

# Direct C-Arylation of Free (NH)-Indoles and Pyrroles Catalyzed by Ar-Rh(III) Complexes Assembled In Situ

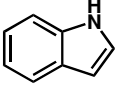
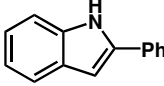
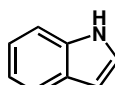
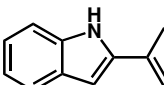
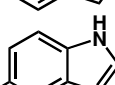
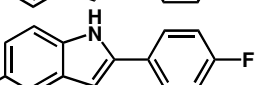
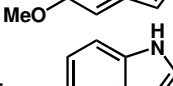
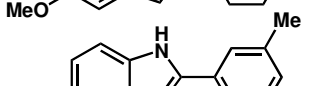
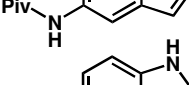
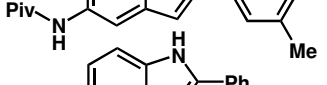
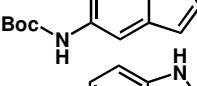
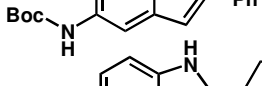
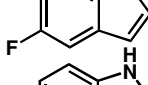
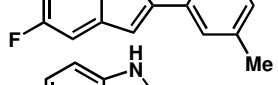
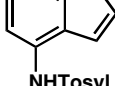
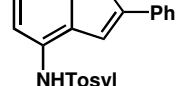
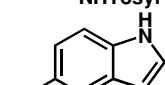
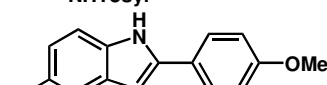
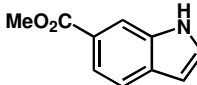
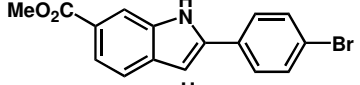
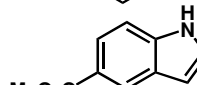
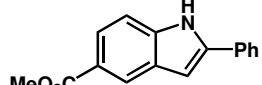

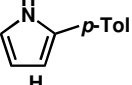

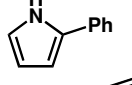
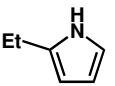
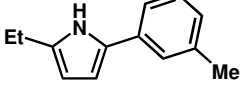


Xiang Wang, Benjamin S. Lane, Dalibor Sames\*

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## Supporting Information

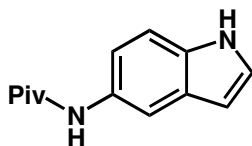
**Materials and General Methods.** Small-scale (<100 mg) arylation reactions were carried out in capped glass vials (VWR, 8 mL) equipped with a Teflon-coated septum, heated in a 34-well reaction block (Chemglass). Large-scale (>1g) arylation reactions were performed in resalable pressure tubes equipped with a Teflon cap and glass plunger (Ace glass), heated in an oil bath. NMR spectra were obtained on a Bruker spectrometer operating at 400 MHz or 300 MHz for  $^1\text{H}$  NMR, 100 MHz or 75 MHz for  $^{13}\text{C}\{^1\text{H}\}$  NMR and 121MHz for  $^{31}\text{P}$  NMR in  $\text{CDCl}_3$  unless otherwise noted. IR spectra were obtained on a Bomen MB-100 FT IR spectrometer. Gas chromatography was performed on an Agilent Technologies 6890N gas chromatograph equipped with a 25 m polydimethylsiloxane capillary column and 5973 Mass Selective Detector. Flash column chromatography was performed employing 200-400 mesh silica gel (EM). Thin layer chromatography (TLC) was performed on silica gel 60 F<sub>254</sub> eluting with a 5:1 mixture of hexanes and ethyl acetate unless noted otherwise.  $[\text{4-(CF}_3\text{)C}_6\text{H}_4\text{]}_3\text{P}$  (**L**)<sup>1</sup> and  $[\text{Rh}(\text{coe})_2\text{Cl}]_2$  (**1**)<sup>2</sup> were synthesized employing known procedures and were as effective as those obtained commercially from Strem.  $\text{CsOPiv}$ ,<sup>3</sup> 1-indole- $d_1$ ,<sup>4</sup> 2-indole- $d_1$ <sup>5</sup> and 3-indole- $d_1$ <sup>5</sup> were synthesized employing known procedures. 1,4-dioxane (Anhydrous, Aldrich), haloarenes (Aldrich) and all other reagents were obtained commercially and used as received.

**Table 1.** Complete Substrate and Functional Group Scope.<sup>a</sup>

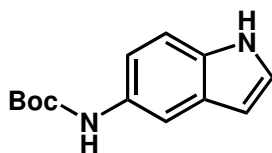
Entry	Azole	Product	Isolated Yield
1			82%
2			75% <sup>b</sup>
3			89%
4			87% 88% <sup>c</sup>
5			78%
6			59%
7			76%
8			65%
9			74% 72% <sup>c</sup>
10			58%
11			59%
12			81%
13			78%
14			67%
15			44%

<sup>a</sup> Reaction conditions: 1 equiv of azole, ArI (1.2 equiv), CsOPiv (1.4 equiv), **1** (2.5 mol%), L (15 mol%), Dioxane/120 °C/18-36h, L= [p-(CF<sub>3</sub>)-C<sub>6</sub>H<sub>4</sub>]<sub>3</sub>P. <sup>b</sup> 1.17 g indole, **1** (1 mol%), L (6 mol%), all reagents weighed in air, 120 °C/56 h. <sup>c</sup> All reagents weighed in air.

## Synthesis of Functionalized Indole Substrates



***N*-(5-Indolyl)-2,2-dimethyl-propionamide:** Trimethyl acetyl chloride (300 mg, 2.29 mmol) was added to the mixture of 5-aminoindole (264 mg, 2.00 mmol), triethylamine (1 mL) and CH<sub>2</sub>Cl<sub>2</sub> (5 mL). The resulting suspension was stirred at room temperature for 3 h, quenched by H<sub>2</sub>O (10 mL), extracted (EtOAc, 10 mL×3), dried (MgSO<sub>4</sub>) and concentrated. Ether (15 mL) was then added to precipitate colorless needles, which were further washed by ether (10 mL×3) to give *N*-(5-indolyl)-2,2-dimethyl-propionamide (298 mg, 69%) as white needles. <sup>1</sup>H NMR (300 MHz, DMSO-*d*<sub>6</sub>): δ 10.98 (s, 1 H), 9.02 (s, 1 H), 7.79 (s, 1 H), 7.20-7.30 (m, 3 H), 6.36 (s, 1 H), 1.24 (s, 9 H). <sup>13</sup>C NMR (75 MHz, DMSO-*d*<sub>6</sub>): δ 175.4, 132.4, 130.7, 127.0, 125.4, 116.1, 112.1, 110.5, 100.8, 27.5. LRMS (APCI) for C<sub>13</sub>H<sub>17</sub>N<sub>2</sub>O (MH<sup>+</sup>) calcd (found): 217.13 (217.23).



***N*-(5-Indolyl)-carbamic acid tert-butyl ester:** A solution of 5-aminoindole (264 mg, 2.00 mmol) and di(*t*-butyl)oxide dicarbonyl (450 mg, 2.06 mmol) in EtOAc (15 mL) was stirred at room temperature for 12 h, diluted (EtOAc, 30 mL), washed (H<sub>2</sub>O, 10 mL×3), dried (MgSO<sub>4</sub>) and concentrated. The resulting oil was dry loaded to a column, and flash chromatographed (2:1 Hexanes:EtOAc) to give *N*-(5-indolyl)-carbamic acid tert-butyl ester (441 mg, 95%) as a white solid. <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>): δ 8.47 (broad s, 1 H), 7.76 (broad s, 1 H), 7.16-7.27 (m, 3 H), 6.66 (broad s, 1 H), 6.53 (broad s, 1 H), 1.67 (s, 9 H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>): δ 133.2, 120.9, 128.4, 125.6, 116.2, 112.0, 111.7, 102.7, 80.6, 29.2. IR (film, cm<sup>-1</sup>): 3320, 2978, 1706, 1540, 1483, 1327, 1249, 1166, 1052, 886, 761, 719. LRMS (APCI) for C<sub>13</sub>H<sub>17</sub>N<sub>2</sub>O<sub>2</sub> (MH<sup>+</sup>) calcd (found): 233.13 (233.25).



***N*-(4-Indolyl)-4-methyl-benzenesulfonamide:** A suspension of tosyl chloride (200 mg, 1.10 mmol) in CH<sub>2</sub>Cl<sub>2</sub> (1 mL) was added slowly to the suspension of 5-aminoindole (132 mg, 1.00 mmol) in CH<sub>2</sub>Cl<sub>2</sub> (1 mL) at 0 °C. The resulting mixture was warmed up to room temperature, stirred for 30 minutes, quenched (H<sub>2</sub>O, 15 mL), extracted (EtOAc, 15 mL×3), dried (MgSO<sub>4</sub>), concentrated and chromatographed (3:1→2:1 hexanes:EtOAc) to give *N*-(4-indolyl)-4-methyl-benzenesulfonamide (156 mg, 43%) as a tan solid. IR (film, cm<sup>-1</sup>): 3403, 3267, 1700, 1503, 1156, 751. <sup>1</sup>H NMR (300 MHz, methanol-*d*<sub>4</sub>): δ 7.66 (d, *J* = 8.1 Hz, 2 H), 7.24 (d, *J* = 8.1 Hz, 2 H), 7.16 (d, *J* = 3.6 Hz, 1 H), 7.04 (t, *J* = 7.8 Hz, 1 H), 6.96 (d, *J* = 7.5 Hz, 1 H), 6.46 (d, *J* = 3.0 Hz, 1 H), 2.39 (s, 3 H). <sup>13</sup>C NMR (75 MHz, methanol-*d*<sub>4</sub>): δ 143.6, 137.7, 137.6, 129.3, 129.0, 127.3, 124.3, 123.6, 121.3, 114.0, 109.1, 99.0. LRMS (APCI) for C<sub>15</sub>H<sub>15</sub>N<sub>2</sub>O<sub>2</sub>S (MH<sup>+</sup>) calcd (found): 287.09 (287.25).

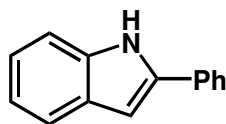
### Arylation of Indoles and Pyrroles: Representative Procedures

**Small scale:** In an argon-filled glovebox, indole (29.3 mg, 0.25 mmol), **1** (4.5 mg, 6.3  $\mu$ mol), [4-(CF<sub>3</sub>)C<sub>6</sub>H<sub>4</sub>]<sub>3</sub>P (**L**, 18.0 mg, 39  $\mu$ mol), CsOPiv (82.0 mg, 0.35 mmol) and PhI (61.0 mg, 0.30 mmol) were charged into a vial, followed by the addition of 1,4-dioxane (0.2 mL). The vial was capped, brought out the glovebox, and heated at 120 °C in a reaction block for 24 h. The reaction mixture was cooled to room temperature, and passed through a short plug of silica gel (3cm×0.5cm, L×ID), eluting with EtOAc (10 mL). The resulting solution was concentrated, dry loaded to a column, and flash chromatographed (15:1, hexanes:EtOAc) to give 2-phenyl indole (39.6 mg, 82%) as a white powder.

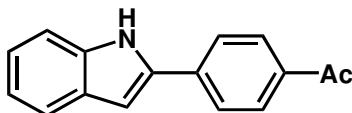
**Small scale (Reagents weighed in air):** On benchtop, **1** (4.5 mg, 6.3  $\mu$ mol), [4-(CF<sub>3</sub>)C<sub>6</sub>H<sub>4</sub>]<sub>3</sub>P (**L**, 18.0 mg, 39  $\mu$ mol), CsOPiv (82.0 mg, 0.35 mmol), 5-bromoindole (49.0 mg, 0.25 mmol) and 4-iodoanisole (70.2 mg, 0.30 mmol) were rapidly charged into a vial. The vial was subsequently capped, evacuated with a needle through the septum, refilled with argon, and 1,4-dioxane (0.2 mL) was then added via a syringe through the septum. The vial was then heated at 120 °C in a reaction block for 24h. The reaction mixture was cooled to room temperature, and passed through a short plug of silica gel (3cm×0.5cm, L×ID), eluting with EtOAc (10 mL). The resulting solution was concentrated, dry loaded to a column, and flash chromatographed (8:1→5:1, hexanes:EtOAc) to give 5-bromo-2-(4-methoxyphenyl) indole (53.5 mg, 72%) as a pale yellow solid.

**Gram scale:** On bench top, a mixture of indole (1.17g, 10.0 mmol), **1** (71.7 mg, 0.10 mmol), [4-(CF<sub>3</sub>)C<sub>6</sub>H<sub>4</sub>]<sub>3</sub>P (279 mg, 0.30 mmol), CsOPiv (3.26 g, 14.0 mmol) and PhI (2.45 g, 12.0 mmol) were charged into into a 20 mL threaded pressure tube (Ace glass). The tube was then capped, evacuated, refilled with argon, and 1,4-dioxane (8 mL) was added under a flow of argon. The tube was purged with argon for 2 min, capped and heated at 120 °C with vigorous stirring. After 52h, the reaction mixture were cooled to room temperature and filtered through a plug of silica gel (4cm×5cm, L×ID), eluting with EtOAc (30 mL). The resulting solution was concentrated to give a dark colored solid.

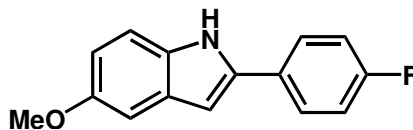
This solid was then washed with hexanes/ether (50:1, 10mL×3) afforded 2-phenyl indole (1.45g, 75%) as a tan powder (>98% pure by GC-MS).



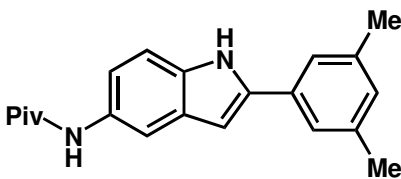
**2-Phenyl indole:**<sup>6</sup> <sup>1</sup>H NMR (300 MHz, DMSO-*d*<sub>6</sub>): δ 11.6 (s, 1 H), 7.87 (d, *J* = 8.4 Hz, 2 H), 7.52 (d, *J* = 7.8 Hz, 1 H), 7.41-7.49 (m, 3 H), 7.29-7.34 (m, 1 H), 7.09-7.14 (m, 1 H), 6.99-7.04 (m, 1 H), 6.91 (d, *J* = 0.9 Hz, 1 H). <sup>13</sup>C NMR (75 MHz, DMSO-*d*<sub>6</sub>): δ 131.3, 136.8, 131.9, 128.3, 127.0, 124.7, 121.2, 119.7, 110.1, 111.0, 98.4. IR (film, cm<sup>-1</sup>): 3435, 1451, 741, 689. LRMS (APCI) for C<sub>14</sub>H<sub>12</sub>N (MH<sup>+</sup>) calcd (found): 194.10 (194.21).



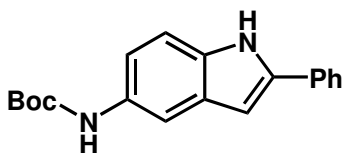
**2-(4-Acetylphenyl)-indole:**<sup>6</sup> <sup>1</sup>H NMR (300 MHz, acetone-*d*<sub>6</sub>): δ 10.91 (s, 1 H), 8.05-8.16 (m, 4 H), 7.69 (d, *J* = 5.1 Hz, 1 H), 7.52 (d, *J* = 5.1 Hz, 1 H), 7.24 (t, *J* = 6.6 Hz, 1 H), 7.17-7.26 (m, 2 H), 2.70 (s, 3 H). <sup>13</sup>C NMR (75 MHz, acetone-*d*<sub>6</sub>): δ 196.7, 138.3, 137.2, 137.0, 136.2, 129.5, 129.4, 125.2, 123.0, 121.0, 120.3, 111.8, 101.5, 26.2. IR (film, cm<sup>-1</sup>): 3351, 1669, 1602, 1427, 1192, 791. LRMS (APCI) for C<sub>16</sub>H<sub>14</sub>NO (MH<sup>+</sup>) calcd (found): 236.11 (236.26).



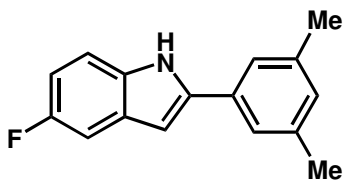
**2-(4-Fluoro-phenyl)-5-methoxy-indole:** <sup>1</sup>H NMR (300 MHz, DMSO-*d*<sub>6</sub>): δ 11.39 (s, 1 H), 7.86 (dd, *J* = 2.7, 8.7 Hz, 2 H), 7.26-7.32 (m, 3 H), 7.01 (d, *J* = 1.5 Hz, 1 H), 6.73-6.77 (m, 2 H), 3.75 (s, 3 H). <sup>13</sup>C NMR (75 MHz, DMSO-*d*<sub>6</sub>): δ 162.6, 159.4, 153.2, 136.8, 131.9, 128.7, 126.5 (d, *J*<sub>F-C</sub> = 7.8 Hz), 115.5 (d, *J*<sub>F-C</sub> = 21.4 Hz), 111.6 (d, *J*<sub>F-C</sub> = 8.7 Hz), 101.3, 98.4, 55.2. IR (film, cm<sup>-1</sup>): 3432, 1589, 1425, 1213, 792. LRMS (APCI) for C<sub>15</sub>H<sub>13</sub>N (MH<sup>+</sup>) calcd (found): 242.10 (242.25).



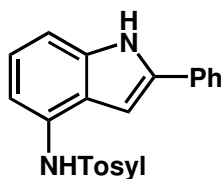
***N*-[2-(3,5-dimethyl-phenyl)-1H-5-indolyl]-2,2-dimethyl-propionamide:**  $^1\text{H}$  NMR (300 MHz,  $\text{DMSO}-d_6$ ):  $\delta$  11.31 (s, 1 H), 8.99 (s, 1 H), 7.76 (s, 1 H), 7.45 (s, 2 H), 7.23-7.25 (m, 2 H), 6.92 (s, 1 H), 6.78 (s, 1 H), 2.33 (s, 3 H), 1.24 (s, 9 H).  $^{13}\text{C}$  NMR (75 MHz,  $\text{DMSO}-d_6$ ):  $\delta$  176.8, 139.1, 138.7, 134.8, 132.9, 132.3, 129.7, 129.2, 123.6, 117.7, 112.9, 111.5, 99.4, 28.3, 21.9. IR (film,  $\text{cm}^{-1}$ ): 3331, 2993, 1702, 1508, 1150. LRMS (APCI) for  $\text{C}_{21}\text{H}_{25}\text{N}_2\text{O}$  ( $\text{MH}^+$ ) calcd (found): 321.20 (321.37).



