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ONE-POT SYNTHESIS OF 2,3-DIARYLTHIENO[2,3-*b*]-, -[2,3-*c*]- OR -[3,2-*c*]PYRIDINES FROM THE RESPECTIVE ARYL(CHLOROPYRIDINYL)METHANONES

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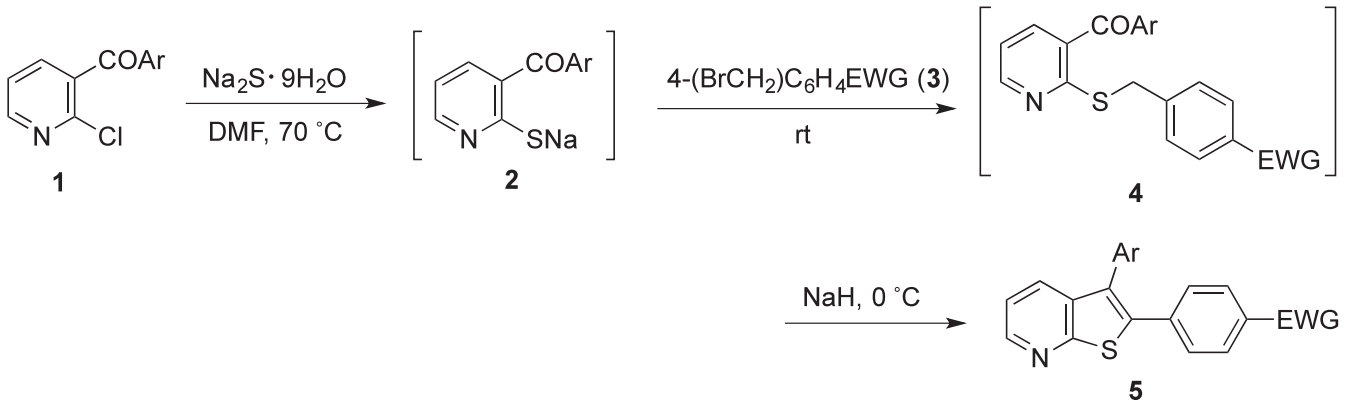
Abstract – The title three types of 2,3-diarylthienopyridines can be conveniently prepared from the respective aryl(chloropyridinyl)methanones in one-pot. The starting ketones react with sodium sulfide nonahydrate to generate aryl[(sodiosulfanyl)pyridinyl]methanones, which are treated successively with 4-($BrCH_2$)C_6H_4EWGs and sodium hydride to give rise to the desired products in generally good yields.

Since thienopyridine derivatives have received much attention because of their significant biological utilities,[1] a number of efficient approaches for their construction have been developed.[2,3] We previously developed a facile one-pot route to 2,3-disubstitued thieno[2,3-*b*]-, -[2,3-*c*]- or -[3,2-*c*]pyridines through the reaction of aryl(2-, 3-, or 4-halopyridin-3-, 4-, or 3-yl)methanones, respectively, with sodium sulfide nonahydrate, followed by successive treatment of the resulting corresponding pyridinethiolates with $BrCH_2$EWGs (EWG = CN, CO_2t-Bu, and Bz) and sodium hydride.[3a] As an extension of this work, we hoped to develop a route to 2,3-diarylthieno[2,3-*b*]-, -[2,3-*c*]- or -[3,2-*c*]pyridines, since there are, as far as we are aware, no general methods for their preparation, though some biological active derivatives have been synthesized.[4] We have now describes the results of our investigation, which provide a facile one-pot route to these 2,3-diarylthienopyridines (**5**), (**7**), or (**9**) from the respective aryl(chloropyridinyl)-methanones (**1**), (**6**), or (**8**) and 4-($BrCH_2$)C_6H_4EWGs (**3**) (EWG = CN, NO_2, CO_2t-Bu, and Bz).

