Supporting Information for:

Oxaziridine-Mediated Intramolecular Amination of sp^3-Hybridized C–H bonds

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I. General Information

$CuCl_2$ and LiCl were purchased from Aldrich and used without further purification. Acetone was purified by distillation from K_2CO_3. C–H amination reactions were performed in two-dram vials fitted with Teflon screwcaps. All other air- and moisture-sensitive reactions were performed under an atmosphere of nitrogen in glassware that had been oven-dried for at least 1 h prior to use. Chromatography was performed with SiliaFlash P60 silica gel (230–400 mesh) using the method of Still.[1]

Diastereomer ratios for all compounds were determined by ^{1}H NMR analysis of the unpurified reaction mixtures. ^{1}H and ^{13}C NMR data for all previously uncharacterized compounds were obtained using Varian Inova-500 and Varian Unity-500 spectrometers and are referenced to TMS (0.00 ppm) and $CDCl_3$ (77.23 ppm), respectively. IR spectral data were obtained using a Bruker Vector 22 spectrometer (thin film on NaCl or ATR). Melting points were obtained using a Mel-Temp II (Laboratory Devices, Inc., USA) melting point apparatus. Mass spectrometry was performed with a Micromass LCT (electrospray ionization, time-of-flight analyzer or electron impact). These facilities are funded by the NSF (CHE-9974839, CHE-9304546) and the University of Wisconsin.

II. Synthesis of oxaziridine substrates

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N-(Benzensulfonyl)-3-(2-pentylphenyl)oxaziridine (**1**). To a solution of 780 mg (4.42 mmol) 2-*n*-pentylbenzaldehyde[2] and 695 mg (4.42 mmol) benzenesulfonamide in 90 mL CH_2Cl_2 was added 2.75 mL (13.3 mmol) $Ti(OEt)_4$ dropwise. The reaction mixture was filtered through a short plug of silica gel, rinsing with several portions of EtOAc. The filtrate was concentrated to afford the *N*-benzenesulfonimine, which was dissolved in 80 mL toluene and added to a solution of 5.13 g (37.1 mmol) K_2CO_3 in 40 mL water. The biphasic mixture was subjected to vigorous mechanical stirring, and a solution of 4.35 g (7.07 mmol) oxone in 40 mL water was added slowly. After 30 min, the reaction was poured into a separatory funnel and the phases were separated. The aqueous layer was washed twice with Et_2O, and the combined organic extracts were washed with brine, dried over $MgSO_4$, and concentrated by rotary evaporation. Purification by chromatography on SiO_2 (15:1 to 10:1 hexanes:EtOAc) afforded 1.07 g (3.23 mmol, 73% yield) of the oxaziridine as a colorless liquid. IR (neat) 1449, 1353, 1173, 1089, 785, 732, 685; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.06–8.03 (m, 2H), 7.75–7.72 (m, 1H), 7.63–7.60 (m, 2H), 7.34 (td, J = 7.4, 1.4 Hz, 1H), 7.26–7.24 (m, 1H), 7.22–7.18 (m, 2H), 5.70 (s, 1H), 2.85–2.74 (m, 2H), 1.70–1.60 (m, 2H), 1.40–1.35 (m, 4H), 0.93–0.90 (m, 3H); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 143.3, 135.2, 134.8, 130.9, 129.9, 129.6, 128.3, 127.0, 126.6, 74.3, 32.6, 31.8, 31.7, 22.7, 14.2; HRMS (EI^+) calculated for [$C_{18}H_{21}NO_3SH^+$] requires *m/z* 332.1315, found *m/z* 332.1306.

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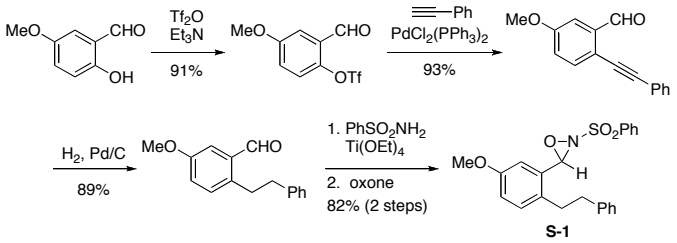
Table 1, entry 1 (**4**). 2-Phenethylbenzaldehyde was prepared as previously described.[3] To a solution of 1.84 g aldehyde (8.75 mmol) and 1.44 g benzenesulfonamide (9.19 mmol) in 90 mL CH_2Cl_2 was added 5.44 mL $Ti(OEt)_4$ (26.2 mmol) dropwise. The reaction was allowed to stir under N_2 overnight. The reaction mixture was filtered through a short plug of silica gel, rinsing with several portions of EtOAc. The filtrate was concentrated to afford the *N*-benzenesulfonimine, which was dissolved in 160 mL toluene and added to a solution of 10.2 g K_2CO_3 (73.5 mmol) in 80 mL water. The biphasic mixture was subjected to vigorous mechanical stirring, and a solution of 8.62 g oxone (14 mmol) in 80 mL water was added slowly. After 30 min, equivalent portions of aqueous K_2CO_3 and oxone were added, and after an additional 30 min, the reaction was poured into a separatory funnel and the phases were separated. The aqueous layer was washed twice with Et_2O, and the combined organic extracts were washed with brine, dried over $MgSO_4$, and concentrated by rotary evaporation. Purification by chromatography on SiO_2 (9:1 to 8:1 hexanes:EtOAc) afforded 3.05 g (8.35 mmol, 95% yield) of oxaziridine **4** as a white solid (m.p. 77–78 °C). IR (ATR) 1500, 1453, 1351, 1244, 1173, 1091, 830, 758, 699; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.06–8.04 (m, 2H), 7.77–7.73 (m, 1H), 7.64–7.60 (m, 2H), 7.35 (td, J = 7.3, 1.5 Hz, 1H), 7.31–7.18 (m, 8H), 5.63 (s, 1H), 3.17–3.05 (m, 2H), 3.02–2.96 (m, 1H), 2.94–2.88 (m, 1H); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 142.0, 141.0, 135.2, 134.8, 131.0, 130.2, 129.6, 128.7, 128.6, 127.2, 126.9, 126.5, 74.5, 38.3, 34.8; HRMS (EI^+) calculated for [$C_{21}H_{19}O_3NSH^+$] requires *m/z* 366.1159, found *m/z* 366.1160.



S-1

Table 1, entry 2 (**S-1**). A solution of 910 mg 5-methoxysalicylaldehyde (5.98 mmol) and 1.25 mL Et_3N (8.97 mmol,) in 12 mL CH_2Cl_2 was cooled to –5 °C and treated with 1.51 mL triflic anhydride (8.97 mmol). After 20 min, the reaction was diluted with CH_2Cl_2, washed successively with sat. aq. $NaHCO_3$ and brine, dried over $MgSO_4$, and concentrated by rotary evaporation. The product was purified by chromatography on SiO_2 (5:1 hexanes:EtOAc) to afford 1.55 g (5.45 mmol, 91% yield) of the triflate as a colorless oil. Spectral properties were identical to those previously reported.[4]

A solution of 1.30 g aryl triflate (4.57 mmol) and 654 mg phenyl acetylene (6.40 mmol) in 14 mL DMF was treated with 64 mg $PdCl_2(PPh_3)_2$ (92 μmol) and 2.90 mL Et_3N (20.6 mmol), and the reaction was warmed to 90 °C for 3 h. After cooling to room temperature, the reaction was diluted with water and extracted with EtOAc (3 x 15 mL), and the combined organics were washed with water and brine, dried over $MgSO_4$, and concentrated by rotary evaporation. Purification by chromatography on SiO_2 (20:1 to 10:1 hexanes:EtOAc) afforded 1.00 g (4.23 mmol, 93% yield) of the alkyne as a yellow solid (m.p. 79–81 °C). IR (ATR) 1687, 1596, 1500, 1324, 1279, 1227, 1157, 1029, 829, 764, 693; ^{1}H NMR (500 MHz, $CDCl_3$) δ 10.61 (s, 1H), 7.57–7.52 (m, 3H), 7.43 (d, J = 2.7 Hz, 1H), 7.38–7.36 (m, 3H), 7.14 (dd, J = 8.6, 2.9 Hz, 1H), 3.88 (s, 3H); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 191.8, 160.0, 137.4, 134.8, 131.7, 129.0, 128.7, 122.9, 121.9, 119.8, 95.0, 85.0, 55.8; HRMS (EI^+) calculated for $[C_{16}H_{12}O_2^+]$ requires *m/z* 236.0832, found *m/z* 236.0832.

A solution of 410 mg (1.74 mmol) of the alkyne in 30 mL EtOAc was treated with 60 mg Pd/C (5% Pd). The reaction was sealed, evacuated, and purged twice with an atmosphere of H_2. The mixture was allowed to stir under a balloon of H_2 gas for 1.5 h. An additional 40 mg Pd/C was added, and the reaction was allowed to continue for 3 h more. The reaction was then filtered through a pad of celite and concentrated by rotary evaporation. Purification by chromatography on SiO_2 (10:1 hexanes/EtOAc) afforded 370 mg (1.54 mmol, 89% yield) of the alkane as a clear oil. IR (neat) 1685, 1607, 1497, 1265, 1163, 1038, 824; ^{1}H NMR (500 MHz, $CDCl_3$) δ 10.14 (s, 1H), 7.34 (d, J = 2.9 Hz, 1H), 7.28–7.25 (m, 2H), 7.21–7.18 (m, 1H), 7.15–7.12 (m, 3H), 7.05 (dd, J = 8.4, 2.8 Hz, 1H), 3.84 (s, 3H), 3.26–3.23 (m, 2H), 2.90–2.86 (m, 2H); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 191.7, 158.5, 141.2, 137.0, 134.7, 132.6, 128.8, 128.6, 126.4, 121.1, 114.3, 55.7, 39.0, 33.8; HRMS (ESI^+) calculated for $[C_{16}H_{16}O_2Na^+]$ requires *m/z* 263.1043, found *m/z* 263.1050.

To a solution of 370 mg aryl aldehyde (1.54 mmol) and 242 mg benzenesulfonamide (1.54 mmol) in CH_2Cl_2 was added 960 μL $Ti(OEt)_4$ (4.62 mmol) dropwise. The reaction was allowed to stir under N_2 overnight. The reaction mixture was filtered through a short plug of silica gel, rinsing with several portions of EtOAc. The filtrate was concentrated to afford the *N*-benzenesulfonimine, which was dissolved in 45 mL toluene and added to a solution of 1.79 g K_2CO_3 (12.9 mmol) in 20 mL water. The biphasic mixture was subjected to vigorous mechanical stirring, and a solution of oxone 1.52 g (2.46 mmol) in 20 mL water was added slowly. After 30 min, equivalent portions of aqueous K_2CO_3 and oxone were added, and after an additional 30 min, the reaction was poured into a separatory funnel. The phases were separated, the aqueous layer was washed twice with Et_2O, and the combined organic extracts were washed with brine, dried over $MgSO_4$, and concentrated by rotary evaporation. ^{1}H NMR analysis of the residue showed incomplete oxidation of the imine, and the reaction mixture was twice resubjected to oxidation. Purification by chromatography on SiO_2 (9:1 to 7:1 hexanes:EtOAc) afforded 500 mg (1.26 mmol, 82% yield) of the oxaziridine as a white solid (m.p. 90–92 °C). IR (neat) 1613, 1504, 1449, 1352, 1289, 1225, 1171, 1088, 1038, 734, 699; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.05–8.03 (m, 2H), 7.75–7.72 (m, 1H), 7.62–7.59 (m, 2H), 7.30–7.27 (m, 2H), 7.24–7.17 (m, 3H), 7.08 (d, J = 8.3 Hz, 1H), 6.88 (dd, J = 8.4, 2.8 Hz, 1H), 6.77 (d, J = 2.7 Hz, 1H), 5.58 (s, 1H), 3.72 (s, 3H), 3.09–2.83 (m, 4H); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 158.5, 141.0, 135.2, 134.7, 134.1, 131.4, 129.6(0), 129.5(8), 129.5, 128.7(4), 128.6(8), 126.4, 117.6, 111.3, 74.4, 55.6, 38.5, 34.0; HRMS (EI^+) calculated for $[C_{22}H_{21}SO_4N^+]$ requires *m/z* 395.1186, found *m/z* 395.1181.

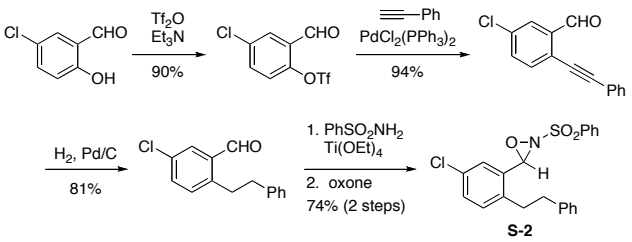


Table 1, entry 3 (**S-2**). A solution of 1.00 g 5-chlorosalicylaldehyde (6.39 mmol) and 1.34 mL Et_3N (9.58 mmol) in 15 mL CH_2Cl_2 was cooled to –5 °C and treated with 1.61 mL triflic anhydride (9.58 mmol). After 50 min, the reaction was diluted with CH_2Cl_2, washed successively with sat. aq. $NaHCO_3$ and brine, dried over $MgSO_4$, and concentrated by rotary evaporation. The product was purified by chromatography on SiO_2 (10:1 hexanes:EtOAc) to afford 1.66 g (5.75 mmol, 90% yield) of the triflate as a colorless oil. Spectral properties were identical to those previously reported.[4]

A solution of 800 mg aryl triflate (2.77 mmol) and 396 mg phenyl acetylene (3.88 mmol) in 9 mL DMF was treated with 39 mg $PdCl_2(PPh_3)_2$ (55 μmol) and 1.74 mL Et_3N (12.5 mmol), and the reaction was warmed to 90 °C for 2 h. After cooling to room temperature, the reaction was diluted with water and extracted with EtOAc (3 x 15 mL), and the combined organics were washed with water and brine, dried over $MgSO_4$, and concentrated by rotary evaporation. Purification by chromatography on SiO_2 (20:1 hexanes:EtOAc) afforded 627 mg of the diaryl acetylene (2.61 mmol, 94% yield) as a yellow solid (m.p. 95–96 °C). IR (neat) 1691, 1584, 1492, 1245, 1183, 1105, 901, 840, 752, 666; ^{1}H NMR (500 MHz, $CDCl_3$) δ 10.57 (s, 1H), 7.90 (d, J = 2.1 Hz, 1H), 7.58–7.52 (m, 4H), 7.42–7.36 (m, 3H); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 190.5, 137.1, 135.3, 134.6, 134.0, 131.9, 129.5, 128.8, 127.5, 125.3, 122.2, 97.5, 84.1; HRMS (ESI^+) calculated for [$C_{15}H_9OClNa^+$] requires *m/z* 263.0235, found *m/z* 263.0238.

A solution of 505 mg (2.10 mmol) of the alkyne in 25 mL EtOAc was treated with 90 mg Pd/C (5% Pd). The reaction was sealed, evacuated, and purged twice with an atmosphere of H_2. The mixture was allowed to stir under a balloon of H_2 gas for 4.5 h. The reaction was then filtered through a pad of celite and concentrated by rotary evaporation. Purification by chromatography on SiO_2 (20:1 hexanes/EtOAc) afforded 415 mg (1.70 mmol, 81% yield) of the alkane as a clear oil. IR (neat) 1701, 1594, 1561, 1480, 1453, 1197, 897, 822, 699, 666; ^{1}H NMR (500 MHz, $CDCl_3$) δ 10.08 (s, 1H), 7.78 (d, J = 2.4 Hz, 1H), 7.43 (dd, J = 8.2, 2.5 Hz, 1H), 7.28–7.24 (m, 2H), 7.22–7.19 (m, 1H), 7.15–7.13 (m, 3H), 3.30–3.27 (m, 2H), 2.90–2.87 (m, 2H); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 190.8, 142.7, 140.7, 135.2, 133.8, 133.0, 132.9, 131.5, 128.8, 128.7, 126.5, 38.4, 34.2; HRMS (ESI^+) calculated for [$C_{15}H_{13}OClNa^+$] requires *m/z* 267.0548, found *m/z* 267.0542.

To a solution of 410 mg aryl aldehyde (1.68 mmol) and 263 mg benzenesulfonamide (1.68 mmol) in CH_2Cl_2 was added 1.04 mL $Ti(OEt)_4$ (5.03 mmol) dropwise. The reaction was allowed to stir under N_2 overnight. The reaction mixture was filtered through a plug of silica gel, rinsing with several portions of EtOAc. The filtrate was concentrated to afford the *N*-benzenesulfonimine, which was dissolved in 40 mL toluene and added to a solution of 1.94 g K_2CO_3 (14.1 mmol) in 20 mL water. The biphasic mixture was subjected to vigorous mechanical stirring, and a solution of oxone 1.65 g (2.68 mmol) in 20 mL water was added slowly. After 30 min, equivalent portions of aqueous K_2CO_3 and oxone were added, and after an additional 30 min, the reaction was poured into a separatory funnel. The phases were separated, the aqueous layer was washed twice with Et_2O, and the combined organic extracts were washed with brine, dried over $MgSO_4$, and concentrated by rotary evaporation. ^{1}H NMR analysis of the residue showed incomplete oxidation of the imine, and the reaction mixture was twice resubjected to oxidation. Purification by chromatography on SiO_2 (10:1 hexanes:EtOAc) afforded 500 mg (1.25 mmol, 74% yield) of oxaziridine as a white solid (m.p. 118–120 °C). IR (ATR) 1490, 1451, 1343, 1250, 1164, 1090, 828, 745, 701; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.06–8.03 (m, 2H), 7.78–7.75 (m, 1H), 7.65–7.62 (m, 2H), 7.31–7.21 (m, 6H), 7.17–7.15 (m, 2H), 7.10 (d, J = 8.2 Hz, 1H), 3.15–2.95 (m, 3H), 2.92–2.85 (m, 1H); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 140.5, 140.4, 135.4, 134.8, 132.9, 131.6, 131.0, 130.5, 129.7, 129.6 128.8(1), 128.7(6), 127.2, 126.6, 73.6, 38.1, 34.3; HRMS (ESI^+) calculated for [$C_{21}H_{18}O_3SClNNH_4^+$] requires *m/z* 417.1035, found *m/z* 417.1032.

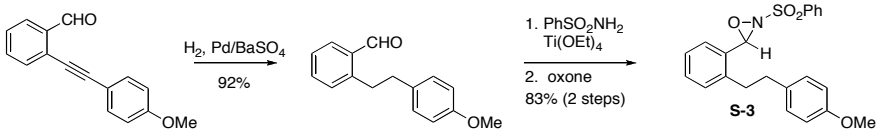


Table 1, entry 4 (**S-3**).

2-(4-Methoxyphenylethynyl)benzaldehyde was prepared as previously described.[5]

A solution of 670 mg (2.84 mmol) of the alkyne in 50 mL THF was treated with 200 mg $Pd/BaSO_4$ (5% Pd). The reaction vessel was sealed, evacuated, and purged twice with an atmosphere of H_2. The mixture was allowed to stir under a balloon of H_2 gas. The reaction was then filtered through a pad of Celite® and concentrated by rotary evaporation. Purification by chromatography on SiO_2 (9:1 hexanes/EtOAc) afforded 629 mg (2.62 mmol, 92% yield) of the alkane as a clear oil. IR (neat) 1696, 1611, 1512, 1245, 1178, 1035, 822, 757; ^{1}H NMR (500 MHz, $CDCl_3$) δ 10.20 (s, 1H), 7.82 (dd, J = 7.7, 1.3 Hz, 1H), 7.48 (td, J = 7.4, 1.5 Hz, 1H), 7.38 (td, J = 7.5, 1.1 Hz, 1H), 7.21 (d, J = 7.3 Hz, 1H), 7.11–7.08 (m, 2H), 6.83–6.80 (m, 2H), 3.78 (s, 3H), 3.30–3.27 (m, 2H), 2.86–2.83 (m, 2H); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 192.5, 158.2, 144.6, 134.0, 133.9, 133.5, 132.5, 131.5, 129.7, 126.9, 114.0, 55.5, 37.6, 35.3; HRMS (ESI^+) calculated for $[C_{16}H_{16}O_2Na^+]$ requires *m/z* 263.1043, found *m/z* 263.1041.

To a solution of 290 mg aryl aldehyde (1.21 mmol) and 190 mg benzenesulfonamide (1.21 mmol) in 20 mL CH_2Cl_2 was added 0.751 mL $Ti(OEt)_4$ (4.62 mmol) dropwise. The reaction was allowed to stir under N_2 overnight. The mixture was filtered through a plug of silica gel, rinsing with several portions of EtOAc. The filtrate was concentrated to afford the *N*-benzenesulfonimine, which was dissolved in 40 mL toluene and added to a solution of 1.40 g K_2CO_3 (10.2 mmol) in 15 mL water. The biphasic mixture was subjected to vigorous mechanical stirring, and a solution of 1.20 g Oxone® (1.94 mmol) in 15 mL water was added slowly. After 30 min, equivalent portions of aqueous K_2CO_3 and Oxone® were added, and after an additional 30 min, the reaction was poured into a separatory funnel. The phases were separated, the aqueous layer was washed twice with Et_2O, and the combined organic extracts were washed with brine, dried over $MgSO_4$, and concentrated by rotary evaporation. ^{1}H NMR analysis of the residue showed incomplete oxidation of the imine, and the reaction mixture was twice resubjected to oxidation. Purification by chromatography on SiO_2 (9:1 hexanes:EtOAc) afforded 395 mg (1.00 mmol, 83% yield) of oxaziridine as a white solid (m.p. 86–87 °C). IR (thin film) 1611, 1513, 1449, 1352, 1247, 1175, 1088, 1036, 824, 730, 685; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.05–8.03 (m, 2H), 7.73 (tt, J = 7.6, 1.2 Hz, 1H), 7.62–7.58 (m, 2H), 7.33 (td, J = 7.5, 1.5 Hz, 1H), 7.26 (dd, J = 7.8, 1.4 Hz, 1H), 7.24–7.17 (m, 2H), 7.11–7.08 (m, 2H), 6.85–6.82 (m, 2H), 5.61 (s, 1H), 3.79 (s, 3H), 3.12–3.01 (m, 2H), 2.95–2.82 (m, 2H); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 158.3, 142.1, 135.2, 134.8, 133.0, 130.9, 130.2, 129.6(4), 129.5(7), 129.5, 128.6, 127.1, 126.8, 114.1, 74.5, 55.4, 37.4, 35.1; HRMS (ESI^+) calculated for $[C_{22}H_{21}SO_4NH^+]$ requires *m/z* 396.1265, found *m/z* 396.1277.

