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SYNTHESIS OF 2-(ALKYL(OR ARYL)SULFANYL)BENZO[*b*]THIOPHEN-3-AMINES BY LDA-MEDIATED CYCLIZATION OF 2-{[(ALKYL(OR ARYL)SULFANYL)METHYL]SULFANYL}BENZONITRILES

Kazuhiro Kobayashi* and Keita Yamashita

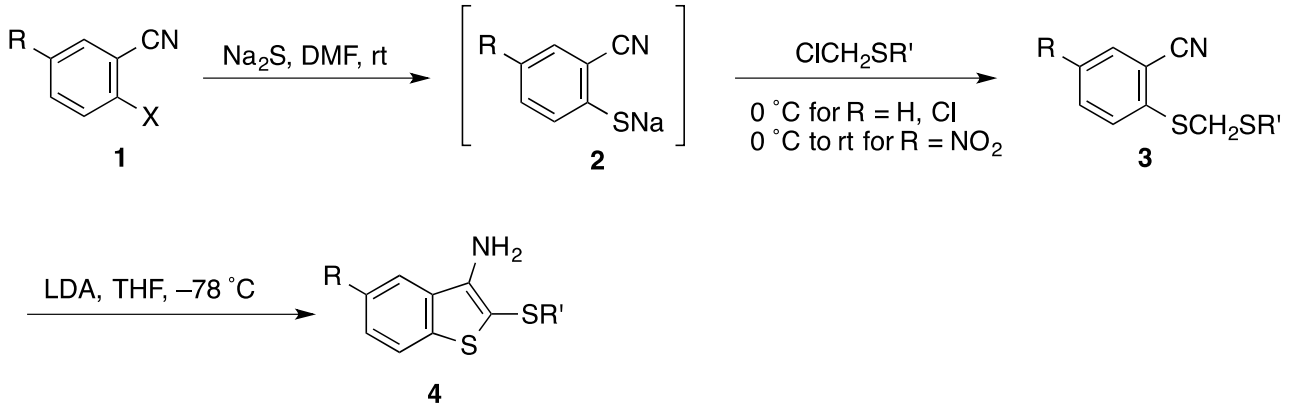
Division of Applied Chemistry, Department of Chemistry and Biotechnology, Graduate School of Engineering, Tottori University, 4-101 Koyama-minami, Tottori 680-8552, Japan; E-mail: kkoba@chem.tottori-u.ac.jp

Abstract – A new and convenient method for the preparation of 2-(alkyl(or aryl)sulfanyl)benzo[*b*]thiophen-3-amines has been developed. Thus, 2-{[(alkyl(or aryl)sulfanyl)methyl]sulfanyl}benzonitriles, prepared by successive treatment of 2-halobenzonitriles with anhydrous disodium sulfide and chloromethyl sulfides, are cyclized to the desired products *via* lithiation of the carbon between two sulfur atoms with LDA, followed by addition of the resulting carbanion to the nitrile carbon.

New and efficient methods for the general preparation of benzo[*b*]thiophenes have been being developed[1,2] due to importance of these derivatives in heterocyclic chemistry. However, there have been no general methods for the preparation of 2-(alkyl(or aryl)sulfanyl)benzo[*b*]thiophen-3-amines of potential biological interest so far, though the synthesis of 2-(ethylsulfanyl)- and 2-(butylsulfanyl)benzo[*b*]thiophen-3-amines by the reaction of 3-azidobenzo[*b*]thiophene with ethanethiol and butanethiol, respectively, has been reported by Toselli *et al*.[3] Accordingly, development of a new and convenient method for the general preparation of 2-(alkyl(or aryl)sulfanyl)benzo[*b*]thiophen-3-amines is meaningful. In this paper, we wish to report the results of our study that offers a novel and facile route to 2-(alkyl(or aryl)sulfanyl)benzo[*b*]thiophen-3-amines. We have found that the treatment of 2-{[(alkyl(or aryl)sulfanyl)methyl]sulfanyl}benzonitriles (**3**) with lithium diisopropylamide (LDA) provides the corresponding 2-(alkyl(or aryl)sulfanyl)benzo[*b*]thiophen-3-amines (**4**). It should be noted that constructions of 2-substituted benzo[*b*]thiophen-3-amine structures by

cyclization of 2-[(aryl-, nitro-, and alkoxycarbonyl-methyl)sulfanyl]benzonitriles with appropriate bases have been reported.[4]

