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HAL Id: hal-02394491

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MPHT Promoted Bromocyclization of Ortho Substituted Arylalkynes: Application to the Synthesis of 2-Substituted-3-Bromo-Benzofurans and -Benzo[b]thiophenes

Maud Jacubert,^[a] Abdellatif Tikad,^[a] Olivier Provot,^[a] Abdallah Hamze,^[a] Jean-Daniel Brion^[a] and Mouâd Alami^{*[a]}

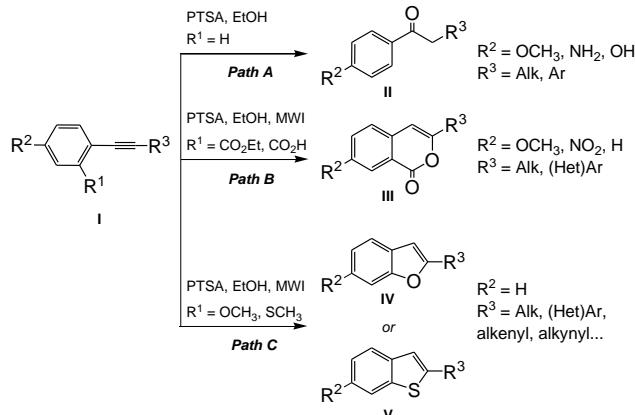
Keywords: Enynes / Enediynes / Alkynes / Benzofurans / Benzothiophenes / MPHT / Cyclization.

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 with high to excellent yields.

Subsequent functionalization by palladium-catalyzed coupling reactions at the C-Br bond afforded a 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 the 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 afforded in good yields a large variety of ketones according to Markovnikov's rules (Path A, Scheme 1).



Scheme 1. Reaction of substituted arylalkynes with PTSA

molecular cyclization reaction, promoted by PTSA, of ortho substituted diarylalkynes. With substrates bearing on the *ortho* position an ethoxycarbonyl or a carboxylic acid function (CO₂Et, COOH), 3-substituted isocoumarins were obtained in good to excellent yields (path B, Scheme 1).^[4a] When applying this environmentally 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 (path C, Scheme 1).^[4b] In these cyclisation reactions,^[5] PTSA activated the triple bond, and a 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]

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 these class of 2,3-disubstituted heterocycles. Generally, 2-substituted 3-halo-benzofurans and -benzo[b]thiophenes either are prepared by electrophilic cyclization of 2-alkynylphenol,^[9] -ether,^[6e,f, 10] and sulfide derivatives^[10a, 11] with a range of electrophiles (I₂, ICl,...). Alternative methods are based on treatment of 2-substituted benzothiophene derivatives with molecular Br₂.^[7c] Our continuing interest in the electrophilic cyclization of ortho substituted arylalkynes encouraged us to further examine 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-bromo-benzofurans and -benzo[b]thiophene. MPHT complex is a stable solid that smoothly liberates bromine in organic solvents. It presents several advantages than molecular bromine: (*i*) MPHT can be stored several month at room temperature with no decrease in the free bromine titer, (*ii*) it is not corrosive, not necrosive, and therefore easy to weigh and to handle. Because MPHT is a mild reagent, we envisioned to used it in the bromocyclization of highly unsaturated alkynes, including 1,3-enynes and 1,3-diyynes to provide 3-bromo-benzofurans and benzo[b]thiophenes having an alkenyl or an alkynyl chain on the C-2 position, respectively. To our knowledge, only one example of the

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bromocyclization of an enyne substrate is described in the literature. Larock reported that a 2-thiomethylarylenyne substrate was bromocyclized using NBS for two days, whereas the bromocyclization was unsuccessful with Br₂ probably "because Br₂ addition to the carbon-carbon double bond is

occurring faster than cyclization".^[11b,c] We report herein an easy and versatile process for the synthesis of 2-substituted-3-bromo-benzofurans and benzothiophenes from the electrophilic MPHT promoted cyclization of 1,3-enynes and 1,3-diyne as well as diarylalkynes.

Table 1. MPHT promoted the bromocyclization of ortho substituted conjugated enynes **1** and diynes **3**.

The reaction scheme shows the MPHT-promoted bromocyclization of ortho-substituted alkynes and diarylalkynes. For alkynes **1**, the reaction conditions are MPHT 1.2 eq, CH₂Cl₂, r.t., 1 h. The product is a 2-substituted-3-bromo-heterocycle **2** and H₃C—Br. For diarylalkynes **3**, the reaction conditions are MPHT 4.2 eq, CH₂Cl₂, 15 h. The product is a 2-substituted heterocycle **4**. The structures of the substrates and products are shown with their respective chemical formulas.

Entry	Ortho substituted alkyne 1 or 3	2-Substituted-3-bromo-heterocycle 2 or 4	Yield (%) ^a
1	1a	2a	81 ^c
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
	3	4	
10	3a	4a	96
11	3b	4b	97
12	3c	4c	99
13	3d	4d	88 ^b

^a Isolated yields. ^b 1.5 eq of MPHT were used for 5 h. ^c A complex mixture was obtained with Br₂ (1.2 equiv) and 35% of **2b** was obtained using NBS (1.2 equiv) instead of MPHT, but after 36 h at room temperature.

This method furnished heterocycles bearing various substituents on the C-2 position and a bromine atom at the C-3 position useful for further palladium-catalyzed coupling reactions.

