

Supporting Information for:

**Highly Regioselective Catalytic Oxidative Coupling Reactions: Synthetic and Mechanistic Investigations**

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## I. General Procedures and Materials and Methods

**General Procedures:** NMR spectra were obtained on a Varian Inova 500 (499.90 MHz for  $^1\text{H}$ ; 125.70 MHz for  $^{13}\text{C}$ ), a Varian Inova 400 (399.96 MHz for  $^1\text{H}$ ; 100.57 MHz for  $^{13}\text{C}$ ; 376.34 MHz for  $^{19}\text{F}$ ), or a Varian Mercury 300 (300.07 MHz for  $^1\text{H}$ ; 75.45 MHz for  $^{13}\text{C}$  NMR; 282.35 MHz for  $^{19}\text{F}$ ) spectrometer.  $^1\text{H}$  and  $^{13}\text{C}$  NMR chemical shifts are reported in parts per million (ppm) relative to TMS, with the residual solvent peak used as an internal reference ( $\nu_{^{13}\text{C}}^{\text{obs}}$  is 125.7015602599, 100.5718255687, 75.45387632423 Mz for the Varian 500, 400, and Mercury 300, respectively);  $^{19}\text{F}$  NMR are referenced based on the residual solvent peak in the  $^1\text{H}$  NMR spectrum ( $\delta_{\text{F}} = 94.094011$ ).<sup>\*</sup> Multiplicities are reported as follows: singlet (s), doublet (d), doublet of doublets (dd), doublet of doublet of doublets (ddd), doublet of triplets (dt), doublet of quartets (dq), triplet (t), triplet of doublets (td), quartet (q), quartet of doublets (qd), and multiplet (m). Unless otherwise indicated, the  $^1\text{H}$  and  $^{13}\text{C}$  NMR spectra were recorded at room temperature.

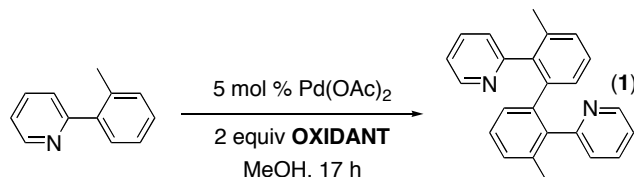
**Materials and Methods:** 2-Phenylpyridine was obtained from commercial sources and used as received. 2-*o*-Bromophenylpyridine was prepared by palladium-catalyzed *ortho*-bromination of 2-phenylpyridine.<sup>1</sup> The remainder of the arylpyridine/heteroarylpyridine substrates were prepared by Suzuki cross coupling between 2-bromopyridine or 2-bromo-3-methylpyridine and the corresponding boronic acid.<sup>2</sup> Oxone was obtained from Acros and used without further purification.  $\text{Pd}(\text{OAc})_2$  was obtained from Pressure Chemical or Frontier Scientific and used as received. Solvents were obtained from Fisher Scientific and used without purification. 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 F<sub>254</sub>. Gas chromatographs were obtained on a Shimadzu 17A using a Restek Rtx®-5 (Crossbond 5% diphenyl – 95% dimethyl polysiloxane; 15 m, 0.25 mm ID, 0.25 mm ID, 0.25  $\mu\text{m}$  df) column. pH measurements were determined using an Accumet AB15 pH meter.

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<sup>\*</sup> For more information of referencing NMR spectra using this method, see the following website: [www.iupac.org/publications/pac/2001/7311/7311x1795.html](http://www.iupac.org/publications/pac/2001/7311/7311x1795.html)

## II. Reaction Optimization

**Table S1.** Variation of Oxidant

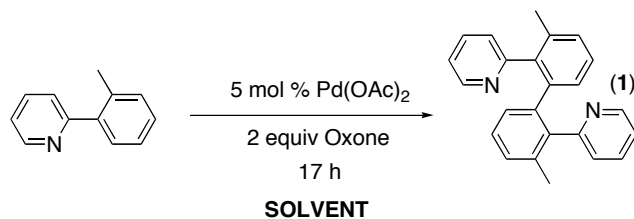


Entry	Oxidant	% Yield (GC) RT <sup>a</sup>	% Yield (GC) 60 °C <sup>a</sup>
1	Oxone	78% <sup>b</sup>	65% <sup>b</sup>
2	K <sub>2</sub> S <sub>2</sub> O <sub>8</sub>	57% <sup>b</sup>	37% <sup>b</sup>
3	PhI(OAc) <sub>2</sub>	7% <sup>b</sup>	0% <sup>b</sup>
4	H <sub>2</sub> O <sub>2</sub> •urea	0%	0% <sup>b</sup>
5	Benzoquinone	0%	0%
6	AgF	0%	0%
7	AgOAc	0%	0%
8	Cu(OAc) <sub>2</sub>	0%	0%
9	CuCl <sub>2</sub>	0%	0%
10	air	0%	0%

<sup>a</sup> % yield determined based on methyl naphthalene as an internal standard

<sup>b</sup> The corresponding *o*-OMe product was also observed by GC and GCMS (see ref. 3)

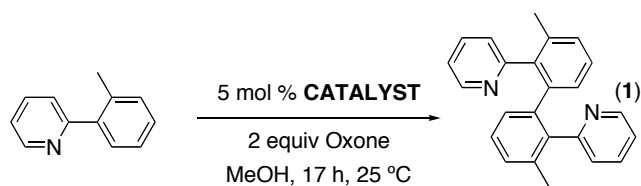
**Table S2.** Variation of Solvent



Entry	Solvent	% Yield (GC) RT <sup>a</sup>	% Yield (GC) 60 °C <sup>a</sup>
1	<i>i</i> -PrOH	76%	69% <sup>b</sup>
2	MeOH	71% <sup>b</sup>	63% <sup>b</sup>
3	Dichloroethane	60%	16%
4	AcOH	35% <sup>b</sup>	14% <sup>b</sup>
5	DMF	32%	40%
6	CH <sub>3</sub> NO <sub>2</sub>	30%	48%
7	Trifluoroethanol	19%	13% <sup>b</sup>
8	DMSO	2%	1%

<sup>a</sup> % yield determined based on methyl naphthalene as an internal standard

<sup>b</sup> The corresponding *o*-OR (OR = *Oi*-Pr, OMe, OCH<sub>2</sub>CF<sub>3</sub>, OAc) was also observed by GC and GCMS (see ref. 3)

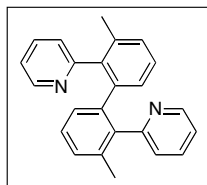
**Table S3.** Variation of Catalyst

Entry	Catalyst	% Yield (GC) <sup>a</sup>
1	Pd(OAc) <sub>2</sub>	71% <sup>b</sup>
2	Pd(TFA) <sub>2</sub>	60% <sup>b</sup>
3	(IMes)Pd(OAc) <sub>2</sub>	41%
4	PdCl <sub>2</sub>	23%
5	PdCl <sub>2</sub> (MeCN) <sub>2</sub>	15%
6	PdCl <sub>2</sub> (PhCN) <sub>2</sub>	8%
7	Pd(bipy)Cl <sub>2</sub>	1%
8	PdBr <sub>2</sub>	0%

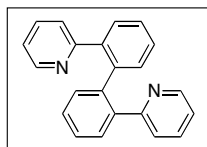
<sup>a</sup> % yield determined based on methyl naphthalene as an internal standard

<sup>b</sup> The corresponding *o*-OMe product was also observed by GC and GCMS (see ref. 3)

### III. Experimental Procedures

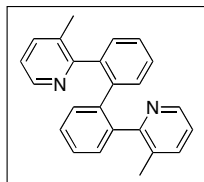


**Product 1.** 2-*o*-Tolylpyridine (100 mg, 0.59 mmol, 1 equiv), Oxone (710 mg, 1.15 mmol, 2.0 equiv) and Pd(OAc)<sub>2</sub> (6.5 mg, 0.029 mmol, 5.0 mol %) were combined in *i*-PrOH (5.0 mL) in a 20 mL scintillation vial equipped with a Teflon stirbar. The reaction mixture was stirred at room temperature for 17 h. GC analysis of the crude reaction mixture showed a >100 : 1 ratio of **1** to 2-*o*-tolylpyridine and traces of the *o*-isopropylether product. The resulting pale yellow suspension was diluted with ethyl acetate (100 mL) and washed three times with 10% Na<sub>2</sub>SO<sub>3</sub> and one time with brine. The organic layer was dried over MgSO<sub>4</sub> and concentrated, and the resulting orange oil was purified by chromatography on silica gel (*R*<sub>f</sub> = 0.4 in 50% hexanes/50% ethyl acetate). Product **1** was isolated as a white solid (85 mg, 86% yield, mp = 152.4-154.5 °C). <sup>1</sup>H NMR (400 MHz, DMSO-*d*<sub>6</sub>, 60 °C): δ 8.53 (ddd, *J* = 4.8, 1.6, 0.8 Hz, 2H), 7.63 (td, *J* = 7.7, 1.7 Hz, 2H), 7.37 (d, *J* = 7.6 Hz, 2H), 7.16 (ddd, *J* = 7.6, 5.1, 1.1 Hz, 2H), 7.06 (d, *J* = 7.6 Hz, 2H), 6.94 (t, *J* = 7.8 Hz, 2H), 6.68 (d, *J* = 7.2 Hz, 2H), 1.99 (s, 6H); <sup>13</sup>C NMR (75 MHz, 59 °C, DMSO-*d*<sub>6</sub>): δ 158.55, 148.28, 139.63, 139.57, 135.30, 135.18, 128.14, 128.04, 126.01, 125.13, 121.08, 19.79. HRMS ESI with Formic Acid (*m/z*): [M+H]<sup>+</sup> calcd for C<sub>24</sub>H<sub>21</sub>N<sub>2</sub>, 337.1705; found, 337.1695.