(2-Chloropyridin-3-yl)phenylmethanone (**1a**), prepared by lithiation of commercially available 2-chloropyridne followed by treatment of the resulting 2-chloro-3-lithiopyridine with *N*,*N*-dimethylbenzamide as described previously,[3b] was initially chosen as the substrate for the present

one-pot synthesis. As illustrated in Scheme 1, treatment of **1a** with sodium sulfide nonahydrate in DMF at 70 ˚C generated phenyl[2-(sodiosulfanyl)pyridin-3-yl]methanone (**2a**; Ar = Ph), which was allowed to react with 4-($BrCH_2$)C_6H_4EWGs (**3**) to afford substitution intermediates (**4**). Cyclization of these intermediates with an equivalent of sodium hydride proceeded cleanly and smoothly in general to give, after aqueous workup and the subsequent purification by column chromatography on silica gel, the corresponding 2,3-diarylthieno[2,3-*b*]pyridines (**5a-d**) in yields listed in Table 1, Entries 1–4. The yields were relatively good in general, while that of the product using 1-bromomethyl-4-nitrobenzene was rather lower than those of the others (Entry 2); the reaction gave a rather complicated mixture of products. It should be noted that the sequence using 2-(bromomethyl)benzonitrile resulted in the formation of an intractable mixture of products. This may be ascribed to the steric crowdedness between 2- and 3-aryl groups of the expected product. The other three 2,3-diarylthieno[2,3-*b*]pyridines (**5e-g**) were similarly obtained from aryl(2-chloropyridin-3-yl)methanones (**1b**) and (**1c**) (Entries 5-7).



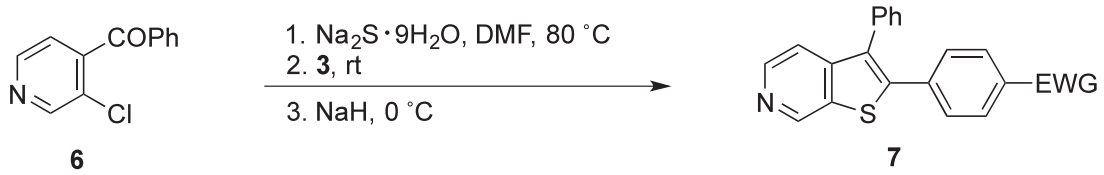
Scheme 1

Table 1. Preparation of 2,3-Diarylthienopyridines (**5**), (**7**), and (**9**)

Entry	**1, 6, 8**	EWG	**5, 7, 9**	Yield/%[a]
1	**1a** (Ar = Ph)	CN	**5a**	77
2	**1a**	NO_2	**5b**	47
3	**1a**	CO_2t-Bu	**5c**	69
4	**1a**	Bz	**5d**	78
5	**1b** (Ar = *p*-Tol)	CN	**5e**	79
6	**1b**	NO_2	**5f**	46
7	**1c** (Ar = 4-$MeOC_6H_4$)	CN	**5g**	70
8	**6**	CN	**7a**	67
9	**6**	Bz	**7b**	65
10	**8a** (Ar = Ph)	CN	**9a**	86
11	**8a**	NO_2	**9b**	60
12	**8a**	Bz	**9c**	82
13	**8b** (Ar = 3-ClC_6H_4)	CN	**9d**	87
14	**8c** (Ar = 4-$MeOC_6H_4$)	CN	**9e**	79
15	**8c**	Bz	**9f**	76

[a] Yields of isolated products.

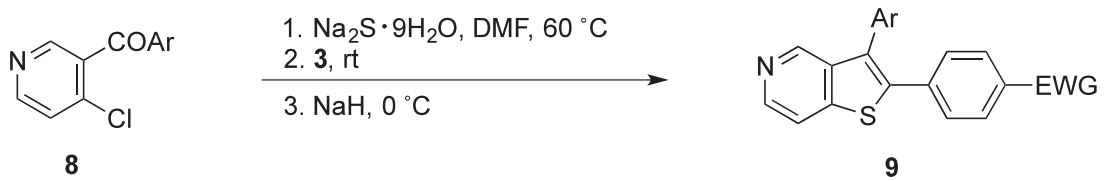
We then tried to prepare 2,3-diarylthieno[2,3-*c*]pyridines (**7**) from (3-chloropyridin-4-yl)phenylmethanone (**6**). Scheme 2 shows that the reaction of **6** with sodium sulfide nonahydrate required slightly higher reaction temperature than that of **1**, and the resulting sodium thiolate intermediate was similarly treated with 4-($BrCH_2$)C_6H_4EWGs (**3**) (EWG = CN and Bz) and then sodium hydride as described for the preparation of **5** to provide the corresponding required products (**7a**) and (**7b**) in somewhat lower yields than those of **5** as can be seen from Table 1, Entries 8 and 9.



