A General and Efficient Synthesis of Sulfonylbenzotriazoles from *N*-
Chlorobenzotriazole and Sulfinic acid salts

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SUPPORTING INFORMATION

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Experimental Section

Melting points were uncorrected. ^1H (300 MHz) and ^{13}C (75 MHz) NMR spectra were recorded on a 300 MHz NMR spectrometer in chloroform-*d* solution. Column chromatography was performed on silica gel. THF was distilled from sodium-benzophenone ketyl prior to use. All the reactions were performed under a nitrogen atmosphere and in oven dried glasswares. Commercially available Grignard reagents were used for the preparation of sulfinic acid salts. Organolithium reagents were prepared following literature methods.¹⁹ All sulfinic acid salts were prepared from organo magnesium or lithium reagents and commercially available sulfur dioxide²¹ following the method described by Pinnick and co-workers.¹⁶

General procedure for the preparation of sulfonyl benzotriazoles 3a–k: Sulfur dioxide was bubbled to a solution of the organometallic reagent (7 mmol) in THF (20 mL) at $-78\text{ }^{\circ}\text{C}$ until a sample to the solution no longer gave a basic pH test. The mixture was stirred at that temperature for 15 min, then at room temperature for 1 h. *N*-Chlorobenzotriazole (1.07 g, 7 mmol) was now added in one portion and the mixture was stirred for 2 h at rt. Triethylamine (0.92 mL, 7 mmol) was now added followed by stirring at rt for 10 h. Water (ca 100 mL) was added and extracted with ethyl acetate (3×100 mL). The combined organic layers were washed with water, brine, dried over anhydrous sodium sulfate and filtered. Concentration under reduced pressure gave an oil, which was further purified either by re-crystallization or column chromatography over silica gel (200–400 Mesh).

1-(Cyclohexylsulfonyl)-1*H*-1,2,3-benzotriazole (3b): Purified by column chromatography with hexanes/EtOAc = 2:1 as eluent and obtained as colorless prisms (71%), mp 117–119 °C. ¹H NMR δ 1.10–1.30 (m, 3H), 1.50–1.70 (m, 3H), 1.85–1.90 (m, 2H), 2.02–2.06 (m, 2H), 3.51–3.62 (m, 1H), 7.52 (t, *J* = 7.2 Hz, 1H), 7.66 (t, *J* = 7.2 Hz, 1H), 8.01 (d, *J* = 8.4 Hz, 1H), 8.16 (d, *J* = 8.1 Hz, 1H). ¹³C NMR δ 24.6, 24.7, 25.8, 65.2, 112.1, 120.5, 125.8, 130.3, 132.6, 145.0. Anal. Calcd For C₁₂H₁₅N₃O₂S: C, 54.32; H, 5.70; N, 15.84. Found: C, 54.47; H, 5.68; N, 15.71.

1-(Isobutylsulfonyl)-1*H*-1,2,3-benzotriazole (3c): Purified by column chromatography with hexanes/EtOAc = 4:1 as eluent and obtained as brown oil (75%). ¹H NMR δ 1.09 (d, *J* = 6.9 Hz, 6H), 2.30 (sep, *J* = 6.6 Hz, 1H), 3.51 (d, *J* = 6.6 Hz, 2H), 7.53 (t, *J* = 7.2 Hz, 1H), 7.68 (t, *J* = 7.2 Hz, 1H), 8.03 (d, *J* = 8.4 Hz, 1H), 8.16 (d, *J* = 8.4 Hz, 1H). ¹³C NMR δ 22.1, 24.6, 63.2, 111.9, 120.5, 125.9, 130.4, 132.0, 145.1. Anal. Calcd For C₁₀H₁₃N₃O₂S: C, 50.19; H, 5.48; N, 17.56. Found: C, 50.08; H, 5.23; N, 17.55.

1-[(4-Methylphenyl)sulfonyl]-1*H*-1,2,3-benzotriazole (3d):²⁰ Colorless needles (from EtOAc, 93%), mp 126–129 °C (Lit. mp 128–129 °C).² ¹H NMR δ 2.39 (s, 3H), 7.32 (d, *J* = 8.1 Hz, 2H), 7.48 (t, *J* = 7.7 Hz, 1H), 7.66 (t, *J* = 7.8 Hz, 1H), 8.00 (d, *J* = 8.1 Hz, 2H), 8.10 (t, *J* = 9.6 Hz, 2H). ¹³C NMR δ 21.7, 112.0, 120.5, 125.8, 128.0, 130.2, 130.3, 131.5, 134.0, 145.4, 146.7.

