Supporting Information for:

A Mild Negishi Cross-Coupling of 2-Heterocyclic Organozinc Reagents and Aryl Chlorides

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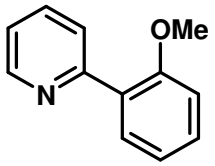
General Information. Unless otherwise noted, all reagents and solvents were obtained commercially and used without further purification. Tetrahydrofuran (THF) was dried with 4 Å molecular sieves. Extracts were dried over $MgSO_4$ and solvents were removed in vacuo via a rotary evaporator at aspirator pressure. Reactions were monitored by HPLC (C-18 column, 4.6 x 100 mm, 2.7 µm particle column; 35 °C; Mobile phase: (A) 0.1% H_3PO_4/water; (B) Acetonitrile. Gradient, 10-95% B in 6 min and hold at 95% B for 2 minutes. Flow rate, 1.8 mL/min. UV = 210 nm) and/or TLC (0.25mm silica gel plates with UV indicator). Compounds were purified by forced flow column chromatography using silica gel (230-400 mesh). ^{1}H and ^{13}C NMR spectra were recorded on a 400 MHz spectrometer at 400 MHz and 100 MHz and are internally referenced to residual protio solvent signals. Data for ^{1}H NMR are reported as follows: chemical shift (δ ppm), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet), integration and coupling constant (Hz). Data for ^{13}C NMR are reported in terms of chemical shift. HRMS data was obtained from an LC/MSD TOF spectrometer.

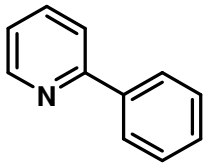
Representative procedure for the synthesis of 2-pyridyl and 2-thienylzinc chloride. A 3-neck round-bottom flask with a stirbar was charged with isopropylmagnesium chloride (2.0 M, 2.75 mL, 5.5 mmol, 1.1 eq). To this mixture was added neat 2-bromopyridine (0.476 mL, 5 mmol, 1.0 eq) or 2-bromothiophene (0.479 mL, 5 mmol, 1.0 eq) dropwise with the temperature not exceeding 30 °C. After 3-4 hrs, zinc chloride (0.5 M, 12 mL, 6 mmol, 1.2 eq) was added dropwise with the temperature not exceeding 30 °C. After 1 hr at room temperature, the mixture was used as is for subsequent cross-coupling.

Representative procedure for the Negishi cross-coupling. A solution of $Pd_2(dba)_3$ (18.3 mg, 0.02 mmol, 2 mol%) and XPhos (38.1 mg, 0.08 mmol, 8 mol%) in 2.72 mL of THF under nitrogen was heated and stirred to 65 ^{o}C. To this solution was added an aryl chloride substrate (1 mmol). After stirring for 15 minutes, an organozinc reagent (1.5 mmol) was added dropwise. The reaction was monitored by HPLC and/or TLC and upon completion was cooled to room temperature. The reaction was then quenched with 3 mL $NaHCO_3$ and 3 mL H_2O. After separation, the aqueous layer was extracted 3 times with EtOAc. The combined organic layers were washed with H_2O, dried over $MgSO_4$, filtered, and concentrated by rotary evaporation. The crude product was purified by column chromatography on silica gel with a gradient of EtOAc in hexanes.



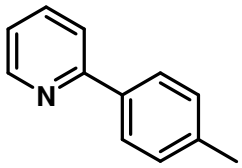
3a

Table 2, entry 3a:[1] Reaction time: 2 h. Yellow oil, purified by column chromatography on silica gel with a gradient of 0-25 % EtOAc in hexanes (182.6 mg, 97 % yield). ^{1}H NMR ($CDCl_3$, 400 MHz) ∂ 8.71 (d, 1H, *J* = 4.6 Hz), 7.82 (d, 1H, *J* = 8.0 Hz), 7.78 (dd, 1H, *J* = 7.6, 1.6 Hz), 7.71 (td, 1 H, *J* = 7.8, 1.7 Hz), 7.40-7.36 (m, 1H), 7.27-7.19 (m, 1H), 7.09 (t, 1H, *J* = 7.5 Hz), 7.01 (d, 1H, *J* = 8.3 Hz), 3.87 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz) ∂ 157.0, 156.2, 149.4, 135.6, 131.2, 129.9, 129.2, 125.1, 121.7, 121.1, 111.4, 55.6. HRMS calc'd for $C_{12}H_{11}NOH^+$: 186.0913, found: 186.0919.



