Synthesis M. Nayak et al. Paper

Regiospecific Synthesis of 5- and 6-Acylated Naphtho[1,2-*b*]benzofurans via Intramolecular Alkyne Carbonyl Metathesis

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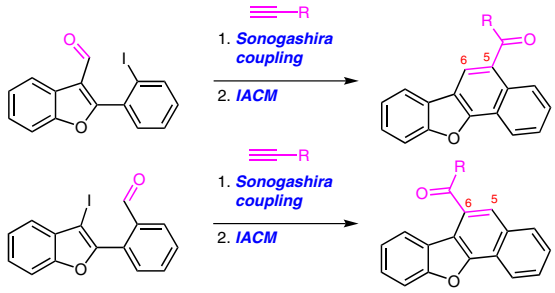

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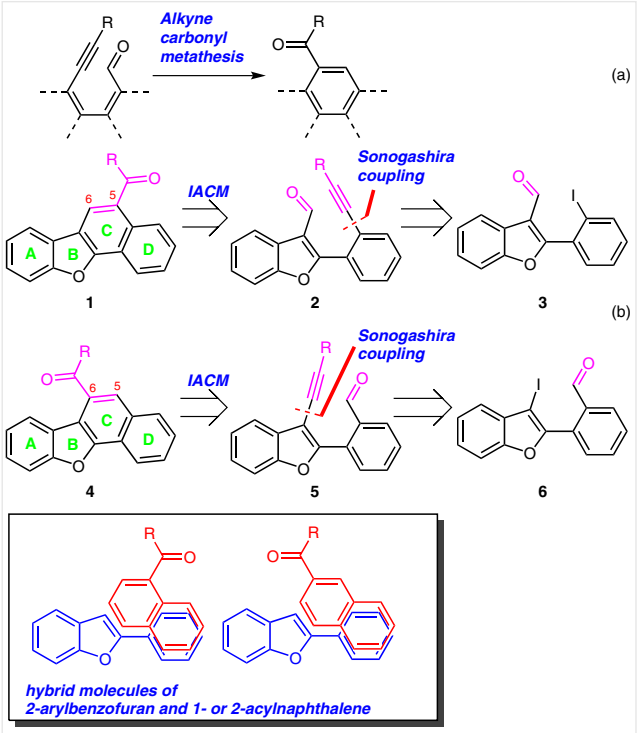
Abstract Straightforward access to various 5- and 6-acylated naphtho[1,2-*b*]benzofurans was achieved by successive Sonogashira coupling and intramolecular alkyne carbonyl metathesis to assemble the central aromatic C ring of naphtho[1,2-*b*]benzofurans regiospecifically substituted with an acyl group at the C5 or C6 position.

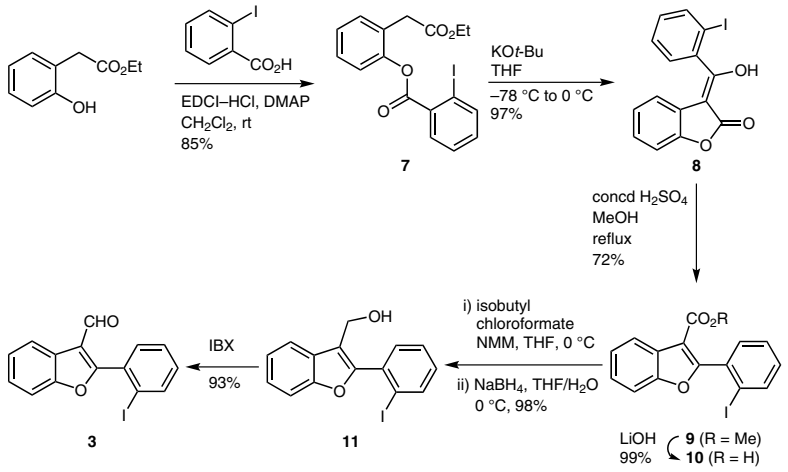
Key words naphtho[1,2-*b*]benzofuran, Sonogashira coupling, alkyne carbonyl metathesis, intramolecular reaction, regiospecific reaction

Intramolecular alkyne carbonyl metathesis (IACM) of an alkyne and a carbonyl spatially arranged within one molecular skeleton provides an efficient way to make carbo- or heterocycles with an enone functional group (Scheme 1, a).[1] Recently, we have employed this strategy for the synthesis of benzo-fused indolizines, pyrrolo[1,2-*a*]quinolines,[2] as well as natural products, such as brazilin, deguelin, and munduserone,[3] constructing the pyridine ring in the former and 3- or 4-acylchromene in the latter.

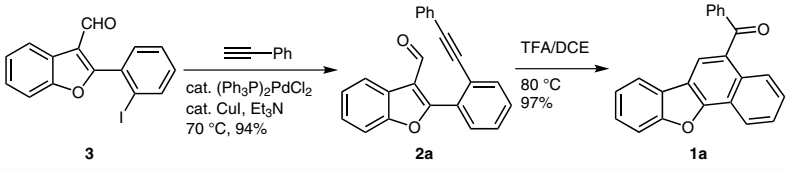
As an extension, we decided to investigate IACM-based modular synthesis of polyaromatic heterocycles,[4] an important class of chemicals in the area of pharmaceuticals and functional materials. Since IACM typically allows the regiospecific introduction of an acyl moiety in the newly formed ring systems, we hoped to construct polyheterocycles with an acyl group positioned at a specific site, which is quite difficult to achieve by any other synthetic methods such as intermolecular Friedel–Crafts acylation. As part of our continued interest in polyfunctionalized benzofurans[5] we wish to describe here a synthetic approach to naphtho[1,2-*b*]benzofurans[6] with an acyl unit at the C5 or C6 position[7] through IACM (Scheme 1, b). As 2-arylbenzofuran, 1-acylnaphthalene, and 2-acylnaphthalene have been employed as key pharmacophores in the area of small-molecule drug discovery, we expected that these two hybrid structures would be useful in the discovery of new interesting biological activities.[8] Retrosynthetically, 2-arylbenzofurans, **2** and **5**, having both alkyne and aldehyde groups were required for this purpose. In turn, we expected that Sonogashira cross-coupling of **3** and **6** with terminal alkynes would give rise to **2** and **5**, respectively.



Scheme 1 Synthetic plans



Scheme 2 Synthesis of **3**



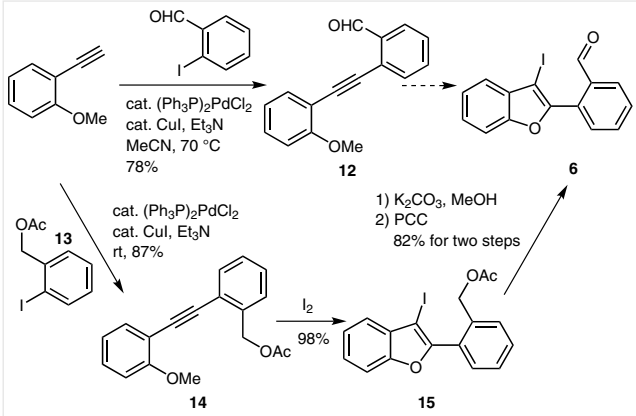
Scheme 3 Sonogashira coupling/IACM of **3**

To validate our proposal, preparation of the requisite **3** was first attempted. After several unsuccessful attempts, we finally resorted to Chi's protocol (Scheme 2).[9] First, ethyl (2-hydroxyphenyl)acetate was coupled with 2-iodobenzoic acid under modified Steglich esterification conditions[10] to give ester **7**. Exposure of **7** to excess *t*-BuOK resulted in β-keto ester **8** in its enol form in excellent yield, which was smoothly converted into methyl 2-(2-iodophenyl)benzofuran-3-carboxylate (**9**) by treatment of MeOH and concentrated H_2SO_4. The ester moiety in **9** was transformed into the desired aldehyde to furnish **3** in good overall yield by a three-step sequence: hydrolysis, $NaBH_4$ reduction of the mixed anhydride formed in situ, and IBX oxidation.

When **3** was subjected to Sonogashira coupling conditions with phenylacetylene, **2a** was isolated in 94% yield (Scheme 3). After screening of several ACM catalyst conditions, we were pleased to find that heating of **2a** in TFA/DCE at 80 °C for 1 hour deliver the desired product **1a** in excellent yield.

