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Supporting Information

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Practical Synthesis of Amides from In Situ Generated Copper(I) Acetylides and Sulfonyl Azides

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NMR spectra were recorded on either Bruker DRX-500, Bruker AMX-400, or Varian Inova-400 instruments and calibrated using residual undeuterated solvent as an internal reference. Proton magnetic resonance (^{1}H NMR) spectra were recorded at 400 MHz. Data are presented as follows: chemical shift (ppm), multiplicity (*s* = singlet, *d* = doublet, *t*= triplet, *q* = quartet, *m* = multiplet, *b* = broad), coupling constant (Hz) and integration. Carbon magnetic resonance (^{13}C NMR) spectra were recorded at 125 or 100 MHz. Data for ^{13}C NMR are reported in terms of chemical shifts (ppm). High-resolution mass spectra (HRMS) were recorded at the mass spectrometry facility at The Scripps Research Institute, La Jolla. HPLC was performed on an Agilent 1100 LC/MSD with an Agilent 1100 SL mass spectrometer, eluting with 0.1 % trifluoroacetic acid (TFA) in H_2O and 0.05 % TFA in CH_3CN. Melting points (m.p.) are uncorrected and were determined using a Thomas Hoover, uni-melt, capillary melting point apparatus.

***N*-(4-acetamidophenylsulfonyl)-2-(1-hydroxycyclohexyl)acetamide (Entry 1).** Prepared as a white solid (mp 225-227 °C) in 60% yield. ^{1}H NMR (400 MHz, [D_6]DMSO) δ 11.7 (s, 1H), 10.6 (s, 1H), 7.81 (d, 4H, *J* = 1.2 Hz), 2.28 (s, 2H), 2.09 (s, 2H), 1.47 (m, 2H), 1.39-1.23 (m, 7H), 1.10-1.06 (m, 1 H); ^{13}C NMR (100 MHz, [D_6]DMSO) δ 169.5, 169.2, 143.8, 132.6, 128.7, 118.1, 69.6, 47.8, 36.8, 25.1, 24.1, 21.4; Anal. calcd for $C_{16}H_{22}N_2O_5S$: C, 54.22; H, 6.26; N, 7.90; found: C, 53.93, H, 6.34, N, 7.82.

2-(4-(4-acetamidophenylsulfonamido)-4-oxobutylcarbamoyl)benzoic acid (Entry 2). Prepared in 67% yield as an off-white solid with m.p. 113-115 °C (dec.); ^{1}H NMR (400 MHz, [D_6]DMSO) δ 12.9 (bs, 1H), 11.9 (s, 1H), 10.4 (s, 1H), 8.25 (t, 1H, *J* = 5.6 Hz), 7.84 (d, 2H, *J* = 9.2 Hz), 7.77 (d, 2H, *J* = 9.2 Hz), 7.74 (m, 1H), 7.55 (dt, 1H, *J* = 1.2, 7,6 Hz), 7.49 (td, 1H, *J* = 1.6, 7.6 Hz), 7.37 (dd, 1H, *J* = 1.2, 7.6 Hz), 3.10 (q, 2H, *J* = 6.8 Hz), 2.28 (t, 2H, *J* = 7.2 Hz), 2.09 (s, 3H),

1.62 (p, 2H, *J* = 7.2 Hz); ^{13}C NMR (100 MHz, [D_6]DMSO) δ 171.3, 169.1, 168.5, 167.8, 143.7, 138.7, 132.7, 131.2, 130.4, 129.1, 128.9, 128.8, 127.6, 118.3, 38.1, 32.8, 24.1, 23.8; HRMS (ESI-TOF): calcd for $C_{20}H_{21}N_3O_7S^+$ [*M*+H^+]: 448.1173; found: 448.1175.

***N1,N7*-bis(4-acetamidophenylsulfonyl)heptanediamide (Entry 3).** Prepared in 74% yield as an off-white solid with m.p. 226 °C (dec.); ^{1}H NMR (400 MHz, [D_6]DMSO) δ 11.9 (s, 1H), 10.3 (s, 1H), 7.77 (d, 4H, *J* = 8.8 Hz), 7.71 (d, 4H, *J* = 8.8 Hz), 2.06 (t, 4H, *J* = 7.6 Hz), 2.04 (s, 6H), 1.26 (p, 4H, *J* = 7.6 Hz), 0.96 (p, 2H, *J* = 7.6 Hz); ^{13}C NMR (100 MHz, [D_6]DMSO) δ 171.3, 169.0, 143.7, 132.7, 128.7, 118.3, 34.9, 27.4, 24.0, 23.5; HRMS (ESI-TOF) calcd for $C_{23}H_{28}N_4O_8S_2^+$ [*M*+H^+]: 553.1421; found: 553.1406.

