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Ruthenium(II)-Catalyzed C3 Arylation of 2-Aroylbenzofurans with Arylboronic Acids/Aryltrifluoroborates via Carbonyl-Directed C−H Bond Activation

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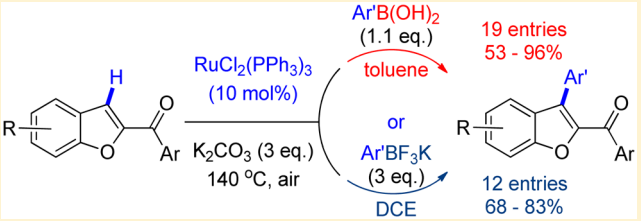
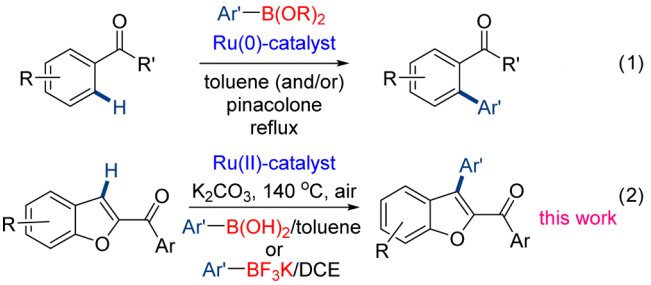
Supporting Information

ABSTRACT: The Ru(II)-catalyzed carbonyl-directed C−H activation with (hetero)arylboron reagents has been executed for the synthesis of 2-aroyl-3-(hetero)arylbenzofurans. A hypothesis founded upon the involvement of an active carbonatoruthenium(II) complex for a coordinative insertion and the aerobic oxidation of the *in situ* generated Ru(0) to Ru(II), to continue the catalytic cycle, has been extended.



The direct and directed catalytic activation of aryl C−H bonds and their functionalization with various electrophiles is one of the contemporary approaches for the construction of various types of C−C and C−heteroatom bonds.[1] The step and atom economies associated with this C−H activation approach have led to a revolution in synthetic methodologies, and a plethora of new methods that can competitively replace several classical catalytic cross-coupling reactions have been documented, and a wide-range of metal complexes have been explored in this pursuit.[2] Arguably, the ruthenium complexes, because of their cost, compatibility with many oxidants, stability, and ready suitability at least for some of the complexes to carry the reactions even in water, have emerged as powerful catalysts in this "C−H activation and functionalization" domain.[3]

Benzofuran is one of the commonly encountered structural units in natural products.[4] In recent years, benzofuran derivatives have seen applications in the development of pharmaceutical agents and functionalized materials.[5] Particularly, the 2-aroyl-3-arylbenzofuran structural motifs are present in many natural products and have been shown to display a range of biological activities.[6] General approaches reported for the synthesis of these 2-aroyl-3-arylbenzofuran substrates involve the use of classical acid/base-mediated condensations and subsequent aroylation or arylation.[7] Despite the fact that the core of 2-aroylbenzofuran is integrated with a readily required carbonyl-directing group, the utilization of this handle for the directed alkylation or arylation has not been used until recently.[8−10] Recently, the Bertounesque and Doucet groups documented the Pd-catalyzed C3-arylation of C2-substituted benzofurans using aryl bromides,[9] and alkylation with acrylates was documented by our group using Ru complexes.[10] Given their significant biological activities and also considering the fact that the ruthenium complexes are cheaper and stable with air and moisture, the possibility of Ru-catalyzed C3-arylation of C2-aroylbenzofurans has been undertaken.[10−13] There was only a single report on the carbonyl-directed arylation with the Ru complexes. In 2003, Kakiuchi described the Ru(0)-catalyzed carbonyl-directed ortho arylation of acetophenones with arylboronates (eq 1).[14] Apart from, and to the best of our



knowledge, there has been no report so far on this aspect. Herein we describe the Ru(II)-catalyzed carbonyl-directed C3-arylation of 2-aroylbenzofurans either with arylboronic acids or with aryl-BF_3K salts (eq 2).[15,16]

Initially, the feasibility of arylation of benzofuran **1a** with 4-acetylphenylboronic acid **2a** was examined in the presence of the $RuCl_2(PPh_3)_3$/AgOAc catalyst system under the conditions that have been earlier established for the alkylation of **1a** with acrylates.[10] The reaction was conducted by heating a mixture of substrates **1a** and **2a** in the presence of catalyst $RuCl_2(PPh_3)_3$ (10 mol %), K_2CO_3 (3.0 equiv), and cocatalyst AgOAc (30 mol %) in toluene at 140 °C for 24 h in a screw-capped sealed tube under the argon atmosphere. However, the reaction was incomplete and afforded the required **3aa** in 13% yield (Table 1, entry 1). With this initial optimiztic result, the reaction was explored by varying the co-oxidants like $Cu(OAc)_2{\cdot}2H_2O$/$AgSbF_6$ and Ad-CO_2H (Table 1, entries 2 and 3). With the former, the yield of **3aa** was improved up to 37%. Surprisingly,

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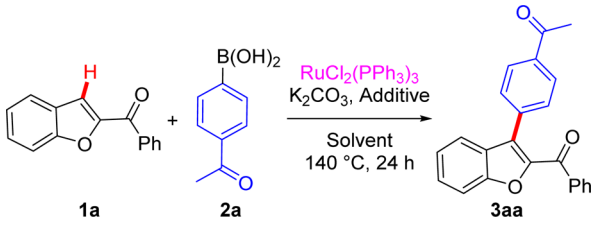
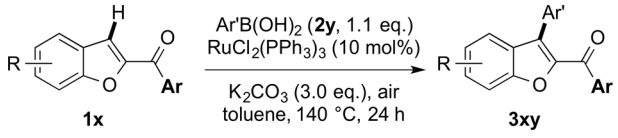
Table 1. Optimization of C3-Arylation of Benzofuran 1a with Boronic Acid 2a[a]

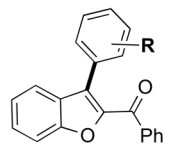


entry	additive	base	solvent	yield (%)[c]
1[b]	AgOAc	K_2CO_3	toluene	13(71)[d]
2[b]	Ad-CO_2H	K_2CO_3	toluene	–
3[b]	$Cu(OAc)_2{\cdot}2H_2O$, $AgSbF_6$	K_2CO_3	toluene	37(78)[d]
4	–	**K_2CO_3**	**toluene**	**87**
5	–	K_2CO_3	DCE	81
6	–	K_2CO_3	1,4-dioxane	42(83)[d]
7	–	K_2CO_3	NMP	53(84)[d]
8	–	K_2CO_3	DMF	11(58)[d]
9	–	Na_2CO_3	toluene	78
10	–	Cs_2CO_3	toluene	68(79)[d]

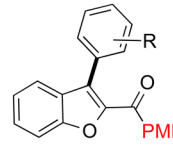
[a]Reaction conditions: **1a** (0.2 mmol), **2a** (0.22 mmol), $RuCl_2(PPh_3)_3$ (0.02 mmol), base (0.6 mmol), and additive (0.06 mmol); 140 °C, 24 h, solvent (2 mL). [b]Under argon atmosphere. [c]Isolated yields. [d]Yields (based on recovered **1a**).

Table 2. Reaction Scope of C3-Arylation with Boronic Acids 2

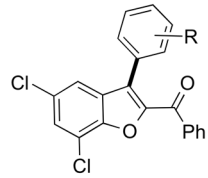




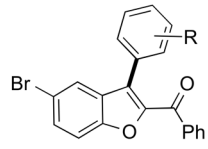
3aa, 87% (R = 4-Ac)
3ab, 89% (R = 3-OMe)
3ac, 71% (R = 4-Br)



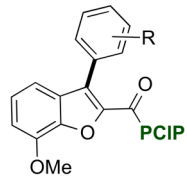
3bb, 89% (R = 3-OMe)
3bd, 79% (R = 4-F)
3be, 58% (R = 3-NO_2)
3bf, 93% (R = 3,4-dichloro)
3bg, 85% (R = 3-Ac)
(PMP = 4-methoxyphenyl)



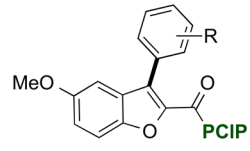
3ca, 96% (R = 4-Ac)
3cb, 93% (R = 3-OMe)
3cd, 81% (R = 4-F)
3cg, 92% (R = 3-Ac)
3ch, 92% (R = 3,4-dimethoxy)



3df, 83% (R = 3,4-dichloro)
3dh,86% (R = 3,4-dimethoxy)



3ea, 64% (R = 4-Ac)
3eb, 53% (R = 3-OMe)



3fa, 68% (R = 4-Ac)
3fg, 75% (R = 3-Ac)
(**PCIP = 4-chlorophenyl**)

the reaction in the presence of Ad-CO_2H was sluggish, and no product formation was noticed. Quite interestingly, when the reaction was conducted only in the presence of catalyst/K_2CO_3 and without any other additive, the complete consumption of starting **1a** was noticed and provided **3aa** in 87% isolated yield. With these promising results in hand, we next examined the compatibility of other solvents like 1,2-dichloroethane (DCE), 1,4-dioxane, NMP, and DMF (Table 1, entries 4–8) as well as other bases. It was found that toluene was the best solvent for the present arylation reaction. As far as the other bases examined, Na_2CO_3 and Cs_2CO_3 gave 78% and 68% yield respectively (Table 1, entries 9 and 10).

