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New method for the acylation of benzofurans toward the synthesis of 6*H*-indeno[2,1-*b*]benzofuran-6-ones and 2,2-bibenzofurans

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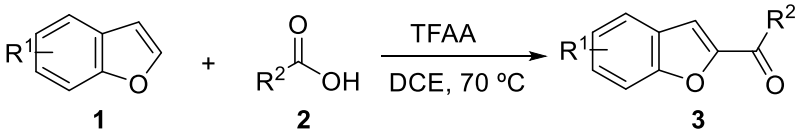
Abstract

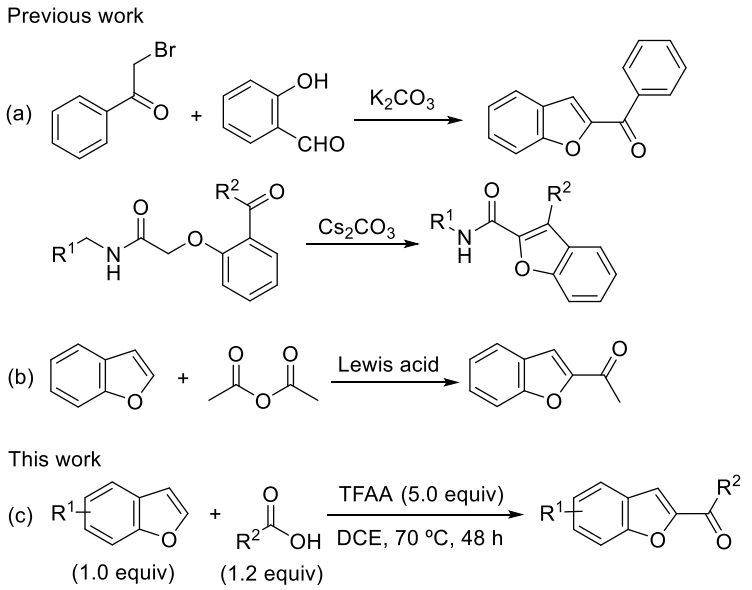
We have developed a TFAA-mediated acylation of benzofurans using carboxylic acids as acylating agents. The reaction does not require the aid of Lewis acid catalysts, and lead to the regioselective formation of 2-acyl benzofurans. Among these, 2-bromophenylacyl benzofurans and 2-(2-bromophenyl)acetyl benzofurans could be converted into 6*H*-indeno[2, 1-*b*]benzofuran-6-ones and 2, 2'-bibenzofurans, respectively.



Keywords: TFAA, 2-acyl benzofurans, 6*H*-indeno[2, 1-*b*]benzofuran-6-ones, 2, 2'-bibenzofurans

Introduction

2-Substituted benzofurans have shown unique anti-fungal,[1,2] anti-viral,[3] anti-diabetic,[4] anti-tumor,[5,6] anti-osteoporosis[7] and anti-Alzheimer's disease activities.[8] Besides, many medical products such as amiodarone hydrochloride[9] are also derived from 2-substituted benzofurans. A number of strategies for the synthesis of 2-substituted benzofurans have been developed. The base-catalyzed intermolecular or intramolecular condensation reactions to construct a fused furan ring to form 2-substituted benzofuran derivatives is the most common synthetic method (Scheme 1a).[10,11] 2-Acylbenzofurans can also be obtained by Lewis acid catalyzed acylation of benzofurans using acid anhydrides or acyl chlorides as acylating agents (Scheme 1b).[12-15] The trifluoroacetic anhydride (TFAA)-mediated acylation[16] using carboxylic acids as the acylating agent have been applied to arenes[17] and heteroarenes including thiophenes,[18] benzothiophenes,[19] pyrroles,[20] and carbazoles.[21] However, to the best of our knowledge, this protocol has never been used with benzofurans, although a single literature precedent with furans as substrates has been reported.[22] Herein, we report the TFAA-mediated acylation of benzofurans using carboxylic acids as the acylating agent. The reaction does not require the aid of Lewis acid catalysts, and leads to the regioselective formation of 2-acyl benzofurans (Scheme 1c).



