

Stereoselective Vinylation of Aryl *N*-(2-Pyridylsulfonyl) Aldimines with 1-Alkenyl-1,1-Heterobimetallic Reagents

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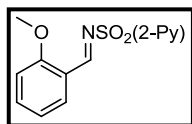
I. General Methods. All reactions were performed under a nitrogen atmosphere with oven-dried glassware. All manipulations involving dicyclohexylborane, diethylzinc, and dimethylzinc were carried out under an inert atmosphere in a Vacuum Atmospheres drybox with an attached MO-40 Dritrain or by using standard Schlenk or vacuum line techniques. Chemicals were obtained from Aldrich, Acros, or Strem Chemicals unless otherwise specified. Solvents were purchased from Fischer Scientific.

and dichloromethane were dried through activated alumina columns. Tetrahydrofuran was distilled from sodium and benzophenone under N₂. Liquid substrates were distilled and degassed prior to use. B(pin)-substituted alkynes¹ and *N*-(2-pyridyl) sulfonyl imines² were prepared by literature methods. Dimethylzinc and diethylzinc were obtained from Akzo Nobel and 2.0 M solution in toluene were prepared and stored in a Vacuum Atmospheres drybox. NMR spectra were obtained on Brüker 300 or 500 MHz Fourier transform spectrometer at the University of Pennsylvania NMR facility. ¹H and ¹³C{¹H} NMR spectra were referenced to residual solvent. ¹¹B{¹H} NMR spectra were referenced to BF₃·OEt₂. The infrared spectra were obtained using a Perkin-Elmer 1600 series spectrometer. HRMS data was obtained on a Waters LC-TOF mass spectrometer (model LCT-XE Premier) using electrospray ionization in positive or negative mode, depending on analyte. Melting points were determined on a Uni-melt Thomas Hoover melting point apparatus and are uncorrected. Thin-layer chromatography was performed on Whatman precoated silica gel 60 F-254 plates and visualized by ultraviolet light or by staining with ceric ammonium molybdate, phosphomolybdic acid, or potassium permanganate solutions. Silica gel (Silicaflash, P60, 40-63 μm, Silicycle) was used for air-flashed chromatography.

Caution. Dialkylzinc reagents are pyrophoric. Care must be used when handling them.

(1) Brown, H. C.; Bhat, N. G.; Srebnik, M. *Tetrahedron Lett.* **1988**, *29*, 2631. (b) Kim, M.; Lee, D. *Org. Lett.* **2005**, *7*, 1865. (c) Renaud, J.; Graf, C.; Oberer, L. *Angew. Chem. Int. Ed.* **2000**, *39*, 3101. (d) Brown, H. C.; Sinclair, J. A. *J. Organomet. Chem.* **1977**, *131*, 163. (d) Hansen, E. C.; Lee, D. *J. Am. Chem. Soc.* **2005**, *127*, 3252. (e) Buettner, M. W.; Naetscher, J. B.; Burschka, C.; Tacke, R. *Organometallics* **2007**, *26*, 4835.
(2) Esquivias, J.; Arrayás, R. G.; Carretero, J. C. *Angew. Chem. Int. Ed.* **2006**, *45*, 629.

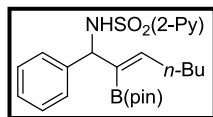
II. Characterization of *N*-Pyridyl Sulfonyl Imine:



***N*-(2-Methoxybenzylidene)pyridine-2-sulfonamide (6).** The product was prepared according to literature procedure² using *o*-methoxybenzaldehyde (2.5 mmol, 0.34 g) to give the title compound as a crystalline solid (0.42 g, 74% yield). m.p. 111-114 °C. ¹H NMR (500 MHz, CDCl₃) δ 9.75 (s, 1H), 8.75 – 8.73 (m, 1H), 8.24 (d, *J* = 7.9 Hz, 1H), 8.08 (dd, *J* = 8.0, 1.7 Hz, 1H), 7.96 (td, *J* = 7.8, 1.7 Hz, 1H), 7.62-7.57 (m, 1H), 7.54 – 7.51 (m, 1H), 6.98 (d, *J* = 8.2 Hz, 2H), 3.95 (s, 3H); ¹³C{¹H} NMR (125 MHz, CDCl₃) δ 170.5, 162.3, 156.5, 150.6, 150.1, 138.2, 137.7, 129.8, 127.3, 123.5, 121.1, 111.8, 56.0; IR (neat) 3430, 1639, 1588, 1479, 1324, 1254, 1172 cm⁻¹; HRMS *m/z* 277.0648 [(MH)⁺; calcd for C₁₃H₁₃N₂O₃S : 277.0641].

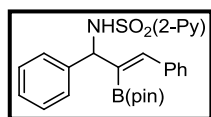
III. Synthesis and Characterization of B(pin)-substituted Allylic Amines:

General Procedure A: Synthesis of B(pin)-substituted Allylic Amines. To a suspension of HBCy₂ (53.4 mg, 0.30 mmol) in toluene (1.0 mL) under N₂ was added alkyne-4,4,5,5-tetramethyl-[1,3,2]-dioxaborolane¹ (0.30 mmol) and the reaction mixture was stirred for 30 min at rt, after which it was homogeneous. The reaction vessel was cooled to –78 °C and treated with Me₂Zn (0.15 mL, 2.0 M in toluene, 0.30 mmol) for 30 – 45 min. The solution was then warmed to –18 °C, and a solution of *N*-(2-pyridyl) sulfonyl imine² (0.2 mmol) in dichloromethane (4 ml) was added slowly to the solution over 10 min. The reaction mixture was stirred at –18 °C until TLC showed complete consumption of the imines (5–18 h). The reaction mixture was warmed to 0 °C, diluted with EtOAc (2 mL) and quenched with saturated NH₄Cl (2 mL). The organic layer was separated and the aqueous solution was extracted with EtOAc (3 x 5 mL). The combined organic layer was dried over MgSO₄, filtered through Celite and the solvent was removed under reduced pressure. The crude product was purified by flash column chromatography on silica gel (hexanes:EtOAc = 80:20) to give the desired B(pin)-substituted allylic amine.



