JOC The Journal of Organic Chemistry

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CuI/TMEDA-Catalyzed Annulation of 2-Bromo Alkynylbenzenes with Na_2S: Synthesis of Benzo[*b*]thiophenes

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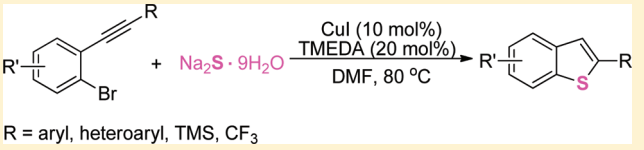
Supporting Information

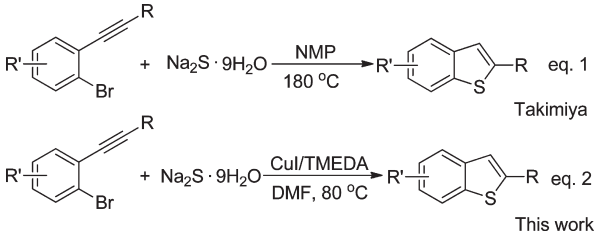
ABSTRACT: A copper-catalyzed thiolation annulation reaction of 2-bromo alkynylbenzenes with sodium sulfide has been developed. In the presence of CuI and TMEDA, a variety of 2-substituted benzo[*b*]thiophenes were readily prepared in moderate to good yields by the reaction of 2-bromo alkynylbenzenes and $Na_2S \cdot 9H_2O$.



Benzo[*b*]thiophenes are an important class of heterocyclic compounds due to their wide range of biological properties[1] and also various applications in materials science.[2] The benzo[*b*]thiophene ring system and its derivatives are the core of numerous medicinal molecules, such as clinically used raloxifene,[3] arzoxifene,[4] and zileuton.[5] For this reason, synthesis of this privileged structure has recently attracted much attention and many efficient methods have been developed. Most of these approaches are focused on (1) electrophilic cyclization reaction of *o*-alkynyl thioanisole[6] and (2) coupling cyclization reaction of *o*-bromo alkynylbenzenes with various thiol surrogates upon lithium−halogen exchange at −78 °C.[7] In 2009, Takimiya and co-workers also reported the synthesis of benzo[*b*]thiophene from the annulation of *o*-haloethynylbenzene with sodium sulfide at 180 °C (Scheme 1, eq 1).[8] However, the utility and applicability of the above reactions suffer from the harsh reaction conditions. Recently, transition-metal-catalyzed carbon−sulfur bond forming reactions have been extensively studied,[9] which would provide a more convenient and efficient route for the construction of the benzo[*b*]thiophene skeleton.[10] Our group also developed a copper-catalyzed double thiolation reaction of 1,4-dihalides with metal sulfides for the synthesis of 2-trifluoromethyl benzo[*b*]thiophenes and benzo[*b*]thiazoles.[11] As a continuing interest in the synthesis of sulfur-containing compounds,[12] we wish to prepare various different 2-substituted benzo[*b*]thiophenes using a practical method. Herein, we report a copper-catalyzed cyclization between 2-bromo alkynylbenzenes and easily available sodium sulfide for the synthesis of 2-substituted benzo[*b*]thiophenes (Scheme 1, eq 2).

The reaction of 1-bromo-2-(phenylethynyl)benzene (**1a**) with Na_2S was screened to optimize reaction conditions, and the results are summarized in Table 1. Our investigation began with an attempted annulation of substrate **1a** with Na_2S in DMF at 80 °C in the absence of any catalyst; the desired product **2a** could be isolated only in 18% yield (entry 1). This result demonstrated that high reaction temperature is essential in Takimiya's procedure[8] and encouraged us to develop efficient catalytic systems. Subsequently, a variety of copper salts were examined to optimize the reaction conditions. The results displayed that both cuprous salts and cupric