Next, the scope and limitations of the ruthenium-catalyzed arylation reaction have been examined by employing variously substituted benzofurans and arylboronic acids. Functional groups like acetyl, bromo, chloro, fluoro, and methoxy on the phenylboronic acid unit were found to be tolerated under these conditions and gave the corresponding products in excellent yields. These results indicated that the reaction is not sensitive to the electronic properties of the substituents present on the any boronic acids. Coming to the effect of the substituents on the benzofuran reactivity, 5,7-dichloro-substituted benzofuran **3c** delivered the arylation products in excellent yields (Table 2, entries **3ca**–**3ch**). It has been observed that the yields are moderate when the benzofuran ring contains electron-donating substituents like the methoxy group (Table 2, entries **3ea**, **3eb**, **3fa**, **3fg**), which is expected as the C3–H bond should be less acidic and more difficult to deprotonate. The successful reaction of 4-bromophenylboronic acid (**2c**) with benzofuran **1a** is noteworthy, since the reaction specifically worked with the boronic acid counterpart and not with the bromide (Table 2, entry **3ac**).

Having established the arylation with various arylboronic acids, we next focused our attention on the arylation with potassium aryltrifluoroborates considering the superior air and moisture stability and the better nucleophilicity over the corresponding aryl boronic acid derivatives.[16c] In the first instance, the reaction was carried under the conditions optimized with the arylboronic acids (3.0 equiv K_2CO_3 in toluene at 140 °C for 24 h). The reaction proceeded smoothly and afforded the required **3ai** in moderate yield (Table 3, entry 1). Like with the boronic acids, the presence of carboxylic acid additives has a negative effect (Table 3, entries 2–6). Among the various solvents screened, in DCE the yield has been further improved (Table 3, entries 7–10). The variation in base did not show any promising effect on the reaction (Table 3, entries 11 and 12). To this end, when we employed 3.0 equiv of **2i**, the yield was improved from 67% to 83% (Table 3, entry 13). The requirement of excess of **2i** may be due to its lower solubility as has been seen earlier.[16a]

Table 4 reveals the scope of the C2 arylation of various 2-aroylbenzofurans **1** with potassium (hetero)aryltrifluoroborates **2**. As has been seen earlier, the nature of the substituents on the aryl ring does not have much influence on the reaction outcome. Impressively, the reaction with 3-furyltrifluoroborate **2k** also proceeded smoothly and provided the corresponding products in very good yields.

Next we proceeded further to understand the course of the reaction mechanism. As mentioned earlier, the only available reports on the Ru(0)-catalyzed carbonyl-directed C–H arylation are from Kakiuchi's group where arylboronates were employed as the electrophiles.[14] The *in situ* generation of a

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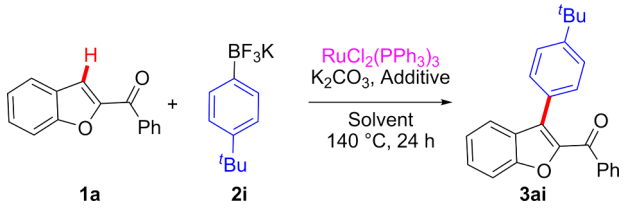
Table 3. Optimization of C3 Arylation of Benzofuran 1a with Aryltrifluoroborate Salt 2i[a]

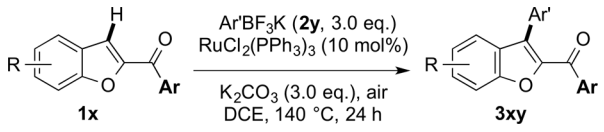


1a 2i 3ai

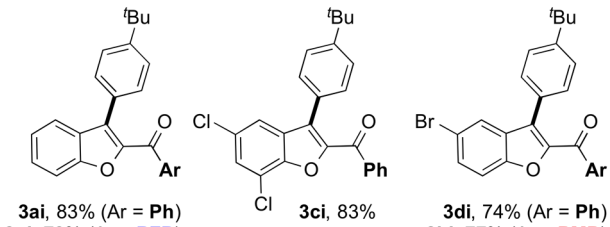
entry	additive	base	solvent	yield (%)[c]
1	–	K_2CO_3	toluene	58
2[b]	AgOAc	K_2CO_3	toluene	35(76)[d]
3[b]	AgOTf	K_2CO_3	toluene	28(68)[d]
4[b]	Ad-CO_2H	K_2CO_3	1,4-dioxane	9(63)[d]
5[b]	$Cu(OAc)_2{\cdot}2H_2O$, $AgSbF_6$	K_2CO_3	toluene	–
6[b]	KPF_6	K_2CO_3	toluene	15(64)[d]
7	–	K_2CO_3	DCE	67
8	–	K_2CO_3	1,4-dioxane	32
9	–	K_2CO_3	NMP	42
10	–	K_2CO_3	DMF	–
11	–	Na_2CO_3	DCE	44
12	–	Cs_2CO_3	DCE	51
13	–	**K_2CO_3**	**DCE**	**83**[e]

[a]Reaction conditions: **1a** (0.2 mmol), **2i** (0.24 mmol), $RuCl_2(PPh_3)_3$ (0.02 mmol), base (0.6 mmol), and additive (0.06 mmol); 140 °C, 24 h, solvent (2 mL). [b]Under argon atmosphere. [c]Isolated yields. [d]Yields (based on recovered **1a**). [e]**2i** 0.6 mmol was used.

Table 4. Reaction Scope of C3-Arylation with Potassium Aryltrifluorolborates 2



1x 3xy



3ai, 83% (Ar = **Ph**)
3gi, 79% (Ar = **PFP**)

3ci, 83%

3di, 74% (Ar = **Ph**)
3hi, 77% (Ar = **PMP**)

3aj, 68% (Ar = **Ph**)
3bj, 69% (Ar = **PMP**)
3gj, 73% (Ar = **PFP**)

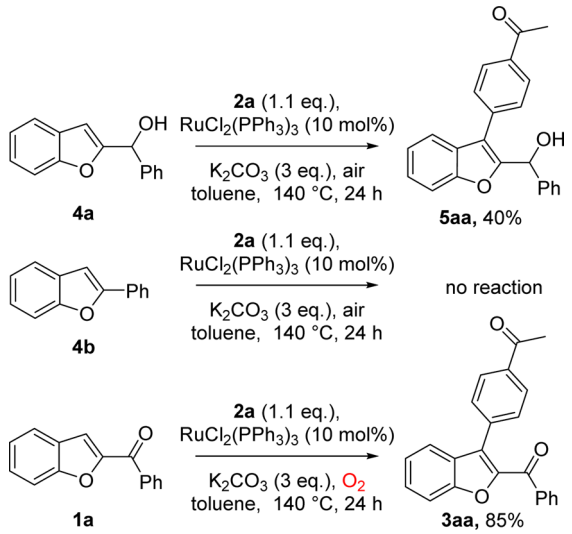
3ak, 70% (Ar = **Ph**)
3bk, 83% (Ar = **PMP**)

3dk, 81% (R = Br, Ar = **Ph**)
3fk, 73% (R = OMe, Ar = **PCIP**)

PFP = 4-fluorophenyl; **PMP** = 4-methoxyphenyl; **PCIP** = 4-chlorophenyl

Ru(0) complex from the employed $RuH_2(CO)(PPh_3)_3$ complex and the subsequent carbonyl-directed oxidative insertion across the Ar–H bond has been proposed as the key step. It has been proposed that the reduction of one molecule of either of the acetophenone substrates or an added aliphatic ketone to the corresponding alcohol is inevitable for the hydride transfer from the initially generated Ar–Ru–H species and the resulting alcohol assists the transfer of the aryl group from the boronate to the Ru-center. A final reductive elimination results in the formation of product and the regeneration of initial Ru(0)-complex to continue the catalytic cycle. Coming to the current conditions for the carbonyl-directed arylation, both the substrate and boronic acid were employed in equal molar proportions, and the yields were excellent. An examination of the course of the reaction with HPLC revealed that there is no formation of the corresponding alcohol **4a**, which is expected if the Ru–H intermediate is involved. In addition, we examined the arylation of **4a** with **2a** under established reaction conditions (Scheme 1). The reaction

Scheme 1. Control Experiments



was sluggish, and the arylation product **5aa** was obtained 40% yield along with portion of **4a** being recovered. The HPLC analysis of this reaction mixture revealed that there were no traces of **3aa** or **1a** resulting from the oxidation of either product **5aa** or starting **4a**. When simple 2-phenylbenzofuran **4b** was used as a substrate, there was no arylation under these conditions. This revealed that the current arylation needs a carbonyl as a directing group. Now, the important question is about the oxidation of the resulting Ru(0)-species after the final reductive elimination, thus completing the catalytic cycle. At this stage, some reports on aerobic oxidation by palladium[17] and rhodium[18] catalysts and also a recent report on ruthenium from Ackermann's group[19] revealing the reoxidation of Ru(0) by molecular oxygen in a Ru(II)-catalyzed oxidative alkyne annulation have rescued our hypothesis. Considering this, the arylation of **1a** with **2a** was examined under the established conditions, albeit purging the reaction mixture with oxygen prior to heating. Under these conditions, the reaction proceeded smoothly and provided the expected arylation product **3aa** in 85% yield. This suggests that the aerobic oxidation of the intermediate Ru(0)-complex in the presence of bi/carbonate regenerates the carbonatoruthenium(II) complex (**I**), to continue the catalytic cycle.

