 (3)	0.034 (3)	0.007 (2)	0.013 (2)	0.003 (2)
C3	0.058 (3)	0.049 (3)	0.038 (3)	0.012 (2)	0.017 (2)	0.006 (2)
C4	0.043 (2)	0.042 (2)	0.047 (3)	0.012 (2)	0.014 (2)	0.007 (2)
C5	0.056 (3)	0.048 (3)	0.059 (3)	0.016 (2)	0.027 (3)	0.011 (2)
C6	0.050 (3)	0.037 (2)	0.068 (4)	0.007 (2)	0.021 (3)	0.005 (2)
C7	0.049 (3)	0.046 (3)	0.057 (3)	0.004 (2)	0.007 (2)	0.000 (2)
C8	0.052 (3)	0.045 (3)	0.051 (3)	0.003 (2)	0.017 (2)	0.000 (2)
C9	0.040 (2)	0.040 (3)	0.048 (3)	0.0076 (19)	0.012 (2)	0.003 (2)
C10	0.052 (3)	0.047 (3)	0.050 (3)	0.008 (2)	0.008 (2)	0.002 (2)
O11	0.073 (2)	0.095 (3)	0.042 (2)	−0.016 (2)	0.0125 (18)	−0.0123 (19)
C12	0.042 (2)	0.044 (2)	0.043 (3)	0.008 (2)	0.006 (2)	−0.001 (2)
C13	0.056 (3)	0.064 (3)	0.043 (3)	0.002 (3)	0.001 (3)	−0.005 (2)
C14	0.044 (3)	0.071 (3)	0.063 (4)	−0.005 (2)	0.002 (3)	−0.005 (3)
C15	0.045 (3)	0.049 (3)	0.059 (3)	0.002 (2)	0.010 (2)	0.002 (2)
C16	0.062 (3)	0.064 (3)	0.044 (3)	−0.008 (3)	0.008 (3)	−0.003 (2)
C17	0.045 (3)	0.058 (3)	0.051 (3)	−0.008 (2)	0.008 (2)	−0.002 (2)
Cl18	0.0611 (8)	0.0974 (10)	0.0795 (10)	−0.0114 (7)	0.0261 (7)	0.0049 (8)
O19	0.070 (2)	0.092 (3)	0.044 (2)	−0.007 (2)	0.0203 (19)	−0.0046 (19)
Br20	0.0535 (3)	0.0522 (3)	0.1076 (5)	0.0021 (2)	0.0364 (3)	0.0067 (3)
O21	0.0570 (19)	0.062 (2)	0.042 (2)	−0.0063 (16)	0.0098 (16)	−0.0054 (15)
C22	0.063 (3)	0.056 (3)	0.030 (3)	−0.005 (2)	0.006 (2)	−0.001 (2)
C23	0.076 (3)	0.055 (3)	0.029 (3)	−0.001 (3)	0.010 (3)	0.007 (2)
C24	0.060 (3)	0.045 (3)	0.039 (3)	−0.001 (2)	0.010 (2)	0.006 (2)
C25	0.070 (3)	0.047 (3)	0.047 (3)	0.004 (2)	0.020 (3)	0.007 (2)
C26	0.058 (3)	0.047 (3)	0.053 (3)	−0.003 (2)	0.013 (3)	0.013 (2)
C27	0.066 (3)	0.058 (3)	0.046 (3)	−0.008 (3)	0.004 (3)	0.000 (2)
C28	0.067 (3)	0.061 (3)	0.045 (3)	−0.004 (3)	0.016 (3)	−0.006 (2)
C29	0.062 (3)	0.049 (3)	0.038 (3)	−0.005 (2)	0.010 (2)	0.002 (2)
C30	0.070 (3)	0.051 (3)	0.041 (3)	0.000 (3)	0.000 (3)	0.003 (2)
O31	0.080 (2)	0.088 (3)	0.045 (2)	−0.006 (2)	0.0018 (19)	−0.0140 (19)
C32	0.063 (3)	0.050 (3)	0.043 (3)	−0.005 (2)	0.000 (3)	0.000 (2)
C33	0.074 (3)	0.066 (3)	0.049 (3)	−0.012 (3)	−0.001 (3)	−0.011 (3)
C34	0.062 (3)	0.090 (4)	0.074 (4)	−0.019 (3)	0.000 (3)	−0.010 (3)
C35	0.062 (3)	0.073 (4)	0.063 (4)	−0.012 (3)	0.011 (3)	−0.004 (3)
C36	0.068 (3)	0.086 (4)	0.051 (3)	−0.017 (3)	0.010 (3)	−0.014 (3)
C37	0.062 (3)	0.071 (3)	0.049 (3)	−0.016 (3)	0.000 (3)	−0.006 (3)
Cl38	0.0789 (10)	0.1375 (15)	0.1097 (13)	−0.0319 (10)	0.0336 (9)	−0.0211 (11)
O39	0.093 (3)	0.084 (3)	0.043 (2)	−0.009 (2)	0.021 (2)	−0.0099 (18)
Br40	0.0627 (3)	0.0649 (3)	0.0813 (4)	−0.0056 (3)	0.0145 (3)	0.0078 (3)

Geometric parameters ($\text{\AA}$, $^\circ$)

O1—C2	1.398 (4)	O21—C22	1.400 (5)
O1—C9	1.373 (4)	O21—C29	1.367 (5)