6 **7**

Scheme 2

The preparation of 2,3-diarylthieno[3,2-*c*]pyridines (**9**) from aryl(4-chloropyridin-3-yl)methanone (**8)** was also similarly conducted as shown in Scheme 3. Compounds (**8**) reacted with sodium sulfide nonahydrate most cleanly at the lowest temperature of the sequences for the preparation of the three types of 2,3-diarylthienopyridines to generate the corresponding sodium thiolate intermediates, of which treatment with 4-($BrCH_2$)C_6H_4EWGs (**3**) (EWG = CN, NO_2, and Bz) and then sodium hydride afforded the desired products (**9**) in good yields in general (Table 1, Entries 10–15), though the product (**9b**) using 1-bromomethyl-4-nitrobenzene was also only moderate-to-fair (Entry 11).



8 **9**

Scheme 3

In the present work, we have developed a versatile method that allows access to three types of 2,3-diarylthienopyridines. The operational simplicity, together with readily availability of the starting materials, makes the present procedure attractive.

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 Spectrum65 FTIR spectrophotometer. ^{1}H NMR spectra were recorded in $CDCl_3$ using TMS as an internal reference with a JEOL ECP500 FT NMR spectrometer operating at 500 MHz or a JEOL LA400FT NMR spectrometer operating at 400 MHz. ^{13}C NMR spectra were recorded in $CDCl_3$ using TMS as an internal reference with a JEOL ECP500 FT NMR

spectrometer operating at 125 MHz or a JEOL LA400FT NMR spectrometer operating at 100 MHz. High-resolution MS spectra (DART, positive) were measured by a Thermo Scientific Exactive spectrometer. 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. Butyllithium was supplied by Asia Lithium Corporation. All other chemicals used in this study were commercially available.

Aryl(chloropyridinyl)methanones (1), (6), and (8). These compounds were prepared by treating the respective chlorolithiopyridines[5] with *N*,*N*-dimethylbenzamides under the conditions reported previously.[3] Physical, spectral, and analytical data for new compounds follow.

(2-Chloropyridin-3-yl)(4-methylphenyl)methanone (1b): yield: 56%; a pale-yellow oil; R_f 0.33 (AcOEt–hexane 1:4); IR (neat) 1670, 1604 cm^{-1}; ^1H NMR (400 MHz) δ 2.44 (s, 3H), 7.29 (d, J = 7.8 Hz, 2H), 7.38 (dd, J = 7.8, 4.9 Hz, 1H), 7.70 (d, J = 7.8 Hz, 2H), 7.73 (dd, J = 4.9, 2.0 Hz, 1H), 8.54 (dd, J = 4.9, 2.0 Hz, 1H). Anal. Calcd for $C_{13}H_{10}ClNO$: C, 67.39; H, 4.35; N, 6.05. Found: C, 67.37; H, 4.42; N, 6.08.

(3-Chlorolphenyl)(4-chloropyridin-3-yl)methanone (8b): yield: 58%; a pale-yellow oil; R_f 0.39 (AcOEt–hexane 1:3); IR (neat) 1678 cm^{-1}; ^1H NMR (400 MHz) δ 7.39–7.45 (m, 2H), 7.60 (d, J = 9.2 Hz, 1H), 7.64 (d, J = 7.4 Hz, 1H), 7.79 (br s, 1H), 8.60 (s, 1H), 8.65 (d, J = 5.2 Hz, 1H). Anal. Calcd for $C_{12}H_7Cl_2NO$: C, 57.17; H, 2.80; N, 5.56. Found: C, 57.03; H, 2.93; N, 5.54.

