**Exploring New Uses for C-H Amination:
Ni-Catalyzed Cross Coupling of Cyclic Sulfamates**

Supplementary Material
(10 pages)

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General. All reagents were obtained commercially unless otherwise noted. Reactions were performed using oven-dried glassware under an atmosphere of dry nitrogen. Air- and moisture-sensitive liquids and solutions were transferred via syringe or stainless steel cannula. Organic solutions were concentrated under reduced pressure (ca. 15 mm Hg) by rotary evaporation. Dichloromethane, acetonitrile, and pyridine were freshly distilled from CaH₂ immediately prior to use. Tetrahydrofuran (THF), diethyl ether (Et₂O), and 1,2-dimethoxyethane (DME) were freshly distilled from sodium benzophenone ketyl immediately prior to use. Benzene was distilled from sodium metal. *N,N*-Dimethylformamide (DMF) and *N,N*-Dimethylacetamide (DMA) were dried over activated 4 Å molecular sieves. Chlorosulfonyl isocyanate was obtained from Acros Chemicals, transferred via cannula to a Schlenk flask, and stored at -20 °C. Light magnesium oxide was flame-dried under reduced pressure (1 mm Hg) prior to use. Chromatographic purification of products was accomplished using forced-flow chromatography on EM Science Geduran silica gel 60 (35–75 µm). Compounds purified by chromatography on silica gel were typically applied to the adsorbent bed using the indicated solvent conditions with a minimum amount of added chloroform as needed for solubility. Thin layer chromatography was performed on EM Science silica gel 60 F₂₅₄ plates (250 µm). Visualization of the developed chromatogram was accomplished by fluorescence quenching and by staining with ethanolic anisaldehyde, aqueous potassium permanganate, or aqueous ceric ammonium molybdate (CAM) solution.

NMR spectra were acquired on a Varian Mercury-400 operating at 400 and 100 MHz or a Varian Inova-500 operating at 500 and 125 MHz for ¹H and ¹³C, respectively, and are referenced internally according to residual solvent signals. Data for ¹H NMR are recorded as follows: chemical shift (δ, ppm), multiplicity (s, singlet; d, doublet; t, triplet; q, quartet; sept, septet; m, multiplet), integration, coupling constant (Hz). Data for ¹³C are reported in terms of chemical shift (δ, ppm). Infrared spectra were recorded as thin films using NaCl salt plates on a Perkin-Elmer Paragon 500 FTIR spectrometer or a Thermo-Nicolet IR300 spectrometer and are reported in frequency of absorption. High-resolution mass spectra were obtained from following facilities: the Mass Spectrometry Facility, University of California at San Francisco, supported by the NIH Division of Research and Resources, the High Resolution Mass Spectrometry Facility, University of California at Riverside, and the Vincent Coates Foundation Mass Spectrometry Laboratory, Stanford University.

Characterization Data for Sulfamate Esters and Corresponding Amination Products¹

Purified by chromatography on silica gel (4:1 hexanes/EtOAc); white solid (83%): TLC R_f = 0.23 (4:1 hexanes/EtOAc); ¹H NMR (CDCl₃, 500 MHz) δ 7.37 (dd, 1H, *J* = 7.8, 1.8 Hz), 7.31 (dd, 1H, *J* = 7.5, 2.0 Hz), 7.27–7.19 (m, 2H), 5.08 (br s, 2H), 2.76 (q, 2H, *J* = 7.5 Hz), 1.24 (t, 3H, *J* = 7.5 Hz) ppm; ¹³C NMR (CDCl₃, 125 MHz) δ 148.6, 137.3, 130.3, 127.6, 127.4, 121.9, 23.3, 14.5 ppm; IR (thin film) ν 3390, 3291, 2972, 2876, 1550, 1370, 1189, 1155, 877, 780 cm⁻¹; HRMS (EI) calcd for C₈H₁₁NO₃S 201.0460 found 201.0453 (M⁺).

Purified by chromatography on silica gel (2:3 hexanes/CH₂Cl₂); tan solid (78%): TLC R_f = 0.18 (2:3 hexanes/CH₂Cl₂); ¹H NMR (CDCl₃, 500 MHz) δ 7.31 (dddd, 1H, *J* = 11.5, 6.5, 2.6, 0.6 Hz), 7.24–7.18 (m, 2H), 6.99 (dd, 1H, *J* = 8.3, 0.8 Hz), 4.90 (q, 1H, *J* = 7.0 Hz), 4.58 (br s, 1H), 1.72 (d, 3H, *J* = 7.0 Hz) ppm; ¹³C NMR (CDCl₃, 125 MHz) δ 150.9, 129.5, 126.2, 125.4, 123.5, 118.7, 53.0, 20.1 ppm; IR (thin film) ν 3271, 1425, 1386, 1174, 869, 758 cm⁻¹; HRMS (EI) calcd for C₈H₉NO₃S 199.0303 found 199.0312 (M⁺).

Purified by chromatography on silica gel (4:1 hexanes/EtOAc); white solid (92%): TLC R_f = 0.29 (4:1 hexanes/EtOAc); ^1H NMR (CDCl_3 , 400 MHz) δ 7.17 (d, 1H, J = 7.3 Hz), 7.11 (t, 1H, J = 7.8 Hz), 7.02 (d, 1H, J = 7.6 Hz), 5.18 (br s, 2H), 2.88-2.75 (m, 4H), 1.85-1.72 (m, 4H) ppm; ^{13}C NMR (CDCl_3 , 100 MHz) δ 148.5, 140.0, 130.6, 128.0, 126.0, 118.4, 29.3, 23.6, 22.4, 22.2 ppm; IR (thin film) ν 3391, 3286, 2935, 2860, 1574, 1457, 1374, 1179, 1015, 904, 809 cm^{-1} ; HRMS (EI) calcd for $\text{C}_{10}\text{H}_{13}\text{NO}_3\text{S}$ 227.0616 found 227.0606 (M^+).