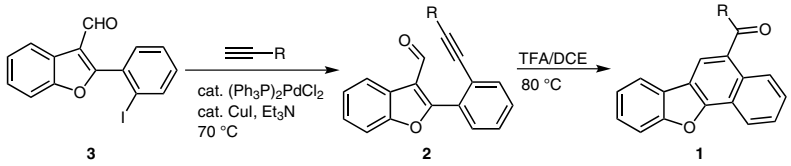
With these optimized conditions in hand, substrate scope was examined with different terminal alkynes (Table 1). Sonogashira cross-coupling of **3** with several (hetero)arylalkynes proceeded well to give the corresponding alkynes **2** in excellent yields. Subsequent IACM of **2** under the optimized conditions furnished the desired 5-acylnaphtho[1,2-*b*]benzofurans in good yields except for **2f** (entry 5). The formation of **1f′** can be interpreted as a consequence of domino alkyne carbonyl metathesis/Nazarov cyclization.[11]

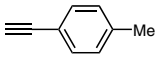
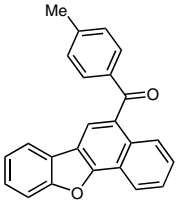
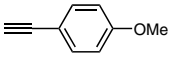
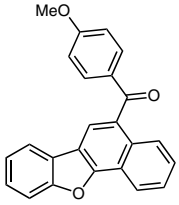
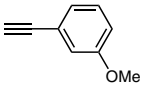
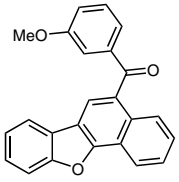
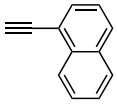
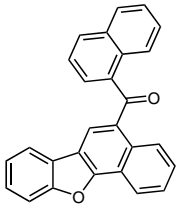
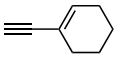
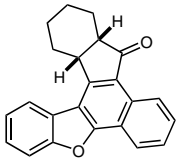
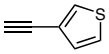
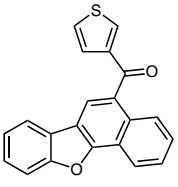
Next, **6** was synthesized for the synthesis of 6-acylnaphtho[1,2-*b*]benzofurans **4** (Scheme 4). Sonogashira coupling of 1-ethynyl-2-methoxybenzene with 2-iodobenzaldehyde afforded the corresponding product **12** in 78% yield. To our disappointment, however, no desired 3-iodobenzofuran **6** was observed from the reaction of **12** under several iodocyclization conditions, which might be ascribed to the competitive participation of the formyl group in **12** in iodine-



Scheme 4 Synthesis of **6**

Table 1 Synthesis of Diverse 5-Acylnaphtho[1,2-*b*]benzofurans[a]



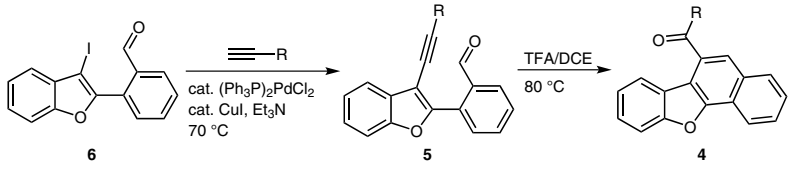
Entry	Alkyne	**2** (yield,[b] %)	Product	**1** (yield,[b] %)
1		**2b** (98)		**1b** (97)
2		**2c** (96)		**1c** (90)
3		**2d** (94)		**1d** (93)
4		**2e** (98)		**1e** (93)
5		**2f** (75)		**1f′** (68)
6		**2g** (95)		**1g** (87)

[a] Reaction conditions: 1. **3** (0.14 mmol), terminal alkyne (0.16 mmol), $(Ph_3P)_2PdCl_2$ (0.1 equiv), CuI (0.05 equiv), Et_3N (2 mL), 70 °C, 12 h; 2. **2** (0.1 mmol), TFA/DCE (1:2, 3 mL); 80 °C 1 h.
[b] Isolated yield.

mediated cyclization.[12] These difficulties in preparing **6** were overcome by replacing the coupling partner by 2-iodobenzyl acetate (**13**). Thus, when 1-ethynyl-2-methoxybenzene was treated with **13** in the presence of $(Ph_3P)_2PdCl_2$ (0.1 equiv) and CuI (0.05 equiv) in Et_3N at room temperature, the cross-coupled product **14** was obtained in excellent yield. Smooth iodocyclization took place upon exposure of **14** to I_2 (4 equiv), affording the cyclized product **15** in 98% yield. Deacetylation of **15** and subsequent PCC oxidation gave **6**, setting the stage for sequential Sonogashira coupling/IACM for the synthesis of 6-acylnaphtho[1,2-*b*]benzofuran.

As shown in Table 2, Sonogashira coupling of **6** with phenylacetylene under the similar reaction conditions employed for the synthesis of **2** led to **5a** in 92% yield (entry 1). Again, subjection of **5a** in TFA/DCE at 80 °C for 1 hour produced the desired product **4a** in excellent yield. The reaction scope was also investigated with different (hetero)aryl- and alkylalkynes under the same reaction sequence. Various 6-acylnaphtho[1,2-*b*]benzofurans **4** were synthesized in good overall yields. The IACM reaction with a substrate bearing an electron-deficient aryl group on the alkyne **5f** also worked well under these conditions to give **4f** in 90% yield (entry 6). When **5g** having a cyclohex-1-enyl group was exposed to TFA at 80 °C, hexacyclic compound **4g′** was obtained as the major product due to Nazarov reaction after IACM (entry 7).

Table 2 Synthesis of Diverse 6-Acylnaphtho[1,2-*b*]benzofurans[a]



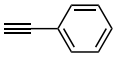
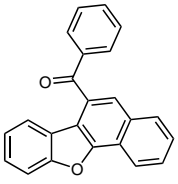
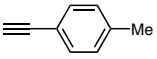
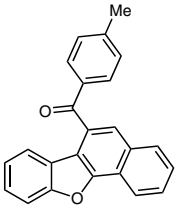
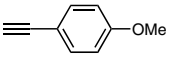
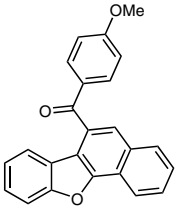
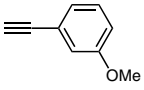
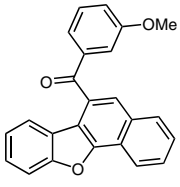
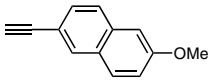
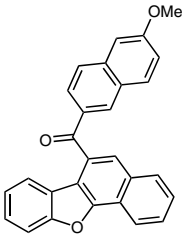
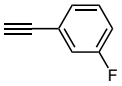
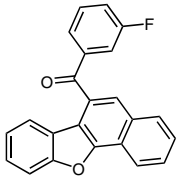
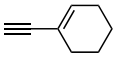
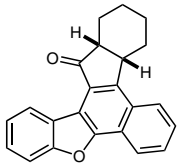
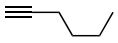
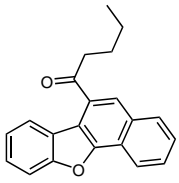
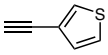
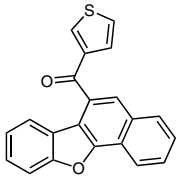
Entry	Alkyne	**5** (yield,[b] %)	Product	**4** (yield,[b] %)
1		**5a** (92)		**4a** (90)
2		**5b** (85)		**4b** (95)
3		**5c** (83)		**4c** (90)
4		**5d** (85)		**4d** (88)

Table 2 (continued)

Entry	Alkyne	**5** (yield,[b] %)	Product	**4** (yield,[b] %)
5		**5e** (76)		**4e** (89)
6		**5f** (82)		**4f** (90)
7		**5g** (88)		**4g′** (82)
8		**5h** (96)		**4h** (97)
9		**5i** (96)		**4i** (87)

[a] Reaction conditions: 1. **6** (0.14 mmol), terminal alkyne (0.16 mmol), $(Ph_3P)_2PdCl_2$ (0.1 equiv), CuI (0.05 equiv), Et_3N (2 mL), 70 °C, 12 h; 2. **5** (0.1 mmol), TFA/DCE (1:2, 3 mL); 80 °C, 1 h.
[b] Isolated yield.

In summary, we have established an expeditious route to 5- and 6-acylated naphtho[1,2-*b*]benzofurans, hybrid structures of 2-arylbenzofuran and 1- or 2-acylnaphthalene, by utilizing a sequential Sonogashira coupling/intramolecular alkyne carbonyl metathesis reaction where the benzene ring C of this scaffold was formed with an acyl substituent at the specific position. Both aryl- and alkylalkynes were employed in this sequence to generate a wide variety of new 6-acylnaphtho[1,2-*b*]benzofurans, exhibiting good functional group tolerance. Application of this protocol for the synthesis of other polyaromatic heterocycles as well as evaluation of these compounds in biomedical sciences are underway in our laboratory.