1-(2-Pyridinylsulfonyl)-1*H*-1,2,3-benzotriazole (3e): Purple needles (from EtOAc, 71%), mp 132–135 °C. ¹H NMR δ 7.48–7.59 (m, 2H), 7.67–7.73 (m, 1H), 8.02 (dt, *J* = 7.8, 1.8 Hz, 1H), 8.08–8.12 (m, 1H), 8.21–8.25 (m, 1H), 8.36 (dt, *J* = 8.1, 0.9 Hz, 1H), 8.59 (ddd, *J* = 4.8, 1.5, 0.6 Hz, 1H). ¹³C NMR δ 112.7, 120.4, 123.4, 126.0, 128.6, 130.4,

132.7, 138.7, 145.4, 150.7, 154.7. Anal. Calcd For $C_{11}H_8N_4O_2S$: C, 50.76; H, 3.10; N, 21.53. Found: C, 50.81; H, 3.05; N, 21.51.

1-(3-Pyridinylsulfonyl)-1*H*-1,2,3-benzotriazole (3f): Cream needles (from EtOAc, 41%), mp 128–129 °C. 1H NMR δ 7.49–7.56 (m, 2H), 7.64–7.74 (m, 1H), 8.10–8.15 (m, 2H), 8.42 (ddd, J = 8.1, 2.4, 1.8 Hz, 1H), 8.87 (dd, J = 4.8, 1.8 Hz, 1H), 9.30–9.31 (m, 1H). ^{13}C NMR 111.9, 120.8, 124.1, 126.3, 130.8, 131.5, 134.1, 135.7, 145.5, 148.4, 155.5. Anal. Calcd For $C_{11}H_8N_4O_2S$: C, 50.76; H, 3.10; N, 21.52. Found: C, 50.60; H, 3.01; N, 21.13.

1-(2-Furylsulfonyl)-1*H*-1,2,3-benzotriazole (3g): Amber needles (from EtOAc, 83%), mp 107–109 °C. 1H NMR δ 6.60 (dd, J = 3.6, 1.8 Hz, 1H), 7.51–7.56 (m, 2H), 7.60–7.61 (m, 1H), 7.71 (dt, J = 8.1, 0.9 Hz, 1H), 8.11 (t, J = 8.6 Hz, 2H). ^{13}C NMR δ 112.0, 112.3, 120.6, 121.1, 126.1, 130.5, 131.5, 144.9, 145.4, 149.1. Anal. Calcd For $C_{10}H_7N_3O_3S$: C, 48.19; H, 2.83; N, 16.86. Found: C, 47.82; H, 2.57; N, 16.52.

1-(2-Thienylsulfonyl)-1*H*-1,2,3-benzotriazole (3h): Purple needles (from EtOAc, 82%), mp 143–144 °C. 1H NMR δ 7.13 (dd, J = 5.1, 3.9 Hz, 1H), 7.48–7.54 (m, 1H), 7.66–7.72 (m, 1H), 7.76 (dd, J = 5.1, 1.2 Hz, 1H), 7.96 (dd, J = 3.6, 1.2 Hz, 1H), 8.08–8.09 (m, 1H), 8.10–8.12 (m, 1H). ^{13}C NMR δ 112.0, 120.6, 126.0, 128.2, 130.4, 131.2, 135.8, 136.3, 136.4, 145.4. Anal. Calcd For $C_{10}H_7N_3O_2S_2$: C, 45.27; H, 2.66; N, 15.84. Found: C, 45.36; H, 2.34; N, 15.71.

1-[(1-Methyl-1*H*-indol-2-yl)sulfonyl]-1*H*-1,2,3-benzotriazole (3i): Purified by column chromatography with hexanes/EtOAc = 6:1 as eluent and obtained as colorless prisms (20%), mp 150–152 °C. 1H NMR δ 4.08 (s, 3H), 7.19 (t, J = 6.9 Hz, 1H), 7.33–7.51 (m,

3H), 7.60–7.69 (m, 3H), 8.06–8.11 (m, 2H). ^{13}C NMR δ 31.7, 110.7, 112.0, 113.6, 120.7, 121.9, 123.2, 124.6, 126.0, 127.3, 129.5, 130.3, 131.2, 140.2, 145.6. Anal. Calcd For $\text{C}_{15}\text{H}_{12}\text{N}_4\text{O}_2\text{S}$: C, 57.68; H, 3.87; N, 17.94. Found: C, 57.54; H, 3.76; N, 17.82.