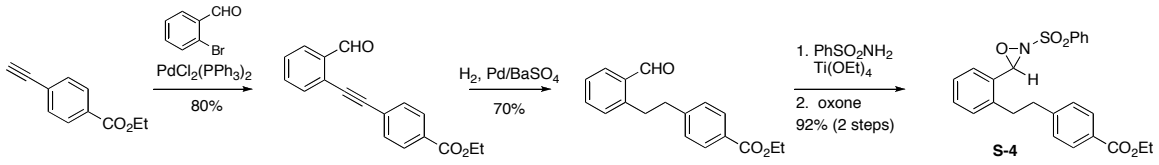


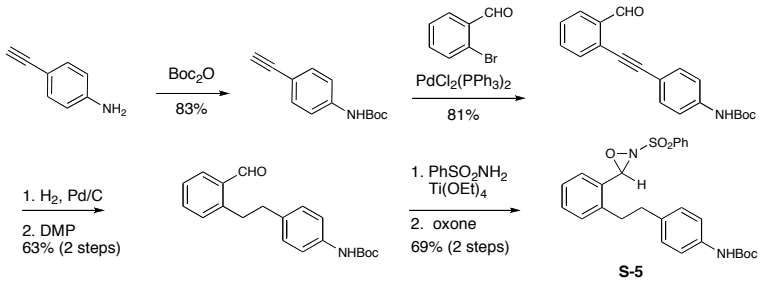
Table 1, entry 5 (**S-4**)

A dry 50–mL flask was charged with 706 mg ethyl 4-ethynylbenzoate (4.05 mmol), 600 mg 2-bromobenzaldehyde (3.24 mmol), 91 mg $PdCl_2(PPh_3)_2$ (0.310 mmol), and 15 mL Et_3N. The reaction was allowed to stir under N_2 for five minutes, at which time 12.4 mg CuI was added (0.065 mmol), and the reaction was brought to 50 °C and stirred for 3 hours. Upon completion, the reaction was filtered through a plug of silica gel, washed with EtOAc, and concentrated. Purification by chromatography on SiO_2 (20:1 to 10:1 hexanes:EtOAc) afforded 720 mg (2.59 mmol, 80% yield) of the alkyne as a yellow solid (m.p. 95–97 °C). IR (ATR) 1708, 1592, 1475, 1407, 1282, 1192, 1107, 1024, 859, 769, 694; ^{1}H NMR (500 MHz, $CDCl_3$) δ 10.64 (d, J = 1.0 Hz, 1H), 8.06 (dt, J = 8.6, 1.7 Hz, 2H), 7.97 (dd, J = 7.8, 1.0 Hz, 1H), 7.67 (dd, J = 7.7, 1.0 Hz, 1H), 7.64–7.62 (m, 2H), 7.60 (dd, J = 7.7, 1.3 Hz, 1H), 7.50 (t, J = 7.6 Hz, 1H), 4.40 (q, J = 7.1 Hz, 2H), 1.42 (t, J = 7.1 Hz, 3H); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 191.6,

166.1, 136.2, 134.0, 133.6, 131.8, 130.8, 129.8, 129.3, 127.7, 127.0, 126.3, 95.5, 87.8, 61.5, 14.5; HRMS (ESI^+) calculated for $[C_{18}H_{14}O_3Na^+]$ requires *m/z* 301.0836, found *m/z* 301.0825. (Procedure from Dai, G.; Larock, R. C. *Org. Lett.* **2001**, *3*, 4035.)

A solution of 580 mg (2.08 mmol) of the alkyne in 50 mL EtOAc was treated with 60 mg Pd/C (5% Pd). The reaction vessel was sealed, evacuated, and purged twice with an atmosphere of H_2 gas. The mixture was allowed to stir under a balloon of H_2 gas for 13h. After 5h, an additional 20 mg Pd/C was added. The reaction was then filtered through a pad of Celite® and concentrated by rotary evaporation. Purification by chromatography on SiO_2 (20:1 to 10:1 hexanes:EtOAc) afforded 410 mg (1.45 mmol, 70% yield) of the alkane as a clear oil. IR (neat) 1715, 1600, 1367, 1277, 1178, 1106, 1022, 766, 665; ^{1}H NMR (500 MHz, $CDCl_3$) δ 10.20 (s, 1H), 7.96–7.94 (m, 2H), 7.82 (dd, J = 7.6, 1.5 Hz, 1H), 7.48 (td, J = 7.5, 1.5 Hz, 1H), 7.41 (td, J = 7.5, 1.2 Hz, 1H), 7.25 (d, J = 7.6 Hz, 2H), 7.18 (d, J = 7.3 Hz, 1H), 4.37 (q, J = 7.1 Hz, 2H), 3.37–3.32 (m, 2H), 2.97–2.94 (m, 2H), 1.39 (t, J = 7.2 Hz, 3H); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 192.9, 166.9, 146.8, 143.9, 134.0(1), 133.9(5), 133.7, 131.5, 129.9, 128.8, 128.7, 127.1, 61.0, 38.2, 35.0, 14.6; HRMS (ESI^+) calculated for $[C_{18}H_{18}O_3Na^+]$ requires *m/z* 305.1154, found *m/z* 305.1154.

To a solution of 400 mg aryl aldehyde (1.42 mmol) and 234 mg benzenesulfonamide (1.49 mmol) in 20 mL CH_2Cl_2 was added 0.88 mL $Ti(OEt)_4$ (4.25 mmol) dropwise. The reaction was allowed to stir under N_2 overnight. The mixture was filtered through a plug of silica gel, rinsing with several portions of EtOAc. The filtrate was concentrated to afford the *N*-benzenesulfonimine, which was dissolved in 20 mL toluene and added to a solution of 1.64 g K_2CO_3 (11.9 mmol) in water. The biphasic mixture was subjected to vigorous stirring, and a solution of 1.40 g Oxone® (2.27 mmol) in 20 mL water was added slowly. After 30 min, equivalent portions of aqueous K_2CO_3 and Oxone® were added, and after an additional 30 min, the reaction was poured into a separatory funnel. The phases were separated, the aqueous layer was washed twice with Et_2O, and the combined organic extracts were washed with brine, dried over $MgSO_4$, and concentrated by rotary evaporation. Purified by chromatography on SiO_2 (7:1 hexanes:EtOAc) to afford 570 mg (1.30 mmol, 92% yield) of the oxaziridine as a waxy white semi-solid. IR (neat) 1715, 1611, 1449, 1352, 1278, 1175, 1104, 1022, 732; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.05–8.03 (m, 2H), 7.97 (m, 2H), 7.76–7.73 (m, 1H), 7.63–7.60 (m, 2H), 7.33 (td, J = 7.5, 1.5 Hz, 1H), 7.28 (dd, J = 7.8, 1.4 Hz, 1H), 7.25–7.21 (m, 3H), 7.14 (d, J = 7.6 Hz, 1H), 5.65 (s, 1H), 4.37 (q, J = 7.2 Hz, 2H), 3.18–2.93 (m, 4H), 1.39 (t, J = 7.2 Hz, 3H); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 166.8, 146.2, 141.1, 135.3, 134.8, 130.1, 130.2, 130.0, 129.6(1), 129.5(5), 128.8(0), 128.7(5), 128.5, 127.4, 127.1, 74.5, 61.0, 38.1, 34.4, 14.5; HRMS (ESI^+) calculated for $[C_{24}H_{23}NO_5SH^+]$ requires *m/z* 438.1370, found *m/z* 438.1353.



S-5

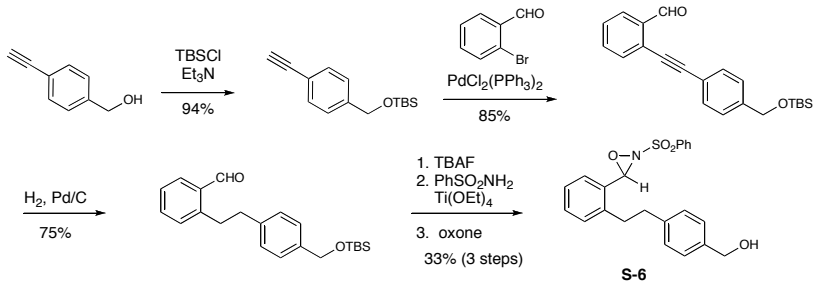
Table 1, entry 6 **(S-5)**

To a solution of 502 mg (4.29 mmol) ethynyl aniline in 5 mL of THF added 930 mg (4.26 mmol) di-*tert*-butyl carbonate and refluxed for 6h. After removal of the solvent, the crude mixture was purified via chromatography on SiO_2 (15:1 hexanes:EtOAc) affording 774 mg (3.57 mmol, 83% yield) of the alkyne as white solid. Spectral properties of the product were identical were found to be identical to those previously reported.[6]

A dry 50–mL flask was charged with 770 mg *N*-Boc 4-ethynylaniline (3.55 mmol), 518 mg 2-bromobenzaldehyde (2.80 mmol), 80 mg $PdCl_2(PPh_3)_2$ (0.114 mmol), and 11 mL Et_3N. The reaction was allowed to stir under N_2 for five minutes, at which time 10.0 mg CuI was added (0.053 mmol), and the reaction was brought to 50 °C and stirred for 2 hours. Upon completion, the reaction was filtered through a plug of silica gel, washed with EtOAc, and concentrated. Purification by chromatography on SiO_2 (20:1 to 10:1 hexanes:EtOAc) afforded 720 mg (2.24 mmol, 81% yield) of the alkyne as a yellow solid (m.p. 118-120 °C). IR (neat) 3331, 2978, 2212, 1729, 1697, 1590, 1523; ^{1}H NMR (500 MHz, $CDCl_3$) δ 10.65 (s, 1H), 7.95 (d, J = 7.7 Hz, 1H), 7.63 (d, J = 7.6 Hz, 1H), 7.58 (t, J = 7.5 Hz, 1H), 7.51 (d, J = 8.7 Hz, 2H), 7.46-7.41 (m, 3H), 6.67 (br s, 1H), 1.53 (s, 9H); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 192.1, 152.6, 139.5, 135.9, 134.0, 133.3, 132.8, 128.9 127.5, 127.4, 118.3, 116.7, 96.7, 84.4, 81.2, 28.5; HRMS (ESI^+) calculated for $[C_{20}H_{19}NO_3Na^+]$ requires *m/z* 344.1258, found *m/z* 344.1251.

A solution of 379 mg (1.18 mmol) of the alkyne in 20 mL MeOH was treated with 100 mg Pd/C (10% Pd). The reaction vessel was sealed, evacuated, and purged three times with an atmosphere of H_2 gas. The mixture was allowed to stir under a pressure of 15 psi for 13h. After 5h, an additional 29 mg Pd/C was added. The reaction was then filtered through a pad of Celite® and concentrated by rotary evaporation. The crude mixture was dissolved in 9 ml CH_2Cl_2 and added dropwise to a solution of Dess-Martin periodinane (DMP, 424 mg, 1.00 mmol) at room temperature. After the addition of 200 mg (0.472 mmol) of DMP, the reaction was stopped by the addition of saturated $NaHCO_3$ solution. The aqueous phase was extracted twice with CH_2Cl_2, the combined organic extracts were dried with Na_2SO_4 and concentrated by rotary evaporation. Purification by chromatography on SiO_2 (10:1 to 5:1 hexanes:EtOAc) afforded 272 mg (0.747 mmol, 63% yield) of the alkane as yellow solids (m.p. 109-110°C). IR (neat) 3332, 2975, 2926, 1724, 1696, 1597, 1525; ^{1}H NMR (500 MHz, $CDCl_3$) δ 10.21 (s, 1H), 7.84 (dd, J = 7.6, 1.5 Hz, 1H), 7.50 (td, J = 7.4, 1.6 Hz, 1H), 7.38 (td, J = 7.5, 1.6 Hz, 1H), 7.28-7.27 (m, 2H), 7.22 (d, J = 7.9 Hz, 1H), 7.11 (d, J = 8.2 Hz, 2H), 6.40 (br s, 1H), 3.32-3.29 (m, 2H), 2.88-2.85 (m, 2H), 1.53 (s, 9H); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 192.6, 153.0, 144.5, 136.6, 136.1, 133.9(5), 134.0(1), 132.6, 131.5, 129.3, 126.9, 118.9, 37.8, 28.6; HRMS (ESI^+) calculated for [$C_{20}H_{23}NO_3Na^+$] requires *m/z* 348.1571, found *m/z* 348.1561.

To a solution of 353 mg aryl aldehyde (1.08 mmol) and 188 mg benzenesulfonamide (1.20 mmol) in 21 mL CH_2Cl_2 was added 0.70 mL $Ti(OEt)_4$ (2.7 mmol) dropwise. The reaction was allowed to stir under N_2 for 8h, after which additional 51 mg of benzenesulfonamide (0.32 mmol) was added followed by 0.11 mL $Ti(OEt)_4$ (0.42 mmol). The mixture was filtered through a plug of silica gel, rinsing with several portions of EtOAc. The filtrate was concentrated to afford the *N*-benzenesulfonimine, which was dissolved in 35 mL toluene and added to a solution of 1.3 g K_2CO_3 (9.4 mmol) in 15 mL water. The biphasic mixture was subjected to vigorous stirring, and a solution of 1.2 g Oxone® (1.95 mmol) in 15 mL water was added slowly. After 10 min, equivalent portions of aqueous K_2CO_3 and Oxone® were added, and after an additional 10 min, the reaction was poured into a separatory funnel. The phases were separated, the aqueous layer was washed twice with Et_2O, and the combined organic extracts were washed with brine, dried over $MgSO_4$, and concentrated by rotary evaporation. Purified by chromatography on SiO_2 (6:1 to 3:1 hexanes:EtOAc) to afford 362 mg (0.75 mmol, 69% yield) of the oxaziridine as a yellow solid (m.p. 111-114°C (dec)). IR (neat) 2979, 1722, 1596, 1523, 1448, 1392; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.04 (d, J = 7.4 Hz, 2H), 7.74 (t, J = 7.4 Hz, 1H), 7.62 (t, J = 7.8 Hz, 2H), 7.33 (t, J = 7.4 Hz, 1H), 7.28-7.26 (m, 3H), 7.23-7.20 (m, 1H), 7.16 (d, J = 7.6 Hz, 1H), 7.09 (d, J = 8.2 Hz, 2H), 6.42 (br s, 1H), 5.61 (s, 1H), 3.12-3.01 (m, 2H), 2.96-2.82 (m, 2H), 1.52 (s, 9H); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 153.0, 142.0, 136.8, 135.7, 135.3, 134.8, 131.0, 130.3, 129.6 129.3, 128.6, 127.2, 126.9, 119.0, 74.6, 37.6, 34.9, 28.6; HRMS (ESI^+) calculated for [$C_{26}H_{32}N_3O_5S^+$] [$M+NH_4^+$] requires *m/z* 498.2058, found *m/z* 498.2057.



S-6

Table 1, entry 7 **(S-6)**

To a solution of 1.32 g (10.0 mmol) ethynyl benzyl alcohol in 30 mL of THF added 4.5 mL (32.2 mmol) Et_3N and cooled to 0 °C. The solution was warmed to room temperature after the dropwise addition of 2.23 g (14.8 mmol) TBSCl in 10 mL THF. After 48 h, TLC indicated full conversion. The solids were removed via filtration and the solvent via rotary evaporation and the crude mixture was purified via chromatography on SiO_2 (20:1 hexanes:EtOAc) affording 2.32 g (9.41 mmol, 94% yield) of the alkyne as yellowish oil. IR (neat): 3300, 2955, 2932, 2889, 2858, 2108, 1506, 1472, 1463, 1255; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.46 (d, J = 8.1 Hz, 2H), 7.27 (d, J = 8.1 Hz, 2H), 4.73 (s, 2H), 3.04 (s, 1H), 0.94 (s, 9H), 0.09 (s, 6H); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 142.6, 132.3, 126.1, 120.7, 84.0, 76.9, 64.8, 26.1, 18.6, -5.1; HRMS (EI^+) calculated for [$C_{15}H_{21}OSi^+$] requires *m/z* 245.1357, found *m/z* 245.1355.

A dry 50–mL flask was charged with 2.15 g TBS-ethynyl benzyl alcohol (8.72 mmol), 1.08 g 2-bromobenzaldehyde (5.83 mmol), 164 mg $PdCl_2(PPh_3)_2$ (0.233 mmol), and 20 mL Et_3N. The reaction was allowed to stir under N_2 for five minutes, at which time 23.0 mg CuI was added (0.121 mmol), and the reaction was brought to reflux and stirred for one hour. Upon completion, the reaction was filtered through a plug of silica gel, washed

with EtOAc, and concentrated. Purification by chromatography on SiO_2 (20:1 hexanes:EtOAc) afforded 1.73 g (4.93 mmol, 85% yield) of the alkyne as a greyish solid (m.p. 37-38 °C). IR (neat): 2954, 2931, 2888, 2856, 2215, 1697, 1594, 1510, 1472, 1288; ^{1}H NMR (500 MHz, $CDCl_3$) δ 10.66 (s, 1H), 7.95 (d, J = 7.7 Hz, 1H), 7.64 (d, J = 7.7 Hz, 1H), 7.58 (t, J = 7.7 Hz, 1H), 7.53 (d, J = 8.2 Hz, 2H), 7.44 (t, J = 7.7 Hz, 1H), 7.24 (d, J = 8.2 Hz, 2H), 4.77 (s, 2H), 0.95 (s, 9H), 0.12 (s, 6H); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 192.0, 143.0, 136.0, 134.0, 133.4, 131.8, 128.7, 127.4, 127.3, 126.3, 120.9, 96.8, 84.7, 64.8, 26.1, 18.6, -5.1; HRMS (ESI$^+$) calculated for [$C_{22}H_{26}O_2SiNa^+$] requires *m/z* 373.1595, found *m/z* 373.1600.

A solution of 897 mg (2.56 mmol) of the alkyne in 50 mL MeOH was treated with 285 mg Pd/C (10% Pd). The reaction vessel was sealed, evacuated, and purged three times with an atmosphere of H_2 gas. The mixture was allowed to stir under a pressure of 15 psi for 2h. The reaction was then filtered through a pad of Celite® and concentrated by rotary evaporation. Purification by chromatography on SiO_2 (20:1 hexanes:EtOAc) afforded 701 mg (1.98 mmol, 77% yield) of the alkane as a clear liquid. IR (neat) 2954, 2930, 2856, 1606, 1589, 1565, 1323; ^{1}H NMR (500 MHz, $CDCl_3$) δ 10.22 (s, 1H), 7.82 (dd, J = 7.6, 1.1 Hz, 1H), 7.48 (td, J = 7.5, 1.4 Hz, 2H), 7.38 (td, J = 7.5, 1.4 Hz, 2H), 7.25-7.21 (m, 3H), 7.16 (d, J = 8.2 Hz, 2H), 4.72 (s, 2H), 3.33-3.30 (m, 2H), 2.90-2.87 (m, 2H), 0.94 (s, 9H), 0.09 (s, 6H); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 192.6, 144.6, 140.0, 139.5, 134.0, 133.9, 132.6, 131.5, 128.6, 126.9, 126.4, 65.1, 38.2, 35.2, 26.2, 18.6, -5.0; HRMS (ESI$^+$) calculated for [$C_{22}H_{34}NO_2Si^+$] [M+NH_4^+] requires *m/z* 372.2354, found *m/z* 372.2354.

To a solution of 660 mg aryl aldehyde (1.86 mmol) was added 2.4 mL TBAF (1M in THF) dropwise. The reaction was allowed to stir under N_2 for 10 min, after which the solution was concentrated and passed through a plug of silica using 1:1 hexane:EtOAc as an eluent. 301 mg of this reaction mixture was dissolved in 18 mL CH_2Cl_2 along with 148 mg benzenesulfonamide (0.943 mmoles). 0.750 mL $Ti(OEt)_4$ (2.5 mmol) was added dropwise and the reaction was allowed to stir under N_2 overnight. The mixture was filtered through a short plug of silica gel, rinsing with several portions of ethyl acetate. The filtrate was concentrated to afford the *N*-benzenesulfonimine, which was dissolved in 30 mL toluene and added to a solution of 1.6 g K_2CO_3 (11.6 mmol) in 10 mL water. The biphasic mixture was subjected to vigorous stirring, and a solution of 1.3 g Oxone® (2.11 mmol) in 13 mL water was added slowly. After 10 min, an additional portion of aqueous Oxone® was added, followed by additional 10 min stirring. The reaction mixture was poured into a separatory funnel, the phases were separated, the aqueous layer was washed twice with Et_2O, and the combined organic extracts were washed with brine, dried over Na_2SO_4, and concentrated by rotary evaporation. Purified by chromatography on SiO_2 (2:1 to 1:1 hexanes:EtOAc) to afford 123.9 mg (0.313 mmol, 33% yield) of the oxaziridine as a colorless liquid. IR (neat): 3584, 3062, 2921, 1692, 1601, 1583, 1449, 1350, 1247; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.03 (dd, J = 8.6, 1.0 Hz, 2H), 7.75 (t, J = 7.5 Hz, 1H), 7.62 (t, J = 7.5 Hz, 2H), 7.36 (td, J = 7.5, 1.0 Hz, 1H), 7.30 (d, J = 8.0 Hz, 2H), 7.25 (m, 1H), 7.22 (t, J = 7.4 Hz, 2H), 7.14 (d, J = 8.0 Hz, 2H), 5.47 (s, 1H), 4.67 (s, 2H), 3.10 (m, 2H), 2.97 (m, 2H), 1.73 (br s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 142.0, 140.4, 139.2, 135.3, 134.9, 131.1, 130.3, 129.6, 129.6, 129.0, 128.7, 127.7, 127.3, 127.0, 74.4, 65.5, 38.1, 34.8; HRMS (ESI$^+$) calculated for [$C_{22}H_{21}NO_4SNa^+$] requires *m/z* 418.1084, found *m/z* 418.1080.