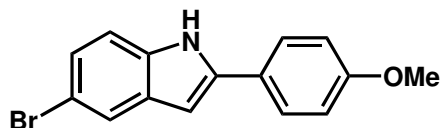
**(2-Phenyl-5-indolyl)-carbamic acid *tert*-butyl ester:**  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ ):  $\delta$  8.29 (s, 1 H), 7.63-7.67 (m, 3 H), 7.43 (t,  $J = 7.5$  Hz, 3 H), 7.26-7.34 (m, 2 H), 7.09 (dd,  $J = 1.8, 8.7$  Hz, 1 H), 6.74 (d,  $J = 1.5$  Hz, 1 H), 6.46 (s, 1 H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ ):  $\delta$  154.9, 139.0, 132.6, 131.6, 129.9, 129.3, 128.0, 125.5, 116.3, 111.4, 100.4, 80.5, 29.1. IR (film,  $\text{cm}^{-1}$ ): 3321, 2972, 1698, 1478, 1159, 760. LRMS (APCI) for  $\text{C}_{19}\text{H}_{21}\text{NO}_2$  ( $\text{MH}^+$ ) calcd (found): 309.16 (309.35).



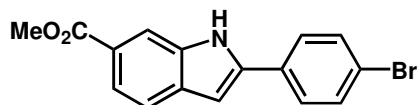
**2-(3,5-Dimethyl-phenyl)-5-fluoroindole:**  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ ):  $\delta$  8.29 (s, 1 H), 7.26-7.31 (m, 4 H), 7.00 (broad s, 1 H), 6.94 (dt,  $J = 2.4, 9.0$  Hz, 1H), 6.76-6.77 (m, 1 H), 2.41 (s, 3 H).  $^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ ):  $\delta$  160.1, 157.0, 140.4, 139.1, 133.6, 132.3, 130.2, 123.5, 111.8. IR (film,  $\text{cm}^{-1}$ ): 3419, 2921, 1602, 1454, 1191, 785, 675. LRMS (APCI) for  $\text{C}_{16}\text{H}_{15}\text{FN}$  ( $\text{MH}^+$ ) calcd (found): 240.12 (240.28).



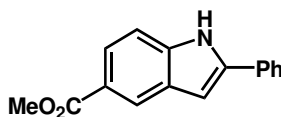
**4-Methyl-N-(2-phenyl-4-indolyl)-benzenesulfonamide:**  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  8.41 (s, 1 H), 7.70 (d,  $J = 6.3$  Hz, 2 H), 7.58 (d,  $J = 6.9$  Hz, 2 H), 7.43 (t,  $J = 5.7$  Hz, 2 H), 7.31-7.35 (m, 1 H), 7.16-7.20 (m, 3 H), 7.06 (t,  $J = 5.7$  Hz, 1 H), 7.10 (d,  $J = 5.7$  Hz, 1 H), 6.75 (s, 1 H), 6.59 (d,  $J = 0.9$  Hz, 1 H), 2.31 (s, 3 H).  $^{13}\text{C}$  NMR (75 MHz,  $\text{DMSO}-d_6$ ):  $\delta$  143.7, 138.8, 138.2, 137.7, 132.8, 129.3, 128.5, 127.5, 127.4, 125.1, 121.7, 115.1, 109.1, 96.4, 20.3. IR (film,  $\text{cm}^{-1}$ ): 3321, 2972, 1698, 1478, 1159, 760. LRMS (APCI) for  $\text{C}_{21}\text{H}_{19}\text{N}_2\text{O}_2\text{S}$  ( $\text{MH}^+$ ) calcd (found): 363.12 (363.36).



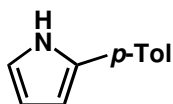
**5-Bromo-2-(4-methoxy-phenyl)-indole:**  $^1\text{H}$  NMR (300 MHz,  $\text{DMSO}-d_6$ ):  $\delta$  11.59 (s, 1 H), 7.75-7.78 (m, 2 H), 7.64 (d,  $J = 1.8$  Hz, 1 H), 7.31 (d,  $J = 7.6$  Hz, 1 H), 7.14 (dd,  $J = 1.8, 7.6$  Hz, 1 H), 7.02 (d,  $J = 8.7$  Hz, 2 H), 6.72 (d,  $J = 1.8$  Hz, 1 H), 3.80 (s, 3 H).  $^{13}\text{C}$  NMR (75 MHz,  $\text{DMSO}-d_6$ ):  $\delta$  159.8, 140.1, 136.4, 131.5, 127.4, 125.1, 124.2, 122.5, 115.3, 113.8, 112.6, 97.8, 56.3. IR (film,  $\text{cm}^{-1}$ ): 3453, 2855, 1628, 1554, 1200, 855. LRMS (APCI) for  $\text{C}_{15}\text{H}_{13}\text{BrNO}$  ( $\text{MH}^+$ ) calcd (found): 302.02, 304.02 (302.19, 304.20).



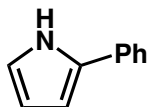
**2-(4-Bromo-phenyl)-1H-indole-6-carboxylic acid methyl ester:**  $^1\text{H}$  NMR (300 MHz,  $\text{DMSO}-d_6$ ):  $\delta$  11.98 (s, 1 H), 8.06 (s, 1 H), 7.85-7.88 (m, 2 H), 7.71-7.73 (m, 2 H), 7.64 (s, 1 H), 7.07 (d,  $J = 0.9$  Hz, 1 H), 3.89 (s, 3 H).  $^{13}\text{C}$  NMR (75 MHz,  $\text{DMSO}-d_6$ ):  $\delta$  168.0, 141.0, 137.3, 133.1, 132.9, 131.6, 128.3, 123.6, 122.2, 121.1, 120.9, 114.0, 100.7, 52.7. IR (film,  $\text{cm}^{-1}$ ): 3521, 2923, 1718, 726. LRMS (APCI) for  $\text{C}_{16}\text{H}_{14}\text{BrNO}_2$  ( $\text{MH}^+$ ) calcd (found): 330.01, 330.11 (330.15, 330.25).



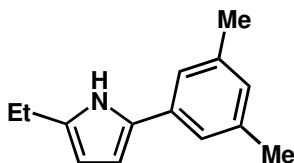
**2-Phenyl-5-indole-carboxylic acid methyl ester:**<sup>7</sup>  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ ):  $\delta$  8.57 (s, 1 H), 8.39 (s, 1 H), 7.91 (dd,  $J = 1.8, 5.4$  Hz, 1 H), 7.68 (d,  $J = 7.5$  Hz, 2 H), 7.47 (t,  $J = 4.5$  Hz, 1 H), 7.34-7.43 (m, 3 H), 6.91 (d,  $J = 1.8$  Hz, 1 H), 3.91 (s, 3 H).  $^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ ):  $\delta$  168.5, 139.7, 132.1, 129.5, 129.2, 128.6, 125.7, 124.2, 124.0, 122.8, 111.0, 101.4, 52.3. IR (film,  $\text{cm}^{-1}$ ): 3342, 1687, 755, 687. LRMS (APCI) for  $\text{C}_{16}\text{H}_{14}\text{NO}_2$  ( $\text{MH}^+$ ) calcd (found): 252.10 (252.26).



**2-(4-Tolyl)-pyrrole:**<sup>8</sup>  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ ):  $\delta$  8.38 (s, 1 H), 7.38 (d,  $J = 8.1$  Hz, 2 H), 7.18 (d,  $J = 7.8$  Hz, 2 H), 6.84-6.86 (m, 1 H), 6.48-6.51 (m, 1 H), 6.30 (dd,  $J = 2.7, 6.0$  Hz, 1 H).  $^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ ):  $\delta$  136.3, 132.7, 130.4, 130.0, 124.3, 118.8, 110.4, 105.8, 21.5. IR (film,  $\text{cm}^{-1}$ ): 3435, 1707, 1507, 1362, 1225, 1120, 907, 820, 797, 734. LRMS (APCI) for  $\text{C}_{11}\text{H}_{12}\text{N}$  ( $\text{MH}^+$ ) calcd (found): 158.10 (158.19).

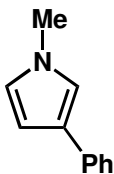


**2-Phenyl-pyrrole:**<sup>9</sup>  $^1\text{H}$  NMR (300 MHz,  $\text{DMSO}-d_6$ ):  $\delta$  8.46 (s, 1 H), 7.51-7.54 (m, 2 H), 7.39-7.45 (m, 2 H), 7.21-7.29 (m, 1 H), 6.90-6.92 (m, 1 H), 6.58-6.60 (m, 1 H), 6.36 (dd,  $J = 3.6, 8.0$  Hz, 1 H).  $^{13}\text{C}$  NMR (75 MHz,  $\text{DMSO}-d_6$ ):  $\delta$  133.2, 132.5, 133.2, 132.5, 129.3, 126.6, 124.3, 119.3, 110.5, 106.4. IR (film,  $\text{cm}^{-1}$ ): 3421, 3372, 1463, 1109, 904, 755, 725, 605. LRMS (APCI) for  $\text{C}_{10}\text{H}_{10}\text{N}$  ( $\text{MH}^+$ ) calcd (found): 144.08 (144.17).



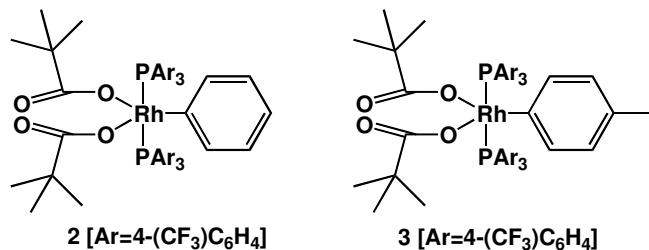
**2-(3,5-Dimethyl-phenyl)-5-ethyl-1H-pyrrole:**  $^1\text{H}$  NMR (300 MHz,  $\text{DMSO}-d_6$ ):  $\delta$  8.13 (s, 1 H), 7.09 (s, 2 H), 6.85 (s, 1 H), 6.42 (t,  $J = 3.0$  Hz, 1 H), 6.00 (t,  $J = 2.7$  Hz, 1 H),

2.72 (q,  $J = 7.5$  Hz, 2 H), 2.37 (s, 3 H), 1.33 (t,  $J = 7.5$  Hz, 3 H).  $^{13}\text{C}$  NMR (75 MHz, DMSO- $d_6$ ):  $\delta$  138.7, 135.7, 133.3, 131.2, 127.9, 106.5, 106.2, 21.8, 21.4, 14.0. IR (film,  $\text{cm}^{-1}$ ): 3404, 2968, 2916, 1602, 1503, 1322, 1193, 1036, 899, 761. LRMS (APCI) for  $\text{C}_{14}\text{H}_{18}\text{N}$  ( $\text{MH}^+$ ) calcd (found): 200.14 (200.27).



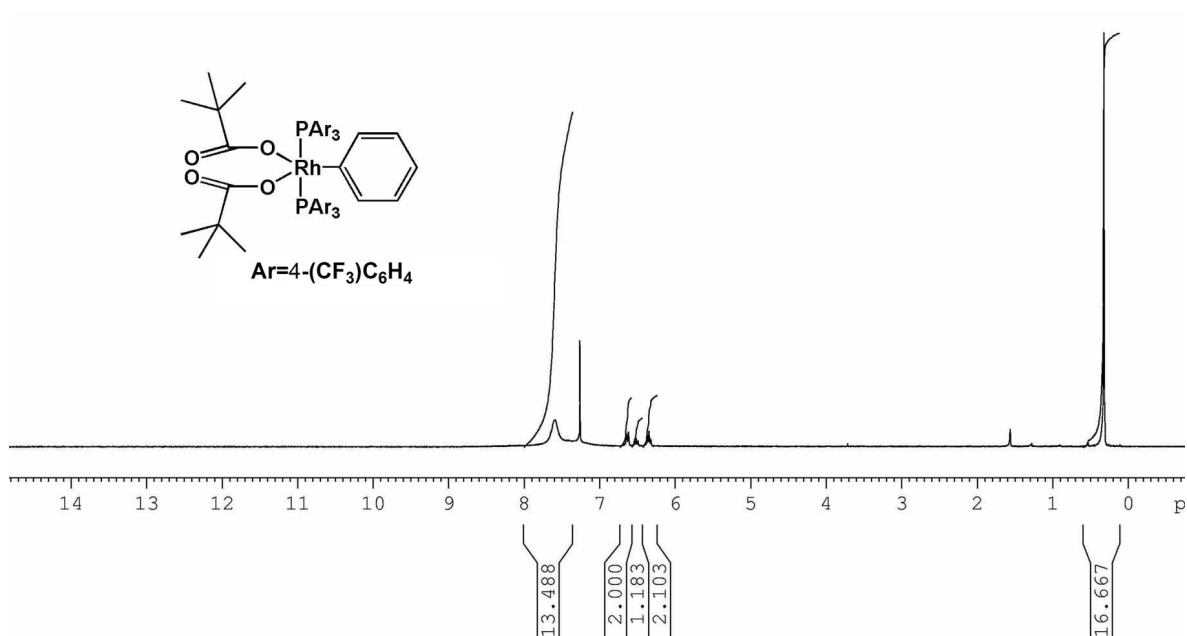
**1-Methyl-3-phenyl-pyrrole:**  $^{9-11}$   $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ ):  $\delta$  7.49-7.52 (m, 2 H), 7.33 (t,  $J = 7.5$  Hz, 2 H), 7.13-7.18 (m, 1 H), 6.92 (t,  $J = 2.1$  Hz, 1 H), 6.64 (t,  $J = 2.4$  Hz, 1 H), 6.45 (t,  $J = 2.1$  Hz, 1 H), 3.71 (s, 3 H).  $^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ ):  $\delta$  136.3, 131.0, 129.0, 125.7, 125.4, 123.1, 119.0, 106.7, 36.8. IR (film,  $\text{cm}^{-1}$ ): 2914, 1704, 1605, 1211. LRMS (APCI) for  $\text{C}_{11}\text{H}_{12}\text{N}$  ( $\text{MH}^+$ ) calcd (found): 158.10 (158.23).

## Mechanistic Studies of Rh-Catalyzed Arylation of Free Azoles.

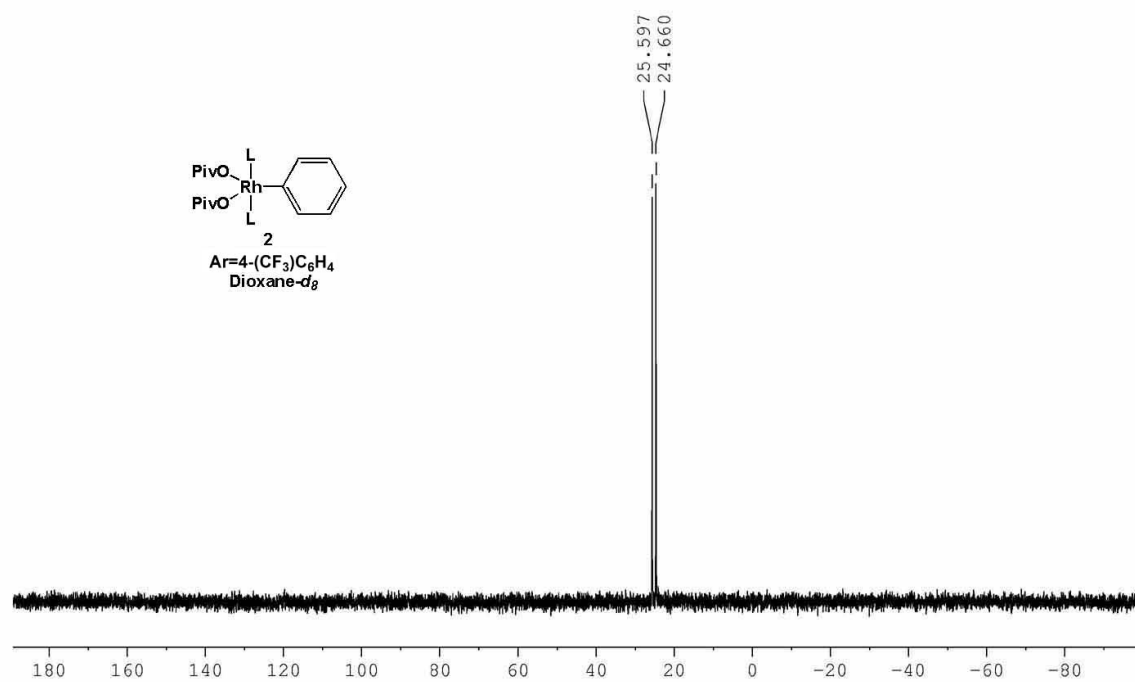


**Synthesis of Complex 2.** [Rh(coe)<sub>2</sub>Cl]<sub>2</sub> (180 mg, 0.25 mmol) and P[4-(CF<sub>3</sub>)C<sub>6</sub>H<sub>4</sub>]<sub>3</sub> (700 mg, 1.50 mmol), PhI (204 mg, 1.0 mmol), CsOPiv (930 mg, 4.0 mmol) and 1,4-dioxane (5 mL) were subsequently charged into a screw-capped vial in an argon-filled glovebox. The vial was subsequently capped, brought out the glovebox and heated at 120 °C for 10 min with vigorous stirring. The resulting yellowish mixture was then cooled to room temperature, and diluted with hexanes (15 ml). The yellow precipitation was collected on a frit, sequentially washed (hexanes/10mL×2, H<sub>2</sub>O/10mL×3, hexanes/10mL×2) and then dried on high vacuum for 60 min to give **2** (585 mg, 89%) as a fine yellowish powder. <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>): δ 6.72-8.30 (broad s, 24 H), 6.63 (d, *J* = 7.8 Hz, 2 H), 6.51 (t, *J* = 7.2 Hz, 1 H), 6.34 (t, *J* = 7.5 Hz, 2 H), 0.32 (s, 18 H). <sup>31</sup>P NMR (121 MHz, Dioxane-*d*<sub>8</sub>): δ 25.2 (d, *J*<sub>Rh-P</sub> = 113 Hz). IR (film, cm<sup>-1</sup>): 1712, 1609, 1400, 1323, 1131, 1062. MS (FAB) for C<sub>53</sub>H<sub>38</sub>F<sub>18</sub>O<sub>2</sub>P<sub>2</sub>Rh (M<sup>+</sup>-OPiv) calcd (found): 1213.1 (1213.2).