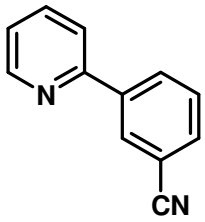
3b

Table 2, entry 3b:[2] Reaction time: 4.5 h. Yellow oil, purified by column chromatography on silica gel with a gradient of 0-15 % EtOAc in hexanes (132.9 mg, 86 % yield). ^{1}H NMR ($CDCl_3$, 400 MHz) ∂ 8.72-8.70 (m, 1 H), 8.02-7.99 (m, 2H), 7.76-7.74 (m, 2H), 7.51-7.47 (m, 2H), 7.44-7.40 (m, 1H), 7.27-7.22 (m, 1H). ^{13}C NMR ($CDCl_3$, 100 MHz) ∂ 157.5, 149.7, 139.5, 136.7, 129.0, 128.8 (2C), 126.9 (2C), 122.1, 120.6. HRMS calc'd for $C_{11}H_9NH^+$: 156.0808, found: 156.0810.



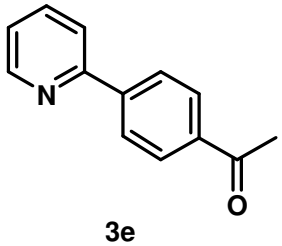
3c

Table 2, entry 3c:[3] Reaction time: 24 h. Yellow oil, purified by column chromatography on silica gel with a gradient of 0-10 % EtOAc in hexanes (150.4 mg, 89 % yield). ^{1}H NMR ($CDCl_3$, 500 MHz) ∂ 8.69 (d, 1H, *J* = 4.55 Hz), 7.91 (d, 2H, *J* = 8.2 Hz), 7.75-7.70 (m, 2H), 7.30 (d, 2H, *J* = 7.9 Hz), 7.21 (t, 1H, *J* = 4.0 Hz), 2.42 (s, 3H). ^{13}C NMR ($CDCl_3$, 125 MHz) ∂ 157.6, 149.7, 139.2, 137.0, 136.7, 129.7 (2C), 127.0 (2C), 122.0, 120.5, 21.4. HRMS calc'd for $C_{12}H_{11}NH^+$: 170.0964, found: 170.0972.



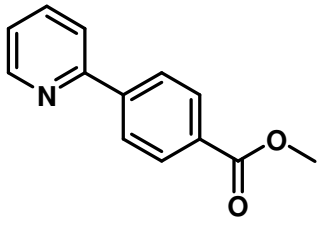
3d

Table 2, entry 3d:[4] Reaction time: 1.5 h. Yellow solid, purified by preparatory TLC on silica in a 25 % EtOAc in hexanes solvent system (160.1 mg, 89 % yield). ^{1}H NMR ($CDCl_3$, 400 MHz) ∂ 8.72 (dq, 1H, *J* = 4.8, 0.9 Hz), 8.32 (t, 1H, *J* = 1.5 Hz), 8.23 (dt, 1H, *J* = 8.1, 1.5 Hz), 7.81 (td, 1H, *J* = 7.7, 1.7 Hz), 7.74 (dt, 1H, *J* = 8.0, 1.9 Hz), 7.69 (dt, 1H, *J* = 6.4, 1.4 Hz), 7.59 (t, 1H, *J* = 7.7 Hz), 7.31 (qd, 1H, *J* = 4.4, 1.1 Hz). ^{13}C NMR ($CDCl_3$, 100 MHz) ∂ 154.9, 150.0, 140.4, 137.2, 132.2, 131.1, 130.6, 129.6, 123.2, 120.5, 118.7, 113.1. HRMS calc'd for $C_{12}H_8N_2H^+$: 181.0760, found: 181.0755.



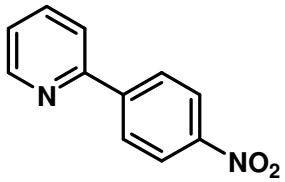
3e

Table 2, entry 3e:[3] Reaction time: 1 h. White solid, purified by column chromatography on silica gel with a gradient of 0-25 % EtOAc in hexanes (183.4 mg, 93 % yield). ^{1}H NMR ($CDCl_3$, 400 MHz) ∂ 8.76 (dt, 1H, *J* = 4.8, 1.3 Hz), 8.13 (dt, 2H, *J* = 10.0, 1.3 Hz), 8.09 (dt, 2H, *J* = 8.6, 1.8 Hz), 7.82 (dd, 2H, *J* = 4.0, 1.5 Hz), 7.32-7.29 (m, 1H), 2.68 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz) ∂ 197.8, 156.1, 150.0, 143.6, 137.2, 136.9, 128.8 (2C), 127.0 (2C), 122.9, 121.0, 27.7. HRMS calc'd for $C_{13}H_{11}NOH^+$: 198.0913, found: 198.0917.



