

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

by Kazuhiro Kobayashi*, Teruhiko Suzuki, and Yuko Egara

Division of Applied Chemistry, Department of Chemistry and Biotechnology, Graduate School of Engineering, Tottori University, 4–101 Koyama-minami, Tottori 680-8552, Japan
(phone/fax: +81(857)315263; e-mail: kkoba@chem.tottori-u.ac.jp)

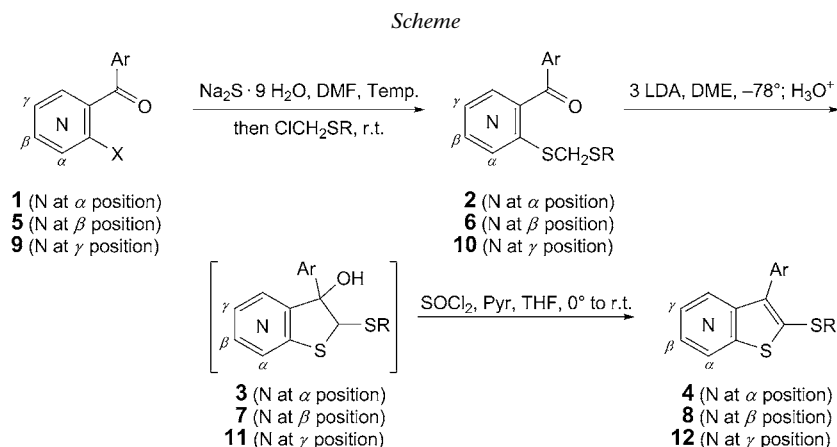
A convenient three-step procedure for the synthesis of three types of 3-aryl-2-sulfanylthienopyridines **4**, **8**, and **12** has been developed. The first step of the synthesis of thieno[2,3-*b*]pyridine derivatives **4** is the replacement of the halo with a (sulfanylmethyl)sulfanyl group in aryl(2-halopyridin-3-yl)methanones **1** by successive treatment with $\text{Na}_2\text{S} \cdot 9 \text{H}_2\text{O}$ 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 properties¹⁾. Although the syntheses of thieno[2,3-*b*]pyridine²⁾, thieno[2,3-*c*]pyridine³⁾, and thieno[3,2-*c*]pyridine derivatives⁴⁾ have been reported by a number of groups, there have been few reports on methods for preparing the corresponding 2-sulfanylated derivatives⁵⁾, 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

- 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 $\text{Na}_2\text{S} \cdot 9 \text{H}_2\text{O}$ 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 anions⁶), generated by treatment of **2** with 3 mol-equiv. of LDA⁷ 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 as mixtures of diastereoisomers, 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*).