**Synthesis of Complex 3** was isolated in 55% yield employing a procedure analogous to that was used for **2**, with the exception that washing by hexanes was carried out at -78 °C due to the much higher solubility of **3** in organic solvents. X-ray quality crystals were grown from chloroform/hexanes solution. <sup>1</sup>H NMR (300 MHz, Dioxane-*d*<sub>8</sub>): δ 7.01-8.90 (m, 24 H), 6.65 (d, *J* = 8.1 Hz, 2 H), 6.23 (d, *J* = 8.1 Hz, 2 H), 2.09 (s, 3 H), 0.41 (s, 18 H). <sup>31</sup>P NMR (121 MHz, Dioxane-*d*<sub>8</sub>): δ 24.8 (d, *J*<sub>Rh-P</sub> = 113 Hz). IR (film, cm<sup>-1</sup>): 1717, 1610, 1480, 1325, 1172, 1133, 1063.

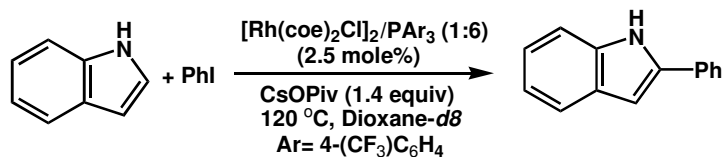


**Figure S1.** <sup>1</sup>H NMR (CDCl<sub>3</sub>) of Rh(OPiv)<sub>2</sub>{P[4-(CF<sub>3</sub>)C<sub>6</sub>H<sub>4</sub>]<sub>3</sub>}<sub>2</sub>Ph (**2**).

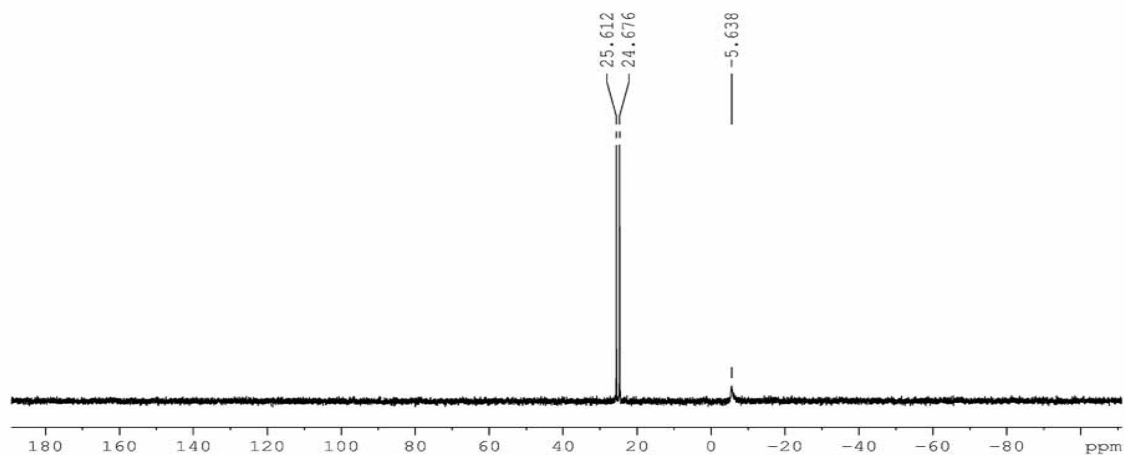


**Figure S2.** <sup>31</sup>P NMR of Rh(OPiv)<sub>2</sub>{P[4-(CF<sub>3</sub>)C<sub>6</sub>H<sub>4</sub>]<sub>3</sub>}<sub>2</sub>Ph (**2**) in dioxane-*d*<sub>8</sub>.

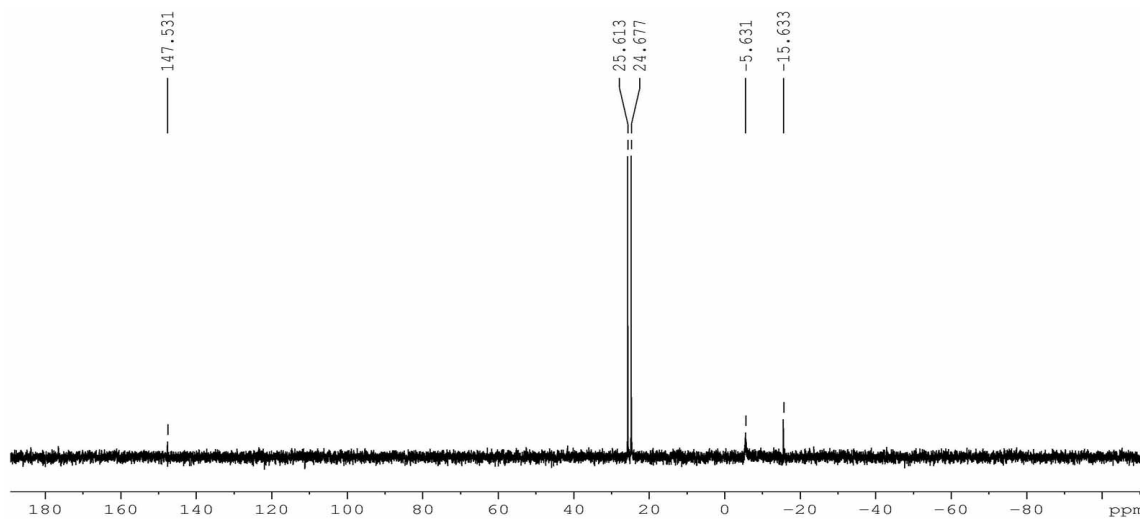
## NMR Monitoring of Catalytic Reaction



The above reaction ([Indole]=0.50 M, [PhI]=0.60 M, [1]=25 mM, [phos]<sub>total</sub>=150 mM) was carried out in an argon-filled J-Young NMR tube at 120°C in dioxane- $d_8$ . <sup>31</sup>P NMR was taken at room temperature.

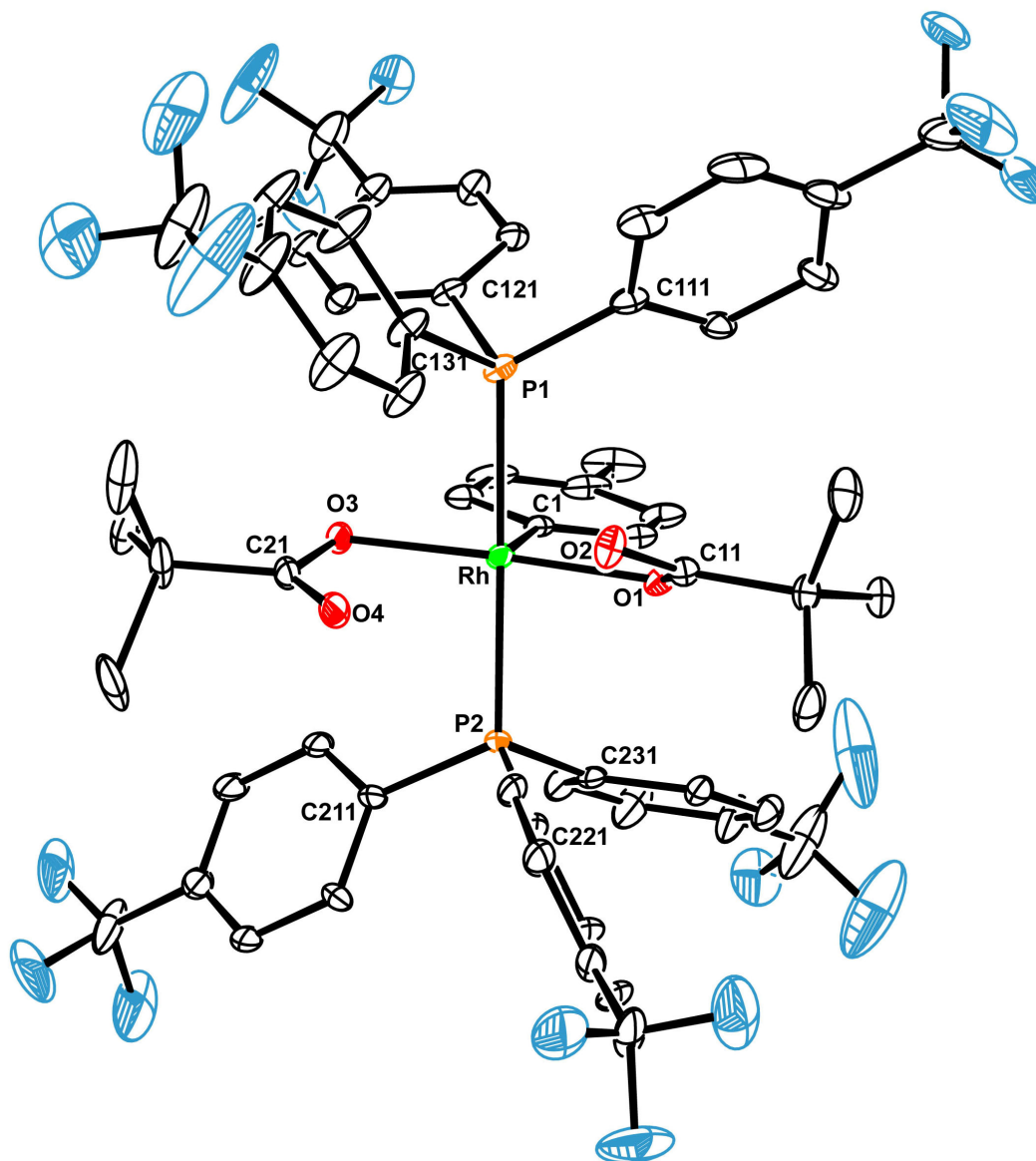


**Figure S3.** <sup>31</sup>P NMR of catalytic reaction mixture taken after 30 min of heating, dioxane- $d_8$ . Free phosphine L ( $\delta$  -5.64ppm)



**Figure S4.** <sup>31</sup>P NMR of catalytic reaction mixture taken after 8h of heating in dioxane- $d_8$ .

Although the decomposition of phosphine is evident after prolonged heating, complex **2** remained as the only observable Rh-phosphine species (rhodium phosphine coupling).



Ortep Drawing of **3**. A molecule of solvent and conformation isomers for fluoroines were omitted. For selected bond length and angles see table 2&3. For complete data see the CIF file.

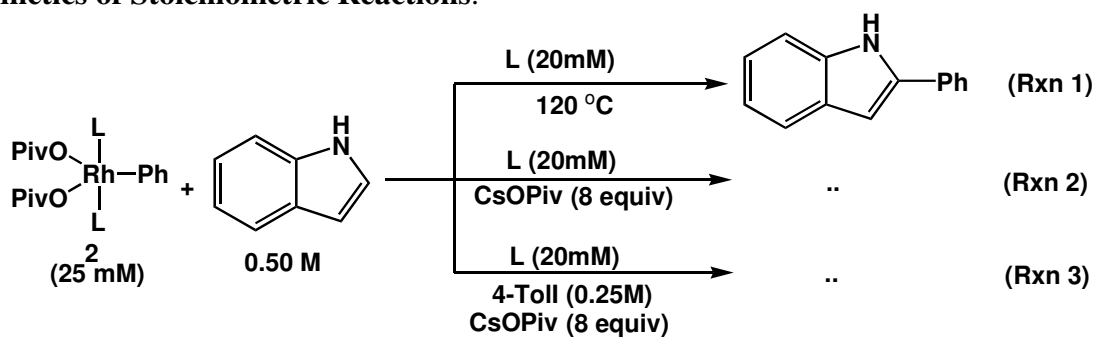
Table 2. Selected Bond Lengths (Angstroms) for **3**

Atom	A	B	Dist	A	B	Dist
	O1	C11	1.298	P2	Rh	2.346
	O1	Rh	2.034	Rh	C1	1.989
	O2	C11	1.226	Rh	O1	2.034
	O3	C21	1.288	Rh	O3	2.055
	O3	Rh	2.055	Rh	P2	2.346
	O4	C21	1.218	Rh	P1	2.357
	P1	Rh	2.357			

Table 3. Selected Bond Angles for **3**

Atom	A	B	C	Angle	A	B	C	Angle
	C2	C1	Rh	122.61	C231	P2	C221	104.46
	C6	C1	Rh	120.73	C231	P2	C211	103.88
	O2	C11	O1	120.24	C231	P2	Rh	112.85
	O2	C11	C12	123.02	C221	P2	C211	104.81
	O1	C11	C12	116.74	C221	P2	Rh	112.67
	O4	C21	O3	121.9	C211	P2	Rh	116.96
	O4	C21	C22	121.58	C1	Rh	O1	89.31
	O3	C21	C22	116.48	C1	Rh	O3	92.81
	C11	O1	Rh	111.83	C1	Rh	P2	91.89
	C21	O3	Rh	105.5	C1	Rh	P1	90.58
	C111	P1	C121	103.53	O1	Rh	O3	177.25
	C111	P1	C131	103.49	O1	Rh	P2	84.39
	C111	P1	Rh	119	O1	Rh	P1	95.72
	C121	P1	C131	103.42	O3	Rh	P2	93.79
	C121	P1	Rh	112.77	O3	Rh	P1	86.01
	C131	P1	Rh	112.98	P2	Rh	P1	177.53

## Kinetics of Stoichiometric Reactions.

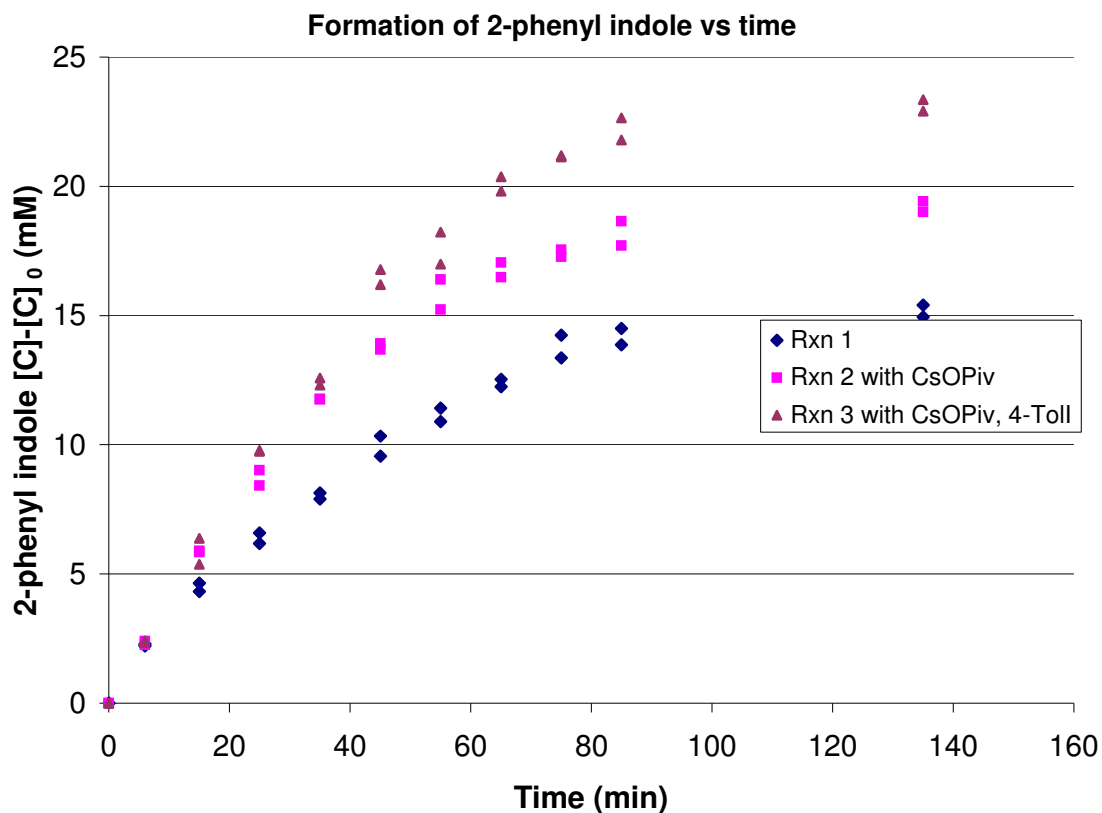


A stock solution (**Stock A**) was prepared by mixing the following solutions: **L** (1.0 mL, 1.0 M in 1,4-dioxane), indole (16.0 mL, 1.25 M in 1,4-dioxane) and dodecane (1.60 mL, 72.5 mg/ mL) and then was diluted by dioxane to a total volume of 20.0 mL.

For reaction 1: A reaction vial was charged with **2** (16.4 mg, 12.5 μmol), **stock A** (250 μL) and dioxane (250 μL). The vial was capped with a Teflon septum-equipped cap, heated at 120 °C for 3 minutes and the reaction was then monitored by GC-MS.

For reaction 2: A reaction vial was charged with **2** (16.4 mg, 12.5 μmol), **stock A** (250 μL), CsOPiv (23 mg, 0.10 mmol) and dioxane (250 μL). The vial was capped with a Teflon septum-equipped cap, heated at 120 °C for 3 minutes and the reaction was then monitored by GC-MS.

For reaction 3: A reaction vial was charged with **2** (16.4 mg, 12.5 μmol), **stock A** (250 μL), 4-TolI (100 μL, 1.25 M) and dioxane (150 μL). The vial was capped with a Teflon septum-equipped cap, heated at 120 °C for 3 minutes and the reaction was then monitored by GC-MS. Each of the above experiments was performed twice (**Figure S5**).



**Figure S5.** Stoichiometric Reaction of **2** and Indole.

Initial conditions:

Rxn 1: [2]=25 mM, [indole]=0.5 M, [L] = 25 mM.<sup>1</sup>

Rxn 2: [2]=25 mM, [indole]=0.5 M, [L] = 25 mM, CsOPiv (heterogeneous, 8 equiv)

Rxn 3: [2]=25 mM, [indole]=0.5 M, [L] = 25 mM, CsOPiv (heterogeneous, 8 equiv), [4-Toll]= 0.25M.<sup>2</sup>

Initial rate for the formation of 2-phenyl indole(first 300 seconds)

**Rxn 1=0.375(7) mM\*min<sup>-1</sup>.**

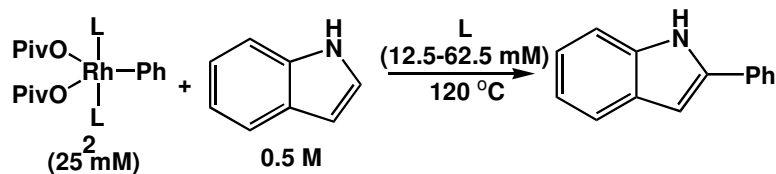
**Rxn 2=0.387(9) mM\*min<sup>-1</sup>**

**Rxn 3=0.397(5) mM\*min<sup>-1</sup>**

<sup>1</sup> 1 equivalence of phosphine **L** was added to maintain the concentration of free phosphine.

