

Supporting Information

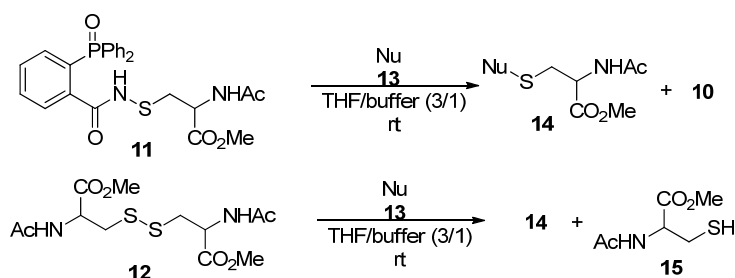
Disulfide formation via sulfenamides

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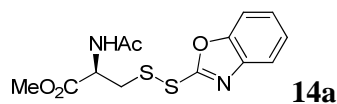
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Materials and Methods: All solvents were reagent grade. Tetrahydrofuran (THF) was freshly distilled from sodium/benzophenone under argon. Reactions were magnetically stirred and monitored by thin layer chromatography (TLC) with 0.25 mm pre-coated silica gel plates. Flash chromatography was performed with silica gel 60 (particle size 0.040-0.062mm). Yields refer to chromatographically and spectroscopically pure compounds, unless otherwise stated. Proton and carbon-13 NMR spectra were recorded on a 300 MHz spectrometer. Chemical shifts are reported relative to chloroform (δ 7.26) for ^1H NMR and chloroform (δ 77.0) for ^{13}C NMR.

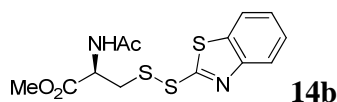
General procedure for the reactions shown in Table 1



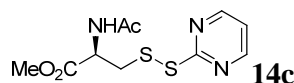
To a stirred solution of sulfenamide **11** or disulfide **12** (0.3 mmol) in 4 mL THF/PBS buffer (pH 7.4) (3:1) was added nucleophile **13** (0.33 mmol). The reaction mixture was stirred at room temperature for 0.5 to 2 hours and monitored by TLC. After the reaction was completed, the mixture was diluted with dichloromethane (15 mL) and washed with brine (15 mL). The organic layer was then dried over anhydrous Na_2SO_4 and concentrated. The product was purified by flash column chromatography.



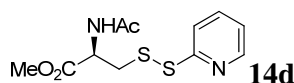
14a: White solid; m.p. 151-152 °C; ¹H NMR (300 MHz, CDCl₃): δ 7.69-7.66 (1H, m), 7.59 (1H, d, *J* = 7.8 Hz), 7.52-7.49 (1H, m), 7.36-7.32 (2H, m), 4.99-4.94 (1H, m), 3.72 (3H, s), 3.65 (1H, dd, *J*₁ = 14.6 Hz, *J*₂ = 5.3 Hz), 3.41 (1H, dd, *J*₁ = 14.6, *J*₂ = 4.8 Hz), 2.07 (3H, s); ¹³C NMR (75 MHz, CDCl₃): δ 170.8, 170.4, 164.2, 152.8, 141.5, 125.4, 125.2, 119.3, 110.8, 53.1, 51.6, 42.1, 23.3; IR (thin film) cm⁻¹ 3280, 3063, 1747, 1660, 1538, 1504, 1452, 1237, 1216, 1127, 1094, 745; MS m/z 327.4 [M+H⁺].



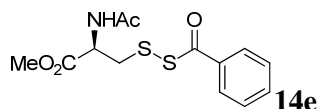
14b: White solid; m.p. 153 °C; ¹H NMR (300 MHz, CDCl₃): δ 7.89 (1H, dd, *J*₁ = 8.1 Hz, *J*₂ = 0.6 Hz), 7.81 (1H, dd, *J*₁ = 8.0 Hz, *J*₂ = 0.6 Hz), 7.46 (1H, dt, *J*₁ = 7.8 Hz, *J*₂ = 1.2 Hz), 7.35 (1H, dt, *J*₁ = 7.8 Hz, *J*₂ = 1.2 Hz), 6.90 (1H, d, *J* = 7.2 Hz), 4.99-4.94 (1H, m), 3.75 (3H, s), 3.50 (2H, d, *J* = 4.8 Hz), 2.04 (3H, s); ¹³C NMR (75 MHz, CDCl₃): δ 170.7, 170.7, 170.2, 154.7, 136.1, 126.7, 125.2, 122.4, 121.5, 53.2, 52.0, 41.7, 23.4; IR (thin film) cm⁻¹ 3275, 3061, 1747, 1660, 1540, 1459, 1426, 1236, 1216, 1006, 758; HRMS m/z 343.0247 [M+H⁺], calcd for C₁₃H₁₅N₂O₃S₃ 343.0239.