Purified by chromatography on silica gel (3:7 hexanes/ CH_2Cl_2); white solid (75%): TLC R_f = 0.29 (3:7 hexanes/ CH_2Cl_2); ^1H NMR (CDCl_3 , 400 MHz) δ 7.23 (t, 1H, J = 7.9 Hz), 6.96 (d, 1H, J = 6.8 Hz), 6.84 (d, 1H, J = 8.2 Hz), 4.77 (td, 1H, J = 11.6, 4.9 Hz), 4.26 (br d, 1H, J = 11.2 Hz), 2.98-2.78 (m, 2H), 2.42-2.34 (m, 1H), 2.18-2.08 (m, 1H), 1.98-1.83 (m, 1H), 1.61 (qd, 1H, J = 12.3, 3.4 Hz) ppm; ^{13}C NMR (CDCl_3 , 100 MHz) δ 151.9, 137.6, 129.0, 125.1, 119.9, 114.9, 53.3, 27.9, 27.6, 21.2 ppm; IR (thin film) ν 3257, 2949, 2867, 1452, 1420, 1369, 1187, 978, 817 cm^{-1} ; HRMS (EI) calcd for $\text{C}_{10}\text{H}_{11}\text{NO}_3\text{S}$ 225.0460 found 225.0463 (M^+).

Purified by chromatography on silica gel (4:1 hexanes/EtOAc); white solid: TLC R_f = 0.25 (4:1 hexanes/EtOAc); ^1H NMR (CDCl_3 , 400 MHz) δ 7.36 (dd, 2H, J = 8.0, 1.6 Hz), 7.27 (dt, 1H, J = 7.6, 1.2 Hz), 7.20 (dt, 1H, J = 8.0, 2.0 Hz), 5.19 (br s, 2H), 3.39 (sept, 1H, J = 6.8 Hz), 1.23 (d, 6H, J = 7.2 Hz) ppm; ^{13}C NMR (CDCl_3 , 125 MHz) δ 147.4, 141.6, 127.5, 127.4, 126.8, 121.5, 26.8, 23.2 ppm; IR (thin film) ν 3376, 3281, 3070, 2961, 2870, 1487, 1360, 1185, 1157, 1033, 780 cm^{-1} ; HRMS (ES^+) calcd for $\text{C}_9\text{H}_{13}\text{NO}_3\text{S}$ 215.0616 found 238.0514 (MNa^+).

Purified by chromatography on silica gel (gradient elution: 1:1 $\rightarrow$ 2:3 hexanes/ CH_2Cl_2); tan solid (86%): mp 89–92 $^\circ\text{C}$; TLC R_f = 0.31 (3:7 hexanes/ CH_2Cl_2); ^1H NMR (CDCl_3 , 500 MHz) δ 7.33-7.21 (m, 3H), 6.99 (d, 1H, J = 8.0 Hz), 4.90 (br s, 1H), 1.75 (s, 6H) ppm; ^{13}C NMR (CDCl_3 , 125 MHz) δ 149.2, 129.2, 127.8, 126.4, 125.6, 119.1, 60.2, 30.7 ppm; IR (thin film) ν 3274, 2984, 1425, 1360, 1176, 850 cm^{-1} ; HRMS (ES^+) calcd for $\text{C}_9\text{H}_{11}\text{NO}_3\text{S}$ 213.0460 found 236.0357 (MNa^+).

Purified by chromatography on silica gel (4:1 hexanes/EtOAc); white solid (94%): TLC R_f = 0.28 (4:1 hexanes/EtOAc); ^1H NMR (CDCl_3 , 500 MHz) δ 7.43-7.38 (m, 1H), 7.31-7.23 (m, 3H), 4.79 (ddt, 1H, J = 17.0, 10.5, 6.5 Hz), 5.14-5.08 (m, 2H), 5.05 (br s, 2H), 3.51 (d, 2H, J = 6.5 Hz) ppm; ^{13}C NMR (CDCl_3 , 125 MHz) δ 148.4, 136.2, 132.9, 131.1, 127.7, 127.3, 121.8, 116.7, 34.2 ppm; IR (thin film) ν 3391, 3290, 3080, 2979, 1486, 1375, 1188, 1155, 877, 776 cm^{-1} ; HRMS (EI) calcd for $\text{C}_9\text{H}_{11}\text{NO}_3\text{S}$ 213.0460 found 213.0463 (M^+).

Purified by chromatography on silica gel (4:1 hexanes/EtOAc); tan solid (83%): TLC R_f = 0.20 (4:1 hexanes/EtOAc); ^1H NMR (CDCl_3 , 400 MHz) δ 7.35 (t, 1H, J = 7.5 Hz), 7.30-7.16 (m, 3H), 3.92 (dd, 1H, J = 15.3, 2.0 Hz), 3.42-3.26 (m, 2H), 2.60 (d, 1H, J = 4.7 Hz), 2.43 (d, 1H, J = 4.5 Hz) ppm; ^{13}C NMR (CDCl_3 , 100 MHz) δ 148.4, 131.0, 129.8, 127.9, 126.9, 122.2, 44.3, 35.1, 30.4 ppm; IR (thin film) ν 3066, 3012, 2921, 1488, 1376, 1271, 1186, 1157, 1103, 869, 785 cm^{-1} ; HRMS (EI) calcd for $\text{C}_9\text{H}_9\text{NO}_3\text{S}$ 211.0303 found 211.0307 (M^+).