With this available information in hand, and based upon the earlier studies, we propose the following tentative mechanism (Scheme 2).[20] First, the catalyst $RuCl_2(PPh_3)_3$ reacts with K_2CO_3 to form the active carbonatoruthenium(II) complex **I**.[21] Then the Ru-metal reversibly coordinates with carbonyl to

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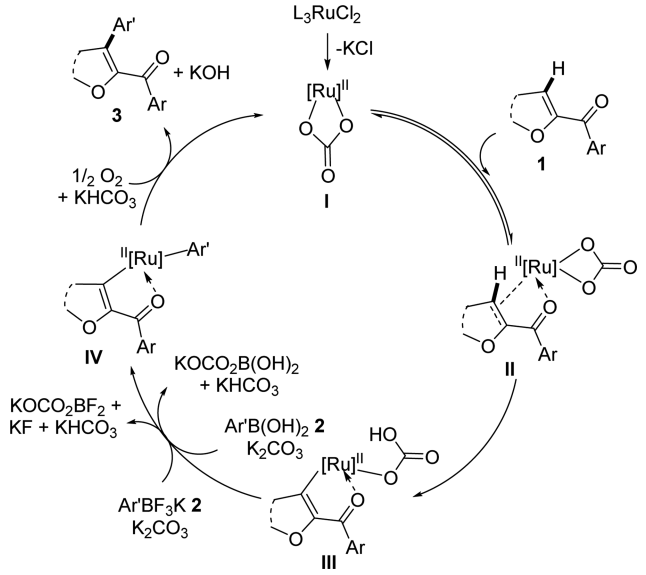
Scheme 2. Plausible Reaction Mechanism



form the intermediate **II**. Next, the ruthenium interacts with the ortho-carbon atom to favor the concerted metalation deprotonation by the coordinated carbonate to deliver the cyclometalated intermediate **III**.[22] Subsequently, the transmetalation of **III** takes place with the arylboronic reagents to yield the Ru−Ar′ species **IV**. Poor yields were obtained when AgOAc was employed, and the complete lack of reactivity when Ad-CO_2H was employed as an additive reveals that the steric crowding around the Ru-center in the intermediate metallacycle **III** is detrimental in the transmetalation with the arylboron reagents **2**, leading to the [Ru]−Ar′ species **IV**. Finally, the intermediate species **IV** undergoes a reductive elimination reaction resulting in the arylation product **3** and a Ru(0)-complex, which was subsequently oxidized by molecular oxygen to Ru(II)-complex (**I**) that continues the catalytic cycle.

In conclusion, a carbonyl-directed ruthenium(II)-catalyzed C3−H activation and (hetero)arylation of 2-aroylbenzofurans employing either (hetero)aryl-boronic acids or their corresponding trifluoroborate salts, has been documented. The reactions proceed smoothly in the presence of K_2CO_3, and added carboxylates were found to be detrimental to the reactivity. This has been attributed to the steric crowding caused by the corresponding carboxylate during the transmetalation step. The control experiments revealed that the directing group is essential and that crucial reoxidation of Ru(0) with molecular oxygen assists to continue the catalytic cycle.

EXPERIMENTAL SECTION

General Information. Reactions were carried out in anhydrous solvents in oven-dried glassware. NMR spectra were recorded on 200, 400, and 500 MHz spectrometers. TMS was used as an internal standard, and chemical shifts were reported in parts per million (δ) relative to internal standard TMS (0 ppm) and for $CDCl_3$, 25 °C (7.25 ppm for ^{1}H NMR; and central peak is 77.0 ppm in $CDCl_3$ for ^{13}C NMR). Mass spectroscopy was carried out on Hybrid Quadrupole-TOF LC/MS/MS. Melting points are uncorrected.

General Procedure. 2-Aroylbenzofuran (0.2 mmol) was placed in a screw cap pressure tube and dissolved in anhydrous solvent (2 mL). To the reaction vessel arylboronic acid (0.22 mmol) or potassium aryltrifluoroborate (0.6 mmol), K_2CO_3 (0.6 mmol), and $RuCl_2(PPh_3)_3$ (10 mol %) were added. The solution was then stirred at 140 °C (bath temperature) for 24 h. The reaction mixture was cooled to room temperature. The solvent was evaporated, and the crude mixture was purified by silica gel (230−400 mesh) column chromatography (0 → 15% pet. ether/EtOAc).

1-(4-(2-Benzoylbenzofuran-3-yl)phenyl)ethan-1-one (***3aa***).[9b] Pale yellow solid; 87% yield (60 mg); mp 87−89 °C; R_f = 0.2 (pet. ether/EtOAc = 9:1); ^{1}H NMR (500 MHz, $CDCl_3$): δ 2.62 (s, 3H), 7.36−7.41 (m, 3H), 7.51−7.56 (m, 2H), 7.62−7.67 (m, 4H), 7.94 (d, J = 7.6 Hz, 2H), 7.99 (d, J = 8.2 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 26.7 (q), 112.5 (d), 122.0 (d), 124.3 (d), 127.6 (s), 128.2 (s), 128.3 (d, 2C), 128.3 (d, 2C), 128.5 (d), 129.9 (d, 2C), 130.2 (d, 2C), 133.0 (d), 136.0 (s), 136.6 (s), 137.0 (s), 147.5 (s), 154.5 (s), 185.4 (s), 197.6 (s) ppm; IR ($CHCl_3$) 3022, 1681, 1649, 1606, 1567, 1367, 1265, 1008, 766 cm^{-1}; HRMS (ESI) calcd for $C_{23}H_{17}O_3$ $(M + H)^+$ 341.1172, found 341.1173.

(3-(3-Methoxyphenyl)benzofuran-2-yl)(phenyl)methanone (***3ab***). White solid; 89% yield (59 mg); mp 84−86 °C; R_f = 0.4 (pet. ether/EtOAc = 9:1); ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.74 (s, 3H), 6.87 (ddd, J = 0.9, 2.3, 8.2 Hz, 1H), 6.98 (dd, J = 1.3, 2.3 Hz, 1H), 7.07(dt, J = 1.1, 7.6 Hz, 1H), 7.27(t, J = 7.9 Hz, 1H), 7.31−7.37 (m, 3H), 7.47 (tt, J = 1.4, 7.5 Hz, 1H), 7.53 (ddd, J = 1.4, 7.3, 8.3 Hz, 1H), 7.64 (d, J = 8.2 Hz, 1H), 7.72 (d, J = 7.8 Hz, 1H), 7.84−7.86 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 55.3 (q), 112.4 (d), 114.3 (d), 115.4 (d), 122.4 (d), 122.4 (d), 123.9 (d), 128.0 (s), 128.1 (d, 2C), 128.2 (d), 129.2 (s), 129.4 (d), 129.8 (d, 2C), 132.1 (s), 132.7 (d), 137.3 (s), 147.1 (s), 154.6 (s), 159.5 (s), 185.9 (s) ppm; IR ($CHCl_3$) 3021, 1646, 1597, 1481, 1436, 1217, 1170, 1021, 760 cm^{-1}; HRMS (ESI) calcd for $C_{22}H_{17}O_3$ $(M + H)^+$ 329.1172, found 329.1170.

