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Synthesis and Transformation of 5-Acetyl-2-aryl-6-hydroxybenzofurans into Furanoflavanone Derivatives

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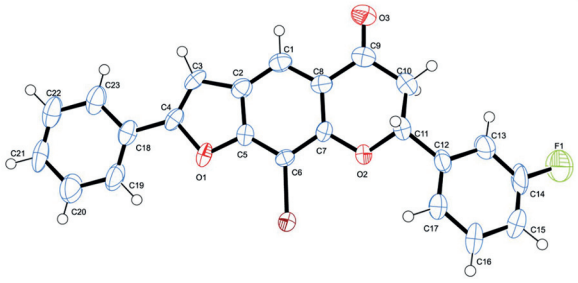

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Abstract Tandem palladium-catalyzed Sonogashira cross-coupling and heteroannulation of 3-bromo-2,4-dihydroxy-5-iodoacetophenone with arylacetylenes followed by the base-mediated Claisen–Schmidt aldol condensation of the intermediate 5-acetyl-2-aryl-7-bromo-6-hydroxybenzofurans with benzaldehyde derivatives afforded the corresponding linear 2-arylbenzofuranchalcone hybrids. The presence of the *o*-hydroxy-*trans*-α,β-unsaturated carbonyl moiety in the prepared furanochalcone hybrids facilitated acid-mediated cycloisomerization into the corresponding linear furanoflavanones. The structures of the prepared compounds were confirmed using a combination of spectrometric techniques complemented with single crystal XRD analysis.

Keywords 3-bromo-2,4-dihydroxy-5-iodoacetophenone, Sonogashira cross-coupling, furanochalcones, furanoflavanones, X-ray

Although 2-phenylbenzofuran derivatives are widely distributed in plants and constitute basic structure of neolignans,[2] majority of the naturally occurring linear and angular furanoflavanoids lack an aryl substituent on the C-2 position of the five-membered ring.[3] Cissampeloflavone (**1a**) and ridiculuflavonylchalcone B (**1b**) shown in Figure 1 represent the first examples of furanoflavonoids substituted with an aryl group at C-2 position of ring D.[4] These 2,3-dicarbo-substituted furanoflavanoids were first isolated from a Venezuelan plant *Cissampelos pareira* and Brazilian plant *Aristolochia ridicula*, respectively, along with the analogous 6-aryl-8*H*-furo[2,3-*g*]chromen-8-one derivatives.[5–7] The most commonly used approach towards linear[8–10] and angular benzofuran-appended chalcone hybrids[11,12] and their corresponding furanoflavanones,[9,12] furanoflavones,[11] and furanoflavonol derivatives[8,13] involves the use of the *o*-hydroxy acetylbenzofurans as the key intermediates for the syntheses.[14,15] However, the methodology is limited to the synthesis of C-2 unsubstituted or 3-carbo-substituted derivatives. Conventional methods for the synthesis of *o*-hydroxy acetylbenzofurans involve multiple steps that result in reduced yields or mixtures of the isomeric 5-acetyl-4-hydroxybenzofuran and 5-acetyl-6-hydroxybenzofuran derivatives.[16]

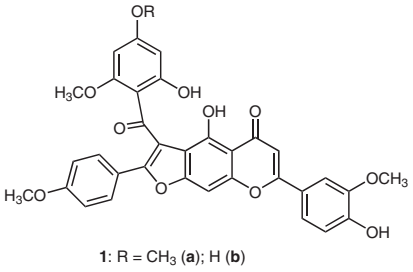

Figure 1 Structures of cissampeloflavone (**1a**) and ridiculuflavonylchalcone B (**1b**), respectively

The first total synthesis of analogues of cissampeloflavone (**1a**) was reported recently and it involved C-3 benzoylation of 2-(4-methoxyphenyl)-5*H*-furo[3,2-*g*]chromen-5-one **3**, prepared in turn, in 45% yield via palladium chloride-catalyzed intramolecular C–H cyclization of 7-{[2-bromo-1-(4-methoxyphenyl)vinyl]oxy}-5-hydroxy-4*H*-chromen-4-one **2** as shown in Scheme 1.[17] *ortho*-Halogenated phenols constitute important scaffolds for transition-metal-catalyzed carbon–carbon and/or carbon–heteroatom bond formation to afford either linear or angular benzofuran derivatives, exclusively.[18–28] Among the cross-coupling reactions, tandem palladium-catalyzed Sonogashira cross-coupling of

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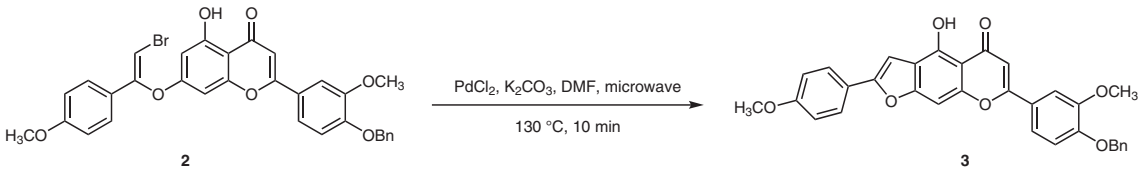
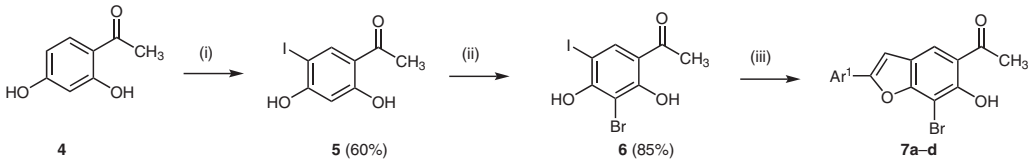


Scheme 1 Synthesis of 2-(4-methoxyphenyl)-5*H*-furo[3,2-*g*]chromen-5-one derivative **3**

o-halogenophenols with terminal acetylenes and subsequent cycloisomerization of the intermediate alkynylated derivative represents the most convenient and efficient method for the construction of linear or angular 2-arylbenzofurans in the presence[22,24] or absence[24–28] of the protective groups. We have initiated a research program to exploit this valuable methodology for the synthesis of polycyclic flavonoid derivatives.

In continuation with our research on the reactivity of mixed dihalogenated *o*-hydroxyacetophenones,[27,28] we decided to prepare 3-bromo-2,4-dihydroxy-5-iodoacetophenone for use as a scaffold for tandem Sonogashira cross-coupling with arylacetylenes. The main aim was to employ the resultant *o*-hydroxy acetylbenzofurans as scaffolds for sequential Claisen–Schmidt aldol condensation and cycloisomerization or oxidative cyclization of the intermediate furanochalcones to append a six-membered heterocyclic moiety onto the benzofuran moiety.

Literature search revealed several reagents for the iodination of 2,4-dihydroxyacetophenone, which include the use of iodine monochloride in acetic acid at room temperature,[22] 2 equivalents of pyridinium iodochloride in methanol under reflux,[25] or I_2/HIO_3 mixture in aqueous ethanol under reflux for 5 minutes[26,27] to afford 2,4-dihydroxy-3,5-diiodoacetophenone. Sodium iodide/potassium iodate (NaI/KIO_3) mixture in acetic acid at room temperature, on the other hand, afforded a mixture of 2,4-dihydroxy-3-iodoacetophenone and 2,4-dihydroxy-3,5-diiodoacetophenone in 74% and 7% yield, respectively.[21] 2,4-Dihydroxy-3-iodoacetophenone, was isolated in 98% directly from the reaction of 2,4-dihydroxyacetophenone with iodine and potassium iodate mixture in aqueous ethanol.[29] The isomeric 5-iodo-substituted derivative was only accessible from the 2,4-bis(methoxymethoxy)acetophenone with 1.2 equivalents of *N*-iodosuccinamide (NIS) in dimethylformamide (DMF) at 50 °C.[29,30] We required the 3-bromo-2,4-dihydroxy-5-iodoacetophenone as a precursor for the site-selective Sonogashira cross-coupling with terminal acetylenes to afford the 5-acetyl-2-aryl-7-bromo-6-hydroxybenzofurans without the need for protection of the hydroxyl group(s). Protection of the phenolic functionality was found to be essential to achieve good yields of the benzofuran derivatives in the case of Sonogashira cross-coupling reactions of mono- or diiodinated resorcinol or 2,4-dihydroxyacetophenone.[31] Attempted C-5 iodination of 2,4-dihydroxyacetophenone (**4**) with NIS in DMF or acetonitrile at room temperature afforded in our hands 2,4-dihydroxy-3,5-diiodoacetophenone (90%) as the sole product. Treatment of **4** with NIS (1 equiv) in acetic acid at room temperature for 18 hours followed by aqueous workup and purification by silica gel column chromatography afforded two products in sequence characterized using NMR and IR spectroscopy as 2,4-dihydroxy-5-iodoacetophenone (**5**, 40%) and 2,4-dihydroxy-3,5-diiodoacetophenone (**5′**, 30%). We then opted for the use of 1.0 equivalent of *p*-toluenesulfonic acid (*p*-TsOH) as an additive to a mixture of **4** and NIS (1 equiv) in acetonitrile at room temperature. To our delight, we isolated after 14 hours by silica gel column chromatography compound **5** as the major product (60%) along with the 2,4-dihydroxy-3,5-diiodoacetophenone as the minor product (15%). The ^{1}H NMR spectrum of 2,4-dihydroxy-5-iodoacetophenone (**5**) revealed the presence of a set of singlets in the aromatic region at δ = 6.41 and 8.14 corresponding to H-3 and H-6, respectively. These signals distinguished this compound from the isomeric 3-iodo- or the 2,4-dihydroxy-3,5-diiodoacetophenone, which were the main products formed when using other iodinating agents.[21,23,25,32,33] 2,4-Dihydroxy-5-iodoacetophenone (**5**) was, in turn, treated with 1.0 equivalent of *N*-bromosuccinimide (NBS) in acetic acid at room temperature for 30 minutes to afford 3-bromo-2,4-dihydroxy-5-iodoacetophenone (**6**) in 85% yield. The ^{1}H NMR spectrum of this mixed 3,5-dihalogenated 2,4-dihydroxyacetophenone revealed the presence of a singlet in the aromatic region at δ = 8.25, which corresponds to H-6. We took advantage of the ease of Csp^2–I bond to undergo transition-metal-catalyzed cross-coupling in the presence of other halogen atoms[33] and subjected compound **6** to the Sonogashira cross-coupling reaction conditions. The use of tetrakis(triphenylphosphine)palldium(0) [$Pd(PPh_3)_4$] as source of active Pd(0) catalyst in the presence of CuI as co-catalyst and cesium carbonate as a base in THF or DMF at room temperature led to recovery of the substrate. The more active dichlorobis(triphenylphosphine)palladium(II) [$PdCl_2(PPh_3)_2$] was then used as the source of active Pd(0) catalyst in the presence of copper iodide (CuI) as co-catalyst and cesium carbonate as a base in 4:1 DMF/water (Scheme 2). The reaction was found to be slow at room temperature, but to be complete within 1 hour at 50 °C to afford upon silica gel column chromatography in sequence traces of the dimer and the cross-coupled product. The ^{1}H NMR spectra of the cross-coupled products revealed the presence of increased num-



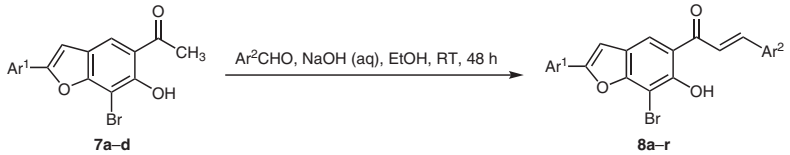
Scheme 2 Sequential halogenation of **4** into **6** followed by alkynylation–heteroannulation into **7a–d** [Ar^1 = C_6H_5 (**7a**), 3-FC_6H_4 (**7b**), 4-FC_6H_4 (**7c**), and 4-$CH_3OC_6H_4$ (**7d**)]. *Reagents and conditions*: (i) NIS, *p*-TsOH, RT, CH_3CN, 14 h; (ii) NBS, AcOH, RT, 3 h; (iii) $Ar^1C{\equiv}CH$, $PdCl_2(PPh_3)_2$, Cs_2CO_3, aq DMF, 50 °C, 1 h.