Experimental Procedures and Characterization Data for *N*-Alkylation Reactions

General Procedure: A flask was charged with substrate (10 mmol), anhydrous K_2CO_3 (5.5 g, 40 mmol, 4 equiv), and 30 mL of DMF. To the resulting suspension was added dropwise the alkyl halide (20 mmol, 2 equiv). The reaction vessel was wrapped in aluminum foil and stirred until starting material was consumed, as judged by TLC (4–48 h). The reaction was poured into a separatory funnel containing 300 mL of H_2O and extracted with 4 x 50 mL of Et_2O . The combined organic extracts were washed with 1 x 50 mL of saturated aqueous NaCl, dried over MgSO_4 , filtered, and concentrated under reduced pressure. Purification of the oily residue by chromatography on silica gel furnished the desired product.

Purified by chromatography on silica gel (3:2 hexanes/ CH_2Cl_2); pale yellow oil (78%): TLC R_f = 0.20 (3:2 hexanes/ CH_2Cl_2); ^1H NMR (CDCl_3 , 400 MHz) δ 7.35-7.28 (m, 1H), 7.20 (d, 2H, J = 4.1 Hz), 7.00 (d, 1H, J = 8.1 Hz), 5.01 (q, 1H, J = 7.1 Hz), 2.82 (s, 3H), 1.73 (d, 3H, J = 7.2 Hz) ppm; ^{13}C NMR (CDCl_3 , 50 MHz) δ 150.4, 129.4, 127.2, 125.4, 121.4, 118.1, 58.4, 34.2, 18.5 ppm; IR (thin film) ν 2989, 2939, 1579, 1451, 1391, 1217, 1164, 908, 856, 756 cm^{-1} ; HRMS (EI) calcd for $\text{C}_9\text{H}_{11}\text{NO}_3\text{S}$ 213.0460 found 213.0463 (M^+).

Purified by chromatography on silica gel (95:5 hexanes/EtOAc); tan solid (85%): mp 74–76 $^\circ\text{C}$; TLC R_f = 0.45 (4:1 hexanes/EtOAc); ^1H NMR (CDCl_3 , 500 MHz) δ 7.40-7.32 (m, 5H), 7.30 (tdd, 1H, J = 7.5, 1.5, 0.5 Hz), 7.18 (td, 1H, J = 7.5, 1.3 Hz), 7.09 (dd, 1H, J = 7.3, 0.5 Hz), 7.03 (dd, 1H, J = 8.0, 1.0 Hz), 4.74 (d, 1H, J = 14.5 Hz), 4.63 (q, 1H, J = 7.2 Hz), 4.07 (d, 1H, J = 14.5 Hz), 1.65 (d, 3H, J = 7.5 Hz) ppm; ^{13}C NMR (CDCl_3 , 125 MHz) δ 152.2, 135.0, 129.1, 128.8, 128.3, 127.8, 125.4, 122.2, 118.6, 58.3, 54.6, 21.8 ppm; IR (thin film) ν 3033, 1485, 1396, 1175, 1109, 864, 759 cm^{-1} ; HRMS (EI) calcd for $\text{C}_{15}\text{H}_{15}\text{NO}_3\text{S}$ 289.0773 found 289.0779 (M^+).

Purified by chromatography on silica gel (17:3 hexanes/EtOAc); white solid (52%): mp 85–88 $^\circ\text{C}$; TLC R_f = 0.33 (4:1 hexanes/EtOAc); ^1H NMR (CDCl_3 , 400 MHz) δ 7.32-7.24 (m, 3H), 7.17 (td, 1H, J = 7.5, 0.9 Hz), 7.08 (d, 1H, J = 7.6 Hz), 7.02 (d, 1H, J = 8.2 Hz), 6.89 (m, 2H), 4.68 (d, 1H, J = 14.0 Hz), 4.61 (q, 1H, J = 7.0 Hz), 4.00 (d, 1H, J = 14.1 Hz), 3.82 (s, 3H), 1.63 (d, 3H, J = 7.3 Hz) ppm; ^{13}C NMR (CDCl_3 , 100 MHz) δ 159.5, 150.1, 129.7, 129.0,

127.7, 126.6, 125.3, 122.2, 118.4, 114.1, 57.8, 55.2, 54.1, 21.8 ppm; IR (thin film) ν 2938, 1612, 1514, 1395, 1248, 1176, 1033, 864, 756 cm^{-1} ; HRMS (EI) calcd for $\text{C}_{16}\text{H}_{17}\text{NO}_4\text{S}$ 319.0878 found 319.0880 (M^+).

Purified by chromatography on silica gel (17:3 hexanes/ CH_2Cl_2); white solid (96%): mp 59–61 °C; TLC R_f = 0.41 (7:3 hexanes/ CH_2Cl_2); ^1H NMR (CDCl_3 , 400 MHz) δ 7.29 (tdd, 1H, J = 6.8, 2.6, 0.6 Hz), 7.21–7.14 (m, 2H), 6.99 (dd, 1H, J = 8.2, 0.6 Hz), 4.74 (q, 1H, J = 7.2 Hz), 3.18 (dd, 1H, J = 13.8, 9.0 Hz), 2.80 (dd, 1H, J = 13.6, 6.0 Hz), 2.02–1.87 (m, 1H), 1.79 (d, 3H, J = 7.2 Hz), 1.01 (d, 3H, J = 6.4 Hz), 0.95 (d, 3H, J = 6.8 Hz) ppm; ^{13}C NMR (CDCl_3 , 100 MHz) δ 150.4, 129.1, 127.5, 125.1, 122.3, 118.5, 60.0, 58.6, 27.9, 21.4, 19.9, 19.8 ppm; IR (thin film) ν 2964, 2873, 1485, 1397, 1188, 1163, 860, 758 cm^{-1} ; HRMS (EI) calcd for $\text{C}_{12}\text{H}_{17}\text{NO}_3\text{S}$ 255.0929 found 255.0940 (M^+).