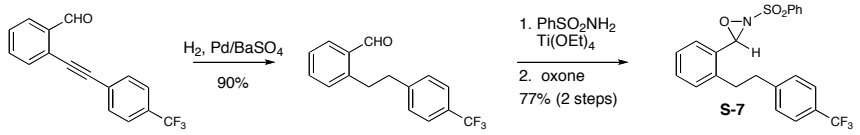


Table 1, entry 8 **(S-7)**

2-(4-(Trifluoromethyl)phenylethynyl)benzaldehyde was prepared as previously described.[5]

A solution of 710 mg (2.59 mmol) of the alkyne in 13 mL THF was treated with 120 mg Pd/$BaSO_4$ (5% Pd). The reaction vessel was sealed, evacuated, and purged twice with an atmosphere of H_2. The mixture was allowed to stir under a balloon of H_2 gas. Three recycles were required, in which 80 mg, 160 mg, and 100 mg of additional Pd/$BaSO_4$ were added. The reaction was then filtered through a pad of Celite® and concentrated by rotary evaporation. Purification by chromatography on SiO_2 (20:1 to 10:1 hexanes/EtOAc) afforded 651 mg (2.34 mmol, 90% yield) of the alkane as a clear oil. IR (neat) 1696, 1601, 1326, 1163, 1116, 1067, 825, 756, 666; ^{1}H NMR (500 MHz, $CDCl_3$) δ 10.19 (s, 1H), 7.83 (dd, J = 7.5, 1.4 Hz, 1H), 7.53 (d, J = 7.9 Hz, 2H), 7.50 (td, J = 7.5, 1.5 Hz, 1H), 7.43 (td, J = 7.5, 1.0 Hz, 1H), 7.33 (d, J = 7.9 Hz, 1H), 7.20 (d, J = 7.3 Hz, 1H), 3.35–3.32 (m, 2H), 2.96–2.93 (m, 2H); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 193.0, 145.7, 143.7, 134.1, 133.9(8), 133.9(7), 129.1 (2C), 128.6 (q, J = 32 Hz), 127.2, 125.5 (q, J = 4 Hz), 124.6 (q, J = 272 Hz), 37.9, 35.2; HRMS (ESI$^+$) calculated for [$C_{16}H_{13}OF_3Na^+$] requires *m/z* 301.0811, found *m/z* 301.0823.

To a solution of 645 mg (2.32 mmol) aryl aldehyde and 364 mg benzenesulfonamide (2.32) in 40 mL CH_2Cl_2 was added 1.44 mL $Ti(OEt)_4$ (6.95 mmol) dropwise. The reaction was allowed to stir under N_2 overnight. The mixture was filtered through a plug of silica gel, rinsing with several portions of ethyl acetate. The filtrate was concentrated to afford the *N*-benzenesulfonimine, which was dissolved in 75 mL toluene and added to a solution of 2.69 g K_2CO_3 (19.5 mmol) in 40 mL water. The biphasic mixture was subjected to vigorous stirring, and a solution of 2.29 g Oxone® (3.71 mmol) was added slowly. After 30 min, equivalent portions of aqueous K_2CO_3 and Oxone® were added, and after an additional 30 min, the reaction was poured into a separatory funnel. The phases were separated, the aqueous layer was washed twice with Et_2O, and the combined organic extracts were washed with brine, dried over $MgSO_4$, and concentrated by rotary evaporation. ^{1}H NMR analysis of the residue showed incomplete oxidation of the imine, and the reaction mixture was twice resubjected to oxidation. Purification by chromatography on SiO_2 (9:1 hexanes:EtOAc) afforded 770 mg (1.78 mmol, 77% yield) of the oxaziridine as a clear oil. IR (neat) 1618, 1450, 1326, 1169, 1088, 826, 733, 666; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.04–8.02 (m, 2H), 7.75–7.71 (m, 1H), 7.62–7.58 (m, 2H), 7.53 (d, J = 7.9 Hz, 2H), 7.33 (td, J = 7.3, 1.5 Hz, 1H), 7.28 (d, J = 9.5 Hz, 3H), 7.22 (t, J = 7.5 Hz, 1H), 7.16 (d, J = 7.6 Hz, 1H), 5.65 (s, 1H), 3.18–3.02 (m, 3H), 2.98–2.91 (m, 1H); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 145.0, 141.3, 135.3, 134.7, 131.1, 130.2, 129.6, 129.5, 129.1(5), 129.0(9), 128.8 (q, J = 33 Hz), 128.5, 127.4, 127.1, 125.6 (q, J = 3 Hz), 124.5 (q, J = 272 Hz), 38.0, 34.4; HRMS (EI) calculated for $[C_{22}H_{18}F_3NO_3S^+]$ requires *m/z* 433.0955, found *m/z* 433.0948.

S-8

Table 1, entry 9 **(S-8)**

2-(Phenylmethyl)benzaldehyde was prepared as previously described.[7]

To a solution of 300 mg (1.56 mmol) aryl aldehyde and 246 mg benzenesulfonamide (1.56 mmol) in 15 mL CH_2Cl_2 was added 0.960 mL $Ti(OEt)_4$ (4.56 mmol) dropwise. The reaction was allowed to stir under N_2 overnight or until reaction went to completion (as per NMR aliquot). The mixture was filtered through a short plug of silica gel, rinsing with several portions of ethyl acetate. The filtrate was concentrated to afford the *N*-benzenesulfonimine, which was dissolved in 30 mL toluene and added to a solution of 1.78 g K_2CO_3 (12.9 mmol) in 15 mL water. The biphasic mixture was subjected to vigorous stirring, and a solution of 1.51 g Oxone® (2.40 mmol) was added slowly. After 30 min, equivalent portions of aqueous K_2CO_3 and Oxone® were added, and after an additional 30 min, the reaction was poured into a separatory funnel. The phases were separated, the aqueous layer was washed twice with Et_2O, and the combined organic extracts were washed with brine, dried over $MgSO_4$, and concentrated by rotary evaporation. Purification by chromatography on SiO_2 (7:1 hexanes/EtOAc) afforded 520 mg (1.48 mmol, 95% yield) of the oxaziridine as a white solid (m.p. 93–94 °C). IR (ATR) 1584, 1495, 1451, 1348, 1246, 1163, 1090, 837, 768, 728, 685; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.95–7.93 (m, 2H), 7.73–7.69 (m, 1H), 7.58–7.55 (m, 2H), 7.38 (td, J = 7.5, 1.5 Hz, 1H), 7.33–7.30 (m, 3H), 7.27–7.21 (m, 3H), 7.14 (d, J = 7.0 Hz, 2H), 5.58 (s, 1H), 4.19 (ABq, $\Delta\nu_{AB}$ = 13 Hz, J_{AB} = 15.9 Hz, 2H); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 140.8, 139.5, 135.2, 134.3, 131.1, 130.9, 129.6, 129.5, 129.2, 129.0, 128.9, 127.4, 127.3, 126.8, 74.5, 38.4; HRMS (ESI^+) calculated for $[C_{20}H_{17}O_3NSNH_4^+]$ requires *m/z* 369.1268, found *m/z* 369.1265.

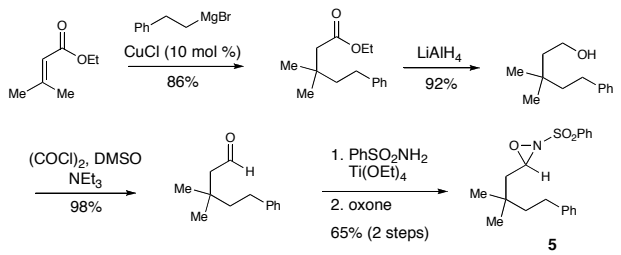


Table 2, entry 1 (**5**)

To a solution of 1.00 g ethyl 3,3-dimethylacrylate (7.80 mmol) in 13 mL THF was added 1.18 mL TMSCl (9.36 mmol) and 77 mg CuCl (0.78 mmol). The reaction was brought to –15 °C in a MeOH/H_2O(s) bath. Phenylethylmagnesium bromide (7 mL of 1.56M in Et_2O, 10.9 mmol) was added via syringe pump over 1h. The reaction was allowed to stir an additional 90 min, at which time saturated aqueous NH_4Cl was added, followed by 1N HCl. The reaction was allowed to stir for 5 min and was subsequently poured into a separatory funnel and diluted with water and Et_2O. The phases were separated, and the aqueous phase was extracted twice with Et_2O. The combined organic extracts were washed with brine, dried over $MgSO_4$, and concentrated by rotary evaporation. Purification by chromatography on SiO_2 (20:1 to 10:1 hexanes:EtOAc) afforded 1.57 g (6.70 mmol, 86% yield) of the ester as a clear oil. IR (neat) 1731, 1604, 1454, 1230, 1117, 1038, 699; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.28–7.24 (m, 2H), 7.19–7.15 (m, 3H), 4.13 (q, J = 7.2 Hz, 2H), 2.62–2.58 (m, 2H), 2.27 (s, 2H), 1.64–1.61 (m, 2H), 1.26 (t, J = 7.2 Hz, 3H), 1.08 (s, 6H); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 172.2, 142.9, 128.3, 125.6, 59.9, 45.8, 44.4, 33.4, 30.7, 27.4, 14.3; HRMS (ESI$^+$) calculated for [$C_{15}H_{22}O_2Na^+$] requires *m/z* 257.1512, found *m/z* 257.1517.

To a stirring suspension of 293 mg $LiAlH_4$ (7.71 mmol) in 20 mL Et_2O at 0 °C was added a solution of 1.39 g (5.93 mmol) of the ester in 5 mL Et_2O dropwise. The reaction was stirred for approximately 5 min before being brought to reflux for 1h. The mixture was cooled to 0 °C, and water (mL equivalent to g $LiAlH_4$) was carefully added dropwise, followed by 6M NaOH (mL equivalent to g $LiAlH_4$), additional water, and $MgSO_4$ sufficient to sequester excess water. The slurry was stirred 30–60 min and filtered through Celite®. The cake was washed with Et_2O and the filtrate was washed with brine, dried over $MgSO_4$, filtered and concentrated. Purification by chromatography on SiO_2 (4:1 hexanes:EtOAc) afforded 1.05 g (5.46 mmol, 92% yield) of the alcohol as a clear liquid. IR (neat) 3331 (br), 1736, 1654, 1497, 1366, 1031, 740, 698; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.28–7.24 (m, 2H), 7.18–7.15 (m, 3H), 3.71 (t, J = 7.6 Hz, 2H), 2.59–2.55 (m, 2H), 1.61–1.58 (m, 2H), 1.53–1.50 (m, 2H), 1.33 (s, 1H), 0.98 (s, 6H); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 143.3, 128.5(4), 128.4(9), 125.8, 60.0, 45.0, 44.5, 32.6, 30.9, 27.6; HRMS (ESI$^+$) calculated for [$C_{13}H_{20}ONa^+$] requires *m/z* 215.1407, found *m/z* 215.1411.

Oxalyl chloride (0.77 mL, 8.77 mmol) was dissolved in 25 mL CH_2Cl_2 and brought to –78 °C. A solution of 1.00 mL DMSO (14.3 mmol) in CH_2Cl_2 (3 mL) was added dropwise, and the reaction was allowed to stir for 5 min. A solution of 1.25 g (6.50 mmol) of the alcohol in CH_2Cl_2 (3 mL) was added over 20 min via syringe pump, and the reaction was allowed to stir an additional 40 min. Over 45 min, 4.53 mL Et_3N (32.5 mmol) was added via syringe pump. After 5 min, the reaction was allowed to warm to room temperature. The reaction mixture was transferred to a separatory funnel and washed with 1N HCl. The phases were separated, and the aqueous phase was extracted with several portions of CH_2Cl_2. The combined organic extracts were washed with saturated $NaHCO_3$ and brine, dried over $MgSO_4$, and concentrated by rotary evaporation. Purification by chromatography on SiO_2 (10:1 to 8:1 hexanes:EtOAc) afforded 1.21 g (6.36 mmol, 98% yield) of the aldehyde as a clear liquid. IR (neat) 1720, 1604, 1497, 1455, 1369, 1261, 1076, 1031, 745, 699; ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.87 (t, J = 3.1 Hz, 1H), 7.29–7.24 (m, 2H), 7.19–7.16 (m, 3H), 2.61–2.58 (m, 2H), 2.34 (d, J = 3.2 Hz, 2H), 1.66–1.63 (m, 2H), 1.13 (s, 6H); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 177.8, 142.6, 128.6, 128.5(5), 128.4(8), 126.0, 125.9, 54.9, 45.7, 45.1, 44.5, 33.9, 33.6, 30.9, 30.8, 27.7, 27.5; HRMS (ESI$^+$) calculated for [$C_{13}H_{18}ONa^+$] requires *m/z* 213.1250, found *m/z* 213.1245.

A solution of 870 mg aliphatic aldehyde (4.57 mmol), 719 mg benzenesulfonamide (4.57 mmol), and 815 mg sodium *p*-toluenesulfinate (4.57 mmol) in 5 mL formic acid and 9 mL water was allowed to stir for several days. Upon completion, the precipitate was filtered, washed with several portions of water and extracted with hexanes. The precipitate was redissolved in CH_2Cl_2 and was added to a saturated solution of K_2CO_3, and the mixture was allowed to stir for 2h. The phases were separated, and the aqueous phase was extracted with several portions of CH_2Cl_2. The combined organic extracts were washed with brine, dried over Na_2SO_4, and concentrated by rotary evaporation. The residue was dissolved in 120 mL toluene and added to a solution of 5.31 g K_2CO_3 (38.4 mmol) in 75 mL water. The biphasic mixture was subjected to vigorous stirring, and a solution of 4.50 g Oxone® (7.63 mmol) was added slowly. After 30 min, equivalent portions of aqueous K_2CO_3 and Oxone® were added, and after

an additional 30 min, the reaction was poured into a separatory funnel. The phases were separated, the aqueous layer was extracted twice with Et_2O. The combined organic extracts were washed with brine, dried over $MgSO_4$, and concentrated by rotary evaporation. Purification by chromatography on SiO_2 (10:1 to 8:1 hexanes:EtOAc) afforded 1.03 g (2.98 mmol, 65% yield) of the oxaziridine as a white solid (m.p. 64–65 °C). IR (ATR) 1739, 1583, 1347, 1227, 1171, 837, 793, 724, 681; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.99–7.97 (m, 2H), 7.70–7.67 (m, 1H), 7.58–7.55 (m, 2H), 7.29–7.26 (m, 2H), 7.18–7.16 (m, 3H), 4.76 (t, J = 5.5 Hz, 1H), 2.62–2.51 (m, 2H), 1.73 (qd, J = 14.6, 5.3 Hz, 2H), 1.63–1.58 (m, 2H), 1.09 (d, J = 3.1 Hz, 6H); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 142.6, 135.0(4), 135.0(1), 129.5, 129.3, 128.6, 128.5, 126.0, 76.5, 44.9, 42.6, 33.0, 30.7, 27.4; HRMS (ESI$^+$) calculated for [$C_{18}H_{23}O_3NSNa^+$] requires *m/z* 368.1291, found *m/z* 368.1282.

Table 1, entry 2 **(S-9)**

A solution of 1.00 g 5-phenylpentanal (6.16 mmol), 0.98 g benzenesulfonamide (6.22 mmol), and 1.10 g sodium *p*-toluenesulfinate (6.16 mmol) in 10 mL formic acid and 10 mL water was allowed to stir for several days. Upon completion, the precipitate was filtered, washed with several portions of water and extracted with hexanes. The precipitate was redissolved in CH_2Cl_2 and was added to a saturated solution of K_2CO_3, and the mixture was allowed to stir for 2h. The phases were separated, and the aqueous phase was extracted with several portions of CH_2Cl_2. The combined organic extracts were washed with brine, dried over Na_2SO_4, and concentrated by rotary evaporation. The residue was dissolved in 120 mL toluene and added to a solution of 8.88 g K_2CO_3 (64.2 mmol) in 75 mL water. The biphasic mixture was subjected to vigorous stirring, and a solution of 4.70 g Oxone® (7.63 mmol) was added slowly. After 30 min, equivalent portions of aqueous K_2CO_3 and Oxone® were added, and after an additional 30 min, the reaction was poured into a separatory funnel. The phases were separated, the aqueous layer was extracted twice with Et_2O. The combined organic extracts were washed with brine, dried over $MgSO_4$, and concentrated by rotary evaporation. Purified by chromatography using a solvent gradient (10:1 to 8:1 hexanes:EtOAc to afford 1.00 g (3.15 mmol, 51% yield) of the oxaziridine as a clear liquid. IR (neat) 1603, 1496, 1449, 1351, 1170, 1090, 848, 735, 691; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.99–7.97 (m, 2H), 7.73–7.70 (m, 1H), 7.61–7.57 (m, 2H), 7.29–7.25 (m, 2H), 7.20–7.15 (m, 3H), 4.68 (t, J = 4.9 Hz, 1H), 2.61 (t, J = 7.6 Hz, 2H), 1.85–1.81 (m, 2H), 1.71–1.65 (m, 2H), 1.55–1.48 (m, 2H); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 142.0, 135.1, 135.0, 129.5, 129.4, 128.6, 126.1, 78.3, 35.7, 31.0, 31.0, 30.8(0), 30.7(8), 23.3(2), 23.3(0); HRMS (ESI$^+$) calculated for [$C_{17}H_{19}NO_3SNH_4^+$] requires *m/z* 335.1424, found *m/z* 335.1420.

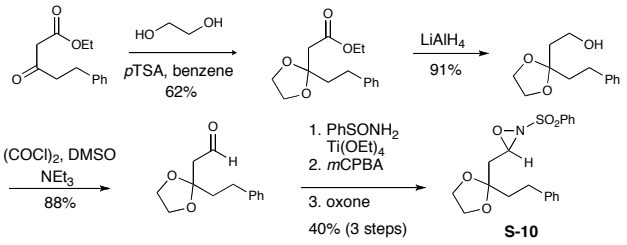


Table 2, entry 3 (**S-10**)

Ethyl 3-oxo-5-phenylpentanoate was prepared as previously described.[8]

The β-ketoester (1.01 g, 4.58 mmol), 845 mg ethylene glycol (13.8 mmol), and 9.0 mg *p*-toluenesulfonic acid monohydrate (0.0458 mmol) were dissolved in 30 mL benzene and allowed to reflux in a Dean-Stark apparatus under N_2 for 1.5 days. Additional ethylene glycol (500 mg) was added after 14 h. The reaction was cooled to room temperature and quenched with saturated, aqueous $NaHCO_3$. The mixture was transferred to a separatory funnel, the phases were separated and the aqueous phase was extracted with Et_2O (3 x 25 mL). The combined organic extracts were washed sequentially with water and brine, dried over $MgSO_4$, and concentrated by rotary evaporation. Purification by chromatography on SiO_2 (8:1 to 6:1 hexanes:EtOAc) afforded 750 mg (2.84 mmol, 62% yield) of the

ketal as a clear liquid. IR (neat) 2981, 1735, 1497, 1369, 1222, 1032, 750, 701, 666; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.29–7.26 (m, 2H), 7.21–7.16 (m, 2H), 4.16 (q, J = 7.1 Hz, 2H), 4.07–4.00 (m, 4H), 2.75–2.72 (m, 2H), 2.70 (s, 2H), 2.17–2.13 (m, 2H), 1.28 (t, J = 7.1 Hz, 3H); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 169.6, 142.0, 128.6, 126.0, 109.2, 65.4, 60.8, 43.0, 39.7, 29.9, 14.4; HRMS (ESI^+) calculated for [$C_{15}H_{20}O_4Na^+$] requires *m/z* 287.1254, found *m/z* 287.1253.

To a stirring suspension of 134 mg $LiAlH_4$ (3.54 mmol) in 20 mL Et_2O at 0 °C was added a solution of 720 mg (2.72 mmol) of the ester in 5 mL Et_2O dropwise. The reaction was stirred for approximately 5 min before being brought to reflux for 1h. The mixture was cooled to 0 °C, and water (150 μL) was carefully added dropwise, followed by 6M NaOH (150 μL), additional water, and $MgSO_4$ sufficient to sequester excess water. The slurry was stirred 30–60 min and filtered through Celite®. The cake was washed with Et_2O and the filtrate was washed with brine, dried over $MgSO_4$, filtered and concentrated. Purification by chromatography on SiO_2 (3:1 to 2:1 hexanes:acetone) afforded 550 mg (2.47 mmol, 91% yield) of the alcohol as a clear liquid. IR (neat) 3423 (br), 1497, 1454, 1312, 1044, 666; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.30–7.26 (m, 2H), 7.20–7.17 (m, 3H), 4.06–4.00 (m, 4H), 3.78 (q, J = 5.6 Hz, 2H), 2.74 (t, J = 5.6 Hz, 1H), 2.71–2.67 (m, 2H), 1.99–1.96 (m, 4H); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 142.0, 128.7, 128.5, 126.1, 112.0, 65.2, 59.1, 39.2, 38.6, 30.2; HRMS (EI^+) calculated for [$C_{13}H_{18}O_3^+$] requires *m/z* 222.1251, found *m/z* 222.1245.

