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Halocyclization of 2-alkynylthioanisoles by cupric halides: synthesis of 2-substituted 3-halobenzo[*b*]thiophenes

Wen-Der Lu[b] and Ming-Jung Wu[a,*]

[a]*Faculty of Medicinal and Applied Chemistry, Kaohsiung Medical University, Kaohsiung, Taiwan*
[b]*Graduate Institute of Pharmaceutical Science, Kaohsiung Medical University, Kaohsiung, Taiwan*

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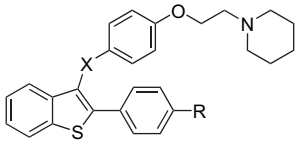
Abstract—Reaction of 2-alkynylthioanisoles **3** with 2 equiv of CuX_2 (X=Br or Cl) in refluxing CH_3CN for 2.5 h gave the 2-substituted 3-halobenzo[*b*]thiophenes **4** in good yields.

1. Introduction

The benzo[*b*]thiophenes have attracted much attention as the synthetic target molecules due to the wide spectrum of biological activities. These compounds often exhibit as potent antimitotic,[1] antipsychotic,[2] and antiinflammatory[3] agents or herpes virus inhibitors.[4] For instance, Arzoxifene (**1**) and Raloxifene (**2**) were found to be the unique selective estrogen receptor modulators (SERMs) and antitubulin agents.[5,6] To synthesize these biological active compounds, the 2-substituted 3-halobenzo[*b*]thiophenes appear to be the key synthetic intermediates. Although the efficient synthesis of the iodo and bromo derivatives has recently been reported by Flynn[7] and Larock,[8] no chlorinating agent was described in these papers. We herein wish to report an efficient method to prepare the 2-substituted 3-chlorobenzo[*b*]thiophenes as well as the bromo analogs using commercially available copper halides as the promotors.



X = O, R = OMe: Arzoxifene (**1**)
X = CO, R = OH: Raloxifene (**2**)

2. Results and discussion

The precursors, 2-alkynylthioanisoles (**3a–l**), were prepared from the 2-iodothioanisole by the Sonogashira coupling reaction[9] with terminal alkynes using $Pd(PPh_3)_4$ as the catalyst. The first attempt for the halocyclization was carried out by treatment of 2-phenylethynylthioanisole (**3a**) with 2 equiv of $CuCl_2$ in CH_3CN at room temperature for 18 h. 2-Phenyl-3-chlorobenzo[*b*]thiophene (**4aa**) was obtained in 65% yield. When the reaction was carried out under refluxing temperature of acetonitrile, the reaction time could be reduced to 2.5 h and the isolated yield of compound **4aa** increased to 71%. On the other hand, treatment of $CuBr_2$ with **3a** under the same reaction conditions gave **4ab** in 76% yield. CuF_2 has also been tested for the halocyclization of **3a** and no product was formed even after stirring for 48 h. After finding that $CuCl_2$ and $CuBr_2$ are effective reagents for the halocyclization of 2-phenylethynylthioanisole (**3a**), we turned our attention to explore the generality of this cyclization reaction. Thus, various 2-(2-substituted ethynyl)-thioanisoles **3b–l** were carried out for the halocyclization reactions. The results are summarized in Table 1.

From the results, we can see that all reactions work well under the optimized conditions. The aryl group bearing either the electron-donating or withdrawing group on the phenyl ring has little effect on the cyclization reaction (entries 3–6). It also works well when the substituent at the terminus alkyne is pyrrole or thiophene ring (entries 7 and 8). The alkyl substituent at the terminus alkyne also provided the 3-halobenzo[*b*]thiophenes in good yields. Only when the substituent is *tert*-butyl group, the reaction of **3k** with $CuBr_2$ gave the cyclization product **4kb** in 57% yield along with 25% of the bromine addition adduct **5kb**.[10] A similar result was also found by reaction of *o*-(2-trimethylsilylethynyl)-thioanisole (**3l**) with $CuBr_2$. The cyclization product **4lb** and the desilylated adduct **6lb**[11] were isolated in 10% and 26% yields, respectively. A majority (45%) of the bromine addition adduct **5lb** was obtained (Eq. 1). The structure of **5lb** was unambiguously determined by single crystal X-ray analysis[12] as shown in Figure 1.

* Corresponding author. Tel.: +886 7 3121101x2220; fax: +886 7 3125339; e-mail: mijuwu@kmu.edu.tw

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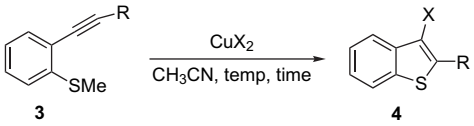
Table 1. CuX_2 promoted cyclization of 2-alkynylthioanisoles



3 4

R	Temp	Time (h)	Products, yields[a] (%)
3a, R=C_6H_5	rt	18	**4aa**, 65
	Reflux	2.5	**4aa**, 71 (**4ab**, 76)
3b, R=4-$MeOC_6H_4$	Reflux	2.5	**4ba**, 71 (**4bb**, 87)
3c, R=4-HOC_6H_4	Reflux	2.5	**4ca**, 81 (**4cb**, 81)
3d, R=4-MeC_6H_4	Reflux	2.5	**4da**, 75 (**4db**, 79)
3e, R=4-CNC_6H_4	Reflux	2.5	**4ea**, 99 (**4eb**, 99)
3f, R=3-$(C_5H_4)N$	Reflux	2.5	**4fa**, 78 (**4fb**, 82)
3g, R=2-$(C_4H_3)S$	Reflux	2.5	**4ga**, 90 (**4gb**, 90)
3h, R=$(CH_2)_5CH_3$	Reflux	2.5	**4ha**, 87 (**4hb**, 80)
3i, R=$(CH_2)_4OH$	Reflux	2.5	**4ia**, 75 (**4ib**, 78)
3j, R=$CH_2CH(CH_3)_2$	Reflux	2.5	**4ja**, 71 (**4jb**, 79)
3k, R=*t*-Bu	Reflux	2.5	**4ka**, 87
3l, R=$SiMe_3$	Reflux	2.5	**4la**, 71

[a] The numbers in parentheses are yields of the bromination products.