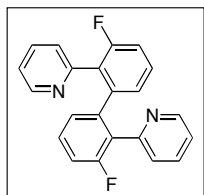


**Product 2.** 2-Phenylpyridine (82 μL, 0.57 mmol, 1 equiv), Oxone (390 mg, 0.63 mmol, 1.1 equiv) and Pd(OAc)<sub>2</sub> (6.5 mg, 0.029 mmol, 5.0 mol %) were combined in MeOH (5.0 mL) in a 20 mL scintillation vial equipped with a Teflon stirbar. The reaction mixture was stirred at room temperature for 17 h. GC analysis of the crude reaction mixture showed an ~2.4 : 1 ratio of **2** to 2-phenylpyridine along with traces of the *o*-methylether product. The resulting pale yellow suspension was diluted with ethyl acetate (100 mL) and washed three times with 10% Na<sub>2</sub>SO<sub>3</sub> and one time with brine. The organic layer was dried over MgSO<sub>4</sub> and concentrated, and the resulting orange oil was purified by chromatography on silica gel (*R*<sub>f</sub> = 0.1 in 50% hexanes/50% ethyl acetate). Product **2** was isolated as a white solid (36 mg, 41% yield, mp = 136-136.5 °C). Note: electrospray mass spectrometry of the crude reaction mixture showed the presence of further oligomers of 2-phenylpyridine (predominantly *n* = 3 and *n* = 4). <sup>1</sup>H NMR (400 MHz, acetone-*d*<sub>6</sub>): δ 8.38 (ddd, *J* = 4.8, 1.6, 0.8 Hz, 2H), 7.60 (dd, *J* = 3.5, 1.4 Hz, 2H), 7.47 (td, *J* =

7.7, 1.9 Hz, 2H), 7.37 (td,  $J = 7.6, 1.2$  Hz, 2H), 7.27 (td,  $J = 7.6, 1.5$  Hz, 2H), 7.18 (dt,  $J = 8.0, 1.1$  Hz, 2H), 7.12–7.05 (multiple peaks, 4H);  $^{13}\text{C}$  NMR (100 MHz, acetone- $d_6$ ):  $\delta$  159.70, 149.88, 141.48, 141.06, 136.19, 132.22, 131.07, 128.71, 127.95, 125.29, 122.17. HRMS ESI with Formic Acid ( $m/z$ ):  $[\text{M}+\text{H}]^+$  calcd for  $\text{C}_{22}\text{H}_{17}\text{N}_2$ , 309.1392; found, 309.1385.

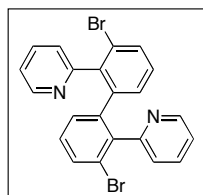


**Product 3.** 3-Methyl-2-phenylpyridine (95 mg, 0.58 mmol, 1 equiv), Oxone (710 mg, 1.15 mmol, 2.0 equiv) and  $\text{Pd}(\text{OAc})_2$  (6.5 mg, 0.029 mmol, 5.0 mol %) were combined in MeOH (5.0 mL) in a 20 mL scintillation vial equipped with a Teflon stirbar. The reaction mixture stirred at room temperature for 17 h. GC analysis of the crude reaction mixture showed a  $>100 : 1$  ratio of **3** to 2-phenyl-3-methylpyridine and traces of the *o*-methylether product. The resulting pale yellow suspension was diluted with ethyl acetate (100 mL) and washed three times with 10%  $\text{Na}_2\text{SO}_3$  and one time with brine. The organic layer was dried over  $\text{MgSO}_4$  and concentrated, and the resulting orange oil was purified by chromatography on silica gel ( $R_f = 0.07$  in 50% hexanes/50% ethyl acetate). Product **3** was isolated as a white solid (83 mg, 86% yield, mp = 178.4–179.3 °C).  $^1\text{H}$  NMR (400 MHz,  $\text{DMSO}-d_6$ , 59 °C):  $\delta$  8.17 (d,  $J = 4.5$  Hz, 2H), 7.48 (d,  $J = 7.2$  Hz, 2H), 7.26–7.06 (multiple peaks, 10H), 1.92 (s, 6H);  $^{13}\text{C}$  NMR (75 MHz,  $\text{DMSO}-d_6$ , 59 °C):  $\delta$  158.27, 145.34, 139.25, 139.13, 137.24, 131.23, 131.19, 129.40, 126.37, 125.87, 121.48, 18.78. HRMS ESI with Formic Acid ( $m/z$ ):  $[\text{M}+\text{H}]^+$  calcd for  $\text{C}_{24}\text{H}_{21}\text{N}_2$ , 337.1705; found, 337.1691.

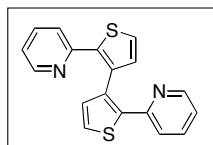


**Product 4.** 2-(*o*-Fluorophenyl)pyridine (100 mg, 0.58 mmol, 1 equiv), Oxone (710 mg, 1.15 mmol, 2.0 equiv) and  $\text{Pd}(\text{OAc})_2$  (6.5 mg, 0.029 mmol, 5.0 mol %) were combined in  $\text{MeNO}_2$  (5.0 mL) in a 20 mL scintillation vial equipped with a Teflon stirbar. The reaction mixture stirred at 60 °C for 17 h. GC analysis of the crude reaction mixture showed a  $>100 : 1$  ratio of **4** to 2-*o*-fluorophenylpyridine. The resulting pale yellow suspension was diluted with ethyl acetate (100 mL) and washed three times with 10%  $\text{Na}_2\text{SO}_3$  and one time with brine. The organic layer was dried over  $\text{MgSO}_4$  and concentrated, and the resulting orange oil. was purified by chromatography on silica gel ( $R_f = 0.4$  in 50% hexanes/50% ethyl

acetate). Product **4** was isolated as a white solid (82 mg, 82% yield, mp = 126.5-127.2 °C).  $^1\text{H}$  NMR (300 MHz, acetone- $d_6$ ):  $\delta$  8.49 (ddd,  $J$  = 5.1, 1.8, 0.9 Hz, 2H), 7.65 (td,  $J$  = 7.5, 1.5 Hz, 2H), 7.50 (dd,  $J$  = 7.8, 1.2 Hz, 2H), 7.22-7.05 (multiple peaks, 6H), 6.80 (dd,  $J$  = 7.4, 1.4 Hz, 2H);  $^{13}\text{C}$  NMR (75 MHz, acetone- $d_6$ ):  $\delta$  160.96 (d,  $J_{\text{CF}}$  = 234.9 Hz), 154.64, 149.86, 142.77 (t,  $J_{\text{CF}}$  = 2.9 Hz), 136.51, 129.61 (d,  $J_{\text{CF}}$  = 8.8 Hz), 129.45 (d,  $J_{\text{CF}}$  = 15.4 Hz), 127.79 (d,  $J_{\text{CF}}$  = 3.6 Hz), 127.00 (d,  $J_{\text{CF}}$  = 2.1 Hz), 123.01, 115.14 (d,  $J_{\text{CF}}$  = 22.7 Hz);  $^{19}\text{F}$  NMR (282 MHz, acetone- $d_6$ ): -117.78 (dd,  $J$  = 9.3, 5.9 Hz). HRMS ESI with Formic Acid ( $m/z$ ):  $[\text{M}+\text{H}]^+$  calcd for  $\text{C}_{22}\text{H}_{15}\text{F}_2\text{N}_2$ , 345.1203; found, 345.1190.

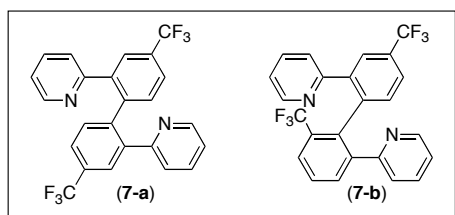


**Product 5.** 2-(2-Bromophenyl)pyridine (135 mg, 0.58 mmol, 1 equiv), Oxone (710 mg, 1.15 mmol, 2.0 equiv) and  $\text{Pd}(\text{OAc})_2$  (6.5 mg, 0.029 mmol, 5.0 mol %) were combined in MeOH (5.0 mL) in a 20 mL scintillation vial equipped with a Teflon stirbar. The reaction mixture was stirred at room temperature for 17 h. The resulting pale yellow suspension was diluted with ethyl acetate (100 mL) and washed three times with 10%  $\text{Na}_2\text{SO}_3$  and one time with brine. The organic layer was dried over  $\text{MgSO}_4$  and concentrated, and the resulting orange oil was purified by chromatography on silica gel ( $R_f$  = 0.56 in 50% hexanes/50% ethyl acetate). Product **5** was isolated as a white solid (91 mg, 67% yield, mp = 193.1-195.2 °C).  $^1\text{H}$  NMR (300 MHz, DMSO- $d_6$ , 50 °C):  $\delta$  8.52 (d,  $J$  = 4.2 Hz, 2H), 7.70 (td,  $J$  = 7.5, 0.9 Hz, 2H), 7.51 (dd,  $J$  = 7.8, 1.2 Hz, 2H), 7.44 (d,  $J$  = 7.5 Hz, 2H), 7.21 (ddd,  $J$  = 7.5, 4.8, 1.2 Hz, 2H), 7.02 (t,  $J$  = 7.8 Hz, 2H), 6.93 (d,  $J$  = 7.5, 2H);  $^{13}\text{C}$  NMR (75 MHz, DMSO- $d_6$ , 50 °C):  $\delta$  157.35, 148.39, 140.81, 140.12, 135.63, 131.22, 129.71, 128.24, 125.29, 122.25, 122.15. HRMS ESI with Formic Acid ( $m/z$ ):  $[\text{M}+\text{H}]^+$  calcd for  $\text{C}_{22}\text{H}_{15}\text{Br}_2\text{N}_2$ , 464.9602; found, 464.9592.



**Product 6.** 2-(2-Thiophenyl)pyridine (175 mg, 1.1 mmol, 1 equiv), Oxone (1.3 g, 2.1 mmol, 1.9 equiv) and  $\text{Pd}(\text{OAc})_2$  (24 mg, 0.11 mmol, 10 mol %) were combined in trifluoroethanol (10 mL) in a 20 mL scintillation vial equipped with a Teflon stirbar. The reaction mixture was stirred at room temperature for 17 h. GC analysis of the crude reaction mixture showed an  $\sim$  1.3 : 1 ratio of **6** to 2-(2-thiophenyl)pyridine. The reaction was quenched with 10%  $\text{Na}_2\text{SO}_3$  (7 mL) and diluted with ethyl acetate

(20 mL). The phases were separated, and the aqueous layer was extracted with ethyl acetate (3 x 20 mL). The combined organic layers were then washed with 10% Na<sub>2</sub>SO<sub>3</sub> (3 x 20 mL) and one time with brine. The organic layer was dried over MgSO<sub>4</sub> and concentrated, and the resulting oil was purified by chromatography on silica gel ( $R_f$  = 0.26 in 30% ethyl acetate/70% hexanes). Product **6** was isolated as a pale yellow solid (76 mg, 44% yield, mp = 171.0-171.6 °C). <sup>1</sup>H NMR (300 MHz, DMSO-*d*<sub>6</sub>) δ 8.48 (ddd,  $J$  = 4.8, 1.8, 0.9 Hz, 2H), 7.78 (d,  $J$  = 5.4, 2H), 7.54 (td,  $J$  = 7.8, 1.8 Hz, 2H), 7.17 (ddd, 7.5, 4.8, 1.0 Hz, 2H), 7.03 (d,  $J$  = 5.4 Hz, 2H), 6.92 (d,  $J$  = 8.1 Hz, 2H). <sup>13</sup>C NMR (75 MHz, DMSO-*d*<sub>6</sub>): δ 151.43, 149.42, 140.41, 136.78, 134.01, 130.88, 128.50, 122.29, 119.05. HRMS ESI with Formic Acid ( $m/z$ ): [M+H]<sup>+</sup> calcd for C<sub>18</sub>H<sub>13</sub>N<sub>2</sub>S<sub>2</sub>, 321.0520; found, 321.0516.