<sup>2</sup> Formation of 2-(4-Tolyl) indole was also observed after 30 minutes via the generation of complex **3**.

### Determination of Reaction Order Based on Initial Rate Dependence on Reagent Concentration:<sup>3</sup>



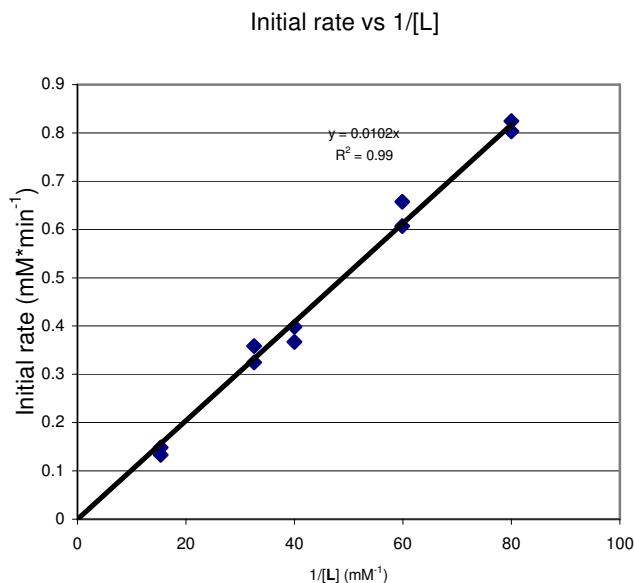
#### Rate dependence on phosphine [L] (12.5-65.2 mM):

**Stock solution B** was prepared as following: Indole (2.40 mL, 1.25 M in dioxane), dodecane (240  $\mu\text{L}$ , 72.5 mg/ mL) and dioxane (diluted to a total amount of 3.0 mL)

Five different amounts of **L** (25.0  $\mu\text{L}$ , 33.5  $\mu\text{L}$ , 50.0  $\mu\text{L}$ , 61.5  $\mu\text{L}$ , 135.5  $\mu\text{L}$ , 0.50 M in dioxane), **2** (16.4 mg, 12.5  $\mu\text{mol}$ ), stock B (250  $\mu\text{L}$ ) and five different amounts of dioxane (225  $\mu\text{L}$ , 216  $\mu\text{L}$ , 200  $\mu\text{L}$ , 188  $\mu\text{L}$ , 114  $\mu\text{L}$ ) were charged into 5 reaction vials, respectively. Vials were capped and heated at 120  $^\circ\text{C}$ . Monitoring starts after 3 min of preheating and initial rates recorded for first 300 seconds (5 minutes, conversion <10%). Experiments were repeated once. Data are plotted in **Figure S6**.

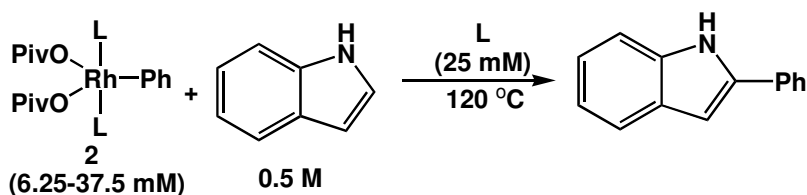
[L] (mM)	12.5	16.7	25	30.7	65.2
1/[L] ( $\text{mM}^{-1}$ )	80.0	59.9	40.0	32.6	15.3
Initial rate ( $\text{mM}\cdot\text{min}^{-1}$ )	0.803	0.658	0.398	0.324	0.149
Initial rate ( $\text{mM}\cdot\text{min}^{-1}$ )	0.825	0.607	0.367	0.358	0.133

Conditions: [indole] = 0.50 M, [**2**] = 25 mM, [L] (12.5-65.2 mM) .



**Figure S6.** Initial Rates-Inversed-first order plot on phosphine [L]

<sup>3</sup> Due to the decomposition of **2** in the absence of CsOPiv and PhI (trapping effect), reaction order for the stoichiometric reaction of **2** and indole was determined using initial rate kinetics.



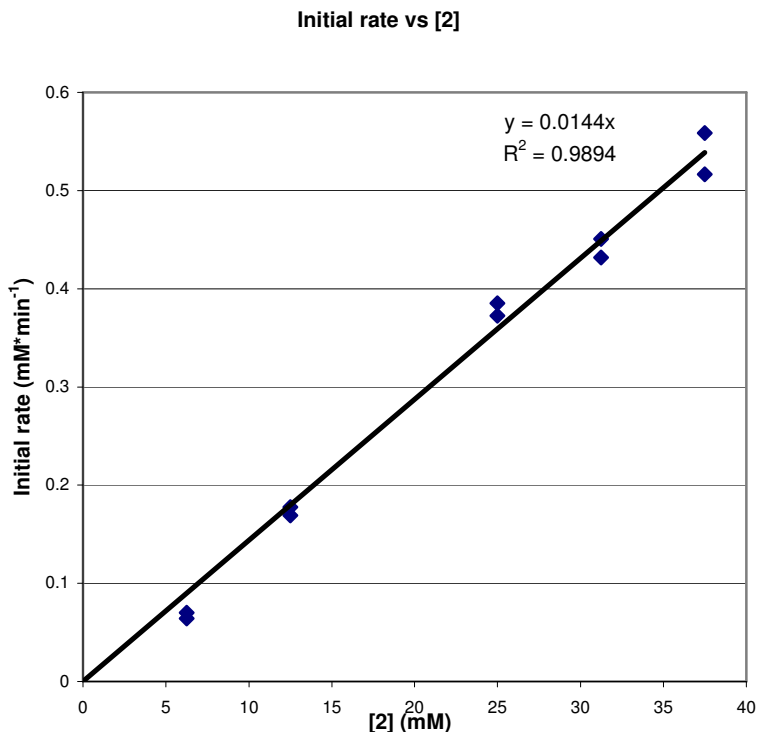
**Rate dependence on [2] (6.25-37.5mM):**

**Stock solution C:** Indole (2.4 mL, 1.25 M in dioxane), dodecane (240  $\mu\text{L}$ , 72.5 mg/mL), **L** (150.0  $\mu\text{L}$ , 1.0 M in dioxane) and dioxane (diluted to a total amount of 3.0 mL).

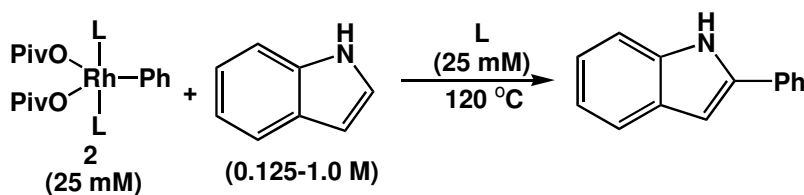
Five different amount of **2** (4.1 mg, 8.2 mg, 16.4 mg, 20.5 mg, 24.6 mg), stock C (250  $\mu\text{L}$ ) and dioxane (250  $\mu\text{L}$ ) were charged into five reaction vials, respectively. Vials were capped and heated at 120  $^\circ\text{C}$ . Monitoring starts after 3 min of preheating and initial rates recorded for first 300 seconds (5 minutes, conversion <10%). Experiments were repeated once. Data are plotted in **Figure S7**.

[2] (mM)	6.25	12.5	25	31.25	37.5
Initial rate (mM*min <sup>-1</sup> )	0.064	0.178	0.373	0.451	0.559
Initial rate (mM*min <sup>-1</sup> )	0.070	0.169	0.385	0.432	0.517

Conditions: [indole] = 0.50 M, [L] = 25 mM.



**Figure S7.** First order plot on [2]



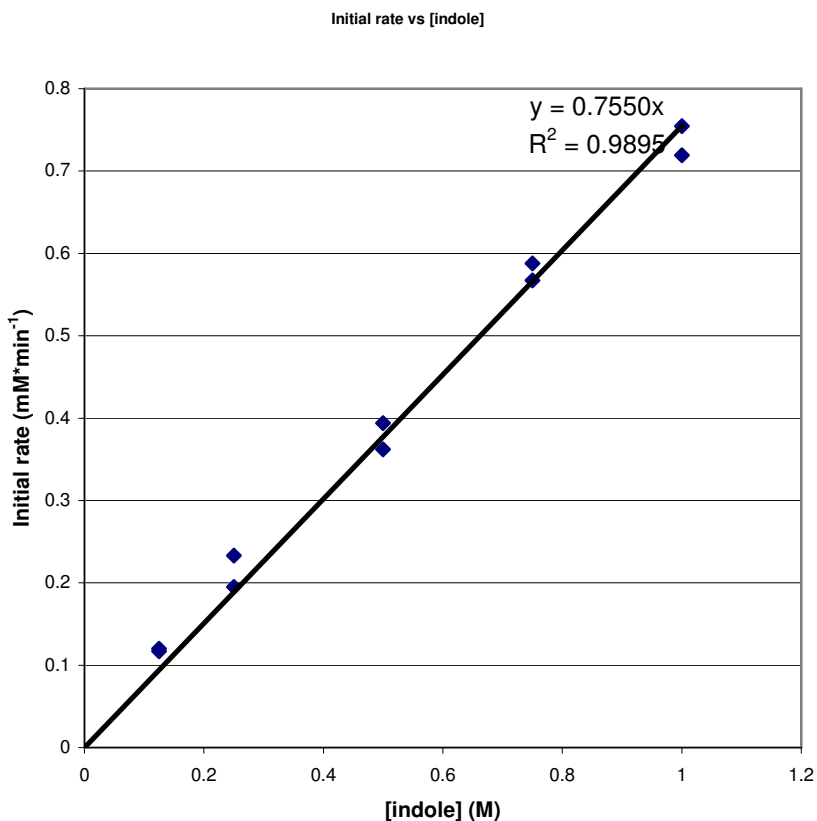
**Rate dependence on [indole] (0.125-1.0 M):**

**Stock solution D:** L (75.0  $\mu\text{L}$ , 1.0 M in dioxane), dodecane (120  $\mu\text{L}$ , 72.5 mg/ mL) and dioxane (diluted to a total amount of 3.00 mL).

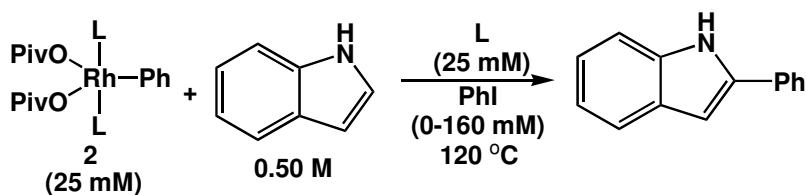
Five different amounts of indole (50.0  $\mu\text{L}$ , 100  $\mu\text{L}$ , 200  $\mu\text{L}$ , 300  $\mu\text{L}$ , 400  $\mu\text{L}$ , 1.25 M in dioxane), **2** (16.4 mg, 12.5  $\mu\text{mol}$ ), stock D (50  $\mu\text{L}$ ) and five different amounts of dioxane (400  $\mu\text{L}$ , 350  $\mu\text{L}$ , 250  $\mu\text{L}$ , 150  $\mu\text{L}$ , 50  $\mu\text{L}$ ) were charged into 5 reaction vials, separately. Vials were capped and heated at 120  $^{\circ}\text{C}$ . Monitoring starts after 3 min of preheating and initial rates recorded for first 300 seconds (5 minutes, conversion <10%). Experiments were repeated once. Data are plotted in **Figure S8**.

[Indole] (M)	0.125	0.25	0.5	0.75	1.0
Initial rate ( $\text{mM}\cdot\text{min}^{-1}$ )	0.117	0.233	0.362	0.567	0.719
Initial rate ( $\text{mM}\cdot\text{min}^{-1}$ )	0.120	0.195	0.394	0.588	0.755

Conditions: [**2**] = 25.0 mM, [L] = 25.0 mM.



**Figure S8.** First Order Plot on [Indole].

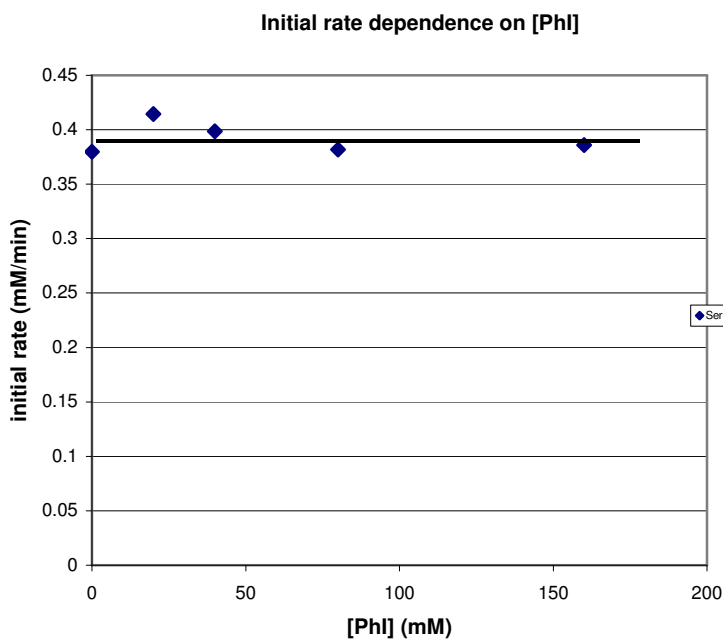


### Rate dependence on [PhI] (0-160mM):

Five different amounts of PhI (0  $\mu\text{L}$ , 20  $\mu\text{L}$ , 40  $\mu\text{L}$ , 80  $\mu\text{L}$ , 160  $\mu\text{L}$ , 1.0 M in dioxane), **2** (16.4 mg, 12.5  $\mu\text{mol}$ ), stock A (250  $\mu\text{L}$ ) and five different amounts of dioxane (250  $\mu\text{L}$ , 230  $\mu\text{L}$ , 210  $\mu\text{L}$ , 170  $\mu\text{L}$ , 90  $\mu\text{L}$ ) were charged into 5 reaction vials, separately. Vials were capped and heated at 120  $^\circ\text{C}$ . Monitoring starts after 3 min of preheating and initial rates recorded for first 300 seconds (5 minutes, conversion <10%). Experiments were performed once due to apparent zero order dependence on [PhI]. Data plotted in **Figure S9**.

[PhI] (mM)	0	20	40	80	160
Initial rate (mM $\cdot\text{min}^{-1}$ )	0.380	0.414	0.399	0.382	0.386

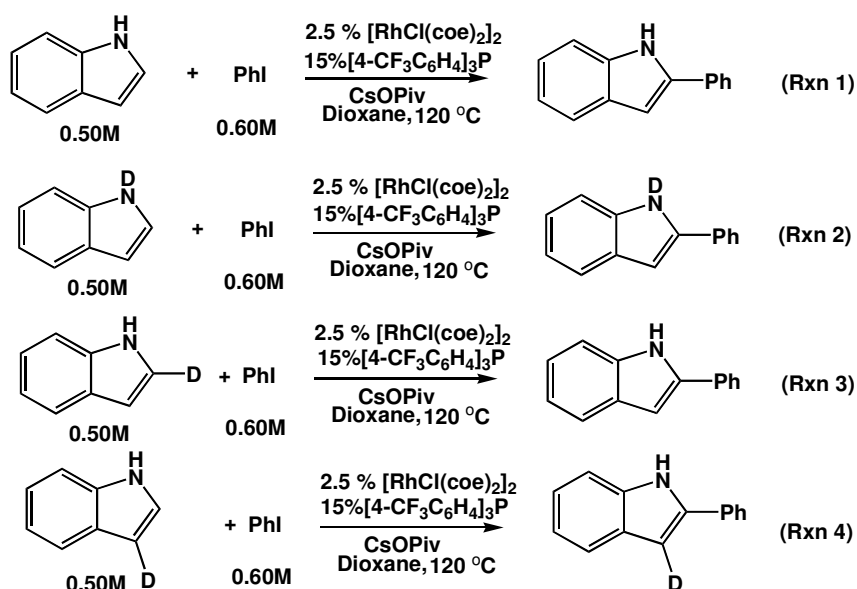
Conditions: [indole] = 0.50 M, [**2**] = 25.0 mM, [L] = 25.0 mM.



**Figure S9.** Zero order Plot on [PhI]

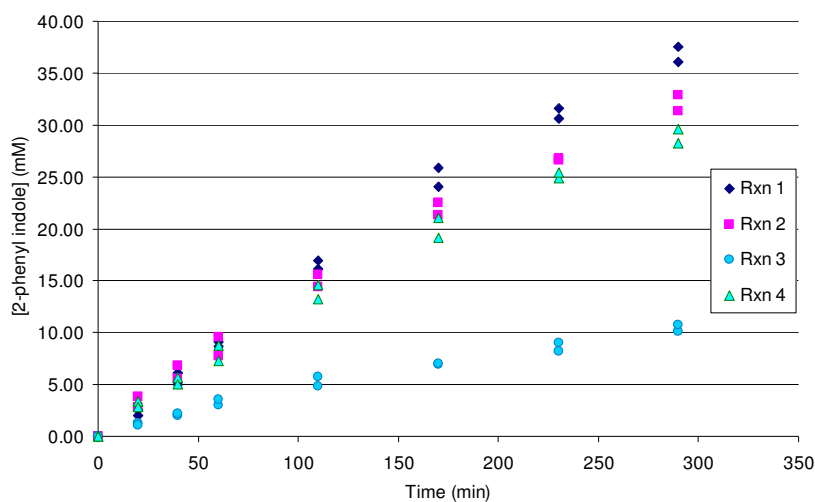
## Kinetics of Catalytic Reactions<sup>4</sup>

Measurement of H/D kinetic isotope effect: In an argon filled glovebox, **1** (9.0 mg, 0.0125 mmol), P[4-(CF<sub>3</sub>)C<sub>6</sub>H<sub>4</sub>]<sub>3</sub> (**L**, 36.0 mg, 0.075 mmol), indole (58.5 mg, 0.50 mmol), benzophenone (internal standard, 29 mg), CsOPiv (164 mg, 0.70 mmol) and PhI (122 mg, 0.60 mmol) was charged into a vial, followed by the addition of 1,4-dioxane (1.0 mL). Similarly, reaction mixture were loaded into three other vials with 1-indole-*d*<sub>1</sub> (59.0 mg, 0.50 mmol), 2-indole-*d*<sub>1</sub> (59.0 mg, 0.50 mmol) and 3-indole-*d*<sub>1</sub> (59.0 mg, 0.50 mmol), respectively. The vials were capped, brought out the glovebox, and heated at 120 °C in a reaction block. After 5 minutes of preheating, reaction samples were taken periodically via syringe and their component concentration was analyzed via a GC/FID. H/D scrambling of indole was checked via GC/MS detector separately. Data are plotted in **Figure S10**. Initial rates are plotted in **Figure S11**.