C2—C3	1.366 (5)	C22—C23	1.352 (6)
C2—C10	1.431 (6)	C22—C30	1.427 (6)
C3—C4	1.421 (6)	C23—C24	1.432 (6)
C3—O19	1.332 (5)	C23—O39	1.345 (5)
C4—C5	1.395 (5)	C24—C25	1.393 (6)
C4—C9	1.392 (5)	C24—C29	1.392 (6)
C5—H5	0.9300	C25—H25	0.9300
C5—C6	1.364 (6)	C25—C26	1.364 (6)
C6—C7	1.389 (6)	C26—C27	1.397 (6)
C6—Br20	1.899 (4)	C26—Br40	1.902 (4)
C7—H7	0.9300	C27—H27	0.9300
C7—C8	1.389 (5)	C27—C28	1.374 (6)
C8—H8	0.9300	C28—H28	0.9300
C8—C9	1.384 (5)	C28—C29	1.378 (6)
C10—O11	1.256 (5)	C30—O31	1.268 (5)
C10—C12	1.473 (6)	C30—C32	1.469 (6)
C12—C13	1.394 (5)	C32—C33	1.388 (6)
C12—C17	1.383 (5)	C32—C37	1.395 (6)
C13—H13	0.9300	C33—H33	0.9300
C13—C14	1.369 (6)	C33—C34	1.365 (6)
C14—H14	0.9300	C34—H34	0.9300
C14—C15	1.373 (6)	C34—C35	1.369 (6)
C15—C16	1.370 (6)	C35—C36	1.376 (6)
C15—Cl18	1.738 (5)	C35—Cl38	1.724 (5)
C16—H16	0.9300	C36—H36	0.9300
C16—C17	1.374 (6)	C36—C37	1.366 (6)
C17—H17	0.9300	C37—H37	0.9300
O19—H19	0.86 (5)	O39—H39	0.90 (6)
C9—O1—C2	105.2 (3)	C29—O21—C22	105.3 (3)
O1—C2—C10	124.8 (4)	O21—C22—C30	124.2 (4)
C3—C2—O1	110.2 (4)	C23—C22—O21	109.9 (4)
C3—C2—C10	125.0 (4)	C23—C22—C30	125.9 (4)
C2—C3—C4	108.0 (4)	C22—C23—C24	108.7 (4)
O19—C3—C2	126.6 (4)	O39—C23—C22	126.1 (4)
O19—C3—C4	125.3 (4)	O39—C23—C24	125.2 (5)
C5—C4—C3	135.4 (4)	C25—C24—C23	136.3 (5)
C9—C4—C3	104.8 (4)	C29—C24—C23	103.9 (4)
C9—C4—C5	119.8 (4)	C29—C24—C25	119.8 (4)
C4—C5—H5	121.4	C24—C25—H25	121.4
C6—C5—C4	117.2 (4)	C26—C25—C24	117.2 (4)
C6—C5—H5	121.4	C26—C25—H25	121.4
C5—C6—C7	122.8 (4)	C25—C26—C27	122.7 (4)
C5—C6—Br20	118.5 (4)	C25—C26—Br40	119.7 (4)
C7—C6—Br20	118.8 (4)	C27—C26—Br40	117.7 (4)
C6—C7—H7	119.5	C26—C27—H27	119.7
C8—C7—C6	121.0 (4)	C28—C27—C26	120.6 (4)
C8—C7—H7	119.5	C28—C27—H27	119.7

C7—C8—H8	122.0	C27—C28—H28	121.5
C9—C8—C7	116.0 (4)	C27—C28—C29	116.9 (4)
C9—C8—H8	122.0	C29—C28—H28	121.5
O1—C9—C4	111.8 (4)	O21—C29—C24	112.1 (4)
O1—C9—C8	125.0 (4)	O21—C29—C28	125.0 (4)
C8—C9—C4	123.2 (4)	C28—C29—C24	122.8 (4)
C2—C10—C12	125.8 (4)	C22—C30—C32	126.1 (4)
O11—C10—C2	114.6 (4)	O31—C30—C22	114.3 (5)
O11—C10—C12	119.6 (4)	O31—C30—C32	119.6 (4)
C13—C12—C10	118.5 (4)	C33—C32—C30	119.3 (4)
C17—C12—C10	123.0 (4)	C33—C32—C37	117.1 (5)
C17—C12—C13	118.4 (4)	C37—C32—C30	123.6 (4)
C12—C13—H13	119.7	C32—C33—H33	119.2
C14—C13—C12	120.7 (4)	C34—C33—C32	121.6 (5)
C14—C13—H13	119.7	C34—C33—H33	119.2
C13—C14—H14	120.2	C33—C34—H34	120.1
C13—C14—C15	119.6 (4)	C33—C34—C35	119.8 (5)
C15—C14—H14	120.2	C35—C34—H34	120.1
C14—C15—Cl18	119.0 (4)	C34—C35—C36	120.4 (5)
C16—C15—C14	121.0 (4)	C34—C35—Cl38	120.4 (4)
C16—C15—Cl18	120.1 (4)	C36—C35—Cl38	119.2 (4)
C15—C16—H16	120.3	C35—C36—H36	120.3
C15—C16—C17	119.4 (4)	C37—C36—C35	119.4 (5)
C17—C16—H16	120.3	C37—C36—H36	120.3
C12—C17—H17	119.5	C32—C37—H37	119.2
C16—C17—C12	121.0 (4)	C36—C37—C32	121.6 (4)
C16—C17—H17	119.5	C36—C37—H37	119.2
C3—O19—H19	102 (4)	C23—O39—H39	99 (4)
O1—C2—C3—C4	−1.0 (4)	O21—C22—C23—C24	−1.3 (5)
O1—C2—C3—O19	179.5 (4)	O21—C22—C23—O39	179.0 (4)
O1—C2—C10—O11	−176.3 (4)	O21—C22—C30—O31	−177.9 (4)
O1—C2—C10—C12	5.1 (6)	O21—C22—C30—C32	3.6 (7)
C2—O1—C9—C4	−0.1 (4)	C22—O21—C29—C24	−0.6 (5)
C2—O1—C9—C8	−179.6 (4)	C22—O21—C29—C28	179.4 (4)
C2—C3—C4—C5	−178.8 (4)	C22—C23—C24—C25	−177.8 (5)
C2—C3—C4—C9	0.8 (4)	C22—C23—C24—C29	0.9 (5)
C2—C10—C12—C13	−169.9 (4)	C22—C30—C32—C33	−178.1 (4)
C2—C10—C12—C17	12.6 (6)	C22—C30—C32—C37	3.8 (7)
C3—C2—C10—O11	4.6 (6)	C23—C22—C30—O31	2.3 (7)
C3—C2—C10—C12	−174.0 (4)	C23—C22—C30—C32	−176.2 (4)
C3—C4—C5—C6	179.7 (4)	C23—C24—C25—C26	178.5 (5)
C3—C4—C9—O1	−0.5 (4)	C23—C24—C29—O21	−0.1 (5)
C3—C4—C9—C8	179.1 (4)	C23—C24—C29—C28	179.9 (4)
C4—C5—C6—C7	1.0 (6)	C24—C25—C26—C27	0.7 (6)
C4—C5—C6—Br20	−179.6 (3)	C24—C25—C26—Br40	179.6 (3)
C5—C4—C9—O1	179.3 (3)	C25—C24—C29—O21	178.8 (4)
C5—C4—C9—C8	−1.2 (6)	C25—C24—C29—C28	−1.2 (7)