(3-(4-Bromophenyl)benzofuran-2-yl)(phenyl)methanone (***3ac***). White solid; 71% yield (54 mg); mp 115−117 °C; R_f = 0.4 (pet. ether/EtOAc = 9.5:0.5); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.34−7.45 (m, 5H), 7.52−7.55 (m, 4H), 7.64 (t, J = 7.9 Hz, 2H), 7.91 (d, J = 7.8 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 112.5 (d), 122.0 (d), 122.6 (s), 124.1 (d), 127.8 (s), 128.2 (d, 2C), 128.4 (d), 128.4 (s), 129.7 (s), 129.9 (d, 2C), 131.5 (d, 2C), 131.6 (d, 2C), 132.9 (d), 137.1 (s), 147.2 (s), 154.5 (s), 185.4 (s) ppm; IR ($CHCl_3$) 3022, 1648, 1596, 1485, 1432, 1216, 1116, 764, 672 cm^{-1}; HRMS (ESI) calcd for $C_{21}H_{14}BrO_2$ $(M + H)^+$ 377.0172, found 377.0168.

(4-Methoxyphenyl)(3-(3-methoxyphenyl)benzofuran-2-yl)-methanone (***3bb***). Yellow oil; 89% yield (63 mg); R_f = 0.4 (pet. ether/EtOAc = 9:1); ^{1}H NMR (500 MHz, $CDCl_3$): δ 3.76 (s, 3H), 3.84 (s, 3H), 6.84 (d, J = 8.8 Hz, 2H), 6.89 (dd, J = 2.2, 8.1 Hz, 1H), 7.03 (s, 1H), 7.10 (d, J = 7.5 Hz, 1H), 7.30 (t, J = 8.0 Hz, 1H), 7.34 (t, J = 7.5 Hz, 1H), 7.51 (t, J = 7.4 Hz, 1H), 7.63 (d, J = 8.4 Hz, 1H), 7.73 (d, J = 8.0 Hz, 1H), 7.91 (d, J = 8.8 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 55.3 (q), 55.5 (q), 112.3 (d), 113.5 (d, 2C), 114.1 (d), 115.4 (d), 122.2 (d), 122.4 (d), 123.8 (d), 127.8 (d), 128.0 (s), 128.1 (s), 129.4 (d), 130.0 (s), 132.3 (d, 2C), 132.3 (s), 147.5 (s), 154.4 (s), 159.5 (s), 163.5 (s), 184.3 (s) ppm; IR ($CHCl_3$) 3022, 1639, 1598, 1425, 1254, 1216, 1119, 765 cm^{-1}; HRMS (ESI) calcd for $C_{23}H_{19}O_4$ $(M + H)^+$ 359.1278, found 359.1274.

(3-(4-Fluorophenyl)benzofuran-2-yl)(4-methoxyphenyl)-methanone (***3bd***). White solid; 79% yield (54 mg); mp 114−116 °C; R_f = 0.5 (pet. ether/EtOAc = 9:1); ^{1}H NMR (500 MHz, $CDCl_3$): δ 3.86 (s, 3H), 6.88 (d, J = 8.7 Hz, 2H), 7.10 (t, J = 8.6 Hz, 2H), 7.35 (t, J = 7.5 Hz, 1H), 7.52 (t, J = 6.4 Hz, 3H), 7.63(d, J = 8.5 Hz, 1H), 7.66 (d, J = 7.9 Hz, 1H), 7.96 (d, J = 8.5 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 55.5 (q), 112.4 (d), 113.6 (d, 2C), 115.5 (d, J = 21.9 Hz, 2C), 122.0 (d), 124.0 (d), 127.1 (d, J = 2.9 Hz), 127.5 (s), 128.0 (d), 128.0 (s), 129.8 (s), 131.8 (d, J = 8.6 Hz, 2C), 132.4 (d, 2C), 147.6 (s), 154.4 (s), 162.6 (d, J = 248.0 Hz), 163.6 (s), 184.0 (s) ppm; IR ($CHCl_3$) 3021, 1643, 1601, 1568, 1423, 1221, 1025, 765 cm^{-1}; HRMS (ESI) calcd for $C_{22}H_{16}FO_3$ $(M + H)^+$ 347.1078, found 347.1078.

(4-Methoxyphenyl)(3-(3-nitrophenyl)benzofuran-2-yl)-methanone (***3be***). Pale yellow solid; 58% yield (43 mg); mp 131−133 °C; R_f = 0.3 (pet. ether/EtOAc = 9:1); ^{1}H NMR (500 MHz, $CDCl_3$): δ 3.87 (s, 3H), 6.93 (d, J = 8.8 Hz, 2H), 7.40 (t, J = 7.4 Hz, 1H), 7.56 (t, J = 7.5 Hz, 1H), 7.60−7.68 (m, 3H), 7.93 (d, J = 7.6 Hz, 1H), 8.03 (d, J = 8.8 Hz, 2H), 8.25 (d, J = 8.2 Hz, 1H), 8.45 (s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 55.5 (q), 112.6 (d), 113.7 (d, 2C), 121.5 (d),

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123.1 (d), 124.4 (d), 124.9 (d), 126.2 (s), 127.4 (s), 128.4 (d), 129.3 (d), 129.6 (s), 132.5 (d, 2C), 133.1 (s), 136.2 (d), 148.2 (s), 148.3 (s), 154.3 (s), 163.8 (s), 183.5 (s) ppm; IR ($CHCl_3$) 3022, 1642, 1597, 1527, 1425, 1217, 1027, 766 cm^{-1}; HRMS (ESI) calcd for $C_{22}H_{16}NO_5$ $(M + H)^+$ 374.1023, found 374.1022.

*(3-(3,4-Dichlorophenyl)benzofuran-2-yl)(4-methoxyphenyl)-methanone (**3bf**).* White solid; 93% yield (73 mg); mp 119−121 °C; R_f = 0.4 (pet. ether/EtOAc = 9:1); ^1H NMR (500 MHz, $CDCl_3$): δ 3.88 (s, 3H), 6.92 (d, J = 8.7 Hz, 2H), 7.36−7.41 (m, 2H), 7.49 (d, J = 8.3 Hz, 1H), 7.53 (t, J = 7.3 Hz, 1H), 7.63−7.66 (m, 3H), 8.00 (d, J = 8.6 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 55.5 (q), 112.5 (d), 113.7 (d, 2C), 121.7 (d), 124.2 (d), 126.1 (s), 127.6 (s), 128.2 (d), 129.4 (d), 129.7 (s), 130.4 (d), 131.2 (s), 131.6 (d), 132.4 (d, 2C), 132.4 (s), 132.6 (s), 147.9 (s), 154.3 (s), 163.8 (s), 183.6 (s) ppm; IR ($CHCl_3$) 3021, 1639, 1597, 1469, 1421, 1217, 1027, 762 cm^{-1}; HRMS (ESI) calcd for $C_{22}H_{15}Cl_2O_3$ $(M + H)^+$ 397.0393, found 397.0394.

*1-(3-(2-(4-Methoxybenzoyl)benzofuran-3-yl)phenyl)ethan-1-one (**3bg**).* White solid; 85% yield (62 mg); mp 81−83 °C; R_f = 0.5 (pet. ether/EtOAc = 8.5:1.5); ^1H NMR (200 MHz, $CDCl_3$): δ 2.59 (s, 3H), 3.85 (s, 3H), 6.85−6.89 (m, 2H), 7.32−7.40 (m, 1H), 7.48−7.58 (m, 2H), 7.63−7.68 (m, 2H), 7.77 (dt, J = 1.5, 7.6 Hz, 1H), 7.96 (d, J = 8.8 Hz, 3H), 8.12 (t, J = 1.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 26.7 (q), 55.5 (q), 112.4 (d), 113.6 (d, 2C), 121.9 (d), 124.1 (d), 127.6 (s), 127.8 (s), 128.0 (d), 128.1 (d), 128.7 (d), 129.8 (s), 130.0 (d), 131.7 (s), 132.4 (d, 2C), 134.6 (d), 137.2 (s), 147.8 (s), 154.4 (s), 163.6 (s), 183.9 (s), 197.7 (s) ppm; IR ($CHCl_3$) 3022, 1684, 1600, 1426, 1298, 1218, 1026, 767 cm^{-1}; HRMS (ESI) calcd for $C_{24}H_{19}O_4$ $(M + H)^+$ 371.1278, found 371.1278.

*1-(4-(2-Benzoyl-5,7-dichlorobenzofuran-3-yl)phenyl)ethan-1-one (**3ca**).* White solid; 96% yield (81 mg); mp 168−170 °C; R_f = 0.2 (pet. ether/EtOAc = 9:1); ^1H NMR (500 MHz, $CDCl_3$): δ 2.63 (s, 3H), 7.45 (t, J = 7.8 Hz, 2H), 7.52−7.59 (m, 3H), 7.61 (d, J = 8.2 Hz, 2H), 8.01−8.03 (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 26.7 (q), 118.8 (s), 120.0 (d), 127.7 (s), 128.3 (d), 128.5 (d, 2C), 128.6 (d, 2C), 129.9 (s), 130.0 (d, 4C), 130.3 (s), 133.6 (d), 134.7 (s), 136.3 (s), 137.0 (s), 148.9 (s), 149.0 (s), 184.3 (s), 197.5 (s) ppm; IR ($CHCl_3$) 3024, 1678, 1592, 1418, 1217, 1119, 761 cm^{-1}; HRMS (ESI) calcd for $C_{23}H_{14}Cl_2O_3Na$ $(M+Na)^+$ 431.0212, found 431.0214.