Unless specified, all reagents and starting materials were purchased from commercial sources and used as received without purification. 'Concentrated' refers to the removal of volatile solvents via distillation using a rotary evaporator. 'Dried' refers to pouring onto, or passing through, anhyd $MgSO_4$ followed by filtration. Flash chromatography was performed using silica gel (230–400 mesh) with hexanes, EtOAc, and CH_2Cl_2 as eluent. All reactions were monitored by TLC on 0.25-mm silica plates (F-254) visualizing with UV light. Melting points were measured using a capillary melting point apparatus. ^1H and ^{13}C NMR spectra were recorded on 400 MHz NMR spectrometer. HRMS were measured with electrospray ionization (ESI) and Q-TOF mass analyzer.

2-(2-Ethoxy-2-oxoethyl)phenyl 2-Iodobenzoate (7)

To a stirred solution of ethyl (2-hydroxyphenyl)acetate (1.2 g, 6.66 mmol) in anhyd CH_2Cl_2 (25 mL) were added 2-iodobenzoic acid (1.98 g, 7.99 mmol), EDCI-HCl (1.53 g, 7.99 mmol), and DMAP (163 mg, 1.33 mmol) at rt and the mixture was stirred overnight. The mixture was washed with 1 M HCl and water followed by sat. aq $NaHCO_3$ solution. The organic layer was dried ($MgSO_4$) and concentrated in vacuo to yield the crude product which was purified by flash chromatography (silica gel, hexanes/EtOAc, 9:1) give **7** (2.33 g, 85%) as a colorless liquid.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.09 (t, *J* = 8.1 Hz, 2 H), 7.49 (t, *J* = 7.6 Hz, 1 H), 7.35–7.39 (m, 2 H), 7.21–7.30 (m, 3 H), 4.08 (q, *J* = 7.1 Hz, 2 H), 3.64 (s, 2 H), 1.14 (t, *J* = 7.1 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 170.7, 164.4, 149.2, 141.9, 133.7, 133.4, 131.7, 131.5, 128.7, 128.19, 126.8, 126.5, 122.6, 94.9, 61.1, 36.7, 14.2.

HRMS (ESI-QTOF): *m*/*z* [M + H]$^+$ calcd for $C_{17}H_{16}IO_4$: 411.0088; found: 411.0090.

3-[Hydroxy(2-iodophenyl)methylene]benzofuran-2(3*H*)-one (8)

To a mixture of KO*t*-Bu (862 mg, 7.68 mmol) in anhyd THF (40 mL) under a N_2 atmosphere was dropwise added a solution of **7** (2.1 g, 5.12 mmol) in THF (5 mL) at –78 °C. The mixture was stirred for 10 min at –78 °C, and then it was warmed to 0 °C and stirred for 2 h at this temperature. The mixture was quenched with 1 M HCl (20 mL), diluted with EtOAc (30 mL), and washed with water (2 × 20 mL). The organic layer was dried ($MgSO_4$) and concentrated in vacuo to yield the product (1.81 g, 97%) as a greenish yellow solid, which was used for the next step without further purification; mp 129.4–131.5 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.04 (d, *J* = 8.0 Hz, 1 H), 7.55 (t, *J* = 7.6 Hz, 1 H), 7.45 (d, *J* = 7.6 Hz, 1 H), 7.30 (d, *J* = 7.6 Hz, 1 H), 7.16–7.23 (m, 2 H), 6.93 (t, *J* = 7.2 Hz, 1 H), 6.31 (d, *J* = 7.2 Hz, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 173.4, 171.2, 151.1, 140.3, 138.1, 132.3, 129.3, 128.9, 127.6, 124.2, 121.9, 120.2, 111.0, 100.1, 94.5.

HRMS (ESI-QTOF): *m*/*z* [M + H]$^+$ calcd for $C_{15}H_{10}IO_3$: 364.9669; found: 364.9668.

Methyl 2-(2-Iodophenyl)benzofuran-3-carboxylate (9)

To a stirred solution of **8** (1.3 g, 3.57 mmol) in anhyd MeOH (40 mL) was slowly added concd H_2SO_4 (4.5 mL) at r.t. The resulting mixture was refluxed for 24 h, cooled to r.t., and concentrated under reduced pressure. The residue was diluted with EtOAc (20 mL) and washed with water (2 × 10 mL) and sat. aq $NaHCO_3$ solution (2 × 10 mL). The combined organic layers were dried ($MgSO_4$) and concentrated in vacuo to yield the crude product which was purified by flash chromatography (silica gel, hexanes/EtOAc, 19:1) afforded **9** (970 mg, 72%) as a white solid; mp 99.5–101.6 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.13–8.15 (m, 1 H), 7.99 (d, *J* = 7.8 Hz, 1 H), 7.56–7.58 (m, 1 H), 7.47–7.49 (m, 2 H), 7.40–7.43 (m, 2 H), 7.18–7.22 (m, 1 H), 3.83 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 163.7, 162.2, 154.2, 139.3, 136.1, 131.7, 131.4, 127.8, 125.9, 125.7, 124.4, 122.6, 111.6, 111.1, 98.3, 51.8.

HRMS (ESI-QTOF): *m*/*z* [M + H]$^+$ calcd for $C_{16}H_{12}IO_3$: 378.9826; found: 378.9823.

2-(2-Iodophenyl)benzofuran-3-carboxylic Acid (10)

To a stirred solution of **9** (1 g, 2.64 mmol) in THF/H_2O (1:1, 20 mL) was added LiOH·H_2O (555 mg, 13.22 mmol). The mixture was stirred at 80 °C for 12 h, and then it was cooled to r.t., acidified with 2 M HCl, and extracted with EtOAc (20 mL). The organic layer was dried ($MgSO_4$) and concentrated in vacuo to yield the product (960 mg, 99%) as a white solid which was used for the next step without further purification; mp 194.7–196.2 °C.

^{1}H NMR (400 MHz, DMSO-d_6): δ = 8.07 (d, *J* = 6.7 Hz, 1 H), 8.01 (d, *J* = 7.8 Hz, 1 H), 7.70 (d, *J* = 6.8 Hz, 1 H), 7.52–7.59 (m, 2 H), 7.41–7.47 (m, 2 H), 7.30 (t, *J* = 7.3 Hz, 1 H).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 163.9, 161.7, 153.6, 138.6, 135.8, 131.8, 131.7, 127.9, 125.9, 125.7, 124.4, 122.2, 111.6, 111.3, 99.2.

HRMS (ESI-QTOF): *m*/*z* [M + H]$^+$ calcd for $C_{15}H_{10}IO_3$: 364.9669; found: 364.9668.

[2-(2-Iodophenyl)benzofuran-3-yl]methanol (11)

To a stirred solution of **10** (960 mg, 2.65 mmol) in THF (20 mL) at 0 °C were added isobutyl chloroformate (0.414 mL, 3.18 mmol) and *N*-methylmorpholine (0.35 mL, 3.18 mmol). The resulting mixture was stirred for 2 min, and the precipitate obtained was filtered through a pad of Celite and washed with THF (5 mL). The combined filtrates were added to another round bottom flask and cooled to 0 °C. To this solution was added dropwise $NaBH_4$ (200 mg, 5.30 mmol) dissolved in water (0.5 mL). The mixture was stirred for 5 min at 0 °C, and then it was quenched with water (10 mL) and extracted with EtOAc (3 × 20 mL). The combined organic layers were dried ($MgSO_4$) and concentrated in vacuo to yield the crude product which was purified by flash chromatography (silica gel, hexanes/EtOAc, 4:1) to afford **11** (905 mg, 98%) as an off-white solid; mp 98.3–100.4 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.00 (d, *J* = 7.9 Hz, 1 H), 7.81 (d, *J* = 7.2 Hz, 1 H), 7.54 (d, *J* = 8.0 Hz, 1 H), 7.44–7.48 (m, 2 H), 7.31–7.39 (m, 2 H), 7.17–7.20 (m, 1 H), 4.75 (s, 2 H), 1.81 (s, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 154.5, 154.3, 139.8, 135.6, 132.2, 131.2, 128.2, 125.1, 123.2, 120.6, 117.0, 111.6, 99.1, 56.4.

HRMS (ESI-QTOF): *m*/*z* [M + Na]$^+$ calcd for $C_{15}H_{11}NaIO_2$: 372.9696; found: 372.9697.