Oxalyl chloride (0.318 mL, 3.64 mmol) was dissolved in 15 mL CH_2Cl_2 and brought to –78 °C. A solution of 0.38 mL DMSO (5.34 mmol) in 3 mL CH_2Cl_2 was added dropwise, and the reaction was allowed to stir for 5 min. A solution of 540 mg (2.43 mmol) of the alcohol in CH_2Cl_2 (3 mL) was added over 20 min via syringe pump, and the reaction was allowed to stir an additional 40 min. Over 45 min, 1.69 mL Et_3N (12.1 mmol) was added via syringe pump. After 5 min, the reaction was allowed to warm to room temperature. The reaction mixture was transferred to a separatory funnel and washed with saturated $NaHCO_3$. The phases were separated, and the aqueous phase was extracted with several portions of CH_2Cl_2. The combined organic extracts were washed with saturated $NaHCO_3$ and brine, dried over $MgSO_4$, and concentrated by rotary evaporation. Purification by chromatography on SiO_2 (5:1 to 4:1 hexanes:EtOAc) afforded 470 mg (2.13 mmol, 88% yield) of the aldehyde as a clear oil. IR (neat) 2889, 1724, 1603, 1498, 1455, 1294, 1142, 1052, 702, 666; ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.76 (t, J = 3.1 Hz, 1H), 7.29–7.25 (m, 2H), 7.20–7.17 (m, 3H), 4.06–4.03 (m, 4H), 2.73–2.70 (m, 4H), 2.04–2.01 (m, 2H); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 200.4, 141.6, 128.7, 128.5, 126.2, 109.2, 65.4, 60.0, 40.5, 29.9; HRMS (ESI^+) calculated for [$C_{13}H_{16}O_3Na^+$] requires *m/z* 243.0992, found *m/z* 243.1003.

To a solution of 400 mg (1.82 mmol) of the aldehyde and 269 mg benzenesulfinamide (1.91 mmol) in 25 mL CH_2Cl_2 was added 0.753 mL $Ti(OEt)_4$ (3.63 mmol) dropwise. The reaction was allowed to stir under N_2 for 3.5h. The mixture was filtered through a plug of silica gel, rinsing with several portions of ethyl acetate. The filtrate was concentrated to afford the *N*-benzenesulfinimine, which was dissolved in 10 mL CH_2Cl_2. To this solution was added 435 mg (2.27 mmol) freshly purified *m*CPBA (>90%) in one portion. Upon completion, the reaction was concentrated by rotary evaporation. The crude reaction mixture was dissolved in 25 mL toluene and added to a solution of 2.11 g K_2CO_3 (15.3 mmol) in 25 mL water. The biphasic mixture was subjected to vigorous stirring, and a solution of 1.79 g Oxone® (2.91 mmol) was added slowly. After 30 min, equivalent portions of aqueous K_2CO_3 and Oxone® were added, and after an additional 30 min, the reaction was poured into a separatory funnel. The phases were separated, the aqueous layer was extracted twice with Et_2O. The combined organic extracts were washed with brine, dried over $MgSO_4$, and concentrated by rotary evaporation. Purification by chromatography on SiO_2 (5:1 to 4:1 hexanes:acetone) afforded 270 mg (0.72 mmol, 40% yield) of the oxaziridine as a clear oil. IR (neat) 2889, 1497, 1449, 1351, 1170, 1031, 686; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.00–7.98 (m, 2H), 7.73–7.69 (m, 1H), 7.61–7.57 (m, 2H), 7.29–7.25 (m, 2H), 7.19–7.17 (m, 3H), 4.88 (t, J = 5.2 Hz, 1H), 4.09–4.02 (m, 4H), 2.73–2.64 (m, 2H), 2.21–2.12 (m, 2H), 2.01–1.94 (m, 2H); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 141.6, 135.1, 135.0, 129.5(0), 129.4(5), 128.7, 128.5, 126.2, 109.1, 75.6, 65.5, 40.1, 39.4, 30.0; HRMS (ESI^+) calculated for [$C_{19}H_{21}NO_5SNa^+$] requires *m/z* 398.1033, found *m/z* 398.1015.

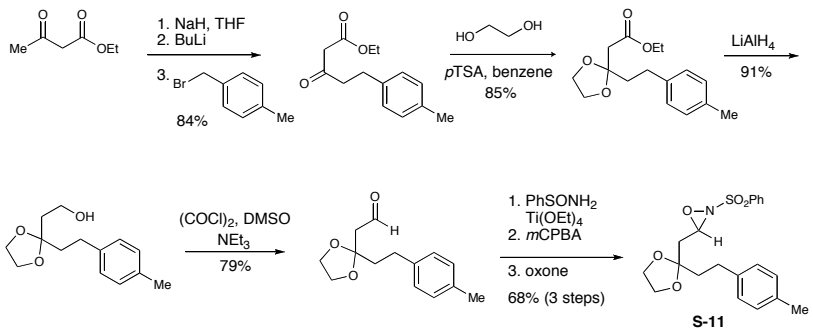


Table 2, entry 4 (**S-11**)

To a flame-dried, 50 mL flask was added 440 mg NaH (60% in mineral oil, 11.0 mmol) and 25 mL THF under a current of N_2. The mixture was cooled to 0 °C, and 1.27 mL ethyl acetoacetate (10.0 mmol) was added dropwise with vigorous evolution of H_2. The reaction was stirred for 10 minutes, at which time 8.4 mL *n*BuLi (1.25 M in hexanes, 10.5 mmol) was added dropwise. After an additional 10 minutes, at 0 °C, a solution of 3.32 g (15.0 mmol) 4-methylbenzyl bromide in 2 mL THF was added quickly to the reaction, and the ice bath was removed. The reaction was stirred an additional 30 minutes before being quenched with a solution of concentrated HCl (2 mL) in water (5 mL). The reaction mixture was diluted with Et_2O and water, and the phases were separated. The aqueous phase was extracted with Et_2O (2 x 20 mL), and the combined organic extracts were washed with saturated, aqueous $NaHCO_3$ and brine, dried over $MgSO_4$, and concentrated by rotary evaporation. Purification by chromatography on SiO_2 (10:1 hexanes:EtOAc) afforded 1.96 g (8.37 mmol, 84% yield) of the β-ketoester as a yellow liquid. IR (thin film) 1745, 1716, 1516, 1367, 1315, 1181, 1080, 1036; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.10-7.06 (m, 4H), 4.18 (q, J = 7.2 Hz, 2H), 3.41 (s, 2H), 2.90-2.83 (m, 4H), 2.31 (s, 3H), 1.26 (t, J = 7.1 Hz, 3H); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 202.2, 167.3, 137.6, 135.9, 129.4(2), 129.3(9), 61.6, 49.7, 44.9, 29.2, 21.2, 14.3; HRMS (EI^+) calculated for [$C_{14}H_{18}O_3^+$] requires *m/z* 234.1251, found *m/z* 234.1247.

The β-ketoester (1.75 g, 7.5 mmol), 1.39 g ethylene glycol (22.4 mmol), and 14.3 mg *p*-toluenesulfonic acid monohydrate (0.075 mmol) were dissolved in 50 mL benzene and allowed to reflux in a Dean-Stark apparatus under N_2 for 24 h. The reaction was cooled to room temperature and quenched with saturated, aqueous $NaHCO_3$. The mixture was transferred to a separatory funnel, the phases were separated and the aqueous phase was extracted with Et_2O (3 x 25 mL). The combined organic extracts were washed sequentially with water and brine, dried over $MgSO_4$, and concentrated by rotary evaporation. Purification by chromatography on SiO_2 (7:1 to 6:1 hexanes:EtOAc) afforded 1.78 g (6.4 mmol, 85% yield) of the ketal as a yellow liquid. IR (thin film) 1737, 1516, 1454, 1369, 1222, 1095, 1046, 950, 889, 809, 666; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.11-7.07 (m, 4H), 4.16 (q, J = 7.2 Hz, 2H), 4.06-3.99 (m, 4H), 2.71-2.67 (m, 4H), 2.31 (s, 3H), 2.14-2.10 (m, 2H), 1.27 (t, J = 7.1 Hz, 3H); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 169.7, 139.0, 135.5, 129.3, 128.5, 109.2, 65.4, 60.8, 43.0, 39.9, 29.5, 21.2, 14.4; HRMS (ESI^+) calculated for [$C_{16}H_{22}O_4$] requires *m/z* 278.1513, found *m/z* 278.1514.

To a stirring suspension of 290 mg $LiAlH_4$ (7.64 mmol) in 60 mL Et_2O at 0 °C was added a solution of 1.62 g (5.82 mmol) of the ester in 5 mL Et_2O dropwise. The reaction was stirred for approximately 5 min before being brought to reflux for 1h. The mixture was cooled to 0 °C, and water (300 μL) was carefully added dropwise, followed by 6M NaOH (300 μL), additional water, and $MgSO_4$ sufficient to sequester excess water. The slurry was stirred 30–60 min and filtered through Celite®. The cake was washed with Et_2O and the filtrate was washed with brine, dried over $MgSO_4$, filtered and concentrated. Purification by chromatography on SiO_2 (3:1 to 2:1 hexanes:acetone) afforded 550 mg (2.47 mmol, 91% yield) of the alcohol as a clear liquid. IR (thin film) 1515, 1453, 1366, 1301, 1209, 1132, 1047, 948, 897, 810, 666; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.10-7.07 (m, 4H), 4.06-3.99 (m, 4H), 3.77 (t, J = 5.5 Hz, 2H), 2.75 (br s, 1H), 2.67-2.63 (m, 2H), 2.31 (s, 3H), 1.99-1.93 (m, 4H); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 202.2, 167.3, 137.6, 135.9, 129.4, 128.4, 61.6, 49.7, 44.9, 29.2, 21.2, 14.3; HRMS (ESI^+) calculated for [$C_{14}H_{20}O_3Na^+$] requires *m/z* 259.1305, found *m/z* 259.1308.

Oxalyl chloride (0.76 mL, 8.7 mmol) was dissolved in 47 mL CH_2Cl_2 and brought to –78 °C. A solution of 0.91 mL DMSO (12.8 mmol) in 3 mL CH_2Cl_2 was added dropwise, and the reaction was allowed to stir for 5 min. A solution of 1.37 g (5.8 mmol) of the alcohol in CH_2Cl_2 (3 mL) was added over 20 min via syringe pump, and the reaction was allowed to stir an additional 40 min. Over 45 min, 4.07 mL Et_3N (29.0 mmol) was added via syringe pump. After 5 min, the reaction was allowed to warm to room temperature. The reaction mixture was transferred to a separatory funnel and washed with saturated $NaHCO_3$. The phases were separated, and the aqueous phase was

extracted with several portions of CH_2Cl_2. The combined organic extracts were washed with saturated $NaHCO_3$ and brine, dried over $MgSO_4$, and concentrated by rotary evaporation. Purification by chromatography on SiO_2 (5:1 hexanes:EtOAc) afforded 1.07 g (4.57 mmol, 79% yield) of the aldehyde as a clear liquid (m.p. 34–36 °C). IR (ATR) 1716, 1517, 1298, 1281, 1160, 1115, 1055, 1024, 946, 894, 812; ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.76 (t, J = 2.9 Hz, 1H), 7.10-7.06 (m, 4H), 4.06-4.03 (m, 4H), 2.73 (d, J = 2.9 Hz, 2H), 2.69-2.66 (m, 2H), 2.31 (s, 3H), 2.02-1.98 (m, 2H); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 200.5, 138.5, 135.7, 129.4, 128.4, 109.3, 65.4, 51.0, 40.6, 29.4, 21.2; HRMS (ESI^+) calculated for $[C_{14}H_{18}O_3Na^+]$ requires *m/z* 257.1149, found *m/z* 257.1158.

To a solution of 200 mg (0.85 mmol) of the aldehyde and 130 mg benzenesulfinamide (0.90 mmol) in 12 mL CH_2Cl_2 was added 0.35 mL $Ti(OEt)_4$ (1.7 mmol) dropwise. The reaction was allowed to stir under N_2. The mixture was filtered through a plug of silica gel, rinsing with several portions of ethyl acetate. The filtrate was concentrated to afford the *N*-benzenesulfinimine, which was dissolved in 10 mL CH_2Cl_2. To this solution was added 180 mg (1.06 mmol) freshly purified *m*CPBA (>90%) in one portion. Upon completion, the reaction was concentrated by rotary evaporation. The crude reaction mixture was dissolved in 25 mL toluene and added to a solution of 0.99 g K_2CO_3 (7.14 mmol) in 25 mL water. The biphasic mixture was subjected to vigorous stirring, and a solution of 0.84 g Oxone® (1.36 mmol) was added slowly. After 30 min, equivalent portions of aqueous K_2CO_3 and Oxone® were added, and after an additional 30 min, the reaction was poured into a separatory funnel. The phases were separated, the aqueous layer was extracted twice with Et_2O. The combined organic extracts were washed with brine, dried over $MgSO_4$, and concentrated by rotary evaporation. Purification by chromatography on SiO_2 (5:1 to 3:1 hexanes:acetone) afforded 226 mg (0.58 mmol, 68% yield) of the oxaziridine as a white solid (m.p. 110–112 °C). IR (thin film) 1513, 1450, 1170, 1089, 1044, 726, 665, 612; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.00-7.98 (m, 2H), 7.73-7.70 (m, 1H), 7.61-7.58 (m, 2H), 7.10-7.06 (m, 4H), 4.87 (t, J = 5.2 Hz, 1H), 4.06-4.04 (m, 4H), 2.66-2.63 (m, 2H), 2.31 (s, 3H), 2.16 (qd, J = 14.5, 5.2 Hz, 2H), 1.96 (dd, J = 10.6, 6.1 Hz, 2H); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 138.5, 135.6, 135.1, 135.0, 129.5(1), 129.4(8), 129.3, 109.2, 75.6, 65.5, 40.3, 39.4, 29.5, 21.2; HRMS (ESI^+) calculated for $[C_{20}H_{23}O_5NSNH_4^+]$ requires *m/z* 407.1636, found *m/z* 407.1633.

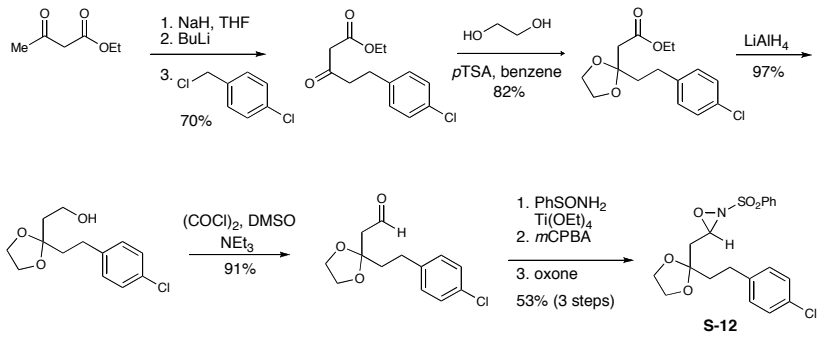


Table 2, entry 5 (**S-12**)

To a flame-dried, 50 mL flask was added 440 mg NaH (60% in mineral oil, 11.0 mmol) and 25 mL THF under a current of N_2. The mixture was cooled to 0 °C, and 1.27 mL ethyl acetoacetate (10.0 mmol) was added dropwise with vigorous evolution of H_2. The reaction was stirred for 10 minutes, at which time 8.4 mL *n*BuLi (1.25 M in hexanes, 10.5 mmol) was added dropwise. After an additional 10 minutes, at 0 °C, a solution of 2.42 g (15.0 mmol) 4-chlorobenzyl chloride in 2 mL THF was added quickly to the reaction, and the ice bath was removed. The reaction was stirred an additional 30 minutes before being quenched with a solution of concentrated HCl (2 mL) in water (5 mL). The reaction mixture was diluted with Et_2O and water, and the phases were separated. The aqueous phase was extracted with Et_2O (2 x 20 mL), and the combined organic extracts were washed with saturated, aqueous $NaHCO_3$ and brine, dried over $MgSO_4$, and concentrated by rotary evaporation. Purification by chromatography on SiO_2 (9:1 to 8:1 hexanes:EtOAc) afforded 1.78 g (6.99 mmol, 70% yield) of the β-ketoester as a clear liquid. IR (neat) 2983, 1744, 1716, 1647, 1493, 1319, 1093, 1016, 814; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.243 (d, J = 8.4 Hz, 2H), 7.11 (d, J = 8.4 Hz, 2H), 4.17 (q, J = 7.1 Hz, 2H), 3.41 (s, 2H), 2.91–2.84 (m, 4H), 1.26 (t, J = 7.1 Hz, 3H); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 201.7, 167.2, 139.2, 132.2, 129.9(3), 129.8(9), 128.8, 61.7, 49.6, 44.4, 28.9, 14.3; HRMS (EI^+) calculated for $[C_{13}H_{15}ClO_3^+]$ requires *m/z* 254.0705, found *m/z* 254.0716.

The β-ketoester (1.76 g, 6.91 mmol), 1.29 g ethylene glycol (20.7 mmol), and 13 mg *p*-toluenesulfonic acid monohydrate (0.069 mmol) were dissolved in 50 mL benzene and allowed to reflux in a Dean-Stark apparatus under

N_2 for 41 h. Additional ethylene glycol (1.25 g) was added after 18 h. The reaction was cooled to room temperature and quenched with saturated, aqueous $NaHCO_3$. The mixture was transferred to a separatory funnel, the phases were separated and the aqueous phase was extracted with Et_2O (3 x 25 mL). The combined organic extracts were washed sequentially with water and brine, dried over $MgSO_4$, and concentrated by rotary evaporation. Purification by chromatography on SiO_2 (5:1 to 4:1 hexanes:EtOAc) afforded 1.70 mg (5.69 mmol, 82% yield) of the ketal as a clear liquid. IR (neat) 2981, 1735, 1492, 1370, 1221, 1093, 1044; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.24 (d, J = 8.4 Hz, 2H), 7.13 (d, J = 8.4 Hz, 2H), 4.16 (q, J = 7.1 Hz, 2H), 4.06–3.98 (m, 4H), 2.72–2.68 (m, 2H), 2.68 (s, 2H), 2.14–2.11 (m, 2H), 1.27 (t, J = 7.1 Hz, 3H); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 169.6, 140.5, 131.7, 129.0, 128.7, 109.0, 65.4, 60.8, 43.0, 39.5, 29.3, 14.4; HRMS (EI^+) calculated for [$C_{15}H_{19}ClO_4^+$] requires *m/z* 298.0968, found *m/z* 298.0970.

To a stirring suspension of 277 mg $LiAlH_4$ (7.31 mmol) in 50 mL Et_2O at 0 °C was added a solution of 1.68 g (5.62 mmol) of the ester in 5 mL Et_2O dropwise. The reaction was stirred for approximately 5 min before being brought to reflux for 1h. The mixture was cooled to 0 °C, and water (300 μL) was carefully added dropwise, followed by 6M NaOH (300 μL), additional water, and $MgSO_4$ sufficient to sequester excess water. The slurry was stirred 30–60 min and filtered through Celite®. The cake was washed with Et_2O and the filtrate was washed with brine, dried over $MgSO_4$, filtered and concentrated. Purification by chromatography on SiO_2 (3:1 to 2:1 hexanes:acetone) afforded 1.40 g (5.45 mmol, 97% yield) of the alcohol as a clear liquid. IR (neat) 3443 (br), 2957, 2887, 1492, 1132, 1093, 1046, 949; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.25 (d, J = 8.4 Hz, 2H), 7.11 (d, J = 8.4 Hz, 2H), 4.07–3.98 (m, 4H), 3.77 (q, J = 5.5 Hz, 2H), 2.71 (t, J = 5.5 Hz, 1H), 2.68–2.64 (m, 2H), 1.98–1.93 (m, 4H); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 140.5, 131.8, 129.8, 128.7, 111.8, 65.2, 59.0, 39.1, 38.6, 29.6; HRMS (ESI^+) calculated for [$C_{13}H_{17}ClO_3H^+$] requires *m/z* 257.0939, found *m/z* 257.0945.

Oxalyl chloride (0.56 mL, 6.4 mmol) was dissolved in 21 mL CH_2Cl_2 and brought to –78 °C. A solution of 0.84 mL DMSO (11.9 mmol) in 3 mL CH_2Cl_2 was added dropwise, and the reaction was allowed to stir for 5 min. A solution of 1.38 g (2.43 mmol) of the alcohol in CH_2Cl_2 (3 mL) was added over 20 min via syringe pump, and the reaction was allowed to stir an additional 40 min. Over 45 min, 3.79 mL Et_3N (27.0 mmol) was added via syringe pump. After 5 min, the reaction was allowed to warm to room temperature. The reaction mixture was transferred to a separatory funnel and washed with saturated $NaHCO_3$. The phases were separated, and the aqueous phase was extracted with several portions of CH_2Cl_2. The combined organic extracts were washed with saturated $NaHCO_3$ and brine, dried over $MgSO_4$, and concentrated by rotary evaporation. Purification by chromatography on SiO_2 (2:1 hexanes:EtOAc) afforded 1.24 g (4.87 mmol, 91% yield) of the aldehyde as a clear liquid. IR (neat) 2890, 1724, 1492, 1297, 1093, 1052, 949; ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.76 (t, J = 2.9 Hz, 1H), 7.25 (d, J = 8.4 Hz, 2H), 7.11 (d, J = 8.4 Hz, 2H), 4.05 (s, 4H), 2.73 (d, J = 2.9 Hz, 2H), 2.70–2.67 (m, 2H), 2.01–1.97 (m, 2H); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 200.3, 140.0, 131.9, 129.9, 128.8, 109.1, 65.5, 51.0, 40.4, 29.2; HRMS (EI^+) calculated for [$C_{13}H_{15}ClO_3^+$] requires *m/z* 254.0705, found *m/z* 254.0710.