Scheme 1



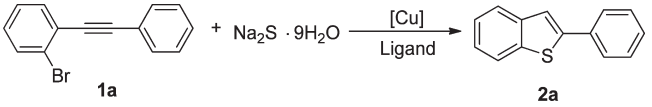
salts could mediate the cyclization reaction (entries 2−6). CuI was proved to be superior to other copper salts, including CuCl, CuBr, $Cu(OTf)_2$, and $Cu(OAc)_2$. The target product **2a** could be obtained in 47% yield when substrate **1a** was treated with Na_2S and 10 mol % of CuI in DMF at 80 °C (entry 3). Encouraged by these results, we investigated various N,N-bidentate ligands, such as *N*,*N*,*N*′,*N*′-tetramethylethylenediamine (TMEDA), 1,10-phenanthroline (1,10-phen), *N*,*N*′-dimethylethanediamine (DMEDA), and 2,2′-bipyridine (entries 7−10). To our delight, all of these ligands could promote the thiolation annulation reaction and TMEDA provided the best result. Treatment of substrate **1a** with Na_2S, 10 mol % of CuI, and 20 mol % of TMEDA in DMF at 80 °C afforded the target product **2a** in 83% yield (entry 7). Finally, the effects of solvents and reaction temperatures were evaluated, and the results showed that DMSO, NMP, and toluene were less effective than DMF (entries 11−13). A low yield was also found when the reaction was carried out at 60 °C, but identical results were observed when the reaction was carried out at 80 or 100 °C (entries 14 and 15). The yield of **2a** was reduced obviously when using 5 mol % loading of CuI and 10 mol % of TMEDA (entry 16).

With the optimal reaction conditions in hand, we explored the scope of 2-bromo alkynylbenzenes for the thiolation annulation reaction (Table 2). Initially, R substituents at the terminal alkyne

Received: May 31, 2011
Published: August 03, 2011

   dx.doi.org/10.1021/jo201081v | *J. Org. Chem.* 2011, 76, 7546–7550

Table 1. Screening Conditions[a]

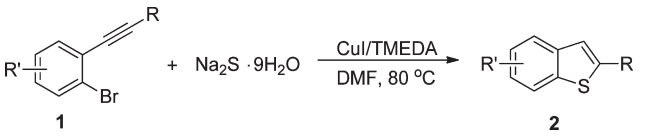


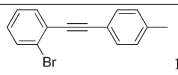
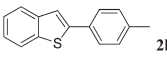
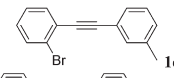
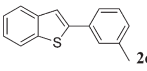
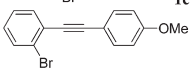
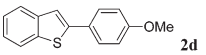
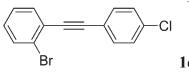
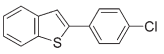
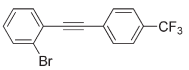
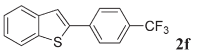
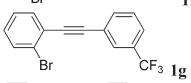
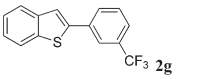
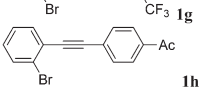
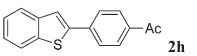
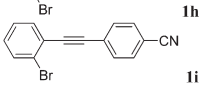
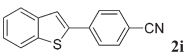
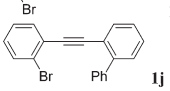
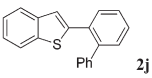
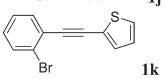
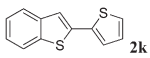
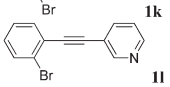
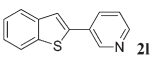
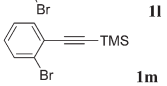
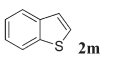
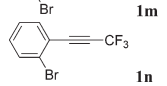
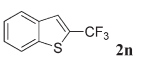
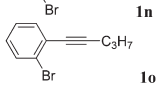
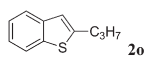
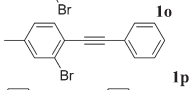
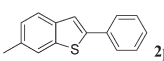
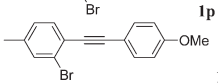
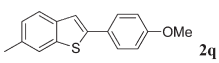
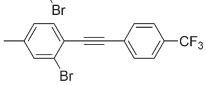
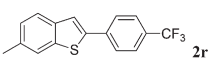
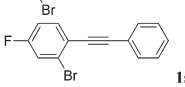
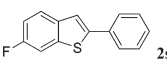
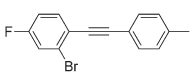
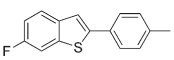
entry	[Cu]	ligand	solvent	T (°C)	yield (%)[b]
1			DMF	80	18
2	CuCl		DMF	80	35
3	CuBr		DMF	80	31
4	CuI		DMF	80	47
5	$Cu(OTf)_2$		DMF	80	27
6	$Cu(OAc)_2$		DMF	80	39
7	CuI	TMEDA	DMF	80	83
8	CuI	1,10-phen	DMF	80	75
9	CuI	DMEDA	DMF	80	63
10	CuI	2,2′-bipyridine	DMF	80	73
11	CuI	TMEDA	DMSO	80	65
12	CuI	TMEDA	NMP	80	62
13	CuI	TMEDA	toluene	80	trace
14	CuI	TMEDA	DMF	100	82
15	CuI	TMEDA	DMF	60	54
16[c]	CuI	TMEDA	DMF	80	67

