Supporting Information

Copper-Catalyzed Hydrative Amide Synthesis with Terminal Alkyne, Sulfonyl Azide, and Water

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General Methods Unless otherwise stated, all commercial reagents and solvents were used without additional purification. Analytical thin layer chromatography (TLC) was performed on Merck precoated silica gel 60 F₂₅₄ plates. Visualization on TLC was achieved by the use of UV light (254 nm) and treatment with phosphomolybdic acid or anisaldehyde stain followed by heating. Flash column chromatography was undertaken on silica gel (Merck Kieselgel 60 F₂₅₄ 400-630 mesh). ¹H NMR was recorded on Bruker FT AM 400 (400 MHz). Chemical shifts were quoted in parts per million (ppm) referenced to the appropriate solvent peak or 0.0 ppm for tetramethylsilane (TMS). The following abbreviations were used to describe peak patterns when appropriate: br = broad, s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet. Coupling constant, *J*, was reported in Hertz unit (Hz). ¹³C NMR was recorded on Bruker FT AM 400 (100 MHz) and was fully decoupled by broad band decoupling. Chemical shifts were reported in ppm referenced to the center line of a triplet at 77.0 ppm of chloroform-*d*. Infrared (IR) spectra were recorded neat in a 0.5 mm path length NaCl cell on Bruker EQUINOX 55. Frequencies are given in reciprocal centimeters (cm⁻¹) and only selected absorbance is reported. High resolution mass spectra were recorded on a Jeol JMS-HX110/110A by using FAB method.

General Procedure for the Test Reactions (Table 1 and Table S1). To a stirred mixture of *p*-toluenesulfonyl azide (0.6 mmol), phenylacetylene (0.5 mmol), catalyst (0.05 mmol) and H₂O (1.25 mmol) in a solvent (1 mL) was slowly added base (0.6 mmol) at room temperature under an N₂ atmosphere. After stirring the reaction mixture for 12 h at room temperature under N₂, it was diluted by adding CH₂Cl₂ (2 mL) and saturated NH₄Cl solution (3 mL). The mixture was stirred for additional 30 min and two layers were separated. The aqueous layer was extracted with CH₂Cl₂ (3 mL x 3). The combined organic layers were dried over MgSO₄, filtered, and concentrated in *vacuo*. The NMR yield was determined by integration using an internal standard (*p*-anisole).

Table S1. Hydrative Amide Synthesis under Various Conditions

$ \begin{array}{c} \text{Ph}-\text{C}\equiv\text{C} + \text{Ts}-\text{N}_3 + \text{H}_2\text{O} \xrightarrow[\text{solvent, 25 }^\circ\text{C, 12 h}]{\text{catalyst, base}} \text{Ph}-\text{CH}_2-\text{C}(=\text{O})-\text{NH}-\text{Ts} \\ \text{1a} \qquad \qquad \text{2a} \qquad \qquad \qquad \qquad \qquad \qquad \qquad \qquad \qquad \qquad \qquad \qquad \qquad \text{3a} \end{array} $				
Entry	Catalyst	Base	Solvent	Yield (%) ^a
1	CuI	-	CHCl ₃	<1
2	CuI	Et ₃ N	CHCl ₃	94
3	CuI	Et ₃ N (0.2eq)	CHCl ₃	27
4	CuI	(i-Pr) ₂ NEt	CHCl ₃	47
5	CuI	Pyridine	CHCl ₃	35
6	CuI	K ₃ PO ₄	CHCl ₃	<1
7	CuI	Et ₃ N	THF	30
8	CuI	Et ₃ N	CH ₃ CN	54
9	CuI	Et ₃ N	1,4-dioxane	32
10	CuI	Et ₃ N	DMF	49
11	CuI	Et ₃ N	CH ₂ Cl ₂	61
12	CuBr•SMe ₂	Et ₃ N	CHCl ₃	67
13 ^b	Cu(tfac) ₂	Et ₃ N	CHCl ₃	75
14	CuCl	Et ₃ N	CHCl ₃	61
15	Cu(OTf)•C ₆ H ₅	Et ₃ N	CHCl ₃	57

^a NMR yield based on an internal standard (*p*-anisole). ^b tfac: trifluoroacetylacetone.