General Procedure for the Preparation of 2,3-Diarylthienopyridines (5), (7), and (9). A mixture of **1**, **6**, or **8** (1.0 mmol) in DMF (6 mL) containing $Na_2S{\cdot}9H_2O$ (0.26 g, 1.1 mmol) was heated at 70 °C for **1**, 80 °C for **6**, or 60 °C for **8** under stirring until consumption of the starting material had been confirmed by TLC analyses (silica gel; AcOEt–hexane 1:2; *ca*. 3 h). To the cooled (rt) mixture was added a solution of 4-$(BrCH_2)C_6H_4$EWG (0.90 mmol) in DMF (2 mL) and the mixture was stirred for 10 min. Then, the mixture was cooled to 0 °C and NaH (60 % in mineral oil; 40 mg, 1.0 mmol) was added in portions. After 5 min, saturated aqueous NH_4Cl (15 mL) was added and the mixture was extracted with AcOEt (3 × 10 mL). The combined extracts were washed with brine (2 × 10 mL) and brine (10 mL), dried (Na_2SO_4), and concentrated by evaporation. The residue was purified column chromatography on silica gel (THF–hexane 3:10) to give the desired products.

4-(3-Phenylthieno[2,3-*b*]pyridin-2-yl)benzonitrile (5a): a white solid; mp 176–178 °C (hexane–CH_2Cl_2); IR (KBr) 2226, 1600 cm^{-1}; ^1H NMR (500 MHz) δ 7.27–7.33 (m, 3H), 7.42–7.45 (m, 5H), 7.55 (d, J = 8.6 Hz, 2H), 7.89 (d, J = 8.0 Hz, 1H), 8.61 (d, J = 2.9 Hz, 1H); ^{13}C NMR (125 MHz) δ 111.52, 118.45, 120.09, 128.28, 129.14, 129.98, 130.14, 131.19, 132.17, 132.89, 133.71, 134.15, 136.89, 138.40, 147.48, 160.86. HR-MS. Calcd for $C_{20}H_{13}N_2S$ (M+H): 313.0799. Found: *m*/*z* 313.0781. Anal.

Calcd for $C_{20}H_{12}N_2S$: C, 76.90; H, 3.87; N, 8.97. Found: C, 77.03; H, 4.15; N, 8.71.

2-(4-Nitrophenyl)-3-phenylthieno[2,3-*b*]pyridine (5b): a yellow solid; mp 178–181 ˚C (hexane–Et_2O); IR (KBr) 1518, 1345 cm^{-1}; ^1H NMR (500 MHz) δ 7.29–7.31 (m, 2H), 7.34 (dd, *J* = 8.0, 4.6 Hz, 1H), 7.44–7.47 (m, 3H), 7.49 (d, *J* = 8.6 Hz, 2H), 7.90 (dd, *J* = 8.0, 1.7 Hz, 1H), 8.12 (d, *J* = 8.6 Hz, 2H), 8.63 (dd, *J* = 4.6, 1.7 Hz, 1H); ^{13}C NMR (125 MHz) δ 120.19, 123.73, 128.41, 129.23, 130.01, 130.34, 131.33, 133.42, 133.70, 134.18, 136.48, 140.41, 147.09, 147.65, 160.98. HR-MS. Calcd for $C_{19}H_{13}N_2O_2S$ (M+H): 333.0697. Found: *m/z* 333.0696. Anal. Calcd for $C_{19}H_{12}N_2O_2S$: C, 68.66; H, 3.64; N, 8.43. Found: C, 68.61; H, 3.68; N, 8.29.

