Sulfur-Silicon Bond Activation Catalysed by Cl/Br Ions: Waste-Free Synthesis of Unsymmetrical Thioethers by Replacing Fluoride Catalysis and Fluorinated Substrates in S_NAr Reactions

Xiaojuan Jia, Lei Yu, Jianping Liu, Qing Xu, Marcel Sickert, Lianhui Chen, and Mark Lautens

Zhejiang Key Laboratory of Carbon Materials, College of Chemistry and Materials Engineering, Wenzhou University, Wenzhou, Zhejiang 325035, China
Davenport Chemistry Laboratories, Department of Chemistry, University of Toronto, 80 St. George Street, Toronto, ON, M5S 3H6, Canada
School of Chemistry and Chemical Engineering, Yangzhou University, Yangzhou, Jiangsu 225002, China

Emails: qing-xu@wzu.edu.cn; mlautens@chem.utoronto.ca

Contents

Experimental..........................................................................................................................S2
Typical Procedures for Small and Large Scale Reactions, Characterization of the Products and Byproduct Me_3SiCl and Their References...........................................................................S2
Detailed Condition Screening Table.....................................................................................S13
Copies of ^1H and ^13C NMR Spectra of the Products and a Byproduct..............................S14
Experimental

General. Unless otherwise noted, substrates, catalysts, and solvents were all purchased and used without further purification. Except PhSSiMe₃, other S-Si reagents were prepared according to the reported literature procedure (Bull. Chem. Soc. Jpn. 1978, 51, 2183; Org. Lett. 2012, 14, 1846). Small scale reactions were carried out in sealed Schlenk tubes under nitrogen atmosphere using degassed commercial solvents and then monitored by TLC and/or GC-MS. Products were purified by column chromatography on silica gel using petroleum ether and ethyl acetate as the eluent. Unless otherwise noted, ¹H and ¹³C NMR spectra were measured on a Bruker Avance-III 500 instrument (500 MHz for ¹H, 125.4 MHz for ¹³C NMR spectroscopy) using CDCl₃ as the solvent. Dry CDCl₃ was obtained by distillation under nitrogen after dried over CaCl₂, and then stored in a sealed Schlenk tube over dry molecular sieves under nitrogen protection. Chemical shifts for ¹H and ¹³C NMR were referred to internal Me₄Si (0 ppm) as the standard. Mass spectra were measured on a Shimadzu GC-MS-QP2010 Plus spectrometer (EI). HRMS (ESI) analysis was measured on a Bruker micrOTOF-Q II instrument.

Typical Procedure of TBAB-Catalysed S_NAr Reaction of 2-Chloropyridine with Phenylthiotrimethylsilane for Heteroaryl Aryl Thioether Synthesis. The mixture of 2-chloropyridine 3a (0.047 ml, 0.5 mmol), phenylthiotrimethylsilane 1a (0.104 ml, 0.55 mmol, 1.1 equiv.), and TBAB (0.0161 g, 10 mol%) in acetonitrile (0.5 mL) was sealed under nitrogen in a Schlenk tube (10 mL, see the picture below for the apparatus) and then stirred at 100 °C for 48 h. The reaction was monitored by TLC and/or GC-MS. After completion of the reaction, solvent was evaporated under vacuum. The residue was then purified by flash column chromatography on silica gel using petroleum ether and ethyl acetate as the eluent. The target product 6aa was obtained in 96% isolated yield.
2-(Phenylthio)pyridine (6aa). Colorless oil. $^1$H NMR (500 MHz, CDCl$_3$): $\delta$ 8.43 (dd, $J = 5.0$ Hz, $J = 1.0$ Hz, 1H), 7.61-7.58 (m, 2H), 7.46 (dd, $J = 8.0$ Hz, $J = 2.0$ Hz, 1H), 7.44-7.41 (m, 3H), 6.99 (ddd, $J = 7.5$ Hz, $J = 5.0$ Hz, $J = 1.0$ Hz, 1H), 6.89 (d, $J = 8.0$ Hz, 1H). $^{13}$C NMR (125.4 MHz, CDCl$_3$): $\delta$ 161.5, 149.6, 136.7, 134.9, 131.1, 129.6, 129.0, 121.4, 119.9. MS (EI): m/z (%) 187 (25), 186 (100), 154 (1), 115 (5), 109 (2), 93 (5), 78 (7), 65 (4), 52 (3), 51 (12). This compound was known: S. Yasuike, M. Nishioka, N. Kakusawa, J. Kurita, *Tetrahedron Lett.* 2011, 52, 6403-6406.

4-Methyl-2-(phenylthio)pyridine (6ab). Yellow oil. $^1$H NMR (500 MHz, CDCl$_3$): $\delta$ 8.28 (d, $J = 5.0$ Hz, 1H), 7.59-7.56 (m, 2H), 7.43-7.38 (m, 3H), 6.82 (d, $J = 5.0$ Hz, 1H), 6.74 (s, 1H), 2.20 (s, 3H). $^{13}$C NMR (125.4 MHz, CDCl$_3$): $\delta$ 160.9, 149.3, 148.0, 134.7, 131.4, 129.5, 128.8, 122.2, 121.3, 20.9. MS (EI): m/z (%) 201 (26), 200 (100), 186 (4), 115 (2), 109 (3), 100 (4), 77 (4), 65 (19), 51 (6). This compound was known: B. Sreedhar, P. S. Reddy, M. A. Reddy, *Synthesis* 2009, 1732-1738.