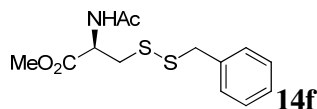
14c: Colorless thick oil; ¹H NMR (300 MHz, CDCl₃): δ 8.65 (2H, d, *J* = 4.8 Hz), 7.23 (1H, s), 7.16 (1H, t, *J* = 4.8 Hz), 4.95-4.89 (1H, m), 3.71 (3H, s), 3.53 (1H, dd, *J*₁ = 14.4 Hz, *J*₂ = 4.8 Hz), 3.29 (1H, dd, *J*₁ = 14.4 Hz, *J*₂ = 4.8 Hz), 2.06 (3H, s); ¹³C NMR (75 MHz, CDCl₃): δ 171.6, 171.0, 170.0, 158.2, 118.4, 52.9, 51.5, 41.2, 23.4; IR (thin film) cm⁻¹ 3276, 3063, 1744, 1656, 1554, 1380, 1218, 1037, 773; MS m/z 287.8 [M+H⁺].



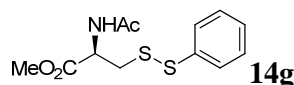
14d: Colorless thick oil; ^1H NMR (300 MHz, CDCl_3): δ 8.55-8.52 (1H, m), 7.65 (1H, dt, $J_1 = 8.1$ Hz, $J_2 = 1.8$ Hz), 7.52 (1H, d, $J = 8.1$ Hz), 7.43 (1H, d, $J = 7.2$ Hz), 7.16 (1H, ddd, $J_1 = 7.2$ Hz, $J_2 = 4.8$ Hz, $J_3 = 1.2$ Hz), 4.94-4.89 (1H, m), 3.72 (3H, s), 3.44 (1H, dd, $J_1 = 14.4$ Hz, $J_2 = 4.8$ Hz), 3.29 (1H, dd, $J_1 = 14.4$ Hz, $J_2 = 4.8$ Hz), 2.02 (3H, s); ^{13}C NMR (75 MHz, CDCl_3): δ 171.0, 170.2, 159.2, 150.1, 137.4, 121.6, 121.3, 52.9, 51.9, 41.6, 23.3; IR (thin film) cm^{-1} 3267, 3049, 2953, 1746, 1659, 1574, 1561, 1447, 1418, 1216, 1118, 763; MS m/z 286.9 $[\text{M}+\text{H}^+]$.



14e: White solid; m.p. 104-105 °C; ^1H NMR (300 MHz, CDCl_3): δ 7.96-7.93 (2H, m), 7.62 (1H, dt, $J_1 = 7.5$ Hz, $J_2 = 1.5$ Hz), 7.49-7.44 (2H, m), 7.16 (1H, d, $J = 7.5$ Hz), 4.87-4.81 (1H, m), 3.68 (3H, s), 3.44 (1H, dd, $J_1 = 14.4$ Hz, $J_2 = 4.8$ Hz), 3.13 (1H, dd, $J_1 = 14.4$ Hz, $J_2 = 4.8$ Hz), 2.07 (3H, s); ^{13}C NMR (75 MHz, CDCl_3): δ 171.1, 170.1, 167.5, 136.8, 129.5, 128.5, 127.7, 53.0, 51.9, 40.8, 23.2; IR (thin film) cm^{-1} 3287, 3062, 2953, 1747, 1686, 1540, 1448, 1206, 1176, 887, 679; MS m/z 314.0 $[\text{M}+\text{H}^+]$.



