A Palladium-Catalyzed Three-Component Coupling of Arylboronic Acids, Sulfur Dioxide, and Hydrazines

Shengqing Ye† and Jie Wu*†,‡

† Department of Chemistry, Fudan University, 220 Handan Road, Shanghai 200433, China
‡ State Key Laboratory of Organometallic Chemistry, Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences, Shanghai 200032, China

jie_wu@fudan.edu.cn

Supporting Information

1. General experimental methods (S2).
2. General experimental procedure and characterization data (S2-S7).
3. $^1$H and $^{13}$C NMR spectra of compounds 3 (S8-S43).
**General experimental methods:**

Unless otherwise stated, all commercial reagents were used as received. All solvents were dried and distilled according to standard procedures. Flash column chromatography was performed using silica gel (60-Å pore size, 32–63 µm, standard grade). Analytical thin–layer chromatography was performed using glass plates pre-coated with 0.25 mm 230–400 mesh silica gel impregnated with a fluorescent indicator (254 nm). Thin layer chromatography plates were visualized by exposure to ultraviolet light. Organic solutions were concentrated on rotary evaporators at ~20 Torr at 25–35°C. Nuclear magnetic resonance (NMR) spectra are recorded in parts per million from internal tetramethylsilane on the δ scale. ¹H and ¹³C NMR spectra were recorded in CDCl₃ on a Bruker DRX-400 spectrometer operating at 400 MHz and 100 MHz, respectively. All chemical shift values are quoted in ppm and coupling constants quoted in Hz. High resolution mass spectrometry (HRMS) spectra were obtained on a micrOTOF II Instrument.

*General experimental procedure for the palladium-catalyzed three-component reaction of arylboronic acids 1, DABCO-bis(sulfur dioxide), with amines 2.*

Hydrazine 2 (0.5 mmol) in 1,4-dioxane (2.0 mL) was added to a mixture of arylboronic acids 1 (1.0 mmol), DABCO·(SO₂)₂ (1.0 mmol)¹, Pd(OAc)₂ (0.025 mmol), and TBAB (0.75 mmol) under a balloon of O₂. The reaction was stirred at 80 °C for 12 hours. After completion of the reaction as indicated by TLC, the residue was purified directly by flash chromatography on silica gel to afford aryl N-aminosulfonamides 3.

4-Methyl-N-morpholinobenzensulfonamide (3a)

$^1$H NMR (400 MHz, CDCl$_3$) δ 2.43 (s, 3H), 2.62 (d, $J = 3.2$ Hz, 4H), 3.59 (d, $J = 3.2$ Hz, 4H), 5.97 (s, 1H), 7.31 (d, $J = 7.8$ Hz, 2H), 7.85 (d, $J = 7.8$ Hz, 2H); $^{13}$C NMR (100 MHz, CDCl$_3$) δ 21.5, 56.5, 66.5, 128.0, 129.4, 135.5, 143.9; HRMS (ESI) calcd for C$_{11}$H$_{17}$N$_2$O$_3$S: 257.0954 (M + H$^+$), found: 257.0964.

2-Methyl-N-morpholinobenzensulfonamide (3b)

$^1$H NMR (400 MHz, CDCl$_3$) δ 2.64 (s, 4H), 2.69 (s, 3H), 3.56 (s, 4H), 5.98 (s, 1H), 7.29-7.35 (m, 2H), 7.46 (d, $J = 7.3$ Hz, 1H), 8.06 (d, $J = 7.8$ Hz, 1H); $^{13}$C NMR (100 MHz, CDCl$_3$) δ 20.6, 56.5, 66.5, 126.0, 130.9, 132.2, 133.1, 136.4, 137.8; HRMS (ESI) calcd for C$_{11}$H$_{17}$N$_2$O$_3$S: 257.0954 (M + H$^+$), found: 257.0975.