5-Methyl-2-(phenylthio)pyridine (6ac). Brown oil. $^1$H NMR (500 MHz, CDCl$_3$): $\delta$ 8.27 (d, $J = 2.0$ Hz, 1H), 7.56-7.54 (m, 2H), 7.40-7.36 (m, 3H), 7.28 (dd, $J = 8.0$ Hz, $J = 2.0$ Hz, 1H), 6.85 (d, $J = 8.5$ Hz, 1H), 2.25 (s, 3H). $^{13}$C NMR (125.4 MHz, CDCl$_3$): $\delta$ 157.5, 149.9, 137.5, 134.2, 132.0, 129.7, 129.4, 128.6, 121.7, 17.8. MS (EI): m/z (%) 201 (27), 200 (100), 185 (2), 156 (1), 109 (3), 93 (2), 77 (4), 65 (18), 51 (6). This compound was known: S. Arai, M. Yamazaki, M. Hida, *J. Heterocyclic Chem.* 1990, 27, 1073-1078.

2-(Phenylthio)pyridin-3-amine (6ad). Brown oil. $^1$H NMR (500 MHz, CDCl$_3$): $\delta$ 8.02 (d, $J = 3.5$ Hz, 1H), 7.28-7.24 (m, 4H), 7.21-7.17 (m, 1H), 7.07 (dd, $J = 8.0$ Hz, $J = 4.5$ Hz, 1H), 7.00 (dd, $J = 8.0$ Hz, $J = 1.5$ Hz, 1H), 4.23 (b, 2H). $^{13}$C NMR (125.4 MHz, CDCl$_3$): $\delta$ 144.2, 140.3, 139.0, 134.0, 129.4, 129.1, 126.6, 124.2, 122.0. MS (EI): m/z (%) 202 (46), 201 (100), 186 (7), 168 (5), 140 (1), 115 (2), 101 (6), 77 (4), 66 (10), 51 (4). This compound was known: X. Xu, S. Guo, Q. Dang, J. Chen, X. Bai, *J. Comb. Chem.* 2007, 9, 773-782.
2-(Phenylthio)pyridin-4-amine (6ae). Brown oil. $^1$H NMR (500 MHz, CDCl$_3$): $\delta$ 8.05 (d, $J$ = 5.5 Hz, 1H), 7.59-7.57 (m, 2H), 7.40-7.39 (m, 3H), 6.27 (dd, $J$ = 5.5 Hz, $J$ = 2.0 Hz, 1H), 6.09 (d, $J$ = 2.0 Hz, 1H), 4.07 (b, 2H). $^{13}$C NMR (125.4 MHz, CDCl$_3$): $\delta$ 161.7, 153.4, 149.8, 134.9, 131.5, 129.5, 128.9, 107.0, 106.4. MS (EI): m/z (%) 202 (26), 201 (100), 184 (6), 140 (3), 108 (2), 93 (3), 77 (3), 66 (9), 52 (3), 51 (4). HRMS Calcd for C$_{11}$H$_{11}$N$_2$S (M+H): 203.0604; found: 203.0637.

6-(Phenylthio)pyridin-3-amine (6af). Yellow oil. $^1$H NMR (500 MHz, CDCl$_3$): $\delta$ 8.02 (d, $J$ = 2.5 Hz, 1H), 7.42-7.41 (m, 1H), 7.40-7.39 (m, 1H), 7.33-7.29 (m, 2H), 7.27-7.24 (m, 1H), 7.02 (d, $J$ = 8.5 Hz, 1H), 6.88 (dd, $J$ = 8.0 Hz, $J$ = 2.5 Hz, 1H), 3.22 (b, 2H). $^{13}$C NMR (125.4 MHz, CDCl$_3$): $\delta$ 146.6, 141.0, 137.5, 134.9, 131.8, 129.2, 127.3, 125.9, 123.1. MS (EI): m/z (%) 203 (10), 202 (46), 201 (100), 184 (5), 174 (8), 173 (4), 147 (3), 101 (3), 77 (4), 66 (7). This compound was known: H. C. Winter, F. E. Reinhart. J. Am. Chem. Soc. 1940, 62 (12), 3508–3511.

3-Chloro-2-(phenylthio)pyridine (6ag). Brown oil. $^1$H NMR (500 MHz, CDCl$_3$): $\delta$ 8.20 (dd, $J$ = 4.5 Hz, $J$ = 1.5 Hz, 1H), 7.57-7.54 (m, 3H), 7.43-7.40 (m, 3H), 6.95 (dd, (dd, $J$ = 8.0 Hz, $J$ = 4.5 Hz, 1H). $^{13}$C NMR (125.4 MHz, CDCl$_3$): $\delta$ 157.5, 147.4, 136.2, 135.4, 129.7, 129.1, 129.0, 128.7, 120.6. MS (EI): m/z (%) 221 (29), 220 (100), 185 (15), 140 (2), 115 (5), 85 (2), 76 (7), 65 (6), 52 (1), 51 (9). This compound was known: X. Zhang, X. Zhang, S. Guo, J. Sulfur Chem. 2011, 32, 23-35.

4-Chloro-2-(phenylthio)pyridine (6ah). Yellow oil. $^1$H NMR (500 MHz, CDCl$_3$): $\delta$ 8.11 (d, $J$ = 5.0 Hz, 1H), 7.57-7.55 (m, 2H), 7.52-7.46 (m, 3H), 6.90 (d, $J$ = 1.0 Hz, 1H), 6.85 (dd, $J$ = 5.5 Hz, $J$ = 2.0 Hz, 1H). $^{13}$C NMR (125.4 MHz, CDCl$_3$): $\delta$ 153.8, 151.9, 148.9, 135.4, 130.19, 130.16, 128.4, 120.2, 119.4. MS (EI): m/z (%) 221 (100), 186 (44), 158 (6), 140 (14), 115 (25), 109 (19), 93 (7), 85 (10), 77 (21) 65 (22), 51 (34). HRMS Calcd for C$_{11}$H$_{9}$ClNS (M+H): 222.0139; found:222.0116.
2,4-Bis(phenylthio)pyridine (6ah'). Yellow oil. $^1$H NMR (500 MHz, CDCl$_3$): $\delta$ 8.14 (d, $J = 5.5$ Hz, 1H), 7.49-7.47 (m, 2H), 7.42-7.40 (m, 2H), 7.39-7.37 (m, 1H), 7.36-7.31 (m, 5H), 6.66 (dd, $J = 5.5$ Hz, $J = 2.0$ Hz, 1H), 6.40 (d, $J = 1.5$ Hz, 1H). $^{13}$C NMR (125.4 MHz, CDCl$_3$): $\delta$ 161.9, 151.4, 148.8, 135.2, 135.0, 130.4, 129.8, 129.64, 129.57, 129.1, 128.9, 117.3, 117.1. MS (EI): m/z (%) 295 (36), 294 (100), 260 (1), 217 (4), 185 (12), 173 (4), 147 (5), 115 (10), 77 (8), 51 (7). HRMS Caled for C$_{17}$H$_{14}$NS$_2$ (M+H): 296.0562; found: 296.0531.

