Supporting Information for:

Insights into Directing Group Ability in Palladium-Catalyzed C-H Bond Functionalization

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IA. General Procedures

NMR spectra were obtained on a Varian Inova 400 (399.96 MHz for ^{1}H; 100.57 MHz for ^{13}C; 376.34 MHz for ^{19}F) unless otherwise noted. ^{1}H NMR chemical shifts are reported in parts per million (ppm) relative to TMS, with the residual solvent peak used as an internal reference. Multiplicities are reported as follows: singlet (s), doublet (d), doublet of doublets (dd), doublet of doublets of doublets (ddd), doublet of triplets (dt), triplet (t), quartet (q), quintet (quin), multiplet (m), and broad resonance (br). IR spectra were obtained on a Perkin-Elmer spectrum BX FT-IR spectrometer.

IB. Materials and Methods

$Pd(OAc)_2$ was obtained from Pressure Chemical and used as received, and $PhI(OAc)_2$ was obtained from Merck Research Laboratories and used as received. Solvents were obtained from Fisher Chemical and used without further purification unless otherwise noted. THF was purified using an Innovative Technology (IT) solvent purification system composed of activated alumina, copper catalyst, and molecular sieves. Flash chromatography was performed on EM Science silica gel 60 (0.040–0.063 mm particle size, 230–400 mesh) and thin layer chromatography was performed on Merck TLC plates pre-coated with silica gel 60 F254. Melting points were determined with a Mel-Temp 3.0, a Laboratory Devices Inc, USA instrument and are uncorrected. HRMS data were obtained on a Micromass AutoSpec Ultima Magnetic Sector mass spectrometer. Gas chromatography was carried out on a Shimadzu 17A using a Restek Rtx®-5 (Crossbond 5% diphenyl – 95 % dimethyl polysiloxane; 15 m, 0.25 mm ID, 0.25 μm df) column. UV-vis kinetics were conducted on a UV-1601 Spectrometer Shimadzu TCC-240A using a quartz rectangular 10 mm cell sealed with a stopper.

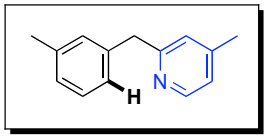
II. Synthesis and Characterization of Substrates 1a-16a

Synthesis of Benzyl Substrates 1a-8a, 14a, 16a and 16a-d_5

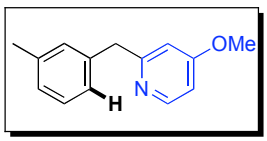
Substrates **1a-8a**, and **14a** were prepared via Pd-catalyzed Negishi coupling of (3-methylbenzyl)zinc bromide with the corresponding halopyridine derivative using a modification of a literature procedure.[1] The halopyridines were all commercially available except for 2-chloro-4-methoxypyridine, which was prepared according to a literature method.[2] Substrates **16a** and **16a-d_5** were prepared via Negishi coupling of benzyl bromide (or the deuterated benzyl bromide) with the corresponding halopyridine.

Synthesis of Zn reagent: A three-necked flask was charged with purified zinc dust[3] (1.2 equiv) and anhydrous THF. The mixture was heated to reflux, and 1,2-dibromoethane (0.04 equiv) was added. After heating at reflux for 15 min, the reaction was cooled to room temperature and TMSCl (0.05 equiv) was added. The resulting mixture was stirred at room temperature for 30 min, and then a solution of *m*-bromoxylenes (1 equiv) in anhydrous THF was added dropwise over a period of 2 h.

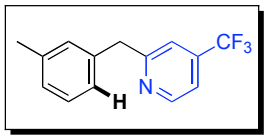
Negishi coupling. In a Schlenk flask, $Pd(OAc)_2$ (0.05 equiv) and P(*o*-tolyl)$_3$ (0.1 equiv) were dissolved in anhydrous THF, and this mixture was stirred for 10 min. The halopyridine (1.0 equiv) was then added, and the resulting mixture was cooled to 0 ºC. The aryl zinc reagent (2.0 equiv) was added dropwise to this solution over the course of 15 min, and the reaction was allowed to warm to room temperature and stirred overnight. Importantly, **1a-8a**, **14a**, **16a** and **16a-d_5** were purified by distillation to remove all residual palladium.



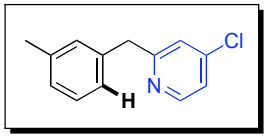
Substrate **1a** was obtained as a colorless oil (R_f = 0.26 in 80% hexanes/20% ethyl acetate). ^{1}H NMR ($CDCl_3$): δ 8.40 (d, *J* = 5.2 Hz, 1H), 7.20 (t, *J* = 7.6 Hz, 1H), 7.10-7.03 (multiple peaks, 3H), 6.94-6.92 (multiple peaks, 2H), 4.08 (s, 2H), 2.33 (s, 3H), 2.28 (s, 3H). $^{13}C\{^1H\}$ NMR ($CDCl_3$): δ 160.73, 148.94, 147.50, 139.47, 138.03, 129.77, 128.35, 127.00, 126.01, 123.87, 122.18, 44.44, 21.32, 20.91. HRMS electrospray (m/z): $[M-H]^+$ calcd for $C_{14}H_{15}N$, 196.1126; found, 196.1125.



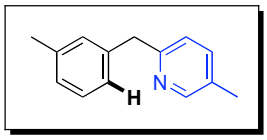
Substrate **2a** was obtained as a pale yellow oil (R_f = 0.22 in 70% hexanes/30% ethyl acetate). ^{1}H NMR ($CDCl_3$): δ 8.37 (d, *J* = 5.6 Hz, 1H), 7.19 (t, *J* = 7.2 Hz, 1H), 7.09-7.02 (multiple peaks, 3H), 6.65-6.62 (multiple peaks, 2H), 4.06 (s, 2H), 3.77 (s, 3H), 2.32 (s, 3H). $^{13}C\{^1H\}$ NMR ($CDCl_3$): δ 166.07, 162.67, 150.51, 139.21, 138.08, 129.79, 128.39, 127.08, 126.02, 109.11, 107.28, 54.92, 44.63, 21.34. HRMS electrospray (m/z): $[M-H]^+$ calcd for $C_{14}H_{15}NO$, 212.1075; found, 212.1070.



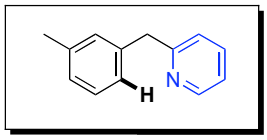
Substrate **3a** was obtained as a colorless oil (R_f = 0.26 in 90% hexanes/10% ethyl acetate). ^{1}H NMR ($CDCl_3$): δ 8.74 (d, J = 4.4 Hz, 1H), 7.36-7.34 (multiple peaks, 2H), 7.23 (t, J = 1.9 Hz, 1H), 7.11-7.07 (multiple peaks, 3H), 4.21 (s, 2H), 2.35 (s, 3H). ^{13}C{^{1}H} NMR ($CDCl_3$): δ 162.68, 150.29, 138.71 (q, $^2J_{CF}$ = 33.7 Hz), 138.40, 138.28, 129.80, 128.63, 127.50, 126.04, 122.80 (q, $^1J_{CF}$ = 271 Hz), 118.56 (q, $^3J_{CF}$ = 3.6 Hz), 116.84 (q, $^3J_{CF}$ = 2.9 Hz), 44.58, 21.32. ^{19}F{^{1}H} NMR ($CDCl_3$): δ –64.78. HRMS electrospray (m/z): $[M-H]^+$ Calcd for $C_{14}H_{12}F_3N$, 250.0843; Found, 250.0842.



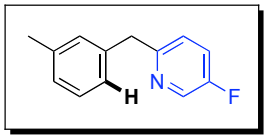
Substrate **4a** was obtained as a colorless oil (R_f = 0.26 in 80% hexanes/20% ethyl acetate). ^{1}H NMR ($CDCl_3$): δ 8.45 (d, J = 6.0 Hz, 1H), 7.22 (t, J = 7.6 Hz, 1H), 7.14-7.12 (multiple peaks, 2H), 7.08-7.07 (multiple peaks, 2H), 7.07 (s, 1H), 4.11 (s, 2H), 2.34 (s, 3H). ^{13}C{^{1}H} NMR ($CDCl_3$): δ 162.78, 150.14, 144.38, 138.42, 138.31, 129.83, 128.56, 127.40, 126.08, 123.30, 121.63, 44.36, 21.35. HRMS electrospray (m/z): $[M-H]^+$ Calcd for $C_{13}H_{12}ClN$, 216.0580; Found, 216.0581.



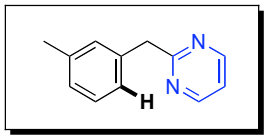
Substrate **5a** was obtained as a colorless oil (R_f = 0.26 in 80% hexanes/20% ethyl acetate). ^{1}H NMR ($CDCl_3$): δ 8.38 (d, J = 2.0 Hz, 1H), 7.38 (dd, J = 8.0, 2.4 Hz, 1H), 7.20 (t, J = 7.6 Hz, 1H), 7.09-7.00 (multiple peaks, 4H), 4.09 (s, 2H), 2.32 (s, 3H) 2.28 (s, 3H). ^{13}C{^{1}H} NMR ($CDCl_3$): δ 158.05, 149.54, 139.63, 138.02, 137.04, 130.34, 129.72, 128.34, 126.95, 125.95, 122.49, 44.09, 21.31, 17.94. HRMS electrospray (m/z): $[M-H]^+$ Calcd for $C_{14}H_{15}N$, 196.1126; Found, 196.1128.



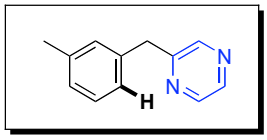
Substrate **6a** was obtained as a clear oil (R_f = 0.28 in 70% hexanes/30% ethyl acetate). ^{1}H NMR ($CDCl_3$): δ 8.56 (dd, J = 4.4, 1.2 Hz, 1H), 7.56 (dt, J = 7.6, 2.0 Hz, 1H), 7.20 (t, J = 7.6 Hz, 1H), 7.13-7.03 (multiple peaks, 5H), 4.13 (s, 2H), 2.33 (s, 3H). ^{13}C{^{1}H} NMR ($CDCl_3$): δ 161.02, 149.23, 139.30, 138.06, 136.40, 129.78, 128.34, 127.03, 126.02, 122.99, 121.08, 44.59, 21.30. HRMS electrospray (m/z): $[M-H]^+$ calcd for $C_{13}H_{13}N$, 182.0970; found, 182.0970.



Substrate **7a** was obtained as a colorless oil (R_f = 0.26 in 92% hexanes/8% ethyl acetate). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.41 (d, J = 2.8 Hz, 1H), 7.29 (td, J = 8.6, 3.2 Hz, 1H), 7.21 (t, J = 7.2 Hz, 1H), 7.11 (dd, J = 8.4, 4.4 Hz, 1H), 7.07-7.06 (multiple peaks, 2H), 7.04 (s, 1H), 4.11 (s, 2H), 2.33 (s, 3H). ^{13}C{^{1}H} NMR ($CDCl_3$): δ 158.08 (d, $^1J_{C\text{-}F}$ = 252.8 Hz), 157.07 (d, $^3J_{C\text{-}F}$ = 4.4 Hz), 139.19, 138.23, 137.22 (d, $^2J_{C\text{-}F}$ = 22.7 Hz), 129.73, 128.50, 127.22, 125.96, 123.74 (d, $^4J_{C\text{-}F}$ = 3.6 Hz), 123.23 (d, $^2J_{C\text{-}F}$ = 18.3 Hz), 43.74, 21.33. ^{19}F{^{1}H} NMR ($CDCl_3$): δ –131.23. HRMS electrospray (m/z): $[M\text{-}H]^+$ Calcd for $C_{13}H_{12}FN$, 200.0875; Found, 200.0872.