C5—C6—C7—C8	−1.0 (7)	C25—C26—C27—C28	−0.3 (7)
C6—C7—C8—C9	−0.1 (6)	C26—C27—C28—C29	−0.8 (7)
C7—C8—C9—O1	−179.4 (3)	C27—C28—C29—O21	−178.4 (4)
C7—C8—C9—C4	1.2 (6)	C27—C28—C29—C24	1.6 (7)
C9—O1—C2—C3	0.7 (4)	C29—O21—C22—C23	1.1 (5)
C9—O1—C2—C10	−178.5 (4)	C29—O21—C22—C30	−178.7 (4)
C9—C4—C5—C6	0.1 (6)	C29—C24—C25—C26	0.0 (6)
C10—C2—C3—C4	178.2 (4)	C30—C22—C23—C24	178.6 (4)
C10—C2—C3—O19	−1.3 (7)	C30—C22—C23—O39	−1.2 (7)
C10—C12—C13—C14	−177.4 (4)	C30—C32—C33—C34	−179.2 (5)
C10—C12—C17—C16	176.6 (4)	C30—C32—C37—C36	178.5 (4)
O11—C10—C12—C13	11.6 (6)	O31—C30—C32—C33	3.5 (7)
O11—C10—C12—C17	−166.0 (4)	O31—C30—C32—C37	−174.6 (4)
C12—C13—C14—C15	0.2 (7)	C32—C33—C34—C35	0.9 (8)
C13—C12—C17—C16	−1.0 (6)	C33—C32—C37—C36	0.4 (7)
C13—C14—C15—C16	0.0 (7)	C33—C34—C35—C36	0.0 (8)
C13—C14—C15—Cl18	179.8 (4)	C33—C34—C35—Cl38	179.4 (4)
C14—C15—C16—C17	−0.8 (7)	C34—C35—C36—C37	−0.6 (8)
C15—C16—C17—C12	1.3 (7)	C35—C36—C37—C32	0.4 (8)
C17—C12—C13—C14	0.3 (6)	C37—C32—C33—C34	−1.0 (7)
Cl18—C15—C16—C17	179.5 (3)	Cl38—C35—C36—C37	180.0 (4)
O19—C3—C4—C5	0.7 (8)	O39—C23—C24—C25	2.0 (8)
O19—C3—C4—C9	−179.6 (4)	O39—C23—C24—C29	−179.4 (4)
Br20—C6—C7—C8	179.6 (3)	Br40—C26—C27—C28	−179.2 (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>
O19—H19 $\cdots$ O11	0.86 (5)	1.87 (5)	2.631 (5)	147 (5)
C17—H17 $\cdots$ O1	0.93	2.29	2.951 (5)	128
O39—H39 $\cdots$ O31	0.91 (6)	1.80 (6)	2.627 (6)	150 (7)
C37—H37 $\cdots$ O21	0.93	2.25	2.926 (6)	129
C36—H36 $\cdots$ O11	0.93	2.40	3.235 (6)	149
C8—H8 $\cdots$ O39 ⁱ	0.93	2.67	3.434 (6)	140

Symmetry code: (i) *x*, $-\gamma+1/2$, *z*−1/2.

(5-Bromo-3-hydroxybenzofuran-2-yl)(4-bromophenyl)methanone (4c)

Crystal data

C₁₅H₈Br₂O₃*M_r* = 396.03Triclinic, *P*1*a* = 7.0725 (4) Å*b* = 7.0884 (5) Å*c* = 14.6069 (8) Å α = 92.230 (5)° β = 103.091 (5)° γ = 101.219 (6)°*V* = 696.98 (8) Å³*Z* = 2*F*(000) = 384*D_x* = 1.887 Mg m^{−3}Mo *K*α radiation, λ = 0.71073 Å

Cell parameters from 3969 reflections

 θ = 2.9–25.0° μ = 5.82 mm^{−1}*T* = 294 K

Plate, yellow

0.35 × 0.15 × 0.05 mm

Data collection

Rigaku OD SuperNova Single source
diffractometer with an Eos detector
Radiation source: micro-focus sealed X-ray
tube, SuperNova (Mo) X-ray Source
Mirror monochromator
Detector resolution: 15.9631 pixels mm⁻¹
 ω scans
Absorption correction: multi-scan
(CrysAlis PRO; Rigaku OD, 2018)

$T_{\min} = 0.523$, $T_{\max} = 1.000$
14183 measured reflections
2840 independent reflections
1867 reflections with $I > 2\sigma(I)$
 $R_{\text{int}} = 0.046$
 $\theta_{\max} = 26.4^\circ$, $\theta_{\min} = 2.9^\circ$
 $h = -8 \rightarrow 8$
 $k = -8 \rightarrow 8$
 $l = -18 \rightarrow 18$

Refinement

Refinement on F^2
Least-squares matrix: full
 $R[F^2 > 2\sigma(F^2)] = 0.046$
 $wR(F^2) = 0.109$
 $S = 1.03$
2840 reflections
185 parameters
0 restraints

Hydrogen site location: mixed
H atoms treated by a mixture of independent
and constrained refinement
 $w = 1/[\sigma^2(F_o^2) + (0.0415P)^2 + 0.4345P]$
where $P = (F_o^2 + 2F_c^2)/3$
 $(\Delta/\sigma)_{\max} = 0.001$
 $\Delta\rho_{\max} = 0.44 \text{ e } \text{\AA}^{-3}$
 $\Delta\rho_{\min} = -0.40 \text{ e } \text{\AA}^{-3}$

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.

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

	<i>x</i>	<i>y</i>	<i>z</i>	$U_{\text{iso}}^*/U_{\text{eq}}$
O1	0.2698 (4)	0.5503 (4)	0.38600 (19)	0.0488 (7)
C2	0.2236 (6)	0.3699 (6)	0.4205 (3)	0.0451 (10)
C3	0.1893 (6)	0.2269 (6)	0.3496 (3)	0.0492 (10)
C4	0.2133 (6)	0.3147 (6)	0.2657 (3)	0.0467 (10)
C5	0.1950 (6)	0.2465 (7)	0.1721 (3)	0.0538 (11)
H5	0.162112	0.115376	0.152601	0.065*
C6	0.2283 (6)	0.3842 (8)	0.1110 (3)	0.0603 (13)
C7	0.2745 (7)	0.5815 (8)	0.1380 (3)	0.0644 (13)
H7	0.294088	0.668302	0.093245	0.077*
C8	0.2919 (7)	0.6517 (7)	0.2302 (3)	0.0583 (12)
H8	0.322333	0.783073	0.249141	0.070*
C9	0.2605 (6)	0.5113 (6)	0.2925 (3)	0.0470 (10)
C10	0.2117 (6)	0.3412 (6)	0.5157 (3)	0.0471 (10)
O11	0.1679 (5)	0.1689 (4)	0.5325 (2)	0.0672 (9)
C12	0.2445 (5)	0.4957 (6)	0.5920 (3)	0.0432 (10)
C13	0.2243 (6)	0.4393 (7)	0.6802 (3)	0.0528 (11)
H13	0.190559	0.308580	0.688378	0.063*
C14	0.2529 (6)	0.5720 (7)	0.7550 (3)	0.0562 (12)
H14	0.239823	0.532483	0.813584	0.067*
C15	0.3015 (6)	0.7652 (7)	0.7422 (3)	0.0516 (11)
C16	0.3218 (6)	0.8272 (7)	0.6564 (3)	0.0538 (11)