To a solution of 490 mg (1.82 mmol) of the aldehyde and 344 mg benzenesulfinamide (2.44 mmol) in 25 mL CH_2Cl_2 was added 1.20 mL $Ti(OEt)_4$ (5.81 mmol) dropwise. The reaction was allowed to stir under N_2 for 2 h. The mixture was filtered through a plug of silica gel, rinsing with several portions of ethyl acetate. The filtrate was concentrated to afford the *N*-benzenesulfinimine, which was dissolved in 10 mL CH_2Cl_2. To this solution was added 706 mg (3.48 mmol) freshly purified *m*CPBA (>90%) in one portion. Additional, equivalent portions of mCPBA were added both after 30 min and 1 h. Upon completion, the reaction was concentrated by rotary evaporation. The crude reaction mixture was dissolved in 25 mL toluene and added to a solution of 2.70 g K_2CO_3 (19.5 mmol) in 25 mL water. The biphasic mixture was subjected to vigorous stirring, and a solution of 2.29 g Oxone® (3.71 mmol) was added slowly. After 30 min, equivalent portions of aqueous K_2CO_3 and Oxone® were added, and after an additional 30 min, the reaction was poured into a separatory funnel. The phases were separated, the aqueous layer was extracted twice with Et_2O. The combined organic extracts were washed with brine, dried over $MgSO_4$, and concentrated by rotary evaporation. Purification by chromatography on SiO_2 (1:0 to 20:1 toluene:EtOAC) afforded 500 mg (1.22 mmol, 53% yield) of the oxaziridine as a white solid (m.p. 102–103 °C). IR (ATR) 1355, 1180, 1087, 1020, 848, 754; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.99 (dd, J = 8.2, 1.1 Hz, 2H), 7.72 (tt, J = 7.5, 1.1, 1H), 7.60 (t, J = 7.9, 2H), 7.22 (d, J = 8.4, 2H), 7.11 (d, J = 8.4 Hz, 2H), 4.87 (t, J = 5.2 Hz, 1H), 4.09–4.01 (m, 4H), 2.67–2.63 (m, 2H), 2.18–2.10 (m, 2H), 1.97–1.94 (m, 2H); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 140.0, 135.1, 134.9, 131.9, 129.9, 129.5, 129.4, 128.7, 108.9, 75.5, 65.5, 39.9, 39.4, 29.3; HRMS (EI^+) calculated for [$C_{19}H_{20}ClNO_5^+$] requires *m/z* 409.0746, found *m/z* 409.0736.

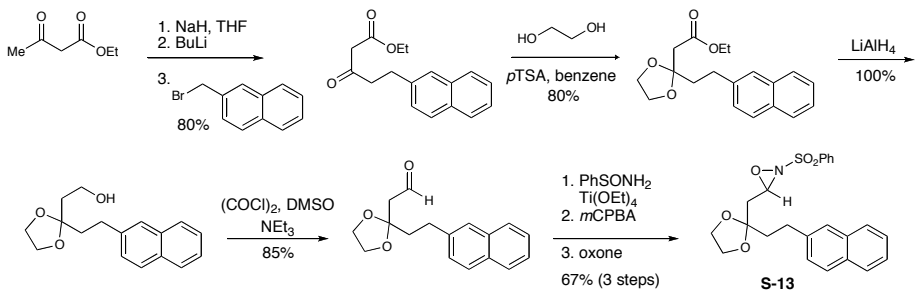


Table 2, entry 6 (**S-13**)

To a flame-dried, 50 mL flask was added 440 mg NaH (60% in mineral oil, 11.0 mmol) and 25 mL THF under a current of N_2. The mixture was cooled to 0 °C, and 1.27 mL ethyl acetoacetate (10.0 mmol) was added dropwise with vigorous evolution of H_2. The reaction was stirred for 10 minutes, at which time 8.4 mL *n*BuLi (1.25 M in hexanes, 10.5 mmol) was added dropwise. After an additional 10 minutes, at 0 °C, a solution of 3.32 g (15.0 mmol) 2-(bromomethyl)naphthalene in 2 mL THF was added quickly to the reaction, and the ice bath was removed. The reaction was stirred an additional 30 minutes before being quenched with a solution of concentrated HCl (2 mL) in water (5 mL). The reaction mixture was diluted with Et_2O and water, and the phases were separated. The aqueous phase was extracted with Et_2O (2 x 20 mL), and the combined organic extracts were washed with saturated, aqueous $NaHCO_3$ and brine, dried over $MgSO_4$, and concentrated by rotary evaporation. Purifcation by chromatography on SiO_2 (8:1 to 7:1 hexanes:EtOAc) afforded 2.15 g (7.95 mmol, 80% yield) of the β-ketoester as a clear liquid. IR (neat) 2983, 1743, 1715, 1409, 1367, 1035, 857; ^{1}H NMR (500 MHz, $CDCl_3$) (keto isomer) δ 7.80–7.78 (m, 3H), 7.62 (s, 1H), 7.47–7.40 (m, 2H), 7.31 (dd, J = 8.4, 1.6 Hz, 1H), 4.16 (q, J = 7.3 Hz, 2H), 3.43 (s, 2H), 3.09 (t, J = 7.4 Hz, 2H), 2.96 (t, J = 7.5 Hz, 2H), 1.24 (t, J = 7.1 Hz, 3H); ^{13}C NMR (125.7 MHz, $CDCl_3$) (keto isomer) δ 167.3, 138.2, 133.8, 132.3, 128.4, 127.8, 127.7, 127.2, 126.7, 126.3, 125.6, 61.6, 49.7, 44.6, 29.8, 14.3; HRMS (ESI$^+$) calculated for $[C_{17}H_{18}O_3Na]^+$ requires *m/z* 293.1149, found *m/z* 293.1140.

The β-ketoester (2.13 g, 7.88 mmol), 7.24 g ethylene glycol (118 mmol), and 15 mg *p*-toluenesulfonic acid monohydrate (0.079 mmol) were dissolved in 55 mL benzene and allowed to reflux in a Dean-Stark apparatus under N_2 for 25 h. The reaction was cooled to room temperature and quenched with saturated, aqueous $NaHCO_3$. The mixture was transferred to a separatory funnel, the phases were separated and the aqueous phase was extracted with Et_2O (3 x 25 mL). The combined organic extracts were washed sequentially with water and brine, dried over $MgSO_4$, and concentrated by rotary evaporation. Purification by chromatography on SiO_2 (5:1 to 4:1 hexanes:EtOAc) afforded 1.99 g (6.33 mmol, 80% yield) of the ketal as a clear liquid. IR (neat) 2980, 1733, 1509, 1369, 1046, 950, 750; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.79 (d, J = 7.7 Hz, 1H), 7.76 (d, J = 8.4 Hz, 2H), 7.64 (s, 1H), 7.45–7.39 (m, 2H), 7.35 (dd, J = 8.4, 1.7 Hz, 1H), 4.16 (q, J = 7.2 Hz, 2H), 4.08–4.01 (m, 4H), 2.92–2.88 (m, 2H), 2.72 (s, 2H), 2.26–2.22 (m, 2H), 1.26 (t, J = 7.2 Hz, 3H); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 169.6, 139.6, 133.8, 132.2, 128.1, 127.8, 127.6, 127.5, 126.5, 126.1, 125.3, 109.2, 65.5, 60.8, 43.0, 39.6, 30.1, 14.4; HRMS (EI$^+$) calculated for $[C_{19}H_{22}O_4^+]$ requires *m/z* 314.1513, found *m/z* 314.1521.

To a stirring suspension of 342 mg $LiAlH_4$ (9.00 mmol) in 55 mL Et_2O at 0 °C was added a solution of 1.97 g (6.27 mmol) of the ester in 5 mL Et_2O dropwise. The reaction was stirred for approximately 5 min before being brought to reflux for 1h. The mixture was cooled to 0 °C, and water (350 μL) was carefully added dropwise, followed by 6M NaOH (350 μL), additional water, and $MgSO_4$ sufficient to sequester excess water. The slurry was stirred 30–60 min and filtered through Celite®. The cake was washed with Et_2O and the filtrate was washed with brine, dried over $MgSO_4$, filtered and concentrated. Purification by chromatography on SiO_2 (1:1 to 0:1 hexanes:EtOAc) afforded 1.71 g (6.27 mmol, 100% yield) of the alcohol as a clear liquid. IR (neat) 3424 (br), 2955, 1600, 1364, 1127, 1047, 820, 750; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.80 (d, J = 7.9 Hz, 1H), 7.77 (d, J = 8.4 Hz, 2H), 7.63 (s, 1H), 7.46-7.40 (m, 2H), 7.33 (dd, J = 8.5, 1.5 Hz, 1H), 4.08–4.01 (m, 4H), 3.80 (q, J = 5.5 Hz, 2H), 2.87–2.84 (m, 2H), 2.78 (t, J = 5.6 Hz, 1H), 2.08–2.05 (m, 2H), 2.01 (t, J = 5.4 Hz, 2H); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 139.5, 133.8, 132.2, 128.2, 127.8, 127.6, 127.4, 126.4, 126.2, 125.4, 112.0, 65.2, 59.1, 39.1, 38.6, 30.4; HRMS (EI$^+$) calculated for $[C_{17}H_{20}O_3^+]$ requires *m/z* 272.1407, found *m/z* 272.1405.

Oxalyl chloride (0.82 mL, 9.36 mmol) was dissolved in 50 mL CH_2Cl_2 and brought to –78 °C. A solution of 0.975 mL DMSO (13.7 mmol) in 3 mL CH_2Cl_2 was added dropwise, and the reaction was allowed to stir for 5 min. A solution of 1.70 g (6.24 mmol) of the alcohol in CH_2Cl_2 (3 mL) was added over 20 min via syringe pump,

and the reaction was allowed to stir an additional 40 min. Over 45 min, 4.35 mL Et_3N (31.2 mmol) was added via syringe pump. After 5 min, the reaction was allowed to warm to room temperature. The reaction mixture was transferred to a separatory funnel and washed with saturated $NaHCO_3$. The phases were separated, and the aqueous phase was extracted with several portions of CH_2Cl_2. The combined organic extracts were washed with saturated $NaHCO_3$ and brine, dried over $MgSO_4$, and concentrated by rotary evaporation. Purification by chromatography on SiO_2 (3:1 to 2:1 hexanes:EtOAc) afforded 1.43 g (5.29 mmol, 85% yield) of the aldehyde as a clear liquid. IR (neat) 2958, 2889, 1723, 1509, 1143, 1053, 821, 751; ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.78 (t, J = 2.9 Hz, 1H), 7.79 (d, J = 7.7 Hz, 1H), 7.76 (d, J = 8.1 Hz, 2H), 7.62 (s, 1H), 7.46–7.40 (m, 2H), 7.32 (dd, J = 8.6, 1.5 Hz, 1H), 4.09–4.03 (m, 4H), 2.89–2.86 (m, 2H), 2.76 (dd, J = 2.9 Hz, 2H), 2.13–2.07 (m, 2H); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 200.4, 139.0, 133.8, 132.2, 128.2, 127.8, 127.6, 127.3, 126.5, 126.2, 125.5, 109.2, 65.5, 51.0, 40.4, 30.1; HRMS (EI^+) calculated for [$C_{17}H_{18}O_3^+$] requires *m/z* 270.1251, found *m/z* 270.1247.

To a solution of 1.41 g (5.22 mmol) of the aldehyde and 773 mg benzenesulfinamide (5.48 mmol) in 55 mL CH_2Cl_2 was added 2.70 mL $Ti(OEt)_4$ (13.0 mmol) dropwise. The reaction was allowed to stir under N_2 for 2 h. The mixture was filtered through a plug of silica gel, rinsing with several portions of ethyl acetate. The filtrate was concentrated to afford the *N*-benzenesulfinimine, which was dissolved in 30 mL CH_2Cl_2. To this solution was added 1.50 g (7.82 mmol) freshly purified *m*CPBA (>90%) in one portion. Upon completion, the reaction was concentrated by rotary evaporation. The crude reaction mixture was dissolved in 60 mL toluene and added to a solution of 6.06 g K_2CO_3 (43.8 mmol) in 60 mL water. The biphasic mixture was subjected to vigorous stirring, and a solution of 5.14 g Oxone® (8.35 mmol) was added slowly. After 30 min, equivalent portions of aqueous K_2CO_3 and Oxone® were added, and after an additional 30 min, the reaction was poured into a separatory funnel. The phases were separated, the aqueous layer was extracted twice with Et_2O. The combined organic extracts were washed with brine, dried over $MgSO_4$, and concentrated by rotary evaporation. Purification by chromatography on SiO_2 (1:0 to 20:1 toluene:EtOAC) afforded 1.49 g (3.50 mmol, 67% yield) of the oxaziridine as a clear liquid, which solidifies somewhat at temperatures below 0 °C. IR (neat) 2957, 2889, 1478, 1351, 1171, 1089, 1045, 734; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.00–7.98 (m, 2H), 7.80–7.78 (m, 1H), 7.76 (d, J = 7.8 Hz, 2H), 7.71–7.67 (m, 1H), 7.62 (s, 1H), 7.59–7.56 (m, 2H), 7.46–7.40 (m, 2H), 7.32 (dd, J = 8.5, 1.7 Hz, 1H), 4.90 (t, J = 5.4 Hz, 1H), 4.13–4.04 (m, 4H), 2.89–2.80 (m, 2H), 2.19 (m, 2H), 2.09–2.06 (m, 2H); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 139.1, 135.1, 135.0, 133.8, 132.2, 129.5, 129.4, 128.2, 127.8, 127.6, 127.4, 126.5, 126.2, 125.4, 109.2, 75.6, 65.6, 40.0, 39.4, 30.1; HRMS (ESI^+) calculated for [$C_{23}H_{23}NO_5SNH_4^+$] requires *m/z* 443.1637, found *m/z* 443.1644.

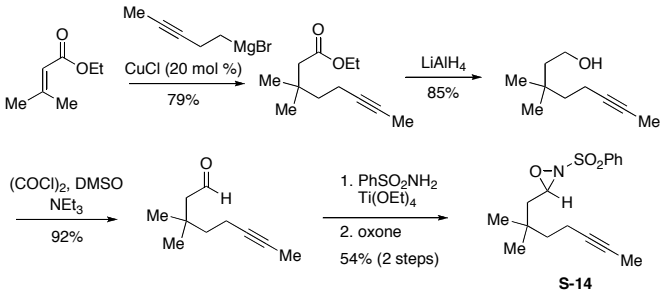


Table 2, entry 7 (**S-14**)

A 25 mL flask containing 408 mg magnesnium turnings (16.8 mmol) was charged with a solution of 1.80 g 1-bromo-3-pentyne[9] (12 mmol) in 12 mL THF. The reaction was refluxed under argon for 1.5 h. In a separate 50 mL flask, 125 mg CuCl (1.26 mmol) was dissolved in 1 mL THF and cooled to–78 °C. The Grignard reagent was added to the flask containing the CuCl solution over 15 min, followed by 1.1 mL TMSCl (8.67 mmol) in one portion. After 5 min, 873 mg ethyl 3,3-dimethylacrylate (6.81 mmol) in 0.5 mL THF was added to the reaction in one portion. The reaction was allowed to warm up to room temperature overnight, and then quencehd by addition of sat. aq. NH_4Cl, followed by 1N HCl. The reaction was allowed to stir for 5 min and was subsequently poured into a separatory funnel. The phases were separated, and the aqueous phase was extracted twice with chloroform. The combined organic extracts were dried over Na_2SO_4 and concentrated by rotary evaporation. Purification by chromatography on SiO_2 (40:1 to 20:1 hexanes:EtOAc) afforded 1.06 g (5.40 mmol, 79% yield) of the ester as a clear oil. IR (neat) 2962, 1733, 1454, 1369, 1149, 1118, 1043; ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.12 (q, J = 7.2 Hz, 2H), 2.19 (s, 2H), 2.13 (tq, J = 8.4, 2.4 Hz, 2H), 1.77 (t, J = 2.4 Hz, 3H), 1.57 (t, J =8.4 Hz, 2H), 1.26 (t, J = 7.2 Hz,

3H), 1.00 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 172.2, 79.6, 75.5, 60.2, 46.0, 41.7, 33.3, 27.2, 14.5, 14.1, 3.7; HRMS (ESI^+) calculated for $[C_{12}H_{20}O_2Na^+]$ requires *m/z* 219.1356, found *m/z* 219.1351.

To a stirring suspension of 320 mg $LiAlH_4$ (8.43 mmol) in 20 mL Et_2O at 0 °C was added a solution of 1.06 g (5.40 mmol) of the ester in 10 mL Et_2O dropwise. The reaction was stirred for approximately 5 min before being brought to reflux for 1h. The mixture was cooled to 0 °C, and 1 mL water was carefully added dropwise, followed by 1 mL 6M NaOH, additional water, and $MgSO_4$ sufficient to sequester excess water. The slurry was stirred 30–60 min and filtered through Celite®. The cake was washed with Et_2O and the filtrate was washed with brine, dried over $MgSO_4$, filtered and concentrated. Purification by chromatography on SiO_2 (4:1 hexanes:EtOAc) afforded 713 mg (4.63 mmol, 85% yield) of the alcohol as a clear liquid. IR (neat) 3346 (br), 2958, 1471, 1367, 1036; ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.67 (t, J = 7.7 Hz, 2H), 2.09 (tq, J = 8.4, 2.5 Hz, 2H), 1.77 (t, J = 2.5 Hz, 3H), 1.49 (m, 5H), 0.90 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 79.9, 75.4, 59.8, 44.2, 41.9, 32.3, 27.2, 14.0, 3.6.

Oxalyl chloride (0.65 mL, 7.68 mmol) was dissolved in 6 mL CH_2Cl_2 and brought to –78 °C. A solution of 1.00 mL DMSO (14.3 mmol) in CH_2Cl_2 (8 mL) was added dropwise, and the reaction was allowed to stir for 5 min. A solution of 713 mg (4.63 mmol) of the alcohol in CH_2Cl_2 (18 mL) was added over 45 min via syringe pump, and the reaction was allowed to stir an additional 15 min. Over 45 min, 1.9 mL Et_3N (13.6 mmol) was added via syringe pump. After 5 min, the reaction was allowed to warm to room temperature. The reaction mixture was transferred to a separatory funnel and washed with water. The phases were separated, and the aqueous phase was extracted with several portions of diethyl ether. The combined organic extracts were dried over Na_2SO_4, and concentrated by rotary evaporation. Purification by chromatography on SiO_2 (20:1 hexanes:EtOAc) afforded 647 g (4.25 mmol, 92% yield) of the aldehyde as a clear liquid. IR (neat) 2961, 2922, 1707, 1470, 1390, 1370, 1254; ^{1}H NMR (500 MHz, $CDCl_3$) 9.85 (t, J = 3.1 Hz, 1H), 2.29 (d, J = 3.1 Hz, 2H), 2.14 (tq, J = 8.1, 2.5 Hz, 2H), 1.76 (t, J = 2.5 Hz, 3H), 1.60 (t, J = 8.1 Hz, 2H), 1.05 (s, 6H); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 203.4, 79.3, 76.0, 54.6, 42.0, 33.6, 27.4, 14.1, 3.6.

A solution of 647 mg aliphatic aldehyde (4.25 mmol) and 680 mg benzenesulfonamide (4.33 mmol) was mixed together in 60 mL CH_2Cl_2. To this solution, 2.1 mL $Ti(OEt)_4$ (8.5 mmoles) was added dropwise. At 1 and 2h, additional 0.3 mL $Ti(OEt)_4$ was added, and at 3 hours, the reaction mixture was passed through a silica plug followed by ample of EtOAc. The combined organic filtrate was concentrated by rotary evaporation, and the residue was dissolved in 100 mL toluene and added to a solution of 5.00 g K_2CO_3 (36.2 mmol) in 40 mL water. The biphasic mixture was subjected to vigorous stirring, and a solution of 4.30 g Oxone® (6.99 mmol) was added slowly. After 10 min, equivalent portion of aqueous Oxone® was added, followed by another portion after an additional 10 min. The reaction was poured into a separatory funnel. The phases were separated, the aqueous layer was extracted once with toluene. The combined organic extracts were dried over Na_2SO_4, and concentrated by rotary evaporation. Purification by chromatography on SiO_2 (20:1 to 10:1 hexanes:EtOAc) afforded 697 g (2.27 mmol, 54% yield) of the oxaziridine as a clear liquid. IR (neat) 2960, 2921, 1449, 1301, 1234, 1171, 1060; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.00 (d, J = 7.5 Hz, 2H), 7.73 (t, J = 7.5 Hz, 1H), 7.61 (t, J = 7.5 Hz, 2H), 4.77 (t, J = 5.5 Hz, 1H), 2.11 (tq, J = 8.0, 2.5 Hz, 2H), 1.77 (t, J = 2.5 Hz, 3H), 1.74 (dd, J = 14.5, 5.5 Hz, 1H), 1.63 (dd, J = 14.5, 5.5 Hz, 1H), 1.57 (m, 2H), 1.02 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 135.1, 135.1, 129.5, 129.4, 79.3, 76.5, 76.0, 42.6, 41.9, 32.9, 27.2, 27.2, 14.0, 3.6; HRMS (ESI^+) calculated for $[C_{16}H_{21}O_3NSNH_4^+]$ requires *m/z* 325.1581, found *m/z* 325.1591.