(E)-N-(1-Phenyl-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)hept-2-enyl)pyridine-2-sulfonamide (1a). The product was prepared by General Procedure

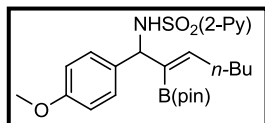
A using *N*-benzylidenepyridine-2-sulfonamide (49.3 mg, 0.2 mmol) and 2-hex-1-ynyl-4,4,5,5-tetramethyl-[1,3,2]-dioxaborolane (62.4 mg, 0.3 mmol). The crude product was purified by flash column chromatography on silica gel (hexanes:EtOAc = 80:20) to afford the title compound (73.0 mg, 80% yield). ^1H NMR (500 MHz, CDCl_3) δ 8.62 (dt, $J = 4.7, 0.8$ Hz, 1H), 7.90 (d, $J = 7.8$ Hz, 1H), 7.78 (td, $J = 7.7, 1.2$ Hz, 1H), 7.38 (dd, $J = 7.6, 4.7$ Hz, 1H), 7.27-7.26 (m, 2H), 7.19 (t, $J = 7.6$ Hz, 2H), 7.14-7.12 (m, 1H), 6.28 (d, $J = 9.8$ Hz, 1H), 5.98 (t, $J = 7.5$ Hz, 1H), 5.05 (d, $J = 9.8$ Hz, 1H), 2.26 – 2.15 (m, 1H), 2.01 (m, 1H), 1.24 – 1.16 (m, 4H), 1.13 (s, 6H), 1.03 (s, 6H), 0.85 (t, $J = 7.0$ Hz, 3H); $^{13}\text{C}\{^1\text{H}\}$ NMR (125 MHz, CDCl_3) δ 158.7, 150.3, 150.1, 141.6, 137.7, 128.1, 127.0, 126.8, 126.3, 122.3, 83.6, 64.6, 31.8, 30.5, 24.9, 24.4, 22.4, 14.1 (the quaternary vinyl C bearing the boron group is not observed); $^{11}\text{B}\{^1\text{H}\}$ NMR (CDCl_3 , 128 MHz) δ 28.6; IR (neat) 3312, 2977, 1634, 1427, 1339, 1178, 1141 cm^{-1} ; HRMS m/z 457.2333 [(MH) $^+$; calcd for $\text{C}_{24}\text{H}_{34}\text{BN}_2\text{O}_4\text{S}$: 457.2327].



(E)-N-(1,3-Diphenyl-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)allyl)pyridine-2-sulfonamide (1b). The product was prepared by General Procedure A using *N*-

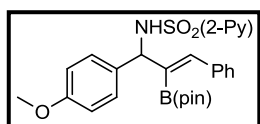
benzylidenepyridine-2-sulfonamide (49.3 mg, 0.20 mmol) and 4,4,5,5-tetramethyl-2-(phenylethynyl)-[1,3,2]-dioxaborolane (45.6 mg, 0.30 mmol). The crude product was purified by flash column chromatography on silica gel (hexanes:EtOAc = 80:20) to afford the title compound (64.8 mg, 68% yield). ^1H NMR (300 MHz, CDCl_3) δ 8.59 – 8.52 (m, 1H), 7.90 (d, $J = 7.8$ Hz, 1H), 7.66 (td, $J = 7.8, 1.7$ Hz, 1H), 7.35 (d, $J = 7.3$ Hz, 2H), 7.26 – 7.18 (m, 7H), 7.13 – 7.06 (m, 2H), 6.79 (s, 1H), 6.20 (d, $J = 9.7$ Hz, 1H), 5.29 (d, $J = 9.7$ Hz, 1H), 1.03 (s, 6H), 0.93 (s, 6H); $^{13}\text{C}\{^1\text{H}\}$ NMR (125 MHz, CDCl_3) δ 158.1, 149.9, 144.3, 140.1, 137.4, 136.8, 128.6, 128.1, 128.0, 127.6, 127.2, 126.7, 126.1, 122.1, 83.9, 64.6, 24.4, 24.1 (the quaternary vinyl C bearing the boron group is not observed). $^{11}\text{B}\{^1\text{H}\}$ NMR (CDCl_3 , 128 MHz)

δ 28.7; IR (neat) 3304, 2978, 1627, 1494, 1427, 1335, 1177, 1141 cm^{-1} ; $^1\text{HRMS}$ m/z 499.1828 $[(\text{M}+\text{Na})^+]$; calcd for $\text{C}_{26}\text{H}_{29}\text{BN}_2\text{NaO}_4\text{S}$: 499.1833].



(E)-N-(1-(4-Methoxyphenyl)-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)hept-2-enyl)pyridine-2-sulfonamide (1c). The product was prepared by

