Three-Step Synthesis of 3-Aryl-2-sulfanylthieno[2,3-*b*]-, -[2,3-*c*]-, or -[3,2-*c*]pyridines from the Corresponding Aryl(halopyridinyl)methanones

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A convenient three-step procedure for the synthesis of three types of 3-aryl-2-sulfanylthienopyridines **4**, **8**, and **12** has been developed. The first step of the synthesis of thieno[2,3-*b*]pyridine derivatives **4** is the replacement of the halo with a (sulfanylmethyl)sulfanyl group in aryl(2-halopyridin-3-yl)methanones **1** by successive treatment with $Na_2S \cdot 9\ H_2O$ and chloromethyl sulfides to give aryl{2-[(sulfanylmethyl)sulfanyl]pyridin-3-yl}methanones **2**. In the second step, these were treated with LDA (LiN^iPr_2) to give 3-aryl-2,3-dihydro-2-sulfanylthieno[2,3-*b*]pyridin-3-ols **3**, which were dehydrated in the last step with $SOCl_2$ in the presence of pyridine to give the desired products. Similarly, thieno[2,3-*c*]pyridine and thieno[3,2-*c*]pyridine derivatives, **8** and **12**, respectively, can be prepared from aryl(3-chloropyridin-4-yl)methanones **5** and aryl(4-chloropyridin-3-yl)methanones **9**, respectively.

Introduction. – Recently, thienopyridine derivatives have attracted intense interest from synthetic and medicinal chemists due to their biological properties[1]). Although the syntheses of thieno[2,3-*b*]pyridine[2]), thieno[2,3-*c*]pyridine[3]), and thieno[3,2-*c*]pyridine derivatives[4]) have been reported by a number of groups, there have been few reports on methods for preparing the corresponding 2-sulfanylated derivatives[5]), which may also be of potential importance from a biological point of view [9]. Therefore, we became interested in developing a synthetic approach applicable to all of these three 2-sulfanylated thieno-pyridine derivatives as an extension of our previous work, in which 2-sulfanylated 3-arylbenzo[*b*]thiophenes were synthesized by intramolecular cyclization of aryl{2-[(sulfanylmethyl)sulfanyl]phenyl}methanones using 2 mol-equiv. of LiN^iPr_2 (LDA) and subsequent dehydration of the resulting 3-aryl-2,3-dihydro-2-sulfanylbenzo[*b*]thiophen-3-ols [10]. We herein describe the results of our

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1) For recent reports on the biological activity of compounds having the thieno[2,3-*b*]pyridine moiety, see [1] and also pertinent references cited in [2] and [3]. For recent reports on the biological activity of compounds having the thieno[2,3-*c*]pyridine moiety, see [4] and also pertinent references cited in [3]. For recent reports on the biological activity of compounds having the thieno[3,2-*c*]pyridine moiety, see [5] and [4a], as well as pertinent references cited in [3].

2) For recent reports on the synthesis of thieno[2,3-*b*]pyridine derivatives, see [6], and also [2] and [3] and pertinent references cited therein.

3) For recent reports on the synthesis of thieno[2,3-*c*]pyridine derivatives, see [7] and [3] and pertinent references cited therein.

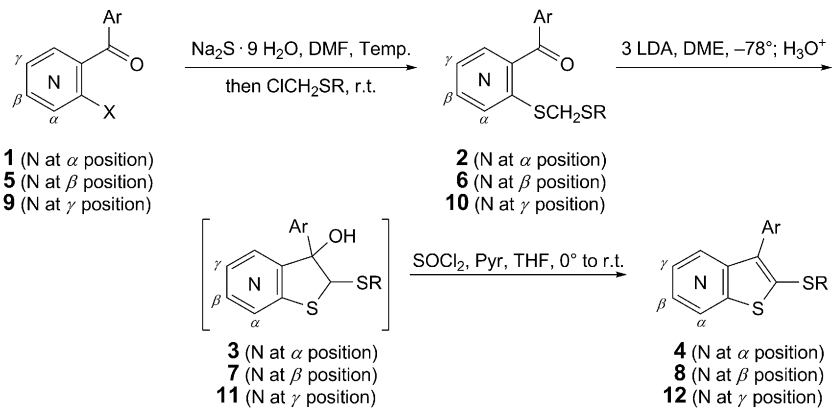
4) For recent reports on the synthesis of thieno[3,2-*c*]pyridine derivatives, see [3] and pertinent references cited therein.

5) 2-(Methylsulfanyl)thienopyridine-3-carboxylic acid derivatives were synthesized previously [8].

study, which provide a convenient synthetic route to 3-aryl-2-sulfanylthieno[2,3-*b*]-, -[2,3-*c*]-, or -[3,2-*c*]pyridines starting from the respective aryl(halopyridinyl)methanones, employing this 2-sulfanylated-thiophene ring-forming methodology.