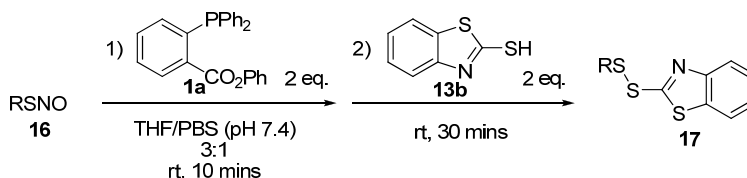
14f: White solid; m.p. 89-90 °C; ^1H NMR (300 MHz, CDCl_3): δ 7.36-7.28 (5H, m), 7.30 (1H, d, $J = 6.9$ Hz), 4.80-4.74 (1H, m), 3.89 (2H, s), 3.73 (3H, s), 2.89-2.75 (2H, m), 2.02 (3H, s); ^{13}C NMR (75 MHz, CDCl_3): δ 171.2, 170.1, 137.0, 129.6, 128.9, 127.9, 52.9, 51.8, 43.7, 40.0, 23.4; IR (thin film) cm^{-1} 3281, 3030, 1747, 1656, 1541, 1215, 700; MS m/z 300.0 $[\text{M}+\text{H}^+]$.



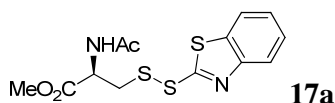
14g: Colorless thick oil; ^1H NMR (300 MHz, CDCl_3): δ 7.70-7.55 (1H, m), 7.54-7.47 (2H, m), 7.37-7.31 (2H, m), 7.28-7.22 (1H, m), 6.35 (1H, d, $J = 7.2$ Hz), 4.91-4.82 (1H, m), 3.73 (3H, s), 3.23 (1H, q, $J = 2.4$ Hz), 1.93 (3H, s); ^{13}C NMR (75 MHz,

CDCl₃): δ 171.1, 170.1, 167.5, 136.8, 129.5, 128.5, 127.7, 53.0, 51.9, 40.8, 23.2; IR (thin film) cm⁻¹ 3275, 3060, 1747, 1660, 1539, 1438, 1217, 1024, 744; MS m/z 285.9 [M+H⁺].

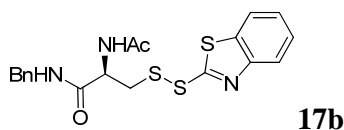
General procedure for one-pot disulfide formation from RSNO



To a stirred solution of freshly prepared RSNO **16** (0.3 mmol) in 4 mL THF/PBS buffer (pH 7.4) 3:1 was added phosphine **1a** (0.6 mmol). The mixture was stirred for 10 minutes at rt. Thiol **13b** (0.33 mmol) was then added into the reaction. The reaction mixture was stirred at rt for another 30 minutes and then diluted with dichloromethane (25 mL) and washed with brine (25 mL). The organic layer was dried over anhydrous Na₂SO₄ and concentrated. The product was purified by flash column chromatography.

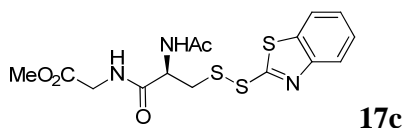


17a is compound **14b**.

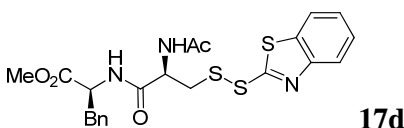


17b: White solid; m.p. 223-224 °C; ¹H NMR (300 MHz, CDCl₃): δ 8.69 (1H, t, *J* = 6.0 Hz), 8.39 (1H, dd, *J* = 7.8 Hz), 8.04 (1H, d, *J* = 7.8 Hz), 7.84 (1H, d, *J* = 8.1 Hz), 7.48 (1H, t, *J* = 7.2 Hz), 7.48 (1H, t, *J* = 7.2 Hz), 7.30-7.21 (5H, m), 4.70-4.63 (1H, m), 4.27 (2H, d, *J* = 5.7 Hz), 3.39 (1H, dd, *J*₁ = 13.5 Hz, *J*₂ = 5.7 Hz), 3.18 (1H, dd, *J*₁ = 13.5 Hz, *J*₂ = 5.7 Hz), 1.87 (3H, s); ¹³C NMR (75 MHz, CDCl₃): δ 170.4, 169.7, 137.8, 129.1, 129.0, 128.1, 127.8, 126.8, 126.8, 125.3, 121.7, 121.6, 52.8, 44.0, 42.8, 23.4; IR (thin film) cm⁻¹ 3276, 1647, 1541, 1426, 1006, 698; HRMS(ESI) m/z 418.0739

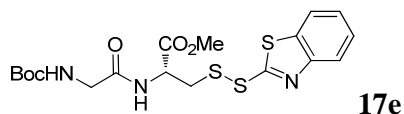
[M+H⁺], calcd for C₁₉H₂₀N₃O₂S₃ 418.0712.