Reaction Profile Studies.

Amidine - To a stirred mixture of *p*-toluenesulfonyl azide (0.99 g, 5.0 mmol), phenylacetylene (0.55 mL, 5.0 mmol) and CuI (95 mg, 0.5 mmol) in THF (10.0 mL) was slowly added benzyl amine (0.66 mL, 6.0 mmol) at room temperature under an N₂ atmosphere.

Amide - To a stirred mixture of *p*-toluenesulfonyl azide (0.99 g, 5.0 mmol), phenylacetylene (0.55 mL, 5.0 mmol), H₂O (0.24 mL, 12.5 mmol) and CuI (95 mg, 0.5 mmol) in CHCl₃ (10.0 mL) was slowly added Et₃N (0.84 mL, 6.0 mmol) at room temperature under an N₂ atmosphere.

Progress of each reaction was monitored for the product formation of either amidine or amide by ¹H NMR (300 MHz) using an internal standard (1,4-dimethoxybenzene).

General Procedure for the Preparation of Amide (Table 2). To a stirred mixture of sulfonyl azide (0.6 mmol), alkyne (0.5 mmol), H₂O (1.25 mmol) and CuI (0.05 mmol) in CHCl₃ (1 mL) was slowly added Et₃N (0.6 mmol) at room temperature under an N₂ atmosphere. After stirring the reaction mixture for 12 h at room temperature under N₂, it was diluted by adding CH₂Cl₂ (2 mL) and saturated NH₄Cl solution (3 mL). The mixture was stirred for additional 30 min and two layers were separated. The aqueous layer was extracted with CH₂Cl₂ (3 mL x 3). The combined organic layers were dried over MgSO₄, filtered, and concentrated in *vacuo*. The crude residue was purified by flash column chromatograph on silica gel with an appropriate eluting solvent system (CH₂Cl₂/MeOH, 20~40:1 depending on substrates).

4-Methyl-*N*-(phenylacetyl)benzenesulfonamide (Table 2, 3a): white solid (94%); m.p. 146–148 °C; ¹H NMR (400 MHz, CDCl₃) δ 8.47 (br s, 1H), 7.85 (d, *J* = 8.3 Hz, 2H), 7.26 (m, 5H), 7.10 (m, 2H), 3.54 (s, 2H), 2.41 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 168.7, 145.1, 135.2, 132.3, 129.5, 129.3, 129.0, 128.3, 127.7, 43.04, 21.6; IR (KBr) ν 3447, 3091, 2881, 1678, 1597, 1456, 1345, 1163, 552 cm⁻¹; HRMS (FAB) *m/z* calcd. for C₁₅H₁₆NO₃S [*M*+*H*]⁺: 290.0851, found: 290.0847.

4-Methyl-*N*-(*p*-tolylacetyl)benzenesulfonamide (Table 2, 3b): white solid (82%); m.p. 173–175 °C; ¹H NMR (400 MHz, CDCl₃) δ 8.10 (br s, 1H), 7.86 (d, *J* = 8.3 Hz, 2H), 7.29 (d, *J* = 8.1 Hz, 2H), 7.12 (d, *J* = 7.8 Hz, 2H), 7.00 (d, *J* = 7.9 Hz, 2H), 3.52 (s, 2H), 2.42 (s, 3H), 2.32 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 168.5, 145.1, 137.9, 135.3, 130.1, 129.5, 129.2, 129.1, 128.5, 43.4, 21.7, 21.1; IR (KBr) ν 3448, 3115, 2919, 1685, 1595, 1460, 1352, 1163, 549 cm⁻¹; HRMS (FAB) *m/z* calcd. for C₁₆H₁₈NO₃S [*M*+*H*]⁺: 304.1007, found: 304.1005.