Results and Discussion. – Our syntheses of 3-aryl-2-sulfanylthienopyridines **4**, **8**, and **12** were conducted following the procedure outlined in the *Scheme* and the results obtained are compiled in the *Table*. First, preparation of 3-aryl-2-sulfanylthieno[2,3-*b*]pyridines **3** from aryl(2-halopyridin-3-yl)methanones **1**, which could be easily prepared from 2-chloropyridine or 2-bromopyridine according to the methods described in [2][3][11], was carried out. The reaction of **1** with $Na_2S \cdot 9\ H_2O$ in DMF at 70°, followed by sulfanylmethylation with chloromethyl sulfides at room temperature, furnished aryl{2-[(sulfanylmethyl)sulfanyl]pyridin-3-yl}methanones **2** in moderate yields. Cyclization *via* the addition of the carbanions between the two S-atoms (dithioacetal anions[6])), generated by treatment of **2** with 3 mol-equiv. of LDA[7]) in DME at −78°, to the C=O group proceeded relatively cleanly by raising the reaction temperature to 0° to give, after aqueous workup, the corresponding 2,3-dihydrothieno[2,3-*b*]pyridin-3-ols **3** as mixtures of diastereisomers, as judged by TLC analyses (SiO_2). These crude alcohols, without any purification, were subjected to the dehydration with $SOCl_2$ in THF in the presence of pyridine (0° – room temperature) to afford the desired products **4** in acceptable overall yields from **2** (*Table*, *Entries 1–5*).

Scheme



1 (N at α position)
5 (N at β position)
9 (N at γ position)

2 (N at α position)
6 (N at β position)
10 (N at γ position)

3 (N at α position)
7 (N at β position)
11 (N at γ position)

4 (N at α position)
8 (N at β position)
12 (N at γ position)

Next, the synthesis of 3-aryl-2-sulfanylthieno[2,3-*c*]pyridines **8** from aryl(3-chloropyridin-4-yl)methanones **5** was carried out. The preparation of **5** has also been

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6) For recent relevant reports on the synthesis utilizing dithioacetal anions (*Corey–Seebach* reaction), see [12].

7) The use of 3 equiv. of LDA was essential for satisfactory formation of the desired products. When 2 equiv. of LDA were used for the preparation of benzo[*b*]thiophenes [10], mixtures containing only lower yields of the alcohols and considerable amounts of recovered **2** were obtained, from which the desired products were isolated in yields which never exceeded 20%, though the reason for this is not clear yet.

Table. *Preparation of 3-Aryl-2-sulfanylthienopyridines* **4**, **8**, *and* **12**

Entry	**1**	R	Temp.	**2**, **6**, **10**	Yield[a]) [%]	**4**, **8**, **12**	Yield[a]) [%]
1	**1a** (N = α, Ar = Ph, X = Br)	Ph	70°	**2a**	51	**4a**	54
2	**1a**	Me	70°	**2b**	55	**4b**	50
3	**1a**	^{t}Bu	70°	**2c**	51	**4c**	48
4	**1b** (N = α, Ar = 3-Cl–C_6H_4, X = Br)	Ph	70°	**2d**	52	**4d**	47
5	**1c** (N = α, Ar = 3,4-(OCH_2O)–C_6H_3, X = Cl)	Ph	70°	**2e**	48	**4e**	52
6	**5a** (N = β, Ar = Ph, X = Cl)	Ph	80°	**6a**	74	**8a**	59
7	**5a**	Me	80°	**6b**	73	**8b**	57
8	**5b** (N = β, Ar = thiophen-2-yl, X = Cl)	Ph	80°	**6c**	71	**8c**	55
9	**5b**	^{t}Bu	80°	**6d**	77	**8d**	56
10	**9a** (N = γ, Ar = Ph, X = Cl)	Ph	60°	**10a**	79	**12a**	51
11	**9a**	^{t}Bu	60°	**10b**	74	**12b**	52
12	**9b** (N = γ, Ar = 4-MeO–C_6H_4, X = Cl)	Ph	60°	**10c**	78	**12c**	52
13	**9b**	Me	60°	**10d**	75	**12d**	49

[a]) Yields of isolated products.

achieved by the method described in [3][11]. The reaction of **5** with $Na_2S \cdot 9\ H_2O$ proceeded more smoothly and cleanly than that of **1** but at somewhat higher temperature to give, after treatment with chloromethyl sulfides, aryl{[3-(sulfanylmethyl)sulfanyl]pyridin-4-yl}methanones **6** in fair-to-good yields. These ketones were treated with LDA, and the resulting 2,3-dihydrothieno[2,3-*c*]pyridin-3-ols **7** were dehydrated in a manner similar to that described for the preparation of **4** to give the desired products **8** in reasonable overall yields from **6** (*Table*, *Entries 6–9*).