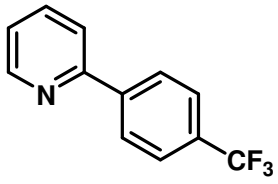
3f

Table 2, entry 3f:[5] Reaction time: 24 h. White solid, purified by column chromatography on silica gel with a gradient of 0-20 % EtOAc in hexanes (153.6 mg, 72 % yield). ^{1}H NMR ($CDCl_3$, 400 MHz) ∂ 8.73 (dt, 1H, *J* = 4.7, 1.3 Hz), 8.15 (d, 2H, *J* = 8.6 Hz), 8.08 (d, 2H, *J* = 8.6 Hz), 7.79 (d, 2H, *J* = 4.6, 1.4 Hz), 7.30-7.26 (m, 1H), 3.98 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz) ∂ 166.9, 156.3, 149.9, 143.5, 136.9, 130.4, 130.1 (2C), 126.8 (2C), 122.9, 121.0, 52.2. HRMS calc'd for $C_{13}H_{11}NO_2H^+$: 214.0863, found: 214.0860.



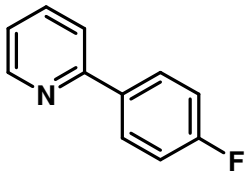
3g

Table 2, entry 3g:[6] Reaction time: 1 h. Yellow solid, purified by column chromatography on silica gel with a gradient of 0-25 % EtOAc in hexanes (141.5 mg, 70 % yield). ^{1}H NMR ($CDCl_3$, 400 MHz) ∂ 8.76 (dt, 1H, J = 4.7, 1.3 Hz), 8.34 (dt, 2H, J = 8.9, 2.2 Hz), 8.19 (dt, 2H, J = 9.0, 2.2 Hz), 7.84-7.80 (m, 2H), 7.37-7.33 (m, 1H). ^{13}C NMR ($CDCl_3$, 100 MHz) ∂ 154.9, 150.2, 148.2, 145.3, 137.1, 127.7 (2C), 124.0 (2C), 123.5, 121.2. HRMS calc'd for $C_{11}H_8N_2O_2H^+$: 201.0659, found: 201.0650.



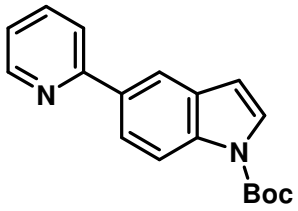
3h

Table 2, entry 3h:[7] Reaction time: 2.5 h. Yellow solid, purified by column chromatography on silica gel with a gradient of 0-15 % EtOAc in hexanes (192.6 mg, 86 % yield). ^{1}H NMR ($CDCl_3$, 400 MHz) ∂ 8.74 (dt, 1H, J = 4.8, 1.4 Hz), 8.13 (d, 2H, J = 8.1 Hz), 7.82-7.77 (m, 2H), 7.76-7.73 (m, 2H), 7.32-7.28 (m, 1H). ^{13}C NMR ($CDCl_3$, 100 MHz) ∂ 155.9, 150.0, 142.7, 137.0, 131.0, 130.7, 127.2, 125.7, 123.0, 120.9. HRMS calc'd for $C_{12}H_8F_3NH^+$: 224.0682, found: 224.0685.



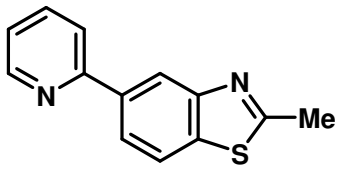
3i

Table 2, entry 3i:[7] Reaction time: 24 h. Yellow oil, purified by column chromatography on silica gel with a gradient of 0-15 % MTBE in hexanes (149.8 mg, 87 % yield). ^{1}H NMR ($CDCl_3$, 400 MHz) ∂ 8.68 (dq, 1H, J = 4.8, 1.0 Hz), 8.01-7.96 (m, 2H), 7.76-7.72 (m, 1H), 7.68 (dt, 1H, J = 8.0, 1.0 Hz), 7.24-7.21 (m, 1H), 7.18-7.14 (m, 2H). ^{13}C NMR ($CDCl_3$, 100 MHz) ∂ 163.6 (J = 247 Hz), 156.5, 149.7, 136.8, 135.6 (J = 3.0 Hz), 128.7, 122.0, 120.2, 115.7 (J = 22 Hz). HRMS calc'd for $C_{11}H_8FNH^+$: 174.0714, found: 174.0715.