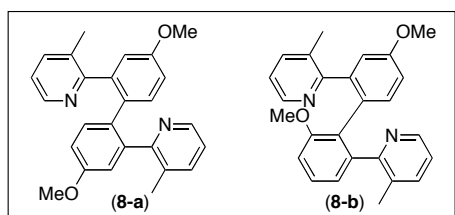


**Products 7-a and 7-b.** 2-(*m*-Trifluoromethylphenyl)pyridine (129 mg, 0.58 mmol, 1 equiv), Oxone (710 mg, 1.1 mmol, 2 equiv) and Pd(OAc)<sub>2</sub> (6.5 mg, 0.029 mmol, 5 mol %) were combined in MeOH (5 mL) in a 25 mL round bottom flask equipped with a Teflon stirbar. The reaction mixture was stirred at room temperature for 17 h. GC analysis of the crude reaction mixture showed an ~1.3 : 1 ratio of **7-a** + **7-b** : 2-(*m*-trifluoromethylphenyl)pyridine and an ~2.5 : 1 ratio of **7-a** + **7-b** : the *o*-methylether product. The reaction was quenched with 10% Na<sub>2</sub>SO<sub>3</sub> (15 mL) and diluted with ethyl acetate (15 mL). The phases were separated, and the aqueous layer was extracted with ethyl acetate (3 x 15 mL). The combined organic layers were then washed with 10% Na<sub>2</sub>SO<sub>3</sub> (3 x 15 mL) and one time with brine. The organic layer was dried over MgSO<sub>4</sub> and concentrated, and the resulting oil was purified by chromatography on silica gel ( $R_f$  for **7-a** = 0.6 in 50% ethyl acetate/ 50% hexanes;  $R_f$  for **7-b** = 0.2 in 50% ethyl acetate/50% methanol). Product **7-a** was isolated as a white solid and **7-b** was isolated as white semi-solid (58 mg, 44% combined yield, ratio of **7-a** : **7-b** = 1.7 : 1).

**Characterization data for 7-a:** mp = 132.5-135.8 °C. <sup>1</sup>H NMR (400 MHz, acetone-*d*<sub>6</sub>): δ 8.39 (ddd,  $J$  = 4.8, 1.8, 1.0 Hz, 2H), 7.92 (dd,  $J$  = 1.2, 0.4 Hz, 2H), 7.70 (ddd,  $J$  = 8.0, 2.0, 0.8 Hz, 2H), 7.58 (td,  $J$  = 7.7, 1.9 Hz, 2H), 7.40 (d,  $J$  = 8.0 Hz, 2H), 7.26 (dt,  $J$  = 7.9, 1.1 Hz, 2H), 7.20 (ddd,  $J$  = 7.6, 4.8, 1.2 Hz, 2H); <sup>19</sup>F NMR (376 MHz, acetone-*d*<sub>6</sub>): δ -62.96 (s); <sup>13</sup>C NMR (100 MHz, acetone-*d*<sub>6</sub>): δ 157.59, 150.23, 144.32, 141.78, 136.93, 133.03, 130.27 (q,  $J_{CF}$  = 32.2 Hz), 127.75 (q,  $J_{CF}$  = 4.4 Hz) 125.57 (q,  $J_{CF}$  = 3.7 Hz), 125.30 (q,  $J_{CF}$  = 269.8 Hz), 125.25, 123.16; HRMS ESI with Formic Acid ( $m/z$ ): [M+H]<sup>+</sup> calcd for C<sub>24</sub>H<sub>15</sub>F<sub>6</sub>N<sub>2</sub>, 445.1139; found, 445.1136.



**Characterization data for 7-b:**  $^1\text{H}$  NMR (400 MHz,  $\text{DMSO}-d_6$ , 75 °C):  $\delta$  8.35 (d,  $J$  = 4.0 Hz, 1H), 8.25 (d,  $J$  = 4.8 Hz, 1H), 7.89 (s, 1H), 7.85 (d,  $J$  = 7.6 Hz, 1H), 7.75-7.66 (multiple peaks, 3H), 7.57-7.46 (multiple peaks, 3H), 7.17 (dd,  $J$  = 7.4, 4.6 Hz, 1H), 7.13-7.08 (multiple peaks, 2H), 6.93 (d,  $J$  = 8.0 Hz, 1H);  $^{19}\text{F}$  NMR (376 MHz,  $\text{DMSO}-d_6$ , 75 °C):  $\delta$  -55.92 (s), -61.21 (s);  $^{13}\text{C}$  NMR (100 MHz,  $\text{DMSO}-d_6$ , 75 °C):  $\delta$  156.51, 155.12, 148.42, 148.06, 141.64, 140.07, 139.30, 136.77 (app. d,  $J$  = 1.0 Hz), 135.57, 135.23, 133.31, 132.60, 128.4 (q,  $J_{\text{CF}}$  = 31.9 Hz), 128.13, 127.58 (q,  $J_{\text{CF}}$  = 28.5 Hz), 125.8 (q,  $J_{\text{CF}}$  = 5.1 Hz), 125.20 (app. d,  $J_{\text{CF}}$  = 2.9), 123.69 (q,  $J_{\text{CF}}$  = 272.4 Hz), 123.68, 123.60 (q,  $J_{\text{CF}}$  = 274.8 Hz), 123.1 (app. d,  $J_{\text{CF}}$  = 2.9), 122.81, 121.78, 121.48. HRMS ESI with Formic Acid ( $m/z$ ):  $[\text{M}+\text{H}]^+$  calcd for  $\text{C}_{24}\text{H}_{15}\text{F}_6\text{N}_2$ , 445.1139; found, 445.1140.

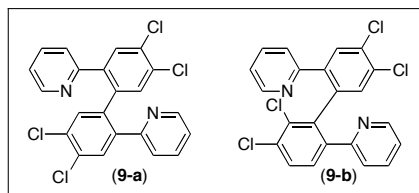


**Products 8-a and 8-b.** 3-Methyl-2-(3-methoxyphenyl)pyridine (115 mg, 0.58 mmol, 1 equiv), Oxone (710 mg, 1.15 mmol, 2.0 equiv) and  $\text{Pd}(\text{OAc})_2$  (6.5 mg, 0.029 mmol, 5.0 mol %) were combined in *i*-PrOH (5.0 mL) in a 20 mL scintillation vial equipped with a Teflon stirbar. The reaction mixture was stirred at room temperature for 17 h. The resulting pale orange suspension was diluted with ethyl acetate (100 mL) and washed three times with 10%  $\text{Na}_2\text{SO}_3$  and one time with brine. The organic layer was dried over  $\text{MgSO}_4$  and concentrated, and the resulting orange oil was purified by chromatography on silica gel ( $R_f$  for **8-a** = 0.27 in 95% ethyl acetate/5% methanol;  $R_f$  for **8-b** = 0.04 in 95% ethyl acetate/5% methanol). Products **8-a** and **8-b** were isolated as white solids (87 mg, 76% combined yield, ratio of **8a** : **8-b** = 1 : 1.3).

**Characterization data for 8-a:** mp = 61.2-62.6 °C.  $^1\text{H}$  NMR (400 MHz,  $\text{DMSO}-d_6$ , 50 °C):  $\delta$  8.20 (d,  $J$  = 4.2 Hz, 2H), 7.49 (d,  $J$  = 7.5 Hz, 2H), 7.11 (dd,  $J$  = 7.7, 4.7 Hz, 2H), 6.93 (d,  $J$  = 8.7 Hz, 2H), 6.72-6.64 (multiple peaks, 4H), 3.69 (s, 6H), 1.97 (s, 6H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{DMSO}-d_6$ , 50 °C):  $\delta$  158.41, 156.96, 145.50, 140.47, 137.35, 132.39, 131.28, 128.06, 121.69, 114.60, 112.46, 54.85, 18.94. HRMS ESI with Formic Acid ( $m/z$ ):  $[\text{M}+\text{H}]^+$  calcd for  $\text{C}_{26}\text{H}_{25}\text{N}_2\text{O}_2$ , 397.1916; found, 397.1919.

**Characterization data for 8-b:** mp: begins to sublime at 158 °C and then decomposes at 202.8-206.8 °C.  $^1\text{H}$  NMR (400 MHz,  $\text{DMSO}-d_6$ , 48 °C):  $\delta$  8.20 (d,  $J$  = 3.6 Hz, 1H), 8.00 (d,  $J$  = 4.5 Hz, 1H), 7.51 (d,  $J$  = 7.8 Hz, 1H), 7.41 (d,  $J$  = 7.5 Hz, 1H), 7.20-7.12 (multiple peaks, 2H), 7.09-7.01 (multiple peaks, 2H), 6.79 (d,  $J$  = 8.1 Hz, 1H), 6.72 (dd,  $J$  = 8.4, 2.8 Hz, 1H), 6.66-6.64 (multiple peaks, 2H), 3.69 (s, 3H), 3.41 (s, 3H), 1.97 (s, 3H), 1.92 (s, 3H);  $^{13}\text{C}$  NMR (75 MHz,  $\text{DMSO}$ , 55 °C):  $\delta$  158.48, 158.12,

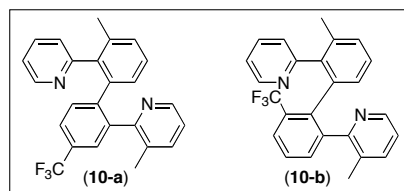
156.85, 156.52, 144.97, 144.74, 141.15, 140.74, 137.28, 137.12, 134.12, 131.50, 131.00, 128.54, 127.44, 126.87, 121.50, 121.35, 121.23, 114.36, 111.64, 109.66, 54.80, 54.69, 19.05, 18.72. HRMS ESI with Formic Acid ( $m/z$ ):  $[M+H]^+$  calcd for  $C_{26}H_{25}N_2O_2$ , 397.1916; found, 397.1913.



**Products 9-a and 9-b.** 2-(3,4-Dichlorophenyl)pyridine (130 mg, 0.58 mmol, 1 equiv), Oxone (710 mg, 1.15 mmol, 2.0 equiv) and  $Pd(OAc)_2$  (6.5 mg, 0.029 mmol, 5.0 mol %) were combined in MeOH (5.0 mL) in a 20 mL scintillation vial equipped with a Teflon stirbar. The reaction mixture was stirred at room temperature for 17 h. The resulting pale orange suspension was diluted with ethyl acetate (100 mL) and washed three times with 10%  $Na_2SO_3$  and one time with brine. The organic layer was dried over  $MgSO_4$  and concentrated, and the resulting orange oil was purified by chromatography on silica gel ( $R_f$  for **9-a** = 0.40 in 50% hexanes/50% ethyl acetate;  $R_f$  for **9-b** = 0.29 in 50% hexanes/50% ethyl acetate). Products **9-a** and **9-b** were isolated as white solids (75 mg, 58% combined yield, ratio of **9-a** : **9-b** = 1.1 : 1).