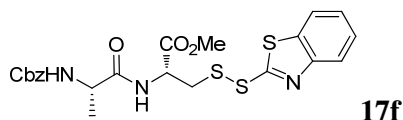
17c: Colorless thick oil; ¹H NMR (300 MHz, CDCl₃): δ 8.09 (1H, t, *J* = 5.6 Hz), 7.86 (1H, d, *J* = 8.1 Hz), 7.78 (1H, dd, *J*₁ = 8.1 Hz, *J*₂ = 0.8 Hz), 7.44 (1H, dt, *J*₁ = 7.8 Hz, *J*₂ = 1.2 Hz), 7.33 (1H, dt, *J*₁ = 7.7 Hz, *J*₂ = 1.2 Hz), 7.19 (1H, d, *J* = 7.8 Hz), 4.95 (1H, q, *J* = 6.8 Hz), 4.07 (2H, dd, *J*₁ = 5.7 Hz, *J*₂ = 0.9 Hz), 3.72 (3H, s), 3.45 (1H, dd, *J*₁ = 14.3 Hz, *J*₂ = 5.9 Hz), 3.22 (1H, dd, *J*₁ = 14.1 Hz, *J*₂ = 6.9 Hz), 1.99 (3H, s); ¹³C NMR (75 MHz, CDCl₃): δ 170.8, 170.4, 170.0, 153.9, 136.2, 126.7, 125.2, 122.0, 121.6, 52.6, 52.6, 42.4, 41.6, 23.3; IR (thin film) cm⁻¹ 3289, 3061, 2952, 1750, 1652, 1538, 1426, 1122, 1006, 758, 729; MS *m/z* 399.9 [M+H⁺].



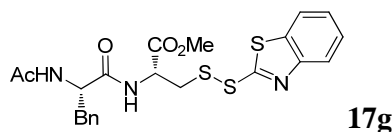
17d: White solid; m.p. 193-194 °C; ¹H NMR (300 MHz, CDCl₃): δ 7.75 (1H, dd, *J*₁ = 7.8 Hz, *J*₂ = 0.9 Hz), 7.70 (1H, dd, *J*₁ = 7.8 Hz, *J*₂ = 0.9 Hz), 7.64 (1H, d, *J* = 7.5 Hz), 7.38 (1H, dt, *J*₁ = 7.5 Hz, *J*₂ = 1.2 Hz), 7.30 (1H, dt, *J*₁ = 7.5 Hz, *J*₂ = 1.2 Hz), 7.26-7.08 (6H, m), 4.92 (1H, dd, *J*₁ = 14.1 Hz, *J*₂ = 6.0 Hz), 4.83 (1H, dd, *J*₁ = 13.2 Hz, *J*₂ = 6.9 Hz), 3.67 (3H, s), 3.41 (1H, dd, *J*₁ = 14.1 Hz, *J*₂ = 6.0 Hz), 3.20 (2H, dt, *J*₁ = 13.8 Hz, *J*₂ = 6.0 Hz), 3.06 (1H, dd, *J*₁ = 13.8 Hz, *J*₂ = 6.9 Hz), 1.92 (3H, s); ¹³C NMR (75 MHz, CDCl₃): δ 171.6, 170.8, 170.7, 169.9, 154.2, 136.2, 136.0, 129.5, 128.8, 127.3, 126.7, 125.1, 122.2, 121.5, 54.1, 52.7, 52.6, 42.7, 37.8, 23.3; IR (thin film) cm⁻¹ 3285, 3061, 1743, 1648, 1541, 1426, 1215, 1006, 757; MS *m/z* 489.9 [M+H⁺].



17e: Colorless thick oil; ^1H NMR (300 MHz, CDCl_3): δ 7.90 (1H, dd, $J_1 = 8.4$ Hz, $J_2 = 0.6$ Hz), 7.83 (1H, dd, $J_1 = 8.1$ Hz, $J_2 = 0.6$ Hz), 7.46 (1H, dt, $J_1 = 7.2$ Hz, $J_2 = 1.2$ Hz), 7.36 (1H, dt, $J_1 = 7.5$ Hz, $J_2 = 1.2$ Hz), 7.33 (1H, s), 5.16-5.15 (1H, m), 4.98-4.92 (1H, m), 3.86 (2H, d, $J = 5.7$ Hz), 3.75 (3H, s), 3.50 (2H, ddd, $J_1 = 21.3$ Hz, $J_2 = 14.4$ Hz, $J_3 = 1.5$ Hz), 1.46 (9H, s); ^{13}C NMR (75 MHz, CDCl_3): δ 170.3, 169.8, 154.8, 136.1, 126.7, 125.2, 122.5, 121.5, 53.2, 51.9, 41.3, 28.5; IR (thin film) cm^{-1} 3314, 3062, 2978, 1745, 1678, 1518, 1427, 1367, 1250, 1169, 1006, 758, 728; MS m/z 457.8 $[\text{M}+\text{H}^+]$.