5-Chloro-2-(phenylthio)pyridine (6ai). Yellow oil. $^1$H NMR (500 MHz, CDCl$_3$): $\delta$ 8.37 (d, $J = 2.5$ Hz, 1H), 7.59-7.57 (m, 2H), 7.43-7.40 (m, 4H), 6.83 (d, $J = 8.5$ Hz, 1H). $^{13}$C NMR (125.4 MHz, CDCl$_3$): $\delta$ 159.6, 148.2, 136.4, 134.9, 130.7, 129.7, 129.3, 128.3, 122.1. MS (EI): m/z (%) 221 (28), 220 (100), 185 (13), 158 (1), 140 (4), 93 (11), 76 (12), 65 (10), 51 (12). This compound was known: R. E. Tenbrink, S. W. Kortum, W. O. Patent, 2003072548, 2003.

2-Chloro-6-(phenylthio)pyridine (6aj). Yellow oil. $^1$H NMR (500 MHz, CDCl$_3$): $\delta$ 7.61-7.59 (m, 2H), 7.45-7.43 (m, 3H), 7.38-7.35 (m, 1H), 6.99 (d, $J = 7.5$ Hz, 1H), 6.69 (d, $J = 8.0$ Hz, 1H). $^{13}$C NMR (125.4 MHz, CDCl$_3$): $\delta$ 162.8, 150.8, 138.8, 135.1, 130.0, 129.8, 129.6, 119.8, 119.1. MS (EI): m/z (%) 221 (54), 220 (100), 186 (20), 153 (4), 140 (8), 115 (10), 109 (10), 93 (9), 76 (15), 65 (13), 51 (17). This compound was known: S. Kato, A. Masui, S. Ishida, *Nippon Noyaku Gakkaishi* 1989, 14, 11-22.

2,6-Bis(phenylthio)pyridine (6aj'). White solid. $^1$H NMR (300 MHz, CDCl$_3$): $\delta$ 7.58-7.55 (m, 4H), 7.39-7.38 (m, 6H), 7.17 (m, 1H), 6.51 (d, $J = 8.1$ Hz, 2H). $^{13}$C NMR (125.4 MHz, CDCl$_3$): $\delta$ 161.5, 136.9, 135.0, 130.7, 129.5, 129.0, 117.0. MS (EI): m/z (%) 296 (24), 295 (88), 294 (100), 216 (16), 186 (58), 185 (36), 115 (22), 109 (16), 77 (17), 65 (11), 51 (11). This compound was known: Y. G. Zhang, K. C. Ngeow, J. Y. Ying, *Org. Lett.* 2007, 9, 3495-3498.
2-(Phenylthio)isonicotinonitrile (6ak). White solid. $^1$H NMR (500 MHz, CDCl$_3$): $\delta$ 8.55 (d, $J = 5.0$ Hz, 1H), 7.62-7.60 (m, 2H), 7.51-7.47 (m, 3H), 7.17 (dd, $J = 5.0$ Hz, $J = 1.0$ Hz, 1H), 6.98 (s, 1H). $^{13}$C NMR (125.4 MHz, CDCl$_3$): $\delta$ 164.4, 150.2, 135.4, 130.12, 130.09, 128.8, 121.9, 121.0, 120.5, 116.2. MS (EI): m/z (%) 212 (26), 211 (100), 184 (2), 109 (4), 92 (2), 82 (1), 77 (5), 65 (6), 51 (9). HRMS Calcd for C$_{12}$H$_9$N$_2$S (M+H): 213.0481; found: 213.0439.

6-(Phenylthio)nicotinonitrile (6al). White solid. $^1$H NMR (500 MHz, CDCl$_3$): $\delta$ 8.62 (d, $J = 2.0$ Hz, 1H), 7.65-7.63 (m, 1H), 7.61-7.59 (m, 2H), 7.51-7.49 (m, 3H), 6.90 (d, $J = 8.5$ Hz, 1H). $^{13}$C NMR (125.4 MHz, CDCl$_3$): $\delta$ 167.8, 152.0, 138.8, 135.4, 130.1, 130.0, 128.4, 120.0, 116.7, 104.9. MS (EI): m/z (%) 212 (29), 211 (100), 179 (1), 140 (7), 109 (4), 92 (2), 82 (2), 77 (7), 69 (4), 51 (10). HRMS Calcd for C$_{12}$H$_9$N$_2$S (M+H): 213.0481; found: 213.0438.

5-Nitro-2-(phenylthio)pyridine (6am). White solid. $^1$H NMR (500 MHz, CDCl$_3$): $\delta$ 9.19 (d, $J = 2.5$ Hz, 1H), 8.18 (dd, $J = 9.0$ Hz, $J = 3.0$ Hz, 1H), 7.63-7.61 (m, 2H), 7.63-7.49 (m, 3H), 6.94 (d, $J = 9.0$ Hz, 1H). $^{13}$C NMR (125.4 MHz, CDCl$_3$): $\delta$ 170.2, 145.0, 141.0, 135.5, 131.1, 130.3, 130.1, 128.4, 119.7. MS (EI): m/z (%) 232 (38), 231 (100), 201 (11), 185 (49), 173 (5), 115 (11), 109 (29), 77 (10), 65 (17), 52 (1), 51 (8). This compound was known: E. A. Hamed, A. A. El-Bardan, E. F. Saad, G. A. Gohar, G. A. Hassan, *J. Chem. Soc., Perkin Trans. 2*, 1997, 2415-2422.

