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SILICA GEL-ASSISTED PREPARATION OF (BROMO)(CHLORO)(IODO)BENZO[*b*]THIOPHENES BEARING HALOGEN ATOMS AT THE 2-, 4-, AND 7-POSITIONS

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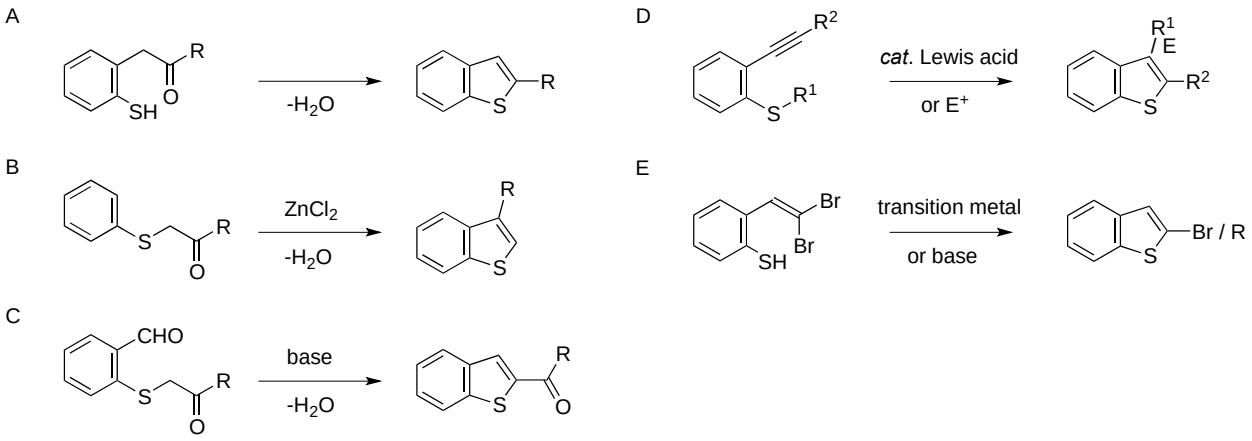
Abstract – Six types of (bromo)(chloro)(iodo)benzo[*b*]thiophenes bearing halogen atoms at the 2-, 4-, and 7-positions were prepared from the corresponding 2-(1-adamantylsulfanyl)-1,4-dihalo-3-(haloethynyl)benzene derivatives, by treatment with silica gel under thermal conditions. 4,7-Dihalobenzo[*b*]thiophenes, bearing two different halogen atoms (chlorine, bromine, or iodine), were also prepared from 2-(1-adamantylsulfanyl)-3-(ethynyl)-1,4-dihalobenzene derivatives.

INTRODUCTION

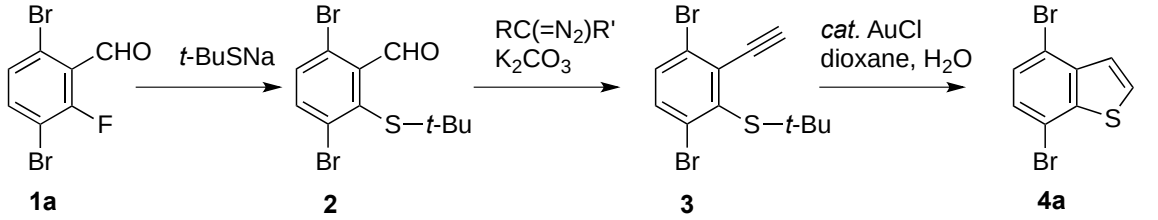
Benzo[*b*]thiophenes are currently of interest as useful building blocks. Utilization and functionalization of benzo[*b*]thiophene derivatives have been extensively explored in the fields of synthetic chemistry,[1] medicinal chemistry,[2] as well as materials science,[3] because they provide many valuable compounds in these fields. Consequently, several synthetic methods have been developed as shown in Scheme 1.



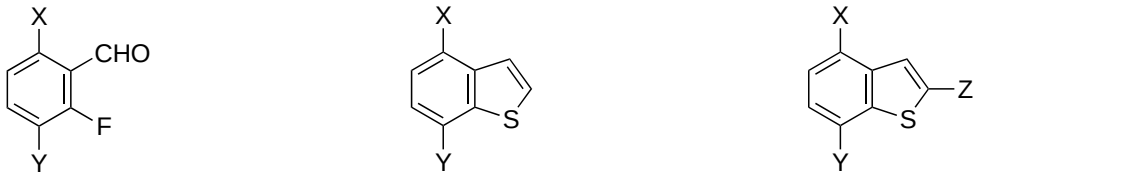
Scheme 1. Some typical synthetic methods of benzo[*b*]thiophene derivatives

Various benzo[*b*]thiophene derivatives have been synthesized by cyclodehydration (Scheme 1, methods A–C)[4a,b] as well as some specific methods.[4c–g] More recently, many 3-substituted benzo[*b*]thiophenes have been prepared from 1-alkynyl-2-sulfanylbenzene derivatives (method D), by utilization of suitable reagents such as halogen reagents,[5] Lewis acidic transition metal catalysts,[6] or sulfur reagents.[5a,7] 2-Substituted benzo[*b*]thiophenes have been prepared also from 1-alkynyl-2-sulfanylbenzene derivatives[8] (method D) as well as from 1-alkenyl-2-sulfanylbenzene derivatives (method E).[9]

In the course of our research in development of ring-fused thiopehene building blocks,[10] we have reported a preparation of 4,7-dihalobenzo[*b*]thiophenes from (ethynyl)(*t*-butylsulfanyl)benzene derivative (Scheme 2)[10b] as follows: 3,6-Dibromo-2-fluorobenzaldehyde (**1a**) was converted to the corresponding *t*-butylsulfanylbenzaldehyde **2** by using *t*-butyl mercaptan (2-methyl-2-propanethiol) sodium salt. Compound **2** reacted with Ohira-Bestmann reagent [$PhCOC(=N_2)P(O)(OMe)_2$] to give **3**, which was cyclized by addition of AuCl catalyst to give 4,7-dibromobenzo[*b*]thiophene (**4a**). Lithiation of **4a** with lithium *N*,*N*-diisopropylamide (LDA) followed by treatment with iodomethane gave **5a** (Chart 1, X = Y = Br, Z = Me), while lithiation of **4a** with butyllithium followed by treatment with 1,2-diiodoethane afforded **4c** (X = Br, Y = I).



Scheme 2. Previously reported preparation of 4,7-dibromobenzo[*b*]thiophene



1a: X = Br, Y = Br (Ref. 11a)
1b: X = Br, Y = Cl (Ref. 11b)
1c: X = Br, Y = I (Ref. 11c)
1d: X = Cl, Y = Br (Ref. 11d)
1e: X = Cl, Y = I
1f: X = I, Y = Cl
1g: X = I, Y = Br (Ref. 11e)

4a: X = Br, Y = Br (Ref. 10b)
4b: X = Br, Y = Cl
4c: X = Br, Y = I (Ref. 10b)
4d: X = Cl, Y = Br
4e: X = Cl, Y = I
4f: X = I, Y = Cl
4g: X = I, Y = Br

5a: X = Br, Y = Br, Z = Me (Ref. 10b)
5b: X = Br, Y = Cl, Z = I
5c: X = Br, Y = I, Z = Cl
5d: X = Cl, Y = Br, Z = I
5e: X = Cl, Y = I, Z = Br
5f: X = I, Y = Cl, Z = Br
5g: X = I, Y = Br, Z = Cl
5h: X = Br, Y = Cl, Z = Br

Chart 1. Structures of compounds **1**, **4**, and **5**

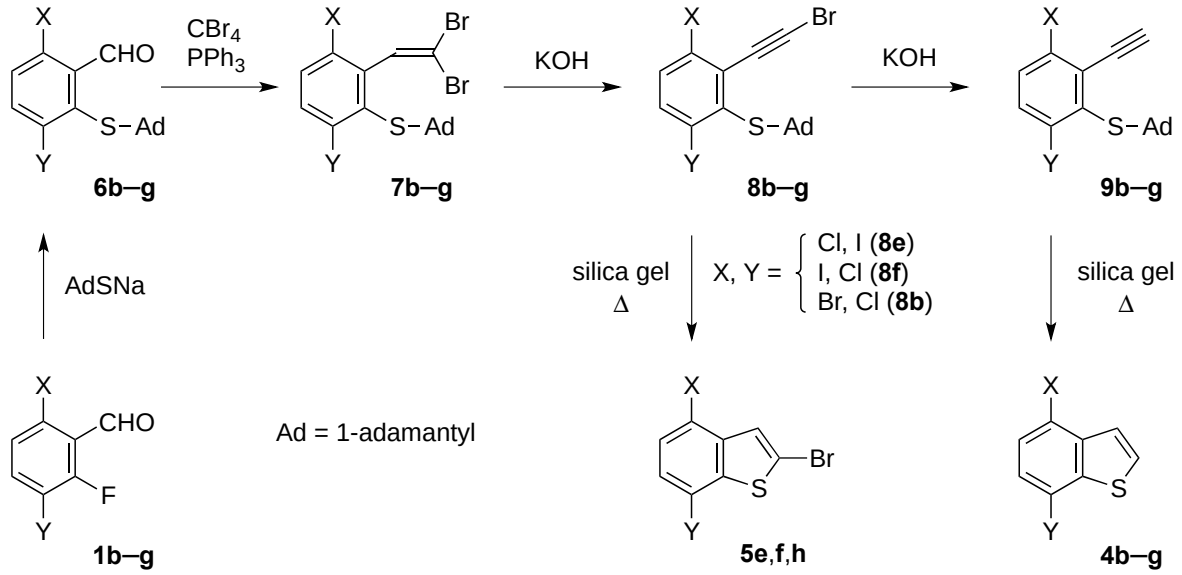
The compound **4c** bearing different halogen atoms is expected to possess several reaction site of different reactivity, which makes **4c** a promising regioselective building block: Dihalo- or trihalo-aromatic compounds, whose halogen atoms are different each other, are potentially *regioselective* building blocks, taking the difference in reactivity in cross coupling reactions into account.