Purified by chromatography on silica gel (9:1 hexanes/EtOAc); white solid (96%): TLC R_f = 0.35 (4:1 hexanes/EtOAc); ^1H NMR (CDCl_3 , 400 MHz) δ 7.19 (t, 1H, J = 7.9 Hz), 6.93 (d, 1H, J = 7.6 Hz), 6.77 (d, 1H, J = 8.2 Hz), 5.18 (dd, 1H, J = 11.3, 4.9 Hz), 3.25–3.18 (m, 1H), 2.95–2.78 (m, 3H), 2.30–2.22 (m, 1H), 2.18–2.10 (m, 1H), 1.96–1.76 (m, 2H), 1.67–1.51 (m, 2H), 0.90 (t, 3H, J = 7.4 Hz) ppm; ^{13}C NMR (CDCl_3 , 100 MHz) δ 151.4, 138.6, 128.9, 125.0, 117.9, 114.8, 58.6, 47.7, 28.4, 26.7, 23.2, 21.8, 11.0 ppm; IR (thin film) ν 2963, 2876, 1578, 1451, 1393, 1190, 966, 814, 763 cm^{-1} ; HRMS (EI) calcd for $\text{C}_{13}\text{H}_{17}\text{NO}_3\text{S}$ 267.0929 found 267.0941 (M^+).

Purified by chromatography on silica gel (9:1 hexanes/EtOAc); white solid (94%): TLC R_f = 0.38 (4:1 hexanes/EtOAc); ^1H NMR (CD_3CN , 500 MHz, 75 °C) δ 7.43–7.40 (m, 1H), 7.38–7.26 (m, 6H), 7.21–7.17 (m, 2H), 4.22 (d, 1H, J = 15.8 Hz), 4.12 (d, 1H, J = 15.8 Hz), 3.61–3.56 (m, 1H), 3.43–3.34 (m, 2H), 3.38 (s, 3H), 3.07 (d, 2H, 5.8 Hz) ppm; ^{13}C NMR (CD_3CN , 125 MHz, 75 °C) δ 150.6, 137.6, 134.0, 132.7, 129.9, 129.6, 129.1(2), 128.8, 124.6, 80.6, 57.9, 54.5, 49.8, 34.1 ppm; IR (thin film) ν 3032, 2935, 1455, 1381, 1182, 1162, 1110, 873, 792 cm^{-1} ; HRMS (EI) calcd for $\text{C}_{17}\text{H}_{19}\text{NO}_4\text{S}$ 333.1035 found 333.1026 (M^+).

Purified by chromatography on silica gel (95:5 hexanes/EtOAc); white solid (92%): mp 104–106 °C; TLC R_f = 0.65 (4:1 hexanes/EtOAc); ^1H NMR (CD_3CN , 500 MHz, 75 °C) δ 7.37 (dd, 1H, J = 7.0, 2.0 Hz), 7.38–7.27 (m, 2H), 7.25 (dd, 1H, J = 7.8, 1.8 Hz), 4.29–4.24 (m, 1H), 3.48 (dd, 1H, J = 15.3, 2.8 Hz), 3.29 (dd, 1H, J = 15.5, 6.0 Hz), 3.06–2.94 (m, 2H), 2.71 (s, 3H), 0.95 (s, 9H), 0.22 (s, 3H), 0.16 (s, 3H) ppm; ^{13}C NMR (CD_3CN , 125 MHz, 75 °C) δ 150.6, 134.3, 132.5, 129.5, 128.5, 124.7, 72.5, 55.8, 39.0, 37.9, 26.6, 19.0, -4.2, -4.4 ppm; IR (thin film) ν 2930, 2857, 1386, 1186, 1101, 1003, 856, 780 cm^{-1} ; HRMS (EI) calcd for $\text{C}_{16}\text{H}_{27}\text{NO}_4\text{SSi}$ 357.1430 found 300.0706 ($\text{M}^+ - \text{C}_4\text{H}_9$).

Purified by chromatography on silica gel (gradient elution: 7:3→3:2 hexanes/CH₂Cl₂); pale yellow oil (90%): TLC R_f = 0.31 (3:2 hexanes/CH₂Cl₂); ¹H NMR (CDCl₃, 400 MHz) δ 7.31-7.19 (m, 3H), 7.00 (dd, 1H, J = 7.8, 1.0 Hz), 3.02 (s, 3H), 1.72 (s, 6H) ppm; ¹³C NMR (CDCl₃, 100 MHz) δ 148.3, 129.0, 128.9, 127.2, 125.6, 118.8, 64.0, 30.5, 28.0 ppm; IR (thin film) ν 2990, 2943, 1448, 1363, 1174, 1089, 864, 760 cm⁻¹; HRMS (ES⁺) calcd for C₁₀H₁₃NO₃S 227.0616 found 250.0514 (MNa⁺).

Purified by chromatography on silica gel (9:1 hexanes/EtOAc); white solid (87%): mp 87–89 °C; TLC R_f = 0.25 (9:1 hexanes/EtOAc); ¹H NMR (CDCl₃, 400 MHz) δ 7.77-7.73 (m, 2H), 7.59 (tt, 1H, J = 7.3, 1.6 Hz), 7.51-7.45 (m, 2H), 7.39-7.19 (m, 3H), 7.12 (d, 1H, J = 7.4 Hz), 6.05 (q, 1H, J = 7.1 Hz), 1.85 (d, 3H, J = 6.8 Hz) ppm; ¹³C NMR (CDCl₃, 100 MHz) δ 169.3, 149.1, 134.5, 132.7, 129.4, 128.6, 128.3, 127.0, 126.6, 125.9, 118.7, 55.9, 21.4 ppm; IR (thin film) ν 3065, 2982, 1697, 1411, 1266, 1176, 1122, 805 cm⁻¹; HRMS (ES⁺) calcd for C₁₅H₁₃NO₄S 303.0565 found 326.0463 (MNa⁺).

