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MPHT-Promoted Bromocyclization of *ortho*-Substituted Arylalkynes: Application to the Synthesis of 2-Substituted 3-Bromobenzofurans and -Benzo[*b*]thiophenes

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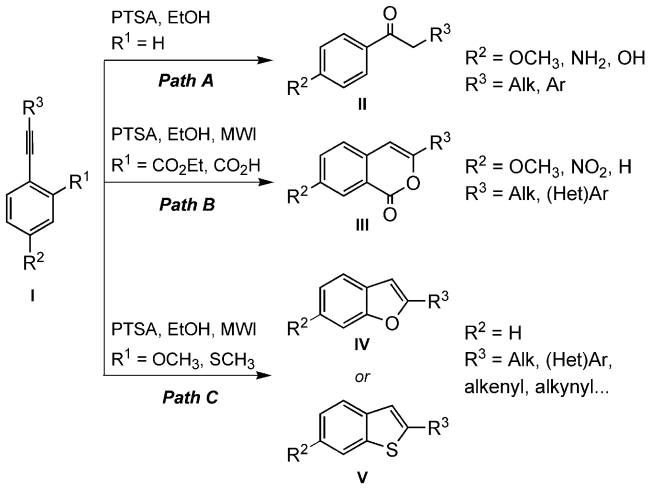
A convenient and general approach to the synthesis of 2-substituted 3-bromobenzofurans and -benzothiophenes was developed. The procedure is based on the cyclization of *ortho*-substituted arylalkynes in the presence of *N*-methylpyrrolidin-2-one hydrotribromide (MPHT) as a soft and easy-to-handle electrophilic brominating reagent. Under mild reaction conditions, MPHT promoted the bromocyclization of various enynes and diynes as well as arylalkynes to give 2-substituted 3-bromobenzofurans and -benzothiophenes in high to excellent yields. Subsequent functionalization by palladium-catalyzed coupling reactions at the C–Br bond afforded general access to 2,3-disubstituted benzofurans and benzothiophenes of biological interest.

Introduction

As part of a program focusing on the functionalization of arylalkynes,[1] we have recently reported their reactivity with *p*-toluenesulfonic acid (PTSA) in EtOH.[2] There are two main strands to this work, which consist of triple-bond hydration[3] or cyclization reactions,[4] depending on the alkyne substrates. In the hydration process promoted by PTSA, the reaction takes place rapidly in EtOH or water and regioselectively affords in good yields a large variety of ketones according to Markovnikov's rules (Scheme 1, Path A).

The second string of this program involves an intramolecular cyclization reaction, promoted by PTSA, of *ortho*-substituted diarylalkynes. With substrates bearing an ethoxycarbonyl or a carboxylic acid function (CO_2Et, COOH) at the *ortho* position, 3-substituted isocoumarins were obtained in good to excellent yields (Scheme 1, Path B).[4a] When applying this environmentally friendly, metal-free procedure to *ortho*-(1-alkynyl)-anisole or -thioanisole derivatives, a series of 2-substituted benzofurans and benzothiophenes was prepared in good to excellent yields, respectively (Scheme 1, Path C).[4b] In these cyclization reactions,[5] PTSA activated the triple bond, and subsequent regioselective 5- or 6-*endo-dig* cyclization with the *ortho* substituent afforded the required 2-substituted heterocycle. It should be noted that 2-substituted as well as 2,3-disubstituted benzofurans and benzothiophenes are attractive synthetic target molecules due to the wide spectrum of their biological activities,[6] including antimitotic properties.[7]



Scheme 1. Reaction of substituted arylalkynes with PTSA.

In continuation of our studies concerning the design and the preparation of anticancer agents,[1i,8] we were interested in developing a novel access to this class of 2,3-disubstituted heterocycles. Generally, 2-substituted 3-halobenzofurans and -benzo[*b*]thiophenes are prepared by electrophilic cyclization of 2-alkynylphenol,[9] ether,[6e,6f,10] and sulfide derivatives[10a,11] with a range of electrophiles (I_2, ICl, etc.). Alternative methods are based on treatment of 2-substituted benzothiophene derivatives with molecular Br_2.[7c] Our continuing interest in the electrophilic cyclization of *ortho*-substituted arylalkynes encouraged us to further ex-

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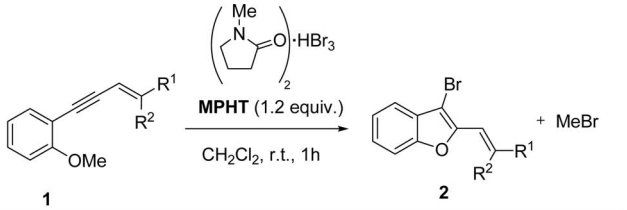
amine the use of *N*-methylpyrrolidin-2-one hydrotribromide (MPHT), developed in our lab[12] as a mild electrophile, in the preparation of 2-substituted 3-bromobenzofurans and -benzothiophenes. MPHT complex is a stable solid that smoothly liberates bromine in organic solvents. It presents several advantages over molecular bromine: (i) MPHT can be stored for several months at room temperature with no decrease in the free bromine titer. (ii) It is not corrosive or necrosive, and therefore, it is easy to weigh and handle. Because MPHT is a mild reagent, we envisioned to use it in the bromocyclization of highly unsaturated alkynes, including 1,3-enynes and 1,3-diynes to provide 3-bromobenzofurans and -benzo[*b*]thiophenes having an alkenyl or an alkynyl chain at the C-2 position, respectively. To the best of our knowledge, only one example of the bromocyclization of an enyne substrate is described in the literature. Larock reported that 2-thiomethylarylenyne underwent bromocyclization in the presence of NBS over 2 d, whereas the bromocyclization was unsuccessful with Br_2 probably "*because Br_2 addition to the carbon–carbon double bond is occurring faster than cyclization*".[11b,11c] We report herein an easy and versatile process for the synthesis of 2-substituted 3-bromobenzofurans and -benzothiophenes from the electrophilic MPHT-promoted cyclization of 1,3-enynes and 1,3-diynes as well as diarylalkynes. This method furnished heterocycles bearing various substituents at the C-2 position and a bromine atom at the C-3 position useful for further palladium-catalyzed coupling reactions.

Results and Discussion

Required 1,3-enynes **1**[13] and 1,3-diynes **3**[14] were prepared by Pd-catalyzed coupling reactions, according to literature procedures. Initially, 1,3-enyne substrates were evaluated in the MPHT bromocyclization process, and the results of this study are reported in Table 1. From these results, we can see that all reactions work well in CH_2Cl_2 at room temperature for 1 h. Enyne **1a** bearing no substituent on the styryl moiety reacted cleanly and rapidly with MPHT (1.2 equiv.) to give expected (*E*)-2-styryl-3-bromobenzofuran (**2a**) in a good 81% yield (Table 1, Entry 1). It is noteworthy that no product resulting from the bromination of the carbon–carbon double or triple bond of **1a** was detected in the crude mixture, as judged by ^{1}H NMR spectroscopy. When (*E*)- or (*Z*)-enynes **1b** were employed as substrates for the bromocyclization, a single (*E*)-styrylbenzofuran **2b** was obtained probably for thermodynamic considerations (Table 1, Entries 2 and 3). Enynes **1** having either electron-donating (Table 1, Entries 2–4 and 7) or electron-withdrawing substituents (Table 1, Entries 5 and 6) on the styryl moiety were evaluated and gave satisfactory yields in the corresponding (*E*)-2-substituted 3-bromobenzofurans **2b**–**f**. A thiophene nucleus was also tolerated on enyne **1g** and expected benzofuran **2g** was obtained in a satisfactory 56% yield (Table 1, Entry 8). Finally, the reaction was successfully achieved with enyne **1h** bearing two methyl substituents on the double bond, thus demonstrating the general character of the method (Table 1, Entry 9).

Table 1. MPHT-promoted bromocyclization of *ortho*-substituted conjugated enynes **1**.