ber of proton signals in the aromatic region and a singlet around δ = 13.20 corresponding to the hydroxyl proton. Their ^{13}C NMR spectra revealed the absence of the Csp^2–I signal around δ = 75.2 and the absence of two singlets in the region δ = 80–100 typical for the acetylene moiety, thus ruling out the structure of the alkynyl isomer. Moreover, their high-resolution mass spectra revealed the presence of the ^{79}Br and ^{81}Br containing molecular ions in the ratio 1:1 thus confirming carbon–carbon bond formation through the weak Csp^2–I bond. A combination of these spectroscopic data corroborated the structures of the cross-coupled products as the 5-acetyl-2-aryl-7-bromo-6-hydroxybenzofurans **7a–d** (Scheme 2). The presence of a lipophilic bromine atom on the fused benzo ring of a benzofuran moiety has been found to impart significant biological activity for the 2-carbo-substituted arylbenzofuran derivatives.[34]

The benzofuran derivatives **7a–d** contain the acetyl moiety, which could facilitate Claisen–Schmidt aldol condensation to afford chalcone derivatives substituted with a hydroxyl group *ortho* to the *trans*-α,β-unsaturated carbonyl framework. Surprisingly, examples of such benzofuran-chalcone hybrids are less documented in the literature.[9,10] Compounds **7a–d** were, in turn, subjected to Claisen–Schmidt aldol condensation with benzaldehyde derivatives in the presence of aqueous 30% NaOH in ethanol at room temperature for 48 hours to afford after aqueous workup and silica gel column chromatography, the corresponding 2-arylbenzofuran-appended chalcones **8a–r** in appreciable yields (Scheme 3, Table 1). The *E*-geometry around the vinylic framework of these chalcones was confirmed by the typical set of doublets around δ = 7.60 and 7.90 with coupling constant values J_{trans} = 15.3–15.5 Hz, which correspond to the α-H and β-H, respectively. Moreover, single crystal X-ray diffraction (XRD) analysis of compound **8e** distinctly confirmed their structure and the *E*-geometry around the olefinic framework (Figure 2).[35] In the context of the X-ray analyses, crystallographic numbering has been used in place of the systematic numbering. There is intramolecular hydrogen bonding between the oxygen acceptor (O1) and the α-hydrogen bond donor [d(O(2)–H(2)·O(3) = 1.74 Å].

Table 1 Substitution Pattern and Percentage Yields of the Furanochalcones **8a–r**

Ar^1	Ar^2	Yield (%)
C_6H_5	C_6H_5	87 (**8a**)
3-FC_6H_4	C_6H_5	88 (**8b**)
4-FC_6H_4	C_6H_5	88 (**8c**)
4-$CH_3OC_6H_4$	C_6H_5	84 (**8d**)
C_6H_5	3-FC_6H_4	91 (**8e**)
3-FC_6H_4	3-FC_6H_4	92 (**8f**)
4-FC_6H_4	3-FC_6H_4	92 (**8g**)
C_6H_5	4-FC_6H_4	87 (**8h**)
3-FC_6H_4	4-FC_6H_4	92 (**8i**)
4-FC_6H_4	4-FC_6H_4	92 (**8j**)
4-$CH_3OC_6H_4$	4-FC_6H_4	81 (**8k**)
C_6H_5	4-ClC_6H_4	95 (**8l**)
4-FC_6H_4	4-ClC_6H_4	89 (**8m**)
4-$CH_3OC_6H_4$	4-ClC_6H_4	86 (**8n**)
C_6H_5	4-$CH_3OC_6H_4$	88 (**8o**)
3-FC_6H_4	4-$CH_3OC_6H_4$	93 (**8p**)
4-FC_6H_4	4-$CH_3OC_6H_4$	82 (**8q**)
4-$CH_3OC_6H_4$	4-$CH_3OC_6H_4$	86 (**8r**)



Scheme 3 Synthesis of furanochalcones **8a–r**

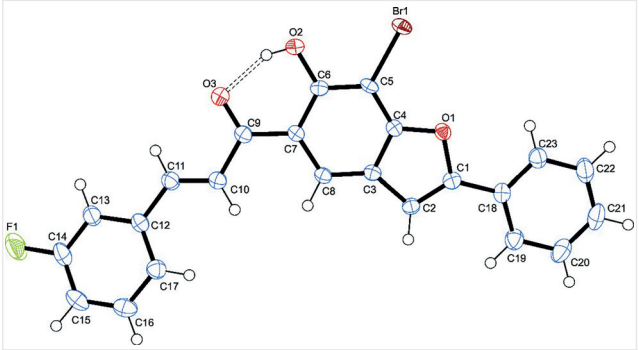
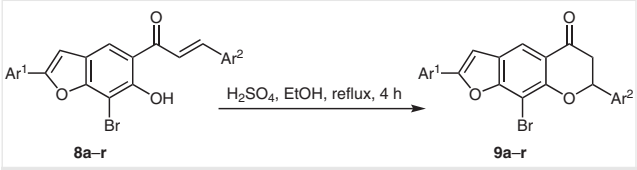


Figure 2 Oak Ridge Thermal Ellipsoid Plot (ORTEP) diagram (50% probability level) of **8e**; for clarity, hydrogen atoms are omitted

Very few examples of the naturally occurring furanoflavanoid derivatives substituted at the C-2 position of the benzofuran moiety with carbon-based substituent have been reported in the literature[36–39] and their synthesis remain surprisingly less explored.[4,18,39,40] The *o*-hydroxy-*trans*-α,β-unsaturated carbonyl moiety represents suitable scaffold for possible cycloisomerization or oxidative cyclization to afford analogues of the naturally occurring furanoflavanones, furanoflavones, furanoisoflavones, and furanoflavonols. We took advantage of the proximity of the nucleophilic hydroxyl group to the *trans*-α,β-unsaturated carbonyl moiety in compounds **8a–r** to effect cycloisomerization to append a six-membered heterocyclic ring onto the benzofuran scaffold. Compound **8a** was subjected to standard cycloisomerization conditions, which involved the use of sulfuric acid in ethanol under reflux for 4 hours to afford upon aqueous workup and purification by silica gel column chromatography a product characterized using a combination of NMR and IR spectroscopic techniques as the furanoflavanone **9a** in 50% yield (Scheme 4, Table 2). These reaction conditions were extended to furanochalcones **8b–r** to afford novel furanoflavanones **9b–r**. The ^{1}H NMR spectral data of compounds **9a–r** are distinguished from those of the corresponding chalcone precursors by the absence of a set of doublets corresponding to the olefinic proton signals and the presence in the aliphatic region of two sets of doublet of doublets (dd) for the diastereotopic methylene protons around δ = 3.01 and 3.20 as well as the methine proton signal around δ = 5.60. In all cases, the methine proton exhibits significantly different vicinal H–H coupling constants, J_{vic} = 3.40–4.50 Hz and J_{vic} = 11.00–12.00 Hz, which indicates that different torsion angles exist between this proton and each of the methylene protons. This observation would require the methine proton (7-H_X) to be *gauche* to one of the methylene protons (6-H_a) with J_{vic} = 3.40–4.50 Hz (vicinal axial equatorial coupling constant) and *anti* to the other (6-H_b) with J_{vic} = 11.00–12.00 Hz (vicinal diaxial coupling constant) in a quasi-chair conformation of the flavanone ring with phenyl substituent in equatorial positions. The coupling constant values of C(7)H proton, J = 3.2 Hz and 12.4 Hz (vicinal diaxial coupling) indicated it to be axial in the quasi chair conformation of the flavanone ring, with the phenyl substituent (Ar^2) in equatorial position. This quasi-chair conformation is, in fact, evident in the single crystal X-ray diffraction structure of furanoflavanone **9e** shown in Figure 3.[41]



Scheme 4 Cycloisomerization of *o*-hydroxyfuranochalcones **8a–r** into furanoflavanones **9a–r**

Table 2 Substitution Pattern and Percentage Yields of the Furanoflavanones **9a–r**

Ar^1	Ar^2	Yield (%)
C_6H_5	C_6H_5	50 (**9a**)
3-FC_6H_4	C_6H_5	60 (**9b**)
4-FC_6H_4	C_6H_5	55 (**9c**)
4-$CH_3OC_6H_4$	C_6H_5	60 (**9d**)
C_6H_5	3-FC_6H_4	55 (**9e**)
3-FC_6H_4	3-FC_6H_4	50 (**9f**)
4-FC_6H_4	3-FC_6H_4	55 (**9g**)
C_6H_5	4-FC_6H_4	60 (**9h**)
3-FC_6H_4	4-FC_6H_4	50 (**9i**)
4-FC_6H_4	4-FC_6H_4	70 (**9j**)
4-$CH_3OC_6H_4$	4-FC_6H_4	60 (**9k**)
C_6H_5	4-ClC_6H_4	50 (**9l**)
4-FC_6H_4	4-ClC_6H_4	50 (**9m**)
4-$CH_3OC_6H_4$	4-ClC_6H_4	60 (**9n**)
C_6H_5	4-$CH_3OC_6H_4$	55 (**9o**)
3-FC_6H_4	4-$CH_3OC_6H_4$	60 (**9p**)
4-FC_6H_4	4-$CH_3OC_6H_4$	60 (**9q**)
4-$CH_3OC_6H_4$	4-$CH_3OC_6H_4$	60 (**9r**)

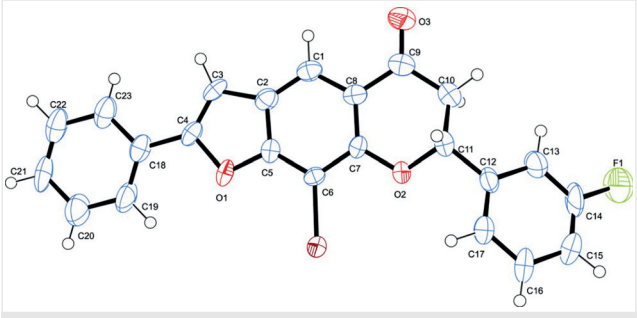


Figure 3 ORTEP diagram (50% probability level) of **9e**; for clarity, hydrogen atoms are omitted

In summary, 3-bromo-2,4-dihydroxy-5-iodoacetophenone (**6**) undergoes tandem palladium-catalyzed Sonogashira cross-coupling–heteroannulation to afford *o*-hydroxy acetylbenzofurans **7**. The reaction is high yielding without the need for protection of the phenolic functionality, an essential step in the case of Sonogashira cross-coupling reactions of mono- or diiodinated resorcinol or the 2,4-dihydroxyacetophenone.[31] Claisen–Schmidt aldol condensation of the *o*-hydroxy acetylbenzofurans **7** with benzaldehyde derivatives afforded novel benzofuran–chalcone hybrids **8** appended with a *trans*-α,β-unsaturated carbonyl moiety adjacent the hydroxyl group. The presence of the *o*-hydroxy-*trans*-α,β-unsaturated carbonyl moiety in the prepared furanochalcone hybrids **8** facilitated annulation of the six-membered heterocyclic ring onto the benzofuran framework to afford the 2-aryl-substituted furanoflavanones **9** in moderate to high yields. Efforts are currently underway in the laboratory to employ this strategy towards the synthesis of analogues of the naturally occurring cissampeloflavone (**1a**).

Melting points were recorded on a Thermocouple digital melting point apparatus and are uncorrected. IR spectra were recorded as powders using a Bruker VERTEX 70 FT-IR spectrophotometer (Bruker Optics, Billerica, MA, USA) with a diamond ATR (attenuated total reflectance) accessory by using the thin-film method. Merck Kieselgel 60 (0.063–0.200 mm) (Merck KGaA, Frankfurt, Germany) was used as stationary phase for column chromatography. NMR spectra were obtained as $CDCl_3$ or DMSO-d_6 solutions using Varian 300 MHz NMR spectrometer (Varian Inc., Palo Alto, CA, USA) or 500 MHz NMR spectrometers (Agilent Technologies, Oxford, UK) and the chemical shifts are quoted relative to the TMS peak. High-resolution mass spectra (ESMS) were recorded using Waters Synapt G2 Quadrupole Time-of-flight mass spectrometer (Waters Corp., Milford, MA, USA) at the University of Stellenbosch Central Analytical Facility (CAF).