H16	0.354165	0.958359	0.648961	0.065*
C17	0.2934 (6)	0.6921 (6)	0.5815 (3)	0.0485 (10)
H17	0.307233	0.732746	0.523116	0.058*
Br18	0.34142 (8)	0.94907 (8)	0.84645 (4)	0.0757 (2)
O19	0.1385 (5)	0.0365 (5)	0.3552 (3)	0.0671 (9)
Br20	0.20857 (10)	0.30111 (10)	−0.01643 (4)	0.0906 (3)
H19	0.127 (9)	0.030 (8)	0.411 (4)	0.10 (2)*

Atomic displacement parameters (Å²)

	U^{11}	U^{22}	U^{33}	U^{12}	U^{13}	U^{23}
O1	0.0533 (18)	0.0470 (17)	0.0475 (16)	0.0062 (14)	0.0175 (13)	0.0085 (13)
C2	0.044 (2)	0.044 (3)	0.048 (2)	0.008 (2)	0.0135 (19)	0.009 (2)
C3	0.051 (3)	0.048 (3)	0.053 (3)	0.011 (2)	0.020 (2)	0.010 (2)
C4	0.038 (2)	0.053 (3)	0.052 (3)	0.011 (2)	0.0147 (19)	0.009 (2)
C5	0.051 (3)	0.056 (3)	0.055 (3)	0.010 (2)	0.015 (2)	0.002 (2)
C6	0.054 (3)	0.084 (4)	0.044 (2)	0.016 (3)	0.012 (2)	0.006 (3)
C7	0.064 (3)	0.075 (4)	0.056 (3)	0.011 (3)	0.019 (2)	0.021 (3)
C8	0.067 (3)	0.057 (3)	0.052 (3)	0.007 (2)	0.021 (2)	0.014 (2)
C9	0.040 (2)	0.057 (3)	0.046 (2)	0.008 (2)	0.0142 (19)	0.007 (2)
C10	0.045 (3)	0.049 (3)	0.048 (2)	0.010 (2)	0.0123 (19)	0.013 (2)
O11	0.099 (3)	0.0453 (19)	0.0565 (19)	0.0070 (18)	0.0227 (17)	0.0145 (15)
C12	0.036 (2)	0.052 (3)	0.043 (2)	0.010 (2)	0.0116 (18)	0.013 (2)
C13	0.056 (3)	0.054 (3)	0.053 (3)	0.011 (2)	0.018 (2)	0.018 (2)
C14	0.056 (3)	0.069 (3)	0.047 (3)	0.011 (2)	0.018 (2)	0.014 (2)
C15	0.046 (3)	0.060 (3)	0.049 (3)	0.008 (2)	0.013 (2)	0.002 (2)
C16	0.055 (3)	0.047 (3)	0.058 (3)	0.006 (2)	0.013 (2)	0.008 (2)
C17	0.050 (3)	0.052 (3)	0.044 (2)	0.009 (2)	0.0131 (19)	0.011 (2)
Br18	0.0838 (4)	0.0774 (4)	0.0631 (3)	0.0050 (3)	0.0248 (3)	−0.0112 (3)
O19	0.102 (3)	0.046 (2)	0.059 (2)	0.0128 (18)	0.031 (2)	0.0083 (16)
Br20	0.1167 (5)	0.1131 (5)	0.0462 (3)	0.0303 (4)	0.0227 (3)	0.0072 (3)

Geometric parameters (Å, °)

O1—C2	1.399 (5)	C7—C8	1.387 (6)
O1—C9	1.368 (5)	C8—C9	1.394 (6)
C2—C3	1.367 (6)	C10—O11	1.248 (5)
C2—C10	1.432 (5)	C10—C12	1.478 (6)
C3—C4	1.425 (5)	C12—C13	1.394 (5)
C3—O19	1.338 (5)	C12—C17	1.391 (6)
C4—C5	1.400 (6)	C13—C14	1.365 (6)
C4—C9	1.387 (6)	C14—C15	1.376 (6)
C5—C6	1.370 (6)	C15—C16	1.372 (6)
C6—C7	1.393 (7)	C15—Br18	1.899 (4)
C6—Br20	1.896 (4)	C16—C17	1.379 (6)
C9—O1—C2	105.3 (3)	O1—C9—C4	112.3 (3)
O1—C2—C10	124.7 (4)	O1—C9—C8	124.3 (4)