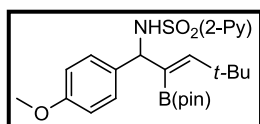
General Procedure A using *N*-(4-methoxybenzylidene)pyridine-2-sulfonamide (55.2 mg, 0.20 mmol) and 2-hex-1-ynyl-4,4,5,5-tetramethyl-[1,3,2]-dioxaborolane (62.4 mg, 0.30 mmol). The crude product was purified by flash column chromatography on silica gel (hexanes:EtOAc = 80:20) to afford the title compound as a white solid (84.6 mg, 87% yield). m.p. 108-111 $^{\circ}\text{C}$. ^1H NMR (500 MHz, CDCl_3) δ 8.63 (d, J = 4.4 Hz, 1H), 7.90 (d, J = 7.8 Hz, 1H), 7.80 (td, J = 7.7, 1.7 Hz, 1H), 7.40 (ddd, J = 7.7, 4.7, 1.2 Hz, 1H), 7.18 (d, J = 8.5 Hz, 2H), 6.74 (d, J = 8.8 Hz, 2H), 6.27 (d, J = 9.8 Hz, 1H), 5.95 (t, J = 7.6 Hz, 1H), 5.00 (d, J = 9.7 Hz, 1H), 3.76 (s, 3H), 2.24 – 2.13 (m, 1H), 2.08 – 1.95 (m, 1H), 1.32 – 1.23 (m, 2H), 1.23 – 1.17 (m, 2H), 1.15 (s, 6H), 1.06 (s, 6H), 0.86 (t, J = 7.0 Hz, 3H); $^{13}\text{C}\{^1\text{H}\}$ NMR (125 MHz, CDCl_3) δ 158.4 (two overlapping carbon signals), 149.8, 149.5, 137.3, 133.6, 127.7, 125.9, 122.1, 113.2, 83.3, 63.8, 55.2, 31.5, 30.2, 24.7, 24.2, 22.1, 13.8 (the quaternary vinyl C bearing the boron group is not observed); $^{11}\text{B}\{^1\text{H}\}$ NMR (CDCl_3 , 128 MHz) δ 30.5; IR (neat) 3310, 2958, 1611, 1511, 1427, 1339, 1250, 1177, 1141 cm^{-1} ; HRMS m/z 509.2244 $[(\text{M}+\text{Na})^+]$; calcd for $\text{C}_{25}\text{H}_{35}\text{BN}_2\text{NaO}_5\text{S}$: 509.2252].



(E)-N-(1-(4-Methoxyphenyl)-3-phenyl-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)allyl)pyridine-2-sulfonamide (1d). The product was prepared

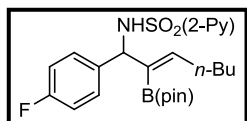
by General Procedure A using *N*-(4-methoxybenzylidene)pyridine-2-sulfonamide (55.2 mg, 0.20 mmol) and 4,4,5,5-tetramethyl-2-(phenylethynyl)-1,3,2-dioxaborolane (45.6 mg, 0.30 mmol). The crude product was purified by flash column chromatography on silica gel (hexanes:EtOAc = 80:20) to afford the title compound as a white solid (94.1 mg, 93% yield). m.p. 145-147 $^{\circ}\text{C}$. ^1H NMR (500 MHz, CDCl_3) δ 8.60 – 8.54 (m, 1H), 7.89 (dd, J = 7.9, 1.1 Hz, 1H), 7.67 (td, J = 7.7, 1.7 Hz, 1H), 7.27 – 7.20 (m, 6H), 7.11 –

7.09 (m, 2H), 6.78 – 6.75 (m, 3H), 6.15 (d, $J = 9.7$ Hz, 1H), 5.24 (d, $J = 9.7$ Hz, 1H), 3.76 (s, 3H), 1.05 (s, 6H), 0.96 (s, 6H); $^{13}\text{C}\{^1\text{H}\}$ NMR (125 MHz, CDCl_3) δ 159.0, 158.3, 150.1, 144.1, 137.7, 137.0, 132.4, 128.8, 128.2, 128.2, 127.9, 126.3, 122.4, 113.7, 84.1, 64.3, 55.5, 24.7, 24.4 (the quaternary vinyl C bearing the boron group is not observed); $^{11}\text{B}\{^1\text{H}\}$ NMR (CDCl_3 , 128 MHz) δ 28.5; IR (neat) 3294, 2979, 1611, 1511, 1427, 1337, 1251, 1177, 1141 cm^{-1} ; HRMS m/z 529.1932 [(M+Na) $^+$; calcd for $\text{C}_{27}\text{H}_{31}\text{BN}_2\text{NaO}_5\text{S}$: 529.1931].



(E)-N-(1-(4-Methoxyphenyl)-4,4-dimethyl-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pent-2-enyl)pyridine-2-sulfonamide (1e). The product was

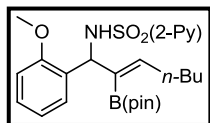
prepared by General Procedure A using *N*-(4-methoxybenzylidene)pyridine-2-sulfonamide (55.2 mg, 0.20 mmol) and 2-(3,3-dimethylbut-1-ynyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (62.4 mg, 0.30 mmol). The crude product was purified by flash column chromatography on silica gel (hexanes:EtOAc = 80:20) to afford the title compound as a white solid (58.4 mg, 60% yield). m.p. 166-168 °C. ^1H NMR (500 MHz, CDCl_3) δ 8.65 (d, $J = 4.3$ Hz, 1H), 7.91 (d, $J = 7.7$ Hz, 1H), 7.80 (t, $J = 7.4$ Hz, 1H), 7.40 (dd, $J = 7.4, 4.7$ Hz, 1H), 7.21 (d, $J = 8.6$ Hz, 2H), 6.75 (d, $J = 8.6$ Hz, 2H), 6.12 (d, $J = 9.2$ Hz, 1H), 5.81 (s, 1H), 4.98 (d, $J = 9.2$ Hz, 1H), 3.75 (s, 3H), 1.03 (s, 6H), 1.01 (s, 6H), 0.91 (s, 9H); $^{13}\text{C}\{^1\text{H}\}$ NMR (125 MHz, CDCl_3) δ 158.9 (two overlapping carbon signals), 157.0, 150.2, 137.7, 133.1, 128.3, 126.3, 122.3, 113.6, 84.0, 65.3, 55.5, 33.6, 30.5, 24.8 (the quaternary vinyl C bearing the boron group is not observed); IR (neat) 3308, 2956, 1611, 1510, 1427, 1340, 1250, 1177, 1142 cm^{-1} ; HRMS m/z 509.2247 [(M+Na) $^+$; calcd for $\text{C}_{25}\text{H}_{35}\text{BN}_2\text{NaO}_5\text{S}$: 509.4210].