1 2

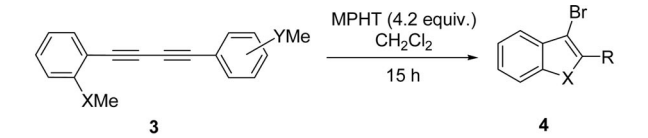
Entry	Alkyne **1**	Bromoheterocycle **2**	Yield [%][a]
1	**1a**	**2a**	81[b]
2	(*E*)-**1b**	**2b**	58
3	(*Z*)-**1b**	**2b**	51
4	**1c**	**2c**	56
5	**1d**	**2d**	70
6	**1e**	**2e**	62
7	**1f**	**2f**	50
8	**1g**	**2g**	56
9	**1h**	**2h**	51

[a] Isolated yield. [b] A complex mixture was obtained with Br_2 (1.2 equiv.), and 35% of **2b** was obtained by using NBS (1.2 equiv.) instead of MPHT, but after 36 h at room temperature.

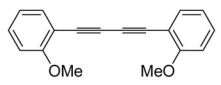
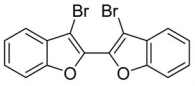
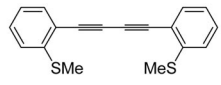
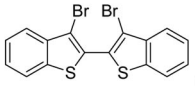
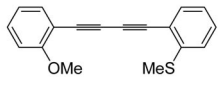
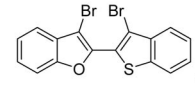
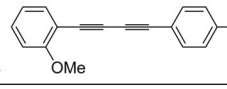
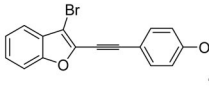
Next, 1,3-diynes **3a** and **3b** were evaluated in the presence of 4.2 equiv. of MPHT (Table 2, Entries 1 and 2). We were pleased to observe the quantitative formation of bis(3-bromobenzofuran) **4a** and bis(3-bromobenzothiophene) **4b**, which were used as starting materials for the synthesis of benzannulated phospholes,[15] dibenzothienopyrroles,[16] dithienosiloles,[17] and functionalized phenanthrenes[18] of physical interest. Unsymmetrical diyne **3c** reacted cleanly with MPHT to afford expected heterocycle **4c**, again with excellent yield (Table 2, Entry 3). Finally, the selectivity observed in the presence of conjugated diyne **3d** must be espe-

cially underlined, as the bromocyclization reaction efficiently occurred to provide **4d**, with no addition of bromine to the second carbon–carbon triple bond (Table 2, Entry 4).

Table 2. MPHT-promoted bromocyclization of *ortho*-substituted conjugated diynes **3**.

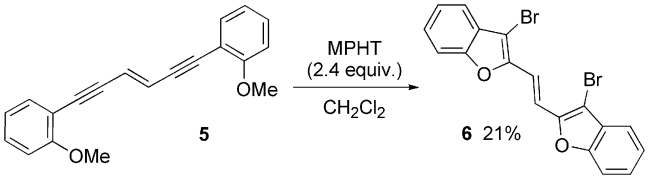


3 **4**

Entry	Alkyne **3**	Bromoheterocycle **4**	Yield [%][a]
1	 **3a**	 **4a**	96
2	 **3b**	 **4b**	97
3	 **3c**	 **4c**	99
4	 **3d**	 **4d**	88[b]

[a] Isolated yield. [b] 1.5 equiv. of MPHT were used for 5 h.

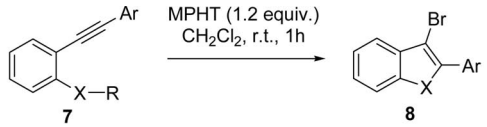
Having demonstrated the efficiency of MPHT to promote the bromocyclization of conjugated enynes **1** and diynes **3**, we sought to extend the cyclization reaction with highly conjugated (*E*)-enediyne **5**.[19] Thus, after stirring with MPHT (2.4 equiv.) at room temperature for 3 h, we were pleased to observe the formation of 1,2-ethenyl bis(benzofuran) **6**, which was isolated in a moderate 21% yield, despite the fact that the reaction conditions were unoptimized (Scheme 2). Further cyclization of **6** (or its benzothiophene analog) would provide a set of fused thiepins,[20] as well as 1-sila-, 1-germa-, 1-selenacyclohepta-2,4,6-trienes[21] of biological interest.



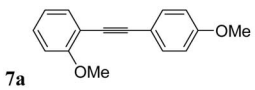
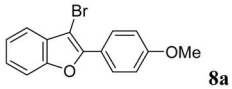
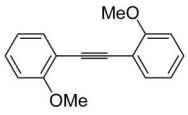
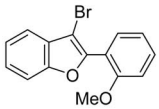
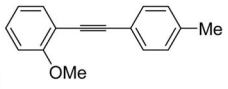
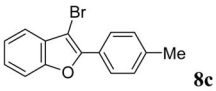
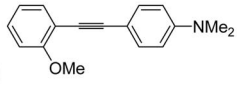
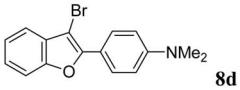
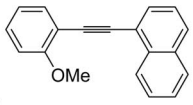
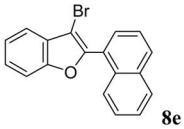
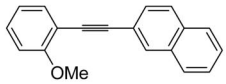
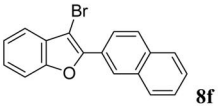
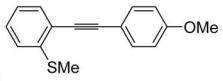
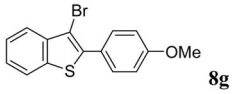
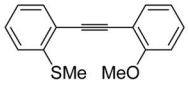
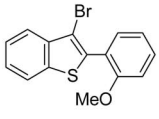
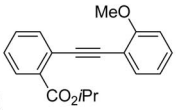
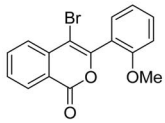
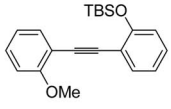
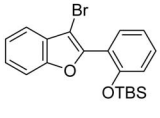
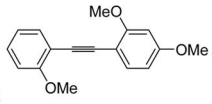
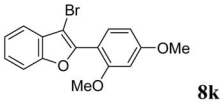
Scheme 2. Bromocyclization of (*E*)-enediyne **5** with MPHT.

Having succeeded in developing an efficient bromocyclization of conjugated enyne, diyne, and enediyne substrates, we next examined the reaction with a range of *ortho*-substituted diarylalkynes **7**, which were prepared by Pd-catalyzed coupling reactions according to literature procedures.[22] The results of this study are summarized in Table 3. Under the above reaction conditions, MPHT-promoted annulations of 2-methoxydiarylalkynes **7a**–**f** provided good

Table 3. MPHT-promoted bromocyclization of *ortho*-substituted diarylalkynes **7**.



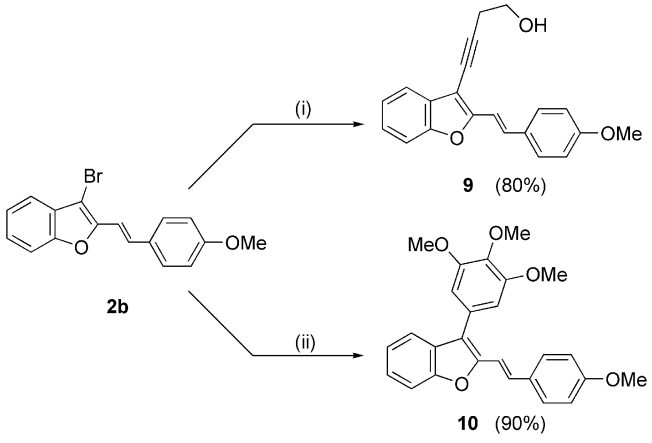
7 **8**

Entry	Alkyne **7**	Bromoheterocycle **8**	Yield [%][a]
1	 **7a**	 **8a**	98
2	 **7b**	 **8b**	79
3	 **7c**	 **8c**	80
4	 **7d**	 **8d**	74[b]
5	 **7e**	 **8e**	75
6	 **7f**	 **8f**	61
7	 **7g**	 **8g**	97
8	 **7h**	 **8h**	81
9	 **7i**	 **8i**	98
10	 **7j**	 **8j**	93
11	 **7k**	 **8k**	94