Our investigations began with the preparation of **3** from commercially available 2-halobenzonitriles **1**. As shown in Scheme 1, compounds (**1**) were treated with anhydrous disodium sulfide in DMF at room temperature, and the resulting sodium 2-cyanobenznethiolates (**2**) were allowed to react with alkyl(or aryl) chloromethyl sulfides to afford **3** in moderate yields, as compiled in Table 1. As can be seen from it, the yields of the products from 2,5-dichlorobenzonitrile (**1b**) (Entries 6–10) were somewhat lower than those from 2-fluorobenzonitrile (**1a**) and 2-chloro-5-nitrobenzonitrile (**1c**) (Entries 1–5 and 11).



Scheme 1

Table 1. Preparation of 2-(alkyl(or aryl)sulfanyl)benzo[*b*]thiophen-3-amines (**4**)

Entry	**1**	R'	**3**	Yield/%[a]	**4**	Yield/%[a]
1	**1a** (X = F, R = H)	Me	**3a**	55	**4a**	72
2	**1a**	*t*-Bu	**3b**	63	**4b**	84
3	**1a**	Ph	**3c**	54	**4c**	83
4	**1a**	4-ClC_6H_4	**3d**	63	**4d**	79
5	**1a**	4-$MeOC_6H_4$	**3e**	59	**4e**	86
6	**1b** (X = R = Cl)	Me	**3f**	41	**4f**	76
7	**1b**	*t*-Bu	**3g**	41	**4g**	80
8	**1b**	Ph	**3h**	40	**4h**	80
9	**1b**	4-ClC_6H_4	**3i**	40	**4i**	56
10	**1b**	4-$MeOC_6H_4$	**3j**	37	**4j**	79
11	**1c** (X = Cl, R = NO_2)	Ph	**3k**	54	**4k**	60

[a] Yields of isolated products.

The reaction of sulfanylated benzonitriles (**3**), thus obtained, with two equivalent of LDA in THF at –78 ˚C caused cyclization quickly through attack of the resulting carbanion between two sulfur atoms on the nitrile carbon. After aqueous work up followed by purification of the crude products using column chromatography on silica gel, the desired products (**4**) were obtained. The yields are summarized in Table 1 as well. Entry 9 indicates that the yield of the product (**4i**) is somewhat lower than those of the others,

though the reason for this is not clear. It should be noted that the use of an equivalent of LDA caused decrease in the yields of the products; considerable quantities of the starting materials were recovered.

In conclusion, we have demonstrated that 2-(alkyl(or aryl)sulfanyl)benzo[*b*]thiophen-3-amines can be prepared from 2-halobenzonitriles utilizing a two-step sequence. The present method may be of value in organic synthesis because of the simple experimental operations and may offer interesting pharmacophores.

EXPERIMENTAL

All melting points were obtained on a Laboratory Devices MEL-TEMP II melting apparatus and are uncorrected. IR spectra were recorded with a Perkin/Elmer Spectrum 65 FTIR spectrophotometer. ^{1}H NMR and ^{13}C NMR spectra were recorded in $CDCl_3$ (unless otherwise stated) using TMS as an internal reference with a Bruker Biospin AVANCE II 600 spectrometer operating at 600 MHz and 150 MHz, respectively, or a JEOL ECP500 FT NMR spectrometer operating at 500 and 125 MHz, respectively. High-resolution MS spectra were measured by a JEOL JMS-T100GCV spectrometer (EI or FI, TOF; 70eV or 2100V, respectively) or a Thermo Scientific Exactive spectrometer (ESI, positive). Elemental analyses were performed with an Elementar Vario EL II instrument. TLC was carried out on Merck Kieselgel 60 PF_{254}. Column chromatography was performed using WAKO GEL C-200E. All of the organic solvents used in this study were dried over appropriate drying agents and distilled prior to use.