During our continuing effort of preparation of various 4,7-dihalobenzothiophenes, we fortunately found efficient and practical preparative methods of 4,7-dihalobenzo[*b*]thiophenes and 2,4,7-trihalobenzo[*b*]thiophenes. We report here preparation of trihalobenzo[*b*]thiophenes **5b**–**g** (Chart 1, where X ≠ Y ≠ Z) bearing different halogen atoms at the 2-, 4-, and 7-positions, which may work as 'quasi T-shape' scaffolds regarding to the directions of the carbon–halogen bonds. We also describe preparation of 4,7-dihalobenzo[*b*]thiophenes **4b**–**g** (where X ≠ Y). In both cases, silica gel was effectively utilized for preparations under thermal conditions.

RESULTS AND DISCUSSION

Preparation of 2,4,7-trihalobenzo[*b*]thiophenes

In the present study, we sought some improvements in our preparation of multihalo-benzothiophenes. In the first place, we utilized 1-adamantanethiol instead of *t*-butyl mercaptan. 1-Adamantanethiol is a solid at room temperature and has only slight and gentle perfume. Thus, handling of 1-adamantanethiol is much easier, compared to a liquid and bad smelling *t*-butyl mercaptan: an introduction of adamantylsulfanyl group into **1b**–**g**[11] was performed with its sodium salt to give **6b**–**g** in moderate to excellent yields (64–96%) (Scheme 3, Table 1).



Scheme 3. Preparations of 4,7-dihalobenzo[*b*]thiophenes and 2,4,7-trihalobenzo[*b*]thiophenes

Table 1. Summary of the yield (%) of the products **4**–**13**[a]

compound	(X	Y)	**6**	**7**	**8**	**9**[b,c]	**4**	(X	Y	Z)	**10**	**11**	**12**	**13**	**5**
b	Br	Cl	87	90	98[d]	86	89	Br	Cl	I	–	–	71	95	75[e]
c	Br	I	64	86	–	77	98	Br	I	Cl	(67)[f,g]	(90)[g]	–	–	89[h]
d	Cl	Br	91	93	–	87	97	Cl	Br	I	–	–	70	95	80[e]
e	Cl	I	89	86	91[i]	96	66	Cl	I	Br	–	–	–	–	90[b]
f	I	Cl	84	92	99[i]	93	79[b]	I	Cl	Br	–	–	–	–	74[b]
g	I	Br	96	93	–	99	93	I	Br	Cl	(67)[f,g]	(99)[g]	–	–	80[h]
h								Br	Cl	Br	–	–	–	–	69[j]

[a]Isolated yield, unless otherwise specified. [b]Yield based on **7**. [c]Reaction in acetone-H_2O (intermediate **8** was not isolated). [d]Reaction in THF-H_2O. [e]Yield based on **13**. [f]Data obtained in Scheme 4, method B. [g]Approximate yield due to difficulty in separation of **10** and **15**; determined by ^{1}H NMR. [h]Yield based on **11**. [i]Reaction in 1,4-dioxane-H_2O. [j]Yield based on **8b**.

In the second place, we investigated a modified Corey-Fuchs alkynation of the aldehydes **6**, instead of Ohira-Bestmann type alkynation. In our previous preparation of **4a**,[10b] the alkyne **3** was introduced by the reaction of the aldehyde **2** with Ohira-Bestmann reagent, which has a reactive diazo group in the molecule, demanding a careful handling in experiments. In the present study, we sought safe and easy-handling preparation of alkynes from aldehydes via the corresponding dibromoethenyl derivatives **7**. Thus, the aldehydes **6b**–**g** were treated with carbon tetrabromide and triphenylphosphine to give the corresponding dibromoalkenes **7b**–**g** (86–93%).

We then tried to prepare terminal alkynes by reaction of **7** with a base, by a method reported by Zhao *et al*.[12] When **7b** was treated with Cs_2CO_3 in DMSO at 115 °C for 20 min under N_2, we obtained a corresponding terminal alkyne **9b** (31% yield), 2-bromobenzo[*b*]thiophene derivative **5h** (34%), and a trace amount of bromoalkyne **8b** (1%), after silica gel column chromatography (Kanto Chemical Co. Ltd., spherical silica gel 60N, neutral; eluent: hexane-$CHCl_3$ 95:5 to 83:17). At this stage, we recognized that **5h** was formed during the silica gel column chromatographic treatment, because ^{1}H NMR spectrum of the crude product before column chromatography showed signals only due to **8b** and **9b** (about 1:2 ratio); signals due to **5h** were not detected before the column chromatography. We were interested in this easy formation of **5h** losing the adamantyl group. In many reported synthetic methods of benzo[*b*]thiophenes, a metal catalyst or iodine is needed for this kind of cyclization of *o*-(alkynyl)(sulfanyl)benzene derivatives, to give *3-substituted* benzo[*b*]thiophenes.[5,6] In our case, formation of 3-adamantylbenzo[*b*]thiophene was not observed. Thus we examined the reaction conditions in detail.

For the purpose of investigation of the reaction conditions, we tried to prepare the alkynes **8** and **9** in better yields and this was done by tuning the bases, solvents, and reaction time as follows:[13] When the dibromoalkene **7b** was reacted with aqueous KOH solution *in acetone* at room temperature for 3 h in air,

the terminal alkyne **9b** was obtained in 86% yield (Table 1). On the other hand, when **7b** was reacted with aqueous KOH solution *in THF* at room temperature for 40 h, **8b** was obtained nearly quantitatively. It should be mentioned that information of 1-(haloethynyl)-2-(sulfanyl)benzene derivatives has been limited until recently.[5g,6f,9h,14]

When **8b** thus formed was stirred with silica gel in toluene at room temperature for 16 h, formation of **5h** was confirmed by ^{1}H NMR and **5h** was obtained in 17% yield after basic alumina column chromatography (hexane-$CHCl_3$ 4:1). A significant acceleration occurred, when **8b** was heated with silica gel in toluene at 90 °C for 16 h, to give **5h** in 69% yield (Table 1). In the *absence* of silica gel in toluene at 90 °C for 16 h, most of **8b** remained unchanged (checked by ^{1}H NMR spectroscopy) and only a small amount of a complex mixture including **5h** was obtained after column chromatography.

Probably, silica gel as an acid activates the triple bond under thermal conditions (Figure 1, A, B; hydrogen bondings among the Si-OH groups and incorporated H_2O are omitted in the drawing) to form sulphonium ion intermediate (C), and then contact ion pair (D).[6c] At the same time, the proximate Si-OH or water acts as a trapping reagent of the adamantyl portion, preventing rearrangement of the substituents into the 2- or 3-positions. Actually, in some cases, a small amount of 1-adamantanol was obtained by eluting the silica gel with MeOH after reaction.

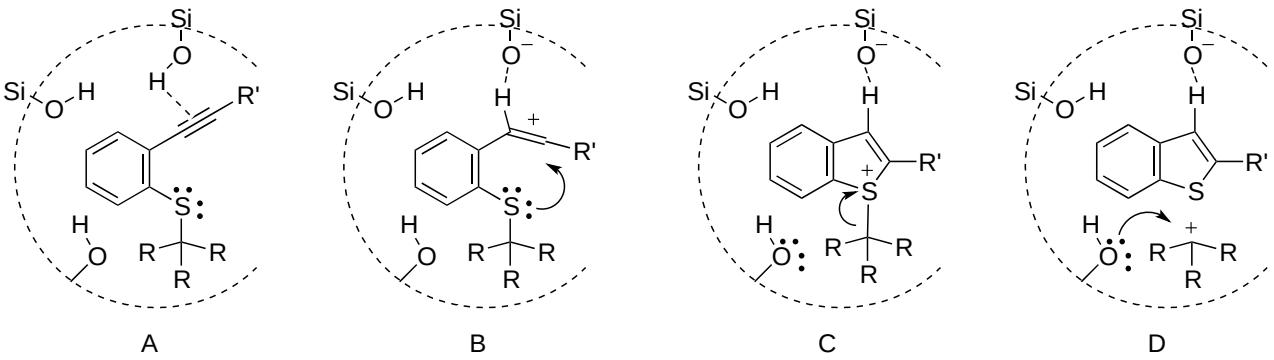


Figure 1. Plausible reaction mechanism

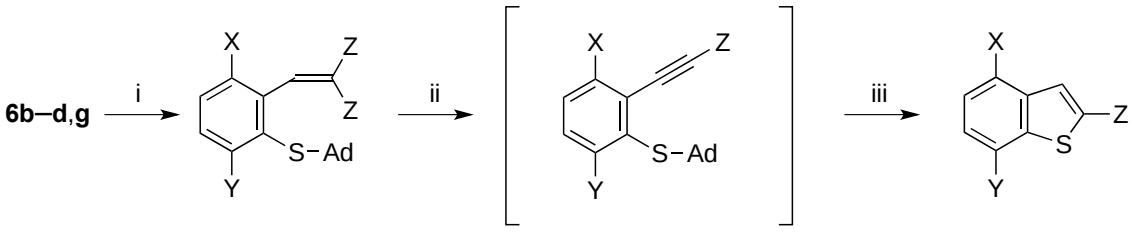
Analogous results were obtained with silica gel of other supplier (Merck 1.07734, silica gel 60; 76% yield, or Sigma-Aldrich 288594, silica gel 60 Å; 71% yield), and with alumina (Merck 1.01076, aluminium oxide 90 active basic; *ca*. 10% conversion by ^{1}H NMR at room temperature for 16 h). When the silica gel was pre-washed with MeOH and dried to remove inorganic salts, **5h** was obtained in 68% yield under similar conditions, suggesting that silica gel itself catalyzed the cyclization as an acid. However, we do not exclude the possibility that trace amount of salts or metals in silica gel causes the cyclization, because complete removal of salt or metal impurities from silica gel is generally very difficult.

We then tried to prepare benzo[*b*]thiopehenes **5b**–**g** bearing three different halogen atoms at the 2-, 4-,

and 7-positions, by this method (Chart 1, X ≠ Y ≠ Z). 2-Bromo-4,7-dihalobenzo[*b*]thiophenes **5e**,**f** were obtained in good yields from the corresponding (2,2-dibromoethenyl)benzene derivatives **7e**,**f**, by treatment of the intermediates **8e**,**f** with silica gel under thermal conditions (Scheme 3): **5e**, 90% yield based on **7e** (2 steps); **5f**, 74% based on **7f** (2 steps).