4-Methyl-*N*-[(4-trifluoromethylphenyl)acetyl]benzenesulfonamide (Table 2, 3c): white solid (83%); m.p. 113–115 °C; ¹H NMR (400 MHz, CDCl₃) δ 8.91 (br s, 1H), 7.86 (d, *J* = 8.3 Hz, 2H), 7.49 (d, *J* = 8.2 Hz, 2H), 7.29 (dd, *J* = 8.1, 4.7 Hz, 2H), 7.24 (dd, *J* = 5.0, 2.8 Hz, 3H), 3.61 (s, 2H), 2.41 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 167.8, 145.5, 143.8, 138.9, 136.2, 135.0, 130.1, 129.8, 129.8, 129.7, 128.3, 126.4, 125.8, 125.8, 125.7, 125.7, 125.3, 122.6, 42.8, 21.6, 21.5; IR (KBr) ν 3445, 3319, 2952, 1732, 1599, 1440, 1330, 1175, 548 cm⁻¹; HRMS (FAB) *m/z* calcd. for C₁₆H₁₅F₃NO₃S [*M*+*H*]⁺: 358.0725, found: 358.0723.

***N*-Hexanoyl-4-methylbenzenesulfonamide (Table 2, 3d):** white solid (78%); m.p. 65–66 °C; ¹H NMR (400 MHz, CDCl₃) δ 8.88 (br s, 1H), 7.92 (d, *J* = 8.3 Hz, 2H), 7.31 (d, *J* = 8.2 Hz, 2H), 2.41 (s, 3H), 2.21 (t, *J* = 7.4 Hz, 2H), 1.53 (m, 2H), 1.18 (m, 4H), 0.79 (t, *J* = 7.1 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 171.2, 145.1, 135.6, 129.6, 128.3, 36.2, 30.9, 23.9, 22.2, 21.6, 13.7; IR (KBr) ν 3447, 3081, 2927, 1684, 1598, 1458, 1342, 1152, 553 cm⁻¹; HRMS (FAB) *m/z* calcd. for C₁₃H₂₀NO₃S [*M*+*H*]⁺: 270.1164, found: 270.1160.

***N*-(3,3-Dimethylbutanoyl)-4-methylbenzenesulfonamide (Table 2, 3e):** white solid (87%); m.p. 120–122 °C; ¹H NMR (400 MHz, CDCl₃) δ 9.04 (br s, 1H), 7.92 (d, *J* = 8.3 Hz, 2H), 7.31 (d, *J* = 8.1 Hz, 2H), 2.41 (s, 3H), 2.06 (s, 3H), 0.92 (s, 9H); ¹³C NMR (100 MHz, CDCl₃) δ 169.8, 145.0, 135.6, 129.5, 128.3, 49.6, 31.3, 29.4, 21.6; IR (KBr) ν 3251, 2964, 1714, 1599, 1434, 1168, 549 cm⁻¹; HRMS (FAB) *m/z* calcd. for C₁₃H₂₀NO₃S [*M*+*H*]⁺: 270.1164, found: 270.1160.

4-Methyl-*N*-(3-thiopheneacetyl)benzenesulfonamide (Table 2, 3f): white solid (84%); m.p. 138–140 °C; ^1H NMR (400 MHz, CDCl_3) δ 8.63 (br s, 1H), 7.86 (d, J = 8.4 Hz, 2H), 7.27 (m, 3H), 7.06 (d, J = 2.0 Hz, 1H), 6.87 (dd, J = 4.9, 1.2 Hz, 1H), 3.58 (s, 2H), 2.41 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ 168.3, 145.2, 135.2, 131.9, 129.6, 128.4, 128.1, 126.9, 124.1, 37.9, 21.6; IR (KBr) ν 3447, 3299, 3110, 2924, 1724, 1594, 1420, 1330, 1160, 542 cm^{-1} ; HRMS (FAB) m/z calcd. for $\text{C}_{13}\text{H}_{14}\text{NO}_3\text{S}_2$ [$M+H$] $^+$: 296.0415, found: 296.0413.