Iodination of 2,4-Dihydroxyacetophenone (4)

A stirred solution of **4** (2.00 g, 13.1 mmol) in CH_3CN (20 mL) was treated with *p*-TsOH·H_2O (2.50 g, 13.1 mmol) at 0 °C and after 5 min, NIS (2.96 g, 13.1 mmol) was added. The reaction mixture was allowed to warm up to RT and stirred at this temperature for 14 h. The mixture was quenched with an ice-cold aq $Na_2S_2O_3$ solution. The resulting precipitate was filtered and purified by silica gel column chromatography with 9:1 toluene/$CHCl_3$ mixture (v/v) as an eluent to afford 1-(2,4-dihydroxy-5-iodophenyl)ethanone (**5**) and 1-(2,4-dihydroxy-3,5-diiodophenyl)ethanone (**5′**) in sequence.

1-(2,4-Dihydroxy-5-iodophenyl)ethanone (5)

White solid; yield: 2.19 g (60%); mp 184–186 °C.

IR (ATR): 889, 1190, 1223, 1314, 1579, 1614, 1634, 3263 cm^{-1}.

^1H NMR (300 MHz, DMSO-d_6): δ = 2.54 (3 H, s, CH_3), 6.41 (1 H, s, H-3), 8.14 (1 H, s, H-6), 11.50 (1 H, s, 4-OH), 12.36 (1 H, s, 2-OH).

^{13}C NMR (75 MHz, DMSO-d_6): δ = 27.3, 74.0, 102.5, 115.9, 142.1, 163.5, 163.9, 202.1.

HRMS (ES^-): *m*/*z* [M – H]$^-$ calcd for $C_8H_6IO_3$: 276.9362; found: 276.9351.

1-(2,4-Dihydroxy-3,5-diiodophenyl)ethanone (5′)

Yellow solid; yield: 0.80 g (15%); mp 173–175 °C (Lit.[42] mp 177 °C).

IR (ATR): 677, 730, 796, 1037, 1076, 1142, 1253, 1281, 1319, 1349, 1362, 1404, 1453, 1613 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 2.60 (3 H, s, CH_3), 6.42 (1 H, br s, 4-OH), 8.07 (1 H, s, H-6), 13.59 (1 H, s, 2-OH).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 26.2, 69.1, 75.5, 116.2, 141.0, 159.7, 163.5, 201.4.

1-(3-Bromo-2,4-dihydroxy-5-iodophenyl)ethanone (6)

A stirred solution of **5** (1.00 g, 3.60 mmol) in AcOH (25 mL) was treated with NBS (0.64 g, 3.60 mmol) and left to stir at RT for 30 min. The mixture was then poured into ice-cold H_2O and the resulting precipitate was filtered and washed with H_2O to afford **6** as a pale yellow solid; yield: 1.09 g (85%); mp 171–173 °C (EtOH).

IR (ATR): 795, 1044, 1149, 1256, 1285, 1411, 1621, 3252 cm^{-1}.

^1H NMR (300 MHz, DMSO-d_6): δ = 2.61 (3 H, s, CH_3), 8.25 (1 H, s, 6-H), 11.06 (1 H, br s, 4-OH), 13.38 (1 H, br s, 2-OH).

^{13}C NMR (75 MHz, DMSO-d_6): δ = 26.9, 75.2, 98.3, 115.9, 140.6, 159.8, 160.7, 203.3.

HRMS (ES^-): *m*/*z* [M – H]$^-$ calcd for $C_8H_5{}^{79}BrIO_3$: 354.8467; found: 354.8470.

Tandem Sonogashira Cross-Coupling and Heteroannulation of 6; General Procedure

A mixture of **6** (0.50 g, 1.40 mmol), $PdCl_2(PPh_3)_2$ (0.05 g, 0.07 mmol), CuI (0.03 g, 0.14 mmol), Cs_2CO_3 (0.55 g, 1.68 mmol) in 4:1 DMF/H_2O (v/v, 20 mL) was placed in a two-necked round-bottomed flask equipped with a condenser and a rubber septum. The mixture was flushed with argon for 30 min and a solution of the required phenylacetylene derivative (1.2 equiv) in DMF (2 mL) was introduced by means of a syringe via a rubber septum. A balloon filled with argon was connected at the top of the condenser and the mixture was left to stir at 50 °C for 1 h. The mixture was allowed to cool, poured into crushed ice, and the product was extracted with $CHCl_3$. The combined organic phases were dried (anhyd $MgSO_4$) and filtered. The solvent was evaporated under reduced pressure on a rotary evaporator and the residue was purified by silica gel column chromatography with 4:1 hexane/EtOAc (v/v) as an eluent to afford the desired product **7**.

1-[7-Bromo-6-hydroxy-2-phenylbenzofuran-5-yl]ethanone (7a)

Yellow solid; yield: 0.28 g (60%); mp 162–164 °C.

IR (ATR): 758, 1061, 1153, 1243, 1330, 1368, 1415, 1638 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 2.72 (3 H, s, CH_3), 7.00 (1 H, s, H-3), 7.38–7.49 (3 H, m, H-4′ and H-3′,5′), 7.84 (2 H, dd, *J* = 1.2, 8.3 Hz, H-2′,6′), 7. 92 (1 H, s, H-4), 13.21 (1 H, br s, OH).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 26.9, 93.0, 101.3, 117.4, 121.9, 122.2, 124.9, 128.9, 129.1, 129.2, 156.8, 157.3, 157.6, 203.9.

HRMS (ES^-): *m*/*z* [M – H]$^-$ calcd for $C_{16}H_{10}{}^{79}BrO_3$: 328.9814; found: 328.9821.

1-[7-Bromo-2-(3-fluorophenyl)-6-hydroxybenzofuran-5-yl]ethanone (7b)

Yellow solid; yield: 0.32 g (66%); mp 189–191 °C.

IR (ATR): 776, 861, 1056, 1177, 1218, 1364, 1417, 1483, 1577, 1608, 1643 cm^{-1}.

^{1}H NMR (500 MHz, DMSO-d_6): δ = 2.74 (3 H, s, CH_3), 7.24 (1 H, t, J = 8.0 Hz, H-4′), 7.52–7.56 (2 H, m, H-3 and H-6′), 7.64–7.69 (2 H, m, H-2′,3′), 8.28 (1 H, s, H-4), 13.13 (1 H, br s, OH).

^{13}C NMR (125 MHz, DMSO-d_6): δ = 27.5, 92.0, 104.5, 111.6 (d, $^2J_{C,F}$ = 23.8 Hz), 116.3 (d, $^2J_{C,F}$ = 21.2 Hz), 118.1, 121.0 (d, $^4J_{C,F}$ = 2.7 Hz), 121.8, 124.9, 131.4 (d, $^3J_{C,F}$ = 8.7 Hz), 131.7 (d, $^3J_{C,F}$ = 8.6 Hz), 155.3 (d, $^4J_{C,F}$ = 3.2 Hz), 156.2, 157.3, 162.9 (d, $^1J_{C,F}$ = 243.9 Hz), 205.6.

HRMS (ES$^-$): [M – H]$^-$ calcd for $C_{16}H_9{}^{79}BrFO_3$: 346.9719; found: 346.9723.

1-[7-Bromo-2-(4-fluorophenyl)-6-hydroxybenzofuran-5-yl]ethanone (7c)

Yellow solid; yield: 0.30 g (62%); mp 202–204 °C.

IR (ATR): 797, 835, 1063, 1155, 1218, 1372, 1419, 1504, 1613, 1635 cm^{-1}.

^{1}H NMR (300 MHz, DMSO-d_6): δ = 2.76 (3 H, s, CH_3), 7.35 (2 H, t, J = 8.9 Hz, H-3′,5′), 7.51 (1 H, s, H-3), 7.93 (2 H, dd, J = 5.4, 8.9 Hz, H-2′,6′), 8.31 (1 H, s, H-4), 13.19 (1 H, br s, OH).

^{13}C NMR (75 MHz, DMSO-d_6): δ = 27.6, 92.0, 103.0, 116.7 (d, $^2J_{C,F}$ = 22.1 Hz), 118.0, 122.1, 124.7, 125.8 (d, $^4J_{C,F}$ = 3.2 Hz), 127.3 (d, $^3J_{C,F}$ = 8.5 Hz), 155.8, 156.2, 157.1, 162.9 (d, $^1J_{C,F}$ = 247.0 Hz), 206.7.

HRMS (ES$^-$): m/z [M – H]$^-$ calcd for $C_{16}H_9{}^{79}BrFO_3$: 346.9719; found: 346.9725.

1-[7-Bromo-6-hydroxy-2-(4-methoxyphenyl)benzofuran-5-yl]ethanone (7d)

Yellow solid; yield: 0.34 g (67%); mp 180–182 °C.

IR (ATR): 823, 1018, 1154, 1247, 1373, 1417, 1504, 1613, 1635 cm^{-1}.

^{1}H NMR (300 MHz, DMSO-d_6): δ = 2.71 (3 H, s, CH_3), 3.80 (3 H, s, OCH_3), 7.02 (2 H, d, J = 8.5 Hz, H-3′,5′), 7.25 (1 H, s, H-3), 7.74 (2 H, d, J = 8.5 Hz, H-2′,6′), 8.16 (1 H, s, H-4), 13.12 (1 H, br s, OH).

^{13}C NMR (75 MHz, DMSO-d_6): δ = 27.4, 55.5, 91.7, 100.8, 114.7, 117.5, 121.6, 122.2, 123.7, 126.4, 155.9, 156.6, 156.7, 160.2, 205.4.

HRMS (ES$^-$): m/z [M – H]$^-$ calcd for $C_{17}H_{12}{}^{79}BrO_4$: 358.9919; found: 358.9937.

Base-Catalyzed Claisen–Schmidt Condensation of 7a–d; (*E*)-1-(7-Bromo-6-hydroxy-2-phenylbenzofuran-5-yl)-3-phenylprop-2-en-1-one (8a); Typical Procedure

A mixture of benzofuran **7a** (0.20 g, 0.60 mmol) and benzaldehyde (0.127 g, 1.2 mmol, 1.2 equiv) was dissolved in EtOH (10 mL), and 30% (w/v) aq KOH (3 mL) was added. The mixture was left to stir for 48 h at RT and then poured onto ice-cold dilute HCl. The resultant precipitate was filtered on a Büchner funnel and then purified by column chromatography on silica gel using 4:1 toluene/EtOAc (v/v) as an eluent to afford **8a** as an orange solid; yield: 0.22 g (87%); mp 243–244 °C.

IR (ATR): 720, 760, 856, 1145, 1280, 1422, 1571, 1641 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.05 (1 H, s, H-3), 7.37–7.50 (6 H, m, α-H and ArH), 7.69–7.74 (3 H, m, ArH), 7.86–7.89 (2 H, m, ArH), 7.99 (1 H, d, J_{trans} = 15.5 Hz, H-β), 8.14 (1 H, s, H-4), 13.86 (1 H, br s, OH).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 93.3, 101.4, 117.8, 119.9, 121.2, 122.0, 124.9, 128.8, 128.9, 129.1, 129.2, 129.2, 131.2, 134.4, 146.2, 157.0, 157.4, 158.8, 193.1.

HRMS (ES$^-$): m/z [M – H]$^-$ calcd for $C_{23}H_{14}{}^{79}BrO_3$: 417.0127; found: 417.0115.

(*E*)-1-[7-Bromo-2-(3-fluorophenyl)-6-hydroxybenzofuran-5-yl]-3-phenylprop-2-en-1-one (8b)

Orange solid; yield: 0.22 g (88%); mp 245–247 °C.