C3—C2—O1	109.8 (3)	C4—C9—C8	123.4 (4)
C3—C2—C10	125.5 (4)	C2—C10—C12	125.6 (4)
C2—C3—C4	108.2 (4)	O11—C10—C2	114.9 (4)
O19—C3—C2	127.2 (4)	O11—C10—C12	119.5 (4)
O19—C3—C4	124.6 (4)	C13—C12—C10	117.3 (4)
C5—C4—C3	135.0 (4)	C17—C12—C10	124.5 (3)
C9—C4—C3	104.4 (4)	C17—C12—C13	118.2 (4)
C9—C4—C5	120.6 (4)	C14—C13—C12	121.3 (4)
C6—C5—C4	116.2 (4)	C13—C14—C15	119.0 (4)
C5—C6—C7	123.1 (4)	C14—C15—Br18	118.7 (3)
C5—C6—Br20	118.2 (4)	C16—C15—C14	121.6 (4)
C7—C6—Br20	118.7 (4)	C16—C15—Br18	119.6 (3)
C8—C7—C6	121.5 (4)	C15—C16—C17	119.0 (4)
C7—C8—C9	115.2 (5)	C16—C17—C12	120.8 (4)
O1—C2—C3—C4	0.0 (5)	C7—C8—C9—C4	−0.6 (6)
O1—C2—C3—O19	−179.0 (4)	C9—O1—C2—C3	0.5 (4)
O1—C2—C10—O11	179.8 (4)	C9—O1—C2—C10	−178.7 (4)
O1—C2—C10—C12	0.5 (6)	C9—C4—C5—C6	0.6 (6)
C2—O1—C9—C4	−0.8 (4)	C10—C2—C3—C4	179.2 (4)
C2—O1—C9—C8	178.3 (4)	C10—C2—C3—O19	0.2 (7)
C2—C3—C4—C5	−178.7 (4)	C10—C12—C13—C14	179.6 (4)
C2—C3—C4—C9	−0.4 (4)	C10—C12—C17—C16	−179.9 (4)
C2—C10—C12—C13	179.3 (4)	O11—C10—C12—C13	0.0 (6)
C2—C10—C12—C17	−0.6 (6)	O11—C10—C12—C17	−179.9 (4)
C3—C2—C10—O11	0.7 (6)	C12—C13—C14—C15	0.4 (6)
C3—C2—C10—C12	−178.6 (4)	C13—C12—C17—C16	0.2 (6)
C3—C4—C5—C6	178.7 (4)	C13—C14—C15—C16	0.0 (6)
C3—C4—C9—O1	0.8 (4)	C13—C14—C15—Br18	−179.9 (3)
C3—C4—C9—C8	−178.4 (4)	C14—C15—C16—C17	−0.3 (6)
C4—C5—C6—C7	−1.1 (6)	C15—C16—C17—C12	0.2 (6)
C4—C5—C6—Br20	179.3 (3)	C17—C12—C13—C14	−0.5 (6)
C5—C4—C9—O1	179.4 (3)	Br18—C15—C16—C17	179.7 (3)
C5—C4—C9—C8	0.2 (6)	O19—C3—C4—C5	0.3 (7)
C5—C6—C7—C8	0.7 (7)	O19—C3—C4—C9	178.6 (4)
C6—C7—C8—C9	0.2 (7)	Br20—C6—C7—C8	−179.7 (3)
C7—C8—C9—O1	−179.7 (4)		

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

$D\cdots H\cdots A$	$D\cdots H$	$H\cdots A$	$D\cdots A$	$D\cdots H\cdots A$
O19—H19 $\cdots$ O11	0.84 (6)	1.93 (6)	2.669 (5)	146 (5)
C17—H17 $\cdots$ O1	0.93	2.28	2.948 (5)	129
O19—H19 $\cdots$ O11 ⁱ	0.84 (6)	2.60 (6)	3.174 (5)	127
C14—H14 $\cdots$ Br20 ⁱⁱ	0.93	3.05	3.959 (5)	165
C16—H16 $\cdots$ O11 ⁱⁱⁱ	0.93	2.61	3.287 (6)	130

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

(4-Bromophenyl)(3-hydroxy-5-iodobenzofuran-2-yl)methanone (4h)

Crystal data

 $C_{15}H_8BrIO_3$ $M_r = 443.02$ Monoclinic, $P2_1/a$ $a = 26.4214$ (8) Å $b = 4.76309$ (13) Å $c = 46.6213$ (14) Å $\beta = 106.034$ (3)° $V = 5638.9$ (3) Å³ $Z = 16$ $F(000) = 3360$ $D_x = 2.087$ Mg m⁻³Mo $K\alpha$ radiation, $\lambda = 0.71073$ Å

Cell parameters from 11835 reflections

 $\theta = 2.7\text{--}27.2^\circ$ $\mu = 5.11$ mm⁻¹ $T = 293$ K

Needle, yellow

 $0.35 \times 0.15 \times 0.05$ mm

Data collection

Rigaku OD SuperNova Single source

diffractometer with an Eos detector

Radiation source: micro-focus sealed X-ray

tube, SuperNova (Mo) X-ray Source

Mirror monochromator

Detector resolution: 15.9631 pixels mm⁻¹ ω scans

Absorption correction: gaussian

(CrysAlis PRO; Rigaku OD, 2018)

 $T_{\min} = 0.582$, $T_{\max} = 1.000$

30966 measured reflections

5733 independent reflections

4448 reflections with $I > 2\sigma(I)$ $R_{\text{int}} = 0.036$ $\theta_{\max} = 26.4^\circ$, $\theta_{\min} = 2.7^\circ$ $h = -32 \rightarrow 33$ $k = -5 \rightarrow 5$ $l = -58 \rightarrow 58$

Refinement

Refinement on F^2

Least-squares matrix: full

 $R[F^2 > 2\sigma(F^2)] = 0.048$ $wR(F^2) = 0.123$ $S = 1.07$

5733 reflections

369 parameters

2 restraints

Primary atom site location: dual

Hydrogen site location: mixed

H atoms treated by a mixture of independent

and constrained refinement

 $w = 1/[\sigma^2(F_o^2) + (0.0486P)^2 + 38.6563P]$ where $P = (F_o^2 + 2F_c^2)/3$ $(\Delta/\sigma)_{\max} = 0.002$ $\Delta\rho_{\max} = 1.78$ e Å⁻³ $\Delta\rho_{\min} = -1.21$ e Å⁻³

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.

Fractional atomic coordinates and isotropic or equivalent isotropic displacement parameters (Å²)

	<i>x</i>	<i>y</i>	<i>z</i>	$U_{\text{iso}}^*/U_{\text{eq}}$
O1	0.31437 (17)	−0.1296 (9)	0.62348 (9)	0.0509 (10)
C2	0.3471 (2)	0.0161 (13)	0.60926 (12)	0.0440 (14)
C3	0.3360 (2)	−0.0703 (13)	0.58016 (13)	0.0442 (14)
C4	0.2954 (2)	−0.2773 (12)	0.57509 (12)	0.0423 (13)
C5	0.2670 (2)	−0.4364 (13)	0.55069 (14)	0.0501 (15)
H5	0.274146	−0.425178	0.532280	0.060*
C6	0.2279 (3)	−0.6110 (14)	0.55498 (14)	0.0519 (16)
C7	0.2174 (3)	−0.6343 (15)	0.58299 (16)	0.0606 (18)
H7	0.191032	−0.755200	0.585119	0.073*