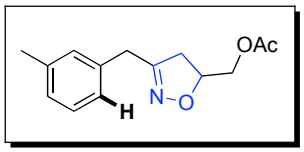


Substrate **8a** was obtained as a pale yellow oil (R_f = 0.28 in 70% hexanes/30% ethyl acetate). ^{1}H NMR ($CDCl_3$): δ 8.66 (d, J = 4.8 Hz, 2H), 7.21-7.15 (multiple peaks, 3H), 7.08 (t, J = 4.8 Hz, 1H), 7.02 (d, J = 6.8 Hz, 1H), 4.26 (s, 2H), 2.31 (s, 3H). ^{13}C{^{1}H} NMR ($CDCl_3$): δ 170.02, 157.17, 138.00, 129.76, 128.32, 127.26, 126.02, 118.48, 45.92, 21.28. Two carbons coincidentally overlap. HRMS electrospray (m/z): $[M\text{-}H]^+$ calcd for $C_{12}H_{12}N_2$, 183.0922; found, 183.0920.

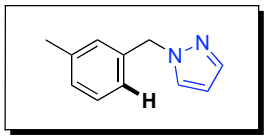


Substrate **14a** was obtained as a clear oil (R_f = 0.28 in 75% hexanes/25% ethyl acetate). ^{1}H NMR ($CDCl_3$): δ 8.50- 8.47 (multiple peaks, 2H), 8.40 (d, J = 2.8 Hz, 1H), 7.21 (t, J = 7.6 Hz, 1H), 7.08-7.04 (multiple peaks, 3H), 4.13 (s, 2H), 2.32 (s, 3H). ^{13}C{^{1}H} NMR ($CDCl_3$): δ 156.53, 144.70, 144.00, 142.24, 138.34, 137.93, 129.67, 128.57, 127.44, 125.94, 41.84, 21.28. HRMS electrospray (m/z): $[M\text{-}H]^+$ calcd for $C_{12}H_{12}N_2$, 183.0922; found, 183.0920.

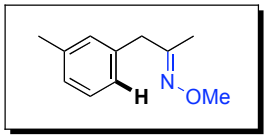
Synthesis of Substrates 9a-13a and 15a



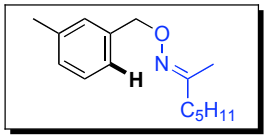
Substrate **9a** was prepared from 2-*m*-tolylacetaldehyde according to a literature procedure.[4] Substrate **9a** was obtained as a yellow oil (R_f = 0.28 in 70% hexanes/30% ethyl acetate). ^{1}H NMR ($CDCl_3$): δ 7.21 (t, J = 7.4 Hz, 1H), 7.09-7.01 (multiple peaks, 3H), 4.76 (m, 1H), 4.08 (qd, J = 12.0, 4.8 Hz, 2H), 3.64-3.59 (multiple peaks, 2H), 2.93 (dd, J = 17.2, 11.2 Hz, 1H), 2.60 (dd, J = 17.2, 6.8 Hz, 1H), 2.33 (s, 3H), 2.02 (s, 3H). ^{13}C{^{1}H} NMR ($CDCl_3$): δ 170.77, 157.56, 138.57, 135.36, 129.49, 128.72, 127.91, 125.72, 77.36, 65.04, 38.56, 33.85, 21.32, 20.07. IR (thin film): 1742 (br) cm^{-1}. HRMS electrospray (m/z): $[M]^+$ calcd for $C_{14}H_{17}NO_3$, 247.1208; found, 247.1201.



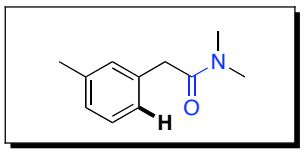
Substrate **10a** was prepared from pyrazole and α-bromoxylenes according to a literature procedure.[5] Substrate **10a** was obtained as a red oil (R_f = 0.24 in 90% hexanes/10% ethyl acetate). ^{1}H NMR ($CDCl_3$): δ 7.56 (d, *J* = 1.6 Hz, 1H), 7.38 (d, *J* = 2.4 Hz, 1H), 7.24 (t, *J* = 7.6 Hz, 1H), 7.12 (d, *J* = 7.6 Hz, 1H), 7.04-7.01 (multiple peaks, 2H), 6.28 (t, *J* = 2.0 Hz, 1H), 5.28 (s, 2H), 2.33 (s, 3H). ^{13}C{^{1}H} NMR ($CDCl_3$): δ 139.41, 138.45, 136.47, 129.11, 128.69, 128.62, 128.34, 124.67, 105.82, 55.85, 21.31. HRMS electrospray (m/z): $[M-H]^+$ calcd for $C_{11}H_{12}N_2$, 171.0922; found, 171.0925.



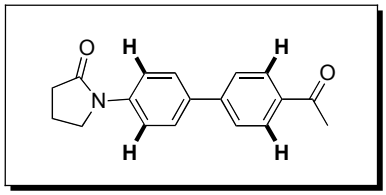
Substrate **11a** was prepared from 3-methylphenylacetone and methoxylamine hydrochloride according to a literature procedure.[6] Substrate **11a** was obtained as a clear oil as a 1 : 0.4 mixture of oxime isomers. Major oxime isomer: ^{1}H NMR ($CDCl_3$): δ 7.20 (m, 1H), 7.07-6.99 (multiple peaks, 3H), 3.91 (s, 3H), 3.44 (s, 2H), 2.35 (s, 3H), 1.75 (s, 3H). ^{13}C{^{1}H} NMR ($CDCl_3$): δ 156.62, 138.16, 136.78, 129.73, 128.39, 127.44, 126.04, 61.23, 41.97, 21.34, 13.52. HRMS electrospray (m/z): $[M]^+$ calcd for $C_{11}H_{15}NO$, 177.1153; found, 177.1156.



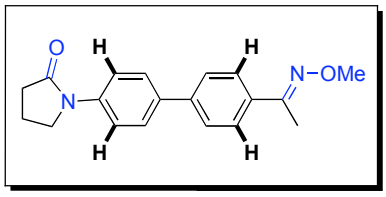
Substrate **12a** was prepared from 2-heptanone, hydroxylamine hydrochloride, and α-bromoxylenes according to a literature procedure.[7] Substrate **12a** was obtained as a clear oil as a 1 : 0.9 mixture of oxime isomers (R_f = 0.26 in 97% hexanes/3% ethyl acetate). Major oxime isomer: ^{1}H NMR ($CDCl_3$): δ 7.27 (t, *J* = 7.6 Hz, 1H), 7.20-7.17 (multiple peaks, 2H), 7.12 (d, *J* = 7.2 Hz, 1H), 5.07 (s, 2H), 2.39 (s, 3H), 2.19 (dd, *J* = 8.0, 7.6 Hz, 2H), 1.89 (s, 3H), 1.56-1.48 (multiple peaks, 2H), 1.37-1.27 (multiple peaks, 4H), 0.91 (m, 3H). ^{13}C{^{1}H} NMR ($CDCl_3$): δ 158.92, 138.18, 137.77, 128.61, 128.25, 128.12, 124.83, 75.15, 35.75, 31.30, 26.15, 22.38, 21.36, 14.07, 13.92. HRMS electrospray (m/z): $[M]^+$ calcd for $C_{15}H_{23}NO$, 233.1780; found, 233.1777.



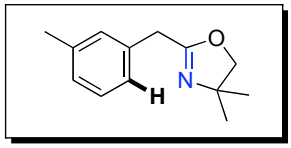
Substrate **13a** was prepared from *m*-tolylacetic acid and dimethylamine according to a literature procedure.[8] The ^{1}H NMR and ^{13}C NMR data for **13a** were identical to those reported in the literature.[9]



This compound was prepared via the Cu-catalyzed reaction of pyrrolidinone with 1-(4'-bromobiphenyl-4-yl) ethanone according to a literature procedure.[10] The product was obtained as a yellow solid. ^{1}H NMR ($CDCl_3$): δ 8.02 (d, J = 8.0 Hz, 2H), 7.73 (d, J = 8.8 Hz, 2H), 7.69-7.63 (multiple peaks, 4H), 3.92 (t, J = 6.8 Hz, 2H), 2.67-2.63 (multiple peaks, 5H), 2.20 (quin, J = 7.6 Hz, 2H). ^{13}C{^{1}H} NMR ($CDCl_3$): δ 197.70, 174.37, 144.97, 139.52, 135.64, 135.60, 128.95, 127.58, 126.84, 120.07, 48.65, 32.76, 26.66, 17.97. IR (thin film): 1694, 1682 cm^{-1}. HRMS electrospray (m/z): [M]$^{+}$ calcd for $C_{18}H_{17}NO_2$, 279.1259; found, 279.1264.



Substrate **15a** was prepared from the corresponding ketone (above) and methoxylamine hydrochloride according to a literature procedure.[6] Substrate **15a** was obtained as a yellow solid. ^{1}H NMR ($CDCl_3$): δ 7.73-7.69 (multiple peaks, 4H), 7.63-7.57 (multiple peaks, 4H), 4.02 (s, 3H), 3.90 (t, J = 6.8 Hz, 2H), 2.64 (t, J = 8.0 Hz, 2H), 2.24 (s, 3H), 2.19 (m, 2H). ^{13}C{^{1}H} NMR ($CDCl_3$): δ 174.25, 154.21, 140.94, 138.86, 136.37, 135.33, 127.27, 126.73, 126.41, 120.09, 61.93, 48.68, 32.72, 17.97, 12.51. IR (thin film): 1685 cm^{-1}. HRMS electrospray (m/z): [M]$^{+}$ calcd for $C_{19}H_{20}N_2O_2$, 308.1525; found, 308.1518.

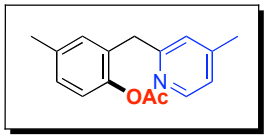


Substrate **17a** was prepared from 2-*m*-tolylacetic acid according to a literature procedure[11]. Substrate **17a** was obtained as a yellow oil (R_f = 0.20 in 80% hexanes/20% ethyl acetate). 300 MHz ^{1}H NMR ($CDCl_3$): δ 7.22 (t, J = 8.0 Hz, 1H), 7.12-7.06 (multiple peaks, 3H), 3.92 (s, 2H), 3.56 (s, 2H), 2.35 (s, 3H), 1.29 (s, 6H). ^{13}C{^{1}H} NMR ($CDCl_3$): δ 164.55, 138.42, 135.44, 129.79, 128.69, 127.91, 125.95, 79.54, 67.21, 35.11, 28.56, 21.58. IR (thin film): 1664 cm^{-1}. HRMS electrospray (m/z): [M+H]$^{+}$ calcd for $C_{13}H_{17}NO$, 204.1388; found, 204.1379.

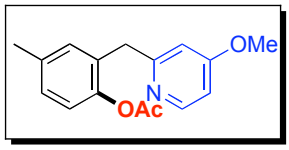
III. Synthesis and Characterization of Acetoxylated Products 1b-15b

Typical procedure for Pd-catalyzed C–H activation/acetoxylation

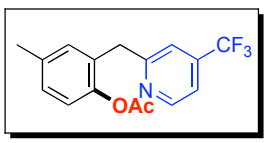
In a 20 mL vial, $PhI(OAc)_2$ (0.49-0.86 mmol, 1.02-1.80 equiv) and $Pd(OAc)_2$ (1.08 mg, 0.0048 mmol, 0.01 equiv) were combined in a mixture of AcOH (2.0 mL) and Ac_2O (2.0 mL). Substrate (0.48 mmol, 1.0 equiv) was added, the vial was sealed with a Teflon-lined cap, and the resulting solution was heated at 100 ºC for 3-24 h. The reaction was cooled to room temperature, and the solvent was removed under vacuum. The resulting brown oil was purified by chromatography on silica gel. Each substrate was optimized for reaction time and equiv of the oxidant, as indicated below.