IR (ATR): 721, 773, 841, 854, 1144, 1205, 1280, 1361, 1396, 1422, 1570, 1639 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.05–7.13 (2 H, overlapping signals, H-3 and 4′), 7.41–7.49 (4 H, m, α-H and ArH), 7.53–7.67 (1 H, m, ArH), 7.63–7.67 (1 H, m, ArH), 7.68–7.74 (3 H, m, ArH), 8.00 (1 H, d, J_{trans} = 15.4 Hz, β-H), 8.15 (1 H, s, H-4), 13.84 (1 H, br s, OH).

^{13}C NMR (75 MHz, DMSO-d_6): δ = 92.4, 104.7, 111.8 (d, $^2J_{C,F}$ = 23.9 Hz), 116.4 (d, $^2J_{C,F}$ = 21.2 Hz), 121.1 (d, $^4J_{C,F}$ = 2.9 Hz), 121.5, 124.5, 128.6, 129.3, 129.5, 129.9, 131.5 (d, $^3J_{C,F}$ = 8.6 Hz), 131.7, 131.8 (d, $^3J_{C,F}$ = 8.5 Hz), 134.8, 146.4, 155.3, 156.5, 158.8, 163.0 (d, $^1J_{C,F}$ = 243.7 Hz), 194.0.

HRMS (ES$^+$): m/z [M + H]$^+$ calcd for $C_{23}H_{15}{}^{79}BrFO_3$: 437.0189; found: 437.0191.

(*E*)-1-[7-Bromo-2-(4-fluorophenyl)-6-hydroxybenzofuran-5-yl]-3-phenylprop-2-en-1-one (8c)

Orange solid; yield: 0.22 g (88%); mp 209–211 °C.

IR (ATR): 723, 834, 1147, 1233, 1422, 1515, 1573, 1603, 1640 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 6.97 (1 H, s, H-3), 7.17 (2 H, t, J = 8.8 Hz, H-3′,5′), 7.46–7.48 (3 H, m, ArH), 7.68–7.73 (3 H, m, α-H and ArH), 7.84 (2 H, t, J = 8.8 Hz, H-2′,6′), 7.99 (1 H, d, J_{trans} = 15.4 Hz, β-H), 8.12 (1 H, s, H-4), 13.86 (1 H, br s, OH).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 93.3, 101.1, 116.1 (d, $^2J_{C,F}$ = 22.2 Hz), 117.8, 119.8, 121.1, 121.9, 125.6 (d, $^4J_{C,F}$ = 3.4 Hz), 126.9 (d, $^3J_{C,F}$ = 8.4 Hz), 128.8, 129.1, 131.2, 134.4, 146.2, 156.4, 157.9 (d, $^1J_{C,F}$ = 256.4 Hz), 158.8, 164.8, 193.1.

HRMS (ES$^-$): m/z [M – H]$^-$ calcd for $C_{23}H_{13}F^{79}BrO_3$: 435.0032; found: 435.0021.

(*E*)-1-[7-Bromo-6-hydroxy-2-(4-methoxyphenyl)benzofuran-5-yl]-3-phenylprop-2-en-1-one (8d)

Brown solid; yield: 0.21 g (84%); mp 202–204 °C.

IR (ATR): 853, 1035, 1145, 1249, 1422, 1569, 1614, 1640 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.86 (3 H, s, OCH_3), 6.87 (1 H, s, H-3), 6.98 (2 H, d, J = 8.7 Hz, H-3′,5′), 7.42–7.47 (3 H, m, ArH), 7.66–7.71 (3 H, m, α-H and H-2″,6″), 7.78 (2 H, d, J = 8.7 Hz, H-2′,6′), 7.96 (1 H, d, J_{trans} = 15.5 Hz, H-β), 8.06 (1 H, s, H-4), 13.85 (1 H, br s, OH).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 55.4, 93.2, 99.6, 114.3, 117.7, 119.9, 120.7, 122.0, 122.3, 126.5, 128.8, 129.1, 131.1, 134.5, 146.0, 156.8, 157.5, 158.6, 160.4, 193.1.

HRMS (ES$^-$): m/z [M – H]$^-$ calcd for $C_{24}H_{16}{}^{79}BrO_4$: 447.0232; found: 447.0218.

(*E*)-1-(7-Bromo-6-hydroxy-2-phenylbenzofuran-5-yl)-3-(3-fluorophenyl)prop-2-en-1-one (8e)

Red solid; yield: 0.24 g (91%); mp 210–212 °C.

IR (ATR): 756, 851, 980, 1146, 1230, 1421, 1574, 1640 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.01 (1 H, s, H-3), 7.13–7.19 (1 H, m, H-4′), 7.35–7.48 (6 H, m, ArH), 7.65 (1 H, d, J_{trans} = 15.5 Hz, α-H), 7.82–7.92 (3 H, m, β-H and ArH), 8.06 (1 H, s, H-4), 13.73 (1 H, br s, OH).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 93.3, 101.4, 114.6 (d, $^2J_{C,F}$ = 21.9 Hz), 117.6, 118.0 (d, $^2J_{C,F}$ = 21.4 Hz), 121.1, 121.2, 122.0, 124.9, 125.0 (d, $^4J_{C,F}$ = 2.9 Hz), 128.9, 129.1, 129.2, 130.7 (d, $^3J_{C,F}$ = 8.2 Hz), 136.6 (d, $^3J_{C,F}$ = 7.8 Hz), 144.5 (d, $^4J_{C,F}$ = 2.8 Hz), 157.0, 157.4, 158.8, 163.0 (d, $^1J_{C,F}$ = 247.4 Hz), 192.7.

HRMS (ES⁻): *m*/*z* [M – H]⁻ calcd for $C_{23}H_{13}{}^{79}BrFO_3$: 435.0032; found: 435.0034.

(*E*)-1-[7-Bromo-2-(3-fluorophenyl)-6-hydroxybenzofuran-5-yl]-3-(3-fluorophenyl)prop-2-en-1-one (8f)

Orange solid; yield: 0.24 g (92%); mp 223–225 °C.

IR (ATR): 776, 873, 1140, 1238, 1264, 1360, 1425, 1446, 1486, 1571, 1616, 1640 cm^{-1}.

^1H NMR (300 MHz, DMSO-d_6): δ = 7.20–7.34 (2 H, m, H-6′ and H-6″), 7.48–7.56 (3 H, m, H-3 and ArH), 7.72 (3 H, d, *J* = 7.9 Hz, ArH), 7.82–7.90 (2 H, m, α-H and ArH), 8.22 (1 H, d, J_{trans} = 15.5 Hz, β-H), 8.68 (1 H, s, H-4), 13.79 (1 H, br s, OH).

^{13}C NMR (75 MHz, DMSO-d_6): δ = 92.7, 104.6, 111.7 (d, $^2J_{C,F}$ = 24.1 Hz), 115.4 (d, $^2J_{C,F}$ = 22.1 Hz), 116.2 (d, $^2J_{C,F}$ = 21.2 Hz), 118.2 (d, $^2J_{C,F}$ = 20.8 Hz), 121.0, 123.4 (d, $^4J_{C,F}$ = 2.1 Hz), 123.4 (d, $^4J_{C,F}$ = 1.9 Hz), 124.4, 126.5, 131.3 (d, $^3J_{C,F}$ = 8.3 Hz), 131.5 (d, $^3J_{C,F}$ = 8.8 Hz), 131.7 (d, $^3J_{C,F}$ = 8.5Hz), 137.4 (d, $^3J_{C,F}$ = 7.9 Hz), 144.2 (d, $^4J_{C,F}$ = 2.9 Hz), 155.0 (d, $^4J_{C,F}$ = 3.9 Hz), 156.7, 158.4 (d, $^1J_{C,F}$ = 241.3 Hz), 161.3, 164.6, 167.7 (d, $^1J_{C,F}$ = 226.0 Hz), 193.6.

HRMS (ES⁻): *m*/*z* [M – H]⁻ calcd for $C_{23}H_{12}{}^{79}BrF_2O_3$: 452.9938; found: 452.9919.

(*E*)-1-[7-Bromo-2-(4-fluorophenyl)-6-hydroxybenzofuran-5-yl]-3-(3-fluorophenyl)prop-2-en-1-one (8g)

Orange solid; yield: 0.24 g (92%); mp 254–255 °C.

IR (ATR): 833, 846, 1147, 1232, 1360, 1402, 1421, 1503, 1576, 1601, 1643 cm^{-1}.

^1H NMR (500 MHz, DMSO-d_6): δ = 7.31–7.40 (3 H, m, H-4″ and H-3′,5′), 7.49 (1 H, s, H-3), 7.53 (1 H, dd, *J* = 7.7, 9.0 Hz, H-3″), 7.75 (1 H, d, *J* = 7.7 Hz, H-6″), 7.87–7.94 (2 H, m, α-H and H-2″), 7.98 (2 H, t, *J* = 7.7 Hz, H-2′,6′), 8.24 (1 H, d, J_{trans} = 15.4 Hz, β-H), 8.76 (1 H, s, H-4), 13.77 (1 H, br s, OH).

^{13}C NMR (125 MHz, DMSO-d_6): δ = 92.4, 103.0, 115.4 (d, $^2J_{C,F}$ = 22.0 Hz), 116.7 (d, $^2J_{C,F}$ = 22.1 Hz), 118.3 (d, $^2J_{C,F}$ = 21.4 Hz), 118.5, 122.2, 123.1, 124.2, 125.9 (d, $^4J_{C,F}$ = 2.8 Hz), 126.6 (d, $^4J_{C,F}$ = 2.2 Hz), 127.5 (d, $^3J_{C,F}$ = 8.4 Hz), 131.4 (d, $^3J_{C,F}$ = 8.5 Hz), 137.4 (d, $^3J_{C,F}$ = 8.5 Hz), 144.6, 155.9, 157.6 (d, $^1J_{C,F}$ = 257.5 Hz), 159.4, 162.0 (d, $^4J_{C,F}$ = 3.3 Hz), 162.9 (d, $^1J_{C,F}$ = 243.9 Hz), 193.9.

HRMS (ES⁻): *m*/*z* [M – H]⁻ calcd for $C_{23}H_{12}{}^{79}BrF_2O_3$: 452.9938; found: 452.9932.

(*E*)-1-(7-Bromo-6-hydroxy-2-phenylbenzofuran-5-yl)-3-(4-fluorophenyl)prop-2-en-1-one (8h)

Brown solid; yield: 0.23 g (87%); mp 217–219 °C.

IR (ATR): 757, 827, 1144, 1222, 1401, 1420, 1507, 1576, 1638 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 7.02 (1 H, s, H-3), 7.15 (2 H, t, *J* = 8.6 Hz, H-3″,5″), 7.35–7.40 (1 H, m, H-4′), 7.46 (2 H, t, *J* = 7.3 Hz, ArH), 7.60 (1 H, d, J_{trans} = 15.4 Hz, α-H), 7.69 (2 H, t, *J* = 8.6 Hz, H-2″,6″), 7.81–7.87 (2 H, m, ArH), 7.92 (1 H, d, J_{trans} = 15.4 Hz, β-H), 8.08 (1 H, s, H-4), 13.82 (1 H, br s, OH).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 93.3, 101.4, 116.3 (d, $^2J_{C,F}$ = 22.0 Hz), 117.7, 119.5 (d, $^4J_{C,F}$ = 2.4 Hz), 121.1, 122.0, 124.9, 128.9, 129.1, 129.2, 130.7, 130.7 (d, $^3J_{C,F}$ = 9.0 Hz), 144.8, 156.9, 157.4, 158.8, 164.4 (d, $^1J_{C,F}$ = 252.8 Hz), 192.8.

HRMS (ES⁻): [M – H]⁻ calcd for $C_{23}H_{13}{}^{79}BrFO_3$: 435.0032; found: 435.0021.

(*E*)-1-[7-Bromo-2-(3-fluorophenyl)-6-hydroxybenzofuran-5-yl]-3-(4-fluorophenyl)prop-2-en-1-one (8i)

Orange solid; yield: 0.24 g (92%); mp 232–234 °C.