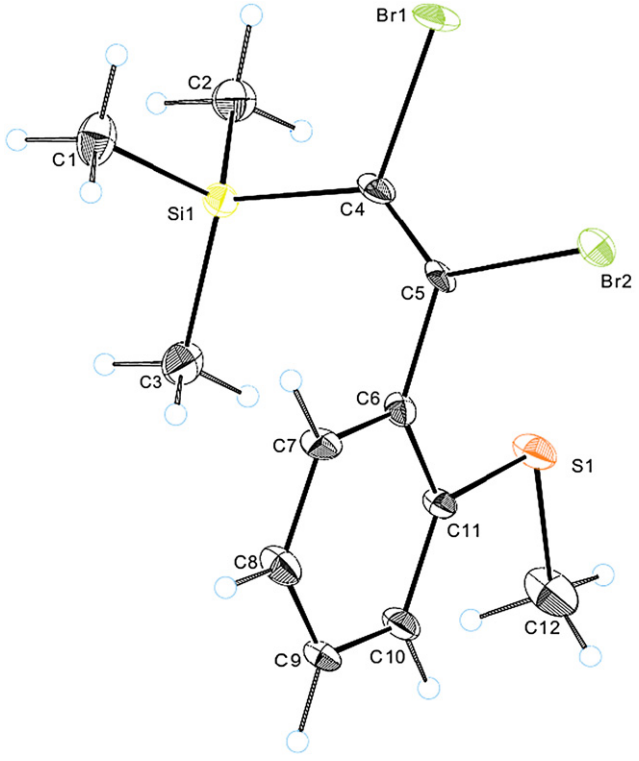
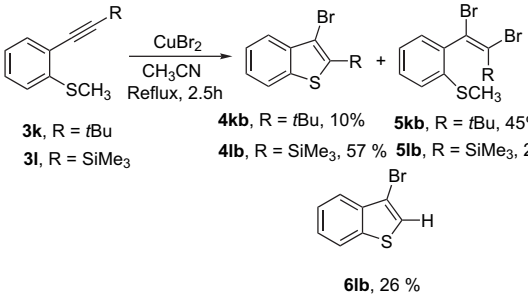
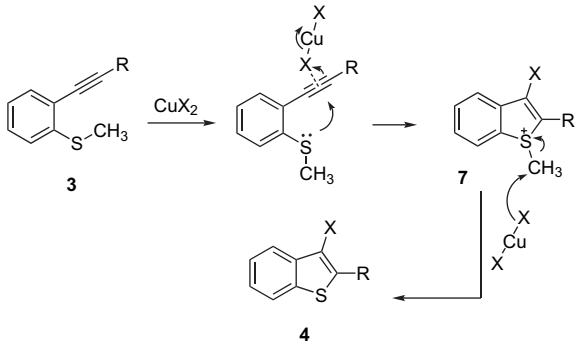


Figure 1. ORTEP plots for X-ray crystal structures of **5lb**.



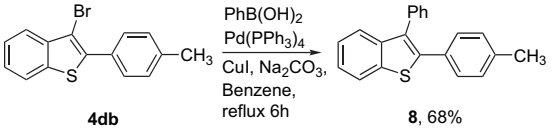
(1)

It was reported that cupric bromide in refluxing acetonitrile would produce bromine and cupric chloride is not prone to decomposition to generate chlorine at that temperature.[13] A plausible mechanism for the chlorocyclization reaction is shown in Scheme 1. First of all, the cupric chloride forms a 1:1 complex with **3** followed by *anti* attack of the sulfur on the thiomethyl group to the alkyne to give the sulfonium salt **7**. Finally, removal of the methyl group by chloride via S_N2 displacement would give the 3-chlorobenzo[*b*]thiophenes **4**. However, the formation of 2-substituted 3-bromobenzo[*b*]-thiophenes could either proceed as the same reaction mechanism as above or by bromine promoted pathway reported by Larock.[8]



Scheme 1.

To explore the synthetic utility of these halobenzo[*b*]thiophenes, one of the cyclization product, 2-(4-methylphenyl)-3-bromobenzo[*b*]thiophene (**4ib**), was converted to the 2,3-diarylbenzo[*b*]thiophene **8**[14] by Suzuki cross-coupling reaction with phenylboronic acid in 68% yield (Eq. 2).



(2)

In conclusion, we have demonstrated that cupric bromide and cupric chloride are efficient halocyclization agents of 2-alkynylthioanisoles. These cyclization reactions gave the 2-substituted 3-halobenzo[*b*]thiophenes in good yields.

3. Experimental section

3.1. Typical procedure for Sonogashira coupling reaction of 1-octyne with 2-iodothioanisole

Method A: 1-octyne (3.2 mmol), 2-iodothioanisole (3.2 mmol), $Pd(PPh_3)_4$ (5 mol %), CuI (2 mol %), and *n*-$BuNH_2$ (1.5 mmol) in ether (20 mL) were stirred at room temperature for 4 h. The saturated aqueous solutions of NH_4Cl and $NaHCO_3$ were added subsequently into the reaction mixture and extracted with EtOAc. The combined organic extracts were dried over anhydrous $MgSO_4$(s). After filtration and removal of solvent, the residue was purified by column chromatography to give the products.

3.2. Typical procedure for the halocyclization of 2-phenyl-3-chlorobenzo[*b*]thiophene

Method B: to a stirred solution of 2-alkynylthioanisole (1 mmol) in CH_3CN (5 mL) was added $CuCl_2$ (2 mmol) or $CuBr_2$ (2 mmol), the solution was heated to reflux and stirred at this temperature for 2.5 h. After cooling to room temperature, the saturated aqueous solution of NH_4Cl was added subsequently into the reaction mixture and extracted with EtOAc. The combined organic extracts were dried over anhydrous $MgSO_4$(s). After filtration and removal of solvent, the residue was purified by column chromatography to give the products.