(E)-N-(1-(4-Fluorophenyl)-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)hept-2-enyl)pyridine-2-sulfonamide (1f). The product was prepared by General

Procedure A using *N*-(4-fluorobenzylidene)pyridine-2-sulfonamide (52.8 mg, 0.20 mmol) and 2-hex-1-ynyl-4,4,5,5-tetramethyl-[1,3,2]-dioxaborolane (62.4 mg, 0.30 mmol). The crude product was purified by

flash column chromatography on silica gel (hexanes:EtOAc = 80:20) to afford the title compound as a white solid (66.4 mg, 70% yield). m.p. 102-105 °C. ¹H NMR (500 MHz, CDCl₃) δ 8.66 – 8.61 (m, 1H), 7.91 (d, *J* = 7.8 Hz, 1H), 7.81 (td, *J* = 7.7, 1.6 Hz, 1H), 7.41 (dd, *J* = 7.5, 4.7 Hz, 1H), 7.28-7.22 (m, 2H), 6.89 (t, *J* = 8.7 Hz, 2H), 6.29 (d, *J* = 9.8 Hz, 1H), 5.96 (t, *J* = 7.6 Hz, 1H), 5.01 (d, *J* = 9.8 Hz, 1H), 2.23-2.13 (m, 1H), 2.05 – 1.95 (m, 1H), 1.21 – 1.15 (m, 4H), 1.15 (s, 6H), 1.04 (s, 6H), 0.85 (t, *J* = 7.0 Hz, 3H); ¹³C{¹H} NMR (125 MHz, CDCl₃) δ 163.0, 161.0, 158.5, 150.6 (d, *J* = 60 Hz), 137.7, 137.5 (d, *J* = 2.9 Hz), 128.4 (d, *J* = 7.9 Hz), 126.4, 122.3, 114.9 (d, *J* = 21.4 Hz), 83.7, 64.0, 31.8, 30.4, 24.9, 24.4, 22.4, 14.1 (the quaternary vinyl C bearing the boron group is not observed); IR (neat) 3308, 2956, 1611, 1510, 1427, 1340, 1250, 1177, 1142 cm⁻¹; HRMS *m/z* 497.2055 [(M+Na)⁺; calcd for C₂₄H₃₂BFN₂NaO₄S : 497.2052].

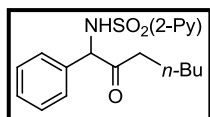


(*E*)-*N*-(1-(2-Methoxyphenyl)-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)hept-2-enyl)pyridine-2-sulfonamide (1g). The product was prepared by General Procedure

A using *N*-(2-methoxybenzylidene)pyridine-2-sulfonamide (55.2 mg, 0.20 mmol) and 2-hex-1-ynyl-4,4,5,5-tetramethyl-[1,3,2]-dioxaborolane (64.4 mg, 0.30 mmol). The crude product was purified by flash column chromatography on silica gel (hexanes:EtOAc = 80:20) to afford the title compound as a oil (51.6 mg, 53% yield). ¹H NMR (500 MHz, CDCl₃) δ 8.49 – 8.46 (m, 1H), 7.77 (d, *J* = 7.8 Hz, 1H), 7.65 (td, *J* = 7.7, 1.6 Hz, 1H), 7.29 – 7.22 (m, 1H), 7.10 (d, *J* = 7.5 Hz, 1H), 7.06 – 6.99 (m, 1H), 6.68 (t, *J* = 7.5 Hz, 1H), 6.60 (d, *J* = 8.2 Hz, 1H), 6.37 (d, *J* = 10.0 Hz, 1H), 6.01 (t, *J* = 7.6 Hz, 1H), 5.32 (d, *J* = 10.0 Hz, 1H), 3.68 (s, 3H), 2.17 – 2.07 (m, 2H), 1.23 – 1.15 (m, 16H), 0.84 (t, *J* = 6.8 Hz, 3H); ¹³C{¹H} NMR (125 MHz, CDCl₃) δ 158.2, 156.5, 149.8, 147.1, 137.3, 128.8, 128.6, 128.3, 126.0, 122.3, 120.0, 110.5, 83.5, 59.6, 55.3, 31.9, 30.6, 25.1, 24.7, 22.3, 14.1 (the quaternary vinyl C bearing the boron group is not observed); IR (neat) 3308, 2957, 1600, 1493, 1427, 1343, 1246, 1178, 1142 cm⁻¹; HRMS *m/z* 509.2249 [(M+Na)⁺; calcd for C₂₅H₃₅BN₂NaO₅S : 509.2252].

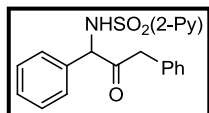
IV. Synthesis and Characterization of α -Amino Ketones:

General Procedure B: Synthesis of α -Amino Ketones. To a solution of allylic amine boronate ester (0.10 mmol) in a 1:1 mixture of THF : H₂O (1 mL each) was added NaBO₃·H₂O (0.30 mmol) at rt. The resulting suspension was stirred at rt until the reaction was complete by TLC (2–6 h). Water was added (1 mL) and the solution was extracted with Et₂O (3 x 10 mL). The combined diethyl ether phase was washed with brine, dried with anhydrous Na₂SO₄, and the solvent was removed under reduced pressure. The crude product was purified by flash column chromatography on silica gel to obtain the pure α -amino ketone.