[a] Isolated yield. [b] 3 h were required.

yields of the corresponding 2-aryl-3-bromobenzofurans **8a**–**f** (Table 3, Entries 1–6). Similarly, 2-thioanisole derivative **7g** underwent rapid cyclization to give 2-aryl-3-bromobenzothiophene **8g** in nearly quantitative yield (97%; Table 3, Entry 7). To determine the relative reactivity of various substituents toward the bromocyclization, the MPHT protocol was applied to unsymmetrically 2,2′-disubstituted diarylalkynes **7h**–**k**. Alkyne **7h** with *ortho*-methoxy and *ortho′*-thiomethyl substituents underwent bromocyclization at the sulfur atom to give selectively benzothiophene **8h** in good yield (Table 3, Entry 8). A similar selectivity was observed with diarylalkyne **7i** having an *ortho* ester function (Table 3, Entry 9). In this case, the 6-*endo*-*dig* cyclization proceeded selectively to provide exclusively isocoumarin **8i** in an excellent 98% yield. We observed total hierarchy of a OMe substituent versus a OTBDMS group towards the bromocyclization, and the reaction gave 3-bromobenzofuran **8j** having a OTBDMS substituent at C-2′ (Table 3, Entry 10). Surprisingly, starting from *o*,*o′*,*p*-trimethoxyalkyne **7k**, single cyclization product **8k** was formed, showing a significant difference in reactivity between the two *ortho*-methoxy substituents of **7k** (94%; Table 3, Entry 11).

To increase the synthetic utility of these 2-substituted 3-bromobenzofurans, the cyclization product (*E*)-2-(4-methoxystyryl)-3-bromobenzofuran (**2b**) was converted into 2-alkenyl-3-alkynylbenzofuran **9** and 2-alkenyl-3-arylbenzofuran **10** by Sonogashira and Suzuki cross-coupling reactions with but-1-yn-4-ol and 3,4,5-trimethoxyphenylboronic acid, respectively, in good yields (Scheme 3). One can note that compound **10** may be regarded as a conformationally restricted analog of vinylogous combretastatin A-4 of biological interest.[23]



Scheme 3. Cross-coupling reactions of **2b** under palladium catalysis. Reagents and conditions: (i) CuI (10 mol-%), $PdCl_2(PPh_3)_2$ (5 mol-%), but-1-yn-4-ol (1.6 equiv.), Et_3N, 50 °C, 12 h; (ii) 3,4,5-trimethoxyphenylboronic acid (1.2 equiv.), $Pd(PPh_3)_4$ (5 mol-%), K_2CO_3 (2 equiv.), toluene/H_2O (2:1), 100 °C.

Conclusions

In summary, we have shown that MPHT in CH_2Cl_2 is a soft and compatible reagent to promote the bromocyclization of *ortho*-substituted alkynes at room temperature. Under these mild conditions, it was demonstrated that various conjugated enyne, diyne, enediyne, and arylalkyne substrates were successfully cyclized in good to excellent yields to provide structurally interesting 2-substituted 3-bromobenzofuran and -benzothiophene derivatives. By further chemical manipulations, our synthetic approach should allow rapid access to a wide range of 2,3-disubstituted benzofurans and benzothiophenes amenable for biological evaluations.

Experimental Section

General Comments: All glassware was oven-dried at 140 °C, and all reactions were conducted under a nitrogen atmosphere. Solvents were dried by standard methods and distilled before use. Piperidine was dried and distilled from potassium hydroxide prior to use. $Pd(PPh_3)_4$ was prepared following a literature procedure.[24] The compounds were all identified by usual physical methods, that is, ^1H NMR, ^{13}C NMR, and IR spectroscopy, MS, and elemental analysis. ^1H and ^{13}C NMR spectra were measured in $CDCl_3$ with a Bruker Avance 300 or Bruker ARX 400. ^1H chemical shifts are reported in ppm from the peak of residual chloroform (δ =7.27 ppm) and coupling constants J were measured in Hz. The following abbreviations are used: m (multiplet), s (singlet), d (doublet), t (triplet) dd (doublet of doublet), br. s (broad singlet). ^{13}C chemical shifts are reported in ppm from the central peak of deuteriochloroform (δ =77.14 ppm). IR spectra were measured with a Bruker Vector 22 spectrophotometer as neat samples. Elemental analyses (for all new cyclized products) were performed with a Perkin–Elmer 240 analyzer. Mass spectra were obtained by using a Bruker Esquire electrospray ionization apparatus. Analytical TLC was performed on Merck precoated silica gel 60F plates. Merck silica gel 60 (230–400 mesh) was used for column chromatography. Enynes **1a**–**c** and **1e**–**g**, enediynes **3a** and **3b**, and diarylalkynes **5a**–**k** were prepared according to literature procedures.

Experimental Procedures

(*E*)-1-Fluoro-4-[4-(2-methoxyphenyl)but-1-en-3-ynyl]benzene (1d): To a mixture of (*E*)-1-(4-chlorobut-3-en-1-ynyl)-2-methoxybenzenechloroenyne (192 mg, 1 mmol) in toluene (4 mL) and EtOH (2 mL) was successively added 4-fluorophenylboronic acid (168 mg, 1.2 mmol), K_2CO_3 (276 mg, 2 mmol), and $Pd(PPh_3)_4$ (58 mg, 0.05 mmol). The reaction mixture was heated at 100 °C under vigorous stirring and monitored by TLC until complete disappearance of the starting material. The solvent was evaporated in vacuo and water (10 mL) was added. After extraction with CH_2Cl_2 (3 × 10 mL), the combined organic layer was dried with $MgSO_4$, and the solvent was removed under reduced pressure. The crude material was purified by column chromatography to afford expected enyne **1d**. Yield: 214 mg, 85%. ^1H NMR (300 MHz, $CDCl_3$): δ = 3.91 (s, 3 H, OCH_3), 6.37 (d, J = 16.2 Hz, 1 H, H_{vinyl}), 6.88–6.96 (m, 2 H, H_{arom}), 7.00–7.06 (m, 3 H, $H_{arom+vinyl}$), 7.30 (dt, J = 7.9, 1.7 Hz, 1 H, H_{arom}), 7.39 (dd, J = 8.8, 5.4 Hz, 2 H, H_{arom}), 7.45 (dd, J = 7.5, 1.7 Hz, 1 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 55.9 (CH_3), 88.2 (C_q), 92.8 (C_q), 108.4 (CH), 110.7 (CH), 112.6 (C_q), 115.8 ($J_{C,F}$ = 21.8 Hz, 2 CH), 120.6 (CH), 128.0 ($J_{C,F}$ = 8.1 Hz, 2 CH), 129.9 (CH), 132.8 ($J_{C,F}$ = 3.1 Hz, C_q), 133.6 (CH), 139.7 (CH), 160.0 (C_q), 162.9 ($J_{C,F}$ = 248.6 Hz, C_q) ppm. IR: $\tilde{\nu}$ = 1597, 1490, 1434, 1228, 1158, 1024, 954, 813, 750 cm^{-1}. MS (APCI+): m/z = 253.0 $[M + H]^+$.