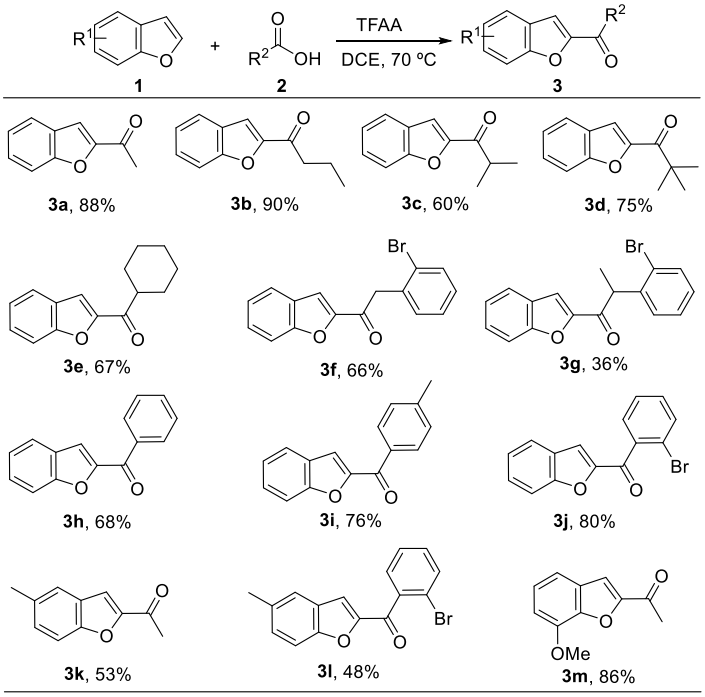
Scheme 1. Synthetic routes toward 2-substituted benzofuran derivatives.

Results and Discussion

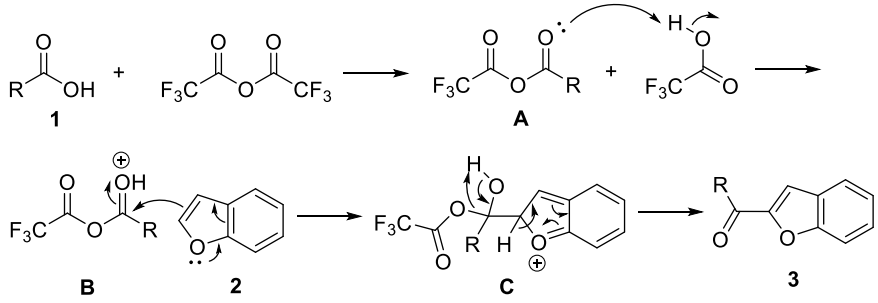
Our optimization of reaction conditions commenced with acetic acid as the acylating agent. The reaction was complete in different solvents such as *N*,*N*-dimethylformamide (DMF), dichloromethane (DCM) and 1,2-dichloroethane (DCE) under appropriate temperature conditions in the presence of 5 equivalent of TFAA. It was found that the optimum yield was 88% when the solvent was DCE and acylation reaction system of benzofuran with acetic acid reacted at 70 °C under TFAA-mediated conditions. Next, the substrate scope was examined and the results were shown in Table 1. Acylation with a variety of aliphatic carboxylic acids provided the corresponding 2-acylbenzofurans **3a**-**e** in good to excellent isolated yields. While acylation with 2-(2-

bromophenyl)acetic acid gave **3f** in 66% isolated yield, reaction of 2-(2-bromophenyl)proponic acid was less satisfactory and resulted in the formation of **3g** in 36% yield only. Under the reaction conditions, acylation with aromatic acids proceeded as expected to provide **3h**-**j** in good isolated yields. Finally, acylation of representative substituted benzofurans were examined, which resulted in the formation of **3k-m** in moderate to excellent isolated yields.

Table 1. Substrate scope of acylation reaction



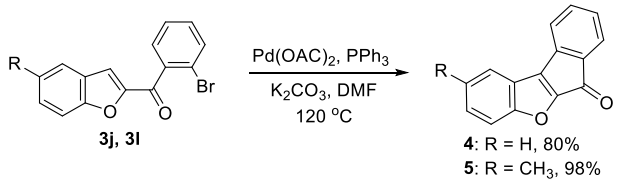
Based on the results obtained above and literature reports,[16,20,23] a plausible mechanism is depicted in Scheme 2. Mixed anhydride formation from acid **1** and TFAA provided **A** and trifluoroacetic acid (TFA). Because of the strong eletron-withdrawing nature of the trifluoromethyl group, protonation of the alternative carbonyl group by TFA generated the acylating agent **B**, which reacted with benzofuran **2** to provide **3** via intermediate **C**. The fact that no trifluoroacylation product was observed could be attributed to the inability for TFAA to be protonated.