4-Methoxy-N-morpholinobenzensulfonamide (3c)

$^1$H NMR (400 MHz, CDCl$_3$) δ 2.63 (s, 4H), 3.60 (s, 4H), 3.88 (s, 3H), 5.78 (s, 1H), 6.98 (d, $J = 7.3$ Hz, 2H), 7.90 (d, $J = 7.3$ Hz, 2H); $^{13}$C NMR (100 MHz, CDCl$_3$) δ 55.5, 56.5, 66.6, 113.9, 130.0, 130.2, 163.2; HRMS (ESI) calcd for C$_{11}$H$_{17}$N$_2$O$_4$S: 273.0904 (M + H$^+$), found: 273.0912.

4-(tert-Butyl)-N-morpholinobenzensulfonamide (3d)

$^1$H NMR (400 MHz, CDCl$_3$) δ 1.35 (s, 9H), 2.64 (s, 4H), 3.61 (s, 4H), 6.00 (s, 1H), 7.52 (d, $J = 7.3$ Hz, 2H), 7.90 (d, $J = 7.3$ Hz, 2H); $^{13}$C NMR (100 MHz, CDCl$_3$) δ 31.0, 35.1, 56.5, 66.5, 125.7, 127.8, 135.5, 156.9; HRMS (ESI) calcd for C$_{14}$H$_{23}$N$_2$O$_3$S: 299.1424 (M + H$^+$), found: 299.1446.
**N-Morpholinobenzenesulfonamide (3e)**

\(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 2.62 (d, \(J = 3.6\) Hz, 4H), 3.59 (d, \(J = 3.2\) Hz, 4H), 5.87 (s, 1H), 7.53 (t, \(J = 7.3\) Hz, 2H), 7.62 (t, \(J = 7.3\) Hz, 1H), 7.98 (d, \(J = 7.3\) Hz, 2H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) 56.5, 66.5, 128.0, 128.8, 133.1, 138.5; HRMS (ESI) calcd for C\(_{10}\)H\(_{13}\)N\(_2\)O\(_3\)S: 243.0798 (M + H\(^+\)), found: 243.0812.

**N-Morpholinonaphthalene-1-sulfonamide (3f)**

\(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 2.53 (d, \(J = 2.7\) Hz, 4H), 3.46 (d, \(J = 2.7\) Hz, 4H), 6.04 (s, 1H), 7.55-7.61 (m, 2H), 7.67 (t, \(J = 7.8\) Hz, 1H), 7.93 (d, \(J = 7.8\) Hz, 1H), 8.09 (d, \(J = 7.8\) Hz, 1H), 8.39 (d, \(J = 8.7\) Hz, 1H), 8.80 (d, \(J = 8.7\) Hz, 1H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) 56.6, 66.4, 124.1, 125.0, 126.8, 128.1, 128.4, 128.8, 131.3, 133.4, 133.9, 134.7; HRMS (ESI) calcd for C\(_{14}\)H\(_{17}\)N\(_2\)O\(_3\)S: 293.0954 (M + H\(^+\)), found: 293.0956.

**N-Morpholinonaphthalene-2-sulfonamide (3g)**

\(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 2.64 (d, \(J = 3.2\) Hz, 4H), 3.57 (d, \(J = 3.2\) Hz, 4H), 6.03 (s, 1H), 7.60-7.68 (m, 2H), 7.91-7.99 (m, 4H), 8.57 (s, 1H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) 56.6, 66.5, 123.1, 127.5, 127.8, 128.9, 129.0, 129.2, 129.6, 131.9, 134.9, 135.4; HRMS (ESI) calcd for C\(_{14}\)H\(_{17}\)N\(_2\)O\(_3\)S: 293.0954 (M + H\(^+\)), found: 293.0960.

**4-Fluoro-N-morpholinobenzenesulfonamide (3h)**

\(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 2.64 (s, 4H), 3.62 (s, 4H), 5.53 (s, 1H), 7.21 (t, \(J = 7.8\) Hz, 2H), 7.99 (d, \(J = 5.5\) Hz, 2H); \(^{13}\)C NMR (100 MHz, CD\(_3\)OD) \(\delta\) 56.3, 66.4, 116.7 (d, \(J_F = 22.9\) Hz), 131.1 (d, \(J_F = 9.5\) Hz), 136.1, 164.9 (d, \(J_F = 250.7\) Hz); HRMS (ESI) calcd for C\(_{14}\)H\(_{17}\)N\(_2\)O\(_3\)S: 293.0954 (M + H\(^+\)), found: 293.0960.
calcd for C\textsubscript{10}H\textsubscript{14}FN\textsubscript{2}O\textsubscript{3}S: 261.0704 (M + H\textsuperscript{+}), found: 261.0709.