IR (ATR): 777, 827, 1139, 1157, 1218, 1237, 1418, 1446, 1509, 1565, 1600, 1638 cm^{-1}.

^1H NMR (300 MHz, DMSO-d_6): δ = 7.26–7.37 (3 H, m, H-3′ and H-2′,6′), 7.50–7.60 (1 H, m, H-4′), 7.62 (1 H, s, H-3), 7.76 (2 H, d, *J* = 8.0 Hz, H-3″,5″), 7.92 (1 H, d, J_{trans} = 15.4 Hz, α-H), 8.02–8.07 (2 H, dd, *J* = 5.6, 8.0 Hz, H-2″,6″), 8.15 (1 H, d, J_{trans} = 15.4 Hz, β-H), 8.77 (1 H, s, H-4), 13.89 (1 H, br s, OH).

^{13}C NMR (75 MHz, DMSO-d_6): δ = 92.4, 104.6, 111.8 (d, $^2J_{C,F}$ = 23.9 Hz), 116.4 (d, $^2J_{C,F}$ = 21.4 Hz), 116.5 (d, $^2J_{C,F}$ = 21.8 Hz), 118.5, 121.2 (d, $^3J_{C,F}$ = 7.9 Hz), 122.0, 124.4, 131.4, 131.5, 131.5, 131.8 (d, $^3J_{C,F}$ = 8.7 Hz), 132.3 (d, $^3J_{C,F}$ = 8.8 Hz), 145.2, 155.4 (d, $^4J_{C,F}$ = 3.2 Hz), 156.5, 158.7, 163.0 (d, $^1J_{C,F}$ = 243.7 Hz), 164.2 (d, $^1J_{C,F}$ = 250.2 Hz), 193.9.

HRMS (ES⁻): *m*/*z* [M – H]⁻ calcd for $C_{23}H_{12}{}^{79}Br\ F_2O_3$: 452.9938; found: 452.9910.

(*E*)-1-[7-Bromo-6-hydroxy-2-(4-fluorophenyl)benzofuran-5-yl]-3-(4-fluorophenyl)prop-2-en-1-one (8j)

Orange solid; yield: 0.24 g (92%); mp 227–229 °C.

IR (ATR): 715, 734, 824, 1029, 1157, 1200, 1217, 1402, 1421, 1503, 1576, 1641 cm^{-1}.

^1H NMR (500 MHz, DMSO-d_6): δ = 7.35 (4 H, dt, *J* = 8.8, 11.0 Hz, H-3″,5″, H-3′,5′), 7.48 (1 H, s, H-3), 7.92 (1 H, d, J_{trans} = 15.5 Hz, α-H), 7.97 (2 H, t, *J* = 8.8 Hz, H-2″,6″), 8.04 (2 H, t, *J* = 8.8 Hz, H-2′,6′), 8.13 (1 H, d, J_{trans} = 15.5 Hz, β-H), 8.73 (1 H, s, H-4), 13.88 (1 H, br s, OH).

^{13}C NMR (125 MHz, DMSO-d_6): δ = 92.3, 103.0, 116.5 (d, $^2J_{C,F}$ = 21.7 Hz), 116.6 (d, $^2J_{C,F}$ = 22.0 Hz), 118.3, 122.2, 124.0, 127.4 (d, $^3J_{C,F}$ = 8.5 Hz), 128.6, 129.3, 131.5 (d, $^4J_{C,F}$ = 3.1 Hz), 132.3 (d, $^3J_{C,F}$ = 8.8 Hz), 145.1, 155.9, 156.5, 158.5, 162.9 (d, $^1J_{C,F}$ = 247.1 Hz), 164.2 (d, $^1J_{C,F}$ = 250.0 Hz), 193.9.

HRMS (ES⁻): *m*/*z* [M – H]⁻ calcd for $C_{23}H_{12}{}^{79}BrF_2O_3$: 452.9938; found: 452.9955.

(*E*)-1-[7-Bromo-6-hydroxy-2-(4-methoxyphenyl)benzofuran-5-yl]-3-(4-fluorophenyl)prop-2-en-1-one (8k)

Brown solid; yield: 0.21 g (81%); mp 223–225 °C.

IR (ATR): 826, 1144, 1221, 1251, 1424, 1505, 1568, 1613, 1639 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 3.86 (3 H, s, OCH_3), 6.86 (1 H, s, H-3), 6.98 (2 H, d, *J* = 8.8 Hz, H-3′,5′), 7.15 (2 H, t, *J* = 8.5 Hz, H-3″,5″), 7.60 (1 H, d, J_{trans} = 15.4 Hz, α-H), 7.69 (2 H, t, *J* = 8.5 Hz, H-2″,6″), 7.77 (2 H, d, *J* = 8.8 Hz, H-2′,6′), 7.92 (1 H, d, J_{trans} = 15.4 Hz, β-H), 8.03 (1 H, s, H-4), 13.82 (1 H, br s, OH).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 55.4, 93.2, 99.6, 114.2, 114.3, 116.3 (d, $^2J_{C,F}$ = 22.0 Hz), 119.6 (d, $^4J_{C,F}$ = 2.2 Hz), 120.6, 122.0, 122.3, 126.5, 127.6, 130.7 (d, $^3J_{C,F}$ = 8.6 Hz), 133.2, 144.6, 157.5, 158.5 (d, $^1J_{C,F}$ = 242.0 Hz), 158.6, 160.4, 192.9.

HRMS (ES⁻): *m*/*z* [M – H]⁻ calcd for $C_{24}H_{15}{}^{79}BrFO_4$: 465.0138; found: 465.0157.

(*E*)-1-(7-Bromo-6-hydroxy-2-phenylbenzofuran-5-yl)-3-(4-chlorophenyl)prop-2-en-1-one (8l)

Red solid; yield: 0.26 g (95%); mp 214–216 °C.

IR (ATR): 730, 818, 1091, 1142, 1401, 1420, 1490, 1563, 1637 cm^{-1}.

^{1}H NMR (300 MHz, DMSO-d_6): δ = 7.42–7.56 (6 H, m, H-3, ArH), 7.85–7.92 (3 H, m, α-H and H-3″,5″), 7.98 (2 H, d, J = 8.4 Hz, H-2″,6″), 8.18 (1 H, d, J_{trans} = 15.4 Hz, β-H), 8.73 (1 H, s, H-4), 13.86 (1 H, br s, OH).

^{13}C NMR (75 MHz, DMSO-d_6): δ = 92.3, 103.1, 118.2, 121.9, 122.2, 124.1, 125.1, 129.1, 129.4, 129.5, 129.7, 131.5, 133.7, 136.2, 144.8, 156.5, 156.8, 158.5, 193.8.

HRMS (ES$^-$): m/z [M – H]$^-$ calcd for $C_{23}H_{13}{}^{79}Br^{35}ClO_3$: 450.9737; found: 450.9724.

(*E*)-1-[7-Bromo-2-(4-fluorophenyl)-6-hydroxybenzofuran-5-yl]-3-(4-chlorophenyl)prop-2-en-1-one (8m)

Orange solid; yield: 0.24 g (89%); mp 252–254 °C.

IR (ATR): 820, 1146, 1203, 1229, 1275, 1422, 1504, 1567, 1579, 1643 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 6.99 (1 H, s, H-3), 7.18 (2 H, t, J = 8.7 Hz, H-3′,5′), 7.45 (2 H, d, J = 8.5 Hz, H-3″,5″), 7.64 (2 H, d, J = 8.5 Hz, H-2″,6″), 7.69 (1 H, d, J_{trans} = 15.4 Hz, α-H), 7.86 (2 H, t, J = 8.7 Hz, H-2′,6′), 7.94 (1 H, d, J_{trans} = 15.4 Hz, β-H), 8.12 (1 H, s, H-4), 13.76 (1 H, br s, OH).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 93.4, 101.1, 116.10 (d, $^2J_{C,F}$ = 22.1 Hz), 117.8, 120.4, 121.1, 122.0, 125.6 (d, $^4J_{C,F}$ = 3.4 Hz), 126.9 (d, $^3J_{C,F}$ = 8.3 Hz), 129.4, 129.9, 132.9, 137.1, 144.6, 156.6, 157.0, 158.9, 163.2 (d, $^1J_{C,F}$ = 250.0 Hz), 192.9.

HRMS (ES$^-$): m/z [M – H]$^-$ calcd for $C_{23}H_{12}{}^{79}Br^{35}ClFO_3$: 468.9642; found: 468.9661.

(*E*)-1-[7-Bromo-6-hydroxy-2-(4-methoxyphenyl)benzofuran-5-yl]-3-(4-chlorophenyl)prop-2-en-1-one (8n)

Red solid; yield: 0.25 g (86%); mp 215–217 °C.

IR (ATR): 819, 1025, 1090, 1141, 1249, 1420, `505, 1562, 1615, 1636 cm^{-1}.

^{1}H NMR (300 MHz, DMSO-d_6): δ = 3.86 (3 H, s, OCH_3), 6.84 (1 H, s, H-3), 6.96 (2 H, d, J = 8.5 Hz, H-3′,5′), 7.42 (2 H, d, J = 8.5 Hz, H-3″,5″), 7.57–7.66 (3 H, m, α-H, H-2″,6″), 7.75 (2 H, d, J = 8.5 Hz, H-2′,6′), 7.87 (1 H, d, J_{trans} = 15.5 Hz, β-H), 7.99 (1 H, s, H-4), 13.78 (1 H, br s, OH).

^{13}C NMR (75 MHz, DMSO-d_6): δ = 55.4, 93.2, 99.5, 114.3, 117.5, 120.2, 120.6, 121.9, 122.3, 126.4, 129.4, 129.9, 132.9, 137.0, 144.4, 156.8, 157.5, 158.5, 160.3, 192.7.

HRMS (ES$^-$): m/z [M – H]$^-$ calcd for $C_{24}H_{15}{}^{79}Br^{35}ClO_4$: 480.9842; found: 480.9843.

(*E*)-1-(7-Bromo-6-hydroxy-2-phenylbenzofuran-5-yl)-3-(4-methoxyphenyl)prop-2-en-1-one (8o)

Orange solid; yield: 0.24 g (88%); mp 187–189 °C.

IR (ATR): 826, 1025, 1141, 1172, 1223, 1421, 1510, 1560, 1603, 1632 cm^{-1}.

^{1}H NMR (300 MHz, DMSO-d_6): δ = 3.84 (3 H, s, OCH_3), 7.05 (2 H, d, J = 8.8 Hz, H-3″ and H-5″), 7.41–7.55 (4 H, m, H-3, H-4′ and H-3′,5′), 7.88–7.95 (5 H, m, α-H, H-2′,6′ and H-2″,6″), 8.05 (1 H, d, J_{trans} = 15.4 Hz, β-H), 8.74 (1 H, s, H-4).

^{13}C NMR (75 MHz, DMSO-d_6): δ = 55.9, 92.3, 103.2, 114.9, 118.3, 118.5, 122.1, 123.8, 125.1, 127.5, 129.2, 129.5, 129.6, 132.0, 146.5, 156.3, 156.6, 158.6, 162.4, 193.8.

HRMS (ES$^-$): m/z [M – H]$^-$ calcd for $C_{24}H_{16}{}^{79}BrO_4$: 447.0232; found: 447.0252.

(*E*)-1-[7-Bromo-2-(3-fluorophenyl)-6-hydroxybenzofuran-5-yl]-3-(4-methoxyphenyl)prop-2-en-1-one (8p)

Brown solid; yield: 0.25 g (93%); mp 215–218 °C.