[a] Reaction conditions: **1a** (0.2 mmol), $Na_2S·9H_2O$ (0.6 mmol), [Cu] (10 mol %), and ligand (20 mol %) in solvent (2 mL) under N_2 atmosphere for 24 h. [b] Isolated yield. [c] 5 mol % of CuI was added.

moiety of 2-(1-alkynyl)bromobenzene were evaluated (entries 1−14). The results demonstrated that both electron-deficient and electron-rich phenyl group were compatible, but the reaction of 2-bromo alkynylbenzene bearing electron-deficient substituent provided a lower yield (entries 1−8). For example, substrates **1b** and **1h**, bearing a 4-methylphenyl or 4-acetylphenyl group, underwent the thiolation annulation with Na_2S smoothly to afford the corresponding benzo[*b*]thiophene in 80 and 50% yields, respectively (entries 1 and 7). We found that the steric effect of substituents affected the reaction, and only trace product was detected when R was the bulky (1,1′-biphenyl)-2-yl group (entry 9). We were also pleased to find that substrates bearing a heteroaryl group (such as pyridin-3-yl and thiophen-2-yl) were tolerated very well to provide corresponding product in good yields (entries 10 and 11). However, a low yield was observed in the annulation reaction of substrate **1m** or **1n**, bearing a TMS or CF_3 group at the terminal of the triple bond (entries 12 and 13). Similarly, substrate **1o** bearing an aliphatic alkyl group did not work under the standard conditions (entry 14). Subsequently, various multisubstituted 2-bromo alkynylbenzenes were examined. The results displayed that the thiolation reaction of 2-bromo alkynylbenzenes bearing a substituent (such as methyl, Cl, and F atom) at the 4-position of the benzene ring proceeded smoothly to afford product in good yields. For example, substrates **1q** and **1r**, both bearing a methyl at the 4-position of the bromobenzene moiety, were treated with Na_2S, CuI, and TMEDA to afford corresponding product in 70 and 75% yields, respectively (entries 16 and 17). All thiolation annulation reactions of 4-halo (Cl, F)-2-bromo alkynylbenzenes with Na_2S were conducted successfully. For example, substrate **1u** or **1v** was reacted with Na_2S under the standard conditions to provide corresponding product in 84 and 74% yields, respectively (entries 20 and 21).

Table 2. CuI-Catalyzed Annulation of 2-Bromo Alkynylbenzenes with Na_2S[a]

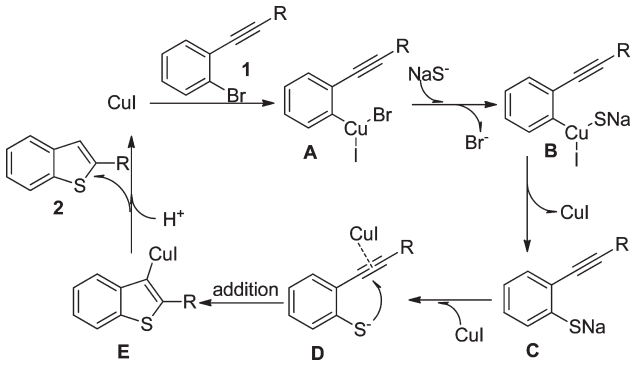


Entry	Substrate **1**	Product **2**	Yield (%)[b]
1	 **1b**	 **2b**	80
2	 **1c**	 **2c**	82
3	 **1d**	 **2d**	71
4	 **1e**	 **2e**	82
5	 **1f**	 **2f**	52
6	 **1g**	 **2g**	54
7	 **1h**	 **2h**	50
8	 **1i**	 **2i**	48
9[c]	 **1j**	 **2j**	5<
10	 **1k**	 **2k**	73
11	 **1l**	 **2l**	70
12	 **1m**	 **2m**	30
13	 **1n**	 **2n**	42
14	 **1o**	 **2o**	0
15	 **1p**	 **2p**	75
16	 **1q**	 **2q**	70
17	 **1r**	 **2r**	75
18	 **1s**	 **2s**	70
19	 **1t**	 **2t**	68
20	**1u**	**2u**	84
21	**1v**	**2v**	74