Subsequently, attempts were made at obtaining 3-aryl-2-sulfanylthieno[3,2-*c*]pyridines **12** from aryl(4-chloropyridin-3-yl)methanones **9** employing a sequence similar to those for the preparation of **4** and **8**. As can be seen from the *Table*, it was found that the reaction of **9** with $Na_2S \cdot 9\ H_2O$ proceeded smoothly at the lowest temperature of the present three sequences to give the corresponding aryl{[4-(sulfanylmethyl)sulfanyl]pyridin-3-yl}methanones **10** in yields comparable to **6**. Similarly, treatment of these ketones **10** with 3 mol-equiv. of LDA, followed by aqueous workup and subsequent dehydration of the resulting alcohol derivatives **11**, gave the desired products **12** in satisfactory overall yields from **10** (*Table*, *Entries 10–13*).

In conclusion, we have demonstrated that three types of 3-aryl-2-sulfanylthienopyridines can be obtained in reasonable overall yields from the respective aryl(halopyridinyl)methanones employing the essentially same three-step sequence. The present approach has the advantage that the operations are very simple, and the starting materials are readily available.

Experimental Part

General. All of the org. solvents used in this study were dried over appropriate drying agents and distilled prior to use. TLC: *Merck* silica gel *60 PF_{254}*. Column chromatography (CC): *Wako Gel C-200E*. M.p.: *Laboratory Devices MEL-TEMP II* melting point apparatus; uncorrected. IR Spectra: *Shimadzu FTIR-8300* spectrophotometer. ^{1}H-NMR Spectra: in $CDCl_3$ with TMS as an internal reference with a *JEOL ECP500* FT NMR spectrometer, at 500 MHz, or a *JEOL LA400* FT NMR spectrometer, at

400 MHz. ^{13}C-NMR Spectra: in $CDCl_3$ with TMS as an internal reference with a *JEOL ECP500* FT NMR spectrometer, at 125 MHz. LR-MS (EI, 70 eV): with *JEOL JMS AX505 HA* spectrometer.

Aryl(halopyridinyl)methanones **1**, **5**, *and* **9**. These compounds, excluding **5a**, were prepared by the appropriate procedures reported previously by us (**1a** and **1b**: [2], **1c**, **5b**, and **9b**: [3]; **9a**: [11]). BuLi was supplied by *Asia Lithium Corporation*. All other chemicals used in this study were commercially available.

(3-Chloropyridin-4-yl)(phenyl)methanone (**5a**) [13]. This compound was prepared from 3-chloro-4-lithiopyridine [14] with *N,N*-dimethylbenzamide under conditions as described for the preparation of **9a** and **9b** [3][11]. Yield: 61%. Colorless crystals. M.p. 48–49° (hexane). IR (KBr): 1669. ^{1}H-NMR (500 MHz): 7.29 (*d*, *J* = 5.0, 1 H); 7.51 (*dd*, *J* = 8.2, 7.3, 2 H); 7.60 (*tt*, *J* = 7.3, 1.4, 1 H); 7.80 (*d*, *J* = 8.2, 1.4, 2 H); 8.64 (*d*, *J* = 5.0, 1 H); 8.73 (*s*, 1 H).

Aryl[(sulfanylmethylsulfanyl)pyridinyl]methanones **2**, **6**, *and* **10**. *General Procedure*. A mixture of **1**, **5**, or **9** (3.0 mmol) and $Na_2S \cdot 9\,H_2O$ (0.79 g, 3.3 mmol) in DMF (7 ml) was heated at the temp. indicated in the *Table*, under stirring until complete consumption of the starting material was confirmed by TLC (SiO_2) analysis. After cooling to r.t., the appropriate chloromethyl sulfide (3.3 mmol) was added, and the resulting mixture was stirred for 1 h at the same temp., before H_2O (20 ml) was added. The org. materials were extracted with AcOEt (3 × 10 ml), and the combined extracts were washed with H_2O (3 × 10 ml) and then brine (10 ml), dried (Na_2SO_4), and concentrated by evaporation. The residue was purified by CC (SiO_2; THF/hexane 1:5) to afford the desired product.

Phenyl(2-{[(phenylsulfanyl)methyl]sulfanyl}pyridin-3-yl)methanone (**2a**). Yellow solid. M.p. 105–109° (hexane/CH_2Cl_2). IR (KBr): 1661, 1626. ^{1}H-NMR (500 MHz): 4.73 (*s*, 2 H); 7.12 (*dd*, *J* = 7.3, 4.6, 1 H); 7.19 (*tt*, *J* = 7.3, 1.4, 1 H); 7.25 (*dd*, *J* = 7.8, 7.3, 2 H); 7.41 (*dd*, *J* = 7.8, 1.4, 2 H); 7.47 (*dd*, *J* = 7.8, 7.3, 2 H); 7.58 (*t*, *J* = 7.3, 1 H); 7.71–7.74 (*m*, 3 H); 8.62 (*dd*, *J* = 4.6, 1.3, 1 H). Anal. calc. for $C_{19}H_{15}NOS_2$ (337.46): C 67.62, H 4.48, N 4.15; found: C 67.57, H 4.62, N 4.12.