2-(2-Iodophenyl)benzofuran-3-carbaldehyde (3)

To a stirred solution of **11** (990 mg, 2.83 mmol) in EtOAc (20 mL) was added IBX (2.4 g, 8.49 mmol). The mixture was refluxed for 3 h, and then it was cooled to r.t., filtered through a pad of Celite, and washed with EtOAc. The filtrate was washed with sat. aq $NaHCO_3$ (3 × 10 mL) and water (2 × 10 mL). The combined organic layers were dried ($MgSO_4$) and concentrated in vacuo to give the crude product which was purified by flash chromatography (silica gel, hexanes/EtOAc, 9:1) to afford **3** (914 mg, 93%) as a white solid; mp 104.9–106.9 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.98 (s, 1 H), 8.29 (d, *J* = 8.0 Hz, 1 H), 8.05–8.07 (m, 1 H), 7.59–7.61 (m, 1 H), 7.53–7.54 (m, 2 H), 7.41–7.47 (m, 2 H), 7.26–7.30 (m, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 186.6, 166.8, 154.4, 140.3, 133.9, 132.6, 132.3, 128.3, 126.4, 125.1, 124.4, 122.9, 118.9, 111.6, 98.2.

HRMS (ESI-QTOF): *m*/*z* [M + H]$^+$ calcd for $C_{15}H_{10}IO_2$: 348.9720; found: 348.9723.

2-[2-(Phenylethynyl)phenyl]benzofuran-3-carbaldehyde (2a); Typical Procedure

To a mixture of **3** (50 mg, 0.14 mmol) in Et_3N (2 mL) were added phenylacetylene (0.018 mL, 0.16 mmol), $(Ph_3P)_2PdCl_2$ (10 mg, 0.014 mmol), and CuI (1.33 mg, 0.007 mmol). The mixture was stirred at 70 °C for 12 h, and then it was concentrated in vacuo to yield the

crude product. Purification by flash chromatography (silica gel, hexanes/EtOAc, 49:1) afforded **2a** (43.5 mg, 94%) as an off-white solid; mp 102.3–104.6 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 10.26 (s, 1 H), 8.31–8.32 (m, 1 H), 7.70–7.75 (m, 2 H), 7.49–7.58 (m, 3 H), 7.40–7.42 (m, 2 H), 7.31–7.33 (m, 2 H), 7.25–7.27 (m, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 187.0, 164.2, 154.7, 133.6, 131.7, 130.8, 130.8, 130.4, 128.9, 128.6, 128.5, 126.2, 125.1, 124.9, 124.1, 122.9, 122.4, 118.7, 111.4, 94.0, 87.4.

HRMS (ESI-QTOF): *m*/*z* [M + H]$^+$ calcd for $C_{23}H_{15}O_2$: 323.1067; found: 323.1066.

2-[2-(*p*-Tolylethynyl)phenyl]benzofuran-3-carbaldehyde (2b)

White solid; yield: 47.5 mg (98%); mp 112.2–114.4 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 10.28 (s, 1 H), 8.33–8.34 (m, 1 H), 7.72–7.76 (m, 2 H), 7.49–7.60 (m, 3 H), 7.42–7.43 (m, 2 H), 7.23 (d, *J* = 7.6 Hz, 2 H), 7.08 (d, *J* = 7.6 Hz, 2 H), 2.32 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 187.0, 164.2, 154.7, 139.2, 133.4, 131.6, 130.8, 130.7, 130.3, 129.3, 128.4, 126.1, 125.2, 124.9, 124.3, 122.9, 119.3, 118.6, 111.3, 94.3, 86.9, 21.7.

HRMS (ESI-QTOF): *m*/*z* [M + H]$^+$ calcd for $C_{24}H_{17}O_2$: 337.1223; found: 337.1226.

2-{2-[(4-Methoxyphenyl)ethynyl]phenyl}benzofuran-3-carbaldehyde (2c)

Pale yellow solid; yield: 48.6 mg (96%); mp 96.2–98.6 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 10.27 (s, 1 H), 8.31–8.32 (m, 1 H), 7.70 (br s, 2 H), 7.48–7.58 (m, 3 H), 7.40–7.41 (m, 2 H), 7.25 (d, *J* = 8.0 Hz, 2 H), 6.78 (d, *J* = 8.0 Hz, 2 H), 3.77 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 187.1, 164.3, 160.2, 154.7, 133.3, 133.2, 130.7, 130.1, 128.2, 126.1, 125.1, 124.9, 124.5, 122.9, 118.6, 114.5, 114.2, 111.3, 94.2, 86.3, 55.4.

HRMS (ESI-QTOF): *m*/*z* [M + H]$^+$ calcd for $C_{24}H_{17}O_3$: 353.1172; found: 353.1174.

2-{2-[(3-Methoxyphenyl)ethynyl]phenyl}benzofuran-3-carbaldehyde (2d)

Off-white solid; yield: 47.5 mg (94%); mp 161.4–163.2 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 10.28 (s, 1 H), 8.31–8.33 (m, 1 H), 7.72–7.76 (m, 2 H), 7.52–7.60 (m, 3 H), 7.41–7.43 (m, 2 H), 7.17 (t, *J* = 7.6 Hz, 1 H), 6.94 (d, *J* = 7.4 Hz, 1 H), 6.83–6.86 (m, 2 H), 3.73 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 187.0, 164.2, 159.4, 154.7, 133.4, 130.8, 130.8, 130.5, 129.6, 128.6, 126.2, 125.1, 124.9, 124.2, 124.1, 123.4, 122.9, 118.7, 116.0, 111.4, 93.9, 87.2, 55.4.

HRMS (ESI-QTOF): *m*/*z* [M + H]$^+$ calcd for $C_{24}H_{17}O_3$: 353.1172; found: 353.1178.

2-[2-(Naphthalen-1-ylethynyl)phenyl]benzofuran-3-carbaldehyde (2e)

Yellow solid; yield: 52.5 mg (98%); mp 150.1–153.4 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 10.28 (s, 1 H), 8.36–8.37 (m, 1 H), 7.94 (d, *J* = 8.3 Hz, 1 H), 7.89 (d, *J* = 8.3 Hz, 1 H), 7.79–7.80 (m, 2 H), 7.74 (d, *J* = 7.4 Hz, 1 H), 7.53–7.63 (m, 4 H), 7.37–7.47 (m, 4 H), 7.15–7.19 (m, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 186.9, 164.7, 154.8, 133.7, 133.1, 133.1, 131.2, 130.9, 130.9, 130.2, 129.4, 128.6, 128.3, 126.9, 126.5, 126.3, 126.0, 125.3, 125.06, 125.0, 124.4, 122.9, 120.1, 119.1, 111.6, 92.4, 92.1.

HRMS (ESI-QTOF): *m*/*z* [M + H]$^+$ calcd for $C_{27}H_{17}O_3$: 373.1223; found: 373.1227.

2-[2-(Cyclohex-1-en-1-ylethynyl)phenyl]benzofuran-3-carbaldehyde (2f)

Pale yellow solid; yield: 35.0 mg (75%); mp 103.1–105.2 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 10.20 (s, 1 H), 8.30–8.31 (m, 1 H), 7.67 (d, *J* = 7.2 Hz, 1 H), 7.64–7.62 (d, *J* = 7.5 Hz, 1 H), 7.55–7.57 (m, 1 H), 7.40–7.51 (m, 4 H), 6.08 (s, 1 H), 2.02–2.06 (m, 4 H), 1.49–1.61 (m, 4 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 187.1, 164.3, 154.6, 136.8, 133.3, 130.6, 130.6, 130.1, 128.0, 126.0, 125.1, 124.8, 124.6, 122.9, 120.3, 118.5, 111.3, 96.0, 84.9, 28.7, 25.9, 22.2, 21.4.

HRMS (ESI-QTOF): *m*/*z* [M + H]$^+$ calcd for $C_{23}H_{19}O_2$: 327.1380; found: 327.1382.

2-[2-(Thiophen-3-ylethynyl)phenyl]benzofuran-3-carbaldehyde (2g)

Off-white solid; yield: 45.0 mg (95%); mp 93.5–95.8 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 10.29 (s, 1 H), 8.33–8.34 (m, 1 H), 7.72–7.74 (m, 2 H), 7.52–7.59 (m, 3 H), 7.40–7.43 (m, 3 H), 7.23 (s, 1 H), 7.01 (d, *J* = 4.6 Hz, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 187.1, 164.0, 154.7, 133.3, 130.7, 130.3, 129.7, 129.7, 128.5, 126.2, 125.6, 125.1, 124.9, 124.1, 122.9, 121.5, 118.6, 111.3, 89.3, 87.0.