![Structure](image)

4-Chloro-N-morpholinobenzenesulfonamide (3i)

\(^1\)H NMR (400 MHz, CDCl\textsubscript{3}) \(\delta\) 2.65 (s, 4H), 3.62 (s, 4H), 5.68 (s, 1H), 7.51 (d, \(J = 7.3\) Hz, 2H), 7.92 (d, \(J = 7.3\) Hz, 2H); \(^{13}\)C NMR (100 MHz, CDCl\textsubscript{3}) \(\delta\) 56.7, 66.6, 129.1, 129.5, 137.0, 139.7; HRMS (ESI) calcd for C\textsubscript{10}H\textsubscript{14}ClN\textsubscript{2}O\textsubscript{3}S: 277.0408 (M + H\textsuperscript{+}), found: 277.0425.

![Structure](image)

4-Bromo-N-morpholinobenzenesulfonamide (3j)

\(^1\)H NMR (400 MHz, CDCl\textsubscript{3}) \(\delta\) 2.64 (d, \(J = 3.2\) Hz, 4H), 3.62 (d, \(J = 2.8\) Hz, 4H), 5.72 (s, 1H), 7.67 (d, \(J = 7.3\) Hz, 2H), 7.84 (d, \(J = 7.3\) Hz, 2H); \(^{13}\)C NMR (100 MHz, CDCl\textsubscript{3}) \(\delta\) 56.7, 66.6, 128.3, 129.2, 132.1, 132.1, 137.6; HRMS (ESI) calcd for C\textsubscript{10}H\textsubscript{14}BrN\textsubscript{2}O\textsubscript{3}S: 320.9903 (M + H\textsuperscript{+}), found: 320.9912.

![Structure](image)

4-Hydroxy-N-morpholinobenzenesulfonamide (3k)

\(^1\)H NMR (400 MHz, CD\textsubscript{3}OD) \(\delta\) 2.54 (s, 4H), 3.55 (s, 4H), 4.89 (br, 2H), 6.90 (d, \(J = 7.8\) Hz, 2H), 7.75 (d, \(J = 7.8\) Hz, 2H); \(^{13}\)C NMR (100 MHz, CD\textsubscript{3}OD) \(\delta\) 56.0, 66.5, 115.0, 129.1, 130.1, 161.9; HRMS (ESI) calcd for C\textsubscript{10}H\textsubscript{15}N\textsubscript{2}O\textsubscript{4}S: 259.0747 (M + H\textsuperscript{+}), found: 259.0765.

![Structure](image)

3-Amino-N-morpholinobenzenesulfonamide (3l)

\(^1\)H NMR (400 MHz, CD\textsubscript{3}OD) \(\delta\) 2.56 (s, 4H), 3.56 (s, 4H), 4.88 (s, 3H), 6.88 (d, \(J = 7.3\) Hz, 1H), 7.14 (d, \(J = 6.8\) Hz, 1H), 7.21-7.25 (m, 2H); \(^{13}\)C NMR (100 MHz, CDCl\textsubscript{3}) \(\delta\) 56.7, 66.6, 113.7, 117.6, 119.2, 129.7, 139.4, 147.0; HRMS (ESI) calcd for C\textsubscript{10}H\textsubscript{16}N\textsubscript{3}O\textsubscript{3}S: 258.0907 (M + H\textsuperscript{+}), found: 258.0918.
(E)-N-Morpholino-2-phenylethanesulfonamide (3m)

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 2.88 (s, 4H), 3.72 (s, 4H), 5.72 (s, 1H), 6.83 (d, $J$ = 15.6 Hz, 1H), 7.43-7.50 (m, 5H), 7.60 (d, $J$ = 15.6 Hz, 1H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 57.3, 66.5, 123.4, 128.3, 129.1, 131.1, 132.4, 143.7; HRMS (ESI) calcd for C$_{12}$H$_{17}$N$_2$O$_3$: 269.0954 (M + H$^+$), found: 269.0965.