(2-{[(Methylsulfanyl)methyl]sulfanyl}pyridin-3-yl)(phenyl)methanone (**2b**). Yellow oil. R_f (THF/hexane 1:4) 0.30. IR (neat): 1659. ^{1}H-NMR (500 MHz): 2.18 (*s*, 3 H); 4.37 (*s*, 3 H); 7.12 (*dd*, *J* = 7.3, 4.6, 1 H); 7.49 (*dd*, *J* = 8.2, 7.3, 1 H); 7.59 (*tt*, *J* = 7.3, 1.4, 1 H); 7.70 (*dd*, *J* = 7.3, 1.8, 1 H); 7.76 (*dd*, *J* = 8.2, 1.4, 2 H); 8.62 (*dd*, *J* = 4.6, 1.8, 1 H). Anal. calc. for $C_{14}H_{13}NOS_2$ (275.39): C 61.06, H 4.76, N 5.09; found: C 60.84, H 4.76, N 5.01.

*(2-{[(*tert*-Butylsulfanyl)methyl]sulfanyl}pyridin-3-yl)(phenyl)methanone* (**2c**). Yellow oil. R_f (THF/hexane 1:5) 0.42. IR (neat): 1659. ^{1}H-NMR (500 MHz): 1.36 (*s*, 9 H); 4.40 (*s*, 2 H); 7.10 (*dd*, *J* = 7.3, 4.6, 1 H); 7.48 (*dd*, *J* = 7.8, 7.3, 2 H); 7.60 (*tt*, *J* = 7.3, 1.4, 1 H); 7.69 (*dd*, *J* = 7.3, 1.8, 1 H); 7.75 (*dd*, *J* = 8.2, 1.4, 2 H); 8.61 (*dd*, *J* = 4.6, 1.8, 1 H). Anal. calc. for $C_{17}H_{19}NOS_2$ (317.47): C 64.32, H 6.03, N 4.41; found: C 64.07, H 6.07, N 4.39.

(3-Chlorophenyl)(2-{[(phenylsulfanyl)methyl]sulfanyl}pyridin-3-yl)methanone (**2d**). Yellow solid. M.p. 110–111° (hexane/CH_2Cl_2). IR (KBr): 1655. ^{1}H-NMR (500 MHz): 4.73 (*s*, 2 H); 7.14 (*dd*, *J* = 7.8, 5.0, 1 H); 7.20 (*tt*, *J* = 7.3, 1.4, 1 H); 7.26 (*dd*, *J* = 7.8, 7.3, 2 H); 7.39–7.43 (*m*, 3 H); 7.55–7.60 (*m*, 2 H); 7.69–7.71 (*m*, 2 H); 8.64 (*dd*, *J* = 5.0, 1.8, 1 H). Anal. calc. for $C_{19}H_{14}ClNOS_2$ (371.90): C 61.36, H 3.79, N 3.77; found: C 61.26, H 3.81, N 3.60.

(1,3-Benzodioxol-5-yl)(2-{[(phenylsulfanyl)methyl]sulfanyl}pyridin-3-yl)methanone (**2e**). Yellow oil. R_f (THF/hexane 1:2) 0.42. IR (neat): 1651, 1603. ^{1}H-NMR (500 MHz): 4.72 (*s*, 2 H); 6.07 (*s*, 2 H); 6.82 (*d*, *J* = 8.2, 1 H); 7.12 (*dd*, *J* = 7.3, 5.0, 1 H); 7.19 (*t*, *J* = 7.3, 1 H); 7.23–7.27 (*m*, 3 H); 7.32 (*d*, *J* = 1.8, 1 H); 7.40 (*dd*, *J* = 7.8, 1.4, 2 H); 7.64 (*dd*, *J* = 7.3, 1.8, 1 H); 8.60 (*dd*, *J* = 5.0, 1.8, 1 H). Anal. calc. for $C_{20}H_{15}NO_3S_2$ (381.47): C 62.97, H 3.96, N 3.67; found: C 63.02, H 4.03, N 3.64.

Phenyl(3-{[(phenylsulfanyl)methyl]sulfanyl}pyridin-4-yl)methanone (**6a**). Yellow oil. R_f (THF/hexane 2:3) 0.28. IR (neat): 1668. ^{1}H-NMR (400 MHz): 4.26 (*s*, 2 H); 7.22–7.33 (*m*, 6 H); 7.47 (*t*, *J* = 7.8, 2 H); 7.63 (*t*, *J* = 7.8, 1 H); 7.75 (*d*, *J* = 7.8, 2 H); 8.65 (*d*, *J* = 4.9, 1 H); 8.83 (*s*, 1 H). Anal. calc. for $C_{19}H_{15}NOS_2$ (337.46): C 67.62, H 4.48, N 4.15; found: C 67.53, H 4.48, N 4.03.

(3-{[(Methylsulfanyl)methyl]sulfanyl}pyridin-4-yl)(phenyl)methanone (**6b**). Yellow oil. R_f (THF/hexane 1:4) 0.25. IR (neat): 1668. ^{1}H-NMR (400 MHz): 2.07 (*s*, 3 H); 3.91 (*s*, 2 H); 7.26 (*d*, *J* = 4.9, 1 H); 7.49 (*t*, *J* = 7.8, 2 H); 7.64 (*t*, *J* = 7.8, 1 H); 7.79 (*d*, *J* = 7.8, 2 H); 8.65 (*d*, *J* = 4.9, 1 H); 8.85 (*s*, 1 H). Anal. calc. for $C_{14}H_{13}NOS_2$ (275.39): C 61.06, H 4.76, N 5.09; found: C 61.04, H 4.77, N 5.02.