***N*-(5-Chloropentanoyl)-4-methylbenzenesulfonamide (Table 2, 3g):** white solid (83%); m.p. 95–96 °C; ^1H NMR (400 MHz, CDCl_3) δ 9.0–8.2 (br s, 1H), 7.90 (d, J = 8.2 Hz, 2H), 7.30 (d, J = 8.2 Hz, 2H), 3.40 (t, J = 5.8 Hz, 2H), 2.39 (s, 1H), 2.27 (t, J = 6.8 Hz, 2H), 1.65 (m, 4H); ^{13}C NMR (100 MHz, CDCl_3) δ 171.0, 145.1, 135.4, 129.6, 128.1, 44.2, 35.0, 31.3, 21.5, 21.4; IR (KBr) ν 3448, 3301, 2928, 1732, 1597, 1426, 1329, 1171, 558 cm^{-1} ; HRMS (FAB) m/z calcd. for $\text{C}_{12}\text{H}_{17}\text{ClNO}_3\text{S}$ [$M+H$] $^+$: 290.0618, found: 290.0615.

***N*-(5-Acetyloxypentanoyl)-4-methylbenzenesulfonamide (Table 2, 3h):** white solid (75%); m.p. 94–95 °C; ^1H NMR (400 MHz, CDCl_3) δ 9.27 (s, 1H), 7.89 (d, J = 8.4 Hz, 2H), 7.30 (d, J = 8.1 Hz, 2H), 3.97 (t, J = 6.1 Hz, 2H), 2.40 (s, 3H), 2.27 (t, J = 6.9 Hz, 2H), 2.00 (s, 3H), 1.58 (m, 4H); ^{13}C NMR (100 MHz, CDCl_3) δ 171.4, 170.7, 145.0, 129.5, 128.2, 63.8, 35.4, 27.6, 21.6, 20.9, 20.6; IR (KBr) ν 3226, 2961, 1730, 1714, 1599, 1454, 1344, 1173, 551 cm^{-1} ; HRMS (FAB) m/z calcd. for $\text{C}_{14}\text{H}_{20}\text{NO}_5\text{S}$ [$M+H$] $^+$: 314.1063, found: 314.1060.

***N*-[(5-Triisopropylsilyloxy)pentanoyl]-4-methylbenzenesulfonamide (Table 2, 3i):** white solid (84%); ^1H NMR (400 MHz, CDCl_3) δ 9.21 (br s, 1H), 7.90 (d, J = 8.0 Hz, 2H), 7.29 (d, J = 8.2 Hz, 2H), 3.60 (t, J = 6.2 Hz, 2H), 2.40 (s, 3H), 2.27 (t, J = 7.3 Hz, 2H), 1.59 (m, 2H), 1.44 (m, 2H), 1.02 (s, 21H); ^{13}C NMR (100 MHz, CDCl_3) δ 171.1, 144.9, 135.7, 129.5, 128.2, 62.8, 35.9, 21.6, 21.0, 17.9, 11.8; IR (KBr) ν 3252, 2971, 1731, 1600, 1455, 1347, 1174, 552 cm^{-1} ; HRMS (FAB) m/z calcd. for $\text{C}_{21}\text{H}_{38}\text{NO}_4\text{SSi}$ [$M+H$] $^+$: 428.2292, found: 428.2296.

***N*-(3-Methoxypropanoyl)-4-methylbenzenesulfonamide (Table 2, 3j):** light green solid (74%); ^1H NMR (400 MHz, CDCl_3) δ 9.19 (br s, 1H), 7.90 (d, J = 8.3 Hz, 2H), 7.28 (d, J = 8.2 Hz, 2H), 3.53 (t, J = 5.6 Hz, 2H), 3.36 (s, 3H), 2.45 (t, J = 5.6 Hz, 2H), 2.39 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ 169.3, 144.9, 129.5, 128.4, 67.2, 59.0, 37.1, 21.6; IR (KBr) ν 3064, 2856, 1719, 1458, 1334, 1143, 547 cm^{-1} ; HRMS (FAB) m/z calcd. for $\text{C}_{11}\text{H}_{16}\text{NO}_4\text{S}$ [$M+H$] $^+$: 258.0801, found: 258.0805.