Starting Materials. 2-[(Chloromethyl)sulfanyl]-2-methylpropane,[5] 1-chloro-4-[(chloromethyl)sulfanyl]-benzene,[2] and 1-[(chloromethyl)sulfanyl]-4-methoxybenzene[6] were prepared according to the appropriate reported procedures. *n*-BuLi was supplied by Asia Lithium Corporation. All chemicals used in this study were commercially available.

Typical Procedure for the Preparation of 2-{[(Alkyl(or aryl)sulfanyl)methyl]sulfanyl}benzonitriles (3a-j). 2-[(Methylsulfanyl)methylsulfanyl]benzonitrile (3a). To a stirred suspension of anhydrous Na_2S (0.31 g, 4.0 mmol) in DMF (6 mL) at rt was added 2-fluorobenzonitrile (0.48 g, 4.0 mmol) and stirring was continued overnight. The mixture was then cooled to 0 ˚C and $ClCH_2SMe$ (0.39 g, 4.0 mmol) was added dropwise. After 5 min, saturated aqueous NH_4Cl (40 mL) was added and the mixture was extracted with AcOEt (3 × 20 mL). The combined extracts were washed with H_2O (3 × 20 mL) and brine (20 mL), dried (Na_2SO_4), and concentrated by evaporation. The residue was purified by column chromatography on SiO_2 to afford **3a** (0.41 g, 55%); a pale-yellow oil; R_f 0.27 (Et_2O/hexane 1:7); IR (neat) 2223 cm^{-1}; ^{1}H NMR (500 MHz) δ 2.28 (s, 3H), 4.09 (s, 2H), 7.36 (td, *J* = 7.4, 1.1 Hz, 1H), 7.55 (ddd, *J* = 8.0, 7.4, 1.1 Hz, 1H), 7.59 (d, *J* = 7.4 Hz, 1H), 7.66 (d, *J* = 8.0 Hz, 1H); ^{13}C NMR (125 MHz) δ 15.24, 40.65, 115.69, 117.11, 127.39, 131.91, 132.28, 133.71, 139.29. MR-MS (EI). Calcd for $C_9H_9NS_2$ (M): 195.0176. Found: *m/z* 195.0167.

2-{[(1,1-Dimethylethyl)sulfanyl]methylsulfanyl}benzonitrile (3b): a pale-yellow oil; R_f 0.38 (Et_2O/hexane 1:7); IR (neat) 2223 cm^{-1}; ^1H NMR (500 MHz) δ 1.40 (s, 9H), 4.16 (s, 2H), 7.32 (td, J = 7.4, 1.7 Hz, 1H), 7.54 (ddd, J = 8.0, 7.4, 1.7 Hz, 1H), 7.57 (dd, J = 7.4, 1.7 Hz, 1H), 7.65 (d, J = 8.0 Hz, 1H); ^{13}C NMR (125 MHz) δ 30.89, 34.07, 44.33, 114.27, 117.11, 126.84, 130.53, 132.86, 133.70, 140.55. HR-MS (EI). Calcd for $C_{12}H_{15}NS_2$ (M): 237.0646. Found: *m/z* 237.0654.

2-[(Phenylsulfanyl)methylsulfanyl]benzonitrile (3c): a light brown oil; R_f 0.34 (CH_2Cl_2/hexane 1:2); IR (neat) 2223 cm^{-1}; ^1H NMR (500 MHz) δ 4.44 (s, 2H), 7.27 (t, J = 7.4 Hz, 1H), 7.31–7.36 (m, 3H), 7.44 (d, J = 7.4 Hz, 2H), 7.53 (t, J = 7.4 Hz, 1H), 7.56 (d, J = 7.4 Hz, 1H), 7.65 (d, J = 7.4 Hz, 1H); ^{13}C NMR (125 MHz) δ 40.58, 115.31, 117.00, 127.44, 127.64, 129.13, 131.23, 131.80, 132.83, 133.78, 133.97, 139.19. HR-MS (EI). Calcd for $C_{14}H_{11}NS_2$ (M): 257.0333. Found: *m/z* 257.0327.