Results and Discussion

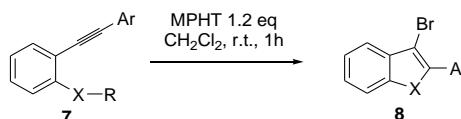
The required 1,3-enynes **1**^[13] and 1,3-diyne **3**^[14] were prepared by Pd-catalyzed coupling reactions, according to literature procedures. Initially, 1,3-enyne substrates were evaluated in the

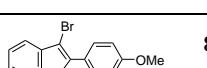
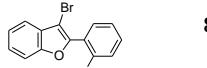
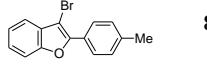
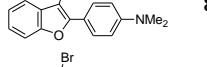
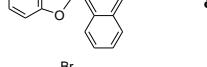
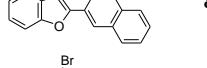
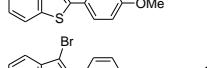
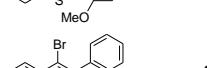
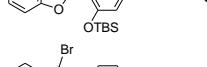
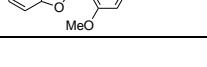
MPHT bromocyclization process and the results of this study are reported in Table 1. From these results, we can see that all reactions work well in CH₂Cl₂ at room temperature for 1 h. As shown in entry 1, enyne **1a** bearing no substituent on the styryl moiety reacted cleanly and rapidly with MPHT (1.2 equiv) to give the expected (E)-2-styryl-3-bromobenzofuran **2a** in a good 81% yield. 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 as judged by ¹H NMR. When (E)- or (Z)-enynes **1b** were employed as substrates for the

bromocyclization, a single (*E*)-styrylbenzofuran **2b** was obtained probably for thermodynamic considerations (entries 2 and 3). Enynes **1** having either electron donating (entries 2–4 and 7) or electron withdrawing substituents (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 the enyne **1g** and the expected benzofuran **2g** was obtained in a satisfactory 56% yield (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 (entry 9).

Next, 1,3-diyne **3a** and **3b** were evaluated in the presence of 4.2

Table 2. MPHT promoted the bromocyclization of *ortho*-substituted diarylalkynes **7**



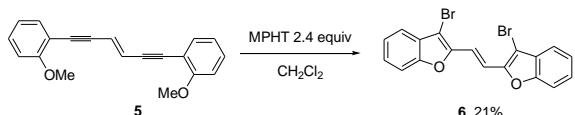
Entry	Alkyne 7	Bromoheterocycle 8	Yield (%) ^a
1	7a		8a 98
2	7b		8b 79
3	7c		8c 80
4	7d		8d 74 ^b
5	7e		8e 75
6	7f		8f 61
7	7g		8g 97
8	7h		8h 81
9	7i		8i 98
10	7j		8j 93
11	7k		8k 94

^a Isolated yields. ^b 3 h were required.

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

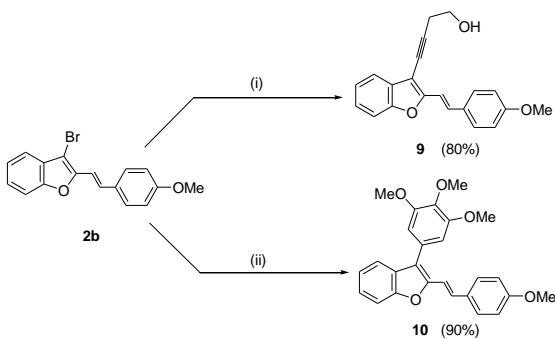
equiv. of MPHT (Table 1). We were pleased to observe the quantitative formation of *bis*-3-bromobenzofuran **4a** and *bis*-3-bromobenzothiophene **4b** which have been used as starting materials for the synthesis of benzannelated phospholes,^[15] dibenzothienopyrroles,^[16] dithienosiloles^[17] and functionalized phenanthrenes^[18] of physical interest. Example depicted in entry 12 showed that unsymmetrical diyne **3c** reacted cleanly with MPHT to afford the expected heterocycle **4c**, again with excellent yield. Finally, the selectivity observed in the presence of conjugated diyne **3d** must be especially underlined as the bromocyclization reaction efficiently occurred to provide **4d**, with no addition of bromine to the second carbon–carbon triple bond (entry 13).

conditions have not been optimized (Scheme 2). A further cyclization of **6** (or its benzothiophene analogue) 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 2. Under the above reaction conditions, MPHT promoted annulations of 2-methoxy diarylalkynes **7a-f** and provided good yields of the corresponding 2-aryl-3-bromobenzofurans **8a-f** (entries 1-6). Similarly, 2-thioanisole derivative **7g** undergoes a rapid cyclization to give 2-aryl-3-bromobenzothiophene **8g** in a nearly quantitative yield (entry 7, 97%). 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 an ortho methoxy- and ortho' thiomethyl- substituents undergoes bromocyclization at the sulphur atom to give selectively benzothiophene **8h** in a good yield (entry 8). A similar selectivity was observed with diarylalkyne **7i** having an ortho ester function (entry 9). In this case, the 6-*endo*-dig cyclization proceeded selectively to provide exclusively isocoumarin **8i** in an excellent 98% yield. In example depicted in entry 10, we have observed a total hierarchy of a OMe substituent versus a OTBDMS group toward the bromocyclization and the reaction gave 3-bromobenzofuran **8j** having a OTBDMS substituent on the C-2'. Surprisingly, starting from *o,o'*-*p*-trimethoxyalkyne **7k**, a single cyclization product **8k** was formed showing a significant difference in reactivity between the two ortho methoxy substituents of **7k** (entry 11, 94%).



Scheme 3. Cross-coupling reactions of **2b** under palladium catalysis. Reagents and conditions: (i). CuI (10 mol%), PdCl₂(PPh₃)₂ (5 mol%), but-1-yn-4-ol (1.6 equiv), Et₃N, 50 °C, 12 h. (ii) 3,4,5-trimethoxyphenylboronic acid (1.2 equiv), Pd(PPh₃)₄ (5 mol%), K₂CO₃ (2 equiv), toluene-H₂O (2/1), 100 °C.

To increase the synthetic utility of these 2-substituted-3-bromobenzofurans, one the cyclization product, (*E*)-2-(4-methoxystyryl)-3-bromobenzofuran **2b** was converted to 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 analogue of vinylogous combretastatin A-4 of biological interest.^[23]

Conclusions

In summary, we have showed that MPHT in CH₂Cl₂ 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 details