***N*-(1-Cyclohexenylacetyl)-4-methylbenzenesulfonamide (Table 2, 3k):** white solid (75%); m.p. 94–95 °C; ¹H NMR (400 MHz, CDCl₃) δ 8.60 (s, 1H), 7.96 (d, *J* = 8.3 Hz, 2H), 7.30 (d, *J* = 8.2 Hz, 2H), 5.55 (s, 1H), 2.84 (s, 2H), 2.41 (s, 3H), 1.98–1.97 (m, 2H), 1.77 (m, 2H), 1.56–1.48 (m, 4H); ¹³C NMR (100 MHz, CDCl₃) δ 169.0, 145.0, 135.4, 130.0, 129.5, 128.3, 128.3, 46.3, 28.1, 25.2, 22.4, 21.6, 21.6; IR (KBr) ν 3445, 3256, 2933, 1731, 1681, 1455, 1348, 1171, 1089, 550 cm⁻¹; HRMS (FAB) *m/z* calcd. for C₁₅H₂₀NO₃S [*M*+*H*]⁺: 294.1165, found: 294.1164.

***N*-(4,4-Diethoxycarbonyl-6-heptenoyl)-4-methylbenzenesulfonamide (Table 2, 3l):** light yellow oil (89%); ¹H NMR (400 MHz, CDCl₃) δ 9.13 (br s, 1H), 7.90 (d, *J* = 8.3 Hz, 2H), 7.30 (d, *J* = 8.1 Hz, 2H), 5.55 (m, 1H), 5.04 (d, *J* = 3.8 Hz, 1H), 5.01 (s, 1H), 4.10 (m, 4H), 2.54 (d, *J* = 7.4 Hz, 2H), 2.40 (s, 3H), 2.30 (t, *J* = 7.2 Hz, 2H), 2.06 (t, *J* = 8.3 Hz, 2H), 1.19 (m, 6H); ¹³C NMR (100 MHz, CDCl₃) δ 170.8, 170.0, 144.9, 135.6, 131.7, 129.5, 128.4, 119.5, 61.6, 38.2, 31.5, 27.1, 21.6, 13.9; IR (KBr) ν 3446, 3258, 2985, 1730, 1598, 1446, 1346, 1176, 1089, 548 cm⁻¹; HRMS (FAB) *m/z* calcd. for C₂₀H₂₈NO₇S [*M*+*H*]⁺: 426.1587, found: 426.1583.

***N*-[5-(2-Butynyloxy)pentanoyl]-4-methylbenzenesulfonamide (Table 2, 3m):** white solid (77%); ¹H NMR (400 MHz, CDCl₃) δ 9.36 (br s, 1H), 7.89 (d, *J* = 8.3 Hz, 2H), 7.26 (d, *J* = 8.1 Hz, 2H), 3.97 (s, 2H), 3.38 (t, *J* = 6.1 Hz, 2H), 2.37 (s, 3H), 2.24 (t, *J* = 7.1 Hz, 2H), 1.76 (s, 3H), 1.58 (m, 2H), 1.47 (m, 2H); ¹³C NMR (100 MHz, CDCl₃) δ 171.2, 144.8, 135.7, 129.5, 128.2, 82.4, 69.3, 58.5, 35.7, 28.2, 21.5, 21.3; IR (KBr) ν 3226, 2925, 1727, 1599, 1455, 1346, 1173 cm⁻¹; HRMS (FAB) *m/z* calcd. for C₁₆H₂₂NO₄S [*M*+*H*]⁺: 324.1271, found: 324.1266.

4-Methyl-*N*-(phenylacetyl)benzenesulfonamide (Table 2, 3n): white yellow solid (74%); m.p. 121–123 °C; ¹H NMR (400 MHz, CDCl₃) δ 8.06 (br s, 1H), 7.31 (m, 5H), 7.24 (d, 2H), 7.12 (m, 2H), 4.55 (s, 2H), 3.43 (s, 2H); ¹³C NMR (100 MHz, CDCl₃) δ 170.0, 132.1, 130.6, 129.3, 129.2, 128.9, 128.0, 127.8, 58.6, 43.6; IR (KBr) ν 1716, 1456, 1347, 1115, 697 cm⁻¹; HRMS (FAB) *m/z* calcd. for C₁₅H₁₆NO₃S [*M*+*H*]⁺: 290.0852, found: 290.0851.