HRMS (ESI-QTOF): *m*/*z* [M + H]$^+$ calcd for $C_{21}H_{13}O_2S$: 329.0631; found: 329.0632.

Naphtho[1,2-*b*]benzofuran-5-yl(phenyl)methanone (1a)

To a solution of **2a** (32 mg, 0.1 mmol) in DCE (2.0 mL) was added TFA (1.0 mL) and the resulting solution was stirred at 80 °C for 1 h. Then the mixture was cooled down to r.t. and concentrated in vacuo to yield the crude product. Purification by flash chromatography (silica gel, hexanes/EtOAc, 49:1) afforded **1a** (31 mg, 97%) as an off-white solid; mp 167.4–168.9 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.56 (d, *J* = 8.0 Hz, 1 H), 8.33 (d, *J* = 8.2 Hz, 1 H), 8.17 (s, 1 H), 7.94–7.95 (m, 3 H), 7.69–7.77 (m, 2 H), 7.59–7.66 (m, 2 H), 7.51–7.52 (m, 3 H), 7.39–7.43 (m, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 197.8, 156.5, 138.9, 133.3, 132.0, 131.2, 130.7, 128.6, 127.5, 127.2, 127.0, 126.9, 124.7, 123.6, 122.1, 121.7, 121.4, 120.6, 117.8, 112.2.

HRMS (ESI-QTOF): *m*/*z* [M + Na]$^+$ calcd for $C_{23}H_{14}NaO_2$: 346.0886; found: 346.0888.

Naphtho[1,2-*b*]benzofuran-5-yl(*p*-tolyl)methanone (1b)

Off-white solid; yield: 33.0 mg (97%); mp 163.4–165.6 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.55 (d, *J* = 8.0 Hz, 1 H), 8.28 (d, *J* = 8.4 Hz, 1 H), 8.15 (s, 1 H), 7.95 (d, *J* = 7.2 Hz, 1 H), 7.84 (d, *J* = 7.6 Hz, 2 H), 7.68–7.76 (m, 2 H), 7.50–7.61 (m, 2 H), 7.40 (t, *J* = 7.2 Hz, 1 H), 7.30 (d, *J* = 7.6 Hz, 2 H), 2.46 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 197.5, 156.4, 144.3, 136.3, 132.4, 131.1, 130.8, 129.4, 127.4, 127.1, 126.9, 126.9, 124.8, 123.5, 121.7, 121.5, 121.4, 120.56, 117.8, 112.2, 21.9.

HRMS (ESI-QTOF): *m*/*z* [M + Na]$^+$ calcd for $C_{24}H_{16}NaO_2$: 359.0042; found: 359.0043.

(4-Methoxyphenyl)(naphtho[1,2-*b*]benzofuran-5-yl)methanone (1c)

White solid; yield: 31.5 mg (90%); mp 154.2–156.4 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.54 (d, *J* = 8.0 Hz, 1 H), 8.22 (d, *J* = 8.3 Hz, 1 H), 8.14 (s, 1 H), 7.91–7.97 (m, 3 H), 7.67–7.76 (m, 2 H), 7.50–7.60 (m, 2 H), 7.39–7.43 (m, 1 H), 6.97 (d, *J* = 8.5 Hz, 2 H), 3.89 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 196.5, 163.9, 156.4, 153.5, 133.0, 132.7, 131.6, 131.1, 127.3, 127.1, 126.9, 126.9, 124.8, 123.5, 121.7, 121.4, 120.9, 120.5, 117.9, 113.9, 112.1, 55.7.

HRMS (ESI-QTOF): *m*/*z* [M + Na]$^+$ calcd for $C_{24}H_{16}NaO_3$: 375.0991; found: 375.0994.

(3-Methoxyphenyl)(naphtho[1,2-*b*]benzofuran-5-yl)methanone (1d)

Off-white solid; yield: 32.6 mg (93%); mp 147.3–149.6 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.55 (d, *J* = 8.3 Hz, 1 H), 8.32 (d, *J* = 8.5 Hz, 1 H), 8.17 (s, 1 H), 7.95 (d, *J* = 7.5 Hz, 1 H), 7.69–7.77 (m, 2 H), 7.50–7.63 (m, 3 H), 7.35–7.43 (m, 3 H), 7.18 (d, *J* = 7.7 Hz, 1 H), 3.87 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 197.6, 159.9, 156.5, 153.8, 140.3, 132.1, 131.2, 129.6, 127.5, 127.2, 127.0, 126.9, 124.7, 123.8, 123.6, 122.0, 121.7, 121.4, 120.6, 120.0, 117.8, 114.3, 112.2, 55.7.

HRMS (ESI-QTOF): *m*/*z* [M + H]$^+$ calcd for $C_{24}H_{17}O_3$: 353.1172; found: 353.1172.

Naphthalen-1-yl(naphtho[1,2-*b*]benzofuran-5-yl)methanone (1e)

Gray solid; yield: 34.5 mg (93%); mp 182.5–184.6 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.82 (d, *J* = 8.3 Hz, 1 H), 8.57–8.59 (m, 2 H), 8.20 (s, 1 H), 8.07 (d, *J* = 8.1 Hz, 1 H), 7.98–7.99 (m, 1 H), 7.81 (d, *J* = 7.1 Hz, 1 H), 7.68–7.75 (m, 4 H), 7.59–7.62 (m, 2 H), 7.47–7.51 (m, 2 H), 7.35 (t, *J* = 7.5 Hz, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 199.3, 156.4, 154.5, 137.8, 134.1, 133.0, 132.5, 131.5, 131.5, 130.2, 128.6, 128.1, 128.0, 127.3, 127.1, 127.0, 126.7, 126.0, 124.9, 124.6, 123.6, 121.8, 121.4, 120.6, 117.8, 112.1.

HRMS (ESI-QTOF): *m*/*z* [M + H]$^+$ calcd for $C_{27}H_{17}O_2$: 373.1223; found: 373.1220.

(10a*S*,14a*R*)-10a,11,12,13,14,14a-Hexahydro-10*H*-benzo[1,2]fluoreno[3,4-*b*]benzofuran-10-one (1f')

Off-white solid; yield: 22.4 mg (68%); mp 189.3–191.5 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.29 (d, *J* = 7.7 Hz, 1 H), 8.47 (d, *J* = 7.7 Hz, 1 H), 8.04 (d, *J* = 7.1 Hz, 1 H), 7.67–7.78 (m, 3 H), 7.46–7.56 (m, 2 H), 3.94–4.02 (m, 1 H), 3.04 (br s, 1 H), 2.52–2.62 (m, 2 H), 1.79–1.90 (m, 1 H), 1.65–1.74 (m, 2 H), 1.45–1.54 (m, 1 H), 1.28–1.32 (m, 1 H), 1.08–1.17 (m, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 206.7, 157.8, 156.4, 156.3, 129.5, 128.9, 126.9, 126.8, 125.3, 125.1, 124.0, 121.7, 121.4, 120.7, 116.0, 112.4, 49.0, 38.4, 31.4, 23.2, 22.7, 22.4.

HRMS (ESI-QTOF): *m*/*z* [M + H]$^+$ calcd for $C_{23}H_{19}O_2$: 327.1380; found: 327.1382.

Naphtho[1,2-*b*]benzofuran-5-yl(thiophen-3-yl)methanone (1g)

Gray solid; yield: 28.6 mg (87%); mp 184.9–186.6 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.54 (d, *J* = 7.4 Hz, 1 H), 8.36 (d, *J* = 8.4 Hz, 1 H), 8.25–8.28 (m, 1 H), 7.97 (d, *J* = 6.1 Hz, 1 H), 7.92 (s, 1 H), 7.68–7.75 (m, 3 H), 7.48–7.65 (m, 2 H), 7.39–7.44 (m, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 191.0, 156.4, 153.7, 143.6, 135.4, 132.8, 130.8, 128.6, 127.5, 127.2, 126.9, 126.7, 126.6, 124.7, 123.6, 121.8, 121.4, 121.2, 120.5, 117.7, 112.2.

HRMS (ESI-QTOF): *m*/*z* [M + H]$^+$ calcd for $C_{21}H_{13}O_2S$: 329.0631; found: 329.0635.