*(5,7-Dichloro-3-(3-methoxyphenyl)benzofuran-2-yl)(phenyl)-methanone (**3cb**).* Brown solid; 93% yield (76 mg); mp 113−115 °C; R_f = 0.4 (pet. ether/EtOAc = 9:1); ^1H NMR (400 MHz, $CDCl_3$): δ 3.77 (s, 3H), 6.92 (dd, J = 2.3, 8.3 Hz, 1H), 6.97 (t, J = 2.2 Hz, 1H), 7.04 (d, J = 7.7 Hz, 1H), 7.32 (t, J = 7.8 Hz, 1H), 7.39 (t, J = 7.8 Hz, 2H), 7.51−7.55 (m, 2H), 7.58 (d, J = 1.9 Hz, 1H), 7.92−7.94 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 55.3 (q), 114.5 (d), 115.4 (d), 118.6 (s), 120.4 (d), 122.1 (d), 128.0 (d), 128.3 (d, 2C), 128.5 (s), 129.7 (d), 129.9 (s), 129.9 (d, 2C), 130.3 (s), 131.0 (s), 133.2 (d), 136.6 (s), 148.7 (s), 149.0 (s), 159.6 (s), 184.7 (s) ppm; IR ($CHCl_3$) 3021, 1718, 1595, 1571, 1457, 1217, 1168, 1045, 764 cm^{-1}; HRMS (ESI) calcd for $C_{22}H_{15}Cl_2O_3$ $(M + H)^+$ 397.0393, found 397.0396.

*(5,7-Dichloro-3-(4-fluorophenyl)benzofuran-2-yl)(phenyl)-methanone (**3cd**).* Pale yellow solid; 81% yield (64 mg); mp 140−142 °C; R_f = 0.3 (pet. ether/EtOAc = 9.5:0.5); ^1H NMR (200 MHz, $CDCl_3$): δ 7.12 (tt, J = 2.1, 8.5 Hz, 2H), 7.38−7.42 (m, 1H), 7.43−7.47 (m, 2H), 7.48−7.61 (m, 4H), 7.94−7.99 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 115.8 (d, J = 21.9 Hz, 2C), 118.7 (s), 120.1 (d), 125.7 (d, J = 2.9 Hz), 127.8 (s), 128.1 (d), 128.4 (d, 2C), 130.0 (d, 2C), 130.0 (s), 130.3 (s), 131.7 (d, J = 7.6 Hz, 2C), 133.4 (d), 136.5 (s), 148.7 (s), 148.9 (s), 162.9 (d, J = 243.2 Hz), 184.5 (s) ppm; IR ($CHCl_3$) 3022, 1717, 1654, 1595, 1449, 1218, 1088, 762 cm^{-1}; HRMS (ESI) calcd for $C_{21}H_{12}Cl_2FO_2$ $(M + H)^+$ 385.0193, found 385.0189.

*1-(3-(2-Benzoyl-5,7-dichlorobenzofuran-3-yl)phenyl)ethan-1-one (**3cg**).* White solid; 92% yield (78 mg); mp 164−166 °C: R_f = 0.2 (pet. ether/EtOAc = 9:1); ^1H NMR (500 MHz, $CDCl_3$): δ 2.60 (s, 3H), 7.42 (t, J = 7.7 Hz, 2H), 7.51 (d, J = 1.8 Hz, 1H), 7.54−7.57 (m, 3H), 7.71(d, J = 7.6 Hz, 1H), 7.97−7.99 (m, 3H), 8.07 (s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 26.7 (q), 118.8 (s), 120.0 (d), 127.9 (s), 128.3 (d), 128.4 (d, 2C), 128.7(d), 129.0 (d), 129.8 (d), 130.0 (d, 2C), 130.0 (s), 130.1 (s), 130.2 (s), 130.4 (s), 133.4 (d), 134.2 (d), 136.4 (s), 137.4 (s), 148.9 (s), 184.4 (s), 197.4 (s) ppm; IR ($CHCl_3$) 3020, 1687, 1599, 1424, 1216, 1017, 771 cm^{-1}; HRMS (ESI) calcd for $C_{23}H_{15}Cl_2O_3$ $(M + H)^+$ 409.0393, found 409.0392.

*(5,7-Dichloro-3-(3,4-dimethoxyphenyl)benzofuran-2yl) (phenyl)-methanone (**3ch**).* Yellow solid; 92% yield (81 mg); mp 145−147 °C; R_f = 0.3 (pet. ether/EtOAc = 9:1); ^1H NMR (500 MHz, $CDCl_3$): δ 3.81 (s, 3H), 3.91 (s, 3H), 6.92 (d, J = 8.3 Hz, 1H), 6.96 (d, J = 1.9 Hz, 1H), 7.09 (dd, J = 1.9, 8.2 Hz, 1H), 7.39 (t, J = 7.9 Hz, 2H), 7.51−7.54 (m, 2H), 7.59 (d, J = 1.8 Hz, 1H), 7.93 (d, J = 8.0 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 56.0 (q), 56.0 (q), 111.2 (d), 113.3 (d), 118.6 (s), 120.5 (d), 122.1 (s), 122.5 (d), 128.0 (d), 128.3 (d, 2C), 128.7 (s), 129.8 (s), 129.9 (d, 2C), 130.5 (s), 133.2 (d), 136.8 (s), 148.4 (s), 148.9 (s), 149.0 (s), 149.6 (s), 184.8 (s) ppm; IR ($CHCl_3$) 3022, 1651, 1592, 1456, 1252, 1218, 1154, 764 cm^{-1}; HRMS (ESI) calcd for $C_{23}H_{17}Cl_2O_4$ $(M + H)^+$ 427.0498, found 427.0499.

*(5-Bromo-3-(3,4-dichlorophenyl)benzofuran-2-yl)(phenyl)-methanone (**3df**).* White solid; 83% yield (74 mg); mp 118−120 °C: R_f = 0.4 (pet. ether/EtOAc = 9:1); ^1H NMR (500 MHz, $CDCl_3$): δ 7.35 (dd, J = 1.7, 8.4 Hz, 1H), 7.43 (t, J = 7.7 Hz, 2H), 7.48−7.53(m, 2H), 7.55−7.64 (m, 3H), 7.76 (d, J = 1.5 Hz, 1H), 7.91 (d, J = 7.7 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 114.1 (d), 117.5 (s), 124.3 (d), 126.0 (s), 128.4 (d, 2C), 129.1 (d), 129.4 (s), 129.8 (d, 2C), 130.2 (s), 130.5 (d), 131.6 (d, 2C), 132.8 (s), 133.0 (s), 133.3 (d), 136.6 (s), 148.3 (s), 153.0 (s), 184.9 (s) ppm; IR ($CHCl_3$) 3022, 1678, 1594, 1425, 1216, 1122, 1024, 766, 670 cm^{-1}; HRMS (ESI) calcd for $C_{21}H_{12}BrCl_2O_2$ $(M + H)^+$ 444.9397, found 444.9405.

*(5-Bromo-3-(3,4-dimethoxyphenyl)benzofuran-2-yl) (phenyl)-methanone (**3dh**).* White solid; 86% yield (75 mg); mp 118−120 °C; R_f = 0.4 (pet. ether/EtOAc = 9:1); ^{1}HNMR (400 MHz, $CDCl_3$): δ 3.77 (s, 3H), 3.90 (s, 3H), 6.90 (dd, J = 2.9, 4.8 Hz, 2H), 7.08 (dd, J = 2.0, 8.3 Hz, 1H), 7.34 (t, J = 7.8 Hz, 2H), 7.46−7.52 (m, 2H), 7.60 (dd, J = 2.0, 8.8 Hz, 1H), 7.82−7.85 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 56.0 (q, 2C), 111.2 (d), 113.4 (d), 114.0 (d), 117.1 (s), 122.5 (d), 122.6 (s), 125.0 (d), 128.2 (d, 2C), 128.3 (s), 129.8 (d, 2C), 130.1 (s), 131.2 (d), 132.9 (d), 137.1 (s), 147.7 (s), 148.9 (s), 149.5 (s), 153.3 (s), 185.6 (s) ppm; IR ($CHCl_3$) 3021, 1646, 1594, 1452, 1255, 1217, 1153, 758 cm^{-1}; HRMS (ESI) calcd for $C_{23}H_{18}BrO_4$ $(M + H)^+$ 437.0383, found 437.0384.