[a] Reaction conditions: **1** (0.2 mmol), $Na_2S·9H_2O$ (0.6 mmol), CuI (10 mol %), and TMEDA (20 mol %) in DMF (2 mL) at 80 °C under N_2 atmosphere for 24 h. [b] Isolated yield. [c] Detected by GC−MS.

dx.doi.org/10.1021/jo201081v |*J. Org. Chem.* 2011, 76, 7546–7550

Scheme 2



On the basis of the present results and the reported mechanism,[9b] a possible mechanism was proposed as outlined in Scheme 2. Oxidative addition of CuI to substrate **1** afforded intermediate **A**; the following ligand exchange with sodium sulfide might provide intermediate **B**, which could then undergo reductive elimination to form intermediate **C** and regenerate CuI. The coordination of CuI with intermediate **C** might provide copper complex **D**, subsequent addition to C−C triple bond gave intermediate **E**. Protonolysis of intermediate **E** formed benzo[*b*]thiophenes **2** and regenerated the active CuI. Study of the detailed mechanism is in progress.

In conclusion, we have developed a practical CuI/TMEDA-catalyzed thiolation annulation method for the synthesis of 2-substituted benzo[*b*]thiophenes. In the presence of CuI and TMEDA, a variety of 2-bromo alkynylbenzene derivatives underwent the annulation reaction with $Na_2S·9H_2O$ at 80 °C to give the corresponding benzo[*b*]thiophenes in moderate to good yields. In contrast to harsh reaction conditions (−78 or 180 °C) of the traditional methods,[7,8] the mild reaction conditions of the present procedure will be a new optional route for constructing the benzo[*b*]thiophene ring.

EXPERIMENTAL SECTION

Typical Experimental Procedure for the CuI-Catalyzed Thiolation Annulation Reaction. A mixture of 2-bromo alkynylbenzene **1** (0.2 mmol), CuI (3.8 mg, 10 mol %), TMEDA (4.7 mg, 20 mol %), and $Na_2S·9H_2O$ (144 mg, 3 equiv) in DMF (2 mL) was evacuated and backfilled with nitrogen (3 cycles) and then stirred at 80 °C until complete consumption of starting material was indicated by TLC or GC−MS analysis. After the reaction was completed, the mixture was filtered through a glass filter and washed with ethyl acetate. The mixture was washed with brine and extracted with ethyl acetate. The organic layers were dried with anhydrous Na_2SO_4 and evaporated under vacuum, and the residue was purified by flash column chromatography (hexane/ethyl acetate) to give product **2**.

2-Phenylbenzo[b]thiophene[8] (***2a***): White solid (34.8 mg, 83%), mp 172.2−173.0 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.82 (d, J = 7.5 Hz, 1H), 7.76 (d, J = 7.5 Hz, 1H), 7.71 (d, J = 7.5 Hz, 2H), 7.54 (s, 1H), 7.43−7.40 (m, 2H), 7.36−7.27 (m, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 144.2, 140.7, 139.5, 134.3, 128.9, 128.2, 126.5, 124.5, 124.3, 123.5, 122.3, 119.4; IR (neat, cm^{-1}) 3051, 3023, 1487, 1457, 1429, 1335; LRMS (EI, 70 eV) m/z (%) 210 (M$^+$, 100), 165 (21), 178 (12), 105 (13).