(3-{[(Phenylsulfanyl)methyl]sulfanyl}pyridin-4-yl)(thiophen-2-yl)methanone (**6c**). Yellow oil. R_f (THF/hexane 1:2) 0.26. IR (neat): 1645. ^{1}H-NMR (400 MHz): 4.32 (*s*, 2 H); 7.12 (*dd*, *J* = 4.9, 3.9, 1 H); 7.22–7.29 (*m*, 4 H); 7.33–7.36 (*m*, 3 H); 7.80 (*dd*, *J* = 3.9, 1.4, 1 H); 8.65 (*d*, *J* = 4.9, 1 H); 8.83 (*s*, 1 H). Anal. calc. for $C_{17}H_{13}NOS_3$ (343.49): C 59.44, H 3.81, N 4.08; found: C 59.44, H 3.81, N 4.11.

*[3-({[(*tert*-Butyl)sulfanyl]methyl}sulfanyl)pyridin-4-yl](thiophen-2-yl)methanone* (**6d**). Yellow oil. R_f (THF/hexane 1:2) 0.24. IR (neat): 1649. ^{1}H-NMR (400 MHz): 1.30 (*s*, 9 H); 4.03 (*s*, 2 H); 7.15 (*dd*, *J* = 4.9, 3.9, 1 H); 7.34 (*d*, *J* = 4.9, 1 H); 7.40 (*d*, *J* = 3.9, 1 H); 7.81 (*d*, *J* = 4.9, 1 H); 8.64 (*d*, *J* = 4.9, 1 H); 8.88 (*s*, 1 H). Anal. calc. for $C_{15}H_{17}NOS_3$ (323.50): C 55.69, H 5.30, N 4.33; found: C 55.60, H 5.37, N 4.28.

Phenyl(4-{[(phenylsulfanyl)methyl]sulfanyl}pyridin-3-yl)methanone (**10a**). Pale-yellow oil. R_f (THF/hexane 1:3) 0.23. IR (neat): 1651. ^{1}H-NMR (500 MHz): 4.37 (*s*, 2 H); 7.25–7.31 (*m*, 3 H); 7.41–7.51 (*m*, 5 H); 7.61 (*tt*, *J* = 7.3, 1.4, 1 H); 7.78 (*dd*, *J* = 7.8, 1.4, 2 H); 8.58 (*d*, *J* = 5.2, 1 H); 8.62 (*s*, 1 H). Anal. calc. for $C_{19}H_{15}NOS_2$ (337.46): C 67.62, H 4.48, N 4.15; found: C 67.56, H 4.50, N 4.12.

*[4-({[(*tert*-Butyl)sulfanyl]methyl}sulfanyl)pyridin-3-yl](phenyl)methanone* (**10b**). Yellow oil. R_f (THF/hexane 1:3) 0.24. IR (neat): 1655. ^{1}H-NMR (400 MHz): 1.38 (*s*, 9 H), 4.07 (*s*, 2 H), 7.46 (*d*, *J* = 5.9, 1 H), 7.50 (*t*, *J* = 7.8, 2 H); 7.63 (*t*, *J* = 7.8, 1 H); 7.79 (*d*, *J* = 7.8, 2 H); 8.57 (*d*, *J* = 5.9, 1 H); 8.60 (*s*, 1 H). Anal. calc. for $C_{17}H_{19}NOS_2$ (317.47): C 64.32, H 6.03, N 4.41; found: C 64.18, H 6.13, N 4.36.

(4-Methoxyphenyl)(4-{[(phenylsulfanyl)methyl]sulfanyl}pyridin-3-yl)methanone (**10c**). Pale-yellow oil. R_f (THF/hexane 1:3) 0.31. IR (neat): 1651. ^{1}H-NMR (400 MHz): 3.89 (*s*, 3 H); 4.36 (*s*, 2 H); 6.96 (*d*, *J* = 8.8, 2 H); 7.23–7.30 (*m*, 3 H); 7.40–7.44 (*m*, 3 H); 7.79 (*d*, *J* = 8.8, 2 H); 8.567 (*d*, *J* = 5.2, 1 H); 8.572 (*s*, 1 H). Anal. calc. for $C_{20}H_{17}NO_2S_2$ (367.48): C 65.37, H 4.66, N 3.81; found: C 65.21, H 4.89, N 3.58.