The reaction was run for 4 h with 1.1 equiv of $PhI(OAc)_2$. The product **1b** was obtained as a yellow oil (91.9 mg, 75% yield, R_f = 0.27 in 64% hexanes/36% ethyl acetate). ^{1}H NMR ($CDCl_3$): δ 8.36 (d, J = 5.2 Hz, 1H), 7.07-7.04 (multiple peaks, 2H), 6.94-6.90 (multiple peaks, 2H), 6.84 (s, 1H), 4.00 (s, 2H), 2.29 (s, 3H), 2.24 (s, 3H), 2.16 (s, 3H). ^{13}C{^{1}H} NMR ($CDCl_3$): δ 169.40, 159.59, 148.81, 147.47, 146.76, 135.75, 131.71, 130.98, 128.31, 123.65, 122.29, 122.21, 39.10, 20.89, 20.80, 20.70. IR (thin film): 1760 cm^{-1}. HRMS electrospray (m/z): [M+Na$^+$] Calcd for $C_{16}H_{17}NO_2$, 278.1157; Found, 278.1147.

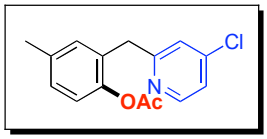


The reaction was run for 4 h with 1.02 equiv of $PhI(OAc)_2$. The product **2b** was obtained as a yellow oil (91.2 mg, 70% yield, R_f = 0.27 in 45% hexanes/55% ethyl acetate). ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.36 (d, J = 5.6 Hz, 1H), 7.09-7.07 (multiple peaks, 2H), 6.95 (d, J = 8.0 Hz, 1H), 6.66 (dd, J = 6.0, 2.4 Hz, 1H), 6.55 (d, J = 2.4 Hz, 1H), 4.01 (s, 2H), 3.77 (s, 3H), 2.32 (s, 3H) 2.20 (s, 3H). ^{13}C{^{1}H} NMR (500 MHz $CDCl_3$): δ 169.36, 166.05, 161.53, 150.25, 146.78, 135.74, 131.65, 130.72, 128.35, 122.21, 108.74, 107.56, 54.86, 39.19, 20.76, 20.70. IR (thin film): 1759 cm^{-1}. HRMS electrospray (m/z): [M+Na$^+$] Calcd for $C_{16}H_{17}NO_3$, 294.1106; Found, 294.1108.

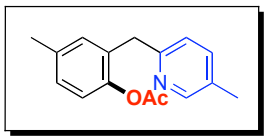


The reaction was run for 4.5 h with 1.02 equiv of $PhI(OAc)_2$. The product **3b** was obtained as a colorless oil (135.1 mg, 91% yield, R_f = 0.27 in 79% hexanes/21% ethyl acetate). ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.71 (d, J = 5.5 Hz, 1H), 7.34 (d, J = 5.0 Hz, 1H), 7.29 (s, 1H), 7.11-7.09 (multiple peaks, 2H), 6.96 (d, J = 8.5 Hz, 1H), 4.12 (s, 2H), 2.33 (s, 3H), 2.19 (s, 3H). ^{13}C{^{1}H} NMR ($CDCl_3$): δ 169.26, 161.59, 150.22, 146.82, 138.66 (q, $^2J_{C\text{-}F}$ = 33.7 Hz), 136.06, 131.71, 129.95, 128.88, 122.76 (q, $^1J_{C\text{-}F}$ = 271.7 Hz), 122.43, 118.47 (q, $^3J_{C\text{-}F}$ = 3.7 Hz), 116.96 (q, $^3J_{C\text{-}F}$

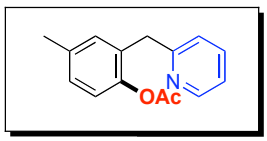
= 3.7 Hz), 39.47, 20.82, 20.71. $^{19}F\{^{1}H\}$ NMR ($CDCl_3$): δ –64.85. IR (thin film): 1753 cm^{-1}. HRMS electrospray (m/z): [M+Na^+] Calcd for $C_{16}H_{14}F_3NO_2$, 332.0874; Found, 332.0868.



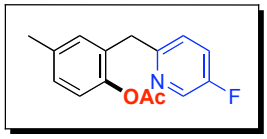
The reaction was run for 6 h with 1.02 equiv of $PhI(OAc)_2$. The product **4b** was obtained as a yellow oil (97.9 mg, 74% yield, R_f = 0.27 in 80% hexanes/20% ethyl acetate). ^{1}H NMR ($CDCl_3$): δ 8.42 (d, *J* = 5.2 Hz, 1H), 7.13 (dd, *J* = 5.6 Hz, 2.0 Hz, 1H), 7.09-7.07 (multiple peaks, 2H), 7.06 (d, *J* = 2.0 Hz, 1H), 6.95 (d, *J* = 8.8 Hz, 1H), 4.03 (s, 2H), 2.32 (s, 3H), 2.20 (s, 3H). $^{13}C\{^{1}H\}$ NMR ($CDCl_3$): δ. 169.32, 161.62, 149.98, 146.76, 144.35, 136.97, 131.68, 130.06, 128.74, 123.16, 122.36, 121.75, 39.09, 20.80, 20.74. IR (thin film): 1760 cm^{-1}. HRMS electrospray (m/z): [M+Na^+] Calcd for $C_{15}H_{14}ClNO_2$, 298.0611; Found, 298.0600.



The reaction was run for 4 h with 1.1 equiv of $PhI(OAc)_2$. The product **5b** was obtained as a yellow oil (90.7 mg, 74% yield, R_f = 0.27 in 64% hexanes/36% ethyl acetate). ^{1}H NMR ($CDCl_3$): δ 8.36 (t, *J* = 0.8 Hz, 1H), 7.37 (dd, *J* = 8.0 Hz, 2.4 Hz, 1H), 7.08-7.05 (multiple peaks, 2H), 6.94 (d, *J* = 2.0 Hz, 1H), 6.92 (d, *J* = 1.6 Hz, 1H), 4.01 (s, 2H), 2.30 (s, 3H), 2.28 (s, 3H) 2.18 (s, 3H). $^{13}C\{^{1}H\}$ NMR ($CDCl_3$): δ 169.43, 156.89, 149.43, 146.75, 137.02, 135.76, 131.66, 131.14, 130.46, 128.27, 122.29, 122.19, 38.75, 20.80, 20.76, 17.96 IR (thin film): 1760 cm^{-1}. HRMS electrospray (m/z): [M+Na^+] Calcd for $C_{16}H_{17}NO_2$, 278.1157; Found, 278.1150.

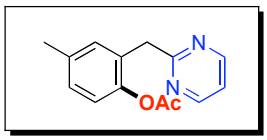


The reaction was run for 6 h with 1.02 equiv of $PhI(OAc)_2$. The product **6b** was obtained as a yellow oil (86.9 mg, 75% yield, R_f = 0.27 in 70% hexanes/30% ethyl acetate). ^{1}H NMR ($CDCl_3$): δ 8.52 (dd, *J* = 4.8, 1.6 Hz, 1H), 7.54 (dt, *J* = 7.6, 1.6 Hz, 1H), 7.11-7.02 (multiple peaks, 4H), 6.94 (d, *J* = 8.0 Hz, 1H), 4.06 (s, 2H), 2.30 (s, 3H), 2.16 (s, 3H). $^{13}C\{^{1}H\}$ NMR ($CDCl_3$): δ 169.37, 159.88, 149.03, 146.79, 136.44, 135.78, 131.72, 130.83, 128.38, 122.85, 122.24, 121.24, 39.21, 20.78, 20.69. IR (thin film): 1759 cm^{-1}. HRMS electrospray (m/z): $[M+H]^+$ calcd for $C_{15}H_{15}NO_2$, 242.1181; found, 242.1177.

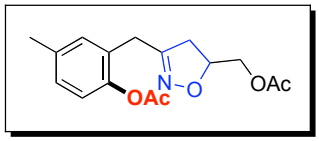


The reaction was run for 10 h with 1.02 equiv of $PhI(OAc)_2$. The product **7b** was obtained as a colorless oil (115.7 mg, 93% yield, R_f = 0.27 in 80% hexanes/20% ethyl acetate). ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.38 (d, *J* = 3.0 Hz, 1H), 7.29 (td, *J* = 8.5, 3.0 Hz, 1H), 7.09-7.07 (multiple peaks, 2H), 7.04 (dd, *J* = 8.8, 4.5 Hz, 1H), 6.94 (d, *J* = 8.0 Hz, 1H), 4.03 (s, 2H), 2.31 (s, 3H),

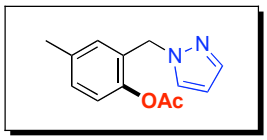
2.20 (s, 3H). $^{13}C\{^{1}H\}$ NMR ($CDCl_3$): δ 169.47, 158.15 (d, $^{1}J_{C\text{-}F}$ = 252.7 Hz), 155.94 (d, $^{3}J_{C\text{-}F}$ = 4.2 Hz), 146.81, 137.10 (d, $^{2}J_{C\text{-}F}$ = 23.4 Hz), 135.99, 131.65, 130.80, 128.61, 123.65 (d, $^{4}J_{C\text{-}F}$ = 4.4 Hz), 123.31 (d, $^{2}J_{C\text{-}F}$ = 18.3 Hz), 122.38, 38.49, 20.86, 20.80. $^{19}F\{^{1}H\}$ NMR ($CDCl_3$): δ –130.93. IR (thin film): 1760 cm^{-1}. HRMS electrospray (m/z): [M+Na^+] Calcd for $C_{15}H_{14}FNO_2$, 282.0906; Found, 282.0905.



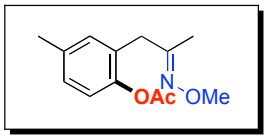
The reaction was run for 3 h with 1.02 equiv of $PhI(OAc)_2$. The product **8b** was obtained as a yellow oil (104.7 mg, 90% yield, R_f = 0.28 in 55% hexanes/45% ethyl acetate). ^{1}H NMR ($CDCl_3$): δ 8.62 (d, *J* = 1.6 Hz, 2H), 7.20 (s, 1H), 7.08-7.04 (multiple peaks, 2H), 6.92 (d, *J* = 8.4 Hz, 1H), 4.19 (s, 2H), 2.31 (s, 3H), 2.18 (s, 3H). $^{13}C\{^{1}H\}$ NMR ($CDCl_3$): δ 169.28, 169.14, 157.01, 146.73, 135.60, 131.84, 129.86, 128.47, 122.12, 118.51, 40.88, 20.72. Two carbons coincidentally overlap. IR (thin film): 1757 cm^{-1}. HRMS electrospray (m/z): $[M+H]^+$ calcd for $C_{14}H_{14}N_2O_2$, 243.1134; found, 243.1135.