2-[(2-Methoxyphenyl)ethynyl]benzaldehyde (12)

To a solution of 2-iodobenzaldehyde (250 mg, 1.08 mmol) in MeCN (3 mL) were added 1-ethynyl-2-methoxybenzene (157 mg, 1.19 mmol), $(Ph_3P)_2PdCl_2$ (76 mg, 0.108 mmol), CuI (10 mg, 0.054 mmol), and Et_3N (0.45 mL, 3.24 mmol). The mixture was stirred at 70 °C for 2 h, and then it was concentrated in vacuo to yield the crude product. Purification by flash chromatography (silica gel, hexanes/EtOAc, 9:1) afforded **12** (198 mg, 78%) as an off-white solid; mp 80.7–83.2 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 10.74 (s, 1 H), 7.95 (d, *J* = 7.7 Hz, 1 H), 7.65 (d, *J* = 7.6 Hz, 1 H), 7.57 (t, *J* = 7.6 Hz, 1 H), 7.52 (d, *J* = 7.5 Hz, 1 H), 7.43 (t, *J* = 7.4 Hz, 1 H), 7.35 (t, *J* = 7.8 Hz, 1 H), 6.92–6.98 (m, 2 H), 3.93 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 192.7, 160.5, 136.0, 133.8, 133.4, 133.1, 130.7, 128.5, 127.5, 127.1, 120.7, 111.7, 110.8, 93.2, 89.2, 55.9.

HRMS (ESI-QTOF): *m*/*z* [M + H]$^+$ calcd for $C_{16}H_{13}O_2$: 237.0910; found: 237.0914.

2-[(2-Methoxyphenyl)ethynyl]benzyl Acetate (14)

To a mixture of **13** (500 mg, 1.81 mmol) in Et_3N (5 mL) were added 1-ethynyl-2-methoxybenzene (251 mg, 1.90 mmol), $(Ph_3P)_2PdCl_2$ (127 mg, 0.181 mmol), and CuI (17 mg, 0.091 mmol). The mixture was stirred at r.t. for 2 h, and then it was concentrated in vacuo to yield the crude product. Purification by flash chromatography (silica gel, hexanes/EtOAc, 9:1) afforded **14** (440 mg, 87%) as a colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.58 (d, *J* = 6.8 Hz, 1 H), 7.49 (d, *J* = 7.8 Hz, 1 H), 7.42–7.43 (m, 1 H), 7.29–7.35 (m, 3 H), 6.87–6.96 (m, 2 H), 5.41 (s, 2 H), 3.93 (s, 3 H), 2.13 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 171.1, 160.3, 137.5, 133.3, 132.1, 130.6, 130.1, 128.4, 128.2, 128.1, 123.1, 120.6, 112.4, 110.8, 77.4, 65.2, 55.9, 21.1.

HRMS (ESI-QTOF): *m*/*z* [M + H]$^+$ calcd for $C_{18}H_{17}O_3$: 281.1172; found: 281.1176.

2-(3-Iodobenzofuran-2-yl)benzyl Acetate (15)

To a stirred solution of **14** (440 mg, 1.57 mmol) in CH_2Cl_2 (10 mL) was added I_2 (1.59 g, 6.28 mmol) and the resulting mixture was stirred at r.t. for 12 h. Then sat. aq. $Na_2S_2O_3$ solution was added to the mixture and extracted with CH_2Cl_2 (3 × 15 mL). The combined organic layers were washed with brine, dried ($MgSO_4$), and concentrated in vacuo to yield the crude product. Purification by flash chromatography (silica gel, hexanes/EtOAc, 9:1) afforded **15** (604 mg, 98%) as a colorless gum.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.68 (d, *J* = 7.7 Hz, 1 H), 7.45–7.57 (m, 5 H), 7.33–7.41 (m, 2 H), 5.23 (s, 2 H), 1.97 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 170.8, 154.7, 154.6, 136.0, 131.7, 131.4, 130.3, 129.3, 129.1, 128.2, 125.9, 123.8, 121.9, 111.5, 65.4, 64.6, 20.9.

HRMS (ESI-QTOF): *m*/*z* [M + H]$^+$ calcd for $C_{17}H_{14}IO_3$: 392.9982; found: 392.9981.

2-(3-Iodobenzofuran-2-yl)benzaldehyde (6)

To a stirred solution of **15** (600 mg, 1.53 mmol) in MeOH (50 mL) was added K_2CO_3 (1.06 g, 7.65 mmol) and the resulting mixture was stirred at r.t. for 30 min. Then the solvent was removed in vacuo. Water was added to the mixture and it was extracted with EtOAc (3 × 25 mL). The combined organic layers were washed with brine, dried (Na_2SO_4), and concentrated in vacuo to yield the crude product. To the crude product dissolved in CH_2Cl_2 (50 mL) was added PCC (493 mg, 2.29 mmol) and the mixture was stirred at r.t. for 2 h. Purification by flash chromatography (silica gel, hexanes/EtOAc, 9:1) afforded **6** (439 mg, 82%) as an off-white solid; mp 77.4–79.2 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 10.09 (s, 1 H), 8.12 (d, *J* = 7.5 Hz, 1 H), 7.82 (d, *J* = 7.5 Hz, 1 H), 7.74 (t, *J* = 7.5 Hz, 1 H), 7.64 (t, *J* = 7.2 Hz, 1 H), 7.39–7.51 (m, 4 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 191.3, 154.96, 152.4, 134.8, 133.6, 132.6, 131.6, 131.5, 130.3, 128.2, 126.5, 124.1, 122.2, 111.7, 67.9.

HRMS (ESI-QTOF): *m*/*z* [M + H]$^+$ calcd for $C_{15}H_{10}IO_2$: 348.9720; found: 348.9723.

Compound **5** was prepared by following the same procedure for the synthesis of **2**.

2-[3-(Phenylethynyl)benzofuran-2-yl]benzaldehyde (5a)

Off-white solid; yield: 41.5 mg (92%); mp 102.5–103.6 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 10.42 (s, 1 H), 8.13 (d, *J* = 7.8 Hz, 1 H), 8.06 (d, *J* = 7.8 Hz, 1 H), 7.82 (d, *J* = 7.4 Hz, 1 H), 7.74 (t, *J* = 7.6 Hz, 1 H), 7.52–7.62 (m, 4 H), 7.36–7.46 (m, 5 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 191.5, 154.6, 154.4, 134.1, 133.5, 132.3, 131.7, 130.0, 129.9, 129.1, 128.8, 128.5, 128.2, 126.3, 123.98, 122.7, 120.99, 111.7, 104.9, 95.9, 79.7.

HRMS (ESI-QTOF): *m*/*z* [M + H]$^+$ calcd for $C_{23}H_{15}O_2$: 323.1067; found: 323.1065.

2-[3-(*p*-Tolylethynyl)benzofuran-2-yl]benzaldehyde (5b)

White solid; yield: 40.0 mg (85%); mp 106.5–108.0 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 10.41 (s, 1 H), 8.12 (d, *J* = 7.7 Hz, 1 H), 8.06 (d, *J* = 7.8 Hz, 1 H), 7.81 (d, *J* = 7.3 Hz, 1 H), 7.73 (t, *J* = 7.6 Hz, 1 H), 7.56–7.61 (m, 2 H), 7.37–7.45 (m, 4 H), 7.16 (d, *J* = 7.8 Hz, 2 H), 2.37 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 191.5, 154.6, 154.2, 139.1, 134.1, 133.5, 132.3, 131.6, 130.1, 129.8, 129.3, 129.2, 128.2, 126.3, 123.9, 121.0, 119.7, 111.7, 105.1, 96.2, 79.0, 21.7.

HRMS (ESI-QTOF): *m*/*z* [M + H]$^+$ calcd for $C_{24}H_{17}O_2$: 337.1223; found: 337.1226.

2-{3-[(4-Methoxyphenyl)ethynyl]benzofuran-2-yl}benzaldehyde (5c)

Off-white solid; yield: 40.9 mg (83%); mp 140.1–142.2 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 10.41 (s, 1 H), 8.12 (d, *J* = 7.6 Hz, 1 H), 8.04 (d, *J* = 7.6 Hz, 1 H), 7.81 (d, *J* = 7.2 Hz, 1 H), 7.73 (t, *J* = 7.2 Hz, 1 H), 7.56–7.60 (m, 2 H), 7.38–7.47 (m, 4 H), 6.88 (d, *J* = 8.0 Hz, 2 H), 3.83 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 191.5, 160.1, 154.6, 153.9, 134.1, 133.5, 133.2, 132.4, 130.0, 129.7, 129.2, 128.2, 126.2, 123.9, 121.0, 114.8, 114.2, 111.7, 105.3, 96.0, 78.3, 55.5.

HRMS (ESI-QTOF): *m*/*z* [M + H]$^+$ calcd for $C_{24}H_{17}O_3$: 353.1172; found: 353.1173.