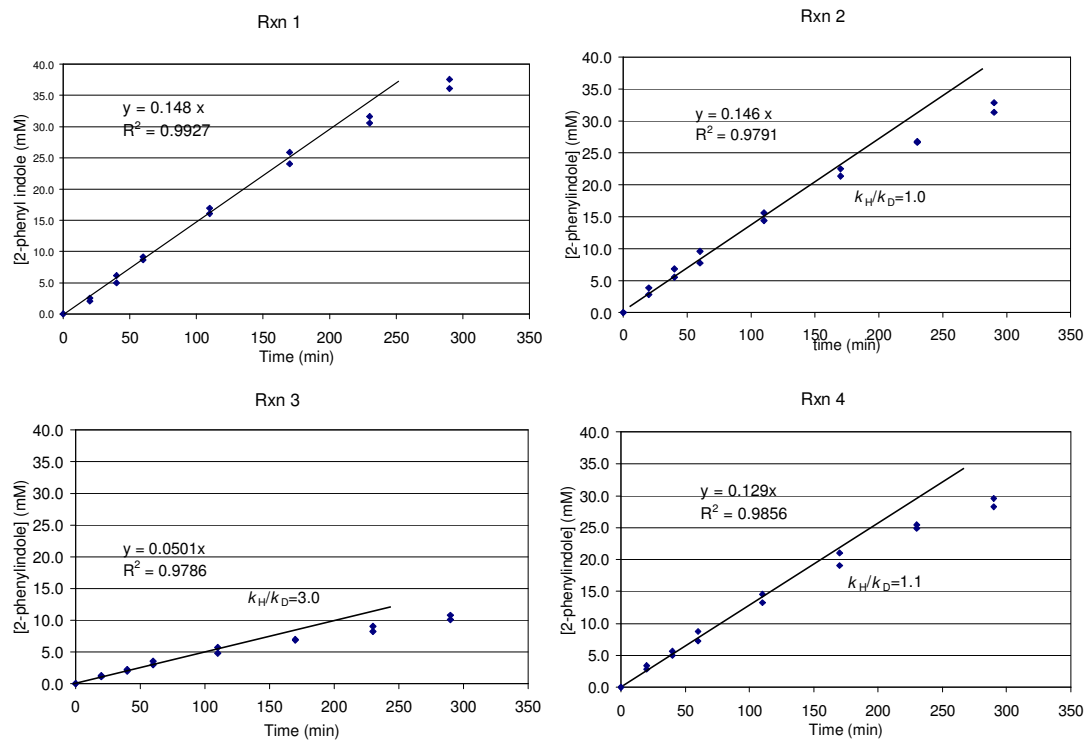


<sup>4</sup> Due to the gradual decomposition of phosphine (erosion) during reaction process, direct measurements of  $k_{\text{H}}$  and  $k_{\text{D}}$  from individual reactions were not feasible. Initial rate kinetics were applied instead.

# Reaction of Isotope-Incorporated Indole with PhI at Initial Stage



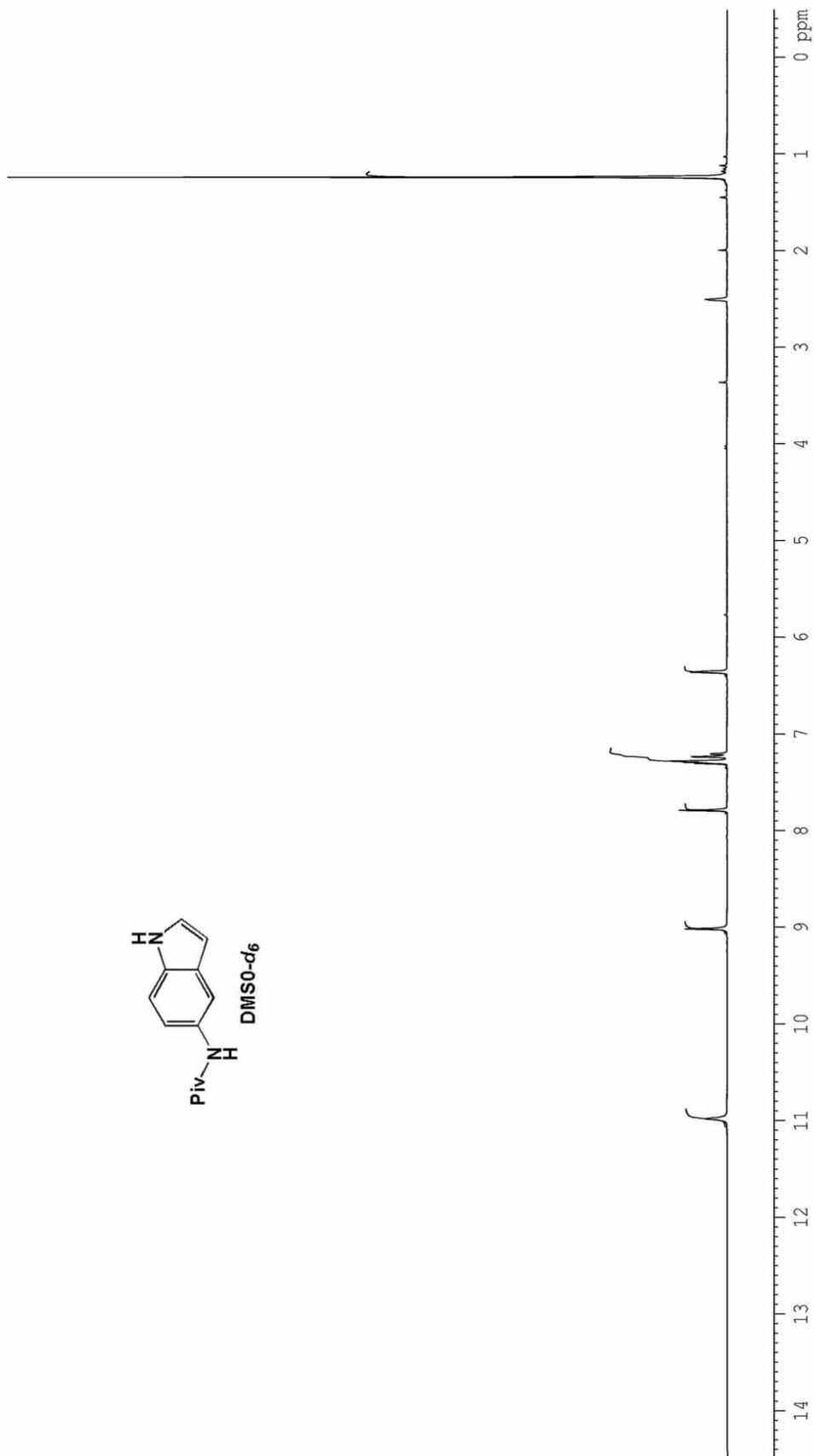
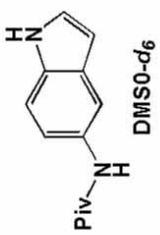
**Figure S10.** Initial conditions: [1] = 12.5  $\mu$ M, [L] = 37.5  $\mu$ M, [Indole] = 0.50 M, [PhI] = 0.60 M.



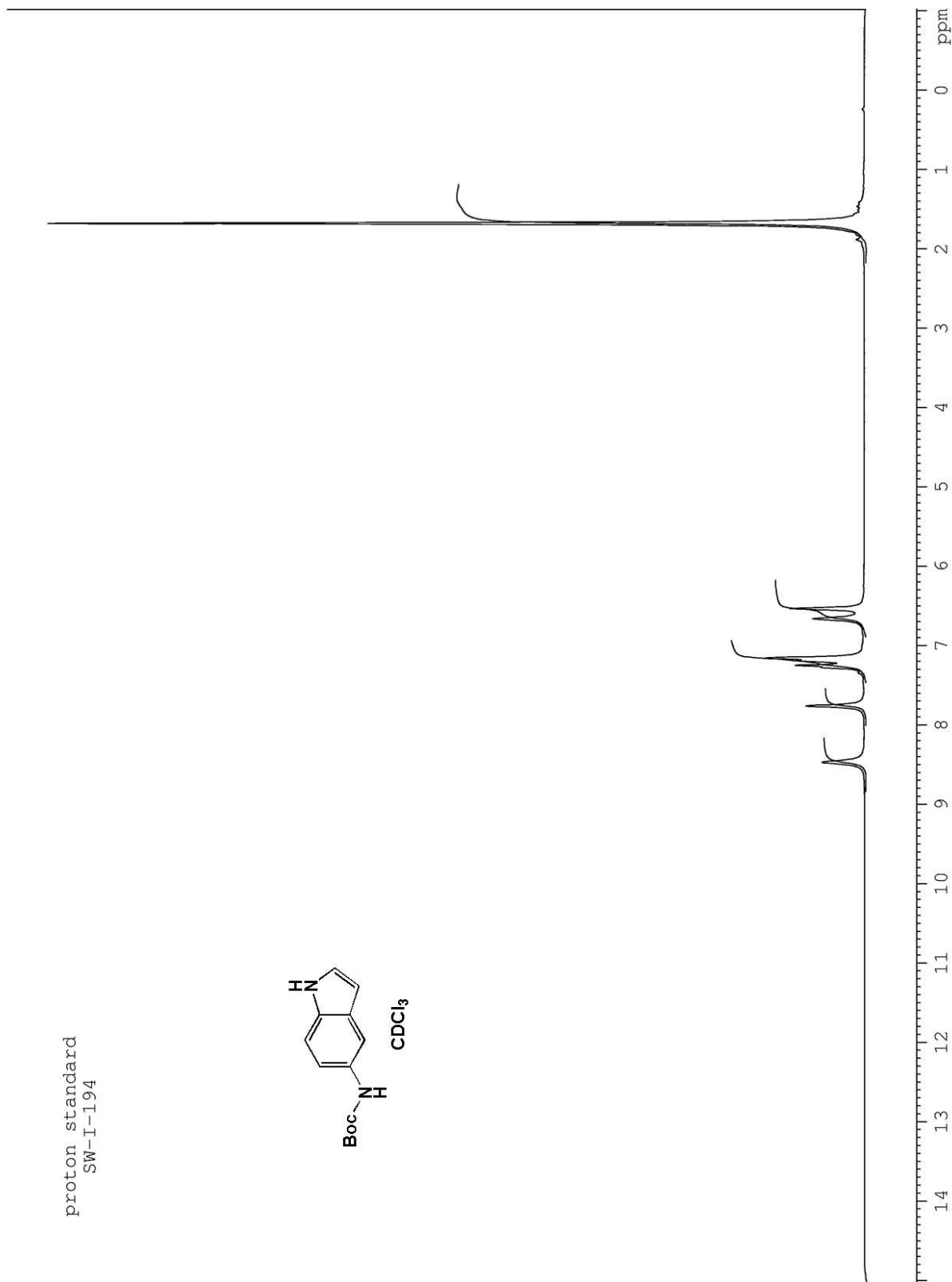
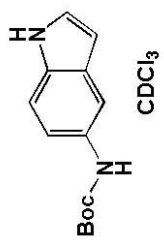
**Figure S11**

D/H scrambling was monitored by GC/MS separately. 1-indole- $d_1$  lost ~20% deuterium after 200 min, 2-indole- $d_1$  lost <5% deuterium after 200 min, 3-indole- $d_1$  lost ~30% deuterium in 200 minutes. Partial loss of deuterium from 1-indole- $d_1$  and 3-indole- $d_1$  does not cause significant deviation in KIE measurement, as KIE at both positions are close to 1 ( $k_D \approx k_H$ ).

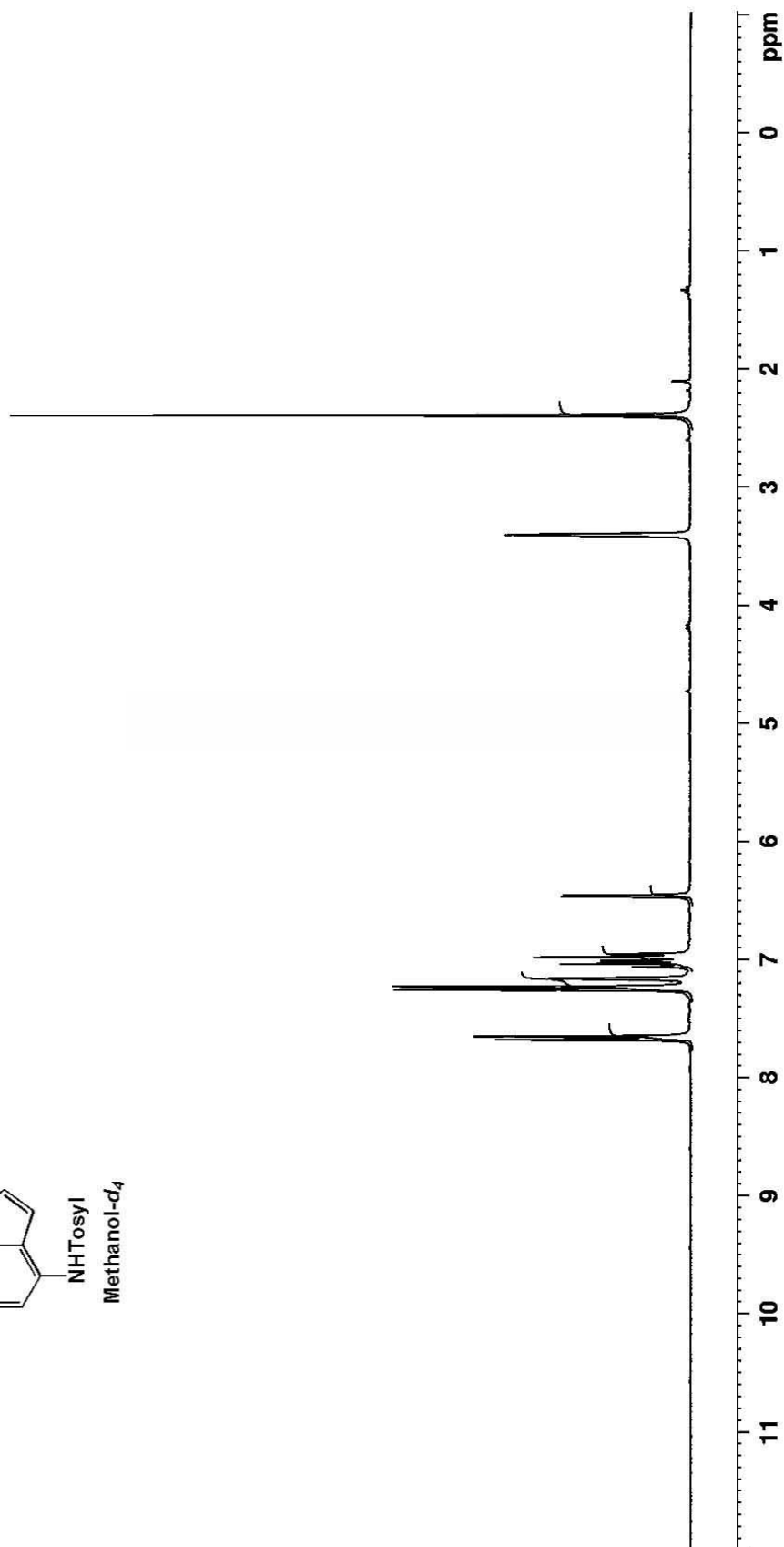
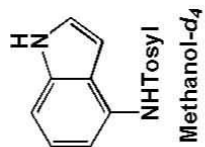
SW-I-129  
MSO wb30