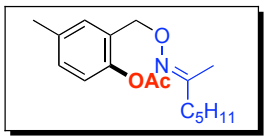
The reaction was run for 6 h with 1.1 equiv of $PhI(OAc)_2$. The product **9b** was obtained as a yellow oil (96.5 mg, 69% yield, R_f = 0.28 in 70% hexanes/30% ethyl acetate). ^{1}H NMR ($CDCl_3$): δ 7.09 (dd, *J* = 8.0, 2.0 Hz, 1H), 7.06 (s, 1H), 6.91 (d, *J* = 8.0 Hz, 1H), 4.71 (m, 1H), 4.10-4.01 (multiple peaks, 2H), 3.56 (s, 2H), 2.84 (dd, *J* = 17.2, 10.8 Hz, 1H), 2.51 (dd, *J* = 17.2, 7.6 Hz, 1H), 2.31 (s, 3H), 2.28 (s, 3H), 2.02 (s, 3H). $^{13}C\{^{1}H\}$ NMR ($CDCl_3$): δ 170.61, 169.68, 156.63, 146.98, 136.14, 131.18, 129.21, 127.10, 122.57, 77.48, 64.86, 38.38, 29.01, 20.69, 20.57. One carbon coincidentally overlaps. IR (thin film): 1746 (br) cm^{-1}. HRMS electrospray (m/z): $[M+Na]^+$ calcd for $C_{16}H_{19}NO_5$, 328.1161; found, 328.1150.



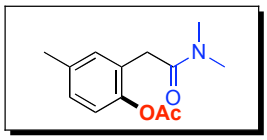
The reaction was run for 10 h with 1.02 equiv of $PhI(OAc)_2$. The product **10b** was obtained as a yellow oil (97.3 mg, 88% yield, R_f = 0.28 in 75% hexanes/25% ethyl acetate). ^{1}H NMR ($CDCl_3$): δ 7.53 (d, *J* = 1.6 Hz, 1H), 7.32 (d, *J* = 2.4 Hz, 1H), 7.14 (dd, *J* = 8.4, 1.6 Hz, 1H), 6.98 (d, *J* = 8.4 Hz, 1H), 6.95 (d, *J* = 1.6 Hz, 1H), 6.26 (t, *J* = 2.0 Hz, 1H), 5.23 (s, 2H), 2.30 (s, 3H), 2.26 (s, 3H). $^{13}C\{^{1}H\}$ NMR ($CDCl_3$): δ 169.07, 146.32, 139.18, 136.04, 130.11, 129.85, 129.14, 128.08, 122.34, 105.90, 50.73, 20.57, 20.50. IR (thin film): 1760 cm^{-1}. HRMS electrospray (m/z): $[M+Na]^+$ calcd for $C_{13}H_{14}N_2O_2$, 253.0953; found, 253.0953.



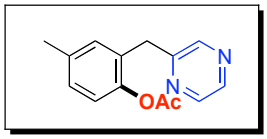
The reaction was run for 4.5 h with 1.1 equiv of $PhI(OAc)_2$. The product **11b** was obtained as a yellow oil as a 1 : 0.42 mixture of oxime isomers (89.2 mg, 79% yield, R_f = 0.28 in 89% hexanes/11% ethyl acetate). Major oxime isomer: ^1H NMR ($CDCl_3$): δ 7.06 (d, *J* = 8.4 Hz, 1H), 7.01 (s, 1H), 6.92 (d, *J* = 8.4 Hz, 1H), 3.88 (s, 3H), 3.57 (s, 2H), 2.32 (s, 3H), 2.28 (s, 3H), 1.71 (s, 3H). $^{13}C\{^1H\}$ NMR ($CDCl_3$): δ 169.45, 155.09, 146.92, 135.95, 131.52, 128.53, 128.42, 122.12, 61.21, 29.85, 20.86, 20.73, 19.37. IR (thin film): 1763 cm^{-1}. HRMS electrospray (m/z): $[M+Na]^+$ calcd for $C_{13}H_{17}NO_3$, 258.1106; found, 258.1100. Minor oxime isomer: ^1H NMR ($CDCl_3$): δ 7.08-7.05 (multiple peaks, 2H), 6.92 (d, *J* = 8.0 Hz, 1H), 3.87 (s, 3H), 3.37 (s, 2H), 2.32 (s, 3H), 2.30 (s, 3H), 1.70 (s, 3H). $^{13}C\{^1H\}$ NMR ($CDCl_3$): δ 169.60, 155.70, 147.18, 135.90, 131.52, 128.74, 128.47, 122.40, 61.24, 36.91, 20.90, 20.83, 13.33.



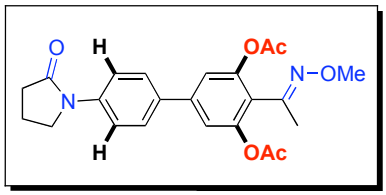
The reaction was run for 8 h with 1.1 equiv of $PhI(OAc)_2$. The product **12b** was obtained as a yellow oil as a 1 : 0.39 mixture of oxime isomers (97.9 mg, 70% yield, R_f = 0.28 in 90% hexanes/10% ethyl acetate). Major oxime isomer: ^1H NMR ($CDCl_3$): δ 7.23 (d, *J* = 1.6 Hz, 1H), 7.11 (dd, *J* = 8.0, 1.6 Hz, 1H), 6.94 (d, *J* = 8.0 Hz, 1H), 4.99 (s, 2H), 2.34 (s, 3H), 2.28 (s, 3H), 2.14 (t, *J* = 7.6 Hz, 2H), 1.83 (s, 3H), 1.48 (m, 2H), 1.34-1.24 (multiple peaks, 4H), 0.88 (t, *J* = 7.2 Hz, 3H). $^{13}C\{^1H\}$ NMR ($CDCl_3$): δ 169.33, 158.35, 146.63, 135.40, 130.40, 129.70, 129.24, 121.97, 70.47, 35.63, 31.23, 26.05, 22.29, 20.80, 20.73, 13.85. One carbon coincidentally overlaps. IR (thin film): 1757 cm^{-1}. HRMS electrospray (m/z): $[M+Na]^+$ calcd for $C_{17}H_{25}NO_3$, 314.1732; found, 314.1729. Minor oxime isomer: ^1H NMR ($CDCl_3$): δ 7.23 (d, *J* = 1.6 Hz, 1H), 7.11 (dd, *J* = 8.0, 1.6 Hz, 1H), 6.94 (d, *J* = 8.0 Hz, 1H), 4.96 (s, 2H), 2.34-2.28 (multiple peaks, 8H), 1.84 (s, 3H), 1.47 (m, 2H), 1.34-1.26 (multiple peaks, 4H), 0.88 (t, *J* = 7.2 Hz, 3H). $^{13}C\{^1H\}$ NMR ($CDCl_3$): δ 169.54, 159.15, 146.54, 135.55, 130.50, 130.36, 129.37, 121.04, 70.54, 35.74, 31.78, 29.29, 25.29, 22.41, 20.88, 20.86, 19.88.



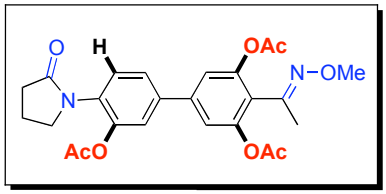
The reaction was run for 10 h with 1.1 equiv of $PhI(OAc)_2$. The product **13b** was obtained as a yellow oil (87 mg, 77% yield, R_f = 0.28 in 30% hexanes/70% ethyl acetate). ^1H NMR ($CDCl_3$): δ 7.07-7.06 (multiple peaks, 2H), 6.93 (d, *J* = 8.8 Hz, 1H), 3.52 (s, 2H), 2.96 (s, 3H), 2.93(s, 3H), 2.30 (s, 3H), 2.29 (s, 3H). $^{13}C\{^1H\}$ NMR ($CDCl_3$): δ 170.16, 169.45, 146.49, 135.98, 130.63, 128.64, 127.00, 122.09, 37.55, 35.82, 35.57, 20.84. IR (thin film): 1759, 1645 cm^{-1}. HRMS electrospray (m/z): $[M+Na]^+$ calcd for $C_{13}H_{17}NO_3$, 258.1106; found, 258.1101.



The reaction was run for 24 h with 1.8 equiv of $PhI(OAc)_2$. The product **14b** was obtained as a yellow oil (86.1 mg, 74% yield, $R_f = 0.28$ in 60% hexanes/40% ethyl acetate). ^1H NMR ($CDCl_3$): δ 8.38 (s, 2H), 8.30 (s, 1H), 7.05 (s, 1H), 7.00 (d, $J = 8.0$ Hz, 1H), 6.89 (d, $J = 9.5$, 8.0 Hz, 1H), 3.99 (s, 2H), 2.23 (s, 3H), 2.13 (s, 3H). $^{13}C\{^1H\}$ NMR ($CDCl_3$): δ 168.79, 155.19, 146.43, 144.30, 143.59, 142.01, 135.54, 131.24, 129.44, 128.42, 122.06, 36.39, 20.41, 20.38. IR (thin film): 1760 cm^{-1}. HRMS electrospray (m/z): $[M+H]^+$ calcd for $C_{14}H_{14}N_2O_2$, 243.1134; found, 243.1132.

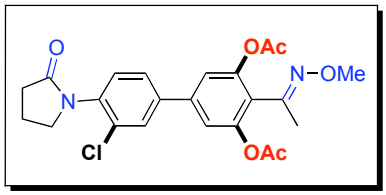


Substrate **15a** (308 mg, 1.0 mmol, 1.0 equiv), $Pd(OAc)_2$ (6.7 mg, 0.03 mmol, 0.03 equiv), and $PhI(OAc)_2$ (902 mg, 2.0 mmol, 2.0 equiv) were combined in a 20 mL vial and were dissolved in a 1 : 1 mixture of AcOH and Ac_2O (8 mL). The vial was sealed with a Teflon-lined cap, and the mixture was heated at 100 ºC for 12 h. The reaction was cooled to room temperature, the solvent was removed under vacuum, and the resulting brown oil was purified by column chromatography. The product **15b** was obtained as a yellow solid (305 mg, 72% yield, $R_f = 0.30$ in 20% hexanes/80% ethyl acetate, mp = 234-237 °C). ^1H NMR ($CDCl_3$): δ 7.72 (d, $J = 8.8$ Hz, 2H), 7.57 (d, $J = 8.8$ Hz, 2H), 7.28 (s, 2H), 3.95 (s, 3H), 3.92 (t, $J = 7.6$ Hz, 2H), 2.66 (t, $J = 8.0$ Hz, 2H), 2.31 (s, 6H), 2.21 (quin, $J = 7.6$ Hz, 2H), 2.07 (s, 3H). $^{13}C\{^1H\}$ NMR ($CDCl_3$): δ 174.30, 168.74, 149.90, 149.23, 142.09, 139.48, 134.50, 127.33, 122.82, 119.88, 118.58, 62.03, 48.57, 32.72, 20.87, 17.88, 15.50. IR (thin film): 1769, 1686 cm^{-1}. HRMS electrospray (m/z): $[M+H]^+$ calcd for $C_{23}H_{24}N_2O_6$, 425.1713; found, 425.1705.

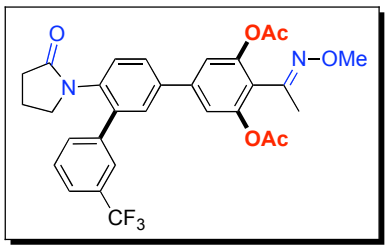


Substrate **15b** (51 mg, 0.12 mmol, 1.0 equiv), $Pd(OAc)_2$ (1.3 mg, 0.006 mmol, 0.03 equiv) and $PhI(OAc)_2$ (121 mg, 0.24 mmol, 2.0 equiv) were combined in a 20 mL vial and were dissolved in a 1 : 1 mixture of AcOH and Ac_2O (1 mL). The vial was sealed with a Teflon-lined cap, and the mixture was heated at 100 ºC for 12 h. The reaction was cooled to room temperature, the solvent was removed under vacuum, and the resulting brown oil was purified by column chromatography. The product **15b-OAc** was obtained as a yellow solid as a 1 : 0.2 mixture of oxime isomers (34 mg, 59% yield, $R_f = 0.25$ in 10% hexanes/90% ethyl acetate, mp = 64.5-70.1 °C). Major oxime isomer: ^1H NMR ($CDCl_3$): δ 7.43 (dd, $J = 8.0$, 2.0 Hz, 1H), 7.36-7.34 (multiple peaks, 2H), 7.21 (s, 2H), 3.95 (s, 3H), 3.76 (t, $J = 6.8$ Hz, 2H), 2.54 (t, $J = 8.0$ Hz, 2H), 2.28-2.22 (multiple peaks, 9H), 2.18 (m, 2H), 2.06 (s, 3H). $^{13}C\{^1H\}$ NMR ($CDCl_3$): δ 174.12, 168.64, 149.76, 149.27, 147.68, 145.93, 141.03, 138.87, 130.92, 128.25, 127.31, 125.04, 123.55,

122.51, 122.40, 118.95, 118.80, 62.05, 49.91, 31.10, 20.91, 20.83, 19.93, 19.24, 15.46. IR (thin film): 1770, 1700 cm^{-1}. HRMS electrospray (m/z): $[M+Na]^+$ calcd for $C_{25}H_{26}N_2O_8$, 505.1587; found, 505.1577.