2-(Phenylthio)isonicotinic acid (6an). White solid. $^1$H NMR (500 MHz, d$_6$-DMSO): $\delta$ 8.58 (dd, $J = 5.0$ Hz, $J = 1.0$ Hz, 1H), 7.64-7.62 (m, 2H), 7.54-7.53 (m, 4H), 7.29 (s, 1H). $^{13}$C NMR (125.4 MHz, d$_6$-DMSO): $\delta$ 165.6, 161.5, 150.4, 139.8, 134.8, 130.0, 129.7, 129.4, 119.4, 119.2. This compound was known: M. Ryozo, H. Katsumi, Patent, 19730515, 1973.
**6-(Phenylthio)nicotinic acid (6ao).** White solid. $^1$H NMR (500 MHz, $d_6$-DMSO): $\delta$ 8.85 (s, 1H), 8.06 (d, $J = 8.5$ Hz, 1H), 7.63-7.61 (m, 2H), 7.53-7.52 (m, 3H), 6.95 (d, $J = 8.5$ Hz, 1H). $^{13}$C NMR (125.4 MHz, $d_6$-DMSO): $\delta$ 163.9, 150.3, 137.7, 134.92, 134.89, 130.01, 129.98, 129.71, 129.67, 129.3, 119.9. This compound was known: M. Ryozo, H. Katsumi. Patent, 19730515, 1973.

![Structure of 6-(Phenylthio)nicotinic acid (6ao)]

**4-(Phenylthio)pyridine (6ap).** Brown oil. $^1$H NMR (500 MHz, CDCl$_3$): $\delta$ 8.34 (dd, $J = 4.5$ Hz, $J = 1.5$ Hz, 2H), 7.56-7.54 (m, 2H), 7.46-7.44 (m, 3H), 6.94 (dd, $J = 4.5$ Hz, $J = 1.5$ Hz, 2H). $^{13}$C NMR (125.4 MHz, CDCl$_3$): $\delta$ 150.3, 149.3, 135.1, 129.9, 129.6, 129.5, 120.8. MS (EI): m/z (%): 187 (100), 186 (68), 160 (7), 154 (7), 134 (2), 128 (3), 115 (14), 65 (7), 52 (2), 51 (28). This compound was known: G. R. Alfonso, F. I. M. Angeles, R. G. Arrayas, J. C. Carretero, *Chem. Eur. J.* 2011, 17, 3567-3570.

![Structure of 4-(Phenylthio)pyridine (6ap)]

**2-(Phenylthio)quinoline (6aq).** Yellow oil. $^1$H NMR (500 MHz, CDCl$_3$): $\delta$ 7.94 (d, $J = 8.5$ Hz, 1H), 7.86 (d, $J = 9.0$ Hz, 1H), 7.68-7.63 (m, 4H), 7.45-7.41 (m, 4H), 6.97 (d, $J = 8.5$ Hz, 1H). $^{13}$C NMR (125.4 MHz, CDCl$_3$): $\delta$ 161.5, 148.0, 136.4, 135.1, 130.8, 129.9, 129.6, 129.1, 128.3, 127.5, 125.8, 125.7, 119.5. MS (EI): m/z (%): 237 (44), 236 (100), 204 (3), 165 (2), 128 (13), 119 (5), 101 (17), 65 (3), 51 (6). This compound was known: R. Saari, J. C. Toermae, T. Nevalainen, *Bioorg. Med. Chem.* 2011, 19, 939-950.

![Structure of 2-(Phenylthio)quinoline (6aq)]

**2-(Phenylthio)pyrimidine (6ar).** Brown oil. $^1$H NMR (500 MHz, CDCl$_3$): $\delta$ 8.48 (d, $J = 5.0$ Hz, 2H), 7.64-7.62 (m, 2H), 7.45-7.42 (m, 3H), 6.95 (t, $J = 5.0$ Hz, 1H). $^{13}$C NMR (125.4 MHz, CDCl$_3$): $\delta$ 172.8, 157.5, 135.2, 129.4, 129.3, 116.9. MS (EI): m/z (%): 188 (35), 187 (100), 160 (3), 135 (4), 109 (10), 77 (16), 65 (9), 63 (4), 51 (11). This compound was known: M. Egi, L. S. Liebeskind, *Org. Lett.* 2003, 5, 801-802.

![Structure of 2-(Phenylthio)pyrimidine (6ar)]

**2-Phenyl-4-(phenylthio)quinazoline (6as).** White solid. $^1$H NMR (500 MHz, CDCl$_3$): $\delta$ 8.24-8.21 (m, 2H), 8.19-8.18 (m, 1H), 8.02 (d, $J = 8.5$ Hz, 1H), 7.86-7.83 (m, 1H), 7.73-7.69 (m, 2H), 7.59-7.51 (m, 4H), 7.41-7.34 (m, 3H). $^{13}$C NMR (125.4 MHz, CDCl$_3$): $\delta$ 171.0, 159.0, 149.4, 137.7,

2-(Phenylthio)benzo[d]thiazole (6at). Yellow oil. $^1$H NMR (500 MHz, CDCl$_3$): $\delta$ 7.87 (d, $J = 8.0$ Hz, 1H), 7.74-7.72 (m, 2H), 7.63 (d, $J = 8.0$ Hz, 1H), 7.52-7.44 (m, 3H), 7.40-7.37 (m, 1H), 7.26-7.23 (m, 1H). $^{13}$C NMR (125.4 MHz, CDCl$_3$): $\delta$ 169.5, 153.9, 135.5, 135.2, 130.4, 130.0, 129.8, 126.1, 124.3, 121.9, 120.7. MS (EI): m/z (%) 243 (56), 242 (100), 209 (2), 121 (8), 108 (9), 82 (4), 77 (6), 65 (8), 51 (8). This compound was known: C. Dai, Z. Xu, F. Huang, Z. Yu, Y. Gao, *J. Org. Chem.* **2012**, 77, 4414-4419.