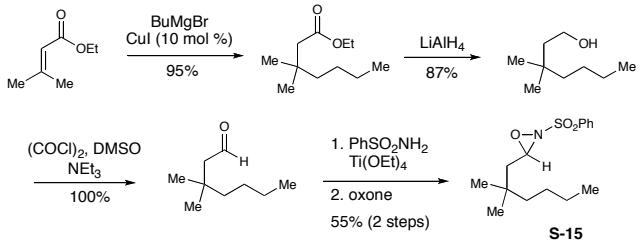


Table 2, entry 7 (**S-15**)

To a solution of 1.10 g ethyl 3,3-dimethylacrylate (8.58 mmol) in 15 mL THF was added 1.31 mL TMSCl (10.3 mmol) and 85 mg CuI (0.86 mmol). The reaction was brought to –15 °C in a MeOH/H_2O(s) bath. Butylmagnesium chloride (5.2 mL, 2.0M in Et_2O, 10.3 mmol) was added via syringe pump over 1h. The reaction was allowed to stir an additional 90 min, at which time saturated aqueous NH_4Cl was added, followed by 1N HCl. The reaction was allowed to stir for 5 min and was subsequently poured into a separatory funnel and diluted with water and Et_2O. The phases were separated, and the aqueous phase was extracted twice with Et_2O. The combined

organic extracts were washed with brine, dried over $MgSO_4$, and concentrated by rotary evaporation. Purification by chromatography on SiO_2 (10:1 hexanes:EtOAc) afforded 1.512 g (8.11 mmol, 95% yield) of the ester as a clear liquid. IR (neat) 1735, 1469, 1368, 1223, 1130, 1097, 1077; ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.11 (q, J = 14.2, 7.0 Hz, 2H), 2.18 (s, 2H), 1.31–1.24 (m, 9H), 0.98 (s, 6H), 0.90 (t, J = 7 Hz, 3H); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 172.6, 60.0, 46.3, 42.3, 33.4, 27.5, 26.5, 23.6, 14.5, 14.3; GCMS: *m/z* 45.1 (*M* – 141.2), 57.1 (*M* – 129.2), 88.1, (*M* – 99.2 + 1), 99.2 (*M* – 87.1), 129.2 (*M* – 57.1), 141.2 (*M* – 45.1).

To a stirring suspension of 380 mg $LiAlH_4$ (9.99 mmol) in 29 mL Et_2O at 0 °C was added a solution of 1.43 g (7.69 mmol) of the ester in 5 mL Et_2O dropwise. The reaction was stirred for approximately 5 min before being brought to reflux for 1h. The mixture was cooled to 0 °C, and water (400 μL) was carefully added dropwise, followed by 6M NaOH (400 μL), additional water, and $MgSO_4$ sufficient to sequester excess water. The slurry was stirred 30–60 min and filtered through Celite®. The cake was washed with Et_2O and the filtrate was washed with brine, dried over $MgSO_4$, filtered and concentrated. Purification by chromatography on SiO_2 (5:1 to 3:1 to 2:1 hexanes:EtOAc) afforded 0.97 g (6.72 mmol, 87% yield) of the alcohol as a clear liquid. IR (neat) 3347 (br), 2931, 1470, 1365, 1053, 1029; ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.69 (t, J = 6.6 Hz, 2H), 1.53–1.50 (m, 2H), 1.31–1.16 (m, 7H), 0.90 (t, J = 7.2 Hz, 3H), 0.88 (s, 6H); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 60.1, 44.7, 42.4, 32.3, 27.7, 26.5, 23.8, 14.4; GCMS: *m/z* 45.1 (*M* – 99.2), 57.1 (*M* – 87.1), 87.1, (*M* – 57.1), 99.2 (*M* –45.1).

Oxalyl chloride (0.73 mL, 8.35 mmol) was dissolved in 25 mL CH_2Cl_2 and brought to –78 °C. A solution of 0.97 mL DMSO (13.6 mmol) in 3 mL CH_2Cl_2 was added dropwise, and the reaction was allowed to stir for 5 min. A solution of 892 mg (6.18 mmol) of the alcohol in CH_2Cl_2 (3 mL) was added over 20 min via syringe pump, and the reaction was allowed to stir an additional 40 min. Over 45 min, 4.31 mL Et_3N (30.9 mmol) was added via syringe pump. After 5 min, the reaction was allowed to warm to room temperature. The reaction mixture was transferred to a separatory funnel and washed with saturated $NaHCO_3$. The phases were separated, and the aqueous phase was extracted with several portions of CH_2Cl_2. The combined organic extracts were washed with saturated $NaHCO_3$ and brine, dried over $MgSO_4$, and concentrated by rotary evaporation. Purification by chromatography on SiO_2 (8:1 hexanes:EtOAc) afforded 0.88 g (6.18 mmol, 100% yield) of the aldehyde as a clear liquid. IR (neat) 1707, 1649, 1546, 1469, 1368, 1125; ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.84 (t, J = 3.2 Hz, 1H), 2.25 (d, J = 3.4 Hz, 2H), 1.34–1.23 (m, 6H), 1.04 (s, 6H), 0.90 (t, J = 6.8 Hz, 3H); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 204.1, 55.0, 42.7, 33.7, 27.8, 26.4, 23.6, 14.3, 14.3; GCMS: *m/z* 57.1 (*M* – 85.1), 85.1 (*M* – 57.1).

The aldehyde (850 mg, 5.97 mmol) and 986 mg benzenesulfonamide (6.27 mmol) were dissolved in 55 mL CH_2Cl_2. To this solution was added 3.76 mL $Ti(OEt)_4$ (17.9 mmol) dropwise. The reaction was allowed to stir under N_2 for 1 h. Upon completion, the mixture was filtered through a short plug of silica gel and washed with several portions of ethyl acetate. The filtrate was concentrated by rotary evaporation, and the residue was dissolved in 130 mL toluene. The dissolved crude was added to a solution of 6.93 g K_2CO_3 (50.1 mmol) in 70 mL water. The biphasic mixture was subjected to vigorous stirring, and a solution of 5.88 g Oxone® (9.55 mmol) in 70 mL water was added slowly. After 45 min, the reaction was poured into a separatory funnel. The phases were separated, the aqueous layer was extracted twice with Et_2O. The combined organic extracts were washed with brine, dried over $MgSO_4$, and concentrated by rotary evaporation. Purification by chromatography on SiO_2 (10:1 hexanes:EtOAc) afforded 980 mg (3.29 mmol, 55% yield) of the oxaziridine as a clear liquid. IR (neat) 2931, 1707, 1353, 1171, 1090; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.00–7.98 (m, 2H), 7.73–7.70 (m, 1H), 7.61–7.58 (m, 2H), 4.73 (t, J = 5.5 Hz, 1H), 1.66 (qd, J = 14.0, 5.5 Hz, 2H), 1.31–1.18 (m, 6H), 1.00 (d, J = 3.7 Hz, 6H), 0.90 (t, J = 7.2 Hz, 3H); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 135.1, 135.0, 129.5, 129.3, 76.7, 42.7, 42.4, 32.8, 27.5, 26.3, 23.5, 14.3; HRMS (ESI^+) calculated for [$C_{15}H_{23}O_3SNNa^+$] requires *m/z* 320.1291, found *m/z* 320.1303.

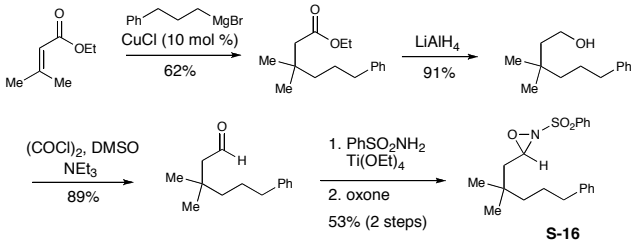


Table 2, entry 8 (**S-16**)

To a solution of 800 mg ethyl 3,3-dimethylacrylate (6.24 mmol) in 12 mL THF was added 0.947 mL TMSCl (7.49 mmol) and 119 mg CuCl (0.624 mmol). The reaction was brought to –15 °C in a MeOH/H_2O(s) bath. Hydrocinnamylmagnesium bromide (7 mL, 1.25M in Et_2O, 8.74 mmol) was added via syringe pump over 1 h. The reaction was allowed to stir an additional 90 min, at which time saturated aqueous NH_4Cl was added, followed by 1N HCl. The reaction was allowed to stir for 5 min and was subsequently poured into a separatory funnel and diluted with water and Et_2O. The phases were separated, and the aqueous phase was extracted twice with Et_2O. The combined organic extracts were washed with brine, dried over $MgSO_4$, and concentrated by rotary evaporation. Purification by chromatography on SiO_2 (20:1 to 10:1 hexanes:EtOAc) to afford 0.96 g (3.86 mmol, 62% yield) of the ester as a clear liquid. IR (neat) 1732, 1497, 1454, 1368, 1227, 1116, 1032, 749, 699, 666; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.31-7.26 (m, 2H), 7.20-7.17 (m, 3H), 4.10 (q, J = 7.1 Hz, 2H), 2.58 (t, J = 7.7 Hz, 2H), 2.20 (s, 2H), 1.67-1.56 (m, 2H), 1.39-1.33 (m, 2H), 1.24 (t, J = 7.2 Hz, 3H), 0.98 (s, 6H); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 172.6, 142.9, 128.6, 128.5, 125.9, 60.0, 46.3, 42.2, 36.8, 33.5, 27.5, 26.4, 14.5; HRMS (ESI^+) calculated for [$C_{16}H_{24}O_2Na^+$] requires *m/z* 271.1669, found *m/z* 271.1677.

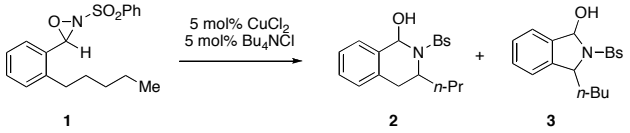
To a stirring suspension of 113 mg $LiAlH_4$ (2.98 mmol) in 12 mL Et_2O at 0 °C was added a solution of 570 mg (2.29 mmol) of the ester in 5 mL Et_2O dropwise. The reaction was stirred for approximately 5 min before being brought to reflux for 1h. The mixture was cooled to 0 °C, and water (125 μL) was carefully added dropwise, followed by 6M NaOH (125 μL), additional water, and $MgSO_4$ sufficient to sequester excess water. The slurry was stirred 30–60 min and filtered through Celite®. The cake was washed with Et_2O and the filtrate was washed with brine, dried over $MgSO_4$, filtered and concentrated. Purification by chromatography on SiO_2 (8:1 to 6:1 hexanes:EtOAc) afforded 430 mg (2.08 mmol, 91% yield) of the alcohol as a clear liquid. IR (neat) 3417 (br), 1636, 1497, 1453, 1365, 1031, 697, 666; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.29–7.26 (m, 2H), 7.19–7.16 (m, 3H), 3.66–3.63 (m, 2H), 2.57 (t, J = 7.7 Hz, 2H), 1.62–1.55 (m, 2H), 1.52–1.49 (m, 2H), 1.27–1.23 (m, 2H), 1.17 (s, 1H), 0.88 (s, 6H); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 142.9, 128.6, 128.5, 60.0, 44.6, 42.3, 36.9, 32.3, 27.7, 26.3; HRMS (EI^+) calculated for [$C_{14}H_{22}O^+$] requires *m/z* 206.1666, found *m/z* 206.1667.

Oxalyl chloride (0.27 mL, 3.05 mmol) was dissolved in 10 mL CH_2Cl_2 and brought to –78 °C. A solution of 0.32 mL DMSO (4.48 mmol) in 3 mL CH_2Cl_2 was added dropwise, and the reaction was allowed to stir for 5 min. A solution of 420 mg (2.04 mmol) of the alcohol in CH_2Cl_2 (3 mL) was added over 20 min via syringe pump, and the reaction was allowed to stir an additional 40 min. Over 45 min, 1.42 mL Et_3N (10.2 mmol) was added via syringe pump. After 5 min, the reaction was allowed to warm to room temperature. The reaction mixture was transferred to a separatory funnel and washed with 1N HCl. The phases were separated, and the aqueous phase was extracted with several portions of CH_2Cl_2. The combined organic extracts were washed with saturated $NaHCO_3$ and brine, dried over $MgSO_4$, and concentrated by rotary evaporation. Purification by chromatography on SiO_2 (10:1 hexanes:EtOAc) to afford 370 mg (1.81 mmol, 89% yield) of the aldehyde as a clear liquid. IR (neat) 1719, 1496, 1453, 1388, 1369, 750, 699, 666; ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.80 (t, J = 3.1 Hz, 1H), 7.29–7.26 (m, 2H), 7.20–7.17 (m, 3H), 2.59 (t, J = 7.7 Hz, 2H), 2.24 (d, J = 3.2 Hz, 2H), 1.65–1.58 (m, 2H), 1.40–1.36 (m, 2H), 1.03 (s, 6H); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 203.7, 142.5, 128.5(2), 128.5(0), 126.0, 54.9, 42.5, 36.7, 33.6, 27.7, 26.2; HRMS (EI^+) calculated for [$C_{14}H_{20}O^+$] requires *m/z* 204.1509, found *m/z* 204.1511.

The aldehyde (310 mg, 1.52 mmol) and 250 mg benzenesulfonamide (1.59 mmol) were dissolved in 40 mL CH_2Cl_2. To this solution was added 0.944 mL $Ti(OEt)_4$ (4.55 mmol) dropwise. The reaction was allowed to stir under N_2 for 2 h. Upon completion, the mixture was filtered through a short plug of silica gel and washed with several portions of ethyl acetate. The filtrate was concentrated by rotary evaporation, and the residue was dissolved in 20 mL toluene. The dissolved crude was added to a solution of 1.76 g K_2CO_3 (12.8 mmol) in 20 mL water. The biphasic mixture was subjected to vigorous stirring, and a solution of 1.50 g Oxone® (2.43 mmol) in 20 mL water was added slowly. After 45 min, the reaction was poured into a separatory funnel. The phases were separated, the aqueous layer was extracted twice with Et_2O. The combined organic extracts were washed with brine, dried over

$MgSO_4$, and concentrated by rotary evaporation. Purification by chromatography on SiO_2 (10:1 hexanes:EtOAc) afforded 290 mg (0.81 mmol, 53% yield) of the oxaziridine as a clear liquid. IR (neat) 1497, 1352, 1171, 1090, 733, 689, 666; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.99–7.97 (m, 2H), 7.74–7.70 (m, 1H), 7.61–7.58 (m, 2H), 7.29–7.25 (m, 2H), 7.20–7.17 (m, 3H), 4.71 (t, J = 5.5, 1H), 2.64–2.54 (m, 2H), 1.70–1.55 (m, 4H), 1.38–1.34 (m, 2H), 1.00 (d, J = 7.9, 6H); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 142.6, 135.1, 135.1, 129.5, 129.4, 128.6, 128.5, 126.0, 76.6, 42.7, 42.3, 36.7, 32.8, 27.6, 27.5, 26.2; HRMS (ESI^+) calculated for $[C_{20}H_{25}NO_3SNH_4^+]$ requires *m/z* 377.1894, found *m/z* 377.1899.

III. Cu-catalyzed intramolecular C–H aminations



1 2 3

Exploratory reaction (eq 1):

A stock solution was prepared of 16.1 mg (0.12 mmol) $CuCl_2$, 33.3 mg (0.12 mmol) Bu_4NCl in 1.2 mL CH_2Cl_2. This solution was allowed to stir for 30 minutes, at which time 0.40 mL of this solution was added to a 1.5 dram vial containing 265.2 mg (0.8 mmol) oxaziridine **1**. The reaction was stirred 4 h, at which time it was quenched with aqueous NH_4Cl and diluted with EtOAc. The phases were separated, and the aqueous phase was extracted twice with EtOAc. The combined organic extracts were washed with brine, dried over $MgSO_4$, and concentrated by rotary evaporation. An internal standard, 1,4-bis(trimethylsilyl)benzene (11.3 mg, 0.0508 mmol) was added, and the entire mixture was dissolved in minimal $CDCl_3$. An aliquot was diluted with additional $CDCl_3$ in an NMR tube, and a ^1H NMR spectrum with recycle delay of 4 s revealed a yield of 18% compared to the internal standard with a regioselectivity of 1.63:1, favoring the six-membered cyclization product (**2**). Major regioisomer (**2**): white solid, m.p. 116–117 °C; IR (ATR) 1450, 1409, 1328, 1168, 1091, 1016, 919, 867, 787, 728, 670; ^1H NMR (500 MHz, $CDCl_3$) δ 7.86–7.82 (m, 2H), 7.56–7.45 (m, 4H), 7.29–7.22 (m, 2H), 7.04 (d, J = 7.3 Hz, 1H), 6.20 (d, J = 3.8 Hz, 1H), 4.25–4.21 (m, 1H), 3.52 (d, J = 3.9 Hz, 1H), 2.69–2.61 (m, 2H), 1.73–1.64 (m, 1H), 1.50–1.34 (m, 3H), 0.86 (t, J = 7.2 Hz, 3H); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 141.1, 133.2, 132.9, 132.1, 129.5, 129.2, 128.7, 128.3, 127.2, 126.9, 76.3, 51.4, 36.4, 33.1, 20.2, 14.0; HRMS (ESI^+) calculated for [$C_{18}H_{21}NO_3SNa^+$] requires *m/z* 354.1135, found *m/z* 354.1149. Minor regioisomer (**3**): Isolated as clear liquid; IR (neat) 3457 (br), 2928, 1636, 1340, 1163, 1022, 719; ^1H NMR (500 MHz, $CDCl_3$) δ 7.91–7.89 (m, 2H), 7.57–7.54 (m, 1H), 7.51–7.48 (m, 2H), 7.41–7.40 (m, 1H), 7.37–7.31 (m, 2H), 7.13 (d, J = 7.3 Hz, 1H), 6.46 (d, J = 4.8 Hz, 1H), 4.87–4.86 (m, 1H), 3.35 (d, J = 4.6 Hz, 1H), 2.15–2.08 (m, 1H), 1.94–1.88 (m, 1H), 1.42–1.33 (m, 1H), 1.26–1.19 (m, 2H), 0.94–0.83 (m, 1H), 0.79 (t, J = 7.4 Hz, 3H); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 140.1, 139.1, 137.1, 133.2, 129.9, 129.5, 128.4, 127.4, 124.3, 122.5, 87.2, 65.0, 35.2, 25.3, 22.8, 14.1; HRMS (ESI^+) calculated for [$C_{18}H_{21}NO_3SNa^+$] requires *m/z* 354.1135, found *m/z* 354.1122.

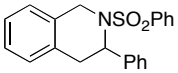
General Procedure **A**: Intramolecular C–H amination for aromatic oxaziridines (Table 1)

A solution of $CuCl_2$ (2 mol%) and LiCl (4 mol%) in acetone was added to a 1.5 dram vial containing the oxaziridine substrate. The vial was sealed with a Teflon cap, and the reaction was allowed to stir for the indicated period of time. Upon completion, the solution was diluted with ethyl acetate and washed with saturated aqueous NH_4Cl. The aqueous layer was extracted twice with EtOAc, and the combined organic layers were washed with brine, dried over $MgSO_4$, and concentrated by rotary evaporation. The residue was then dissolved in THF and stirred under an atmosphere of nitrogen. HCl (2 M in Et_2O, 4.0 equiv) was added dropwise. After 20 min, $NaBH(OAc)_3$ (2.0 equiv) was added in one portion. After 75 min, the reaction was quenched with aqueous 1 N HCl. The mixture was neutralized with aqueous $NaHCO_3$, the THF was removed by rotary evaporation, and the remaining aqueous solution was extracted twice with EtOAc. The organic extracts were washed with brine, dried over $MgSO_4$, and concentrated by rotary evaporation. Purification by flash column chromatography on SiO_2 afforded the product.

General Procedure **B**: Intramolecular C–H amination for aliphatic oxaziridines (Table 2)

A solution of $CuCl_2$ and LiCl in acetone was added to a 1.5 dram vial containing the oxaziridine substrate. The vial was sealed with a Teflon cap, and the reaction was allowed to stir for the indicated period of time. Upon completion, the solvent was removed by rotary evaporation, and the residue was dissolved in CH_2Cl_2. HCl (2 M in Et_2O, 4.0 equiv) was added dropwise. After 20 min, the reaction mixture was partitioned between EtOAc and aqueous 1 N HCl. The aqueous layer was extracted twice with EtOAc, and the combined organic layers were washed with brine, dried over $MgSO_4$, and concentrated by rotary evaporation. Purification by flash column chromatography on SiO_2 afforded the product.