General comments

All glasswares were 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(PPh₃)₄ was prepared following literature procedure.^[24] The compounds were all identified by usual physical methods, i.e. ¹H-NMR, ¹³C-NMR, IR, MS and elemental analysis. ¹H and ¹³C NMR spectra were measured in CDCl₃ with a Bruker Avance 300 or Bruker ARX 400. ¹H chemical shifts are reported in ppm from the peak of residual chloroform (7.27 ppm) and coupling constants *J* were measured in Hz. The following abbreviation are use: m (multiplet), s (singlet), d (doublet), t (triplet) dd (doublet of doublet), bs (broad singlet). ¹³C chemical shifts are reported in ppm from the central peak of deuteriochloroform (77.14). IR spectra were measured on a Bruker Vector 22 spectrophotometer (neat, cm⁻¹). Elemental analyses (for all new cyclized products) were performed with a Perkin-Elmer 240 analyser. Mass spectra were obtained 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**, **1e-g**, enediynes **3a-b** 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) (214 mg; 85%). To a mixture of (*E*)-1-(4-chlorobut-3-en-1-ynyl)-2-methoxybenzenecloroynone (192 mg, 1 mmol) in toluene (4 mL) and EtOH (2 mL), were successively added 4-fluorophenylboronic acid (168 mg, 1.2 mmol), K₂CO₃ (276 mg, 2 mmol) and Pd(PPh₃)₄ (58 mg, 0.05 mmol). The reaction was heated at 100 °C, under vigorous stirring and monitored by TLC until complete disappearance of starting material. The solvent was evaporated in vacuo and 10 mL of water were added. After extraction with CH₂Cl₂ (3 x 10 mL), the combined organic layers were dried over MgSO₄ and the solvent was removed under reduced pressure. The crude material was purified by column chromatography to afford the expected enyne **1d**. ¹H NMR (CDCl₃, 300 MHz): δ 3.91 (s, 3H, OCH₃), 6.37 (d, *J* = 16.2 Hz, 1H, H_{viny}), 6.88-6.96 (m, 2H, H_{arom}), 7.00-7.06 (m, 3H, H_{arom+viny}), 7.30 (dt, *J* = 7.9 Hz, *J* = 1.7 Hz, 1H, H_{arom}), 7.39 (dd, *J* = 8.8 Hz, *J* = 5.4 Hz, 2H, H_{arom}), 7.45 (dd, *J* = 7.5, *J* = 1.7 Hz, 1H). ¹³C NMR (CDCl₃, 75MHz): δ 55.9 (CH₃), 88.2 (Cq), 92.8 (Cq), 108.4 (CH), 110.7 (CH), 112.6 (Cq), 115.8 (2CH, J_{CF}

δ = 21.8 Hz), 120.6 (CH), 128.0 (2CH, J_{CF} = 8.1 Hz), 129.9 (CH), 132.8 (Cq, J_{CF} = 3.1 Hz), 133.6 (CH), 139.7 (CH), 160.0 (Cq), 162.9 (Cq, J_{CF} = 248.6 Hz). IR (ν cm⁻¹): 1597, 1490, 1434, 1228, 1158, 1024, 954, 813, 750. MS (APCI+) m/z 253.0 ([M+H]⁺).

1-Methoxy-2-(4-methylpent-3-en-1-ynyl)benzene (1h) (312 mg; 70%).

To a solution of PdCl₂(PPh₃)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 μ L; 2.4 mmol). The stirred reaction was refluxed for 20 h and treated with a saturated NH₄Cl solution (10 mL). The aqueous layer was extracted with EtOAc (3 x 10 mL) and the combined organic layers were dried over MgSO₄ and concentrated under vacuum. Purification by flash chromatography afforded the expected enyne **1h**. R_f = 0.41 (Cyclohexane/CH₂Cl₂: 8/2). NMR ¹H (CDCl₃, 300 MHz): δ 1.87 (s, 3H, CH₃), 2.01 (s, 3H, CH₃), 3.88 (s, 3H, OCH₃), 5.54 (bs, 1H, H_{viny}l), 6.87 (d, J = 8.2 Hz, 1H, H_{arom}), 6.90 (t, J = 7.5 Hz, 1H, H_{arom}), 7.25 (t, J = 7.9 Hz, 1H, H_{arom}), 7.40 (d, J = 7.5 Hz, 1H, H_{arom}). NMR ¹³C (CDCl₃, 75 MHz): δ 21.2 (CH₃); 25.0 (CH₃), 55.9 (OCH₃), 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). IR (ν cm⁻¹): 2908, 1593, 1434, 1268, 1240, 1119, 1047, 749. MS (APCI+) m/z 373.0 ([2M+H]⁺), 187.0 ([M+H]⁺).

Preparation of unsymmetrical diynes (3c-d) To a solution of CuI (0.1 mmol) in pyrrolidine (10 mL) was added successively at 0 °C, 1 mmol of iodoarylalkyne and 2 mmol of terminal arylalkyne. The stirred reaction was kept at room temperature for a night and treated with a saturated NH₄Cl solution (15 mL). The aqueous layer was extracted with EtOAc (3 x 10 mL) and the combined organic layers were dried over MgSO₄ 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] (152 mg; 70%). Prepared from CuI (14.8 mg, 0.08 mmol), 1-(2-iodoethynyl)-2-methoxybenzene (200 mg, 0.78 mmol) and 2-thiomethylphenylacetylene. Mp = 82-83 °C. R_f = 0.22 (Cyclohexane/EtOAc: 94/6). NMR ¹H (CDCl₃, 400 MHz): δ 2.51 (s, 3H, SCH₃), 3.91 (s, 3H, OCH₃), 6.89 (d, J = 8.7 Hz, 1H, H_{arom}), 6.92 (t, J = 7.5 Hz, 1H, H_{arom}), 7.09 (t, J = 7.5 Hz, 1H, H_{arom}), 7.17 (d, J = 7.9 Hz, 1H, H_{arom}), 7.29-7.36 (m, 2H, H_{arom}), 7.48-7.51 (m, 2H, H_{arom}). NMR ¹³C (CDCl₃, 100 MHz): δ 15.4 (SCH₃), 56.0 (OCH₃), 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. IR (ν cm⁻¹): 2938, 1594, 1492, 1464, 1433, 1248, 1022, 733, 703. MS (APCI+) m/z 279.0 ([M+H]⁺).