IR (ATR): 773, 820, 1035, 1142, 1172, 1238, 1259, 1510, 1564, 1607, 1635 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.88 (3 H, s, OCH_3), 6.97 (2 H, d, J = 8.8 Hz, H-3″,5″), 7.04 (1 H, s, H-3), 7.06–7.19 (1 H, m, H-4′), 7.38–7.56 (3 H, m, H-2′,6′ and H-3′), 7.60 (1 H, d, J_{trans} = 15.3 Hz, α-H), 7.66 (2 H, d, J = 8.8 Hz, H-2″,6″), 7.95 (1 H, d, J_{trans} = 15.3 Hz, β-H), 8.10 (1 H, s, H-4), 14.02 (1 H, br s, OH).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 55.5, 93.2, 102.6, 111.8 (d, $^2J_{C,F}$ = 23.8 Hz), 114.6, 115.9 (d, $^2J_{C,F}$ = 21.3 Hz), 117.1, 118.1, 120.5 (d, $^4J_{C,F}$ = 3.0 Hz), 121.3, 121.5, 127.1, 130.5 (d, $^3J_{C,F}$ = 8.5 Hz), 130.7, 131.3 (d, $^3J_{C,F}$ = 8.3 Hz), 146.2, 155.8, 156.8, 159.0, 162.2, 163.0 (d, $^1J_{C,F}$ = 246.0 Hz), 193.0.

HRMS (ES$^-$): m/z [M – H]$^-$ calcd for $C_{24}H_{15}{}^{79}BrFO_4$: 465.0138; found: 465.0126.

(*E*)-1-[7-Bromo-2-(4-fluorophenyl)-6-hydroxybenzofuran-5-yl]-3-(4-methoxyphenyl)prop-2-en-1-one (8q)

Brown solid; yield: 0.22 g (82%); mp 238–239 °C.

IR (ATR): 820, 1032, 1175, 1226, 1286, 1423, 1504, 1567, 1605, 1639 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.88 (3 H, s, OCH_3), 6.98 (3 H, m, H-3 and H-3″,5″), 7.16 (2 H, t, J = 8.5 Hz, H-3′,5′), 7.57 (1 H, d, J_{trans} = 15.3 Hz, α-H), 7.66 (2 H, d, J = 8.5 Hz, H-2″,6″), 7.84 (2 H, t, J = 8.5 Hz, H-2′,6′), 7.96 (1 H, d, J_{trans} = 15.3 Hz, β-H), 8.10 (1 H, s, H-4), 14.01 (1 H, br s, OH).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 55.5, 93.2, 101.2, 114.6, 116.0 (d, $^2J_{C,F}$ = 22.1 Hz), 117.2, 118.0, 120.9, 121.8, 125.7 (d, $^4J_{C,F}$ = 3.4 Hz), 126.8 (d, $^3J_{C,F}$ = 8.3 Hz), 127.2, 130.7, 146.1, 156.3, 156.7, 158.8, 162.2, 163.1 (d, $^1J_{C,F}$ = 249.8 Hz), 193.0.

HRMS (ES$^-$): m/z [M – H]$^-$ calcd for $C_{24}H_{15}{}^{79}BrFO_4$: 465.0138; found: 465.0129.

(*E*)-1-[7-Bromo-6-hydroxy-2-(4-methoxyphenyl)benzofuran-5-yl]-3-(4-methoxyphenyl)prop-2-en-1-one (8r)

Red solid; yield: 0.25 g (86%); mp 199–201 °C.

IR (ATR): 820, 1030, 1224, 1249, 1423, 1501, 1511, 1567, 1606, 1633 cm^{-1}.

^{1}H NMR (300 MHz, DMSO-d_6): δ = 3.85 (3 H, s, OCH_3), 3.87 (3 H, s, OCH_3), 6.83 (1 H, s, H-3), 6.95 (4 H, d, J = 8.8 Hz, H-3′,5′ and H-3″,5″), 7.52 (1 H, d, J_{trans} = 15.3 Hz, α-H), 7.63 (2 H, d, J = 8.8 Hz, H-2″,6″), 7.75 (2 H, d, J = 8.8 Hz, H-2′,6′), 7.91 (1 H, d, J_{trans} = 15.3 Hz, β-H), 8.00 (1 H, s, H-4).

^{13}C NMR (75 MHz, DMSO-d_6): δ = 55.4, 55.5, 93.0, 99.6, 114.3, 114.5, 117.2, 117.7, 120.5, 122.1, 126.4, 127.2, 130.7, 133.2, 145.8, 156.6, 157.3., 158.5, 160.3, 162.1, 192.9.

HRMS (ES$^-$): m/z [M – H]$^-$ calcd for $C_{25}H_{18}{}^{79}BrO_5$: 477.0338; found: 477.0353.

Furanoflavanones 9a–r; 9-Bromo-6,7-dihydro-2,7-diphenylfuro[3,2-*g*]chromen-5-one (9a); Typical Procedure

A stirred solution of furanochalcone **8a** (0.20 g, 0.48 mmol) in EtOH (10 mL) was treated with concd H_2SO_4 (2 mL). The mixture was refluxed for 4 h and then poured into ice-cold H_2O. The precipitate was

filtered and then purified by column chromatography on silica gel using 9:1 toluene/EtOAc (v/v) as an eluent to afford **9a** as a cream solid; yield: 0.10 g (50%); mp 213–214 °C.

IR (ATR): 753, 881, 1006, 1160, 1185, 1276, 1354, 1414, 1469, 1494, 1571, 1616, 1683 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 3.06 (1 H, dd, *J* = 3.4, 16.9 Hz, 6-H_a), 3.15 (1 H, dd, *J* = 12.1, 16.9 Hz, 6-H_b), 5.65 (1 H, dd, *J* = 3.4, 12.1 Hz, H-7), 7.07 (1 H, s, H-3), 7.40 (2 H, t, *J* = 7.2 Hz, ArH), 7.44–7.52 (4 H, m, ArH), 7.56 (2 H, d, *J* = 7.2 Hz, ArH), 7.88 (2 H, d, *J* = 7.2 Hz, ArH), 8.13 (1 H, s, H-4).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 44.1, 80.0, 93.4, 101.9, 118.5, 119.1, 124.5, 125.0, 125.9, 128.6, 128.8, 128.9, 129.2, 129.3, 138.4, 155.9, 157.0, 157.8, 191.2.

HRMS (ES$^+$): *m*/*z* [M + H]$^+$ calcd for $C_{23}H_{16}{}^{79}BrO_3$: 419.0283; found: 419.0285.

9-Bromo-2-(3-fluorophenyl)-6,7-dihydro-7-phenylfuro[3,2-*g*]chromen-5-one (9b)

Yellow solid; yield: 0.12 g (60%); mp 220–222 °C.

IR (ATR): 691, 752, 776, 839, 1161, 1192, 1269, 1282, 1336, 1413, 1474, 1575, 1617, 1681 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 3.07 (1 H, dd, *J* = 3.4, 16.9, Hz, 6-H_a), 3.15 (1 H, dd, *J* = 12.1, 16.9 Hz, 6-H_b), 5.65 (1 H, dd, *J* = 3.4, 12.1 Hz, H-7), 7.06–7.12 (2 H, m, H-3 and H-4′), 7.40–7.48 (4 H, m, ArH), 7.56 (3 H, d, *J* = 7.7 Hz, C_6H_5), 7.64 (1 H, d, *J* = 7.7 Hz, C_6H_5), 8.13 (1H, s, H-4).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 44.1, 80.0, 93.4, 103.0, 111.9 (d, $^2J_{C,F}$ = 23.8 Hz), 116.1 (d, $^2J_{C,F}$ = 21.4 Hz), 118.8, 119.3, 120.7 (d, $^4J_{C,F}$ = 3.1 Hz), 124.2, 125.9, 128.7, 128.9, 130.6 (d, $^3J_{C,F}$ = 8.4 Hz), 131.3 (d, $^3J_{C,F}$ = 8.4 Hz), 138.3, 156.1, 156.3 (d, $^4J_{C,F}$ = 3.1 Hz), 157.0, 163.1 (d, $^1J_{C,F}$ = 247.0 Hz), 191.1.

HRMS (ES$^+$): *m*/*z* [M + H]$^+$ calcd for $C_{23}H_{15}{}^{79}BrFO_3$: 437.0189; found: 437.0193.

9-Bromo-2-(4-fluorophenyl)-6,7-dihydro-7-phenylfuro[3,2-*g*]chromen-5-one (9c)

Pale yellow solid; yield: 0.11 g (55%); mp 251–254 °C.

IR (ATR): 751, 820, 1159, 1181, 1232, 1282, 1340, 1377, 1408, 1419, 1473, 1506, 1615, 1683 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 3.05 (1 H, dd, *J* = 3.9, 17.0 Hz, 6-H_a), 3.15 (1 H, dd, *J* = 11.6, 17.0 Hz, 6-H_b), 5.65 (1 H, dd, *J* = 3.9, 11.6 Hz, H-7), 7.00 (1 H, s, H-3), 7.16 (2 H, t, *J* = 8.8 Hz, H-3′,5′), 7.39–7.50 (3 H, m, C_6H_5), 7.53–7.58 (2 H, m, C_6H_5), 7.85 (2 H, t, *J* = 8.8 Hz, H-2′,6′), 8.11 (1 H, s, H-4).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 44.1, 80.0, 93.4, 101.6, 116.1 (d, $^2J_{C,F}$ = 22.1 Hz), 118.5, 119.1, 124.4, 125.6 (d, $^4J_{C,F}$ = 3.7 Hz), 125.9, 127.0 (d, $^3J_{C,F}$ = 8.4 Hz), 128.7, 128.9, 138.3, 154.4 (d, $^1J_{C,F}$ = 244.2 Hz), 155.9, 156.8, 164.9, 191.2.

HRMS (ES$^+$): *m*/*z* [M + H]$^+$ calcd for $C_{23}H_{15}{}^{79}BrFO_3$: 437.0189; found: 437.0191.

9-Bromo-6,7-dihydro-2-(4-methoxyphenyl)-7-phenylfuro[3,2-*g*]chromen-5-one (9d)

Yellow solid; yield: 0.12 g (60%); mp 227–230 °C.

IR (ATR): 752, 827, 1002, 1015, 1151, 1181, 1250, 1339, 1412, 1452, 1470, 1506, 1612, 1678 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 3.04 (1 H, dd, *J* = 3.9, 17.0 Hz, 6-H_a), 3.14 (1,H, dd, *J* = 11.6, 17.0 Hz, 6-H_b), 3.87 (3 H, s, OCH_3), 5.63 (1 H, dd, *J* = 3.9, 11.6 Hz, H-7), 6.90 (1 H, s, H-3), 6.99 (2 H, d, *J* = 8.9 Hz, H-3′,5′), 7.39–7.48 (3 H, m, C_6H_5), 7.54–7.57 (2 H, m, C_6H_5), 7.80 (2 H, d, *J* = 8.9 Hz, H-2′,6′), 8.07 (1 H, s, H-4).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 44.1, 55.4, 79.9, 93.2, 100.1, 114.3, 118.0, 119.0, 122.1, 124.8, 125.9, 126.6, 128.6, 128.8, 138.5, 155.6, 156.9, 157.9, 160.5, 191.3.

HRMS (ES$^+$): *m*/*z* [M + H]$^+$ calcd for $C_{24}H_{18}{}^{79}BrO_4$: 449.0388; found: 449.0397.

9-Bromo-7-(3-fluorophenyl)-6,7-dihydro-2-phenylfuro[3,2-*g*]chromen-5-one (9e)

Brown solid; yield: 0.11 g (55%); mp 177–179 °C.

IR (ATR): 759, 782, 1147, 1184, 1229, 1280, 1333, 1413, 1444, 1469, 1491, 1568, 1592, 1616, 1684 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 3.04 (1 H, dd, *J* = 4.5, 16.8 Hz, 6-H_a), 3.11 (1 H, dd, *J* = 11.0, 16.8 Hz, 6-H_b), 5.63 (1 H, dd, *J* = 4.5, 11.0 Hz, H-7), 7.06–7.12 (2 H, m, H-3 and H-4″), 7.28–7.50 (6 H, m, ArH), 7.83–7.88 (2 H, m, ArH), 8.11 (1 H, s, H-4).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 44.0, 79.1, 93.4, 101.8, 113.1 (d, $^2J_{C,F}$ = 22.9 Hz), 115.6 (d, $^2J_{C,F}$ = 21.1 Hz), 118.5, 119.0, 121.4 (d, $^4J_{C,F}$ = 3.0 Hz), 124.7, 125.0, 128.9, 129.2, 129.3, 130.5 (d, $^3J_{C,F}$ = 8.2 Hz), 140.9 (d, $^3J_{C,F}$ = 7.9 Hz), 155.5, 157.0, 157.9, 163.0 (d, $^1J_{C,F}$ = 247.0 Hz), 190.7.