(4-Methoxyphenyl)(4-{[(methylsulfanyl)methyl]sulfanyl}pyridin-3-yl)methanone (**10d**). Pale-yellow oil. R_f (THF/hexane 1:3) 0.31. IR (neat): 1649. ^{1}H-NMR (400 MHz): 2.19 (*s*, 3 H); 3.90 (*s*, 3 H); 4.04 (*s*, 2 H); 6.97 (*d*, *J* = 8.8, 2 H); 7.42 (*d*, *J* = 5.9, 1 H); 7.81 (*d*, *J* = 8.8, 2 H); 8.565 (*s*, 1 H); 8.571 (*d*, *J* = 5.9, 1 H). Anal. calc. for $C_{15}H_{15}NO_2S_2$ (305.42): C 58.99, H 4.95, N 4.59; found: C 58.97, H 5.00, N 4.43.

*3-Phenyl-2-(phenylsulfanyl)thieno[2,3-*b*]pyridine* (**4a**; *Representative Procedure*). To a stirred soln. of LDA (1.8 mmol), generated from BuLi and ^{i}Pr$_2$NH by the standard method, in DME (4 ml) at −78° was added a soln. of **2a** (0.20 g, 0.59 mmol) dropwise. After 30 min, the temp. was raised gradually to 0°, and then the reaction was quenched by adding sat. aq. NH_4Cl (10 ml). The mixture was extracted with Et_2O (3 × 10 ml). The combined extracts were washed with brine (10 ml), dried (Na_2SO_4), and concentrated by evaporation. The residue (crude **3a**) was dissolved in THF (4 ml) and pyridine (0.47 g, 5.9 mmol), the soln. was cooled to 0°, and then $SOCl_2$ (0.14 g, 1.2 mmol) was added. After stirring the mixture at r.t. for 1 h, sat. aq. $NaHCO_3$ (10 ml) was added. The mixture was worked up as described above to give a residue, which was purified by PLC (SiO_2) to afford **4a** (0.10 g, 54%). Yellow oil. R_f (Et_2O/hexane 1:3) 0.27. IR (neat): 1371. ^{1}H-NMR (500 MHz): 7.24–7.30 (*m*, 4 H); 7.34 (*dd*, *J* = 7.8, 1.4, 2 H); 7.42–7.46 (*m*, 3 H); 7.50 (*dd*, *J* = 7.8, 7.3, 2 H); 7.85 (*dd*, *J* = 7.8, 1.4, 1 H); 8.55 (*dd*, *J* = 5.5, 1.4, 1 H). ^{13}C-NMR: 119.9; 127.4; 128.3; 128.6 (two overlapped Cs); 129.2; 129.9; 130.0; 130.7; 132.5; 133.4; 135.7; 138.6; 147.1; 162.3. MS: 319 (100, M^+). Anal. calc. for $C_{19}H_{13}NS_2$ (319.44): C 71.44, H 4.10, N 4.38; found: C 71.29, H 4.15, N 4.21.

*2-(Methylsulfanyl)-3-phenylthieno[2,3-*b*]pyridine* (**4b**). Pale-yellow solid. M.p. 102–103° (hexane/CH_2Cl_2). IR (KBr): 1374. ^{1}H-NMR (500 MHz): 2.55 (*s*, 3 H); 7.24 (*dd*, *J* = 8.2, 4.6, 1 H); 7.43–7.47 (*m*, 3 H); 7.52 (*dd*, *J* = 7.8, 7.3, 2 H); 7.79 (*dd*, *J* = 8.2, 1.4, 1 H); 8.50 (*dd*, *J* = 4.6, 1.4, 1 H). ^{13}C-NMR: 19.4; 119.9; 128.0; 128.6; 129.6; 129.8; 133.7; 133.7; 133.8; 136.5; 145.9; 161.2. MS: 257 (100, M^+). Anal. calc. for $C_{14}H_{11}NS_2$ (257.37): C 65.33, H 4.31, N 5.44; found: C 65.08, H 4.49, N 5.49.

*2-[(*tert*-Butyl)sulfanyl]-3-phenylthieno[2,3-*b*]pyridine* (**4c**). White solid. M.p. 74–75° (hexane/Et_2O). IR (KBr): 1368. ^{1}H-NMR (400 MHz): 1.24 (*s*, 9 H); 7.27 (*dd*, *J* = 7.8, 4.9, 1 H); 7.41–7.44 (*m*, 3 H); 7.50 (*dd*, *J* = 7.8, 7.3, 2 H); 7.85 (*dd*, *J* = 7.8, 1.5, 1 H); 8.60 (*dd*, *J* = 4.9, 1.5, 1 H). ^{13}C-NMR: 31.1; 49.5; 119.7; 127.8; 128.2; 130.7; 131.1; 131.2; 133.3; 134.0; 141.8; 147.4; 162.4. MS: 299 (13, M^+), 243 (100). Anal. calc. for $C_{17}H_{17}NS_2$ (299.45): C 68.18, H 5.72, N 4.68; found: C 68.04, H 5.82, N 4.52.