2-Chloro-4,7-dihalobenzo[*b*]thiophene **5g** was obtained as follows: Dichloroalkene **10g** (Scheme 4) was prepared by reaction of **6g** with CCl_4 (or $CBrCl_3$)[15] and PPh_3. In the reaction of **6g** with CCl_4 and PPh_3, a small amount (*ca*. 5%) of (*E*)-(2-chloroethenyl)benzene **14g** (Chart 2) was obtained as a by-product, which was not fully removed either by column chromatography or recrystallization.

In the case of reaction of **6g** with $CBrCl_3$ and PPh_3, a significant amount of (2-bromo-2-chloroethenyl)benzene **15g** was formed as a by-product (*ca*. 21% yield by ^{1}H NMR, as (*E*)- and (*Z*)-mixture), besides the desired **10g** (*ca*. 67% yield by ^{1}H NMR).



10c: X = Br, Y = I, Z = Cl
10g: X = I, Y = Br, Z = Cl

11c: X = Br, Y = I, Z = Cl
11g: X = I, Y = Br, Z = Cl

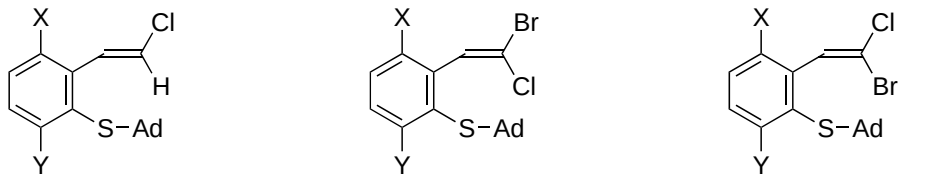
5c: X = Br, Y = I, Z = Cl
5g: X = I, Y = Br, Z = Cl

12b: X = Br, Y = Cl, Z = I
12d: X = Cl, Y = Br, Z = I

13b: X = Br, Y = Cl, Z = I
13d: X = Cl, Y = Br, Z = I

5b: X = Br, Y = Cl, Z = I
5d: X = Cl, Y = Br, Z = I

Scheme 4. *Reagents and conditions*: i, method A, CCl_4, PPh_3, reflux, 43 h (Z = Cl), method B, $CBrCl_3$, PPh_3, MeCN, 50 °C, 20 h (Z = Cl), method C, $(EtO)_2P(O)CH_2I$, I_2, $(Me_3Si)_2NLi$, THF, –78 °C, 0.5 h, then rt, 3 h (Z = I); ii, *t*-BuOK, THF, –78 °C, 0.5 h (Z = I) or 1.5 h (Z = Cl); iii, silica gel, toluene, 90 °C, 19 h (Z = I) or 20 h (Z = Cl)



(*E*)-**14c**: X = Br, Y = I
(*E*)-**14g**: X = I, Y = Br

(*E*)-**15c**: X = Br, Y = I
(*E*)-**15g**: X = I, Y = Br

(*Z*)-**15c**: X = Br, Y = I
(*Z*)-**15g**: X = I, Y = Br

Chart 2

However, to our delight, when the crude mixture of **10g**, (*E*)-**15g**, and (*Z*)-**15g** were reacted with KOH, only (chloroethynyl)benzene derivative **11g** was formed as a product and the corresponding (bromoethynyl)benzene derivative was not detected by ^{1}H NMR. It should be mentioned that an attempted isolation of **11g** by column chromatography failed, because partial isomerization to **5g** occurred

during the chromatographic treatment, even with alumina. This facile isomerization of **11g** favors the preparation of **5g**: By heating **11g** (generated by the latter method) with silica gel in toluene at 90 °C for 20 h followed by silica gel column chromatography, **5g** was obtained in pure form (80% yield based on **11g**). Similar results were obtained in the preparation of **5c** (89% yield based on **11c**).

2-Iodo-4,7-dihalobenzo[*b*]thiophenes **5b**,**d** were obtained as follows: Diiodoalkenes **12b**,**d** were prepared from **6b**,**d** in pure form (71% and 70% yield, respectively) by using $(EtO)_2P(O)CH_2I$, Tms_2NLi, and I_2.[16] Compounds **5b**,**d** were then obtained by analogous method from **12b**,**d** via **13b**,**d** (Table 1). It should be noted that compounds **5b**,**d** could also be obtained by lithiation of **4b**,**d** followed by iodination (see below).

Preparation of 4,7-dihalobenzo[*b*]thiophenes

Next, we studied a cyclization reaction of **9b**–**g** for preparation of 4,7-dihalobenzo[*b*]thiophenes **4b**–**g**, bearing different halogen atoms at the 4- and 7-positions (Scheme 3, where X ≠ Y). A preliminary examination suggested that cyclization of the terminal alkynes **9b**–**g** did not proceed so smoothly at room temperature, as that of haloalkynes **8**, **11**, or **13**. Thus, we sought suitable reaction conditions using **9g** as a probe (Table 2). Highly polar solvents did not give good results (entries 1–4, 9). Chloroform as well as some hydrophobic solvents such as benzene and toluene gave better yield at 60 °C (entries 5–7). Hexane (60 °C) and toluene (90 °C) afforded **4g** nearly quantitatively (entries 8, 10). The reaction is

Table 2. Preparation of **4g** from **9g**[a]

Entry	Solvent	Temp./°C	Conv./%b
1	THF	60	n.d.
2	DMSO		n.d.
3	MeCN		5
4	MeOH		36
5	$CHCl_3$		72
6	benzene		51
7	toluene		75
8	hexane		> 99
9	DMSO	90	n.d.
10	toluene		> 99
11[c]	toluene		22
12	toluene	rt	3
13[d]	toluene	110	n.d.

[a]**9g** (0.021 mmol), silica gel (1 g), solv. (5 mL), 15 h in air. [b]Determined by ^{1}H NMR; n.d. = not detected. [c]Silica gel (26 mg) was used. [d]Without silica gel.

very slow at room temperature (entry 12). With less amount of silica gel, the reaction proceeds insufficiently (entry 11), while the reaction did not proceed without silica gel even at 110 °C (entry 13). Taking the above results into account, compounds **4b**–**f** were also obtained in 66–98% isolated yields (Table 1) by analogous reaction conditions of **4g** (Table 2, entry 10). It should be mentioned that preparations of 2,3-*unsubstituted* benzo[*b*]thiophenes from (alkynyl)(sulfanyl)benzenes are rarely reported[10b] except for those from trialkylsilyl-protected (ethynyl)(sulfanyl)benzenes followed by desilylation[5d,8a] or desilylation-deiodination process.[5e]

As mentioned above, compounds **4** can be converted into the corresponding 2-substituted compounds **5** by alternative methods. For example, lithiation of **4b**,**d** with LDA followed by treatment with 1,2-diiodoethane afforded **5b**,**d** in 97% and 95% yields, respectively.

In summary, we have prepared all possible (bromo)(chloro)(iodo)benzo[*b*]thiophenes bearing halogen atoms at the 2-, 4-, and 7-positions, from the corresponding 1-(1-adamantylsulfanyl)-2-(haloethynyl)-benzene derivatives, by a practical and rather safe method using silica gel under thermal conditions. 4,7-Dihalobenzo[*b*]thiophene derivatives, whose halogen atoms are different each other (either chlorine, bromine, or iodine), were also prepared from 1-(1-adamantylsulfanyl)-2-(ethynyl)benzene derivatives. The trihalobenzo[*b*]thiophenes obtained in this paper are promising scaffolds for regioselective introduction of different substituents by cross coupling reaction. Further investigation concerning their reactivities and applications are currently in progress.

EXPERIMENTAL

Melting points were measured on a Yanagimoto MP-J3 micro melting point apparatus and are not corrected. ^{1}H (400 MHz) and ^{13}C (100 MHz) NMR spectra were recorded on a Bruker Avance III-400 spectrometer. MS spectra were taken on a Bruker solariX spectrometer or a JEOL JMS-T spectrometer. Elemental analyses were performed at Research and Analytical Center for Giant Molecules, Graduate School of Science, Tohoku University. Silica gel (either Kanto Chemical spherical silica gel 60N, Merck 1.07734, silica gel 60, or Sigma-Aldrich 288594, silica gel 60 Å) and alumina (Merck 1.01076; aluminium oxide 90 active basic) were purchased and used as it is, unless otherwise specified. Compounds **1b**–**d**,**g** have been known[11] and were prepared by a standard method.

Typical Procedure for the Preparation of Products 1e,**f. 6-Chloro-2-fluoro-3-iodobenzaldehyde (1e).** 4-Chloro-2-fluoro-1-iodobenzene (5.0127 g, 19.55 mmol) in THF (35 mL) was cooled to –63 °C with a dry ice-$CHCl_3$ bath under nitrogen atmosphere. LDA (23.1 mmol; 1.10 M solution in hexane-THF) was slowly added to the solution and the reaction mixture was stirred at –63 °C for 1 h. DMF (2.3 mL, 29.89 mmol) was slowly added to the reaction mixture and the mixture was stirred at

–63 °C for 1.5 h, warmed to room temperature. The mixture was slowly poured into 50 mL of 4 M hydrochloric acid at 0 °C with stirring. The resulting mixture was extracted with hexane-EtOAc (1:1). The organic phase was separated, dried over $MgSO_4$, and the solvent was removed under reduced pressure. Recrystallization of the crude product from hexane followed by silica gel column chromatographic treatment (hexane-$CHCl_3$ 80:20 to 50:50) afforded **1e** (4.5746 g, 16.08 mmol) in 82% yield; a pale yellow solid; mp 115–116 °C; ^{1}H NMR ($CDCl_3$) δ 7.08 (1H, dd, ^3J = 8.4 Hz, J = 1.4 Hz), 7.87 (1H, dd, ^3J = 8.4 Hz, $^4J_{FH}$ = 6.2 Hz), 10.4 (1H, d, J = 1.2 Hz, CHO); ^{13}C{^{1}H} NMR ($CDCl_3$) δ 81.0 (d, $^2J_{FC}$ = 26.0 Hz), 122.2 (d, $^2J_{FC}$ = 12.4 Hz), 128.2 (d, $^4J_{FC}$ = 4.9 Hz), 137.2 (d, $^3J_{FC}$ = 2.5 Hz), 143.9 (d, $^3J_{FC}$ = 3.7 Hz), 162.1 (d, $^1J_{FC}$ = 260.9 Hz), 186.0 (s, CHO). Found: *m*/*z* 284.8974. Calcd for $C_7H_4{}^{35}ClFIO$: $(M+H)^+$, 284.8974.