**Characterization data for 9-a.** mp = 201.6-202.6 °C.  $^1H$  NMR (400 MHz,  $CDCl_3$ ):  $\delta$  8.32 (dd,  $J$  = 4.9, 1.7, 0.7 Hz, 2H), 7.62 (s, 2H), 7.50 (s, 2H), 7.43 (td,  $J$  = 7.7, 1.7 Hz, 2H), 7.10 (ddd,  $J$  = 7.6, 4.8, 1.2 Hz, 2H), 6.76 (d,  $J$  = 8.0 Hz, 2H);  $^{13}C$  NMR (100 MHz,  $CDCl_3$ ):  $\delta$  155.28, 149.24, 139.41, 137.44, 135.99, 132.85, 132.69, 132.47, 131.95, 124.01, 122.12. HRMS ESI with Formic Acid ( $m/z$ ):  $[M+H]^+$  calcd for  $C_{22}H_{13}N_2Cl_4$ , 444.9833; found, 444.9829.

**Characterization data for 9-b.** mp = 155.9-157.0 °C.  $^1H$  NMR (400 MHz,  $CDCl_3$ ):  $\delta$  8.39-8.37 (multiple peaks, 2H), 7.72 (s, 1H), 7.54 (d,  $J$  = 8.4 Hz, 1H), 7.50-7.40 (multiple peaks, 2H), 7.41 (d,  $J$  = 8.4 Hz, 1H), 7.35 (s, 1H), 7.13-7.08 (multiple peaks, 2H), 7.01 (dt,  $J$  = 8.0, 1.0 Hz, 1H), 6.93 (d,  $J$  = 8.0 Hz, 1H);  $^{13}C$  NMR (100 MHz,  $CDCl_3$ ):  $\delta$  156.43, 155.47, 149.12, 149.04, 140.44, 140.01, 138.53, 136.01, 136.00, 135.87, 133.54, 133.26, 132.64, 132.28, 132.22, 131.55, 129.98, 129.13, 124.22, 123.42, 122.30, 122.11. HRMS ESI with Formic Acid ( $m/z$ ):  $[M+H]^+$  calcd for  $C_{22}H_{13}N_2Cl_4$ , 444.9833; found, 444.9833.

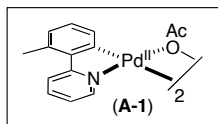


**Products 11-a and 11-b.** Complex **A-1** [400 mg, 0.6 mmol, 0.5 equiv (1 equiv based on [Pd])], Oxone (1.424 g, 2.40 mmol, 2 equiv), and substrate **E** (569 mg, 2.40 mmol, 2 equiv) were combined in MeOH (10 mL), and the mixture was stirred at room temperature for 12 h. The resulting red suspension was diluted with ethyl acetate (100 mL) and washed three times with 10% Na<sub>2</sub>SO<sub>3</sub> and one time with brine. The organic layer was dried over MgSO<sub>4</sub> and concentrated, and the resulting orange oil was purified by chromatography on silica gel (*R<sub>f</sub>* for **11-a** = 0.23 in 20% ethyl acetate/ 80% hexanes; *R<sub>f</sub>* for **11-b** = 0.15 in 75% ethyl acetate/ 25% methylene chloride).

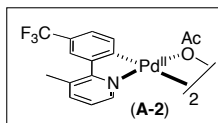
**Characterization data for 11-a.** mp = 45.0–50.2 °C. <sup>1</sup>H NMR (400 MHz, DMSO-*d*<sub>6</sub>, 80 °C): δ 8.53 (d, *J* = 4.0 Hz, 1H), 8.26 (d, *J* = 4.0 Hz, 1H), 7.62–7.55 (multiple peaks, 2H), 7.52 (d, *J* = 1.2 Hz, 1H), 7.41 (app. d, *J* = 8.0 Hz, 2H), 7.20–7.10 (multiple peaks, 4H), 7.02 (t, *J* = 7.6 Hz, 1H), 6.78 (d, *J* = 7.6 Hz, 1H), 2.11 (s, 3H), 2.03 (s, 3H); <sup>13</sup>C NMR (100 MHz, DMSO-*d*<sub>6</sub>, 80 °C) δ 157.95, 156.58, 148.01, 145.71, 144.07, 139.96, 139.17, 137.80, 137.41 (app. d, *J* = 2.9 Hz), 135.58, 135.16, 132.07, 131.03, 128.84, 126.95, 126.64 (q, *J* = 31.5 Hz), 126.21, 125.67 (m), 125.05, 123.65 (q, *J* = 271 Hz), 122.70 (m), 121.94 (bs), 121.18, 19.56, 18.50; <sup>19</sup>F NMR (376 MHz, DMSO-*d*<sub>6</sub>): δ –61.03 (s). HRMS ESI with Formic Acid (*m/z*): [M+H]<sup>+</sup> calcd for C<sub>25</sub>H<sub>20</sub>F<sub>3</sub>N<sub>2</sub>, 405.1579; found, 405.1573.

**Characterization data for 11-b.** <sup>1</sup>H NMR (400 MHz, DMSO-*d*<sub>6</sub>, 80 °C): δ 8.40 (d, *J* = 4.8 Hz, 1H), 8.07 (d, *J* = 4.4 Hz, 1H), 7.64 (d, *J* = 7.6 Hz, 1H), 7.55–7.45 (multiple peaks, 4H), 7.40 (d, *J* = 7.6 Hz, 1H), 7.12–6.97 (multiple peaks, 5H), 1.97 (s, 3H), 1.82 (bs, 3H); <sup>13</sup>C NMR (100 MHz, DMSO-*d*<sub>6</sub>, 80 °C): δ 157.10, 156.53, 147.70, 144.90, 140.83, 138.91, 138.18, 137.13 (app. d, *J* = 2.7 Hz), 135.17, 134.67, 134.51, 132.42, 130.94, 129.14, 128.49 (q, *J* = 30.0 Hz), 127.78 (bm), 126.77, 125.23, 125.14 (app. d, *J* = 5.7 Hz), 124.63, 123.68 (q, *J* = 274 Hz), 121.50, 120.77, 19.96, 18.60; <sup>19</sup>F NMR (376 MHz, DMSO-*d*<sub>6</sub>, 80 °C): δ –55.27. HRMS ESI with Formic Acid (*m/z*): [M+H]<sup>+</sup> calcd for C<sub>25</sub>H<sub>20</sub>F<sub>3</sub>N<sub>2</sub>, 405.1579; found, 405.1575.

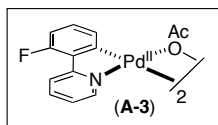
The new palladacycles **A-1** and **A-3** were synthesized according to the literature procedure for complex **A**.<sup>4</sup> The new palladacycle **A-2** was prepared by an alternative route based on a literature procedure.<sup>5</sup> They were characterized by <sup>1</sup>H NMR spectroscopy by breaking up the acetate-bridged dimer *in situ* with pyridine-*d*<sub>5</sub>.



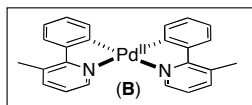
**Complex A-1.**  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$  with several drops of pyridine- $d_5$ ):  $\delta$  8.77 (d,  $J = 1.5$  Hz, 1H), 8.11-8.05 (multiple peaks, 2H), 7.37 (m, 1H), 6.91 (d,  $J = 7.5$  Hz, 1H), 6.78 (t,  $J = 7.0$  Hz, 1H), 6.15 (d,  $J = 7.5$  Hz, 1H), 2.66 (s, 3H), 1.77 (s, 3H).



**Complex A-2.**  $^1\text{H}$  NMR (500 MHz, acetone- $d_6$  with several drops of pyridine- $d_5$ ):  $\delta$  8.72 (bs, 1H), 8.01 (s, 1H), 7.92 (d,  $J = 7.5$  Hz, 1H), 7.35 (d,  $J = 7.5$  Hz, 1H), 7.23 (d,  $J = 8.0$  Hz, 1H), 6.53 (d,  $J = 7.5$  Hz, 1H), 2.79 (s, 3H), 1.82 (s, 3H). Complex A-2 was palladated with >20:1 selectivity at the less sterically hindered position.



**Complex A-3.**  $^1\text{H}$  NMR (400 MHz,  $\text{CD}_3\text{OD}$  with several drops of pyridine- $d_5$ ):  $\delta$  8.12 (d,  $J = 8.4$  Hz, 1H), 8.01 (td,  $J = 6.4, 1.6$  Hz, 1H), 7.56 (d,  $J = 13.6$  Hz, 1H), 7.20 (td,  $J = 7.6, 1.2$  Hz, 1H), 6.98-6.87 (multiple peaks, 2H), 5.89 (dd,  $J = 7.6, 1.2$  Hz, 1H), 1.90 (s, 3H);  $^{19}\text{F}$  NMR (376 MHz,  $\text{CD}_3\text{OD}$  with several drops of pyridine- $d_5$ ):  $\delta$  -113.80 (multiplet).

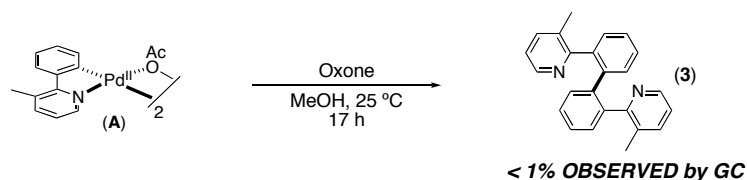


**Complex B** was prepared according to a literature procedure for closely related phenylpyridine complexes.<sup>6</sup>  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ ):  $\delta$  8.52 (dd,  $J = 5.5, 1.5$  Hz, 2H), 8.16 (dd,  $J = 7.5, 1.0$  Hz, 2H), 7.73 (dd,  $J = 7.5, 1.0$  Hz, 2H), 7.60 (dd,  $J = 7.5, 1.0$  Hz, 2H), 7.27 (td,  $J = 7.5, 1.5$  Hz, 2H), 7.16-7.11 (multiple peaks, 4H), 2.73 (s, 6H).