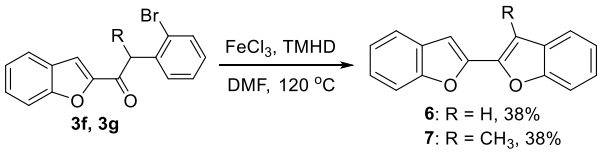
Scheme 2. Proposed mechanism.

Having established the method, we then turned our attention to the transformation of the products into other useful molecules. First, palladium-catalyzed C–H activation[24,25] of **3j, 3l** provided fluorenores **4** and **5** in

80% and 98% isolated yields, respectively (Scheme 3). Second, under the joint action of $FeCl_3$ and 2,2,6,6-tetramethyl-3,5-heptanedione (TMHD), **3f, 3g** could be converted into 2, 2'-bibenzofurans **6** and **7**, respectively, in moderate isolated yields (Scheme 4). The pharmacological activities of 2,2'-bibenzofurans have attracted much attention.[5] Literature methods for the synthesis of 2, 2'-bibenzofurans include homogeneous coupling of benzofurans[26,27] or 2-(2,2-dibromovinyl)phenols,[28] and condensation of 2-acetylbenzofurans with benzoquinones.[29] However, these either suffered from limited substrate scope or could only be applied to the synthesis of symmetrical 2, 2'-bibenzofurans. The method reported herein provided a new entry to access unsymmetrically substituted 2, 2'-bibenzofurans.



Scheme 3. Synthesis of 6*H*-indeno[2,1-*b*]benzofuran-6-ones **4** and **5**.



Scheme 4. Synthesis of 2,2'-bibenzofurans **6** and **7**.

Conclusions

We have developed a TFAA-mediated approach for the acylation of benzofurans using carboxylic acid as the acylating agent. A series of 2-acyl benzofuran derivatives have been synthesized. Among these, **3j**, **3l** and **3f**, **3g** could be further converted into 6*H*-indeno[2,1-*b*]benzofuran-6-ones **4**, **5** and 2,2'-bibenzofurans **6**, **7**, respectively.

Experimental Section

General. Melting points were determined on a XT4A hot-stage apparatus and are uncorrected. IR spectra were obtained using a PerkinElmer FT/IR spectrometer. ^1H and ^{13}C NMR spectra were obtained on a Agilent AV400 instrument. High-resolution mass spectra were recorded on a Micromass Q-TOF mass spectrometer.

General procedure for the preparation of 3a-m. TFAA (5.0 mmol) was added to a solution of benzofurans **1a-m** (1.0 mmol) and acids **2a-m** (1.2 mmol) in DCE (25 mL).The resulting mixture was heated at 70 °C until the reaction was completed (reaction monitored by TLC). The mixture was poured into water (20 mL), neutralized with saturated aqueous $NaHCO_3$ (20 mL), then extracted with EtOAc (3 x 40 mL). The combined organic extracts were dried over anhydrous sodium sulfate, filtered, and then evaporated *in vacuo.* The residue was purified by column chromatograph on silica gel to afford **3a-m**.

1-(Benzofuran-2-yl)ethan-1-one (3a).[30] The title compound was prepared according to the general pr[oc]edure by stirring a mixture of benzofuran (110 µL, 1.0 mmol), acetic acid (69 µL, 1.2 mmol) and TFAA (705 µL, 5.0 mmol) in DCE (25 mL) at 70 ºC for 48 h. The crude product was purified by column chromatography on silica gel (0.5% EtOAc in petroleum ether) to afford compound **3a** (141 mg, 88%) as a colorless solid: mp 61–62 °C; IR (neat, cm^{-1}): ν_{max} 3120, 1673, 1555, 1295, 928; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.71 (d, *J* 7.8 Hz, 1H), 7.58 (d, *J* 8.4 Hz, 1H), 7.51 (s, 1H), 7.48 (t, *J* 7.8 Hz, 1H), 7.32 (t, *J* 7.6 Hz, 1H), 2.62 (s, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 188.7, 155.7, 152.6, 128.3, 127.1, 123.9, 123.3, 113.1, 112.5, 26.5 ppm; HRMS (ESI): *m/z* calcd for $C_{10}H_9O_2$ $[M+H]^+$ 161.0597; found 161.0596.