1-Methoxy-2-(4-methylpent-3-en-1-ynyl)benzene (1h): To a solution of $PdCl_2(PPh_3)_2$ (104 mg, 0.15 mmol), CuI (56.4 mg, 0.3 mmol), and bromo-1-methylpropene (400 mg, 3 mmol) in THF (10 mL) and piperidine (1.2 mL, 11.9 mmol) was slowly added 2-methoxyphenylacetylene (461 μL, 2.4 mmol). The stirred reaction was heated at reflux for 20 h and treated with a saturated NH_4Cl solution (10 mL). The aqueous layer was extracted with EtOAc (3 × 10 mL), and the combined organic layer was dried with $MgSO_4$ and concentrated under vacuum. Purification by flash chromatography afforded expected enyne **1h**. Yield: 312 mg, 70%. R_f = 0.41 (cyclohexane/CH_2Cl_2, 8:2). ^1H NMR (300 MHz, $CDCl_3$): δ = 1.87 (s, 3 H, CH_3), 2.01 (s, 3 H, CH_3), 3.88 (s, 3 H, OCH_3), 5.54 (br. s, 1 H, H_{vinyl}), 6.87 (d, J = 8.2 Hz, 1 H, H_{arom}), 6.90 (t, J = 7.5 Hz, 1 H, H_{arom}), 7.25 (t, J = 7.9 Hz, 1 H, H_{arom}), 7.40 (d, J = 7.5 Hz, 1 H, H_{arom}) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 21.2 (CH_3), 25.0 (CH_3), 55.9 (OCH_3), 87.8 (C), 92.1 (C), 105.7 (CH), 110.7 (CH), 113.4 (C), 120.5 (CH), 129.2 (CH), 133.2 (CH), 148.8 (C), 159.7 (C) ppm. IR: $\tilde{\nu}$ = 2908, 1593, 1434, 1268, 1240, 1119, 1047, 749 cm^{-1}. MS (APCI+): m/z = 373.0 $[2M + H]^+$, 187.0 $[M + H]^+$.

Preparation of Unsymmetrical Diynes 3c and 3d: To a solution of CuI (0.1 mmol) in pyrrolidine (10 mL) was added successively at 0 °C the iodoarylalkyne (1 mmol) and the terminal arylalkyne (2 mmol). The stirred reaction was kept at room temperature for one night and treated with a saturated NH_4Cl solution (15 mL). The aqueous layer was extracted with EtOAc (3 × 10 mL), and the combined organic layer was dried with $MgSO_4$ and concentrated under vacuum. Purification by flash chromatography afforded the expected diynes.

{2-[4-(2-Methoxyphenyl)buta-1,3-diynyl]phenyl}(methyl) Sulfane (3c):[25] Prepared from CuI (14.8 mg, 0.08 mmol), 1-(2-iodoethynyl)-2-methoxybenzene (200 mg, 0.78 mmol), and 2-thiomethylphenylacetylene. Yield: 152 mg, 70%. M.p. 82–83 °C. R_f = 0.22 (cyclohexane/EtOAc, 94:6). ^1H NMR (400 MHz, $CDCl_3$): δ = 2.51 (s, 3 H, SCH_3), 3.91 (s, 3 H, OCH_3), 6.89 (d, J = 8.7 Hz, 1 H, H_{arom}), 6.92 (t, J = 7.5 Hz, 1 H, H_{arom}), 7.09 (t, J = 7.5 Hz, 1 H, H_{arom}), 7.17 (d, J = 7.9 Hz, 1 H, H_{arom}), 7.29–7.36 (m, 2 H, H_{arom}), 7.48–7.51 (m, 2 H, H_{arom}) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 15.4 (SCH_3), 56.0 (OCH_3), 77.7, 79.5, 80.1, 80.4, 110.8, 111.2, 120.5, 120.7, 124.5, 124.6, 129.5, 130.9, 133.7, 134.6, 143.2, 161.5 ppm. IR: $\tilde{\nu}$ = 2938, 1594, 1492, 1464, 1433, 1248, 1022, 733, 703 cm^{-1}. MS (APCI+): m/z = 279.0 $[M + H]^+$.

1-(2-Methoxyphenyl)-4-(4-methoxyphenyl)buta-1,3-diyne (3d): Prepared from CuI (40.6 mg, 0.21 mmol), 1-(2-iodoethynyl)-2-methoxybenzene (550 mg, 0.78 mmol), and 4-methoxyphenylacetylene. Yield: 131 mg, 64%. M.p. 109–110 °C. R_f = 0.24 (cyclohexane/acetone, 95:5). ^1H NMR (300 MHz, $CDCl_3$): δ = 3.82 (s, 3 H, OCH_3), 3.90 (s, 3 H, OCH_3), 6.84–6.94 (m, 4 H, H_{arom}), 7.32 (t, J = 7.6 Hz, 1 H, H_{arom}), 7.45–7.48 (m, 3 H, H_{arom}) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 55.4 (OCH_3), 55.9 (OCH_3), 73.2, 77.7, 78.0, 82.5, 110.8, 111.3, 114.0, 114.2, 120.6, 130.6, 134.1, 134.4, 160.4, 161.5 ppm. IR: $\tilde{\nu}$ = 2936, 2837, 1601, 1508, 1489, 1247, 1171, 1024, 750 cm^{-1}. MS (APCI+): m/z = 263.0 $[M + H]^+$.

General Procedure for the Electrophilic Cyclization with MPHT: To a solution of **1**, **3**, or **5** in CH_2Cl_2 (1 mmol) was added MPHT (for quantity, see text), and the resulting solution was stirred at room temperature until disappearance of the starting material (as judged by TLC). The reaction mixture was next treated with a saturated $Na_2S_2O_3$ solution. The organic layer was washed with HCl 10% (3 × 10 mL) and dried with $MgSO_4$. Removal of the solvent yielded a crude product, which was purified by silica gel flash chromatography to afford **2**, **4**, **6**, or **8**.

(*E*)-3-Bromo-2-styrylbenzofuran (2a): Yield: 242 mg, 81%. R_f = 0.57 (cyclohexane/CH_2Cl_2, 95:5). ^1H NMR (400 MHz, $CDCl_3$): δ = 7.14 (d, J = 16.2 Hz, 1 H, H_{vinyl}), 7.28–7.43 (m, 5 H, H_{arom}), 7.41 (d, J = 16.2 Hz, 1 H, H_{vinyl}), 7.47 (d, J = 8.1 Hz, 1 H, H_{arom}), 7.50 (d, J = 7.6 Hz, 1 H, H_{arom}), 7.59 (d, J = 7.6 Hz, 2 H, H_{arom}) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 97.0, 111.3, 113.8, 119.7, 123.6, 126.0, 127.1, 128.7, 128.9, 129.0, 132.0, 136.5, 151.5, 153.7 ppm. IR: $\tilde{\nu}$ = 3058, 2924, 1446, 1013, 1001, 954, 741, 689 cm^{-1}. MS (APCI+): m/z = 220.0 $[M – Br + H]^+$. $C_{16}H_{11}BrO$ (299.16): calcd. C 64.24, H 3.71; found C 64.09, H 3.56.

(*E*)-2-(4-Methoxystyryl)-3-bromobenzofuran (2b): Yield: 191 mg, 58%. Beige solid. M.p. 85–86 °C. ^1H NMR (300 MHz, $CDCl_3$): δ = 3.85 (s, 3 H, CH_3), 6.93 (d, J = 8.6 Hz, 2 H, H_{arom}), 6.99 (d, J = 16.2 Hz, 1 H, H_{vinyl}), 7.28–7.39 (m, 3 H, $H_{vinyl+arom}$), 7.44–7.50 (m, 2 H, H_{arom}), 7.53 (d, J = 8.6 Hz, 2 H, H_{arom}) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 55.5 (CH_3), 96.0 (C), 111.1 (CH), 111.6 (CH), 114.4 (2 CH), 119.5 (CH), 123.5 (CH), 125.6 (CH), 128.5 (2 CH), 129.1 (C), 129.2 (C), 131.6 (CH), 151.8 (C_q), 153.6 (C), 160.2 (C) ppm. IR: $\tilde{\nu}$ = 821, 953, 1014, 1173, 1243, 1450, 1505, 1599, 2926 cm^{-1}. MS (APCI+): m/z = 329.0 $[M + H]^+$ (^{79}Br), 331.0 $[M + H]^+$ (^{81}Br), 250.0 $[M – Br + H]^+$. $C_{17}H_{13}BrO_2$ (329.19): calcd. C 62.03, H 3.98; found C 61.91, H 3.84.