4-Methoxy-N-(piperidin-1-yl)benzenesulfonamide (3n)

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 1.29 (s, 2H), 1.49 (d, $J$ = 4.1 Hz, 4H), 2.53 (s, 4H), 3.88 (s, 3H), 6.97 (d, $J$ = 7.8 Hz, 2H), 7.90 (d, $J$ = 7.8 Hz, 2H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 22.9, 25.5, 55.5, 57.6, 113.7, 130.2, 130.3, 162.9; HRMS (ESI) calcd for C$_{12}$H$_{19}$N$_2$O$_3$: 271.1111 (M + H$^+$), found: 271.1124.

4-Hydroxy-N-(piperidin-1-yl)benzenesulfonamide (3o)

$^1$H NMR (400 MHz, CD$_2$OD) $\delta$ 1.27 (s, 2H), 1.45 (d, $J$ = 5.0 Hz, 4H), 2.49 (s, 4H), 4.90 (br, 2H), 6.90 (d, $J$ = 7.8 Hz, 2H), 7.74 (d, $J$ = 7.8 Hz, 2H); $^{13}$C NMR (100 MHz, CD$_2$OD) $\delta$ 23.0, 25.6, 56.9, 114.9, 129.3, 130.1, 161.7; HRMS (ESI) calcd for C$_{11}$H$_{17}$N$_2$O$_3$: 257.0954 (M + H$^+$), found: 257.0968.

4-Methoxy-N'-methyl-N'-phenylbenzenesulfonohydrazide (3p)

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 2.93 (s, 3H), 3.84 (s, 3H), 6.31 (s ,1H), 6.85-6.87 (m, 3H), 6.94 (d, $J$ = 7.3 Hz, 2H), 7.17 (t, $J$ = 7.3 Hz, 2H), 7.87 (d, $J$ = 7.3 Hz, 2H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 42.4, 55.6, 114.2, 114.3, 120.8, 128.8, 129.8, 130.3, 149.7, 163.4; HRMS (ESI) calcd for C$_{14}$H$_{17}$N$_2$O$_3$: 293.0954 (M + H$^+$), found: 293.0964.
4-(tert-Butyl)-N'-methyl-N'-phenylbenzenesulfonyldrazide (3q)

$^1$H NMR (400 MHz, CDCl$_3$) δ 1.31 (s, 9H), 2.93 (s, 3H), 6.50 (s, 1H), 6.80-6.84 (m, 3H), 7.12 (t, $J = 7.3$ Hz, 2H), 7.46 (d, $J = 8.3$ Hz, 2H), 7.85 (d, $J = 7.8$ Hz, 2H); $^{13}$C NMR (100 MHz, CDCl$_3$) δ 30.9, 35.1, 42.4, 114.3, 120.7, 126.0, 127.9, 128.7, 135.4, 149.6, 157.2; HRMS (ESI) calcd for C$_{17}$H$_{23}$N$_2$O$_2$S: 319.1475 (M + H$^+$), found: 319.1487.

4-Fluoro-N'-methyl-N'-phenylbenzenesulfonyldrazide (3r)

$^1$H NMR (400 MHz, CDCl$_3$) δ 2.97 (s, 3H), 6.46 (s, 1H), 6.81-6.88 (m, 3H), 7.12-7.17 (m, 4H), 7.94 (t, $J = 6.9$ Hz, 2H); $^{13}$C NMR (100 MHz, CDCl$_3$) δ 42.8, 114.3, 116.3 (d, $J_F = 22.9$ Hz), 121.0, 128.9, 130.9 (d, $J_F = 9.5$ Hz), 134.4, 149.4, 165.4 (d, $J_F = 254.6$ Hz); HRMS (ESI) calcd for C$_{13}$H$_{14}$FN$_2$O$_2$S: 281.0755 (M + H$^+$), found: 281.0764.