Experimental Procedures and Characterization Data for Ni-Catalyzed Cross-Coupling of Cyclic Sulfamates

General procedure: A 10 mL Schlenk flask was charged with cyclic sulfamate (0.4 mmol) and 5 mol% of Ni(dppp)Cl₂.² The vessel was sealed with a glass stopper, the contents placed briefly under vacuum (~1 torr), and the flask back-filled with N₂. This evacuation/fill cycle was repeated three times. The gas inlet hose was then exchanged with a rubber septum and a N₂ bleed, and 4 mL of C₆H₆ was added via syringe. To the resulting red suspension was added an ethereal solution (0.5–2 M) of RMgX (0.8 mmol, 2 equiv). The mixture was stirred at 55 °C for 15 h, following which time the reaction was cooled to 25 °C and quenched by the addition of 500 μ L of MeOH. After stirring vigorously for 5 min, the contents were transferred to a recovery flask and all volatiles were removed by concentration under reduced pressure. The oily residue was treated with 2 mL of anhydrous 2 M methanolic HCl and the resulting orange solution was stirred at 55 °C for 6 h. Once cooled to 25 °C, the contents were poured carefully into a separatory funnel containing 10 mL of saturated aqueous NaHCO₃. The organic phase was collected and the aqueous solution was extracted with 3 x 15 mL of EtOAc. The combined organics were washed with 1 x 10 mL of saturated aqueous NaCl, dried over MgSO₄, filtered, and concentrated under reduced pressure. Purification of the isolated material by chromatography on silica gel afforded the desired product. In specific cases (as indicated below), the unpurified amine was first treated with (CF₃CO₂)₂O or Boc₂O and the *N*-acylated derivative then purified.

Acylation with (CF₃CO)₂O: The unpurified amine was dissolved in 5 mL of CH₂Cl₂ and treated sequentially with 225 μ L of Et₃N (1.6 mmol, 4 equiv) and 115 μ L of (CF₃CO)₂O (0.8 mmol, 2 equiv). The mixture was stirred for 1 h and then carefully poured into a separatory funnel containing 10 mL of saturated aqueous NaHCO₃. The contents were extracted with 3 x 15 mL of EtOAc. The combined organics were washed with 1 x 10 mL of saturated aqueous NaCl, dried over MgSO₄, filtered, and concentrated under reduced pressure. The oily residue was purified by chromatography on silica gel to furnish the desired trifluoroacetamide product.

Acylation with Boc₂O: The unpurified amine was dissolved in 8 mL of a biphasic solution consisting of equal parts saturated aqueous NaHCO₃ and CH₂Cl₂. The solution was stirred vigorously while 175 mg of Boc₂O (0.8 mmol, 2

equiv) was added. After 1 h, the mixture was transferred to a separatory funnel containing 10 mL of H₂O and extracted with 3 x 15 mL of CH₂Cl₂. The combined organic extracts were washed 1 x 10 mL of saturated aqueous NaCl, dried over MgSO₄, filtered, and concentrated under reduced pressure. Purification of the isolated material by chromatography on silica gel afforded the desired carbamate.

Purified by chromatography on silica gel (97:3 hexanes/Et₂O); pale yellow oil (72%): TLC R_f = 0.30 (95:5 hexanes/Et₂O); ¹H NMR (CDCl₃, 500 MHz) δ 7.39-7.35 (m, 1H), 7.29-7.24 (m, 2H), 7.23-7.19 (m, 1H), 5.89 (q, 1H, *J* = 7.0 Hz), 2.65 (q, 3H, *J* = 1.7 Hz), 2.19 (s, 3H), 1.56 (d, 3H, *J* = 7.0 Hz) ppm; ¹³C NMR (CDCl₃, 125 MHz) δ 156.4 (q, *J*_{CF} = 35.2 Hz), 137.8, 135.7, 130.9, 128.3, 127.1, 126.0, 116.6 (q, *J*_{CF} = 286.7 Hz), 51.1, 28.8 (q, *J*_{CF} = 4.0 Hz), 18.8, 15.2 ppm; IR (thin film) ν 2979, 1688, 1461, 1417, 1244, 118, 1142, 1084, 739 cm⁻¹; HRMS (ES⁺) calcd for C₁₂H₁₄F₃NO 245.1027 found 268.0925 (MNa⁺).

Purified by chromatography on silica gel (97:3 hexanes/Et₂O); clear oil (79%): TLC R_f = 0.38 (95:5 hexanes/Et₂O); ¹H NMR (CDCl₃, 400 MHz) δ 7.36 (d, 1H, *J* = 7.2 Hz), 7.34-7.30 (m, 2H), 7.25-7.19 (m, 1H), 6.05 (q, 1H, *J* = 6.9 Hz), 2.64 (q, 3H, *J* = 1.6 Hz), 2.53 (tt, 1H, *J* = 11.3, 3.2 Hz), 1.84-1.66 (m, 4H), 1.54 (d, 3H, *J* = 6.8 Hz), 1.51-1.18 (m, 6H) ppm; ¹³C NMR (CD₃CN, 100 MHz) δ 156.6 (q, *J*_{CF} = 34.8 Hz), 148.5, 135.4, 129.5, 128.5, 127.9, 126.7, 117.7 (q, *J*_{CF} = 285.9 Hz), 51.2, 39.5, 35.1, 34.9, 29.6 (q, *J*_{CF} = 4.6 Hz), 27.9, 27.6, 26.7, 15.7 ppm; IR (thin film) ν 2927, 2853, 1687, 1450, 1242, 1143, 1081 cm⁻¹; HRMS (EI) calcd for C₁₇H₂₂F₃NO 313.1653 found 313.1643 (M⁺).