1,1-Dimethylethyl 4-(3-Phenylthieno[2,3-*b*]pyridin-2-yl)benzoate (5c): a pale-yellow solid; mp 201–203 ˚C (hexane–CH_2Cl_2); IR (KBr) 1712, 1605 cm^{-1}; ^1H NMR (400 MHz) δ 1.58 (s, 9H), 7.26–7.30 (m, 3H), 7.37–7.42 (m, 4H), 7.86–7.89 (m, 4H), 8.59 (d, *J* = 4.6 Hz, 1H); ^{13}C NMR (125 MHz) δ 28.12, 81.17, 119.87, 127.93, 128.95, 129.43, 129.50, 130.09, 130.87, 131.36, 131.93, 134.18, 134.30, 137.70, 138.36, 147.02, 160.89, 165.19. HR-MS. Calcd for $C_{24}H_{22}NO_2S$ (M+H): 388.1371. Found: *m/z* 388.1372. Anal. Calcd for $C_{24}H_{21}NO_2S$: C, 74.39; H, 5.46; N, 3.61. Found: C, 74.30; H, 5.56; N, 3.46.

Phenyl[4-(3-phenylthieno[2,3-*b*]pyridin-2-yl)phenyl]methanone (5d): a white solid; mp 182–185 ˚C (hexane–CH_2Cl_2); IR (KBr) 1654 cm^{-1}; ^1H NMR (500 MHz) δ 7.17–7.23 (m, 3H), 7.31–7.40 (m, 7H), 7.49 (t, *J* = 7.4 Hz, 1H), 7.62 (d, *J* = 8.0 Hz, 2H), 7.69 (d, *J* = 8.0 Hz, 2H), 7.80 (dd, *J* = 8.0, 1.1 Hz, 1H), 8.50 (dd, *J* = 4.6, 1.1 Hz, 1H); ^{13}C NMR (125 MHz) δ 119.92, 128.01, 128.26, 128.99, 129.43, 129.89, 130.05, 130.20, 130.95, 132.19, 132.46, 134.07, 134.31, 136.66, 137.29, 137.79, 138.01, 147.12, 160.85, 195.92. HR-MS. Calcd for $C_{26}H_{18}NOS$ (M+H): 392.1109. Found: *m/z* 392.1092. Anal. Calcd for $C_{26}H_{17}NOS$: C, 79.77; H, 4.38; N, 3.58. Found: C, 79.70; H, 4.28; N, 3.38.

4-[3-(4-Methylphenyl)thieno[2,3-*b*]pyridin-2-yl]benzonitrile (5e): a pale-yellow solid; mp 176–178 ˚C (hexane–AcOEt); IR (KBr) 2226, 1603 cm^{-1}; ^1H NMR (400 MHz) δ 2.43 (s, 3H), 7.16 (d, *J* = 7.8 Hz, 2H), 7.25 (d, *J* = 7.8 Hz, 2H), 7.31 (dd, *J* = 8.2, 4.4 Hz, 1H), 7.44 (d, *J* = 8.3 Hz, 2H), 7.55 (d, *J* = 8.3 Hz, 2H), 7.89 (dd, *J* = 8.2, 1.5 Hz, 1H), 8.61 (dd, *J* = 4.4, 1.5 Hz, 1H); ^{13}C NMR (125 MHz) δ 21.31, 111.46, 118.51, 120.04, 129.84, 129.87, 130.14, 130.70, 131.26, 132.17, 132.99, 134.31, 136.60, 138.18, 138.60, 147.42, 160.91. HR-MS. Calcd for $C_{21}H_{15}N_2S$ (M+H): 327.0956. Found: *m/z* 327.0964. Anal. Calcd for $C_{21}H_{14}N_2S$: C, 77.27; H, 4.32; N, 8.58. Found: C, 77.03; H, 4.37; N, 8.57.

3-(4-Methylphenyl)-2-(4-nitrophenyl)thieno[2,3-*b*]pyridine (5f): an orange-yellow solid; mp 199–202 ˚C (hexane–AcOEt); IR (KBr) 1513, 1346 cm^{-1}; ^1H NMR (400 MHz) δ 2.43 (s, 3H), 7.18 (d, *J* = 7.8 Hz, 2H), 7.25 (d, *J* = 7.8 Hz, 2H), 7.32 (dd, *J* = 7.8, 3.9 Hz, 1H), 7.50 (d, *J* = 8.8 Hz, 2H), 7.90 (dd, *J* = 7.8, 1.9 Hz, 1H), 8.13 (d, *J* = 8.8 Hz, 2H), 8.62 (dd, *J* = 3.9, 1.9 Hz, 1H); ^{13}C NMR (125 MHz) δ 21.32, 120.11, 123.70, 129.84, 129.93, 130.30, 130.63, 131.36, 133.49, 134.28, 136.14, 138.31, 140.58, 147.03, 147.58, 160.99. HR-MS. Calcd for $C_{20}H_{15}N_2O_2S$ (M+H): 347.0854. Found: *m/z* 347.0839. Anal. Calcd for