*3-(3-Chlorophenyl)-2-(phenylsulfanyl)thieno[2,3-*b*]pyridine* (**4d**). Yellow crystal. M.p. 106–107° (hexane/CH_2Cl_2). IR (KBr): 1373. ^{1}H-NMR (500 MHz): 7.27–7.36 (*m*, 7 H); 7.42–7.43 (*m*, 3 H); 7.82 (*dd*, *J* = 8.2, 1.4, 1 H); 8.56 (*dd*, *J* = 4.6, 1.4, 1 H). ^{13}C-NMR: 120.0; 127.8; 128.1; 128.4; 129.3 (two overlapped Cs); 129.9; 130.3; 130.5; 133.1; 133.9; 134.5; 135.1; 135.2; 136.4; 147.2; 162.1. MS: 353 (100, M^+). Anal. calc. for $C_{19}H_{12}ClNS_2$ (353.89): C 64.48, H 3.42, N 3.96; found: C 64.40, H 3.45, N 3.92.

*3-(1,3-Benzodioxol-5-yl)-2-(phenylsulfanyl)thieno[2,3-*b*]pyridine* (**4e**). Pale-yellow oil. R_f (Et_2O/hexane 1:2) 0.32. IR (neat): 1371, 1234. ^{1}H-NMR (500 MHz): 6.04 (*s*, 2 H); 6.90–6.94 (*m*, 3 H); 7.23–7.31 (*m*, 4 H); 7.34 (*d*, *J* = 7.3, 2 H); 7.86 (*dd*, *J* = 7.8, 1.4, 1 H); 8.55 (*dd*, *J* = 4.6, 1.4, 1 H). ^{13}C-NMR: 101.3; 108.5; 110.2; 119.8; 123.7; 126.9; 127.5; 129.2; 130.0; 130.6; 132.3; 133.4; 135.6; 138.0; 147.1; 147.6; 147.8; 162.2. MS: 363 (100, M^+). Anal. calc. for $C_{20}H_{13}NO_2S_2$ (363.45): C 66.09, H 3.61, N 3.85; found: C 66.12, H 3.43, N 4.04.

*3-Phenyl-2-(phenylsulfanyl)thieno[2,3-*c*]pyridine* (**8a**). Pale-yellow oil. R_f (AcOEt/hexane 1:3) 0.25. IR (neat): 1573, 1439. ^{1}H-NMR (400 MHz): 7.31–7.34 (*m*, 3 H); 7.42–7.58 (*m*, 8 H); 8.44 (*d*, *J* = 4.9, 1 H); 8.96 (*s*, 1 H). ^{13}C-NMR: 116.8; 128.3; 128.4; 128.7; 129.4; 129.8; 131.8; 133.0; 134.2; 136.6; 137.2; 143.3; 143.7; 145.0; 145.2. MS: 319 (100, M^+). Anal. calc. for $C_{19}H_{13}NS_2$ (319.44): C 71.44, H 4.10, N 4.38; found: C 71.19, H 4.16, N 4.25.

*2-(Methylsulfanyl)-3-phenylthieno[2,3-*c*]pyridine* (**8b**). Pale-yellow oil. R_f (AcOEt/hexane 1:2) 0.33. IR (neat): 1601, 1576, 1433. ^{1}H-NMR (400 MHz): 2.59 (*s*, 3 H); 7.42 (*d*, *J* = 5.9, 1 H); 7.43–7.48 (*m*, 3 H); 7.53 (*dd*, *J* = 7.8, 7.3, 2 H); 8.43 (*d*, *J* = 5.9, 1 H); 9.03 (*s*, 1 H). ^{13}C-NMR: 18.9; 116.1; 128.2; 128.8; 129.7 (two overlapped Cs); 133.2; 133.9; 135.6; 143.4; 143.8; 145.3. MS: 257 (100, M^+). Anal. calc. for $C_{14}H_{11}NS_2$ (257.37): C 65.33, H 4.31, N 5.44; found: C 65.10, H 4.29, N 5.45.

*2-(Phenylsulfanyl)-3-(thiophen-2-yl)thieno[2,3-*c*]pyridine* (**8c**). Yellow oil. R_f (AcOEt/hexane 1:2) 0.41. IR (neat): 1576, 1440. ^{1}H-NMR (400 MHz): 7.22 (*dd*, *J* = 4.9, 3.9, 1 H); 7.30 (*d*, *J* = 2.9, 1 H); 7.33–7.41 (*m*, 3 H); 7.47–7.51 (*m*, 3 H); 7.70 (*d*, *J* = 5.9, 1 H); 8.48 (*d*, *J* = 5.9, 1 H); 8.92 (*s*, 1 H). ^{13}C-NMR: 116.7; 126.8; 127.4; 127.8; 128.5; 128.8; 129.0; 129.6; 132.3; 133.1; 133.5; 136.0; 143.6; 144.0; 144.9. MS: 325 (100, M^+). Anal. calc. for $C_{17}H_{11}NS_3$ (325.47): C 62.73, H 3.41, N 4.30; found: C 62.71, H 3.42, N 4.30.