***N*-(Phenylacetyl)butanesulfonamide (Table 2, 3o):** white solid (87%); m.p. 117–120 °C; ¹H NMR (400 MHz, CDCl₃) δ 8.72 (s, 1H), 7.29 (m, 5H), 3.60 (s, 2H), 3.36 (t, *J* = 7.9 Hz, 2H), 1.64 (m, 2H), 1.37 (m, 2H), 0.86 (t, *J* = 7.3 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 170.2, 132.4, 129.3, 129.0, 127.7, 52.8, 43.4, 24.9, 21.1, 13.4; IR (KBr) ν 3121, 1684, 1463, 1348,

1138, 709 cm^{-1} ; HRMS (FAB) m/z calcd. for $\text{C}_{12}\text{H}_{18}\text{NO}_3\text{S}$ $[M+H]^+$: 256.1008, found: 256.1003.

***N*-(Phenylacetyl)-2-(trimethylsilyl)ethanesulfonamide (Table 2, 3p):** light yellow oil (97%); ^1H NMR (400 MHz, CDCl_3) δ 8.72 (br s, 1H), 7.29 (m, 5H), 3.61 (s, 2H), 3.29 (m, 2H), 0.83 (m, 2H), 0.01 (s, 9H); ^{13}C NMR (100 MHz, CDCl_3) δ 170.2, 132.6, 129.2, 129.0, 127.8, 49.7, 43.4, 9.8; IR (KBr) ν 3231, 1718, 1343, 1457, 1343, 1252, 1174, 1116, 857, 763, 697, 545 cm^{-1} ; HRMS (FAB) m/z calcd. for $\text{C}_{13}\text{H}_{22}\text{NO}_3\text{SSi}$ $[M+H]^+$: 300.1091, found: 300.1087.

***N*-(Phenylacetyl)-(1*S*)-(+)-10-camphorsulfonamide (Table 2, 3q):** white solid (77%); ^1H NMR (400 MHz, CDCl_3) δ 8.95 (br s, 1H), 7.27 (m, 5H), 3.79 (d, $J = 13.6$ Hz, 1H), 3.66 (s, 2H), 3.33 (d, $J = 14.0$ Hz, 1H), 2.31 (m, 1H), 2.21 (m, 1H), 2.05 (m, 2H), 1.94 (m, 1H), 0.98 (s, 3H), 0.81 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ 215.3, 170.4, 132.6, 129.5, 128.8, 127.5, 58.6, 50.6, 48.5, 43.4, 42.6, 42.5, 26.7, 25.3, 19.6, 19.4; IR (KBr) ν 1744, 1454, 1348, 1157, 1113, 866, 764, 565 cm^{-1} ; HRMS (FAB) m/z calcd. for $\text{C}_{18}\text{H}_{24}\text{NO}_4\text{S}$ $[M+H]^+$: 350.1427, found: 350.1429.

Experimental Procedure for the Solid-Phase Synthesis of Amide (eq. 2). [The general procedure of attaching alcohol to resin and detaching the amide product from the resin was referred from a literature (Yadav, V.; Chu, C. K.; Rais, R. H.; Al Safarjalani, O. N.; Guarcello, V.; Naguib, F. N. M.; el Kouni, M. H. *J. Med. Chem.* **2004**, *47*, 1987-1996)].

A solution of 4-ethynylbenzyl alcohol (0.96 g, 7.3 mmol) in dry pyridine (3 mL) was added dropwise to a suspension of 2-chlorotrityl chloride resin (0.65 g, 0.6 mmol/g), which was swollen before use in CH_2Cl_2 (5 mL) for 2 h at room temperature in pyridine (13 mL). The mixture was shaken at room temperature for 48 h under N_2 atmosphere, filtered, washed several times with pyridine, methylene chloride, methanol, and dry diethyl ether, and dried in *vacuo* to afford the corresponding alkyne resin (IR (KBr): 3289 cm^{-1}).