$C_{20}H_{14}N_2O_2S$: C, 69.35; H, 4.07; N, 8.09. Found: C, 69.05; H, 4.29; N, 7.99.

4-[3-(4-Methoxyphenyl)thieno[2,3-*b*]pyridin-2-yl]benzonitrile (5g): a pale-yellow solid; mp 198–201 °C (hexane–AcOEt); IR (KBr) 2225, 1604 cm^{-1}; ^1H NMR (400 MHz) δ 3.87 (s, 3H), 6.98 (d, *J* = 8.8 Hz, 2H), 7.20 (d, *J* = 8.8 Hz, 2H), 7.32 (dd, *J* = 8.3, 4.4 Hz, 1H), 7.44 (d, *J* = 8.3 Hz, 2H), 7.56 (d, *J* = 8.3 Hz, 2H), 7.89 (dd, *J* = 8.3, 1.5 Hz, 1H), 8.60 (dd, *J* = 4.4, 1.5 Hz, 1H); ^{13}C NMR (125 MHz) δ 55.31, 111.44, 114.62, 118.51, 120.04, 125.80, 130.13, 131.16 (2C), 131.22, 132.19, 134.35, 136.44, 138.65, 147.42, 159.54, 160.88. HR-MS. Calcd for $C_{21}H_{15}N_2OS$ (M+H): 343.0905. Found: *m/z* 343.0887. Anal. Calcd for $C_{21}H_{14}N_2OS$: C, 73.66; H, 4.12; N, 8.18. Found: C, 73.64; H, 4.24; N, 8.18.

4-(3-Phenylthieno[2,3-*c*]pyridin-2-yl)benzonitrile (7a): a yellow solid; mp 155–158 °C (hexane–CH_2Cl_2); IR (KBr) 2227 cm^{-1}; ^1H NMR (500 MHz) δ 7.27–7.30 (m, 2H), 7.44–7.46 (m, 5H), 7.51 (dd, *J* = 5.7, 1.1 Hz, 1H), 7.57 (d, *J* = 8.6 Hz, 2H), 8.52 (d, *J* = 5.7 Hz, 1H), 9.19 (d, *J* = 1.1 Hz, 1H); ^{13}C NMR (125 MHz) δ 112.09, 117.56, 118.29, 128.40, 129.16, 129.96, 130.20, 132.26, 133.21, 134.40, 135.50, 137.99, 142.25, 143.88, 144.44, 145.66. HR-MS. Calcd for $C_{20}H_{13}N_2S$ (M+H): 313.0799. Found: *m/z* 313.0784. Anal. Calcd for $C_{20}H_{12}N_2S$: C, 76.90; H, 3.87; N, 8.97. Found: C, 76.84; H, 4.07; N, 8.87.

Phenyl[4-(3-phenylthieno[2,3-*c*]pyridin-2-yl)phenyl]methanone (7b): a pale-yellow solid; mp 179–180 °C (hexane–CH_2Cl_2); IR (KBr) 1658 cm^{-1}; ^1H NMR (500 MHz) δ 7.32 (dd, *J* = 8.0, 1.7 Hz, 2H), 7.39–7.52 (m, 8H), 7.59 (t, *J* = 7.4 Hz, 1H), 7.73 (d, *J* = 8.6 Hz, 2H), 7.79 (d, *J* = 8.6 Hz, 2H), 8.51 (d, *J* = 5.7 Hz, 1H), 9.18 (s, 1H); ^{13}C NMR (125 MHz) δ 117.42, 126.28, 128.14, 128.28, 129.01, 129.47, 129.88, 130.02, 130.23, 132.53, 133.58, 133.71, 135.48, 137.15, 137.31, 143.49, 143.69, 144.31, 145.84, 195.81. HR-MS. Calcd for $C_{26}H_{18}NOS$ (M+H): 392.1109. Found: *m/z* 392.1093. Anal. Calcd for $C_{26}H_{17}NOS$: C, 79.77; H, 4.38; N, 3.58. Found: C, 80.00; H, 4.61; N, 3.29.