1-(Benzofuran-2-yl)butan-1-one (3b). The title compound was prepared according to the general procedure by stirring a mixture of benzofuran (110 µL, 1.0 mmol), butyric acid (106 mg, 1.2 mmol) and TFAA (705 µL, 5.0 mmol) in DCE (25 mL) at 70 °C for 48 h. The crude product was purified by column chromatography on silica gel (0.5% EtOAc in petroleum ether) to afford compound **3b** (169 mg, 90%) as a colorless solid: mp 56–57 °C; IR (neat, cm^{-1}): ν_{max} 2965, 1682, 1561, 1158, 743; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.70 (d, *J* 7.9 Hz, 1H), 7.57 (d, *J* 8.4 Hz, 1H), 7.49 (s, 1H), 7.48 – 7.44 (m, 1H), 7.30 (t, *J* 7.4 Hz, 1H), 2.93 (t, *J* 7.4 Hz, 2H), 1.81 (m, 2H), 1.02 (t, *J* 7.4 Hz, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 191.7, 155.7, 152.8, 128.2, 127.2, 123.9, 123.4, 112.7, 112.6, 40.9, 17.9, 14.0 ppm; HRMS (ESI): *m/z* calcd for $C_{12}H_{13}O_2$ $[M+H]^+$ 189.0910; found 189.0912.

1-(Benzofuran-2-yl)-2-methylpropan-1-one (3c).[31] The title compound was prepared according to the general procedure by stirring a mixture of benzofuran (110 µL, 1.0 mmol), isobutyric acid (106 mg, 1.2 mmol) and TFAA (705 µL, 5.0 mmol) in DCE (25 mL) at 70 °C for 48 h. The crude product was purified by column chromatography on silica gel (0.5% EtOAc in petroleum ether) to afford compound **3c** (113 mg, 60%) as a light brown oil: IR (neat, cm^{-1}): ν_{max} 3423, 2972, 1680, 1553, 1003; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.69 (d, *J* 7.9 Hz, 1H), 7.56 (d, *J* 8.4 Hz, 1H), 7.50 (s, 1H), 7.45 (t, *J* 7.8 Hz, 1H), 7.29 (t, *J* 7.5 Hz, 1H), 3.50– 3.45 (m, 1H), 1.26 (d, *J* 6.9 Hz, 6H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 195.6, 155.6, 152.1, 128.1, 127.1, 123.9, 123.3, 112.9, 112.5, 36.7, 18.9 ppm; HRMS (ESI): *m/z* calcd for $C_{12}H_{13}O_2$ $[M+H]^+$ 189.0910; found 189.0909.

1-(Benzofuran-2-yl)-2,2-dimethylpropan-1-one (3d).[31] The title compound was prepared according to the general procedure by stirring a mixture of benzofuran (110 µL, 1.0 mmol), pivalic acid (122 mg, 1.2 mmol) and TFAA (705 µL, 5.0 mmol) in DCE (25 mL) at 70 °C for 48 h. The crude product was purified by column chromatography on silica gel (1% EtOAc in petroleum ether) to afford compound **3d** (151 mg, 75%) as a bright yellow oil: IR (neat, cm^{-1}): ν_{max} 3429, 2971, 1671, 1546, 1132; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.70 (d, *J* 7.9 Hz, 1H), 7.59 – 7.55 (m, 1H), 7.54 (d, *J* 1.0 Hz, 1H), 7.48 – 7.43 (m, 1H), 7.32 – 7.28 (m, 1H), 1.43 (s, 9H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 196.9, 155.2, 152.8, 127.8, 126.9, 123.8, 123.2, 113.8, 112.4, 43.6, 26.9 ppm; HRMS (ESI): *m/z* calcd for $C_{13}H_{15}O_2$ $[M+H]^+$ 203.1067; found 203.1065.

Benzofuran-2-yl(cyclohexyl)methanone (3e). The title compound was prepared according to the general procedure by stirring a mixture of benzofuran (110 µL, 1.0 mmol), cyclohexanecarboxylic acid (153 mg, 1.2 mmol) and TFAA (705 µL, 5.0 mmol) in DCE (25 mL) at 70 °C for 48 h. The crude product was purified by column chromatography on silica gel (0.5% EtOAc in petroleum ether) to afford compound **3e** (152 mg, 67%) as a colorless solid: mp 61–62 °C; IR (neat, cm^{-1}): ν_{max} 3114, 2940, 2858, 1666, 987; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.69 (d, *J* 7.9 Hz, 1H), 7.58 (d, *J* 8.4 Hz, 1H), 7.52 – 7.50 (m, 1H), 7.49 – 7.43 (m, 1H), 7.32 – 7.28 (m, 1H), 3.24 – 3.17 (m, 1H), 2.00 – 1.91 (m, 2H), 1.89 – 1.83 (m, 2H), 1.77 – 1.72 (m, 1H), 1.61 – 1.51 (m, 2H), 1.46 – 1.35 (m, 2H), 1.34 – 1.25 (m, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 194.9, 155.7, 152.3; 128.1, 127.2, 123.9, 123.3, 112.9, 112.6, 46.8, 29.9, 25.9, 25.9 ppm; HRMS (ESI): *m/z* calcd for $C_{15}H_{17}O_2$ $[M+H]^+$ 229.1223; found 229.1225.