2-p-Tolylbenzo[b]thiophene[13] (***2b***): White solid (35.8 mg, 80%), mp 166.1−168.2 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.81 (d, J = 8.0 Hz, 1H), 7.74 (d, J = 8.0 Hz, 1H), 7.60 (d, J = 8.0 Hz, 2H), 7.49 (s, 1H), 7.35−7.26 (m, 2H), 7.22 (d, J = 8.0 Hz, 2H), 2.38 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 144.4, 140.8, 139.3, 138.3, 131.5, 129.6, 126.4, 124.4, 124.1, 123.4, 122.2, 118.8, 21.2; IR (neat, cm^{-1}) 2914, 1559, 1460, 1438, 809; LRMS (EI, 70 eV) m/z (%) 224 (M$^+$, 100), 189 (5), 178 (5), 112 (9).

2-m-Tolylbenzo[b]thiophene[14] (***2c***): White solid (36.7 mg, 82%), mp 117.0−118.0 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.82 (d, J = 8.0 Hz, 1H), 7.75 (d, J = 7.5 Hz, 1H), 7.52−7.51 (m, 3H), 7.35−7.29 (m, 3H), 7.15 (d, J = 7.5 Hz, 1H), 2.41 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 144.4, 140.7, 139.5, 138.6, 134.2, 129.1, 128.8, 127.2, 124.4, 124.2, 123.7, 123.5, 122.2, 119.3, 21.4; IR (neat, cm^{-1}) 3052, 1604, 1486, 1454, 782; LRMS (EI, 70 eV) m/z (%) 224 (M$^+$, 100), 189 (5), 112 (9).

2-(4-Methoxyphenyl)benzo[b]thiophene[13] (***2d***): White solid (34.1 mg, 71%), mp 191.3−193.5 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.81 (d, J = 8.0 Hz, 1H), 7.74 (d, J = 8.0 Hz, 1H), 7.65 (d, J = 9.0 Hz, 2H), 7.43 (s, 1H), 7.33−7.26 (m, 2H), 6.96 (d, J = 9.0 Hz, 2H), 3.85 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 159.8, 144.1, 140.9, 139.2, 127.7, 127.1, 124.4, 123.9, 123.2, 122.2, 118.2, 114.4, 55.4; IR (neat, cm^{-1}) 2956, 1604, 1499, 1464, 1247, 1177, 1031, 820; LRMS (EI, 70 eV) m/z (%) 240 (M$^+$, 100), 225 (69), 197 (39), 165 (20).

2-(4-Chlorophenyl)benzo[b]thiophene[15] (***2e***): White solid (40.0 mg, 82%), mp 190.5−192.1 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.80 (d, J = 8.0 Hz, 1H), 7.75 (d, J = 7.5 Hz, 1H), 7.61 (d, J = 8.5 Hz, 2H), 7.49 (s, 1H), 7.37 (d, J = 8.5 Hz, 2H), 7.33−7.30 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 142.8, 140.6, 139.5, 134.1, 132.8, 129.1, 127.6, 124.6, 124.5, 123.6, 122.3, 119.9; IR (neat, cm^{-1}) 3058, 1486, 1432, 1094, 1010, 815; LRMS (EI, 70 eV) m/z (%) 246 (M$^+$, 39), 244 (M$^+$, 100), 208 (19), 165 (17).

2-(4-(Trifluoromethyl)phenyl)benzo[b]thiophene[13] (***2f***): White solid (28.9 mg, 52%), mp 216.1−217.4 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.85 (d, J = 7.5 Hz, 1H), 7.82−7.80 (m, 3H), 7.67 (d, J = 8.0 Hz, 2H), 7.63 (s, 1H), 7.40−7.34 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 142.3, 140.5, 139.9, 137.8, 130.1 (q, J_{C-F} = 32.5 Hz), 126.6, 125.9 (q, J_{C-F} = 3.8 Hz), 125.0, 124.8, 124.1 (q, J_{C-F} = 270.3 Hz), 124.0, 122.4, 121.1; IR (neat, cm^{-1}) 3068, 2933, 1611, 1599, 1454, 1322; LRMS (EI, 70 eV) m/z (%) 278 (M$^+$, 100), 233 (8), 208 (10), 114 (14).