1-[(1-Methyl-1*H*-imidazol-2-yl)sulfonyl]-1*H*-1,2,3-benzotriazole (3j): Purified by column chromatography with hexanes/EtOAc = 3:7 as eluent and obtained as colorless prisms (80%), mp 147–150 °C. ^1H NMR δ 4.18 (s, 3H), 7.13 (d, J = 3.6 Hz, 2H), 7.51 (t, J = 7.5 Hz, 1H), 7.69 (t, J = 7.2 Hz, 1H), 8.09 (d, J = 8.1 Hz, 1H), 8.19 (d, J = 8.4 Hz, 1H). ^{13}C NMR δ 36.1, 112.5, 120.4, 126.2, 127.9, 130.6, 130.7, 131.6, 138.5, 145.3. Anal. Calcd For $\text{C}_{10}\text{H}_9\text{N}_5\text{O}_2\text{S}$: C, 45.62; H, 3.45; N, 26.60. Found: C, 45.64; H, 3.35; N, 26.49.

General procedure for the preparation of sulfonamides 7–15: The respective sulfonyl benzotriazole **3** (1 equiv.) was heated at the established temperature in the chosen solvent with the appropriate primary or secondary amine (1 equiv.) for the established time. (See Table II) Water (ca 100 mL) was added and extracted with ethyl acetate (3×100 mL). The combined organic layers were washed with water, 1M HCl, brine, dried over anhydrous sodium sulfate and filtered. Concentration under reduced pressure gave a solid, which was further purified either by re-crystallization or column chromatography over silica gel (200–400 Mesh).

***N*-Benzyl-*N*,2-dimethyl-1-propanesulfonamide (8):** Purified by column chromatography with hexanes/Et₂O = 6:1 as eluent and obtained as colorless needles (72%), mp 32–34 °C. ^1H NMR δ 1.13 (d, J = 6.6 Hz, 6H), 2.32 (sep, J = 6.6 Hz, 1 H),

2.76 (s, 3H), 2.83 (d, $J = 6.6$ Hz, 2H), 4.32 (s, 2H), 7.31–7.36 (m, 5H). ^{13}C NMR δ 22.7, 24.5, 34.1, 53.7, 57.4, 127.9, 128.3, 128.7, 135.9. Anal. Calcd For $\text{C}_{12}\text{H}_{19}\text{NO}_2\text{S}$: C, 59.72; H, 7.93; N, 5.80. Found: C, 59.88; H, 8.10; N, 5.92.

1-(2-Thienylsulfonyl)piperidine (9): Purified by column chromatography with CHCl_3 as eluent and obtained as colorless prisms (85%), mp 76–77 °C. ^1H NMR δ 1.41–1.49 (m, 2H), 1.64–1.72 (m, 4H), 3.04 (t, $J = 5.6$ Hz, 4H), 7.14 (dd, $J = 4.8, 3.6$ Hz, 1H), 7.52 (dd, $J = 3.6, 1.2$ Hz, 1H), 7.61 (dd, $J = 4.8, 1.2$ Hz, 1H). ^{13}C NMR δ 23.4, 25.0, 47.0, 127.5, 131.7, 132.1, 136.7. Anal. Calcd For $\text{C}_9\text{H}_{13}\text{NO}_2\text{S}_2$: C, 46.73; H, 5.66; N, 6.05. Found: C, 46.98; H, 5.64; N, 6.15.

N-(1-Methylbutyl)-2-furansulfonamide (10): Purified by column chromatography with hexanes/EtOAc = 4:1 as eluent and obtained as cream prisms (100%), mp 57–58 °C. ^1H NMR δ 0.82–0.87 (m, 3H), 1.08 (d, $J = 6.6$ Hz, 3H), 1.21–1.38 (m, 4H), 3.33–3.45 (m, 1H), 4.45 (d, $J = 7.8$ Hz, 1H), 6.50 (dd, $J = 3.3, 1.8$ Hz, 1H), 7.03 (d, $J = 3.3$ Hz, 1H), 7.55 (d, $J = 1.8$ Hz, 1H). ^{13}C NMR δ 13.6, 18.6, 21.9, 39.5, 50.2, 103.4, 111.2, 116.0, 145.7. Anal. Calcd For $\text{C}_9\text{H}_{15}\text{NO}_3\text{S}$: C, 49.75; H, 6.96; N, 6.45. Found: C, 49.95; H, 6.97; N, 6.37.

1-(3-Pyridinylsulfonyl)piperidine (11): Purified by column chromatography with hexanes/EtOAc/ CHCl_3 = 4:1:5 as eluent and obtained as white prisms (100%), mp 88–89 °C. ^1H NMR δ 1.43–1.49 (m, 2H), 1.63–1.71 (m, 4H), 3.05 (t, $J = 5.6$ Hz, 4H), 7.49 (dd, $J = 2.7, 5.1$ Hz, 1H), 8.05 (dt, $J = 8.1, 1.8$ Hz, 1H), 8.82 (dd, $J = 4.8, 1.5$ Hz, 1H), 8.99 (d, $J = 2.1$ Hz, 1H). ^{13}C NMR δ 23.4, 25.1, 46.8, 123.6, 133.3, 135.2, 148.4, 153.2. Anal. Calcd For $\text{C}_{10}\text{H}_{14}\text{N}_2\text{O}_2\text{S}$: C, 53.08; H, 6.24; N, 12.38. Found: C, 53.10; H, 6.32; N, 11.96.