3-Chloro-2-fluoro-6-iodobenzaldehyde (1f): 83% yield from 1-chloro-2-fluoro-4-iodobenzene; a colorless solid; mp 61–63 °C; ^{1}H NMR ($CDCl_3$) δ 7.30 (1H, dd, ^3J = 8.6 Hz, $^4J_{FH}$ = 7.4 Hz), 7.75 (1H, dd, ^3J = 8.6 Hz, $^5J_{FH}$ = 1.8 Hz), 10.1 (1H, d, ^5J = 0.4 Hz, CHO); ^{13}C{^{1}H} NMR ($CDCl_3$) δ 94.0 (s, C-I), 123.4 (d, $^2J_{FC}$ = 18.5 Hz), 125.3 (d, $^2J_{FC}$ = 8.7 Hz), 135.9 (s), 137.2 (d, J_{FC} = 5.0 Hz), 158.7 (d, $^1J_{FC}$ = 265.8 Hz), 189.7 (d, $^3J_{FC}$ = 3.7 Hz, CHO). Found: *m*/*z* 284.8974. Calcd for $C_7H_4{}^{35}ClFIO$: $(M+H)^+$, 284.8974.

Typical Procedure for the Preparation of Products 6b–g. 2-(1-Adamantylsulfanyl)-6-bromo-3-chlorobenzaldehyde (6b). NaH (0.3687 g, *ca*. 60% in mineral oil, *ca*. 9.2 mmol) was washed with hexane under nitrogen atmosphere. 1-Adamantanethiol (1.5670 g, 9.218 mmol) in DMF (15 mL) was slowly added to the NaH at 0 °C and the reaction mixture was stirred at 0 °C for 15 min. After cooling the mixture to –40 °C, **1b** (1.9756 g, 8.320 mmol) in THF (8 mL) was added and the resulting mixture was stirred at –40 °C for 6 h then warmed to room temperature. The solution was poured into a saturated aqueous NaCl solution (brine), then worked up with a hexane-AcOEt (4:1) solution. The organic phase was separated, dried over Na_2SO_4, and the solvent was removed under reduced pressure. Silica gel column chromatographic treatment of the residue (hexane-$CHCl_3$ 7:3) afforded **6b** (2.7929 g, 7.240 mmol, 87% yield); a pale yellow solid; mp 97–99 °C; ^{1}H NMR ($CDCl_3$) δ 1.25–1.66 (6H, m, Ad), 1.86–1.87 (6H, m, Ad), 2.02 (3H, s, Ad), 7.51 (1H, d, ^3J = 8.8 Hz), 7.63 (1H, d, ^3J = 8.8 Hz), 10.46 (1H, s, CHO); ^{13}C{^{1}H} NMR ($CDCl_3$) δ 30.3 (Ad), 35.9 (Ad), 44.1 (Ad), 54.9 (Ad), 118.8 (C-Br), 133.2, 133.8, 135.9, 142.7, 143.2, 192.2 (CHO). Found: *m*/*z* 406.9842. Calcd for $C_{17}H_{18}{}^{79}Br{}^{35}ClNaOS$: $(M+Na)^+$, 406.9843. Anal. Calcd for $C_{17}H_{18}BrClOS$: C, 52.93; H, 4.70; Br, 20.71; Cl, 9.19; S, 8.31%. Found: C, 52.83; H, 4.73; Br, 20.78; Cl, 9.15; S, 8.23%.

2-(1-Adamantylsulfanyl)-6-bromo-3-iodobenzaldehyde (6c): Reaction with AdSNa at –40 °C; 64% yield; a pale yellow solid; mp 148–150 °C; ^{1}H NMR ($CDCl_3$) δ 1.58–1.66 (6H, m, Ad), 1.88 (6H, br s, Ad), 2.02 (3H, s, Ad), 7.39 (1H, dd, ^3J = 8.4 Hz and ^5J = 0.8 Hz), 7.98 (1H, d, ^3J = 8.4 Hz), 10.32 (1H, d,

^5J = 0.8 Hz, CHO); $^{13}C\{^1H\}$ NMR ($CDCl_3$) δ 30.6 (Ad), 36.0 (Ad), 44.4 (Ad), 55.9 (Ad), 115.1 (C-I), 121.3 (C-Br), 136.4, 140.3, 142.7, 143.2, 192.9 (CHO). Found: *m*/*z* 498.9199. Calcd for $C_{17}H_{18}{}^{79}BrINaOS$: $(M+Na)^+$, 498.9204. Anal. Calcd for $C_{17}H_{18}BrIOS$: C, 42.79; H, 3.80; Br, 16.74; I, 26.59; S, 6.72%. Found: C, 42.86; H, 3.76; Br, 16.93; I, 26.68; S, 6.66%.

2-(1-Adamantylsulfanyl)-3-bromo-6-chlorobenzaldehyde (6d): Reaction with AdSNa at –78 °C; 91% yield; a yellow-green solid; mp 108–109 °C; ^1H NMR ($CDCl_3$) δ 1.62 (6H, m, Ad), 1.88 (6H, m, Ad), 2.03 (3H, m, Ad), 7.35 (1H, m), 7.79 (1H, d, ^3J = 8.8 Hz), 10.5 (1H, s, CHO); $^{13}C\{^1H\}$ NMR ($CDCl_3$) δ 30.2 (Ad), 35.7 (Ad), 44.0 (Ad), 55.0 (Ad), 131.9, 132.8 (CH), 133.7, 135.8, 136.3 (CH), 141.5, 191.7 (CHO). Found: *m*/*z* 406.9842. Calcd for $C_{17}H_{18}{}^{79}Br{}^{35}ClNaOS$: $(M+Na)^+$, 406.9843.

2-(1-Adamantylsulfanyl)-6-chloro-3-iodobenzaldehyde (6e): Reaction with AdSNa at –63 °C; 89% yield; a colorless solid; mp 150–153 °C; ^1H NMR ($CDCl_3$) δ 1.62 (6H, m, Ad), 1.88 (6H, m, Ad), 2.02 (3H, s, Ad), 7.20 (1H, d, ^3J = 8.3 Hz, ^5J = 0.5 Hz), 8.07 (1H, d, ^3J = 8.3 Hz), 10.42 (1H, d, ^5J = 0.5 Hz, CHO); $^{13}C\{^1H\}$ NMR ($CDCl_3$) δ 30.6 (Ad), 36.0 (Ad), 44.4 (Ad), 56.8 (Ad), 114.0 (C-I), 133.2, 133.6, 140.3, 141.1, 143.1, 192.4 (CHO). Found: *m*/*z* 432.9884. Calcd for $C_{17}H_{19}{}^{35}ClIOS$: $(M+H)^+$, 432.9884.

2-(1-Adamantylsulfanyl)-3-chloro-6-iodobenzaldehyde (6f): Reaction with AdSNa at –63 °C; 84% yield; a pale yellow solid; mp 124–126 °C; ^1H NMR ($CDCl_3$) δ 1.62 (6H, m, Ad), 1.85 (6H, m, Ad), 2.02 (3H, s, Ad), 7.35 (1H, d, ^3J = 8.6 Hz), 7.95 (1H, d, ^3J = 8.6 Hz, ^5J = 0.8 Hz), 10.36 (1H, d, ^5J = 0.6 Hz, CHO); $^{13}C\{^1H\}$ NMR ($CDCl_3$) δ 30.5 (Ad), 36.0 (Ad), 44.1 (Ad), 54.9 (Ad), 90.5 (C-I), 133.8, 134.2, 143.0, 144.1, 145.2, 193.4 (CHO). Found: *m*/*z* 432.9884. Calcd for $C_{17}H_{19}{}^{35}ClIOS$: $(M+H)^+$, 432.9884.

2-(1-Adamantylsulfanyl)-3-bromo-6-iodobenzaldehyde (6g): Reaction with AdSNa at –15 °C; 96% yield; a pale yellow solid; mp 89–91 °C; ^1H NMR ($CDCl_3$) δ 1.62 (6H, m, Ad), 1.86 (6H, s, Ad), 2.02 (3H, s, Ad), 7.53 (1H, d, ^3J = 8.4 Hz), 7.86 (1H, dd, ^3J = 8.4 Hz and ^5J = 0.4 Hz), 10.31 (1H, d, ^5J = 0.4 Hz, CHO); $^{13}C\{^1H\}$ NMR ($CDCl_3$) δ 30.5 (Ad), 36.0 (Ad), 44.2 (Ad), 55.2 (Ad), 77.4 (C-I), 91.5 (C-Br), 136.4, 137.1, 143.2, 145.4, 193.5 (CHO). Found: *m*/*z* 498.9198. Calcd for $C_{17}H_{18}{}^{79}BrINaOS$: $(M+Na)^+$, 498.9204. Anal. Calcd for $C_{17}H_{18}BrIOS$: C, 42.79; H, 3.80; Br, 16.74; I, 26.59; S, 6.72%. Found: C, 42.87; H, 3.70; Br, 16.85; I, 26.34; S, 6.60%.

Typical Procedure for the Preparation of Products 7b–g. 2-(1-Adamantylsulfanyl)-4-bromo-1-chloro-3-(2,2-dibromoethenyl)benzene (7b). A solution of PPh_3 (2.5328 g, 9.656 mmol) in CH_2Cl_2 (11 mL) was slowly added to a mixture of **6b** (1.5063 g, 3.905 mmol) and CBr_4 (1.5610 g, 4.707 mmol) in CH_2Cl_2 (9 mL) at 0 °C under nitrogen atmosphere. During stirring for 10 min at 0 °C, the color of the mixture changed yellow to brown. The mixture was stirred at room temperature for 2 h and 20 mL of water was added. The resulting mixture was extracted with CH_2Cl_2, the organic phase was washed with brine, and dried over Na_2SO_4. The solvent was removed under reduced pressure, and the residue was

treated with silica gel column chromatography (hexane-$CHCl_3$ 4:1) to give 1.9056 g (3.519 mmol, 90% yield) of **7b**; a colorless solid; mp 108–110 °C; ^{1}H NMR ($CDCl_3$) δ 1.65–1.66 (6H, m, Ad), 1.90–1.96 (6H, m, Ad), 2.03 (3H, s, Ad), 7.38 (1H, d, ^3J = 8.4 Hz), 7.49 (1H, s, CH=CBr_2), 7.54 (1H, d, ^3J = 8.4 Hz); ^{13}C{^{1}H} NMR ($CDCl_3$) δ 30.5 (Ad), 36.2 (Ad), 44.5 (Ad), 54.3 (Ad), 96.2 (CBr_2), 121.5 (C-Br), 130.8, 132.3, 134.4, 138.1, 142.6, 145.9; Found: *m*/*z* 560.8260. Calcd for $C_{18}H_{18}{}^{79}Br_3{}^{35}ClNaS$: $(M+Na)^+$, 560.8260. Anal. Calcd for $C_{18}H_{18}Br_3ClS$: C, 39.92; H, 3.35; Br, 44.26; Cl, 6.55; S, 5.92%. Found: C, 40.01; H, 3.36; Br, 44.07; Cl, 6.39; S, 5.83%.