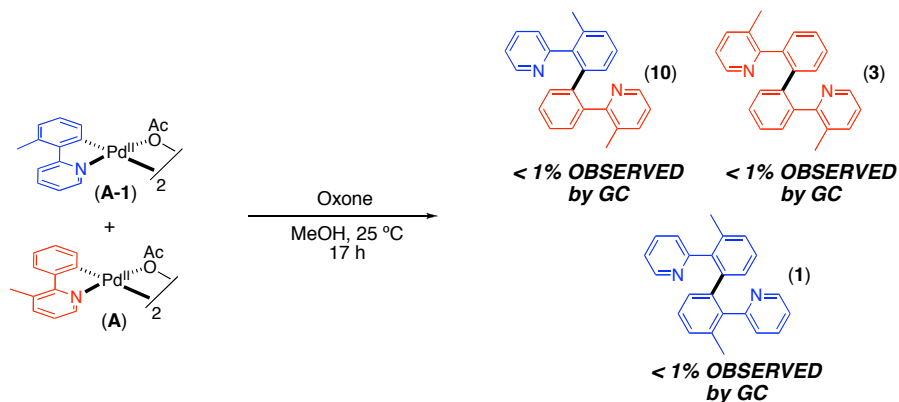
## IV. Mechanistic Experiments

**A. Cross-Over Experiments.** A series of stoichiometric experiments were carried out to probe whether mechanisms I or II (involving exchange of cyclometalated ligands between Pd centers)<sup>†</sup> are operating. In both mechanisms I or II, cross-over of ligands on adjacent Pd complexes is required prior to C–C bond formation. As summarized in Figure S1, the stoichiometric reaction of **A** with Oxone (in the absence of external arylpyridine substrate) afforded <1% of the oxidative coupling products. Similarly, reaction of two different cyclometalated dimers (**A-1** and **A**) with Oxone (in the absence of external arylpyridine substrate) afforded <1% of each of the oxidative coupling products (Figure S2). The lack of C–C bond formation in these systems is evidence against mechanisms involving direct exchange of cyclometalated ligands between Pd<sup>II</sup> complex **A** and its analogues.

**Figure S1.** Cross-over experiments of **A** in the absence of added substrate



**Figure S2.** Cross-over experiments of **A** and **A-1** in the absence of added substrate



The experiments above were carried out in the absence of external substrate, which is clearly in large excess during the catalytic reactions. The substrate could be critical for promoting transmetalation, possibly by breaking up the dimeric Pd complexes **A** and **A-1**. As a result, an analogous cross-over experiment was also carried out in the presence of 2 equiv of free 2-*o*-tolylpyridine (Figure S3). However,

<sup>†</sup> For recent examples of other Pd-mediated/catalyzed reactions that involve similar transmetalation/disproportionation steps, see: (a) Cardenas, D. J.; Martin-Matute, B.; Echavarren, A. M. *J. Am. Chem. Soc.* **2006**, *128*, 5033; (b) Grushin, V. V.; Marshall, W. J. *J. Am. Chem. Soc.* **2006**, *128*, 4632; (c) Lane, B. S.; Sames, D. *Org. Lett.* **2004**, *6*, 2897 and references therein.

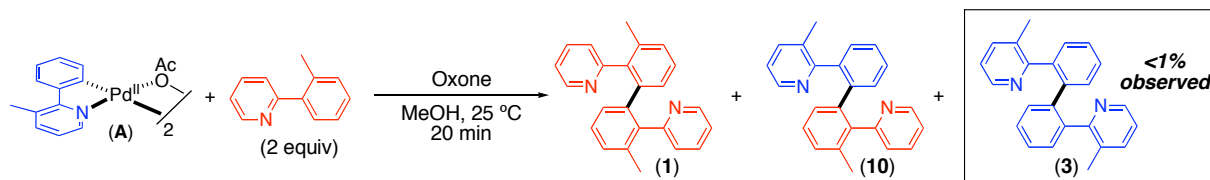
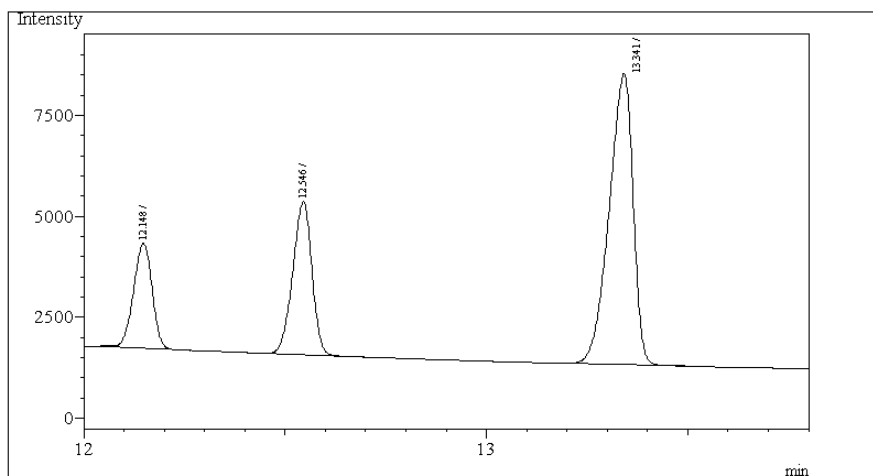
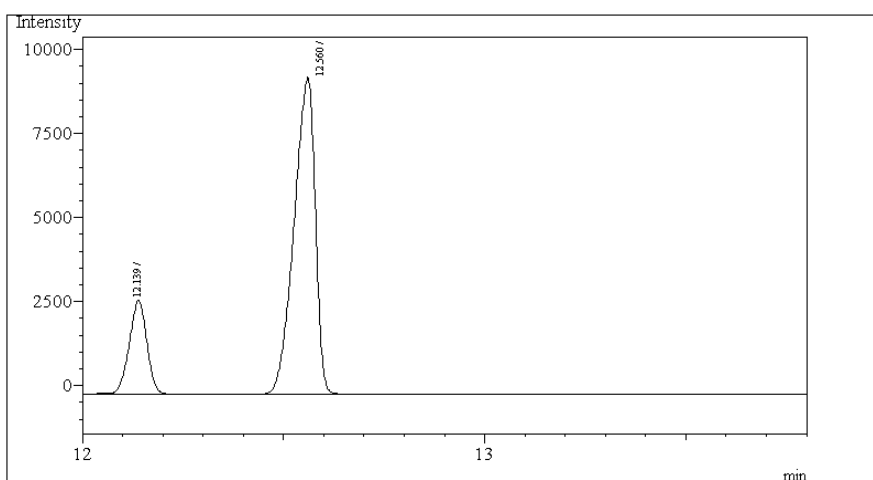
<1% of product **3** was observed in this experiment as well. GC traces associated with this experiment (which (i) confirm that the three oxidative coupling products are separable and readily observable by GC and (ii) show the experimental data) are shown in Figures S4 and S5, respectively.

#### **Experimental for Cross-over Experiments in Figures S1-S3**

**Figure S1:** Complex **A** [4.8 mg, 0.007 mmol, 0.5 equiv (1 equiv based on [Pd])], Oxone (17.7 mg, 0.029 mmol, 2 equiv), and AcOH (0 equiv, 1 equiv or 20 equiv) were combined in MeOH (0.5 mL), and the mixture was stirred at room temperature for 17 h. Methyl naphthalene (5  $\mu$ L), 10% aqueous Na<sub>2</sub>SO<sub>3</sub> (0.5 mL), and ethyl acetate (2 mL) were then added, and the resulting biphasic mixture was stirred for 30 min. The organic layer was analyzed by gas chromatography, which revealed <1% of the oxidative coupling product **3**.

**Figure S2:** Complex **A** [2.4 mg, 0.0035 mmol, 0.25 equiv (0.5 equiv based on [Pd])], complex **A-1** [2.4 mg, 0.0035 mmol, 0.25 equiv (0.5 equiv based on [Pd])], Oxone (17.7 mg, 0.029 mmol, 2 equiv), and AcOH (0 equiv, 1 equiv or 20 equiv) were combined in MeOH (0.5 mL), and the mixture was stirred at room temperature for 17 h. Methyl naphthalene (5  $\mu$ L), 10% aqueous Na<sub>2</sub>SO<sub>3</sub> (0.5 mL), and ethyl acetate (2 mL) were then added, and the resulting biphasic mixture was stirred for 30 min. The organic layer was analyzed by gas chromatography, which revealed <1% of each of the oxidative coupling products **1**, **3**, or **10**.

**Figure S3:** Complex **A** [4.8 mg, 0.07 mmol, 0.5 equiv (1 equiv based on [Pd])], 2-*o*-tolylpyridine (4.9 mg, 0.029 mmol, 2 equiv), Oxone (17.7 mg, 0.029 mmol, 2 equiv), and AcOH (0 equiv, 1 equiv or 20 equiv) were combined in MeOH (0.5 mL), and the mixture was stirred at room temperature for 20 min. Methyl naphthalene (5  $\mu$ L), 10% aqueous Na<sub>2</sub>SO<sub>3</sub> (0.5 mL), and ethyl acetate (2 mL) were then added, and the resulting biphasic mixture was stirred for 30 min. The organic layer was analyzed by gas chromatography (GC from this reaction is shown in Figure S5), which revealed the presence of **1** and **10** but showed <1% of compound **3**.

**Figure S3.** Cross-over experiment in the presence of 2 equiv of 2-*o*-tolylpyridine**Figure S4.** GC trace of authentic mixture of **1** (12.15 min), **10** (12.55 min) and **3** (13.41 min)**Figure S5.** GC trace from the cross-over experiment shown in **Figure S3** [note that <1% of product **3** is observed in the reaction]

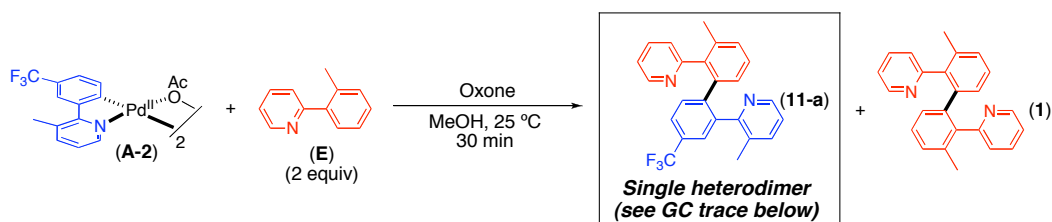
**B. Regioselectivity Experiments.** To probe the origin of the unusual regioselectivity observed in the catalytic reactions, stoichiometric reactions of the *m*-CF<sub>3</sub> substrate **E** and its Pd complex **A-2** were investigated. As shown in Figures S6 and S7, the regioselectivity is not due to the initial cyclometallation step, as complex **A-2** (>20:1 of a single regioisomer as determined by <sup>1</sup>H NMR spectroscopy) reacted with 2-*o*-tolylpyridine to afford heterodimer **11-a** (with <1% of the regioisomeric heterodimer **11-b** formed in this reaction). In contrast, when complex **A-1** was reacted with substrate **E**, regioisomeric products **11-a** and **11-b** were formed in a 5 : 1 ratio. This result suggests against a mechanism involving transmetalation between Pd complexes (with the regioisomeric mixture resulting from an unselective transmetalation step). Instead it suggests that the unusual regiochemistry is determined by a second, much less selective C–H activation event occurring subsequent to the initial cyclometallation reaction.