4-[(1-Methyl-1*H*-imidazol-2-yl)sulfonyl]morpholine (12): Colorless oil (91%). ¹H NMR δ 3.40 (t, *J* = 4.8 Hz, 4H), 3.72 (t, *J* = 4.8 Hz, 4H), 3.85 (s, 3H), 6.91 (s, 1H), 7.01 (s, 1H). ¹³C NMR δ 34.7, 46.5, 66.2, 124.6, 128.4, 141.9. Anal. Calcd For C₈H₁₃N₃O₃S: C, 41.55; H, 5.67; N, 18.17. Found: C, 41.45; H, 6.04; N, 15.99.

1-[(4-Methylphenyl)sulfonyl]piperidine (13): White prisms (from EtOAc, 100%), mp 93 °C. ¹H NMR δ 1.36–1.45 (m, 2H), 1.60–1.67 (m, 4H), 2.43 (s, 3H), 2.97 (t, *J* = 5.7 Hz, 4H), 7.32 (d, *J* = 8.1 Hz, 2H), 7.64 (d, *J* = 8.1 Hz, 2H). ¹³C NMR δ 21.5, 23.4, 25.1, 46.9, 127.6, 129.5, 133.2, 143.2. Anal. Calcd For C₁₂H₁₇NO₂S: C, 60.22; H, 7.16; N, 5.85. Found: C, 60.01; H, 7.27; N, 5.95.

***N*-(1,5-Dimethylhexyl)-1-methyl-1*H*-imidazole-2-sulfonamide (14):** Purified by column chromatography with hexanes/EtOAc = 3:1 as eluent and obtained as white prisms (64%), mp 82–84 °C. ¹H NMR δ 0.84 (d, *J* = 6.6 Hz, 6H), 1.06–1.35 (m, 7H), 1.38–1.55 (m, 3H), 3.46–3.55 (m, 1H), 3.94 (s, 3H), 5.25 (s, 1H), 6.96 (s, 1H), 7.09 (s, 1H). ¹³C NMR δ 21.4, 22.5, 23.3, 27.8, 35.1, 37.7, 38.5, 51.1, 124.6, 128.1, 143.4. Anal. Calcd For C₁₂H₂₃N₃O₂S: C, 52.72; H, 8.48; N, 15.37. Found: C, 52.54; H, 8.07; N, 15.84.

***N*-Phenethyl-2-thiophenesulfonamide (15):** Purified by column chromatography with hexanes/EtOAc = 3:1 as eluent and obtained as yellow oil (80%). ¹H NMR δ 2.81 (t, *J* = 6.9 Hz, 2H), 3.32 (q, *J* = 6.6 Hz, 2H), 4.54 (br s, 1H), 7.06–7.13 (m, 3H), 7.20–7.32 (m, 3H), 7.56–7.59 (m, 2H). ¹³C NMR δ 35.6, 44.4, 126.9, 127.4, 128.7, 128.8, 131.8, 132.1, 137.5, 140.9. Anal. Calcd For C₁₂H₁₃NO₂S₂: C, 53.91; H, 4.90; N, 5.24. Found: C, 54.21; H, 4.89; N, 5.59.

Figure 1. ^1H NMR spectrum for compound **3a**.

Figure 2. ^1H NMR spectrum for compound **3b**.

Figure 3. ^1H NMR spectrum for compound **3c**.

Figure 4. ^1H NMR spectrum for compound **3d**.

Figure 5. ¹H NMR spectrum for compound **3e**

Figure 6. ^1H NMR spectrum for compound **3e**

Figure 7. ^1H NMR spectrum for compound **3f**.

Figure 8. ^1H NMR spectrum for compound **3f**.

Figure 9. ^1H NMR spectrum for compound **3g**

Figure 9. ¹H NMR spectrum for compound **3h**

Figure 10. ^1H NMR spectrum for compound **3h**

Figure 11. ¹H NMR spectrum for compound **3i**.

Figure 12. ¹H NMR spectrum for compound **3j**.

Figure 13. ¹H NMR spectrum for compound **7**.

Figure 14. ^1H NMR spectrum for compound **8**.

Figure 15. ^1H NMR spectrum for compound **9**

Fi

Figure 16. ^1H NMR spectrum for compound **10**.

Figure 17. ^1H NMR spectrum for compound **11**.

Figure 18. ^1H NMR spectrum for compound **12**.

Figure 19. ^1H NMR spectrum for compound **13**.

Figure 20. ¹H NMR spectrum for compound 14.

Figure 21. ¹H NMR spectrum for compound **15**.