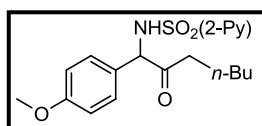
***N*-(2-Oxo-1-phenylheptyl)pyridine-2-sulfonamide (2a).** The product was prepared by General Procedure B using **1a** (45.6 mg, 0.10 mmol). The crude product was purified by flash column chromatography on silica gel (hexanes:EtOAc = 70:30) to afford the title compound as a white solid (27.7 mg, 80% yield). m.p. 100-102 °C. ¹H NMR (500 MHz, CDCl₃) δ 8.52 (d, J = 4.7 Hz, 1H), 7.67 – 7.62 (m, 2H), 7.35 – 7.28 (m, 1H), 7.22 – 7.15 (m, 3H), 7.14 – 7.09 (m, 2H), 6.37 (d, J = 6.3 Hz, 1H), 5.38 (d, J = 6.3 Hz, 1H), 2.41 – 2.22 (m, 2H), 1.51 – 1.44 (m, 1H), 1.42 – 1.35 (m, 1H), 1.18 – 1.11 (m, 2H), 1.10 – 1.02 (m, 2H), 0.78 (t, J = 7.2 Hz, 3H); ¹³C{¹H} NMR (125 MHz, CDCl₃) δ 204.5, 158.3, 149.8, 137.8, 135.4, 129.1, 128.8, 128.3, 126.5, 121.8, 66.5, 39.6, 31.2, 23.5, 22.4, 14.0; IR (neat) 3280, 2929, 2855, 1721, 1579, 1455, 1427, 1335, 1246, 1176, 1121 cm⁻¹; HRMS m/z 347.1435 [(MH)⁺; calcd for C₁₈H₂₃N₂O₃S : 347.1424].

Synthesis of **2a** in a tandem procedure: After completion of the addition step as judged by TLC, the reaction was removed under vacuum pressure. THF/H₂O (1 mL each) was added followed by NaBO₃·H₂O (29.9 mg, 0.30 mmol). The crude product was purified by flash column chromatography on silica gel (hexanes:EtOAc = 70:30) to obtain the α -amino ketone as a white solid (23.5 mg, 68% yield).



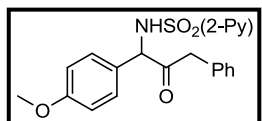
***N*-(2-Oxo-1,3-diphenylpropyl)pyridine-2-sulfonamide (2b).** The product was prepared by General Procedure B using **1b** (47.6 mg, 0.10 mmol). The crude product

was purified by flash column chromatography on silica gel (hexanes:EtOAc = 70:30) to afford the title compound as a white solid (27.5 mg, 75% yield). m.p. 159-160 °C. ¹H NMR (500 MHz, CDCl₃) δ 8.45 – 8.42 (m, 1H), 7.69 – 7.58 (m, 2H), 7.35 – 7.28 (m, 1H), 7.27 – 7.21 (m, 6H), 7.15 (dd, *J* = 7.4, 2.2 Hz, 2H), 6.96 (dd, *J* = 6.5, 2.8 Hz, 2H), 6.39 (s, 1H), 5.52 (s, 1H), 3.63 (s, 2H); ¹³C{¹H} NMR (125 MHz, CDCl₃) δ 201.8, 158.1, 149.8, 137.8, 135.0, 132.8, 129.6, 129.3, 129.0, 128.9, 128.6, 127.5, 126.5, 121.7, 65.9, 46.2; IR (neat) 3138, 2906, 2851, 1724, 1580, 1456, 1427, 1340, 1178, 1120 cm⁻¹; HRMS *m/z* [(MH)⁺; calcd for C₂₀H₁₉N₂O₃S : 367.1111].



***N*-(1-(4-Methoxyphenyl)-2-oxoheptyl)pyridine-2-sulfonamide (2c).** The product was prepared by General Procedure B using **1c** (48.6 mg, 0.10 mmol).

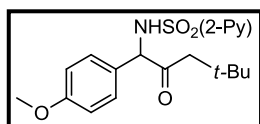
The crude product was purified by flash column chromatography on silica gel (hexanes:EtOAc = 70:30) to afford the title compound as a white solid (36.1 mg, 96% yield). m.p. 91-94 °C. ¹H NMR (500 MHz, CDCl₃) δ 8.57 – 8.54 (m, 1H), 7.73 – 7.63 (m, 2H), 7.39 – 7.32 (m, 1H), 7.04 (d, *J* = 8.7, 1.4 Hz, 2H), 6.71 (d, *J* = 8.7, 1.3 Hz, 2H), 6.36 (d, *J* = 6.3 Hz, 1H), 5.34 (d, *J* = 6.4 Hz, 1H), 3.75 (s, 3H), 2.39 – 2.25 (m, 2H), 1.54 – 1.44 (m, 1H), 1.44 – 1.35 (m, 1H), 1.21 – 1.13 (m, 2H), 1.13 – 1.05 (m, 2H), 0.81 (t, *J* = 7.2, 1.2 Hz, 3H); ¹³C{¹H} NMR (125 MHz, CDCl₃) δ 204.7, 160.0, 158.4, 149.8, 137.8, 129.6, 127.4, 126.4, 121.9, 114.5, 65.8, 55.5, 39.5, 31.2, 23.5, 22.4, 14.0; IR (neat) 3273, 2928, 2857, 1718, 1609, 1512, 1427, 1340, 1254, 1176 cm⁻¹; HRMS *m/z* 377.1546 [(MH)⁺; calcd for C₁₉H₂₅N₂O₄S : 377.1530].