***tert*-butyl 3-(4-acetamidophenylsulfonamido)-3-oxopropylcarbamate (Entry 4).** Prepared in 83% yield as a yellow solid with m.p. 203-205 °C (dec.); ^{1}H NMR (400 MHz, [D_6]DMSO) δ 11.9 (s, 1H), 10.4 (s, 1H), 7.82 (d, 2H, *J* = 8.9 Hz), 7.77 (d, 2H, *J* = 9.0 Hz), 6.74 (bt, 1H, *J* = 5.3 Hz), 3.01 (dt, 2H, *J* = 6.0, 6.7 Hz), 2.36 (t, 2H, *J* = 6.9 Hz), 2.09 (s, 3H), 1.34 (s, 9H); ^{13}C NMR (100 MHz, [D_6]DMSO) δ 169.7, 169.0, 155.3, 143.7, 132.6, 128.7, 118.2, 77.6, 35.5, 35.2, 28.1, 24.0; HRMS (ESI-TOF) calcd for $C_{16}H_{23}N_3O_6S^+$ [*M*+Na^+]: 408.1200; found: 408.1196.

***N*-(4-acetamidophenylsulfonyl)-2-phenylacetamide (Entry 5).** Prepared in 64% as an off-white solid with m.p. 232-234 °C (dec.), lit 239 °C[1]; ^{1}H NMR (400 MHz, [D_6]DMSO) δ 12.2 (s, 1H), 10.3 (s, 1H), 7.77 (d, 2H, *J* = 9.2 Hz), 7.70 (d, 2H, *J* = 8.8 Hz), 7.24-7.15 (m, 3H), 7.09 (m, 2H), 3.48 (s, 2H), 2.04 (s, 3H); ^{13}C NMR (100 MHz, [D_6]DMSO) δ 169.2, 169.0, 143.8, 133.9, 132.4, 129.2, 128.8, 128.2, 126.7, 118.2, 41.9, 24.1.

***N*-(4-acetamidophenylsulfonyl)-3-tert-butoxybutanamide (Entry 6).** Prepared in 83% as a white solid with m.p. 204-206 °C (dec.); ^{1}H NMR (400 MHz, [D_6]DMSO) δ 11.9 (s, 1H), 10.5 (s, 1H), 7.77 (d, 4H, *J* = 3.6 Hz), 3.82 (m, 1H), 2.24 (dd, 1H, *J* = 7.2, 14.0 Hz), 2.14 (dd, 1H, *J* = 6.0, 14.0 Hz), 2.04 (s, 3H), 0.91 (s, 9H), 0.88 (d, 3H, *J* = 6.0 Hz); ^{13}C NMR (100 MHz, [D_6]DMSO) δ 169.4, 169.1, 142.8, 132.5, 128.9, 118.2, 72.9, 64.1, 45.1, 28.0, 24.1, 23.1; Anal. calcd for $C_{16}H_{24}N_2O_5S$: C, 53.91; H, 6.79; N, 7.86; found: C, 54.10; H, 6.85; N, 7.89.

***N*-(4-acetamidophenylsulfonyl)-2-cyclohexenylacetamide (Entry 7).** Prepared in 54% yield as a tan solid with m.p. 227 °C (dec.); ^{1}H NMR (400 MHz, [D_6]DMSO) δ 11.9 (s, 1H), 10.4 (s,

1H), 7.81 (d, 2H, *J* = 9.2 Hz), 7.77 (d, 2H, *J* = 9.2 Hz), 5.38 (bs, 1H), 2.80 (s, 2H), 2.09 (s, 3H), 1.89 (m, 2H), 1.75 (m, 2H), 1.44 (m, 4H); ^{13}C NMR (100 MHz, [D_6]DMSO) δ 169.3, 169.0, 143.7, 132.5, 130.8, 128.7, 124.9, 118.2, 44.3, 27.6, 24.6, 24.0, 22.1, 21.4; Anal. calcd for $C_{16}H_{20}N_2O_4S$: C, 57.12; H, 5.99; N, 8.33; found: C, 56.95; H, 5.98; N, 8.20.