2-{[(4-Chlorophenyl)sulfanyl]methylsulfanyl}benzonitrile (3d): a white solid; mp 71–73 ˚C (hexane/CH_2Cl_2); IR (KBr) 2224 cm^{-1}; ^1H NMR (500 MHz) δ 4.42 (s, 2H), 7.30 (d, J = 8.0 Hz, 2H), 7.36–7.40 (m, 3H), 7.52–7.56 (m, 2H), 7.67 (dd, J = 7.4, 1.7 Hz, 1H); ^{13}C NMR (125 MHz) δ 40.90, 115.57, 117.01, 127.68, 129.28, 132.12, 132.29, 132.73, 132.89, 133.85, 133.92, 138.72. Anal. Calcd for $C_{14}H_{10}ClNS_2$: C, 57.62; H, 3.45; N, 4.80. Found: C, 57.32; H, 3.51; N, 4.76.

2-{[(4-Methoxyphenyl)sulfanyl]methylsulfanyl}benzonitrile (3e): a white solid; mp 63–65 ˚C (hexane/CH_2Cl_2); IR (KBr) 2221 cm^{-1}; ^1H NMR (500 MHz) δ 3.81 (s, 3H), 4.34 (s, 3H), 6.86 (d, J = 8.6 Hz, 2H), 7.32 (ddd, J = 8.0, 6.3, 2.3 Hz, 1H), 7.43 (d, J = 8.6 Hz, 2H), 7.51–7.55 (m, 1H), 7.64 (d, J = 8.0 Hz, 1H); ^{13}C NMR (125 MHz) δ 42.39, 55.34, 114.72, 114.84, 117.06, 123.98, 127.10, 131.20, 132.81, 133.75, 135.09, 139.63, 160.01. Anal. Calcd for $C_{15}H_{13}NOS_2$: C, 62.69; H, 4.56; N, 4.87. Found: C, 62.51; H, 4.55; N, 4.86.

5-Chloro-2-[(methylsulfanyl)methylsulfanyl]benzonitrile (3f): a yellow liquid; R_f 0.30 (CH_2Cl_2/hexane 1:2); IR (neat) 2226 cm^{-1}; ^1H NMR (500 MHz) δ 2.27 (s, 3H), 4.07 (s, 2H), 7.53 (br s, 2H), 7.64 (br s, 1H); ^{13}C NMR (125 MHz) δ 15.19, 40.89, 115.91, 117.14, 133.15, 133.17, 133.31, 133.61, 137.67. HR-MS (EI). Calcd for $C_9H_8ClNS_2$ (M): 228.9787. Found: *m/z* 228.9790.

5-Chloro-2-{[(1,1-dimethylethyl)sulfanyl]methylsulfanyl}benzonitrile (3g): a yellow oil; R_f 0.29 (CH_2Cl_2/hexane 1:4); IR (neat) 2223 cm^{-1}; ^1H NMR (600 MHz) δ 1.39 (s, 9H), 4.13 (s, 2H), 7.49–7.51 (m, 2H), 7.62 (t, J = 1.3 Hz, 1H); ^{13}C NMR (150 MHz) δ 30.92, 34.40, 44.48, 115.89, 115.92, 132.13, 133.04, 133.17, 133.19, 139.05. HR-MS (ESI). Calcd for $C_{12}H_{14}ClNNaS_2$ (M+Na): 294.0154. Found: *m/z* 294.0148.

5-Chloro-2-[(phenylsulfanyl)methylsulfanyl]benzonitrile (3h): a yellow oil; R_f 0.31 (CH_2Cl_2/hexane 1:4); IR (neat) 2225 cm^{-1}; ^1H NMR (500 MHz) δ 4.42 (s, 2H), 7.27–7.34 (m, 3H), 7.42 (d, J = 7.4 Hz, 2H), 7.48 (br s, 2H), 7.60 (br s, 1H); ^{13}C NMR (125 MHz) δ 40.85, 115.82, 116.83, 127.77, 129.18,

131.35, 133.11, 133.25, 133.34, 133.60, 133.69, 137.53. Anal. Calcd for $C_{14}H_{10}ClNS_2$: C, 57.62; H, 3.45; N, 4.80. Found: C, 57.67; H, 3.74; N, 4.78.