Purified by chromatography on silica gel (97:3 hexanes/Et₂O); clear oil (85%): TLC R_f = 0.38 (95:5 hexanes/Et₂O); ¹H NMR (CDCl₃, 400 MHz) δ 7.35 (dd, 1H, *J* = 7.6, 0.8 Hz), 7.21 (td, 1H, *J* = 7.4, 1.5 Hz), 7.13 (td, 1H, *J* = 7.4, 1.3 Hz), 7.03 (dd, 1H, *J* = 7.6, 1.6 Hz), 5.86 (q, 1H, *J* = 6.9 Hz), 2.67 (q, 3H, *J* = 1.6 Hz), 2.04 (d, 1H, *J* = 14.0 Hz), 1.94 (d, 1H, *J* = 14.0 Hz), 1.51 (d, 3H, *J* = 7.2 Hz), 0.00 (s, 9H) ppm; ¹³C NMR (CDCl₃, 100 MHz) δ 156.5 (q, *J*_{CF} = 34.9 Hz), 140.9, 133.5, 129.7, 128.1, 127.7, 124.1, 116.6 (q, *J*_{CF} = 286.7 Hz), 50.7, 28.7 (q, *J*_{CF} = 3.8 Hz), 22.8, 15.2, -1.6 ppm; IR (thin film) ν 2927, 2853, 1687, 1450, 1242, 1143, 1081 cm⁻¹; HRMS (EI) calcd for C₁₅H₂₂F₃NOSi 317.1423 found 302.1189 (M⁺-CH₃).

Purified by chromatography on silica gel (85:15 hexanes/EtOAc); pale yellow oil (96%): TLC R_f = 0.31 (4:1 hexanes/EtOAc); ¹H NMR (CDCl₃, 400 MHz) δ 7.58 (dd, 1H, *J* = 7.6, 1.2 Hz), 7.35-7.22 (m, 6H), 7.17 (td, 1H, *J* = 7.2, 1.5 Hz), 7.09 (dd, 1H, *J* = 7.4, 1.4 Hz), 4.14 (q, 1H, *J* = 6.5 Hz), 3.65 (s, 2H), 2.46 (dd, 1H, *J* = 13.6, 7.6 Hz), 2.42 (dd, 1H, *J* = 13.6, 6.8 Hz), 1.73 (sept, 1H, *J* = 6.8 Hz), 1.62 (br s, 1H), 1.36 (d, 3H, *J* = 6.8 Hz), 0.89 (d, 3H, *J* = 6.8 Hz), 0.87 (d, 3H, *J* = 6.8 Hz) ppm; ¹³C NMR (CDCl₃, 100 MHz) δ 143.5, 140.6, 138.9, 130.4, 128.3, 128.1, 126.8, 126.4, 126.1, 125.4, 51.8, 51.6, 41.8, 30.0, 23.9, 22.6, 22.4 ppm; IR (thin film) ν 3025, 2955, 2925, 2866, 1453, 1366, 1116, 758, 697 cm⁻¹; HRMS (EI) calcd for C₁₉H₂₅N 267.1987 found 267.1980 (M⁺).

Reaction was stirred for 6 h at 25 °C. Purified by chromatography on silica gel (9:1 hexanes/EtOAc); pale yellow oil (91%): TLC R_f = 0.21 (9:1 hexanes/EtOAc); ^1H NMR (CDCl_3 , 500 MHz) δ 7.44-7.27 (m, 10H), 3.87 (q, 1H, J = 6.7 Hz), 3.72 (d, 1H, J = 13.3 Hz), 3.65 (d, 1H, J = 13.3 Hz), 1.66 (br s, 1H), 1.43 (d, 3H, J = 6.5 Hz) ppm; ^{13}C NMR (CDCl_3 , 100 MHz) δ 145.5, 140.6, 128.4, 128.3, 128.1, 126.9, 126.8, 126.7, 57.5, 51.6, 24.5 ppm; IR (thin film) ν 3026, 2962, 2924, 1492, 1451, 1119, 1027, 698 cm^{-1} ; HRMS (EI) calcd for $\text{C}_{15}\text{H}_{17}\text{N}$ 211.1361 found 211.1367 (M^+).

Purified by chromatography on silica gel (85:15 hexanes/EtOAc); pale yellow oil (94%): TLC R_f = 0.10 (4:1 hexanes/EtOAc); ^1H NMR (CDCl_3 , 400 MHz) δ 7.54 (d, 1H, J = 8.2 Hz), 7.26-7.11 (m, 5H), 6.86-6.81 (m, 2H), 4.11 (q, 1H, J = 6.5 Hz), 3.78 (s, 3H), 3.57 (s, 2H), 2.58 (dt, 1H, J = 14.0, 7.9 Hz), 2.54 (dt, 1H, J = 14.0, 7.7 Hz), 1.56 (br s, 1H), 1.53-1.44 (m, 2H), 1.39-1.29 (m, 5H), 0.91 (t, 3H, J = 7.4 Hz) ppm; ^{13}C NMR (CDCl_3 , 100 MHz) δ 158.5, 143.0, 140.2, 132.8, 129.4, 129.2, 126.4, 126.3, 125.4, 113.7, 55.2, 51.8, 51.0, 33.9, 32.3, 24.0, 22.8, 14.0 ppm; IR (thin film) ν 2957, 2869, 1611, 1511, 1463, 1247, 1176, 1037, 757 cm^{-1} ; HRMS (EI) calcd for $\text{C}_{20}\text{H}_{27}\text{NO}$ 297.2093 found 297.2099 (M^+).