1-(Benzofuran-2-yl)-2-(2-bromophenyl)ethan-1-one (3f). The title compound was prepared according to the general procedure by stirring a mixture of benzofuran (110 µL, 1.0 mmol), 2-(2-bromophenyl)acetic acid (257 mg, 1.2 mmol) and TFAA (705 µL, 5.0 mmol) in DCE (25 mL) at 70 ºC for 48 h. The crude product was purified

by column chromatography on silica gel (0.5% EtOAc in petroleum ether) to afford compound **3f** (207 mg, 66%) as a colorless solid: mp 126–127 ºC; IR (neat, cm^{-1}): ν_{max} 3424, 1678, 1159, 1138, 1020; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.11 (s, 1H), 7.89 (d, *J* 7.9 Hz, 1H), 7.77 (d, *J* 8.4 Hz, 1H), 7.65 (d, *J* 7.9 Hz, 1H), 7.58 – 7.37 (m, 1H), 7.46 (dd, *J* 7.6, 1.8 Hz, 1H), 7.43 – 7.37 (m, 2H), 7.27 (td, *J* 7.8, 1.7 Hz, 1H), 4.57 (s, 2H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 187.3, 155.8, 152.3, 134.2, 133.0, 131.9, 129.1, 128.5, 127.7, 127.2, 125.2, 124.1, 123.5, 113.5, 112.6, 46.0 ppm; HRMS (ESI): *m/z* calcd for $C_{16}H_{12}{}^{79}BrO_2$ $[M+H]^+$ 315.0015; found 315.0017.

1-(Benzofuran-2-yl)-2-(2-bromophenyl)propan-1-one (3g). The title compound was prepared according to the general procedure by stirring a mixture of benzofuran (110 µL, 1.0 mmol), 2-(2-bromophenyl)propanoic acid (273 mg, 1.2 mmol) and TFAA (705 µL, 5.0 mmol) in DCE (25 mL) at 70 °C for 48 h. The crude product was purified by column chromatography on silica gel (0.5% EtOAc in petroleum ether) to afford compound **3g** (118 mg, 36%) as a light yellow solid: mp 105–106 ºC; IR (neat, cm^{-1}): ν_{max} 2927, 1673, 1547, 1160, 755; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.65 (d, *J* 7.9 Hz, 1H), 7.61 (dd, *J* 8.0, 1.0 Hz, 1H), 7.56 – 7.53 (m, 1H), 7.51 (s, 1H), 7.46 – 7.40 (m, 1H), 7.29 – 7.21 (m, 3H), 7.08 (ddd, *J* 7.9, 7.2, 1.9 Hz, 1H), 5.10 (q, *J* 6.9 Hz, 1H), 1.54 (d, *J* 6.9 Hz, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 190.6, 155.7, 151.8, 140.4, 133.3, 128.8, 128.6, 128.4, 128.2, 127.0, 124.2, 123.9, 123.4, 114.0, 112.6, 47.5, 17.6 ppm; HRMS (ESI): *m/z* calcd for $C_{17}H_{14}{}^{79}BrO_2$ $[M+H]^+$: 329.0172; found 329.0174.

Benzofuran-2-yl(phenyl)methanone (3h).[32] The title compound was prepared according to the general procedure by stirring a mixture of benzofuran (110 µL, 1.0 mmol), benzoic acid (146 mg, 1.2 mmol) and TFAA (705 µL, 5.0 mmol) in DCE (25 mL) at 70 °C for 48 h. The crude product was purified by column chromatography on silica gel (0.5% EtOAc in petroleum ether) to afford compound **3h** (150 mg, 68%) as a yellow solid: mp 83–84 °C; IR (neat, cm^{-1}): ν_{max} 2958, 2925, 2853, 1689, 1291; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.06 – 8.03 (m, 2H), 7.73 (d, *J* 7.9 Hz, 1H), 7.64 (t, *J* 7.4 Hz, 2H), 7.57 – 7.48 (m, 4H), 7.34 (t, *J* 7.4 Hz, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 184.6, 156.1, 152.3, 137.3, 133.0, 129.6, 128.7, 128.5, 127.1, 124.1, 123.5, 116.7, 112.7 ppm; HRMS (ESI): *m/z* calcd for $C_{15}H_{11}O_2$ $[M+H]^+$ 223.0754; found 223.0757.