The above obtained resin was swollen before use with CHCl_3 (2 mL) for 1 h at room temperature. To a suspension of the resin in CHCl_3 (2 mL) were added CuI (28.5 mg, 0.15 mmol), *p*-toluenesulfonyl azide (730 mg, 3.7 mmol), H_2O (0.15 mL, 7.4 mmol), and Et_3N (0.52 mL, 3.7 mmol) at room temperature. After shaking the reaction mixture for 48 h at room temperature under N_2 atmosphere, it was diluted by adding CH_2Cl_2 (3 mL) and saturated NH_4Cl solution (3 mL). The mixture was stirred for an additional 30 min at the

same temperature, filtered, and then washed with CH₂Cl₂ and methanol several times each. The filtered solid was dried at room temperature for 6 h in *vacuo*.

To a suspension of the dried resin in CH₂Cl₂ (5 mL) was added triisopropylsilane (0.25 mL) and trifluoroacetic acid (0.1 mL) at room temperature. The reaction mixture was stirred for 2 h at the same temperature and was diluted with CH₂Cl₂ (3 mL) and saturated aqueous NaHCO₃ solution (2 mL) to neutralize excessive trifluoroacetic acid. The organic layer was separated, washed with brine (10 mL x 3), dried over MgSO₄, and concentrated in *vacuo* to afford *N*-[4-(hydroxymethyl)phenylacetyl]-4-methylbenzenesulfonamide (**3r**) as a white solid (56.5 mg, 46% over three steps based on the amounts of the employed resin; ¹H NMR (400 MHz, CD₃OD) δ 7.81 (dd, *J* = 8.3, 1.8 Hz, 2H), 7.33 (dd, *J* = 7.9, 1.7 Hz, 2H), 7.23 (d, *J* = 8.0 Hz, 2H), 7.09 (d, *J* = 8.2 Hz, 2H), 4.54 (s, 2H), 3.49 (s, 2H), 2.40 (s, 3H); ¹³C NMR (100 MHz, CD₃OD) δ 171.5, 146.1, 141.7, 137.7, 133.8, 130.5, 130.2, 129.5, 128.2, 127.2, 64.9, 43.4, 21.5, 18.5, 13.2; IR (KBr) ν 2942, 2866, 1789, 1714, 1681, 1599, 1554, 1455, 1140, 1084, 813, 750, 663, 543 cm⁻¹.

Representative Experimental Procedure of Gram Scale Reaction (eq. 3). To a stirred mixture of *p*-toluenesulfonyl azide (**1a**, 2.36 g, 12.0 mmol), *tert*-butyl *N*-(2-propynyl)-carbamate (1.55 g, 10.0 mmol), H₂O (0.45 mL, 25 mmol) and CuI (57 mg, 0.03 mmol) in CHCl₃ (10.0 mL) was slowly added Et₃N (1.7 mL, 12.0 mmol) at 0 °C under an N₂ atmosphere. After stirring the reaction mixture for 12 h at room temperature under nitrogen atmosphere, it was diluted by adding CH₂Cl₂ (9 mL) and saturated NH₄Cl solution (12 mL). The mixture was stirred for an additional 30 min at the same temperature and then two layers were separated. The aqueous layer was extracted with CH₂Cl₂ (5 mL x 3). The combined organic layers were dried over MgSO₄, filtered, and concentrated in *vacuo*. The crude residue was purified by flash column chromatograph on silica gel (CH₂Cl₂/MeOH, 40:1) to afford *N*-[3-(*tert*-butoxycarbonyl)propanoyl]-4-methylbenzenesulfonamide (**3s**) as a light yellow foam (2.76 g, 81%): ¹H NMR (400 MHz, CDCl₃) δ 9.94 (s, 1H), 7.95 (d, *J* = 8.3 Hz, 2H), 7.35 (d, *J* = 8.0 Hz, 2H), 5.33 (s, 1H), 3.37 (q, *J* = 6.1, 6.0 Hz, 2H), 2.55 (t, *J* = 5.9 Hz, 2H), 2.46 (s, 3H), 1.44 (s, 9H); ¹³C NMR (100 MHz, CDCl₃) δ 170.4, 156.2, 144.8, 135.7, 129.5, 128.1, 79.6, 36.3, 35.4, 28.2, 21.5; IR (KBr) ν 3384, 3209, 1685, 1597, 1449, 1161, 1088, 661, 548 cm⁻¹; HRMS (FAB) *m/z* calcd. for C₁₅H₂₂N₂O₅SNa [*M*+*Na*]⁺: 365.1147, found: 365.1146.