*2-[(*tert*-Butyl)sulfanyl]-3-(thiophen-2-yl)thieno[2,3-*c*]pyridine* (**8d**). Pale-yellow oil. R_f (AcOEt/hexane 1:4) 0.29. IR (neat): 1573, 1454, 1161. ^{1}H-NMR (400 MHz): 1.32 (*s*, 9 H); 7.20 (*dd*, *J* = 4.9, 2.9, 1 H); 7.27 (*d*, *J* = 2.9, 1 H); 7.49 (*d*, *J* = 4.9, 1 H); 7.74 (*d*, *J* = 5.9, 1 H); 8.51 (*d*, *J* = 5.9, 1 H); 9.07 (*s*, 1 H). ^{13}C-NMR: 31.1; 50.3; 117.5; 126.8; 127.0; 128.9; 133.7; 135.1; 137.3; 138.5; 143.6; 143.7; 144.4. MS: 305 (35, M^+), 249 (100). Anal. calc. for $C_{15}H_{15}NS_3$ (305.48): C 58.98, H 4.95, N 4.59; found: C 58.72, H 5.01, N 4.42.

*3-Phenyl-2-(phenylsulfanyl)thieno[3,2-*c*]pyridine* (**12a**). Pale-yellow solid. M.p. 131–133° (hexane/CH_2Cl_2). IR (neat): 1566, 1437. ^{1}H-NMR (500 MHz): 7.26–7.33 (*m*, 5 H); 7.45–7.54 (*m*, 5 H); 7.68 (*dd*, *J* = 5.2, 1.1, 1 H); 8.47 (*d*, *J* = 5.2, 1 H); 8.87 (*d*, *J* = 1.1, 1 H). ^{13}C-NMR: 116.6; 127.5; 128.5; 128.6; 129.2; 129.9; 130.0; 132.8; 133.2; 135.6; 135.7; 139.8; 143.4; 145.7; 148.2. MS: 319 (100, M^+). Anal. calc. for $C_{19}H_{13}NS_2$ (319.44): C 71.44, H 4.10, N 4.38; found: C 71.36, H 4.13, N 4.56.

*2-[(*tert*-Butyl)sulfanyl]-3-phenylthieno[3,2-*c*]pyridine* (**12b**). Yellow oil. R_f (AcOEt/hexane 1:3) 0.44. IR (neat): 1570, 1427, 1163. ^{1}H-NMR (400 MHz): 1.22 (*s*, 9 H); 7.42–7.55 (*m*, 5 H); 7.73 (*d*, *J* = 5.9, 1 H); 8.48 (*d*, *J* = 5.9, 1 H); 8.86 (*s*, 1 H). ^{13}C-NMR: 31.0; 49.6; 116.3; 128.1; 128.3; 130.8; 131.9 (two overlapped Cs); 133.4; 143.2; 143.4; 146.3; 148.5. MS: 299 (13, M^+), 243 (100). Anal. calc. for $C_{17}H_{17}NS_2$ (299.45): C 68.18, H 5.72, N 4.68; found: C 68.14, H 5.73, N 4.52.

*3-(4-Methoxyphenyl)-2-(phenylsulfanyl)thieno[3,2-*c*]pyridine* (**12c**). White solid. M.p. 123–125° (hexane/CH_2Cl_2). IR (KBr): 1611, 1573, 1523, 1438, 1249. ^{1}H-NMR (500 MHz): 3.88 (*s*, 3 H); 7.04 (*d*, *J* = 8.6, 2 H); 7.25–7.32 (*m*, 5 H); 7.43 (*dd*, *J* = 8.6, 2 H); 7.67 (*d*, *J* = 5.7, 1 H); 8.46 (*d*, *J* = 5.7, 1 H); 8.88 (*s*, 1 H). ^{13}C-NMR: 55.3; 114.1; 116.6; 125.0; 127.4; 129.2; 129.8; 131.1; 132.3; 135.8; 135.8; 139.8; 143.4; 145.8; 148.3; 159.7. MS: 349 (100, M^+). Anal. calc. for $C_{20}H_{15}NOS_2$ (349.47): C 68.74, H 4.33, N 4.01; found: C 68.70, H 4.35, N 3.87.

*3-(4-Methoxyphenyl)-2-(methylsulfanyl)thieno[3,2-*c*]pyridine* (**12d**). White solid. M.p. 82–84° (hexane/CH_2Cl_2). IR (KBr): 1610, 1523, 1433, 1249. ^{1}H-NMR (400 MHz): 2.51 (*s*, 3 H); 3.90 (*s*, 3 H); 7.07 (*d*, *J* = 8.8, 2 H); 7.43 (*d*, *J* = 8.8, 2 H); 7.70 (*d*, *J* = 5.9, 1 H); 8.43 (*d*, *J* = 5.9, 1 H); 8.82 (*s*, 1 H). ^{13}C-NMR: 19.8; 55.3; 114.1; 116.4; 125.3; 131.1 (two overlapped Cs); 135.6; 136.1; 142.6; 144.9; 146.9; 159.5. MS: 287 (100, M^+). Anal. calc. for $C_{15}H_{13}NOS_2$ (287.40): C 62.69, H 4.56, N 4.87; found: C 62.62, H 4.58, N 5.01.

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