*1-(4-(2-(4-Chlorobenzoyl)-7-methoxybenzofuran-3-yl)phenyl)-ethan-1-one (**3ea**).* Brown solid; 64% yield (50 mg); mp 151−153 °C; R_f = 0.3 (pet. ether/EtOAc = 8:2); ^1H NMR (500 MHz, $CDCl_3$): δ 2.64 (s, 3H), 4.04 (s, 3H), 7.02 (d, J = 7.9 Hz, 1H), 7.22 (d, J = 7.9 Hz, 1H), 7.29 (d, J = 7.9 Hz, 1H), 7.42 (d, J = 8.6 Hz, 2H), 7.66 (d, J = 8.1 Hz, 2H), 7.99 (d, J = 8.5 Hz, 2H), 8.01 (d, J = 8.3 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 26.7 (q), 56.2 (q), 109.7 (d), 113.7 (d), 125.1 (d), 128.4 (d, 2C), 128.7 (d, 2C), 129.3 (s), 130.2 (d, 2C), 130.3 (s), 131.4 (d, 2C), 135.3 (s), 135.9 (s), 136.7 (s), 139.6 (s), 144.2 (s), 146.1 (s), 147.3 (s), 183.5 (s), 197.6 (s) ppm; IR ($CHCl_3$) 3021, 1678, 1592, 1492, 1437, 1217, 1095, 766 cm^{-1}; HRMS (ESI) calcd for $C_{24}H_{18}ClO_4$ $(M + H)^+$ 405.0888, found 405.0880.

*(4-Chlorophenyl)(7-methoxy-3-(3-methoxyphenyl)benzofuran-2-yl)methanone (**3eb**).* Yellow oil; 53% yield (40 mg); R_f = 0.5 (pet. ether/EtOAc = 8:2); ^1H NMR (500 MHz, $CDCl_3$): δ 3.80 (s, 3H), 4.05 (s, 3H), 6.93 (ddd, J = 8.4, 2.7, 0.9 Hz, 1H), 7.01 (dd, J = 7.0, 1.8 Hz, 1H), 7.05 (m, 1H), 7.10 (dd, J = 7.6, 1.2 Hz, 1H), 7.27 (d, J = 3.9 Hz, 1H), 7.28 (d, J = 1.8 Hz, 1H), 7.32 (t, J = 7.9 Hz, 1H), 7.33−7.37 (m, 2H), 7.88−7.90 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 55.3 (q), 56.2 (q), 109.6 (d), 114.2 (d, 2 C), 115.6 (d), 122.4 (d), 124.7 (d), 128.5 (d, 2C), 129.5 (d), 129.6 (s), 131.3 (d, 2C), 131.4 (s), 132.0 (s), 135.6 (s), 139.2 (s), 144.3 (s), 146.1 (s), 147.0 (s), 159.5 (s), 183.9 (s) ppm; IR ($CHCl_3$) 3020, 1649, 1591, 1491, 1386, 1218, 1095, 918, 764 cm^{-1}; HRMS (ESI) calcd for $C_{23}H_{18}ClO_4$ $(M + H)^+$ 393.0888, found 393.0882.

*1-(4-(2-(4-Chlorobenzoyl)-5-methoxybenzofuran-3-yl)phenyl)-ethan-1-one (**3fa**).* Brown oil; 68% yield (53 mg); R_f = 0.4 (pet. ether/EtOAc = 8:2); ^1H NMR (500 MHz, $CDCl_3$): δ 2.64 (s, 3H), 3.82 (s, 3H), 6.98 (d, J = 2.2 Hz, 1H), 7.17 (dd, J = 8.9, 2.5 Hz, 1H), 7.39 (d, J = 8.4 Hz, 2H), 7.53 (d, J = 9.1 Hz, 1H), 7.63 (d, J = 8.2 Hz, 2H), 7.92 (d, J = 8.4 Hz, 2H), 8.03 (d, J = 8.0 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 26.7 (q), 56.9 (q), 102.4 (d), 113.2 (d), 119.0 (d), 128.1 (s), 128.4 (d, 2C), 128.6 (d, 2C), 128.7 (s), 130.1 (d, 2C),

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131.3 (d, 2C), 135.4 (s), 136.0 (s), 136.7 (s), 139.4 (s), 147.9 (s), 149.7 (s), 157.1 (s), 183.6 (s), 197.6 (s) ppm; IR ($CHCl_3$) 3021, 1681, 1599, 1488, 1219, 1095, 1016, 767 cm^{-1}; HRMS (ESI) calcd for $C_{24}H_{18}ClO_4$ $(M + H)^+$ 405.0888, found 405.0879.

*1-(3-(2-(4-Chlorobenzoyl)-5-methoxybenzofuran-3-yl)phenyl)-ethan-1-one (**3fg**).* Brown solid; 75% yield (58 mg); mp 139−141 °C; R_f = 0.4 (pet. ether/EtOAc = 8:2); ^1H NMR (400 MHz, $CDCl_3$): δ 2.61 (s, 3H), 3.82 (s, 3H), 6.98 (d, J = 2.6 Hz, 1H), 7.17 (dd, J = 9.2, 2.7 Hz, 1H), 7.37 (br d, J = 8.6 Hz, 2H), 7.53 (d, J = 9.0 Hz, 1H), 7.55 (t, J = 7.8 Hz, 1H), 7.75 (td, J = 7.6, 1.4 Hz, 1H), 7.89 (br d, J = 8.6 Hz, 2H), 8.00 (td, J = 7.8, 1.6 Hz, 1H), 8.11 (t, J = 1.8 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 26.7 (q), 55.9 (q), 102.5 (d), 113.2 (d), 119.0 (d), 128.1 (s), 128.3 (d), 128.5 (d, 2C), 128.8 (d), 128.9 (s), 129.9 (d), 131.3 (d, 2C), 131.6 (s), 134.4 (d), 135.5 (s), 137.3 (s), 139.2 (s), 147.9 (s), 149.7 (s), 157.1 (s), 183.7 (s), 197.6 (s) ppm; IR ($CHCl_3$) 3019, 1685, 1588, 1485, 1436, 1216, 1177, 755 cm^{-1}; HRMS (ESI) calcdfor $C_{24}H_{18}ClO_4$ $(M + H)^+$ 405.0888, found 405.0880.

*(3-(4-(tert-Butyl)phenyl)benzofuran-2-yl)(phenyl)methanone (**3ai**).* Yellow oil; 83% yield (60 mg); R_f = 0.5 (pet. ether/EtOAc = 9.5:0.5); ^1H NMR (500 MHz, $CDCl_3$): δ 1.32 (s, 9H), 7.30 (t, J = 7.7 Hz, 2H), 7.34−7.36 (m, 3H), 7.40−7.45 (m, 3H), 7.52 (t, J = 7.3 Hz, 1H), 7.63 (d, J = 8.4 Hz, 1H), 7.73 (d, J = 7.9 Hz, 1H), 7.83 (d, J = 7.6 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 31.2 (q, 3C), 34.6 (s), 112.4 (d), 122.6 (d), 123.8 (d), 125.2 (d, 2C), 127.8 (s), 128.0 (d, 2C), 128.1 (s), 128.2 (d), 129.6 (s), 129.7 (d, 2C), 129.8 (d, 2C), 132.4 (d), 137.3 (s), 147.1 (s), 151.3 (s), 154.6 (s), 185.9 (s) ppm; IR ($CHCl_3$) 3021, 1717, 1646, 1565, 1457, 1218, 1004, 764 cm^{-1}; HRMS (ESI) calcd for $C_{25}H_{23}O_2$ $(M + H)^+$ 355.1693, found 355.1693.

*(3-(3-Fluorophenyl)benzofuran-2-yl)(phenyl)methanone (**3aj**).*[9b] Yellow oil; 68% yield (43 mg); R_f = 0.4 (pet. ether/EtOAc = 9.5:0.5); ^1H NMR (400 MHz, $CDCl_3$): δ 7.05 (ddt, J = 1.4, 2.8, 8.5 Hz, 1H), 7.23 (dt, J = 1.7, 9.6 Hz, 1H), 7.27 (dt, J = 1.0, 7.7 Hz, 1H), 7.31−7.40 (m, 4H), 7.49−7.56 (m, 2H) 7.65 (d, J = 8.3 Hz, 1H), 7.69 (dd, J = 1.1, 8.7 Hz, 1H), 7.88−7.90 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 112.5 (s), 115.3 (d, J = 21.1 Hz), 116.9 (d, J = 23.0 Hz), 122.1 (d), 124.1 (d), 125.8 (d, J = 2.9 Hz), 127.7 (s), 128.0 (d, J = 1.9 Hz), 128.2 (d, 2C), 128.4 (d), 129.8 (d, 2C), 129.9 (d, J = 8.6 Hz), 132.9 (d), 133.0 (d, J = 7.7 Hz), 137.1 (s), 147.3 (s), 154.5 (s), 162.6 (d, J = 246.3 Hz), 185.6 (s) ppm; IR ($CHCl_3$) 3068, 1650, 1614, 1563, 1448, 1292, 1262, 1233, 1168, 1021 cm^{-1}; HRMS (ESI) Calcd for $C_{21}H_{14}FO_2$ $(M + H)^+$ 317.0972, found 317.0971.