2-{3-[(3-Methoxyphenyl)ethynyl]benzofuran-2-yl}benzaldehyde (5d)

Off-white solid; yield: 41.9 mg (85%); mp 121.1–123.0 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 10.42 (s, 1 H), 8.13 (d, *J* = 7.8 Hz, 1 H), 8.02 (d, *J* = 7.8 Hz, 1 H), 7.82 (d, *J* = 7.3 Hz, 1 H), 7.74 (t, *J* = 7.5 Hz, 1 H), 7.57–7.62 (m, 2 H), 7.38–7.46 (m, 2 H), 7.25–7.29 (m, 1 H), 7.12 (d, *J* = 6.8 Hz, 1 H), 7.05 (s, 1 H), 6.91 (d, *J* = 8.2 Hz, 1 H), 3.85 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 191.5, 159.5, 154.6, 154.5, 134.2, 133.6, 132.3, 130.1, 129.9, 129.6, 129.1, 128.2, 126.3, 124.2, 124.0, 123.7, 121.0, 116.4, 115.5, 111.7, 104.9, 95.8, 79.5, 55.5.

HRMS (ESI-QTOF): *m*/*z* [M + H]$^+$ calcd for $C_{24}H_{17}O_3$: 353.1172; found: 353.1171.

2-{3-[(6-Methoxynaphthalen-2-yl)ethynyl]benzofuran-2-yl}benzaldehyde (5e)

Yellow solid; yield: 42.8 mg (76%); mp 161.1–163.0 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 10.46 (s, 1 H), 8.15 (d, *J* = 7.8 Hz, 1 H), 8.09 (d, *J* = 7.8 Hz, 1 H), 7.97 (s, 1 H), 7.86 (d, *J* = 7.0 Hz, 1 H), 7.69–7.78 (m, 3 H), 7.58–7.63 (m, 2 H), 7.52 (d, *J* = 8.4 Hz, 1 H), 7.39–7.47 (m, 2 H), 7.17 (d, *J* = 8.4 Hz, 1 H), 7.12 (s, 1 H), 3.94 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 191.6, 158.6, 154.6, 154.2, 134.5, 134.2, 133.6, 132.4, 131.5, 130.1, 129.8, 129.6, 129.2, 128.9, 128.6, 128.3, 127.1, 126.3, 123.98, 121.1, 119.7, 117.6, 111.7, 105.98, 105.1, 96.6, 79.3, 55.5.

HRMS (ESI-QTOF): *m*/*z* [M + H]$^+$ calcd for $C_{28}H_{19}O_3$: 403.1329; found: 403.1325.

2-{3-[(3-Fluorophenyl)ethynyl]benzofuran-2-yl}benzaldehyde (5f)

Off-white solid; yield: 39.1 mg (82%); mp 129.1–131.2 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 10.39 (s, 1 H), 8.13 (d, *J* = 7.7 Hz, 1 H), 8.03 (d, *J* = 7.8 Hz, 1 H), 7.80 (d, *J* = 7.3 Hz, 1 H), 7.75 (t, *J* = 7.4 Hz, 1 H), 7.58–7.64 (m, 2 H), 7.38–7.47 (m, 2 H), 7.30–7.35 (m, 2 H), 7.21 (d, *J* = 9.2 Hz, 1 H), 7.06 (t, *J* = 7.8 Hz, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 191.4, 163.7, 161.3, 154.8, 154.6, 134.2, 133.6, 132.1, 130.2, 130.14, 130.08, 130.0, 128.9, 128.3, 127.60, 127.57, 126.4, 124.1, 120.9, 118.5, 118.3, 116.3, 116.1, 111.8, 104.6, 94.59, 94.56, 80.7.

HRMS (ESI-QTOF): *m*/*z* [M + H]$^+$ calcd for $C_{23}H_{14}FO_2$: 341.0972; found: 341.0977.

2-[3-(Cyclohex-1-en-1-ylethynyl)benzofuran-2-yl]benzaldehyde (5g)

Colorless oil; yield: 40.2 mg (88%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 10.34 (s, 1 H), 8.09 (d, *J* = 7.8 Hz, 1 H), 8.00 (d, *J* = 7.8 Hz, 1 H), 7.69–7.74 (m, 2 H), 7.53–7.59 (m, 2 H), 7.35–7.42 (m, 2 H), 6.23–6.25 (m, 1 H), 2.12–2.21 (m, 4 H), 1.61–1.71 (m, 4 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 191.5, 154.5, 153.6, 136.3, 133.97, 133.5, 132.4, 129.9, 129.6, 129.2, 128.1, 126.1, 123.8, 120.98, 120.5, 111.6, 105.4, 97.97, 28.9, 25.9, 22.3, 21.6.

HRMS (ESI-QTOF): *m*/*z* [M + H]$^+$ calcd for $C_{23}H_{19}O_2$: 327.1380; found: 327.1383.

2-[3-(Hex-1-yn-1-yl)benzofuran-2-yl]benzaldehyde (5h)

Colorless oil; yield: 40.6 mg (96%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 10.32 (s, 1 H), 8.09 (dd, *J* = 0.8, 7.8 Hz, 1 H), 7.99 (d, *J* = 7.8 Hz, 1 H), 7.68–7.72 (m, 2 H), 7.52–7.59 (m, 2 H), 7.33–7.41 (m, 2 H), 2.45 (t, *J* = 7.0 Hz, 2 H), 1.57–1.61 (m, 2 H), 1.43–1.48 (m, 2 H), 0.94 (t, *J* = 7.3 Hz, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 191.5, 154.5, 153.7, 133.97, 133.4, 132.5, 129.9, 129.6, 129.5, 128.0, 126.0, 123.7, 120.9, 111.6, 105.5, 97.7, 70.7, 30.6, 22.1, 19.5, 13.7.

HRMS (ESI-QTOF): *m*/*z* [M + Na]$^+$ calcd for $C_{21}H_{18}NaO_2$: 325.1199; found: 325.1194.

2-[3-(Thiophen-3-ylethynyl)benzofuran-2-yl]benzaldehyde (5i)

Yellow solid; yield: 44.1 mg (96%); mp 120.6–121.9 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 10.40 (s, 1 H), 8.11 (d, *J* = 7.7 Hz, 1 H), 8.03 (d, *J* = 7.8 Hz, 1 H), 7.80 (d, *J* = 7.5 Hz, 1 H), 7.73 (t, *J* = 7.5 Hz, 1 H), 7.57–7.61 (m, 3 H), 7.37–7.45 (m, 2 H), 7.30–7.32 (m, 1 H), 7.19 (d, *J* = 4.8 Hz, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 191.4, 154.6, 154.3, 134.1, 133.6, 132.3, 130.0, 129.9, 129.8, 129.5, 129.0, 128.2, 126.3, 125.7, 123.98, 121.7, 121.0, 111.7, 104.99, 91.1, 79.2.

HRMS (ESI-QTOF): *m*/*z* [M + H]$^+$ calcd for $C_{21}H_{13}O_2S$: 329.0631; found: 329.0651.

Compound **4** was prepared by following the same procedure for the synthesis of **1**.

Naphtho[1,2-*b*]benzofuran-6-yl(phenyl)methanone (4a)

Yellow solid; yield: 29.0 mg (90%); mp 152.9–154.6 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.53 (d, *J* = 8.3 Hz, 1 H), 7.97–8.05 (m, 5 H), 7.73–7.78 (m, 2 H), 7.61–7.68 (m, 2 H), 7.47–7.56 (m, 3 H), 7.31 (t, *J* = 7.4 Hz, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 196.4, 156.5, 152.8, 137.99, 133.3, 131.5, 131.2, 130.7, 129.5, 128.7, 128.6, 127.2, 127.1, 126.9, 124.0, 123.2, 122.8, 121.3, 117.6, 111.7.

HRMS (ESI-QTOF): *m*/*z* [M + H]$^+$ calcd for $C_{23}H_{15}O_2$: 323.1067; found: 323.1065.

Naphtho[1,2-*b*]benzofuran-6-yl(*p*-tolyl)methanone (4b)

White solid; yield: 32.0 mg (95%); mp 146.8–148.5 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.53 (d, *J* = 8.3 Hz, 1 H), 7.98–8.01 (m, 2 H), 7.91–7.95 (m, 3 H), 7.72–7.77 (m, 2 H), 7.62 (t, *J* = 7.2 Hz, 1 H), 7.48 (t, *J* = 7.8 Hz, 1 H), 7.28–7.34 (m, 3 H), 2.48 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 196.1, 156.4, 152.8, 144.3, 135.3, 130.9, 129.44, 129.39, 128.5, 127.1, 126.8, 126.7, 124.0, 123.9, 123.2, 121.3, 111.7, 21.9.