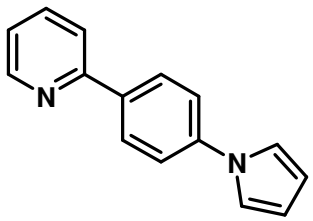
3j

Table 2, entry 3j:[8] Reaction time: 3 h. Yellow oil, purified by column chromatography on silica gel with a gradient of 0-25 % EtOAc in hexanes (277.0 mg, 94 % yield). ^{1}H NMR ($CDCl_3$, 400 MHz) ∂ 8.72 (dq, 1H, *J* = 4.9, 0.9 Hz), 8.25 (d, 1H *J* = 1.9 Hz), 8.23 (bs, 1H), 7.97 (dd, 1H, *J* = 8.7, 1.8 Hz), 7.82-7.75 (m, 2H), 7.64 (d, 1H, *J* = 3.6 Hz), 7.24 (qd, 1H, *J* = 4.8, 1.8 Hz), 6.66 (d, 1H, *J* = 3.6 Hz), 1.70 (s, 9H). ^{13}C NMR ($CDCl_3$, 100 MHz) ∂ 157.7, 149.7, 149.3, 137.1, 135.8, 133.8, 131.1, 126.7, 123.3, 121.7, 120.7, 119.7, 115.4, 107.8, 83.9, 28.2 (3C). HRMS calc'd for $C_{18}H_{18}N_2O_2H^+$: 295.1441, found: 295.1446.



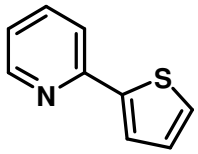
3k

Table 2, entry 3k: Reaction time: 2.5 h. White solid, purified by preparatory TLC on silica in a 25 % EtOAc in hexanes solvent system (145.0 mg, 64 % yield). ^{1}H NMR ($CDCl_3$, 400 MHz) ∂ 8.72 (dq, 1H, *J* = 4.8, 0.8 Hz), 8.51 (d, 1H, *J* = 1.6 Hz), 8.10 (dd, 1H, *J* = 8.4, 1.7 Hz), 7.90 (d, 1H, *J* = 8.4 Hz), 7.81-7.75 (m, 2H), 7.27-7.23 (m, 1H), 2.86 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz) ∂ 167.6, 157.1, 154.0, 149.8, 137.8, 136.9, 136.4, 123.8, 122.2, 121.6, 120.6, 120.6, 20.24. HRMS calc'd for $C_{13}H_{10}N_2SH^+$: 227.0637, found: 227.0631.



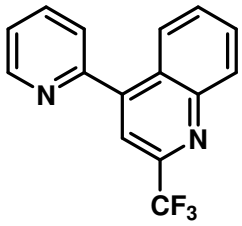
3l

Table 2, entry 3l: Reaction time: 1.5 h. Yellow solid, purified by column chromatography on silica gel with a gradient of 0-25 % EtOAc in hexanes (217.2 mg, 99 % yield). ^{1}H NMR ($CDCl_3$, 400 MHz) ∂ 8.71 (dt, 1H, *J* = 4.8, 1.3 Hz), 8.08 (dt, 2H, *J* = 3.7, 2.3 Hz), 7.78-7.74 (m, 2H), 7.52 (dt, 2H, *J* = 8.6, 2.3 Hz), 7.26-7.23 (m, 1H), 7.18 (t, 2H, *J* = 2.2 Hz), 6.40 (t, 2H, *J* = 2.2 Hz). ^{13}C NMR ($CDCl_3$, 100 MHz) ∂ 156.5, 149.8, 141.2, 136.9, 136.6, 128.1 (2C), 122.2, 120.4 (2C), 120.2, 119.2 (2C), 110.8 (2C). HRMS calc'd for $C_{15}H_{12}N_2H^+$: 221.1073, found: 221.1068.



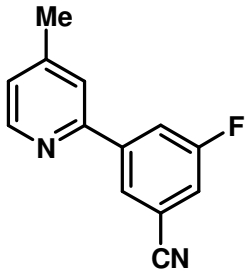
3m

Table 2, entry 3m:[9] Reaction time: 2.5 h. Yellow solid, , purified by column chromatography on silica gel with a gradient of 0-20 % EtOAc in hexanes (141.8 mg, 75 % yield). ^{1}H NMR ($CDCl_3$, 400 MHz) ∂ 8.58 (dt, 1H, J = 4.7, 1.3 Hz), 7.70-7.65 (m, 2H), 7.59 (dd, 1H, J = 5.0, 1.0 Hz), 7.40 (m, 1H), 7.16-7.10 (m, 2H). ^{13}C NMR ($CDCl_3$, 100 MHz) ∂ 152.6, 149.6, 144.9, 136.7, 128.1, 127.6, 124.5, 121.9, 118.8. HRMS calc'd for $C_9H_7NSH^+$: 162.0372, found: 162.0372.