1-(2-Methoxyphenyl)-4-(4-methoxyphenyl)buta-1,3-diyne (3d) (131 mg; 64%). Prepared from CuI (40.6 mg, 0.21 mmol), 1-(2-iodoethynyl)-2-methoxybenzene (550 mg, 0.78 mmol) and 4-methoxyphenylacetylene. Mp = 109-110 °C. R_f = 0.24 (Cyclohexane/Acetone: 95/5). NMR ¹H (CDCl₃, 300 MHz): δ 3.82 (s, 3H, OCH₃), 3.90 (s, 3H, OCH₃), 6.84-6.94 (m, 4H, H_{arom}), 7.32 (t, J = 7.6 Hz, 1H, H_{arom}), 7.45-7.48 (m, 3H, H_{arom}). NMR ¹³C (CDCl₃, 75 MHz): δ 55.4 (OCH₃), 55.9 (OCH₃), 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. IR (ν cm⁻¹): 2936, 2837, 1601, 1508, 1489, 1247, 1171, 1024, 750. 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 CH₂Cl₂ (1 mmol) was added MPHT (for quantity, see text) and the resulting solution was stirred at room temperature until disappearance of starting material (as judged by TLC). The reaction mixture was next treated with a saturated Na₂S₂O₃ solution. The organic layer was washed with HCl 10% (3 x 10 mL) and dried over MgSO₄. 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) (242 mg; 81%). R_f = 0.57 (Cyclohexane/CH₂Cl₂: 95/5). NMR ¹H (CDCl₃, 400 MHz): δ 7.14 (d, J = 16.2 Hz, 1H, H_{viny}l), 7.28-7.43 (m, 5H, H_{arom}), 7.41 (d, J = 16.2 Hz, 1H, H_{viny}l), 7.47 (d, J = 8.1 Hz, 1H, H_{arom}), 7.50 (d, J = 7.6 Hz, 1H, H_{arom}), 7.59 (d, J = 7.6 Hz, 2H, H_{arom}). RMN ¹³C (CDCl₃, 100 MHz): 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. IR (ν cm⁻¹): 3058, 2924, 1446, 1013, 1001, 954, 741, 689. MS (APCI+) m/z 220.0 ([M-Br+H]⁺). Anal. C₁₆H₁₁BrO (299.16): found C 64.09, H 3.56 requires C 64.24, H 3.71.

(E)-2-(4-Methoxystyryl)-3-bromobenzofuran (2b) (191 mg; 58%). Beige solid. Mp 85-86 °C. ¹H NMR (CDCl₃, 300 MHz): δ 3.85 (s, 3H, CH₃), 6.93 (d, 2H, J = 8.6 Hz, H_{arom}), 6.99 (d, 1H, J = 16.2 Hz, H_{viny}l), 7.28-7.39 (m, 3H, H_{viny}l+arom), 7.44-7.50 (m, 2H, H_{arom}), 7.53 (d, 2H, J = 8.6 Hz, H_{arom}). ¹³C NMR (CDCl₃, 75 MHz): δ 55.5 (CH₃), 96.0 (C), 111.1 (CH), 111.6 (CH), 114.4 (2CH), 119.5 (CH), 123.5 (CH), 125.6 (CH), 128.5 (2CH), 129.1 (C), 129.2 (C), 131.6 (CH), 151.8 (Cq), 153.6 (C), 160.2 (C). IR (ν cm⁻¹): 821, 953, 1014, 1173, 1243, 1450, 1505, 1599, 2926. MS (APCI+) m/z 329.0 (M+H)⁺ (⁷⁹Br), 331.0 (M+H)⁺ (⁸¹Br), 250.0 [(M-Br)+H]⁺. C₁₇H₁₃BrO₂ (329.19): found C 61.91, H 3.84 requires C 62.03, H 3.98.

(E)-5-(2-(3-bromobenzofuran-2-yl)vinyl)benzo-[1,3]-dioxole (2c) (192 mg; 56%). Yellow solid. Mp 122-123 °C. ¹H NMR (CDCl₃, 300 MHz): 6.00 (s, 2H, OCH₂O), 6.83 (d, 1H, J = 8.0 Hz, H_{arom}), 6.94 (d, 1H, J = 16.1 Hz, H_{viny}l), 7.03 (dd, 1H, J = 8.0, 1.3 Hz, H_{arom}), 7.12 (d, 1H, J = 1.6 Hz, H_{arom}), 7.27-7.35 (m, 3H, H_{viny}l+arom), 7.43-7.49 (m, 2H, H_{arom}). ¹³C NMR (CDCl₃, 75 MHz): 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). IR (ν cm⁻¹): 746, 931, 1037, 1199, 1250, 1447, 1487, 2360. MS (APCI+) m/z 343.0 (M+H)⁺ (⁷⁹Br), 345.0 (M+H)⁺ (⁸¹Br). Anal. C₁₇H₁₁BrO₃ (343.17): found C 59.41, H 3.16 requires C 59.50, H 3.23.

(E)-2-(4-Fluorostyryl)-3-bromobenzofuran (2d) (222 mg; 70%). Yellow solid. Mp 83-84 °C. ¹H NMR (CDCl₃, 300 MHz): δ 6.94 (d, 1H, J = 16.0 Hz, H_{viny}l), 7.01 (d, 2H, J = 8.6 Hz, H_{arom}), 7.17-7.29 (m, 3H, H_{arom}), 7.36-7.48 (m, 4H, H_{arom}). ¹³C NMR (CDCl₃, 75 MHz): δ 97.0 (C), 111.2 (CH), 113.6 (CH, J_{CF} = 1.5 Hz), 116.0 (2CH, J_{CF} = 21.9 Hz), 119.7 (CH), 123.7 (CH), 126.0 (CH), 128.7 (2CH, J_{CF} = 8.1 Hz), 129.0 (C), 130.7 (CH), 132.7 (Cq, J_{CF} = 3.0 Hz), 151.3 (C), 153.7 (C), 163.0 (Cq, J_{CF} = 249.1 Hz). IR (ν cm⁻¹): 740, 811, 847, 947, 1002, 1151, 1227, 1447, 1501, 1592. MS (APCI+) m/z 317.0 (M+H)⁺ (⁷⁹Br), 319.0 (M+H)⁺ (⁸¹Br). Anal. C₁₆H₁₀BrFO (317.15): found C 60.47, H 3.01 requires C 60.59, H 3.18.