2-(1-Adamantylsulfanyl)-4-bromo-3-(2,2-dibromoethenyl)-1-iodobenzene (7c): 86% yield; a colorless solid; mp 137–138 °C; ^{1}H NMR ($CDCl_3$) δ = 1.66 (6H, s, Ad), 1.96–2.04 (9H, m, Ad), 7.26 (1H, dd, ^3J = 8.8 Hz), 7.54 (1H, br s, CH=CBr_2), 7.83 (1H, d, ^3J = 8.8 Hz); ^{13}C{^{1}H} NMR ($CDCl_3$) δ 30.7 (Ad), 36.2 (Ad), 44.8 (Ad), 55.0 (Ad), 96.3, 114.3, 123.8, 134.8, 138.7, 139.1, 140.6, 144.5. Found: *m*/*z* 654.7596. Calcd for $C_{18}H_{18}{}^{79}Br_2{}^{81}BrINaS$: $(M+Na)^+$, 654.7595. Anal. Calcd for $C_{18}H_{18}Br_3IS$: C, 34.15; H, 2.87; Br, 37.87; I, 20.05; S, 5.06%. Found: C, 34.25; H, 2.87; Br, 38.11; I, 19.89; S, 5.05%.

2-(1-Adamantylsulfanyl)-1-bromo-4-chloro-3-(2,2-dibromoethenyl)benzene (7d): 93% yield; a colorless solid; mp 136–137 °C; ^{1}H NMR (CD_2Cl_2) δ 1.63–1.70 (6H, m, Ad), 1.96 (6H, m, Ad), 2.03 (3H, m, Ad), 7.30 (1H, d, ^3J = 8.4 Hz), 7.58 (1H, s, CH=CBr_2), 7.68 (1H, d, ^3J = 8.4 Hz); ^{13}C{^{1}H} NMR ($CDCl_3$) δ 30.6 (Ad), 36.2 (Ad), 44.6 (Ad), 54.4 (Ad), 96.1 (C=*C*Br_2), 131.5, 132.9, 133.6, 133.8, 134.4, 136.5, 143.8. Found: *m*/*z* 560.8260. Calcd for $C_{18}H_{18}{}^{79}Br_3{}^{35}ClNaS$: $(M+Na)^+$, 560.8260.

2-(1-Adamantylsulfanyl)-4-chloro-3-(2,2-dibromoethenyl)-1-iodobenzene (7e): 86% yield; a colorless solid; mp 152–153 °C; ^{1}H NMR ($CDCl_3$) δ 1.67 (6H, m, Ad), 1.99 (6H, m, Ad), 2.05 (3H, s, Ad), 7.10 (1H, d, ^3J = 8.4 Hz), 7.58 (1H, s, CH=CBr_2), 7.92 (1H, d, ^3J = 8.4 Hz); ^{13}C{^{1}H} NMR ($CDCl_3$) δ 30.7 (Ad), 36.2 (Ad), 44.8 (Ad), 54.9 (Ad), 96.2 (C-I), 113.3, 131.7, 134.2, 137.2, 138.6, 140.3, 142.6. Found: *m*/*z* 588.8280. Calcd for $C_{18}H_{19}{}^{79}Br^{81}Br^{35}ClIS$: $(M+H)^+$, 588.8280.

2-(1-Adamantylsulfanyl)-1-chloro-3-(2,2-dibromoethenyl)-4-iodobenzene (7f): 92% yield; a colorless solid; mp 130–132 °C; ^{1}H NMR ($CDCl_3$) δ 1.65 (6H, m, Ad), 1.92 (6H, m, Ad), 2.03 (3H, s, Ad), 7.22 (1H, d, ^3J = 8.6 Hz), 7.48 (1H, s, CH=CBr_2), 7.78 (1H, d, ^3J = 8.6 Hz); ^{13}C{^{1}H} NMR ($CDCl_3$) δ 30.5 (Ad), 36.2 (Ad), 44.4 (Ad), 54.3 (Ad), 95.9, 96.7, 131.1, 131.6, 140.6, 141.7, 143.8, 149.7. Found: *m*/*z* 588.8280. Calcd for $C_{18}H_{19}{}^{79}Br^{81}Br^{35}ClIS$: $(M+H)^+$, 588.8280.

2-(1-Adamantylsulfanyl)-1-bromo-3-(2,2-dibromoethenyl)-4-iodobenzene (7g): 93% yield; a colorless solid; mp 142–144 °C; ^{1}H NMR ($CDCl_3$) δ 1.66 (6H, s, Ad), 1.90–2.03 (9H, m, Ad), 7.39 (1H, dd, ^3J = 8.4 Hz, ^5J = 0.4 Hz), 7.50 (1H, br s, CH=CBr_2), 7.68 (1H, d, ^3J = 8.4 Hz); ^{13}C{^{1}H} NMR ($CDCl_3$) δ 30.5 (Ad), 36.1 (Ad), 44.5 (Ad), 54.4 (Ad), 96.7, 96.9, 133.6, 134.4, 135.8, 140.7, 141.9, 149.5. Found: *m*/*z* 654.7596. Calcd for $C_{18}H_{18}{}^{79}Br_2{}^{81}BrINaS$: $(M+Na)^+$, 654.7595. Anal. Calcd for $C_{18}H_{18}Br_3IS$:

C, 34.15; H, 2.87; Br, 37.87; I, 20.05; S, 5.06%. Found: C, 34.06; H, 2.83; Br, 37.78; I, 19.83; S, 4.99%.

Typical Procedure for the Preparation of Products 8b,e,f. 2-(1-Adamantylsulfanyl)-4-bromo-3-(2-bromoethynyl)-1-chlorobenzene (8b): A solution of KOH (1.3 g) in water (4.4 mL) was added to a solution of **7b** (733.3 mg, 1.354 mmol) in THF (44 mL) and the resulting mixture was stirred at room temperature for 40 h in air. Brine was added to this mixture and the resulting mixture was extracted with AcOEt. The organic phase was separated, dried over Na_2SO_4, and the solvent was removed under reduced pressure. ^{1}H NMR spectroscopy of the residue (610.4 mg, 1.325 mmol) indicated nearly quantitative formation of **8b**; 98% yield; a pale yellow solid; mp 100–103 °C; ^{1}H NMR ($CDCl_3$) δ 1.65–1.66 (6H, m, Ad), 1.98 (6H, m, Ad), 2.04 (3H, m, Ad), 7.32 (1H, d, ^3J = 8.4 Hz), 7.50 (1H, d, ^3J = 8.4 Hz); ^{13}C{^{1}H} NMR ($CDCl_3$) δ 30.5 (Ad), 36.2 (Ad), 44.4 (Ad), 54.9 (Ad), 60.7 (C≡C), 79.8 (C≡C), 125.0, 130.4, 133.7, 134.7, 135.5, 142.1. Found: *m*/*z* 480.89982. Calcd for $C_{18}H_{17}{}^{79}Br_2{}^{35}ClNaS$: $(M+Na)^+$, 480.89985. Anal. Calcd for $C_{18}H_{17}Br_2ClS$: C, 46.93; H, 3.72; Br, 34.74; Cl, 7.70; S, 6.87%. Found: C, 47.07; H, 3.92; Br, 34.74; Cl, 7.51; S, 6.87%.

2-(1-Adamantylsulfanyl)-3-(2-bromoethynyl)-4-chloro-1-iodobenzene (8e): 91% yield after alumina column chromatography; a colorless solid; mp 145–148 °C; ^{1}H NMR ($CDCl_3$) δ 1.66 (6H, m, Ad), 2.04 (9H, m, Ad), 7.06 (1H, d, ^3J = 8.8 Hz), 7.85 (1H, d, ^3J = 8.8 Hz); ^{13}C{^{1}H} NMR ($CDCl_3$) δ 30.7 (Ad), 36.2 (Ad), 44.7 (Ad), 55.8 (Ad), 61.0 (C≡C), 78.7 (C≡C), 111.9 (C-I), 130.7, 130.8, 138.1, 139.7, 141.8. Found: *m*/*z* 508.9019. Calcd for $C_{18}H_{18}{}^{81}Br^{35}ClIS$: $(M+H)^+$, 508.9019.

2-(1-Adamantylsulfanyl)-3-(2-bromoethynyl)-1-chloro-4-iodobenzene (8f): 99% yield after alumina column chromatography; a colorless solid; mp 99–104 °C (decomp); ^{1}H NMR ($CDCl_3$) δ 1.65 (6H, m, Ad), 1.98 (6H, m, Ad), 2.03 (3H, s, Ad), 7.16 (1H, d, ^3J = 8.4 Hz), 7.73 (1H, d, ^3J = 8.4 Hz); ^{13}C{^{1}H} NMR ($CDCl_3$) δ 30.4 (Ad), 36.1 (Ad), 44.3 (Ad), 54.8 (Ad), 59.8 (C≡C), 83.4 (C≡C), 99.3 (C-I), 130.6, 134.6, 138.8, 139.9, 143.1. Found: *m*/*z* 508.9019. $C_{18}H_{18}{}^{81}Br^{35}ClIS$: $(M+H)^+$, 508.9019.