HRMS (ESI-QTOF): *m*/*z* [M + H]$^+$ calcd for $C_{24}H_{17}O_2$: 337.1223; found: 337.1228.

(4-Methoxyphenyl)(naphtho[1,2-*b*]benzofuran-6-yl)methanone (4c)

Off-white solid; yield: 31.7 mg (90%); mp 154.5–156.2 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.52 (d, *J* = 8.2 Hz, 1 H), 7.99–8.02 (m, 3 H), 7.91–7.93 (m, 2 H), 7.71–7.77 (m, 2 H), 7.63 (t, *J* = 7.6 Hz, 1 H), 7.47 (t, *J* = 7.3 Hz, 1 H), 7.29 (t, *J* = 7.8 Hz, 1 H), 7.00 (d, *J* = 8.8 Hz, 2 H), 3.91 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 195.1, 163.98, 156.4, 152.7, 133.1, 131.64, 131.63, 130.6, 129.3, 128.3, 127.1, 126.8, 126.0, 124.0, 123.7, 123.2, 122.6, 121.3, 117.5, 114.0, 111.7, 55.7.

HRMS (ESI-QTOF): *m*/*z* [M + H]$^+$ calcd for $C_{24}H_{17}O_3$: 353.1172; found: 353.1175.

(3-Methoxyphenyl)(naphtho[1,2-*b*]benzofuran-6-yl)methanone (4d)

Brown solid, yield: 31.0 mg (88%); mp 137.9–139.5 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.53 (d, *J* = 8.2 Hz, 1 H), 8.06 (d, *J* = 7.8 Hz, 1 H), 7.98–8.00 (m, 2 H), 7.73–7.77 (m, 2 H), 7.61–7.64 (m, 2 H), 7.47–7.53 (m, 2 H), 7.41 (t, *J* = 7.9 Hz, 1 H), 7.32 (t, *J* = 7.5 Hz, 1 H), 7.21 (d, *J* = 8.1 Hz, 1 H), 3.89 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 196.2, 159.9, 156.5, 152.8, 139.3, 131.4, 131.1, 129.6, 129.5, 128.6, 127.2, 127.1, 126.9, 123.97, 123.8, 123.2, 122.8, 121.3, 120.0, 117.5, 114.4, 111.7, 55.7.

HRMS (ESI-QTOF): *m*/*z* [M + Na]$^+$ calcd for $C_{24}H_{16}NaO_3$: 375.0992; found: 375.0993.

6-Methoxynaphthalen-1-yl(naphtho[1,2-*b*]benzofuran-6-yl)methanone (4e)

Off-white solid; yield: 35.8 mg (89%); mp 161.3–162.6 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.56 (d, *J* = 7.9 Hz, 1 H), 8.36 (s, 1 H), 8.16 (d, *J* = 8.4 Hz, 1 H), 7.99–8.01 (m, 3 H), 7.88 (d, *J* = 8.5 Hz, 1 H), 7.73–7.77 (m, 3 H), 7.62–7.66 (m, 1 H), 7.47 (t, *J* = 7.8 Hz, 1 H), 7.29 (d, *J* = 7.8 Hz, 1 H), 7.18–7.22 (m, 2 H), 3.97 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 196.2, 160.1, 156.5, 152.8, 137.6, 133.1, 133.0, 131.6, 131.4, 129.4, 128.4, 127.8, 127.5, 127.1, 126.8, 126.6, 124.0, 123.8, 123.3, 122.7, 121.3, 119.98, 117.7, 111.7, 105.98, 55.6.

HRMS (ESI-QTOF): *m*/*z* [M + H]$^+$ calcd for $C_{28}H_{19}O_3$: 403.1329; found: 403.1327.

(3-Fluorophenyl)(naphtho[1,2-*b*]benzofuran-6-yl)methanone (4f)

Off-white solid; yield: 30.6 mg (90%); mp 130.7–132.6 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.54 (d, *J* = 8.2 Hz, 1 H), 8.06 (d, *J* = 7.9 Hz, 1 H), 8.00 (d, *J* = 8.2 Hz, 1 H), 7.97 (s, 1 H), 7.72–7.80 (m, 4 H), 7.64 (t, *J* = 7.5 Hz, 1 H), 7.48–7.52 (m, 2 H), 7.31–7.39 (m, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 195.0, 164.1, 161.6, 156.5, 152.9, 140.2, 140.1, 131.4, 130.6, 130.3, 129.5, 128.9, 127.5, 127.3, 127.0, 126.6, 123.95, 123.89, 123.3, 123.0, 121.4, 120.4, 120.2, 117.5, 117.3, 117.1, 111.8, 55.6.

HRMS (ESI-QTOF): *m*/*z* [M + H]$^+$ calcd for $C_{23}H_{14}FO_2$: 341.0972; found: 341.0977.

(9c*S*,13a*R*)-9c,10,11,12,13,13a-Hexahydro-14*H*-benzo[3,4]fluoreno[2,1-*b*]benzofuran-14-one (4g′)

Colorless oil; yield: 26.8 mg (82%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.91 (d, *J* = 7.4 Hz, 1 H), 8.55 (d, *J* = 8.2 Hz, 1 H), 8.24 (d, *J* = 8.1 Hz, 1 H), 7.81 (t, *J* = 7.3 Hz, 1 H), 7.67–7.72 (m, 2 H), 7.52 (t, *J* = 7.5 Hz, 1 H), 7.45 (t, *J* = 7.2 Hz, 1 H), 4.02–4.08 (m, 1 H), 3.05 (br s, 1 H), 2.53–2.61 (m, 2 H), 1.82–1.88 (m, 1 H), 1.65–1.76 (m, 2 H), 1.42–1.51 (m, 1 H), 1.22–1.31 (m, 1 H), 1.01–1.11 (m, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 207.1, 156.51, 156.49, 152.1, 129.3, 128.6, 128.4, 127.1, 126.9, 125.41, 125.39, 124.5, 124.3, 123.5, 122.3, 115.1, 111.4, 49.4, 38.6, 33.8, 23.8, 23.0, 22.9.

HRMS (ESI-QTOF): *m*/*z* [M + H]$^+$ calcd for $C_{23}H_{19}O_2$: 327.1380; found: 327.1384.

1-Naphtho[1,2-*b*]benzofuran-6-yl)pentan-1-one (4h)

Off-white solid; yield: 29.3 mg (97%); mp 134.6–136.2 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.76 (d, *J* = 7.9 Hz, 1 H), 8.65 (d, *J* = 7.8 Hz, 1 H), 7.76 (d, *J* = 7.8 Hz, 1 H), 7.63–7.72 (m, 4 H), 7.49–7.53 (m, 1 H), 7.43–7.46 (m, 1 H), 2.85 (t, *J* = 7.7 Hz, 2 H), 1.66–1.70 (m, 2 H), 1.45–1.51 (m, 2 H), 0.98 (t, *J* = 7.3 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 182.98, 156.7, 153.9, 146.1, 137.9, 134.6, 132.9, 130.2, 129.7, 127.6, 127.4, 127.2, 126.6, 125.0, 124.6, 122.2, 110.7, 35.8, 32.1, 23.0, 14.2.

HRMS (ESI-QTOF): *m*/*z* [M + H]$^+$ calcd for $C_{21}H_{19}O_2$: 303.1380; found: 303.1378.

Naphtho[1,2-*b*]benzofuran-6-yl(thiophen-3-yl)methanone (4i)

Gray solid; yield: 28.6 mg (87%); mp 137.8–139.6 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.52 (d, *J* = 7.6 Hz, 1 H), 8.02–8.09 (m, 4 H), 7.72–7.78 (m, 3 H), 7.64 (t, *J* = 6.8 Hz, 1 H), 7.47–7.50 (m, 2 H), 7.33 (t, *J* = 6.8 Hz, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 189.7, 156.4, 152.8, 142.3, 135.5, 131.96, 131.5, 129.4, 128.63, 128.56, 127.1, 126.9, 126.8, 126.2, 123.9, 123.3, 122.8, 121.3, 117.2, 111.7.

HRMS (ESI-QTOF): *m*/*z* [M + H]$^+$ calcd for $C_{21}H_{13}O_2S$: 329.0631; found: 329.0635.

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Supporting Information

Supporting Information for this article is available online at http://dx.doi.org/10.1055/s-0036-1588120. ^{1}H and ^{13}C NMR spectra of synthesized compounds are included.

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