(E)-2-(4-Chlorostyryl)-3-bromobenzofuran (2e) (207 mg; 62%). Yellow solid. Mp 114-115 °C. ¹H NMR (CDCl₃, 300 MHz): 7.09 (d, 1H, J = 16.2 Hz, H_{viny}l), 7.29-7.38 (m, 5H, H_{viny}l+arom), 7.45-7.52 (m, 4H, H_{arom}). ¹³C NMR (CDCl₃, 75 MHz): δ 97.5 (C), 111.3 (CH), 114.2 (CH), 119.8 (CH), 123.7

(CH), 126.2 (CH), 128.2 (2CH), 128.9 (C), 129.2 (2CH), 130.5 (CH), 134.3 (C), 135.0 (C), 151.2 (C), 153.8 (C). IR (ν cm $^{-1}$): 812, 954, 1013, 1091, 1192, 1252, 1448, 1489, 1592. MS (APCI+) m/z 333.0 (M+H) $^+$ (^{79}Br), 335.0 (M+H) $^+$ (^{81}Br). Anal. C₁₆H₁₀BrClO (333.61): found C 333.48, H 2.94 requires C 57.60, H 3.02.

(E)-3-Bromo-2-(2-(naphthalen-2-yl)vinyl)benzofuran (2f) (175 mg; 50%). Yellow solid. Mp 141–142 °C. ^1H NMR (CDCl₃, 300 MHz): 7.22–7.39 (m, 3H, H_{vinylic+arom}), 7.48–7.53 (m, 4H, H_{arom+naph}), 7.57 (d, 1H, J = 16.2 Hz, H_{vinyl}), 7.77–7.87 (m, 4H, H_{naph}), 7.94 (s, 1H, H_{naph}). ^{13}C NMR (CDCl₃, 75 MHz): 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 (2CH), 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). IR (ν cm $^{-1}$): 804, 962, 1015, 1195, 1258, 1446. MS (APCI+) m/z 349.0 (M+H) $^+$ (^{79}Br), 351.0 (M+H) $^+$ (^{81}Br). Anal. C₂₀H₁₃BrO (349.22): found C 68.55, H 3.51 requires C 68.79, H 3.75.

(E)-3-Bromo-2-(2-(thiophen-3-yl)vinyl)benzofuran (2g) (171 mg; 56%). Gray solid. Mp 65–66 °C. ^1H NMR (CDCl₃, 300 MHz): 6.95 (d, 1H, J = 16.1 Hz, H_{vinyl}), 7.29–7.34 (m, 2H, H_{vinylic+arom}), 7.35–7.47 (m, 5H, H_{arom}), 7.48–7.51 (m, 1H, H_{arom}). ^{13}C NMR (CDCl₃, 75 MHz): 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). IR (ν cm $^{-1}$): 738, 823, 853, 941, 1014, 1191, 1257, 1404, 1445, 1632. MS (APCI+) m/z 305.0 (M+H) $^+$ (^{79}Br), 307.0 (M+H) $^+$ (^{81}Br). Anal. C₁₄H₉BrOS (305.19): found C 55.19, H 3.06 requires C 55.10, H 2.97.

3-Bromo-2-(2-methylprop-1-enyl)benzofuran (2h) (128 mg; 51%). R_f = 0.62 (Cyclohexane/CH₂Cl₂: 95/5). NMR ^1H (CDCl₃, 300 MHz): δ 2.01 (s, 3H, CH₃), 2.22 (d, 3H, J = 1.3 Hz, CH₃), 6.25 (q, J = 1.3 Hz, 1H, H_{vinyl}), 7.26–7.33 (m, 2H, H_{arom}), 7.41–7.50 (m, 2H, H_{arom}). NMR ^{13}C (CDCl₃, 75 MHz): δ 20.8 (CH₃), 27.8 (CH₃), 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. IR (ν cm $^{-1}$): 2930, 1450, 1259, 1197, 1011, 738. MS (APCI+) 252.0 ([M+H] $^+$). Anal. C₁₂H₁₁BrO (251.12): found C 57.33, H 4.37 requires C 57.39, H 4.42.

3-Bromo-2-(3-bromobenzofuran-2-yl)benzofuran (4a)^[26] (376 mg; 96%).

White solid. Mp 224–225 °C. R_f = 0.43 (Cyclohexane/ CH₂Cl₂: 96/4). NMR ^1H (CDCl₃, 400 MHz): δ 7.38 (t, J = 7.4 Hz, 2H, H_{arom}), 7.45 (t, J = 7.4 Hz, 2H, H_{arom}), 7.59 (d, J = 8.2 Hz, 2H, H_{arom}), 7.64 (d, J = 7.7 Hz, 2H, H_{arom}). RMN ^{13}C (CDCl₃, 100 MHz): δ 98.3 (2C), 111.9 (2C), 120.5 (2C), 124.1 (2C), 126.9 (2C), 128.7 (2C), 142.8 (2C), 154.7 (2C). IR (ν cm $^{-1}$): 2923, 1437, 1260, 1211, 1122, 743. MS (APCI+) m/z 312.0 ([M- $^{79}\text{Br}+\text{H}]^+$), 314.0 ([M- $^{79}\text{Br}+\text{H}]^+$).

3-Bromo-2-(3-bromobenzo[b]thiophen-2-yl)benzo[b]thiophene (4b)^[27] (395 mg; 97%). Yellow solid. R_f = 0.67 (Cyclohexane/ CH₂Cl₂: 9/1). NMR ^1H (CDCl₃, 300 MHz): δ 7.50 (m, 4H, H_{arom}), 7.85 (d, J = 7.6 Hz, 2H, H_{arom}), 7.93 (d, J = 7.7 Hz, 2H, H_{arom}). NMR ^{13}C (CDCl₃, 75 MHz): δ 111.0 (2C), 122.4 (2C), 124.2 (2C), 125.6 (2C), 126.5 (2C), 129.5 (2C), 138.2 (2C), 139.3 (2C).

3-Bromo-2-(3-bromobenzothiophen-2-yl)benzofuran (4c) (99%). Yellow solid. Mp 113–118 °C. R_f = 0.59 (Cyclohexane/EtOAc: 96/4). NMR ^1H (CDCl₃, 300 MHz): δ 7.35–7.64 (m, 6H, H_{arom}), 7.86 (d, J = 7.5 Hz, 1H, H_{arom}), 7.96

(d, J = 8.4 Hz, 1H, H_{arom}). NMR ^{13}C (CDCl₃, 75 MHz): 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 (2CH), 128.7 (C), 138.3 (C), 138.8 (C), 145.4 (C), 148.4 (C), 154.2 (C). IR (ν cm $^{-1}$): 2923, 1454, 1257, 1241, 1040, 978, 737, 720. MS (APCI+) m/z 409.0 ([M+H] $^+$). Anal. C₁₆H₈Br₂OS (408.11): found C 46.89, H 1.89 requires C 47.09, H 1.98.