#### Experimentals for Regioselectivity Experiments

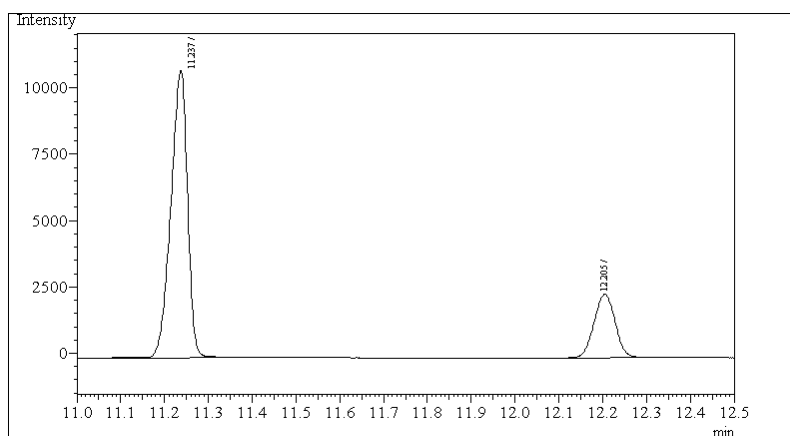
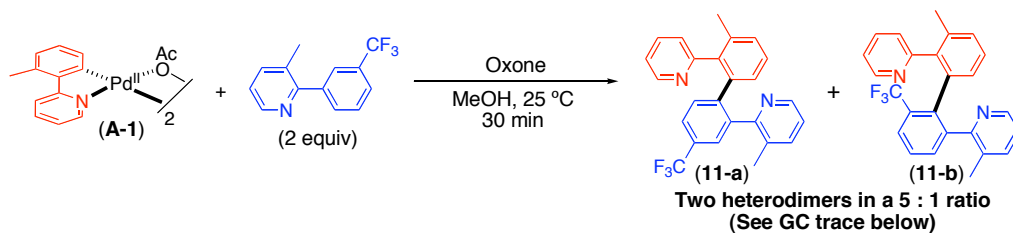
**Figure S6.** Complex **A-2** [5.8 mg, 0.07 mmol, 0.5 equiv (1 equiv based on [Pd])], 2-*o*-tolylpyridine (4.9 mg, 0.029 mmol, 2 equiv), and Oxone (17.7 mg, 0.029 mmol, 2 equiv) were combined in MeOH (0.5 mL), and the mixture was stirred at room temperature for 30 min. 1-Methylnaphthalene (5 μL), 10% aqueous Na<sub>2</sub>SO<sub>3</sub> (0.5 mL), and ethyl acetate (2 mL) were then added, and the resulting biphasic mixture was stirred for 30 min. The organic layer was analyzed by gas chromatography (GC from this reaction is shown in Figure S6), which revealed the presence of **11-a**, but showed <1% of compound **11-b**.

**Figure S7.** Complex **A-1** [4.8 mg, 0.07 mmol, 0.5 equiv (1 equiv based on [Pd])], **E** (6.8 mg, 0.0289 mmol, 2 equiv), and oxone (17.7 mg, 0.029 mmol, 2 equiv) were combined in MeOH (0.5 mL) and the mixture was stirred at room temperature for 30 min. 1-Methylnaphthalene (5 μL), 10% aqueous Na<sub>2</sub>SO<sub>3</sub> (0.5 mL) and ethyl acetate (2 mL) were then added, and the resulting biphasic mixture was stirred for 30 min. The organic layer was analyzed by gas chromatography (GC from this reaction is shown Figure S7) and it shows the presence of **11-a** and **11-b** in a 5 : 1 ratio.

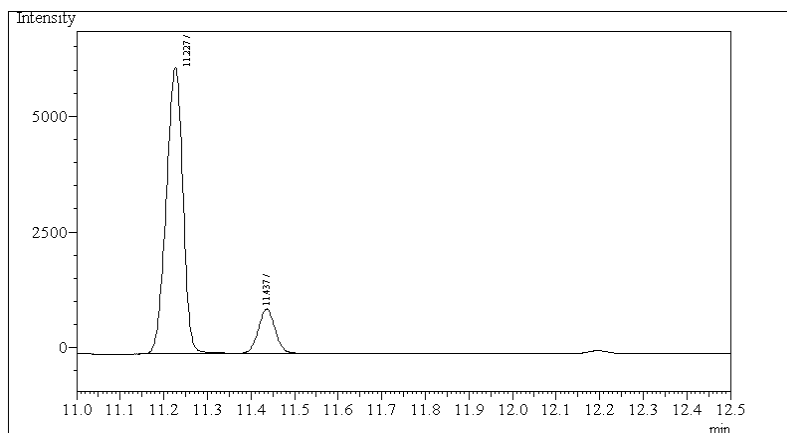


**Figure S6.** GC Trace for reaction of **A-2** with 2-*o*-tolylpyridine

(Reaction after 30 min; Retention times: **11-a** = 11.2 min, **11-b** (expected at 11.4 min, <1% observed), **1** = 12.2 min)

**Figure S7.** GC Trace for reaction of **A-1** with substrate **E**

(Reaction after 30 min; Retention times: **11-a** = 11.2 min, **11-b** = 11.4 min)



**C. Crossover and Equilibration Studies (Part 1).** Stoichiometric experiments were also carried out to probe whether mechanism III (which involves a second C-H activation at Pd<sup>II</sup> prior to oxidation to Pd<sup>IV</sup>) is occurring. Complex **B**<sup>5</sup> was independently synthesized and was subjected to oxidation reactions. Under the standard oxidation conditions (0.06 M Oxone in MeOH at 25 °C), the oxidative coupling product **3** was formed cleanly (Figure S8), as one would expect if mechanism III were operative. However, when 2 equiv of free 2-*o*-tolylpyridine was added to this same reaction, a significant amount of crossover was observed (Figure S9). This latter result shows that **B** is not oxidized directly and quantitatively by Oxone, and instead suggests that a competing process is taking place.

The competing reaction in these systems appears to be protonation of **B** to afford **A** + 2-phenyl-3-methylpyridine. As shown in Figure S10 (and discussed in detail below), this process is rapid and quantitative with 1 equiv of AcOH. In the reactions shown in Figures S8 and S9, AcOH is not present; however, the Oxone, itself, is reasonably acidic (pH of an aqueous Oxone solution = 1.84 when measured at same concentration as in the reaction mixture), and should therefore be capable of promoting the protonation of **B**. Once **A** + 2-phenyl-3-methylpyridine is generated, this reaction is analogous to the stoichiometric reactions discussed in Part A (p. S13) of the Supporting Information. Therefore, no definitive conclusions can be drawn from this experiment regarding whether mechanism III or IV is operating.

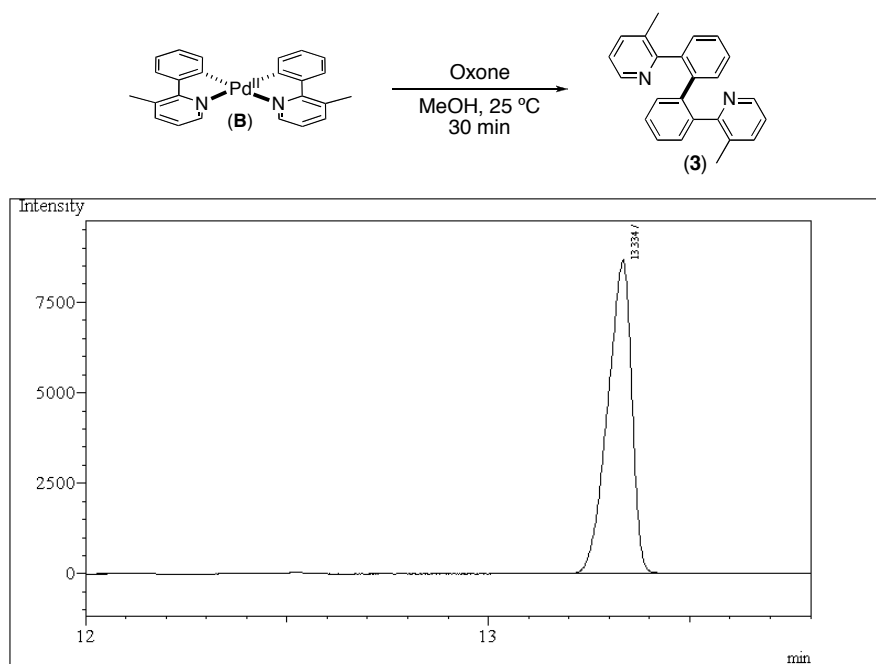
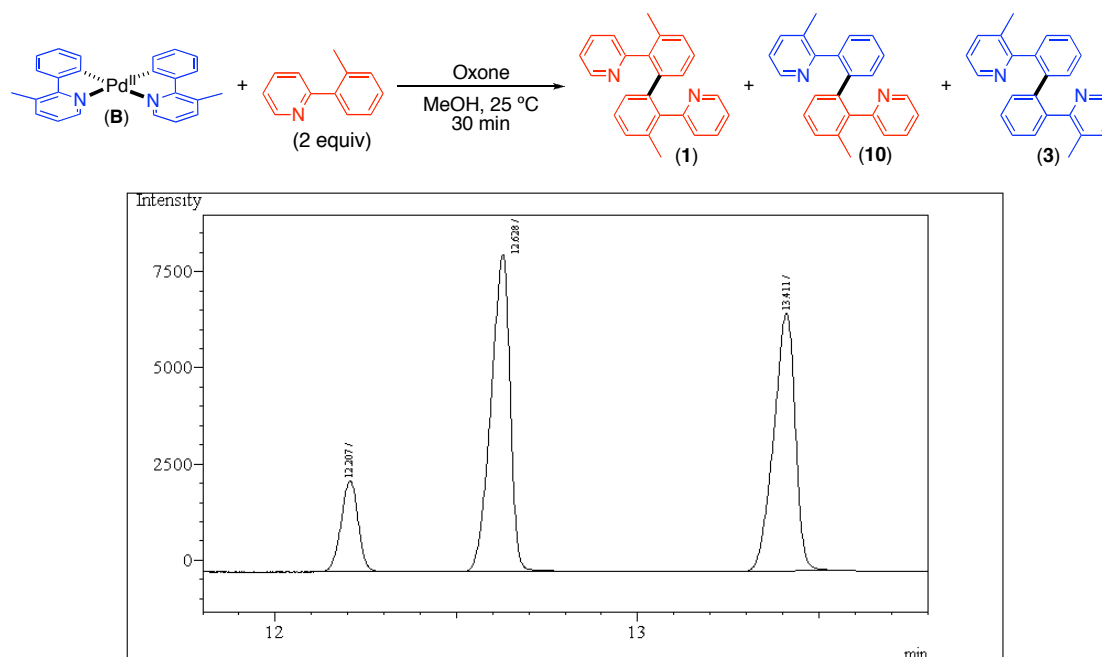
Note:

- The pH of an aqueous 0.06 M solution of Oxone = 1.84. This is the concentration present in the stoichiometric reactions of Figures S8 and S9.
- For comparison, the pH of an aqueous 0.06 M solution of AcOH = 2.78. This is the concentration present in the reaction shown in Figure S10 (which results in quantitative protonation of **B** to form **A** + 2-phenyl-3-methylpyridine).