*(3-(Furan-3-yl)benzofuran-2-yl) (phenyl)methanone (**3ak**).* Pale yellow oil; 70% yield (41 mg); R_f = 0.6 (pet. ether/EtOAc = 9.5:0.5); ^1H NMR (200 MHz, $CDCl_3$): δ 6.87 (dd, J = 0.8, 1.9 Hz, 1H), 7.38 (ddd, J = 1.5, 6.8, 8.1 Hz, 1H), 7.43−7.51 (m, 2H), 7.51−7.63 (m, 4H), 7.84 (br d, J = 7.8 Hz, 1H), 8.00 (br d, J = 6.8 Hz, 2H), 8.13 (dd, J = 0.8, 1.5 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 111.4 (d), 112.4 (d), 115.4 (s), 120.5 (s), 122.4 (d), 123.9 (d), 127.6 (s), 128.2 (d), 128.3 (d, 2C), 129.9 (d, 2C), 132.8 (d), 137.5 (s), 143.0 (d), 143.2 (d), 147.4 (s), 154.5 (s), 185.4 (s) ppm; IR ($CHCl_3$) 3023, 1717, 1601, 1541, 1433, 1216, 1023, 1116, 767 cm^{-1}; HRMS (ESI) calcd for $C_{19}H_{13}O_3$ $(M + H)^+$ 289.0859, found 289.0857.

*(3-(3-Fluorophenyl)benzofuran-2-yl)(4-methoxyphenyl)-methanone (**3bj**).* White solid; 69% yield (47 mg); mp 124−126 °C; R_f = 0.5 (pet. ether/EtOAc = 9:1); ^1H NMR (400 MHz, $CDCl_3$): δ 3.85 (s, 3H), 6.88 (br d, J = 8.9 2H), 7.06 (ddt, J = 1.2, 2.7, 8.6 Hz, 1H), 7.26 (dt, J = 2.1, 9.3 Hz, 1H), 7.30 (dt, J = 1.2, 7.7 Hz, 1H), 7.33−7.39 (m, 2H), 7.52 (ddd, J = 1.2, 7.0, 8.1 Hz, 1H), 7.64 (d, J = 8.4 Hz, 1H), 7.68 (d, J = 7.8 Hz, 1H), 7.96 (br d, J = 8.8 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 55.5 (q), 112.3 (d), 113.5 (d, 2C), 115.1 (d, J = 21.1 Hz), 116.8 (d, J = 23.0 Hz), 121.9 (d), 124.0 (d), 125.8 (d, J = 2.9 Hz), 127.1 (s), 127.7 (s), 128.0 (d), 129.7 (s), 129.9 (d, J = 8.6 Hz), 132.4 (d, 2C), 133.2 (d, J = 8.6 Hz), 147.7 (s), 154.3 (s), 162.6 (d, J = 246.3 Hz), 163.6 (s), 183.9 (s) ppm; IR ($CHCl_3$) 3021, 1717, 1643, 1501, 1479, 1434, 1220, 1168, 1028, 762 cm^{-1}; HRMS (ESI) calcd for $C_{22}H_{16}FO_3$ $(M + H)^+$ 347.1078, found 347.1077.

*(3-(Furan-3-yl)benzofuran-2-yl)(4-methoxyphenyl)methanone (**3bk**).* Brown oil; 83% yield (52 mg); R_f = 0.4 (pet. ether/EtOAc = 9.5:0.5); ^1H NMR (500 MHz, $CDCl_3$): δ 3.89 (s, 3H), 6.86 (s, 1H), 6.96 (d, J = 8.6 Hz, 2H), 7.37 (t, J = 7.5 Hz, 1H), 7.50−7.53 (m, 2H), 7.59 (d, J = 8.4 Hz, 1H), 7.84 (d, J = 8.0 Hz, 1H), 8.04 (d, J = 8.7 Hz, 2H), 8.11 (s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 55.5 (q), 111.4 (d), 112.3 (d), 113.6 (d, 2C), 115.5 (s), 119.7 (s), 122.3 (d), 123.8 (d), 127.6 (s), 127.9 (d), 130.2 (s), 132.4 (d, 2C), 142.9 (d), 143.0 (d), 147.8 (s), 154.3 (s), 163.5 (s), 183.9 (s) ppm; IR ($CHCl_3$) 3021, 1718, 1599, 1456, 1429, 1219, 1117, 761 cm^{-1}; HRMS (ESI) calcd for $C_{20}H_{15}O_4$ $(M + H)^+$ 319.0965, found 319.0966.

*(3-(4-(tert-Butyl)phenyl)-5,7-dichlorobenzofuran-2-yl)-(phenyl)-methanone (**3ci**).* White solid; 83% yield (66 mg); mp 121−123 °C; R_f = 0.3 (pet. ether/EtOAc = 9.5:0.5); ^1H NMR (400 MHz, $CDCl_3$): δ 1.33 (s, 9H), 7.37 (t, J = 7.8 Hz, 2H), 7.41 (m, 4H), 7.49−7.52 (m, 2H), 7.60(d, J = 1.9 Hz, 1H), 7.92 (br d, J = 7.9 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 31.2 (q, 3C), 34.7 (s), 118.5 (s), 120.6 (d), 125.5 (d, 2C), 126.6 (s), 128.0 (d), 128.2 (d, 2C), 129.0 (s), 129.5 (d, 2C), 129.7 (s), 129.9 (d, 2C), 130.4 (s), 133.0 (d), 136.7 (s), 148.6 (s), 149.0 (s), 152.0 (s), 184.8 (s) ppm; IR ($CHCl_3$) 3022, 1678, 1592, 1420, 1216, 1120, 766 cm^{-1}; HRMS (ESI) calcd for $C_{25}H_{21}Cl_2O_2$ $(M + H)^+$ 423.0913, found 423.0913.

*(5-Bromo-3-(4-(tert-butyl)phenyl)benzofuran-2-yl) (phenyl)-methanone (**3di**).* White solid; 74% yield (64 mg); mp 133−135 °C; R_f = 0.5 (pet. ether/EtOAc = 9.5:0.5); ^1H NMR (400 MHz, $CDCl_3$): δ 1.32 (s, 9H), 7.31 (t, J = 7.7 Hz, 2H), 7.37−7.38 (m, 4H), 7.45 (t, J = 7.5 Hz, 1H), 7.51 (d, J = 8.8 Hz, 1H), 7.60 (dd, J = 2.0, 8.8 Hz, 1H), 7.81 (br d, J = 7.6 Hz, 2 H), 7.85 (d, J = 1.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 31.2 (q, 3C), 34.7 (s), 113.9 (d), 117.0 (s), 125.1 (d), 125.4 (d, 2C), 127.1 (s), 128.1 (d, 2C), 128.7 (s), 129.6 (d, 2C), 129.8 (d, 2C), 130.1 (s), 131.1 (d), 132.7 (d), 137.0 (s), 147.9 (s), 151.7 (s), 153.3 (s), 185.6 (s) ppm; IR ($CHCl_3$) 3022, 1648, 1590, 1495, 1433, 1216, 1118, 766, 672 cm^{-1}; HRMS (ESI) calcd for $C_{25}H_{22}BrO_2$ $(M + H)^+$ 433.0803, found 433.0805.

*(5-Bromo-3-(furan-3-yl)benzofuran-2-yl) (phenyl)methanone (**3dk**).* Yellow oil; 81% yield (59 mg); R_f = 0.3 (pet. ether/EtOAc = 9.5:0.5); ^1H NMR (500 MHz, $CDCl_3$): δ 6.82 (s, 1H), 7.48 (t, J = 7.3 Hz, 3H), 7.54 (s, 1H), 7.60 (t, J = 9.7 Hz, 2H), 7.96−7.98 (m, 3H), 8.09 (s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 111.2 (d), 113.9 (d), 114.8 (s), 117.1 (s), 119.7 (s), 125.0 (d), 128.4 (d, 2C), 129.5 (s), 129.9 (d, 2C), 131.2 (d), 133.1 (d), 137.1 (s), 143.2 (d, 2C), 148.3 (s), 153.1 (s), 185.1 (s) ppm; IR ($CHCl_3$) 3020, 1710, 1656, 1423, 1216, 1120, 1022, 769 cm^{-1}; HRMS (ESI) calcd for $C_{19}H_{10}BrO_3$ $(M - H)^+$ 364.9811, found 364.9777.