3-Bromo-2-(2-(4-methoxyphenyl)ethynyl)benzofuran (4d) (288 mg; 88%). Yellow solid. Mp 82–83 °C. R_f = 0.23 (Cyclohexane/ CH₂Cl₂: 9/1). NMR ^1H (CDCl₃, 300 MHz): δ 3.83 (s, 3H, OCH₃), 6.90 (d, J = 7.6 Hz, 2H, H_{arom}), 7.29–7.41 (m, 2H, H_{arom}), 7.45 (d, J = 8.3 Hz, 1H, H_{arom}), 7.50 (d, J = 7.4 Hz, 1H, H_{arom}), 7.56 (d, J = 7.6 Hz, 2H, H_{arom}). NMR ^{13}C (CDCl₃, 75 MHz): δ 55.5 (OCH₃) ; 77.0 (C), 99.5 (C), 102.9 (C), 111.6 (CH), 113.6 (C), 114.3 (2CH), 120.0 (CH), 123.9 (CH), 126.6 (CH), 127.8 (C), 133.6 (2CH), 137.8 (C), 153.8 (C), 160.7 (C). IR (ν cm $^{-1}$): 2208, 1504, 1290, 1249, 1016, 905, 830, 725. MS (APCI+) m/z 328.0 ([M+H] $^+$). Anal. C₁₇H₁₁BrO₂ (327.17): found C 62.13, H 3.10 requires C 62.41, H 3.39.

(E)-3-Bromo-2-(2-(3-bromobenzofuran-2-yl)vinyl)benzofuran (6) (92 mg; 21%). Yellow solid. Mp 232–233 °C. NMR ^1H (CDCl₃, 300 MHz): δ 7.26 (s, 2H, H_{vinyl}), 7.40 (m, 2H, H_{arom}), 7.49 (m, 2H, H_{arom}), 7.56 (dd, 2H, J = 7.7, 0.8 Hz, H_{arom}), 7.73 (d, 2H, J = 8.2 Hz, H_{arom}). NMR ^{13}C (CDCl₃, 75 MHz): 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). IR (ν cm $^{-1}$): 738, 861, 943, 1017, 1106, 1202, 1259, 1343, 1447, 1612. MS (APCI+) m/z 441.0 ([M+Na] $^+$). Anal. C₁₈H₁₀Br₂O₂ (418.08): found C 51.50, H 2.28 requires C 51.71, H 2.41.

3-Bromo-2-(4-methoxyphenyl)benzofuran (8a)^[28] (297 mg; 98%). Yellow solid. Mp 66–67 °C. R_f = 0.51 (Cyclohexane/ CH₂Cl₂: 8/2). NMR ^1H (CDCl₃, 400 MHz): δ 3.88 (d, J = 0.9 Hz, 3H, OCH₃), 7.02 (d, J = 7.9 Hz, 2H, H_{arom}), 7.32 (m, 2H, H_{arom}), 7.50 (m, 2H, H_{arom}), 8.12 (d, J = 7.9 Hz, 2H, H_{arom}). NMR ^{13}C (CDCl₃, 100 MHz): δ 55.5 (OCH₃), 92.3, 111.3, 114.2, (2), 119.7, 122.4, 123.5, 125.3, 128.5 (2), 129.9, 150.7, 153.1, 160.4. IR (ν cm $^{-1}$): 2959, 1609, 1450, 1251, 1117, 1072, 1030, 985, 830, 783. MS (APCI+) m/z 224 ([M-Br+H] $^+$).

3-Bromo-2-(2-methoxyphenyl)benzofuran (8b)^[9b] (239 mg; 79%). R_f = 0.38 (Cyclohexane/ CH₂Cl₂: 8/2). NMR ^1H (CDCl₃, 300 MHz): δ 3.89 (s, 3H, OCH₃), 7.05 (d, J = 8.1 Hz, 1H, H_{arom}), 7.09 (td, J = 7.5 Hz, J = 1.0 Hz, 1H, H_{arom}), 7.35 (m, 2H, H_{arom}), 7.49 (m, 2H, H_{arom}), 7.60 (m, 2H, H_{arom}). NMR ^{13}C (CDCl₃, 75 MHz): δ 55.8 (OCH₃), 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). IR (ν cm $^{-1}$): 2933, 1486, 1447, 1255, 1058, 1044, 1024, 740. MS (ESI+) m/z 224.0 ([M-Br+H] $^+$). Anal. C₁₅H₁₁BrO₂ (303.15): found C 59.19, H 3.76 requires C 59.43, H 3.66.

3-Bromo-2-p-tolylbenzofuran (8c) (229 mg; 80%). Yellow solid. Mp 70–72 °C. R_f = 0.65 (Cyclohexane/ CH₂Cl₂: 9/1). NMR ^1H (CDCl₃, 400 MHz): δ 2.43 (s, 3H, CH₃), 7.32 (m, 4H, H_{arom}), 7.53 (m, 2H, H_{arom}), 8.07 (d, J = 8.3 Hz, 2H, H_{arom}). NMR ^{13}C (CDCl₃, 100 MHz): δ : 21.6 (CH₃), 93.3, 111.3, 119.9, 123.5, 125.5, 126.9 (3), 129.4 (2C), 129.8, 139.4, 150.8, 153.2. IR (ν cm $^{-1}$): 2919, 1503, 1450, 1253, 1204, 1072, 1020, 817, 741. MS (APCI+) m/z 208 ([M-Br+H] $^+$).

4-(3-Bromobenzofuran-2-yl)-N,N-dimethylbenzenamine (8d) (221 mg; 74%). R_f = 0.57 (Cyclohexane/ CH₂Cl₂: 8/2). NMR ^1H (CDCl₃, 300 MHz): δ 3.04 (s, 6H, N-CH₃), 6.80 (d, J = 8.9 Hz,

2H,), 7.29 (m, 2H, H_{arom}), 7.50 (m, 2H, H_{arom}), 8.08 (d, J = 8.7 Hz, 2H,). NMR ^{13}C (CDCl_3 , 75 MHz): 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). IR (v cm $^{-1}$): 2889, 1607, 1510, 1450, 1361, 1194, 816, 742. MS (APCI+) m/z 316 ([M(^{79}Br) $+\text{H}]^+$), 318 ([M(^{81}Br) $+\text{H}]^+$). Anal. $\text{C}_{16}\text{H}_{14}\text{BrNO}$ (299.16): found C 60.54, H 4.29, N 4.23 requires C 60.78, H 4.46, N 4.43.