3.2.1. *o*-(Phenylethynyl)thioanisole (3a). Obtained as a yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.60–7.50 (m, 2H), 7.48 (d, J=1.2 Hz, 1H), 7.38–7.28 (m, 4H), 7.19 (d, J=6.8 Hz, 1H), 7.12 (t, J=6.4 Hz, 1H), 2.52 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 141.6, 132.2, 131.5, 128.7, 128.4, 128.3, 126.0, 124.2, 124.1, 121.3, 113.6, 95.8, 86.8, 15.0; MS (70 eV) *m*/*z* (%): 224 (100) [M$^+$], 223 (75), 221 (13), 208 (19), 147 (16); HMRS (EI) calcd for $C_{15}H_{12}S$ 224.0660, found 224.0657.

3.2.2. *o*-(4-Methoxyphenylethynyl)thioanisole (3b). Obtained as an orange solid; mp 59–60 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.52 (dd, J=9.2, 2.4 Hz, 2H), 7.47 (dd, J=8.8, 2.0 Hz, 1H), 7.28 (t, J=7.6 Hz, 1H), 7.17 (d, J=8.0 Hz, 1H), 7.12 (t, J=7.6 Hz, 1H), 6.89 (dd, J=8.8, 2.0 Hz, 2H), 3.83 (s, 3H), 2.50 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 141.6, 134.2, 133.3, 132.2, 128.6, 127.5, 124.4, 124.2, 118.3, 115.5, 114.2, 113.9, 96.1, 85.8, 55.5, 55.4; MS (70 eV) *m*/*z* (%): 254 (90) [M$^+$], 253 (63), 247 (51), 223 (16), 195 (14), 147 (19); HMRS (EI) calcd for $C_{16}H_{14}OS$ 254.0765, found 254.0775; Anal. Calcd for $C_{16}H_{14}OS$: C, 75.55; H, 5.55; S, 12.61. Found: C, 75.79; H, 5.71; S, 11.39.

3.2.3. *o*-(4-Hydroxyphenylethynyl)thioanisole (3c). Obtained as a brown oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.48–7.44 (m, 3H), 7.30 (t, J=8.0 Hz, 1H), 7.17 (d, J=6.8 Hz, 3H), 7.12 (t, J=7.6 Hz, 1H), 6.82 (d, J=8.8 Hz, 3H), 5.81 (br s, 1H), 2.50 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 156.1, 141.2, 133.2, 131.9, 128.4, 124.2, 124.0, 121.6, 115.5, 115.5, 115.5, 115.2, 95.9, 85.5, 15.1; MS (70 eV) *m*/*z* (%): 240 (35) [M$^+$], 226 (100), 197 (10), 165 (11); HMRS (EI) calcd for $C_{15}H_{12}OS$ 240.0609, found 240.0606.

3.2.4. *o*-(4-Methylphenylethynyl)thioanisole (3d). Obtained as a yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.52–7.49 (m, 3H), 7.33 (t, J=8.4 Hz, 1H), 7.19–7.17 (m, 3H), 7.14 (t, J=7.6 Hz, 1H), 2.52 (s, 3H), 2.39 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 141.5, 138.4, 132.0, 131.4, 131.4, 129.0, 129.0, 128.5, 124.1, 124.0, 121.4, 120.0, 96.0, 86.2, 21.4, 14.9; MS (70 eV) *m*/*z* (%): 238 (100) [M$^+$], 237 (71), 223 (20), 221 (29), 208 (10), 147 (23); HMRS (EI) calcd for $C_{16}H_{14}S$ 238.0816, found 238.0823.

3.2.5. *o*-(4-Cyanophenylethynyl)thioanisole (3e). Obtained as a white solid; mp 66–67 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.63 (d, J=0.4 Hz, 4H), 7.47 (dd, J=7.6, 1.2 Hz, 1H), 7.35 (td, J=7.6, 1.2 Hz, 1H), 7.20 (d, J=7.6 Hz, 1H), 7.18 (td, J=7.2, 1.2 Hz, 1H), 2.51 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 142.2, 132.4, 131.9, 131.8, 131.7, 131.6, 129.5, 128.0, 124.2, 124.0, 120.0, 118.5, 111.4, 93.9, 91.1, 14.9; MS (70 eV) *m*/*z* (%): 249 (100) [M$^+$], 233 (13), 190 (12), 147 (42); HMRS (EI) calcd for $C_{16}H_{11}NS$ 249.0612, found 249.0613; Anal. Calcd for $C_{16}H_{11}NS$: C, 77.07; H, 4.45; S, 12.86; N, 5.62. Found: C, 77.22; H, 4.45; S, 12.98; N, 5.63.

3.2.6. *o*-(3-Pyridinylethynyl)thioanisole (3f). Obtained as a brown oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.81 (br s, 1H), 8.56 (br s, 1H), 7.88 (dt, J=8.0, 2.0 Hz, 1H), 7.50 (dd, J=7.6, 1.6 Hz, 1H), 7.36 (d, J=8.0 Hz, 1H), 7.33–7.29 (m, 1H), 7.20 (d, J=8.0 Hz, 1H), 7.14 (t, J=7.6 Hz, 1H), 2.52 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 151.8, 148.2, 141.9, 138.6, 132.3, 129.3, 129.3, 124.2, 124.0, 123.1, 120.3, 92.0, 90.2, 15.0; MS (70 eV) *m*/*z* (%): 225 (100) [M$^+$], 224 (68), 223 (18), 147 (30), 139 (10); HMRS (EI) calcd for $C_{14}H_{11}NS$ 225.0612, found 225.0616.