5-Chloro-2-{[(4-chlorophenyl)sulfanyl]methylsulfanyl}benzonitrile (3i): a pale-yellow viscous oil; R_f 0.38 (CH_2Cl_2/hexane 1:5); IR (neat) 2207 cm^{-1}; ^1H NMR (600 MHz) δ 4.39 (s, 2H), 7.30 (d, J = 8.3 Hz, 2H), 7.36 (d, J = 8.3 Hz, 2H), 7.48 (d, J = 8.3 Hz, 1H), 7.50 (dd, J = 8.3, 2.1 Hz, 1H), 7.62 (d, J = 2.1 Hz, 1H); ^{13}C NMR (150 MHz) δ 41.18, 115.83, 117.19, 129.39, 132.06, 132.84, 133.21, 133.37, 133.66, 134.06, 134.17, 137.18. HR-MS (FI). Calcd for $C_{14}H_9Cl_2NS_2$ (M): 324.9553. Found: *m/z* 324.9541.

5-Chloro-2-{[(4-methoxyphenyl)sulfanyl]methylsulfanyl}benzonitrile (3j): a pale-yellow oil; R_f 0.22 (CH_2Cl_2/hexane 1:2); IR (neat) 2225 cm^{-1}; ^1H NMR (500 MHz) δ 3.81 (s, 3H), 4.32 (s, 2H), 6.85 (d, J = 8.6 Hz, 2H), 7.40 (d, J = 8.6 Hz, 2H), 7.46 (d, J = 8.6 Hz, 1H), 7.48 (dd, J = 8.6, 1.7 Hz, 1H), 7.59 (d, J = 1.7 Hz, 1H); ^{13}C NMR (125 MHz) δ 42.61, 55.35, 114.75, 115.85, 116.37, 123.66, 132.75, 133.06, 133.18, 133.27, 135.11, 138.05, 160.10. HR-MS (FI). Calcd for $C_{15}H_{12}ClNOS_2$ (M): 321.0049. Found: *m/z* 321.0057.

5-Nitro-2-[(phenylsulfanyl)methylsulfanyl]benzonitrile (3k). To a stirred suspension of anhydrous Na_2S (0.16 g, 2.0 mmol) in DMF (2 mL) at rt was added a solution of 2-chloro-5-nitrobenzonitrile (0.37 g, 2.0 mmol) in DMF (1 mL) and stirring was continued overnight. The mixture was then cooled to 0 ˚C and $ClCH_2SPh$ (0.32 g, 2.0 mmol) was added dropwise, then temperature was raised to rt and stirring was continued for a day. The resulting mixture was worked up as described for the preparation of **3a** and the crude product was purified by column chromatography on SiO_2 to afford **3k** (0.32 g, 54%); a yellow oil; R_f 0.32 (CH_2Cl_2/hexane 2:1); IR (neat) 2229, 1520, 1347 cm^{-1}; ^1H NMR (500 MHz) δ 4.52 (s, 2H), 7.32–7.38 (m, 3H), 7.47 (dd, J = 8.0, 1.7 Hz, 2H), 7.59 (d, J = 9.2 Hz, 1H), 8.35 (dd, J = 9.2, 2.3 Hz, 1H), 8.45 (d, J = 2.3 Hz, 1H); ^{13}C NMR (125 MHz) δ 39.09, 112.54, 114.68, 127.15, 127.67, 128.49, 128.57, 129.40, 132.08, 132.63, 144.92, 149.74. HR-MS (EI). Calcd for $C_{14}H_{10}N_2O_2S_2$ (M): 302.0184. Found: *m/z* 302.0188.

Typical Procedure for the Preparation of 2-(Alkyl(or aryl)sulfanyl)benzo[*b*]thiophen-3-amines (4). 2-(Methylsulfanyl)benzo[*b*]thiophen-3-amine (4a). To a stirred solution of LDA (2.5 mmol), generated from *i*-Pr_2NH and *n*-BuLi by the standard method, in THF (4 mL) at –78 ˚C was added a solution of **3a** (0.25 g, 1.3 mmol) in THF (4 mL) dropwise. After 20 min, saturated aqueous NH_4Cl (15 mL) was added and the mixture was extracted with AcOEt (3 × 15 mL). The combined extracts were washed with brine (15 mL), dried (Na_2SO_4), and concentrated by evaporation. The residue was purified by column chromatography on SiO_2 to afford **4a** (0.18 g, 72%); a beige oil; R_f 0.34 (CH_2Cl_2/hexane 1:2); IR (neat) 3439, 3337, 1606 cm^{-1}; ^1H NMR (500 MHz) δ 2.56 (s, 3H), 4.28 (br s, 2H), 7.32–7.36 (m, 2H), 7.53 (ddd, J = 6.9, 3.4, 2.9 Hz, 1H), 7.69 (ddd, J = 6.9, 3.4, 2.9 Hz, 1H); ^{13}C NMR (125 MHz) δ 20.52, 106.84,