Reaction performed with 4 mmol of substrate, 1.3 equiv of 2 M ethereal $n\text{BuMgCl}$, and 2 mol% Ni(dppp)Cl_2 in 8 mL of C_6H_6 . Purified by chromatography on silica gel (4:1 hexanes/EtOAc); pale yellow oil (86%): TLC R_f = 0.20 (4:1 hexanes/EtOAc); ^1H NMR (CDCl_3 , 400 MHz) δ 7.45 (dd, 1H, J = 7.8, 1.2 Hz), 7.20 (td, 1H, J = 6.6, 2.0 Hz), 7.17-7.10 (m, 2H), 4.04 (q, 1H, J = 6.5 Hz), 2.70-2.58 (m, 2H), 2.35 (dd, 1H, J = 11.4, 6.2 Hz), 2.19 (dd, 1H, J = 11.2, 7.2 Hz), 1.69 (sept, 1H, J = 6.7 Hz), 1.60-1.51 (m, 2H), 1.40 (sext, 2H, J = 7.4 Hz), 1.31 (d, 3H, J = 6.4 Hz), 0.95 (t, 3H, J = 7.2 Hz), 0.88 (d, 3H, J = 6.8 Hz), 0.87 (s, 3H, J = 6.8 Hz) ppm; ^{13}C NMR (CDCl_3 , 100 MHz) δ 143.6, 140.0, 129.3, 126.2, 125.3, 55.9, 52.8, 34.0, 32.3, 28.6, 24.1, 22.8, 20.8, 20.6, 14.0 ppm; IR (thin film) ν 2956, 2930, 2870, 1466, 1135, 756 cm^{-1} ; HRMS (EI) calcd for $\text{C}_{16}\text{H}_{27}\text{N}$ 233.2143 found 233.2150 (M^+).

Purified by chromatography on silica gel (19:1 hexanes/EtOAc); pale yellow oil (75%): TLC R_f = 0.15 (4:1 hexanes/EtOAc); ^1H NMR (CDCl_3 , 500 MHz) δ 7.05 (t, 1H, J = 7.5 Hz), 6.99 (d, 1H, J = 7.5 Hz), 6.92 (d, 1H, J = 7.5 Hz), 3.76 (t, 1H, J = 3.0 Hz), 2.85-2.66 (m, 3H), 2.58 (dt, 1H, J = 11.0, 7.0 Hz), 2.37 (s, 3H), 2.17-2.11 (m, 1H), 1.96 (qdd, 1H, J = 13.0, 5.8, 2.8 Hz), 1.73-1.66 (m, 1H), 1.55-1.46 (m, 3H), 0.94 (t, 3H, J = 7.5 Hz) ppm; ^{13}C NMR (CDCl_3 , 125 MHz) δ 137.7, 137.2, 137.1, 127.9, 127.0, 126.5, 52.4, 50.1, 29.7, 26.4, 23.6, 18.5, 17.0, 12.0 ppm; IR (thin film) ν 2931, 2871, 1587, 1461, 1111, 766 cm^{-1} ; HRMS (EI) calcd for $\text{C}_{14}\text{H}_{21}\text{N}$ 203.1674 found 203.1680 (M^+).

Purified by chromatography on silica gel (70:30:1 hexanes/EtOAc/MeOH); pale yellow oil (84%): TLC R_f = 0.26 (70:30:1 hexanes/EtOAc/MeOH); ^1H NMR (CDCl_3 , 500 MHz) δ 7.31-7.15 (m, 10H), 7.10-7.05 (m, 2H), 7.01-6.96 (m, 1H), 6.74 (d, 1H, J = 7.5 Hz), 3.71 (d, 1H, J = 13.3 Hz), 3.67 (d, 1H, J = 13.3 Hz), 3.40 (qd, 1H, J = 6.8, 3.5

Hz), 3.25 (s, 3H), 2.96 (d, 1H, $J = 13.8$ Hz), 2.92 (d, 1H, $J = 13.8$ Hz), 2.60 (dd, 1H, $J = 14.0, 6.0$ Hz), 2.56 (dd, 1H, $J = 12.3, 3.3$ Hz), 2.50 (dd, 1H, $J = 12.3, 7.3$ Hz), 2.41 (dd, 1H, $J = 13.8, 7.8$ Hz), 1.68 (br s, 1H), 1.35 (s, 3H), 1.34 (s, 3H) ppm; ^{13}C NMR (CDCl_3 , 125 MHz) δ 148.9, 140.3, 137.8, 137.1, 131.5, 130.1, 128.3, 128.1, 127.9, 126.8, 126.1, 126.0, 125.7, 125.3, 81.9, 57.3, 54.0, 52.0, 46.3, 39.4, 35.0, 28.4, 28.3 ppm; IR (thin film) ν 3059, 2964, 2928, 1601, 1494, 1452, 1097, 764, 698 cm^{-1} ; HRMS (EI) calcd for $\text{C}_{27}\text{H}_{33}\text{NO}$ 387.2562 found 387.2559 (M^+).

Purified by chromatography on silica gel (4:1 hexanes/EtOAc); pale yellow oil (88%): TLC $R_f = 0.20$ (4:1 hexanes/EtOAc); ^1H NMR (CD_3CN , 400 MHz, 75 $^\circ\text{C}$) δ 7.43-7.26 (m, 7H), 7.24 (td, 1H, $J = 7.4, 1.5$ Hz), 7.17 (dd, 1H, $J = 7.4, 1.8$ Hz), 3.82-3.73 (m, 1H), 3.11 (dd, 1H, $J = 14.0, 4.4$ Hz), 2.97 (dd, 1H, $J = 14.2, 7.4$ Hz), 2.76 (dd, 1H, $J = 14.2, 4.6$ Hz), 2.70 (s, 3H), 2.61 (dd, 1H, $J = 14.2, 8.6$ Hz), 1.35 (s, 9H) ppm; ^{13}C NMR (CD_3CN , 100 MHz, 75 $^\circ\text{C}$) δ 143.8, 143.3, 137.8, 131.8, 131.2, 130.6, 129.4, 128.5, 128.1, 127.3, 80.2, 72.0, 56.1, 39.7, 36.2, 29.0 ppm; IR (thin film) ν 3434, 2975, 2928, 1693, 1673, 1479, 1393, 1241, 1147, 752 cm^{-1} ; HRMS (EI) calcd for $\text{C}_{21}\text{H}_{27}\text{NO}_3$ 341.1991 found 268.1328 ($\text{M}^+ - \text{OC}_4\text{H}_9$).