2-(3-(Trifluoromethyl)phenyl)benzo[b]thiophene (***2g***): White solid (30.1 mg, 54%), mp 102.6−105.3 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.95 (s, 1H), 7.87−7.83 (m, 2H), 7.79 (d, J = 7.0 Hz, 1H), 7.61−7.58 (m, 2H), 7.56−7.52 (m, 1H), 7.40−7.33 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 142.3, 140.5, 139.7, 135.2, 131.5 (q, J_{C-F} = 32.5 Hz), 129.6, 129.5, 124.9, 124.8, 124.7 (q, J_{C-F} = 3.8 Hz), 124.0 (q, J_{C-F} = 270.8 Hz), 123.9, 123.1 (q, J_{C-F} = 3.8 Hz), 122.3, 120.7; IR (neat, cm^{-1}) 3058, 3039, 1607, 1521, 1456, 1438; LRMS (EI, 70 eV) m/z (%) 278 (M$^+$, 100), 208 (9), 139 (10); HRMS (EI) calcd for $C_{15}H_9F_3S^+$ (M$^+$) 278.0372, found 278.0382.

1-(4-(Benzo[b]thiophen-2-yl)phenyl)ethanone[16] (***2h***): White solid (25.2 mg, 50%), mp 165.2−166.7 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.00 (d, J = 8.5 Hz, 2H), 7.84 (d, J = 7.0 Hz, 1H), 7.81−7.78 (m, 3H), 7.66 (s, 1H), 7.39−7.33 (m, 2H), 2.62 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 197.3, 142.6, 140.4, 139.9, 138.7, 136.4, 129.1, 126.3, 125.0, 124.8, 124.0, 122.3, 121.2, 26.6; IR (neat, cm^{-1}) 3059, 1674, 1600, 1358, 1266, 819, 743; LRMS (EI, 70 eV) m/z (%) 252 (M$^+$, 82), 237 (100), 208 (39), 165 (40).

4-(Benzo[b]thiophen-2-yl)benzonitrile[17] (***2i***): White solid (22.5 mg, 48%), mp 181.1−182.6 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.85 (d, J = 7.5 Hz, 1H), 7.83−7.77 (m, 3H), 7.70 (d, J = 8.5 Hz, 2H), 7.66 (s, 1H), 7.42−7.34 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 141.6, 140.3, 140.0, 138.6, 132.7, 126.7, 125.3, 124.9, 124.1, 122.4, 121.8, 118.6, 111.4; IR (neat, cm^{-1}) 2917, 2217, 1604, 1526, 1494, 1335, 822, 752; LRMS (EI, 70 eV) m/z (%) 235 (M$^+$, 100), 203 (10), 190 (15), 117 (8).

2-(Thiophen-2-yl)benzo[b]thiophene[18] (***2k***): White solid (31.4 mg, 73%), mp 118.1−120.2 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.78 (d, J = 8.0 Hz, 1H), 7.72 (d, J = 7.5 Hz, 1H), 7.40 (s, 1H), 7.30−7.28 (m, 2H), 7.08−7.05 (m, 2H), 7.03−7.01 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 140.4, 139.1, 137.4, 136.2, 127.9, 125.1, 124.7, 124.5, 124.3, 123.4, 122.1, 119.7; IR (neat, cm^{-1}) 3064, 1556, 1499, 1434, 1415, 815, 691; LRMS (EI, 70 eV) m/z (%) 216 (M$^+$, 100), 184 (12), 171 (19), 108 (11).

3-(Benzo[b]thiophen-2-yl)pyridine[19] (***2l***): White solid (29.5 mg, 70%), mp 131.2−132.0 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.99 (s, 1H), 8.57

(d, J = 4.5 Hz, 1H), 7.96 (d, J = 8.0 Hz, 1H), 7.85 (d, J = 7.5 Hz, 1H), 7.81 (d, J = 7.5 Hz, 1H), 7.60 (s, 1H), 7.38−7.34 (m, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 149.2, 147.5, 140.4, 140.2, 139.7, 133.5, 130.3, 124.9, 124.8, 123.8, 123.7, 122.3, 120.7; IR (neat, cm^{-1}) 3055, 1568, 1523, 1478, 1435, 1301,1192; LRMS (EI, 70 eV) m/z (%) 211 (M^+, 100), 167 (12), 139 (17), 79 (9).

Benzo[b]thiophene[8] (***2m***): White solid (8.1 mg, 30%), mp 29.2−31.0 °C.^{1}H NMR (500 MHz, $CDCl_3$) δ 7.89 (d, J = 7.5 Hz, 1H), 7.83 (d, J = 8.0 Hz, 1H), 7.44 (d, J = 5.5 Hz, 1H), 7.38−7.33 (m, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 139.7, 139.6, 126.3, 124.2, 124.1, 123.8, 123.6, 122.5; IR (neat, cm^{-1}) 3049, 1586, 1456, 1414, 1344, 795, 761; LRMS (EI, 70 eV) m/z (%) 134 (M^+, 100), 89 (11), 63 (6).