120.31, 122.62, 123.78, 125.45, 132.41, 139.55, 142.11. HR-MS (EI). Calcd for $C_9H_9NS_2$ (M): 195.0176. Found: *m/z* 195.0177. Anal. Calcd for $C_9H_9NS_2$: C, 55.35; H, 4.65; N, 7.17. Found: C, 55.48; H, 4.58; N, 7.22.

2-[(1,1-Dimethylethyl)sulfanyl]benzo[*b*]thiophen-3-amine (4b): a beige oil; R_f 0.47 (AcOEt/hexane 1:10); IR (neat) 3445, 3351, 1604 cm^{-1}; ^1H NMR (500 MHz) δ 1.38 (s, 9H), 4.34 (br s, 2H), 7.33–7.38 (m, 2H), 7.57 (ddd, *J* = 6.9, 3.4, 2.9 Hz, 1H), 7.71 (ddd, *J* = 6.9, 3.4, 2.9 Hz, 1H); ^{13}C NMR (125 MHz) δ 30.98, 49.66, 103.72, 120.60, 122.39, 123.59, 125.62, 132.23, 140.31, 144.49. HR-MS (EI). Calcd for $C_{12}H_{15}NS_2$ (M): 237.0646. Found: *m/z* 237.0649. Anal. Calcd for $C_{12}H_{15}NS_2$: C, 60.72; H, 6.37; N, 5.90. Found: C, 60.62; H, 6.45; N, 5.76.

2-(Phenylsulfanyl)benzo[*b*]thiophen-3-amine (4c): a white solid; mp 71–73 ˚C (hexane/CH_2Cl_2); IR (KBr) 3342, 3356, 1611 cm^{-1}; ^1H NMR (500 MHz) δ 4.38 (br s, 2H), 7.12 (tt, *J* = 7.4, 1.1 Hz, 1H), 7.15 (dd, *J* = 7.4, 1.1 Hz, 2H), 7.23 (t, *J* = 7.4 Hz, 2H), 7.36–7.42 (m, 2H), 7.60 (dd, *J* = 6.9, 1.7 Hz, 1H), 7.73 (dd, *J* = 6.9, 1.7 Hz, 1H); ^{13}C NMR (125 MHz) δ 100.38, 120.70, 122.84, 123.83, 125.66, 126.03, 126.07, 129.04, 132.08, 137.24, 140.57, 144.61. HR-MS (EI). Calcd for $C_{14}H_{11}NS_2$ (M): 257.0333. Found: *m/z* 257.0336. Anal. Calcd for $C_{14}H_{11}NS_2$: C, 65.34; H, 4.31; N, 5.44; S, 24.91. Found: C, 65.24; H, 4.34; N, 5.45; S, 25.16.

2-[4-Chlorophenyl]sulfanyl]benzo[*b*]thiophen-3-amine (4d): a pale-yellow solid; mp 93–95 ˚C (hexane); IR (KBr) 3453, 3353, 1604 cm^{-1}; ^1H NMR (600 MHz) δ 4.40 (br s, 2H), 7.08 (d, *J* = 8.7 Hz, 2H), 7.19 (d, *J* = 8.7 Hz, 2H), 7.39 (td, *J* = 7.2, 1.3 Hz, 1H), 7.42 (td, *J* = 7.2, 1.3 Hz, 1H), 7.60 (dd, *J* = 7.2, 1.3 Hz, 1H), 7.74 (dd, *J* = 7.2, 1.3 Hz, 1H); ^{13}C NMR (150 MHz) δ 99.74, 120.80, 122.92, 123.98, 126.31, 127.39, 129.16, 131.63, 132.01, 135.90, 140.65, 144.91. HR-MS (EI). Calcd for $C_{14}H_{10}ClNS_2$ (M): 290.9943. Found: *m/z* 290.9931. Anal. Calcd for $C_{14}H_{10}ClNS_2$: C, 57.62; H, 3.45; N, 4.80. Found: C, 57.49; H, 3.50; N, 4.81.