2-($p$-Tolythio)pyridine (6ba). Colorless oil. $^1$H NMR (500 MHz, CDCl$_3$): $\delta$ 8.39 (d, $J = 4.5$ Hz, 1H), 7.48 (d, $J = 8.0$ Hz, 2H), 7.22 (d, $J = 8.0$ Hz, 2H), 6.95 (dd, $J = 8.0$ Hz, $J = 5.0$ Hz, 1H), 6.83 (d, $J = 8.0$ Hz, 1H), 2.38 (s, 3H). $^{13}$C NMR (125.4 MHz, CDCl$_3$): $\delta$ 162.1, 149.3, 139.3, 136.5, 135.1, 130.4, 127.1, 120.7, 119.5, 21.2. MS (EI): m/z (%) 202 (7), 201 (30), 200 (100), 199 (8), 100 (9), 91 (5), 79 (5), 78 (10), 77 (6), 65 (5), 63 (5), 51 (11). This compound was known: A. K. Verma, R. R. Jha, R. Chaudhary, R. K. Tiwari, A. K. Danodia, *Adv. Synth. Catal.* **2013**, 355, 421-438.

2-(4-Methoxyphenylthio)pyridine (6ca). Brown oil. $^1$H NMR (500 MHz, CDCl$_3$): $\delta$ 8.40 (d, $J = 5.0$ Hz, 1H), 7.55-7.52 (m, 2H), 7.44-7.41 (m, 1H), 6.98-6.94 (m, 3H), 6.79 (d, $J = 8.0$ Hz, 1H), 3.85 (s, 3H). $^{13}$C NMR (125.4 MHz, CDCl$_3$): $\delta$ 162.8, 160.7, 149.4, 137.2, 136.6, 121.2, 120.5, 119.4, 115.3, 55.4. MS (EI): m/z (%) 218 (11), 217 (53), 216 (100), 202 (8), 201 (23), 186 (5), 174 (7), 173 (12), 78 (17), 73 (5), 70 (12), 63 (6), 61 (11), 51 (6). This compound was known: C. Robert Lucas. *Can. J. Chem.* **1986**, 64, 1758-1763.

2-(Benzylthio)pyridine. (6da). Yellow oil. $^1$H NMR (500 MHz, CDCl$_3$): $\delta$ 8.45-8.43 (m, 1H), 7.44-7.39 (m, 3H), 7.29-7.26 (m, 2H), 7.23-7.21 (m, 1H), 7.13 (d, $J = 8.0$ Hz, 1H), 6.97-6.94 (m, 1H), 4.43 (s, 2H). $^{13}$C NMR (125.4 MHz, CDCl$_3$): $\delta$ 158.8, 149.3, 137.9, 135.9, 128.9, 128.4, 127.0,
122.0, 119.5, 34.4. MS (EI): m/z (%) 202 (9), 201 (65), 200 (5), 169 (14), 168 (100), 167 (23), 124 (8), 92 (5), 91 (49), 79 (13), 78 (4), 65 (17), 52 (4), 51 (5). This compound was known: K. Mai, G. Patil, J. Org. Chem. 1986, 51, 3545-3548.

**Typical Procedure of TBAC-Catalysed S_NAr Reaction of p-Chloronitrobenzene with Phenylthiotrimethylsilane for Diaryl Thioether Synthesis.** The mixture of p-chloronitrobenzene 7a (0.0788g, 0.5 mmol.), phenylthiotrimethylsilane 1a (0.104 ml, 0.55 mmol, 1.1 equiv.), and TBAC (0.0417 g, 30 mol%) in DMF (0.5 mL) was sealed under nitrogen in a Schlenk tube (10 mL, the same apparatus as in the above picture) and then stirred at 150 °C for 43 h. The reaction was monitored by TLC and/or GC-MS. After completion of the reaction, solvent was evaporated under vacuum. The residue was then purified by flash column chromatography on silica gel using petroleum ether and ethyl acetate as the eluent. The target product 8a was obtained in 95% isolated yield.

![4-(Phenylthio)nitrobenzene (8a)](image)

**4-(Phenylthio)nitrobenzene (8a).** Yellow oil. \(^1^H\) NMR (500 MHz, CDCl\(_3\)): \(\delta\ 8.05\) (d, \(J = 9.0\) Hz, 2H), 7.55-7.52 (m, 2H), 7.47-7.44 (m, 3H), 7.16 (d, \(J = 9.0\) Hz, 2H). \(^1^C\) NMR (125.4 MHz, CDCl\(_3\)): \(\delta\ 148.4, 145.2, 134.7, 130.3, 129.9, 129.6, 126.5, 124.0\). MS (EI): m/z (%) 233 (9), 232 (34), 231 (100), 186 (10), 185 (55), 173 (5), 115 (14), 109 (37), 93 (7), 77 (13), 69 (6), 65 (18), 51 (12). This compound was known: P. Guan, C. S. Cao, Y. Liu, Y. F. Li, P. He, Q. Chen, G. Liu, Y. H. Shi, Tetrahedron Lett. 2012, 53, 5987-5992.