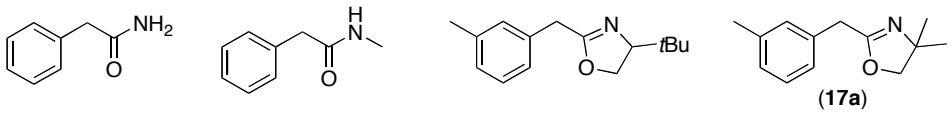
Substrate **15b** (51 mg, 0.12 mmol, 1.0 equiv), $Pd(OAc)_2$ (1.3 mg, 0.006 mmol, 0.05 equiv) and *N*-chlorosuccinimide (32 mg, 0.24 mmol, 2.0 equiv) were combined in a 20 mL vial and were dissolved in AcOH (1 mL). The vial was sealed with a Teflon-lined cap, and the mixture was heated at 100 ºC for 12 h. The reaction was cooled to room temperature, the solvent was removed under vacuum, and the resulting brown oil was purified by column chromatography. The product **15b-Cl** was obtained as a yellow solid as a 1 : 0.5 mixture of oxime isomers (47 mg, 81% yield, R_f = 0.28 in 15% hexanes/85% ethyl acetate, mp = 66.8–73.2 °C). Major oxime isomer: ^{1}H NMR ($CDCl_3$): δ 7.64 (dd, *J* = 5.2, 1.6 Hz, 1H), 7.47 (m, 1H), 7.34 (s, 1H), 7.25 (s, 1H), 7.2 (s, 1H), 3.94 (s, 3H), 3.79 (t, *J* = 6.8 Hz, 2H), 2.58 (t, *J* = 8.0 Hz, 2H), 2.28-2.22 (multiple peaks, 8H), 2.06 (s, 3H). $^{13}C\{^1H\}$ NMR ($CDCl_3$): δ 175.00, 168.57, 149.79, 149.29, 147.59, 141.21, 139.84, 136.19, 132.51, 129.65, 128.98, 128.20, 126.44, 123.80, 118.94, 62.89, 49.84, 32.71, 36.34, 30.91, 20.93, 19.06, 15.41. IR (thin film): 1773, 1694 cm^{-1}. HRMS electrospray (m/z): $[M+Na]^+$ calcd for $C_{23}H_{23}ClN_2O_6$, 481.1142; found, 481.1144.



Substrate **15b** (51 mg, 0.12 mmol, 1.0 equiv), $Pd(OAc)_2$ (1.3 mg, 0.006 mmol, 0.03 equiv) and $[(m\text{-}CF_3C_6H_4)_2I]BF_4$ (32 mg, 0.24 mmol, 2.0 equiv), $NaHCO_3$ (15 mg, 0.18 mmol, 1.5 equiv) were combined in a 20 mL vial and were dissolved in a toluene (1 mL). The vial was sealed with a Teflon-lined cap, and the mixture was heated at 100 ºC for 12 h. The reaction was cooled to room temperature, the solvent was removed under vacuum, and the resulting brown oil was purified by column chromatography. The product **15b-Ar** was obtained as a yellow solid as a 1 : 0.3 mixture of oxime isomers (53 mg, 78% yield, R_f = 0.28 in 25% hexanes/75% ethyl acetate, mp = 62.2-65.8 °C). Major oxime isomer: ^{1}H NMR ($CDCl_3$): δ 7.66-7.57 (multiple peaks, 4H), 7.53-7.49 (multiple peaks, 2H), 7.30 (s, 1H), 7.22 (s, 1H), 7.19 (s, 1H), 3.91 (s, 3H), 3.83 (t, *J* = 6.8 Hz, 1H), 3.25 (t, *J* = 6.8 Hz, 1H), 2.57 (t, *J* = 8.0 Hz, 1H), 2.36 (t, *J* = 8.0 Hz, 1H), 2.23 (s, 6H), 2.12 (t, *J* = 7.4 Hz, 1H), 2.03 (s, 3H), 1.88 (t, *J* = 7.4 Hz, 1H). $^{13}C\{^1H\}$ NMR ($CDCl_3$): δ175.46, 168.54, 168.48, 149.87, 149.31, 149.21, 141.45, 139.47, 138.62, 136.37, 131.81, 130.75 (q, $^2J_{C\text{-}F}$ = 32.2 Hz), 129.25, 129.10, 128.82, 128.23, 127.31, 124.93 (q, $^3J_{C\text{-}F}$ = 3.7 Hz), 124.45 (q, $^3J_{C\text{-}F}$ = 3.8 Hz), 123.90 (q, $^1J_{C\text{-}F}$ = 271 Hz), 119.86, 118.98, 118.55, 61.99, 48.54, 32.69, 20.81, 18.85, 17.85, 15.46. $^{19}F\{^1H\}$ NMR ($CDCl_3$): δ –62.57. IR (thin film): 1771, 1694 cm^{-1}. HRMS electrospray (m/z): $[M+Na]^+$ calcd for $C_{30}H_{27}F_3N_2O_6$, 591.1719; found, 591.1719.

Acetoxylation reactions of the substrates shown in Figure S1 below, with 5 mol % $Pd(OAc)_2$, 1.02 equiv $PhI(OAc)_2$ in $AcOH/Ac_2O$ or benzene at 80 °C, afforded complex mixtures of products. Additionally, many of these products were also formed in the control reaction (in the absence of $Pd(OAc)_2$).

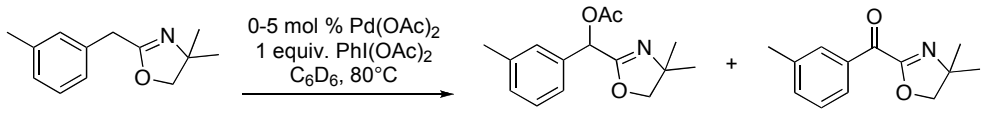
Figure S1. Other Substrates Investigated



(**17a**)

In one example, substrate **17a** forms similar ratios (~4:1) of products **17b** and **17c** under our standard reaction conditions, with and without $Pd(OAc)_2$ as shown in Figure S2. These experiments were conducted on NMR scale with a known standard added. Isolated yields are notably lower due to the instability of the compounds upon purification.

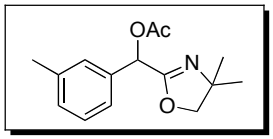
Figure S2. Uncatalyzed Products Under Standard Reaction Conditions: NMR Yields



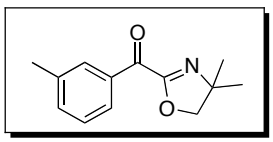
(**17a**) (**17b**) (**17c**)

No $Pd(OAc)_2$: 77%
5 mol% Pd(OAc)2: 62%

No $Pd(OAc)_2$: 19%
5 mol% Pd(OAc)2: 16%



The reaction was run for 12 h with 1.02 equiv of $PhI(OAc)_2$. The product **17b** was obtained as a yellow oil (23 mg, 35% yield, R_f = 0.25 in 70% hexanes/70% ethyl acetate). ^1H NMR ($CDCl_3$): δ 7.33-7.31 (multiple peaks, 3H), 7.19 (m, 1H), 6.23 (s, 1H), 4.01 (d, 8.0 Hz, 1H) 3.93 (d, *J* = 8.4 Hz, 1H), 2.39 (s, 3H), 2.19 (s, 3H), 1.33 (s, 3H), 1.30 (s, 3H). $^{13}C\{^1H\}$ NMR ($CDCl_3$): δ 170.10, 162.84, 138.67, 135.37, 130.06, 128.82, 128.48, 124.81, 79.71, 71.08, 67.61, 28.23, 28.19, 21.58, 21.24. IR (thin film): 1749, 1674 cm^{-1}. HRMS electrospray (m/z): $[M+Na]^+$ calcd for $C_{15}H_{19}NO_3$, 284.1263; found, 284.1257.



The reaction was run for 12 h with 1.02 equiv of $PhI(OAc)_2$. The product **17c** was obtained as a yellow oil (5.7 mg, 10% yield, 87% pure. R_f = 0.25 in 90% hexanes/10% ethyl acetate). ^1H NMR ($CDCl_3$): δ 7.71-7.72 (multiple peaks, 2H), 7.34-7.27 (multiple peaks, 2H), 4.29 (s, 2H), 2.40 (s, 3H), 1.41 (s, 6H). $^{13}C\{^1H\}$ NMR ($CDCl_3$): δ 184.58, 157.98, 138.56, 135.34, 135.14, 130.99,

128.61, 128.33, 79.20, 69.39, 28.41, 21.59. IR (thin film): 1737, 1674 cm^{-1}. HRMS electrospray (m/z): $[M+Na]^+$ calcd for $C_{13}H_{15}NO_2$, 240.1000; found, 240.1003.

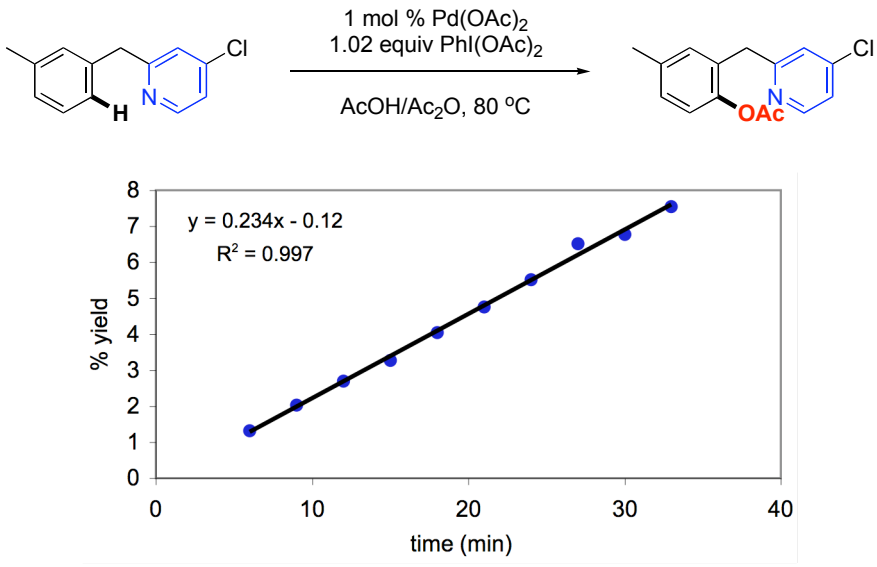
IV. Kinetics Procedures and Representative Kinetics Data

General Information. Each reaction was monitored to ~10% (8.6-11.0%) conversion, and rate constants were calculated for each reaction using the initial rates method. Each kinetics experiment was run in triplicate, and the data shown in the Hammett plots represent an average of these three runs. Error analysis was conducted using standard equations and calculations.[12]

Typical Procedure for Kinetics in AcOH/Ac_2O

Kinetics experiments were run in two dram vials sealed with Teflon-lined caps. Each data point represents a reaction in an individual vial, with each vial containing an identical concentration of oxidant, catalyst, and substrate. The vials were charged with $PhI(OAc)_2$ (0.0158 g, 0.049 mmol, 1.02 equiv, added as a solid), substrate (0.048 mmol, 1.0 equiv, added as a 0.96 M stock solution in AcOH), and $Pd(OAc)_2$ (0.11 mg, 0.00048 mmol, 0.01 equiv, added as a 0.0096 M stock solution in AcOH), and the resulting mixtures were diluted to a total volume of 400 μL of a 1 : 1 mixture of AcOH and Ac_2O. The vials were then heated at 80 ºC for various amounts of time. Reactions were quenched by cooling the vial at 0 ºC for 5 min, followed by the addition of a 2% solution of pyridine in CH_2Cl_2 (2 mL). An internal standard (pyrene) was then added, and the reactions were analyzed by gas chromatography.