Purified by chromatography on silica gel (4:1 hexanes/EtOAc); clear oil (81%): TLC $R_f = 0.25$ (4:1 hexanes/EtOAc); ^1H NMR (CD_3CN , 500 MHz, 75 $^\circ\text{C}$) δ 7.30-7.26 (m, 3H), 7.21-7.12 (m, 6H), 4.11 (d, 1H, $J = 15.5$ Hz), 4.05 (d, 1H, $J = 15.5$ Hz), 4.00-3.93 (m, 1H), 3.28 (dd, 1H, $J = 14.0, 4.0$ Hz), 3.19 (dd, 1H, $J = 13.8, 7.8$ Hz), 2.85 (s, 3H), 2.78 (dd, 1H, $J = 14.5, 4.5$ Hz), 2.61 (dd, 1H, $J = 14.3, 8.3$ Hz), 1.42 (s, 9H) ppm; ^{13}C NMR (CD_3CN , 125 MHz, 75 $^\circ\text{C}$) δ 142.6, 140.7, 138.8, 132.0, 131.7, 130.0, 129.7, 127.6, 127.5, 127.2, 80.3, 72.2, 56.4, 39.8, 39.6, 36.6, 29.0 ppm; IR (thin film) ν 3434, 2975, 2928, 1692, 1672, 1452, 1393, 1148, 878 cm^{-1} ; HRMS (EI) calcd for $\text{C}_{22}\text{H}_{29}\text{NO}_3$ 355.2147 found 282.1510 ($\text{M}^+ - \text{OC}_4\text{H}_9$).

Purified by chromatography on silica gel (gradient elution: 17:3 $\rightarrow$ 3:1 hexanes/EtOAc); colorless oil (30%): TLC $R_f = 0.36$ (7:3 hexanes/EtOAc); ^1H NMR (CD_3CN , 400 MHz, 75 $^\circ\text{C}$) δ 7.34-7.18 (m, 5H), 4.04-3.95 (m, 1H), 3.30 (dd, 1H, $J = 14.0, 4.0$ Hz), 3.17 (dd, 1H, $J = 14.0, 8.0$ Hz), 2.88 (s, 3H), 2.75 (dd, 1H, $J = 13.6, 5.2$ Hz), 2.66 (dd, 1H, $J = 14.0, 7.6$ Hz), 1.42 (s, 9H) ppm; ^{13}C NMR (CD_3CN , 100 MHz, 75 $^\circ\text{C}$) δ 140.5, 130.7, 129.5, 127.3, 80.3, 72.5, 56.2, 42.8, 36.7, 29.0 ppm; IR (thin film) ν 3434, 2975, 2928, 1693, 1672, 1452, 1393, 1148, 878 cm^{-1} ; HRMS (ES^+) calcd for $\text{C}_{15}\text{H}_{23}\text{NO}_3$ 265.1678 found 288.1576 (MNa^+).

Purified by chromatography on silica gel (gradient elution: 17:3 $\rightarrow$ 3:1 hexanes/EtOAc); colorless oil (8%): TLC $R_f = 0.51$ (7:3 hexanes/EtOAc); ^1H NMR (CD_3CN , 500 MHz, 75 $^\circ\text{C}$) δ 7.22 (dd, 1H, $J = 6.8, 2.0$ Hz), 7.18 (dd, 1H, $J = 7.5, 2.0$ Hz), 7.16-7.09 (m, 2H), 4.02-3.95 (m, 1H), 3.35 (dd, 1H, $J = 14.3, 4.3$ Hz), 3.17 (dd, 1H, $J = 13.8, 7.8$ Hz), 2.90 (s, 3H), 2.80 (dd, 1H, $J = 14.3, 4.8$ Hz), 2.72-2.61 (m, 3H), 1.62-1.55 (m, 2H), 1.46-1.38 (m, 2H), 1.43 (s, 9H), 0.96 (t, 3H, $J = 7.5$ Hz) ppm; ^{13}C NMR (CD_3CN , 125 MHz, 75 $^\circ\text{C}$) δ 142.7, 138.2, 131.7, 130.5, 127.5, 126.9, 80.3, 72.5, 56.5, 39.4, 36.7, 34.5, 33.5, 29.1, 23.7, 14.4 ppm; IR (thin film) ν 3435, 2957, 2929, 2871, 1696, 1673, 1453, 1392, 1240, 1147, 750 cm^{-1} ; HRMS (ES^+) calcd for $\text{C}_{19}\text{H}_{31}\text{NO}_3$ 321.2304 found 344.2202 (MNa^+).

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- (1) Preparation of the sulfamate esters and the corresponding products of C–H amination followed the general protocols outlined in: (a) Okada, M.; Iwashita, S.; Koizumi, N. *Tetrahedron Lett.* **2000**, *41*, 7047-7051. (b) Espino, C. G.; Wehn, P. M.; Chow, J.; Du Bois, J. *J. Am. Chem. Soc.* **2001**, *123*, 6935-6936.
  - (2) Ni(dppp)Cl₂ was purchased from Strem Chemicals, Inc; dppp = 1,3-Bis(diphenylphosphino)propane.
  - (3) Despite repeated scans, the ¹³C NMR signal for the ^tBuCO₂- (Boc) carbonyl carbon was not observed in the elevated temperature (75 °C) spectrum.