3-(4-acetamidophenylsulfonamido)-3-oxopropanoic acid (Entry 8). Prepared in 75% yield as an off-white solid with m.p. 261 °C (dec.); ^{1}H NMR (400 MHz, [D_6]DMSO) δ 12.7 (bs, 1H), 12.2 (s, 1H), 10.4 (s, 1H), 7.83 (d, 2H, *J* = 8.8 Hz), 7.77 (d, 2H, *J* = 8.8 Hz), 3.24 (s, 2H), 2.09 (s, 3H); ^{13}C NMR (100 MHz, [D_6]DMSO) δ 169.1, 168.8, 164.7, 143.8, 132.3, 128.9, 118.2, 43.0, 24.1; Anal. calcd for $C_{11}H_{12}N_2O_6S$: C, 44.00; H, 4.03; N, 9.33; found: C, 44.02; H, 4.05; N, 9.14.

***N*-(4-acetamidophenylsulfonyl)-2-((8*R*,9*S*,13*S*,14*S*,17*R*)-3,17-dihydroxy-13-methyl-7,8,9,11,12,13,14,15,16,17-decahydro-*6H*-cyclopenta[*a*]phenanthren-17-yl)acetamide (Entry 9).** Prepared in 68% yield as a tan solid with m.p. 175 °C (dec.); ^{1}H NMR (400 MHz, [D_6]DMSO) δ 11.7 (s, 1H), 10.5 (s, 1H), 9.00 (bs, 1H), 7.92 (d, 2H, *J* = 9.0 Hz), 7,86 (d, 2H, *J* = 9.0 Hz), 7.06 (d, 1H, *J* = 8.5 Hz), 6.56 (m, 1H), 6.48 (m, 1H), 3.17 (s, 1H), 2.68 (m, 2H), 2.46 (d, 1H, *J* = 14.2 Hz), 2.29 (d, 1H, *J* = 14.5 Hz), 2.09 (s, 3H), 2.07-1.95 (m, 2H), 1.73 (m, 2H), 1.54 (m, 2H), 1.37 (d, 1H, *J* = 12.0 Hz), 1.27-1.09 (m, 6H), 0.74 (s, 3H); ^{13}C NMR (100 MHz, [D_6]DMSO) δ 171.2, 169.0, 154.8, 143.8, 137.0, 132.4, 130.1, 128.8, 125.9, 118.2, 114.8, 112.6, 88.9, 81.8, 78.1, 48.5, 46.6, 43.0, 34.3, 31.3, 29.1, 27.0, 25.9, 24.1, 22.7, 14.0; Anal. calcd for $C_{28}H_{34}N_2O_6S$: C, 63.86; H, 6.51; N, 5.32; found: C, 63.93; H, 6.63; N, 5.09.

Prop-2-ynyl 3-(4-acetamidophenylsulfonamido)-3-oxopropanoate (Entry 10). Prepared in 62% yield as a white solid with m.p. 195-197 °C (dec.); ^{1}H NMR (400 MHz, [D_6]DMSO) δ 12.3 (s, 1H), 10.4 (s, 1H), 7.84 (d, 2H, *J* = 9.2 Hz), 7.78 (d, 2H, *J* = 9.2 Hz), 4.67 (d, 2H, *J* = 2.4 Hz), 3.57 (d, 1H, *J* = 2.0 Hz), 3.43 (s, 2H), 2.09 (s, 3H); ^{13}C NMR (100 MHz, [D_6]DMSO) δ 169.1, 165.6, 164.0, 143.9, 132.0, 128.9, 118.3, 78.1, 77.8, 52.5, 42.2, 24.1; Anal. calcd for $C_{14}H_{14}N_2O_6S$: C, 49.70; H, 4.17; N, 8.28; found: C, 49.60, H, 4.29; N, 8.30.

***N*-(4-nitrophenylsulfonyl)-2-phenylacetamide (Entry 11).** Prepared in 27% yield as a pale yellow solid with m.p. 170-171 °C, lit 172-173 °C[2]. ^{1}H NMR (400 MHz, [D_6]DMSO) δ 12.7 (bs, 1H), 8.41 (d, 2H *J* = 8.9 Hz), 8.14 (d, 2H, *J* = 8.9 Hz), 7.29-7.21 (m, 3H), 7.15 (m, 2H), 3.58 (s,

2H); ^{13}C NMR (125 MHz, [D_6]DMSO) δ 169.7, 150.2, 144.2, 133.5, 129.2, 129.1, 128.2, 126.8, 124.4, 41.9.