C8	0.2457 (3)	−0.4804 (15)	0.60729 (15)	0.0592 (18)
H8	0.239390	−0.496240	0.625887	0.071*
C9	0.2837 (3)	−0.3023 (13)	0.60254 (14)	0.0489 (15)
C10	0.3842 (2)	0.2278 (13)	0.62289 (13)	0.0426 (13)
O11	0.40906 (18)	0.3384 (10)	0.60636 (9)	0.0561 (11)
C12	0.3956 (2)	0.3180 (12)	0.65444 (13)	0.0434 (13)
C13	0.4331 (3)	0.5229 (15)	0.66462 (15)	0.0568 (17)
H13	0.449736	0.602010	0.651387	0.068*
C14	0.4469 (3)	0.6151 (15)	0.69416 (15)	0.0577 (17)
H14	0.473533	0.746849	0.700905	0.069*
C15	0.4200 (3)	0.5055 (14)	0.71317 (13)	0.0505 (15)
C16	0.3822 (3)	0.3006 (14)	0.70382 (14)	0.0536 (16)
H16	0.365082	0.225725	0.717047	0.064*
C17	0.3699 (3)	0.2079 (14)	0.67478 (15)	0.0533 (16)
H17	0.344307	0.070224	0.668447	0.064*
Br18	0.43363 (3)	0.64613 (18)	0.75258 (2)	0.0687 (2)
O19	0.3584 (2)	0.0240 (12)	0.55955 (10)	0.0569 (12)
I20	0.18141 (2)	−0.84287 (11)	0.51858 (2)	0.06610 (17)
O21	0.59407 (16)	0.3302 (9)	0.61452 (9)	0.0479 (10)
C22	0.5739 (2)	0.3006 (13)	0.63934 (13)	0.0447 (14)
C23	0.5344 (2)	0.1034 (13)	0.63325 (13)	0.0450 (14)
C24	0.5269 (2)	0.0073 (12)	0.60347 (13)	0.0448 (14)
C25	0.4916 (2)	−0.1762 (14)	0.58424 (13)	0.0481 (14)
H25	0.466170	−0.274141	0.590511	0.058*
C26	0.4964 (3)	−0.2045 (14)	0.55608 (14)	0.0507 (15)
C27	0.5355 (3)	−0.0663 (15)	0.54646 (14)	0.0560 (16)
H27	0.538039	−0.097817	0.527223	0.067*
C28	0.5702 (3)	0.1147 (15)	0.56484 (15)	0.0571 (17)
H28	0.596072	0.208781	0.558524	0.069*
C29	0.5646 (2)	0.1500 (13)	0.59361 (13)	0.0459 (14)
C30	0.5924 (2)	0.4426 (14)	0.66678 (13)	0.0473 (14)
O31	0.57006 (18)	0.3832 (11)	0.68662 (10)	0.0601 (12)
C32	0.6364 (2)	0.6516 (13)	0.67412 (13)	0.0456 (14)
C33	0.6541 (3)	0.7459 (17)	0.70387 (15)	0.066 (2)
H33	0.637978	0.682757	0.718059	0.079*
C34	0.6958 (3)	0.9338 (17)	0.71181 (16)	0.069 (2)
H34	0.707602	0.996950	0.731405	0.082*
C35	0.7195 (2)	1.0266 (14)	0.69098 (15)	0.0523 (16)
C36	0.7020 (3)	0.9403 (15)	0.66182 (16)	0.0592 (17)
H36	0.717881	1.008713	0.647729	0.071*
C37	0.6611 (3)	0.7523 (14)	0.65349 (14)	0.0504 (15)
H37	0.649775	0.691805	0.633777	0.061*
Br38	0.77726 (3)	1.27828 (18)	0.70198 (2)	0.0785 (3)
O39	0.50813 (19)	0.0169 (11)	0.65218 (11)	0.0583 (12)
I40	0.43898 (2)	−0.44310 (11)	0.52517 (2)	0.06144 (16)
H39	0.521 (4)	0.109 (19)	0.6664 (11)	0.14 (5)*
H19	0.372 (4)	0.16 (2)	0.566 (2)	0.12 (4)*

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

	U^{11}	U^{22}	U^{33}	U^{12}	U^{13}	U^{23}
O1	0.063 (3)	0.050 (3)	0.040 (2)	−0.011 (2)	0.016 (2)	−0.0027 (19)
C2	0.050 (3)	0.047 (4)	0.035 (3)	0.001 (3)	0.012 (3)	0.002 (3)
C3	0.046 (3)	0.043 (3)	0.044 (3)	0.010 (3)	0.012 (3)	0.008 (3)
C4	0.047 (3)	0.040 (3)	0.038 (3)	0.008 (3)	0.008 (3)	0.003 (2)
C5	0.052 (4)	0.048 (4)	0.047 (3)	0.014 (3)	0.009 (3)	0.006 (3)
C6	0.050 (4)	0.045 (4)	0.052 (4)	0.003 (3)	0.000 (3)	−0.002 (3)
C7	0.063 (4)	0.053 (4)	0.064 (4)	−0.009 (3)	0.014 (4)	0.001 (3)
C8	0.075 (5)	0.055 (4)	0.051 (4)	−0.013 (4)	0.022 (3)	−0.004 (3)
C9	0.058 (4)	0.041 (4)	0.048 (3)	0.000 (3)	0.014 (3)	−0.001 (3)
C10	0.047 (3)	0.041 (3)	0.043 (3)	0.006 (3)	0.017 (3)	0.007 (3)
O11	0.060 (3)	0.063 (3)	0.047 (2)	−0.010 (2)	0.016 (2)	0.003 (2)
C12	0.041 (3)	0.039 (3)	0.050 (3)	−0.002 (3)	0.013 (3)	0.003 (3)
C13	0.058 (4)	0.059 (4)	0.055 (4)	−0.011 (3)	0.020 (3)	0.000 (3)
C14	0.061 (4)	0.058 (4)	0.054 (4)	−0.015 (3)	0.017 (3)	−0.006 (3)
C15	0.061 (4)	0.047 (4)	0.041 (3)	0.005 (3)	0.009 (3)	−0.001 (3)
C16	0.061 (4)	0.058 (4)	0.046 (3)	−0.009 (3)	0.021 (3)	0.000 (3)
C17	0.058 (4)	0.048 (4)	0.055 (4)	−0.010 (3)	0.017 (3)	0.000 (3)
Br18	0.0813 (5)	0.0782 (5)	0.0436 (4)	−0.0039 (4)	0.0122 (3)	−0.0089 (3)
O19	0.061 (3)	0.070 (3)	0.041 (2)	−0.005 (3)	0.016 (2)	−0.003 (2)
I20	0.0611 (3)	0.0597 (3)	0.0616 (3)	0.0046 (2)	−0.0096 (2)	−0.0056 (2)
O21	0.047 (2)	0.052 (3)	0.047 (2)	−0.009 (2)	0.0178 (19)	−0.005 (2)
C22	0.046 (3)	0.045 (4)	0.042 (3)	0.000 (3)	0.011 (3)	0.003 (3)
C23	0.044 (3)	0.047 (4)	0.046 (3)	0.001 (3)	0.016 (3)	0.008 (3)
C24	0.047 (3)	0.038 (3)	0.048 (3)	0.001 (3)	0.011 (3)	0.005 (3)
C25	0.045 (3)	0.049 (4)	0.047 (3)	−0.001 (3)	0.009 (3)	0.002 (3)
C26	0.050 (4)	0.045 (4)	0.050 (4)	0.001 (3)	0.003 (3)	−0.005 (3)
C27	0.061 (4)	0.063 (4)	0.045 (3)	−0.004 (3)	0.016 (3)	−0.006 (3)
C28	0.062 (4)	0.062 (4)	0.054 (4)	−0.009 (3)	0.025 (3)	−0.010 (3)
C29	0.047 (3)	0.044 (3)	0.047 (3)	−0.005 (3)	0.015 (3)	−0.003 (3)
C30	0.046 (3)	0.049 (4)	0.046 (3)	0.005 (3)	0.012 (3)	0.003 (3)
O31	0.065 (3)	0.072 (3)	0.046 (2)	−0.007 (2)	0.020 (2)	0.003 (2)
C32	0.044 (3)	0.042 (3)	0.048 (3)	0.003 (3)	0.008 (3)	−0.004 (3)
C33	0.079 (5)	0.076 (5)	0.045 (4)	−0.009 (4)	0.021 (4)	−0.015 (4)
C34	0.069 (5)	0.080 (5)	0.050 (4)	−0.005 (4)	0.006 (4)	−0.030 (4)
C35	0.044 (3)	0.049 (4)	0.061 (4)	0.006 (3)	0.011 (3)	−0.014 (3)
C36	0.059 (4)	0.055 (4)	0.068 (4)	−0.010 (3)	0.025 (4)	−0.010 (3)
C37	0.054 (4)	0.053 (4)	0.045 (3)	−0.004 (3)	0.016 (3)	−0.007 (3)
Br38	0.0571 (4)	0.0704 (5)	0.1037 (6)	−0.0097 (4)	0.0152 (4)	−0.0352 (5)
O39	0.066 (3)	0.060 (3)	0.051 (3)	−0.012 (2)	0.019 (2)	0.004 (2)
I40	0.0614 (3)	0.0613 (3)	0.0563 (3)	−0.0061 (2)	0.0073 (2)	−0.0138 (2)