3-Bromo-2-(naphthalen-1-yl)benzofuran (8e) (242 mg; 75%). White solid. Mp 107–109 °C. R_f = 0.65 (Cyclohexane/ CH_2Cl_2 : 9/1). NMR ^1H (CDCl_3 , 300 MHz): δ 7.43 (m, 2H, H_{arom}), 7.62 (m, 5H), 7.87 (d, J = 8.7 Hz, 1H, H_{naph}), 8.00 (m, 3H). NMR ^{13}C (CDCl_3 , 75 MHz): 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). IR (v cm $^{-1}$): 3053, 1449, 1259, 1029, 1014, 968, 800, 772, 743. MS (APCI+) m/z 244.0 ([M-Br+H] $^+$). Anal. $\text{C}_{18}\text{H}_{11}\text{BrO}$ (323.18): found C 66.78, H 3.36 requires C 66.89, H 3.43;

3-Bromo-2-(naphthalen-2-yl)benzofuran (8f) (197 mg; 61%). Yellow solid. Mp 98–102 °C. R_f = 0.56 (Cyclohexane/ CH_2Cl_2 : 9/1). RMN ^1H (CDCl_3 , 300 MHz): δ 7.38 (m, 2H, H_{arom}), 7.57 (m, 4H), 7.87 (m, 4H), 7.96 (m, 2H), 8.30 (d, J = 8.7 Hz, 1H, H_{naph}), 8.68 (s, 1H, H_{naph}). NMR ^{13}C (CDCl_3 , 75 MHz): 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). IR (v cm $^{-1}$): 3058, 1450, 1259, 1065, 994, 857, 815, 742. MS (APCI+) m/z 244.0 ([M-Br+H] $^+$). Anal. $\text{C}_{18}\text{H}_{11}\text{BrO}$ (323.18): found C 67.01, H 3.60 requires C 66.89, H 3.43.

3-Bromo-2-(4-methoxyphenyl)benzo[b]thiophene (8g)^[29] (309 mg; 97%).

Yellow solid. Mp 83 °C. R_f = 0.41 (Cyclohexane/ CH_2Cl_2 : 8/2). NMR ^1H (CDCl_3 , 300 MHz): δ 3.88 (s, 3H, OCH_3), 7.02 (d, J = 8.5 Hz, 2H, H_{arom}), 7.39 (t, J = 7.5 Hz, 1H, H_{arom}), 7.47 (t, J = 7.6 Hz, 1H, H_{arom}), 7.71 (d, J = 8.4 Hz, 2H, H_{arom}), 7.80 (d, J = 7.8 Hz, 1H, H_{arom}), 7.85 (d, J = 8.0 Hz, 1H, H_{arom}). NMR ^{13}C (CDCl_3 , 75 MHz): 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). IR (v cm $^{-1}$): 2922, 1606, 1494, 1433, 1248, 1177, 1032, 831, 802, 749. MS (APCI+) m/z 240 ([M-Br+H] $^+$).

3-Bromo-2-(2-methoxyphenyl)benzo[b]thiophene (8h) (258 mg; 81%).

Beige solid. Mp 85–87 °C. R_f = 0.27 (Cyclohexane). NMR ^1H (CDCl_3 , 300 MHz): δ 3.86 (s, 3H, OCH_3), 7.06 (m, 2H, H_{arom}), 7.45 (m, 4H, H_{arom}), 7.82 (d, J = 7.7 Hz, 1H, H_{arom}), 7.87 (d, J = 8.0 Hz, 1H, H_{arom}). NMR ^{13}C (CDCl_3 , 75 MHz): 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). IR (v cm $^{-1}$): 2938, 1482, 1459, 1432, 1248, 1115, 1024, 889, 748, 725. MS (APCI+) m/z 240 ([M-Br+H] $^+$). Anal. $\text{C}_{15}\text{H}_{11}\text{BrOS}$ (319.22): found C 56.29, H 3.36 requires C 56.44, H 3.47.

4-Bromo-3-(2-methoxyphenyl)-1*H*-isochromen-1-one (8i) (324 mg; 98%). White solid. Mp 129–131 °C. R_f = 0.37 (Cyclohexane/ CH_2Cl_2 : 8/2). NMR ^1H (CDCl_3 , 300 MHz): δ 3.85 (s, 3H, OCH_3), 7.00 (d, J = 8.4 Hz, 1H, H_{arom}), 7.05 (td, J = 7.5, J = 0.9 Hz, 1H, H_{arom}), 7.40–7.49 (m, 2H, H_{arom}), 7.60 (td, J = 7.5 Hz, J = 1.2 Hz, 1H, H_{arom}), 7.84 (td, J = 7.6 Hz, J = 1.3 Hz, 1H, H_{arom}), 7.92 (d, J = 8.1 Hz, 1H, H_{arom}), 8.35 (dd, J = 7.9 Hz, J = 0.8 Hz, 1H, H_{arom}). NMR ^{13}C (CDCl_3 , 75 MHz): 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). IR (v cm $^{-1}$): 2952, 1732, 1279, 1072, 1020, 753. MS (ESI+) m/z 354 ([M+Na] $^+$). Anal. $\text{C}_{16}\text{H}_{11}\text{BrO}_3$ (329.99): found C 57.88, H 3.20 requires C 58.03, H 3.35.

(2-(3-Bromobenzofuran-2-yl)phenoxy)(tert-butyl)dimethylsilane (8j) (375 mg; 93%). R_f = 0.76 (Cyclohexane/ CH_2Cl_2 : 9/1). NMR ^1H (CDCl_3 , 300 MHz): δ 0.06 (s, 6H, CH_3Si), 0.84 (s, 9H, CH_3C), 6.99 (d, J = 8.2 Hz, 1H, H_{arom}), 7.09 (td, J = 7.5 Hz, J = 1.0 Hz, 1H, H_{arom}), 7.36 (m, 3H, H_{arom}), 7.48 (m, 1H, H_{arom}), 7.59 (m, 2H, H_{arom}). NMR ^{13}C (CDCl_3 , 100 MHz): 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). IR (v cm $^{-1}$): 2930, 1483, 1449, 1281, 1258, 916, 887, 826, 780, 743. MS (APCI+) m/z 403 ([M(^{79}Br) $+\text{H}]^+$), 405 ([M(^{81}Br) $+\text{H}]^+$). Anal. $\text{C}_{20}\text{H}_{23}\text{BrO}_2\text{Si}$ (402.07): found C 59.38, H 5.61 requires C 59.55, H 5.75.