Typical Procedure for the Deprotection of *N*-Sulfonamides. A solution of sodium naphthalenide in 1,2-dimethoxyethane (DME) was prepared by adding DME (10 mL) to a

mixture of sodium (0.23 g, 10 mmol) and naphthalene (1.4 g, 11 mmol) followed by stirring the resulting mixture at room temperature for 2 h under N₂ atmosphere. The above prepared DME solution of sodium naphthalenide was added dropwise to a solution of (**3a**, 0.15 g, 0.5 mmol) in DME (2.0 mL) at -78 °C. The reaction mixture was stirred for 1 h at -78 °C and slowly warmed up to room temperature over 30 min. The reaction mixture was quenched with saturated K₂CO₃ solution (3 mL). The mixture was then stirred for additional 6 h at room temperature, filtered, and the precipitates were rinsed with ether several times (3 x 20 mL). The combined filtrates were concentrated under reduced pressure, and the residue was chromatographed on silica gel (CH₂Cl₂/MeOH, 20:1) to afford benzeneacetamide (54 mg, 80%), which was characterized by ¹H and ¹³C NMR.

Appendix I

Spectral Copies of ^1H and ^{13}C NMR of *N*-Sulfonamides Obtained in this Study

4-Methyl-*N*-(phenylacetyl)benzenesulfonamide (Table 2, 3a)

4-Methyl-*N*-(*p*-tolylacetyl)benzenesulfonamide (Table 2, 3b)

4-Methyl-N-[(4-trifluoromethylphenyl)acetyl]benzenesulfonamide (Table 2, 3c)

***N*-Hexanoyl-4-methylbenzenesulfonamide (Table 2, 3d)**

***N*-(3,3-Dimethylbutanoyl)-4-methylbenzenesulfonamide (Table 2, 3e)**

4-Methyl-N-(3-thiopheneacetyl)benzenesulfonamide (Table 2, 3f)

***N*-(5-Chloropentanoyl)-4-methylbenzenesulfonamide (Table 2, 3g)**

***N*-(5-Acetyloxypentanoyl)-4-methylbenzenesulfonamide (Table 2, 3h)**

***N*-[(5-Triisopropylsilyloxy)pentanoyl]-4-methylbenzenesulfonamide (Table 2, 3i)**

***N*-(3-Methoxypropanoyl)-4-methylbenzenesulfonamide (Table 2, 3j)**

***N*-(1-Cyclohexenylacetyl)-4-methylbenzenesulfonamide (Table 2, 3k)**

***N*-(4,4-Diethoxycarbonyl-6-heptenoyl)-4-methylbenzenesulfonamide (Table 2, 3I)**

***N*-[5-(2-Butynyloxy)pentanoyl]-4-methylbenzenesulfonamide (Table 2, 3m)**

4-Methyl-*N*-(phenylacetyl)benzenesulfonamide (Table 2, 3n)

***N*-(Phenylacetyl)butanesulfonamide (Table 2, 3o)**

***N*-(Phenylacetyl)-2-(trimethylsilyl)ethanesulfonamide (Table 2, 3p)**

***N*-(Phenylacetyl)-(1*S*)-(+)-10-camphorsulfonamide (Table 2, 3q)**

***N*-[4-(Hydroxymethyl)phenylacetyl]-4-methylbenzenesulfonamide (eq 2, 3r)**

***N*-[3-(*tert*-Butyloxycarbonyl)propanoyl]-4-methylbenzenesulfonamide (eq 3, 3s)**