Geometric parameters ($\text{\AA}$, $^\circ$)

O1—C2	1.410 (7)	O21—C22	1.409 (7)
O1—C9	1.360 (7)	O21—C29	1.369 (7)

C2—C3	1.370 (8)	C22—C23	1.373 (9)
C2—C10	1.427 (9)	C22—C30	1.410 (9)
C3—C4	1.427 (9)	C23—C24	1.423 (8)
C3—O19	1.339 (7)	C23—O39	1.330 (7)
C4—C5	1.400 (9)	C24—C25	1.404 (9)
C4—C9	1.402 (8)	C24—C29	1.385 (8)
C5—H5	0.9300	C25—H25	0.9300
C5—C6	1.383 (9)	C25—C26	1.360 (9)
C6—C7	1.412 (10)	C26—C27	1.399 (9)
C6—I20	2.111 (6)	C26—I40	2.112 (6)
C7—H7	0.9300	C27—H27	0.9300
C7—C8	1.383 (9)	C27—C28	1.373 (9)
C8—H8	0.9300	C28—H28	0.9300
C8—C9	1.379 (9)	C28—C29	1.400 (9)
C10—O11	1.258 (7)	C30—O31	1.260 (7)
C10—C12	1.481 (8)	C30—C32	1.495 (9)
C12—C13	1.379 (9)	C32—C33	1.409 (9)
C12—C17	1.410 (8)	C32—C37	1.388 (9)
C13—H13	0.9300	C33—H33	0.9300
C13—C14	1.395 (9)	C33—C34	1.388 (11)
C14—H14	0.9300	C34—H34	0.9300
C14—C15	1.383 (9)	C34—C35	1.367 (10)
C15—C16	1.378 (9)	C35—C36	1.372 (9)
C15—Br18	1.894 (6)	C35—Br38	1.897 (7)
C16—H16	0.9300	C36—H36	0.9300
C16—C17	1.375 (9)	C36—C37	1.376 (9)
C17—H17	0.9300	C37—H37	0.9300
O19—H19	0.78 (11)	O39—H39	0.79 (2)
C9—O1—C2	106.3 (4)	C29—O21—C22	104.6 (4)
O1—C2—C10	125.0 (5)	O21—C22—C30	125.5 (5)
C3—C2—O1	109.0 (5)	C23—C22—O21	109.7 (5)
C3—C2—C10	126.0 (6)	C23—C22—C30	124.7 (6)
C2—C3—C4	108.6 (5)	C22—C23—C24	108.4 (5)
O19—C3—C2	126.4 (6)	O39—C23—C22	125.5 (6)
O19—C3—C4	125.1 (6)	O39—C23—C24	126.1 (6)
C5—C4—C3	135.9 (6)	C25—C24—C23	135.4 (6)
C5—C4—C9	119.5 (6)	C29—C24—C23	104.3 (5)
C9—C4—C3	104.6 (5)	C29—C24—C25	120.3 (6)
C4—C5—H5	121.2	C24—C25—H25	121.4
C6—C5—C4	117.5 (6)	C26—C25—C24	117.2 (6)
C6—C5—H5	121.2	C26—C25—H25	121.4
C5—C6—C7	121.8 (6)	C25—C26—C27	122.4 (6)
C5—C6—I20	119.4 (5)	C25—C26—I40	118.2 (5)
C7—C6—I20	118.9 (5)	C27—C26—I40	119.3 (5)
C6—C7—H7	119.5	C26—C27—H27	119.3
C8—C7—C6	121.1 (7)	C28—C27—C26	121.4 (6)
C8—C7—H7	119.5	C28—C27—H27	119.3