3-Bromo-2-(2,4-dimethoxyphenyl)benzofuran (8k) (310 mg; 93%). Yellow solid. Mp 59–61 °C. R_f = 0.26 (Cyclohexane/ EtOAc: 9/1). NMR ^1H (CDCl_3 , 400 MHz): δ 3.87 (s, 3H, OCH_3), 3.88 (s, 3H, OCH_3), 5.61 (m, 2H, H_{arom}), 7.33 (m, 1H, H_{arom}), 7.34 (m, 1H, H_{arom}), 7.51 (m, 1H, H_{arom}), 7.53 (m, 1H, H_{arom}), 7.57 (m, 1H, H_{arom}). NMR ^{13}C (CDCl_3 , 100 MHz): 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. IR (v cm $^{-1}$): 2938, 1616, 1499, 1449, 1209, 1161, 1033, 986, 745. MS (APCI+) m/z 254.0 ([M-Br+H] $^+$). Anal. $\text{C}_{16}\text{H}_{13}\text{BrO}_3$ (333.18): found C 57.55, H 3.66 requires C 57.68, H 3.93.

(E)-4-(2-(4-Methoxystyryl)benzofuran-3-yl)but-3-yn-1-ol (9) (254 mg; 80%). A solution of $\text{PdCl}_2(\text{PPh}_3)_2$ (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 12h. The stirred reaction next treated with saturated NH₄Cl solution (25 mL). The aqueous layer was extracted with diethylether (3 x 20 mL), the combined organic layers were washed successively with aqueous HCl (0.2 M, 15 mL), NaHCO₃ (10 mL) and H₂O (2 x 25 mL), dried over MgSO₄ and concentrated under vacuum.

Brown oil. R_f = 0.50 (Cyclohexane/ EtOAc: 5/5). NMR ^1H (CDCl_3 , 300 MHz): δ 2.86 (t, J = 6.3 Hz, 2H, $\text{CH}_2\text{-C}$), 3.84 (s, 3H, OMe), 3.92 (t, J = 6.3 Hz, 2H, CH_2O), 6.93 (dd, J = 9.0 Hz, J = 2.4 Hz, 2H, H_{arom}), 7.06 (d, J = 16.2 Hz, 1H, H_{vinyl}), 7.63–7.20 (m, 7 H, $H_{arom+vinyl}$). NMR ^{13}C (CDCl_3 , 100 MHz): 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 (2CH), 123.3 (CH), 125.3 (CH), 128.5 (CH), 129.6 (2CH), 131.3 (CH), 153.9 (C), 157.8 (C), 160.2 (C). IR (v cm $^{-1}$): 3448, 2935, 1734, 1602, 1577, 1508, 1452, 1423, 1373, 1245, 1034, 959, 932, 746. Anal. $\text{C}_{21}\text{H}_{18}\text{O}_3$ (318.37): found C 79.00, H 5.36 requires C 79.22, H 5.70.

(E)-2-(4-Methoxystyryl)-3-(3,4,5-trimethoxy-phenyl)benzofuran (10) (374 mg; 90%). To a solution of **2b** (1 mmol) in toluene (4mL) and EtOH (2 mL), were successively added 3,4,5-trimethoxyphenyl boronic acid (254 mg, 1.2 mmol), K₂CO₃ (2 mmol) and Pd(PPh₃)₄ (0.05 mmol). The reaction was heated at 100 °C, under vigorous stirring and monitored by TLC until complete disappearance of starting material. The solvent was evaporated in vacuo and 10 mL of water were added. After

extraction with CH_2Cl_2 (3×10 mL), the combined organic layers were dried over MgSO_4 and the solvent was removed under reduced pressure. The crude material was purified by column chromatography to afford **10**. Yellow oil. $R_f = 0.25$ (Cyclohexane/ EtOAc: 8/2). NMR ^1H (CDCl_3 , 300 MHz): δ 3.72 (s, 3H, OCH_3), 3.82 (s, 6H, OCH_3), 3.90 (s, 3H, OCH_3), 6.71 (s, 2H, H_{arom}), 6.80 (d, $J = 7.8$ Hz, 2H, H_{arom}), 6.98 (d, $J = 16.2$ Hz, 1H, H_{vinyl}), 7.15–7.730 (m, 2H, H_{arom}), 7.35 (d, $J = 16.2$ Hz, 1H, H_{vinyl}), 7.42 (d, $J = 7.8$ Hz, 2H, H_{arom}), 7.36–7.60 (m, 2H, H_{arom}). NMR ^{13}C (CDCl_3 , 100 MHz): δ 55.3 (CH_3), 56.3 (2 CH_3), 61.0 (CH_3), 106.6 (2CH), 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 (2CH), 129.1 (C), 129.5 (C), 130.5 (CH), 137.5 (C), 151.1 (C), 153.6 (C), 154.2 (C), 159.8 (C). IR (ν cm^{-1}): 2932, 2249, 2068, 1602, 1580, 1509, 1452, 1414, 1389, 1307, 1243, 1173, 1125, 1032, 1005, 961, 907, 843, 819. Anal. $\text{C}_{26}\text{H}_{24}\text{O}_5$ (416.47): found C 74.89, H 5.66 requires C 74.98, H 5.81.

Acknowledgment

The Centre National de la Recherche Scientifique (CNRS) is gratefully acknowledged for financial support of this research and Ministère de la Recherche et de l'Enseignement Supérieur (MRES) for a doctoral fellowship to M. J. Thanks also to the Association de Recherche sur le Cancer (ARC) for a post-doctoral grant to A. T. and for financial support. Thanks also to E. Morvan for her help in the NMR experiments.

Notes and references

Received: ((will be filled in by the editorial staff))
Published online: ((will be filled in by the editorial staff))

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