(*E*)-5-[2-(3-Bromobenzofuran-2-yl)vinyl]benzo[1,3]dioxole (2c): Yield: 192 mg, 56%. Yellow solid. M.p. 122–123 °C. ^1H NMR (300 MHz, $CDCl_3$): δ = 6.00 (s, 2 H, OCH_2O), 6.83 (d, J = 8.0 Hz, 1 H, H_{arom}), 6.94 (d, J = 16.1 Hz, 1 H, H_{vinyl}), 7.03 (dd, J = 8.0, 1.3 Hz, 1 H, H_{arom}), 7.12 (d, J = 1.6 Hz, 1 H, H_{arom}), 7.27–7.35 (m, 3 H, $H_{vinyl+arom}$), 7.43–7.49 (m, 2 H, H_{arom}) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 96.4 (C), 101.5 (C), 105.9 (CH), 108.7 (CH), 111.2 (CH), 112.0 (CH), 119.5 (CH), 122.6 (CH), 123.6 (CH), 125.8 (CH), 129.0 (C), 131.0 (C), 131.6 (CH), 148.5 (C), 151.6 (C), 153.6 (C) ppm. IR: $\tilde{\nu}$ = 746, 931, 1037, 1199, 1250, 1447, 1487, 2360 cm^{-1}. MS (APCI+): m/z = 343.0 $[M + H]^+$ (^{79}Br), 345.0 $[M + H]^+$ (^{81}Br). $C_{17}H_{11}BrO_3$ (343.17): calcd. C 59.50, H 3.23; found C 59.41, H 3.16.

(*E*)-2-(4-Fluorostyryl)-3-bromobenzofuran (2d): Yield: 222 mg, 70%. Yellow solid. M.p. 83–84 °C. ^1H NMR (300 MHz, $CDCl_3$): δ = 6.94 (d, J = 16.0 Hz, 1 H, H_{vinyl}), 7.01 (d, J = 8.6 Hz, 2 H, H_{arom}), 7.17–7.29 (m, 3 H, H_{arom}), 7.36–7.48 (m, 4 H, H_{arom}) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 97.0 (C), 111.2 (CH), 113.6 ($J_{C,F}$ = 1.5 Hz, CH), 116.0 ($J_{C,F}$ = 21.9 Hz, 2 CH), 119.7 (CH), 123.7 (CH), 126.0 (CH), 128.7 ($J_{C,F}$ = 8.1 Hz, 2 CH), 129.0 (C), 130.7 (CH), 132.7 ($J_{C,F}$ = 3.0 Hz, C_q), 151.3 (C), 153.7 (C), 163.0 ($J_{C,F}$ = 249.1 Hz, C_q) ppm. IR: $\tilde{\nu}$ = 740, 811, 847, 947, 1002, 1151, 1227, 1447, 1501, 1592 cm^{-1}. MS (APCI+): m/z = 317.0 $[M + H]^+$ (^{79}Br), 319.0 $[M + H]^+$ (^{81}Br). $C_{16}H_{10}BrFO$ (317.15): calcd. C 60.59, H 3.18; found C 60.47, H 3.01.

(*E*)-2-(4-Chlorostyryl)-3-bromobenzofuran (2e): Yield: 207 mg, 62%. Yellow solid. M.p. 114–115 °C. ^1H NMR (300 MHz, $CDCl_3$): δ = 7.09 (d, J = 16.2 Hz, 1 H, H_{vinyl}), 7.29–7.38 (m, 5 H, $H_{vinyl+arom}$), 7.45–7.52 (m, 4 H, H_{arom}) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 97.5 (C), 111.3 (CH), 114.2 (CH), 119.8 (CH), 123.7 (CH), 126.2 (CH), 128.2 (2 CH), 128.9 (C), 129.2 (2 CH), 130.5 (CH), 134.3 (C), 135.0 (C), 151.2 (C), 153.8 (C) ppm. IR: $\tilde{\nu}$ = 812, 954, 1013, 1091, 1192, 1252, 1448, 1489, 1592 cm^{-1}. MS (APCI+): m/z = 333.0 $[M + H]^+$ (^{79}Br), 335.0 $[M + H]^+$ (^{81}Br). $C_{16}H_{10}BrClO$ (333.61): calcd. C 57.60, H 3.02; found C 333.48, H 2.94.

(*E*)-3-Bromo-2-[2-(naphthalen-2-yl)vinyl]benzofuran (2f): Yield: 175 mg, 50%. Yellow solid. M.p. 141–142 °C. ^1H NMR (300 MHz, $CDCl_3$): δ = 7.22–7.39 (m, 3 H, $H_{vinyl+arom}$), 7.48–7.53 (m, 4 H, $H_{arom+naph}$), 7.57 (d, J = 16.2 Hz, 1 H, H_{vinyl}), 7.77–7.87 (m, 4 H, H_{naph}), 7.94 (s, 1 H, H_{naph}) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ

= 97.1 (C), 111.3 (CH), 114.0 (CH), 119.7 (CH), 123.4 (CH), 123.7 (CH), 126.0 (CH), 126.6 (CH), 126.7 (CH), 127.9 (2 CH), 128.4 (CH), 128.7 (CH), 129.0 (C), 132.0 (CH), 133.6 (C), 133.8 (C), 134.0 (C), 151.6 (C), 153.8 (C) ppm. IR: $\tilde{\nu}$ = 804, 962, 1015, 1195, 1258, 1446 cm^{-1}. MS (APCI+): *m*/*z* = 349.0 $[M + H]^+$ (^{79}Br), 351.0 $[M + H]^+$ (^{81}Br). $C_{20}H_{13}BrO$ (349.22): calcd. C 68.79, H 3.75; found C 68.55, H 3.51

(*E*)-3-Bromo-2-[2-(thiophen-3-yl)vinyl]benzofuran (2g): Yield: 171 mg, 56%. Gray solid. M.p. 65–66 °C. ^1H NMR (300 MHz, $CDCl_3$): δ = 6.95 (d, *J* = 16.1 Hz, 1 H, H_{vinyl}), 7.29–7.34 (m, 2 H, $H_{vinyl+arom}$), 7.35–7.47 (m, 5 H, H_{arom}), 7.48–7.51 (m, 1 H, H_{arom}) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 96.6 (C), 111.2 (CH), 113.7 (CH), 119.5 (CH), 123.6 (CH), 124.5 (CH), 125.0 (CH), 125.8 (CH), 126.0 (CH), 126.7 (CH), 129.0 (C), 139.4 (C), 151.4 (C), 153.6 (C) ppm. IR: $\tilde{\nu}$ = 738, 823, 853, 941, 1014, 1191, 1257, 1404, 1445, 1632 cm^{-1}. MS (APCI+): *m*/*z* = 305.0 $[M + H]^+$ (^{79}Br), 307.0 $[M + H]^+$ (^{81}Br). $C_{14}H_9BrOS$ (305.19): calcd. C 55.10, H 2.97; found C 55.19, H 3.06.

3-Bromo-2-(2-methylprop-1-enyl)benzofuran (2h): Yield: 128 mg, 51%. R_f = 0.62 (cyclohexane/CH_2Cl_2, 95:5). ^1H NMR (300 MHz, $CDCl_3$): δ = 2.01 (s, 3 H, CH_3), 2.22 (d, *J* = 1.3 Hz, 3 H, CH_3), 6.25 (q, *J* = 1.3 Hz, 1 H, H_{vinyl}), 7.26–7.33 (m, 2 H, H_{arom}), 741–7.50 (m, 2 H, H_{arom}) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 20.8 (CH_3), 27.8 (CH_3), 95.0 (C), 111.2, 111.5 (CH), 119.3 (CH), 123.4 (CH), 124.9 (CH), 128.3 (C), 141.8 (C), 152.1 (C), 153.4 ppm. IR: $\tilde{\nu}$ = 2930, 1450, 1259, 1197, 1011, 738 cm^{-1}. MS (APCI+): *m*/*z* = 252.0 $[M + H]^+$. $C_{12}H_{11}BrO$ (251.12): calcd. C 57.39, H 4.42; found C 57.33, H 4.37.