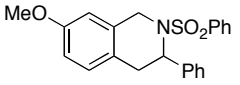
Table 1, entry 1



Prepared according to general procedure **A** using 146.2 mg (0.4 mmol) oxaziridine **4**, 1.1 mg (0.008 mmol) $CuCl_2$, 0.7 mg (0.016 mmol) LiCl, and 0.8 mL acetone, and a reaction time of 2 h. The reductive amination was carried out with 0.8 mL (1.6 mmol) HCl (2M in Et_2O), 170 mg (0.8

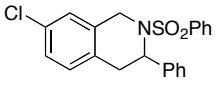
mmol) $NaBH(OAc)_3$, and 5.0 mL THF, and a reaction time of 80 minutes. Purification by chromatography on SiO_2 (5:1 to 4:1 hexanes:acetone) afforded 113.6 mg (0.325 mmol, 81% yield) of the tetrahydroisoquinoline as a white solid (m.p. 120–122 °C). IR (ATR) 1498, 1446, 1325, 1162, 1094, 1057, 935, 750, 723, 693; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.76–7.74 (m, 2H), 7.48–7.44 (m, 1H), 7.37–7.34 (m, 2H), 7.25–7.17 (m, 5H), 7.13–7.10 (m, 2H), 7.04–6.97 (m, 2H), 5.39 (t, J = 4.6 Hz, 1H), 4.73 (d, J = 16.5 Hz, 1H), 4.20 (d, J = 16.5 Hz, 1H), 3.10–3.02 (m, 2H); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 140.3, 140.0, 132.7, 132.6, 132.5, 129.1, 128.8, 128.6, 127.6, 127.4, 127.3, 127.2, 126.6, 126.0, 55.0, 44.3, 32.5; HRMS (ESI^+) calculated for $[C_{21}H_{19}NO_2SNa^+]$ requires *m/z* 372.1029, found *m/z* 372.1026.

Table 1, entry 2



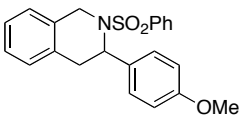
Prepared according to general procedure **A** using 158.2 mg (0.4 mmol) oxaziridine **S-1**, 1.1 mg (0.008 mmol) $CuCl_2$, 0.7 mg (0.016 mmol) LiCl, and 0.8 mL acetone, and a reaction time of 75 min. The reductive amination was carried out with 0.8 mL (1.6 mmol) HCl (2M in Et_2O), 170 mg (0.8 mmol) $NaBH(OAc)_3$, and 7.0 mL THF, and a reaction time of 75 minutes. Purification by chromatography on SiO_2 (4:1 to 3:1 hexanes:EtOAc) afforded 123 mg (0.324 mmol, 81% yield) of the tetrahydroisoquinoline as a clear liquid. IR (neat) 1614, 1506, 1447, 1326, 1237, 1164, 1091, 1052, 929, 729, 666; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.76–7.74 (m, 2H), 7.49–7.45 (m, 1H), 7.39–7.36 (m, 2H), 7.20 (m, 5H), 6.94 (d, J = 8.5 Hz, 1H), 6.69 (dd, J = 8.2, 2.8 Hz, 1H), 6.52 (d, J = 2.7 Hz, 1H), 5.38 (t, J = 4.6 Hz, 1H), 4.70 (d, J = 16.8 Hz, 1H), 4.15 (d, J = 16.8 Hz, 1H), 3.74 (s, 3H), 2.99 (d, J = 4.6 Hz, 2H); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 158.3, 140.4, 139.9, 133.5, 132.6, 129.8, 129.1, 128.6, 127.6, 127.4, 127.3, 124.6, 113.5, 110.9, 55.4, 55.1, 44.4, 31.4; HRMS (EI^+) calculated for $[C_{22}H_{21}SO_3N^+]$ requires *m/z* 379.1237, found *m/z* 379.1234.

Table 1, entry 3



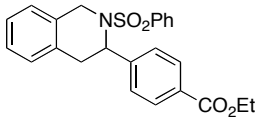
Prepared according to general procedure **A** using 160.0 mg (0.4 mmol) oxaziridine **S-2**, 1.1 mg (0.008 mmol) $CuCl_2$, 0.7 mg (0.016 mmol) LiCl, and 0.8 mL acetone, and a reaction time of 75 min. The reductive amination was carried out with 0.8 mL (1.6 mmol) HCl (2M in Et_2O), 170 mg (0.8 mmol) $NaBH(OAc)_3$, and 7.0 mL THF, and a reaction time of 75 minutes. Purification by chromatography on SiO_2 (4:1 hexanes:EtOAc) afforded 133 mg (0.346 mmol, 87% yield) of the tetrahydroisoquinoline as a white solid (m.p. 129–130 °C). IR (neat) 1601, 1488, 1447, 1347, 1164, 1091, 892, 726, 690; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.76–7.74 (m, 2H), 7.51–7.47 (m, 1H), 7.40–7.37 (m, 2H), 7.24–7.16 (m, 5H), 7.10 (dd, J = 8.2, 2.0 Hz, 1H), 6.99–6.97 (m, 2H), 5.40 (t, J = 4.6 Hz, 1H), 4.70 (d, J = 16.9 Hz, 1H), 4.12 (d, J = 17.2 Hz, 1H), 3.06–2.98 (m, 2H); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 140.2, 139.3, 134.2, 132.8, 132.2, 131.3, 130.1, 129.2, 128.7, 127.8, 127.6, 127.3, 127.2, 126.0, 54.7, 43.8, 31.6; HRMS (ESI^+) calculated for $[C_{21}H_{18}ClNO_2SNa^+]$ requires *m/z* 406.0639, found *m/z* 406.0652.

Table 1, entry 4



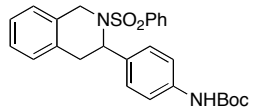
Prepared according to general procedure **A** using 158.2 mg (0.4 mmol) oxaziridine **S-3**, 1.1 mg (0.008 mmol) $CuCl_2$, 0.7 mg (0.016 mmol) LiCl, and 0.8 mL acetone, and a reaction time of 75 min. (The reaction was worked up with $NaHCO_3$ in place of NH_4Cl, and care was taken not to expose the product to acid, which is believed to cause decomposition.) The reductive amination was carried out with 0.8 mL (1.6 mmol) HCl (2M in Et_2O), 170 mg (0.8 mmol) $NaBH(OAc)_3$, and 5.0 mL THF, and a reaction time of 75 minutes. Purification by chromatography on SiO_2 gradient (4:1 to 3:1 hexanes:acetone) afforded 116 mg (0.306 mmol, 76% yield) of the tetrahydroisoquinoline as a white solid (m.p. 106–105 °C). IR (neat) 1611, 1513, 1446, 1332, 1252, 1164, 1091, 1035, 837, 751, 690; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.75–7.74 (m, 2H), 7.47–7.44 (m, 1H), 7.38–7.34 (m, 2H), 7.13–7.09 (m, 4H), 7.05–7.02 (m, 1H), 7.00–6.97 (m, 1H), 6.73–6.70 (m, 2H), 5.37 (dd, J = 5.5, 3.4 Hz, 1H), 4.71 (d, J = 16.5 Hz, 1H), 4.16 (d, J = 16.5 Hz, 1H), 3.72 (s, 3H), 3.07–2.99 (m, 2H); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 159.0, 140.4, 132.8, 132.6, 132.4, 131.7, 129.1, 128.8, 128.6, 127.3, 127.2, 126.6, 126.0, 113.9, 55.4, 54.3, 44.0, 32.3; HRMS (ESI^+) calculated for $[C_{22}H_{21}SO_3NH^+]$ requires *m/z* 380.1315, found *m/z* 380.1309.

Table 1, entry 5



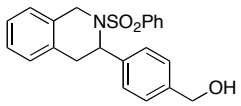
Prepared according to general procedure **A** using 175 mg (0.4 mmol) oxaziridine **S-4**, 1.1 mg (0.008 mmol) $CuCl_2$, 0.7 mg (0.016 mmol) LiCl, and 0.8 mL acetone, and a reaction time of 1 h. The reductive amination was carried out with 0.8 mL (1.6 mmol) HCl (2M in Et_2O), 169.6 mg (0.8 mmol) $NaBH(OAc)_3$, and 7.0 mL THF, and a reaction time of 75 minutes. Purification by chromatography on SiO_2 (20:1 toluene:EtOAc) afforded 125 mg (0.297 mmol, 74% yield) of the oxaziridine as a clear liquid. IR (neat) 1714, 1611, 1446, 1277, 1165, 1105, 726, 666; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.88–7.86 (m, 2H), 7.77–7.75 (m, 2H), 7.51–7.47 (m, 1H), 7.41–7.37 (m, 2H), 7.26–7.25 (m, 2H), 7.14-7.10 (m, 2H), 7.02-7.00 (m, 2H), 5.40 (dd, J = 5.8, 3.7 Hz, 1H), 4.70 (d, J = 16.2 Hz, 1H), 4.33 (q, J = 7.2 Hz, 2H), 4.26 (d, J = 16.2 Hz, 1H), 3.08 (dd, J = 16.2, 6.1 Hz, 1H), 3.03 (dd, J = 16.2, 3.7 Hz, 1H), 1.35 (t, J = 7.2 Hz, 3H); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 166.4, 145.4, 139.9, 132.8, 132.5, 132.4, 129.9, 129.8, 129.2, 128.7, 127.6, 127.3, 127.2, 126.9, 126.1; HRMS (ESI^+) calculated for [$C_{24}H_{23}NO_4SNa^+$] requires *m/z* 443.1240, found *m/z* 443.1231.

Table 1, entry 6



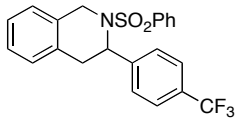
Prepared according to general procedure **A** using 141.5 mg (0.29 mmol) oxaziridine **S-5**, 0.8 mg (0.006 mmol) $CuCl_2$, 0.5 mg (0.012 mmol) LiCl, and 0.6 mL acetone, and a reaction time of 1 h. The reductive amination was carried out with 0.6 mL (1.2 mmol) HCl (2M in Et_2O), 147.0 mg (0.69 mmol) $NaBH(OAc)_3$, and 7.0 mL THF, and a reaction time of 30 minutes. Purification by chromatography on SiO_2 (5:1 to 4:1 hexanes:EtOAc) afforded 98.1 mg (0.21 mmol, 72% yield) of the tetrahydroisoquinoline as a white solid (m.p. 195–198 °C (dec)). IR (neat) 3350, 2972, 2923, 2856, 1718, 1526, 1322, 1236; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.76-7.75 (m, 2H), 7.48-7.45 (m, 1H), 7.38-7.35 (m, 2H), 7.18 (d, J = 8.6 Hz, 2H), 7.12-7.08 (m, 4H), 7.03-6.96 (m, 2H), 6.51 (s, 1H), 5.37-5.35 (m, 1H), 4.7 (d, J = 16.5 Hz, 1H), 4.16 (d, J = 16.9 Hz, 1H), 3.07-3.00 (m, 2H), 1.48 (s, 9H); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 152.9, 140.3, 137.8, 134.2, 132.6, 132.4, 129.1, 128.8, 128.0, 127.3, 127.2, 126.6, 126.0, 118.6, 80.7, 54.4,44.1, 32.3, 28.5; HRMS (ESI^+) calculated for [$C_{26}H_{32}N_3O_4S^+$] [$M+NH_4^+$] requires *m/z* 482.2109, found *m/z* 482.2102.

Table 1, entry 7



Prepared according to general procedure **A** using 112.7 mg (0.28 mmol) oxaziridine **S-6**, 0.8 mg (0.006 mmol) $CuCl_2$, 0.5 mg (0.012 mmol) LiCl, and 0.6 mL acetone, and a reaction time of 1 h. The reductive amination was carried out with 0.6 mL (1.0 mmol) HCl (2M in Et_2O), 136 mg (0.64 mmol) $NaBH(OAc)_3$, and 5.5 mL THF, and a reaction time of 30 minutes. Purification by chromatography on SiO_2 (CH_2Cl_2 to 25:1 CH_2Cl_2:acetone) afforded 72.1 mg (0.19 mmol, 67% yield) of the tetrahydroisoquinoline as a white solid (m.p. 112–115 °C). IR (neat) 3540, 3061, 2922, 2858, 1446, 1330; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.75 (d, J = 7.9 Hz, 2H), 7.47 (t, J = 7.9 Hz, 1H), 7.38 (t, J = 7.9 Hz, 2H), 7.20 (s, 4H), 7.12 (m, 2H), 7.03 (dd, J = 5.0, 2.8 Hz, 1H), 6.98 (dd, J = 5.0, 2.8 Hz, 1H), 5.38 (t, J = 4.4 Hz, 1H), 4.70 (d, J = 16.0 Hz, 1H), 4.60 (s, 2H), 4.21 (d, J = 16.0 Hz, 1H), 3.05 (d, J = 4.4 Hz, 2H), 1.69 (br s, 1H); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 140.3, 140.2, 139.5, 132.7, 132.5, 129.1, 128.8, 127.5, 127.4, 127.3, 127.3, 126.7, 126.1, 65.1, 54.8, 44.4, 32.6;HRMS (ESI^+) calculated for [$C_{22}H_{22}N_2O_3S^+$] [$M+NH_4^+$] requires *m/z* 397.1581, found *m/z* 397.1584.

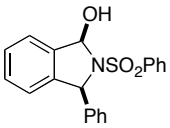
Table 1, entry 8



Prepared according to general procedure **A** using 173.4 mg (0.4 mmol) oxaziridine **S-7**, 1.1 mg (0.008 mmol) $CuCl_2$, 0.7 mg (0.016 mmol) LiCl, and 0.8 mL acetone, and a reaction time of 3.5 h. The reductive amination was carried out with 0.8 mL (1.6 mmol) HCl (2M in Et_2O), 169.6 mg (0.8 mmol) $NaBH(OAc)_3$, and 7.0 mL THF, and a reaction time of 90 minutes. Purification by chromatography on SiO_2 (4:1 hexanes:EtOAc) afforded 102.4 mg (0.245 mmol, 61% yield) of the tetrahydroisoquinoline as a white solid (m.p. 104–105 °C). IR (neat) 1620, 1447, 1326, 1165, 1120, 1069, 723, 666; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.75–7.73 (m, 2H), 7.51–7.47 (m, 1H), 7.46 (d, J = 8.3 Hz, 2H), 7.40–7.37 (m, 2H), 7.31 (d, J = 8.0 Hz, 2H), 7.16–7.11 (m, J = Hz, 2H), 7.04-7.00 (m, 2H), 5.40–5.38 (m, 1H), 4.70 (d, J = 16.3 Hz, 1H), 4.28 (d, J = 16.1 Hz, 1H), 3.09 (dd, J = 16.1, 6.2 Hz, 1H), 3.01 (dd, J = 16.2,

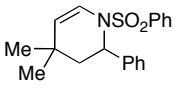
3.3 Hz, 1H); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 144.5, 139.8, 132.9, 132.5, 132.3, 129.8 (q, J = 33 Hz), 129.2, 128.7, 127.7, 127.6, 127.3, 127.0, 126.2, 125.6 (q, J = 4 Hz), 124.2 (q, J = 272 Hz), 55.1, 44.8, 33.2; HRMS (ESI$^+$) calculated for [$C_{22}H_{18}F_3NO_2SNa^+$] requires *m/z* 440.0908, found *m/z* 440.0898.

Table 1, entry 9



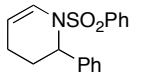
Prepared according to general procedure **A** using 140.6 mg (0.4 mmol) oxaziridine **S-8**, 1.1 mg (0.008 mmol) $CuCl_2$, 0.7 mg (0.016 mmol) LiCl, and 0.8 mL acetone, and a reaction time of 4 h. Saturated $NaHCO_3$ was used in the workup instead of NH_4Cl, and no reductive amination was performed. Purification by chromatography on SiO_2 (3:1 to 2:1 hexanes:EtOAc) afforded 118 mg (0.336 mmol, 84% yield) of the aminal as a white solid, which decomposes readily, especially in the presence of acid. IR (neat) 3448, 1654, 1340, 1160, 1097, 1022, 724; ^{1}H NMR (500 MHz, acetone) δ 7.77–7.72 (m, 2H), 7.52–7.49 (m, 1H), 7.47 (d, J = 8.1 Hz, 1H), 7.42–7.38 (m, 4H), 7.33 (t, J = 7.3 Hz, 1H), 7.28 (td, J = 7.4, 1.2 Hz, 1H), 7.22–7.17 (m, 3H), 6.97 (d, J = 7.6 Hz, 1H), 6.78 (d, J = 6.6 Hz, 1H), 6.03 (d, J = 6.6 Hz, 1H), 5.90 (s, 1H); ^{13}C NMR (125.7 MHz, acetone) δ 142.8, 142.6, 141.9, 139.3, 133.7, 130.7, 130.1, 129.5(1), 129.4(7), 129.1, 128.8, 128.6, 125.5, 124.6, 88.3, 69.4; HRMS (ESI$^+$) calculated for [$C_{20}H_{17}O_3NSNa^+$] requires *m/z* 374.0822, found *m/z* 374.0816. See NOESY-1D data for stereochemical assignment.

Table 2, entry 1



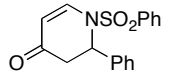
Prepared according to general procedure **B** using 172.7 mg (0.5 mmol) oxaziridine **5**, 1.3 mg (0.010 mmol) $CuCl_2$, 0.9 mg (0.02 mmol) LiCl, 1.0 mL acetone, and a reaction time of 2 h. Purification by chromatography on SiO_2 (5:1 to 4:1 hexanes:EtOAc) afforded 121 mg (0.370 mmol, 74% yield) of the product as clear liquid. IR (neat) 1651, 1496, 1447, 1362, 1265, 1167, 1095, 970, 931, 872, 730, 662; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.78–7.76 (m, 2H), 7.57 (tt, J = 7.5, 1.2 Hz, 1H), 7.51–7.48 (m, 2H), 7.28–7.24 (m, 4H), 7.21–7.17 (m, 1H), 6.78 (dd, J = 8.2, 0.6 Hz, 1H), 4.97–4.93 (m, 2H), 1.92 (ddd, J = 13.8, 5.1, 1.2 Hz, 1H), 1.41 (dd, J = 13.7, 5.5 Hz, 1H), 0.73 (s, 3H), 0.49 (s, 3H); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 140.8, 138.7, 133.0, 129.1, 128.4, 127.3, 127.0, 126.4, 122.4, 121.4, 56.0, 43.2, 31.1, 29.2, 28.6; HRMS (ESI$^+$) calculated for [$C_{19}H_{21}O_2NSNa^+$] requires *m/z* 350.1186, found *m/z* 350.1198.

Table 2, entry 2



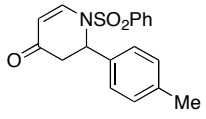
Prepared according to general procedure **B** using 210 mg (0.662 mmol) oxaziridine **S-9**, 1.8 mg (0.013 mmol) $CuCl_2$, 1.1 mg (0.026 mmol) LiCl, 1.3 mL acetone, and a reaction time of 5 h. Purified by chromatography using 2:1 hexanes:dichloromethane (dichloromethane impregnated with NH_3) to afford 26 mg (0.087 mmol, 13% yield) of the product as a white solid (m.p. 125–126 °C). IR (ATR) 1655, 1446, 1336, 1276, 1172, 1097, 941, 724, 689; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.76-7.74 (m, 2H), 7.56–7.52 (m, 1H), 7.47–7.43 (m, 2H), 7.26–7.17 (m, 6H), 6.93–6.91 (m, 1H), 5.19 (s, 1H), 5.07–5.03 (m, 1H), 1.94–1.89 (m, 1H), 1.78 (dt, J = 17.7, 5.8 Hz, 1H), 1.66–1.58 (m, 1H); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 140.3, 139.4, 132.8, 129.2, 128.5, 127.2, 127.1, 126.1, 124.7, 108.9, 56.2, 26.5, 17.1; HRMS (ESI$^+$) calculated for [$C_{17}H_{17}NO_2SH^+$] requires *m/z* 300.1053, found *m/z* 300.1058.

Table 2, entry 3



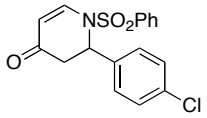
Prepared according to general procedure **B** using 225.3 mg (0.6 mmol) oxaziridine **S-10**, 1.6 mg (0.012 mmol) $CuCl_2$, 1.0 mg (0.024 mmol) LiCl, 1.2 mL acetone, and a reaction time of 2 h. Purification by chromatography on SiO_2 (3:1 hexanes:acetone) afforded 138 mg (0.440 mmol, 73% yield) of the product as white solid (m.p. 133–135 °C). IR (ATR) 1667, 1598, 1370, 1294, 1167, 1054, 764, 730, 689; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.84–7.82 (m, 1H), 7.72–7.70 (m, 2H), 7.59–7.55 (m, 1H), 7.45–7.42 (m, 2H), 7.22–7.13 (m, 5H), 5.55 (d, J = 7.5 Hz, 1H), 5.43 (dd, J = 8.6, 1.2 Hz, 1H), 2.87 (dd, J = 16.5, 7.2 Hz, 1H), 2.70–2.66 (m, 1H); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 190.6, 142.6, 138.7, 137.0, 134.0, 129.6, 129.0, 128.4, 127.2, 126.4, 108.7, 58.0, 42.1; HRMS (ESI$^+$) calculated for [$C_{17}H_{15}NO_3SNa^+$] requires *m/z* 336.0665, found *m/z* 336.0651.