3.2.7. *o*-(2-Thienylethynyl)thioanisole (3g). Obtained as a brown oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.46 (dd, J=7.6, 1.6 Hz, 1H), 7.32–7.28 (m, 3H), 7.19 (d, J=7.6 Hz, 1H), 7.11 (td, J=6.4, 1.2 Hz, 1H), 7.03 (dd, J=5.2, 1.6 Hz, 1H), 2.54 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 141.5, 132.1, 132.0, 128.8, 128.8, 127.5, 127.1, 124.2, 124.1, 121.0, 90.4, 88.9, 15.1; MS (70 eV) *m*/*z* (%): 230 (23) [M$^+$], 229 (100), 228 (86), 197 (16), 171 (19); HMRS (EI) calcd for $C_{13}H_{10}S_2$ 230.0224, found 230.0222.

3.2.8. *o*-(1-Octynyl)thioanisole (3h). Obtained as an orange oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.36 (dd, J=7.6, 1.2 Hz, 1H), 7.34 (td, J=8.0, 0.4 Hz, 1H), 7.12 (d, J=7.6 Hz, 1H), 7.05 (t, J=7.2 Hz, 1H), 2.49 (t, J=7.2 Hz, 2H), 2.47 (s, 3H), 1.68–1.61 (m, 2H), 1.59–1.48 (m, 2H), 1.34–1.31 (m, 4H), 0.93–0.83 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 141.1, 132.2, 127.9, 124.0, 123.7, 122.0, 97.4, 78.0, 31.3, 28.6, 28.5, 22.5, 19.6, 14.9, 14.1; MS (70 eV) *m*/*z* (%): 232 (39) [M$^+$], 217 (100), 173 (11), 162 (14), 147 (74), 115 (17); HMRS (EI) calcd for $C_{15}H_{20}S$ 232.1286, found 232.1292.

3.2.9. *o*-(1-Hydroxyhexynyl)thioanisole (3i). Obtained as a yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.34 (dd, J=6.0, 1.6 Hz, 1H), 7.24 (td, J=6.4, 1.6 Hz, 1H), 7.12 (dd, J=7.2, 0.8 Hz, 1H), 7.04 (td, J=6.4, 1.2 Hz, 1H), 3.72 (t, J=6.4 Hz, 2H), 2.54 (t, J=6.4 Hz, 2H), 2.46 (s, 3H), 1.83–1.57 (m, 4H), 1.45 (br s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 141.0, 132.2, 128.1, 124.1, 123.7, 121.8, 96.8, 78.4, 62.4, 31.8, 24.8, 19.4, 14.9; MS (70 eV) *m*/*z* (%): 220 (25) [M$^+$], 205 (13), 187 (76), 172 (19), 161 (31), 147 (100); HMRS (EI) calcd for $C_{13}H_{16}OS$ 220.0922, found 220.0926.

3.2.10. *o*-(4-Methyl-1-pentynyl)thioanisole (3j). Obtained as an orange oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.37 (d, J=8.0 Hz, 1H), 7.26 (t, J=7.6 Hz, 1H), 7.12 (d, J=7.6 Hz, 1H), 7.04 (t, J=7.6 Hz, 1H), 2.47 (s, 3H), 2.39 (d, J=6.4 Hz, 2H), 1.97 (q, 1H), 1.08 (d, J=6.8 Hz, 3H), 1.07 (d, J=6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 141.1, 132.2, 127.9, 124.0, 123.6, 122.0, 96.3, 78.9, 28.8, 28.2, 22.0, 22.0, 14.9; MS (70 eV) *m*/*z* (%): 204 (17) [M$^+$], 153

(8), 148 (9), 127 (7); HMRS (EI) calcd for $C_{13}H_{16}S$ 204.0973, found 204.0974.

3.2.11. *o*-(*tert*-Butylethynyl)thioanisole (3k). Obtained as a yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.34 (dd, J=6.0, 1.2 Hz, 1H), 7.23 (td, J=6.4, 1.6 Hz, 1H), 7.11 (d, J=7.6 Hz, 1H), 7.04 (td, J=6.0, 1.6 Hz, 1H), 2.46 (s, 3H), 1.36 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 141.2, 131.9, 127.9, 123.9, 123.6, 121.9, 105.5, 31.1, 30.9, 30.6, 30.3, 28.3, 14.8; MS (70 eV) *m*/*z* (%): 204 (19) [M$^+$], 197 (27), 149 (100), 119 (10), 111 (15); HMRS (EI) calcd for $C_{13}H_{16}S$ 204.0973, found 204.0972.

3.2.12. *o*-(Trimethylsilylethynyl)thioanisole (3l). Obtained as a yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.40 (dd, J=7.6, 0.4 Hz, 1H), 7.27 (td, J=6.8, 2.0 Hz, 1H), 7.13 (d, J=8.0 Hz, 1H), 7.05 (td, J=8.8, 1.6 Hz, 1H), 2.47 (s, 3H), 0.27 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 141.9, 132.6, 128.9, 124.0, 123.9, 121.1, 102.0, 101.3, 14.9, −0.06 (3C); MS (70 eV) *m*/*z* (%): 220 (77) [M$^+$], 215 (15), 251 (19), 205 (78), 177 (30), 115 (100); HMRS (EI) calcd for $C_{12}H_{16}SSi$ 220.0742, found 220.0749.

3.2.13. 2-Phenyl-3-chlorobenzo[*b*]thiophene (4aa). Obtained as a white solid, mp 64–65 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.88 (d, J=7.2 Hz, 1H), 7.87–7.79 (m, 3H), 7.51–7.40 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 137.7, 136.7, 136.2, 132.3, 129.2, 129.1, 128.6, 128.5, 125.4, 125.3, 125.0, 122.3, 122.2, 116.3; MS (70 eV) *m*/*z* (%): 244 (100) [M$^+$], 212 (2), 208 (21), 165 (20), 139 (4); HMRS (EI) calcd for $C_{14}H_9ClS$ 244.0113, found 244.0107; Anal. Calcd for $C_{14}H_9ClS$: C, 68.72; H, 3.71; S, 13.10. Found: C, 68.68; H, 3.68; S, 13.09.