C7—C8—H8	121.7	C27—C28—H28	121.8
C9—C8—C7	116.6 (6)	C27—C28—C29	116.3 (6)
C9—C8—H8	121.7	C29—C28—H28	121.8
O1—C9—C4	111.5 (5)	O21—C29—C24	113.1 (5)
O1—C9—C8	124.9 (6)	O21—C29—C28	124.5 (6)
C8—C9—C4	123.6 (6)	C24—C29—C28	122.4 (6)
C2—C10—C12	125.0 (5)	C22—C30—C32	125.5 (6)
O11—C10—C2	115.7 (5)	O31—C30—C22	116.2 (6)
O11—C10—C12	119.3 (6)	O31—C30—C32	118.3 (6)
C13—C12—C10	118.4 (5)	C33—C32—C30	117.6 (6)
C13—C12—C17	117.7 (6)	C37—C32—C30	123.7 (5)
C17—C12—C10	123.8 (6)	C37—C32—C33	118.7 (6)
C12—C13—H13	119.0	C32—C33—H33	120.3
C12—C13—C14	122.0 (6)	C34—C33—C32	119.4 (7)
C14—C13—H13	119.0	C34—C33—H33	120.3
C13—C14—H14	120.9	C33—C34—H34	119.8
C15—C14—C13	118.3 (6)	C35—C34—C33	120.3 (6)
C15—C14—H14	120.9	C35—C34—H34	119.8
C14—C15—Br18	119.6 (5)	C34—C35—C36	120.8 (6)
C16—C15—C14	121.4 (6)	C34—C35—Br38	120.3 (5)
C16—C15—Br18	118.9 (5)	C36—C35—Br38	118.8 (5)
C15—C16—H16	120.3	C35—C36—H36	120.1
C17—C16—C15	119.4 (6)	C35—C36—C37	119.9 (7)
C17—C16—H16	120.3	C37—C36—H36	120.1
C12—C17—H17	119.4	C32—C37—H37	119.6
C16—C17—C12	121.1 (6)	C36—C37—C32	120.8 (6)
C16—C17—H17	119.4	C36—C37—H37	119.6
C3—O19—H19	104 (8)	C23—O39—H39	101 (4)
O1—C2—C3—C4	−0.3 (7)	O21—C22—C23—C24	−2.1 (7)
O1—C2—C3—O19	178.9 (6)	O21—C22—C23—O39	177.5 (6)
O1—C2—C10—O11	−178.5 (5)	O21—C22—C30—O31	−178.4 (6)
O1—C2—C10—C12	2.8 (10)	O21—C22—C30—C32	0.7 (10)
C2—O1—C9—C4	0.5 (7)	C22—O21—C29—C24	0.0 (7)
C2—O1—C9—C8	−179.4 (6)	C22—O21—C29—C28	178.5 (6)
C2—C3—C4—C5	178.4 (7)	C22—C23—C24—C25	−175.9 (7)
C2—C3—C4—C9	0.6 (7)	C22—C23—C24—C29	2.0 (7)
C2—C10—C12—C13	179.0 (6)	C22—C30—C32—C33	−172.1 (6)
C2—C10—C12—C17	−1.4 (10)	C22—C30—C32—C37	6.6 (10)
C3—C2—C10—O11	−1.4 (9)	C23—C22—C30—O31	−1.0 (9)
C3—C2—C10—C12	179.9 (6)	C23—C22—C30—C32	178.1 (6)
C3—C4—C5—C6	−177.0 (6)	C23—C24—C25—C26	177.4 (7)
C3—C4—C9—O1	−0.7 (7)	C23—C24—C29—O21	−1.2 (7)
C3—C4—C9—C8	179.2 (6)	C23—C24—C29—C28	−179.8 (6)
C4—C5—C6—C7	−1.4 (9)	C24—C25—C26—C27	2.1 (10)
C4—C5—C6—I20	177.3 (4)	C24—C25—C26—I40	−173.4 (4)
C5—C4—C9—O1	−178.9 (5)	C25—C24—C29—O21	177.1 (5)
C5—C4—C9—C8	1.0 (10)	C25—C24—C29—C28	−1.5 (10)

C5—C6—C7—C8	0.6 (11)	C25—C26—C27—C28	−2.5 (11)
C6—C7—C8—C9	0.9 (11)	C26—C27—C28—C29	0.7 (10)
C7—C8—C9—O1	178.2 (6)	C27—C28—C29—O21	−177.1 (6)
C7—C8—C9—C4	−1.7 (11)	C27—C28—C29—C24	1.2 (10)
C9—O1—C2—C3	−0.1 (7)	C29—O21—C22—C23	1.3 (6)
C9—O1—C2—C10	177.4 (6)	C29—O21—C22—C30	179.0 (6)
C9—C4—C5—C6	0.6 (9)	C29—C24—C25—C26	−0.2 (9)
C10—C2—C3—C4	−177.8 (6)	C30—C22—C23—C24	−179.8 (6)
C10—C2—C3—O19	1.4 (10)	C30—C22—C23—O39	−0.2 (10)
C10—C12—C13—C14	−178.6 (6)	C30—C32—C33—C34	178.2 (7)
C10—C12—C17—C16	−179.9 (6)	C30—C32—C37—C36	−178.7 (6)
O11—C10—C12—C13	0.4 (9)	O31—C30—C32—C33	7.0 (9)
O11—C10—C12—C17	179.9 (6)	O31—C30—C32—C37	−174.3 (6)
C12—C13—C14—C15	−3.2 (11)	C32—C33—C34—C35	0.0 (12)
C13—C12—C17—C16	−0.3 (10)	C33—C32—C37—C36	0.0 (10)
C13—C14—C15—C16	3.1 (11)	C33—C34—C35—C36	1.2 (11)
C13—C14—C15—Br18	−175.1 (5)	C33—C34—C35—Br38	−178.9 (6)
C14—C15—C16—C17	−1.7 (10)	C34—C35—C36—C37	−1.7 (11)
C15—C16—C17—C12	0.3 (10)	C35—C36—C37—C32	1.1 (11)
C17—C12—C13—C14	1.8 (10)	C37—C32—C33—C34	−0.6 (11)
Br18—C15—C16—C17	176.5 (5)	Br38—C35—C36—C37	178.3 (5)
O19—C3—C4—C5	−0.8 (11)	O39—C23—C24—C25	4.5 (12)
O19—C3—C4—C9	−178.6 (6)	O39—C23—C24—C29	−177.6 (6)
I20—C6—C7—C8	−178.1 (6)	I40—C26—C27—C28	173.0 (5)

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>
O19—H19 $\cdots$ O11	0.76 (10)	2.05 (9)	2.680 (7)	140 (9)
C17—H17 $\cdots$ O1	0.93	2.24	2.919 (8)	129
O39—H39 $\cdots$ O31	0.79 (7)	1.90 (9)	2.617 (7)	151
C37—H37 $\cdots$ O21	0.93	2.28	2.950 (8)	128
C13—H13 $\cdots$ O39 ⁱ	0.93	2.50	3.231 (9)	135

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