Typical Procedure for the Preparation of Products 9b–g. 2-(1-Adamantylsulfanyl)-4-bromo-1-chloro-3-(ethynyl)benzene (9b). A solution of KOH (7.7 g) in water (40 mL) was added to a solution of **7b** (3.1231 g, 5.767 mmol) in acetone (405 mL). The resulting mixture was vigorously stirred at room temperature for 3 h. Brine was added, and the reaction mixture was extracted with hexane-AcOEt (4:1). The organic phase was washed with brine, dried over Na_2SO_4, and the solvent was removed under reduced pressure. The residue was treated with silica gel column chromatography (hexane-$CHCl_3$ 4:1) to give 1.8917 g (4.955 mmol, 86% yield) of **9b**; a pale yellow solid; mp 87–89 °C; ^{1}H NMR ($CDCl_3$) δ 1.64 (6H, s, Ad), 2.01 (9H, m, Ad), 3.67 (1H, s, C≡CH), 7.34 (1H, d, ^3J = 8.4 Hz), 7.53 (1H, d, ^3J = 8.4 Hz); ^{13}C{^{1}H} NMR ($CDCl_3$) δ 30.5 (Ad), 36.2 (Ad), 44.4 (Ad), 55.4 (Ad), 82.6 (C≡C), 87.5 (C≡C), 125.1, 130.6, 133.8, 134.2, 135.3, 142.2. Found: *m*/*z* 402.9893. Calcd for

$C_{18}H_{18}{}^{79}Br^{35}ClNaS$: $(M+Na)^+$, 402.9893. Anal. Calcd for $C_{18}H_{18}BrClS$: C, 56.63; H, 4.75; Br, 20.93; Cl, 9.29; S, 8.40%. Found: C, 56.66; H, 4.75; Br, 21.01; Cl, 9.26; S, 8.40%.

2-(1-Adamantylsulfanyl)-4-bromo-3-(ethynyl)-1-iodobenzene (9c): 77% yield based on **7c**; a pale yellow solid; mp 188–190 °C (decomp); ^{1}H NMR ($CDCl_3$) δ 1.65 (6H, s, Ad), 2.06 (9H, m, Ad), 3.63 (1H, s, C≡CH), 7.25 (1H, d, ^3J = 8.8 Hz), 7.80 (1H, d, ^3J = 8.8 Hz); ^{13}C{^{1}H} NMR ($CDCl_3$) δ 30.6 (Ad), 36.2 (Ad), 44.7 (Ad), 56.3 (Ad), 83.5 (C≡CH), 87.0 (C≡CH), 113.0, 127.4, 132.4, 133.9, 140.2, 141.6. Found: *m*/*z* 494.9250. Calcd for $C_{18}H_{18}{}^{79}BrINaS$: $(M+Na)^+$, 494.9250. Anal. Calcd for $C_{18}H_{18}BrIS$: C, 45.69; H, 3.83; Br, 16.89; I, 26.82; S, 6.77%. Found: C, 45.65; H, 3.86; Br, 16.90; I, 26.63; S, 6.74%.

2-(1-Adamantylsulfanyl)-1-bromo-4-chloro-3-(ethynyl)benzene (9d): 87% yield based on **7d**; a colorless solid; mp 90–91 °C; ^{1}H NMR (CD_2Cl_2) δ 1.65 (6H, m, Ad), 2.02 (9H, m, Ad), 3.71 (1H, s, C≡CH), 7.29 (1H, d, ^3J = 8.4 Hz), 7.63 (1H, d, ^3J = 8.4 Hz); ^{13}C{^{1}H} NMR ($CDCl_3$) δ 30.0 (Ad), 35.7 (Ad), 44.0 (Ad), 54.9 (Ad), 80.4 (C≡C), 87.9 (C≡C), 130.1 (CH), 131.4, 132.5, 133.0, 136.2, 136.8. Found: *m*/*z* 402.9893. Calcd for $C_{18}H_{18}{}^{79}Br^{35}ClNaS$: $(M+Na)^+$, 402.9893.

2-(1-Adamantylsulfanyl)-4-chloro-3-(ethynyl)-1-iodobenzene (9e): 96% yield based on **7e**; a colorless solid; mp 167–170 °C; ^{1}H NMR ($CDCl_3$) δ 1.65 (6H, m, Ad), 2.06 (9H, m, Ad), 3.64 (1H, s, C≡CH), 7.09 (1H, d, ^3J = 8.4 Hz), 7.88 (1H, d, ^3J = 8.4 Hz); ^{13}C{^{1}H} NMR ($CDCl_3$) δ 30.6 (Ad), 36.0 (Ad), 44.7 (Ad), 56.2 (Ad), 81.5 (C≡C), 87.7 (C≡C), 112.0, 130.4, 130.7, 138.1, 140.0, 141.5. Found: *m*/*z* 428.9935. Calcd for $C_{18}H_{19}{}^{35}ClIS$: $(M+H)^+$, 428.9935.

2-(1-Adamantylsulfanyl)-1-chloro-3-(ethynyl)-4-iodobenzene (9f): 93% yield based on **7f**; a colorless solid; mp 125–128 °C; ^{1}H NMR ($CDCl_3$) δ 1.64 (6H, m, Ad), 2.01 (6H, m, Ad), 2.01 (6H, m, Ad), 2.03 (3H, m, Ad), 3.66 (1H, s, C≡CH), 7.18 (1H, d, ^3J = 8.6 Hz), 7.77 (1H, d, ^3J = 8.6 Hz); ^{13}C{^{1}H} NMR ($CDCl_3$) δ 30.5 (Ad), 36.2 (Ad), 44.4 (Ad), 55.3 (Ad), 86.1, 86.4, 99.6, 130.9, 134.5, 138.4, 140.1, 143.2. Found: *m*/*z* 427.9857. Calcd for $C_{18}H_{18}{}^{35}ClIS$: M^+, 427.9857.

2-(1-Adamantylsulfanyl)-1-bromo-3-(ethynyl)-4-iodobenzene (9g): 99% yield based on **7g**; a pale yellow solid; mp 160–162 °C; ^{1}H NMR ($CDCl_3$) δ 1.66 (6H, s, Ad), 2.05 (9H, m, Ad), 3.67 (1H, s, C≡CH), 7.38 (1H, d, ^3J = 8.4 Hz), 7.68 (1H, d, ^3J = 8.4 Hz); ^{13}C{^{1}H} NMR ($CDCl_3$) δ 30.4 (Ad), 36.1 (Ad), 44.4 (Ad), 55.5 (Ad), 86.2 (C≡CH), 86.4 (C≡CH), 100.5, 134.1, 134.9, 136.5, 138.0, 140.1. Found: *m*/*z* 494.9249. Calcd for $C_{18}H_{18}{}^{79}BrINaS$: $(M+Na)^+$, 494.9250. Anal. Calcd for $C_{18}H_{18}BrIS$: C, 45.69; H, 3.83; Br, 16.89; I, 26.82; S, 6.77%. Found: C, 45.54; H, 3.78; Br, 16.87; I, 26.73; S, 6.53%.

Typical Procedure for the Preparation of Products 10c,g. 2-(1-Adamantylsulfanyl)-4-bromo-3-(2,2-dichloroethenyl)-1-iodobenzene (10c): A mixture of **6c** (501.5 mg, 1.051 mmol) and PPh_3 (1.0831 g, 4.129 mmol) in CCl_4 (15 mL) was heated at 80 °C for 44 h. The reaction mixture was allowed to cool to room temperature and the solvent was removed under reduced pressure. The residue

was treated with silica gel column chromatography (hexane-$CHCl_3$ 4:1) to give 411.2 mg (*ca*. 72% yield) of crude **10c**. Recrystallization from hot EtOH afforded 237.2 mg (*ca*. 41% yield, containing 3 mol% of (*E*)-**14c**, by ^{1}H NMR) of **10c** as a colorless solid. **10c**: ^{1}H NMR ($CDCl_3$) δ 1.66 (6H, s, Ad), 1.97 (6H, s, Ad), 2.04 (3H, s, Ad), 6.98 (1H, br s, CH=CCl_2), 7.27 (1H, d, ^3J = 8.4 Hz), 7.82 (1H, dd, ^3J = 8.4 Hz, ^5J = 0.8 Hz); ^{13}C{^{1}H} NMR ($CDCl_3$) δ 30.7 (Ad), 36.2 (Ad), 44.8 (Ad), 54.9 (Ad), 114.2, 124.4, 125.6, 130.8, 134.7, 139.2, 140.6, 142.3. Found: *m*/*z* 564.8626. Calcd for $C_{18}H_{18}{}^{79}Br^{35}Cl_2IS$: M^+, 564.8626.

2-(1-Adamantylsulfanyl)-1-bromo-3-(2,2-dichloroethenyl)-4-iodobenzene (10g): A crude product (*ca*. 83% yield) was recrystallized from hot EtOH to give **10g** (containing 5 mol% of (*E*)-**14g**) in *ca*. 46% yield. **10g**: ^{1}H NMR ($CDCl_3$) δ 1.65 (6H, m, Ad), 1.93 (6H, m, Ad), 2.03 (3H, s, Ad), 6.95 (1H, br s, CH=CCl_2), 7.38 (1H, dd, ^3J = 8.4 Hz, ^5J = 0.8 Hz), 7.68 (1H, d, ^3J = 8.4 Hz); ^{13}C{^{1}H} NMR ($CDCl_3$) δ 30.6 (Ad), 36.2 (Ad), 44.5 (Ad), 54.5 (Ad), 97.5, 125.8, 133.8 (*C*H=CCl_2), 134.2, 134.5, 135.7, 140.8, 147.4. Found: *m*/*z* 564.8627. Calcd for $C_{18}H_{18}{}^{79}Br^{35}Cl_2INaS$: $(M+Na)^+$, 564.8626.

(*E*)-**14g**: ^{1}H NMR ($CDCl_3$) δ 1.6–2.1 (15H, Ad), 6.41 (1H, d, ^3J = 14.0 Hz), 7.00 (1H, d, ^3J = 14.0 Hz), 7.31 (1H, d, ^3J = 8.4 Hz), 7.69 (1H, d, ^3J = 8.4 Hz).