3.2.14. 2-Phenyl-3-bromobenzo[*b*]thiophene (4ab). Obtained as a white solid, mp 62–63 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.89 (d, J=7.2 Hz, 1H), 7.81 (d, J=8.0 Hz, 1H), 7.78–7.76 (m, 2H), 7.51–7.39 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 139.1, 138.2, 137.6, 133.0, 129.6, 129.5, 128.7, 128.5, 128.4, 125.4, 125.2, 123.6, 122.1, 104.9; MS (70 eV) *m*/*z* (%): 287 (97) [M$^+$], 208 (44), 165 (36), 163 (11), 145 (10), 104 (16); HMRS (EI) calcd for $C_{14}H_9BrS$ 287.9608, found 287.9607; Anal. Calcd for $C_{14}H_9BrS$: C, 58.15; H, 3.14; S, 11.09. Found: C, 58.16; H, 3.06; S, 11.14.

3.2.15. 2-(4-Methoxyphenyl)-3-chlorobenzo[*b*]thiophene (4ba). Obtained as a yellow solid, mp 102–103 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.87 (d, J=7.2 Hz, 1H), 7.78 (d, J=7.2 Hz, 1H), 7.74 (d, J=8.8 Hz, 2H), 7.47 (dt, J=7.2, 0.8 Hz, 1H), 7.41 (dt, J=6.8, 1.2 Hz, 1H), 7.03 (d, J=8.8 Hz, 2H), 3.87 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 159.9, 137.8, 136.3, 136.2, 130.5, 130.4, 130.3, 125.1, 124.9, 124.6, 122.1, 121.9, 114.1, 114.0, 55.2; MS (70 eV) *m*/*z* (%): 274 (100) [M$^+$], 261 (17), 259 (43), 231 (32), 195 (16), 152 (14); HMRS (EI) calcd for $C_{15}H_{11}ClOS$ 274.0219, found 274.0214; Anal. Calcd for $C_{15}H_{11}ClOS$: C, 65.57; H, 4.04; S, 11.67. Found: C, 65.53; H, 4.02; S, 11.64.

3.2.16. 2-(4-Methoxyphenyl)-3-bromobenzo[*b*]thiophene (4bb). Obtained as a yellow solid, mp 83–84 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.86 (d, J=7.6 Hz, 1H), 7.80 (d, J=7.6 Hz, 1H), 7.72 (dt, J=8.8, 2.8 Hz, 2H), 7.46 (t, J=6.8 Hz, 1H), 7.40 (t, J=6.8 Hz, 1H), 7.02 (dt, J=9.2, 2.4 Hz, 2H), 3.87 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 160.0, 139.2, 138.1, 137.4, 130.9, 130.7, 125.3, 125.2, 125.1, 123.4, 122.0, 114.1, 114.0, 104.2, 55.3; MS (70 eV) *m*/*z* (%): 317 (96) [M$^+$], 305 (32), 303 (31), 277 (17), 195 (25), 152 (22); HMRS (EI) calcd for $C_{15}H_{11}BrOS$ 317.9714, found 317.9706. Anal. Calcd for $C_{15}H_{11}BrOS$: C, 56.44; H, 3.47; S, 10.04. Found: C, 56.22; H, 3.69; S, 9.85.

3.2.17. 2-(4-Hydroxyphenyl)-3-chlorobenzo[*b*]thiophene (4ca). Obtained as a yellow solid, mp 144–145 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.85 (d, J=8.0 Hz, 1H), 7.80 (d, J=8.4 Hz, 1H), 7.70 (dd, J=6.8, 2.4 Hz, 1H), 7.48 (t, J=7.2 Hz, 1H), 7.40 (t, J=6.4 Hz, 1H), 6.96 (dd, J=6.8, 2.4 Hz, 2H), 5.21 (br s, 1H), 2.50 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 156.0, 137.8, 136.3, 136.1, 130.7, 130.7, 125.2, 124.9, 124.8, 122.1, 122.0, 115.7, 115.6, 115.6; Anal. Calcd for $C_{14}H_9ClOS$: C, 64.49; H, 3.48; S, 12.28. Found: C, 64.52; H, 3.53; S, 11.59.

3.2.18. 2-(4-Hydroxyphenyl)-3-bromobenzo[*b*]thiophene (4cb). Obtained as a yellow solid, mp 125–126 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.85 (d, J=8.0 Hz, 1H), 7.80 (d, J=8.4 Hz, 1H), 7.66 (dd, J=6.8, 2.4 Hz, 2H), 7.48 (t, J=6.8 Hz, 1H), 7.40 (t, J=6.8 Hz, 1H), 6.96 (dd, J=6.8, 2.0 Hz, 2H), 5.81 (br s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 156.3, 139.1, 138.1, 137.3, 131.0, 131.0, 125.3, 125.2, 125.1, 123.4, 122.0, 115.5, 115.5, 104.1; Anal. Calcd for $C_{14}H_9BrOS$: C, 55.10; H, 2.97; S, 10.51. Found: C, 55.49; H, 3.08; S, 10.16.

3.2.19. 2-(4-Methylphenyl)-3-chlorobenzo[*b*]thiophene (4da). Obtained as a white solid, mp 78–79 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.89 (d, J=7.2 Hz, 1H), 7.82 (d, J=8.0 Hz, 1H), 7.72 (d, J=8.0 Hz, 2H), 7.48 (t, J=8.4 Hz, 1H), 7.42 (t, J=6.8 Hz, 1H), 7.39 (d, J=8.0 Hz, 2H), 2.43 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 138.7, 137.8, 136.5, 136.4, 129.4, 129.3, 129.3, 129.0, 129.0, 125.2, 124.9, 122.2, 122.0, 116.2, 21.3; Anal. Calcd for $C_{15}H_{11}ClS$: C, 69.62; H, 4.28; S, 12.39. Found: C, 69.68; H, 4.36; S, 11.70.