![2-(Phenylthio)nitrobenzene (8b)](image)

**2-(Phenylthio)nitrobenzene (8b).** Yellow oil. \(^1^H\) NMR (500 MHz, CDCl\(_3\)): \(\delta\ 8.20\) (dd, \(J = 8.0\) Hz, \(J = 1.5\) Hz, 1H), 7.58-7.56 (m, 2H), 7.50-7.46 (m, 3H), 7.35-7.32 (m, 1H), 7.22-7.19 (m, 1H), 8.36 (dd, \(J = 8.0\) Hz, \(J = 1.0\) Hz, 1H). \(^1^C\) NMR (125.4 MHz, CDCl\(_3\)): \(\delta\ 144.8, 139.4, 135.8, 133.4, 130.8, 130.05, 129.97, 128.3, 125.7, 124.9\). MS (EI): m/z (%) 231 (13), 202 (11), 184 (26), 183 (6), 168 (15), 167 (100), 166 (39), 152 (16), 140 (10), 139 (19), 78 (8), 77 (20), 69 (7), 51 (13). This compound was known: A. Ivachtchenko, E. Golovina, M. Kadicova, O. Mitkin, S. Tkachenko, Bioorg. Med. Chem. 2013, 21, 4614-4627.
4-(Phenylthio)benzonitrile (8c). Yellow oil. $^1$H NMR (500 MHz, CDCl$_3$): $\delta$ 7.52-7.49 (m, 2H), 7.46 (d, $J$ = 6.5 Hz, 2H), 7.44-7.42 (m, 3H), 7.16 (d, $J$ = 6.5 Hz, 2H). $^{13}$C NMR (125.4 MHz, CDCl$_3$): $\delta$ 145.7, 134.5, 132.3, 130.7, 129.9, 129.3, 127.2, 118.7, 108.6. MS (EI): m/z (%) 213 (6), 212 (18), 211 (100), 210 (67), 209 (13), 184 (8), 183 (12), 171 (5), 109 (8), 92 (11), 77 (21), 69 (6), 65 (9), 51 (26), 50 (6). This compound was known: P. Guan, C. S. Cao, Y. Liu, Y. F. Li, P. He, Q. Chen, G. Liu, Y. H. Shi, Tetrahedron Lett. 2012, 53, 5987-5992.

\[\text{CH}_2=\text{CN}\]

2-(Phenylthio)benzonitrile (8d). Yellow oil. $^1$H NMR (500 MHz, CDCl$_3$): $\delta$ 7.62 (dd, $J$ = 7.5 Hz, $J$ = 1.0 Hz, 1H), 7.47-7.45 (m, 2H), 7.42-7.37 (m, 4H), 7.27-7.24 (m, 1H), 7.12 (d, $J$ = 8.0 Hz, 1H). $^{13}$C NMR (125.4 MHz, CDCl$_3$): $\delta$ 142.2, 133.6, 133.5, 132.9, 131.7, 129.8, 129.7, 128.8, 126.4, 116.9, 112.7. MS (EI): m/z (%) 212 (17), 211 (100), 210 (50), 209 (9), 185 (8), 184 (41), 183 (9), 109 (8), 108 (6), 92 (10), 77 (26), 69 (7), 65 (10), 51 (28), 50 (6). This compound was known: P. Guan, C. S. Cao, Y. Liu, Y. F. Li, P. He, Q. Chen, G. Liu, Y. H. Shi, Tetrahedron Lett. 2012, 53, 5987-5992.

\[\text{Me}^+\rightarrow\text{CH}=[\text{CN}]\]

4-(Phenylthio)acetophenone (8e). Yellow solid. $^1$H NMR (500 MHz, CDCl$_3$): $\delta$ 7.81 (d, $J$ = 8.5 Hz, 1H), 7.50-7.48 (m, 2H), 7.42-7.36 (m, 3H), 7.20 (d, $J$ = 8.5 Hz, 1H), 2.54 (s, 3H). $^{13}$C NMR (125.4 MHz, CDCl$_3$): $\delta$ 197.1, 144.9, 134.4, 133.8, 132.0, 129.6, 128.9, 128.7, 127.4, 26.4. MS (EI): m/z (%) 229 (13), 228 (76), 214 (15), 213 (100), 185 (19), 184 (69), 152 (14), 109 (7), 107 (7), 92 (6), 91 (6), 77 (7), 65 (9), 51 (10). This compound was known: S. G. Babu, R. Karvembu, Tetrahedron Lett. 2013, 54, 1677-1680.

\[\text{Cl}^+\rightarrow\text{CH}=[\text{CN}]\]

5-Chloro-2-(phenylthio)acetophenone (8f). Yellow oil. $^1$H NMR (500 MHz, CDCl$_3$): $\delta$ 7.77 (d, $J$ = 2.5 Hz, 1H), 7.52-7.49 (m, 2H), 7.43-7.41 (m, 3H), 7.20 (d, $J$ = 8.5 Hz, 1H), 6.82 (d, $J$ = 8.5 Hz, 1H), 2.65 (s, 3H). $^{13}$C NMR (125.4 MHz, CDCl$_3$): $\delta$ 198.0, 140.2, 135.9, 134.8, 132.8, 131.9, 130.3, 130.1, 129.8, 129.1, 28.2. MS (EI): m/z (%) 264 (35), 263 (17), 262 (100), 249 (22), 247 (57), 212 (52), 185 (31), 184 (67), 183 (17), 173 (22), 171 (60), 152 (17), 139 (33), 77 (13), 69 (11), 51 (20). This compound was known: M. Rajsner, F. Miksik, M. Protiya, Collection Czechoslov.
4-(Phenylthio)benzaldehyde (8g). Yellow oil. $^1$H NMR (500 MHz, CDCl$_3$): $\delta$ 9.91 (s, 1H), 7.72 (d, $J = 8.5$ Hz, 2H), 7.54-7.52 (m, 2H), 7.44-7.41 (m, 3H), 7.23 (d, $J = 8.0$ Hz, 2H). $^{13}$C NMR (125.4 MHz, CDCl$_3$): $\delta$ 191.1, 147.2, 134.3, 133.7, 131.4, 130.1, 129.8, 129.1, 127.3. MS (EI): m/z (%) 216 (6), 215 (18), 214 (100), 213 (53), 186 (9), 185 (37), 184 (57), 152 (14), 109 (8), 77 (12), 69 (7), 65 (10), 51 (19), 50 (7). This compound was known: S. G. Babu, R. Karvembu, Tetrahedron Lett. 2013, 54, 1677-1680.