4-(3-Phenylthieno[3,2-*c*]pyridin-2-yl)benzonitrile (9a): a white solid; mp 180–182 °C (hexane–CH_2Cl_2); IR (KBr) 2225, 1602 cm^{-1}; ^1H NMR (500 MHz) δ 7.33 (d, *J* = 7.4 Hz, 2H), 7.42 (d, *J* = 8.0 Hz, 2H), 7.45–7.47 (m, 3H), 7.56 (d, *J* = 8.0 Hz, 2H), 7.83 (d, *J* = 5.7 Hz, 1H), 8.53 (d, *J* = 5.7 Hz, 1H), 8.90 (s, 1H); ^{13}C NMR (125 MHz) δ 111.76, 116.77, 118.38, 128.53, 129.21, 130.05, 130.12, 132.27, 133.16, 134.37, 136.64, 137.61, 138.05, 143.62, 146.35, 145.39. HR-MS. Calcd for $C_{20}H_{13}N_2S$ (M+H): 313.0799. Found: *m/z* 313.0774. Anal. Calcd for $C_{20}H_{12}N_2S$: C, 76.90; H, 3.87; N, 8.97. Found: C, 76.75; H, 4.01; N, 8.66.

2-(4-Nitrophenyl)-3-phenylthieno[3,2-*c*]pyridine (9b): a yellow solid; mp 162–165 °C (hexane–CH_2Cl_2); IR (KBr) 1518, 1345 cm^{-1}; ^1H NMR (500 MHz) δ 7.35 (d, *J* = 7.4 Hz, 2H), 7.46–7.48 (m, 5H), 7.84 (dd, *J* = 5.7, 1.1 Hz, 1H), 8.13 (d, *J* = 9.2 Hz, 2H), 8.54 (d, *J* = 5.7 Hz, 1H), 8.91 (s, 1H); ^{13}C NMR (125 MHz) δ 116.78, 123.79, 128.63 (2C), 129.27, 130.05, 130.29, 133.09, 134.84, 136.61, 139.98, 143.71, 146.45, 146.49, 147.18. HR-MS. Calcd for $C_{19}H_{13}N_2O_2S$ (M+H): 333.0697. Found: *m/z* 333.0691. Anal. Calcd for $C_{19}H_{12}N_2O_2S$: C, 68.66; H, 3.64; N, 8.43. Found: C, 68.55; H, 3.59; N, 8.46.

Phenyl[4-(3-phenylthieno[3,2-*c*]pyridin-2-yl)phenyl]methanone (9c): a white solid; mp 105–108 °C (hexane–CH_2Cl_2); IR (KBr) 1657 cm^{-1}; ^1H NMR (400 MHz) δ 7.36–7.50 (m, 9H), 7.59 (d, *J* = 7.3 Hz, 1H), 7.73 (d, *J* = 7.8 Hz, 2H), 7.78 (d, *J* = 7.8 Hz, 2H), 7.83 (d, *J* = 5.9 Hz, 1H), 8.52 (d, *J* = 5.9 Hz, 1H), 8.90 (s, 1H); ^{13}C NMR (125 MHz) δ 116.75, 128.27, 128.30, 129.07, 129.42, 129.91, 130.15, 130.29 (2C), 132.52, 133.55, 133.64, 136.86, 137.29, 137.42, 138.78, 143.31, 146.18, 146.33, 195.89. HR-MS. Calcd for $C_{26}H_{18}NOS$ (M+H): 392.1109. Found: *m/z* 392.1123. Anal. Calcd for $C_{26}H_{17}NOS$: C, 79.77; H, 4.38; N, 3.58. Found: C, 79.56; H, 4.70; N, 3.54.