HRMS (ES$^+$): *m*/*z* [M + H]$^+$ calcd for $C_{23}H_{15}{}^{79}BrFO_3$: 437.0189; found: 437.0195.

9-Bromo-2,7-bis(3-fluorophenyl)-6,7-dihydrofuro[3,2-*g*]chromen-5-one (9f)

Yellow solid; yield: 0.10 g (50%); mp 208–210 °C.

IR (ATR): 684, 770, 875, 1169, 1191, 1280, 1336, 1415, 1448, 1487, 1580, 1593, 1618, 1685 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 3.07 (1 H, dd, *J* = 4.3, 16.4 Hz, 6-H_a), 3.12 (1 H, dd, *J* = 10.7, 16.4 Hz, 6-H_b), 5.64 (1 H, dd, *J* = 4.3, 10.7 Hz, H-7), 7.06–7.12 (3 H, m, H-3, H-4′ and H-4″), 7.31 (2 H, t, *J* = 8.3 Hz, H-6′), 7.41–7.46 (2 H, m, H-3′ and H-3″), 7.56 (1 H, d, *J* = 8.0 Hz, ArH), 7.65 (1 H, d, *J* = 8.8 Hz, ArH), 8.13 (1 H, s, H-4).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 44.0, 79.2 (d, $^4J_{C,F}$ = 1.9 Hz), 93.5, 102.9, 112.0 (d, $^2J_{C,F}$ = 23.8 Hz), 113.1 (d, $^2J_{C,F}$ = 22.8 Hz), 115.6 (d, $^2J_{C,F}$ = 21.2 Hz), 116.1 (d, $^2J_{C,F}$ = 21.4 Hz), 118.8, 119.2, 120.7 (d, $^4J_{C,F}$ = 3.1 Hz), 121.4 (d, $^4J_{C,F}$ = 3.1 Hz), 124.4, 130.5 (d, $^3J_{C,F}$ = 8.2 Hz), 130.6 (d, $^3J_{C,F}$ = 8.3 Hz), 131.2 (d, $^3J_{C,F}$ = 8.5 Hz), 140.8 (d, $^3J_{C,F}$ = 7.3 Hz), 155.8, 156.5 (d, $^4J_{C,F}$ = 3.1 Hz), 157.0, 163.0 (d, $^1J_{C,F}$ = 247.0 Hz), 163.1 (d, $^1J_{C,F}$ = 246.4 Hz), 190.6.

HRMS (ES$^-$): *m*/*z* [M – H]$^-$ calcd for $C_{23}H_{12}{}^{79}BrF_2O_3$: 452.9938; found 452.9920.

9-Bromo-7-(3-fluorophenyl)-2-(4-fluorophenyl)-6,7-dihydrofuro[3,2-*g*]chromen-5-one (9g)

Pale yellow solid; yield: 0.11 g (55%); mp 252–254 °C.

IR (ATR): 781, 820, 868, 1147, 1158, 1182, 1229, 1280,1342, 1419, 1506, 1596, 1615, 1685 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 3.06 (1 H, dd, *J* = 4.5, 16.8 Hz, 6-H_a), 3.11 (1 H, dd, *J* = 10.9, 16.8 Hz, 6-H_b), 5.63 (1 H, dd, *J* = 4.5, 10.9 Hz, H-7), 7.00 (1 H, s, H-3), 7.09 (1 H, t, *J* = 8.7 Hz, H-4″), 7.17 (2 H, t, *J* = 8.6

Hz, H-3′,5′), 7.31 (2 H, t, J = 8.7 Hz, H-2″ and H-3″), 7.42 (1 H, dd, J = 8.0, 13.8 Hz, H-6″), 7.85 (2 H, t, J = 8.6 Hz, H-2′,6′), 8.11 (1 H, s, H-4).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 44.0, 79.1 (d, $^4J_{C,F}$ = 1.8 Hz), 93.4, 101.53, 101.54, 113.1 (d, $^2J_{C,F}$ = 22.9 Hz), 115.6 (d, $^2J_{C,F}$ = 21.1 Hz), 116.1 (d, $^2J_{C,F}$ = 22.1 Hz), 118.5, 119.1, 121.3 (d, $^4J_{C,F}$ = 3.0 Hz), 124.6, 125.6 (d, $^4J_{C,F}$ = 3.3 Hz), 127.0 (d, $^3J_{C,F}$ = 8.3 Hz), 130.5 (d, $^3J_{C,F}$ = 8.2 Hz), 140.9 (d, $^3J_{C,F}$ = 7.2 Hz), 155.6, 157.0, 163.0 (d, $^1J_{C,F}$ = 247.0 Hz), 163.3 (d, $^1J_{C,F}$ = 250.2 Hz), 190.6.

HRMS (ES⁻): m/z [M – H]⁻ calcd for $C_{23}H_{12}{}^{79}BrF_2O_3$: 452.9938; found: 452.9930.

9-Bromo-7-(4-fluorophenyl)-6,7-dihydro-2-phenylfuro[3,2-*g*]chromen-5-one (9h)

Cream solid; yield: 0.12 g (60%); mp 230–232 °C.

IR (ATR): 761, 883, 1152, 1226, 1274, 1283, 1338, 1415, 1471, 1513, 1569, 1616, 1682 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.03 (1 H, dd, J = 4.0, 16.9 Hz, 6-H_a), 3.13 (1 H, dd, J = 11.5, 16.9 Hz, 6-H_b), 5.62 (1 H, dd, J = 4.0, 11.5 Hz, H-7), 7.07 (1 H, s, H-3), 7.15 (2 H, t, J = 8.6 Hz, H-3″,5″), 7.38–7.56 (5 H, m, ArH), 7.87 (2 H, dt, J = 2.4, 8.6 Hz, H-2″,6″), 8.12 (1 H, s, H-4).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 44.1, 79.4, 93.3, 101.8, 115.8 (d, $^2J_{C,F}$ = 21.6 Hz), 118.5, 119.0, 124.6, 125.0, 127.8 (d, $^3J_{C,F}$ = 8.2 Hz), 128.9, 129.2, 129.3, 134.2 (d, $^4J_{C,F}$ = 2.9 Hz), 155.7, 157.0, 157.8, 162.8 (d, $^1J_{C,F}$ = 247.6 Hz), 191.0.

HRMS (ES⁺): m/z [M + H]⁺ calcd for $C_{23}H_{15}{}^{79}BrFO_3$: 437.0189; found: 437.0191.

9-Bromo-2-(3-fluorophenyl)-7-(4-fluorophenyl)-6,7-dihydrofuro[3,2-*g*]chromen-5-one (9i)

Yellow solid; yield: 0.10 g (50%); mp 225–227 °C.

IR (ATR): 779, 832, 1162, 1191, 1225, 1285, 1339, 1415, 1486, 1513, 1598, 1619, 1684 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.03 (1 H, dd, J = 4.0, 16.9 Hz, 6-H_a), 3.13 (1 H, dd, J = 11.4, 16.9 Hz, 6-H_b), 5.62 (1 H, dd, J = 4.0, 11.4 Hz, H-7), 7.05–7.10 (2 H, m, H-3 and H-4′), 7.14 (2 H, t, J = 8.5 Hz, H-3″,5″), 7.43 (1 H, dd, $J_{H,H}$ = 8.0 Hz, $J_{H,F}$ = 5.8 Hz, H-6′), 7.51–7.58 (3 H, m, H-3′ and H-2″,6″), 7.64 (1 H, d, J = 8.0 Hz, H-2′), 8.13 (1 H, s, H-4).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 44.0, 79.4, 93.4, 102.9, 111.9 (d, $^2J_{C,F}$ = 23.8 Hz), 115.8 (d, $^2J_{C,F}$ = 21.7 Hz), 116.1 (d, $^2J_{C,F}$ = 20.8 Hz), 118.8, 119.2, 120.7 (d, $^4J_{C,F}$ = 3.0 Hz), 124.3, 127.8 (d, $^3J_{C,F}$ = 8.4 Hz), 130.6 (d, $^3J_{C,F}$ = 8.3 Hz), 131.3 (d, $^3J_{C,F}$ = 8.6 Hz), 134.1 (d, $^4J_{C,F}$ = 3.3 Hz), 155.9, 156.4 (d, $^4J_{C,F}$ = 3.4 Hz), 157.0, 162.8 (d, $^1J_{C,F}$ = 247.9 Hz), 163.1 (d, $^1J_{C,F}$ = 246.5 Hz), 190.9.

HRMS (ES⁻): m/z [M – H]⁻ calcd for $C_{23}H_{12}{}^{79}BrF_2O_3$: 452.9938; found: 452.9918.

9-Bromo-2,7-bis(4-fluorophenyl)-6,7-dihydrofuro[3,2-*g*]chromen-5-one (9j)

Orange solid; yield: 0.14 g (70%); mp 275–277 °C.

IR (ATR): 823, 1156, 1224, 1278, 1360, 1420, 1474, 1505, 1620, 1684 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 3.05 (1 H, dd, J = 3.5, 16.9 Hz, 6-H_a), 3.13 (1 H, dd, J = 12.0, 16.9 Hz, 6-H_b), 5.63 (1 H, dd, J = 3.5, 12.0 Hz, H-7), 7.01 (1 H, s, H-3), 7.15 (2 H, t, J = 8.7 Hz, H-3′,5′), 7.18 (2 H, t, J = 8.7 Hz, H-3″,5″), 7.54 (2 H, dd, $J_{H,H}$ = 8.7 Hz, $J_{H,F}$ = 5.3 Hz, H-2″,6″), 7.86 (2 H, dd, $J_{H,H}$ = 8.7 Hz, $J_{H,F}$ = 5.3 Hz, H-2′,6′), 8.13 (1 H, s, H-4).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 44.0, 79.4, 93.4, 101.6, 115.8 (d, $^2J_{C,F}$ = 21.7 Hz), 116.1 (d, $^2J_{C,F}$ = 22.1 Hz), 118.5, 119.1, 124.6, 125.6 (d, $^4J_{C,F}$ = 3.5 Hz), 127.0 (d, $^3J_{C,F}$ = 8.3 Hz), 127.8 (d, $^3J_{C,F}$ = 8.3 Hz), 134.2 (d, $^4J_{C,F}$ = 3.3 Hz), 155.7, 156.9, 157.0, 163.3 (d, $^1J_{C,F}$ = 250.3 Hz), 164.8 (d, $^1J_{C,F}$ = 255.6 Hz), 190.9.

HRMS (ES⁺): m/z [M + H]⁺ calcd for $C_{23}H_{14}{}^{79}BrF_2O_3$: 455.0094; found: 455.0078.

9-Bromo-7-(4-fluorophenyl)-6,7-dihydro-2-(4-methoxyphenyl)furo[3,2-*g*]chromen-5-one (9k)

Yellow solid; yield: 0.12 g (60%); mp 254–256 °C.

IR (ATR): 827, 1016, 1151, 1183, 1225, 1260, 1341, 1412, 1473, 1506, 1611, 1679 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.03 (1 H, dd, J = 4.0, 16.9 Hz, 6-H_a), 3.12 (1 H, dd, J = 11.4, 16.9 Hz, 6-H_b), 3.88 (3 H, s, OCH_3), 5.61 (1 H, dd, J = 4.0, 11.4 Hz, H-7), 6.91 (1 H, s, H-3), 6.99 (2 H, d, J = 8.7 Hz, H-3′,5′), 7.15 (2 H, t, J = 8.7 Hz, H-3″,5″), 7.54 (2 H, t, J = 8.7 Hz, H-2′,6′), 7.80 (2 H, d, J = 8.9 Hz, H-2″,6″), 8.08 (1 H, s, H-4).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 44.1, 55.4, 79.3, 93.2, 100.0, 114.4, 115.8 (d, $^2J_{C,F}$ = 21.9 Hz), 118.0, 118.9, 122.0, 124.9, 126.6, 127.8 (d, $^3J_{C,F}$ = 8.5 Hz), 129.0, 134.3 (d, $^4J_{C,F}$ = 3.4 Hz), 155.4, 158.1, 158.7 (d, $^1J_{C,F}$ = 271.3 Hz), 164.4, 191.0.