Detailed Procedure for Large Scale Reaction of 2-Chloropyridine and Phenylthiotrimethylsilane Catalysed by TBAC (eq. 1 in the text). A normal distillation apparatus was installed by equipping pre-dried glasswares, such as 50 mL round-bottomed flask with a stirrer, distillation head, condenser, receiving flask, etc. To the round-bottomed flask was added dry TBAC (1.3896 g, 10 mol%). The apparatus was then degassed and charged with nitrogen. Under a flow of nitrogen, 2-chloropyridine 3a (4.7 mL, 50 mmol) and phenylthiotrimethylsilane 1a (9.5 mL, 50 mmol, 1 equiv.) was successively added via syringes with long needles to the round-bottomed flask. The solvent-free mixture was firstly stirred and heated under nitrogen at 100 °C for 2 h. The mixture was then heated to 120 °C to distill out the byproduct trimethylchlorosilane (Me$_3$SiCl). In another 4 h at 120 °C, Me$_3$SiCl was obtained as colorless liquid, and the distillation ceased to finally give a recovery yield of 4.89g (90%) of Me$_3$SiCl, which was then characterized by $^1$H and $^{13}$C NMR analysis in dry CDCl$_3$. The residue of the reaction mixture in the round-bottomed flask was monitored by TLC and GC-MS, showing complete conversion of 2-chloropyridine and phenylthiotrimethylsilane. Column chromatography of the reaction residue gave 8.60 g (92% isolated yield) of 6aa. See Figure S1 in the next page for the distillation apparatus and the freshly collected Me$_3$SiCl.

Large Scale Reaction of 4-Chloronitrobenzene and Phenylthiotrimethylsilane Catalysed by TBAC (eq. 2 in the text). The same procedure as above was then applied to a neat large scale reaction of 4-chloronitrobenzene 7a (3.94 g, 25 mmol) and phenylthiotrimethylsilane 1a (4.75 mL, 25 mmol, 1 equiv.) in the presence of TBAC (2.09 g, 30 mol%). The mixture was firstly heated at 100 °C for 1 h and then 120 °C for 2 h under nitrogen to complete the distillation process, which finally gave 2.26 g (83%) of colourless Me$_3$SiCl. TLC analysis of the reaction residue showed
complete conversion of the reactants. Column chromatography of the reaction residue gave 5.31 g (92% isolated yield) of 8a.

**Large Scale Reaction of 2-Bromopyridine and Phenylthiotrimethylsilane Catalysed by TBAB (eq. 3 in the text).** The same procedure as above was then applied to a neat large scale reaction of 2-bromopyridine 4a (1.9 mL, 20 mmol) and phenylthiotrimethylsilane 1a (3.8 mL, 20 mmol, 1 equiv.) in the presence of TBAB (0.645 g, 10 mol%). The mixture was firstly heated at 100-140 °C under nitrogen for 1 h, but no liquid could be distilled during the time. The mixture was then heated at more than 140 °C, at 140-150 °C. Small amounts of white crystal first appeared in the condenser pipe. A colourless liquid was then distilled as the heating continued. After heated at 140-150 °C for 4 h, the distillation stopped to finally gave 1.60 g (52%) of colourless Me₃SiBr. TLC analysis of the reaction residue showed complete conversion of the reactants. Column chromatography of the reaction residue gave 3.18 g (85% isolated yield) of 6aa. Me₃SiBr is a highly moisture-sensitive chemical with pungent smell and easy to fog and decompose when exposed to air.

**Figure S1. Left:** the distillation apparatus; **Right:** freshly recovered Me₃SiCl

**Trimethylchlorosilane (Me₃SiCl).** Colorless liquid. ¹H NMR (500 MHz, dry CDCl₃): δ 0.44 (S, 9H). ¹³C NMR (125.4 MHz, dry CDCl₃): δ 3.2. Consistent with the known data:
(a) [http://www.sigmaaldrich.com/spectra/fnmr/FNMR009798.PDF](http://www.sigmaaldrich.com/spectra/fnmr/FNMR009798.PDF).
**Table S1.** Condition Optimization for TBAX-Catalysed S-Si Bond Activation in SNAr Reaction of PhS-SiMe\textsubscript{3} (1a) and 2-Halopyridines (2a-5a).\textsuperscript{a}

![Chemical structure](image)