4-[3-(3-Chlorophenyl)thieno[3,2-*c*]pyridin-2-yl]benzonitrile (9d): a white solid; mp 190–192 °C (hexane–CH_2Cl_2); IR (KBr) 2232, 1600 cm^{-1}; ^1H NMR (500 MHz) δ 7.20 (d, *J* = 7.4 Hz, 1H), 7.36–7.43 (m, 5H), 7.60 (d, *J* = 8.0 Hz, 2H), 7.84 (d, *J* = 5.2 Hz, 1H), 8.55 (d, *J* = 5.2 Hz, 1H), 8.69 (s, 1H); ^{13}C NMR (125 MHz) δ 112.13, 116.80, 118.25, 128.33, 128.78, 130.00, 130.12, 130.50, 132.41, 132.62, 134.99, 135.12, 136.28, 137.55, 138.43, 143.80, 146.08, 146.32. HR-MS. Calcd for $C_{20}H_{12}ClN_2S$ (M+H): 347.0409. Found: *m/z* 347.0425. Anal. Calcd for $C_{20}H_{11}ClN_2S$: C, 69.26; H, 3.20; N, 8.08. Found: C, 69.15; H, 3.23; N, 7.87.

4-[3-(4-Methoxyphenyl)thieno[3,2-*c*]pyridin-2-yl]benzonitrile (9e): a yellow solid; mp 203–206 °C (hexane–CH_2Cl_2); IR (KBr) 2225, 1605 cm^{-1}; ^1H NMR (400 MHz) δ 3.88 (s, 3H), 6.99 (d, *J* = 8.8 Hz, 2H), 7.25 (d, *J* = 8.8 Hz, 2H), 7.43 (d, *J* = 7.8 Hz, 2H), 7.57 (d, *J* = 7.8 Hz, 2H), 7.82 (d, *J* = 4.9 Hz, 1H), 8.52 (d, *J* = 4.9 Hz, 1H), 8.91 (s, 1H); ^{13}C NMR (125 MHz) δ 55.30, 111.60, 113.97, 114.66, 116.84, 118.42, 125.09, 130.07, 131.21, 132.26, 134.08, 136.79, 137.12, 138.22, 143.43, 146.35, 159.67. HR-MS. Calcd for $C_{21}H_{15}N_2OS$ (M+H): 343.0905. Found: *m/z* 343.0891. Anal. Calcd for $C_{21}H_{14}N_2OS$: C, 73.66; H, 4.12; N, 8.18. Found: C, 73.50; H, 4.38; N, 8.08.

Phenyl{4-[3-(4-methoxyphenyl)thieno[3,2-*c*]pyridin-2-yl]}phenyl}methanone (9f): a yellow solid; mp 154–158 °C (hexane–CH_2Cl_2); IR (KBr) 1654 cm^{-1}; ^1H NMR (400 MHz) δ 3.87 (s, 3H), 6.98 (d, *J* = 7.8 Hz, 2H), 7.29 (d, *J* = 8.8 Hz, 2H), 7.45 (d, *J* = 8.8 Hz, 2H), 7.49 (t, *J* = 7.4 Hz, 2H), 7.59 (t, *J* = 7.4 Hz, 1H), 7.74 (d, *J* = 7.8 Hz, 2H), 7.79 (d, *J* = 7.4 Hz, 2H), 7.82 (d, *J* = 5.9 Hz, 1H), 8.51 (d, *J* = 5.9 Hz, 1H), 8.91 (s, 1H); ^{13}C NMR (100 MHz) δ 55.27, 114.55, 116.76, 125.58, 128.32, 129.40, 129.93, 130.32, 131.31, 132.52, 133.36, 136.75, 136.98, 137.32, 137.66, 138.24, 143.28, 146.25, 146.31, 159.50, 195.93. HR-MS. Calcd for $C_{27}H_{20}NO_2S$ (M+H): 422.1214. Found: *m/z* 422.1202. Anal. Calcd for $C_{27}H_{19}NO_2S$: C, 76.93; H, 4.54; N, 3.32. Found: C, 77.10; H, 4.30; N, 2.99.

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