***N*-(1-(4-Methoxyphenyl)-2-oxo-3-phenylpropyl)pyridine-2-sulfonamide (2d).**

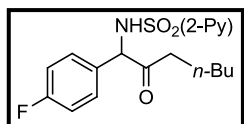
The product was prepared by General Procedure B using **1d** (50.6 mg, 0.10 mmol). The crude product was purified by flash column chromatography on silica gel (hexanes:EtOAc = 70:30) to afford the title compound as a white solid (38.8 mg, 98% yield). m.p. 126-129 °C. ¹H NMR

(500 MHz, CDCl₃) δ 8.44 (d, *J* = 4.6 Hz, 1H), 7.70 – 7.59 (m, 2H), 7.35 – 7.29 (m, 1H), 7.27 – 7.23 (m, 3H), 7.05 (d, *J* = 8.6 Hz, 2H), 6.97-6.97 (m, 2H), 6.74 (d, *J* = 8.6 Hz, 2H), 6.36 (d, *J* = 6.4 Hz, 1H), 5.45 (d, *J* = 6.1 Hz, 1H), 3.78 (s, 3H), 3.62 (s, 2H); ¹³C{¹H} NMR (125 MHz, CDCl₃) δ 202.0, 160.1, 158.2, 149.8, 137.7, 132.9, 129.9, 129.6, 128.9, 127.5, 127.0, 126.4, 121.8, 114.6, 65.2, 55.5, 46.2; IR (neat) 3436, 3279, 3088, 2839, 1724, 1609, 1512, 1427, 1341, 1255, 1177, 1120 cm⁻¹; HRMS *m/z* 397.1229 [(MH)⁺; calcd for C₂₁H₂₁N₂O₄S : 397.1217].



***N*-(1-(4-Methoxyphenyl)-4,4-dimethyl-2-oxopentyl)pyridine-2-sulfonamide (2e)**. The product was prepared by General Procedure B using **1e** (48.6 mg, 0.10

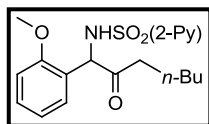
mmol). The crude product was purified by flash column chromatography on silica gel (hexanes:EtOAc = 70:30) to afford the title compound as a oil (32.7 mg, 87% yield). ¹H NMR (500 MHz, CDCl₃) δ 8.55 (m, 1H), 7.71 – 7.60 (m, 2H), 7.36 – 7.31 (m, 1H), 7.02 (d, *J* = 8.7 Hz, 2H), 6.70 (d, *J* = 8.7 Hz, 2H), 6.40 (d, *J* = 6.2 Hz, 1H), 5.24 (d, *J* = 5.9 Hz, 1H), 3.74 (s, 3H), 2.29 (d, *J* = 15.7 Hz, 1H), 2.11 (d, *J* = 15.7 Hz, 1H), 0.89 (s, 9H); ¹³C{¹H} NMR (125 MHz, CDCl₃) δ 203.6, 159.9, 158.4, 149.8, 137.7, 129.8, 127.2, 126.4, 121.9, 114.5, 66.8, 55.5, 51.6, 31.4, 29.7; IR (neat) 3275, 2955, 2870, 1720, 1609, 1512, 1427, 1341, 1254, 1177, 1121 cm⁻¹; HRMS *m/z* 399.1358 [(M+Na)⁺; calcd for C₁₉H₂₄N₂NaO₄S : 399.1349].



***N*-(1-(4-Fluorophenyl)-2-oxoheptyl)pyridine-2-sulfonamide (2f)**. The product was prepared by General Procedure B using **1f** (47.4 mg, 0.10 mmol). The crude

product was purified by flash column chromatography on silica gel (hexanes:EtOAc = 70:30) to afford the title compound as a white solid (25.8 mg, 71% yield). m.p. 83-86 °C. ¹H NMR (500 MHz, CDCl₃) δ 8.58 – 8.51 (m, 1H), 7.80 – 7.63 (m, 2H), 7.41 – 7.35 (m, 1H), 7.19 – 7.08 (m, 2H), 6.90 (t, *J* = 8.3 Hz, 2H), 6.43 (d, *J* = 6.2 Hz, 1H), 5.41 (d, *J* = 5.2 Hz, 1H), 2.44 – 2.22 (m, 2H), 1.57 – 1.46 (m, 1H), 1.45 – 1.41 (m, 1H), 1.23 – 1.15 (m, 2H), 1.13 – 1.03 (m, 2H), 0.81 (t, *J* = 7.2 Hz, 3H); ¹³C{¹H} NMR (125 MHz, CDCl₃) δ 204.3, 163.9 (d, *J* = 248 Hz), 158.3, 149.9, 137.9, 131.5 (d, *J* = 3.1 Hz), 130.2 (d, *J* = 8.4 Hz),

126.6, 121.8, 116.2 (d, $J = 21.8$ Hz), 65.7, 39.6, 31.2, 23.5, 22.4, 14.0; IR (neat) 3273, 2957, 2931, 2871, 1722, 1604, 1580, 1509, 1428, 1341, 1227, 1178, 1121 cm^{-1} ; HRMS m/z 387.1150 [(M+Na) $^+$]; calcd for $\text{C}_{18}\text{H}_{21}\text{FN}_2\text{NaO}_3\text{S}$: 387.1149].



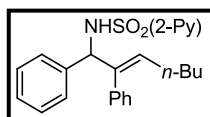
***N*-(1-(2-Methoxyphenyl)-2-oxoheptyl)pyridine-2-sulfonamide (2g).** The product was prepared by General Procedure B using **1g** (48.6 mg, 0.10 mmol). The crude

product was purified by flash column chromatography on silica gel (hexanes:EtOAc = 70:30) to afford the title compound as a oil (32.7 mg, 87% yield). ^1H NMR (500 MHz, CDCl_3) δ 8.51 (d, $J = 4.6$ Hz, 1H), 7.73 – 7.65 (m, 2H), 7.35 – 7.29 (m, 1H), 7.22 – 7.15 (m, 1H), 7.12 (dd, $J = 7.5, 1.7$ Hz, 1H), 6.81 (td, $J = 7.5, 1.1$ Hz, 1H), 6.70 – 6.67 (m, 1H), 6.35 (d, $J = 7.5$ Hz, 1H), 5.45 (d, $J = 7.5$ Hz, 1H), 3.72 (s, 3H), 2.38 – 2.27 (m, 1H), 2.27 – 2.18 (m, 1H), 1.52 – 1.39 (m, 2H), 1.22 – 1.14 (m, 2H), 1.13 – 1.05 (m, 2H), 0.81 (t, $J = 7.2$ Hz, 3H); $^{13}\text{C}\{^1\text{H}\}$ NMR (125 MHz, CDCl_3) δ 204.4, 158.2, 156.8, 149.7, 137.7, 130.8, 130.2, 126.3, 124.2, 121.8, 121.1, 111.0, 63.3, 55.6, 38.8, 31.3, 23.6, 22.5, 14.0; IR (neat) 3284, 2958, 2858, 1724, 1600, 1580, 1494, 1464, 1342, 1252, 1177, 1120 cm^{-1} ; HRMS m/z 377.1549 [(MH) $^+$]; calcd for $\text{C}_{19}\text{H}_{25}\text{N}_2\text{O}_4\text{S}$: 377.1530].