Benzofuran-2-yl(p-tolyl)methanone (3i).[32] The title compound was prepared according to the general procedure by stirring a mixture of benzofuran (110 µL, 1.0 mmol), 4-methylbenzoic acid (283 mg, 1.2 mmol) and TFAA (705 µL, 5.0 mmol) in DCE (25 mL) at 70 ºC for 48 h. The crude product was purified by column chromatography on silica gel (0.5% EtOAc in petroleum ether) to afford compound **3i** (179 mg, 76%) as a colorless solid: mp 74–75 °C; IR (neat, cm^{-1}): ν_{max} 1755, 1610, 1575, 1545; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.97 (d, *J* 8.1 Hz, 2H), 7.72 (d, *J* 7.8 Hz, 1H), 7.64 (d, *J* 8.4 Hz, 1H), 7.52 (s, 1H), 7.51 (t, *J* 7.8 Hz, 1H), 7.35 – 7.31 (m, 3H), 2.46 (s, 3H) ppm; ^{13}C NMR (100MHz, $CDCl_3$): δ 184.2, 156.0, 152.5, 143.9, 134.7, 129.7, 129.4, 128.3, 127.2, 124.0, 123.4, 116.2, 112.6, 21.8 ppm; HRMS (ESI): *m/z* calcd for $C_{16}H_{13}O_2$ $[M+H]^+$ 237.0910; found 237.0912.

Benzofuran-2-yl(2-bromophenyl)methanone (3j). The title compound was prepared according to the general procedure by stirring a mixture of benzofuran (110 µL, 1.0 mmol), 2-bromobenzoic acid (240 mg, 1.2 mmol) and TFAA (705 µL, 5.0 mmol) in DCE (25 mL) at 70 ºC for 48 h. The crude product was purified by column chromatography on silica gel (0.5% EtOAc in petroleum ether) to afford compound **3j** (240 mg, 80%) as a bright yellow oil: IR (neat, cm^{-1}): ν_{max} 3425, 2937, 1665, 1548, 972; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.71 – 7.67 (m, 2H), 7.64 – 7.60 (m, 1H), 7.54 – 7.49 (m, 2H), 7.48 – 7.37 (m, 2H), 7.35 – 7.30 (m, 2H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 184.8, 156.6; 151.7, 139.5, 133.6, 131.9, 129.4, 129.1, 127.3, 127.1, 124.3; 123.7, 120.1, 118.1, 112.9 ppm; HRMS (ESI): *m/z* calcd for $C_{15}H_{10}{}^{79}BrO_2$ $[M+H]^+$ 300.9859; found 300.9856.

1-(5-Methylbenzofuran-2-yl)ethan-1-one (3k). The title compound was prepared according to the general procedure by stirring a mixture of 5-methylbenzofuran (132 mg, 1.0 mmol), glacial acetic acid (69 µL, 1.2 mmol) and TFAA (705 µL, 5.0 mmol) in DCE (25 mL) at 70 °C for 48 h. The crude product was purified by column chromatography on silica gel (0.2% EtOAc in petroleum ether) to afford compound **3k** (92 mg, 53%) as

a colorless solid: mp 74–75 °C; IR (neat, cm^{-1}): ν_{max} 3101, 2919, 1668, 1551, 818; ^1H NMR (400 MHz, $CDCl_3$): δ 7.47 – 7.43 (m, 2H), 7.41 (d, *J* 0.9 Hz, 1H), 7.28 (dd, *J* 8.6, 1.7 Hz, 1H), 2.58 (s, 3H), 2.44 (s, 3H) ppm; ^{13}C NMR (100MHz, $CDCl_3$): δ 188.8, 154.3, 152.9, 133.6, 130.0, 127.3, 122.8, 113.0, 112.1, 26.5, 21.4 ppm; HRMS (ESI): *m/z* calcd for $C_{11}H_{11}O_2$ $[M+H]^+$: 175.0754; found 175.0753.