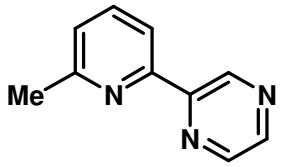
3n

Table 2, entry 3n: Reaction time: 1.5 h. Yellow solid, purified by column chromatography on silica gel with a gradient of 0-25 % EtOAc in hexanes (240.4 mg, 88 % yield). ^{1}H NMR ($CDCl_3$, 400 MHz) ∂ 8.87-8.85 (m, 1H), 8.31 (d, 1H, J = 8.4 Hz), 8.20 (d, 1H, J = 7.5 Hz), 7.92 (td, 1H, J = 7.7, 1.8 Hz), 7.87 (s, 1H), 7.86-7.81 (m, 1H), 7.68-7.64 (m, 2H), 7.47 (ddd, 1H, J = 7.6, 4.8, 1.1 Hz). ^{13}C NMR ($CDCl_3$, 100 MHz) ∂ 155.74, 150.17, 148.27 (J = 39 Hz), 147.67 (J = 35 Hz), 137.0, 130.6, 130.6, 129.0, 126.8, 125.7, 125.0, 123.7, 123.0, 120.2, 117.2. HRMS calc'd for $C_{15}H_9F_3N_2H^+$: 275.0791, found: 275.0795.



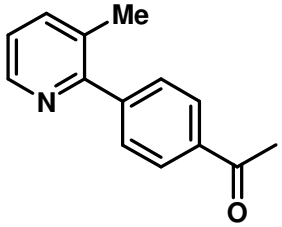
3o

Table 2, entry 3o: Reaction time: 3h. White solid, purified by column chromatography on silica gel with a gradient of 0-25 % EtOAc in hexanes (155 mg, 73% yield). ^{1}H NMR ($CDCl_3$, 400 MHz) ∂ 8.56 (d, 1H, J = 4.0 Hz), 8.09 (s, 1H), 7.98 (d, 1H, J = 8.0 Hz), 7.54 (s, 1H), 7.36 (d, 1H, J = 8.0Hz), 7.16 (d, 1H, J = 4.0 Hz), 2.44 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz) ∂ 162.8, (J = 248 Hz), 153.6, 145.0, 148.7, 143.4 (J = 8.0 Hz), 126.6, (J = 3.0 Hz), 124.9, 121.7, 119.1 (J = 20.0 Hz), 118.8 (J = 17.0 Hz), 117.7 (J = 3.0 Hz), 114.2 (J = 10.0 Hz), 21.4. HRMS calc'd for $C_{13}H_9FN_2H^+$: 213.0823, found: 213.0822.



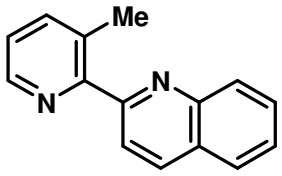
3p

Table 2, entry 3p:[10] Reaction time: 3h. 3.5 eq organozinc reagent used. Light red oil, purified by column chromatography on silica gel with a gradient of 0-25 % EtOAc in hexanes (170 mg, 99% yield). ^{1}H NMR ($CDCl_3$, 400 MHz) ∂ 9.62 (d, 1H, J = 1.0 Hz), 8.57 (dt, 2H, J = 6.6, 2.4 Hz), 8.11 (d, 1H, J = 7.8 Hz), 7.70 (t, 1H, J = 7.8 Hz), 7.19 (d, 1H, J = 7.7 Hz), 2.63 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz) ∂ 158.5, 153.8, 151.6, 144.4, 143.7, 143.6, 137.3, 124.1, 118.6, 24.7. HRMS calc'd for $C_{10}H_9N_3H^+$: 172.0869, found: 172.0877.



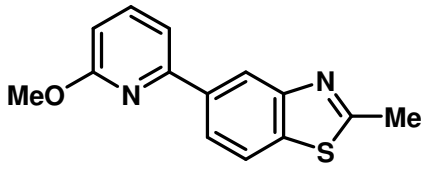
3q

Table 2, entry 3q:[11] Reaction time: 24 h. Light yellow oil, purified by preparatory TLC on silica in a 25 % EtOAc in hexanes solvent system (85.0 mg, 40 % yield). ^{1}H NMR ($CDCl_3$, 400 MHz) ∂ 8.56 (dd, 1H, J = 4.9, 1.2 Hz), 8.05 (dt, 2H, J = 8.2, 2.0 Hz), 7.65-.7.61 (m, 3H), 7.25-7.22 (m, 1H), 2.65 (s, 3H), 2.37 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz) ∂ 197.8, 157.3, 147.0, 145.0, 138.9, 136.5, 131.1, 129.3 (2C), 128.3 (2C), 122.7, 26.7, 19.9. HRMS calc'd for $C_{14}H_{13}NOH^+$: 212.1070, found: 212.1069.