2-[4-Methoxyphenyl]sulfanyl]benzo[*b*]thiophen-3-amine (4e): a yellow solid; mp 103–105 ˚C (hexane); IR (KBr) 3449, 3349, 1607 cm^{-1}; ^1H NMR (500 MHz) δ 3.74 (s, 3H), 4.37 (br, 2H), 6.79 (d, *J* = 8.6 Hz, 2H), 7.17 (d, *J* = 8.6 Hz, 2H), 7.35–7.39 (m, 2H), 7.57 (dd, *J* = 6.9, 2.3 Hz, 1H), 7.71 (dd, *J* = 6.9, 2.3 Hz, 1H); ^{13}C NMR (125 MHz) δ 55.34, 102.84, 114.76, 120.62, 122.77, 123.80, 125.89, 127.70, 128.97, 132.19, 140.30, 143.74, 158.41. HR-MS (EI). Calcd for $C_{15}H_{13}NOS_2$ (M): 287.0439. Found: *m/z* 287.0435. Anal. Calcd for $C_{15}H_{13}NOS_2$: C, 62.69; H, 4.56; N, 4.87. Found: C, 62.42; H, 4.80; N, 4.91.

5-Chloro-2-(methylsulfanyl)benzo[*b*]thiophen-3-amine (4f): a yellow oil; R_f 0.44 (AcOEt/hexane 1:2); IR (neat) 3438, 3339, 1607 cm^{-1}; ^1H NMR (500 MHz) δ 2.36 (s, 3H), 4.23 (br s, 2H), 7.30 (dd, *J* = 8.6, 1.7 Hz, 1H), 7.51 (d, *J* = 1.7 Hz, 1H), 7.59 (d, *J* = 8.6 Hz, 1H); ^{13}C NMR (125 MHz) δ 20.49, 109.20, 120.11, 123.63, 125.74, 130.07, 133.52, 137.56, 141.39. HR-MS (EI). Calcd for $C_9H_8ClNS_2$ (M):

228.9787. Found: *m/z* 228.9787. Anal. Calcd for $C_9H_8ClNS_2$: C, 62.69; H, 4.56; N, 4.87. Found: C, 46.91; H, 3.78; N, 6.03.

5-Chloro-2-[(1,1-dimethylethyl)sulfanyl]benzo[*b*]thiophen-3-amine (4g): a yellow solid; mp 106–108 ˚C (hexane); IR (KBr) 3446, 3350, 1604 cm^{-1}; ^1H NMR (600 MHz) δ 1.38 (s, 9H), 4.29 (br, 2H), 7.32 (dd, *J* = 8.6, 2.0 Hz, 1H), 7.55 (d, *J* = 2.0 Hz, 1H), 7.61 (d, *J* = 8.6 Hz, 1H); ^{13}C NMR (150 MHz) δ 31.03, 49.93, 106.14, 120.43, 123.46, 125.97, 129.94, 133.36, 138.34, 143.80. HR-MS (EI). Calcd for $C_{12}H_{14}ClNS_2$ (M): 271.0256. Found: *m/z* 271.0246. Anal. Calcd for $C_{12}H_{14}ClNS_2$: C, 53.02; H, 5.19; N, 5.15. Found: C, 52.93; H, 5.18; N, 5.14.