(2-Bromophenyl)(5-methylbenzofuran-2-yl)methanone (3l). The title compound was prepared according to the general procedure by stirring a mixture of 5-methylbenzofuran (132 mg, 1.0 mmol), 2-bromobenzoic acid (240 mg, 1.2 mmol) and TFAA (705 µL, 5.0 mmol) in DCE (25 mL) at 70 °C for 48 h. The crude product was purified by column chromatography on silica gel (1% EtOAc in petroleum ether) to afford compound **3l** (150 mg, 48%) as a bright yellow oil: IR (neat, cm^{-1}): ν_{max} 2915, 1651, 1429, 1205, 977; ^1H NMR (400 MHz, $CDCl_3$): δ 7.69 – 7.67 (m, 1H), 7.51 – 7.48 (m, 2H), 7.46 – 7.36 (m, 3H), 7.33 – 7.30 (m, 1H), 7.23 (d, *J* 0.9 Hz, 1H), 2.45 (s, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 184.7, 155.1, 151.9, 139.6, 133.9, 133.6, 131.9, 130.8, 129.4, 127.3, 127.2, 123.0, 120.1, 117.9, 112.4, 21.4 ppm; HRMS (ESI): *m/z* calcd for $C_{16}H_{12}{}^{79}BrO_2$ $[M+H]^+$: 315.0015; found 315.0017.

1-(7-Methoxybenzofuran-2-yl)ethan-1-one (3m). The title compound was prepared according to the general procedure by stirring a mixture of 7-methoxybenzofuran (148 mg, 1.0 mmol), glacial acetic acid (69 µL, 1.2 mmol) and TFAA (705 µL, 5.0 mmol) in DCE (25 mL) at 70 ºC for 48 h. The crude product was purified by column chromatography on silica gel (1% EtOAc in petroleum ether) to afford compound **3m** (163 mg, 86%) as a colorless solid: mp 92–93 °C; IR (neat, cm^{-1}): ν_{max} 3136, 2965, 1655, 1402, 1273; ^1H NMR (400 MHz, $CDCl_3$): δ 7.79 (dd, *J* 8.4, 1.7 Hz, 1H), 7.73 (d, *J* 2.1 Hz, 1H), 7.56 (dd, *J* 2.1, 0.8 Hz, 1H), 6.79 (dd, *J* 8.4, 1.5 Hz, 1H), 4.07 (s, 3H), 2.63 (s, 3H) ppm; ^{13}C NMR (100MHz, $CDCl_3$): δ 197.3, 149.4, 147.1, 144.4, 128.8, 127.9, 123.7, 108.7, 105.3, 56.4, 27.3 ppm; HRMS (ESI): *m/z* calcd for $C_{11}H_{11}O_3$ $[M+H]^+$: 191.0703; found 191.0702.

The preparation of compounds 4-7.

6*H*-Indeno[2, 1-*b*]benzofuran-6-one (**4**).[33] PPh_3 (26.0 mg, 0.1 mmol), K_2CO_3 (276.0 mg, 0.1 mmol) and $Pd(OAC)_2$ (22.5 mg, 0.1 mmol) was added to a solution of **3j** (300.0 mg, 1.0 mmol) in DMF (10 mL). The resulting mixture was heated at 110 °C until the reaction was completed (reaction monitored by TLC). The mixture was poured into water (20 mL), then extracted with EtOAc (3 x 40 mL). The combined organic extracts were washed with brine (3 x 40 mL) and dried over anhydrous sodium sulfate, filtered, and then evaporated *in vacuo*. The crude product was purified by column chromatography on silica gel (0.5% EtOAc in petroleum ether) to afford **4** (176 mg, 80%) as a red solid: mp 97–98 ˚C; IR (neat, cm^{-1}): ν_{max} 1705, 1610, 1399, 1141, 1021; ^1H NMR (400 MHz, $CDCl_3$): δ 7.77 (d, *J* 7.8 Hz, 1H), 7.57 (d, *J* 8.4 Hz, 1H), 7.48 (t, *J* 7.8 Hz, 1H), 7.43 – 7.32 (m, 3H), 7.24 (d, *J* 7.1Hz, 1H), 7.18 (t, *J* 7.5 Hz, 1H) ppm; ^{13}C NMR (100MHz, $CDCl_3$): δ 180.8, 161.7, 154.8, 148.2, 141.5, 136.2, 135.1, 134.0, 128.8, 128.8, 125.0, 124.3, 122.1, 120.4, 114.0 ppm; HRMS (ESI): *m/z* calcd for $C_{15}H_9O_2$ $[M+H]^+$: 221.0597; found 221.0596.