IV. Synthesis and Characterization of Trisubstituted 2-Arylated Allylic Amines:

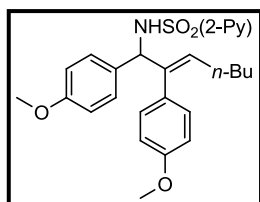
General Procedure C: Suzuki Cross-Coupling of B(pin)-substituted Allylic Amines. To a Schlenk flask was added $\text{Pd}(\text{OAc})_2$ (15 mol %) and PPh_3 (30 mol %) in 1 mL of dry and degassed THF at rt under N_2 and the solution stirred for 30 – 45 min. To this catalyst solution was added 2-B(pin)-substituted allylic amine (0.10 mmol), immediately followed by Cs_2CO_3 (0.30 mmol), 1 mL of degassed H_2O , and aryl bromide (0.30 mmol). The reaction mixture was heated in an oil bath at 75 $^\circ\text{C}$ until the B(pin)-substituted allylic amine had been fully consumed by TLC (12-24 h). The reaction was cooled to rt, diluted with EtOAc (1 mL) and saturated aqueous NH_4Cl (1 mL) was added. The organic layer was separated and the aqueous solution was extracted with EtOAc (3 x 10 mL). The combined organic layer

was washed with brine, dried over MgSO₄, filtered through Celite and the solvent was removed under reduced pressure. The crude product was purified by flash column chromatography on silica gel (hexanes:EtOAc = 80:20) to afford the trisubstituted allylic amine.



(E)-N-(1,2-Diphenylhept-2-enyl)benzenesulfonamide (3a). The product was prepared by General Procedure C using **1a** (45.6 mg, 0.10 mmol) and bromobenzene

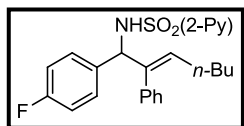
(31.6 μL, 0.30 mmol). The crude product was purified by flash column chromatography on silica gel (hexanes:EtOAc = 80:20) to afford the title compound as a white solid (29.6 mg, 73% yield). m.p. 100-103 °C. ¹H NMR (500 MHz, CDCl₃) δ 8.62 – 8.57 (d, *J* = 4.8 Hz, 1H), 7.86 (d, *J* = 7.8 Hz, 1H), 7.77 (td, *J* = 7.7, 1.7 Hz, 1H), 7.39 (ddd, *J* = 7.5, 4.6, 1.2 Hz, 1H), 7.20 – 7.15 (m, 6H), 7.14 – 7.09 (m, 2H), 6.81 – 6.75 (m, 2H), 5.62 (t, *J* = 7.4 Hz, 1H), 5.36 – 5.28 (m, 2H), 1.80 – 1.72 (m, 2H), 1.21 – 1.13 (m, 4H), 0.78 (t, *J* = 7.0 Hz, 3H); ¹³C{¹H} NMR (125 MHz, CDCl₃) δ 158.0, 150.2, 139.5, 137.8, 137.4, 131.6, 129.4, 128.4, 128.3, 127.6, 127.4 (overlapping carbon signals), 126.5, 122.3, 64.0, 31.9, 28.5, 22.4, 14.1; IR (neat) 3430, 2930, 1645, 1493, 1428, 1335, 1176 cm⁻¹; HRMS *m/z* 407.1794 [(MH)⁺; calcd for C₂₄H₂₇N₂O₂S : 407.1788].



(E)-N-(1,2-Bis(4-methoxyphenyl)hept-2-enyl)benzenesulfonamide (3b). The product was prepared by General Procedure C using **1c** (48.6 mg, 0.10 mmol) and 4-methoxybromobenzene (37.7 μL, 0.30 mmol). The crude product was purified

by flash column chromatography on silica gel (hexanes:EtOAc = 80:20) to afford the title compound as a white solid (32.7 mg, 70% yield). m.p. 117-120 °C. ¹H NMR (500 MHz, CDCl₃) δ 8.61 (d, *J* = 3.6 Hz, 1H), 7.86 (d, *J* = 7.8 Hz, 1H), 7.79 (td, *J* = 7.7, 1.8 Hz, 1H), 7.47 – 7.35 (m, 1H), 7.04 (d, *J* = 8.6 Hz, 2H), 6.85 – 6.60 (m, 6H), 5.55 (t, *J* = 7.3 Hz, 1H), 5.24 (s, 2H), 3.76 (s, 6H), 1.79 – 1.72 (m, 2H), 1.18 – 1.14 (m, 4H), 0.79 (t, *J* = 6.9 Hz, 3H); ¹³C{¹H} NMR (125 MHz, CDCl₃) δ 159.0, 158.8, 158.0, 150.2, 139.0, 137.8, 131.7, 131.2, 130.6, 129.6, 128.6, 126.5, 122.3, 113.8, 63.6, 55.4 (two overlapping carbon signals),

32.0, 28.5, 25.1, 22.4, 14.1; IR (neat) 3278, 2956, 2856, 1609, 1580, 1511, 1247, 1176 cm^{-1} ; HRMS m/z 489.1806 $[(M+Na)^+]$; calcd for $\text{C}_{26}\text{H}_{30}\text{N}_2\text{NaO}_4\text{S}$: 489.1818].