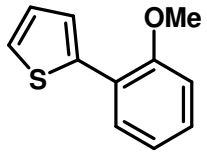
3r

Table 2, entry 3r: Reaction time: 4.5 h. White solid, purified by column chromatography on silica gel with a gradient of 0-25 % EtOAc in hexanes (164.7 mg, 75 % yield). ^{1}H NMR ($CDCl_3$, 400 MHz) ∂ 8.59 (dt, 1H, J = 4.8, 0.7 Hz), 8.28 (d, 1H, J = 8.6 Hz), 8.15 (d, 1H, J = 8.5 Hz), 7.98 (d, 1H, J = 8.5 Hz), 7.86 (dd, 1H, J = 8.2, 0.9 Hz), 7.73 (qd, 1H, J = 6.9, 1.5 Hz), 7.65 (dq, 1H, J = 7.7, 0.7 Hz), 7.57 (qd, 1H, J = 6.9, 1.1 Hz), 7.26 (q, 1H, J = 4.7 Hz), 2.63 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz) ∂ 158.8, 156.3, 147.3, 146.8, 139.4, 136.5, 133.0, 129.7, 129.5, 127.6, 127.3, 126.8, 123.2, 122.0, 20.3. HRMS calc'd for $C_{15}H_{12}N_2H^+$: 221.1073, found: 221.1076.



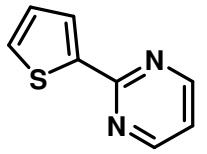
3s

Table 2, entry 3s: Reaction time: 6h. 3.5 eq organozinc reagent used. Light red oil, purified by column chromatography on silica gel with a gradient of 0-25 % EtOAc in hexanes (170 mg, 66% yield). ^{1}H NMR ($CDCl_3$, 400 MHz) ∂ 8.67 (s, 1H), 8.06 (dd, 1H, J = 2.0, 8.0 Hz), 7.86 (d, 1H, J = 8.0 Hz), 7.64 (d, 1H, J = 8.0 Hz), 7.41 (d, 1H, J = 8.0 Hz), 6.71 (d, 1H, J = 8.0 Hz), 4.06 (s, 3H), 2.85 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz) ∂ 167.7, 163.9, 154.3, 154.2, 139.4, 137.6, 136.3, 123.5, 121.5, 120.7, 112.9, 109.7, 53.4, 20.4. HRMS calc'd for $C_{14}H_{12}N_2OSH^+$: 257.0743, found: 257.0752.



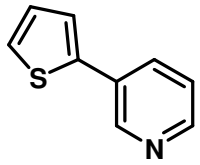
3t

Table 2, entry 3t:[12] Reaction time: 24 h. Yellow oil, purified by preparatory TLC on silica in a 10 % EtOAc in hexanes solvent system (173.3 mg, 91 % yield). ^{1}H NMR ($CDCl_3$, 400 MHz) ∂ 7.64 (dd, 1 H, J = 7.7, 1.8 Hz), 7.49 (dd, 1H, J = 3.6, 1.2 Hz), 7.31 (dd, 1H, J = 5.2, 1.2 Hz), 7.27-7.22 (m, 1H), 7.08-7.06 (m, 1H), 7.00-6.96 (m, 2H), 3.91 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz) ∂ 155.7, 139.5, 128.7, 128.4, 126.8, 125.4, 125.4, 123.4, 121.0, 111.7, 55.6. HRMS calc'd for $C_{11}H_{10}OSH^+$: 191.0525, found: 191.0530.



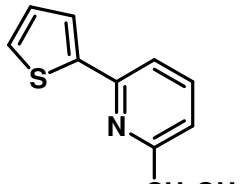
6a

Table 3, entry 6a:[13] Reaction time: 24 h. Light yellow solid, purified by column chromatography on silica gel with a gradient of 0-25 % EtOAc in hexanes (92.0 mg, 57 % yield). ^{1}H NMR ($CDCl_3$, 400 MHz) ∂ 8.70 (d, 2H, J = 4.8 Hz), 8.02 (dd, 1H, J = 3.8, 1.2 Hz), 7.49 (dd, 1H, J = 4.9, 1.2 Hz), 7.16-7.14 (m, 1H), 7.09 (t, 1H, J = 4.9 Hz). ^{13}C NMR ($CDCl_3$, 100 MHz) ∂ 161.6, 157.2 (2C), 143.1, 130.0, 129.1, 128.4, 118.5. HRMS calc'd for $C_8H_6N_2SH^+$: 163.0324, found: 163.0330.