2-(Trifluoromethyl)benzo[b]thiophene[20] (***2n***): White solid (16.9 mg, 42%), mp 49.4−50.1 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.89−7.86 (m, 2H), 7.69 (s, 1H), 7.48−7.42 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 140.2, 137.8, 131.3 (q, J_{C-F} = 32 Hz) 126.6, 125.6 (q, J_{C-F} = 4.0 Hz), 125.2, 125.1, 122.6, 122.5 (q, J_{C-F} = 267.8 Hz); IR (neat, cm^{-1}) 1538, 1336, 1295, 1267, 1156; LRMS (EI, 70 eV) m/z (%) 202 (M^+, 100), 183 (33), 152 (28).

6-Methyl-2-phenylbenzo[b]thiophene[21] (***2p***): White solid (33.6 mg, 75%), mp 145.0−147.4 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.69 (d, J = 7.5 Hz, 1H), 7.65 (d, J = 8.0 Hz, 1H), 7.62 (s, 1H), 7.49 (s, 1H), 7.42−7.39 (m, 2H), 7.33−7.30 (m, 2H), 7.16 (d, J = 8.0 Hz, 1H), 2.47 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 143.0, 139.8, 138.5, 134.3, 133.4, 128.9, 128.0, 126.3, 126.2, 123.2, 122.1, 119.2, 21.6; IR (neat, cm^{-1}) 3023, 2911, 1601, 1524, 1485, 1443, 840, 725; LRMS (EI, 70 eV) m/z (%) 224 (M^+, 100), 189 (6), 147 (7), 112 (8).

2-(4-Methoxyphenyl)-6-methylbenzo[b]thiophene (***2q***): White solid (35.6 mg, 70%), mp 208.0−209.3 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.63−7.60 (m, 4H), 7.37 (s, 1H), 7.15 (d, J = 8.0 Hz, 1H), 6.94 (d, J = 9.0 Hz, 2H), 3.85 (s, 3H), 2.46 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 159.6, 142.9, 139.5, 138.7, 133.9, 127.6, 127.3, 126.1, 122.9, 122.0, 118.0, 114.3, 55.4, 21.6; IR (neat, cm^{-1}) 1604, 1529, 1497, 1255, 1177, 1032; LRMS (EI, 70 eV) m/z (%) 254 (M^+, 100), 239 (67), 211 (27), 207 (38); HRMS (EI) calcd for $C_{16}H_{14}OS^+$ (M^+) 254.0760, found 254.0764.

6-Methyl-2-(4-(trifluoromethyl)phenyl)benzo[b]thiophene (***2r***): White solid (43.8 mg, 75%), mp 184.3−186.1 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.79 (d, J = 8.5 Hz, 1H), 7.69−7.64 (m, 3H), 7.61 (s, 1H), 7.57−7.53 (m, 2H), 7.19 (d, J = 8.0 Hz, 1H), 2.48 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 141.1, 140.2, 138.2, 138.0, 133.6, 129.3 (q, J_{C-F} = 34.0 Hz), 126.4, 125.9 (q, J_{C-F} = 3.8 Hz), 124.1 (q, J_{C-F} = 275.1 Hz), 123.6, 122.2, 120.8, 120.5, 21.6; IR (neat, cm^{-1}) 2920, 2856, 1614, 1595, 1508, 1479; LRMS (EI, 70 eV) m/z (%) 292 (M^+, 100), 246 (8), 221 (11), 192 (6); HRMS (EI) calcd for $C_{14}H_{10}F_3S^+$ (M^+) 292.0528, found 292.0528.