3.2.20. 2-(4-Methylphenyl)-3-bromobenzo[*b*]thiophene (4db). Obtained as a white solid, mp 63–64 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.87 (d, J=8.0 Hz, 1H), 7.81 (d, J=8.0 Hz, 1H), 7.67 (d, J=8.4 Hz, 2H), 7.49 (t, J=7.2 Hz, 1H), 7.41 (t, J=8.4 Hz, 1H), 7.30 (d, J=7.6 Hz, 2H), 2.43 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 139.1, 138.8, 138.3, 137.5, 130.1, 129.4, 129.4, 129.3, 129.3, 125.3, 125.1, 123.5, 122.1, 104.5, 21.3; Anal. Calcd for $C_{15}H_{11}BrS$: C, 59.42; H, 3.66; S, 10.57. Found: C, 59.59; H, 3.68; S, 10.46.

3.2.21. 2-(4-Cyanophenyl)-3-chlorobenzo[*b*]thiophene (4ea). Obtained as a white solid, mp 126–127 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.93–7.89 (m, 1H), 7.91 (d, J=8.0 Hz, 2H), 7.82 (d, J=8.0 Hz, 1H), 7.77 (d, J=8.0 Hz, 2H), 7.51 (t, J=7.0 Hz, 1H), 7.46 (t, J=6.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 137.5, 136.9, 132.3, 132.1, 132.0, 130.8, 129.7, 129.5, 128.7, 126.3, 125.4, 122.6, 122.3, 118.5, 112.0; MS (70 eV) *m*/*z* (%): 269 (100) [M$^+$], 233 (14), 207 (1), 239 (46), 190 (19), 117 (4);

HMRS (EI) calcd for $C_{15}H_8ClNS$ 269.0066, found 269.0064; Anal. Calcd for $C_{15}H_8ClNS$: C, 66.79; H, 2.99; S, 11.89; N, 5.19. Found: C, 66.49; H, 2.92; S, 11.89; N, 5.19.

3.2.22. 2-(4-Cyanophenyl)-3-bromobenzo[*b*]thiophene (4eb). Obtained as a white solid, mp 141–142 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.91–7.85 (m, 1H), 7.90 (d, J=8.4 Hz, 2H), 7.85 (dd, J=8.0, 0.8 Hz, 1H), 7.77 (dt, J=8.0, 0.4 Hz, 2H), 7.51 (td, J=7.6, 0.8 Hz, 2H), 7.46 (t, J=6.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 138.9, 137.8, 137.7, 135.7, 132.3, 132.2, 130.2, 130.1, 126.2, 125.6, 124.0, 122.2, 118.4, 112.2, 106.7; MS (70 eV) *m*/*z* (%): 312 (97) [M$^+$], 235 (25), 233 (39), 207 (6), 190 (76), 188 (16); HMRS (EI) calcd for $C_{15}H_8BrNS$ 312.9561, found 312.9562; Anal. Calcd for $C_{15}H_8BrNS$: C, 57.34; H, 2.57; S, 10.21; N, 4.46. Found: C, 57.79; H, 2.87; S, 9.82; N, 4.24.

3.2.23. 2-(3-Pyridinyl)-3-chlorobenzo[*b*]thiophene (4fa). Obtained as a white solid, mp 73–74 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.02 (br s, 1H), 8.64 (br s, 1H), 8.11 (d, J=8.0 Hz, 1H), 7.88 (d, J=7.2 Hz, 1H), 7.82 (d, J=7.6 Hz, 1H), 7.50–7.40 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 149.5, 149.2, 137.4, 136.8, 136.4, 132.2, 128.8, 125.9, 125.3, 123.4, 122.4, 122.3, 118.1; Anal. Calcd for $C_{13}H_8ClNS$: C, 63.54; H, 3.28; S, 13.01; N, 5.07. Found: C, 63.74; H, 3.44; S, 12.59; N, 5.63.

3.2.24. 2-(3-Pyridinyl)-3-bromobenzo[*b*]thiophene (4fb). Obtained as a white solid, mp 80–81 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.00 (br s, 1H), 8.66 (br s, 1H), 8.09 (d, J=8.0 Hz, 1H), 7.89 (d, J=6.8 Hz, 1H), 7.83 (d, J=8.4 Hz, 1H), 7.51 (t, J=8.0 Hz, 1H), 7.43–7.40 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 149.9, 149.3, 138.8, 137.8, 136.8, 134.1, 129.7, 125.9, 125.4, 125.1, 123.8, 122.2, 106.4; Anal. Calcd for $C_{13}H_8BrNS$: C, 53.81; H, 2.78; S, 11.05; N, 4.83. Found: C, 53.81; H, 2.81; S, 11.00; N, 4.76.

3.2.25. 2-(2′-Thienyl)-3-chlorobenzo[*b*]thiophene (4ga). Obtained as a yellow solid, mp 85–86 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.83 (dd, J=8.0, 0.8 Hz, 1H), 7.75 (dd, J=7.6, 0.8 Hz, 1H), 7.56 (dd, J=4.8, 1.2 Hz, 1H), 7.47–7.43 (m, 2H), 7.41 (t, J=6.8 Hz, 1H), 7.14 (t, J=5.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 137.7, 135.8, 134.0, 130.3, 127.4, 127.2, 127.1, 125.6, 125.1, 122.0, 121.9, 116.3; Anal. Calcd for $C_{12}H_7ClS_2$: C, 57.48; H, 2.81; S, 25.57. Found: C, 57.65; H, 2.84; S, 24.50.