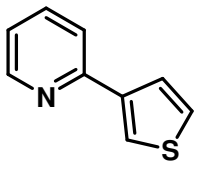
6b

Table 3, entry 6b:[14] Reaction time: 2h. 3.5 eq organozinc reagent used. Yellow oil, purified by column chromatography on silica gel with a gradient of 0-25 % EtOAc in hexanes (160 mg, 99% yield). ^{1}H NMR ($CDCl_3$, 400 MHz) ∂ 8.89 (d, 1H, *J* = 2.0 Hz), 8.51 (d, 1H, *J* = 4.0 Hz), 7.86 (dt, 1H, *J* = 2.0, 8.0 Hz), 7.37 (s, 1H), 7.35 (d, 1H, *J* = 4.0 Hz), 7.30 (q, 1H, *J* = 8.0 Hz), 7.12 (t, 1H, *J* = 8.0 Hz). ^{13}C NMR ($CDCl_3$, 100 MHz) ∂ 148.6, 147.2, 140.6, 133.2, 130.6, 128.4, 126.2, 124.4, 123.8. HRMS calc'd for $C_9H_7NSH^+$: 162.0372, found: 162.0376.



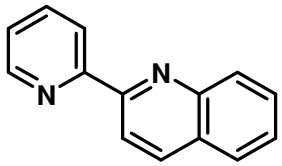
6c

Table 3, entry 6c:[15] Reaction time: 3h. Yellow oil, purified by preparatory TLC on silica in a 25 % EtOAc solvent system (42.1 mg, 81 % yield). ^{1}H NMR (CD_3CN, 400 MHz) ∂ 7.77 (td, 1H, J = 7.7, 1.2 Hz), 7.68-7.64 (m, 2H), 7.48-7.46 (m, 1H), 7.29 (dd, 1H, J = 7.7, 0.7 Hz), 7.14-7.12 (m, 1H), 4.65 (s, 2H), 4.00 (s, 1H). ^{13}C NMR ($CDCl_3$, 100 MHz) ∂ 158.6, 151.4, 144.4, 137.4, 128.1, 127.7, 124.9, 118.5, 117.3, 63.7. HRMS calc'd for $C_{10}H_9NOSH^+$: 192.0478, found: 192.0476.



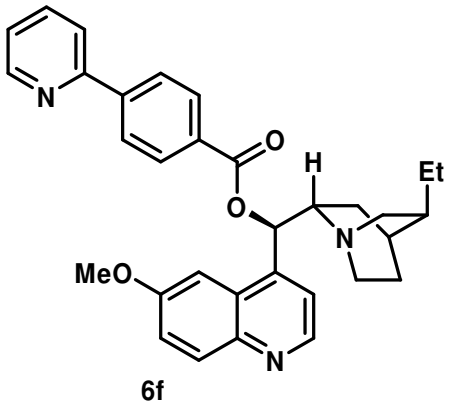
6d

Table 3, entry 6d:[7] Reaction time: 2h. Yellow oil, purified by column chromatography on silica gel with a gradient of 0-25 % EtOAc in hexanes (139 mg, 86% yield). ^{1}H NMR ($CDCl_3$, 400 MHz) ∂ 8.63 (d, 1H, *J* = 4.0 Hz), 7.91 (d, 1H, *J* = 4.0 Hz), 7.72-7.66 (m, 2H), 7.61 (d, 1H, *J* = 8.0 Hz), 7.40 (dd, 1H, *J* = 2.0, 4.0 Hz), 7.17 (dd, 1H, *J* = 2.0, 4.0 Hz). ^{13}C NMR ($CDCl_3$, 100 MHz) ∂ 153.7, 149.8, 142.3, 136.9, 126.5, 126.3, 123.6, 122.0, 120.5. HRMS calc'd for $C_9H_7NSH^+$: 162.0372, found: 162.0378.



6e

Table 3, entry 6e:[16] Reaction time: 0.5 h. Yellow solid, purified by column chromatography on silica gel with a gradient of 0-50 % EtOAc in hexanes (143.3 mg, 70 % yield). ^{1}H NMR ($CDCl_3$, 400 MHz) ∂ 8.76 (dq, 1H, *J* = 4.8, 0.9 Hz), 8.69 (dt, 1H, *J* = 8.0, 0.9 Hz), 8.59 (d, 1H, *J* = 8.6 Hz), 8.30 (d, 1H, *J* = 8.5 Hz), 8.22 (d, 1H, *J* = 8.5 Hz), 7.91-7.85 (m, 2H), 7.75 (qd, 1H, *J* = 6.8, 1.4 Hz), 7.57 (qd, 1H, *J* = 6.8, 1.1 Hz), 7.37 (ddd, 1H, *J* = 7.5, 4.8, 1.1 Hz). ^{13}C NMR ($CDCl_3$, 100 MHz) ∂ 156.2, 156.0, 149.1, 147.8, 137.1, 137.0, 129.8, 129.7, 128.3, 127.6, 126.8, 124.1, 122.0, 119.0. HRMS calc'd for $C_{14}H_{10}N_2H^+$: 207.0917, found: 207.0921.