2-phenyl-*N*-tosylacetamide (Entry 12). Prepared in 69% yield as a tan solid with m.p. 142-144 °C, lit 149 °C[1]. ^{1}H NMR (400 MHz, [D_6]DMSO) δ 12.3 (s, 1H), 7.77 (d, 2H, *J* = 8.0 Hz), 7.40 (d, 2H, *J* = 8.0 Hz), 7.25 (m, 3H), 7.14 (d, 2H, *J* = 6.8 Hz), 3.53 (s, 2H), 2.38 (s, 3H); ^{13}C NMR (100 MHz, [D_6]DMSO) δ 169.2, 144.1, 136.2, 133.8, 129.4, 129.1, 128.2, 127.4, 126.7, 41.9, 20.9.

***N*-(4-acetamidophenylsulfonyl)-N-methyl-2-phenylacetamide** (**11**). To a suspension of **10** (1.66 g, 5 mmol) and potassium carbonate (1.38 g, 10 mmol) in 50 mL of acetonitrile at room temperature was added iodomethane (7.10 g, 50 mmol). The suspension was stirred until LC/MS analysis showed starting material was completely consumed. The solvent was removed in vacuo and water (50 mL) was added slowly with stirring. An off-white solid formed and the suspension was allowed to stir for approximately 1 hour. The product was collected by suction filtration and dried in vacuo, giving 1.41 g of the title compound (81% yield) as an off-white solid (m.p. 134-136 °C) ^{1}H NMR (400 MHz, [D_6]DMSO) δ 10.4 (s, 1H), 7.85 (d, 2H, *J* = 8.8 Hz), 7.78 (d, 2H, *J* = 8.8 Hz), 7.29-7.22 (m, 3H), 7.08 (m, 2H), 3.96 (s, 2H), 3.34 (s, 3 H), 2.09 (s, 3H); ^{13}C NMR (100 MHz, [D_6]DMSO) δ 171.2, 169.2, 144.0, 133.9, 132.0, 129.5, 129.0, 128.2, 126.7, 118.4, 41.7, 33.1, 24.1. HRMS (ESI-TOF) calcd for $C_{17}H_{18}N_2O_4S^+$ [*M*+H^+]: 347.1060; found: 347.1056.

***tert*-butyl 4-(2-phenylacetyl)piperazine-1-carboxylate (12).** Compound **10** (206 mg, 0.59 mmol) and *tert*-butyl piperazine-1-carboxylate (0.110 g, 0.59 mmol) were suspended in toluene (2 mL). The suspension was heated at 100 °C until all starting material was consumed. Chloroform (2 mL) was added and the suspension was stirred at 0 °C for 10 minutes. The cold suspension was filtered and washed with 2 mL of cold chloroform. The filtrate was washed twice with 0.5 M HCl to remove excess piperazine and the organic layer was dried over $MgSO_4$, filtered and concentrated in vacuo to give 175 mg (97% yield) of the title compound as an off-white waxy solid (m.p. 113-115 °C). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32 (m, 2H), 7.25 (m, 3H), 3.74 (s, 2H), 3.60 (m, 2H), 3.37 (m, 4H), 3.20 (m, 2H), 1.43 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.6, 153.4, 133.8, 127.8, 127.5, 125.9, 79.2, 44.9, 40.6, 40.1, 27.3; HRMS (ESI-TOF) calcd for $C_{17}H_{24}N_2O_3^+$ [*M*+H^+]: 305.1860; found: 305.1767.

2-phenylacetic acid (13). Compound **10** (87 mg, 0.323 mmol) was stirred with 1 M NaOH solution (4 mL) and methanol (1 mL). The suspension was heated to 90 °C until LC/MS indicated complete reaction of the starting material. The solution was cooled to room temperature and extracted with ethyl acetate (5 mL). The organic layer was removed and the remaining aqueous material was made acidic with conc. HCl. The solution was extracted with ether and evaporated to give phenylacetic acid (20 mg, 60% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33 (m, 2H), 7.29 (m, 3H), 3.66 (s, 2H). The NMR data is identical to that reported in the literature for 2-phenylacetic acid.[3]

References

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