3.2.26. 2-(2′-Thienyl)-3-bromobenzo[*b*]thiophene (4gb). Obtained as a brown solid, mp 45–46 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.83 (dd, J=8.4, 0.8 Hz, 1H), 7.76 (dd, J=8.4, 0.8 Hz, 1H), 7.60 (dd, J=4.0, 1.6 Hz, 1H), 7.47–7.40 (m, 2H), 7.38 (t, J=6.8 Hz, 1H), 7.15 (t, J=5.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 139.2, 136.6, 134.6, 132.1, 127.9, 127.2, 127.1, 125.6, 125.3, 123.4, 121.9, 104.8; Anal. Calcd for $C_{12}H_7BrS_2$: C, 48.82; H, 2.39; S, 21.72. Found: C, 48.57; H, 2.39; S, 21.44.

3.2.27. 2-Hexyl-3-chlorobenzo[*b*]thiophene (4ha). Obtained as a yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.75 (dd, J=6.8, 1.2 Hz, 2H), 7.41 (td, J=6.8, 0.4 Hz, 1H), 7.33 (td, J=8.0, 1.2 Hz, 1H), 2.94 (t, J=7.6 Hz, 2H), 1.72 (q, J=7.2 Hz, 2H), 1.43–1.26 (m, 6H), 0.89 (t, J=6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 139.0, 136.9, 136.3, 124.6, 124.5, 122.3, 121.2, 117.7, 31.5, 30.2, 28.7, 28.2, 22.5, 14.0; MS (70 eV) *m*/*z* (%): 252 (27) [M$^+$], 183 (27), 181 (100), 149 (12), 147 (27); HMRS (EI) calcd for $C_{14}H_{17}ClS$ 252.0739, found 252.0739.

3.2.28. 2-Hexyl-3-bromobenzo[*b*]thiophene (4hb). Obtained as a yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.75 (dt, J=8.0, 3.6 Hz, 2H), 7.45 (td, J=8.0, 0.8 Hz, 1H), 7.33 (td, J=8.4, 0.8 Hz, 1H), 2.94 (t, J=7.6 Hz, 2H), 1.73 (q, J=7.6 Hz, 2H), 1.57–1.26 (m, 6H), 0.90 (t, J=6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 140.9, 138.3, 137.0, 124.8, 124.6, 122.5, 122.2, 105.6, 31.5, 30.2, 29.9, 28.7, 22.5, 14.0; MS (70 eV) *m*/*z* (%): 296 (45) [M$^+$], 227 (57), 226 (41), 224 (91), 225 (13), 147 (100); HMRS (EI) calcd for $C_{14}H_{17}BrS$ 296.0234, found 296.0241.

3.2.29. 2-Hydroxybutyl-3-chlorobenzo[*b*]thiophene (4ia). Obtained as a yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.75 (dd, J=8.4, 0.4 Hz, 2H), 7.41 (td, J=8.0, 1.2 Hz, 1H), 7.34 (td, J=7.2, 1.2 Hz, 1H), 3.69 (t, J=6.4 Hz, 2H), 2.99 (t, J=7.6 Hz, 2H), 1.82 (q, J=8.0 Hz, 2H), 1.70 (q, J=6.4 Hz, 2H), 1.50 (br s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 138.3, 136.9, 136.3, 124.7, 124.5, 122.3, 121.3, 117.4, 62.4, 31.9, 27.9, 26.5; MS (70 eV) *m*/*z* (%): 240 (27) [M$^+$], 196 (21), 194 (60), 187 (23), 183 (38), 181 (100); HMRS (EI) calcd for $C_{12}H_{13}ClOS$ 240.0376, found 240.0379.

3.2.30. 2-Hydroxybutyl-3-bromobenzo[*b*]thiophene (4ib). Obtained as a yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.75 (dd, J=7.6, 0.4 Hz, 2H), 7.41 (td, J=7.2, 1.2 Hz, 1H), 7.35 (td, J=8.0, 1.2 Hz, 1H), 3.70 (t, J=6.4 Hz, 2H), 2.99 (t, J=7.6 Hz, 2H), 1.87–1.80 (m, 2H), 1.72–1.67 (m, 2H), 1.49 (br s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 140.2, 138.3, 137.0, 124.9, 124.8, 122.6, 122.2, 105.9, 62.5, 31.9, 29.5, 26.5; MS (70 eV) *m*/*z* (%): 283 (43) [M$^+$], 240 (60), 238 (58), 227 (100), 225 (96), 187 (88); HMRS (EI) calcd for $C_{12}H_{13}BrOS$ 283.9870, found 283.9877.

3.2.31. 2-(2-Methyl-propanyl)-3-chlorobenzo[*b*]thiophene (4ja). Obtained as a yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.76–7.73 (m, 2H), 7.43 (t, J=8.0 Hz, 1H), 7.36 (t, J=8.0 Hz, 1H), 2.84 (d, J=7.6 Hz, 2H), 2.17–2.02 (m, 1H), 1.02 (d, J=6.8 Hz, 3H), 1.00 (d, J=6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 137.9, 136.8, 136.5, 124.6, 124.6, 122.2, 121.3, 37.2, 30.1, 29.6, 22.3, 22.3; MS (70 eV) *m*/*z* (%): 224 (27) [M$^+$], 187 (37), 180 (100), 147 (10), 111 (12), 109 (12); HMRS (EI) calcd for $C_{12}H_{13}ClS$ 224.0426, found 224.0425.

3.2.32. 2-(2-Methyl-propanyl)-3-bromobenzo[*b*]thiophene (4jb). Obtained as a yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.58 (d, J=8.0 Hz, 2H), 7.43 (t, J=7.2 Hz, 1H), 7.35 (t, J=8.0 Hz, 1H), 2.85 (d, J=7.2 Hz, 2H), 2.11–2.05 (m, 1H), 1.02 (d, J=6.8 Hz, 3H), 1.00 (d, J=6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 139.8, 138.2, 137.2, 124.7, 124.7, 122.7, 122.1, 106.5, 38.8, 30.1, 22.3, 22.3; MS (70 eV) *m*/*z* (%): 267 (30) [M$^+$], 226 (100), 224 (99), 170 (10), 146 (48), 144 (49); HMRS (EI) calcd for $C_{12}H_{13}BrS$ 267.9921, found 267.9915.