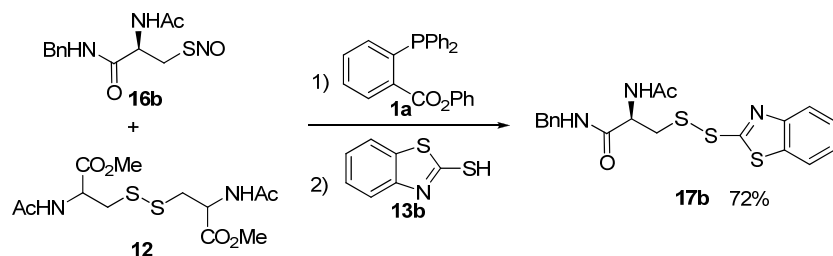


17f: Colorless thick oil; ^1H NMR (300 MHz, CDCl_3): δ 7.90 (1H, d, $J = 8.4$ Hz), 7.80 (1H, d, $J = 7.8$ Hz), 7.44 (1H, dt, $J_1 = 7.8$ Hz, $J_2 = 1.2$ Hz), 7.38-7.30 (7H, m), 5.38 (1H, d, $J = 7.2$ Hz), 5.12 (2H, s), 4.91 (1H, d, $J = 7.2$ Hz), 4.36-4.31 (1H, m), 3.74 (3H, s), 3.54-3.39 (2H, m), 1.41 (3H, d, $J = 6.9$ Hz); ^{13}C NMR (75 MHz, CDCl_3): δ 202.6, 172.4, 170.3, 156.2, 154.7, 136.3, 136.2, 128.7, 128.5, 128.4, 126.7, 125.2, 122.5, 121.5, 67.4, 53.2, 52.1, 50.7, 41.2; IR (thin film) cm^{-1} 3310, 3063, 1718, 1670, 1522, 1237, 1006, 728; MS m/z 506.0 $[\text{M}+\text{H}^+]$.



17g: White solid; m.p. 214-215 °C; ^1H NMR (300 MHz, CDCl_3): δ 7.79 (1H, d, $J = 8.1$ Hz), 7.72 (1H, d, $J = 7.8$ Hz), 7.39-7.10 (8H, m), 6.23 (1H, d, $J = 7.5$ Hz), 4.81-4.71 (2H, m), 3.65 (3H, s), 3.39 (1H, dd, $J_1 = 14.4$ Hz, $J_2 = 4.8$ Hz), 3.27 (1H, dd, $J_1 = 14.1$ Hz, $J_2 = 5.7$ Hz), 3.08-2.94 (2H, m), 1.88 (3H, s); ^{13}C NMR (75 MHz, CDCl_3): δ 171.3, 171.1, 170.5, 170.0, 154.9, 136.5, 136.1, 129.5, 128.9, 127.3, 126.7, 125.2, 122.5, 121.5, 54.5, 53.1, 52.1, 41.1, 38.4, 23.4; IR (thin film) cm^{-1} 3276, 3062, 1747, 1648, 1542, 1426, 1236, 1006, 728; MS m/z 490.0 $[\text{M}+\text{H}^+]$.

Crossover experiment



To a stirred solution of **16b** (0.2 mmol) and disulfide **12** (0.2 mmol) in 3:1 THF/PBS buffer (pH 7.4) (4 mL) was added phosphine **1a** (0.41 mmol). The reaction mixture was stirred for 10 minutes at room temperature. Then **13b** (0.4 mmol) was added into the reaction and the mixture was stirred at room temperature for an additional 30 minutes. After the reaction was completed, the mixture was diluted with dichloromethane (25 mL) and washed with brine (25 mL). The organic solvent was then dried over anhydrous Na₂SO₄ and concentrated. The disulfide product **17b** was isolated in 72% yield and compound **12** was recovered completely by flash column chromatography (dichloromethane/methanol 100:1).