2-Methyl-6*H*-indeno[2, 1-*b*]benzofuran-6-one (5). PPh_3 (26.0 mg, 0.1 mmol), K_2CO_3 (276.0 mg, 0.1 mmol) and $Pd(OAc)_2$ (22.5 mg, 0.1 mmol) was added to a solution of **3l** (314 mg, 1.0 mmol) in DMF (10 mL). The resulting mixture was heated at 110 °C until the reaction was completed (reaction monitored by TLC). The mixture was poured into water (20 mL), then extracted with EtOAc (3 x 40 mL). The combined organic extracts were washed with brine (3 x 40 mL) and dried over anhydrous sodium sulfate, filtered, and then evaporated *in vacuo*. The crude product was purified by column chromatography on silica gel (10% EtOAc in petroleum ether) to afford **5** (229 mg, 98%) as an orange solid: mp 129–130 °C; IR (neat, cm^{-1}): ν_{max} 1705, 1610, 1550, 1260, 1096; ^1H NMR (400 MHz, $CDCl_3$): δ 7.45 (s, 1H), 7.39 – 7.34 (m, 2H), 7.32 – 7.27 (m, 1H), 7.25 – 7.21 (m, 1H), 7.16 – 7.10 (m, 2H), 2.46 (s, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 180.7, 160.2, 154.7, 141.2, 136., 135.1, 134.6, 133.9, 130.3, 128.5, 124.0, 122.0, 121.6, 120.2, 113.3, 21.5 ppm; HRMS (ESI): *m/z* calcd for $C_{16}H_{11}O_2$ $[M+H]^+$: 235.0754; found 235.0755.

2,2'-Bibenzofuran (6).[34] $FeCl_3$ (16.2 mg, 0.1 mmol), TMHD (36.9 mg, 0.2 mmol) was added to a solution of **3f** (314 mg, 1.0 mmol) in DMF (10 mL). The resulting mixture was heated at 120 °C until the reaction was completed (reaction monitored by TLC). The mixture was poured into water (20 mL), then extracted with EtOAc (3 x 40 mL). The combined organic extracts were washed with brine (3 x 40 mL) and dried over anhydrous sodium sulfate, filtered, and then evaporated *in vacuo*. The crude product was purified by column chromatography on silica gel (0.5% EtOAc in petroleum ether) to afford **6** (89 mg, 38%) as a colorless solid: mp 196–197 °C; IR (neat, cm^{-1}): ν_{max} 1468, 1299, 1217, 1171; ^1H NMR (400 MHz, $CDCl_3$): δ 7.77 – 7.63 (m, 2H), 7.58 – 7.54 (m, 2H), 7.36 – 7.32 (m, 2H), 7.30 – 7.26 (m, 2H), 7.17 (s, 2H) ppm; ^{13}C NMR (100 MHz, DMSO): δ 154.5, 146.8, 128.1, 125.6, 123.8, 121.8, 111.3, 104.3 ppm; HRMS (ESI): *m/z* calcd for $C_{16}H_{10}O_2Na$ $[M+Na]^+$: 257.0573; found 257.0569.

3-Methyl-2,2'-bibenzofuran (7). $FeCl_3$ (16.2 mg, 0.1 mmol), TMHD (36.9 mg, 0.2 mmol) was added to a solution of **3g** (328 mg, 1.0 mmol) in DMF (10 mL). The resulting mixture was heated at 120 °C until the reaction was completed (reaction monitored by TLC). The mixture was poured into water (20 mL), then extracted with EtOAc (3 x 40 mL). The combined organic extracts were washed with brine (3 x 40 mL) and dried over anhydrous sodium sulfate, filtered, and then evaporated *in vacuo*. The crude product was purified by column chromatography on silica gel (0.5% EtOAc in petroleum ether) to afford **7** (94 mg, 38%) as a colorless solid: mp 123–124 °C; IR (neat, cm^{-1}): ν_{max} 1442, 1311, 1269, 1221, 1165; ^1H NMR (400 MHz, $CDCl_3$): δ 7.66 – 7.65 (m, 1H), 7.60 – 7.56 (m, 2H), 7.53 (d, *J* 8.0 Hz, 1H), 7.37 – 7.32 (m, 2H), 7.31 – 7.26 (m, 2H), 7.11 (s, 1H), 2.62 (s, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 155.0, 154.5, 148.8, 143.1, 130.5, 128.5, 125.3, 124.8, 123.4, 122.9, 121.3, 119.7, 114.4, 111.4, 111.3, 104.0, 8.9 ppm; HRMS (ESI): *m/z* calcd for $C_{17}H_{13}O_2$ $[M+H]^+$: 249.0910; found 249.0909.

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Supplementary Material

Copies of the ^1H and ^{13}C-NMR spectra are provided in the supplementary material file.

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