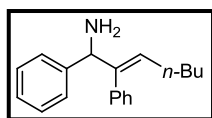


(E)-N-(1-(4-Fluorophenyl)-2-phenylhept-2-enyl)benzenesulfonamide (3c). The

product was prepared by General Procedure C using **1f** (47.4 mg, 0.10 mmol) and bromobenzene (31.6 μL , 0.30 mmol). The crude product was purified by flash column chromatography on silica gel (hexanes:EtOAc = 80:20) to afford the title compound (21.2 mg, 50% yield). ^1H NMR (300 MHz, CDCl_3) δ 8.60-8.54 (m, 1H), 7.89 – 7.72 (m, 2H), 7.48 – 7.34 (m, 1H), 7.22 – 7.15 (m, 3H), 7.16 – 7.03 (m, 2H), 6.86 (t, J = 8.6 Hz, 2H), 6.78 (dd, J = 6.5, 2.9 Hz, 2H), 5.59 (t, J = 7.4 Hz, 1H), 5.40 – 5.27 (m, 2H), 1.84 – 1.67 (m, 2H), 1.22 – 1.09 (m, 4H), 0.78 (t, J = 7.0 Hz, 3H); $^{13}\text{C}\{^1\text{H}\}$ NMR (125 MHz, CDCl_3) δ 163.1, 161.2, 157.8, 150.2, 139.3, 137.9, 137.2, 135.4 (d, J = 3 Hz), 131.8, 129.4, 129.1 (d, J = 8.13 Hz), 128.4, 127.5, 126.6, 122.3, 115.3 (d, J = 21.1 Hz), 63.4, 31.8, 28.5, 22.4, 14.1; IR (neat) 3275, 2957, 2929, 2858, 1604, 1509, 1428, 1339, 1224, 1177 cm^{-1} ; HRMS m/z $[(M+Na)^+]$; calcd for $\text{C}_{24}\text{H}_{25}\text{FN}_2\text{NaO}_2\text{S}$: 447.1513].

VI. Synthesis and Characterization of Trisubstituted 2-Arylated Allylic Primary Amine.

Procedure for the *N*-Deprotection of the (2-Pyridyl)sulfonyl Group:

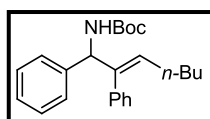


(E)-1,2-Diphenylhept-2-en-1-amine (4). To a solution of compound **3a** (40.6 mg, 0.10 mmol) in anhydrous methanol (4 mL) was added Mg power (24.0 mg, 1.0 mmol)

at rt and the reaction mixture was stirred for 2 hr. Equal volumes of diethyl ether and saturated aq. NH_4Cl were added and the reaction was stirred for 30 minutes. The aqueous layer was extracted with diethyl ether (3 x 10 mL) and the combined organic layers were dried over MgSO_4 , filtered through Celite and the solvent was removed under reduced pressure to give the crude primary amine (24.4 mg, 95% yield).

^1H NMR (500 MHz, CDCl_3) δ 7.32 – 7.17 (m, 8H), 6.92 – 6.85 (m, 2H), 5.76 (t, $J = 7.3$ Hz, 1H), 4.79 (s, 1H), 1.95 – 1.84 (m, 4H), 1.37 – 1.30 (m, 2H), 1.29 – 1.22 (m, 2H), 0.82 (t, $J = 7.2$ Hz, 3H); $^{13}\text{C}\{^1\text{H}\}$ NMR (125 MHz, CDCl_3) δ 144.5, 143.8, 139.3, 129.5, 128.4, 128.3, 128.0, 127.3, 127.0, 126.8, 62.2, 32.2, 28.6, 22.5, 14.1; HRMS m/z 249.1631 $[(\text{M}-\text{NH}_2)^+]$; calcd for $\text{C}_{19}\text{H}_{21}$: 249.1638].

VII. Synthesis and Characterization of Trisubstituted 2-Arylated Boc-protected Allylic Amine:



(*E*)-*N*-(1,2-Diphenylhept-2-enyl)pivalamide (5). Following the above procedure, compound **3a** (40.6 mg, 0.10 mmol) was transformed into the corresponding primary

amine **4** which, without further purification, was subsequently dissolved in CH_2Cl_2 (2 mL) and treated with di-*tert*-butylcarbonate (65.4 mg, 0.30 mmol). The reaction mixture was stirred at rt until TLC showed complete consumption of the primary amine **4** (5-10 h). The reaction solvent was removed under reduced pressure. The residue was purified by flash chromatography (hexanes:EtOAc = 80:20) to afford the title compound as a white solid (30.7 mg, 88% yield). m.p. 55-57 °C. ^1H NMR (500 MHz, CDCl_3) δ 7.34 – 7.27 (m, 2H), 7.26 – 7.19 (m, 6H), 6.95 (d, $J = 7.1$ Hz, 2H), 5.72 (t, $J = 7.4$ Hz, 1H), 5.51 (s, 1H), 4.89 (s, 1H), 2.00 – 1.85 (m, 2H), 1.44 (s, 9H), 1.38 – 1.28 (m, 2H), 1.29 – 1.20 (m, 2H), 0.82 (t, $J = 7.2$ Hz, 3H); $^{13}\text{C}\{^1\text{H}\}$ NMR (125 MHz, CDCl_3) δ 155.1, 140.9, 140.8, 138.7, 129.8, 129.5, 128.6, 128.2, 127.4 (two overlapping carbon peaks), 127.0, 79.7, 61.1, 32.2, 28.6, 28.5, 22.4, 14.1; IR (neat) 3443, 2959, 2930, 2872, 1703, 1601, 1493, 1366, 1249, 1169; HRMS m/z 388.2263 $[(\text{M}+\text{Na})^+]$; calcd for $\text{C}_{24}\text{H}_{31}\text{NNaO}$: 372.2298].

VIII. Spectra Data