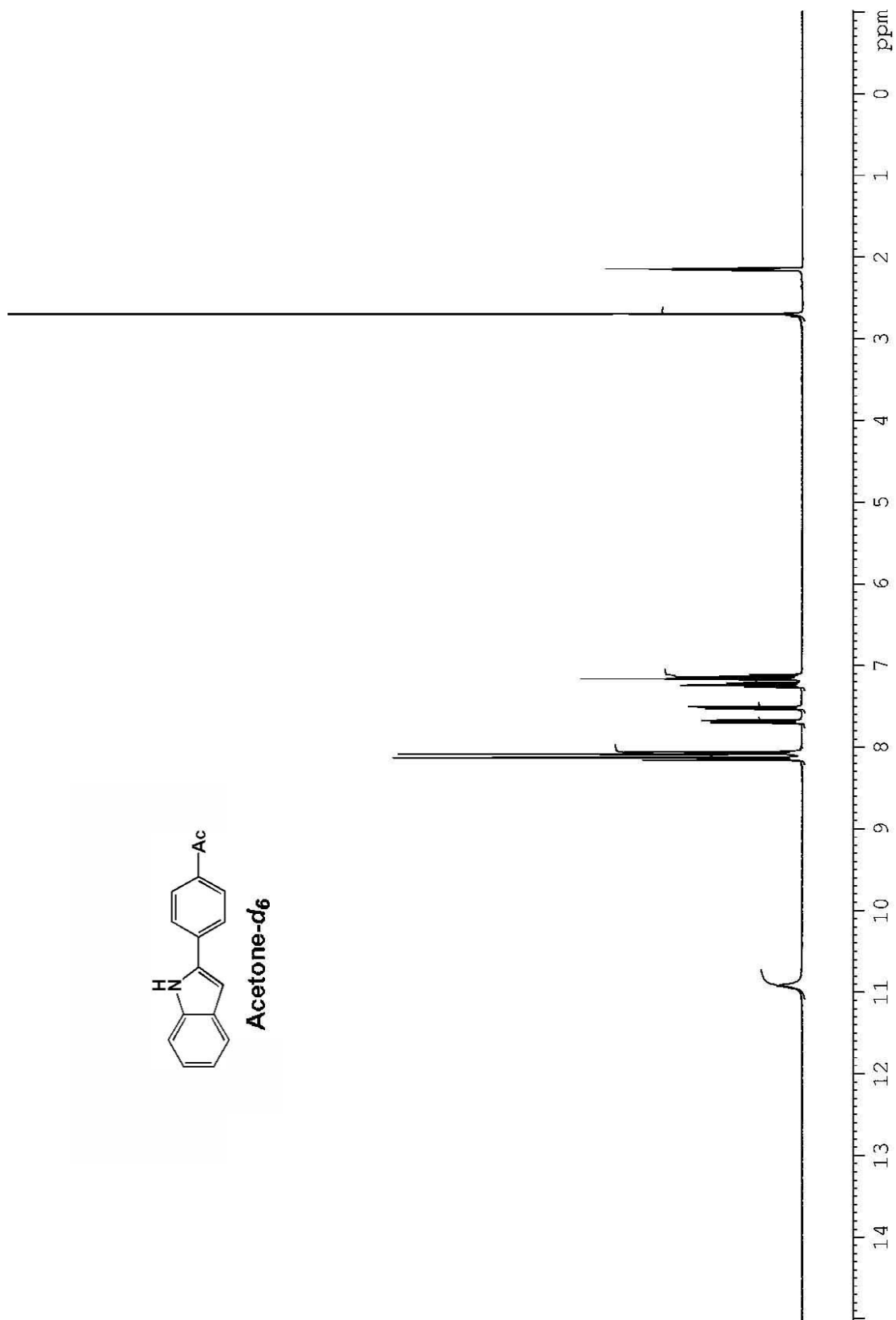
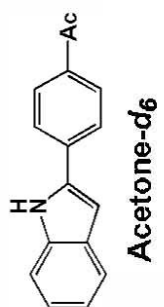


proton standard  
SW-I-194

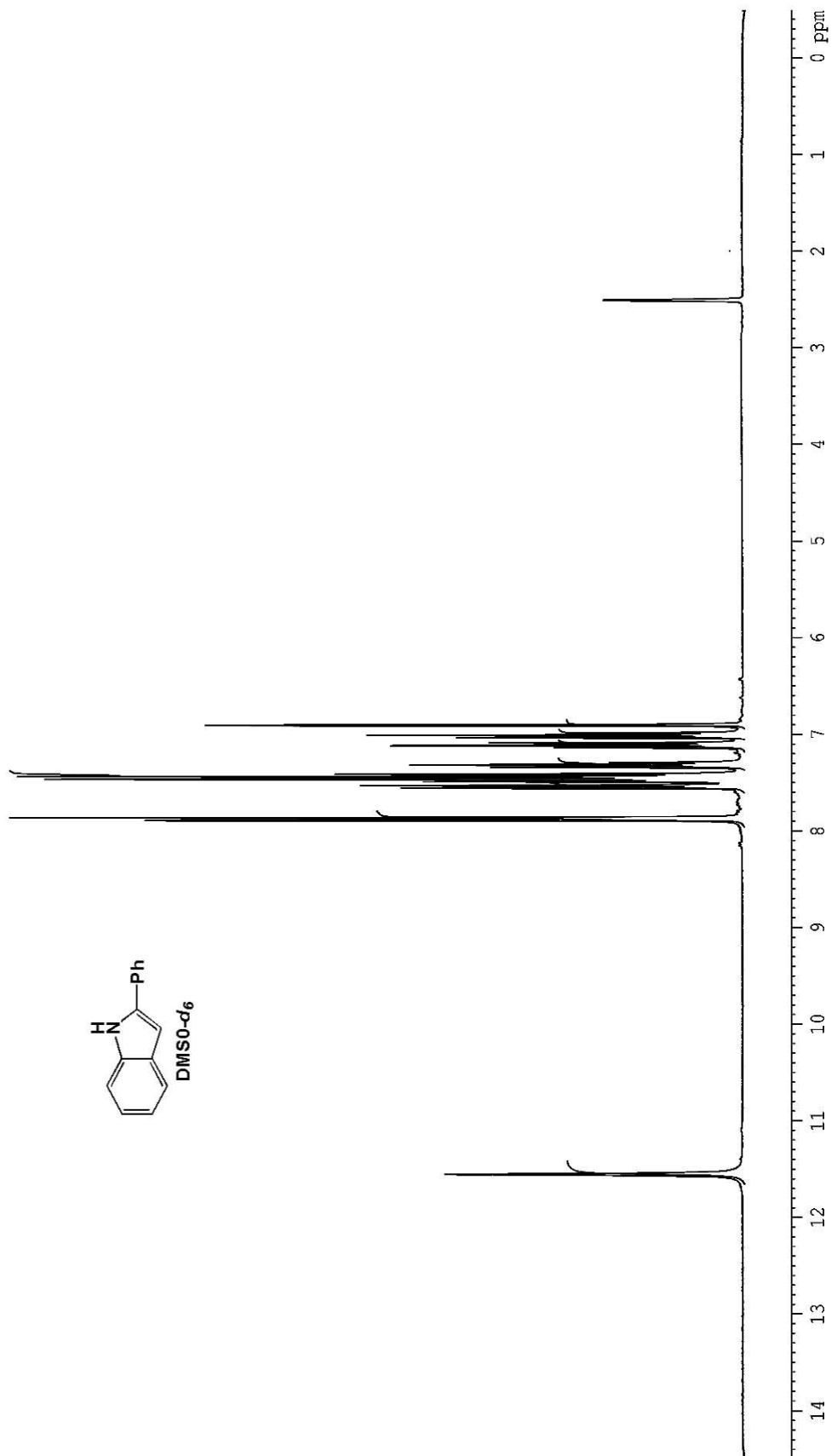
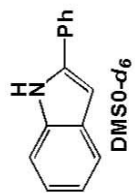


SW-I-141-2  
proton standard

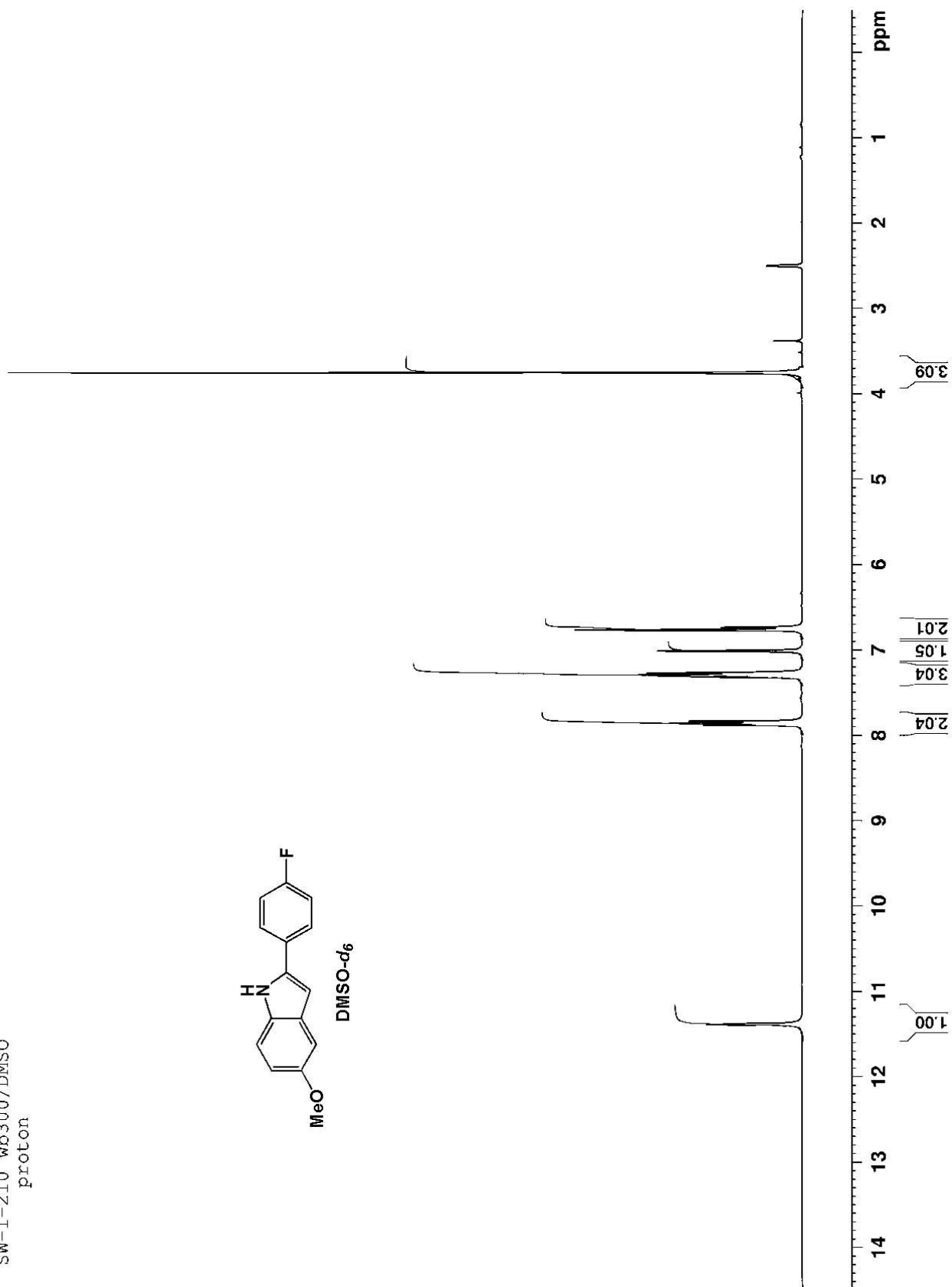
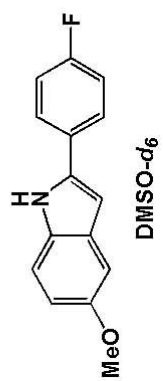


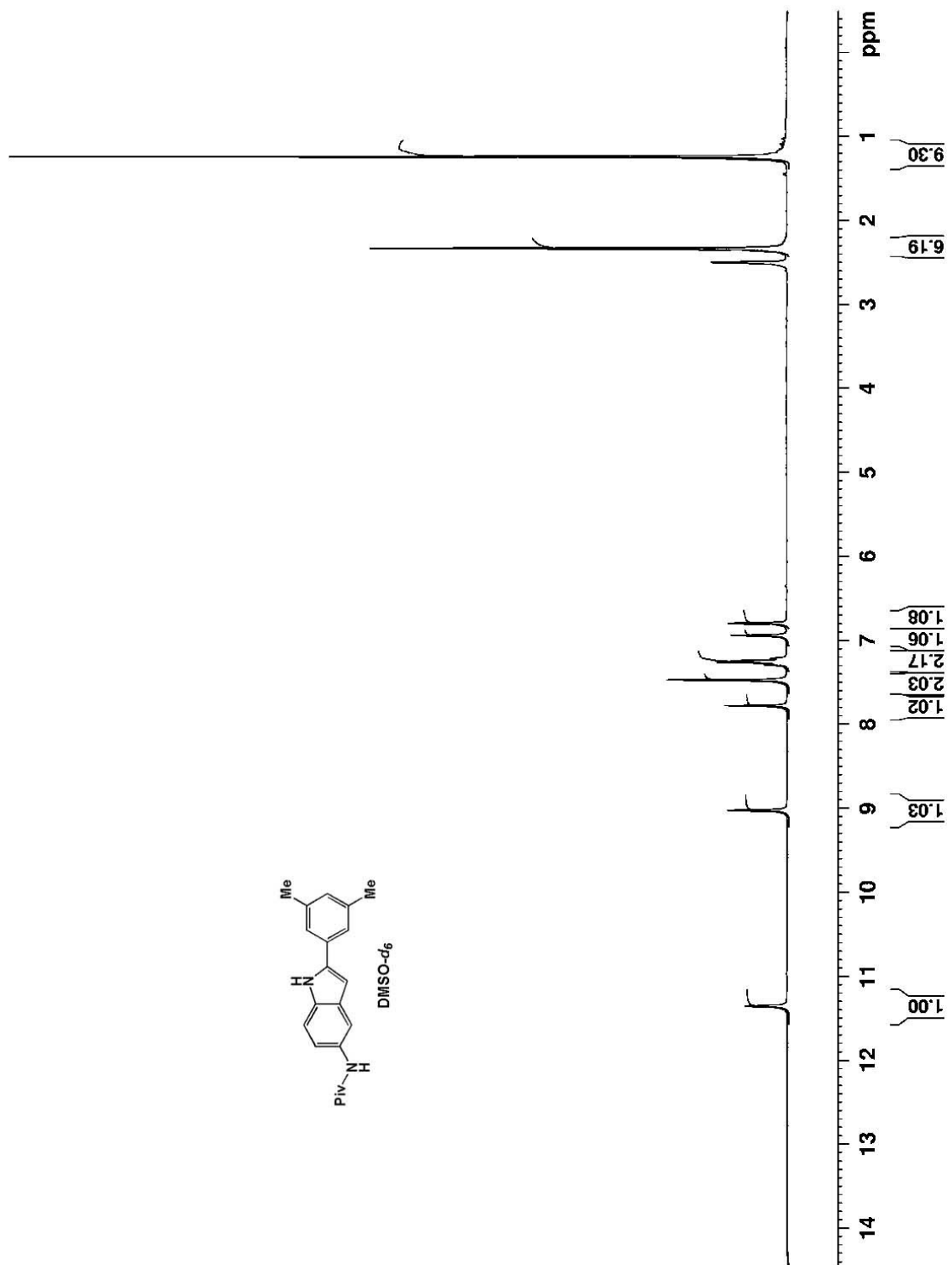


SW-I-175  
proton  
DMSO

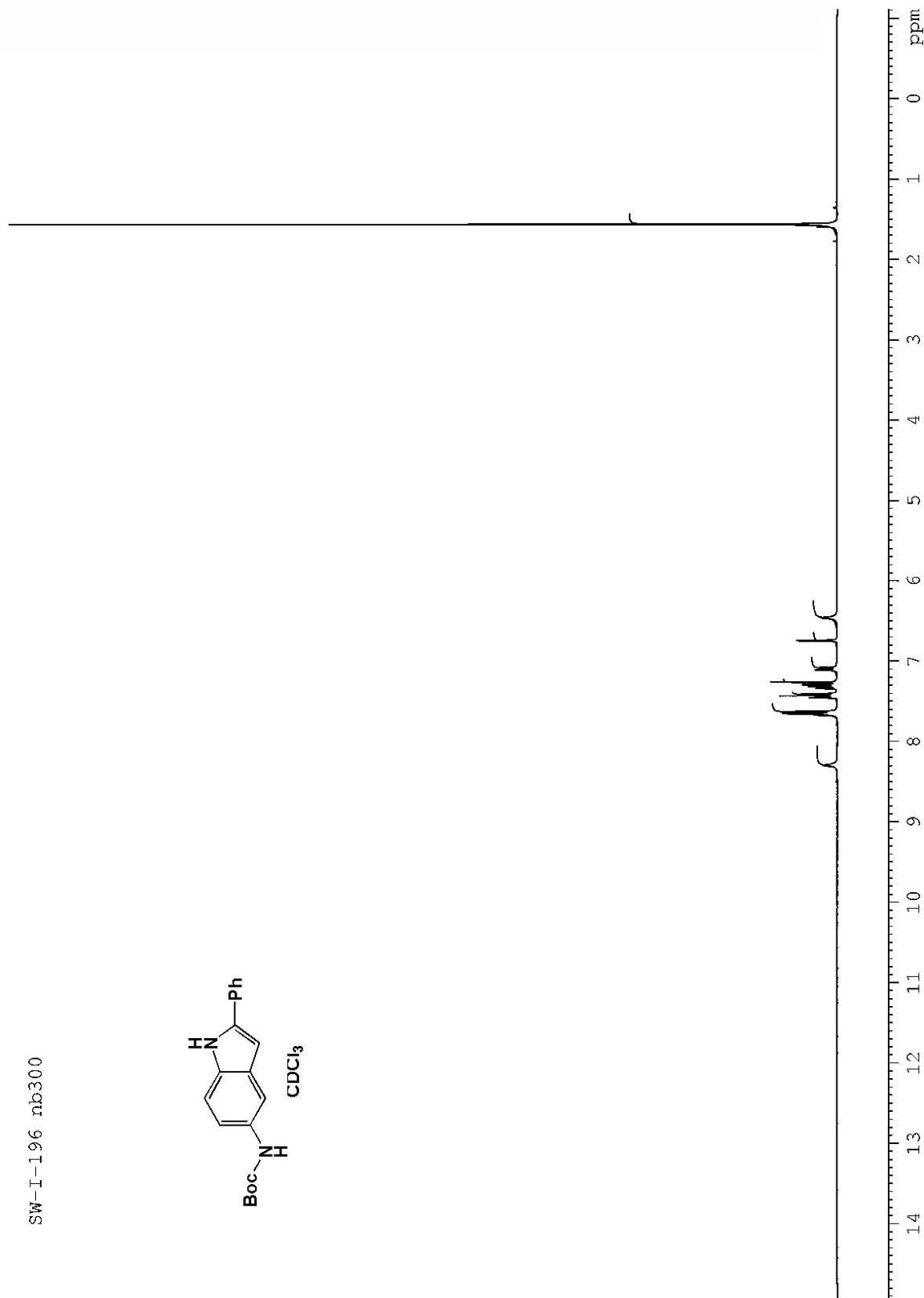
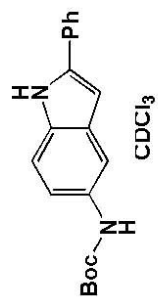