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

- 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 ₆ H ₄ , X = Br)	Ph	70°	2d	52	4d	47
5	1c (N = α , Ar = 3,4-(OCH ₂ O)-C ₆ H 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 ₆ H 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 Na₂S·9 H₂O 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 Na₂S·9 H₂O 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 PF₂₅₄. Column chromatography (CC): Wako Gel C-200E. M.p.: Laboratory Devices MEL-TEMP II melting point apparatus; uncorrected. IR Spectra: Shimadzu FTIR-8300 spectrophotometer. ¹H-NMR Spectra: in CDCl₃ 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. ^1H -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 $\text{Na}_2\text{S} \cdot 9 \text{H}_2\text{O}$ (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. ^1H -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 $\text{C}_{19}\text{H}_{15}\text{NOS}_2$ (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. ^1H -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 $\text{C}_{14}\text{H}_{13}\text{NOS}_2$ (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. ^1H -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 $\text{C}_{17}\text{H}_{19}\text{NOS}_2$ (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. ^1H -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 $\text{C}_{19}\text{H}_{14}\text{ClNOS}_2$ (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. ^1H -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 $\text{C}_{20}\text{H}_{15}\text{NO}_3\text{S}_2$ (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. ^1H -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 $\text{C}_{19}\text{H}_{15}\text{NOS}_2$ (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. ^1H -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 $\text{C}_{14}\text{H}_{13}\text{NOS}_2$ (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. $^1\text{H-NMR}$ (400 MHz): 4.32 (s, 2 H); 7.12 (dd, $J = 4.9, 3.9, 1\text{ H}$); 7.22–7.29 (m, 4 H); 7.33–7.36 (m, 3 H); 7.80 (dd, $J = 3.9, 1.4, 1\text{ H}$); 8.65 (d, $J = 4.9, 1\text{ H}$); 8.83 (s, 1 H). Anal. calc. for $\text{C}_{17}\text{H}_{13}\text{NOS}_3$ (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. $^1\text{H-NMR}$ (400 MHz): 1.30 (s, 9 H); 4.03 (s, 2 H); 7.15 (dd, $J = 4.9, 3.9, 1\text{ H}$); 7.34 (d, $J = 4.9, 1\text{ H}$); 7.40 (d, $J = 3.9, 1\text{ H}$); 7.81 (d, $J = 4.9, 1\text{ H}$); 8.64 (d, $J = 4.9, 1\text{ H}$); 8.88 (s, 1 H). Anal. calc. for $\text{C}_{15}\text{H}_{17}\text{NOS}_3$ (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. $^1\text{H-NMR}$ (500 MHz): 4.37 (s, 2 H); 7.25–7.31 (m, 3 H); 7.41–7.51 (m, 5 H); 7.61 (tt, $J = 7.3, 1.4, 1\text{ H}$); 7.78 (dd, $J = 7.8, 1.4, 2\text{ H}$); 8.58 (d, $J = 5.2, 1\text{ H}$); 8.62 (s, 1 H). Anal. calc. for $\text{C}_{19}\text{H}_{15}\text{NOS}_2$ (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. $^1\text{H-NMR}$ (400 MHz): 1.38 (s, 9 H), 4.07 (s, 2 H), 7.46 (d, $J = 5.9, 1\text{ H}$), 7.50 (t, $J = 7.8, 2\text{ H}$); 7.63 (t, $J = 7.8, 1\text{ H}$); 7.79 (d, $J = 7.8, 2\text{ H}$); 8.57 (d, $J = 5.9, 1\text{ H}$); 8.60 (s, 1 H). Anal. calc. for $\text{C}_{17}\text{H}_{19}\text{NOS}_2$ (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. $^1\text{H-NMR}$ (400 MHz): 3.89 (s, 3 H); 4.36 (s, 2 H); 6.96 (d, $J = 8.8, 2\text{ H}$); 7.23–7.30 (m, 3 H); 7.40–7.44 (m, 3 H); 7.79 (d, $J = 8.8, 2\text{ H}$); 8.567 (d, $J = 5.2, 1\text{ H}$); 8.572 (s, 1 H). Anal. calc. for $\text{C}_{20}\text{H}_{17}\text{NO}_2\text{S}_2$ (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. $^1\text{H-NMR}$ (400 MHz): 2.19 (s, 3 H); 3.90 (s, 3 H); 4.04 (s, 2 H); 6.97 (d, $J = 8.8, 2\text{ H}$); 7.42 (d, $J = 5.9, 1\text{ H}$); 7.81 (d, $J = 8.8, 2\text{ H}$); 8.565 (s, 1 H); 8.571 (d, $J = 5.9, 1\text{ H}$). Anal. calc. for $\text{C}_{15}\text{H}_{15}\text{NO}_2\text{S}_2$ (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 $^i\text{Pr}_2\text{NH}$ 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 \times 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. $^1\text{H-NMR}$ (500 MHz): 7.24–7.30 (m, 4 H); 7.34 (dd, $J = 7.8, 1.4, 2\text{ H}$); 7.42–7.46 (m, 3 H); 7.50 (dd, $J = 7.8, 7.3, 2\text{ H}$); 7.85 (dd, $J = 7.8, 1.4, 1\text{ H}$); 8.55 (dd, $J = 5.5, 1.4, 1\text{ H}$). $^{13}\text{C-NMR}$: 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 $\text{C}_{19}\text{H}_{13}\text{NS}_2$ (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. $102\text{--}103^\circ$ (hexane/ CH_2Cl_2). IR (KBr): 1374. $^1\text{H-NMR}$ (500 MHz): 2.55 (s, 3 H); 7.24 (dd, $J = 8.2, 4.6, 1\text{ H}$); 7.43–7.47 (m, 3 H); 7.52 (dd, $J = 7.8, 7.3, 2\text{ H}$); 7.79 (dd, $J = 8.2, 1.4, 1\text{ H}$); 8.50 (dd, $J = 4.6, 1.4, 1\text{ H}$). $^{13}\text{C-NMR}$: 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 $\text{C}_{14}\text{H}_{11}\text{NS}_2$ (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. $74\text{--}75^\circ$ (hexane/ Et_2O). IR (KBr): 1368. $^1\text{H-NMR}$ (400 MHz): 1.24 (s, 9 H); 7.27 (dd, $J = 7.8, 4.9, 1\text{ H}$); 7.41–7.44 (m, 3 H); 7.50 (dd, $J = 7.8, 7.3, 2\text{ H}$); 7.85 (dd, $J = 7.8, 1.5, 1\text{ H}$); 8.60 (dd, $J = 4.9, 1.5, 1\text{ H}$). $^{13}\text{C-NMR}$: 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 $\text{C}_{17}\text{H}_{17}\text{NS}_2$ (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. $106\text{--}107^\circ$ (hexane/ CH_2Cl_2). IR (KBr): 1373. $^1\text{H-NMR}$ (500 MHz): 7.27–7.36 (m, 7 H); 7.42–7.43 (m, 3 H); 7.82 (dd, $J = 8.2, 1.4, 1\text{ H}$); 8.56 (dd, $J = 4.6, 1.4, 1\text{ H}$). $^{13}\text{C-NMR}$: 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 $\text{C}_{19}\text{H}_{12}\text{ClNS}_2$ (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 (Et₂O/hexane 1:2) 0.32. IR (neat): 1371, 1234. ¹H-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). ¹³C-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 C₂₀H₁₃NO₂S₂ (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. ¹H-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). ¹³C-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 C₁₉H₁₃NS₂ (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. ¹H-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). ¹³C-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 C₁₄H₁₁NS₂ (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. ¹H-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). ¹³C-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 C₁₇H₁₁NS₃ (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. ¹H-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). ¹³C-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 C₁₅H₁₅NS₃ (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/CH₂Cl₂). IR (neat): 1566, 1437. ¹H-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). ¹³C-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 C₁₉H₁₃NS₂ (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. ¹H-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). ¹³C-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 C₁₇H₁₇NS₂ (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/CH₂Cl₂). IR (KBr): 1611, 1573, 1523, 1438, 1249. ¹H-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). ¹³C-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 C₂₀H₁₅NOS₂ (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/CH₂Cl₂). IR (KBr): 1610, 1523, 1433, 1249. ¹H-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). ¹³C-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 C₁₅H₁₃NOS₂ (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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