Typical Procedure for the Preparation of Products 11c,g. 2-(1-Adamantylsulfanyl)-4-bromo-3-(chloroethynyl)-1-iodobenzene (11c): A mixture of **6c** (955.3 mg, 2.002 mmol), $CBrCl_3$ (1.0095 g, 5.092 mmol), and PPh_3 (1.6541 g, 6.306 mmol) in MeCN (100 mL) was heated at 50 °C for 22 h. The reaction mixture was allowed to cool to room temperature and the solvent was removed under reduced pressure. Hexane (hot)-soluble product was collected by decantation and the hexane was evaporated. The residue was treated with silica gel column chromatography (hexane-$CHCl_3$ 9:1) to give a mixture (922.8 mg) containing **10c** (*ca*. 67% yield) and **15c** (*ca*. 16% yield, *E*- and *Z*-forms). The crude mixture (50.8 mg) was dissolved in 2.0 mL of THF and the solution was added to a mixture of *t*-BuOK (50.1 mg, 0.446 mmol) in THF (1 mL) at –78 °C. The reaction mixture was stirred at –78 °C for 1.5 h and quenched with 10 mL of brine, then extracted with AcOEt. The organic phase was separated, dried with Na_2SO_4, and the solvent was removed in vacuo to give 41.8 mg of **11c** (*ca*. 90% yield based on the starting mixture of **10c** and **15c**); a colorless oil; ^{1}H NMR ($CDCl_3$) δ 1.66 (6H, s, Ad), 2.04 (9H, s, Ad), 7.22 (1H, d, ^3J = 8.4 Hz), 7.76 (1H, dd, ^3J = 8.4 Hz); ^{13}C{^{1}H} NMR ($CDCl_3$) δ 30.7 (Ad), 36.2 (Ad), 44.7 (Ad), 55.8 (Ad), 70.2 (C≡C), 87.0 (C≡C), 112.9, 127.3, 132.4, 133.9, 140.0, 141.9. Found: *m*/*z* 528.8860. Calcd for $C_{18}H_{17}{}^{79}Br^{35}ClINaS$: $(M+Na)^+$, 528.8860.

2-(1-Adamantylsulfanyl)-1-bromo-3-(chloroethynyl)-4-iodobenzene (11g): A mixture of **10g** (*ca*. 67% yield) and **15g** (*ca*. 21% yield, *E*- and *Z*-forms) was obtained from **6g**. The mixture was converted to **11g** in *ca*. 99% yield (based on **10g** and **15g**); a colorless oil; ^{1}H NMR ($CDCl_3$) δ 1.65–1.66 (6H, m, Ad), 2.00–2.04 (9H, m, Ad), 7.33 (1H, d, ^3J = 8.4 Hz), 7.63 (1H, d, ^3J = 8.4 Hz); ^{13}C{^{1}H} NMR ($CDCl_3$)

δ 30.6 (Ad), 36.2 (Ad), 44.5 (Ad), 55.2 (Ad), 73.4 (C≡C), 76.9 (C≡C), 100.4, 134.0, 135.0, 134.9, 136.9, 138.2, 140.1. Found: *m*/*z* 528.8860. Calcd for $C_{18}H_{17}{}^{79}BrClINaS$: $(M+Na)^+$, 528.8860.

Typical Procedure for the Preparation of Products 12b,d. 2-(1-Adamantylsulfanyl)-4-bromo-1-chloro-3-(2,2-diiodoethenyl)benzene (12b). A solution of lithium bis(trimethylsilyl)amide (23.8 mmol, 1.3 M solution in THF) was added to THF (90 mL). To the resulting solution was added a solution of I_2 (3.0122 g, 11.868 mmol) in THF (25 mL) at –78 °C. To this mixture was added a solution of diethyl iodomethylphosphonate (3.3203 g, 11.942 mmol) in THF (15 mL) and the resulting solution was stirred at –78 °C for 75 min. This solution was transferred into a THF (30 mL) solution of **6b** (4.1817 g, 10.840 mmol) at –78 °C during a period of 35 min, and the resulting mixture was stirred at that temperature for 3 h. The mixture was then poured into brine and extracted with AcOEt. The organic phase was washed with brine, then with saturated aqueous Na_2SO_3 solution, and dried over $MgSO_4$. The solvent was removed under reduced pressure, and the residue was purified by silica gel column chromatography (hexane-$CHCl_3$ 4:1) to give 4.9157 g (7.734 mmol, 71% yield) of **12b** and 561.4 mg of the starting **6b** (13% recovery). **12b**: a pale yellow solid; mp 113–114 °C; ^{1}H NMR ($CDCl_3$) δ 1.66 (6H, m, Ad), 1.89–1.97 (6H, m, Ad), 2.04 (3H, s, Ad), 7.41 (1H, d, ^3J = 8.8 Hz), 7.54 (1H, d, ^3J = 8.8 Hz), 8.17 (1H, s, CH=CI_2); ^{13}C{^{1}H} NMR ($CDCl_3$) δ 21.9 (C=*C*I_2), 30.5 (Ad), 36.2 (Ad), 44.6 (Ad), 54.4 (Ad), 120.8, 130.7, 131.6, 134.5, 142.8, 150.2, 152.1. Found: *m*/*z* 656.7982. Calcd for $C_{18}H_{18}{}^{79}Br^{35}ClI_2NaS$: $(M+Na)^+$, 656.7983. Anal. Calcd for $C_{18}H_{18}BrClI_2S$: C, 34.02; H, 2.85; Br, 12.57; Cl, 5.58; I, 39.93; S, 5.04%. Found: C, 34.58; H, 3.09; Br, 12.47; Cl, 5.70; I, 39.70; S, 5.06%.

2-(1-Adamantylsulfanyl)-1-bromo-4-chloro-3-(2,2-diiodoethenyl)benzene (12d): 70% yield with 17% recovery of the starting **6d**. **12d**: a pale yellow solid; mp 117–119 °C; ^{1}H NMR ($CDCl_3$) δ 1.67 (6H, m, Ad), 1.93–2.05 (9H, m, Ad), 7.27 (1H, d, ^3J = 8.2 Hz), 7.67 (1H, d, ^3J = 8.2 Hz), 8.24 (1H, s, CH=CI_2); ^{13}C{^{1}H} NMR ($CDCl_3$) δ 21.7 (CH=*C*I_2), 30.5 (Ad), 36.0 (Ad), 44.5 (Ad), 54.4 (Ad), 131.4, 132.0, 133.49, 133.51, 133.7, 147.9, 150.3 (*C*H=CI_2). Found: *m*/*z* 656.7983. Calcd for $C_{18}H_{18}{}^{79}Br^{35}ClI_2NaS$: $(M+Na)^+$, 656.7983.

Typical Procedure for the Preparation of Products 13b,d. 2-(1-Adamantylsulfanyl)-4-bromo-1-chloro-3-(2-iodoethynyl)benzene (13b). A solution of **12b** (512.5 mg, 0.806 mmol) in THF (5 mL) was slowly added to a mixture of *t*-BuOK (450.0 mg, 4.010 mmol) in THF (3 mL) at –78 °C under nitrogen atmosphere and the resulting mixture was stirred for 30 min. Brine was added to this mixture and the resulting mixture was extracted with AcOEt. The organic layer was washed with brine, then with saturated aqueous Na_2SO_3 solution, separated, dried over Na_2SO_4, and the solvent was removed under reduced pressure to give 387.2 mg (0.763 mmol) of **13b** in 95% yield; a colorless solid; mp 138–140 °C; ^{1}H NMR ($CDCl_3$) δ 1.65–1.66 (6H, m, Ad), 1.98–1.99 (6H, m, Ad), 2.04 (3H, m, Ad), 7.30

(1H, d, ^3J = 8.4 Hz), 7.50 (1H, d, ^3J = 8.4 Hz); $^{13}C\{^1H\}$ NMR ($CDCl_3$) δ 19.0 (C≡*C*I), 30.6 (Ad), 36.3 (Ad), 44.5 (Ad), 55.0 (Ad), 93.6 (*C*≡CI), 125.5, 130.4, 133.6, 135.2, 135.9, 142.0. Found: *m*/*z* 528.8860. Calcd for $C_{18}H_{17}BrClINaS$: $(M+Na)^+$, 528.8860. Anal. Calcd for $C_{18}H_{17}{}^{79}Br^{35}ClIS$: C, 42.59; H, 3.38; Br, 15.74; Cl, 6.98; I, 25.00; S, 6.32%. Found: C, 42.73; H, 3.37; Br, 15.79; Cl, 7.09; I, 25.02; S, 6.31%.

2-(1-Adamantylsulfanyl)-1-bromo-4-chloro-3-(iodoethynyl)benzene (13d): 95% yield; a colorless solid; mp 135–137 °C; ^1H NMR ($CDCl_3$) δ 1.66 (6H, m, Ad), 2.02–2.04 (9H, m, Ad), 7.24 (1H, d, ^3J = 8.4 Hz), 7.56 (1H, d, ^3J = 8.4 Hz); $^{13}C\{^1H\}$ NMR ($CDCl_3$) δ 19.5 (C≡*C*I), 30.6 (Ad), 36.3 (Ad), 44.6 (Ad), 55.3 (Ad), 91.9 (*C*≡CI), 130.6, 132.7, 132.9, 133.4, 137.2, 137.9. Found: *m*/*z* 528.8860. Calcd for $C_{18}H_{17}{}^{79}Br^{35}ClINaS$: $(M+Na)^+$, 528.8860.

Typical Procedure for the Preparation of Products 4b–g. 4-Bromo-7-chlorobenzo[*b*]thiophene (4b). A mixture of **9b** (1.8864 g, 4.941 mmol), silica gel 60N (13.0842 g), and toluene (65 mL) was heated at 90 °C for 13 h under nitrogen atmosphere. The reaction mixture was allowed to cool down to room temperature and the silica gel was removed by filtration. The silica gel was washed with 55 mL of $CHCl_3$ and a combined filtrate was evaporated under reduced pressure. Silica gel column chromatographic treatment (hexane) of the residue afforded 1.0919 g (4.411 mmol) of **4b** in 89% yield; a colorless solid; mp 77–79 °C; ^1H NMR ($CDCl_3$) δ 7.22 (1H, d, ^3J = 8.4 Hz), 7.50 (1H, d, ^3J = 8.4 Hz), 7.51 (1H, d, ^3J = 5.6 Hz), 7.58 (1H, d, ^3J = 5.6 Hz); $^{13}C\{^1H\}$ NMR ($CDCl_3$) δ 115.6 (C-Br), 124.8, 125.3, 127.3, 128.4, 128.6, 139.8, 140.5. Found: *m*/*z* 245.8901. Calcd for $C_8H_4{}^{79}Br^{35}ClS$: M^+, 245.8900. Anal. Calcd for C_8H_4BrClS: C, 38.82; H, 1.63; Br, 32.28; Cl, 14.32; S, 12.95%. Found: C, 38.88; H, 1.73; Br, 32.39; Cl, 14.27; S, 12.94%.

4-Bromo-7-iodobenzo[*b*]thiophene (4c):[10b] 98% yield.