*(4-Chlorophenyl)(3-(furan-3-yl)-5-methoxybenzofuran-2-yl)-methanone (**3fk**).* Yellow solid; 73% yield (49 mg); mp 123−125 °C; R_f = 0.5 (pet. ether/EtOAc = 9:1); ^1H NMR (400 MHz, $CDCl_3$): δ 3.94 (s, 3H), 6.91 (s, 1H), 7.19−7.31 (m, 2H), 7.49−755 (m, 3H), 7.61 (s, 1H), 8.00−8.03 (m, 2H), 8.16 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 56.0 (q), 103.3 (d), 111.4 (d), 113.1 (d), 115.4 (s), 118.6 (d), 121.1 (s), 128.1 (s), 128.6 (d, 3C), 131.4 (d, 2C), 135.8 (s), 139.2 (s), 143.1 (d), 147.9 (s), 149.6 (s), 156.9 (s), 183.7 (s) ppm; IR ($CHCl_3$) 3019, 1646, 1591, 1493, 1391, 1234, 1092, 761 cm^{-1}; HRMS (ESI) calcd for $C_{20}H_{14}ClO_4$ $(M + H)^+$ 353.0575, found 353.0571.

*(3-(4-(tert-Butyl)phenyl)benzofuran-2-yl)(4-fluorophenyl)-methanone (**3gi**).* Pale yellow oil; 79% yield (61 mg); R_f = 0.4 (pet. ether/EtOAc = 9.5:0.5); ^1H NMR (400 MHz, $CDCl_3$): δ 1.33 (s, 9H), 6.97 (t, J = 8.7 Hz, 2H), 7.33−7.37 (m, 2H), 7.38 (d, J = 2.0 Hz, 3H), 7.53 (dt, J = 1.1, 8.3 Hz, 1H), 7.64 (d, J = 8.4 Hz, 1H), 7.74 (d, J = 7.9 Hz, 1H), 7.83−7.87 (m, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 31.2 (q, 3C), 34.7 (s), 112.4 (d), 115.1 (d, J = 22.4 Hz, 2C), 122.6 (d), 123.9 (d), 125.3 (d, 2C), 127.7 (s), 128.1 (s), 128.3 (d), 129.7 (d, 2C), 129.9 (s), 132.4 (d, J = 9.3 Hz, 2C), 133.6 (d, J = 3.1 Hz), 146.9 (s), 151.6 (s), 154.7 (s), 165.3 (d, J = 254.3 Hz), 184.3 (s) ppm; IR ($CHCl_3$) 3020, 1728, 1648, 1599, 1465, 1225, 1160, 758 cm^{-1}; HRMS (ESI) calcd for $C_{25}H_{22}FO_2$ $(M + H)^+$ 373.1598, found 373.1602.

*(4-Fluorophenyl)(3-(3-fluorophenyl)benzofuran-2-yl)methanone (**3gj**).* Yellow solid; 73% yield (51 mg); mp 56−58 °C; R_f = 0.4 (pet. ether/EtOAc = 9.5:0.5); ^1H NMR (200 MHz, $CDCl_3$): δ 7.02−7.13 (m, 3H), 7.20−7.22 (m, 1H), 7.26−7.30 (m, 1H), 7.32−7.42 (m, 2H), 7.55 (dt, J = 1.3, 7.0 Hz, 1H), 7.62−7.70 (m, 2H), 7.93−8.00 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 112.4 (d), 115.4 (d, J = 22.0 Hz, 3C), 116.8 (d, J = 22.1 Hz), 122.1 (d), 124.2 (d), 125.8 (d, J = 2.9 Hz), 127.7 (s), 128.1 (s), 128.5 (d), 130.0 (d, J = 8.6 Hz), 132.5 (d, J = 9.6

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Hz, 2C), 132.9 (d, J = 7.7 Hz), 133.3 (d, J = 2.9 Hz), 147.1 (s), 154.5 (s), 162.6 (d, J = 246.3 Hz), 165.6 (d, J = 255.9 Hz), 183.8 (s) ppm; IR ($CHCl_3$) 3022, 1650, 1599, 1494, 1438, 1295, 1221, 1159, 764 cm^{-1}; HRMS (ESI) calcd for $C_{21}H_{13}F_2O_2$ $(M + H)^+$ 335.0878, found 335.0878.

*(5-Bromo-3-(4-(tert-butyl)phenyl)benzofuran-2-yl)(4-methoxyphenyl)methanone (**3hi**).* White solid; 77% yield (70 mg); mp 137−139 °C; R_f = 0.4 (pet. ether/EtOAc = 9:1); ^{1}H NMR (500 MHz, $CDCl_3$): δ 1.33 (s, 9H), 3.82 (s, 3H), 6.82 (d, J = 8.7 Hz, 2H), 7.39 (m, 4H), 7.50 (d, J = 8.7 Hz, 1H), 7.58 (dd, J = 1.8, 8.8 Hz, 1H), 7.88−7.87 (m, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 31.2 (q, 3C), 34.7 (s), 55.4 (q), 113.4 (d, 2C), 113.8 (d), 116.9 (s), 124.9 (d), 125.4 (d, 2C), 127.3 (s), 127.7 (s), 129.6 (d, 2C), 129.7 (s), 130.1 (s), 130.8 (d), 132.3 (d, 2C), 148.3 (s), 151.6 (s), 153.1 (s), 163.5 (s), 184.1 (s) ppm; IR ($CHCl_3$) 3021, 1715, 1643, 1509, 1431, 1217, 1115, 766, 672 cm^{-1}; HRMS (ESI) calcd for $C_{26}H_{24}BrO_3$ $(M + H)^+$ 463.0903, found 463.0902.

*Benzofuran-2-yl(phenyl)methanol (**4a**).* A solution of benzofuran **1a** (250 mg, 1.12 mmol) in methanol was treated with $NaBH_4$ (1.24 mmol) at 0 °C, and then it was stirred at room temperature for 1 h. The reaction mixture was quenched with cold water and portioned between water and EtOAc. The organic phase was separated, and the aqueous phase was extracted with EtOAc (2 × 50 mL). The combined organic phase was washed with brine, dried (Na_2SO_4), and concentrated under reduced pressure. The crude product was purified by silica gel column (pet. ether/EtOAc as eluent) to afford colorless solid; 92% yield (232 mg); ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.91 (br s, 1H), 6.52 (s, 1H), 7.24 (dt, J = 0.9, 7.3 Hz, 1H), 7.29 (dt, J = 1.4, 7.3 Hz, 1H), 7.34−7.42 (m, 3H), 7.46−7.50 (m, 3H), 7.52−7.54 (m, 2H); ^{13}C NMR (50 MHz, $CDCl_3$): δ 70.5 (d), 103.9 (d), 111.2 (d), 121.0 (d), 122.7 (d), 124.2 (d), 126.7 (d, 2C), 127.9 (s), 128.2 (d), 128.5 (d, 2C), 140.2 (s), 155.0 (s), 158.5 (s) ppm.

*1-(4-(2-(Hydroxy(phenyl)methyl)benzofuran-3-yl)phenyl)ethan-1-one (**5aa**).* Brown oil; 40% yield (27 mg); R_f = 0.2 (pet. ether/EtOAc = 7:3); ^{1}H NMR (500 MHz, $CDCl_3$): δ 2.65 (s, 3H), 6.03 (s, 1H), 7.26−7.68 (m, 5H), 7.48 (d, J = 7.3 Hz, 2H), 7.51 (d, J = 8.2 Hz, 1H), 7.59 (d, J = 7.6 Hz, 1H), 7.64 (d, J = 7.9 Hz, 2H), 8.08 (d, J = 7.9 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 26.7 (q), 68.6 (d), 111.8 (d), 118.6 (s), 120.1 (d), 123.3 (d), 125.2 (d), 126.6 (d, 2C), 127.6 (s), 128.2 (d), 128.7 (d, 2C), 128.9 (d, 2C), 129.4 (d, 2C), 136.3 (s), 136.7 (s), 140.5 (s), 152.9 (s), 154.4 (s), 197.6 (s) ppm; IR ($CHCl_3$) 3355, 3021, 1678, 1606, 1451, 1448, 1266, 1217, 760 cm^{-1}; HRMS (ESI) calcd for $C_{23}H_{18}O_3Na$ $(M + Na)^+$ 365.1148, found 365.1138.

HPLC Method. The HPLC was equipped with a Supelgo-C-18, RP 10 × 250 mm, 10 μm column maintained at a temperature of 20 °C. The mobile phase used for was found to be 85% methanol, 15% water with a flow rate of 2.0 mL/min. Note that all solvents were HPLC grade. The volume of sample injected was set at 20 μL, and runtime for each sample was 30 min. The retention time of benzofuran **1a** was 11.822, benzofuran alcohol **4a** was 9.421, arylbenzofuran **3aa** was 14.890, and arylbenzofuran **3aa** in crude reaction mixture was 14.812. In reaction of **4a** with **2a**, retention time of arylbenzofuran **5aa** was 11.045, benzofuran alcohol **4a** was 9.405, and arylbenzofuran **5aa** was 11.191 in crude reaction mixture.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.5b01932.

HPLC plots of control experiments and NMR and HRMS spectra of all new compounds (PDF)

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Notes

The authors declare no competing financial interest.

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