Table 2, entry 4



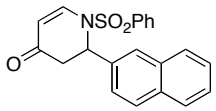
Prepared according to general procedure **B** using 74.5 mg (0.19 mmol) oxaziridine **S-11**, 0.5 mg (0.004 mmol) $CuCl_2$, 0.3 mg (0.008 mmol) LiCl, 0.38 mL acetone, and a reaction time of 2 h. Purification by chromatography on SiO_2 (3:1 hexanes:EtOAc) afforded 56.9 mg (0.17 mmol, 92% yield) of the product as a pale brown solid (m.p. 110–112 °C). IR (thin film) 1669, 1597, 1448, 1366, 1288, 1171, 1090, 1052, 912, 817, 730, 666; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.79 (dd, J = 8.2, 1.3 Hz, 1H), 7.73-7.71 (m, 2H), 7.60-7.57 (m, 1H), 7.46-7.43 (m, 2H), 7.06-6.98 (m, 4H), 5.50 (d, J = 7.1 Hz, 1H), 5.42 (dd, J = 8.2, 1.1 Hz, 1H), 2.81 (dd, J = 16.3, 7.3 Hz, 1H), 2.66 (dt, J = 16.5, 1.7 Hz, 1H), 2.27 (s, 3H); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 190.8, 142.5, 138.9, 138.3, 134.1, 133.9, 129.6(4), 129.5(8), 127.2, 126.4, 108.8, 57.8, 42.0, 29.8, 29.6, 21.2; HRMS (ESI$^+$) calculated for [$C_{17}H_{15}NO_3SNa^+$] requires *m/z* 350.0822, found *m/z* 350.0825.

Table 2, entry 5



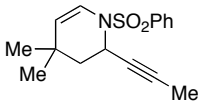
Prepared according to general procedure **B** using 164 mg (0.4 mmol) oxaziridine **S-12**, 1.1 mg (0.008 mmol) $CuCl_2$, 0.7 mg (0.016 mmol) LiCl, 0.8 mL acetone, and a reaction time of 1.5 h. Purification by chromatography on SiO_2 (1:0 to 20:1 dichloromethane:EtOAc) to afford 87 mg (0.250 mmol, 63% yield) of the product as clear liquid. IR (film) 1669, 1597, 1367, 1289, 1172, 1090, 1053, 758; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.81 (dd, J = 8.4, 1.4 Hz, 1H), 7.74–7.72 (m, 2H), 7.64–7.60 (m, 1H), 7.49–7.46 (m, 2H), 7.18–7.15 (m, 2H), 7.11–7.09 (m, 2H), 5.51 (d, J = 7.0 Hz, 1H), 5.44 (dd, J = 8.4, 1.1 Hz, 1H), 2.83 (dd, J = 7.3 Hz, 1H), 2.66–2.62 (m, 1H); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 190.2, 142.4, 138.7, 135.7, 134.5, 134.2, 129.8, 129.1, 127.9, 127.2, 108.8, 57.4, 41.8; HRMS (EI$^+$) calculated for [$C_{17}H_{14}ClNO_3S^+$] requires *m/z* 347.0378, found *m/z* 347.0379.

Table 2, entry 6



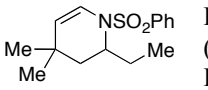
Prepared according to general procedure **B** using 170.2 mg (0.4 mmol) oxaziridine **S-13**, 1.1 mg (0.008 mmol) $CuCl_2$, 0.7 mg (0.016 mmol) LiCl, 0.8 mL acetone, and a reaction time of 1.5 h. Purification by chromatography on SiO_2 (1:0 to 10:1 toluene:EtOAc) to afford 100 mg (0.275 mmol, 69% yield) of the product as white solid (m.p. 161–162 °C). IR (neat) 3061, 1672, 1597, 1171, 1090, 1053, 729; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.88–7.86 (m, 1H), 7.76–7.63 (m, 5H), 7.52 (s, 1H), 7.49–7.42 (m, 3H), 7.36–7.28 (m, 3H), 5.71 (d, J = 7.0 Hz, 1H), 5.47 (dd, J = 8.2, 1.3 Hz, 1H), 2.92 (dd, J = 16.5, 6.8 Hz, 1H), 2.82–2.78 (m, 1H); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 190.6, 142.6, 138.8, 134.2, 134.0, 133.0(8), 133.0(5), 129.6, 129.1, 128.2, 127.7, 127.2, 126.6(9), 126.6(6), 125.8, 124.1, 108.9, 58.2, 41.9; HRMS (EI$^+$) calculated for [$C_{21}H_{17}NO_2S^+$] requires *m/z* 363.0924, found *m/z* 363.0908.

Table 2, entry 7



Prepared according to general procedure **B** using 60.5 mg (0.2 mmol) oxaziridine **S-14**, 2.7 mg (0.02 mmol) $CuCl_2$, 0.8 mg (0.02 mmol) LiCl, 2.0 mL acetone at 40 °C, and a reaction time of 1.5 h. Purified by chromatography using 20:1 to 15:1 hexanes:EtOAc to afford 39.4 mg (0.14 mmol, 69% yield) of the product as clear liquid. IR (neat) 2957, 2921, 1447, 1355, 1254, 1165, 1096, 1062; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.85 (d, J = 7.9 Hz, 2H), 7.56 (t, J = 7.9 Hz, 1H), 7.50 (t, J = 7.9 Hz, 2H), 6.49 (d, J = 8.5 Hz, 1H), 4.87 (d, J = 8.5 Hz, 1H), 4.82 (ddd, J = 5.1, 2.4, 2.1 Hz, 1H), 1.81 (dd, J = 13.3, 2.1 Hz, 1H), 1.58 (dd, J = 13.3, 5.1 Hz, 1H), 1.53 (d, J = 2.4 Hz, 3H), 1.21 (s, 3H), 0.90 (s, 3H); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 139.4, 132.9, 128.9, 127.7, 120.8, 119.4, 81.0, 43.9, 41.2, 31.9, 29.4, 29.3, 3.6; HRMS (ESI$^+$) calculated for [$C_{16}H_{20}NO_2S^+$] requires *m/z* 290.1210, found 290.1205.

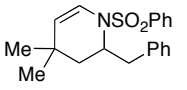
Table 2, entry 8



Prepared according to general procedure **B** using 89.2 mg (0.3 mmol) oxaziridine **S-15**, 2.0 mg (0.015 mmol) $CuCl_2$, 1.3 mg (0.03 mmol) LiCl, 0.6 mL acetone, and a reaction time of 3 h. Purified by chromatography using 10:1 hexanes:EtOAc to afford 31.2 mg (0.112 mmol, 37% yield) of the product as clear liquid. IR (neat) 1647, 1447, 1358, 1244, 1167, 1097, 998, 728, 690; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.81–7.78 (m, 2H), 7.58–7.55 (m, 1H), 7.52–7.48 (m, 2H), 6.46 (dd, J = 8.2, 0.9 Hz, 1H), 4.96 (dd, J = 8.2, 1.5 Hz, 1H), 3.74–3.69 (m, 1H), 1.86–1.77 (m, 1H), 1.60–1.52 (m, 1H), 1.48 (ddd, J = 14.2, 2.9, 1.5 Hz, 1H),

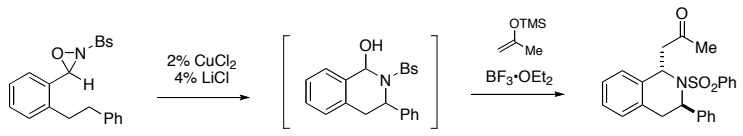
1.01 (s, 3H), 0.98 (t, J = 7.3 Hz, 3H), 0.88 (dd, J = 14.4, 5.5 Hz, 1H), 0.64 (s, 3H); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 139.0, 132.7, 129.0, 127.1, 122.8, 121.3, 55.4, 38.0, 32.3, 29.7, 28.7, 26.7, 11.5; HRMS (ESI^+) calculated for [$C_{18}H_{17}NO_3SNa^+$] requires *m/z* 302.1186, found 302.1197.

Table 2, entry 9

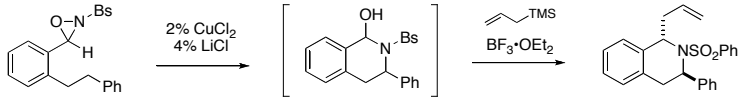


Prepared according to general procedure **B** using 143.8 mg (0.40 mmol) oxaziridine **S-16**, 2.7 mg (0.020 mmol) $CuCl_2$, 1.7 mg (0.040 mmol) LiCl, 0.8 mL acetone, and a reaction time of 3 h. Purification by chromatography on SiO_2 (10:1 to 9:1 hexanes:EtOAc) to afford 55 mg (0.161 mmol, 40% yield) of the product as clear liquid. IR (neat) 1653, 1496, 1357, 1166, 1094, 748, 655; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.81–7.79 (m, 2H), 7.57–7.54 (m, 1H), 7.51–7.48 (m, 2H), 7.33–7.30 (m, 2H), 7.24–7.22 (m, 3H), 6.55 (d, J = 8.3 Hz, 1H), 5.01 (dd, J = 8.2, 1.1 Hz, 1H), 4.03–3.98 (m, 1H), 3.23 (dd, J = 13.6, 5.7 Hz, 1H), 2.89 (dd, J = 13.7, 9.3 Hz, 1H), 1.46 (ddd, J = 14.2, 3.7, 1.2 Hz, 1H), 1.01 (s, 3H), 0.98 (dd, J = 14.2, 5.9 Hz, 1H), 0.60 (s, 3H); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 138.8, 138.7, 132.9, 129.6, 129.1, 128.6, 127.3, 126.6, 122.3, 121.7, 55.1, 40.3, 37.8, 31.9, 30.6, 28.7; HRMS (ESI^+) calculated for [$C_{20}H_{23}NO_2SNa^+$] requires *m/z* 364.1342, found *m/z* 364.1340.

IV. Synthetic Manipulations of the Aminal Intermediate

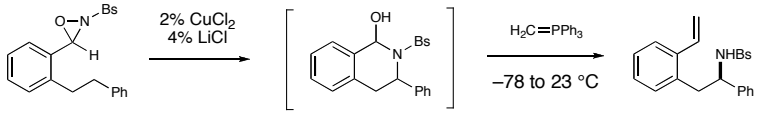


(1*S,3*R**)-1,2,3,4-Tetrahydro-*N*-benzensulfonyl-3-phenyl-1-(2-oxopropyl)isoquinoline (6)**. A solution of 2.0 mg $CuCl_2$ (0.015 mmol) and 1.3 mg LiCl (0.03 mmol) in 1.5 mL acetone was placed in a 2-dram vial and allowed to stir for 15 min. At this time, 274 mg oxaziridine **4** (0.75 mmol) was added. After 1 h, the solvent was removed by rotary evaporation, and the residue was partitioned between ethyl acetate and aqueous NH_4Cl. The aqueous layer was extracted twice with ethyl acetate, and the combined organic extracts were washed with brine, dried over $MgSO_4$, and concentrated by rotary evaporation. The residue was dissolved in dichloromethane (3 mL) and cooled to –78 °C. 2-(Trimethylsilyloxy)propene (0.5 mL, 2.88 mmol) was added, and the reaction was allowed to stir for 5 min under N_2. A 1 M solution of BF_3•OEt_2 in dichloromethane (1.13 mL, 1.13 mmol) was added over 75 minutes via syringe pump, and the reaction was subsequently allowed to gradually warm to 0 °C. The reaction was quenched with aqueous $NaHCO_3$, diluted with EtOAc, and partitioned in a separatory funnel. The aqueous layer was extracted twice with ethyl acetate, and the combined organic layers were washed with brine, dried over $MgSO_4$, and concentrated. ^{1}H NMR analysis of the unpurified reaction mixture in $CDCl_3$ revealed a >10:1 ratio of *trans*:*cis* diastereomers. Purification by flash column chromatography on SiO_2 (5:1 hexanes:EtOAc) afforded 196 mg (0.48 mmol, 64% yield) of the product as a white solid (m.p. 181–183 °C). IR (ATR) 1711, 1450, 1331, 1159, 1124, 1092, 1059, 966, 757, 738, 690; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.34-7.28 (d, 2H), 7.24 (d, J = 10.0 Hz, 2H), 7.16 (t, J = 7.4 Hz, 1H), 7.13-7.07 (m, 2H), 6.99-6.96 (m, 1H), 6.86 (d, J = 7.2 Hz, 1H), 6.81 (t, J = 7.8 Hz, 2H), 6.37 (d, J = 6.9 Hz, 2H), 5.60-5.58 (m, 1H), 5.53-5.51 (m, 1H), 3.69 (dd, J = 17.3, 2.7 Hz, 1H), 3.53 (dd, J = 14.8, 6.1 Hz, 1H), 2.96 (dd, J = 17.4, 9.2 Hz, 1H), 2.85 (dd, J = 15.2, 2.3 Hz, 1H), 2.11 (s, 3H); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 205.7, 140.5, 140.3, 138.7, 132.0, 131.6, 129.4, 128.4, 128.0, 127.9, 127.3, 127.2(4), 127.2(2), 127.1, 126.9, 58.2, 54.1, 53.9, 37.4, 30.8; HRMS (ESI^+) calculated for [$C_{24}H_{22}NO_3S^+$] requires *m/z* 403.1315, found *m/z* 404.1310. The *trans* stereochemistry of the major diastereomer was assigned by NOE correlations.



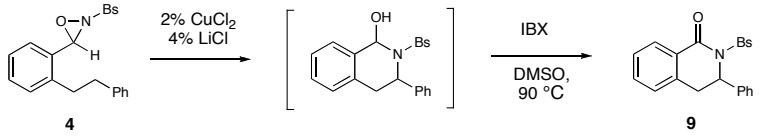
4 7

(1*S,3*R**)-1,2,3,4-Tetrahydro-*N*-benzensulfonyl-3-phenyl-1-(2-propenyl)isoquinoline (7)**. A solution of 4.0 mg $CuCl_2$ (0.03 mmol) and 2.5 mg LiCl (0.06 mmol) in 3 mL acetone was placed in a 2-dram vial and allowed to stir for 15 min. At this time, 548.2 mg oxaziridine **4** (1.5 mmol) was added. After 1h, the solvent was removed by rotary evaporation, and the residue was partitioned between ethyl acetate and aqueous NH_4Cl. The aqueous layer was extracted twice with ethyl acetate, and the combined organic layers were washed with brine, dried over $MgSO_4$, and concentrated. The residue was dissolved in dichloromethane (6 mL) and cooled to –78 °C. Allyltrimethylsilane (958 μL, 6.0 mmol) was added, and the reaction was allowed to stir for 5 min under N_2. A 1 M solution of BF_3•OEt_2 in dichloromethane (2.25 mL, 2.25 mmol) was added over 75 minutes via syringe pump, and the reaction was subsequently allowed to gradually warm to 0 °C. The reaction was quenched with aqueous $NaHCO_3$, diluted with EtOAc, and partitioned in a separatory funnel. The aqueous layer was extracted twice with ethyl acetate, and the combined organic layers were washed with brine, dried over $MgSO_4$, and concentrated. ^{1}H NMR analysis of the unpurified reaction mixture in C_6D_6 revealed a 5:1 ratio of *trans*:*cis* diastereomers. Purification by flash column chromatography using a solvent gradient (10:1 to 9:1 hexanes:EtOAc) afforded 511 mg (1.31 mmol, 87% yield) of both diastereomers of the allylated product as a white solid (m.p. 123–124 °C). Major diastereomer: IR (ATR) 1446, 1333, 1163, 1047, 913, 760, 694; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.30–7.25 (m, 3H), 7.18 (t, J = 7.3 Hz, 1H), 7.12–7.08 (m, 4H), 6.97–6.94 (m, 1H), 6.89 (d, J = 7.6 Hz, 1H), 6.82 (t, J = 7.8 Hz, 2H), 6.49 (d, J = 7.6 Hz, 2H), 5.73–7.65 (m, 1H), 5.42–5.40 (m, 1H), 5.06–4.98 (m, 3H), 3.58 (dd, J = 15.2, 5.9 Hz, 1H), 3.15–3.10 (m, 1H), 2.9 (dd, J = 15.2, 3.2 Hz, 1H), 2.69–2.63 (m, 1H); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 141.4, 140.6, 137.5, 134.5, 132.3, 131.8, 129.5, 128.3, 127.8(0), 127.7(6), 127.3, 127.1(1), 127.0(6), 127.0, 126.6, 118.4, 60.2, 57.9, 43.8, 36.7; HRMS (ESI^+) calculated for [$C_{24}H_{23}NO_2SNa^+$] requires *m/z* 412.1342, found *m/z* 412.1336. The *trans* stereochemistry of the major diastereomer was verified by X-ray crystallographic analysis.



4 8

***N*-(2-*o*-Vinylphenyl-1-phenylethyl) benzenesulfonamide (8).** A solution of 1.2 mg $CuCl_2$ (0.009 mmol) and 0.84 mg LiCl (0.020 mmol) in 0.96 mL acetone was prepared in a flame-dried 2-dram vial, and was allowed to stir for 15 minutes. A separate, 2-dram vial equipped with a stir bar was charged with 59.6 mg oxaziridine **4** (0.16 mmol). To the oxaziridine was added 0.32 mL of the stock solution. The reaction was allowed to stir for 1 h, at which time the solvent was removed by rotary evaporation. The residue was partitioned between ethyl acetate and aqueous NH_4Cl. The phases were separated, and the aqueous layer was extracted three times with ethyl acetate. The combined organic extracts were washed with brine, dried over $MgSO_4$, and concentrated by rotary evaporation. The residue was dissolved in 2.0 mL THF. The Wittig reagent was pre-formed as described[10] from a solution of 246.5 mg methyl triphenylphosphonium bromide (0.16 mmol, 4.3 equiv) in 1.0 mL THF by adding 0.59 mL *n*BuLi (1.08 M in hexanes, 0.64 mmol, 4.0 equiv). The dissolved crude was added to the solution of the ylide at room temperature. The reaction mixture was monitored by TLC and was allowed to stir for 1 h, at which time the ylide was quenched with acetone and the mixture was concentrated by rotary evaporation. Purification by chromatography on SiO_2 (3:1 hexanes:EtOAc) afforded 27.2 mg product (0.075 mmol, 47% yield) as a white semi-solid. IR (thin film) 1626, 1483, 1449, 1323, 1159, 1093, 1059, 990, 911, 837, 753, 721, 699, 688, 612; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.50-7.48 (m, 2H), 7.44-7.41 (m, 1H), 7.36 (d, J = 7.7 Hz, 1H), 7.27 (t, J = 7.8 Hz, 2H), 7.20-7.15 (m, 4H), 7.08-7.05 (m, 3H), 6.84-6.78 (m, 2H), 5.5 (dd, J = 17.5, 1.4 Hz, 1H), 5.27 (dd, J = 11.1, 1.3 Hz, 1H), 4.92 (s, 1H), 4.42 (q, J = 6.8 Hz, 1H), 3.10-3.02 (m, 2H); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 140.8, 140.0, 137.4, 134.2, 134.0, 132.4, 130.7, 128.9, 128.7, 128.1, 127.8, 127.6, 127.1, 126.7, 126.6, 117.0, 58.9, 41.9, 29.9; HRMS (ESI^+) calculated for [$C_{24}H_{22}NO_3SNa^+$] requires *m/z* 386.1186, found *m/z* 386.1180.



4 9

***N*-Benzenesulfonyl-3-phenyl-3,4-dihydro-1(2H)-isoquinolinone (9).** A solution of 2.3 mg $CuCl_2$ (0.018 mmol) and 1.4 mg LiCl (0.034 mmol) in 1.68 mL acetone was prepared in a flame-dried 2-dram vial, and was allowed to stir for 15 minutes. A separate, 2-dram vial equipped with a stir bar was charged with 103.9 mg oxaziridine **4** (0.28 mmol). To the oxaziridine was added 0.56 mL of the stock solution. The reaction was allowed to stir for 2 h, at which time the solvent was removed by rotary evaporation. The residue was partitioned between ethyl acetate and aqueous NH_4Cl. The phases were separated, and the aqueous layer was extracted three times with ethyl acetate. The combined organic extracts were washed with brine, dried over $MgSO_4$, and concentrated by rotary evaporation. The residue was dissolved in 0.7 mL DMSO and 2-iodoxybenzoic acid (627 mg, 2.24 mmol) was added. The reaction was slowly heated to 90 °C and was allowed to stir for 1 h, at which time the mixture was cooled and was diluted with diethyl ether. The reaction mixture was transferred to a separatory funnel and was washed with saturated aqueous $NaHSO_3$, $NaHCO_3$, and brine. The organic extracts were combined, dried over $MgSO_4$, and concentrated by rotary evaporation. Purification by chromatography on SiO_2 (3:1 hexanes:EtOAc) afforded 59.5 mg product (0.16 mmol, 58% yield) as a white solid (m.p. 168–170 °C). IR (thin film) 1685, 1604, 1449, 1353, 1244, 1172, 1115, 1060, 909, 833, 774, 733; ^{1}H (500 MHz, $CDCl_3$) δ 8.03 (d, *J* = 8.3 Hz, 1H), 7.82 (d, *J* = 8.3 Hz, 2H), 7.54 (t, *J* = 7.6 Hz, 1H), 7.39 (t, *J* = 7.6 Hz, 3H), 7.29 (t, *J* = 7.6 Hz, 1H), 7.16 (m, 3H), 7.04 (d, *J* = 7.6 Hz, 1H), 7.02 (d, *J* = 7.6 Hz, 2H), 6.15 (d, *J* = 6.1 Hz, 1H), 3.84 (dd, *J* = 16.7, 6.1 Hz, 1H), 3.20 (d, *J* = 16.7 Hz, 1H),^{13}C NMR (125.7 MHz, $CDCl_3$) δ 163.5, 139.4, 139.0, 136.4, 134.1, 133.8, 129.5, 128.9, 128.8, 128.5, 128.4, 128.1, 127.8, 126.6, 58.5, 36.6; HRMS (ESI^+) calculated for [$C_{21}H_{18}NO_3S^+$] requires *m/z* 364.1002, found *m/z* 364.1014.

V. NOE correlations

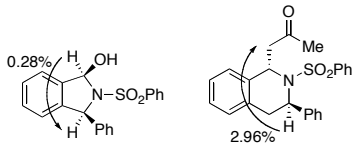


Table 1, entry 9 **6**

VI. References

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