5-Chloro-2-(phenylsulfanyl)benzo[*b*]thiophen-3-amine (4h): a yellow solid; mp 89–91 ˚C (hexane); IR (KBr) 3455, 3359, 1606 cm^{-1}; ^1H NMR (500 MHz) δ 4.33 (br s, 2H), 7.11–7.16 (m, 3H), 7.23 (t, *J* = 7.4 Hz, 2H), 7.35 (dd, *J* = 8.6, 1.7 Hz, 1H), 7.57 (d, *J* = 1.7 Hz, 1H), 7.63 (d, *J* = 8.6 Hz, 1H); ^{13}C NMR (125 MHz) δ 102.84, 120.51, 123.86, 125.89, 126.19, 126.40, 129.11, 130.18, 133.17, 136.77, 138.52, 143.82. HR-MS (EI). Calcd for $C_{14}H_{10}ClNS_2$ (M): 290.9943. Found: *m/z* 290.9953. Anal. Calcd for $C_{14}H_{10}ClNS_2$: C, 57.62; H, 3.45; N, 4.80. Found: C, 57.66; H, 3.53; N, 4.82.

5-Chloro-2-[(4-chlorophenyl)sulfanyl]benzo[*b*]thiophen-3-amine (4i): a pale-yellow solid; mp 109–111 ˚C (hexane/CH_2Cl_2); IR (KBr) 3430, 3346, 1607 cm^{-1}; ^1H NMR (600 MHz) δ 4.35 (br, 2H), 7.07 (d, *J* = 8.6 Hz, 2H), 7.20 (d, *J* = 8.6 Hz, 2H), 7.37 (dd, *J* = 8.6, 2.0 Hz, 1H), 7.58 (d, *J* = 2.0 Hz, 1H), 7.64 (d, *J* = 8.6 Hz, 1H); ^{13}C NMR (150 MHz) δ 102.15, 120.61, 123.95, 126.66, 127.57, 129.25, 130.37, 131.90, 133.09, 135.41, 138.59, 144.01. HR-MS (EI). Calcd for $C_{14}H_9Cl_2NS_2$ (M): 324.9553. Found: *m/z* 324.9551. Anal. Calcd for $C_{14}H_9Cl_2NS_2$: C, 51.54; H, 2.78; N, 4.29. Found: C, 51.60; H, 2.86; N, 4.27.

5-Chloro-2-[(4-methoxyphenyl)sulfanyl]benzo[*b*]thiophen-3-amine (4j): a pale-yellow solid; mp 99–101 ˚C (hexane/CH_2Cl_2); IR (KBr) 3449, 3349, 1607 cm^{-1}; ^1H NMR (500 MHz) δ 3.74 (s, 3H), 4.32 (br s, 2H), 6.79 (d, *J* = 9.2 Hz, 2H), 7.17 (d, *J* = 9.2 Hz, 2H), 7.31 (dd, *J* = 8.6, 2.3 Hz, 1H), 7.54 (d, *J* = 2.3 Hz, 1H), 7.59 (d, *J* = 8.6 Hz, 1H); ^{13}C NMR (125 MHz) δ 55.32, 105.41, 114.80, 120.39, 123.77, 126.17, 127.16, 129.35, 130.11, 133.29, 138.21, 142.84, 158.58. HR-MS (EI). Calcd for $C_{15}H_{12}ClNOS_2$ (M): 321.0049. Found: *m/z* 321.0055. Anal. Calcd for $C_{15}H_{12}ClNOS_2$: C, 55.98; H, 3.76; N, 4.35. Found: C, 55.97; H, 3.75; N, 4.23.

5-Nitro-2-(phenylsulfanyl)benzo[*b*]thiophen-3-amine (4k): a red solid; mp 163–165 ˚C (hexane/CH_2Cl_2); IR (KBr) 3464, 3369, 1621, 1505, 1331 cm^{-1}; ^1H NMR (500 MHz, DMSO-d_6) δ 5.93 (br s, 2H), 6.68–6.72 (m, 3H), 6.83 (d, *J* = 6.9 Hz, 2H), 7.63 (d, *J* = 8.6 Hz, 1H), 7.75 (d, *J* = 8.6 Hz, 1H), 8.63 (s, 1H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 96.12, 118.31, 119.88, 123.81, 125.90, 126.00, 129.26, 131.90, 136.87, 144.43, 145.78, 147.80. HR-MS (EI). Calcd for $C_{14}H_{10}N_2O_2S_2$ (M): 302.0184. Found: *m/z* 302.0182. Anal. Calcd for $C_{14}H_{10}N_2O_2S_2$: C, 55.61; H, 3.33; N, 9.26. Found: C, 55.52; H, 3.45; N, 9.21.

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