Figure S3. Representative Initial Rates Data in AcOH/Ac_2O



Typical Procedure for Kinetics in Benzene

Kinetics experiments were run in two dram vials sealed with Teflon-lined caps. Each data point represents a reaction in an individual vial, with each vial containing a constant concentration of oxidant, catalyst, and substrate. The vials were each sequentially charged with $PhI(OAc)_2$ (0.0158 g, 0.049 mmol, 1.02 equiv, added as a solid), substrate (0.048 mmol, 1.0 equiv, added as a 0.96 M stock solution in C_6H_6), and $Pd(OAc)_2$ (0.54 mg, 0.0024 mmol, 0.05 equiv, added as a 0.0096 M stock solution in C_6H_6), and the resulting mixtures were diluted to a total volume of

400 μL of C_6H_6. The vials were then heated at 80 ºC for various amounts of time. Reactions were quenched by cooling the vial at 0 ºC for 5 min, followed by the addition of a 2% solution of pyridine in CH_2Cl_2 (2 mL). A GC standard (pyrene) was then added, and the reactions were analyzed by gas chromatography.

Figure S4. Representative Initial Rates Data in Benzene

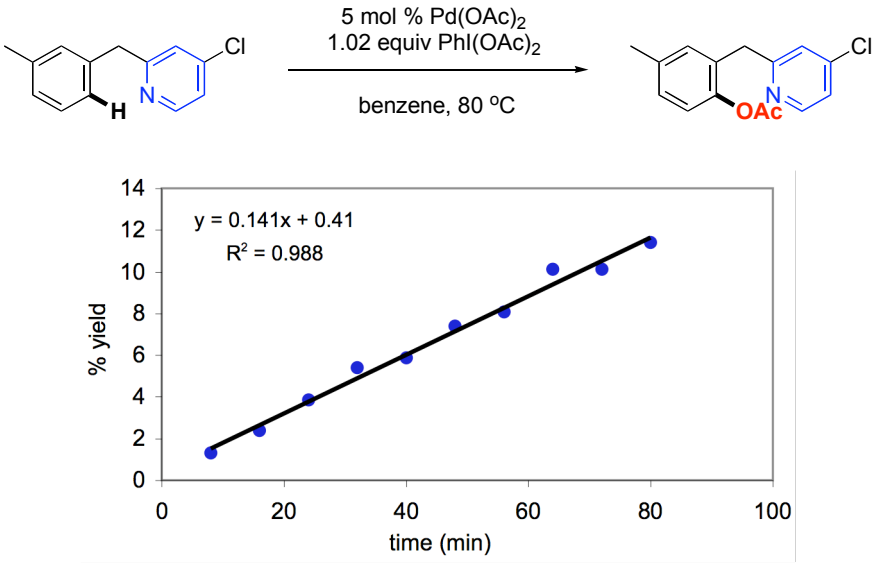
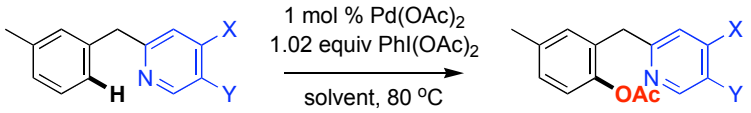


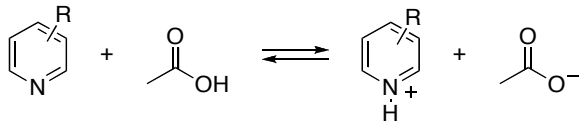
Figure S5. Initial Rate Constants for Substrates **1a-7a** in $AcOH/Ac_2O$ and Benzene



X	Y	k_{obs} ($x10^{-1}$)	
		$AcOH/Ac_2O$	Benzene
CF_3	H	5.01	2.77
H	F	4.01	2.46
Cl	H	2.86	1.44
H	Me	1.85	0.41
Me	H	2.29	0.33
OMe	H	3.82	0.28

Calculations for Obtaining Adjusted Observed Rates in Individual Reactions

The following equations were used in calculating the effective concentration of the substrate. Based on the corrected values of the concentration the adjusted initial rate for the reaction was determined.



$$K_{eq} = \frac{[\text{pyr H}^+]\,[\text{AcO}^-]}{[\text{pyridine}]\,[\text{AcOH}]}$$

$$K_{eq} = \frac{K_{a\ \text{pyridine}}}{K_{a\ \text{AcOH}}}$$

$$\frac{K_{a\ \text{pyridine}}}{1.78 \times 10^{-5}} = \frac{x^2}{(0.12\ \text{M} - x)(8.72\ \text{M} - x)}$$

conc. of free pyridine=(0.12 M – x)

$$\text{rate}_{\text{adjusted}} = k'_{\text{obs}} * [\text{pyridine}]$$

$$k'_{\text{obs}} = k_{\text{obs}} * \frac{[\text{pyridine}_{\text{free}}]}{[\text{pyridine}]}$$

Table S1. Correction for Observed Individual Rate Constant

X	Y	pK_a	k_{obs} x 10^3	k'_{obs} x 10^3 [a]
CF_3	H	2.74	525	234
H	F	2.97	391	139
Cl	H	3.84	298	28
H	Me	5.63	188	0.3
Me	H	6.02	229	0.4
OMe	H	6.55	382	0.1

a. $k'_{obs} = k_{obs} \times \frac{\text{effective concentration}}{\text{actual concentration}}$

Procedure for Determining the Order of Reactions in the Oxidant for Individual Reactions

The kinetics experiments discussed above were conducted using 1.02, 1.5, 2.0 and 2.5 equiv of $PhI(OAc)_2$ (0.049 mmol, 0.072 mmol, 0.096 mmol, and 0.120 mmol, respectively) under otherwise identical conditions. Rate constants were calculated for each reaction using the initial rates method, and the data is plotted below.

Figure S6. Initial Rate Constant as a Function of Oxidant Concentration in $AcOH/Ac_2O$

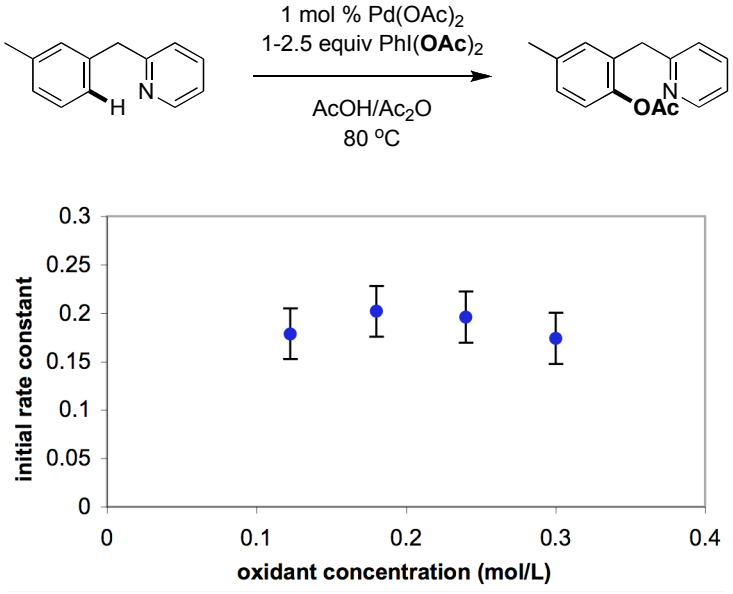
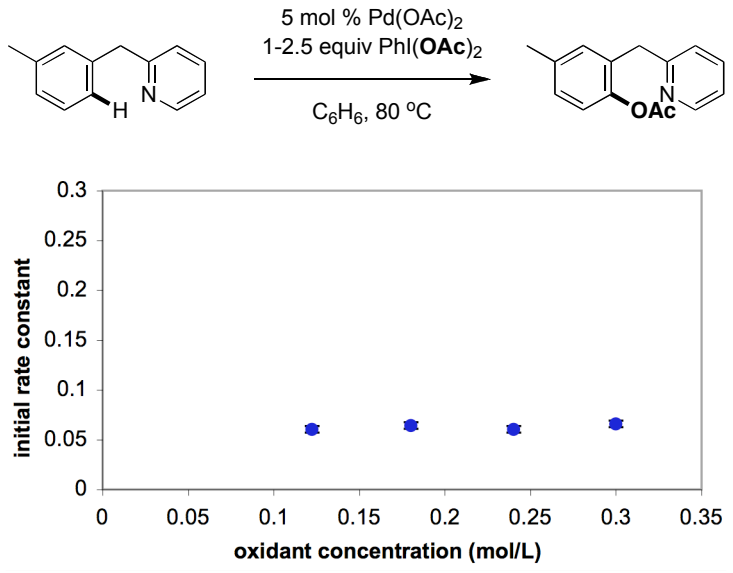


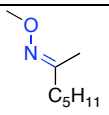
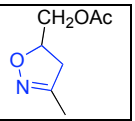
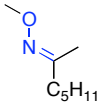
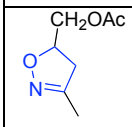
Figure S7. Initial Rate Constant as a Function of Oxidant Concentration in Benzene



Typical Procedure for Competition Studies in AcOH/Ac_2O

A two dram vial was sequentially charged with $PhI(OAc)_2$ (0.0158 g, 0.049 mmol, 1.02 equiv, added as a solid), substrate A (0.048 mmol, 1.0 equiv, added as a 0.96 M stock solution in AcOH), substrate B (0.048 mmol, 1.0 equiv, added as a 0.96 M stock solution in AcOH), and $Pd(OAc)_2$ (0.11 mg, 0.00048 mmol, 0.01 equiv, added as a 0.0096 M stock solution in AcOH), and the resulting mixtures were diluted to a total volume of 400 μL of a 1 : 1 mixture of AcOH and Ac_2O. The reaction was heated at 80 ºC for 12 h, and then cooled to room temperature. A GC standard (pyrene) was added, and the reaction was analyzed by gas chromatography.