**Experimentals for Crossover and Equilibration Studies (Part 1)**

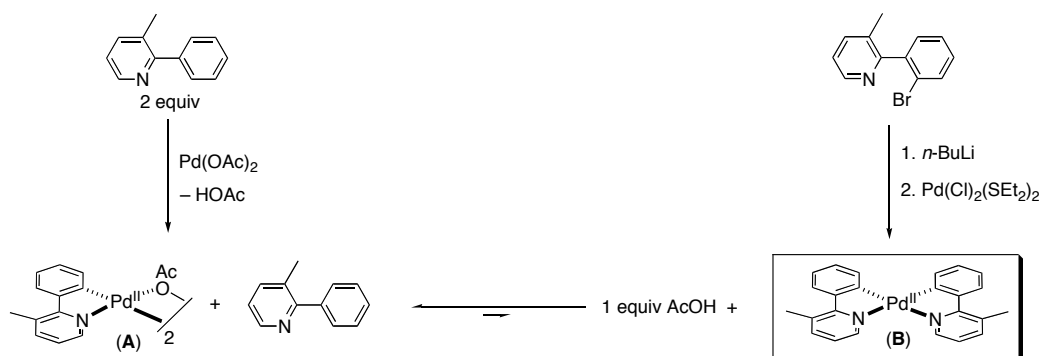
**Figure S8:** Complex **B** (6.4 mg, 0.014 mmol, 1 equiv) and Oxone (17.6 mg, 0.28 mmol, 1 equiv) were combined in MeOH and the reaction mixture was stirred 30 min at 25 °C. 1-Methylnaphalene (5 µL), 10% aqueous Na<sub>2</sub>SO<sub>3</sub> (0.5 mL), and ethyl acetate (2 mL) were then added, and the resulting biphasic mixture was stirred for 30 min. The organic layer was analyzed by gas chromatography (GC from this reaction is shown in Figure S8), which revealed the presence of **3**.

**Figure S9:** Complex **B** (6.4 mg, 0.014 mmol, 1 equiv), 2-*o*-tolylpyridine (4.8 equiv, 0.0289 mmol, 2 equiv), and Oxone (17.6 mg, 0.28 mmol, 1 equiv) were combined in MeOH and the reaction mixture was stirred for 30 min at 25 °C. 1-Methylnaphthalene (5  $\mu$ L), 10% aqueous Na<sub>2</sub>SO<sub>3</sub> (0.5 mL), and ethyl acetate (2 mL) were then added, and the resulting biphasic mixture was stirred for 30 min. The organic layer was analyzed by gas chromatography (GC from this reaction is shown in Figure S9), which revealed the presence of **1**, **3**, and **10**.

**Figure S8.** GC Trace for reaction of **B** with Oxone (Retention time for **3** = 13.41 min)**Figure S9.** GC Trace for reaction of **B** with Oxone in the presence of 2 equiv of 2-*o*-tolylpyridine (the GC retention times are: **1** (12.2 min), **10** (12.6 min) and **3** (13.4 min))

**C. Crossover and Equilibration Studies (Part 2).** Mechanism III requires that **A** converts to **B** (via a second C–H activation reaction) prior to C–C coupling. Independent synthesis of **B**<sup>5</sup> showed that treatment of **B** with 1 equiv of AcOH affords **A** + 2-phenyl-3-methylpyridine (Figure S10). For <sup>1</sup>H spectra of (i) an authentic mixture of **A** + 2-phenyl-3-methylpyridine and (ii) the reaction of **B** with 1 equiv of HOAc, see Figures S11 and S12, respectively. These NMR spectra look nearly identical, and show that the protonation reaction is quantitative. Notably, Ryabov has reported similar results for the reactions of other bis-cyclometalated analogues of **B** with HOAc.<sup>7</sup> This result indicates that the equilibrium between **A** and **B** should lie far to the left (Figure S10).

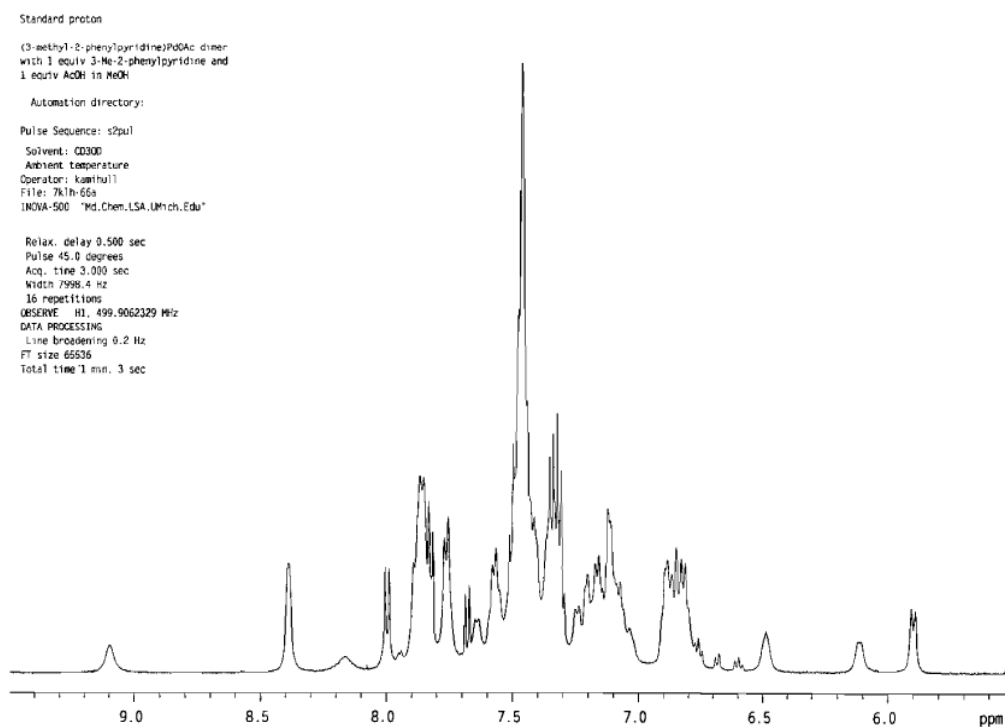
**Figure S10.** Conversion of **B** to **A** in the presence of 1 equiv AcOH



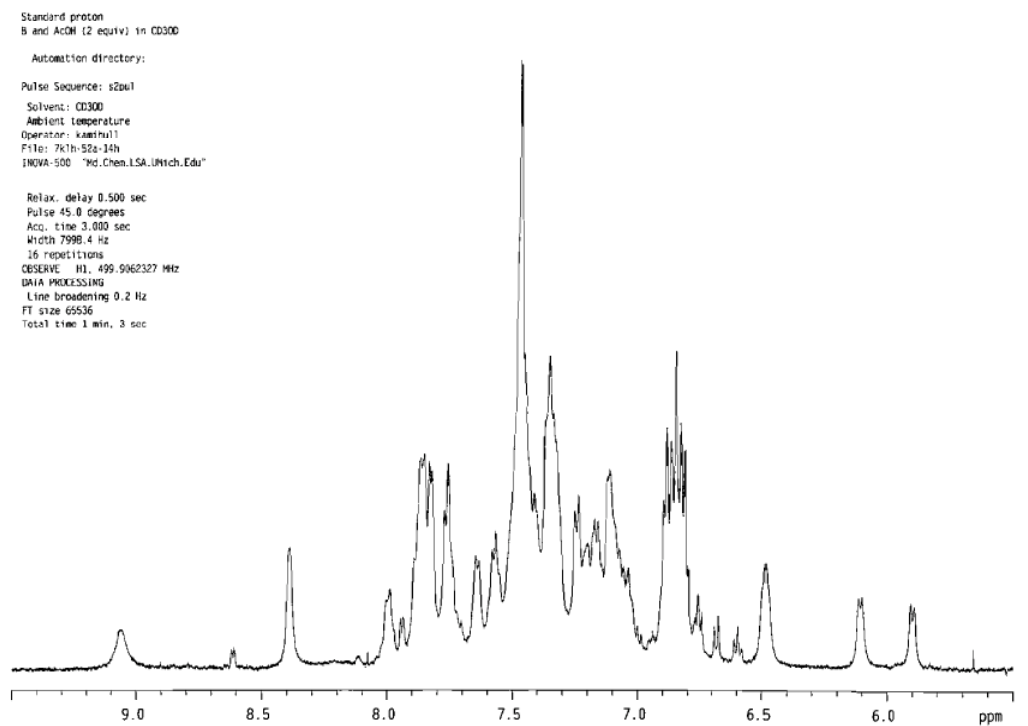
### Experimental for Crossover and Equilibration Studies (Part 2)

**Figure S10:** Complex **B** (6.4 mg, 0.014 mmol, 1 equiv) was placed in an NMR tube in  $\text{CD}_3\text{OD}$ . AcOH (1.95  $\mu\text{L}$ , 1 equiv) was added. A <sup>1</sup>H NMR spectrum was acquired after ~10 min, which showed quantitative conversion to **A** + 2-phenyl-3-methylpyridine (see Figure S12 for a <sup>1</sup>H NMR spectrum of this reaction and Figure S11 for a <sup>1</sup>H NMR spectrum of an authentic mixture of **A** + 1 equiv 2-phenyl-3-methylpyridine).

**Figure S11.**  $^1\text{H}$  NMR spectrum of an authentic 1:1 mixture of **A** and 2-phenyl-3-methylpyridine



**Figure S12.**  $^1\text{H}$  NMR spectrum of the reaction of **B** with 1 equiv of HOAc. (Note: none of the starting material **B** is observed by  $^1\text{H}$  NMR spectroscopy.)

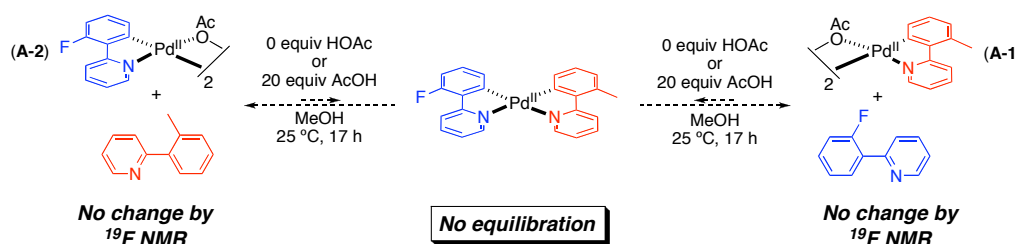


Based on this data, mechanism III would require a fast interconversion between **A** and **B**, followed by trapping of the transient intermediate **B** by the oxidant. As such, in the absence of Oxone, we would expect to see equilibration between the two slightly different cyclometalated Pd complexes **A-1** and **A-3** with the alternate free ligands 2-*o*-fluorophenylpyridine and 2-*o*-tolylpyridine, respectively (Figure S13). However, attempts to approach this equilibrium from either side (*ie*, **A-1** + 1 equiv 2-*o*-fluorophenylpyridine or **A-2** + 1 equiv 2-*o*-tolylpyridine) under our standard reaction conditions resulted in no reaction as monitored by  $^{19}\text{F}$  NMR spectroscopy. (Note: the reactions were examined both in the presence and in the absence of 20 equiv AcOH at room temperature, and this additive had no effect with respect to the lack of equilibration). The  $^{19}\text{F}$  NMR spectrum of a 1:1:1:1 mixture of the 4 components (Figure S14), the  $^{19}\text{F}$  NMR of the reaction of **A-1** with 2-*o*-fluorophenylpyridine in the presence of 20 equiv AcOH (Figure S15), and the  $^{19}\text{F}$  NMR of the reaction of **A-2** with 2-*o*-tolylpyridine in the presence of 20 equiv AcOH (Figure S16) are shown below.