3-Bromo-2-(3-bromobenzofuran-2-yl)benzofuran (4a):[26] Yield: 376 mg, 96%. White solid. M.p. 224–225 °C. R_f = 0.43 (cyclohexane/ CH_2Cl_2, 96:4). ^1H NMR (400 MHz, $CDCl_3$): δ = 7.38 (t, *J* = 7.4 Hz, 2 H, H_{arom}), 7.45 (t, *J* = 7.4 Hz, 2 H, H_{arom}), 7.59 (d, *J* = 8.2 Hz, 2 H, H_{arom}), 7.64 (d, *J* = 7.7 Hz, 2 H, H_{arom}) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 98.3 (2 C), 111.9 (2 C), 120.5 (2 C), 124.1 (2 C), 126.9 (2 C), 128.7 (2 C), 142.8 (2 C), 154.7 (2 C) ppm. IR: $\tilde{\nu}$ = 2923, 1437, 1260, 1211, 1122, 743 cm^{-1}. MS (APCI+): *m*/*z* = 312.0 $[M - {}^{81}Br+H]^+$, 314.0 $[M - {}^{79}Br + H]^+$.

3-Bromo-2-(3-bromobenzo[*b*]thiophen-2-yl)benzo[*b*]thiophene (4b):[27] Yield: 395 mg, 97%. Yellow solid. R_f = 0.67 (cyclohexane/ CH_2Cl_2, 9:1). ^1H NMR (300 MHz, $CDCl_3$): δ = 7.50 (m, 4 H, H_{arom}), 7.85 (d, *J* = 7.6 Hz, 2 H, H_{arom}), 7.93 (d, *J* = 7.7 Hz, 2 H, H_{arom}) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 111.0 (2 C), 122.4 (2 C), 124.2 (2 C), 125.6 (2 C), 126.5 (2 C), 129.5 (2 C), 138.2 (2 C), 139.3 (2 C) ppm.

3-Bromo-2-(3-bromobenzothiophen-2-yl)benzofuran (4c): Yield: 99%. Yellow solid. M.p. 113–118 °C. R_f = 0.59 (cyclohexane/ EtOAc, 96:4). ^1H NMR (300 MHz, $CDCl_3$): δ = 7.35–7.64 (m, 6 H, H_{arom}), 7.86 (d, *J* = 7.5 Hz, 1 H, H_{arom}), 7.96 (d, *J* = 8.4 Hz, 1 H, H_{arom}) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 99.3 (C), 109.9 (C), 111.8 (CH), 120.4 (CH), 122.4 (CH), 124.0 (CH), 124.3 (CH), 125.6 (CH), 126.7 (2 CH), 128.7 (C), 138.3 (C), 138.8 (C), 145.4 (C), 148.4 (C), 154.2 (C) ppm. IR: $\tilde{\nu}$ = 2923, 1454, 1257, 1241, 1040, 978, 737, 720 cm^{-1}. MS (APCI +): *m*/*z* = 409.0 $[M + H]^+$. $C_{16}H_8Br_2OS$ (408.11): calcd. C 47.09, H 1.98; found C 46.89, H 1.89.

3-Bromo-2-[2-(4-methoxyphenyl)ethynyl]benzofuran (4d): Yield: 288 mg, 88%. Yellow solid. M.p. 82–83 °C. R_f = 0.23 (cyclohexane/ CH_2Cl_2, 9:1). ^1H NMR (300 MHz, $CDCl_3$): δ = 3.83 (s, 3 H, OCH_3), 6.90 (d, *J* = 7.6 Hz, 2 H, H_{arom}), 7.29–7.41 (m, 2 H, H_{arom}), 7.45 (d, *J* = 8.3 Hz, 1 H, H_{arom}), 7.50 (d, *J* = 7.4 Hz, 1 H, H_{arom}), 7.56 (d, *J* = 7.6 Hz, 2 H, H_{arom}) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 55.5 (OCH_3), 77.0 (C), 99.5 (C), 102.9 (C), 111.6 (CH), 113.6 (C), 114.3 (2 CH), 120.0 (CH), 123.9 (CH), 126.6 (CH), 127.8 (C), 133.6 (2 CH), 137.8 (C), 153.8 (C), 160.7 (C) ppm. IR: $\tilde{\nu}$ = 2208, 1504, 1290, 1249, 1016, 905, 830, 725 cm^{-1}. MS (APCI+): *m*/*z* = 328.0 $[M + H]^+$. $C_{17}H_{11}BrO_2$ (327.17): calcd. C 62.41, H 3.39; found C 62.13, H 3.10.

(*E*)-3-Bromo-2-[2-(3-bromobenzofuran-2-yl)vinyl]benzofuran (6): Yield: 92 mg, 21%. Yellow solid. M.p. 232–233 °C. ^1H NMR (300 MHz, $CDCl_3$): δ = 7.26 (s, 2 H, H_{vinyl}), 7.40 (m, 2 H, H_{arom}), 7.49 (m, 2 H, H_{arom}), 7.56 (dd, *J* = 7.7, 0.8 Hz, 2 H, H_{arom}), 7.73 (d, *J* = 8.2 Hz, 2 H, H_{arom}) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 99.3 (CH), 115.5 (CH), 116.0 (CH), 120.0 (CH), 123.9 (CH), 126.7 (CH), 129.0 (C), 150.9 (C), 154.1 (C) ppm. IR: $\tilde{\nu}$ = 738, 861, 943, 1017, 1106, 1202, 1259, 1343, 1447, 1612 cm^{-1}. MS (APCI+): *m*/*z* = 441.0 $[M + Na]^+$. $C_{18}H_{10}Br_2O_2$ (418.08): calcd. C 51.71, H 2.41; found C 51.50, H 2.28.

3-Bromo-2-(4-methoxyphenyl)benzofuran (8a):[28] Yield: 297 mg, 98%. Yellow solid. M.p. 66–67 °C. R_f = 0.51 (cyclohexane/ CH_2Cl_2, 8:2). ^1H NMR (400 MHz, $CDCl_3$): δ = 3.88 (d, *J* = 0.9 Hz, 3 H, OCH_3), 7.02 (d, *J* = 7.9 Hz, 2 H, H_{arom}), 7.32 (m, 2 H, H_{arom}), 7.50 (m, 2 H, H_{arom}), 8.12 (d, *J* = 7.9 Hz, 2 H, H_{arom}) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 55.5 (OCH_3), 92.3, 111.3, 114.2 (2 C), 119.7, 122.4, 123.5, 125.3, 128.5 (2 C), 129.9, 150.7, 153.1, 160.4 ppm. IR: $\tilde{\nu}$ = 2959, 1609, 1450, 1251, 1117, 1072, 1030, 985, 830, 783 cm^{-1}. MS (APCI+): *m*/*z* = 224 $[M – Br + H]^+$.

3-Bromo-2-(2-methoxyphenyl)benzofuran (8b):[9b] Yield: 239 mg, 79%. R_f = 0.38 (cyclohexane/ CH_2Cl_2, 8:2). ^1H NMR (300 MHz, $CDCl_3$): δ = 3.89 (s, 3 H, OCH_3), 7.05 (d, *J* = 8.1 Hz, 1 H, H_{arom}), 7.09 (td, *J* = 7.5, *J* = 1.0 Hz, 1 H, H_{arom}), 7.35 (m, 2 H, H_{arom}), 7.49 (m, 2 H, H_{arom}), 7.60 (m, 2 H, H_{arom}) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 55.8 (OCH_3), 96.8 (C), 111.6 (CH), 111.7 (CH), 118.4 (C), 119.9 (CH), 120.6 (CH), 123.3 (CH), 125.3 (CH), 129.1 (CH), 131.5 (CH), 131.8 (CH), 150.6 (C), 154.0 (C), 157.8 (C) ppm. IR: $\tilde{\nu}$ = 2933, 1486, 1447, 1255, 1058, 1044, 1024, 740 cm^{-1}. MS (ESI+): *m*/*z* = 224.0 $[M – Br + H]^+$. $C_{15}H_{11}BrO_2$ (303.15): calcd. C 59.43, H 3.66; found C 59.19, H 3.76.