Table S2. Product Ratios Obtained from Competition Studies in AcOH/Ac_2O

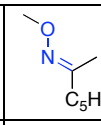
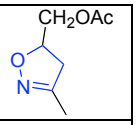
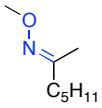
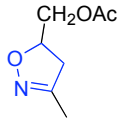
							
	1 : 0.4	1 : 0.3	1 : 0.04	1 : <0.01	1 : <0.01	1 : <0.01	1 : <0.01
	-	1 : 3.3	1 : 1.5	1 : <0.01	1 : <0.01	1 : <0.01	1 : <0.01
	1 : 0.3	-	n/a[a]	1 : <0.01	1 : <0.01	1 : <0.01	1 : <0.01
	0.7 : 1	n/a[a]	-	1 : <0.01	1 : <0.01	1 : <0.01	1 : <0.01
	<0.01 : 1	<0.01 : 1	<0.01 : 1	-	<0.01 : 1	<0.01 : 1	<0.01 : 1
	<0.01 : 1	<0.01 : 1	<0.01 : 1	1 : <0.01	-	<0.01 : 1	<0.01 : 1
	<0.01 : 1	<0.01 : 1	<0.01 : 1	1 : <0.01	1 : <0.01	-	1 : 1
	<0.01 : 1	<0.01 : 1	<0.01 : 1	1 : <0.01	1 : <0.01	1 : 1	-

[a] Ratio not obtained because starting materials and products have identical retention times by GC

Typical Procedure for Competition Studies in Benzene

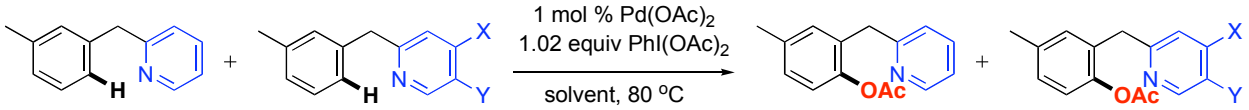
A two dram vial was sequentially charged with $PhI(OAc)_2$ (0.0158 g, 0.049 mmol, 1.02 equiv, added as a solid), substrate A (0.048 mmol, 1.0 equiv, added as a 0.96 M stock solution in C_6H_6), substrate B (0.048 mmol, 1.0 equiv, added as a 0.96 M stock solution in C_6H_6), and $Pd(OAc)_2$ (0.54 mg, 0.0024 mmol, 0.05 equiv, added as a 0.0096 M stock solution in C_6H_6), and the resulting mixtures were diluted to a total volume of 400 μL of C_6H_6. The reaction was heated at 80 ºC for 12 h, and then cooled to room temperature. A GC standard (pyrene) was added, and the reaction was analyzed by gas chromatography.

Table S3. Product Ratios Obtained from Competition Studies in Benzene

							
	1 : 0.06	1 : 0.2	1 : 0.05	1 : <0.01	1 : <0.01	1 : <0.01	1 : <0.01
	-	1 : 4	1 : 2	1 : <0.01	1 : <0.01	1 : <0.01	1 : <0.01
	1 : 0.25	-	n/a[a]	1 : <0.01	1 : <0.01	1 : <0.01	1 : <0.01
	0.5 : 1	n/a[a]	-	1 : <0.01	1 : <0.01	1 : <0.01	1 : <0.01
	<0.01 : 1	<0.01 : 1	<0.01 : 1	-	n/a[b]	<0.01 : 1	<0.01 : 1
	<0.01 : 1	<0.01 : 1	<0.01 : 1	n/a[b]	-	<0.01 : 1	<0.01 : 1
	<0.01 : 1	<0.01 : 1	<0.01 : 1	1 : <0.01	1 : <0.01	-	1 : 1
	<0.01 : 1	<0.01 : 1	<0.01 : 1	1 : <0.01	1 : <0.01	1 : 1	-

[a] Ratio not obtained because starting materials and products have identical retention times by GC
[b] Ratio not obtained because starting materials afford trace amounts of products in benzene

Figure S8. Product Ratios Obtained from Competition Studies of Substituted Benzyl Pyridines

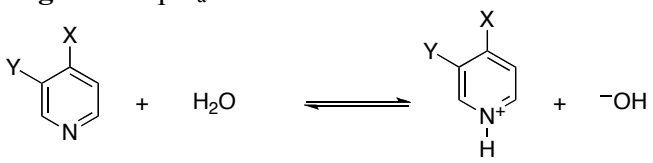


X	Y	AcOH/Ac_2O	Benzene
CF_3	H	0.24 : 1	0.15 : 1
H	F	0.29 : 1	0.13 : 1
Cl	H	0.41 : 1	0.26 : 1
H	Me	1.06 : 1	1.86 : 1
Me	H	1.07 : 1	2.34 : 1
OMe	H	0.77 : 1	3.83 : 1

Adjusted Hammett Plot

Table S4 illustrates the pK_a values used for the various electronically substituted pyridine derivatives to obtain the effective concentrations in $AcOH/Ac_2O$.

Figure S9. pK_a Values for Substrates **1a-7a**[13,14,15]



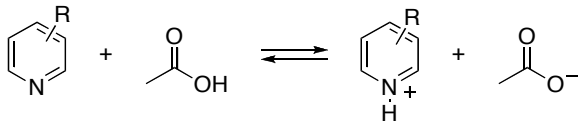
X	Y	pK_a	Ref.
CF_3	H	2.63	12
H	F	2.97	13
Cl	H	3.84	14
H	Me	5.68	13
Me	H	6.02	13
OMe	H	6.62	13
H	H	5.17	13

Table S4. Correction for Unprotonated Benzylpyridine Concentration

X	Y	pK_a	eff. conc	obs. ratio	adj. ratio
CF_3	H	2.74	0.05	0.24	0.003
H	F	2.97	0.04	0.29	0.004
Cl	H	3.84	0.01	0.42	0.02
H	Me	5.63	0.0003	1.06	2.83
Me	H	6.02	0.0001	1.07	7.01
OMe	H	6.55	0.00003	0.77	5.05

Calculations for Obtaining Adjusted Ratios in Competition Reactions

The following equations were used in calculating the effective concentration of the substrate. Based on the corrected values of the concentration the adjusted ratio of products for the competition reaction was determined.



$$K_{eq} = \frac{[\text{pyr H}^+]\,[\text{AcO}^-]}{[\text{pyridine}]\,[\text{AcOH}]}$$

$$K_{eq} = \frac{K_{a\ \text{pyridine}}}{K_{a\ \text{AcOH}}}$$

$$\frac{K_{a\ \text{pyridine}}}{1.78 \times 10^{-5}} = \frac{x^2}{(0.12\ \text{M} - x)(8.72\ \text{M} - x)}$$

conc. of free pyridine=(0.12 M – x)

$$\text{ratio}_{adjusted} = F * \frac{k_R}{k_H}$$

$$F = \frac{[1a_R]}{[1a_H]}$$

Procedure for Determining the Order of Reactions in the Oxidant for Competition Studies

The competition experiments discussed above were conducted with benzylpyridine **6a** and *p*-CF_3benzylpyridine **3a**, using 1.02, 1.5, 2.0 and 2.5 equiv of $PhI(OAc)_2$ (0.049 mmol, 0.072 mmol, 0.096 mmol, and 0.120 mmol, respectively) under otherwise identical conditions. Rate constants were calculated for substrate **6a** in each reaction using the initial rates method, and the data is plotted below.

Figure S10. Initial Rate Constant of **6a** as a Function of Oxidant Concentration in $AcOH/Ac_2O$

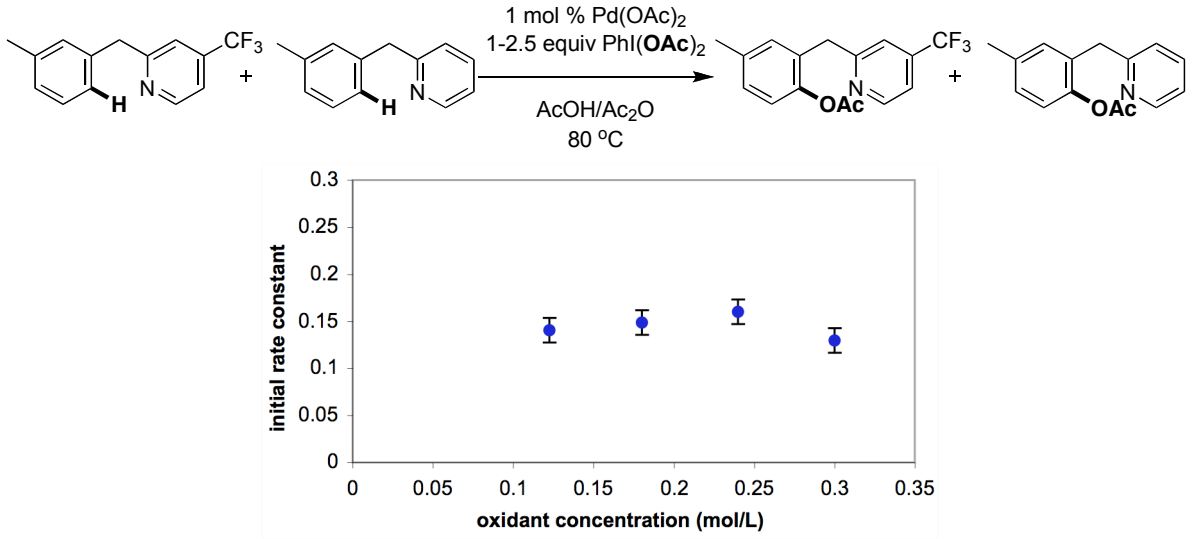
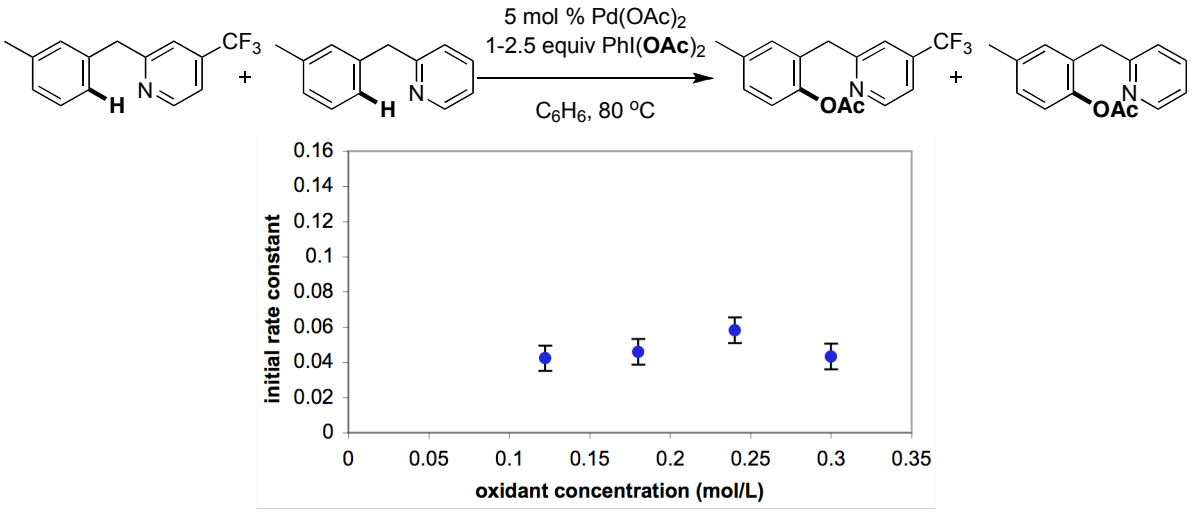


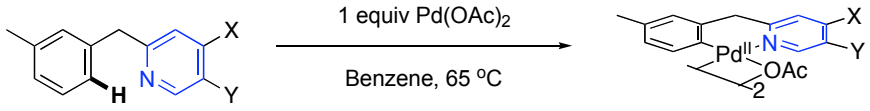
Figure S11. Initial Rate Constant of **6a** as a Function of Oxidant Concentration in Benzene



Procedure for UV-Vis Kinetics of Stoichiometric Cyclopalladation

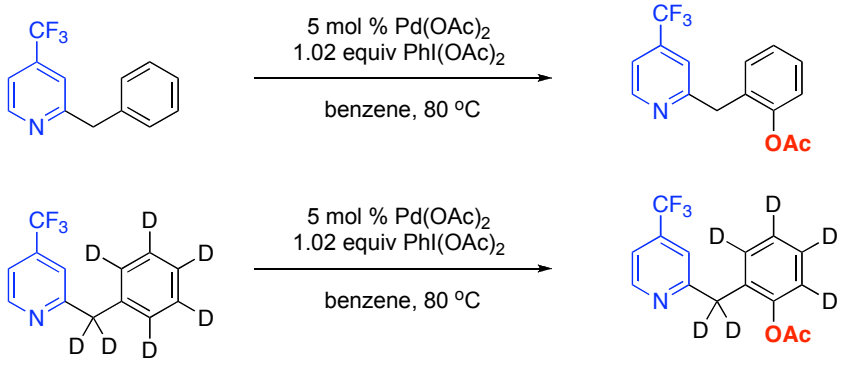
The rate of stoichiometric cyclopalladation of substrates **1a-3a** and **6a-7a** was studied using UV-vis spectroscopy. Each substrate (10 mM, 20 equiv) was added to a solution of $Pd(OAc)_2$ (0.5 mM, 1 equiv) in 3.5 mL of benzene in a 4 mL cuvette (10 mm pathlength), and the resulting solution was heated at 65 °C. The kinetics of the reaction was monitored at the wavelength indicated in Figure S11. Figure S11 also illustrates the rates obtained from the cyclometalation reactions of substrates **1a-3a** and **6a-7a**.