Notably, traces of equilibrated products could be observed under forcing conditions (at 100 °C in  $\text{CD}_3\text{OD}$  with 2 equiv of added  $\text{CD}_3\text{CO}_2\text{D}$  or in neat  $\text{CD}_3\text{CO}_2\text{D}$  at 60 °C). However, we believe that these conditions are not relevant to our catalytic system, since the solvent and temperature are both dramatically different.

Also, note: when these equilibration reactions were performed with Oxone present, the oxidative coupling products were formed (as determined by both  $^{19}\text{F}$  NMR spectroscopy and GC). As such, these reactions are analogous to those shown in Figure S3 and do not provide any additional mechanistic information.

**Figure S13.** Attempts at equilibration of Pd complexes and arylpyridines under standard reaction conditions

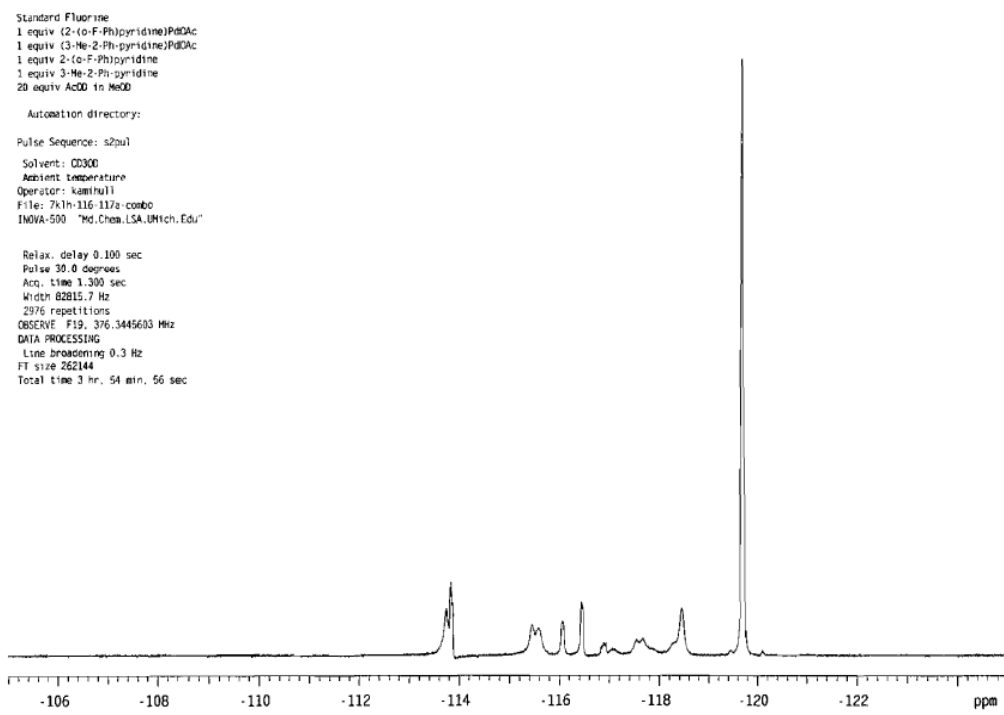


**Figure S13.** The palladium complex [0.007 mmol, 0.5 equiv (1 equiv based on [Pd])], arylpyridine (0.014 mmol, 1 equiv), and  $\text{CD}_3\text{CO}_2\text{D}$  [0 equiv, 20 equiv (16  $\mu\text{L}$ ), or in neat  $\text{CD}_3\text{CO}_2\text{D}$ ] were combined in  $\text{CD}_3\text{OD}$  (0.5 mL, 0.5 mL or 0 mL respectively) in a 4 mL vial equipped with a Teflon stirbar. The vial was fitted with a Teflon-lined cap, and the reaction mixture was stirred at room temperature, 60 °C or 100

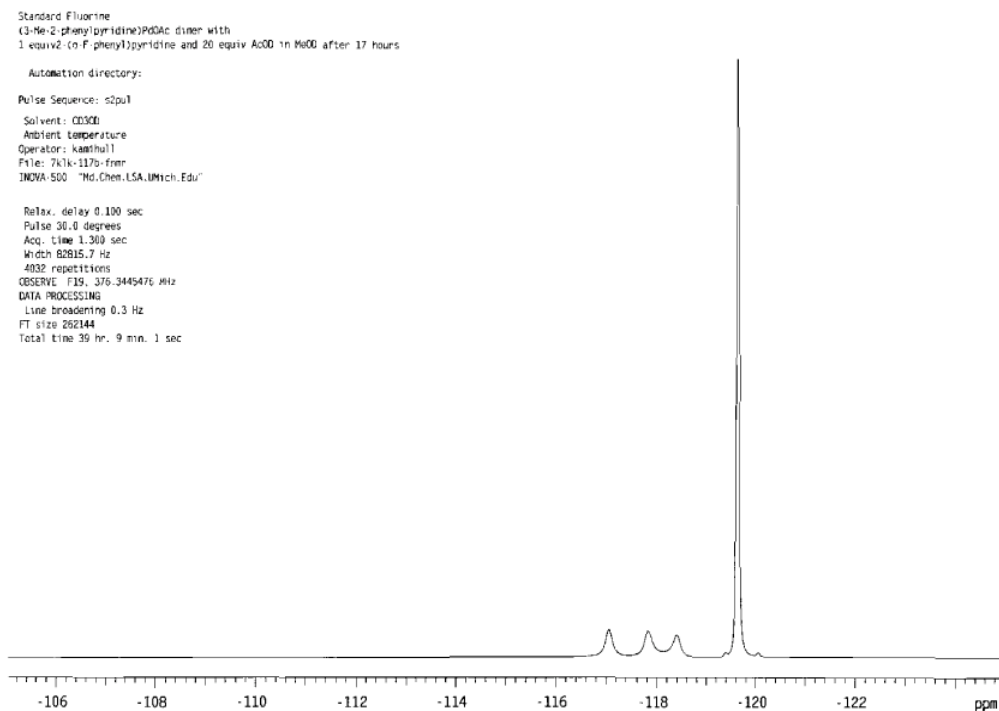
°C for 24 h. The reaction mixture was transferred to an NMR tube, and a  $^{19}\text{F}$  NMR spectrum was acquired. The  $^{19}\text{F}$  NMR spectra for reaction of **A-1** with 2-*o*-fluoropyridine and for the reaction of **A-3** with 2-*o*-tolylpyridine at room temperature are shown in Figures S15 and S16, respectively. It is clear from these spectra (along with the reference spectrum in Figure S14) that neither mixture has equilibrated to any appreciable extent. When the reactions were conducted in  $\text{CD}_3\text{OD}$  with 2 equiv  $\text{CD}_3\text{CO}_2\text{D}$  at 100 °C or in neat  $\text{CD}_3\text{CO}_2\text{D}$  at 60 °C a small amount of equilibration was observed. In neat  $\text{CD}_3\text{CO}_2\text{D}$  at 100 °C a significant amount of equilibration is observed. However, again, these are not conditions that are relevant to the catalytic transformations.



**Figure S14.**  $^{19}\text{F}$  NMR spectrum of an authentic 1:1:1:1 mixture of the four reaction components  
(2-*o*-Tolylpyridine : 2-*o*-Fluoropyridine : Complex **A-1** : Complex **A-3**)  
(Note: Free 2-*o*-fluoropyridine appears at  $-119.7$ )

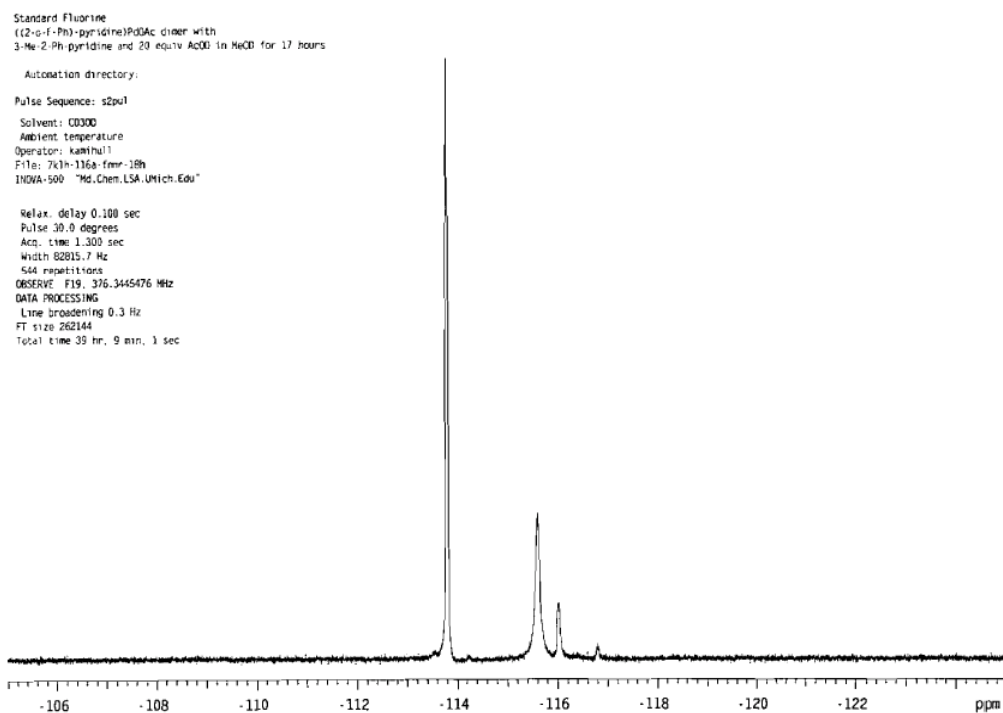


**Figure S15.**  $^{19}\text{F}$  NMR spectrum of reaction of **A-1** with 2-*o*-fluorophenylpyridine in MeOH (24 h)  
(Note: Free 2-*o*-fluoropyridine appears at  $-119.7$ )



**Figure S16.**  $^{19}\text{F}$  NMR spectrum of reaction of **A-2** with 2-*o*-tolylpyridine in MeOH (24 h)

(Note: Free 2-*o*-fluoropyridine appears at  $-119.7$  – not even traces of this free arylpyridine are observed in this spectrum)



## V. References

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