7-Bromo-4-chlorobenzo[*b*]thiophene (4d): 97% yield; a colorless solid; mp 57 °C (sublime); ^1H NMR ($CDCl_3$) δ 7.26 (1H, d, ^3J = 8.0 Hz), 7.42 (1H, d, ^3J = 8.0 Hz), 7.57 (1H, d, ^3J = 5.6 Hz), 7.60 (1H, d, ^3J = 5.6 Hz); $^{13}C\{^1H\}$ NMR ($CDCl_3$) δ 113.9, 123.1, 125.2, 127.4, 127.8, 128.1, 138.2, 142.3. Found: *m*/*z* 245.8900. Calcd for $C_8H_4{}^{79}Br^{35}ClS$: 245.8900.

4-Chloro-7-iodobenzo[*b*]thiophene (4e): 66% yield; a colorless solid; mp 55–57 °C; ^1H NMR ($CDCl_3$) δ 7.10 (1H, d, ^3J = 8.0 Hz), 7.57 (1H+1H, m), 7.73 (1H, d, ^3J = 5.6 Hz); $^{13}C\{^1H\}$ NMR ($CDCl_3$) δ 84.9 (C-I), 124.0, 125.6, 127.8, 129.4, 134.3, 134.3, 137.4, 147.5. Found: *m*/*z* 293.8761. Calcd for $C_8H_4{}^{35}ClIS$: M^+, 293.8761.

7-Chloro-4-iodobenzo[*b*]thiophene (4f): 79% yield based on **7f** (2 steps); a colorless solid; mp 58–59 °C; ^1H NMR ($CDCl_3$) δ 7.06 (1H, d, ^3J = 8.0 Hz), 7.41 (1H, d, ^3J = 5.6 Hz), 7.55 (1H, d, ^3J = 5.6 Hz), 7.69 (1H, d, ^3J = 8.0 Hz); $^{13}C\{^1H\}$ NMR ($CDCl_3$) δ 87.7 (C-I), 125.1, 128.0, 128.6, 128.9, 135.2, 138.5, 143.8. Found: *m*/*z* 293.8761. Calcd for $C_8H_4{}^{35}ClINaS$: M^+, 293.8761.

7-Bromo-4-iodobenzo[*b*]thiophene (4g): 93% yield; a colorless solid; mp 78–79 °C; ^{1}H NMR ($CDCl_3$) δ 7.22 (1H, d, ^3J = 8.4 Hz), 7.50 (1H, d, ^3J = 5.2 Hz), 7.58 (1H, d, ^3J = 5.2 Hz), 7.65 (1H, d, ^3J = 8.4 Hz); ^{13}C{^{1}H} NMR ($CDCl_3$) δ 88.6 (C-I), 116.3, 127.8, 128.2, 129.0, 135.2, 140.9, 143.3. Found: *m*/*z* 337.8257. Calcd for $C_8H_4{}^{79}BrIS$: M^+, 337.8256. Anal. Calcd for C_8H_4BrIS: C, 28.35; H, 1.19; Br, 23.57; I, 37.44; S, 9.46%. Found: C, 28.51; H, 1.26; Br, 23.31; I, 37.44; S, 9.42%.

Typical Procedure for the Preparation of Products 5b–h. 4-Bromo-7-chloro-2-iodobenzo[*b*]thiophene (5b). A mixture of **13b** (149.5 mg, 0.295 mmol), silica gel (1.1098 g), and toluene (5.5 mL) was heated at 90 °C for 19 h under nitrogen atmosphere. The reaction mixture was allowed to cool down to room temperature and the silica gel was removed by filtration. The silica gel was washed with 20 mL of AcOEt and a combined filtrate was washed with saturated aqueous Na_2SO_3 solution and dried over Na_2SO_4. Silica gel column chromatographic treatment (hexane) of the residue afforded 82.3 mg (0.220 mmol) of **5b** in 75% yield; a colorless solid; mp 136–137 °C; ^{1}H NMR ($CDCl_3$) δ 7.15 (1H, d, ^3J = 8.4 Hz), 7.43 (1H, d, ^3J = 8.4 Hz), 7.70 (1H, s); ^{13}C{^{1}H} NMR ($CDCl_3$) δ 81.1 (C-I), 113.8, 125.0, 125.8, 128.9, 135.0, 141.6, 144.2. Found: *m*/*z* 371.7867. Calcd for $C_8H_3{}^{79}Br{}^{35}ClIS$: M^+, 371.7867. Anal. Calcd for $C_8H_3BrClIS$: C, 25.73; H, 0.81; Br, 21.40; Cl, 9.49; I, 33.98; S, 8.59%. Found: C, 29.19; H, 0.91; Br, 21.48; Cl, 9.47; I; 33.97; S, 8.67%.

4-Bromo-2-chloro-7-iodobenzo[*b*]thiophene (5c): 89% yield based on **11c**; a colorless solid; mp 126–128 °C; ^{1}H NMR ($CDCl_3$) δ 7.24 (1H, d, ^3J = 8.4 Hz), 7.47 (1H, d, ^3J = 8.4 Hz), 7.54 (1H, s); ^{13}C{^{1}H} NMR ($CDCl_3$) δ 84.7 (C-I), 116.8, 124.8, 129.4, 133.6, 134.6, 138.2, 145.8. Found: *m*/*z* 371.7866. Calcd for $C_8H_3{}^{79}Br{}^{35}ClIS$: M^+, 371.7867. Anal. Calcd for $C_8H_3BrClIS$: C, 25.73; H, 0.81; Br, 21.40; Cl, 9.49; I, 33.98; S, 8.59%. Found: C, 25.85; H, 0.84; Br, 21.67; Cl, 9.42; I, 33.72; S, 8.57%.

7-Bromo-4-chloro-2-iodobenzo[*b*]thiophene (5d): 80% yield based on **13d**; a colorless solid; mp 132–134 °C; ^{1}H NMR ($CDCl_3$) δ 7.20 (1H, d, ^3J = 8.0 Hz), 7.35 (1H, d, ^3J = 8.0 Hz), 7.78 (1H, s); ^{13}C{^{1}H} NMR ($CDCl_3$) δ 81.1 (C-I), 112.4 (C-Br), 125.9, 126.5, 127.8, 133.2, 139.6, 147.1. Found: *m*/*z* 371.7866. $C_8H_3{}^{79}Br{}^{35}ClIS$: M^+, 371.7867.

2-Bromo-4-chloro-7-iodobenzo[*b*]thiophene (5e): 90% yield based on **7e** (2 steps); a colorless solid; mp 123–124 °C; ^{1}H NMR ($CDCl_3$) δ 7.08 (1H, d, ^3J = 8.0 Hz), 7.54 (1H, d, ^3J = 8.0 Hz), 7.73 (1H, s); ^{13}C{^{1}H} NMR ($CDCl_3$) δ 83.5 (C-I), 117.3, 126.2, 126.6, 128.2, 134.3, 137.5, 148.5. Found: *m*/*z* 371.7866. Calcd for $C_8H_3{}^{79}Br{}^{35}ClIS$: M^+, 371.7867.

2-Bromo-7-chloro-4-iodobenzo[*b*]thiophene (5f): 74% yield based on **7f** (2 steps); a colorless solid; mp 121–125 °C; ^{1}H NMR ($CDCl_3$) δ 7.03 (1H, d, ^3J = 8.0 Hz), 7.42 (1H, s), 7.66 (1H, d, ^3J = 8.0 Hz); ^{13}C{^{1}H} NMR ($CDCl_3$) δ 86.2 (C-I), 117.7, 125.3, 127.4, 131.6, 135.7, 139.4, 143.8. Found: *m*/*z* 371.7866. Calcd for $C_8H_3{}^{79}Br{}^{35}ClIS$: M^+, 371.7867.

7-Bromo-2-chloro-4-iodobenzo[*b*]thiophene (5g): 80% yield based on **11g**; a colorless solid; mp 132–133 °C; ^{1}H NMR ($CDCl_3$) δ 7.18 (1H, d, ^3J = 8.4 Hz), 7.37 (1H, s), 7.62 (1H, d, ^3J = 8.4 Hz); ^{13}C{^{1}H} NMR ($CDCl_3$) δ 87.4 (C-I), 115.3, 128.0, 128.5, 133.9, 135.9, 139.7, 142.5. Found: *m*/*z* 371.7867. Calcd for $C_8H_3{}^{79}Br^{35}ClIS$: M^+, 371.7867. Anal. Calcd for $C_8H_3BrClIS$: C, 25.73; H, 0.81%. Found: C, 25.74; H, 0.88%.

2,4-Dibromo-7-chlorobenzo[*b*]thiophene (5h): 69% yield based on **8b**; a colorless solid; mp 135 °C; ^{1}H NMR ($CDCl_3$) δ 7.18 (1H, d, ^3J = 8.4 Hz), 7.46 (1H, d, ^3J = 8.4 Hz), 7.51 (1H, s); ^{13}C{^{1}H} NMR ($CDCl_3$) δ 114.3, 118.1, 125.1, 126.2, 128.0, 129.2, 140.5, 140.7. Found: *m*/*z* 323.80053. Calcd for $C_8H_3{}^{79}Br_2{}^{35}ClS$: M^+, 323.80053. Anal. Calcd for $C_8H_3Br_2ClS$: C, 29.44; H, 0.93; Br, 48.96; Cl, 10.86; S, 9.82%. Found: C, 29.56; H, 1.02; Br, 49.24; Cl, 10.60; S, 9.80%.

Alternative Preparation of Products 5b,d. To a solution of **4b** (302.0 mg, 1.220 mmol) in 3.5 mL of THF was added 1.452 mmol of LDA (1.10 M solution in hexane-THF, 1.32 mL) at –78 °C under nitrogen atmosphere. The reaction mixture was stirred at –78 °C for 15 min and then at –20 °C for 40 min. To this solution was added a solution of 1,2-diiodoethane (1.691 mmol) in THF (3.4 mL) at –78 °C and the resulting mixture was stirred at –78 °C for 30 min, then at room temperature for 90 min. Saturated aqueous Na_2SO_3 solution was added, and the mixture was extracted with AcOEt. The organic phase was separated and dried over $MgSO_4$. The solvent was removed under reduced pressure and the residue was treated with silica gel column chromatography (hexane) to give 442.1 mg (1.184 mmol, 97% yield) of **5b**. Compound **5d** was obtained from **4d** by an analogous method in 95% yield.

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