HRMS (ES⁻): m/z [M – H]⁻ calcd for $C_{24}H_{15}{}^{79}BrFO_4$: 465.0134; found: 465.0134.

9-Bromo-7-(4-chlorophenyl)-6,7-dihydro-2-phenylfuro[3,2-*g*]chromen-5-one (9l)

Cream solid; yield: 0.10 g (50%); mp 201–203 °C.

IR (ATR): 759, 838, 907, 1014, 1149, 1272, 1339, 1414, 1469, 1492, 1571, 1617, 1682 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.02 (1 H, dd, J = 4.4, 16.9 Hz, 6-H_a), 3.10 (1 H, dd, J = 11.0, 16.9 Hz, 6-H_b), 5.61 (1 H, dd, J = 4.4, 11.0 Hz, H-7), 7.06 (1 H, s, H-3), 7.37–7.53 (7 H, m, ArH), 7.82–7.93 (2 H, m, ArH), 8.09 (1 H, s, H-4).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 44.0, 79.2, 93.4, 101.8, 118.5, 119.0, 124.6, 125.0, 127.3, 128.9, 129.1, 129.2, 129.3, 134.5, 136.9, 155.6, 157.0, 157.9, 190.8.

HRMS (ES⁺): m/z [M + H]⁺ calcd for $C_{23}H_{15}{}^{79}Br{}^{35}ClO_3$: 452.9893; found: 452.9886.

9-Bromo-7-(4-chlorophenyl)-2-(4-fluorophenyl)-6,7-dihydrofuro[3,2-*g*]chromen-5-one (9m)

Cream solid; yield: 0.10 g (50%); mp 260–262 °C.

IR (ATR): 821, 836, 1158, 1227, 1276, 1342, 1412, 1473, 1505, 1602, 1620, 1683 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.03 (1 H, dd, J = 4.3, 16.7 Hz, 6-H_a), 3.11 (1 H, dd, J = 10.9, 16.7 Hz, 6-H_b), 5.62 (1 H, dd, J = 4.3, 10.9 Hz, H-7), 7.00 (1 H, s, H-3), 7.17 (2 H, t, J = 8.8 Hz, H-3′,5′), 7.43 (2 H, d, J = 8.7 Hz, H-3″,5″), 7.50 (2 H, d, J = 8.7 Hz, H-2″,6″), 7.85 (2 H, dd, $J_{H,H}$ = 8.8 Hz, $J_{H,F}$ = 5.2 Hz, H-2′,6′), 8.11 (1 H, s, H-4).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 43.9, 79.3, 93.4, 101.5, 116.1 (d, $^2J_{C,F}$ = 22.1 Hz), 118.5, 119.1, 124.6, 125.6 (d, $^4J_{C,F}$ = 3.4 Hz), 127.0 (d, $^3J_{C,F}$ = 8.4 Hz), 127.3, 129.1, 134.6, 136.8, 155.6, 156.97, 157.98, 163.3 (d, $^1J_{C,F}$ = 250.3 Hz), 190.7.

HRMS (ES⁺): m/z [M + H]⁺ calcd for $C_{23}H_{14}{}^{79}Br{}^{35}ClFO_3$: 470.9799; found: 470.9821.

9-Bromo-7-(4-chlorophenyl)-6,7-dihydro-2-(4-methoxyphenyl)furo[3,2-*g*]chromen-5-one (9n)

Yellow solid; yield: 0.12 g (60%); mp 236–238 °C.

IR (ATR): 822, 1016, 1151, 1183, 1259, 1339, 1412, 1443, 1472, 1506, 1616, 1678 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 3.02 (1 H, dd, *J* = 4.3, 16.8 Hz, 6-H_a), 3.10 (1 H, dd, *J* = 11.0, 16.8 Hz, 6-H_b), 3.87 (3 H, s, OCH_3), 5.62 (1 H, dd, *J* = 4.3, 11.0 Hz, H-7), 6.91 (1 H, s, H-3), 6.99 (2 H, d, *J* = 8.9 Hz, H-3′,5′), 7.43 (2 H, d, *J* = 8.6 Hz, H-3″,5″), 7.50 (2 H, d, *J* = 8.6 Hz, H-2″,6″), 7.80 (2 H, d, *J* = 8.9 Hz, H-2′,6′), 8.06 (1 H, s, H-4).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 44.0, 55.4, 79.2, 93.2, 100.0, 114.4, 118.0, 118.9, 122.0, 125.0, 126.6, 127.3, 129.1, 134.5, 137.0, 155.3, 156.9, 158.0, 160.5, 190.8.

HRMS (ES^+): *m*/*z* $[M + H]^+$ calcd for $C_{24}H_{17}{}^{79}Br^{35}ClO_4$: 482.9999; found: 482.9995.

9-Bromo-6,7-dihydro-7-(4-methoxyphenyl)-2-phenylfuro[3,2-*g*]chromen-5-one (9o)

Orange solid; yield: 0.11 g (55%); mp 177–179 °C.

IR (ATR): 742, 759, 827, 1030, 1150, 1181, 1253, 1339, 1414, 1470, 1516, 1618, 1682 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 3.02 (1 H, dd, *J* = 3.4, 16.9 Hz, 6-H_a), 3.15 (1 H, dd, *J* = 11.9, 16.9 Hz, 6-H_b), 3.84 (3 H, s, OCH_3), 5.58 (1 H, dd, *J* = 3.4, 11.9 Hz, H-7), 6.97 (2 H, d, *J* = 8.0 Hz, H-3″,5″), 7.05 (1 H, s, H-3), 7.35–7.50 (5 H, m, ArH), 7.86 (2 H, d, *J* = 8.0 Hz, H-2″,6″), 8.10 (1 H, s, H-4).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 43.9, 55.3, 79.8, 93.3, 101.9, 114.2, 118.5, 119.1, 124.4, 125.0, 127.5, 128.9, 129.2, 129.3, 130.4, 155.9, 157.0, 157.7, 159.9, 191.5.

HRMS (ES^+): *m*/*z* $[M + H]^+$ calcd for $C_{24}H_{18}{}^{79}BrO_4$: 449.0388; found: 449.0383.

9-Bromo-2-(3-fluorophenyl)-6,7-dihydro-7-(4-methoxyphenyl)furo[3,2-*g*]chromen-5-one (9p)

Orange solid; yield: 0.12 g (60%); mp 192–194 °C.

IR (ATR): 784, 821, 834, 883, 929, 1031, 1171, 1252, 1414, 1464, 1484, 1513, 1615, 1683 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 3.03 (1 H, dd, *J* = 3.5, 16.9 Hz, 6-H_a), 3.16 (1 H, dd, *J* = 11.8, 16.9 Hz, 6-H_b), 3.84 (3 H, s, OCH_3), 5.59 (1 H, dd, *J* = 3.5, 11.8 Hz, H-7), 6.97 (2 H, d, *J* = 8.6 Hz, H-3″,5″), 7.05–7.15 (2 H, m, H-3 and H-4′), 7.43 (1 H, dd, *J* = 2.2, 7.9 Hz, H-6′), 7.47 (2 H, d, *J* = 8.6 Hz, H-2″,6″), 7.55 (1 H, dd, *J* = 2.2, 7.9 Hz, H-2′), 7.62–7.65 (1 H, d, *J* = 8.6 Hz, H-3′), 8.12 (1 H, s, H-4).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 43.8, 55.3, 79.8, 93.4, 103.0, 111.9 (d, $^2J_{C,F}$ = 23.7 Hz), 114.2, 116.0 (d, $^2J_{C,F}$ = 21.3 Hz), 118.8, 119.3, 120.7 (d, $^4J_{C,F}$ = 3.0 Hz), 124.1, 127.5, 130.3, 130.6 (d, $^3J_{C,F}$ = 8.4 Hz), 130.7, 131.3 (d, $^3J_{C,F}$ = 8.6 Hz), 156.2, 157.0, 159.9, 163.1 (d, $^1J_{C,F}$ = 246.1 Hz), 191.4.

HRMS (ES^+): *m*/*z* $[M + H]^+$ calcd for $C_{24}H_{17}{}^{79}BrFO_4$: 467.0294; found: 467.0281.

9-Bromo-2-(4-fluorophenyl)-6,7-dihydro-7-(4-methoxyphenyl)furo[3,2-*g*]chromen-5-one (9q)

Yellow solid; yield: 0.12 g (60%); mp 216–218 °C.

IR (ATR): 813, 831, 1032, 1154, 1176, 1222, 1254, 1335, 1468, 1504, 1516, 1614, 1684 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 3.01 (1 H, dd, *J* = 3.5, 16.9 Hz, 6-H_a), 3.15 (1 H, dd, *J* = 11.9, 16.9 Hz, 6-H_b), 3.84 (3 H, s, OCH_3), 5.58 (1 H, dd, *J* = 3.5, 11.9 Hz, H-7), 6.95–6.99 (3 H, m, H-3 and H-3″,5″), 7.15 (2 H, t, *J* = 8.8 Hz, H-3′,5′), 7.47 (2 H, d, *J* = 8.4 Hz, H-2″,6″), 7.83 (2 H, t, $J_{H,H}$ = 8.8 Hz, $J_{H,F}$ = 5.3 Hz, H-2′,6′), 8.09 (1 H, s, H-4).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 43.8, 55.3, 79.8, 93.3, 101.5, 114.2, 116.1 (d, $^2J_{C,F}$ = 22.2 Hz), 118.4, 119.1, 124.3, 125.6 (d, $^4J_{C,F}$ = 3.4 Hz), 126.9 (d, $^3J_{C,F}$ = 8.5 Hz), 127.5, 130.3, 156.0, 156.7, 156.9, 159.8, 163.2 (d, $^1J_{C,F}$ = 249.9 Hz), 191.5.

HRMS (ES^-): *m*/*z* $[M - H]^-$ calcd for $C_{24}H_{15}{}^{79}BrFO_4$: 465.0138; found: 465.0134.

9-Bromo-6,7-dihydro-2,7-bis(4-methoxyphenyl)furo[3,2-*g*]chromen-5-one (9r)

Orange solid; yield: 0.12 g (60%); mp 175–178 °C.

IR (ATR): 794, 829, 1030, 1151, 1177, 1252, 1338, 1413, 1471, 1507, 1616, 1686 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 3.01 (1 H, dd, *J* = 3.4, 16.9 Hz, 6-H_a), 3.15 (1 H, dd, *J* = 12.0, 16.9 Hz, 6-H_b), 3.84 (3 H, s, OCH_3), 3.87 (3 H, s, OCH_3), 5.58 (1 H, dd, *J* = 3.4, 12.0 Hz, H-7), 6.91 (1 H, s, H-3), 6.97 (2 H, d, *J* = 8.7 Hz, H-3″,5″), 6.99 (2 H, d, *J* = 8.7 Hz, H-3′,5′), 7.47 (2 H, d, *J* = 8.7 Hz, H-2″,6″), 7.80 (2 H, d, *J* = 8.7 Hz, H-2′,6′), 8.07 (1 H, s, H-4).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 43.9, 55.3, 55.4, 79.7, 93.2, 100.1, 114.2, 114.3, 118.0, 119.0, 122.1, 124.7, 126.6, 127.5, 130.5, 155.7, 156.9, 157.8, 159.8, 160.4, 191.6.

HRMS (ES^+): *m*/*z* $[M + H]^+$ calcd for $C_{25}H_{20}{}^{79}BrO_5$: 479.0494; found: 479.0502.

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Supporting Information

Supporting information for this article is available online at https://doi.org/10.1055/s-0039-1690001.

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