6-Fluoro-2-phenylbenzo[b]thiophene (***2s***): White solid (31.8 mg, 70%), mp 161.4−163.8 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.71−7.67 (m, 3H), 7.52−7.49 (m, 2H), 7.44−7.41 (m, 2H), 7.36−7.33 (m, 1H), 7.12−7.08 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 160.5 (d, J_{C-F} = 242.5 Hz), 144.0, 140.4 (d, J_{C-F} = 10.0 Hz), 137.2, 134.0, 129.0, 128.3, 126.4, 124.5 (d, J_{C-F} = 9.0 Hz), 118.8, 113.5 (d, J_{C-F} = 24.0 Hz), 108.4 (d, J_{C-F} = 25.0 Hz); IR (neat, cm^{-1}) 2972, 1713, 1598, 1566, 1468, 1251; LRMS (EI, 70 eV) m/z (%) 228 (M^+, 100), 183 (18), 114 (12), 101 (6); HRMS (EI) calcd for $C_{14}H_9FS^+$ (M^+) 228.0404, found 228.0405.

6-Fluoro-2-p-tolylbenzo[b]thiophene (***2t***): White solid (32.9 mg, 68%), mp 198.4−200.2 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.69−7.66 (m, 1H), 7.57 (d, J = 8.0 Hz, 2H), 7.50−7.48 (m, 1H), 7.44 (s, 1H), 7.23 (d, J = 8.0 Hz, 2H), 7.11−7.07 (m, 1H), 2.39 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 160.4 (d, J_{C-F} = 242.6 Hz), 144.1, 140.2 (d, J_{C-F} = 10.0 Hz), 138.3, 137.2, 131.2, 129.7, 126.2, 124.3 (d, J_{C-F} = 9.0 Hz), 118.2, 113.4 (d, J_{C-F} = 24.0 Hz), 108.4 (d, J_{C-F} = 25.0 Hz), 21.2; IR (neat, cm^{-1}) 3023, 2917, 1606, 1537, 1466, 1248, 850; LRMS (EI, 70 eV) m/z (%) 242 (M^+, 100), 226 (5), 1976 (4), 121 (7); HRMS (EI) calcd for $C_{15}H_{11}FS^+$ (M^+) 242.0560, found 242.0561.

6-Fluoro-2-(4-(trifluoromethyl)phenyl)benzo[b]thiophene (***2u***): White solid (49.6 mg, 84%), mp 163.2−164.0 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.79−7.71 (m, 3H), 7.66 (d, J = 8.0 Hz, 2H), 7.56 (s, 1H), 7.51 (d, J = 8.5 Hz, 1H), 7.14−7.11 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 160.8 (d, J_{C-F} = 244.0 Hz), 142.0, 140.7 (d, J_{C-F} = 10.0 Hz), 137.4, 136.9, 130.0 (q, J_{C-F} = 32.0 Hz), 126.4, 126.0 (q, J_{C-F} = 4.0 Hz), 125.0 (d, J_{C-F} = 9.0 Hz), 124.0 (q, J_{C-F} = 270.4 Hz), 120.4, 113.9 (d, J_{C-F} = 24.0 Hz), 108.5 (d, J_{C-F} = 25.0 Hz); IR (neat, cm^{-1}) 3080, 1617, 1598, 1566, 1469; LRMS (EI, 70 eV) m/z (%) 296 (M^+, 100), 264 (8), 226 (8), 123 (12); HRMS (EI) calcd for $C_{15}H_8F_4S^+$ (M^+) 296.0277, found 296.0287.

6-Chloro-2-phenylbenzo[b]thiophene[22] (***2v***): White solid (36.0 mg, 74%), mp 192.6−194.8 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.79 (s, 1H), 7.69−7.66 (m, 3H), 7.49 (s, 1H), 7.44−7.41 (m, 2H), 7.37−7.34 (m, 1H), 7.31 (d, J = 8.5 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 144.9, 140.5, 139.1, 133.8, 130.3, 129.0, 128.5, 126.4, 125.3, 124.3, 121.8, 118.9; IR (neat, cm^{-1}) 3023, 1520, 1445, 1099, 803; LRMS (EI, 70 eV) m/z (%) 246 (M^+, 38), 244 (M^+, 100), 208 (23), 165 (23).

■ ASSOCIATED CONTENT

Supporting Information. Copies of ^{1}H and ^{13}C NMR of compounds **2a**−**2v**. This material is available free of charge via the Internet at http://pubs.acs.org.

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■ ACKNOWLEDGMENT

We thank the National Natural Science Foundation of China (No. 21002070) and Zhejiang Provincial Natural Science Foundation of China (No. Y4100307) for financial support.

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