3-Bromo-2-*p*-tolylbenzofuran (8c): Yield: 229 mg, 80%. Yellow solid. M.p. 70–72 °C. R_f = 0.65 (cyclohexane/ CH_2Cl_2, 9:1). ^1H NMR (400 MHz, $CDCl_3$): δ = 2.43 (s, 3 H, CH_3), 7.32 (m, 4 H, H_{arom}), 7.53 (m, 2 H, H_{arom}), 8.07 (d, *J* = 8.3 Hz, 2 H, H_{arom}) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.6 (CH_3), 93.3, 111.3, 119.9, 123.5, 125.5, 126.9 (3 C), 129.4 (2 C), 129.8, 139.4, 150.8, 153.2 ppm. IR: $\tilde{\nu}$ = 2919, 1503, 1450, 1253, 1204, 1072, 1020, 817, 741 cm^{-1}. MS (APCI+): *m*/*z* = 208 $[M – Br + H]^+$.

4-(3-Bromobenzofuran-2-yl)-*N*,*N*-dimethylbenzenamine (8d): Yield: 221 mg, 74%. R_f = 0.57 (cyclohexane/ CH_2Cl_2, 8:2). ^1H NMR (300 MHz, $CDCl_3$): δ = 3.04 (s, 6 H, N-CH_3), 6.80 (d, *J* = 8.9 Hz, 2 H), 7.29 (m, 2 H, H_{arom}), 7.50 (m, 2 H, H_{arom}), 8.08 (d, *J* = 8.7 Hz, 2 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 40.3 (2 CH_3), 90.6, 111.0 (CH), 111.9 (2 C), 117.4 (C), 119.3 (CH), 123.3 (CH), 124.6 (CH), 128.1 (2 C), 130.2 (C), 150.8 (C), 151.6 (C), 153.0 (C) ppm. IR: $\tilde{\nu}$ = 2889, 1607, 1510, 1450, 1361, 1194, 816, 742 cm^{-1}. MS (APCI+): *m*/*z* = 316 $[M(^{79}Br) + H]^+$, 318 $[M(^{81}Br) + H]^+$. $C_{16}H_{14}BrNO$ (316.20): calcd. C 60.78, H 4.46, N 4.43; found C 60.54, H 4.29, N 4.23.

3-Bromo-2-(naphthalen-1-yl)benzofuran (8e): Yield: 242 mg, 75%. White solid. M.p. 107–109 °C. R_f = 0.65 (cyclohexane/ CH_2Cl_2, 9:1). ^1H NMR (300 MHz, $CDCl_3$): δ = 7.43 (m, 2 H), 7.62 (m, 5 H), 7.87 (d, *J* = 8.7 Hz, 1 H, H_{naph}), 8.00 (m, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 97.3, 111.7, (CH), 120.1 (CH), 123.7 (CH), 125.1 (C), 125.7 (CH), 126.1 (CH), 126.4 (CH), 126.5 (C), 127.0

(CH), 128.6, (CH), 128.9 (C), 129.7 (CH), 130.6 (CH), 131.6 (C), 133.9 (C), 152.2 (C), 154.1 (C) ppm. IR: $\tilde{\nu}$ = 3053, 1449, 1259, 1029, 1014, 968, 800, 772, 743 cm^{-1}. MS (APCI+): *m*/*z* = 244.0 $[M - Br + H]^+$. $C_{18}H_{11}BrO$ (323.18): calcd. C 66.89, H 3.43; found C 66.78, H 3.36.

3-Bromo-2-(naphthalen-2-yl)benzofuran (8f): Yield: 197 mg, 61%. Yellow solid. M.p. 98–102 °C. R_f = 0.56 (cyclohexane/ CH_2Cl_2, 9:1). ^1H NMR (300 MHz, $CDCl_3$): δ = 7.38 (m, 2 H), 7.57 (m, 4 H), 7.87 (m, 4 H), 7.96 (m, 2 H), 8.30 (d, *J* = 8.7 Hz, 1 H, H_{naph}), 8.68 (s, 1 H, H_{naph}) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 94.4 (C), 110.1 (C), 111.4 (CH), 120.1 (CH), 123.7 (CH), 124.0 (CH), 125.8 (CH), 126.6 (CH), 126.8 (CH), 127.1 (CH), 127.9 (CH), 128.4 (CH), 128.8 (CH), 129.8 (C), 133.2 (C), 133.4 (C), 150.5 (C), 153.4 (C) ppm. IR: $\tilde{\nu}$ = 3058, 1450, 1259, 1065, 994, 857, 815, 742 cm^{-1}. MS (APCI+): *m*/*z* = 244.0 $[M - Br + H]^+$. $C_{18}H_{11}BrO$ (323.18): calcd. C 66.89, H 3.43; found C 67.01, H 3.60.

3-Bromo-2-(4-methoxyphenyl)benzo[*b*]thiophene (8g):[29] Yield: 309 mg, 97%. Yellow solid. M.p. 83 °C. R_f = 0.41 (cyclohexane/ CH_2Cl_2, 8:2). ^1H NMR (300 MHz, $CDCl_3$): δ = 3.88 (s, 3 H, OCH_3), 7.02 (d, *J* = 8.5 Hz, 2 H, H_{arom}), 7.39 (t, *J* = 7.5 Hz, 1 H, H_{arom}), 7.47 (t, *J* = 7.6 Hz, 1 H, H_{arom}), 7.71 (d, *J* = 8.4 Hz, 2 H, H_{arom}), 7.80 (d, *J* = 7.8 Hz, 1 H, H_{arom}), 7.85 (d, *J* = 8.0 Hz, 1 H, H_{arom}) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 55.5 (OCH_3), 104.4 (C), 114.2 (2 C), 122.2 (CH), 123.6 (CH), 125.3 (CH), 125.4 (CH), 125.5 (C), 131.1 (2 C), 137.6 (C), 138.3 (C), 139.4 (C), 160.2 (C) ppm. IR: $\tilde{\nu}$ = 2922, 1606, 1494, 1433, 1248, 1177, 1032, 831, 802, 749 cm^{-1}. MS (APCI+): *m*/*z* = 240 $[M - Br + H]^+$.

3-Bromo-2-(2-methoxyphenyl)benzo[*b*]thiophene (8h): Yield: 258 mg, 81%. Beige solid. M.p. 85–87 °C. R_f = 0.27 (cyclohexane). ^1H NMR (300 MHz, $CDCl_3$): δ = 3.86 (s, 3 H, OCH_3), 7.06 (m, 2 H, H_{arom}), 7.45 (m, 4 H, H_{arom}), 7.82 (d, *J* = 7.7 Hz, 1 H, H_{arom}), 7.87 (d, *J* = 8.0 Hz, 1 H, H_{arom}) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 55.8 (OCH_3), 107.8 (C), 111.6 (CH), 120.6 (CH), 121.9 (C), 122.3 (CH), 123.5 (CH), 125.0 (CH), 125.3 (CH), 130.8 (CH), 132.5 (C), 135.4 (C), 138.5 (C), 138.7 (C), 157.4 (C) ppm. IR: $\tilde{\nu}$ = 2938, 1482, 1459, 1432, 1248, 1115, 1024, 889, 748, 725 cm^{-1}. MS (APCI+): *m*/*z* = 240 $[M - Br + H]^+$. $C_{15}H_{11}BrOS$ (319.22): calcd. C 56.44, H 3.47; found C 56.29, H 3.36.

4-Bromo-3-(2-methoxyphenyl)-1*H*-isochromen-1-one (8i): Yield: 324 mg, 98%. White solid. M.p. 129–131 °C. R_f = 0.37 (cyclohexane/ CH_2Cl_2, 8:2). NMR ^1H (300 MHz, $CDCl_3$): δ = 3.85 (s, 3 H, OCH_3), 7.00 (d, *J* = 8.4 Hz, 1 H, H_{arom}), 7.05 (td, *J* = 7.5, 0.9 Hz, 1 H, H_{arom}), 7.40–7.49 (m, 2 H, H_{arom}), 7.60 (td, *J* = 7.5, 1.2 Hz, 1 H, H_{arom}), 7.84 (td, *J* = 7.6, 1.3 Hz, 1 H, H_{arom}), 7.92 (d, *J* = 8.1 Hz, 1 H, H_{arom}), 8.35 (dd, *J* = 7.9, 0.8 Hz, 1 H, H_{arom}) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 55.8 (OCH_3), 103.9 (C), 111.5 (CH), 120.4 (CH), 121.0 (C), 122.5 (C), 126.5 (CH), 129.2 (CH), 130.0 (CH), 131.3 (CH), 131.9 (CH), 135.4 (CH), 136.6 (C), 150.8 (C), 157.5 (C), 161.7 (C) ppm. IR: $\tilde{\nu}$ = 2952, 1732, 1279, 1072, 1020, 753 cm^{-1}. MS (ESI+): *m*/*z* = 354 $[M + Na]^+$. $C_{16}H_{11}BrO_3$ (329.99): calcd. C 58.03, H 3.35; found C 57.88, H 3.20.