<table>
<thead>
<tr>
<th>run</th>
<th>X</th>
<th>MX (mol%)</th>
<th>Solvent</th>
<th>T, t</th>
<th>6aa%\textsuperscript{b}</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>F</td>
<td>TBAF (30)</td>
<td>CH\textsubscript{3}CN</td>
<td>30 °C, 24 h</td>
<td>trace</td>
</tr>
<tr>
<td>2</td>
<td>F</td>
<td>TBAF (30)</td>
<td>CH\textsubscript{3}CN</td>
<td>60 °C, 24 h</td>
<td>78</td>
</tr>
<tr>
<td>3</td>
<td>Cl</td>
<td>TBAF (30)</td>
<td>CH\textsubscript{3}CN</td>
<td>60 °C, 24 h</td>
<td>30</td>
</tr>
<tr>
<td>4</td>
<td>Cl</td>
<td>TBAF (120)</td>
<td>CH\textsubscript{3}CN</td>
<td>30 °C, 24 h</td>
<td>trace</td>
</tr>
<tr>
<td>5</td>
<td>Cl</td>
<td>TBAF (30)</td>
<td>CH\textsubscript{3}CN</td>
<td>60 °C, 24 h</td>
<td>92</td>
</tr>
<tr>
<td>6</td>
<td>Cl</td>
<td>TBAF (30)</td>
<td>CH\textsubscript{3}CN</td>
<td>80 °C, 24 h</td>
<td>(63)</td>
</tr>
<tr>
<td>7</td>
<td>Cl</td>
<td>TBAF (30)</td>
<td>CH\textsubscript{3}CN</td>
<td>100 °C, 24 h</td>
<td>87 (96)</td>
</tr>
<tr>
<td>8</td>
<td>Cl</td>
<td>CsF (30)</td>
<td>CH\textsubscript{3}CN</td>
<td>100 °C, 24 h</td>
<td>(23)</td>
</tr>
<tr>
<td>9</td>
<td>Cl</td>
<td>NaF (30)</td>
<td>CH\textsubscript{3}CN</td>
<td>100 °C, 24 h</td>
<td>(8)</td>
</tr>
<tr>
<td>10</td>
<td>Cl</td>
<td>KF (30)</td>
<td>CH\textsubscript{3}CN</td>
<td>100 °C, 24 h</td>
<td>(70)</td>
</tr>
<tr>
<td>11</td>
<td>Cl</td>
<td>—</td>
<td>CH\textsubscript{3}CN</td>
<td>100 °C, 24 h</td>
<td>(0)</td>
</tr>
<tr>
<td>12</td>
<td>Cl</td>
<td>TBAF (30)</td>
<td>CH\textsubscript{3}CN (under air)</td>
<td>100 °C, 24 h</td>
<td>trace</td>
</tr>
<tr>
<td>13</td>
<td>Br</td>
<td>TBAF (30)</td>
<td>CH\textsubscript{3}CN</td>
<td>100 °C, 24 h</td>
<td>71</td>
</tr>
<tr>
<td>14</td>
<td>I</td>
<td>TBAF (30)</td>
<td>CH\textsubscript{3}CN</td>
<td>100 °C, 24 h</td>
<td>76</td>
</tr>
<tr>
<td>15</td>
<td>Cl</td>
<td>TBAC (30)</td>
<td>CH\textsubscript{3}CN</td>
<td>100 °C, 48 h</td>
<td>92</td>
</tr>
<tr>
<td>16</td>
<td>Cl</td>
<td>TBAB (30)</td>
<td>CH\textsubscript{3}CN</td>
<td>100 °C, 48 h</td>
<td>94</td>
</tr>
<tr>
<td>17</td>
<td>Cl</td>
<td>TBAI (30)</td>
<td>CH\textsubscript{3}CN</td>
<td>100 °C, 48 h</td>
<td>84</td>
</tr>
<tr>
<td>18</td>
<td>Cl</td>
<td>TBAB (20)</td>
<td>CH\textsubscript{3}CN</td>
<td>100 °C, 48 h</td>
<td>96</td>
</tr>
<tr>
<td>19</td>
<td>Cl</td>
<td>TBAB (10)</td>
<td>CH\textsubscript{3}CN</td>
<td>100 °C, 48 h</td>
<td>96</td>
</tr>
<tr>
<td>20</td>
<td>Cl</td>
<td>TBAB (10)</td>
<td>DMF</td>
<td>100 °C, 48 h</td>
<td>90</td>
</tr>
<tr>
<td>21</td>
<td>Cl</td>
<td>TBAB (10)</td>
<td>DMSO</td>
<td>100 °C, 48 h</td>
<td>15</td>
</tr>
<tr>
<td>22</td>
<td>Cl</td>
<td>TBAB (10)</td>
<td>Toluene</td>
<td>100 °C, 48 h</td>
<td>76</td>
</tr>
<tr>
<td>23</td>
<td>Cl</td>
<td>TBAB (10)</td>
<td>THF</td>
<td>100 °C, 48 h</td>
<td>78</td>
</tr>
<tr>
<td>24</td>
<td>Cl</td>
<td>TBAB (10)</td>
<td>Dioxane</td>
<td>100 °C, 48 h</td>
<td>84</td>
</tr>
</tbody>
</table>

\textsuperscript{a} The mixture of 1a (0.55 mmol, 1.1 equiv.), 2a (0.5 mmol), and MX salt in a solvent (0.5 mL) was sealed under air or N\textsubscript{2} in a 10 mL Schlenk tube and then heated and monitored by TLC and/or GC-MS. \textsuperscript{b} Isolated yields (GC yields in parenthesis) are based on 2a-5a.
$^1$H NMR and $^{13}$C NMR Spectra of All Compounds

$^1$H NMR

$^{13}$C NMR

S14
$^{1}H$ NMR

$^{13}C$ NMR

S16
$^1$H NMR

$^{13}$C NMR
$^1$H NMR

$^{13}$C NMR
**H NMR**

**C NMR**
$^1$H NMR

$^{13}$C NMR

S20
**S21**

**1H NMR**

![1H NMR spectrum](image1)

**13C NMR**

![13C NMR spectrum](image2)
$^1$H NMR

$^{13}$C NMR

S22
$^{1}H$ NMR

$^{13}C$ NMR
$^1$H NMR

$^{13}$C NMR

S26
$^1$H NMR

$^{13}$C NMR

S30
$^1$H NMR

$^{13}$C NMR
$^1$H NMR

$^{13}$C NMR
$^1$H NMR

$^{13}$C NMR

S37
$^1$H NMR

$^13$C NMR

S41
\[ \text{S43} \]

\[ \text{\(^1H\) NMR} \]

\[ \text{\(^{13}C\) NMR} \]
$^{1}H$ NMR

$^{13}C$ NMR
$\text{1}^H$ NMR

$\text{13C NMR}$