3.2.33. 2-*tert*-Butyl-3-chlorobenzo[*b*]thiophene (4ka). Obtained as a yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.76 (d, J=8.0 Hz, 1H), 7.72 (d, J=8.0 Hz, 1H), 7.41 (td, J=7.2, 1.2 Hz, 1H), 7.34 (td, J=8.0, 1.2 Hz, 1H), 1.56 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 147.2, 138.5, 134.8, 124.6, 124.5, 121.9, 121.1, 115.2, 94.4, 35.0, 29.7, 29.5; MS (70 eV) *m*/*z* (%): 224 (4) [M$^+$], 209 (12), 181 (2), 159 (2), 149 (3), 58 (100); HMRS (EI) calcd for $C_{12}H_{13}ClS$ 224.0426, found 224.0425.

3.2.34. 2-*tert*-Butyl-3-bromobenzo[*b*]thiophene (4kb). Obtained as a yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.80 (d, J=8.0 Hz, 1H), 7.74 (d, J=8.4 Hz, 1H), 7.43 (t, J=7.2 Hz, 1H), 7.35 (td, J=8.0 Hz, 1H), 1.59 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 148.7, 139.9, 135.4, 124.7, 124.6, 122.4, 121.7, 102.6, 35.4, 30.5, 29.9, 29.9; MS (70 eV) *m*/*z* (%): 267 (40) [M$^+$], 256 (12), 255 (100), 253 (93), 225 (23), 174 (66); HMRS (EI) calcd for $C_{12}H_{13}BrS$ 267.9921, found 267.9919.

3.2.35. 2-(Trimethylsilyl)-3-chlorobenzo[*b*]thiophene (4la). Obtained as a yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.85 (t, J=7.2 Hz, 1H), 7.83 (t, J=6.8 Hz, 1H), 7.43 (dt, J=7.6, 1.2 Hz, 1H), 7.40 (dt, J=7.6, 1.6 Hz, 1H), 0.45 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 141.2, 138.2, 133.7, 127.2, 125.0, 124.6, 122.3, 121.7, −0.90 (3C); MS (70 eV) *m*/*z* (%): 240 (12) [M$^+$], 224 (15), 163 (15), 149 (23), 135 (37); HMRS (EI) calcd for $C_{11}H_{13}ClSSi$ 240.0196, found 240.0194.

3.2.36. 2-(Trimethylsilyl)-3-bromobenzo[*b*]thiophene (4lb). Obtained as a yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.84 (dd, J=8.0, 1.2 Hz, 2H), 7.44 (t, J=8.0 Hz, 1H), 7.37 (t, J=8.4 Hz, 1H), 0.47 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 141.3, 139.8, 125.1, 125.0, 124.7, 122.9, 122.1, 114.6, −0.80 (3C); MS (70 eV) *m*/*z* (%): 283 (41) [M$^+$], 268 (21), 188 (26), 144 (100), 131 (39), 115 (66); HMRS (EI) calcd for $C_{11}H_{13}BrSSi$ 283.9691, found 283.9699.

3.2.37. 2-[1,2-Dibromo-(2-trimethylsilylethenyl)]thioanisole (5lb). Obtained as a white solid, mp 97–98 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.33 (t, J=8.0 Hz, 1H), 7.17–7.11 (m, 3H), 2.47 (s, 3H), −0.05 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 138.6, 134.2, 130.3, 129.7, 129.5, 124.4, 124.2, 106.9, 15.1, −0.5 (3C); Anal. Calcd for $C_{12}H_{16}Br_2SSi$: C, 37.91; H, 4.24; S, 8.43. Found: C, 37.98; H, 4.20; S, 8.54.

3.2.38. 2-[1,2-Dibromo-(3,3-dimethylbutenyl)]thioanisole (5kb). Obtained as a white solid, mp 74–75 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.29–7.27 (m, 1H), 7.25–7.07 (m, 3H), 2.49 (s, 3H), 1.11 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 143.1, 139.6, 138.0, 129.2, 129.1, 124.2, 124.0, 120.6, 43.2, 31.1 (3C), 14.9; Anal. Calcd for $C_{13}H_{16}Br_2S$: C, 42.88; H, 4.43; S, 8.81. Found: C, 44.72; H, 4.63; S, 9.00.

3.2.39. 3-Bromobenzo[*b*]thiophene (6lb). Obtained as a yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.86–7.83 (m, 2H), 7.49 (ddd, J=7.2, 6.0, 1.2 Hz, 1H), 7.45 (s, 1H), 7.41 (ddd, J=8.0, 6.8, 1.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 138.5, 137.4, 125.2, 124.9, 123.4, 122.9, 122.6, 107.6. These spectral data are identical to those reported in the literature.[11]

3.2.40. 2-(4-Methylphenyl)-3-phenylbenzo[*b*]thiophene (8).[13] Obtained as a white solid, mp 162–163 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.88 (dd, J=6.8, 2.0 Hz, 1H), 7.59 (dd, J=6.8, 1.6 Hz, 1H), 7.43–7.31 (m, 7H), 7.23 (d, J=8.4 Hz, 2H), 7.07 (d, J=7.6 Hz, 2H), 2.32 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 140.9, 139.7, 138.7, 137.6, 135.6, 132.7, 131.2, 130.4, 129.4 (2C), 129.0 (2C), 128.6 (2C), 127.3, 124.3 (3C), 123.2, 122.0, 21.1; Anal. Calcd for $C_{21}H_{16}S$: C, 83.96; H, 5.37; S, 10.67. Found: C, 83.96; H, 5.28; S, 10.87.

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