[2-(3-Bromobenzofuran-2-yl)phenoxy](*tert*-butyl)dimethylsilane (8j): Yield: 375 mg, 93%. R_f = 0.76 (cyclohexane/ CH_2Cl_2, 9:1). ^1H NMR (300 MHz, $CDCl_3$): δ = 0.06 (s, 6 H, CH_3Si), 0.84 (s, 9 H, CH_3C), 6.99 (d, *J* = 8.2 Hz, 1 H, H_{arom}), 7.09 (td, *J* = 7.5, 1.0 Hz, 1 H, H_{arom}), 7.36 (m, 3 H, H_{arom}), 7.48 (m, 1 H, H_{arom}), 7.59 (m, 2 H, H_{arom}) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = –4.5 (2 CH_3), 18.2 (C), 25.6 (3 CH_3), 96.3 (C), 111.5 (CH), 119.8 (CH), 120.8 (CH), 121.3 (CH), 123.3 (CH), 125.3 (CH), 128.8 (2 C), 131.3 (CH), 132.0 (CH), 151.2 (C), 153.8 (C), 154.4 (C) ppm. IR: $\tilde{\nu}$ = 2930, 1483, 1449, 1281, 1258, 916, 887, 826, 780, 743 cm^{-1}. MS (APCI+): *m*/*z* = 403 $[M(^{79}Br) + H]^+$, 405 $[M(^{81}Br) + H]^+$. $C_{20}H_{23}BrO_2Si$ (402.07): calcd. C 59.55, H 5.75; found C 59.38, H 5.61.

3-Bromo-2-(2,4-dimethoxyphenyl)benzofuran (8k): Yield: 310 mg, 93%. Yellow solid. M.p. 59–61 °C. R_f = 0.26 (cyclohexane/ EtOAc, 9:1). ^1H NMR (400 MHz, $CDCl_3$): δ = 3.87 (s, 3 H, OCH_3), 3.88 (s, 3 H, OCH_3), 5.61 (m, 2 H, H_{arom}), 7.33 (m, 1 H, H_{arom}), 7.34 (m, 1 H, H_{arom}), 7.51 (m, 1 H, H_{arom}), 7.53 (m, 1 H, H_{arom}), 7.57 (m, 1 H, H_{arom}) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 55.6 (OCH_3), 55.8 (OCH_3), 96.2, 99.2, 104.9, 111.2, 111.5, 119.7, 123.2, 125.0, 129.1, 132.6, 150.8, 153.8, 159.1, 162.6 ppm. IR: $\tilde{\nu}$ = 2938, 1616, 1499, 1449, 1209, 1161, 1033, 986, 745 cm^{-1}. MS (APCI+): *m*/*z* = 254.0 $[M - Br + H]^+$. $C_{16}H_{13}BrO_3$ (333.18): calcd. C 57.68, H 3.93; found C 57.55, H 3.66.

(*E*)-4-[2-(4-Methoxystyryl)benzofuran-3-yl]but-3-yn-1-ol (9): A solution of $PdCl_2(PPh_3)_2$ (5 mol-%), CuI (10 mol-%), **2b** (329 mg, 1 mmol), and butyn-4-ol (112 mg, 1.6 mmol) in TEA (10 mL) was stirred at 50 °C for 12 h. The stirred reaction was next treated with saturated NH_4Cl solution (25 mL). The aqueous layer was extracted with ethyl ether (3 × 20 mL), the combined organic layer was washed successively with aqueous HCl (0.2 M, 15 mL), $NaHCO_3$ (10 mL), and H_2O (2 × 25 mL), dried with $MgSO_4$, and concentrated under vacuum. Yield: 254 mg, 80%. Brown oil. R_f = 0.50 (cyclohexane/ EtOAc, 5:5). ^1H NMR (300 MHz, $CDCl_3$): δ = 2.86 (t, *J* = 6.3 Hz, 2 H, CH_2-C), 3.84 (s, 3 H, OMe), 3.92 (t, *J* = 6.3 Hz, 2 H, CH_2O), 6.93 (dd, *J* = 9.0, 2.4 Hz, 2 H, H_{arom}), 7.06 (d, *J* = 16.2 Hz, 1 H, H_{vinyl}), 7.63–7.20 (m, 7 H, $H_{arom+vinyl}$) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 24.5 (CH_2), 55.5 (CH_3), 61.5 (CH_2), 73.1 (C), 94.1 (C), 112.7 (CH), 114.4 (CH), 120.1 (2 CH), 123.3 (CH), 125.3 (CH), 128.5 (CH), 129.6 (2 CH), 131.3 (CH), 153.9 (C), 157.8 (C), 160.2 (C) ppm. IR: $\tilde{\nu}$ = 3448, 2935, 1734, 1602, 1577, 1508, 1452, 1423, 1373, 1245, 1034, 959, 932, 746 cm^{-1}. $C_{21}H_{18}O_3$ (318.37): calcd. C 79.22, H 5.70; found C 79.00, H 5.36.

(*E*)-2-(4-Methoxystyryl)-3-(3,4,5-trimethoxy-phenyl)benzofuran (10): To a solution of **2b** (1 mmol) in toluene (4 mL) and EtOH (2 mL) was successively added 3,4,5-trimethoxyphenyl boronic acid (254 mg, 1.2 mmol), K_2CO_3 (2 mmol), and $Pd(PPh_3)_4$ (0.05 mmol). The reaction mixture was heated at 100 °C under vigorous stirring and monitored by TLC until complete disappearance of the starting material. The solvent was evaporated in vacuo, and water (10 mL) was added. After extraction with CH_2Cl_2 (3 × 10 mL), the combined organic layer was dried with $MgSO_4$, and the solvent was removed under reduced pressure. The crude material was purified by column chromatography to afford **10**. Yield: 374 mg, 90%. Yellow oil. R_f = 0.25 (cyclohexane/EtOAc, 8:2). ^1H NMR (300 MHz, $CDCl_3$): δ = 3.72 (s, 3 H, OCH_3), 3.82 (s, 6 H, OCH_3), 3.90 (s, 3 H, OCH_3), 6.71 (s, 2 H, H_{arom}), 6.80 (d, *J* = 7.8 Hz, 2 H, H_{arom}), 6.98 (d, *J* = 16.2 Hz, 1 H, H_{vinyl}), 7.15–7.7.30 (m, 2 H, H_{arom}), 7.35 (d, *J* = 16.2 Hz, 1 H, H_{vinyl}), 7.42 (d, *J* = 7.8 Hz, 2 H, H_{arom}), 7.36–7.60 (m, 2 H, H_{arom}) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 55.3 (CH_3), 56.3 (2 CH_3), 61.0 (CH_3), 106.6 (2 CH), 110.9 (CH), 112.9 (CH), 114.3 (2 CH), 118.8 (C), 119.7 (CH), 123.0 (CH), 124.9 (CH), 127.9 (C), 128.0 (2 CH), 129.1 (C), 129.5 (C), 130.5 (CH), 137.5 (C), 151.1 (C), 153.6 (C), 154.2 (C), 159.8 (C) ppm. IR: $\tilde{\nu}$ = 2932, 2249, 2068, 1602, 1580, 1509, 1452, 1414, 1389, 1307, 1243, 1173, 1125, 1032, 1005, 961, 907, 843, 819 cm^{-1}. $C_{26}H_{24}O_5$ (416.47): calcd. C 74.98, H 5.81; found C 74.89, H 5.66.

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