SW-I-210 wb300/DMSO  
proton

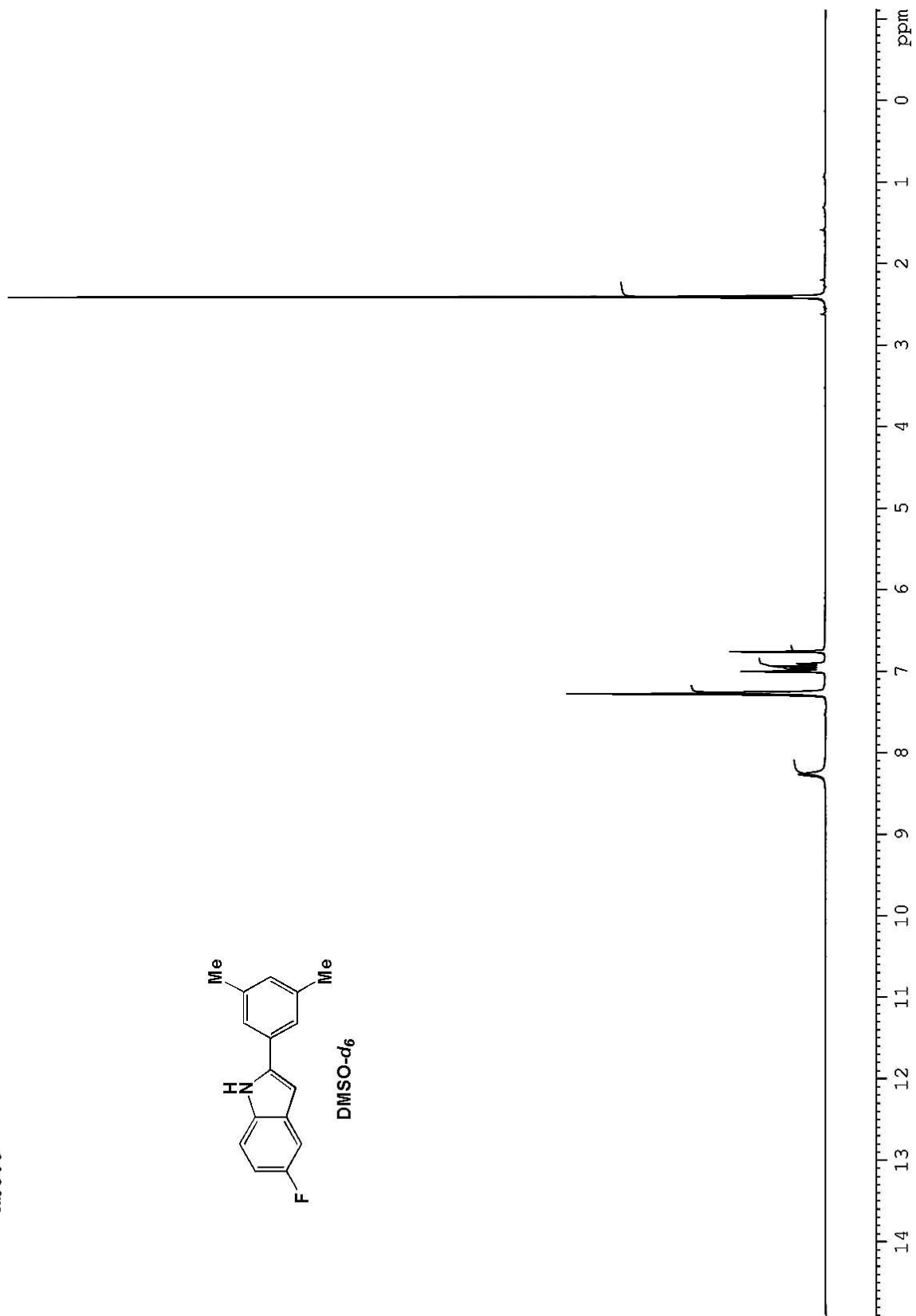
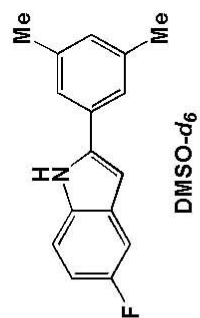


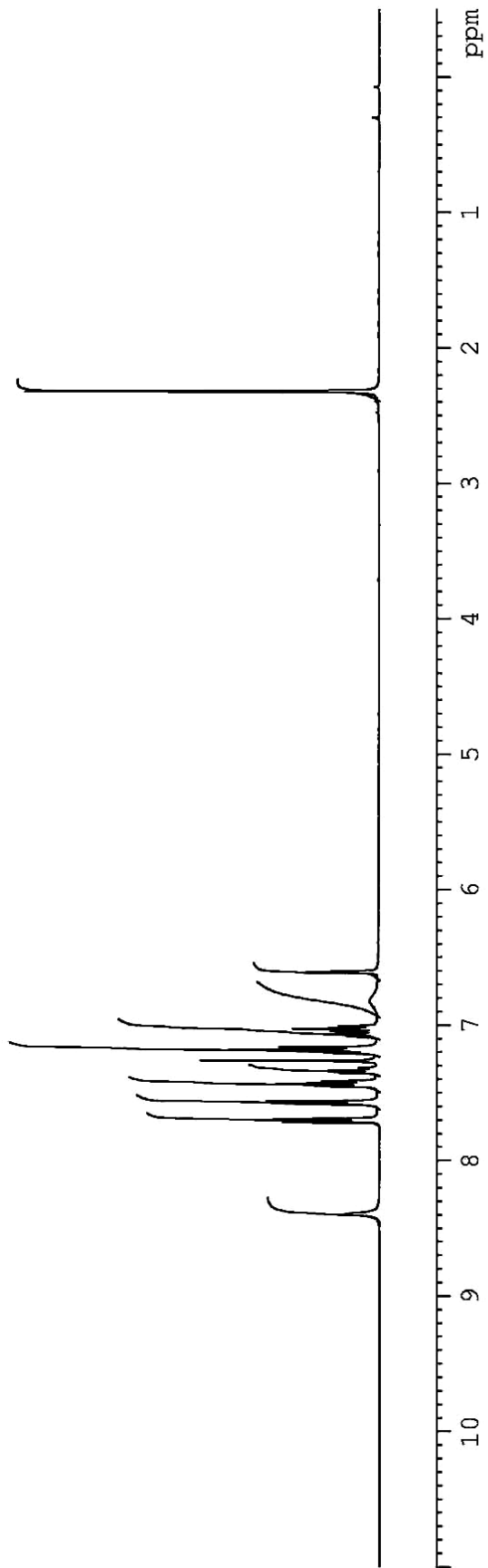


SW-I-196 nb300

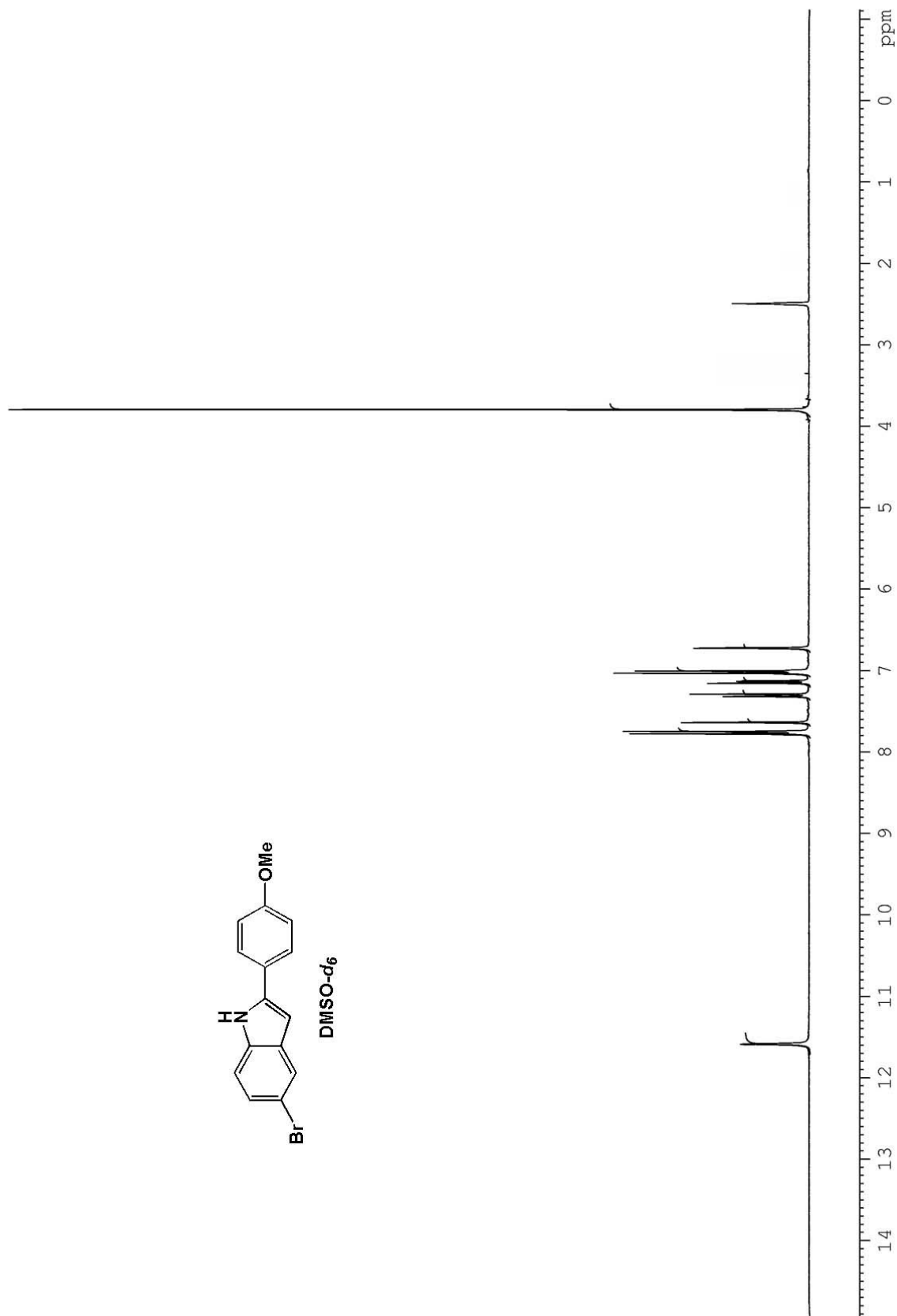
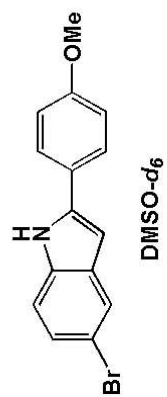


proton standard  
SW-I-209  
nb300

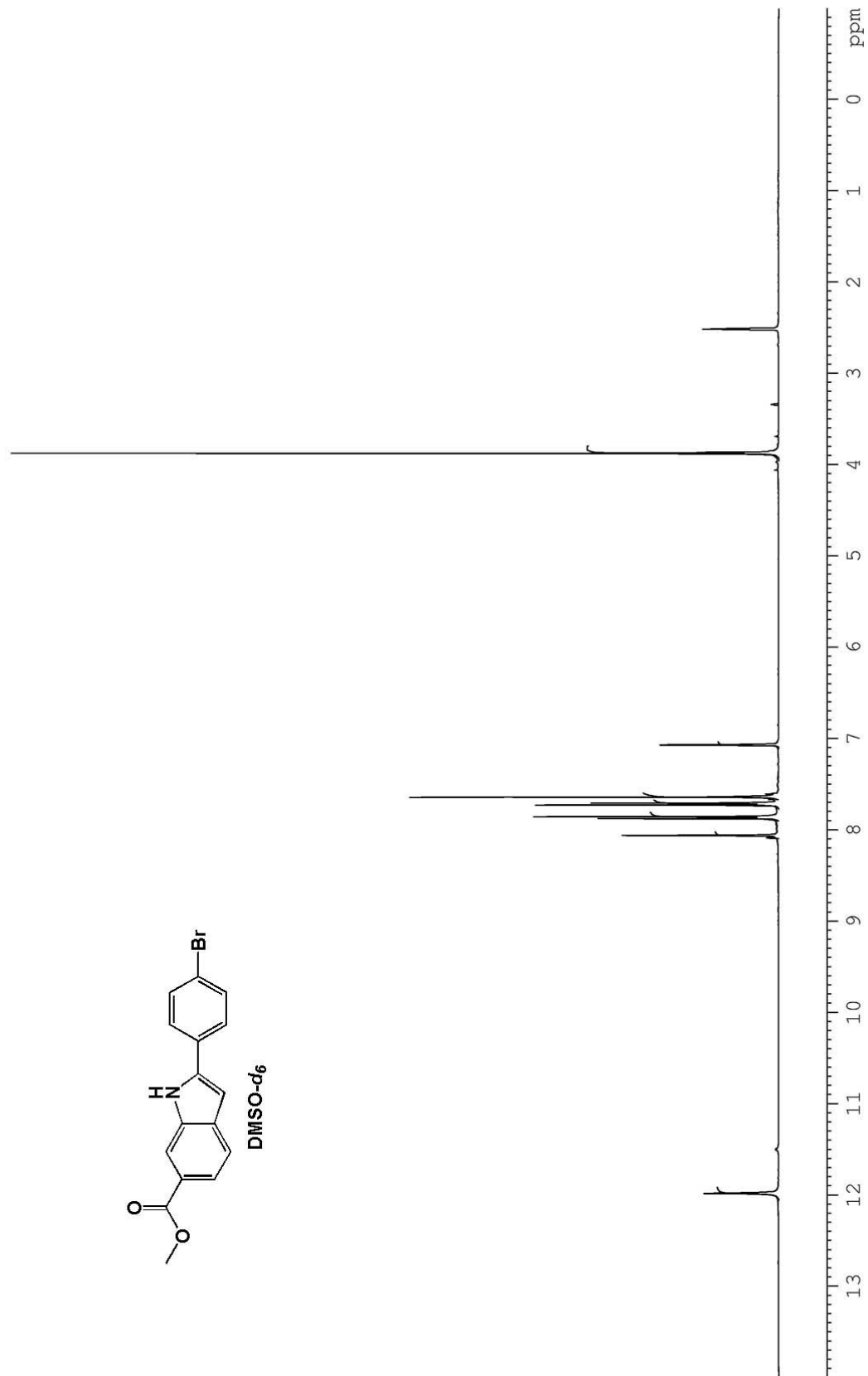
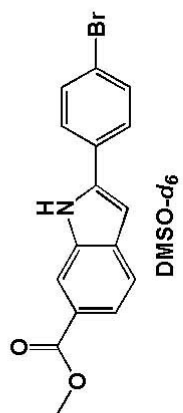




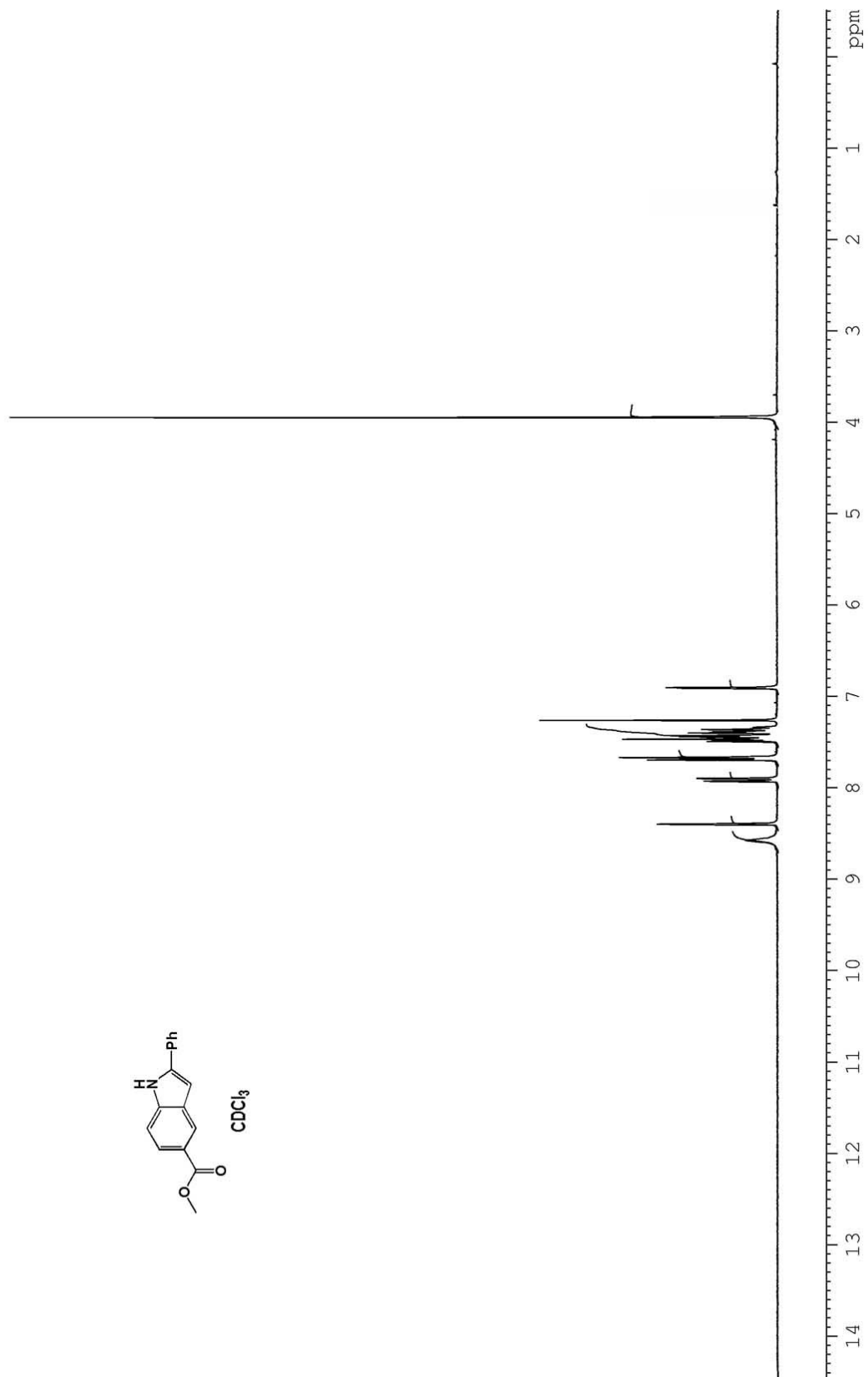
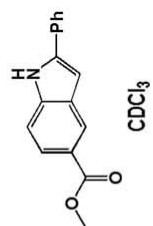
SW-I-211