6f

Table 3, entry 6f: Reaction time: 1h. Yellow foam, purified by column chromatography on silica gel with a gradient of 50-80 % acetone in dichloromethane (245 mg, 97% yield). ^{1}H NMR ($CDCl_3$, 400 MHz) ∂ 8.73 (s, 2H), 8.21 (d, 2H, *J* = 8.0 Hz), 8.12 (d, 2H, *J* = 8.0 Hz), 8.03 (d, 1H, *J* = 8.0 Hz), 7.78 (s, 2H), 7.54 (s, 1H), 7.46 (d, 1H, *J* = 4.0 Hz), 7.38 (dd, 1H, *J* = 4.0, 8.0 Hz), 7.31-7.27 (m, 1H), 6.78 (d, 1H, *J* = 4.0 Hz), 4.00 (s, 3H), 3.51 (dd, 1H, *J* = 4.0, 8.0 Hz), 3.23, bs (1H), 3.08 (dd, 1H, *J* = 12.0, 16.0 Hz), 2.72-2.67 (m, 1H), 2.40 (d, 1H, *J* = 1.0 Hz), 1.88-1.72 (m, 4H), 1.52-1.48 (m, 2H), 1.38-1.33 (m, 2H), 0.87 (t, 3H, *J* = 8.0 Hz). ^{13}C NMR ($CDCl_3$, 100 MHz) ∂ 165.4, 158.0, 156.0, 150.0, 147.5, 144.9, 144.1, 143.7, 137.0, 131.9, 130.1, 130.0, 127.1, 127.0, 123.0, 121.9, 121.0, 118.7, 101.5, 74.8, 59.3, 58.5, 55.7, 53.9, 42.8, 37.5, 29.3, 28.6, 27.8, 25.4, 23.9, 12.1. HRMS calc'd for $C_{32}H_{33}N_3O_3H^+$: 508.2595, found: 508.2599.

References:

1) Mongin, F.; Mojovic, L.; Guillamet, B.; Trécourt, F.; Quéguiner, G. *J. Org. Chem.* **2002**, *67*, 8991-8994.
2) Molander, G. A.; Biolatto, B. *J. Org. Chem.* **2003**, *68*, 4302-4314.
3) Nokami, T.; Tomida, Y.; Kamei, T.; Itami, K.; Yoshida, J. *Org. Lett.* **2006**, *8*, 729-731.
4) Cohen, T.; Deets, G. L. *J. Org. Chem.* **1972**, *37*, 55-58.
5) Bonnet, V.; Mongin, F.; Trécourt, F.; Quéguiner, G.; Knochel, P. *Tetrahedron* **2002**, *58*, 4429-4438.
6) Xu, J.; Cheng, G.; Su, D.; Liu, Y.; Wang, X.; Hu, Y. *Chem. Eur. J.* **2009**, *15*, 13105-13110.
7) Ackermann, L.; Potukuchi, H. K.; Kapdi, A. R.; Schulzke, C. *Chem. Eur. J.* **2010**, *16*, 3300-3303.
8) Çalimsiz, S.; Sayah, M.; Mallik, D.; Organ, M. G. *Angew. Chem. Int. Ed.* **2010**, *49*, 2014-2017.
9) Tingoli, M.; Tiecco, M.; Testaferri, L.; Andrenacci, R.; Balducci, R. *J. Org. Chem. 1993*, *58*, 6097-6102.
10) Uenishi, J.; Tanaka, T.; Nishiwaki, K.; Wakabayashi, S.; Oas, S.; Tsukube, H. *J. Org. Chem.* **1993**, *58*, 4382-4388.
11) Gosmini, C.; Nédélec, J. Y.; Périchon, J. *Tetrahedron Lett.* **2000**, *41*, 5039-5042.
12) Pena, M. A.; Sestelo, J. P.; Sarandeses, L. A. *J. Org. Chem.* **2007**, *72*, 1271-1275.
13) Billingsley, K.; Buchwald, S. L. *J. Am. Chem. Soc.* **2007**, *129*, 3358-3366.
14) Cioffi, C. L.; Spencer, W. T.; Richards, J. J.; Herr, R. J. J. Org. Chem. 2004, 69, 2210-2212.
15) Vacher, B.; Bonnaud, B.; Funes, P.; Jubault, N.; Koek, W.; Assié, M.-B.; Cosi, C. *J. Med. Chem.* **1998**, *41*, 5070-5083.
16) Martínez, R.; Ramón, D. J.; Yus, M. *Tetrahedron* **2006**, *62*, 8988-9001.