Figure S12. Rates of Stoichiometric Cyclopalladation



X	Y	k_{obs} (x10^3)	λ (nm)
CF_3	H	3.75	350
H	F	2.20	330
H	H	0.38	310
Me	H	0.22	320
OMe	H	0.18	325

Figure S13. Representative Data for Proteo and Deutero Substrates in Benzene



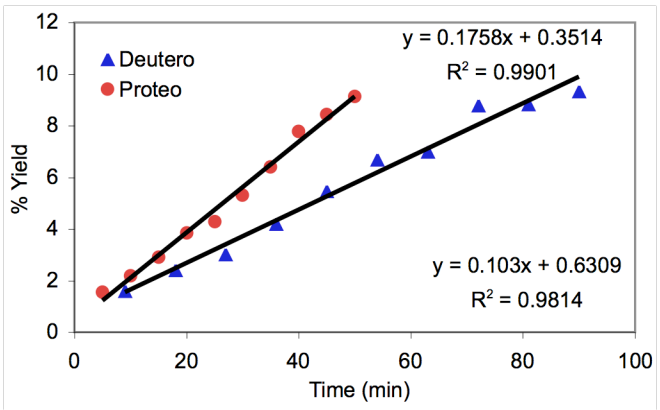


Table S5: Initial Rates and KIE Values Over Three Runs in Benzene

Experiments	Proteo Substrate	Deutero Substrate	KIE
Run 1	0.176	0.103	1.71
Run 2	0.1664	0.0974	1.71
Run 3	0.2506	0.1184	2.12
		Avg. KIE	1.85

Table S6: Initial Rates and KIE Values Over Two Runs in $AcOH/Ac_2O$

Experiments	Proteo Substrate	Deutero Substrate	KIE
Run 1	0.3559	0.0972	3.67
Run 2	0.3575	0.1028	3.48
		Avg. KIE	3.58

Hammett Plots for Competition Experiments: Analyzed at Low Conversion (5-15%)

Figure S14. Hammett Plot in for Competition Studies in AcOH/Ac_2O (Reactions Stopped at Between 10-15% Conversion)

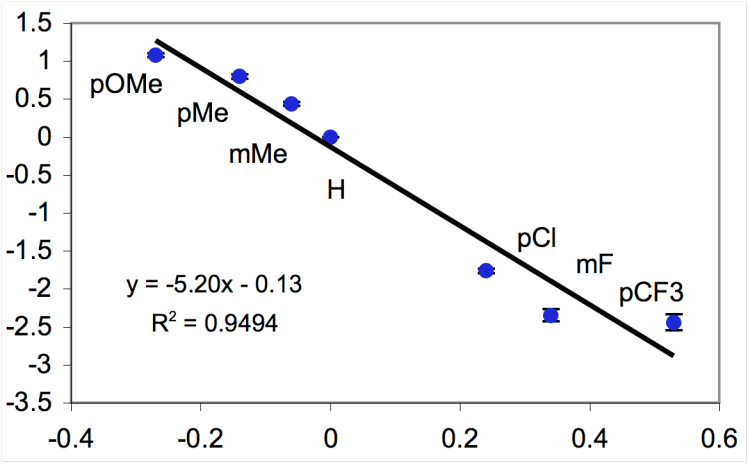
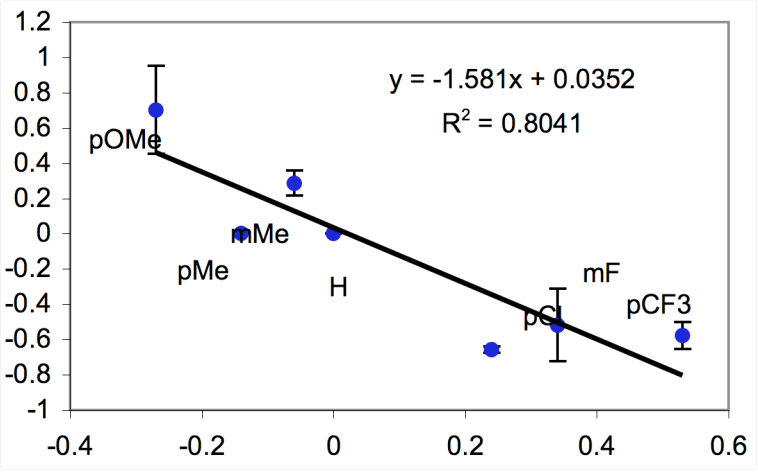
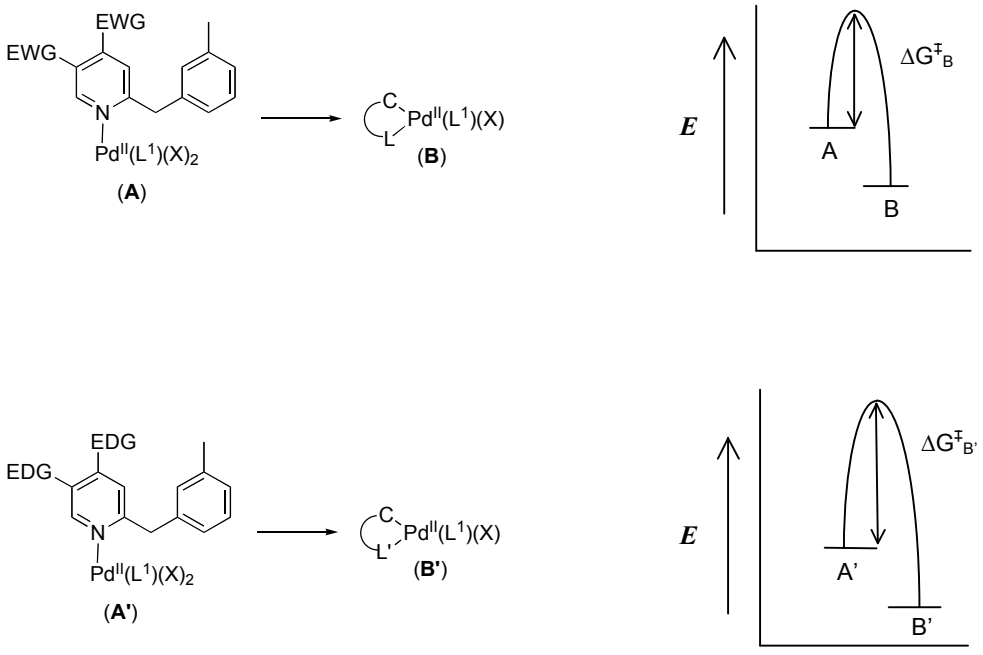


Figure S15. Hammett Plot in for Competition Studies in Benzene (Reactions Stopped at Between 3-7% Conversion)

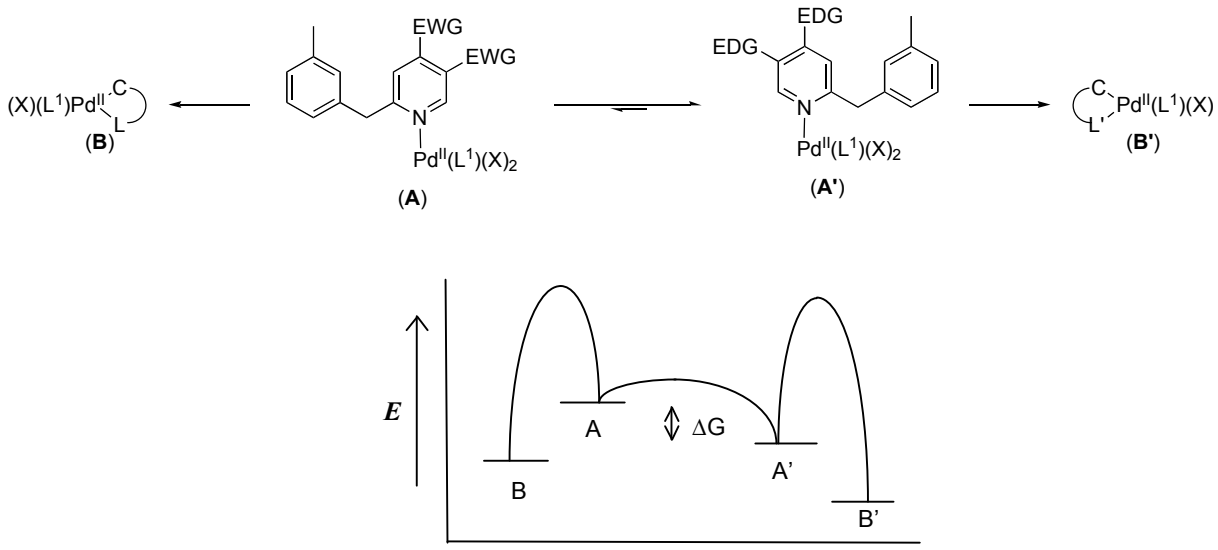


According to the Curtin Hammett principle, the product distribution from these transformations will be determined by the sum of two terms: $\Delta\Delta G^{\dagger\dagger} + \Delta G$. The $\Delta\Delta G^{\dagger\dagger}$ term represents the difference in activation energy for the two C–H activation reactions ($\Delta\Delta G^{\dagger\dagger} = \Delta G^{\dagger\dagger}_{A'} - \Delta G^{\dagger\dagger}_{A}$). (Notably, this is defined such that it will always be positive in sign.) The ΔG term represents the difference in energy between the two coordination complexes **A** and **A'** ($\Delta G = G^{o}_{A'} - G^{o}_{A}$). (This value can be either positive or negative in sign.) If the sum of these two terms is positive in sign then formation of B is favored, while if the sum is negative in sign then the formation of B' is favored. As such, the proposed effects of the equilibrium for ligand exchange in the competition experiments are consistent with the Curtin-Hammett principle as long as the difference in the energy (ΔG) between the two Pd^{II} pyridine coordination complexes is greater than the difference in the activation energies ($\Delta\Delta G^{\dagger\dagger}$) for the C–H activation step (the slow step of these transformations). This is illustrated schematically below.

Figure S16: Illustrating the Curtin Hammett Principle



A reacts faster than A' under individual kinetics conditions



B' is formed to a greater extent than B under competition conditions

V. References

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