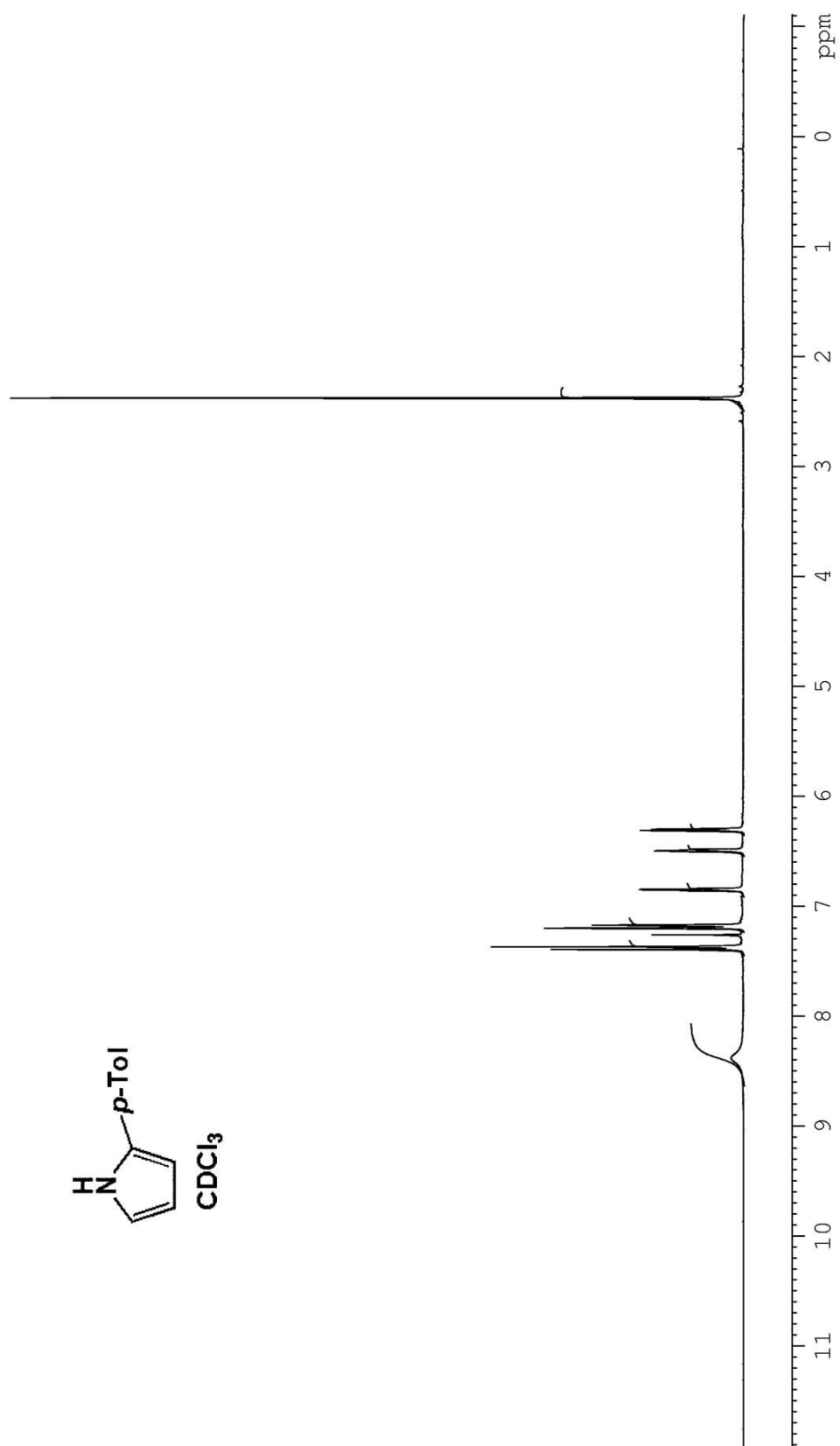


SW-I-220  
proton 400Mhz

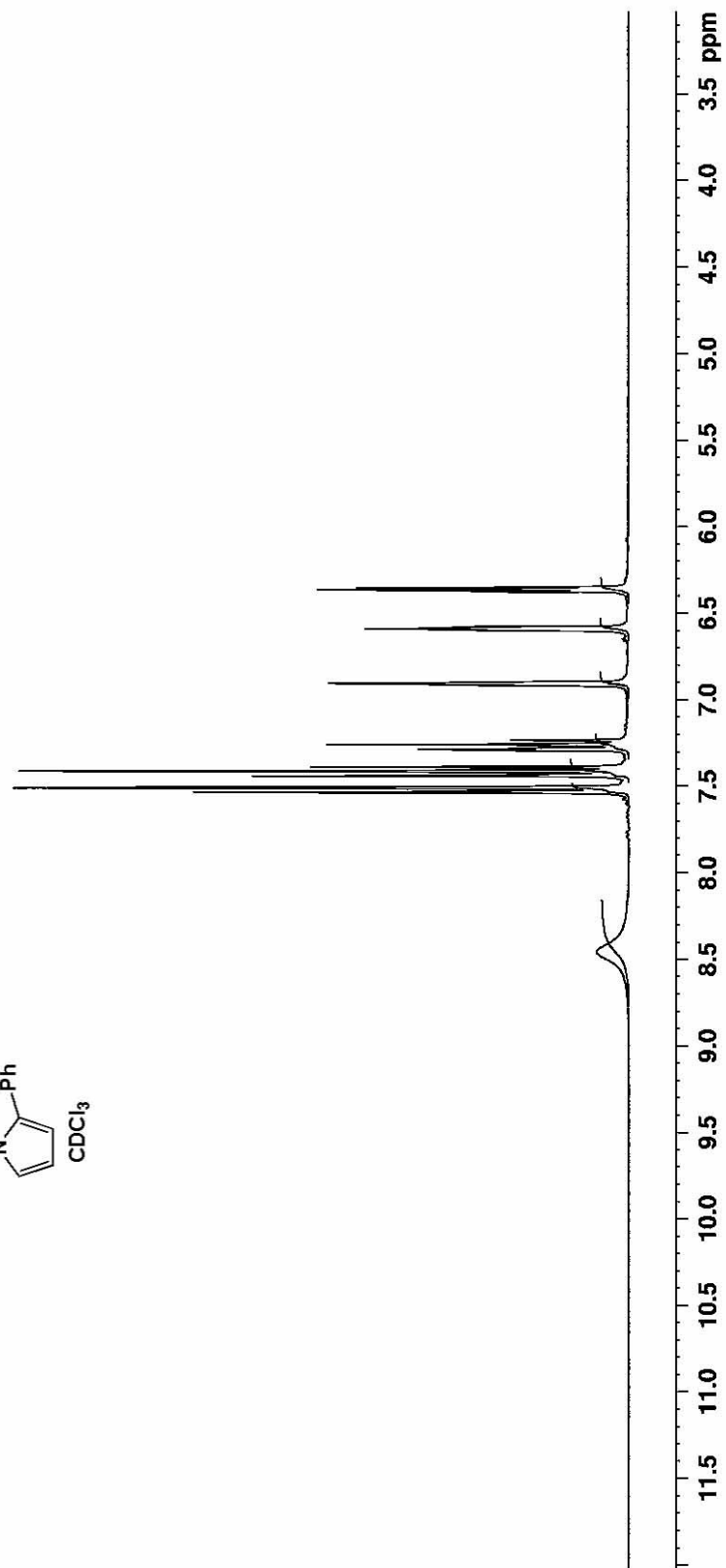
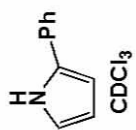


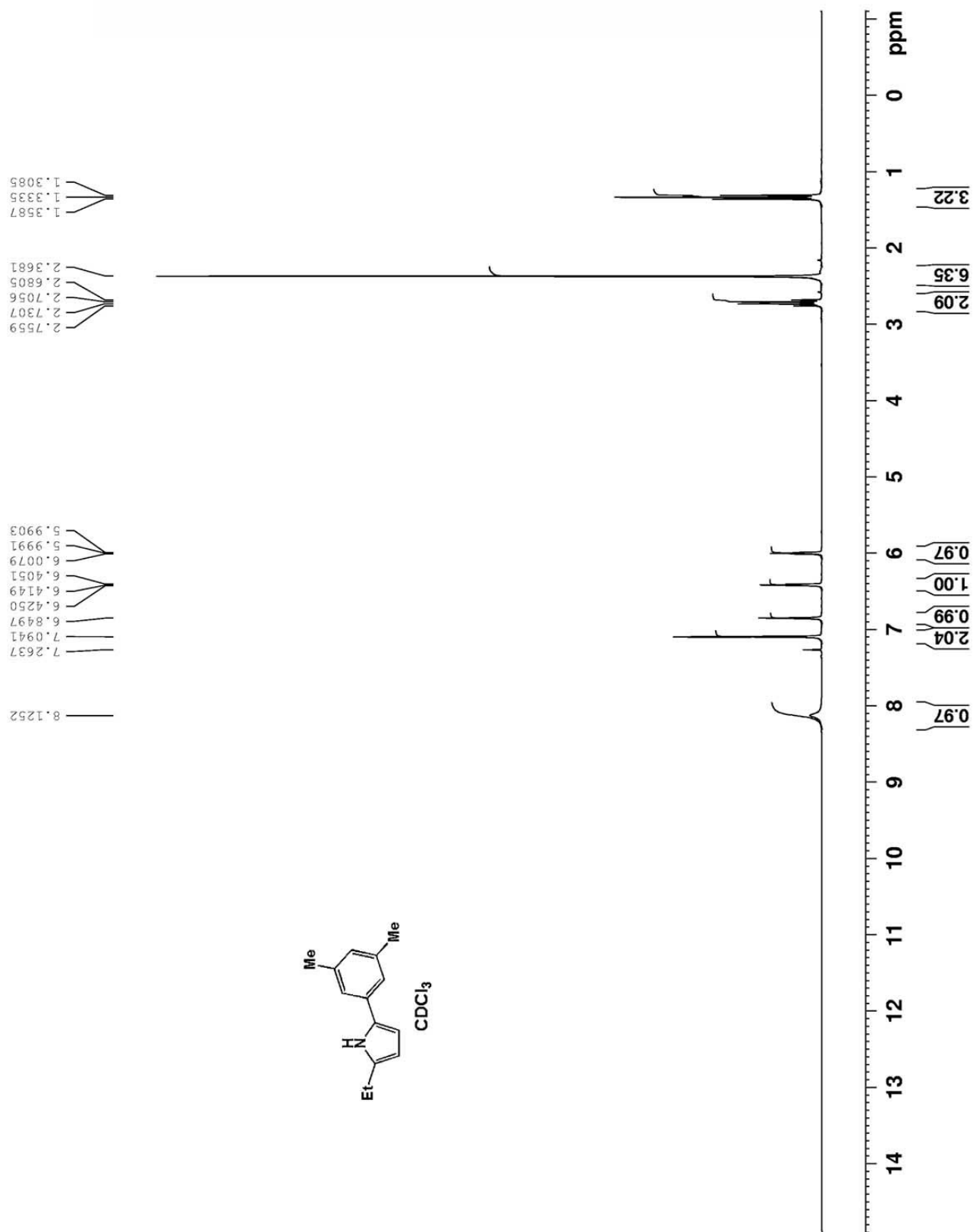
SW-I-89  
proton

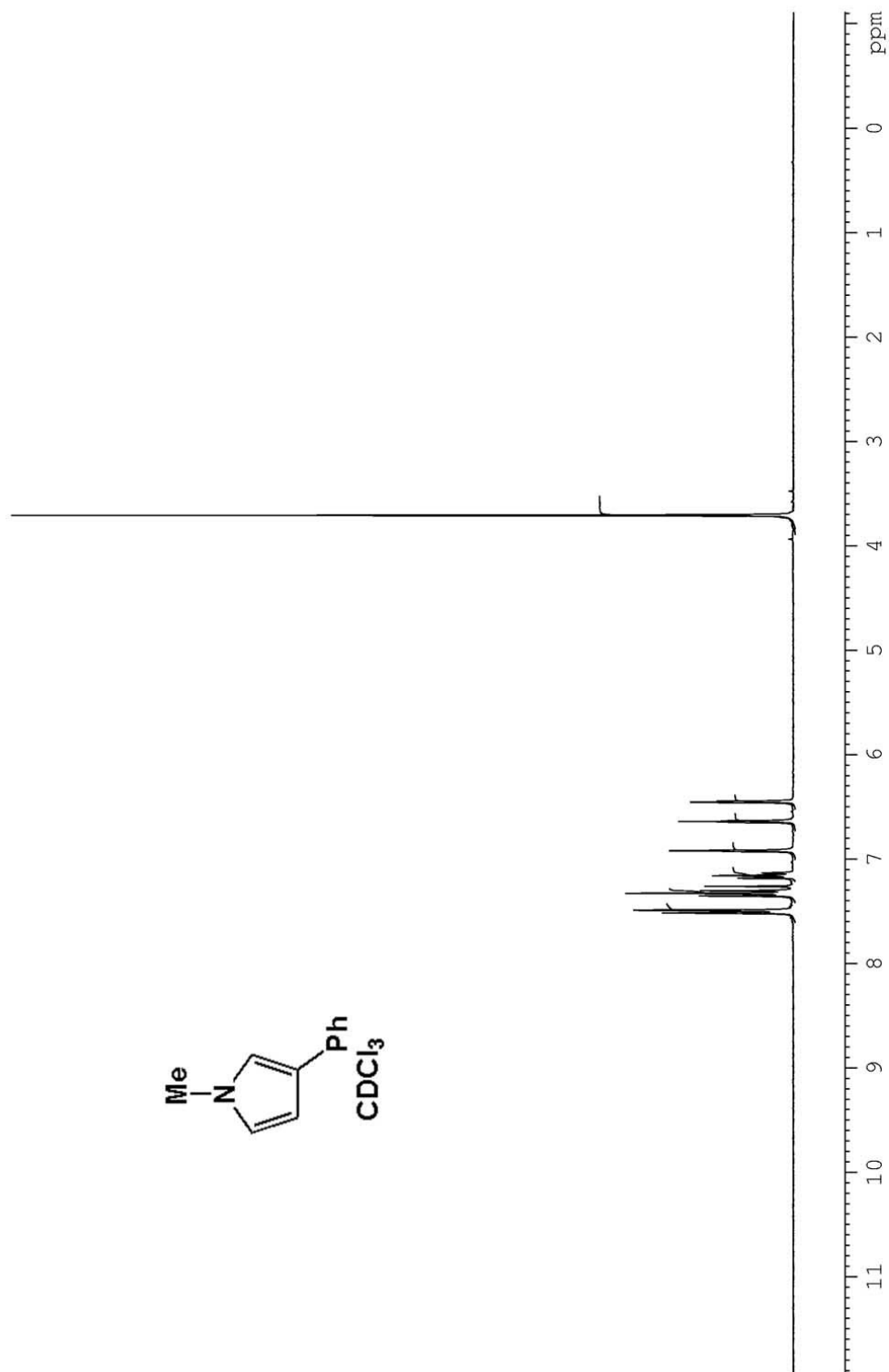




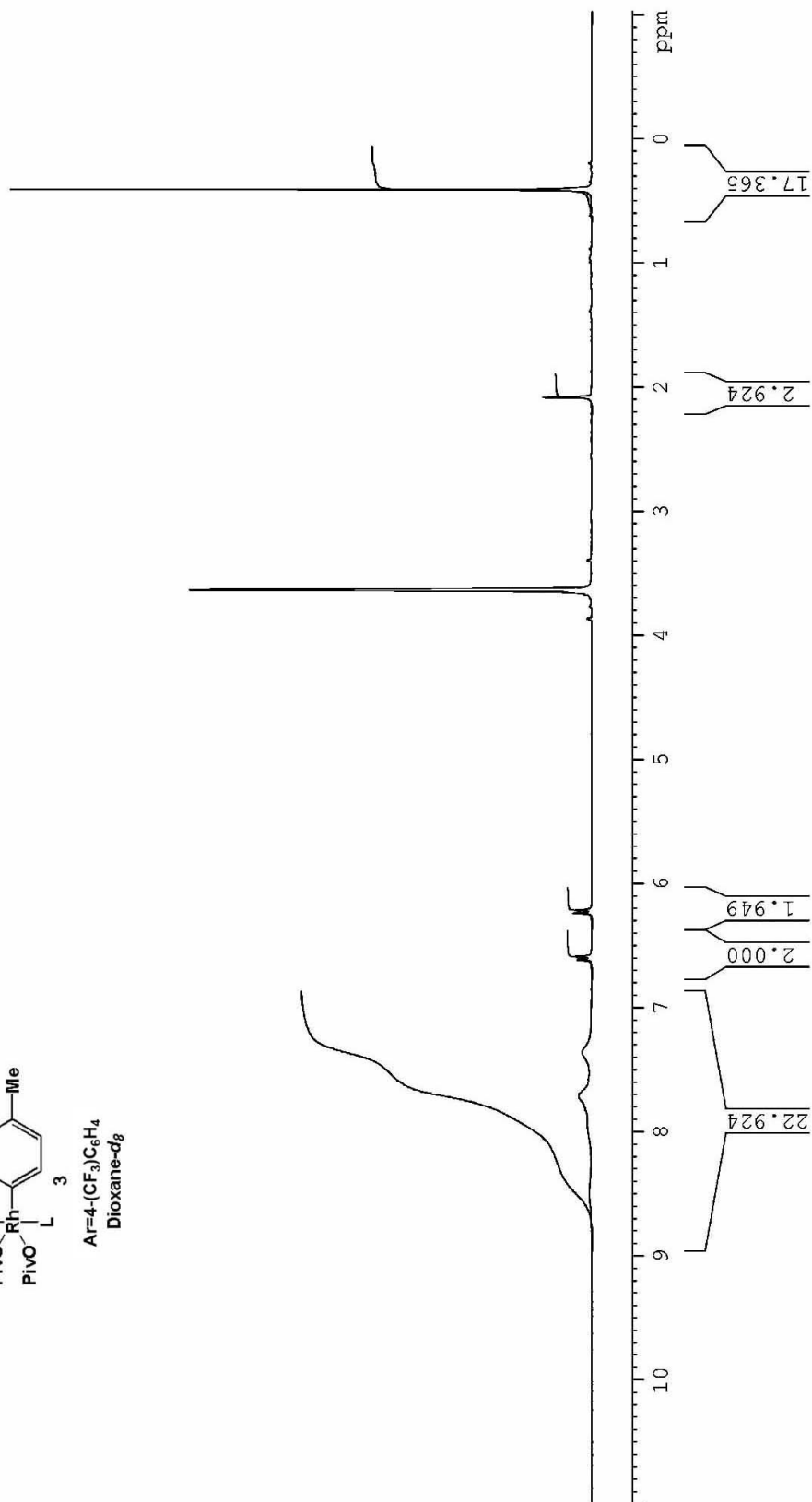
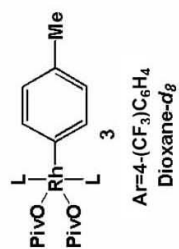
SW-I-143 proton







SW-110-1  
wb300  
proton standard



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